CHEMISTRY FOR HEALTH PROFESSIONS



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Chemistry for Health Professions

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Western Oregon University

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1: MATH FOR INTRODUCTORY CHEMISTRY

1.1: Scientific Notation

1.2: Avogadro's Number and the Mole

1.3: Units of Measurement

1.4: Making Measurements in the Lab

1.5: Chapter Summary

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Making Measurements in Chemistry

Chemistry in the health professions depends on careful measurement, clear communication of quantities, and correct use of units. In this chapter, you will build the “math and measurement toolkit” that you’ll use throughout Allied Health Chemistry. We’ll begin with scientific notation so you can work efficiently with very large and very small values commonly encountered in medicine and laboratory science. Next, you’ll learn the International System of Units (SI), metric prefixes, and the difference between mass and weight, along with key temperature scales and common derived units such as volume, density, and energy. You will then practice how scientists report measurements using accuracy, precision, and significant figures, including scientific rounding (“rounding to the even”) to avoid bias in data sets. Finally, you will apply dimensional analysis and conversion factors to solve real-world problems—such as converting medication doses, working with concentration and volume units, and calculating clinical drip rates—while keeping units consistent and meaningful.

By the end of this chapter, students will be able to:

1. **Use scientific notation correctly** to express, compare, and calculate with very large and very small numbers commonly used in chemistry and healthcare contexts.
2. **Identify and apply SI units and metric prefixes** to report measurements appropriately and convert between related metric units (e.g., g ↔ mg, m ↔ cm, L ↔ mL).
3. **Convert between temperature scales** (°C, K, °F) and explain why Kelvin is used for scientific calculations.
4. **Evaluate and report measurements using accuracy, precision, and significant figures**, including applying scientific rounding (round-to-even) when appropriate.
5. **Perform calculations while maintaining correct significant figures**, using the proper rules for addition/subtraction and multiplication/division.
6. **Use dimensional analysis (conversion factors) to solve applied problems**, including medication dosage conversions and IV drip-rate calculations with drop factors (gtt/mL).

How to Use This Chapter

This chapter is your “math and measurement toolbox” for Chemistry in the Health Professions. You’ll use these skills in every later topic—especially when working with medication doses, lab data, concentrations, and clinical-style calculations—so it’s worth moving carefully and practicing as you go.

- **Start with Section 1.1 (Scientific Notation)** and make sure you can rewrite numbers correctly *before* you try calculations. Small exponent mistakes can change an answer by a factor of 10, 100, or more.
- **In Section 1.2 (Units of Measurement), focus on units and prefixes.** As you read, keep a short list of common prefixes (kilo-, milli-, micro-) and practice moving between them.
- **As you reach Section 1.3 (Making Measurements in the Lab), slow down.** This is where you learn how scientists communicate uncertainty. Pay attention to the difference between **accuracy vs. precision** and how **significant figures** reflect instrument limits.
- **When doing problems, always write units at every step.** Unit cancellations are your built-in error-checking system. If units don’t cancel the way you expect, something is set up incorrectly.

- **Don’t round until the end.** Keep extra digits in intermediate steps, then apply significant-figure rules to the final answer. Use **round-to-even** only when the number you’re rounding is exactly 5 (or 5 followed only by zeros).
- **Practice in short sessions.** A good approach is 15–20 minutes per section: read, do 2–3 practice problems, check your work, then move on. Revisit any section you’ll use often (especially unit conversions and significant figures).

If you treat this chapter as a reference you return to during the term, it will save you time and prevent the most common calculation errors later in the course.

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1.1: Scientific Notation

The study of chemistry can involve numbers that are very large. It can also involve numbers that are very small. Writing out such numbers and using them in their long form is problematic, because we would spend far too much time writing zeroes, and we would probably make a lot of mistakes! There is a solution to this problem. It is called scientific notation.

Scientific notation allows us to express very large and very small numbers using powers of 10.

Recall that:

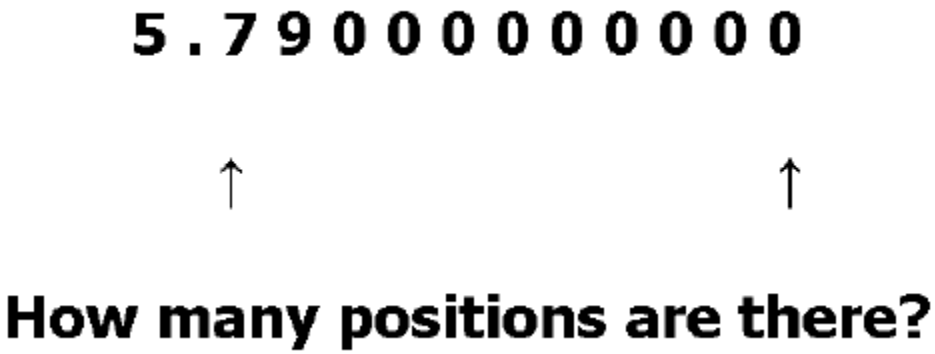
Table 1.1A Defining Factors of Ten - Exponents and Standard Numbers With Large Numbers

Factors of Ten		
$10^0 = 1$	$10^1 = 10$	$10^2 = 100$
$10^3 = 1000$	$10^4 = 10000$	$10^5 = 100000$

As you can see, the power to which 10 is raised is equal to the number of zeroes that follow the 1. This will be helpful for determining which exponent to use when we express numbers using scientific notation.

Let us take a very large number: **579, 000, 000, 000** and express it using scientific notation. First, we find the coefficient, which is a number between 1 and 10 that will be multiplied by 10 raised to some power. **Our coefficient is: 5.79.** This number will be multiplied by 10 that is raised to some power. Now let us figure out what power that is.

We can do this by counting the number of positions that stand between the end of the original number and the new position of the decimal point in our coefficient.



We can see that there are 11 positions between our decimal and the end of the original number. This means that our coefficient, 5.79, will be multiplied by 10 raised to the 11th power. Our number expressed in scientific notation is: **5.79×10^{11}.** But what about very small numbers?

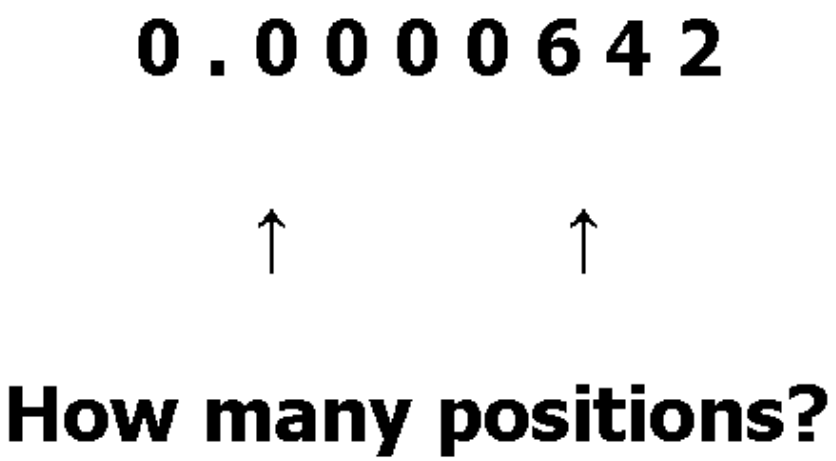
You may recall that:

Table 1.1B Defining Factors of Ten - Exponents and Standard Numbers With Very Small Numbers

Factors of Ten		
$10^{-1} = 0.1$	$10^{-2} = 0.01$	$10^{-3} = 0.001$
$10^{-4} = 0.0001$	$10^{-5} = 0.00001$	$10^{-6} = 0.000001$

The number of spaces to the right of the decimal point for our 1 is equal to the number in the exponent that is behind the negative sign. This is useful to keep in mind when we express very small numbers in scientific notation.

Here is a very small number: **0.0000642.** Let us express this number using scientific notation. **Our coefficient will be 6.42.** This number will be multiplied by 10 raised to some power, which will be negative. Let us figure out the correct power. We can figure this out by counting how many positions stand between the decimal point in our coefficient and the decimal point in our original number.



There are 5 positions between our new decimal point and the decimal point in the original number, so our coefficient will be multiplied by 10 raised to the negative 5th power.

Our number written in scientific notation is: **6.42×10^{-5}.** You can use these methods to express any large or small number using scientific notation.

Here is a short video tutorial to get your started: Scientific Notation Video (opens in new window)

Practice Problems:

1. Express each large number using scientific notation:

a) 2,300,000

b) 45,000

c) 976,000,000,000,000

d) 1,120

2. Express each small number using scientific notation:

a) 0.0012

b) 0.00000326

c) 0.057

d) 0.00000088

3. Fill in the missing exponent

a) 324,000 = 3.24 x $10^{?}$

b) 9,100,000 = 9.1 x $10^{?}$

c) 0.000038 = 3.8 x $10^{?}$

d) 0.0046 = 4.6 x $10^{?}$

Solutions

1. a) 2.3 x 10^{6} b) 4.5 x 10^{4} c) 9.76 x 10^{14} d) 1.12 x 10^{3}

2. a) 1.2 x 10^{-3} b) 3.26 x 10^{-6} c) 5.7 x 10^{-2} d) 8.8 x 10^{-7}

3. a) 5 b) 6 c) -5 d) -3

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1.2: Avogadro's Number and the Mole

Why Do Chemists Use the Mole?

Atoms and molecules are incredibly small. A single drop of water contains more water molecules than there are drops of water in all of Earth's oceans! Because individual atoms and molecules are far too numerous to count directly, chemists use a special counting unit called the **mole**.

A mole is simply a large counting unit, much like a dozen.

Table 1.2A: Common Counting Units in Science

Counting Unit	Number of Objects
Pair	2
Dozen	12
Gross	144
Mole	**6.022×10^{23}**

One mole always contains exactly **6.022×10^{23} representative particles**. This number is called **Avogadro's number** in honor of the Italian scientist Amedeo Avogadro.

The representative particles depend on the substance being measured. Always write the correct representative particle in your final answer.

Table 1.2B: Types of Particles Commonly Represented by Moles

Substance	Representative Particle
Copper	Atoms
Oxygen gas (O_2)	Molecules
Sodium Chloride (NaCl)	Formula Unit
Calcium Ions (Ca^{2+})	Ions

Using Dimensional Analysis

Since the mole is simply another unit, we can use the same dimensional analysis techniques introduced earlier in this chapter. Notice that the units cancel just as they do in any dimensional analysis problem.

Example 1.2.1

Convert 2.00 mol of carbon atoms into atoms.

Solution

$$2.00\ mol\ C\ x\ \frac{6.022\ x\ 10^{23} atoms\ of\ C}{1\ mol\ C} = 1.20\ x\ 10^{24}\ atoms\ of\ C$$

Example 1.2.2

Convert 3.01 × 10^{23} molecules of oxygen (O_2) into moles.

Solution

$$3.01\ x\ 10^{23}\ molecules\ of\ O_2\ x\ \frac{1\ mol\ O_2}{6.022\ x\ 10^{23}\ molecule\ O_2} = 0.500\ mol\ O_2$$

Example 1.2.1

How many formula units are present in 0.250 mol of sodium chloride?

Solution

$$0.250\ mol\ NaCl\ x\ \frac{6.022\ x\ 10^{23}\ formula\ units\ NaCl}{1\ mol\ NaCl} = 1.51\ x\ 10^{23}\ formula\ units\ NaCl$$

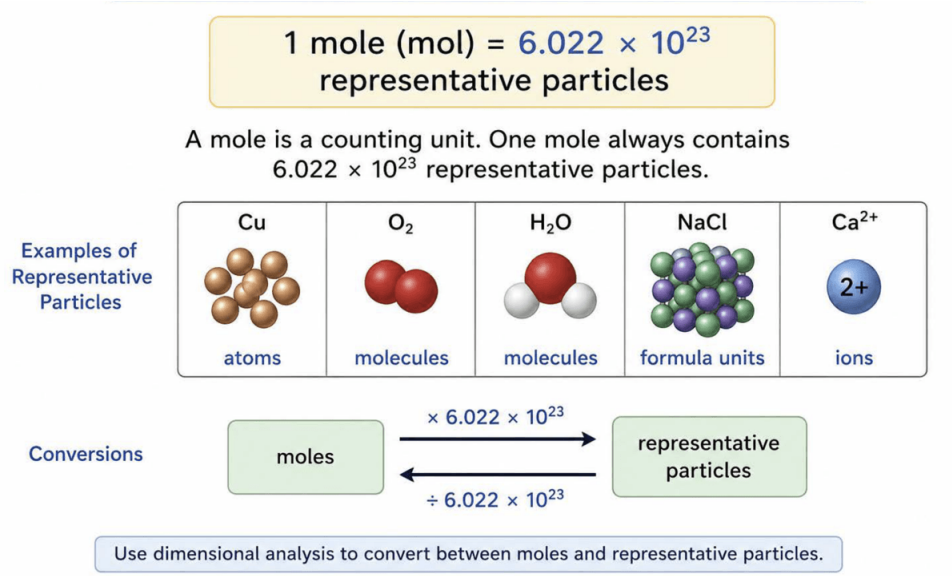


Figure 1.2.1 **Avogadro's Number and the Mole.** One mole is a counting unit equal to **6.022 × 10^{23} representative particles**, known as **Avogadro's number**. Depending on the substance, the representative particles may be atoms, molecules, formula units, or ions. Dimensional analysis can be used to convert between moles and representative particles. The figure states that one mole equals 6.022 × 10^{23} representative particles and explains that a mole is a counting unit. Examples of representative particles include copper atoms, oxygen molecules (O_2), water molecules (H_2O), sodium chloride formula units (NaCl), and calcium ions (Ca^{2+}). A conversion diagram shows that multiplying by 6.022 × 10^{23} converts moles to representative particles, while dividing by 6.022 × 10^{23} converts representative particles to moles. A note at the bottom reminds students to use dimensional analysis for these conversions.

Looking Ahead

In this chapter, the mole is used only as a **counting unit**.

In later chapters, you will learn how to use the mole to:

- convert between mass and moles using molar mass,
- interpret balanced chemical equations using mole ratios,
- predict the amounts of products formed in chemical reactions,
- calculate solution concentrations (molarity).

The mole will become one of the most important tools you use throughout chemistry.

Key Takeaways

After completing this section, you should be able to:

- Define Avogadro's number.
- Explain why chemists use the mole.
- Identify the representative particle for a substance.
- Convert between representative particles and moles using dimensional analysis.
- Express answers using the correct units and significant figures.

Practice Problems

1. Convert **4.50 mol Cu atoms** into atoms.
2. Convert **1.20 × 10^{24} molecules of CO_2** into moles.
3. How many **formula units** are present in **0.800 mol $CaCl_2$**?
4. Convert **6.022 × 10^{23} molecules of H_2O** into moles.
5. Convert **3.50 mol Na^+ ions** into ions.
6. Convert **9.03 × 10^{22} formula units of NaCl** into moles.

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1.3: Units of Measurement

International System of Units and the Metric System

The International System of Units, abbreviated SI from the French Système International D'unités, is the main system of measurement units used in science. Since the 1960s, the International System of Units has been internationally agreed upon as the standard metric system. The SI base units are based on physical standards. The definitions of the SI base units have been and continue to be modified and new base units added as advancements in science are made. Each SI base unit except the kilogram is described by stable properties of the universe.

There are seven base units, which are listed in Table 1.3A. Chemistry primarily uses five of the base units: the mole for amount, the kilogram for mass, the meter for length, the second for time, and the kelvin for temperature. The degree Celsius (^{o}C) is also commonly used for temperature. The numerical relationship between Temperature in Kelvins and Temperature in degrees Celsius is as follows:

$$T_{\mathrm{K}} = T_{^{\circ}\mathrm{C}} + 273.15 \tag{1.3.1}$$

where T_K is degrees Kelvin, and T^{o}_{C} is degrees Celcius

Table 1.3A: Scientific Measurement Base Units

Property	Unit	Abbreviation
Length	**Meter**	**m**
Mass	**Kilogram**	**kg**
Time	**Seconds**	**s**
Amount	**Mole**	**mol**
Temperature	**Kelvin**	**K**
Electric Current	**Ampere**	**amp**
Luminous Intensity	**Candella**	**cd**



Figure 1.3.1**: The Kilogram.** The standard for the kilogram is a platinum-iridium cylinder kept in a special vault in France. Source: wikimedia (opens in new window)

The size of each base unit is defined by international convention. For example, the kilogram is defined as the quantity of mass of a special metal cylinder kept in a vault in France (*Figure 1.3.1*). The other base units have similar definitions. The sizes of the base units are not always convenient for all measurements. For example, a meter is a rather large unit for describing the width of something as narrow as human hair. Instead of reporting the diameter of hair as 0.00012 m or even 1.2×10^{-4} m, SI also provides a series of prefixes that can be attached to the units, creating units that are larger or smaller by powers of 10, known as the metric system.

Common prefixes and their multiplicative factors are listed in *Table 1.5B: Examples of Metric Conversions Using the Gram as the base Unit*. (Perhaps you have already noticed that the base unit kilogram is a combination of a prefix, kilo- meaning 1,000 ×, and a unit of mass, the gram.) Some prefixes create a multiple of the original unit: 1 kilogram equals 1,000 grams (or 1 kg = 1,000 g), and 1 megameter equals 1,000,000 meters (or 1 Mm = 1,000,000 m). Other prefixes create a fraction of the original unit. Thus, 1 centimeter equals 1/100 of a meter, 1 millimeter equals 1/1,000 of a meter, 1 microgram equals 1/1,000,000 of a gram, and so forth.

Table 1.3B provides an example of the correct conversions using the gram as the base unit. In addition, the larger unit, tera- is also included.

Table 1.3B Example of Metric Conversions Using the Gram as the Base Unit

Prefix	Abbr.	example using g as base unit	conversion nearest neighbor
tera-	T	1,000,000,000,000 g = 1 Tg	1,000 Gg = 1 Tg
giga-	G	1,000,000,000 g = 1 Gg	1,000 Mg = 1 Gg
mega-	M	1,000,000 g = 1 Mg	1,000 kg = 1 Mg

Prefix	Abbr.	example using g as base unit	conversion nearest neighbor
kilo-	k	1,000 g = 1 kg	100 Dg = 1 kg
deca-	D	10 g = 1 Dg	
Base Unit		base unit	
deci-	d	10 dg = 1 g	
centi-	c	100 cg = 1 g	10 cg = 1 dg
milli-	m	1,000 mg = 1 g	10 mg = 1 cg
micro-	m	1,000,000 mg = 1 g	1,000 mg = 1 mg
nano-	n	1,000,000,000 ng = 1 g	1,000 ng = 1 mg
pico-	p	1,000,000,000,000 pg = 1 g	1,000 pg = 1 ng
femto-	f	1,000,000,000,000,000 = 1 g	1,000 fg = 1 pg

Mass

The basic unit of mass in the International System of Units is the kilogram. A kilogram is equal to 1000 grams. A gram is a relatively small amount of mass and so larger masses are often expressed in kilograms. When very tiny amounts of matter are measured, we often use milligrams which are equal to 0.001 gram. There are numerous larger, smaller, and intermediate mass units that may also be appropriate. At the end of the 18th century, a kilogram was the mass of a liter of water. In 1889, a new international prototype of the kilogram was made of a platinum-iridium alloy. The kilogram is equal to the mass of this international prototype, which is held in Paris, France.

Mass and weight are not the same thing. Although we often use the terms mass and weight interchangeably, each one has a specific definition and usage. The mass of an object is a measure of the amount of matter in it. The mass (amount of matter) of an object remains the same regardless of where the object is placed. For example, moving a brick to the moon does not cause any matter in it to disappear or be removed.

The weight of an object is determined by the force that gravitation exerts upon the object. The weight is equal to the mass of the object times the local acceleration of gravity. Thus, on the Earth, weight is determined by the force of attraction between the object and the Earth. Since the force of gravity is not the same at every point on the Earth's surface, the weight of an object is not constant. The gravitational pull on the object varies depending on where the object is with respect to the Earth or other gravity-producing object. For example, a man who weighs 180 pounds on Earth would weigh only 45 pounds if he were in a

stationary position, 4,000 miles above the Earth's surface. This same man would weigh only 30 pounds on the moon because the moon's gravity is only one-sixth that of Earth. The mass of this man, however, would be the same in each situation. For scientific experiments, it is important to measure the mass of a substance rather than the weight to retain consistency in the results regardless of where you are performing the experiment.

Length

The SI unit of length is the meter. In 1889, the definition of the meter was a bar of platinum-iridium alloy stored under conditions specified by the International Bureau of Standards. In 1960, this definition of the standard meter was replaced by a definition based on a wavelength of krypton-86 radiation. In 1983, that definition was replaced by the following: the meter is the length of the path traveled by light in a vacuum during a time interval of a second.

Temperature

When used in a scientific context, the words heat and temperature do NOT mean the same thing. Temperature represents the average kinetic energy of the particles that make up a material. Increasing the temperature of a material increases its thermal energy. Thermal energy is the sum of the kinetic and potential energy in the particles that make up a material. Objects do not "contain" heat; rather they contain thermal energy. Heat is the movement of thermal energy from a warmer object to a cooler object. When thermal energy moves from one object to another, the temperature of both objects change.

A thermometer is a device that measures temperature. The name is made up of "thermo" which means heat and "meter" which means to measure. The temperature of a substance is directly proportional to the average kinetic energy it contains. In order for the average kinetic energy and temperature of a substance to be directly proportional, it is necessary that when the temperature is zero, the average kinetic energy must also be zero. It was necessary for use in calculations in science for a third temperature scale in which zero degrees corresponds with zero kinetic energy, that is, the point where molecules cease to move. This temperature scale was designed by Lord Kelvin. Lord Kelvin stated that there is no upper limit of how hot things can get, but there is a limit as to how cold things can get. In 1848, William Lord Kelvin developed the idea of absolute zero, which is the temperature at which molecules stop moving and therefore, have zero kinetic energy. This is known as the Kelvin temperature scale.

The Celsius scale is based on the freezing point and boiling point of water. Thus, 0°C is the freezing point of water, whereas 100°C is the boiling point of water. Most of us are familiar with temperatures that are below the freezing point of water. It should be apparent that even though the air temperature may be -5°C, the molecules of air are still moving (i.e. 0°C is not absolute zero). Substances like oxygen gas and nitrogen gas have already melted and boiled to vapor at temperatures below -150°C.

The Fahrenheit scale is also defined by the freezing point and boiling points of water. However, the scale is different from that of the Kelvin and Celsius scales. In the Fahrenheit scale, the freezing point of water is 32°F and the boiling point of water is 212°F. To convert between the Fahrenheit scale and the Celsius scale , the following conversions can be used:

$$T_{^\circ\mathrm{C}} = (T_{^\circ\mathrm{F}} - 32) \times \frac{5}{9} \qquad \text{or} \qquad T_{^\circ\mathrm{F}} = T_{^\circ\mathrm{C}} \times \frac{9}{5} + 32 \tag{1.3.2}$$

Where T_F is Temperature in degrees Fahrenheit, and $T°_C$ is Temperature in degrees Celcius

The Kelvin temperature scale has its zero at absolute zero (determined to be -273.15°C), and uses the same degree scale as the Celsius scale. Therefore, the mathematical relationship between the Celsius scale and the Kelvin scale is

$$T_{\mathrm{K}} = T_{^\circ\mathrm{C}} + 273.15 \tag{1.3.3}$$

where T_k is Temperature in degrees Kelvin, and $T°_C$ is Temperature in degrees Celcius. In the case of the Kelvin scale, the degree sign is not used. Temperatures are expressed simply as 450 K, and are always positive.

Time

The SI unit for time is the second. The second was originally defined as a tiny fraction of the time required for the Earth to orbit the Sun. It has since been redefined several times. The definition of a second (established in 1967 and reaffirmed in 1997) is: the duration of 9,192,631,770 periods of the radiation corresponding to the transition between the two hyperfine levels of the ground state of the cesium-133 atom.

Amount

Chemists use the term mole to represent a large number of atoms or molecules. Just as a dozen implies 12 things, a mole (mol) represents 6.022×10^{23} things. The number 6.022×10^{23}, called Avogadro's number after the 19th-century chemist Amedeo Avogadro, is the number we use in chemistry to represent macroscopic amounts of atoms and molecules. Thus, if we have 6.022×10^{23} Oxygen atoms, we say we have 1 mol of Oxygen atoms. If we have 2 mol of Na atoms, we have $2 \times (6.022 \times 10^{23})$ Na atoms, or 1.2044×10^{24} Na atoms. Similarly, if we have 0.5 mol of benzene (C_6H_6) molecules, we have $0.5 \times (6.022 \times 10^{23})$ C_6H_6 molecules, or 3.011×10^{23} C_6H_6 molecules.

Derived SI Units

Derived units are combinations of SI base units. Units can be multiplied and divided, just as numbers can be multiplied and divided. For example, the area of a square having a side of 2 cm is 2 cm × 2 cm, or 4 cm^2 (read as "four centimeters squared" or "four square centimeters"). Notice that we have squared a length unit, the centimeter, to get a derived unit for area, the square centimeter.

Table 1.3C: Common Metric to English Conversions

Conversions
1 m = 39.36 in = 3.28 ft = 1.09 yd
1 in = 2.54 cm
1 km = 0.62 mi
1 kg = 2.20 lb
1 lb = 454 g
1 L = 1.06 qt = 0.26 gal

Volume

Volume is an important quantity that uses a derived unit. Volume is the amount of space that a given substance occupies and is defined geometrically as length × width × height. Each distance can be expressed using the meter unit, so volume has the derived unit m × m × m, or m^3 (read as “meters cubed” or “cubic meters”). A cubic meter is a rather large volume, so scientists typically express volumes in terms of 1/1,000 of a cubic meter. This unit has its own name—the liter (L). A liter is a little larger than 1 US quart in volume. (Table 1.3C) gives approximate equivalents for some of the units used in chemistry.) As shown in Figure 1.3.2 “The Liter”, a liter is also 1,000 cm^3. By definition, there are 1,000 mL in 1 L, so 1 milliliter and 1 cubic centimeter represent the same volume.

$$1\,\text{mL} = 1\,\text{cm}^3 \tag{1.3.4}$$

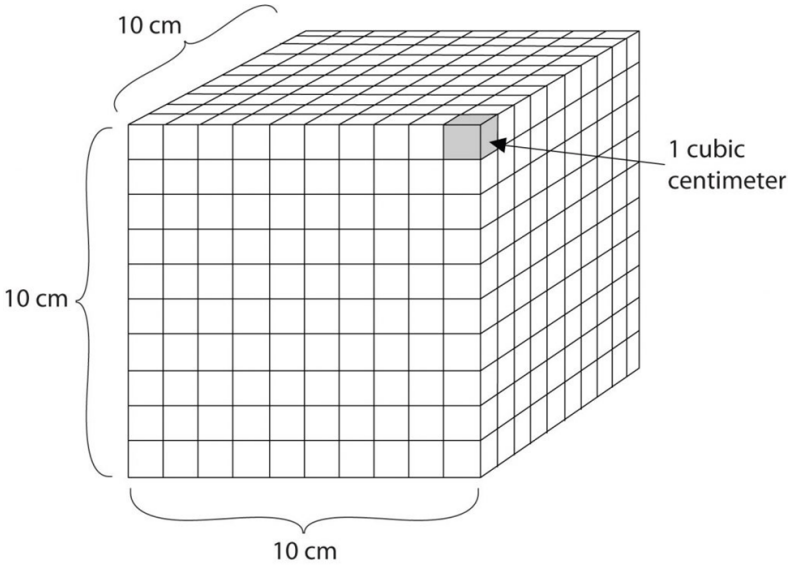


Figure 1.3.2: Volume and the Liter. A liter is defined as a cube that is 10 cm (1/10th of a meter) on a side. A milliliter, 1/1000th of a liter, is equal to 1 cubic centimeter (1 cm^3).

Energy

Energy, another important quantity in chemistry, is the ability to perform work. Moving a box of books from one side of a room to the other side, for example, requires energy. It has a derived unit of kg·m^2/s^2. (The dot between the kg and m^2 units implies the units are multiplied together and then the whole term is divided by s^2.) Because this combination is cumbersome, this collection of units is redefined as a joule (J), which is the SI unit of energy. Thus, 1 J = 1 kg·m^2/s^2. An older unit of energy, the calorie (cal), is also widely used. There are:

$$4.184\ \text{J} = 1\ \text{cal} \tag{1.3.5}$$

Note that this differs from our common use of the big ‘Calorie’or ‘Cal’ listed on food packages in the United States. The big ‘Cal’ is actually a kilocalorie or kcal (Fig 1.3.3) Note that all chemical processes or reactions occur with a simultaneous change in energy and that energy can be stored in chemical bonds. We can think of this in terms of our food molecules. The chemical bonds in proteins, carbohydrates, and fats store a large amount of energy that our bodies can harvest and convert into usable forms of energy to power brain function, muscle contraction, and build new bone, muscle, and other tissues. This energy can be calculated with proteins yielding 4 Cal/g (4 kcal/g), carbohydrates yielding 4 Cal/g (4 kcal/g), and fats yielding 9 Cal/g (9 kcal/g).



Figure 1.3.3: The Difference between kilocalories in Scientific and Common Use. Calories represented on food packaging actually refer to kilocalories in scientific terms.

Thus, we can calculate the amount of energy that we are receiving from each food source. For example, in the food label presented in Figure 1.3.3, there is 4.5 g of fat present. We can calculate how many Calories are generated from this fat using our conversion factor of 9 Cal/g for fat.

$$(4.5 \text{ g fat}) \left(\frac{9 \text{ Cal}}{1 \text{ g fat}} \right) = 40.5 \text{ Cal} \tag{1.3.6}$$

This matches what the manufacturer indicates on the label (40 Cal coming from fat). Note that the manufacturer is rounding down to the evens in this case. This is the scientific way of rounding and is discussed in more detail below in section 1.5.

Density

Density is defined as the mass of an object divided by its volume; it describes the amount of matter contained in a given amount of space. Density (ρ) is calculated using the following equation:

$$\rho = \frac{m}{V} \tag{1.3.7}$$

where:

table: **ρ** = density, **m** = mass, and **V** = volume

Thus, the units of density are the units of mass divided by the units of volume: g/cm^3 or g/mL (for solids and liquids, respectively), g/L (for gases), kg/m^3, and so forth. For example, the density of water is about 1.00 g/mL, while the density of mercury is 13.6 g/mL. Mercury is over 13 times as dense as water, meaning that it contains over 13 times the amount of matter in the same amount of space. The density of air at room temperature is about 1.3 g/L.

Drop Units

Within a hospital setting, medications are often delivered by intravenous fluids (IV). This means that dosages are often calculated by using the number of drops delivered per mL of solution over time. The abbreviation ***gtt*** is used to denote drop and comes from the Latin word for drop which is *gutta*. The *drop factor (gtt/mL)* can be used to determine drip rates when a prescribed volume of medicine is required over a given time period. Note that drop factors will vary depending on the diameter of the IV tubing that is being used.

$$\left(\frac{\textbf{Volume (mL)}}{\textbf{Time (min)}}\right)\left(\textbf{Drop Factor}\ \left(\frac{\textbf{gtt}}{\textbf{mL}}\right)\right) = \textbf{Flow Rate}\ \left(\frac{\textbf{gtt}}{\textbf{min}}\right) \tag{1.3.8}$$

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1.4: Making Measurements in the Lab

Precision vs. Accuracy

It is important to note the different terminology we use when talking in science. One such set of terminology is precision and accuracy. Although precision and accuracy are often used interchangeably in the non-scientific community, the difference between the terms is extremely important to realize. Precision tells you how close two measurements are to one another, while accuracy tells you how close a measurement is to the known value. A measurement can be precise while not being accurate, or accurate but not precise; the two terms are NOT related. A good analogy can be found in a game of darts (Fig. 1.4.1). A player who always hits the same spot just to the left of the dart board would be precise but not very accurate. However, a dart player who is all over the board but hits the center of the board on average would be accurate but not precise. A good darts player, just like a good scientist, wants to be both precise and accurate.

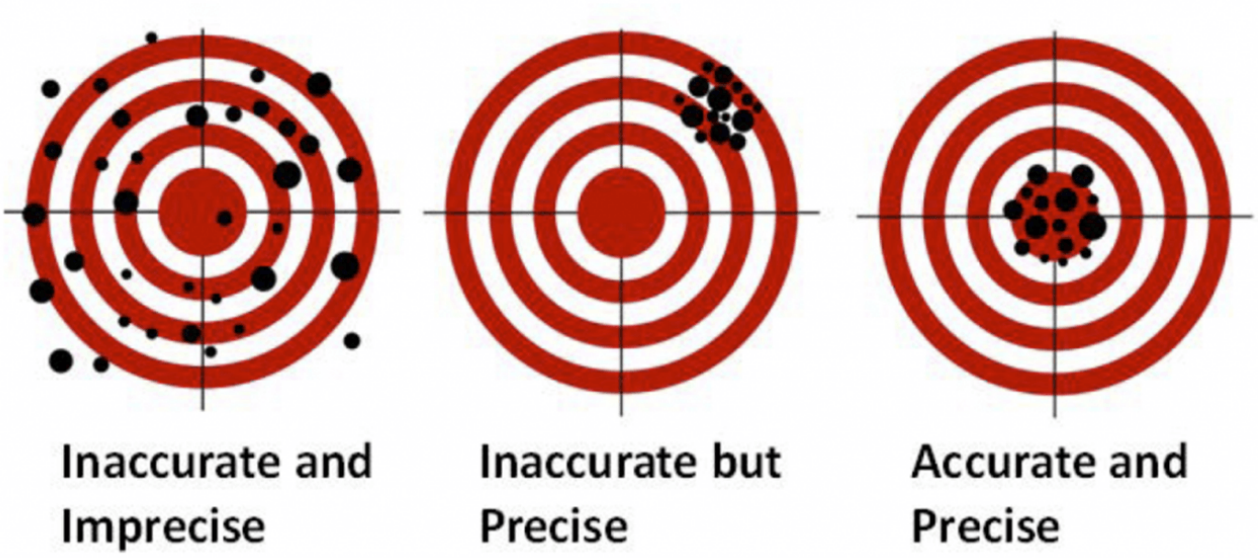


Figure 1.4.1**: Difference Between Accuracy and Precision**. A game of darts can be used to show the difference between accuracy and precision.

Adapted from: wikipedia

Typically within the laboratory, accuracy is a measure of how well your equipment is calibrated. For example, if your balance is not calibrated correctly, you can make very precise, repeated measurements, but the measurements will not represent the true value. Precision, on the otherhand, is usually determined by how careful the scientist is in making measurements. If you are careless and spill part of your sample on the way, your measurements in repeated experiments will not be precise even if your balance is accurate.

Significant Figures

It is important to realize that values in scientific measurements are never 100% accurate. Our instruments only measure to a certain level of accuracy. Thus, we can pick different instruments to make a measurement based upon the level of accuracy we need for the experiment. Due to the inherent inaccuracy in any measured number we must keep track of the different levels of accuracy each number has with significant figures. Significant figures of a measured quantity are defined as all the digits known with certainty and the first uncertain, or estimated, digit. It makes no sense to report any digits after the first uncertain one, so it is the last digit reported in a measurement. Zeros are used when needed to place the significant figures in their correct

positions. Thus, zeros may or may not be significant figures. Significant figures apply in the real world, as they allow us to quantify the accuracy of any type of measurement. To identify how many numbers in a measurement have significance, you can follow a discreet set of rules, shown below and to the right.

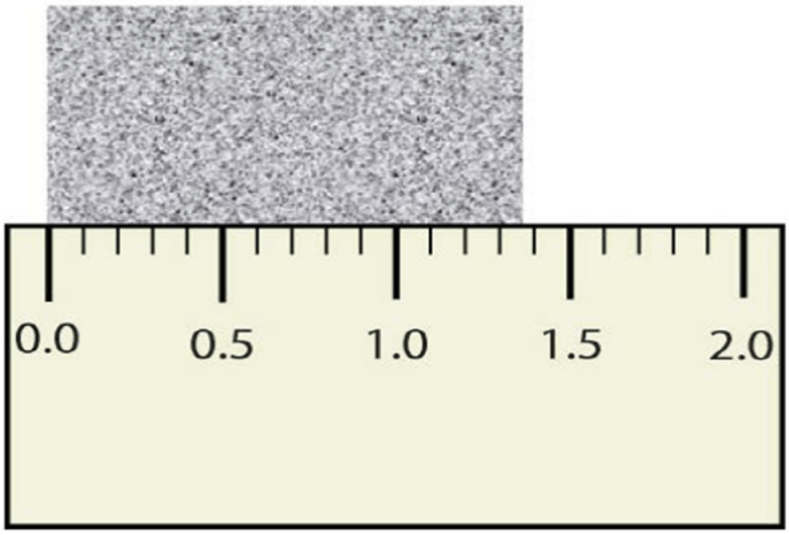


Figure 1.4.2**: Measuring an Object to the Correct Number of Significant Figures.** How many digits should be shown in this measurement? The correct answer is 3! The two that you know for sure, plus the estimated position...for this reading it would be close to 1.37

Exact Numbers

Exact numbers are numbers that are not measured by a scientific instrument. They are either used as definitions to define a concept or terminology, or they are made by counting the total of something present. An example of an exact number, would be the number of eggs in a carton or a defined unit such as there are 100 cm in 1 m. Exact numbers, such as the number of people in a room, DO NOT affect the number of significant figures in calculations made with measured values. **Exact number are treated as having infinite number of significant figures in calculations.**

Here is Some Practice Work

Think About This!
1. An oceanographer needs to go out in a boat to collect an important temperature and salinity data logger that is attached to an underwater buoy. How does each of the following situations illustrate the differences between precision and accuracy?
a. The oceanographer check the weather forecast the night before her trip so she knows what to wear on the boat. The TV forecaster says it will be between 26-31 ^{o}C at noon the next day. The actual temperature reading the next day on the boat at noon is 28 ^{o}C

Think About This!
b. When the oceanographer used her Global Positioning System (GPS) to indicate that she is at the location of the underwater buoy, she anchors the boat and jumps in the water to collect the data logger. However, she can't see the buoy. The other GPS units belonging to her colleagues on the boat also indicate that they are at the correct location. After an extensive search, the oceanographer finds the buoy 50 m from the boat.
c. While on the way back to shore, the oceanographer throws in a fishing line to see if she can catch anything for dinner. She is lucky enough to catch a mahi-mahi. When she pulls it out of the water, her colleagues estimate the weight of the fish. Their estimates are 16.1 kg, 16.8 kg, and 15.9 kg. When they weigh the fish upon returning to shore, the actual weight is 18.2 kg
2. Write your own scenario illustrating the difference between accuracy and precision. Swap your scenario with a classmate. Identify your classmate's scenario measurements as accurate or inaccurate and precise or imprecise.
a. A dart player can see how accurate his or her dart throws are by comparing the location of the thrown darts to the target or the bulls-eye of the dart board.
b. How is this model different from scientists who are measuring a natural phenomenon?
c. Is there a way for scientists to determine how accurate their measurements are? Explain your answer.

Rules for Significant Figures:

1. **Trailing zeros at the end of a number but to the left of the decimal point can act as place holders and may or may not be significant**
   - Example: 39,000 may have 2, 3, 4, or 5 significant figures!
   - The researcher that made the measurement must tell you.
   - If there is no indication, you can only use the fewest significant figures, in this case 2.
2. **All non-zero numbers are significant**
   - Example: 171 has 3 significant figures
3. **Trapped zeros between non-zero numbers are significant**
   - Example: 1,007 has 4 significant figures
4. **Leading zeros are not significant**
   - Example: 0.0017 has 2 significant figures, the zeros to the left of the number are insignificant
5. **Trailing zeros are significant after the decimal place**
   - Example: 17.00 has 4 significant figures
6. **When significant figures are in scientific notation all the numbers shown are significant**
   - Example: 1.70×10^7 has 3 significant figures
7. **A decimal place at the end of a whole number indicates that all values to the left are significant**
   - Examples: 100 has 1 significant figure whereas, 100. has 3 significant figures & 100.0 has 4 significant figures.

Rules of Rounding

In scientific operations, the rules of rounding may be a little bit different than the ones you are used to using. Normal rounding

rules suggest that if a number is below 5, it should be rounded down to the lower number, whereas if it is 5 or higher, it should be rounded up. However, note that 5 is right in the middle and causes a problem when using these conventional rounding rules. If you have a large dataset of numbers that you need to round, using this rounding rule will lead to bias in your dataset (i.e. 4/9th of the time you will be rounding down, and 5/9th of the time you will be rounding up). In a large dataset, this bias is unacceptable.

The rules used in this course for rounding numbers are known as 'rounding to the evens', and are implemented as follows:

1. Increase the final digit by one unit if the digit being dropped is greater than 5
2. Leave the final digit unchanged if the digin being dropped is less than 5
3. If the number to be dropped is exactly 5 (with no other numbers following it) then if the preceding number is odd, increase the number by one. If the preceding number is even, it remains the same.

Example 1.4.1

Round 26.65 to three significant figures.

Solution

When you look at the 4^{th} digit, it is a 5 with no numbers following it. So now you must look at the 3^{rd} digit. In this case it is even, so you would round to the even and the final answer would be 26.6

Example 1.4.2

Round 26.652 to three significant figures.

Solution

When you look at the 4^{th} digit, it is a 5 with a number following it. That means that is it greater than 5. In this case both the 5 and the 2 will be dropped and the remaining digit must be increased by one, so you would round the 6 up and the final answer would be 26.7.

Example 1.4.3

Round 26.7500 to three significant figures.

Solution

When you look at the 4^{th} digit, it is a 5 with only zeros following it. This means it is exactly 5. So now you must look at the 3^{rd} digit. In this case it is odd, so you would round up to the even and the final answer would be 26.8

Calculations with Significant Figures

The first thing to realize before performing any calculations in science is that all measured numbers are only as good as the instrument used to measure them. Even with the best instrument available the measured number will never be 100% exact. Scientists use the “good enough” rule of precision, meaning that we accept an inherent amount of imprecision from every measurement we take as long as the final result is close enough to where we want it to be. This concept becomes dangerous when we begin to use these “good enough” numbers for any calculations, if we aren’t careful to keep track of our significant figures our numbers can quickly lose their “good enough” status. To protect their “good enough” numbers, the scientific community has set forth certain rules for performing any calculations; in this section we need only concern ourselves with two very important rules: the Addition/Subtraction rule, and the Multiplication/Division rule.

Addition/Subtraction Rule with an Example:

Rules:

1. Find the number with the least number of decimals and keep track of the number of decimal place
2. Perform the addition/subtraction
3. Round the final answer to the least number of decimals found in Step 1

Example 1.4.4

If you had a beaker weighing 50.27 g and added 2.5 g of calcium carbonate, what would be the total mass of the filled beaker using the correct number of significant figures?

Solution

1. Identify the number with the fewest decimal places: (2.5 g, in this case).
2. Perform the addition: 50.27 g + 2.5 g = 52.77 g
3. Round your answer to the fewest decimal places identified in step 1: 52.8 g

Multiplication/Division Rule with an Example:

Rules:

1. Count the number of significant figures in each number (keep track of the number of significant figures
2. Perform the multiplication/division
3. Round your final answer to the lowest number of significant figures found in step 1

Example 1.4.5

Suppose you were working with 13.76 ml of water mixed with 2.53 ml of cooking oil in a graduated cylinder and your lab instructor asked you to find the ratio of water to oil. What would the final answer be with the correct number of significant figures?

Solution

1. First, recall that ratios represent division (water/oil)
2. Identify the number of significant figures in each measured value:

13.76 ml of water = 4 sig figs

2.53 ml of oil = 3 sig figs

Final answer needs to have 3 significant figures!!

3. Perform the math operation:

(13.76 ml water)/(2.53 ml oil) = 5.4387 water/oil

4. Round the final answer to the correct number of significant figures (ie the lowest identified from the measured values)

5.4387 water/oil = **5.44** water/oil

Calculating Complicated Problems:

1. Using the order of operations, break the problem up into multiple step
2. Perform any addition/subtraction steps following the Addition/Subtraction rule (Do not round yet, just keep track of the correct number of decimals when finding the number of significant figures.)
3. Perform multiplication/division using the Multiplication/Division rule
4. Round the final answer to the correct number of significant figures

---

Conversions and the Importance of Units

The ability to convert from one unit to another is an important skill. For example, a nurse with 50 mg aspirin tablets who must administer 0.2 g of aspirin to a patient, needs to know that 0.2 g equals 200 mg, so that 4 tablets are needed. Fortunately, there is a simple way to convert from one unit to another.

Conversion Factors

If you learned the SI units and prefixes described in Section 1.4 Units of Measurement", then you know that 1 cm is 1/100th of a meter or:

$$100\,\text{cm} = 1\,\text{m} \tag{1.4.1}$$

Suppose we divide both sides of the equation by 1 m (both the number and the unit; Note that it is critically important to always write out your units! This avoids confusion and mistakes when making conversions.):

$$\frac{100\,\text{cm}}{1\,\text{m}} = 1 \tag{1.4.2}$$

As long as we perform the same operation on both sides of the equals sign, the expression remains an equality. Look at the right side of the equation; it now has the same quantity in the numerator (the top) as it has in the denominator (the bottom). Any fraction that has the same quantity in the numerator and the denominator has a value of 1. We know that 100 cm is 1 m, so we have the same quantity on the top and the bottom of our fraction, although it is expressed in different units. A fraction that has equivalent quantities in the numerator and the denominator but expressed in different units is called a conversion factor. Note that conversion factors can be written with either term in the numerator or denominator, and used as appropriate for the problem that you want to solve. This is because, both terms are equal to 1.

$$\frac{100\,\text{cm}}{1\,\text{m}} = 1 = \frac{1\,\text{m}}{100\,\text{cm}} \tag{1.4.3}$$

Here is a simple example: How many centimeters are there in 3.55 m? Perhaps you can determine the answer in your head. If there are 100 cm in every meter, then 3.55 m equals 355 cm. To solve the problem more formally with a conversion factor, we first write the quantity we are given, 3.55 m. Then we multiply this quantity by a conversion factor, which is the same as multiplying it by 1. We can write 1 as 100cm/1m and multiply:

$$3.55\ \cancel{\text{m}} \times \frac{100\,\text{cm}}{1\ \cancel{\text{m}}} = 355\,\text{cm} \tag{1.4.4}$$

Because m, the abbreviation for meters, occurs in both the numerator and the denominator of our expression, they cancel out. The final step is to perform the calculation that remains once the units have been canceled. Note that it is CRITICAL to retain the right units in the final answer or it will not make sense. A generalized description of this process is as follows:

$$\text{Quantity (old units)} \times \left(\frac{\text{new units}}{\text{old units}}\right) = \text{Quantity (new units)} \tag{1.4.5}$$

You may be wondering why we use a seemingly complicated procedure for a straightforward conversion. In later studies, the conversion problems you will encounter will not always be so simple. If you can master the technique of applying conversion factors, you will be able to solve a large variety of problems.

In the previous example, we used the fraction 100 cm/1 m as a conversion factor. Does the conversion factor 1 m/100 cm also equal 1? Yes, it does; it has the same quantity in the numerator as in the denominator (except that they are flip-flopped). Why did we not use that conversion factor? If we had used the second conversion factor, the original unit would not have canceled, and the result would have been meaningless. Here is what we would have gotten:

$$3.55\,\text{m} \times \frac{1\,\text{m}}{100\,\text{cm}} = \frac{0.0355\,\text{m}^2}{1\,\text{cm}} \tag{1.4.6}$$

INCORRECT USE OF CONVERSION FACTOR!!

You can see that none of the units cancelled out. For the answer to be meaningful, we have to construct the conversion factor in a form that causes the original unit to cancel out. Figure 1.4.3 “A Concept Map for Conversions” shows a concept map for constructing a proper conversion.

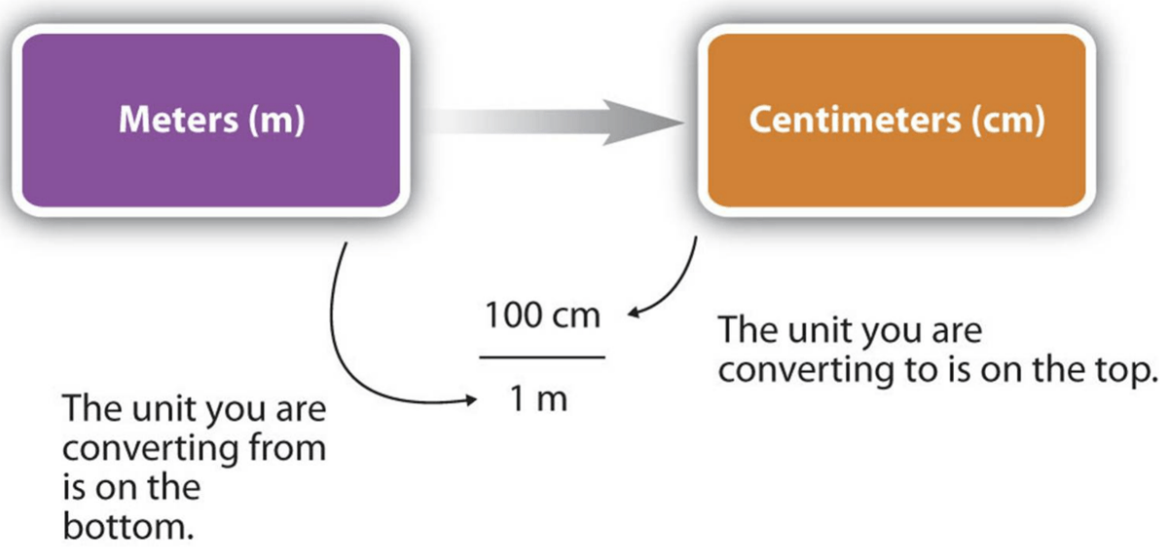


Figure 1.4.3**: A Concept Map for Conversions.** This is how you construct a conversion factor to convert from one unit to another. The units that you are converting from go on the bottom of your fraction, and the units that you are converting to go on the top of your fraction.

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1.5: Chapter Summary

- **Scientific notation** is a useful way to represent very large and very small numbers. Note that when using scientific notation, that all numbers shown are significant figures.
- **The International System of Units (SI)** and the **Metric System** are the standard units of measurement used when making scientific measurements. These include direct measurements for mass (grams), length (meter), temperature (Celcius), time (second), and amount (mole) and the derived units for volume (liter), energy (joule), and density (mass/volume or g/mL).
- The validity of scientific experiments depend on both **precision** and **accuracy**. **Precision** is a measure of the repeatability of the measurements and is usually dependent on how carefully a researcher performs the experiment. **Accuracy** is a measure of the correctness of the collected or analyzed data and is usually dependent on how well the equipment is calibrated and working at the time of the measurements.
- **Significant figures** are used to indicate the accuracy of scientific measurements and are dependent on the equipment used to make the measurement. **Significant figures** in scientific measurements include the first estimated position of a measurement. No additional estimated positions are included.
- When representing a scientific value using significant figures, it may be necessary to round the number to the correct number of digits. For **scientific rounding**, we use the concept of **rounding to the evens**. For numbers below 5 always round down and for numbers larger than 5 always round up. However, if the number you are rounding is exactly 5 or 5 with only zeros following it, round the previous number to the even number. (i.e. 6.5 would be rounded down to 6, whereas 7.5 would be rounded up to 8)
- When making calculations, it is necessary to maintain the correct number of **significant figures** within your answer. The least number of decimal places is critical for finding significant figures after addition and subtraction functions, whereas the least number of significant figures within the starting numbers is important for multiplication and division functions. Recall that only measured numbers are used in the determination of significant figures. Exact numbers such as defined units and conversion factors are not used to determine significant figures. It is also important to only round a calculated number at the final step in the calculation.
- When making calculations, always include the appropriate units within your calculations and utilize appropriate conversion factors when required.

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1.6: Chapter 1 References

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2. Poulsen, T. (2010) Introduction to Chemistry. Published under Creative Commons by-nc-sa 3.0. Available Here

3. OpenStax (2015) Atoms, Isotopes, Ions, and Molecules: The Building Blocks. OpenStax CNX.Available here

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2: ATOMS AND THE PERIODIC TABLE

2.1: Chemistry and Matter

2.2: How Scientists Study Chemistry

2.3: Atomic Theory with Historical Perspectives

2.4: Introduction to Elements and the Periodic Table

2.5: Dimitri Mendeleev and the Periodic Table

2.6: Families of the Periodic Table

2.7: Defining The Atom

2.8: Atomic Number - Protons Determine the Identity of an Element

2.9: Atomic Mass, Isotopes, and Molar Mass

2.10: Periodic Table Trends

2.11: Chapter Summary

2.12: Chapter 2 References

Introduction

Everything around us is made of matter, and chemistry helps us understand what matter is, how it is organized, and how it changes. In this chapter, you will begin building one of the most important foundations in chemistry: the idea that all matter is made of atoms. Although atoms are far too small to see with the naked eye, they determine the properties of the substances we observe every day.

This chapter introduces the structure of matter from both the macroscopic and microscopic perspectives. You will learn how chemists classify matter as elements, compounds, and mixtures, and how physical and chemical properties help us describe and distinguish substances. You will also explore how scientists study the natural world through observation, experimentation, and the scientific method.

From there, the chapter turns to atomic theory and the historical development of our modern understanding of the atom. You will examine how scientists such as Democritus, Dalton, and Mendeleev helped shape chemistry into a predictive science. You will then use the periodic table as a tool to organize elements and understand their properties. Along the way, you will learn about atomic structure, subatomic particles, atomic number, atomic mass, isotopes, molar mass, and several major periodic trends.

By the end of this chapter, you should be able to connect the arrangement of elements on the periodic table with the structure of atoms and explain how that arrangement helps predict chemical behavior. These ideas will be essential as you move into later chapters on chemical bonding, compounds, reactions, and quantitative chemistry.

Learning Goals

After completing this chapter, you should be able to:

1. **Define chemistry** and describe how it relates to other scientific disciplines.
2. **Classify matter** as substances or mixtures, and distinguish between elements, compounds, homogeneous mixtures, and heterogeneous mixtures.
3. **Differentiate between physical and chemical properties** and between physical and chemical changes.
4. **Describe the major states of matter** and explain phase changes using everyday examples.
5. **Identify the basic parts of a chemical reaction**, including reactants, products, coefficients, and subscripts.

6. **Explain how scientists use the scientific method** to investigate questions about the natural world.
7. **Summarize key ideas in the historical development of atomic theory**, including the contributions of Democritus, Dalton, and Mendeleev.
8. **Use the periodic table to identify elements** and describe the general characteristics of metals, nonmetals, and metalloids.
9. **Recognize major families on the periodic table**, including alkali metals, alkaline earth metals, transition metals, halogens, and noble gases.
10. **Describe the structure of the atom** in terms of protons, neutrons, electrons, the nucleus, and electron clouds.
11. **Relate atomic number to the identity of an element** and determine the numbers of protons and electrons in a neutral atom.
12. **Calculate atomic mass and determine the number of neutrons** in an atom when given atomic number and mass number.
13. **Define isotopes** and explain how isotopes of the same element differ from one another.
14. **Interpret average atomic mass** as a weighted average based on isotope abundance.
15. **Define molar mass** and use it to relate atoms, molecules, moles, and grams.
16. **Describe major periodic trends**, including atomic radius, electronegativity, ionization energy, and metallic versus nonmetallic character.
17. **Use periodic position to predict general chemical behavior** of elements.

How to Use This Chapter

This chapter introduces many of the core ideas that support the rest of the chemistry course, so it is helpful to move through it in a careful, step-by-step way.

Begin by focusing on the **big picture of matter**. Make sure you can clearly tell the difference between an element, a compound, and a mixture, and between a physical change and a chemical change. These are foundational ideas that will appear again and again throughout the course.

As you read about **atomic theory and atomic structure**, pay close attention to vocabulary. Terms such as *atom*, *element*, *proton*, *neutron*, *electron*, *atomic number*, *mass number*, *isotope*, and *molar mass* are essential and should become part of your working chemistry language. It may help to create a vocabulary list or concept map as you go.

When studying the **periodic table**, do not try to memorize everything at once. Instead, focus on patterns. Learn how to identify groups and periods, recognize the major families of elements, and understand the general differences between metals, nonmetals, and metalloids. The periodic table is one of the most powerful tools in chemistry because it helps you predict behavior from position alone.

As you work through the sections on **isotopes, atomic mass, and molar mass**, practice the calculations by writing out each step. Chemistry often requires you to move between concepts and numbers, so showing your work carefully will help you avoid confusion later.

Finally, spend extra time on the **periodic trends** section. Rather than memorizing trends as isolated facts, try to connect them to atomic structure. Ask yourself why atomic radius changes across a period, or why ionization energy increases for some elements. Understanding the "why" behind the trend will make the material much easier to remember.

As you move through the chapter, try to:

- pause after each section and summarize the main idea in your own words,
- compare related concepts side by side,
- practice interpreting figures and the periodic table,
- and complete any end-of-section or homework problems to reinforce your understanding.

This chapter lays the groundwork for later topics such as chemical bonding, molecular structure, and chemical reactions. A strong understanding here will make the rest of the course much easier.

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2.1: Chemistry and Matter

What is Chemistry?

Everything around us is made up of chemicals. From the color that makes a rose so red to the gasoline that fills our cars and the silicon chips that power our computers and cell phones...Chemistry is everywhere! Understanding how chemical molecules form and interact to create complex structures enables us to harness the power of chemistry and use it, just like a toolbox, to create many of the modern advances that we see today. This includes advances in medicine, communication, transportation, building infrastructure, food science and agriculture, and nearly every other technical field that you can imagine.

Chemistry is one branch of science. Science is the process by which we learn about the natural universe by observing, testing, and then generating models that explain our observations. is the process by which we learn about the natural universe by observing, testing, and then generating models that explain our observations. Because the physical universe is so vast, there are many different branches of science (Figure 2.1.1). Thus, chemistry is the study of matter, biology is the study of living things, and geology is the study of rocks and the earth. Mathematics is the language of science, and we will use it to communicate some of the ideas of chemistry.

Although we divide science into different fields, there is much overlap among them. For example, some biologists and chemists work in both fields so much that their work is called biochemistry. Similarly, geology and chemistry overlap in the field called geochemistry. Figure 2.1.1 shows how many of the individual fields of science are related.

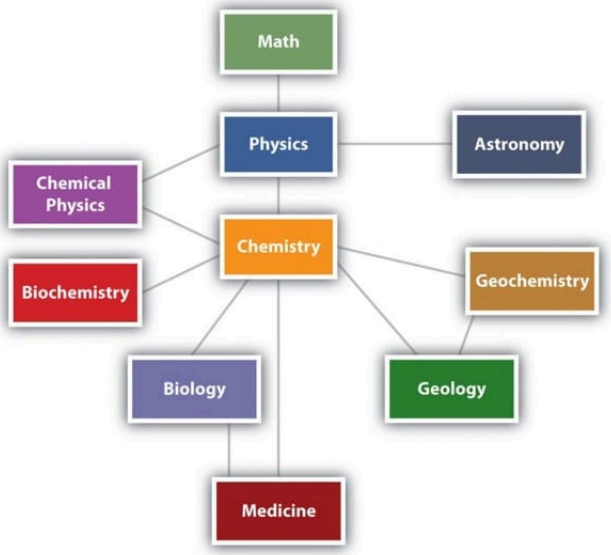


Figure 2.1.1**:The Relationships Between Some of the Major Branches of Science.** Chemistry lies more or less in the middle, which emphasizes its importance to many branches of science. Physical vs. Chemical Properties

---

Part of understanding matter is being able to describe it. One way chemists describe matter is to assign different kinds of properties to different categories. The properties that chemists use to describe matter fall into two general categories. Physical properties are characteristics that describes matter, such as boiling point, melting point and color. Physical Changes, such as melting a solid into a liquid, do not alter the chemical structure of that matter. Chemical properties are characteristics that describe how the chemical structure of matter changes during a chemical reaction. An example of a chemical property is flammability—a materials ability to burn—because burning (also known as combustion) changes the chemical composition of a material.

Elements and Compounds

Any sample of matter that has the same physical and chemical properties throughout the sample is called a substance. There are two types of substances. A substance that cannot be broken down into chemically simpler components is an element. Aluminum, which is used in soda cans, is an element. A substance that can be broken down into chemically simpler components (because it has more than one element) is a compound. Water is a compound composed of the elements hydrogen and oxygen. Today, there are about 118 elements in the known universe which are organized on a fundamental chart called the Periodic Table of Elements (Fig. 2.1.2). In contrast, scientists have identified tens of millions of different compounds to date.

The smallest part of an element that maintains the identity of that element is called an atom. Atoms are extremely tiny; to make a line 1 inch long, you would need 217 million iron atoms! Similarly, the smallest part of a compound that maintains the identity of that compound is called a molecule. Molecules are composed of atoms that are attached together and behave as a unit (Fig. 2.1.2). Scientists usually work with millions of atoms and molecules at a time. When a scientist is working

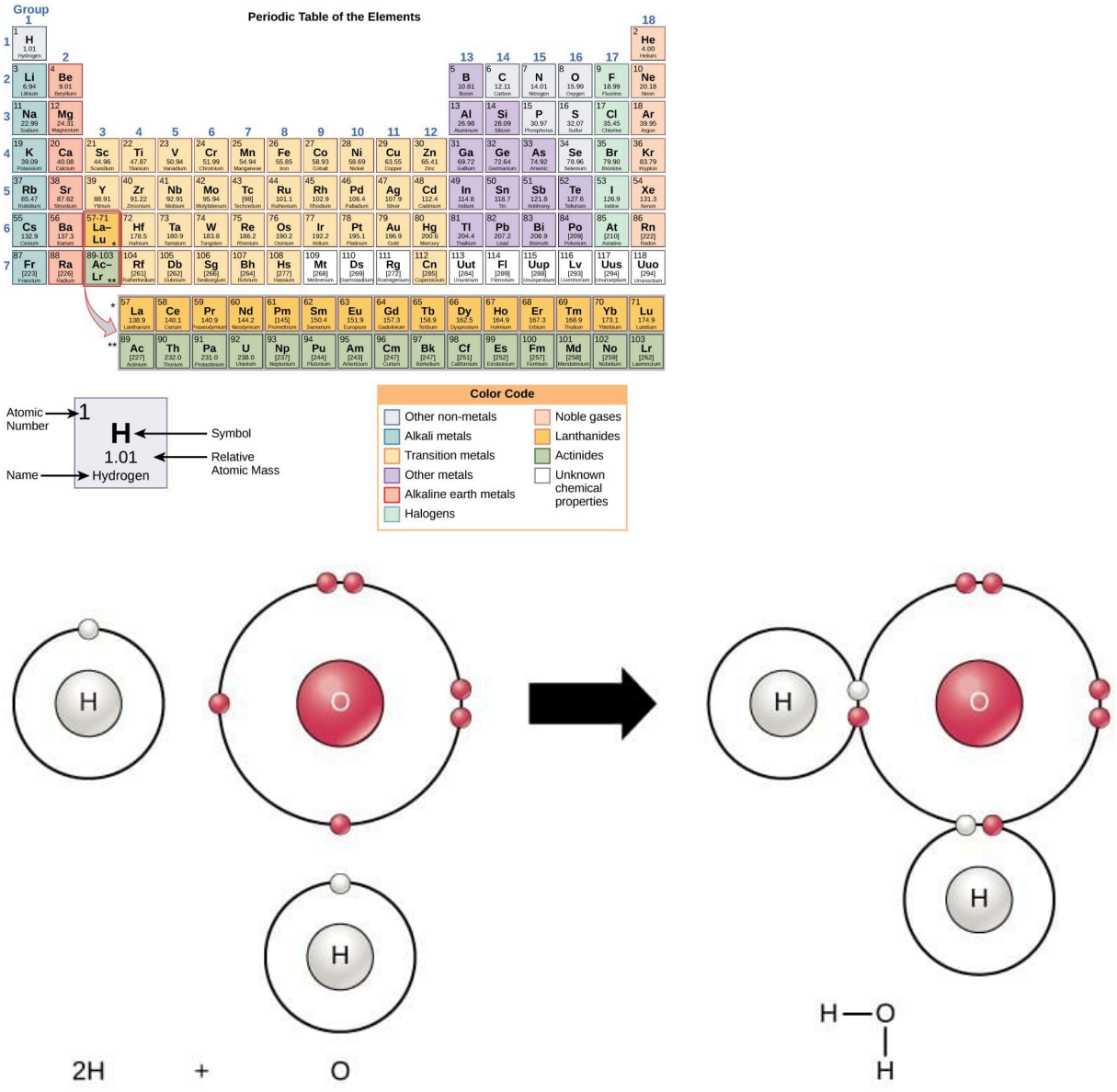


Figure 2.1.2**: (*Upper Panel)* The Periodic Table of the Elements is an organized chart that contains all of the known chemical elements. (*Lower Panel*) To the left of the arrow is shown one atom of oxygen and two atoms of hydrogen.** Each of these represent single elements. When they are combined on the righthand side, they form a single molecule of water (H_2O). Note that water is defined as a compound, because each single molecule is made up of more than one type of element, in

this case, one atom of oxygen with two atoms of hydrogen.

with large numbers of atoms or molecules at a time, the scientist is studying the macroscopic view of the universe. However, scientists can also describe chemical events on the level of individual atoms or molecules, which is referred to as the microscopic viewpoint. We will see examples of both macroscopic and microscopic viewpoints throughout this book (Figure 2.1.3).

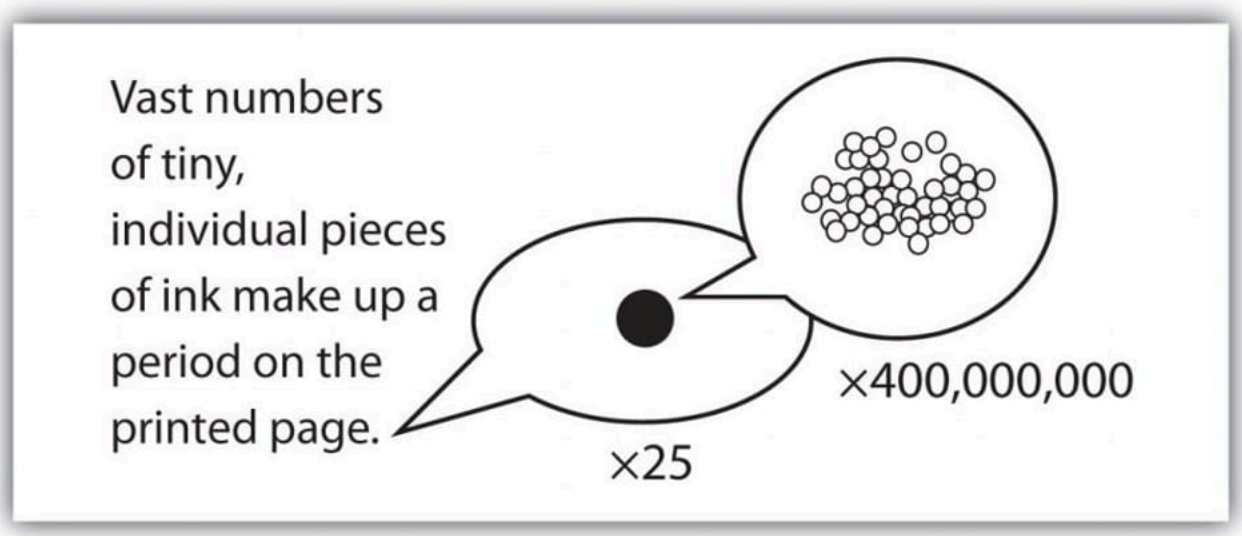


Figure 2.1.3: How many molecules are needed for a period in a sentence? Although we do not notice it from a macroscopic perspective, matter is composed of microscopic particles so tiny that billions of them are needed to make a speck that we can see with the naked eye. The X25 and X400,000,000 indicate the number of times the image is magnified.

Mixtures

A material composed of two or more substances is a mixture. In a mixture, the individual substances maintain their chemical identities. Many mixtures are obvious combinations of two or more substances, such as a mixture of sand and water. Such mixtures are called heterogeneous mixtures. In some mixtures, the components are so intimately combined that they act like a single substance even though they are not. Mixtures with a consistent composition throughout are called homogeneous mixtures Homogeneous mixtures that are mixed so thoroughly that neither component can be observed independently of the other are called solutions. Sugar dissolved in water is an example of a solution. A metal alloy, such as steel, is an example of a solid solution. Air, a mixture of mainly nitrogen and oxygen, is a gaseous solution.

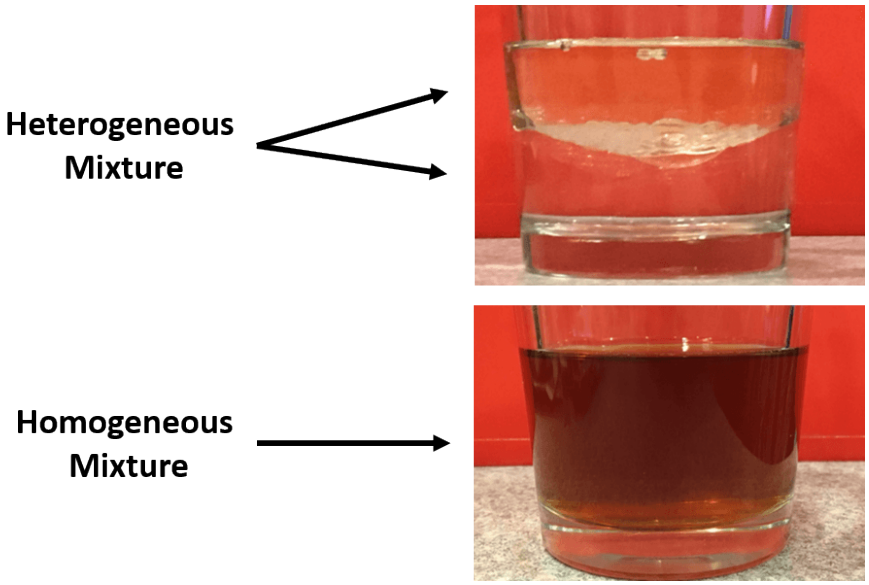


Figure 2.1.4: Heterogeneous vs. Homogeneous Mixtures. A mixture contains more than one substance. In the upper panel you see an example of a heterogeneous mixture of oil and water. The mixture is heterogeneous because you can visibly see two different components in the mixture. In the lower panel, you see an example of a homogeneous mixture, coffee. It is homogeneous because you cannot distinguish the many different components that make up a cup of coffee (water; caffeine; coffee alkaloids and tannins). It looks the same throughout. If the mixture is homogeneous and is also see through or clear, it is called a solution. In our example, the coffee is a solution; however, a concentrated espresso may be very opaque and would only be homogeneous mixture, not a solution.

States of Matter

Another way to classify matter is to describe it as a solid, a liquid, or a gas, which was done in the examples of solutions, above. These three descriptions, each implying that the matter has certain physical properties, represent the three phases of matter. A solid has a definite shape and a definite volume. Liquids have a definite volume but not a definite shape; they take the shape of their containers. Gases have neither a definite shape nor a definite volume, and they expand to fill their containers. We encounter matter in each phase every day. In fact, we regularly encounter water in all three phases: ice (solid), water (liquid), and steam (gas).

We know from our experience with water that substances can change from one phase to another if the conditions are right. Typically, varying the temperature of a substance (and, less commonly, the pressure exerted on it) can cause a phase change or a physical process in which a substance goes from one phase to another (Figure 2.1.5). Phase changes have particular names depending on what phases are involved, as summarized in Table 2.1A.

Table 2.1A: Phase Changes

Change	Name
Solid to Liquid	Melting; Fusion
Solid to Gas	Sublimation
Liquid to Gas	Boiling; Evaporation
Liquid to Solid	Solidification; Freezing
Gas to Liquid	Condensation
Gas to Solid	Deposition



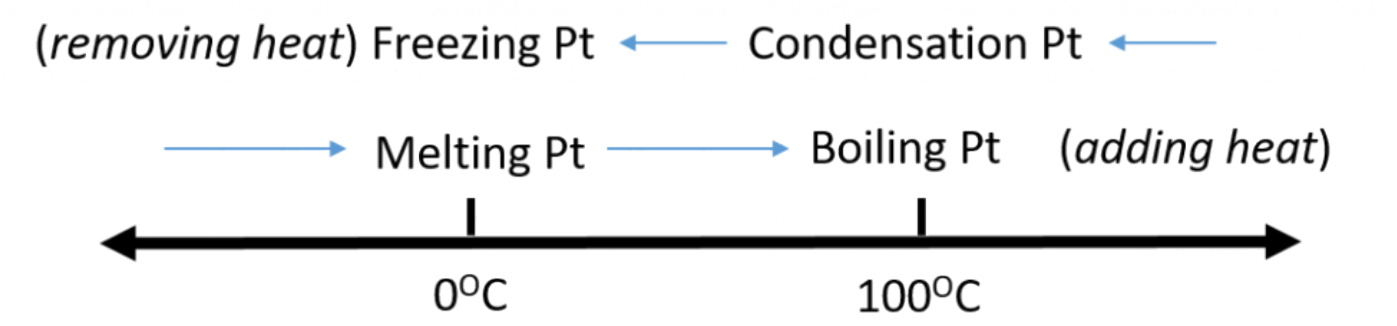


Figure 2.1.5**: Analyzing Phase Changes.** (*Upper panel*) A photo of boiling water demonstrates the phase change of water from the liquid to the gaseous phase. Note that phase changes are a physical property of a molecule. The water is still chemically the same (H_2O) in the solid, liquid, or gaseous state. (*Lower panel*) Change in temperature can cause phase changes . Above is the temperature scale for the phase changes of water. If you add heat to solid ice, water will melt at 0^oC and boil at 100^oC. If you remove heat from gaseous water, it will condense into the liquid state at 100^oC and freeze at 0^oC.

In summary, Figure 2.1.6 “The Classification of Matter” illustrates the relationships between the different ways matter can be classified.

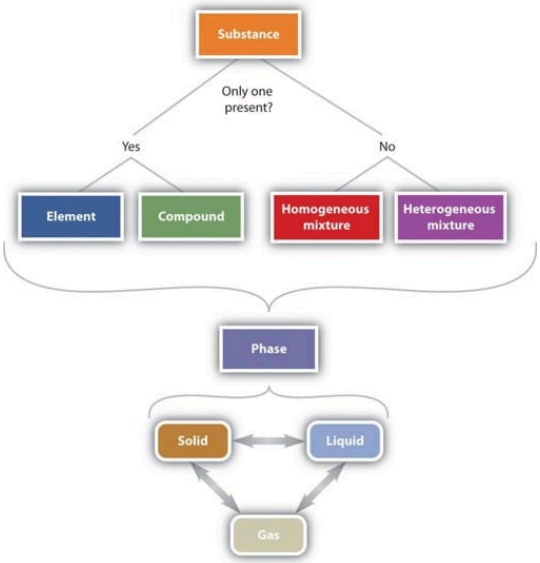


Figure 2.1.6**: The Classification of Matter.** Matter can be classified in a variety of ways depending on its properties

Reactions in Chemistry

Atoms can react chemically with one another to form new compounds and arrangements. When chemical reactions are written, they share some conventional features: (1) The reactants are written on the left hand side of the equation, (2) The products are written on the right hand side of the equation, (3) The reactants and products are separated by an arrow that shows the direction of the reaction, note that some reactions are reversible and are denoted by a double-headed arrow, (4) Conditions that are required for the reaction, such as heat or a *catalyst* (an agent that speeds up the chemical reaction without being used up in the process) are typically indicated above the arrow of the reaction, and (5) the reactants and products can be fully written out, or they can be represented by their chemical structures or by their chemical abbreviations (which you will learn how to formulate in the following chapters).

Reactions are written out with the quantities of the reactants and products in mind as well. During a chemical reaction, matter can never be destroyed. Thus, the atoms that are present on the left hand side of the equation must also be on the right hand side of the equation. They can be rearranged or in different forms, but they must be present. This is known as the ***law of conservation of matter***. To conform to this law, reactions are always written with the minimal amount of reactants required to make the minimal amount of products. An example of a chemical reaction is given below in Figure 2.1.7.

To represent the amounts of atoms present within a chemical reactions, numbers are present as either coefficients or subscripts within the equation. When the number is represented as a subscript, this indicates how many atoms of that element are required to make up a single molecule of the compound. In Figure 1.1.7, the chemical formula for carbon dioxide is given as CO_2 The number 2 subscript next to the oxygen atom indicates that there are two atoms of oxygen within a single molecule of carbon dioxide. When there is no subscript present, this means that there is only one atom present. Thus, for one molecule of carbon dioxide, CO_2, there is one atom of carbon and two atoms of oxygen. The coefficients in front of each substance, indicates how many molecules are required for a single reaction. In Figure 2.1.7, one molecule of methane reacts with 2 molecules of oxygen to yield one molecule of carbon dioxide and two molecules of water.

Since molecules are so small, it is impossible to ever measure out a single molecule when conducting an experiment in a laboratory. Thus, chemists will work with mole quantities of chemicals. The coefficients within chemical equations are also equivalent to mole quantities of each substance. Thus, the equation in Figure 2.1.7 can also be read as, one mole of methane reacts with 2 moles of oxygen to yield one mole of carbon dioxide and two moles of water.

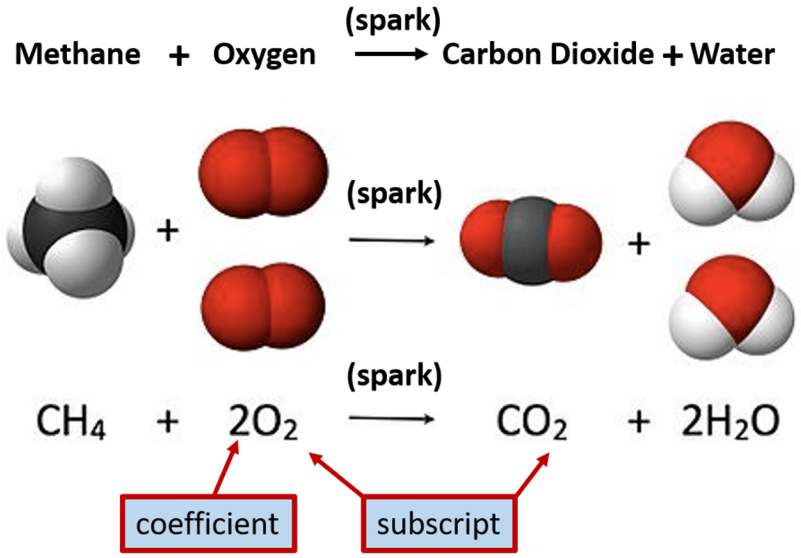


Figure 2.1.7**: Representations of Chemical Reactions.** In the example above the compound methane reacts with oxygen to form the products, carbon dioxide and water. Methane is also known as natural gas and is commonly burned to release usable energy. Subscripts present in the equation represent how many atoms of that element are involved with a chemical bond. If there is no number listed, the number one is implied. (ie in the carbon dioxide (CO_2) molecule denoted above, there is one atom of carbon (C) bonded with two atoms of oxygen (O) to form one molecule of carbon dioxide.) Note that to begin the burning process, a spark is needed to get the reaction started. This spark is noted over the arrow, as it is not a reactant or a product of the reaction. This figure is adapted from *Jynto and Jynto (2013)*(opens in new window).

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2.2: How Scientists Study Chemistry

The Scientific Method

How do scientists work? Generally, they follow a process called the scientific method. The scientific method is an organized procedure for learning answers to questions. To find the answer to a question (for example, "Why do birds fly toward Earth's equator during the cold months?"), a scientist goes through the following steps, which are also illustrated in Figure 2.2.1.

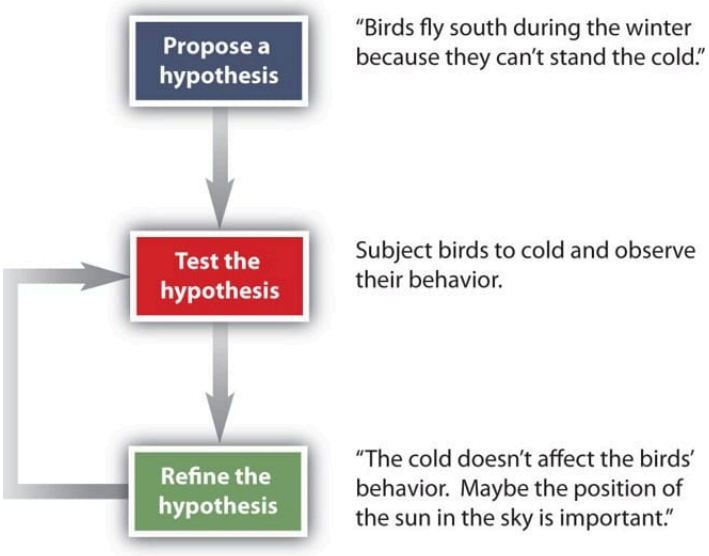


Figure 2.2.1**:The General Steps of the Scientific Method**. The steps may not be as clear-cut in real life as described here, but most scientific work follows this general outline.

Propose a hypothesis. A scientist generates a testable idea, or hypothesis, to try to answer a question or explain how the natural universe works. Some people use the word theory in place of hypothesis, but the word hypothesis is the proper word in science. For scientific applications, the word theory is a general statement that describes a large set of observations and data. A theory represents the highest level of scientific understanding, and is built from a wide array of factual knowledge or data.

Test the hypothesis. A scientist evaluates the hypothesis by devising and carrying out experiments to test it. If the hypothesis passes the test, it may be a proper answer to the question. If the hypothesis does not pass the test, it may not be a good answer.

Refine the hypothesis if necessary. Depending on the results of experiments, a scientist may want to modify the hypothesis and then test it again. Sometimes the results show the original hypothesis to be completely wrong, in which case a scientist will have to devise a new hypothesis.

Not all scientific investigations are simple enough to be separated into these three discrete steps. But these steps represent the general method by which scientist learn about our natural universe.

Exercise 2.2.1

1. Define Science and Chemistry.

2. Define the Scientific Method

Answer available at the end of this section.

Answers

Exercise 2.2.1

1. Science is the process by which we learn about the natural univers by observing, testing and then generating models that explain our observations. Chemistry is the study of matter and how it behaves.
2. The Scientific Method is the general process by which we learn about the natural universe.

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2.3: Atomic Theory with Historical Perspectives

Section 2.3: Atomic Theory with Historical Perspectives

What are the smallest building blocks of everyday objects? This is a question that has interested man since the age of the Greek philosophers. Like the ancient Greeks we can perform a simple thought experiment that raises a very important question for modern chemistry: suppose you were given a piece of aluminum foil and asked to cut the foil in half over and over. How long could you continue cutting, assuming that you had no limitations based on your own abilities? Is there a limit on how small matter can be broken up into, or could you infinitely divide matter into smaller and smaller pieces? This argument dates as far back as the Greek philosophers. Most, like Aristotle, argued that matter could be divided infinitely. However, one brilliant philosopher, Democritus, argued that there is a limit. He proposed that the smallest piece that any element (like aluminum) can be divided into and still be recognized as that element is an ***Atom***, a word derived from the Greek word *atomos,* meaning “indivisible”.

Philosophers, like Democritus (Figure 2.3.1), based most of their ideas off of thought experiments like the one above instead of actual observations and experimentation. It is for this reason that Democritus’ ideas on atoms were dismissed until 1808, when John Dalton, an English scientist, proposed four fundamental assumptions based upon observations that we call ***Dalton’s Atomic Theory.***

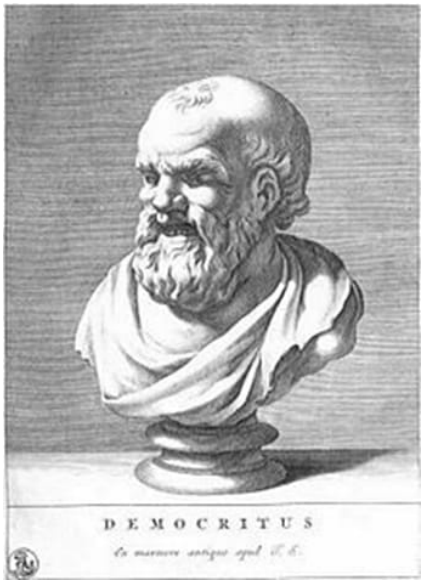


Figure 2.3.1**: Democritus**. Photo taken from: Public Domain(opens in new window)

Dalton proposed that:

- **Matter is made up of tiny particles called atoms**
- **Atoms cannot be broken into smaller pieces. During a chemical reaction, atoms are rearranged, but they do not break apart, nor are they created or destroyed**
- **All atoms of the same element are identical in mass and other properties**
- **Atoms of different elements differ in mass and other properties**

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2.4: Introduction to Elements and the Periodic Table

Types of Elements

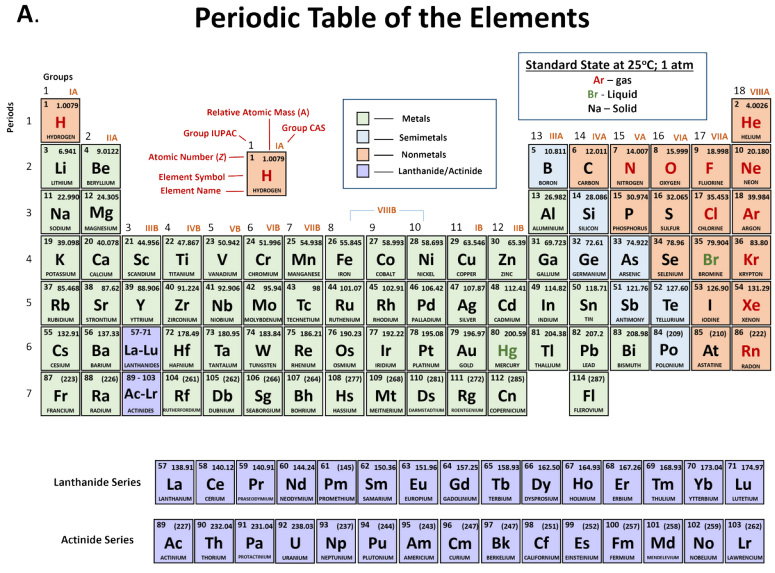
An ***element*** is a substance that cannot be broken down into simpler chemical substances. There are about 90 naturally occurring elements known on Earth. Using technology, scientists have been able to create nearly 30 additional elements that are not readily found in nature. Today, chemistry recognizes a total of 118 elements which are all represented on a standard chart of the elements, called the ***Periodic Table of Elements***. Each element is represented by a one or two letter code, where the first letter is always capitalized and, if a second letter is present, it is written in lowercase. For example, the symbol for Hydrogen is H, and the symbol for carbon is C. Some of the elements have seemingly strange letter codes, such as sodium which is Na. These letter codes are derived from Latin terminology. For example, the symbol for sodium (Na) is derived from the Latin word, natrium, which means sodium carbonate. Elements in the periodic table can be broken up into different general classes based upon similarities in their properties. Going from left to right across the periodic table, the elements can be broken up into ***metals, metalloids, and nonmetals***.

Metals are typically shiny, very dense, and have high melting points. Most metals are ductile (can be drawn out into thin wires), malleable (can be hammered into thin sheets), and good conductors of both heat as well as electricity. All metals are solids at room temperature except for mercury. In chemical reactions, metals easily lose electrons to form positive ions. Examples of metals are silver, gold, and zinc.

Nonmetals are generally brittle, dull, have low melting points, and they are generally poor conductors of heat as well as electricity. In chemical reactions, they tend to gain electrons to form negative ions. Examples of nonmetals are hydrogen, carbon, and nitrogen.

Metalloids have properties of both metals and nonmetals. Metalloids can be shiny or dull. Electricity and heat can travel through metalloids, although not as easily as they can through metals. They are also called ***semimetals***. They are typically semi-conductors, which means that they are elements that conduct electricity better than insulators, but not as well as conductors. They are valuable in the computer chip industry. Examples of metalloids are silicon and boron.

A.



B.

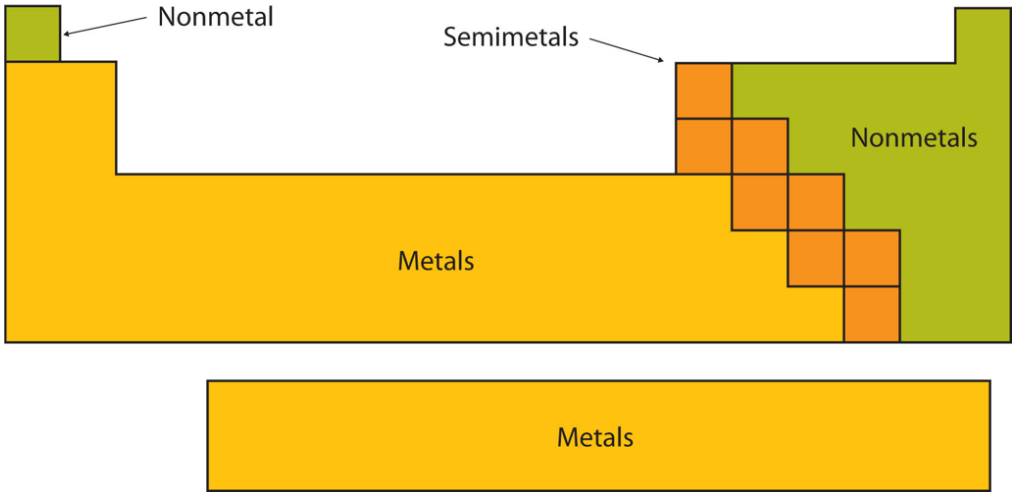


Figure 2.4.1**:Periodic Table of the Elements**. All of the known chemical elements are arranged in the format of a table. The table has been set up in such a way that the characteristics of each different element can be predicted by their position on the table. (A) On this rendition of the periodic table, you can see that the pink elements on the lefthand side of the table are the metals, while the blue elements on the right are the non-metals (Hydrogen is the only exception to this rule and will be explained in the subsequent sections). The metalloids (also termed semi-metals) occur in a stairstep pattern between the metals and nonmetals and are represented in this diagram by the green elements. (B) Shows the positions of the metals, nonmetals and metalloids on the periodic table. During this chapter, you will learn more about these unique characteristics, called *periodic trends*.

Periodic Table Downloadable PDF Version

The elements vary widely in abundance. In the universe as a whole, the most common element is hydrogen (about 90%), followed by helium (most of the remaining 10%). All other elements are present in relatively minuscule amounts, as far as we can detect. On the planet Earth, however, the situation is rather different. Oxygen makes up 46.1% of the mass of Earth's crust (the relatively thin layer of rock forming Earth's surface), mostly in combination with other elements, while silicon makes up 28.5%. Hydrogen, the most abundant element in the universe, makes up only 0.14% of Earth's crust. Table 2.4A lists the relative abundances of elements on Earth as a whole and in Earth's crust. Table 2.4B lists the relative abundances of elements in the human body. If you compare Table 2.4A and 2.4B, you will find disparities between the percentage of each element in the human body and on Earth. Oxygen has the highest percentage in both cases, but carbon, the element with the second highest percentage in the body, is relatively rare on Earth and does not even appear as a separate entry in Table 2.4A; carbon is part of the 0.174% representing "other" elements. How does the human body concentrate so many apparently rare elements?

The relative amounts of elements in the body have less to do with their abundances on Earth than with their availability in a form we can assimilate. We obtain oxygen from the air we breathe and the water we drink. We also obtain hydrogen from water. On the other hand, although carbon is present in the atmosphere as carbon dioxide, and about 80% of the atmosphere is nitrogen, we obtain those two elements from the food we eat, not the air we breathe.

Table 2.4A: Elemental Composition of the Earth

Earth's Crust		Earth Overall	
Element	Percentage	Element	Percentage
Oxygen	46.1	Iron	34.6
Silicon	28.2	Oxygen	29.5
Aluminum	8.23	Silicon	15.2
Iron	5.53	Magnesium	12.7

Earth's Crust		Earth Overall	
Calcium	4.15	Nickel	2.4
Sodium	2.36	Sulfur	1.9
Magnesium	2.33	All Others	3.7
Potassium	2.09		
Titanium	0.565		
Hydrogen	0.14		
Phosphorous	0.105		
All Others	0.174		

Source: D.R. Lide, ed. CRC Handbook of Chemistry and Physics, 89th ed. (Boca Raton, FL; CRC Press, 2008-9), 14-17.

Table 2.4B Elemental Composition of the Human Body

Human Body		Human Body (Continued)	
Element	Percent by Mass	Element	Percent by Mass
Oxygen	61	Sodium	0.14
Carbon	23	Chlorine	0.12
Hydrogen	10	Magnesium	0.027
Nitrogen	2.6	Silicon	0.026
Calcium	1.4	Iron	0.006
Phosphorous	1.1	Fluorine	0.004
Sulfur	0.20	Zinc	0.003
Potassium	0.20	All Others	0.174

Source: D.R. Lide, ed. CRC Handbook of Chemistry and Physics, 89th ed. (Boca Raton, FL; CRC Press, 2008-9), 7-24.

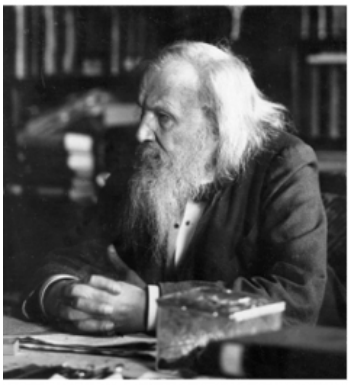
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2.5: Dimitri Mendeleev and the Periodic Table

The First Periodic Table

In the 19th century, many previously unknown elements were discovered, and scientists noted that certain sets of elements had similar chemical properties. For example, chlorine, bromine, and iodine react with other elements (such as sodium) to make similar compounds. Likewise, lithium, sodium, and potassium react with other elements (such as oxygen) to make similar compounds. Why is this so?

In 1864, Julius Lothar Meyer, a German chemist, organized the elements by atomic mass and grouped them according to their chemical properties. Later that decade, Dmitri Mendeleev, a Russian chemist, organized all the known elements according to similar properties. He left gaps in his table for what he thought were undiscovered elements, and he made some bold predictions regarding the properties of those undiscovered elements. Later, when elements were discovered whose properties closely matched Mendeleev's predictions, his version of the table gained favor in the scientific community. Because certain properties of the elements repeat on a regular basis throughout the table (that is, they are periodic), it became known as the *periodic table*.



Dmitri Mendeleev

Reihen	Gruppe I. — R^1O	Gruppe II. — RO	Gruppe III. — R^2O^3	Gruppe IV. RH^4 RO^2	Gruppe V. RH^3 R^2O^5	Gruppe VI. RH^2 RO^3	Gruppe VII. RH R^2O^7	Gruppe VIII. — RO^4
1	H=1							
2	Li=7	Be=9,4	B=11	C=12	N=14	O=16	F=19	
3	Na=23	Mg=24	Al=27,3	Si=28	P=31	S=32	Cl=35,5	
4	K=39	Ca=40	—=44	Ti=48	V=51	Cr=52	Mn=55	Fe=56, Co=59, Ni=59, Cu=63.
5	(Cu=63)	Zn=65	—=68	—=72	As=75	Se=78	Br=80	
6	Rb=85	Sr=87	?Yt=88	Zr=90	Nb=94	Mo=96	—=100	Ru=104, Rh=104, Pd=106, Ag=108.
7	(Ag=108)	Cd=112	In=113	Sn=118	Sb=122	Te=125	J=127	
8	Cs=133	Ba=137	?Di=138	?Ce=140	—	—	—	— — — —
9	(—)	—	—	—	—	—	—	
10	—	—	?Er=178	?La=180	Ta=182	W=184	—	Os=195, Ir=197, Pt=198, Au=199.
11	(Au=199)	Hg=200	Tl=204	Pb=207	Bi=208	—	—	
12	—	—	—	Th=231	—	U=240	—	— — — —

Figure 2.5.1: **Dmitri Medeleev's 1871 Early Version of the Periodic Table**

Photo of Dmitri Medeleev provided by: кабинет академика Михаила Михайловича Шульца – фото любезно передано мне в собственность вдовой М.М.Шульца Ниной Дмитриевной Шульц

Periodic Table provided by: Den fjättrade ankan

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2.6: Families of the Periodic Table

Elements that Share Similarities

Remember that Mendeleev arranged the periodic table so that elements with the most similar properties were placed in the same group. A group, or ***family of elements***, is a vertical column of the periodic table. Elements are placed into families due to their similar properties, characteristics, and reactivities. For example, all of the elements in group 1 (except for hydrogen, which has unique properties) are very reactive and form compounds in the same ratios and with similar properties as other 1 elements. Due to the similarities in their chemical properties, Mendeleev put these elements into the same group and they came to be known as the ***alkali metals.*** The ***alkali metals*** include: lithium, sodium, potassium, rubidium, cesium, and francium. Alkali metals are among the most reactive metals. This is due in part to their larger atomic radii and low ionization energies, that will be discussed in more details in section 2.8 below. They get their name from ancient Arabic (al qali) because "scientists" of the time found that the ashes of the vegetation they were burning contained a large amount of sodium and potassium. In Arabic, *al qali* means *ashes*. Although most metals tend to be very hard, alkali metals have a soft texture, are silvery in color and can be easily cut. They also have low boiling and melting points and are less dense than most elements. Figure 2.6.1 shows some of the most common families on the periodic table.

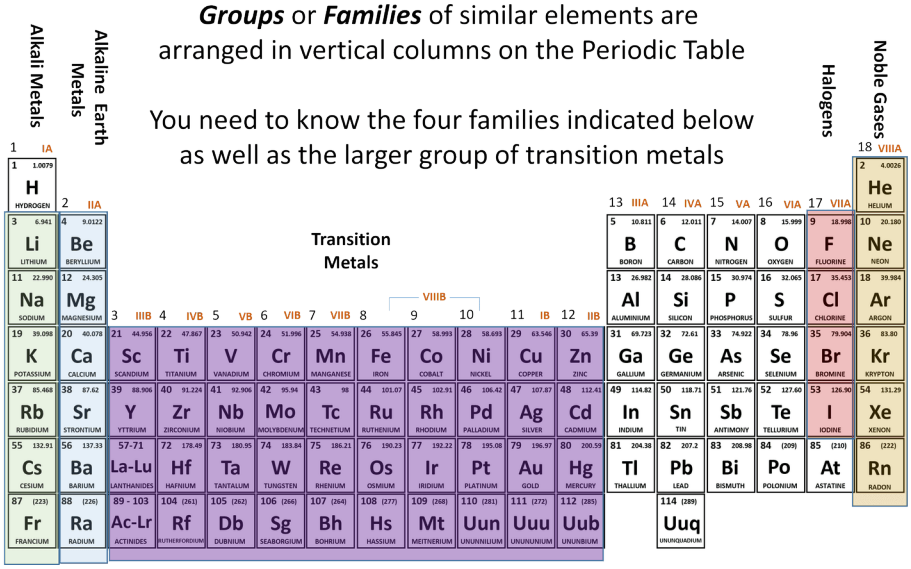


Figure 2.6.1**: Common Families and Groups of the Periodic Table.**

The same pattern is true of other vertical groups on the periodic table. Group 2 is called the ***alkaline earth metals***. Once again these elements have similar properties to each other. ***Alkaline earth metals*** include Beryllium, Magnesium, Calcium, Barium, Strontium and Radium and are soft, silver metals that are less metallic in character than the Group 1 alkali metals. Although many characteristics are common throughout the group, the heavier metals such as Ca, Sr, Ba, and Ra are almost as reactive as the Group 1 alkali metals. They get their name because early "scientists" found that all of the alkaline earth metals were found in the earth's crust.

The ***transition metals*** are the larger block of elements shown in purple on Figure 2.4 extending from Groups 3-12 (also known as the group B elements). Transition elements differ from the main group elements (group A elements) in that they tend to be hard and have high densities. They have high melting points and boiling points and can show various oxidation states when forming chemical bonds (this will be discussed further in chapter 3). They often form colored compounds that are highly stable and they can serve as good *catalysts*. A *catalyst* is an agent that helps to speed up a chemical reaction without itself being changed in the process.

Group 17 elements are also called ***halogens***. This group contains very reactive nonmetals. The ***halogens*** are an interesting group. Halogens are members of Group 17, which is also referred to as 7A. It is the only group in the Periodic Table that contains all of the states of matter at room temperature. Fluorine, F_2 and chlorine, Cl_2 are gases, while Bromine, Br_2, is a liquid and iodine, I_2, and astatine, At, are both solids. Another interesting feature about Group 17 is that it houses four (4) of the seven (7) ***diatomic elements. Diatomic elements*** only exist in nature as a pair of atoms of the same element that are bonded together. The seven diatomic elements are H_2, N_2, O_2, F_2, Cl_2, Br_2, and I_2. Notice that the latter four are Group 17 elements. The word halogen comes from the Greek meaning ***salt forming.*** French chemists discovered that the majority of halogen ions will form salts when combined with metals.

The ***noble gases*** are in group 18. The two most significant properties of noble gases is that they are extremely unreactive, rarely forming compounds, and that they all exist as gases at room temperature. We will learn the reason for their unreactivity when we discuss how compounds form in chapters 3 and 4. The first person to isolate a noble gas was Henry Cavendish, who isolated argon in the late 1700s. The noble gases were actually considered inert gases until the 1960s when a compound was formed between xenon and fluorine which changed the way chemists viewed the “inert” gases. In the English language, inert means to be lifeless or motionless; in the chemical world, inert means *does not react*. Later, the name “noble gas” replaced “inert gas” for the name of Group 18. The elements in this group are also gases at room temperature.

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2.7: Defining The Atom

Basic Atomic Structure – electrons, neutrons, and protons

The modern atomic theory, proposed about 1803 by the English chemist John Dalton, is a fundamental concept that states that all elements are composed of atoms. An atom is the smallest part of an element that maintains the identity of that element. Individual atoms are extremely small; even the largest atom has an approximate diameter of only 5.4×10^{-10} m. With that size, it takes over 18 million of these atoms, lined up side by side, to equal the width of your little finger (about 1 cm).

Most elements in their pure form exist as individual atoms. For example, a macroscopic chunk of iron metal is composed, microscopically, of individual iron atoms. Some elements, however, exist as groups of atoms called molecules. Several important elements exist as two-atom combinations and are called diatomic molecules. In representing a diatomic molecule, we use the symbol of the element and include the subscript 2 to indicate that two atoms of that element are joined together. The elements that exist as diatomic molecules are hydrogen (H_2), oxygen (O_2), nitrogen (N_2), fluorine (F_2), chlorine (Cl_2), bromine (Br_2), and iodine (I_2).

Atoms are made up of extremely small subatomic particles called protons, neutrons, and electrons. *Protons* are positively charged particles with a relative mass of 1.672622×10^{-24}g, which form part of the core *nucleus* of an atom. The other part of the atomic nucleus is made up of *neutrons*, electrically neutral particles with a relative mass almost identical to a proton (1.674927×10^{-24}g). *Electrons* are extremely small (9.109328×10^{-28}g) negatively charged particles that form an electron cloud, which orbits the nucleus.Table 2.7A summarizes some of the general properties of subatomic particles.

Table 2.7A: Properties of Subatomic Particles

Particle	Symbol	Mass (kg)	Relative Mass (Proton = 1)	Relative Charge
Proton	p^+	1.673×10^{-27}	1	+1
Neutron	n^0	1.675×10^{-27}	1	0
Electron	e^-	9.109×10^{-31}	0.00055	-1

Experiment have shown that protons and neutrons are concentrated in a central region of each atom called the nucleus (plural, nuclei). Electrons are outside the nucleus and orbit about it because they are attracted to the positive charge in the nucleus. Figures 2.7.1 and 2.7.2 depict the structure of an atom.

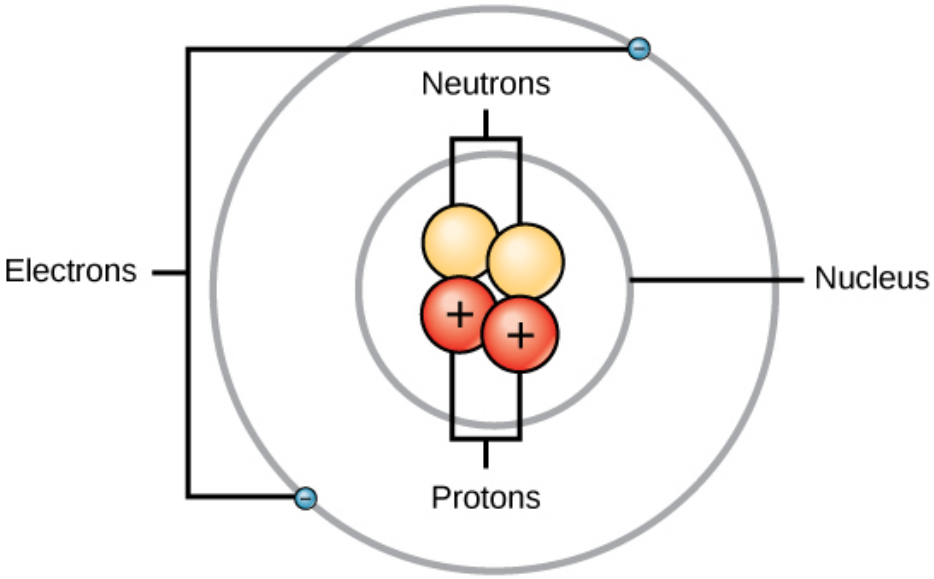


Figure 2.7.1**: The Anatomy of an Atom.** The protons and neutrons of an atom are found clustered at the center of the atom in a structure called the nucleus. The electrons orbit the nucleus of the atom within an electron cloud, or the empty space that surrounds the atom's nucleus. Note that most of the area of an atom is taken up by the empty space of the electron cloud.

Diagram provided by: CNX OpenStax

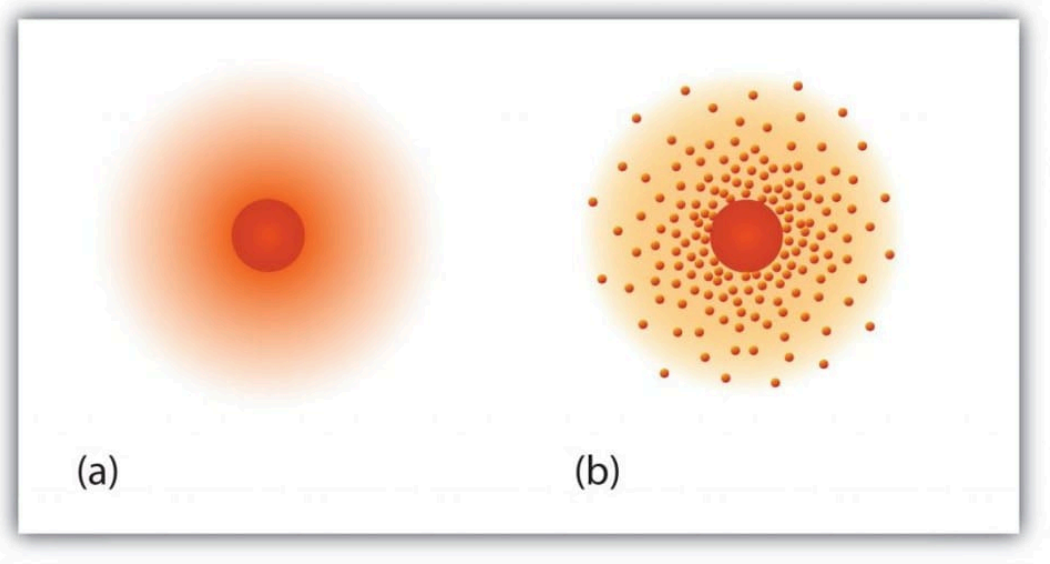


Figure 2.7.2**: The path of the electron in a hydrogen atom.** Electrons are not in discrete orbits like planets around the sun. Instead there is a probability that an electron may occupy a certain space within the electron cloud (a) The darker the color, the higher the probability that the hydrogen's one electron will be at that point at any given time. (b) Similarly, the more crowded the dots, the higher the probability that hydrogen's one electron will be at that point. In both diagrams, the nucleus is in the center of the diagram.

Most of the mass of an atom is in the nucleus, while the orbiting electrons account for an atom's size. As a result, an atom consists largely of empty space. Atomic particles are so small that it is impractical to measure them in grams, instead we use a relative mass scale which makes the numbers much more manageable. We use *Atomic Mass Units (AMU or u)* to measure the mass of atomic particles, one AMU is equal to 1/12th the mass of an atom of carbon-12. You may also see Atomic Mass Units referred

to as *Daltons (Da)* after John Dalton, the English Chemist that first proposed the atomic theory. Carbon-12 has 6 protons and 6 neutrons in its nucleus, meaning that one amu is equal to the average of the masses of a proton and a neutron. The mass of an atom in AMUs is equal to the number of protons and neutrons making up the atom. For example the atomic mass of bromine is roughly 80 amu and its proton number is 35, meaning that bromine has 35 protons and 45 neutrons in its nucleus.

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2.8: Atomic Number - Protons Determine the Identity of an Element

Finding the Atomic Number

When looking at the periodic table you might notice that for each element there are two sets of numbers around the symbol. These symbols correspond to important values that give you important information about each element (Figure 2.8.1). The most important value corresponding to characteristics of an element is the proton number, which is also called ***atomic number*** (represented by the mathematical term, *Z*). As it turns out, the number of protons that an atom holds in its nucleus is the key determining feature for its chemical properties. In short, an element is defined by the number of protons found in its nucleus. If you refer back to the Periodic Table of Elements shown in figure 2.6.1, you will see that the periodic table is organized by the number of protons that an element contains. Thus, as you read across each row of the Periodic Table (left to right), each element increases by one proton (or one Atomic Number, *Z*). When atoms are in their elemental states, their overall charge is zero and the atoms are neutral. Since protons are positively charged and electrons are negatively charged, this means that when atoms are in their elemental form, the number of protons equals the number of electrons. Therefore, if you know the atomic number of an atom, you also know how many electrons are present in that atom when it is in its elemental form. When atoms combine with one another to form compounds, like water (H_2O), they will either share or donate/accept electrons from their bonding partners. It is this movement of electrons that facilitates chemical bond formation. Thus, during bond formation the number of electrons around an atom may change, but the atomic number (or number of protons) remains constant and does not change.

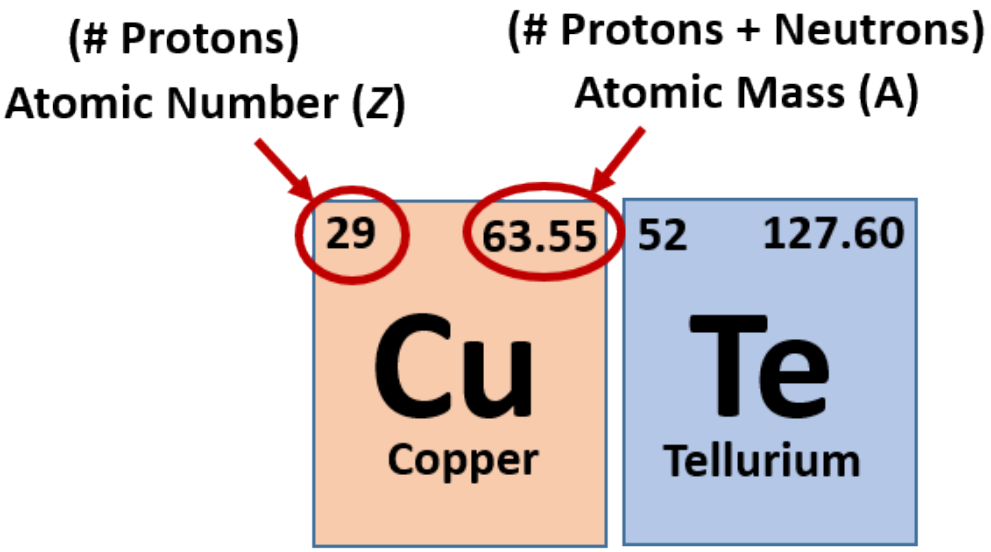


Figure 2.8.1**: Structure of the Periodic Table.** Each element on the periodic table is represented by the atomic symbol (Cu for Copper, and Te for Tellurium). Sometimes the Atomic Number is written in the upper lefthand corner, and the Atomic Mass in the righthand corner, as shown in this figure. Sometimes, periodic tables will show the atomic number above the element symbol and the atomic mass below the element symbol, as shown in the periodic table.

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2.9: Atomic Mass, Isotopes, and Molar Mass

Properties of Atoms

Atomic mass (A) is the total mass of an atom of a specific element and can be calculated by adding up the number of protons and neutrons present within an atom. The electrons are ignored in the mass calculation because they are so small that they barely add any mass to the atom.

$$\text{Mass Number} = \#\,\text{Protons} + \#\,\text{Neutrons} \tag{2.9.1}$$

Thus, if you know any two of the the three values (atomic mass, atomic number, or number of neutrons), you can calculate the third value. For example, nitrogen has an atomic mass of 14.007 and an atomic number of 7. Thus, it contains 7 protons, and 7 neutrons (14.007 – 7 = 7.007, which is then rounded to 7). Note that the number of neutrons in an atom does not have to equal the number of protons in the atom. For example, lead (Pb), contains 82 protons and has an atomic mass of 207.2. Thus it contains 125 neutrons (207.2 – 82 = 125). Thus, if you know the atomic mass and the atomic number of an element, you can calculate the number of neutrons present, or if you know the atomic mass and the number of neutrons, you can calculate the atomic number.

So...how many neutrons are in atoms of a particular element? At first it was thought that the number of neutrons in a nucleus was also defining characteristic of an element. However, it was found that atoms of the same element can have different numbers of neutrons. Atoms of the same element that have different numbers of neutrons are called ***isotopes***. An example of the three common isotopes of hydrogen are shown in Figure 2.8. Note that each of the hydrogen isotopes is known by a unique name, hydrogen, deuterium, and tritium. Not all elemental isotopes have such unique names. Many of the isotopes are distinguished from one another by including the atomic mass in the definition. For example, 99% of the carbon atoms on Earth have 6 neutrons and 6 protons in their nuclei, this is known as carbon-12; just under 1% of the carbon atoms have 7 neutrons and 6 protons in their nuclei, which is known as carbon-13, and an even smaller percent is carbon with 8 neutrons and 6 protons, or carbon-14. Carbon-14 is unstable and will decay over time making it a radioactive form of carbon. The half-life of carbon, or the time it takes for half of the isotope to breakdown is 5,700 years. Overall, there are 15 known isotopes of carbon! Thus, naturally occurring carbon on Earth, therefore, is actually a mixture of isotopes, albeit a mixture that is 99% carbon-12. Isotope composition has proven to be a useful method for dating many rock layers and fossils.

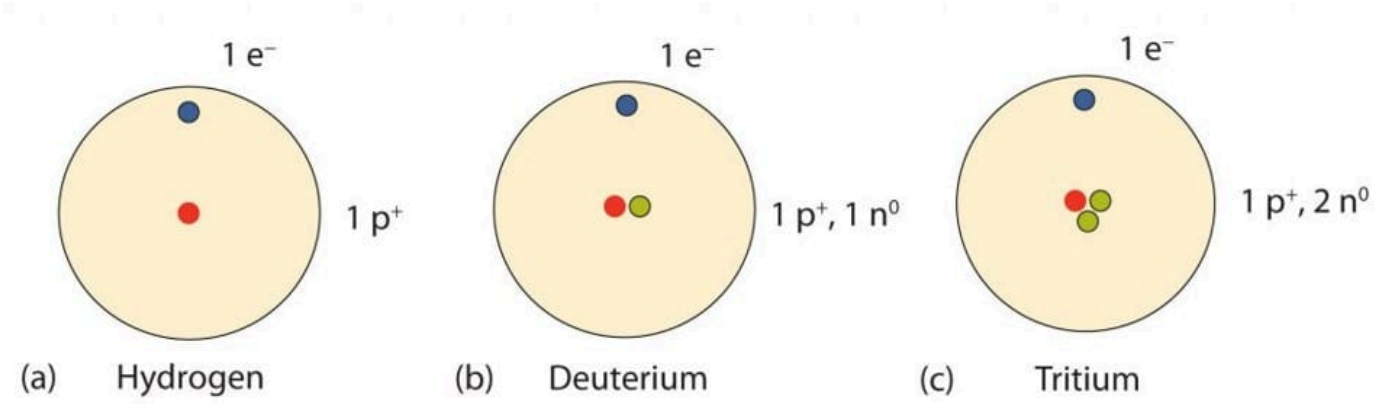
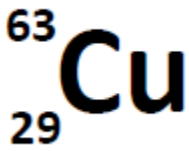


Figure 2.9.1**: Isotopes of Hydrogen.** All hydrogen atoms have one proton and one electron. However, they can differ in the number of neutrons. (a) Most hydrogen atoms only contain one proton and one electron and no neutrons (b) A small amount of hydrogen exists as the isotope deuterium, which has one proton and one neutron in its nucleus, and (c) an even smaller amount contains one proton and two neutrons in its nucleus and is termed Tritium. Note that Tritium is unstable isotope and will breakdown over time. Thus, Tritium is a radioactive element.

Most elements exist as mixtures of isotopes. In fact, there are currently over 3,500 isotopes known for all the elements. When scientists discuss individual isotopes, they need an efficient way to specify the number of neutrons in any particular nucleus. A

simple way of indicating the mass number of a particular isotope is to list it as a superscript on the left side of an element's symbol. Atomic numbers are often listed as a subscript on the left side of an element's symbol. Thus, we might see



which indicates a particular isotope of copper. The 29 is the atomic number, *Z*, (which is the same for all copper atoms), while the 63 is the atomic mass (A) of the isotope. To determine the number of neutrons in this isotope, we subtract 29 from 63: 63 – 29 = 34, so there are 34 neutrons in this atom.

The atomic masses indicated on the periodic table represents an average mass for each element based on the proportion of each isotope present on the Earth. This is why most of the atomic masses on the periodic table are not exact numbers. For example, the atomic mass of copper is 63.546 amu. This mass is an average of an element's atomic masses, weighted by the natural abundance of each isotope. So how could we calculate atomic mass based on the natural abundance of different isotopes of an element?

Example: Calculating Atomic Mass Using Isotope Abundance

Copper has two stable isotopes: ^{63}Cu (A = 62.93 Da) and ^{65}Cu (A = 64.93 Da). On Earth, the abundance of ^{63}Cu is 69.15%, whereas the abundance of ^{65}Cu is 30.85%. From this data, we can calculate the average atomic mass for Cu. Note that the atomic mass values on the periodic table represent the average relative abundance of the isotopes found on Earth.

$$(62.93\,\text{Da})\left(\frac{69.15}{100}\right)+(64.93\,\text{Da})\left(\frac{30.85}{100}\right)=63.55\,\text{Da} \tag{2.9.2}$$

Exercise 2.9.1

Try to work out the atomic mass for boron. Boron exists as a mixture that is 19.9% ^{10}B and 80.1% ^{11}B. Calculate the atomic mass.

Answer available at the end of this section.

Molar Mass

In Chapter 1, you learned that 1 mole of any substance is equivalent to 6.02 X 10^{23} molecules of that substance. But why this number? It seems like a strange number for chemists to work with! However, it turns out that this number of items of any atom or any substance is proportional to the atomic mass of that substance in grams, and this is very useful indeed! Atoms and molecules are way too small to count on an individual scale. However, when you are setting up a chemical reaction in the laboratory, reactions are written such that you know how many of each reactant will react with the other reactant to give you a known number of product molecules. It would be very expensive and wasteful indeed, if we did not have some way to determine how many molecules that we are adding of each substance when we are conducting a chemical reaction. Thus, the relationship of Avogadro's Number to the Molar Mass of a substance provides us with a mechanism to convert the number of molecules present into their gram mass. It is easily possible for us to measure out gram quantities of substances in the laboratory using a simple balance. Thus, by using the relationship of Avogadro's Number with the Molar Mass, we are able to conduct very precise measurements of the substances used in chemical reactions, saving both time and money!

So how does it work? We just learned in the section above that the atomic mass of each element is given on the periodic table, and is determined by the number of protons and neutrons present in the atom. For example the atomic mass of Sodium (Na) is 22.990 Daltons or Atomic Mass Units. If we were to relate this mass to the mass of 1 mole of Na atoms, the mass would be

22.990 grams. This would mean that 6.02 x 10^{23} atoms of Sodium has a mass of 22.990 g! Similarly, for any substance, such as water (H_2O), we need only to add the atomic masses of each element in the substance together to obtain the molar mass of that substance. For water, there are 2 Hydrogen atoms and 1 Oxygen atom. Adding the atomic masses of these elements together, we would get 2(1.0079) + 15.999 = 18.0148 atomic mass units. This is then equivalent to the molar mass of water which is 18.0148 g of water = 1 mole of water = 6.02 x 10^{23} molecules of water. Thus, the overall definition of *molar mass* is that the *molar mass* of a substance is equal to the atomic mass of that substance in grams and is equivalent to 6.02 x 10^{23} molecules of that substance.

Try these problems for little practice:

1. What is the molar mass of glucose ($C_6H_{12}O_6$)?

2. What is the molar mass of Sodium Hydrogen Carbonate ($NaHCO_3$)?

3. How many moles is 42.3 grams of Magnesium (Mg)?

4. How many atoms are in 63 grams of Mercury (Hg)?

Answers

Exercise 2.9.1

Check the Periodic Table for the correct answer!

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2.10: Periodic Table Trends

Now that you have learned about the organization of the periodic table based on the electron configurations of the elements, we can continue to analyze the periodic table for trends that result from this organization.

Atomic Size

One important trend to be aware of is the way that atomic size changes as you move across a period or down a group in the periodic table. Atomic size is typically measured by the radius of the atom starting at the core of the nucleus, and reaching all the way out to the last valence electron. As you may predict, atomic size will increase as you move down a family group, due to the increased number of electron shells. This substantially increases the size of the electron cloud. What you may not so easily predict is that atomic size decreases as you go across a period. Although this may seem counter-intuitive, the decrease in size can be explained by thinking about the valence electron shell as you go across a period; we see that each element across a period has the same valence electron shell that it is filling with valence electrons. While the valence shell stays the same as you go across a period, the number of protons is increasing. Protons, being positively charged, have a pull on the negatively charged electrons out in the electron cloud. As the number of protons and electrons increases across a period, they have an attractive pull on one another. This results in a tightening of the electron cloud and a reduction in the atomic nuclei. In other words, because the outermost electron shell remains the same across a period, that shell gets pulled progressively closer and closer to the nucleus of the atom as you go across a period. So the overall periodic trend for atomic radius (size) is that atoms get smaller as you go across a period, and they get larger as you go down a family group (Figure 2.9.1).

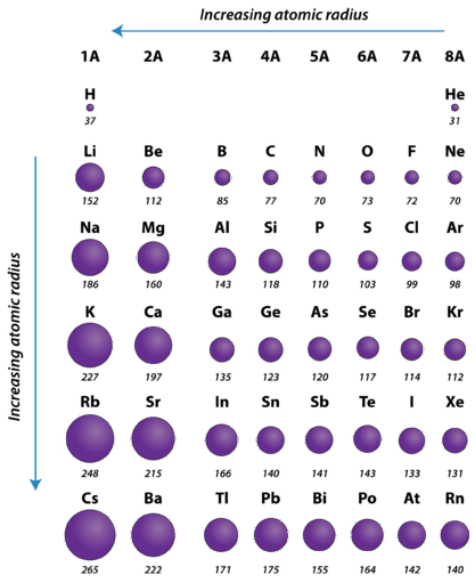


Figure 2.10.1: Atomic Radii of Select Elements Across the Periodic Table

Trends with Atomic Radii

- Atomic radius is determined as half the distance between the nuclei of two identical atoms bonded together.
- The atomic radius of atoms generally decreases from left to right across a period.
- The atomic radius of atoms generally increases from top to bottom within a group.

Electronegativity

Another important periodic trend to be aware of is how electronegativity differences can be identified. *Electronegativity* is the measure of an atom's tendency to attract a bonding pair of electrons. There are various numerical scales for rating electronegativity. Figure 2.9.2 shows one of the most popular—***the Pauling scale***. The Pauling scale assigns fluorine, the most electronegative atom, a 4.0 while less electronegative atoms have smaller grades. We will see in chapters 3 and 4 that electronegativity plays an important role in chemical bonding. The trends for electronegativity in the periodic table are that electronegativity increases as you go across a period, and increases as you go up a group, with fluorine being the most electronegative atom. Noble gases are given an electronegativity rating of 0 due to their inherent stability, which keeps them from forming bonds with other atoms.

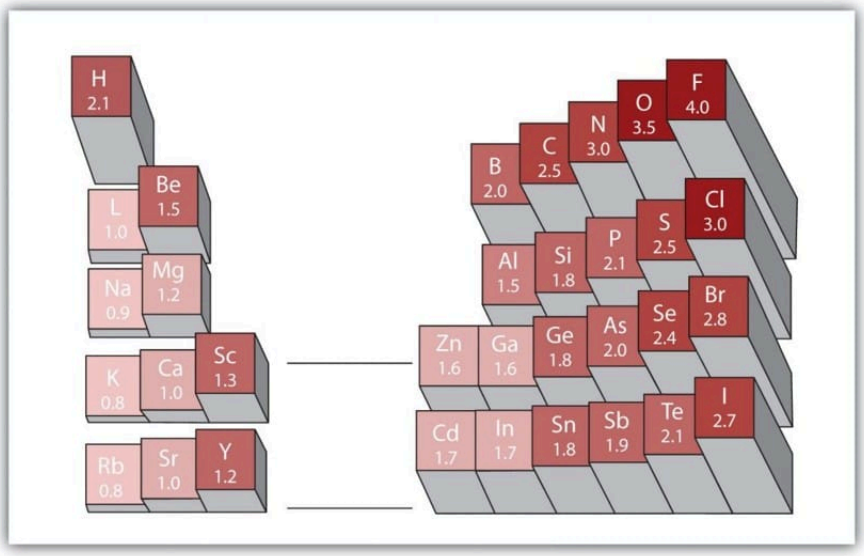
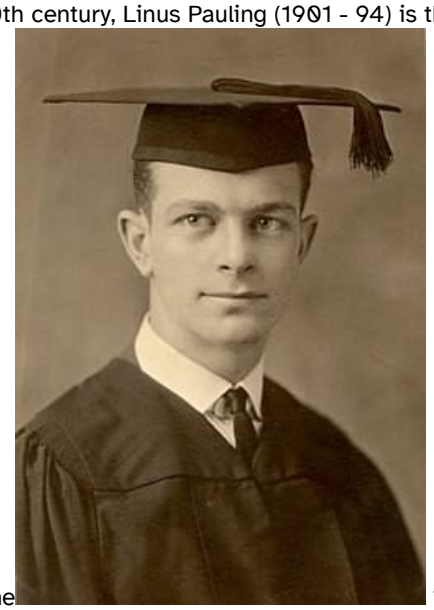


Figure 2.10.2**: Electronegativities of Various Elements.** The Pauling Scale for electronegativities has the value for fluorine atoms set at 4.0, the highest value.

Linus Pauling - A Closer Look

Arguably the most influential chemist of the 20th century, Linus Pauling (1901 - 94) is the only person to have won two



individual (that is unshared) Nobel Prizes. In the 1930s, Pauling used new mathematical theories to enunciate some fundamental principles of the chemical bond. His 1939 book, "*The Nature of the Chemical Bond*", is one of the most significant books every published in chemistry.

By 1935, Pauling's interest turned to biological molecules, and he was awarded the 1954 Nobel Prize in Chemistry for his work on protein structure. (He was also very close to discovering the double helix structure of DNA when James Watson and Francis Crick announced their own discover of its structure in 1953!) He was later awarded the 1962 Nobel Peace Prize for his efforts to ban the testing of nuclear weapons.

In his later years, Pauling became convinced that large doses of vitamin C would prevent disease, including the common cold. Most clinical research failed to show a connection, but Pauling continued to take large doses daily. He died in 1994, having spent a lifetime establishing a scientific legacy that few will ever equal.

Linus Pauling was one of the most influential chemists of the 20th century.

Pauling's Graduation Photo from

Oregon State University in 1922

Ionization Energy

Another periodic trend that you will be expected to know is the trend for ionization energy. ***Ionization energy*** is defined as the amount of energy required to remove the most loosely bound electron of an atom. How tightly bound the electrons of an atom are will affect the amount of energy required to remove one of the valence electrons. Electrons that are closer to the nucleus are going to be more tightly held than those that are further away and will require more energy to pull them off of the atom. For this reason, we see that ionization energy decreases as you go down a family group and the atoms get larger. This same concept can be applied to atoms across a period. We will see that the highest ionization energy will be found on the right side of the period where the atoms are the smallest, and the lowest ionization energy on the left where the atoms have a larger radii. In general, ionization energy decreases as you go down a family group, and increases as you go across a period from left to right (Figure 2.9.3).

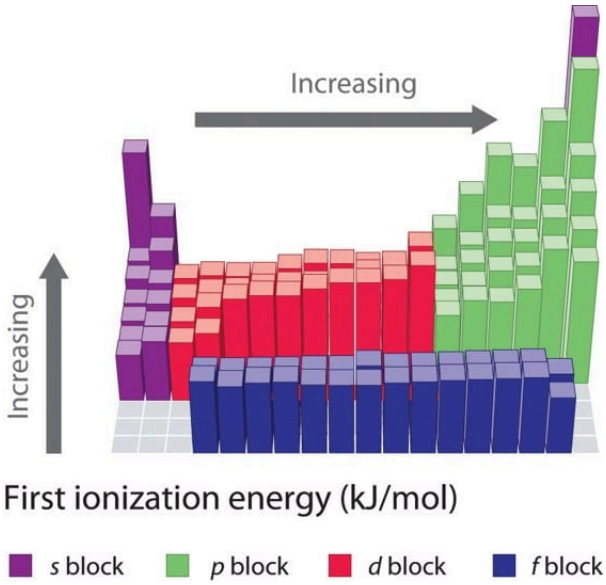


Figure 2.10.3: First Ionization Energies for the Elements of the Periodic Table.

Metallic and Nonmetallic Character

Metallic character refers to the level of reactivity of a metal. Metals tend to lose electrons in chemical reactions, as indicated by their low ionization energies. Within a compound, metal atoms have relatively low attraction for electrons, as indicated by their low electronegativities. By following the trend summary in the figure below, you can see that the most reactive metals would reside in the lower left portion of the periodic table. The most reactive metal is cesium, which is not found in nature as a free element. It reacts explosively with water and will ignite spontaneously in air. Francium is below cesium in the alkali metal group, but is so rare that most of its properties have never been observed.

The metallic character increases as you go down a group. Since the ionization energy decreases going down a group (or increases going up a group), the increased ability for metals lower in a group to lose electrons makes them more reactive. In addition, the atomic radius increases going down a group, placing the outer electrons further away from the nucleus and making that electron less attracted by the nucleus.

Nonmetals tend to gain electrons in chemical reactions and have a high attraction for electrons within a compound. These tendencies are known as ***nonmetallic character***. The most reactive nonmetals reside in the upper right portion of the periodic table. Since the noble gases are a special group because of their lack of reactivity, the element fluorine is the most reactive nonmetal. It is not found in nature as a free element. Fluorine gas reacts explosively with many other elements and compounds and is considered to be one of the most dangerous known substances.

Note that there is no clear division between ***metallic*** and ***nonmetallic*** character. As we move across the periodic table, there is an increasing tendency to accept electrons (nonmetallic) and a decrease in the possibility that an atom would give up one or more electrons.

Metallic and Nonmetallic Character and Periodic Trends:

- Metallic character refers to the level of reactivity of a metal to donate electrons during a chemical reaction.
- Nonmetallic character relates to the tendency of an element to accept electrons during chemical reactions.
- Metallic character increases going down a family group and decreases going across a period.
- Nonmetallic character increases going from left to right across the periodic table and decreases going down a family group.

The following figure summarizes all of the major periodic trends within the periodic table

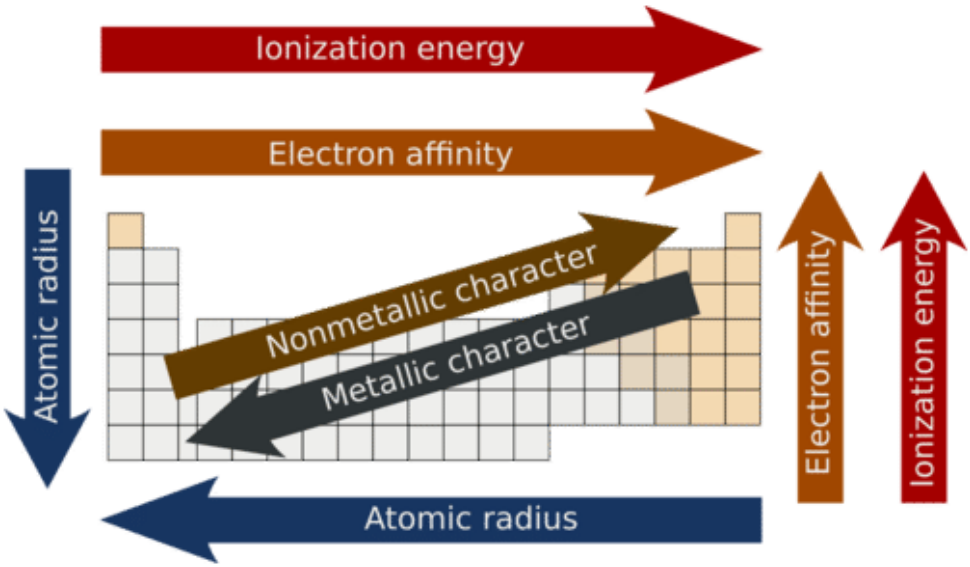


Figure 2.10.4**: Summary of Major Periodic Trends**

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2.11: Chapter Summary

Dalton's Atomic Theory proposed that matter is made up of tiny particles called atoms that cannot be broken into smaller pieces. During a chemical reaction, atoms are rearranged, but they do not break apart, nor are they created or destroyed. An ***element*** is a substance that cannot be broken down into simpler chemical substances. There are about 90 naturally occurring elements known on Earth. The smallest unit of an element is the atom. All atoms of the same element are identical in mass and other properties, whereas atoms of different elements differ in mass and other properties.

The elements can be divided into three major classes: The *metals, metalloids,* and *nonmetals*. ***Metals*** are typically shiny, very dense, have high melting points, and are good conductors. ***Nonmetals*** are generally brittle, dull, have low melting points, and they are generally poor conductors. *Metalloids* have properties of both metals and nonmetals.

Dmitri Mendeleev organized the elements into a chart based on their similar characteristics and properties. Today this chart is known as the *periodic table of the elements*. Within the periodic table group, or ***family of elements***, is a vertical column of the periodic table. Elements are placed into families due to their similar properties, characteristics, and reactivities. Group 1 elements are known as the *alkali metals* and are the most reactive elements of the metal class. *Alkaline earth metals* are found in group 2 and are almost as reactive as the group 1 metals. The *transition metals* are the larger block of elements extending from Groups 3-12 (also known as the group B elements). Transition metals have high melting points and boiling points, often form colored compounds that are highly stable, and they can serve as good *catalysts*. A *catalyst* is an agent that helps to speed up a chemical reaction without itself being changed in the process. Group 17 elements, known as ***halogens***, contains very reactive nonmetals that often exist as diatomic elements (F_2, Cl_2, Br_2, I_2). Group 18 elements, the **noble gases** are extremely stable, unreactive, and rarely form compounds.

Atoms are made up of extremely small subatomic particles called protons, neutrons, and electrons. ***Protons (***positively charged particles), and *neutrons* **(**electrically neutral particles) form the core or ***nucleus*** of an atom. ***Electrons*** are extremely small, negatively charged particles that form an electron cloud, which orbits the nucleus. The ***atomic number* (*Z*)** refers the the number of protons present in an element and is the defining feature of an element. The *atomic mass (A)* of an element is the sum of the protons and neutrons within that element.

Atoms of the same element (have the same atomic number) that have different numbers of neutrons are called ***isotopes.*** Most elements exist as isotopes. In fact, over 3,500 isotopes are known for the different elements. The atomic mass reported on the periodic table is the relative mass of the different isotopes of an element based on their abundance on the Earth.

The *valence shell* of an element is the outermost electron shell. The electrons housed within the valence shell are the most reactive electrons in an atom and are essential for forming chemical bonds with other elements. There are a total of eight electrons that can be housed in the valence shell of any atom.

Due to the organization of the periodic table according to proton and electron configurations, a number of interesting elemental trends can be observed. *Atomic size*, as measured by the atomic radius of an atom, increases and you move down a family group, and decreases as you move from left to right down a period or a row on the periodic table. The ***Electronegativity*** of an atom is the measure of an atom's tendency to attract a bonding pair of electrons, and can be thought of as electron affinity. Electronegativity increases as you go from left to right across the periods of the periodic table and it tends to decrease as you move down family groups. ***Ionization energy*** is defined as the amount of energy required to remove the most loosely bound electron of an atom. Ionization energy tends to increase as you move across the periods of the periodic table from left to right, and decreases as you move down a family group. Metallic character refers to the level of reactivity of a metal, whereas nonmetallic character refers to the level of reactivity of nonmetals. The metallic character of the elements tends to go up as you move down a family group of elements and goes down as you move from left to right across a row of the periodic table. Concomitantly, nonmetallic character tends to go down as you move down a family group of elements and goes up as you move from the left to the right across the periodic table.

Homework Chapter 2:

Part 1: Atomic Structure.

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3: RADIOACTIVITY AND NUCLEAR CHEMISTRY

3.1: Major Forms of Radioactivity

3.2: Radioactive Half Lives

3.3: Biological Effects of Radiation Exposure

3.4: Uses of Radioisotopes

3.5: Chapter Summary

3.6: References

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3.1: Major Forms of Radioactivity

Introduction

Atomic theory in the nineteenth century presumed that nuclei had fixed compositions. But in 1896, the French scientist Henri Becquerel found that a uranium compound placed near a photographic plate made an image on the plate, even if the compound was wrapped in black cloth. He reasoned that the uranium compound was emitting some kind of radiation that passed through the cloth to expose the photographic plate. Further investigations showed that the radiation was a combination of particles and electromagnetic rays, with its ultimate source being the atomic nucleus. These emanations were ultimately called, collectively, ***radioactivity***.

Following the somewhat serendipitous discovery of radioactivity by Becquerel, many prominent scientists began to investigate this new, intriguing phenomenon. Among them were Marie Curie (the first woman to win a Nobel Prize, and the only person to win two Nobel Prizes in different sciences—chemistry and physics), who was the first to coin the term “radioactivity,” and Ernest Rutherford (of gold foil experiment fame), who investigated and named three of the most common types of radiation. During the beginning of the twentieth century, many radioactive substances were discovered, the properties of radiation were investigated and quantified, and a solid understanding of radiation and nuclear decay was developed.

The spontaneous change of an unstable nuclide into another is ***radioactive decay***. The unstable nuclide is called the ***parent nuclide***; the nuclide that results from the decay is known as the ***daughter nuclide***. The daughter nuclide may be stable, or it may decay itself. The radiation produced during radioactive decay is such that the daughter nuclide lies closer to the band of stability than the parent nuclide, so the location of a nuclide relative to the band of stability can serve as a guide to the kind of decay it will undergo (Figure 3.1.1).

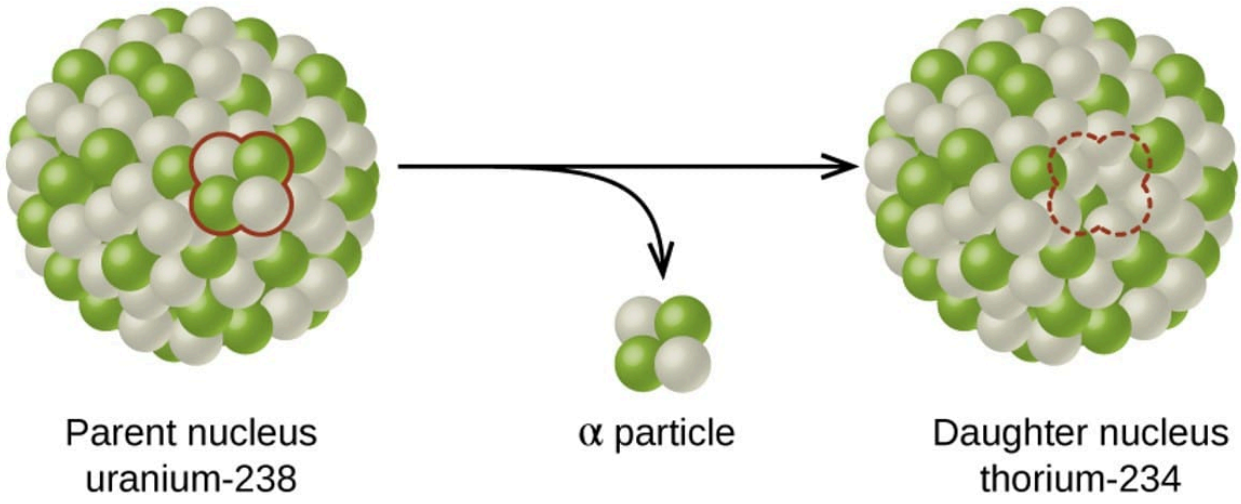


Figure 3.1.1**: A nucleus of uranium-238 (the parent nuclide) undergoes α decay to form thorium-234 (the daughter nuclide).** The alpha particle removes two protons (green) and two neutrons (gray) from the uranium-238 nucleus.

Major Forms of Radioactivity

Alpha Particle (α)

Rutherford's experiments demonstrated that there are three main forms of radioactive emissions. The first is called an ***alpha particle***, which is symbolized by the Greek letter α. An alpha particle is composed of two protons and two neutrons and is the same as a helium nucleus. We often use

$$^{4}_{2}\mathrm{He} \tag{3.1.1}$$

to represent an alpha particle. It has a 2+ charge. When a radioactive atom emits an alpha particle, the original atom's atomic number decreases by two (because of the loss of two protons), and its mass number decreases by four (because of the loss of four nuclear particles). We can represent the emission of an alpha particle with a chemical equation—for example, the alpha-particle emission of uranium-235 is as follows:

$$^{235}_{92}\mathrm{U} \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{231}_{90}\mathrm{Th} \tag{3.1.2}$$

Rather than calling this equation a chemical equation, we call it a ***nuclear equation*** to emphasize that the change occurs in an atomic nucleus. How do we know that a product of this reaction is ^{231}Th? We use the ***law of conservation of matter*****,** which says that matter cannot be created or destroyed. This means we must have the same number of protons and neutrons on both sides of the nuclear equation. If our uranium nucleus loses 2 protons, there are 90 protons remaining, identifying the element as thorium. Moreover, if we lose four nuclear particles of the original 235, there are 231 remaining. Thus we use subtraction to identify the isotope of the Th atom—in this case,

$$^{231}_{90}\mathrm{Th} \tag{3.1.3}$$

Beta Particle (β)

The second type of radioactive emission is called a *beta particle*, which is symbolized by the Greek letter β. A beta particle is an electron ejected from the nucleus (not from the shells of electrons about the nucleus) and has a -1 charge. We can also represent a beta particle as

$$^{0}_{-1}\mathrm{e} \tag{3.1.4}$$

The net effect of beta particle emission on a nucleus is that a neutron is converted to a proton. The overall mass number stays the same, but because the number of protons increases by one, the atomic number goes up by one. Carbon-14 decays by emitting a beta particle:

$$^{14}_{6}\mathrm{C} \longrightarrow {}^{0}_{-1}\mathrm{e} + {}^{14}_{7}\mathrm{N} \tag{3.1.5}$$

Again, the sum of the atomic numbers is the same on both sides of the equation, as is the sum of the mass numbers. (Note that the electron is assigned an "atomic number" of –1, equal to its charge.)

Gamma Radiation (γ)

The third major type of radioactive emission is not a particle but rather a very energetic form of *electromagnetic radiation* called ***gamma rays***, symbolized by the Greek letter γ. Electromagnetic radiation can be characterized into different categories based on the wavelength and photon energies. The electromagnetic spectrum shown in figure 3.2 shows the major categories of electromagnetic radiation. Note that the human sensory adaptations of sight and hearing have evolved to detect electromagnetic radiation, with radio waves having wavelengths between 1 mm and 100 km and visible light having wavelengths between 380 - 700 nm. Technological advances have helped humankind utilize other forms of electromagnetic radiation including X-rays and microwaves.

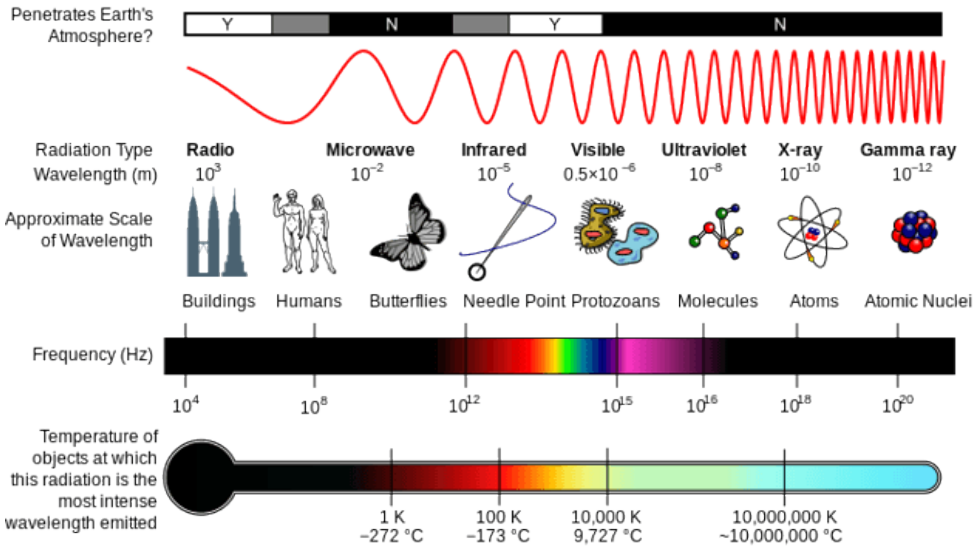


Figure 3.1.2**: The Electromagnetic Spectrum.** A diagram of the electromagnetic spectrum, showing various properties across the range of frequencies and wavelengths. Image Available from Wikipedia

Some electromagnetic radiation with very short wavelengths are active enough that they may knock out electrons out of atoms in a sample of matter and make it electrically charged. The types of radiation that can do this are termed *ionizing radiation*. X-rays and Gamma rays are examples of ionizing radiation. Some radioactive materials, emit gamma radiation during their decay. For example, in the decay of radioactive technetium-99, a gamma ray is emitted. Note that in radioactive decay where the emission of gamma radiation occurs, that the identity of the parent material does not change, as no particles are physically emitted.

$$^{99m}_{43}\mathrm{Tc} \rightarrow {}^{99}_{43}\mathrm{Tc} + \gamma \tag{3.1.6}$$

Sometimes the radioactive decay of a sample can result in the release of multiple forms of radioactivity. For example, in the radioactive decay of radon-222, both alpha and gamma radiation are emitted, with the latter having an energy of 8.2×10^{-14} J per nucleus decayed:

$$^{222}_{86}\mathrm{Rn} \longrightarrow {}^{218}_{84}\mathrm{Po} + {}^{4}_{2}\mathrm{He} + \gamma \tag{3.1.7}$$

This may not seem like much energy, but if 1 mol of Rn atoms were to decay, the gamma ray energy would be 4.9×10^{7} kJ!

Alpha, beta, and gamma emissions have different abilities to penetrate matter. The relatively large alpha particle is easily stopped by matter (although it may impart a significant amount of energy to the matter it contacts). Beta particles penetrate slightly into matter, perhaps a few centimeters at most. Gamma rays can penetrate deeply into matter and can impart a large amount of energy into the surrounding matter. Table 3.1 summarizes the properties of the three main types of radioactive emissions and Figure 3.3 summarizes the ability of each radioactive type to penetrate matter.

Table 3.1A: The Three Main Forms of Radioactive Emissions

Characteristic	Alpha Particles	Beta Particles	Gamma Rays
Symbols	α = $^{4}_{2}$He	β⦻ = $^{0}_{-1}$⦻e	γ
Identity	Helium nucleus	electron	Electromagnetic Radiation
Charge	2^{+}	1^{-}	None
Mass Number	4	0	0
Penetrating Power	Minimal (will not penetrate skin)	Short (will penetrate skin and some tissues slightly)	Deep (will penetrate tissues deeply)

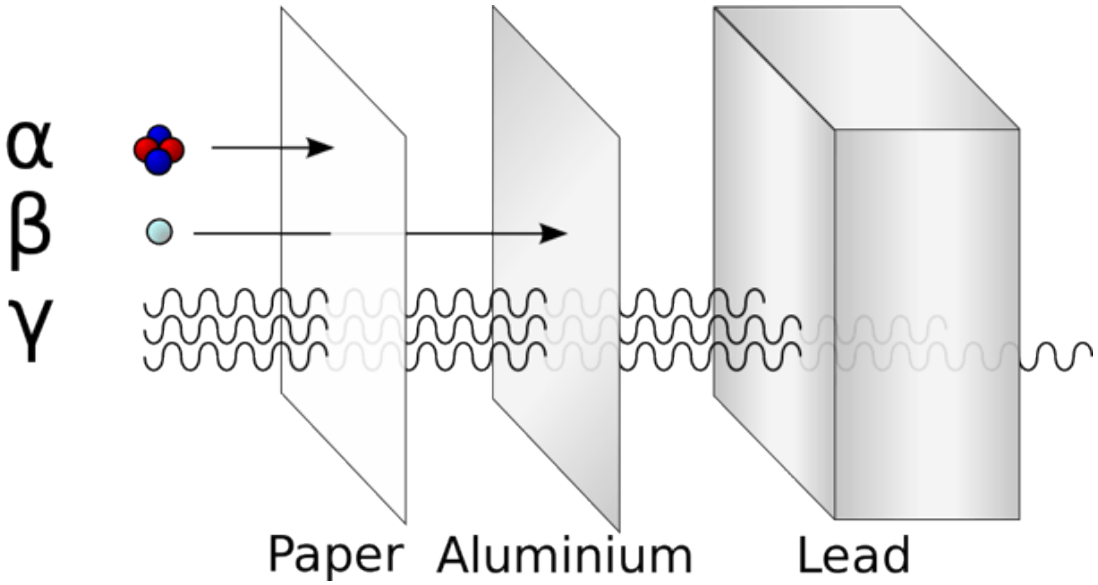


Figure 3.1.3: Illustration of the relative abilities of three different types of ionizing radiation to penetrate solid matter. Typical alpha particles (α) are stopped by a sheet of paper, while beta particles (β) are stopped by an aluminum plate. Gamma radiation (γ) is damped when it penetrates lead. Figure provided by Stannered.

Positron Emission (β^+ decay) and Electron Capture

In addition to the three major types of radioactive particles listed above, two additional less common types of emissions have been discovered. These include **positron emission** and **electron capture**.

Positron emission (β^+ decay) is the emission of a positron from the nucleus. Oxygen-15 is an example of a nuclide that undergoes positron emission:

$$^{15}_{8}\mathrm{O} \longrightarrow {}^{15}_{7}\mathrm{N} + {}^{0}_{+1}\mathrm{e} \tag{3.1.8}$$

Positron emission is observed for nuclides in which the n:p ratio is low. These nuclides lie below the band of stability. Positron decay is the conversion of a proton into a neutron with the emission of a positron. The n:p ratio increases, and the daughter nuclide lies closer to the band of stability than did the parent nuclide. The positron has the mass of an electron, but a positive charge. Thus, the overall mass of the nuclide doesn't change, but the atomic number is decreased by one, which causes a change in the elemental identity of the daughter isotope.

Electron capture occurs when one of the inner electrons in an atom is captured by the atom's nucleus. For example, potassium-40 undergoes electron capture:

$$^{40}_{19}\mathrm{K} + {}^{0}_{-1}\mathrm{e} \longrightarrow {}^{40}_{18}\mathrm{Ar} \tag{3.1.9}$$

Electron capture occurs when an inner shell electron combines with a proton and is converted into a neutron. The loss of an inner shell electron leaves a vacancy that will be filled by one of the outer electrons. As the outer electron drops into the vacancy, it will emit energy. In most cases, the energy emitted will be in the form of an X-ray. Like positron emission, electron capture occurs for "proton-rich" nuclei that lie below the band of stability. Electron capture has the same effect on the nucleus as does positron emission: The atomic number is decreased by one and the mass number does not change. This increases the n:p ratio, and the daughter nuclide lies closer to the band of stability than did the parent nuclide. Whether electron capture or positron emission occurs is difficult to predict. The choice is primarily due to kinetic factors, with the one requiring the smaller activation energy being the one more likely to occur.

Figure 3.1.4 summarizes these types of decay, along with their equations and changes in atomic and mass numbers.

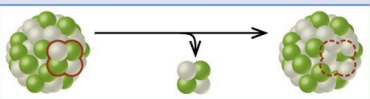
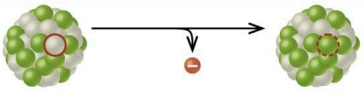
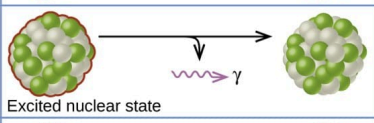
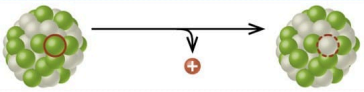
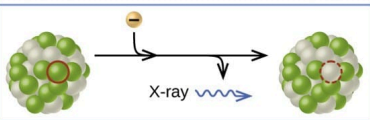
Type	Nuclear equation	Representation	Change in mass/atomic numbers
Alpha decay	${}^{A}_{Z}X \rightarrow {}^{4}_{2}He + {}^{A-4}_{Z-2}Y$		A: decrease by 4 Z: decrease by 2
Beta decay	${}^{A}_{Z}X \rightarrow {}^{0}_{-1}e + {}^{A}_{Z+1}Y$		A: unchanged Z: increase by 1
Gamma decay	${}^{A}_{Z}X \rightarrow {}^{0}_{0}\gamma + {}^{A}_{Z}Y$		A: unchanged Z: unchanged
Positron emission	${}^{A}_{Z}X \rightarrow {}^{0}_{+1}e + {}^{A}_{Y-1}Y$		A: unchanged Z: decrease by 1
Electron capture	${}^{A}_{Z}X \rightarrow {}^{0}_{-1}e + {}^{A}_{Y-1}Y$		A: unchanged Z: decrease by 1

Figure 3.1.4: Summary of the type, nuclear equation, representation, and any changes in the mass or atomic numbers for various types of decay.

Nuclear Fission

Occasionally, an atomic nucleus breaks apart into smaller pieces in a radioactive process called spontaneous fission (or fission). Typically, the daughter isotopes produced by fission are a varied mix of products, rather than a specific isotope as with alpha and beta particle emission. Often, fission produces excess neutrons that will sometimes be captured by other nuclei, possibly inducing additional radioactive events. Uranium-235 undergoes spontaneous fission to a small extent. One typical reaction is:

$$\mathbf{{}^{235}_{92}U + {}^{1}_{0}n \longrightarrow {}^{139}_{56}Ba + {}^{94}_{36}Kr + 2\,{}^{1}_{0}n} \tag{3.1.10}$$

where:

$$\mathbf{{}^{1}_{0}n} \tag{3.1.11}$$

is a neutron. As with any nuclear process, the sums of the atomic numbers and mass numbers must be the same on both sides of the equation. Spontaneous fission is found only in large nuclei. The smallest nucleus that exhibits spontaneous fission is lead-208. (Fission is the radioactive process used in nuclear power plants and one type of nuclear bomb.)

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3.2: Radioactive Half Lives

Each radioactive nuclide has a characteristic, constant **half-life** ($t_{1/2}$), the time required for half of the atoms in a sample to decay. An isotope's half-life allows us to determine how long a sample of a useful isotope will be available, and how long a sample of an undesirable or dangerous isotope must be stored before it decays to a low-enough radiation level that is no longer a problem.

For example,

$$^{60}_{27}\mathrm{Co} \tag{3.2.1}$$

cobalt-60, an isotope that emits gamma rays used to treat cancer, has a half-life of 5.27 years (Figure 3.2.1). In a given cobalt-60 source, since half of the nuclei decay every 5.27 years, both the amount of material and the intensity of the radiation emitted is cut in half every 5.27 years. Note that for a given substance, the intensity of radiation that it produces is directly proportional to the rate of decay of the substance and the amount of the substance. Thus, a cobalt-60 source that is used for cancer treatment must be replaced regularly to continue to be effective.

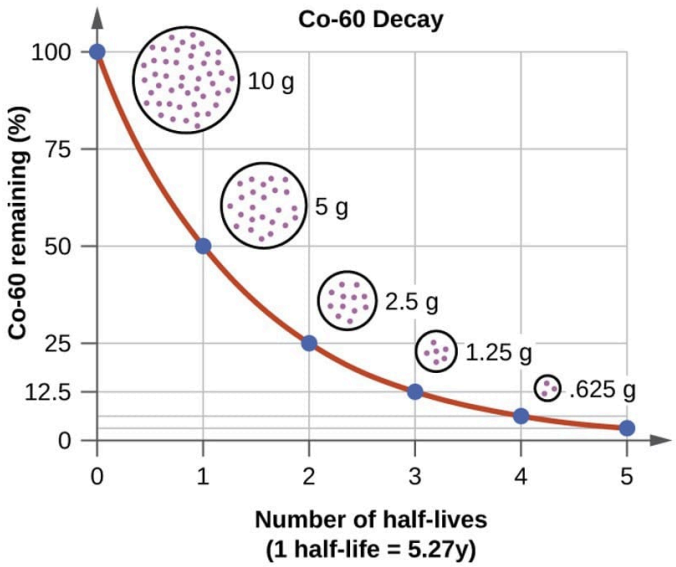


Figure 3.2.1**: The Decay of Cobalt-60.** For cobalt-60, which has a half-life of 5.27 years, 50% remains after 5.27 years (one half-life), 25% remains after 10.54 years (two half-lives), 12.5% remains after 15.81 years (three half-lives), and so on. Note that every half-life is the same length of time.

Since every half-life for a radionuclide is the same length of time, we can use the following equation to calculate how much radioactive nuclide is remaining after the passage of any number (n) of half-lives:

$$\text{Isotope Remaining} = \left(\frac{1}{2}\right)^{n} \times \text{Starting Material} \tag{3.2.2}$$

To find the isotope remaining, it is first necessary to determine how many half-lives have passed, (n). To calculate n, we need to know how much time has elapsed, and the length of time required for one half-life of the isotope in question:

- ***n*** = number of half-lives elapsed
- ***t*** = total time elapsed
- ***t*$_{1/2}$** = half-life of the isotope

Then the relationship is:

$$n = \frac{t}{t_{1/2}} \tag{3.2.3}$$

Let's try a practice problem

Example 3.2.1

The half-life of Zn-71 is 2.4 minutes. If one had 100.0 g at the beginning, how many grams would be left after 7.2 minutes has elapsed?

Solution

Step 1: Identify the information given in the problem and what you need to find.

$$\begin{aligned} t &= 7.2 \text{ min} \\ t_{1/2} &= 2.4 \text{ min} \\ n &= ? \\ \text{Isotope Starting} &= 100.0 \text{ g} \\ \text{Isotope Remaining} &= ? \end{aligned} \tag{3.2.4}$$

Step 2: Determine how many half-lives have elapsed.

Divide the elapsed time by the half-life:

$$\text{Number of half-lives} = \frac{\mathbf{7.2} \text{ min}}{\mathbf{2.4} \text{ min}} = \mathbf{3} \tag{3.2.5}$$

Therefore, **three half-lives** have elapsed or ***n* = 3**.

Step 3: Use the half-life relationship.

After each half-life, one-half of the radioactive isotope remains:

$$\text{Isotope Remaining} = \left(\frac{\mathbf{1}}{\mathbf{2}}\right)^{n} \times \text{Starting Material} \tag{3.2.6}$$

where n is the number of half-lives that have elapsed.

For this problem, *n*=3:

$$\text{Isotope Remaining} = \left(\frac{\mathbf{1}}{\mathbf{2}}\right)^{\mathbf{3}} \times \mathbf{100.0} \text{ g} \tag{3.2.7}$$

Step 4: Calculate the amount remaining.

$$\text{Isotope Remaining} = \frac{\mathbf{1}}{\mathbf{8}} \times \mathbf{100.0} \text{ g} = \mathbf{12.5} \text{ g} \tag{3.2.8}$$

Therefore, after **7.2 minutes**, **12.5 g of Zn-71 remains**.

This equation can also be rearranged using the natural log function to solve for the half-lives passed (*n*). To solve for ***n***, first divide both sides by the starting material:

$$\frac{\text{Isotope Remaining}}{\text{Starting Material}} = \left(\frac{\mathbf{1}}{\mathbf{2}}\right)^{n} \tag{3.2.9}$$

Then take the logarithm of both sides to move *n* out of the superscript position:

$$\ln\left(\frac{\text{Isotope Remaining}}{\text{Starting Material}}\right) = n\ln\left(\frac{1}{2}\right) \tag{3.2.10}$$

Finally, divide by ln(1/2):

$$\ln\left(\frac{\text{Isotope Remaining}}{\text{Starting Material}}\right) = n\ln\left(\frac{1}{2}\right) \tag{3.2.11}$$

So the **rearranged equation to solve directly for the number of half-lives** is:

$$n = \frac{\ln\left(\frac{\text{Isotope Remaining}}{\text{Starting Material}}\right)}{\ln\left(\frac{1}{2}\right)} \tag{3.2.12}$$

By being able to solve for *n* in this way, we can now work problems that ask us to calculate the half-life of an isotope, $t_{1/2}$. Let's work a practice problem:

Example 3.2.2

After 24.0 days, 2.00 milligrams of an original 128.0 milligram sample remain. What is the half-life of the sample?

Solution

Step 1: Identify the information given in the problem and what you need to find.

$$\begin{aligned} t &= 24.0 \text{ days} \\ t_{1/2} &= ? \\ n &= ? \\ \text{Isotope Starting} &= 128.0 \text{ mg} \\ \text{Isotope Remaining} &= 2.00 \text{ mg} \end{aligned} \tag{3.2.13}$$

Step 2: Determine the number of half-lives that have elapsed.

Use the relationship:

$$n = \frac{\ln\left(\frac{\text{Isotope Remaining}}{\text{Starting Material}}\right)}{\ln\left(\frac{1}{2}\right)} \tag{3.2.14}$$

Substitute the known amounts:

$$n = \frac{\ln\left(\frac{2.00 \text{ mg}}{128.0 \text{ mg}}\right)}{\ln\left(\frac{1}{2}\right)} \tag{3.2.15}$$

The milligram units cancel, giving:

$$n = \frac{\ln(0.015625)}{\ln(0.5)} = 6 \tag{3.2.16}$$

Therefore, **6 half-lives** have elapsed, or ***n* = 6**.

Step 3: Determine the length of one half-life.

We know:

$$n = \frac{t}{t_{1/2}} \tag{3.2.17}$$

Rearrange to solve for $t_{1/2}$:

$$t_{1/2} = \frac{t}{n} \tag{3.2.18}$$

The total elapsed time is 24.0 days, and n = 6 from above. Therefore, we can substitute the values and solve for $t_{1/2}$:

$$\text{Half-life} = \frac{\mathbf{24.0}\ \text{days}}{\mathbf{6}} = \mathbf{4.00}\ \text{days} \tag{3.2.19}$$

Therefore, the **half-life ($t_{1/2}$) of the sample is 4.00 days**.

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3.3: Biological Effects of Radiation Exposure

There is a large difference in the magnitude of the biological effects of **nonionizing radiation** (for example, light and microwaves) and **ionizing radiation**, emissions energetic enough to knock electrons out of molecules (for example, α and β particles, γ rays, X-rays, and high-energy ultraviolet radiation) (Figure 3.3.1).

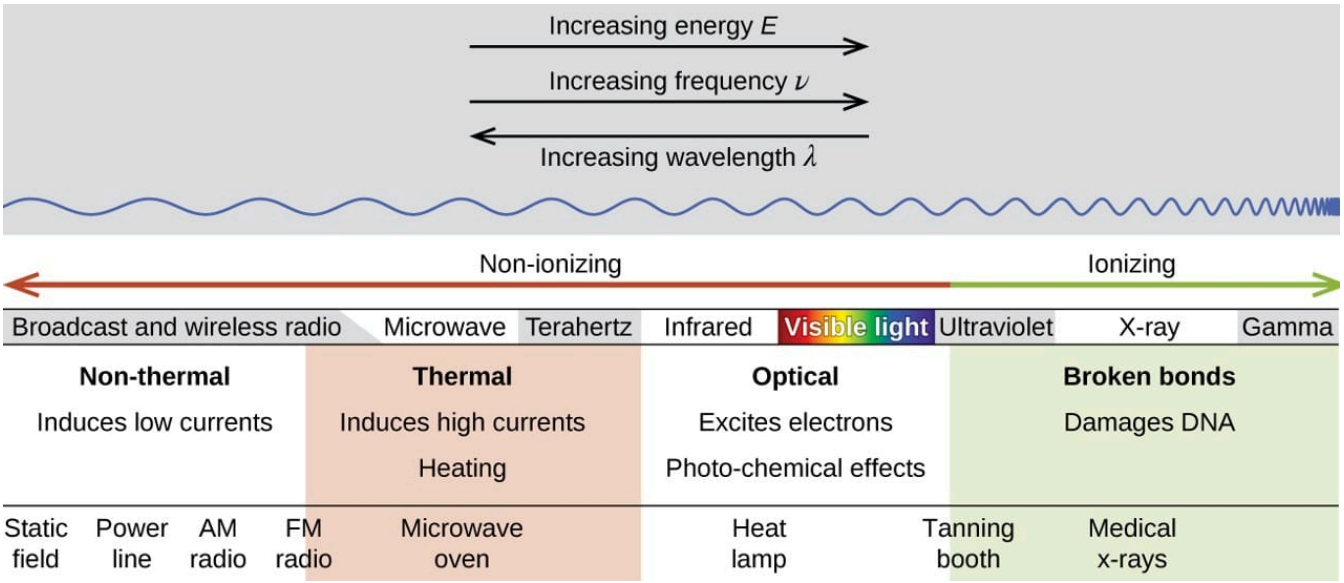


Figure 3.3.1: **Damaging Effects of Ionizing Radiation.** Lower frequency, lower-energy electromagnetic radiation is nonionizing, and higher frequency, higher-energy electromagnetic radiation is ionizing.

Energy absorbed from nonionizing radiation speeds up the movement of atoms and molecules, which is equivalent to heating the sample. Although biological systems are sensitive to heat (as we might know from touching a hot stove or spending a day at the beach in the sun), a large amount of nonionizing radiation is necessary before dangerous levels are reached. Ionizing radiation, however, may cause much more severe damage by breaking bonds or removing electrons in biological molecules, disrupting their structure and function (Figure 3.3.2).

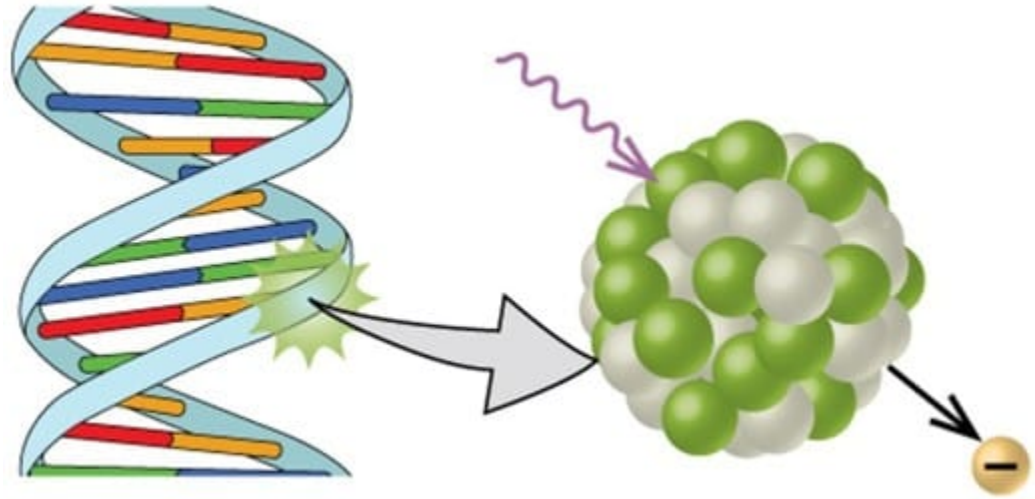


Figure 3.3.2: **Biological Effects of Ionizing Radiation.** Ionizing radiation can directly damage a biomolecule by ionizing it or breaking its bonds.

Radiation can harm either the whole body (somatic damage) or eggs and sperm (genetic damage). Its effects are more pronounced in cells that reproduce rapidly, such as the stomach lining, hair follicles, bone marrow, and embryos. This is why patients undergoing radiation therapy often feel nauseous or sick to their stomach, lose hair, have bone aches, and so on, and why particular care must be taken when undergoing radiation therapy during pregnancy.

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3.4: Uses of Radioisotopes

Radioisotopes have revolutionized medical practice, where they are used extensively. Over 10 million nuclear medicine procedures and more than 100 million nuclear medicine tests are performed annually in the United States. Four typical examples of radioactive tracers used in medicine are technetium-99, thallium-201, iodine-131, and sodium-24. Damaged tissues in the heart, liver, and lungs absorb certain compounds of technetium-99 preferentially. After it is injected, the location of the technetium compound, and hence the damaged tissue, can be determined by detecting the γ rays emitted by the Tc-99 isotope. Thallium-201 (Figure 3.4.1) becomes concentrated in healthy heart tissue, so the two isotopes, Tc-99 and Tl-201, are used together to study heart tissue. Iodine-131 concentrates in the thyroid gland, the liver, and some parts of the brain. It can therefore be used to monitor goiter and treat thyroid conditions, such as Grave's disease, as well as liver and brain tumors. Salt solutions containing compounds of sodium-24 are injected into the bloodstream to help locate obstructions to the flow of blood.

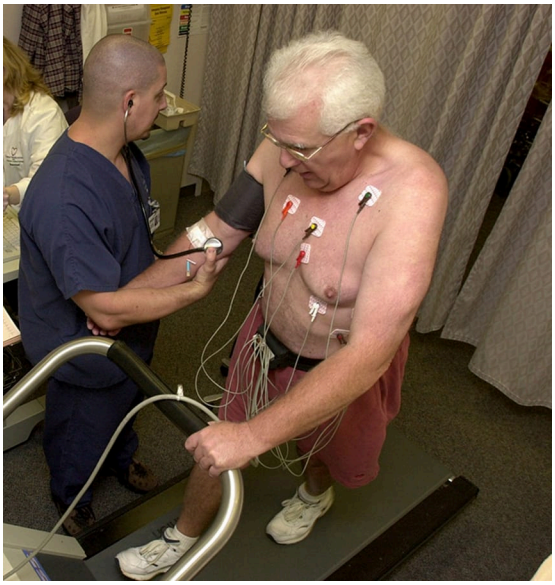


Figure 3.4.1: Administering thallium-201 to a patient and subsequently performing a stress test offer medical professionals an opportunity to visually analyze heart function and blood flow. (credit: modification of work by "Blue0ctane"/Wikimedia Commons)

Radioisotopes used in medicine typically have short half-lives. For example, Tc-99 has a half-life of 6.01 hours. This makes Tc-99 essentially impossible to store and prohibitively expensive to transport, so it is made on-site instead. Hospitals and other medical facilities use Mo-99 (which is primarily extracted from U-235 fission products) to generate Tc-99. Mo-99 undergoes β decay with a half-life of 66 hours, and the Tc-99 is then chemically extracted (Figure 3.4.2). The parent nuclide Mo-99 is part of a molybdate ion (MoO_4^{2-}), when it decays, it forms the pertechnetate ion (TcO_4^-). These two water-soluble ions are separated by column chromatography, with the higher charge molybdate ion adsorbing onto the alumina in the column, and the lower charge pertechnetate ion passing through the column in the solution. A few micrograms of Mo-99 can produce enough Tc-99 to perform as many as 10,000 tests.

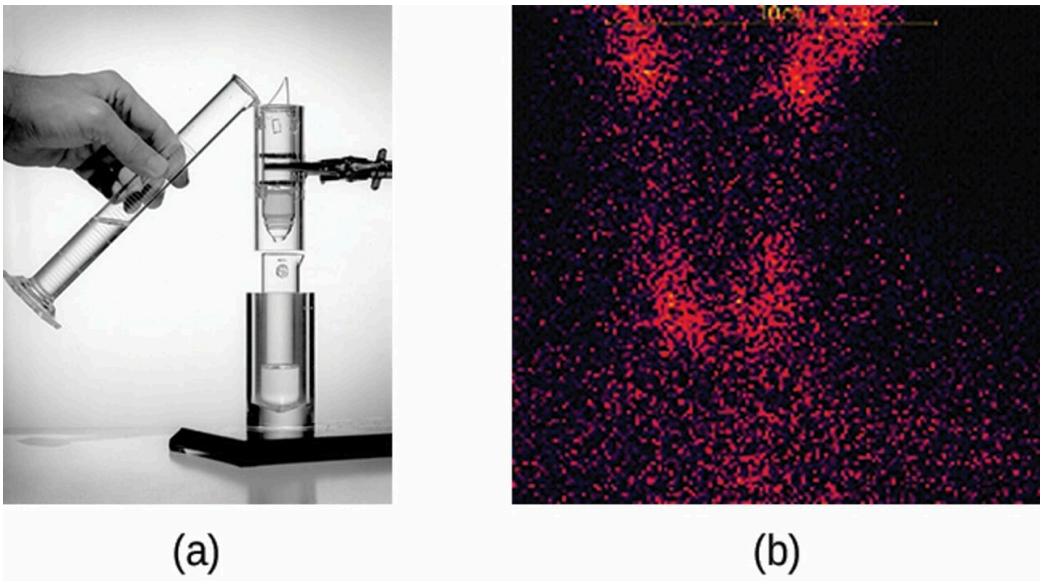


Figure 3.4.2: The formation of Tc-99m from Mo-99 (a) The first Tc-99m generator (circa 1958) is used to separate Tc-99 from Mo-99. The MoO_4^{2-} is retained by the matrix in the column, whereas the TcO_4^-. passes through and is collected. (b) Tc-99 was used in this scan of the neck of a patient with Grave's disease. The scan shows the location of high concentrations of Tc-99. (credit a: modification of work by the Department of Energy; credit b: modification of work by "MBq"/Wikimedia Commons)

Positron emission tomography (PET) scans use radiation to diagnose and track health conditions and monitor medical treatments by revealing how parts of a patient's body function (Figure 3.4.3). To perform a PET scan, a positron-emitting radioisotope is produced in a cyclotron and then attached to a substance that is used by the part of the body being investigated. This "tagged" compound, or **radiotracer**, is then administered to the patient (injected via IV or breathed in as a gas), and how it is used by the tissue reveals how that organ or other area of the body functions.

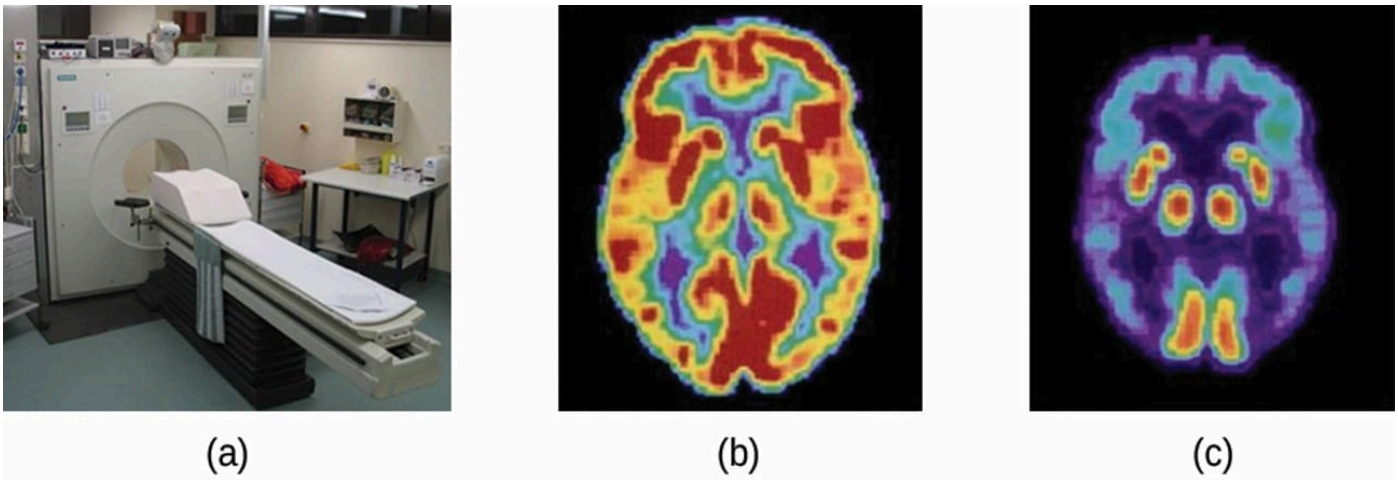


Figure 3.4.3: Positron Emission Scanning. A PET scanner (a) uses radiation to provide an image of how part of a patient's body functions. The scans it produces can be used to image a healthy brain (b) or can be used for diagnosing medical conditions such as Alzheimer's disease (c). (credit a: modification of work by Jens Maus)

For example, F-18 is produced by proton bombardment of ^{18}O and incorporated into a glucose analog called fludeoxyglucose (FDG). How FDG is used by the body provides critical diagnostic information; for example, since cancers use glucose differently than normal tissues, FDG can reveal cancers. The ^{18}F emits positrons that interact with nearby electrons, producing a burst of gamma radiation. This energy is detected by the scanner and converted into a detailed, three-dimensional, color image that

shows how that part of the patient's body functions. Different levels of gamma radiation produce different amounts of brightness and colors in the image, which can then be interpreted by a radiologist to reveal what is going on. PET scans can detect heart damage and heart disease, help diagnose Alzheimer's disease, indicate the part of a brain that is affected by epilepsy, reveal cancer, show what stage it is, and how much it has spread, and whether treatments are effective. Unlike magnetic resonance imaging and X-rays, which only show how something looks, the big advantage of PET scans is that they show how something functions. PET scans are now usually performed in conjunction with a computed tomography scan.

Radioisotopes can also be used, typically in higher doses than as a tracer, as treatment. **Radiation therapy** is the use of high-energy radiation to damage the DNA of cancer cells, which kills them or keeps them from dividing (Figure 3.4.4). A cancer patient may receive **external beam radiation therapy** delivered by a machine outside the body, or **internal radiation therapy (brachytherapy)** from a radioactive substance that has been introduced into the body. Note that **chemotherapy** is similar to internal radiation therapy in that the cancer treatment is injected into the body, but differs in that chemotherapy uses chemical rather than radioactive substances to kill the cancer cells.

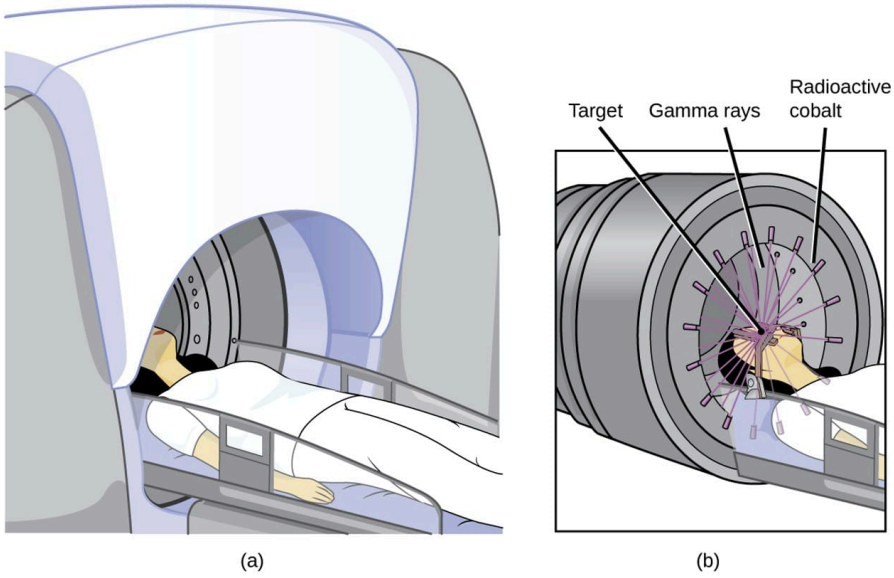


Figure 3.4.4**: Radiation used as a cancer treatment.** The cartoon in (a) shows a cobalt-60 machine used in the treatment of cancer. The diagram in (b) shows how the gantry of the Co-60 machine swings through an arc, focusing radiation on the targeted region (tumor) and minimizing the amount of radiation that passes through nearby regions.

Cobalt-60 is a synthetic radioisotope produced by the neutron activation of Co-59, which then undergoes β decay to form Ni-60, along with the emission of γ radiation. The overall process is:

The overall decay scheme for this is shown graphically in Figure 3.4.5.

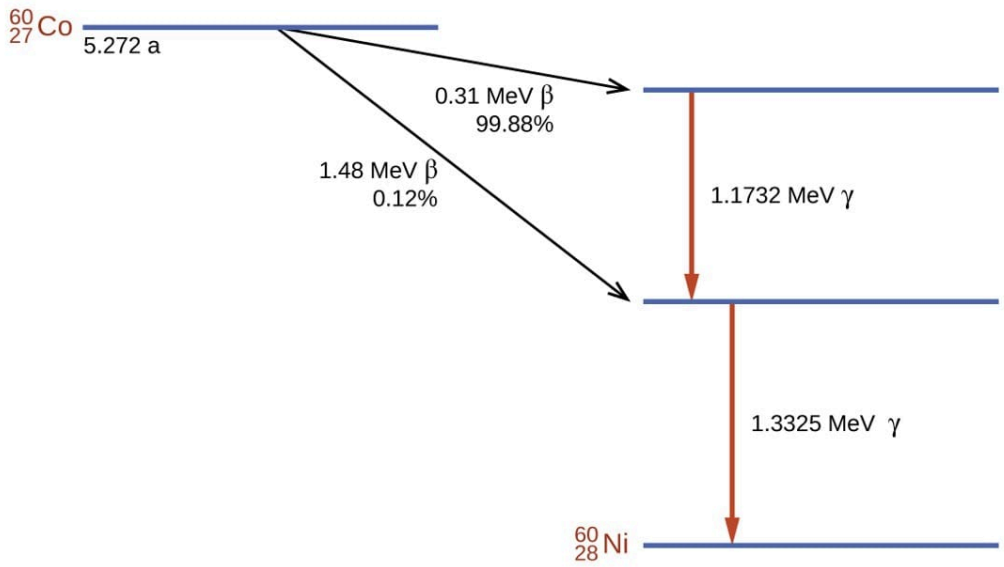


Figure 3.4.5: Co-60 Radioactive decay scheme. Co-60 undergoes a series of radioactive decays. The γ emissions are used for radiation therapy.

Radioisotopes are used in diverse ways to study the mechanisms of chemical reactions in plants and animals. These include labeling fertilizers in studies of nutrient uptake by plants and crop growth, investigations of digestive and milk-producing processes in cows, and studies on the growth and metabolism of animals and plants.

For example, the radioisotope C-14 was used to elucidate the details of how photosynthesis occurs. The overall reaction is:

$$6\,\mathrm{CO_2\,(g)} + 6\,\mathrm{H_2O\,(l)} \longrightarrow \mathrm{C_6H_{12}O_6\,(s)} + 6\,\mathrm{O_2\,(g)} \tag{3.4.1}$$

but the process is much more complex, proceeding through a series of steps in which various organic compounds are produced. In studies of the pathway of this reaction, plants were exposed to CO_2 containing a high concentration of C-14. At regular intervals, the plants were analyzed to determine which organic compounds contained carbon-14 and how much of each compound was present. From the time sequence in which the compounds appeared and the amount of each present at given time intervals, scientists learned more about the pathway of the reaction.

Commercial applications of radioactive materials are equally diverse (Figure 3.4.6). They include determining the thickness of films and thin metal sheets by exploiting the penetration power of various types of radiation. Flaws in metals used for structural purposes can be detected using high-energy gamma rays from cobalt-60 in a fashion similar to the way X-rays are used to examine the human body. In one form of pest control, flies are controlled by sterilizing male flies with γ radiation so that females breeding with them do not produce offspring. Many foods are preserved by radiation that kills microorganisms that cause the foods to spoil.

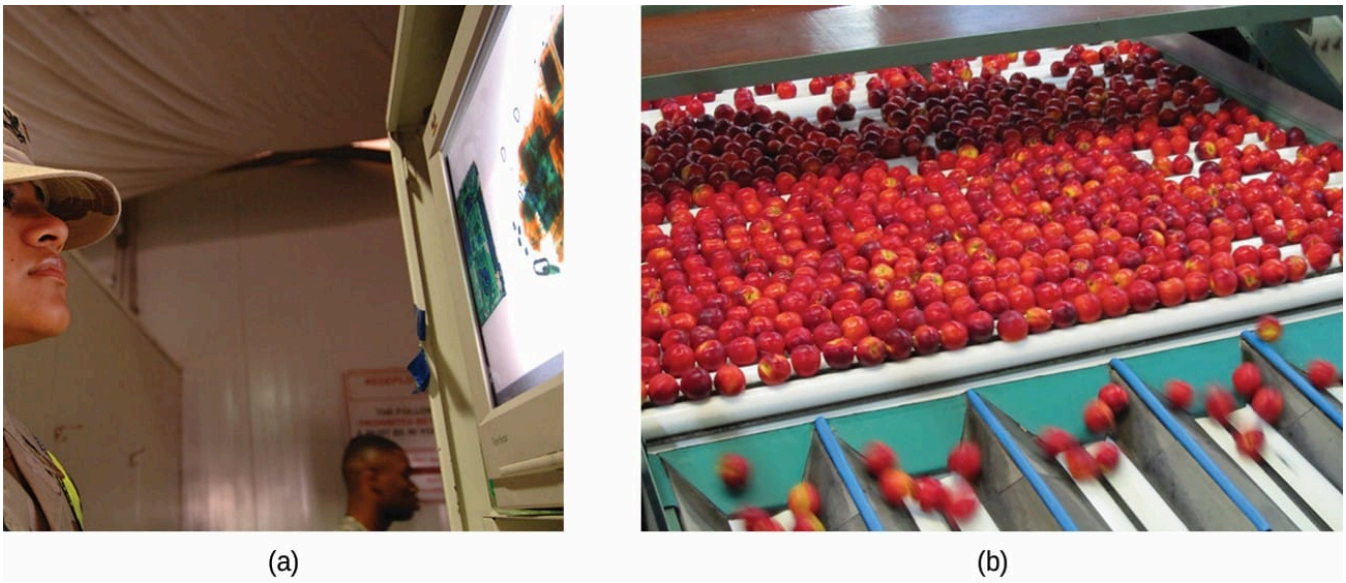


Figure 3.4.6: Examples of radiation used for commercial purposes. Common commercial uses of radiation include (a) X-ray examination of luggage at an airport and (b) preservation of food. (credit a: modification of work by the Department of the Navy; credit b: modification of work by the US Department of Agriculture)

Americium-241, an α emitter with a half-life of 458 years, is used in tiny amounts in ionization-type smoke detectors (Figure 3.4.7). The α emissions from Am-241 ionize the air between two electrode plates in the ionizing chamber. A battery supplies a potential that causes movement of the ions, thus creating a small electric current. When smoke enters the chamber, the movement of the ions is impeded, reducing the conductivity of the air. This causes a marked drop in the current, triggering an alarm.

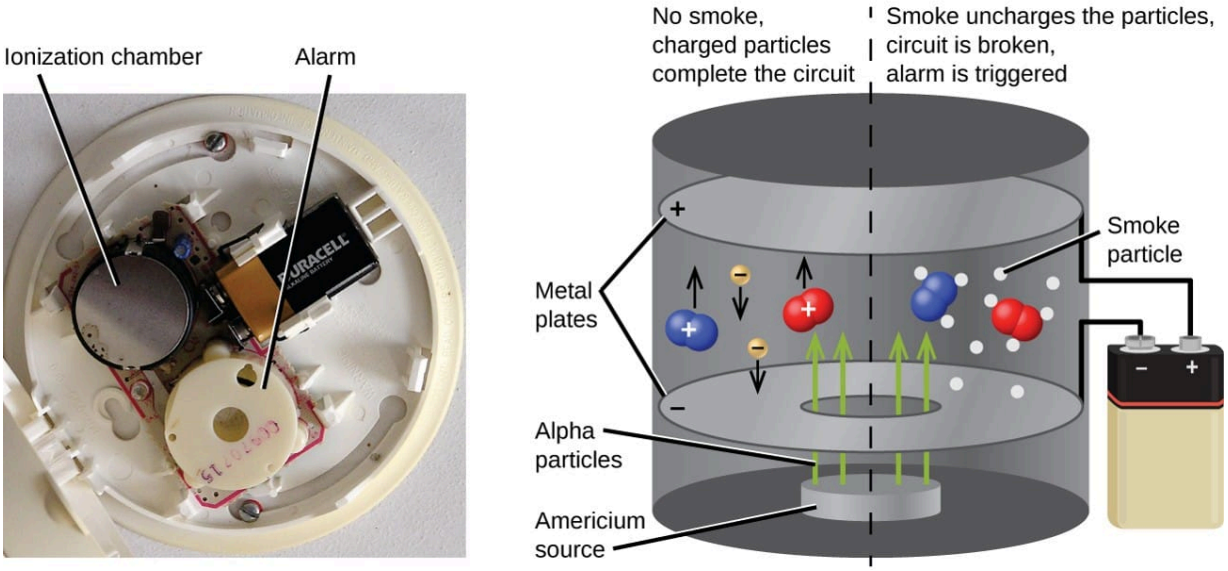


Figure 3.4.7: How radioactivity is used in a common smoke detector. Inside a smoke detector, Am-241 emits α particles that ionize the air, creating a small electric current. During a fire, smoke particles impede the flow of ions, reducing the current and triggering an alarm. (credit a: modification of work by "Muffet"/Wikimedia Commons)

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3.5: Chapter Summary

Radioactivity is defined as the emission of particles and electromagnetic rays from the nucleus of an unstable atom. Six types of radiation produced during nuclear decay were presented within this chapter and include:

· **alpha (α) decay** which is composed of two protons and two neutrons and has a +2 charge.

· **beta (β) decay** which is an electron ejected from the nucleus (not from the shells of electrons about the nucleus) and has a -1 charge and no mass. Within the nucleus a neutron emits the electron and is converted into a proton in the process.

· **gamma (γ) decay** which is characterized by the emission of ionizing radiation and does not contain mass or charge.

· **positron (β^+) emission** which is a positron ejected from the nucleus and has a +1 charge and no mass. Within the nucleus a proton emits the positron and is converted into a neutron in the process.

· **electron capture** occurs when an inner shell electron combines with a proton and is converted into a neutron. The loss of an inner shell electron leaves a vacancy that will be filled by one of the outer electrons. As the outer electron drops into the vacancy, it will emit energy often in the form of X-rays.

· **nuclear fission** occurs when an atomic nucleus breaks apart into smaller pieces in a radioactive process that releases excess neutrons.

Each radioactive nuclide has a characteristic, constant **half-life** ($t_{1/2}$), the time required for half of the atoms in a sample to decay. The equation below can be used to determine how much isotope will remain after the passage of a given number of half-lives:

$$\text{Isotope Remaining} = \left(\frac{1}{2}\right)^n \times \text{Isotope Starting} \tag{3.5.1}$$

Radioactive emissions can cause damage to biological systems by causing the breakdown of proteins and DNA. This can lead to cellular and genetic damage and increase a person's risk for diseases like cancer. However, when used is small quantities and in controlled settings, **radioactive tracers** and treatments have proven to be revolutionary for the medical field. For example, **Radiation therapy** is the use of high-energy radiation to damage the DNA of cancer cells, which kills them or keeps them from dividing. **Radioactive tracers** have also been very useful in evaluating heart disease, thyroid dysfunction, and other blood disorders. **Positron emission tomography (PET)** scans use radiation to diagnose and track health conditions and monitor medical treatments by revealing how parts of a patient's body function and X-rays have long been used to visualize breaks in bones and cavities in teeth.

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3.6: References

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4: CHEMICAL BONDING- HOW ATOMS FORM STABLE COMPOUNDS

4.1: Why do atoms bond?

4.2: Atoms Seek Stable Electron Configurations

4.3: Electron Transfer → Ionic Bonding

4.4: Electron Sharing → Covalent Bonding

4.5: Not All Shared Electrons Are Shared Equally

4.6: Chemistry in the Body- How do Neurons Maintain Ion Gradients?

4.7: Appendix A - Naming Ionic Compounds

4.8: Appendix B - Naming Covalent Compounds

4.9: Chapter Summary

4.10: References

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4.1: Why do atoms bond?

Imagine trying to build a puzzle.

A single puzzle piece is incomplete by itself. Only when it connects with other pieces does the complete picture emerge. Atoms behave in a surprisingly similar way. Although atoms can exist independently, most are more stable when they interact with other atoms to form chemical compounds.

The key to these interactions is **electrons**, especially the electrons located in the atom's outermost energy level. These **valence electrons** determine how an atom will interact with neighboring atoms and ultimately determine the structure and properties of every substance around us.

Water, proteins, DNA, table salt, medications, and even the calcium in your bones all exist because atoms have found stable ways to share or transfer electrons.

Stability: Nature's Goal

One of the fundamental driving forces in chemistry is that systems tend to move toward **lower-energy, more stable arrangements**. Atoms are no exception.

Many atoms have partially filled outer electron shells, making them less stable than atoms with completely filled outer shells. By **gaining, losing, or sharing electrons**, atoms can often achieve electron arrangements similar to those of the noble gases, which have especially stable electron configurations.

As shown in **Figure 4.1.1**, the first energy level can hold a maximum of **two electrons**. Because hydrogen and helium contain only one energy level, they are most stable when that level is filled with **two electrons**, a guideline known as the **duet rule**.

Beginning with the second period of the periodic table, atoms have additional energy levels. For most main-group elements, the outermost energy level is most stable when it contains **eight valence electrons**, a guideline known as the **octet rule**.

Notice in Figure 4.X that atoms become larger as you move down the periodic table because each new period adds another occupied energy level. Although the number of inner electrons increases, it is still the **outermost (valence) electrons** that determine how atoms bond and interact chemically.

Rather than thinking of the duet and octet rules as facts to memorize, think of them as **guidelines that help predict how atoms become more stable through chemical bonding**. In the next sections, we'll see that atoms can achieve these stable electron arrangements by **transferring electrons** or **sharing electrons** with neighboring atoms.

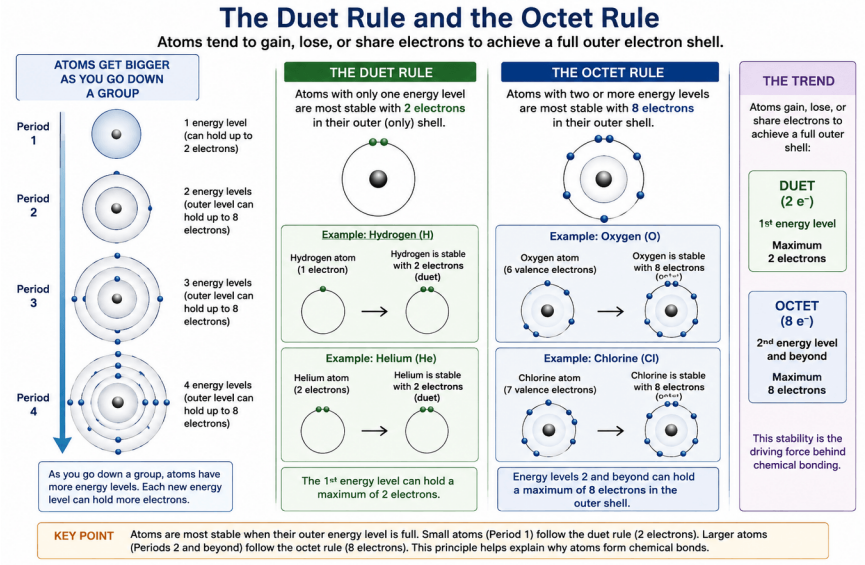


Figure 4.1.1**: The Duet Rule and Octet Rule.** The first energy level can hold a maximum of two electrons, while the outermost energy level of most main-group elements is most stable with eight valence electrons. As atoms become larger down the periodic table, additional energy levels are added, but chemical bonding still occurs through the outermost (valence) electrons. The illustration compares the duet and octet rules. The figure shows that the first energy level holds two electrons, later energy levels hold up to eight valence electrons, and atoms become larger as additional energy levels are added.

Valence Electrons Are the "Social" Electrons

The electrons closest to the nucleus are held tightly by the positively charged nucleus and rarely participate in chemical reactions. These **core electrons** help shield the nucleus but generally do not determine how an atom interacts with other atoms.

The **outermost electrons**, called **valence electrons**, are different. These electrons are the atom's "social" electrons—they are the electrons that are gained, lost, or shared when chemical bonds form. Because chemical bonding depends on valence electrons, chemists have developed a simple way to represent them.

Lewis (Electron-Dot) Symbols

Chemists often use **Lewis (electron-dot) symbols** to represent an atom's valence electrons. The element symbol represents the nucleus and core electrons, while each dot represents one valence electron.

To draw a Lewis symbol:

1. Write the element symbol.
2. Determine the number of valence electrons from the periodic table.
3. Place one electron on each side of the symbol before pairing electrons.

Figure 4.1.2 illustrates Lewis (electron-dot) symbols for several common nonmetals. Notice that the number of dots corresponds to the number of valence electrons. These symbols provide a simple way to visualize the electrons involved in chemical bonding and will be used throughout the remainder of this chapter.



Figure 4.1.2**: Electron Dot Symbols.** Electron Dot Symbols are shown for Carbon through Neon on the Periodic Table. Note that a single electron will be placed in each of the four cardinal directions before electrons will be paired with another electron.

The Lewis symbols shown in Figure 4.1.2 reveal a repeating pattern. As shown in **Figure 4.1.3**, the number of valence electrons for the main-group elements follows a predictable pattern across the periodic table. **Moving from left to right across a period, each successive main group element contains one additional valence electron.** For example, the second period begins with lithium (1 valence electron) and progresses through beryllium (2), boron (3), carbon (4), nitrogen (5), oxygen (6), fluorine (7), and finally neon (8), which has a complete outer electron shell.

Moving down a group, the number of valence electrons remains the same even though additional energy levels are added. For example, lithium, sodium, and potassium each have one valence electron, while fluorine, chlorine, and bromine each have seven valence electrons. Because elements in the same group have the same number of valence electrons, they often exhibit similar chemical properties and form similar types of chemical bonds.

The transition metals (Groups 3–12) are an exception to the simple valence electron pattern of the main-group elements. After the main-group elements reach two valence electrons in Group 2, the transition metals begin filling the inner d orbitals while generally retaining two electrons in their outermost energy level. Because these d electrons can also participate in chemical bonding, transition metals often form multiple ions with different charges, such as Fe^{2+} and Fe^{3+} or Cu^{+} and Cu^{2+}. In this course, we will focus primarily on the predictable bonding patterns of the main-group elements and introduce transition metals only when they are biologically important.

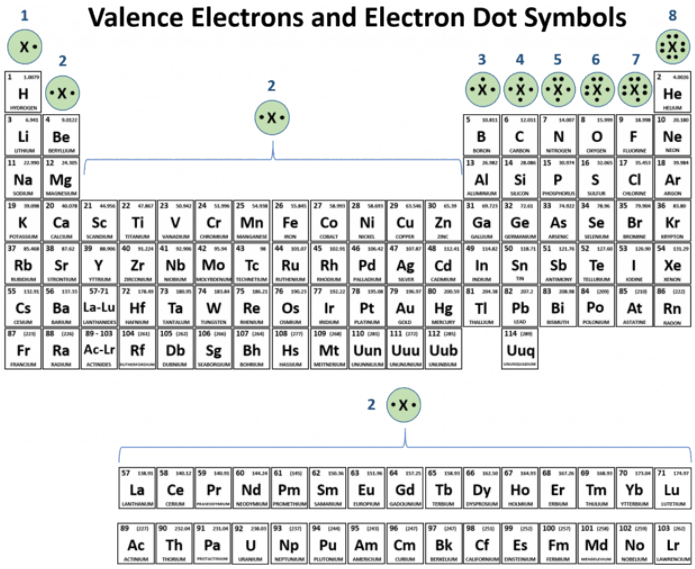


Figure 4.1.3**: Periodic Table with Electron Dot Symbols.** Electron dot symbols are drawn above each family or group of elements on the periodic table, where X indicates any element within that family or group.

The number of valence electrons largely determines:

- whether an atom is likely to form chemical bonds,
- whether it tends to gain, lose, or share electrons,
- how many bonds it can form, and
- the types of compounds it is likely to produce.

Understanding valence electrons is one of the keys to understanding chemistry. Throughout this chapter, we'll see that the behavior of these outermost electrons explains **why atoms bond, what types of bonds they form, and ultimately why different substances have different physical and chemical properties.**

> **Key Idea**
>
> For the main-group elements, **the group number tells you the number of valence electrons**. Groups 1 and 2 have 1 and 2 valence electrons, respectively, while Groups 13–18 have 3–8 valence electrons. Because elements in the same group have the same number of valence electrons, they often have similar chemical properties.

Three Ways Atoms Can Become Stable

Although there are many kinds of chemical compounds, most chemical bonds form in one of three ways.

1. **Electron Transfer** – one atom loses electrons while another gains them, forming **ionic bonds**.
2. **Unequal Sharing of Electrons** – atoms share electrons, but one atom attracts the shared electrons more strongly than the other, forming **polar covalent bonds**.
3. **Equal Sharing of Electrons** – atoms share electrons equally, forming **nonpolar covalent bonds**.

Instead of viewing ionic and covalent bonding as completely different ideas, it is often more useful to think of them as different ways that atoms use electrons to achieve stability.

This chapter will explore each of these bonding strategies and show how they explain the properties of the compounds that make up living organisms and the materials we encounter every day.

Chemistry Connection

Why Does Sodium Become Safe to Eat?

Sodium metal, **Na**, reacts violently with water, while chlorine gas, **Cl_2**, is highly toxic. Yet together they form sodium chloride, **NaCl**, or table salt, an essential nutrient that helps regulate fluid balance and nerve function in the human body.

How can two hazardous elements combine to produce a substance that is safe enough to sprinkle on food?

The answer lies in **chemical bonding**. When sodium transfers an electron to chlorine, both atoms achieve more stable electron arrangements, forming oppositely charged ions that are held together by strong electrostatic attractions. The resulting compound has completely different physical and chemical properties than either element alone.

This remarkable transformation illustrates one of the most important ideas in chemistry:

> **The properties of a compound are often very different from the properties of the elements from which it is formed.**

Looking Ahead...

How do atoms actually achieve stability?

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4.2: Atoms Seek Stable Electron Configurations

Learning Objectives

After completing this section, you should be able to:

- Predict the number of valence electrons in a main-group element using its position on the periodic table.
- Explain how atoms form cations and anions by gaining or losing electrons.
- Use periodic trends to predict the most common ionic charge formed by a main-group element.
- Explain the concept of isoelectronic species and identify ions that have the same electron configuration as a noble gas.

From Stable Atoms to Stable Compounds

In the previous section, we learned that atoms often become more stable by achieving filled outer electron shells. But **how do they actually accomplish this?**

One strategy is surprisingly simple:

> ### One atom gives up one or more electrons, while another atom accepts them.

This process is called **electron transfer**.

Electron transfer occurs most commonly between **metals** and **nonmetals**. Metals tend to lose electrons relatively easily, while nonmetals tend to gain electrons. As a result, both atoms can achieve more stable electron arrangements. Atoms involved in eletron transfer form **ionic bonds**.

A second strategy is to share electrons:

> ### One atom shares one or more electrons with another atom.

Electron sharing occurs most commonly between **two nonmetals**. Atoms that share electrons form **covalent bonds**.

Both strategies are important for chemical bond formation. In this section, we will focus on **electron transfer** and in later sections return to electron sharing.

From Atoms to Ions

When an atom gains or loses electrons, it is no longer electrically neutral. Instead, it becomes a **charged particle called an ion**.

There are two kinds of ions.

Cations

When an atom **loses electrons**, it loses negative charge and becomes **positively charged** due to the new imbalance between the protons and electrons in the atom.

These positively charged ions are called **cations**.

Examples include:

Table 4.2A Examples of Atoms that Form Cations

Atom	Electron Change	Ion
Na	loses 1 electron	Na^{+}
Mg	loses 2 electrons	Mg^{2+}
Ca	loses 2 electrons	Ca^{2+}

Notice that the elements that commonly lose electrons are metals. ***Why would metals prefer to lose electrons, rather than gain them?***

Recall from the previous section that atoms become most stable when their outer energy level is filled. For most main-group elements, this means achieving an **octet** of eight valence electrons.

Sodium provides a useful example (Figure 4.2.1). A neutral sodium atom contains **11 protons and 11 electrons**. During ion formation, sodium loses its single valence electron from the third energy level. The resulting sodium ion (Na^{+}) now contains **11 protons but only 10 electrons**, giving it an overall **+1 charge**.

Most importantly, losing this electron leaves sodium with a completely filled second energy level containing eight electrons (the octet state). In other words, sodium has achieved a much more stable electron configuration.

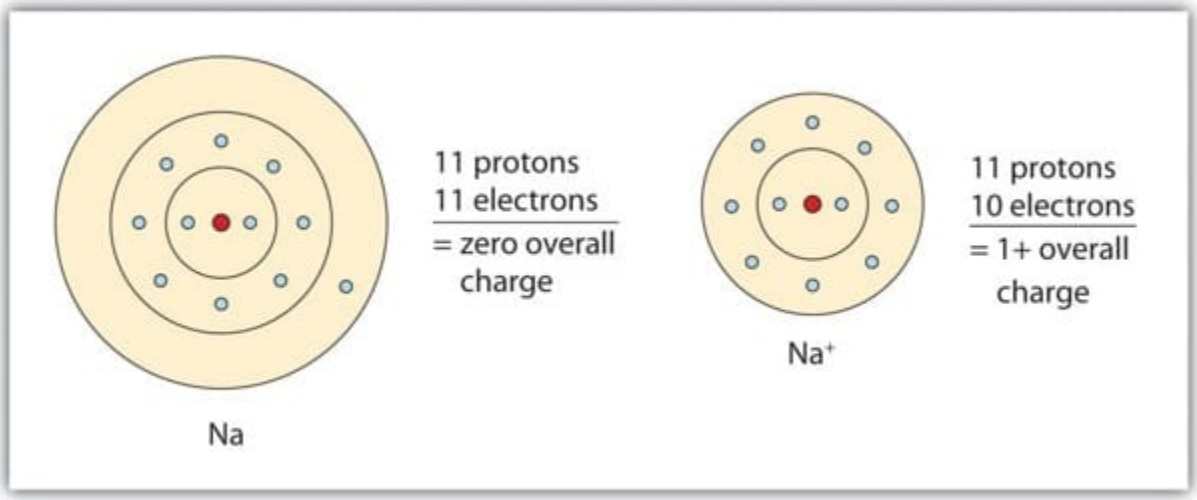


Figure 4.2.1**: The Formation of a Sodium Ion.** Sodium loses its single valence electron from the third energy level, producing a sodium ion (Na^{+}). The sodium ion retains 11 protons but now has only 10 electrons, giving it a net positive charge while achieving a stable octet in its outermost occupied energy level.

Overall, **Group 1A** elements tend to lose one electron, **Group 2A** elements lose two electrons, and **Group 3A (or Group 13)** elements lose three electrons. In each case, electron loss produces a stable electron configuration similar to the noble gas immediately preceding the element in the periodic table.

Notice that although sodium has lost an electron, **it is still sodium**. The nucleus remains unchanged, containing the same number of protons. Only the number of electrons has changed. Cations are named very simply by following the element name with the word 'ion'. Thus, a sodium atom that has lost electrons, is now referred to as a **sodium ion.**

Anions

When an atom **gains electrons**, it gains negative charge and becomes **negatively charged**.

These negatively charged ions are called **anions**.

Examples include:

Table 4.2B Examples of Atoms that Form Anions

Atom	Electron Change	Ion
Cl	gains 1 electron	Cl^-
O	gains 2 electrons	O^{2-}
N	gains 3 electrons	N^{3-}

Unlike metals, **nonmetals** tend to gain electrons in order to complete their outer electron shell.

Chlorine provides a good example (Figure 4.2.2). A neutral chlorine atom contains **17 protons and 17 electrons**. By gaining one additional electron, chlorine becomes the chloride ion (Cl^-), which contains **17 protons and 18 electrons**.

The extra electron completes chlorine's outer electron shell, giving it a stable octet and an overall **–1 charge**.

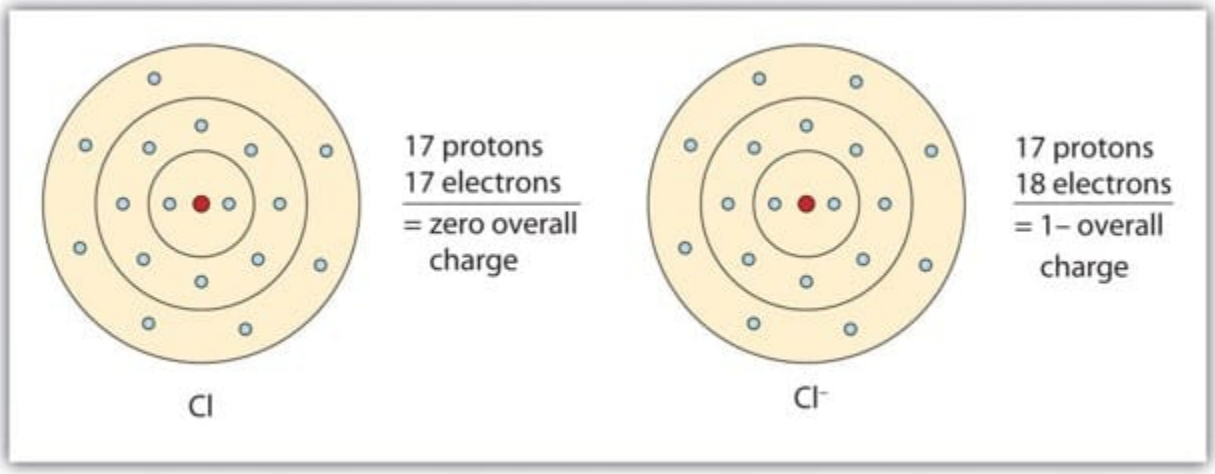


Figure 4.2.2**: The Formation of a Chloride Ion.** Chlorine gains one electron to form a chloride ion (Cl^-). The chloride ion contains 18 electrons and a complete octet in its outermost energy level, resulting in a net negative charge.

Chlorine is now a **chloride ion (Cl^-)**; note the slight change in the suffix (-ide instead of -ine) to create the name of this anion. Similarly, **Group 7A** elements typically gain one electron, **Group 6A** elements gain two electrons, and **Group 5A** elements gain three electrons. In each case, gaining electrons produces a stable electron configuration resembling the noble gas immediately following the element in the periodic table.

Isoelectronic Species

Notice something interesting about both sodium and chlorine.

Although sodium **loses** an electron and chlorine **gains** an electron, **both achieve stable electron configurations by attaining a full outer electron shell**.

Atoms or ions that possess the **same number and arrangement of electrons** are called **isoelectronic**.

For example, each of the following species contains **10 electrons** and has the same electron configuration as neon: N^{3-}, O^{2-}, F^-, Ne, Na^+, Mg^{2+}, and Al^{3+}. Although these species have identical electron configurations, they are **not the same element** because they contain different numbers of protons. Figure 4.2.3 shows the **neon isoelectronic series**.

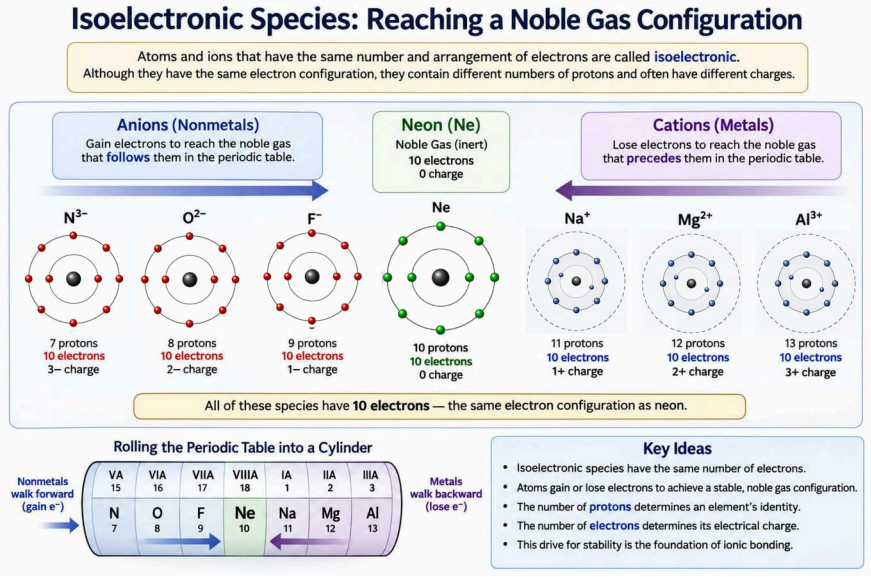


Figure 4.2.3**: The Neon Isoelectronic Series.** Each species contains ten electrons and therefore has the same electron configuration as neon. Although they are isoelectronic, they remain different elements because each contains a different number of protons.

This illustrates an important principle:

Key Idea

The number of protons determines an element's identity. The number of electrons determines its electrical charge.

Thus, sodium ions are chemically very different from neon atoms, even though they are isoelectronic. Likewise, the other members of the neon isoelectronic series have different identities, chemical properties, and biological roles because each contains a different nucleus.

Using the Periodic Table to Predict Ions

Fortunately, you do not need to memorize every common ion. The periodic table provides a simple way to predict how many electrons an atom is likely to gain or lose.

Figure 4.2.4 illustrates a useful way to visualize this idea by imagining the periodic table rolled into a cylinder so that the metals and nonmetals wrap around toward the noble gases.

Notice the pattern:

- **Metals "walk backward"** by losing the fewest electrons necessary to reach the **preceding noble gas**.
- **Nonmetals "walk forward"** by gaining the fewest electrons necessary to reach the **following noble gas**.

Rather than memorizing individual ions, think about which **noble gas configuration** an atom is trying to achieve.

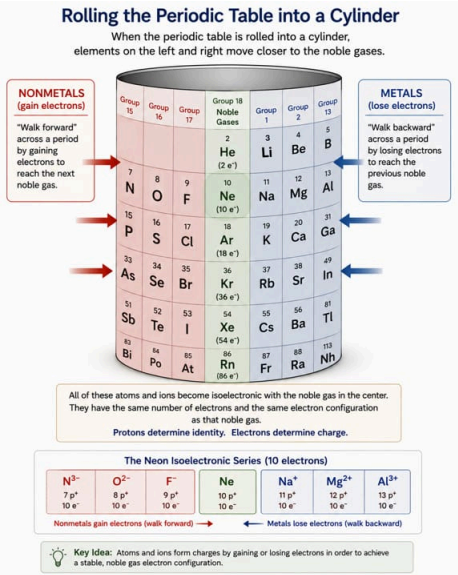


Figure 4.2.4**: Rolling the periodic table into a cylinder highlights a simple trend in ionic bonding.** One way to visualize ion formation is to imagine rolling the periodic table into a cylinder so that the main-group metals and nonmetals wrap toward the noble gases. Main-group metals generally become more stable by **losing the fewest electrons necessary** to reach the preceding noble gas, while main-group nonmetals become more stable by **gaining the fewest electrons necessary** to reach the following noble gas. The resulting ions are **isoelectronic** with the noble gas shown in the center column, meaning they have the same number and arrangement of electrons. Although these ions share the same electron configuration, they remain different elements because **protons determine identity, whereas electrons determine charge.** The "rolling the periodic table into a cylinder" visualization was inspired by a teaching analogy developed by Dr. Ray Dandeneau.

Key Idea

Main-group atoms tend to gain or lose the fewest electrons necessary to achieve the electron configuration of the nearest noble gas. This simple principle explains why many ions form predictable charges and provides a powerful way to understand ionic bonding.

Chemistry Connection

Hydrogen: A Special Case

Hydrogen occupies Group 1 but is **not** an alkali metal. Because it contains only one energy level, hydrogen follows the **duet rule** rather than the octet rule.

Depending on the atoms with which it interacts, hydrogen may:

- lose one electron to form **H**, or
- gain one electron to form **H** (the hydride ion).

The **H ion** is especially important in biology because acids donate hydrogen ions in aqueous solution. We will revisit hydrogen ions and their role in acid-base chemistry later in this textbook.

Naming Simple Ions

Naming simple ions is straightforward.

- **Cations** retain the element name followed by the word **ion** (sodium ion, magnesium ion, calcium ion).
- **Monatomic anions** replace the ending of the element name with **-ide** (chloride ion, oxide ion, nitride ion).

More detailed rules for naming ionic compounds are provided in **Appendix A**.

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4.3: Electron Transfer → Ionic Bonding

Learning Objectives

After completing this section, you should be able to:

- Explain how the electrostatic attraction between oppositely charged ions forms an ionic bond.
- Describe how ionic compounds arrange themselves into repeating crystal lattices.
- Predict the chemical formula of simple ionic compounds using ionic charges.
- Relate the structure of ionic compounds to their physical properties, including high melting points, brittleness, and electrical conductivity.

From Ions to Ionic Compounds

When a metal atom loses an electron, that electron does **not** simply disappear into empty space. Likewise, when a nonmetal gains an electron, it does **not** pull an electron out of nowhere. Instead, electrons are **transferred from one atom to another**.

In ordinary chemical reactions, whenever one atom is **oxidized** (loses electrons), another atom must be **reduced** (gains electrons). These two processes always occur together because **electrons are conserved**. For example, when sodium and chlorine react,

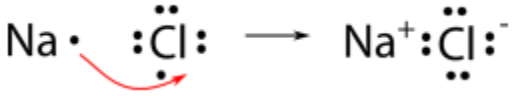
$$\mathrm{Na} \longrightarrow \mathrm{Na^+} + \mathrm{e^-} \tag{4.3.1}$$

and

$$\mathrm{Cl} + \mathrm{e^-} \longrightarrow \mathrm{Cl^-} \tag{4.3.2}$$

occur simultaneously. Combining these two half-reactions gives the overall electron-transfer process:

$$\mathrm{Na} + \mathrm{Cl} \longrightarrow \mathrm{Na^+} + \mathrm{Cl^-} \tag{4.3.3}$$



The formation of these ions creates a new situation—one atom has become **positively charged**, while the other has become **negatively charged**. Because opposite charges attract, the ions are pulled together by a strong **electrostatic force**.

This electrostatic attraction between cations and anions is called an **ionic bond**.

It is important to distinguish **electron transfer** from **ionic bonding**. Electron transfer produces the ions. The **ionic bond** is the attractive force that forms **after** the ions have been created.

Unlike covalent bonds, which involve the sharing of electrons, **ionic bonds** result from the attraction between ions carrying opposite electrical charges.

The Formation of an Ionic Bond Must Result in a Balance of Charges

Once cations and anions have formed, they are attracted to one another because of their opposite electrical charges. However, ionic compounds must satisfy one additional requirement—they must be **electrically neutral overall**.

In other words, the total positive charge contributed by the cations must exactly equal the total negative charge contributed by the anions.

For simple ions, this often occurs naturally. For example, one sodium ion ($Na^{\oplus}$) combines with one chloride ion ($Cl^{\ominus}$).

$$(+1) + (-1) = 0 \tag{4.3.4}$$

The resulting formula is

$$\mathbf{NaCl} \tag{4.3.5}$$

Not all ions have charges of ±1, however.

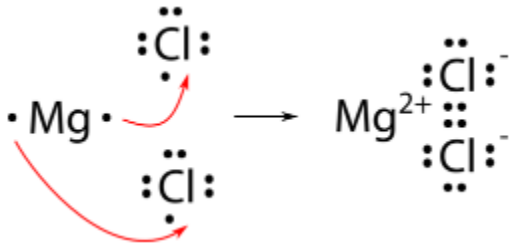
A magnesium ion carries a charge of **+2**, while a chloride ion carries a charge of **–1**. One chloride ion is not enough to balance the charge of a magnesium ion.

Instead, **two chloride ions** are required.

$$(+2) + (-1) + (-1) = 0 \tag{4.3.6}$$

giving the formula

$$\mathbf{MgCl_2} \tag{4.3.7}$$



Likewise, aluminum ions ($Al^{3\oplus}$) and oxide ions ($O^{2\ominus}$) combine in the smallest whole-number ratio that balances the charges.

$$2(+3) + 3(-2) = 0 \tag{4.3.8}$$

producing the formula

$$\mathbf{Al_2O_3} \tag{4.3.9}$$

Notice that the subscripts in an ionic formula do not tell us how many atoms are bonded together as a molecule. In fact, ionic compounds do not exist as individual molecules. Instead, oppositely charged ions arrange themselves into a repeating three-dimensional lattice, where each ion is surrounded by ions of the opposite charge. **The chemical formula represents the smallest whole-number ratio of ions in this lattice, called a formula unit.**

We will see in the next section that **covalent compounds do form discrete molecules**, making their formulas and structures fundamentally different from those of ionic compounds.

Ionic Compounds Form Crystal Lattices

As we noted above, ionic compounds do not exist as individual molecules. That means that a single sodium ion does not bond with only one chloride ion. Instead, each sodium ion is surrounded by multiple chloride ions, and each chloride ion is surrounded by multiple sodium ions. The result is a large, repeating three-dimensional arrangement called a **crystal lattice**.

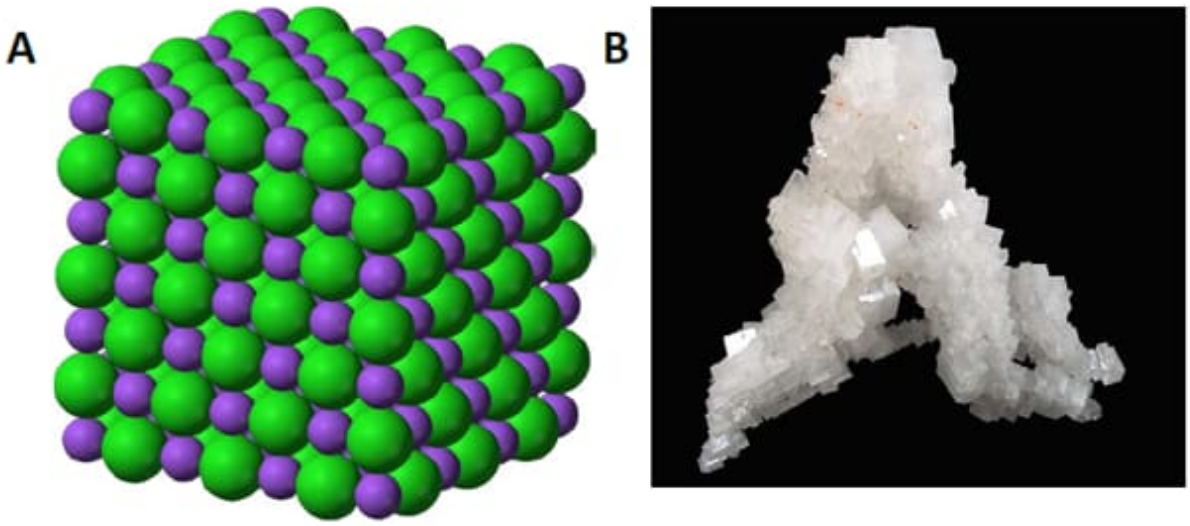


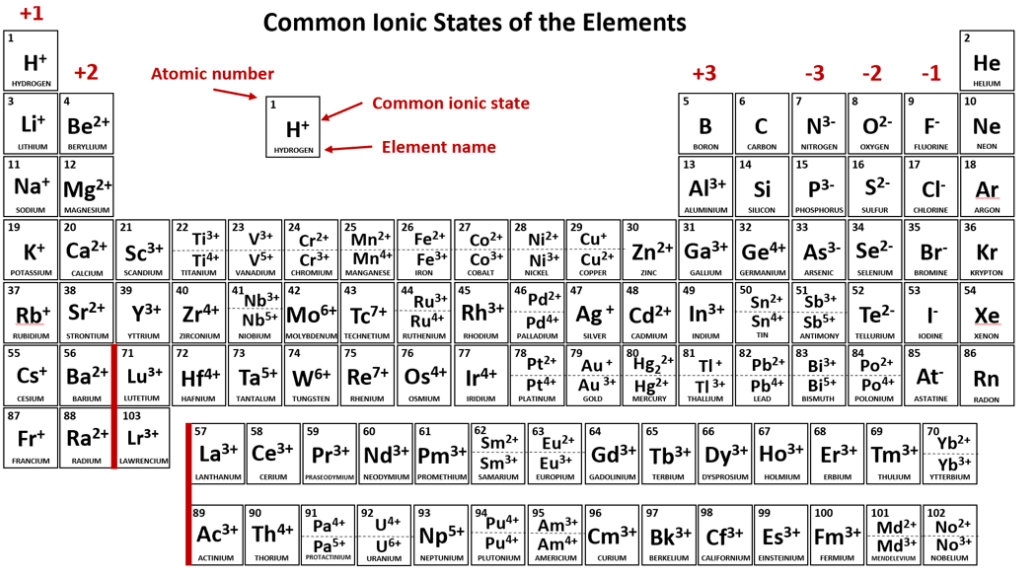
Figure 4.3.X: Ionic Compounds Form Crystal Lattices. (A) In a solid ionic compound, positively and negatively charged ions arrange themselves in a repeating three-dimensional lattice. Each ion is surrounded by ions of the opposite charge rather than being bonded to a single partner in a discrete molecule. **(B)** At the macroscopic level, this ordered arrangement of ions produces the crystalline structures characteristic of ionic compounds. Because the ratio of sodium ions to chloride ions is always **1:1**, the chemical formula is written simply as **NaCl**. This is known as a **formula unit**, representing the simplest whole-number ratio of ions in the crystal.

Predicting Ionic Formulas

Now that we know an ionic formula must represent the **smallest whole-number ratio of ions that produces an electrically neutral compound**, the next question is: **How do we know what charges the ions will have?**

Fortunately, for many main-group elements, we can predict the most common ionic charge directly from the periodic table. As shown in **Figure 4.3.X**, elements within the same group tend to form ions with the same charge because they have the same number of valence electrons.

The periodic table therefore gives us the information we need to predict both **the charges of the ions** and **the ratio in which those ions must combine**.



When ionic compounds form, the total positive charge must exactly balance the total negative charge so that the compound is **electrically neutral**.

Key Idea

- **An ionic formula must contain the smallest whole-number ratio of ions that produces an overall charge of zero**.

For example:

Table 4.3A Ionic Bonding Examples

Cation	Anion	Formula
Na^{+}	Cl^{-}	NaCl
Mg^{2+}	O^{2-}	MgO
Ca^{2+}	Cl^{-}	$CaCl_2$
Al^{3+}	O^{2-}	Al_2O_3

Rather than memorizing these formulas, think about balancing the total positive and negative charges until the compound has **no overall charge**. Here is a 5-step process to help you create correct ionic formulas:

Steps for Predicting an Ionic Formula

1. **Identify the cation and anion** and determine the charge of each ion using your periodic table.
2. **Determine the smallest number of each ion needed** so that the total positive and negative charges are equal.
3. **Write the cation first and the anion second**.
4. **Use subscripts to show the ratio of ions**. Do not write a subcript of 1 (it is implied).
5. **Check your formula**: the total charge should equal zero

---

Exercise 4.3.1

Determine the correct ionic formula when:

1. Calcium and Fluorine combine

2. Potassium and Oxygen combine

Answer available at the end of this section.

Transition Metals Can Form More Than One Ion

The charges formed by many **main-group elements** can be predicted from their position on the periodic table. Transition metals, however, are less predictable.

Many transition metals can lose different numbers of electrons and therefore can form **more than one type of positively charged ion**. For example, iron commonly forms both **Fe^{2+}** and **Fe^{3+}**, while copper commonly forms both **Cu^{+}** and **Cu^{2+}**.

Although these ions have different charges, they are still the same element. Remember that the **number of protons determines the identity of an element**, while changes in the number of electrons determine its charge.

Because a transition metal may form more than one ion, its charge is often indicated using a **Roman numeral** in the ion's name.

Table 4.3B: Transition Metals May Form More Than One Ion

Ion	Name	Charge
Fe^{2+}	Iron (II) ion	+2
Fe^{3+}	Iron (III) ion	+3
Cu^{+}	Copper (I) ion	+1
Cu^{2+}	Copper (II) ion	+2

The Roman numeral tells us the **positive charge of the metal ion**. For example, iron(II) indicates Fe^{2+}, while iron(III) indicates Fe^{3+}.

Key Idea:

- **For metals that can form more than one ion, the Roman numeral identifies the charge of the metal ion**.

This information becomes important when predicting an ionic formula. For example, an **iron(III) ion** has a +3 charge. Because chloride has a –1 charge, three chloride ions are required to produce a neutral compound:

$$(+3) + 3(-1) = 0 \tag{4.3.10}$$

giving the formula:

$$\mathrm{FeCl_3} \tag{4.3.11}$$

In this chapter, our focus is on **using ionic charges to understand and predict formulas**. Additional rules for naming compounds containing transition metals are provided in **Appendix A**.

Some Ions Contain More Than One Atom

So far, most of the ions we have considered have been **monatomic ions**—ions formed from a single atom, such as Na^{+}, Ca^{2+}, Cl^{-}, and O^{2-}.

However, many important ions contain **two or more covalently bonded atoms that together carry an overall electrical charge**. These are called **polyatomic ions**.

A polyatomic ion behaves as a **single charged unit** when it forms an ionic compound. The atoms within the ion remain bonded together as the entire group interacts with ions of the opposite charge.

Polyatomic ions are especially important in biological and health-related chemistry. Rather than memorizing a long list, we will focus on a small group that appears frequently in biological systems, medications, body fluids, and later chapters of this textbook.

Table 4.3C: Important Polyatomic Ions for Health and Biological Systems

Formula	Name	Charge	Biological or Health Connection
NH_4^+	ammonium	+1	nitrogen metabolism and biological systems
OH^-	hydroxide	-1	acids, bases, and pH
NO_3^-	nitrate	-1	nitrogen metabolism, medications, and biological signaling
HCO_3^-	bicarbonate	-1	major buffer in blood
CO_3^{2-}	carbonate	-2	mineral and acid-base chemistry
SO_4^{2-}	sulfate	-2	biological molecules and medications
PO_4^{3-}	phosphate	-3	ATP, DNA, cell chemistry, and bone

Key Idea

- **A polyatomic ion contains several atoms, but the entire group behaves as one charged unit**.

When more than one copy of a polyatomic ion is needed in an ionic formula, the polyatomic ion is placed inside **parentheses**, and the required number is written as a subscript outside the parentheses.

For example, calcium forms Ca^{2+} ions and phosphate is PO_4^{3-}. To produce an electrically neutral compound, three calcium ions are needed for every two phosphate ions:

$$3(+2) + 2(-3) = 0 \tag{4.3.12}$$

The resulting formula is:

$$\mathbf{Ca_3(PO_4)_2} \tag{4.3.13}$$

Notice that the subscript 2 applies to the **entire phosphate ion**, not just to the oxygen atoms. The parentheses keep the polyatomic ion together as a unit.

This compound, **calcium phosphate**, also provides an important connection to human biology: calcium and phosphate are major components of the mineral structure of bones and teeth.

Exercise 4.3.2

Practice building the following formulas:

1. Predict the formula for the ionic compound formed between **iron(III)** and **oxide**.

2. Predict the formula for the ionic compound formed between **copper(II)** and **nitrate**.

Answer available at the end of this section.

Properties of Ionic Compounds

The strong electrostatic attractions within an ionic crystal explain many of the characteristic properties of ionic compounds.

High melting and boiling points

Large amounts of energy are required to separate the strongly attracted ions, so ionic compounds generally have high melting and boiling points.

Brittleness

Although ionic compounds are strong, they are also brittle. When struck, layers of ions may shift so that ions with the same charge become adjacent. Because like charges repel one another, the crystal fractures.

Electrical conductivity

Solid ionic compounds do **not** conduct electricity because the ions are locked into fixed positions within the crystal lattice.

When melted or dissolved in water, however, the ions become free to move and can carry electrical charge. As a result, molten ionic compounds and aqueous ionic solutions conduct electricity.

Chemistry Connection

Electrolytes and the Human Body

Many of the ions discussed in this section are essential electrolytes.

Sodium ($Na^{\diamondsuit}$), potassium ($K^{\diamondsuit}$), calcium ($Ca^{2\diamondsuit}$), magnesium ($Mg^{2\diamondsuit}$), and chloride ($Cl^{\diamondsuit}$) play critical roles in nerve impulses, muscle contraction, maintaining fluid balance, and regulating heartbeat.

When these ionic compounds dissolve in body fluids, they separate into individual ions that conduct electrical signals throughout the body.

This is why electrolyte balance is so important in medicine and why intravenous (IV) fluids contain carefully controlled concentrations of dissolved ionic compounds.

Looking Ahead...

Ionic bonding explains the behavior of compounds formed between metals and nonmetals.

But many biologically important substances—including water, proteins, DNA, sugars, and most pharmaceutical compounds—are **not ionic**.

Instead of transferring electrons, these atoms achieve stability by **sharing electrons**.

In the next section, we'll explore how electron sharing leads to **covalent bonding**, the type of bonding responsible for most of the molecules found in living organisms.

Answers

Exercise 4.3.1

1. One $Ca^{2\diamondsuit}$ requires two $F^{\diamondsuit}$:

$$(+2) + 2(-1) = 0 \tag{4.3.14}$$

Therefore:

$$\mathbf{CaF_2} \tag{4.3.15}$$

2. Two K^+ are required for one O^{2-}

$$2(+1) + (-2) = 0 \tag{4.3.16}$$

Therefore:

$$\mathbf{K_2O} \tag{4.3.17}$$

Exercise 4.3.2

1. Identify the ions and their charges.
Iron(III) means:

$$\mathbf{Fe^{3+}} \tag{4.3.18}$$

Oxide is:

$$\mathbf{O^{2-}} \tag{4.3.19}$$

Determine the smallest whole-number ratio that balances the charges. Two Fe^{3+} ions give a total charge of +6, while three O^{2-} ions give a total charge of –6:

$$2(+3) + 3(-2) = 0 \tag{4.3.20}$$

Write the formula.

$$\mathbf{Fe_2O_3} \tag{4.3.21}$$

2. **Identify the ions and their charges**.
Copper(II) means:

$$\mathbf{Cu^{2+}} \tag{4.3.22}$$

Nitrate is:

$$\mathbf{NO_3{}^-} \tag{4.3.23}$$

Balance the charges.
One Cu^{2+} ion requires two nitrate ions, each with a –1 charge:

$$(+2) + 2(-1) = 0 \tag{4.3.24}$$

Write the formula. Because more than one nitrate ion is needed, the polyatomic ion must be placed in parentheses:

$$\mathbf{Cu(NO_3)_2} \tag{4.3.25}$$

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4.4: Electron Sharing → Covalent Bonding

Learning Objectives

After completing this section, you should be able to:

- Explain how covalent bonds form through the sharing of electrons.
- Distinguish between single, double, and triple covalent bonds.
- Draw Lewis structures for simple molecules.
- Explain how shared electrons help atoms achieve stable electron configurations.
- Predict whether a compound is likely to contain ionic or covalent bonds.

Sharing Electrons

In the previous section, we learned that metals and nonmetals often become stable through **electron transfer**, forming ionic compounds.

However, many atoms—especially **nonmetals**—hold onto their electrons too strongly for complete electron transfer to occur.

Instead of giving electrons away, these atoms solve the problem differently.

> **They share electrons**.

When atoms share one or more pairs of electrons, they form a **covalent bond**.

Unlike ionic bonding, where electrons move completely from one atom to another, covalent bonding allows both atoms to "count" the shared electrons toward filling their outer electron shells.

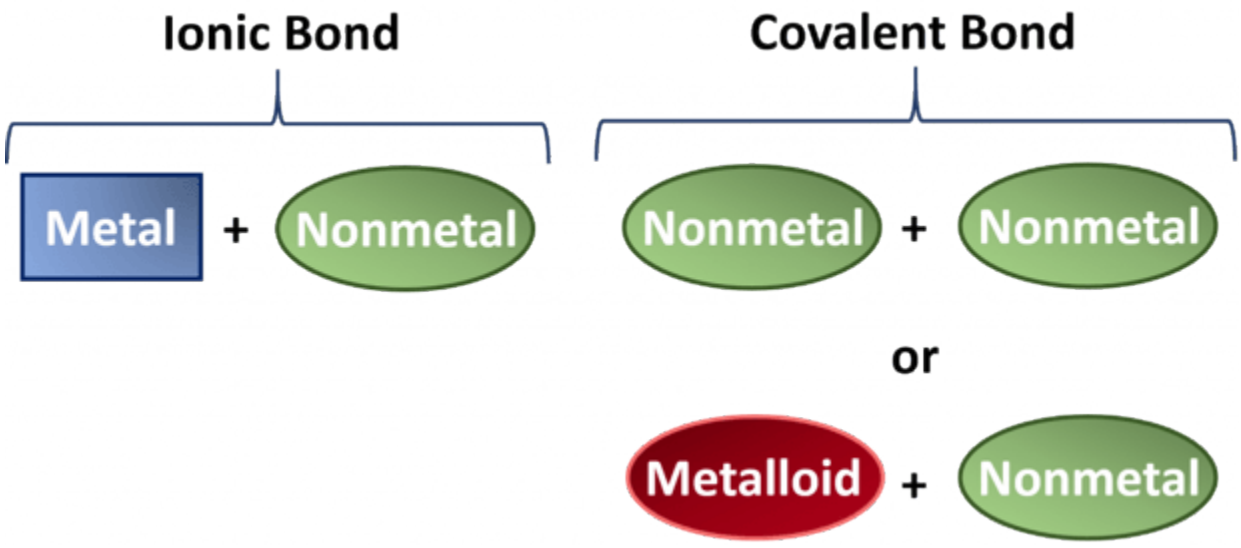


Figure 4.4.1**: Recognizing Ionic vs Covalent Compounds.** Typically compounds that are formed from a combination of a metal with a nonmetal have more ionic bond character whereas compounds formed from two nonmetals or a metalloid and a nonmetal show more covalent character. Although compounds usually lie on a spectrum somewhere between fully ionic and fully covalent character, for naming purposes, this guideline works well.

Elements That Exist as Molecules

Just as an atom is the smallest unit that retains the chemical identity of an element, a **molecule** is a discrete group of atoms held together by covalent bonds. Molecules may contain atoms of the **same element** or atoms of **different elements**.

Several elements naturally exist as **diatomic molecules**, consisting of two atoms of the same element: H_2, N_2, O_2, F_2, Cl_2, Br_2, and I_2. A few elements form larger molecular structures. For example, elemental phosphorus can occur as P_4, while sulfur commonly occurs as S_8 (Figure 4.4.2).

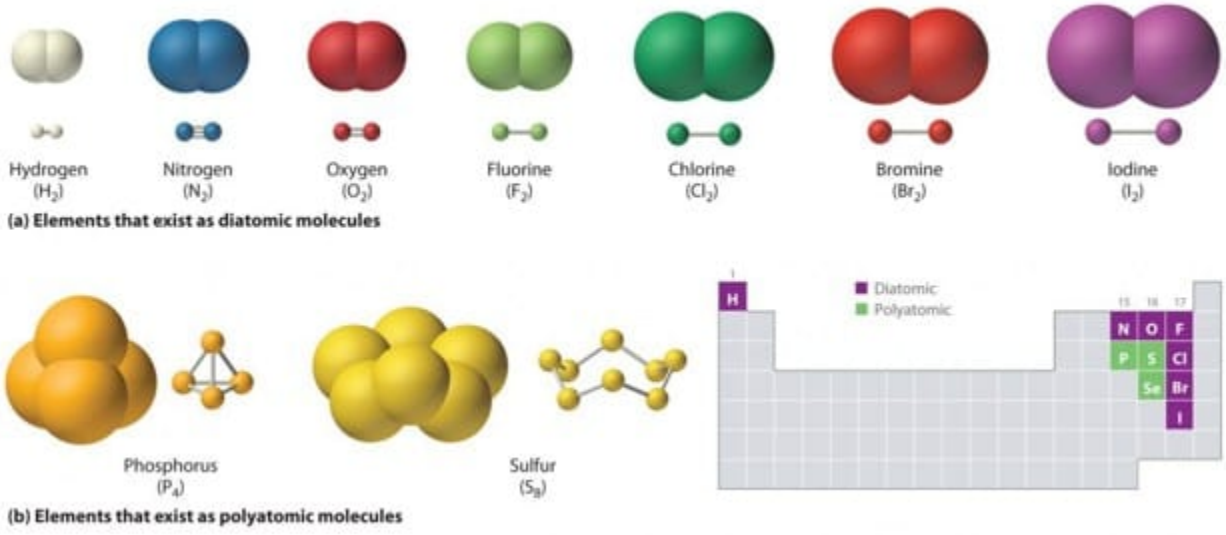


Figure 4.4.2: Elements That Exist as Covalent Molecules. (a) Several elements naturally exist as diatomic molecules, in which two atoms (E) are joined by one or more covalent bonds to form a molecule with the general formula E2. (b) A few elements naturally exist as polyatomic molecules, which contain more than two atoms. For example, phosphorus exists as P4 tetrahedra—regular polyhedra with four triangular sides—with a phosphorus atom at each vertex. Elemental sulfur consists of a puckered ring of eight sulfur atoms connected by single bonds. Selenium is not shown due to the complexity of its structure.

Covalent Bonds Help Atoms Become Stable

In the previous section, you learned how electrons can be transferred from one atom to another so that both atoms have an energy-stable outer electron shell following the ***octet rule***. However, there is another way an atom can achieve a full valence shell: atoms can share electrons to reach the octet state (or the duet state in the case of hydrogen).

This concept can be illustrated by using two hydrogen atoms, each of which has a single electron in its valence shell. (For small atoms such as hydrogen atoms, the valence shell will be the first shell, which holds only two electrons.) Chemists frequently use ***Lewis electron dot diagrams*** to represent covalent bonding in molecular substances. For example, the Lewis diagrams of two hydrogen atoms are shown in Figure 4.4.3C. In this format, the shared electrons can be represented as two dots between the two atoms or a dash can also be used to indicate a single bond. Note that neither hydrogen atom gains or loses an electron. Instead, both atoms share the same pair of electrons.

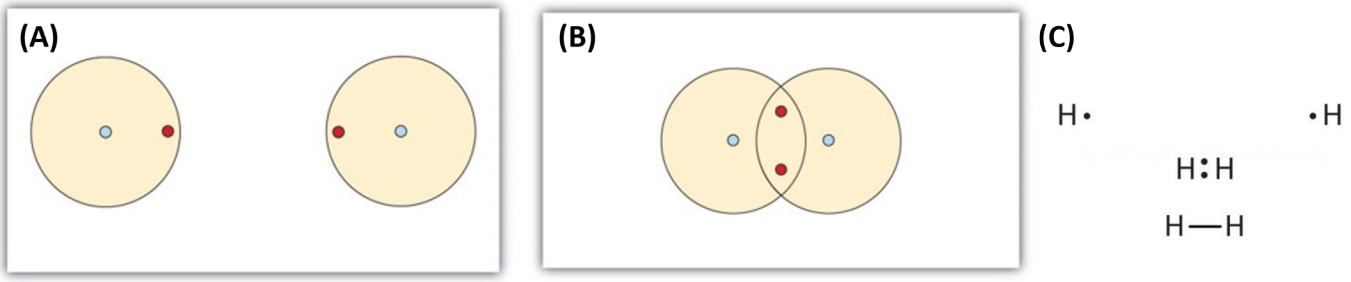


Figure 4.4.3: Hydrogen forming a covalent bond. (A) Two separate hydrogen atoms, (B) two hydrogen atoms sharing electrons in a covalent bond. (C) Lewis structure diagrams of hydrogen covalently bonding. Note that a single line between two atoms indicates a pair of shared electrons.

Another familiar example is **fluorine gas, F_2**. Each fluorine atom has seven valence electrons—just one electron short of a complete octet. As shown in Figure 4.4.4, two fluorine atoms can each contribute one electron to form a **shared pair of electrons** between them. Because both atoms can count the shared pair as part of their valence shell, each fluorine achieves an octet.

The shared pair of electrons forms a **single covalent bond**. Each fluorine atom also retains three pairs of valence electrons that are not involved in the bond. These nonbonding electron pairs are called **lone pairs**.

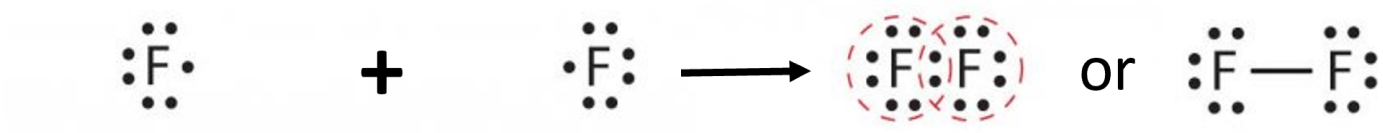


Figure 4.4.4: Formation of a Covalent Bond in F_2. Two fluorine atoms, each with seven valence electrons, share one pair of electrons to form a single covalent bond. Sharing the electron pair allows each fluorine atom to achieve a stable octet. The shared pair may be represented either as **two dots between the atoms** or as a **single line (—)** connecting the two fluorine atoms.

Molecular Compounds

When atoms of **different nonmetal elements** share electrons, they form **molecular compounds**, also called **covalent compounds**. Unlike ionic compounds, which form extended lattices of positively and negatively charged ions, molecular compounds consist of **discrete groups of atoms called molecules**.

For example, a water molecule contains two hydrogen atoms covalently bonded to one oxygen atom:

$$\mathbf{H_2O} \tag{4.4.1}$$

Other familiar molecular compounds include carbon dioxide (CO_2), ammonia (NH_3), and methane (CH_4).

In each case, the atoms share electrons so that they can achieve more stable valence electron configurations. The number of electrons an atom needs to complete its outer shell helps determine **how many covalent bonds it commonly forms**.

Key Idea

- **Ionic compounds form repeating lattices of ions, while covalent compounds form discrete molecules in which atoms are held together by shared electrons.**

The number of covalent bonds an atom commonly forms is closely related to the number of **valence electrons** it contains. Recall

that for main-group elements, the number of valence electrons follows a predictable pattern across the periodic table.

Lewis electron-dot symbols make this pattern especially easy to see. As shown in **Figure 4.4.5**, elements within the same group have the same number of valence electrons and therefore have similar Lewis symbols.

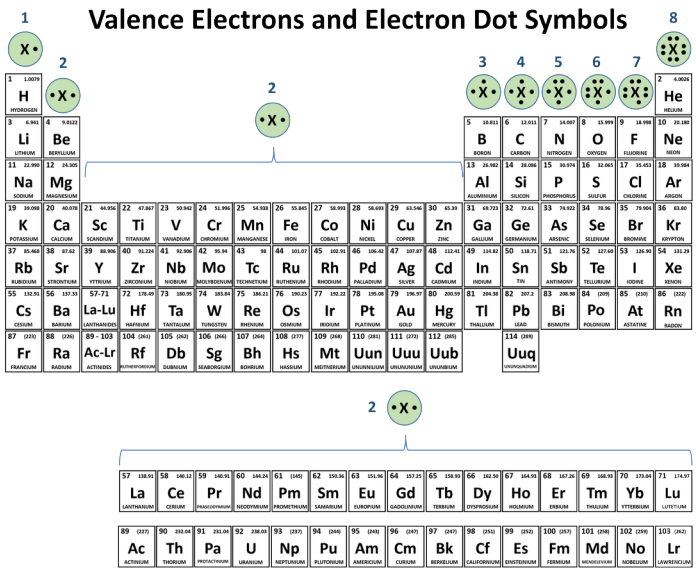


Figure 4.4.5**: Valence Electrons and Lewis Symbols Across the Periodic Table.** Lewis electron-dot symbols show the number of valence electrons associated with each main-group family. Moving from left to right across the periodic table, the number of valence electrons increases from one to eight. For many nonmetals, the number of electrons needed to complete the octet helps predict the number of covalent bonds the element commonly forms.

For many nonmetals, the number of additional **electrons needed to complete an octet** provides a useful clue to the number of covalent bonds the atom commonly forms. For example:

- **Carbon** has 4 valence electrons and commonly forms **4 covalent bonds**.
- **Nitrogen** has 5 valence electrons and commonly forms **3 covalent bonds**.
- **Oxygen** has 6 valence electrons and commonly forms **2 covalent bonds**.
- **Fluorine and the other halogens** have 7 valence electrons and commonly form **1 covalent bond**.

Hydrogen is again a special case. It has one valence electron and needs only one additional electron to satisfy the **duet rule**, so hydrogen commonly forms **one covalent bond**.

Key Idea

- **For many common nonmetals, the number of electrons needed to complete the outer shell helps predict the number of covalent bonds the atom will typically form**.

Single, Double, and Triple Bonds

A single covalent bond allows two atoms to share **one pair of electrons**. But what happens when an atom needs more than one additional electron to complete its octet?

Atoms can share **two or even three pairs of electrons**, producing **double bonds** and **triple bonds**.

Double Bonds: Sharing Two Pairs of Electrons

Consider an oxygen atom. Oxygen has **six valence electrons**, so it needs two additional electrons to achieve a complete octet.

When two oxygen atoms come together, sharing only one pair of electrons would not provide either oxygen with a complete octet. Instead, the two oxygen atoms share **two pairs of electrons**, forming a **double covalent bond**.

A double bond is represented by two lines between the atoms:

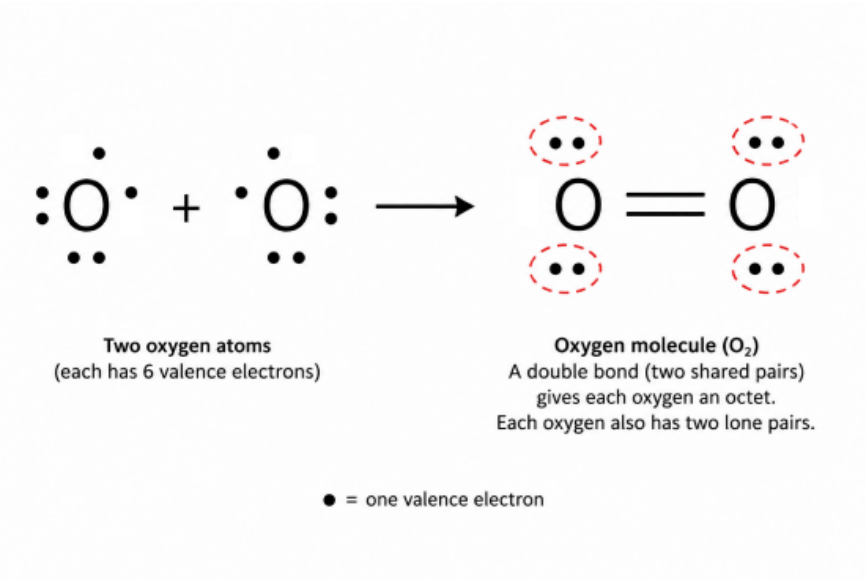


Figure 4.4.6**: Formation of a Double Covalent Bond in O_2.** Each oxygen atom begins with six valence electrons and needs two additional electrons to achieve a stable octet. By sharing **two pairs of electrons**, the oxygen atoms form a **double covalent bond**, represented by two lines between the atoms (O=O). Each oxygen atom also retains **two lone pairs of electrons** that do not participate in bonding.

Each line represents one shared pair of electrons. Therefore, a double bond contains a total of **four shared electrons**. In an oxygen molecule, O_2, each oxygen atom also has **two lone pairs** of electrons that are not involved in bonding.

Triple Bonds: Sharing Three Pairs of Electrons

Nitrogen provides an example of atoms that form a **triple covalent bond**. Each nitrogen atom has five valence electrons and therefore needs three additional electrons to complete its octet.

When two nitrogen atoms bond, they share **three pairs of electrons**, allowing both nitrogen atoms to achieve a complete octet. These three shared pairs form a **triple bond**, represented by three lines between the atoms:

$$\mathrm{N \equiv N} \tag{4.4.2}$$

A triple bond therefore contains **six shared electrons**. Each nitrogen atom also retains **one lone pair** of electrons that does not participate in bonding.

Table 4.4A Comparing Covalent Bonds

Bond Type	Shared Electron Pairs	Shared Electrons	Example
Single bond	1	2	F—F
Double bond	2	4	O=O
Triple bond	3	6	N≡N

As more electrons are shared:

- bonds become **shorter**
- bonds become **stronger**
- more energy is required to break them

Lewis Structures: A Simple Way to Show Bonding

Chemists often use **Lewis structures** to show how valence electrons are arranged in a molecule.

Lewis structures represent:

- shared electron pairs (bonds)
- lone pairs of electrons
- how atoms satisfy the octet (or duet) rule

Water and carbon dioxide provide good examples of Lewis structures.

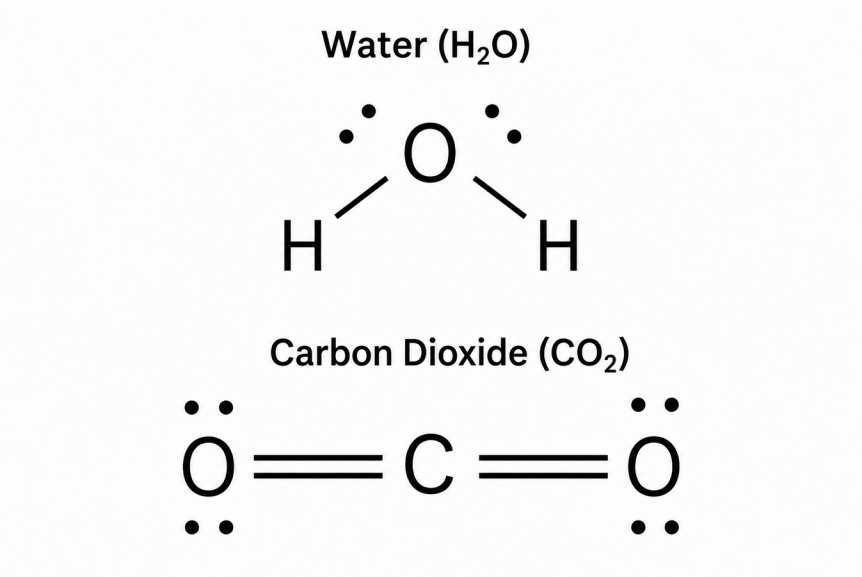


Figure 4.4.7**: Lewis Structures of Water and Carbon Dioxide.** Lewis structures show both the **shared electron pairs that form covalent bonds** and the **lone pairs of electrons** that do not participate in bonding. In H_2O, oxygen forms two single bonds with hydrogen and retains two lone pairs. In CO_2, carbon forms a double bond with each oxygen, while each oxygen retains two lone pairs. In both molecules, the bonding arrangement allows the atoms to achieve stable outer electron configurations.

You may have noticed that the water molecule in Figure 4.4.7 is drawn **bent**, while carbon dioxide is drawn as a **straight, linear molecule**. This difference is not accidental.

Pairs of electrons occupy space around an atom and **repel other electron pairs**. In water, the oxygen atom has two bonding pairs and two lone pairs of electrons. The lone pairs repel the bonding electrons, contributing to the **bent shape of the H_2O molecule**.

Carbon dioxide is different. The central carbon atom has two bonding regions and **no lone pairs**. These bonding regions arrange themselves on opposite sides of the carbon atom as far away from each other as possible, producing a **linear molecule**.

Notice that carbon shares two pairs of electrons with each oxygen atom, forming two double bonds. In this way, each of the atoms can fill their outer electron shell and obtain the **octet** configuration.

Looking Ahead

- **The arrangement of bonding electrons and lone pairs around a central atom determines molecular shape**.

In **Chapter 5**, we will use **Valence Shell Electron Pair Repulsion (VSEPR) theory** to predict molecular shapes and bond angles—and see why molecular shape is so important in determining **polarity, intermolecular forces, and biological function**.

Drawing Simple Lewis Structures

When drawing Lewis structures, follow these general steps.

1. **Determine the number of valence electrons for each atom**. Use the periodic table or Lewis electron-dot symbols to identify the valence electrons contributed by each atom.
2. **Choose the central atom and connect the atoms with single bonds**. The least electronegative atom is usually placed in the center. Hydrogen is never the central atom.
3. **Place the remaining valence electrons around their atoms**. Remember that electrons used to form bonds are **shared between the bonded atoms**.
4. **Check the duet and octet rules.** Hydrogen is complete when it has two electrons around it; most other atoms in these simple structures are most stable with eight.
5. **Form double or triple bonds if needed.** If atoms still have incomplete octets, additional unpaired electrons may be shared to form multiple bonds. Check the structure again to make sure each atom has achieved a stable electron configuration.

Example 4.4.1

Draw the Lewis Structure of CH_2O (formaldehyde)

Solution

Step 1: Count the total number of valence electrons.

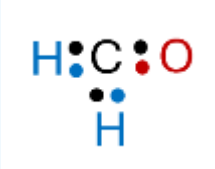
- Carbon: 4 valence electrons
- Two hydrogen atoms: 2 × 1 = 2 valence electrons
- Oxygen: 6 valence electrons



Total = 12 valence electrons.

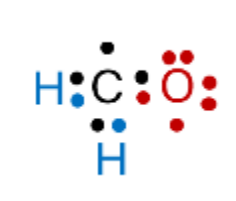
Step 2: Choose the central atom and draw the basic skeleton.

Carbon is the central atom. Hydrogen atoms can form only one bond each, so they must be terminal atoms. Oxygen is more electronegative than carbon. Try placing carbon in the center and draw the other atoms bonded to it with single bonds



Notice that in these three single bonds, each atom involved in the bond shares one electron of the pair with the other atom. So far, we have used **6 of the 12 valence electrons (or 2 electrons per pair)** to join the atoms in single bonds.

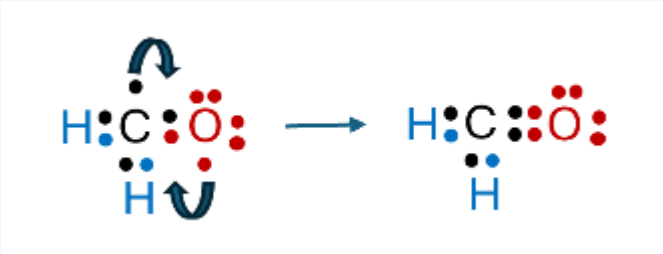
Step 3: Distribute the remaining electrons.



Place the remaining 6 electrons as lone pairs, beginning with oxygen. Oxygen has a total of 6 valence electrons. It is already sharing one electron with the central Carbon atom. Thus, it needs 5 more electrons around it. Each of the hydrogen atoms should have 1 electron, so they are complete, as is. The remaining electron needs to go back to Carbon, as Carbon has 4 valence electrons and currently has 3 accounted for in our current structure.

Step 4: Evaluate the atoms for the completion of an octet, and form multiple bonds as needed.

You should notice at this stage that carbon and oxygen have not achieved an octet. At this stage, both carbon and oxygen have **seven electrons in their valence shells when the shared bonding electrons are counted**. Neither atom has achieved a complete octet. Fold in the lone electrons from the carbon atom and the oxygen atom to form the double bond:

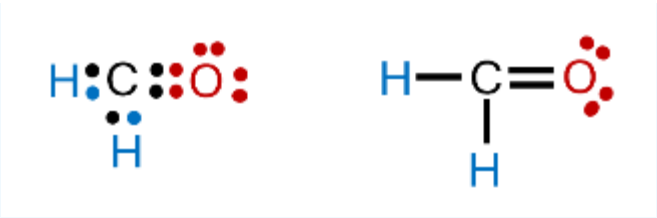


Now evaluate the octet and duet rules for each atom involved in forming the molecule. Each hydrogen is sharing two electrons and has reached the duet stage. And with the formation of the double bond between the carbon and the oxygen, each of these atoms has now reached the octet stage.



Step 5: Present your final structure:

You have now created a stable Lewis structure for formaldehyde! You may replace shared electron pairs with a line, to represent the bond or you may show the electrons, the choice is yours:



Exercise 4.4.1

Draw the Lewis Structure for:

1. Ammonia (NH_3)
2. Hydrogen Cyanide (HCN)

Answer available at the end of this section.

Properties of Covalent Compounds

The properties of covalent compounds can vary considerably, but many differ noticeably from those of ionic compounds. Because covalent compounds consist of atoms joined by shared electrons, many form individual units called **molecules**.

Some common properties of molecular covalent compounds include:

- **Lower melting and boiling points** than many ionic compounds. Many covalent substances are gases, liquids, or relatively soft solids at room temperature.
- **Poor electrical conductivity.** Most covalent compounds do not contain freely moving charged particles and therefore do not conduct electricity well.
- **Variable solubility in water.** Some covalent molecules dissolve readily in water, while others do not. Molecular polarity plays an important role in determining solubility.
- **Formation of discrete molecules.** Unlike ionic compounds, which form extended crystal lattices, many covalent compounds exist as individual molecules with specific numbers of bonded atoms.

The physical properties of covalent substances depend not only on the bonds within each molecule, but also on the attractions **between molecules**. These intermolecular forces will be explored in Chapter 5.

Chemistry Connection: Why Is Carbon So Important?

Carbon forms the backbone of nearly every biological molecule because it forms **four stable covalent bonds**.

This remarkable bonding ability allows carbon atoms to connect into chains, rings, and complex three-dimensional structures.

Proteins, carbohydrates, lipids, DNA, RNA, vitamins, and many medications all depend on carbon's ability to share electrons through covalent bonds.

Without covalent bonding, the chemistry of life would not be possible.

Looking Ahead

So far, we've learned that atoms can become stable by transferring electrons or by sharing them.

But there is still an important question to answer.

When two atoms share electrons,

Do they always share them equally?

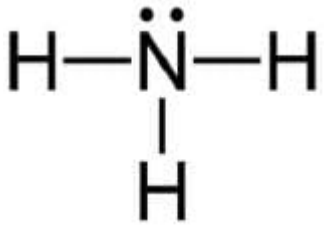
The answer is **no**.

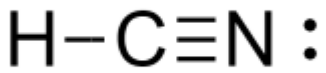
Some atoms attract shared electrons much more strongly than others.

This unequal sharing creates **bond polarity**, one of the most important concepts in chemistry because it helps explain why water dissolves salt, why cell membranes form, why drugs dissolve differently in blood, and why molecules behave the way they do.

Answers

Exercise 4.4.1

1. 

2. 

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4.5: Not All Shared Electrons Are Shared Equally

Learning Objectives

After completing this section, you should be able to:

- Explain why some atoms attract shared electrons more strongly than others.
- Define electronegativity.
- Distinguish between nonpolar covalent and polar covalent bonds.
- Predict bond polarity using electronegativity differences.
- Explain why bond polarity influences the physical and biological properties of compounds.

Who Holds Onto the Shared Electrons?

In the previous section, we learned that atoms can become more stable by **sharing electrons**. At first glance, it might seem that the shared electrons spend exactly the same amount of time around each atom.

In reality, this is often **not true**. Some atoms attract shared electrons more strongly than others. As a result, the shared electrons spend more time closer to one atom than the other. Understanding this unequal sharing is one of the most important ideas in chemistry because it helps explain why water dissolves salt, why cell membranes form, and why many medications dissolve differently in different parts of the body.

Electronegativity

Recall that the tendency of an atom to attract shared electrons toward itself is called **electronegativity**. Think of electronegativity as an atom's "pull" on shared electrons. Atoms with high electronegativity hold shared electrons more strongly. Atoms with low electronegativity hold them less strongly.

In general,

- electronegativity **increases from left to right** across a period,
- electronegativity **decreases down a group**.

Fluorine has the highest electronegativity of any element, while alkali metals have some of the lowest values (Figure 4.5.1).

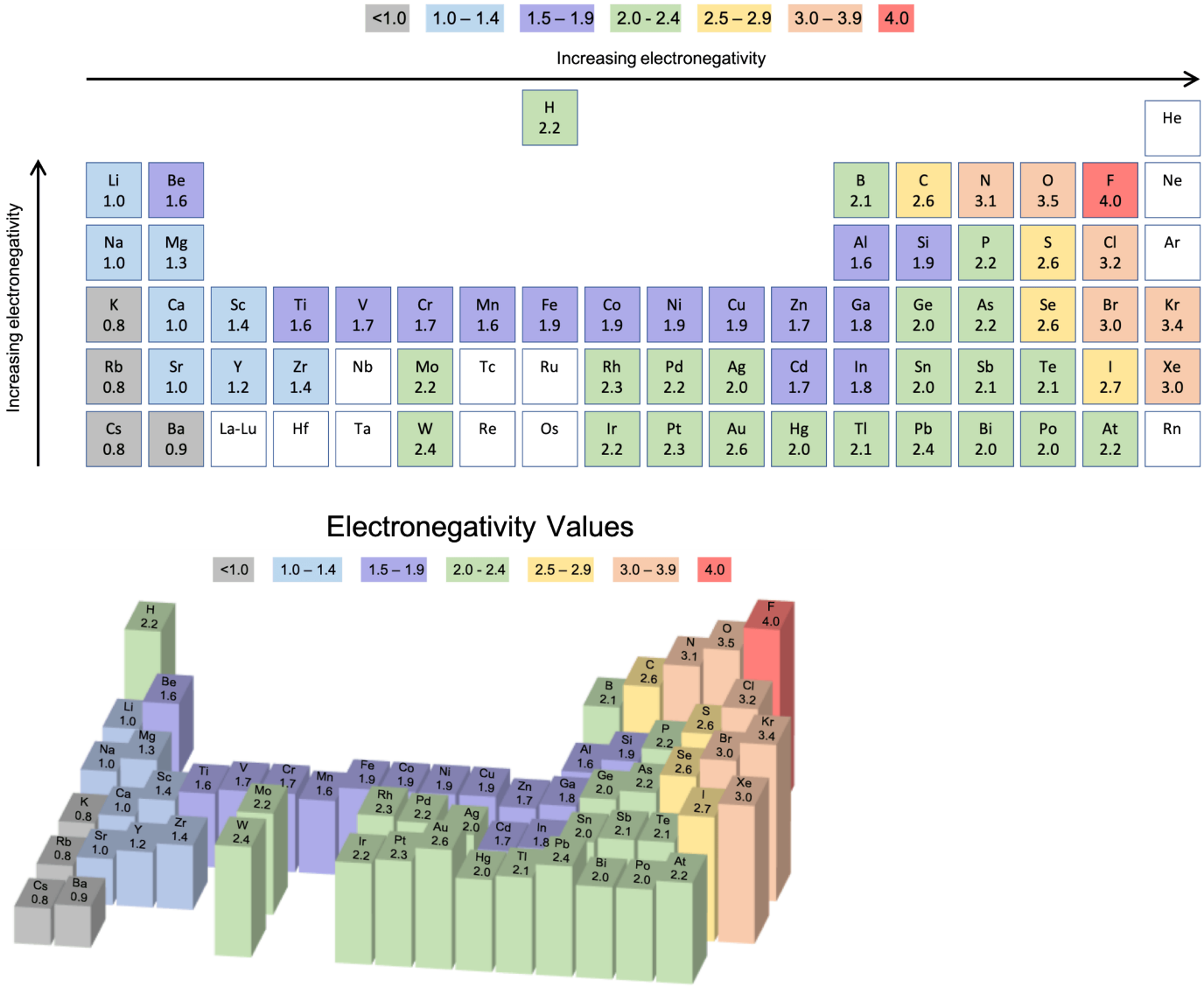


Figure 4.5.1**: Periodic table of the elements with electronegativity values indicated**. Upper panel: The electronegativity values derived by Pauling follow predictable periodic trends with the higher electronegativities toward the upper right of the periodic table. Elements without Pauling electronegativity values are shown with white boxes and no electronegativity value. Lower panel: An alternative view of electronegativity values. In this view, elements without Pauling electronegativity values are excluded. Electronegativity values derived by Pauling follow predictable periodic trends with the higher electronegativities toward the upper right of the periodic table. The height of the bars indicates the electronegativity value. Source: University of Wisconsin Chemistry Book [University of Wisconsin-Madison Chemistry 103].

Rather than memorizing electronegativity values, it is more useful to understand the trend and how it influences bonding. If the two atoms have the **same or very similar electronegativities**, they pull on the shared electrons with approximately equal strength. The electrons are distributed relatively evenly between the two atoms. This produces a **nonpolar covalent bond**.

Equal electron sharing → no permanent bond dipole.

When two bonded atoms have **different electronegativities**, the atom with the higher electronegativity pulls the shared electrons closer to itself. The electrons are still shared between the atoms, but they are **shared unequally**. This produces a **polar covalent bond**.

The unequal distribution of electrons causes the more electronegative atom to develop a slight negative charge, represented by

δ– (delta minus). The less electronegative atom develops a slight positive charge, represented by **δ+ (delta plus)**. These are called **partial charges** because the electrons have not been completely transferred from one atom to another.

Unequal electron sharing → partial charges → a permanent bond dipole.

The greater the difference in electronegativity between the two atoms, the more unequal the sharing of electrons becomes and the more polar the bond becomes.

Key Idea

- **Similar electronegativities → more equal sharing → less polar bond**.
- **Different electronegativities → more unequal sharing → more polar bond**.

In the next section, we will use the **difference in electronegativity (ΔEN)** between two atoms to predict whether a bond is nonpolar covalent, polar covalent, or primarily ionic.

Using Electronegativity to Predict Bond Type

The difference in electronegativity between two bonded atoms can help us predict how equally the bonding electrons are shared. This difference is called the **electronegativity difference**, often written as **ΔEN** ("delta EN").

To calculate the electronegativity difference, subtract the smaller electronegativity value from the larger value:

$$\Delta EN = EN_{\text{higher}} - EN_{\text{lower}} \tag{4.5.1}$$

Because the larger value is always placed first, the electronegativity difference will always be a **positive number or zero**.

The size of the electronegativity difference provides a useful way to estimate the type of bond formed between two atoms:

Table 4.5A Predicting Bond Type Using Electronegativity Differences

Electronegativity Difference (ΔEN)	Predicted Bond Type	Electron Behavior
0–0.4	Nonpolar covalent	Electrons are shared approximately equally
0.5–1.8	Polar covalent	Electrons are shared unequally
Greater than 1.8	Mostly ionic	Electrons are strongly attracted toward one atom

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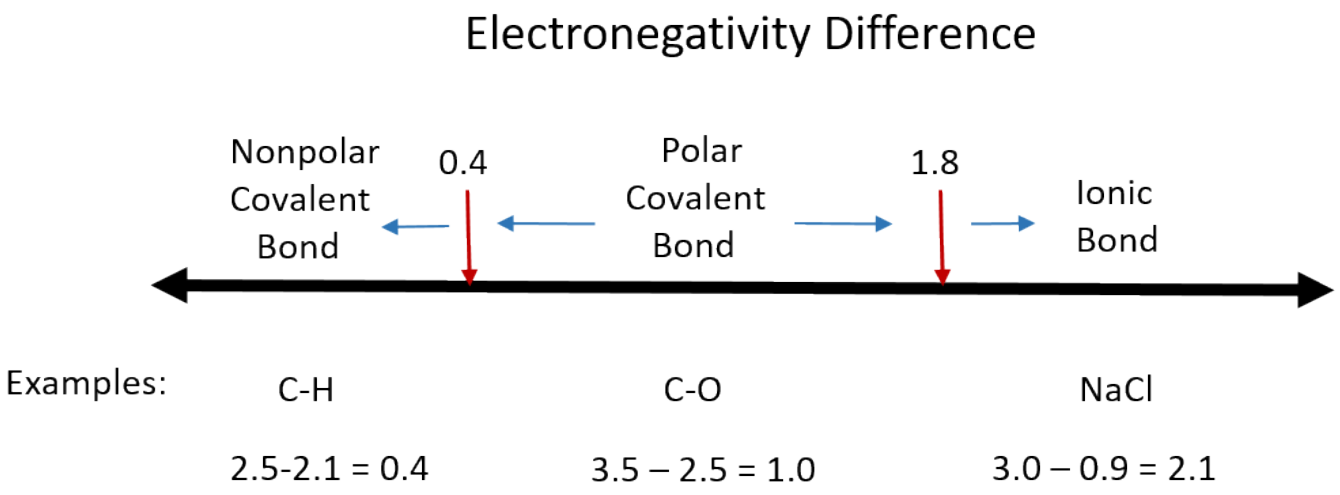


Figure 4.5.2: Chart of electronegativity differences. Electronegativity differences between 0 and 0.4 are treated as nonpolar covalent bonds, whereas differences between 0.4 and 1.8 are considered polar covalent bonds. Above a value of 1.8 the transfer of electrons becomes complete and ionic bonding occurs.

> **These ranges are useful guidelines rather than absolute rules. Chemical bonding exists along a continuum, but these values correctly predict the bonding behavior of most compounds encountered in introductory chemistry**.

Nonpolar Covalent Bonds

When two bonded atoms have the same or very similar electronegativities, the difference in electronegativity is small. Neither atom pulls substantially harder on the shared electrons, so the electrons are shared approximately equally.

For example, consider the bond between two hydrogen atoms. Both hydrogen atoms have an electronegativity of 2.2:

$$\Delta EN = 2.2 - 2.2 = 0 \tag{4.5.2}$$

Because there is no difference in electronegativity, the electrons are shared equally. The H—H bond is therefore a **nonpolar covalent bond**.

A carbon–hydrogen bond also has a relatively small electronegativity difference:

$$\Delta EN = 2.6 - 2.2 = 0.4 \tag{4.5.3}$$

The C—H bond is generally treated as a **nonpolar covalent bond**.

Polar Covalent Bonds

When two atoms have a larger difference in electronegativity, the more electronegative atom pulls more strongly on the shared electrons. The electrons are still **shared**, but they are not shared equally.

Consider the bond between hydrogen and chlorine:

- H = 2.2
- Cl = 3.2

$$\Delta EN = 3.2 - 2.2 = 1.0 \tag{4.5.4}$$

A difference of 1.0 indicates a **polar covalent bond**.

Because chlorine is more electronegative than hydrogen, the shared electrons spend more time near the chlorine atom. This gives chlorine a **partial negative charge (δ–)** and hydrogen a **partial positive charge (δ+)**.

$$\mathrm{H}^{\delta+} - \mathrm{Cl}^{\delta-} \tag{4.5.5}$$

These are called **partial charges** because the electrons have not been completely transferred from one atom to another. The atoms are still connected by a covalent bond.

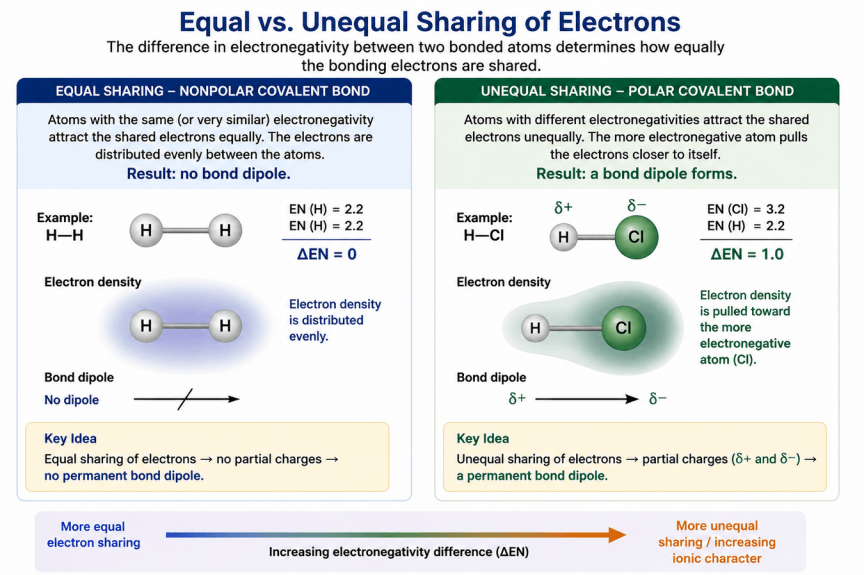


Figure 4.5.3**: Equal and Unequal Sharing of Electrons in Covalent Bonds**. In a nonpolar covalent bond, atoms with the same or similar electronegativities share bonding electrons approximately equally, producing no permanent bond dipole. In a polar covalent bond, the more electronegative atom attracts the shared electrons more strongly, shifting electron density toward that atom. This unequal sharing produces a partial negative charge (δ–) on the more electronegative atom and a partial positive charge (δ+) on the less electronegative atom, creating a permanent bond dipole. As the difference in electronegativity (ΔEN) increases, electron sharing becomes increasingly unequal and the bond develops greater ionic character.

Key Idea

- **The more electronegative atom in a polar covalent bond develops a partial negative charge (δ–), while the less electronegative atom develops a partial positive charge (δ+)**.

Increasing Ionic Character

As the electronegativity difference between two atoms becomes larger, the bonding electrons are pulled more strongly toward the more electronegative atom. The bond therefore develops increasing **ionic character**.

For example, consider sodium and chlorine:

- Na = 0.9
- Cl = 3.2

$$\Delta EN = 3.2 - 0.9 = 2.3 \tag{4.5.6}$$

This very large electronegativity difference indicates that the interaction between sodium and chlorine is best described as **ionic**. Rather than approximately sharing the electrons, sodium transfers an electron to chlorine, producing Na^{+} and Cl^{-} ions.

Thus, bonding can be thought of as a continuum:

Nonpolar covalent → Polar covalent → Increasing ionic character.

As the electronegativity difference increases, electron sharing becomes increasingly unequal.

Predicting the Direction of Bond Polarity

Electronegativity can also tell us **which end of a polar bond is partially positive and which is partially negative**.

Consider an O—H bond:

- O = 3.4
- H = 2.2

Because oxygen is more electronegative, it pulls the shared electrons toward itself.

$$\mathrm{H}^{\delta+} - \mathrm{O}^{\delta-} \tag{4.5.7}$$

The oxygen end of the bond is therefore partially negative, while the hydrogen end is partially positive.

This unequal distribution of electrons is called **bond polarity**.

Key Idea

- **Electronegativity difference tells us how polar a bond is, while the electronegativity values tell us which atom has the stronger pull on the shared electrons**.

Biological Connection: Why Bond Polarity Matters

The difference between nonpolar, polar, and ionic bonding is more than a way to classify chemical bonds. The distribution of electrons within a substance strongly influences how it behaves in **living organisms and medicines**.

Water and Biological Molecules

Many of the bonds found in biological molecules are **polar covalent bonds**. Oxygen and nitrogen are relatively electronegative, so bonds such as **O—H, C—O, and N—H** have an unequal distribution of electrons.

Water is an especially important example. Each O—H bond is polar because oxygen attracts the shared electrons more strongly than hydrogen. This gives oxygen a partial negative charge (δ–) and the hydrogen atoms partial positive charges (δ+).

These partial charges are responsible for many of water's unusual properties and help water interact with ions and other polar substances. Because the human body is largely composed of water, these interactions are essential to biological chemistry.

Nonpolar Bonds and Cell Membranes

Carbon and hydrogen have relatively similar electronegativities, so **C—H bonds are generally treated as nonpolar** in biological chemistry. Molecules or regions of molecules containing many C—H bonds therefore tend to have relatively little separation of electrical charge.

This is particularly important in **lipids**. The long hydrocarbon portions of fatty acids and membrane lipids are largely nonpolar. Their behavior in water helps drive the organization of lipids into biological membranes.

Ionic Interactions in the Body

Ions are also essential to living systems. Sodium ($Na^{\oplus}$), potassium ($K^{\oplus}$), calcium ($Ca^{2\oplus}$), and chloride ($Cl^{\ominus}$) are examples of important biological ions.

Differences in the concentrations and movement of these ions are essential for processes such as **nerve signaling, muscle contraction, fluid balance, and maintenance of normal cellular function**.

Bond Polarity and Medicines

Most medications contain a combination of **polar and nonpolar bonds**. The distribution of these regions can strongly influence how a drug behaves in the body.

Polar regions may interact favorably with water and other polar substances, while nonpolar regions may interact more readily with nonpolar environments such as the interior of cell membranes or hydrophobic regions within proteins.

As a result, the arrangement of polar and nonpolar regions within a drug can influence its **solubility, movement through the body, ability to cross cell membranes, and interactions with its biological target**.

Changes in molecular structure can therefore have important consequences. Even a small chemical modification that changes the distribution of electrons within a molecule may alter how that substance behaves biologically.

Table 4.5B: Analysis of Electronegativity Differences for Biologically Important Bonds

Bond	ΔEN	Bond Type	Why It Matters
C–H	**0.4**	Nonpolar covalent	Hydrocarbons and lipids
C–O	**1.0**	Polar covalent	Sugars and alcohols
O–H	**1.4**	Polar covalent	Water and carbohydrates
N–H	**0.9**	Polar covalent	Proteins and amino acids
P–O	**1.4**	Polar covalent	ATP, DNA, phosphates
S–H	**0.4**	Nonpolar covalent*	Cysteine side chains
Na–Cl	**2.1**	Ionic	Saline solutions
K–Cl	**2.2**	Ionic	Cellular electrolytes
Ca–O	**2.5**	Ionic	Bone minerals
Mg–O	**2.3**	Ionic	Mineral salts

Key Idea

- **The way electrons are distributed within chemical bonds helps determine how substances interact with water, cell membranes, proteins, and other molecules in living systems**.

In Chapter 5, we will build on these ideas by examining how **bond polarity and molecular shape combine to determine the polarity of an entire molecule**, and how molecular polarity influences intermolecular forces and physical properties.

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4.6: Chemistry in the Body- How do Neurons Maintain Ion Gradients?

So far in this chapter, we have examined several different ways that electrons can be distributed between atoms. We have seen that electrons may be transferred to form **ions**, shared approximately equally in **nonpolar covalent bonds**, or shared unequally in **polar covalent bonds**.

These differences in electron distribution have enormous consequences in living systems. One remarkable example occurs in the cells responsible for carrying electrical signals throughout your nervous system: **neurons**.

A **neuron**, or nerve cell, is a specialized cell that receives and transmits information. Neurons allow your brain to communicate with the rest of your body, making it possible to think, sense your surroundings, move your muscles, and respond to changes in your environment.

A typical neuron consists of a **cell body (soma)**, **dendrites**, and an **axon** (Fig 4.6.1) **Dendrites** are thin structures that arise from the cell body, often extending for hundreds of micrometers and branching multiple times, giving rise to a complex "dendritic tree". An **axon**, also called a nerve fiber, is a special cellular extension or process that arises from the cell body at a site called the **axon hillock** and travels for a distance, as far as 1 meter in humans or even more in other species. Most neurons receive signals via the **dendrites** and send out signals down the **axon**. When a neuron fires an electrical signal down the axon, it is called an **action potential**. For an action potential to be sent down the axon, a threshold signal must be received by the dendrites and transmitted to the axon hillock. If the signal is strong enough when it reaches the axon hillock, a single all or nothing action potential will be sent down the axon causing the activation of the neuron's downstream target.

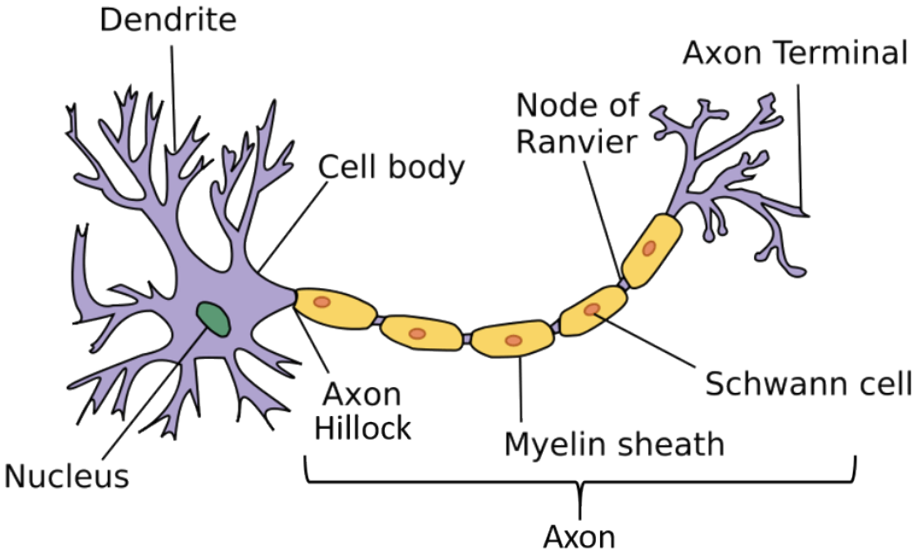


Figure 4.6.1**: Anatomy of a Neuron**. Depicted within the diagram is the neuron with the central cell body (soma) and typical dendrite and axon projections. The dendrites of a neuron are typically where outside signals are received and the axon is the used to transmit the chemical signal to downstream target cells in the communication pathway. Figure adapted from Wikimedia

Neurons Use Ions to Generate Electrical Signals

Like all cells, neurons are surrounded by a **plasma membrane** that separates the fluid inside the cell from the fluid outside the cell. However, the concentrations of dissolved ions on the two sides of this membrane are not the same.

Two particularly important ions are:

- **sodium ions (Na⊕)**, which are present at higher concentrations outside the neuron, and
- **potassium ions (K⊕)**, which are present at higher concentrations inside the neuron.

Other ions, including $Ca^{2⊕}$, Cl⊖, phosphate ions, and negatively charged biological molecules, also contribute to differences between the environments inside and outside the cell.

The unequal distribution of ions, together with the selective permeability of the plasma membrane to different ions, produces a small separation of electrical charge across the membrane. In a resting neuron, the inside of the cell is approximately **70 mV more negative than the outside**, producing a **resting membrane potential of about –70 mV**. The membrane is therefore said to be **polarized**.

How are Na⊕ and K⊕ Gradients Established and Maintained?

Particles in liquids and gases are constantly moving. When particles are more concentrated in one region than another, their random motion results in a **net movement from the region of higher concentration toward the region of lower concentration**. This process is called **diffusion**.

The difference in concentration between two regions is called a **concentration gradient**. Particles naturally tend to move **down their concentration gradient**, from an area where they are more concentrated to an area where they are less concentrated. This movement does not require the cell to supply energy.

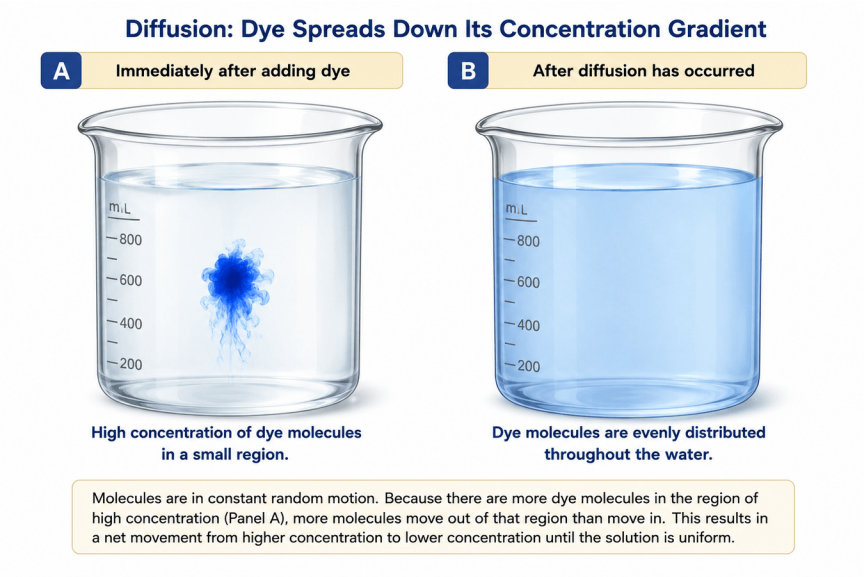


Figure 4.6.2: Diffusion Down a Concentration Gradient. When dye is first added to water, the dye molecules are concentrated within a small region (Panel A). Because molecules are in constant random motion, the dye gradually spreads throughout the water. This produces a **net movement from an area of higher concentration toward areas of lower concentration**, or down the concentration gradient. Eventually, the dye becomes evenly distributed throughout the water (Panel B). The molecules continue to move randomly, but there is no longer a net movement in any one direction.

A useful analogy is water held behind a dam. Water naturally tends to flow downhill. A dam prevents that movement, allowing a large amount of water to accumulate at a higher elevation. The stored water now has **potential energy** because, if a pathway through the dam is opened, the water can rush downhill.

A concentration gradient is similar. When many particles are concentrated in one region and fewer are present in another, there is a tendency for the particles to spread out. If a pathway becomes available, there will be a net movement of particles **down the concentration gradient**.

Moving in the opposite direction is different. Pumping water uphill and back behind a dam requires an input of energy. In the same way, moving particles **against their concentration gradient—from lower concentration toward higher**

concentration—requires energy.

This is exactly what neurons must do with sodium and potassium ions. In order to **stockpile sodium ions outside the cell and potassium ions inside the cell**, neurons must expend energy to pump these ions **against their concentration gradients**. A specialized membrane protein called the **sodium-potassium ATPase (Na⊕/K⊕ ATPase)** uses energy from ATP to accomplish this work. For each transport cycle, the Na⊕/K⊕ ATPase moves **3 Na⊕ ions out of the neuron and 2 K⊕ ions into the neuron**. Over time, this process helps establish and maintain a high concentration of Na⊕ outside the cell and a high concentration of K⊕ inside the cell.

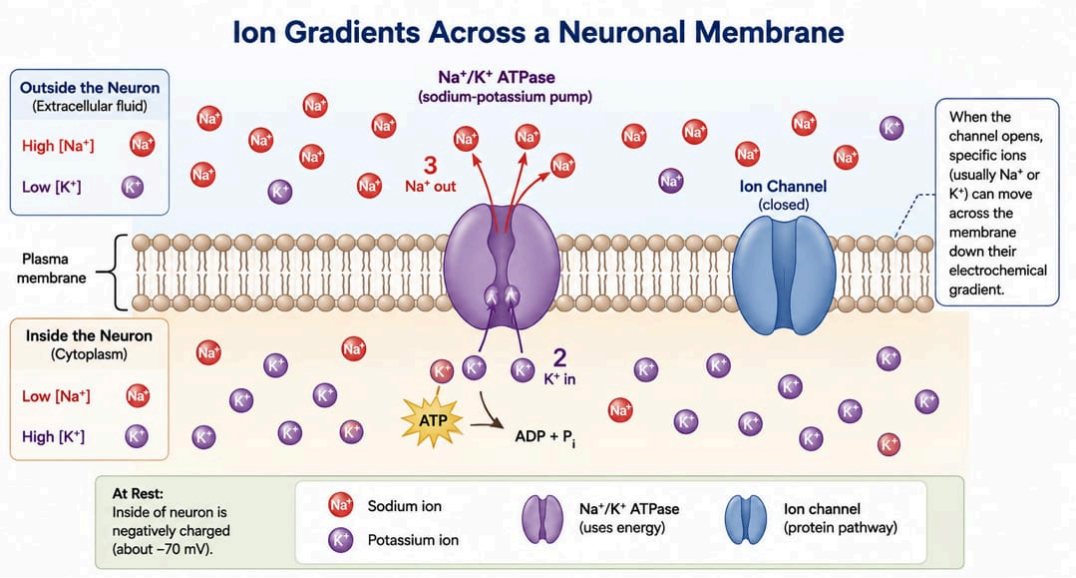


Figure 4.6.3**: Ion gradients across a neuronal membrane.** Neurons maintain different concentrations of Na+ and K+ on opposite sides of the plasma membrane. The Na+/K+ ATPase uses energy from one ATP to transport 3 Na+ out of the cell and 2 K+ into the cell. Because ions cannot readily cross the plasma membrane on their own, these concentration differences can be maintained. Opening specific ion channels allows the controlled movement of ions across the membrane and is essential for electrical signaling.

By continually moving these ions, the Na⊕/K⊕ pump helps maintain a high concentration of Na⊕ outside the neuron and a high concentration of K⊕ inside the neuron. These ion gradients are essential for the electrical activity of nerve and muscle cells.

But Why Don't the Ions Just Move Back?

This raises an important chemical question. If there is a large concentration of Na⊕ outside the neuron and a large concentration of K⊕ inside it, **why don't the ions simply move across the membrane and eliminate these concentration differences?**

The answer is that Na⊕ and K⊕ cannot readily pass directly through the plasma membrane.

Remember that these are **charged particles**. In the watery environments inside and outside cells, ions interact strongly with surrounding polar water molecules. However, the interior of the plasma membrane provides a very different, nonpolar chemical environment that is unfavorable for charged particles.

As a result, ions generally require specialized **transport proteins** to cross the membrane.

Some transport proteins, such as the Na⊕/K⊕ ATPase, use energy to pump ions across the membrane. Other membrane proteins form **ion channels** that can open and close, providing pathways through which particular ions can move down their concentration gradient.

This ability to control when ions cross the membrane is fundamental to the function of neurons.

From Ion Movement to an Electrical Signal

A neuron at rest maintains a separation of charge across its membrane, producing a **resting membrane potential** of approximately –70 mV. The inside of the neuron is electrically negative relative to the outside.

When particular ion channels open, ions can rapidly move across the membrane. Because ions carry electrical charge, their movement changes the electrical potential across the membrane.

If the change is large enough, it can trigger an **action potential**—a rapid electrical signal that travels along the neuron.

Thus, the electrical signals produced by your nervous system ultimately depend on something we have been studying throughout this chapter:

the behavior of charged particles.

The movement of Na^+, K^+, Ca^{2+}, and other ions across cellular membranes allows neurons to transmit the signals that make sensation, movement, thought, and communication possible.

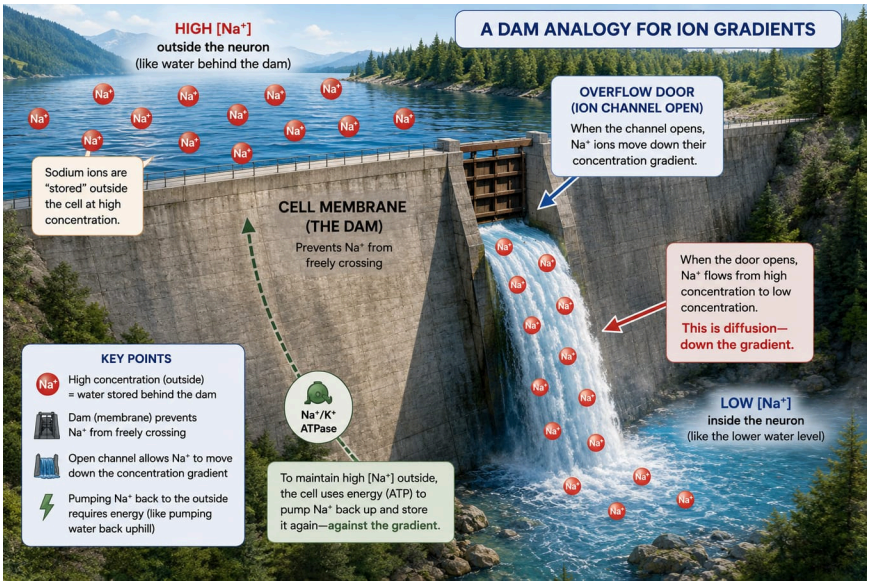


Figure 4.6.4**: A Dam Analogy for Maintaining Ion Concentration Gradients.** A concentration gradient stores potential energy much like water held behind a dam. In a neuron, the plasma membrane acts as a barrier that prevents Na^+ ions from freely moving from their high concentration outside the cell to their lower concentration inside the cell. When an ion channel opens, Na^+ can move **down its concentration gradient**, similar to water flowing through an opened gate in a dam. Maintaining this gradient requires energy: the Na^+/K^+ ATPase uses energy from ATP to transport Na^+ back across the membrane **against its concentration gradient**. The resulting ion gradients provide stored potential energy that cells can use for processes such as electrical signaling.

A Chemical Mystery: What Makes the Membrane a Barrier?

We have answered part of our question, but an important piece of the chemistry is still missing.

We know that:

Na^+ and K^+ are charged.

Water is a polar molecule.

Cell membranes contain many covalently bonded molecules.

And somehow, the plasma membrane forms a barrier that separates ions dissolved in water on one side from ions dissolved in water on the other.

Why?

To answer that question, knowing whether individual bonds are polar is not enough. We must also consider the **three-dimensional shapes of molecules**, whether an **entire molecule is polar or nonpolar**, and the attractive forces that occur **between molecules**.

These concepts—**molecular geometry, molecular polarity, and intermolecular forces**—are the focus of Chapter 5.

As we develop those ideas, we will return to the plasma membrane and begin to uncover the chemistry that allows a neuron to maintain its ion gradients and generate an electrical signal.

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4.7: Appendix A - Naming Ionic Compounds

Why Learn Chemical Names?

Throughout this chapter, we've focused on **how atoms form stable compounds** by transferring or sharing electrons. Chemists, healthcare professionals, and scientists also need a consistent way to communicate about these compounds.

Fortunately, naming ionic compounds follows a few simple rules.

The goal is **recognition**, not memorization. In this course, you should become comfortable reading and writing the names of common compounds encountered in chemistry, biology, and healthcare.

Rule 1: Name the Cation First

The positively charged ion (cation) is always named first.

Formula	Name
NaCl	sodium chloride
KBr	potassium bromide
MgO	magnesium oxide
$CaCl_2$	calcium chloride

Rule 2: Name the Anion Second

For monatomic anions, change the ending to **-ide**.

Ion	Name
Cl^-	chloride
O^{2-}	oxide
S^{2-}	sulfide
N^{3-}	nitride

Polyatomic Ions

Some ions contain more than one atom.

These ions behave as a single charged unit and retain their own names.

You should recognize the most common polyatomic ions encountered in health sciences.

Formula	Name
NH_4^+	ammonium
OH^-	hydroxide

Formula	Name
NO_3^-	nitrate
HCO_3^-	bicarbonate (hydrogen carbonate)
CO_3^{2-}	carbonate
PO_4^{3-}	phosphate
SO_4^{2-}	sulfate

Transition Metals

Some metals can form more than one positive ion.

Roman numerals indicate the charge of the metal.

Formula	Name
$FeCl_2$	iron(II) chloride
$FeCl_3$	iron(III) chloride
Cu_2O	copper(I) oxide
CuO	copper(II) oxide

For CH112, you should recognize these names but extensive memorization of transition-metal charges is **not expected**.

Common Ionic Compounds in Biology

Formula	Name	Biological Importance
NaCl	sodium chloride	electrolyte
KCl	potassium chloride	nerve function
$CaCl_2$	calcium chloride	calcium source
$MgSO_4$	magnesium sulfate	medication (Epsom salts)
$NaHCO_3$	sodium bicarbonate	blood buffer, antacid
$CaCO_3$	calcium carbonate	bone mineral, antacid

Notice that these are compounds you will encounter again in physiology, nutrition, microbiology, and pharmacology.

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4.8: Appendix B - Naming Covalent Compounds

Covalent Compounds

Covalent compounds form when **nonmetals share electrons**.

Unlike ionic compounds, covalent compounds are named using numerical prefixes that indicate the number of atoms present.

Common Prefixes

Number	Prefix
1	mono-
2	di-
3	tri-
4	tetra-
5	penta-
6	hexa-
7	hepta-
8	octa-

General Rules

1. Name the first element.
2. Add a prefix if more than one atom is present.
3. Name the second element using an **-ide** ending.
4. Always use a prefix for the second element.

Examples

Formula	Name
CO	carbon monoxide
CO_2	carbon dioxide
NO	nitrogen monoxide
NO_2	nitrogen dioxide
N_2O	dinitrogen monoxide
SO_2	sulfur dioxide

Common Molecular Compounds

Fortunately, many biologically important covalent compounds are known by their formulas.

Formula	Common Name
H_2O	water
CO_2	carbon dioxide
NH_3	ammonia
CH_4	methane
O_2	oxygen
N_2	nitrogen

These names are encountered so frequently that they quickly become familiar through repeated use.

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4.9: Chapter Summary

- **Chemical bonds form through interactions involving valence electrons**. Atoms tend to form bonds that produce more stable electron configurations, often by achieving a filled outer electron shell.
- **Ionic bonds form through the transfer of electrons**. When one atom loses one or more electrons and another gains them, oppositely charged **cations and anions** are produced. The electrostatic attraction between these ions forms an ionic bond.
- **Ionic compounds are electrically neutral**. Their chemical formulas represent the smallest whole-number ratio of ions needed to balance positive and negative charges. This ratio is called a **formula unit**.
- **Covalent bonds form when atoms share electrons**. A shared pair of electrons forms a **single covalent bond**. Atoms may share two or three pairs of electrons to form **double** or **triple bonds**.
- **Lewis electron-dot symbols and Lewis structures** provide a way to represent valence electrons, bonding pairs, and lone pairs. For many main-group atoms, Lewis structures can be used with the **octet rule** to predict stable bonding arrangements.
- Different elements tend to form characteristic numbers of covalent bonds. Hydrogen commonly forms one bond, oxygen two, nitrogen three, and carbon four. Carbon's ability to form four covalent bonds allows it to produce the enormous variety of molecular structures found in living organisms.
- **Electronegativity** describes the ability of an atom to attract shared electrons toward itself. Electronegativity generally increases from left to right across a period and decreases down a group of the periodic table.
- When bonded atoms have the same or similar electronegativities, electrons are shared approximately equally, producing a **nonpolar covalent bond**. When their electronegativities differ, electrons are shared unequally, producing a **polar covalent bond**.
- In a polar covalent bond, the more electronegative atom develops a **partial negative charge (δ−)** and the less electronegative atom develops a **partial positive charge (δ+)**. This separation of partial charge creates a **bond dipole**.
- The **electronegativity difference (ΔEN)** between two atoms can be used to estimate bond type. Small differences favor nonpolar covalent bonding, intermediate differences produce polar covalent bonding, and very large differences indicate increasing ionic character. Bonding is best understood as a **continuum** rather than as a set of completely separate categories.
- Electron distribution has important consequences in living systems. Polar bonds are common in water and biological molecules, while relatively nonpolar C—C and C—H bonds are abundant in lipids and other organic compounds. The distribution of polar, nonpolar, and charged regions also influences the behavior of medications and their interactions with biological molecules.
- **Diffusion** results from the constant random motion of particles. When a concentration gradient exists, there is a net movement of particles from an area of higher concentration toward an area of lower concentration. Movement **down** a concentration gradient does not require cellular energy, while moving particles **against** a concentration gradient requires an input of energy.
- Neurons use the **Na⊕/K⊕ ATPase** to establish and maintain ion concentration gradients across the plasma membrane. The pump uses energy from ATP to transport **3 Na⊕ out of the cell and 2 K⊕ into the cell** during each transport cycle. These gradients represent stored potential energy that can be used when ion channels open.
- The plasma membrane prevents ions such as Na⊕ and K⊕ from freely moving down their concentration gradients. Controlled movement of ions through membrane proteins contributes to changes in membrane potential and allows neurons to generate **action potentials** and transmit electrical signals.
- Understanding individual bond polarity is only the beginning. To explain why water behaves as it does, why ions cannot readily cross cell membranes, and why molecules interact differently with their surroundings, we must also consider **molecular shape, overall molecular polarity, and intermolecular forces**. These concepts provide the foundation for **Chapter 5**.

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5: MOLECULAR STRUCTURE, POLARITY AND INTERMOLECULAR FORCES

5.1: Introduction

5.2: Molecular Geometry - Using VSEPR Theory to Predict Molecular Shape

5.3: Molecular Polarity

5.4: Intermolecular Forces and Electrostatic Attractions

5.5: Physical Properties of Intermolecular Forces

5.6: Chemistry in the Body- Why Can't Ions Cross the Cell Membrane?

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5.1: Introduction

In the previous chapter, we learned how atoms share electrons to form **covalent bonds** and how to represent those bonds using **Lewis structures**. Lewis structures provide a simple two-dimensional picture of a molecule, showing how atoms are connected and where lone pairs of electrons are located. They also allow us to distinguish between **nonpolar** and **polar covalent bonds** based on differences in electronegativity.

To review, the basic steps for drawing a Lewis structure are:

1. Count the total number of valence electrons for the molecule or polyatomic ion.
2. Identify the central atom and arrange the surrounding atoms around it.
3. Connect the atoms with single bonds.
4. Add lone pairs to the outer atoms to satisfy the octet rule (except for hydrogen).
5. Check whether the central atom has an octet. If necessary, convert lone pairs on surrounding atoms into double or triple bonds.

By following these steps, we can determine how atoms are connected, the types of bonds present, and the locations of lone pairs of electrons. These are essential first steps in understanding the structure of a molecule.

However, Lewis structures have an important limitation—they only show the **connectivity** of atoms, not their actual three-dimensional arrangement in space. In reality, molecules are not flat. Instead, atoms occupy positions in three dimensions that minimize repulsion between regions of electron density.

Each bond and lone pair surrounding the central atom represents a region where electrons are concentrated. These regions, called **electron domains**, repel one another because electrons carry a negative charge. As a result, electron domains arrange themselves as far apart as possible. This simple idea forms the basis of **Valence Shell Electron Pair Repulsion (VSEPR) theory**, which allows us to predict the three-dimensional shape, or **molecular geometry**, of many molecules.

Understanding molecular geometry is about much more than drawing three-dimensional structures. The shape of a molecule determines whether its bond polarities reinforce or cancel one another, which in turn determines whether the molecule is **polar or nonpolar**. Molecular polarity influences how molecules interact with one another, leading to differences in properties such as boiling point, melting point, solubility, and viscosity. By the end of this chapter, you will be able to use a Lewis structure to predict a molecule's geometry, determine whether it is polar, identify its intermolecular forces, and explain many of its physical properties.

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5.2: Molecular Geometry - Using VSEPR Theory to Predict Molecular Shape

Learning Objectives

After completing this section, you should be able to:

- Explain the basic principles of VSEPR theory.
- Distinguish between electron geometry and molecular geometry.
- Predict the molecular geometry of common molecules using a Lewis structure.
- Explain how lone pairs influence molecular shape and bond angles.

From a Lewis Structure to a Molecular Shape

In the previous chapter, you learned how to draw **Lewis structures** to show how atoms are connected within a molecule. Lewis structures provide valuable information about the types of bonds present and the locations of lone pairs of electrons. However, Lewis structures are only **two-dimensional representations** of molecules.

Real molecules exist in **three dimensions**. The arrangement of atoms around the central atom is called the **molecular geometry**, and this three-dimensional shape influences many of a molecule's physical and chemical properties.

To predict molecular geometry, chemists use **Valence Shell Electron Pair Repulsion (VSEPR) theory** (pronounced *vesper*).

The central idea behind VSEPR theory is simple:

Key Idea

- Electron domains repel one another and arrange themselves as far apart as possible.

Because electrons carry a negative charge, regions of high electron density naturally repel one another. The lowest-energy arrangement is therefore the one that minimizes these repulsive forces.

Although VSEPR theory is a simplified model, it accurately predicts the molecular geometry of many small molecules.

Predicting Molecular Geometry

Rather than memorizing dozens of different molecular shapes, it is much easier to follow the same sequence of steps each time to deduce the molecular geometry.

Throughout this chapter, we will use the following five-step strategy.

A Five-Step Strategy for Predicting Molecular Geometry

Step 1. Draw the Lewis structure.



Step 2. Count the electron domains around the central atom.

⬇️

Step 3. Determine the electron geometry.

⬇️

Step 4. Count the number of lone pairs on the central atom.

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Step 5. Determine the molecular geometry.

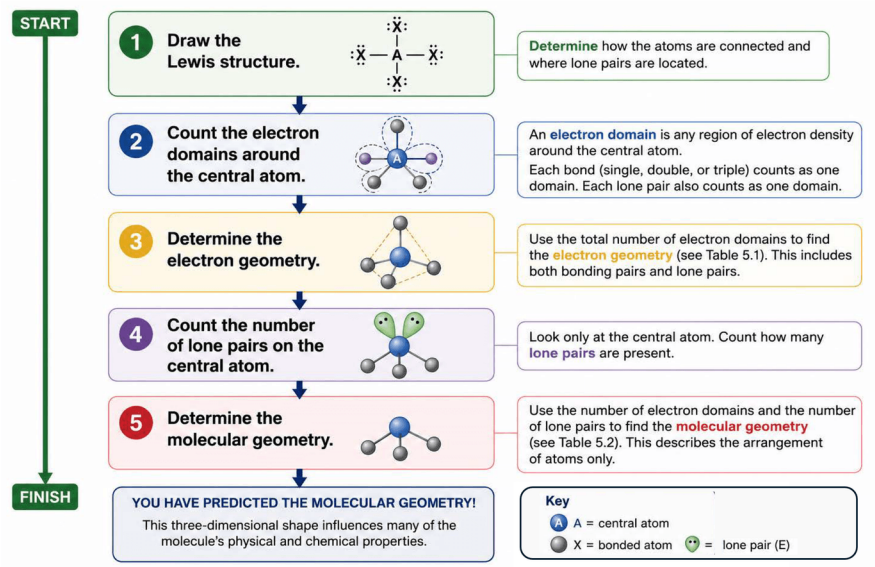


Figure 5.2.1**:** ***Flowchart illustrating the five-step strategy for predicting molecular geometry.*** **1. Draw the Lewis structure** to determine how the atoms are connected and identify the locations of any lone pairs. **2. Count the electron domains** around the central atom. Each single bond, double bond, triple bond, and lone pair counts as one electron domain. **3. Determine the electron geometry** based on the total number of electron domains. Electron geometry includes both bonding pairs and lone pairs. **4. Count the number of lone pairs** on the central atom. **5. Determine the molecular geometry** by combining the electron geometry with the number of lone pairs. Molecular geometry describes the arrangement of the atoms only and does not include lone pairs. The flowchart concludes by noting that the predicted molecular geometry determines many of the molecule's physical and chemical properties.

Step 1: Draw the Lewis Structure

Every molecular geometry problem begins by drawing the **Lewis structure** of the molecule or polyatomic ion. A correct Lewis structure provides the foundation for all of the remaining steps. If the Lewis structure is incorrect, the predicted molecular geometry will also be incorrect.

To draw a Lewis structure:

1. **Count the total number of valence electrons** contributed by all atoms in the molecule or ion. For polyatomic ions, add one

electron for each negative charge or subtract one electron for each positive charge.
2. **Choose the central atom.** In most molecules, the central atom is the least electronegative atom (excluding hydrogen, which is never a central atom).
3. **Connect the surrounding atoms to the central atom** using single covalent bonds.
4. **Complete the octets of the surrounding atoms** by adding lone pairs of electrons.
5. **Place any remaining electrons on the central atom.** If the central atom does not yet have a complete octet, form double or triple bonds as needed by converting lone pairs from surrounding atoms into shared bonding pairs.

Once the Lewis structure is complete, identify the **bonding pairs** and **lone pairs** surrounding the central atom. This information will be used in the remaining steps to predict the molecular geometry.

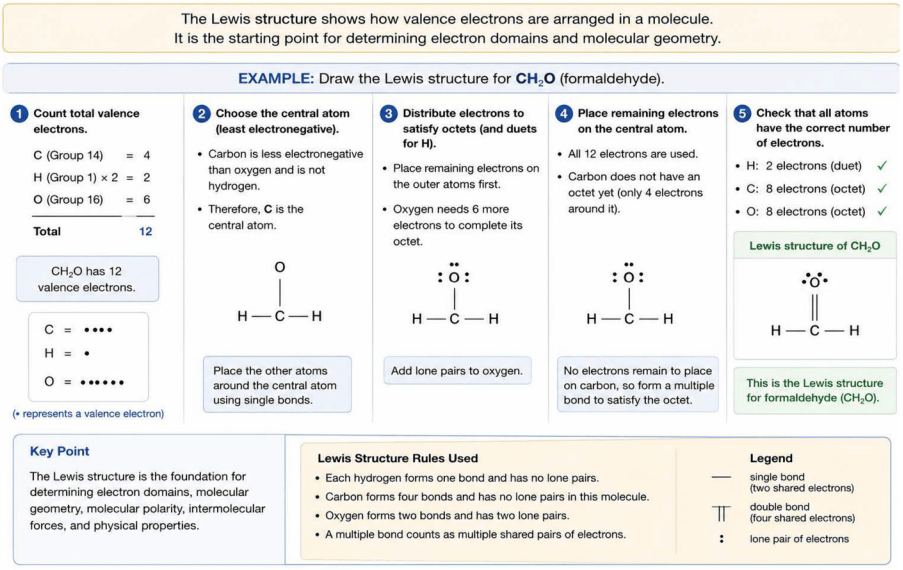


Figure 5.2.2: Drawing the Lewis Structure of Formaldehyde (CH_2O). Five-panel diagram illustrating the steps used to draw the Lewis structure of formaldehyde (CH_2O). Panel 1 counts the total number of valence electrons: carbon contributes 4 electrons, two hydrogen atoms contribute 2 electrons, and oxygen contributes 6 electrons, for a total of 12 valence electrons. Panel 2 identifies carbon as the central atom and connects it to two hydrogen atoms and one oxygen atom with single bonds. Panel 3 places lone pairs on oxygen to satisfy its octet. Panel 4 recognizes that carbon has only six electrons and converts one lone pair on oxygen into a second shared pair, forming a carbon–oxygen double bond. Panel 5 verifies that hydrogen has a duet, while carbon and oxygen each have complete octets. The completed Lewis structure is $H_2C{=}O$, with carbon bonded to two hydrogen atoms by single bonds and to oxygen by a double bond, and oxygen containing two lone pairs.

Note

In VSEPR theory, we are interested only in the electron domains surrounding the **central atom**. Lone pairs located on surrounding atoms do **not** affect the molecular geometry of the central atom.

Step 2: Count the Electron Domains

Next, count the number of **electron domains** surrounding the central atom.

An **electron domain** is any region of electron density around the central atom.

Each of the following counts as **one electron domain**:

- one single bond

- one double bond
- one triple bond
- one lone pair

Notice that double and triple bonds each count as only **one** electron domain because the electrons occupy the same general region of space.

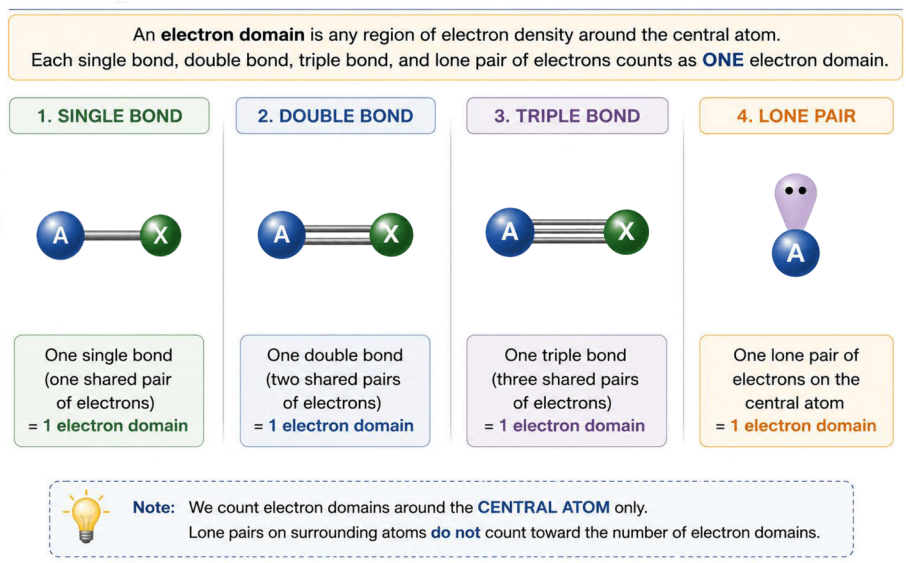


Figure 5.2.3: Each Bond and Lone Pair Counts as One Electron Domain. Four-panel diagram illustrating how electron domains are counted in VSEPR theory. The first panel shows a central atom (A) connected to one bonded atom (X) by a single bond and states that one single bond counts as one electron domain. The second panel shows a double bond between A and X and states that one double bond, although composed of two shared electron pairs, still counts as one electron domain. The third panel shows a triple bond between A and X and states that one triple bond, although composed of three shared electron pairs, also counts as one electron domain. The fourth panel shows a lone pair of electrons (E) on the central atom and states that one lone pair counts as one electron domain. A note at the bottom emphasizes that electron domains are counted only around the central atom; lone pairs on surrounding atoms are not included.

Let's use a water molecule ($\mathbf{H_2O}$) as an example. The oxygen atom is the **central atom** and is bonded to two hydrogen atoms. In addition to these two O–H bonds, the oxygen atom has **two lone pairs of electrons**. Remember that each bond and each lone pair counts as **one electron domain**. Therefore, the oxygen atom in a water molecule has a total of **four electron domains**: two bonding domains and two lone-pair domains (Figure 5.2.4).

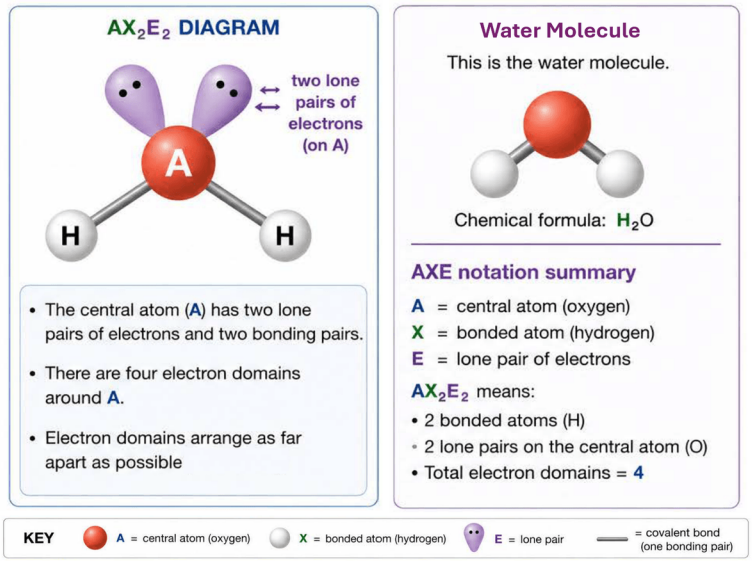
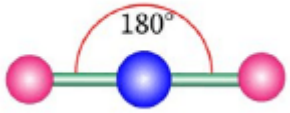
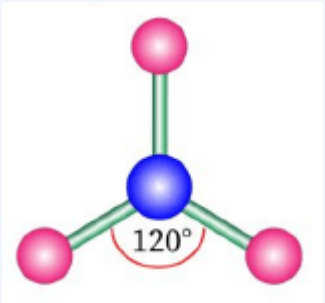


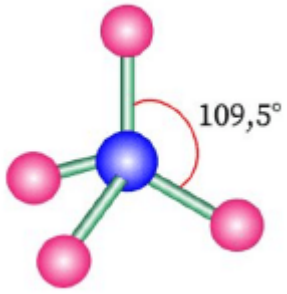
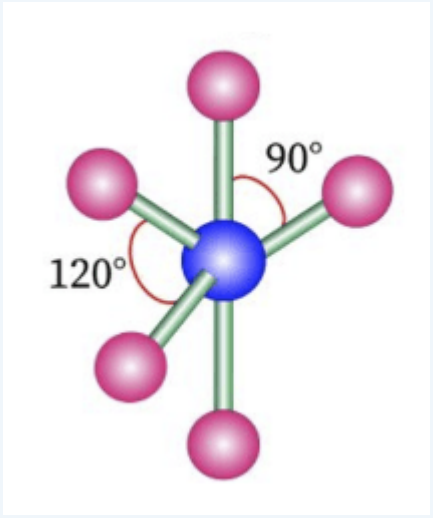
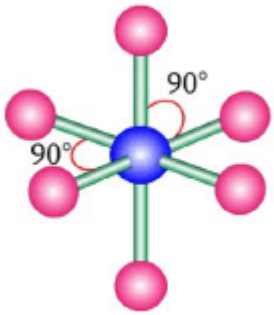
Figure 5.2.4: Identifying Electron Domains in a Water Molecule (H_2O). Diagram of a water molecule (H_2O) illustrating how electron domains are counted using AXE notation. The central oxygen atom (A) is bonded to two hydrogen atoms (X_2) by two single covalent bonds and has two lone pairs of electrons (E_2). The figure explains that A represents the central atom, X represents a bonded atom, and E represents a lone pair of electrons. The notation AX_2E_2 indicates two bonded atoms and two lone pairs surrounding the central atom, for a total of four electron domains. A key identifies the symbols used for the central atom, bonded atoms, lone pairs, and covalent bonds.

Step 3: Determine the Electron Geometry

The number of electron domains determines the **electron geometry**. Electron geometry describes the arrangement of **all electron domains**, including both bonding pairs and lone pairs. Use Table 5.2A to predict the electron geometry of your central atom.

Table 5.2A: Using Electron Domains to Determine Electronic Geometry

Number of Electron Domains	VSEPR Electronic Geometry	Ideal Bond Angle	Visual Representation
2	Linear	180°	
3	Trigonal Planar	120°	

Number of Electron Domains	VSEPR Electronic Geometry	Ideal Bond Angle	Visual Representation
4	Tetrahedral	109.5°	
5	Trigonal Bipyramidal	180°/120°/90°	
6	Octahedral	180°/90°	

Note

To determine the Electronic Geometry, you need to answer one main question: How many **electron domains** are present on the central atom?

Step 4: Count the Lone Pairs

Now count the number of **lone pairs on the central atom**. Lone pairs occupy more space than bonding pairs because their electrons are attracted to only one nucleus rather than being shared between two nuclei. As a result, lone pairs exert stronger repulsive forces than bonding pairs.

The relative strengths of these repulsions are

BP–BP < LP–BP < LP–LP

where

- BP = bonding pair
- LP = lone pair

These stronger repulsions compress nearby bond angles and often change the molecular geometry.

Step 5: Determine the Molecular Geometry

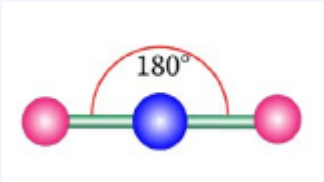
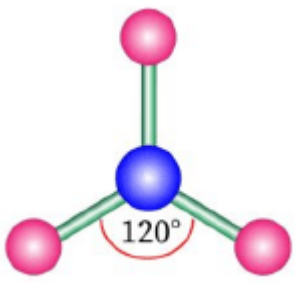
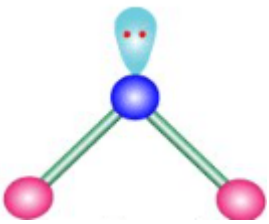
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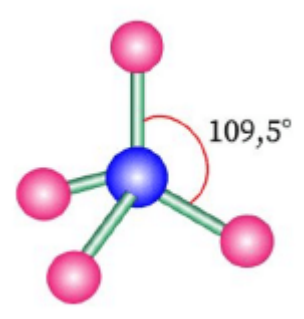
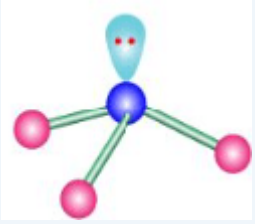
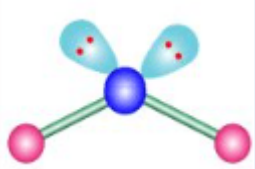
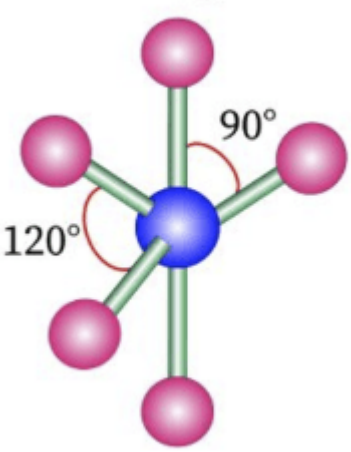
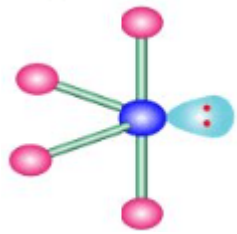
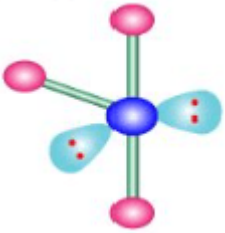
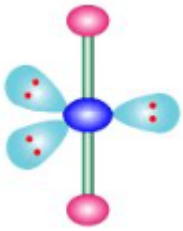
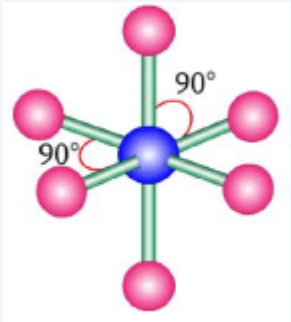
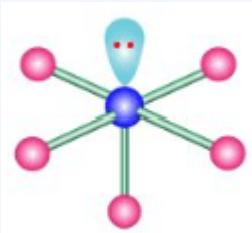
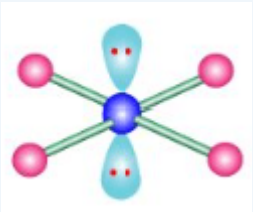
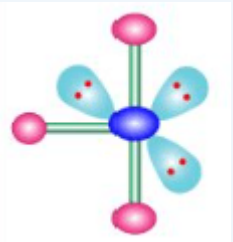
- the number of electron domains, and
- the number of lone pairs

to determine the **molecular geometry**.

Unlike electron geometry, molecular geometry describes only the positions of the **atoms**. Lone pairs influence the shape but are not included when naming the molecular geometry. Table 5.2B summarizes the common molecular geometries. To use this table, slide down the lefthand column to identify the total number of electron domains on your central atom, and then slide across the top row to identify number of lone pairs of electrons on your central atom. Where that row and column meet will identify the appropriate molecular geometry for your central atom.

Table 5.2B: Electron Domains and Lone Pairs of Electrons are Used to Determine Molecular Geometry

	Number of non-bonding electron pairs (or lone pairs) on a central atom			
Total Number of Electron Domains	0	1	2	3
2	Linear 			
3	Trigonal Planar 	Bent 		

Number of non-bonding electron pairs (or lone pairs) on a central atom				
4	Tetrahedral 	Trigonal Pyramidal 	Bent 	
5	Trigonal Bipyramidal 	See-Saw 	T-Shaped 	Linear 
6	Octahedral 	Square Pyramidal 	Square Planar 	T-shaped 

Key Idea

- To determine the Molecular Geometry, follow up with a second question : How many **lone pairs** are attached to the central atom?

Electron Geometry versus Molecular Geometry

One of the most common mistakes students make is confusing **electron geometry** with **molecular geometry**.

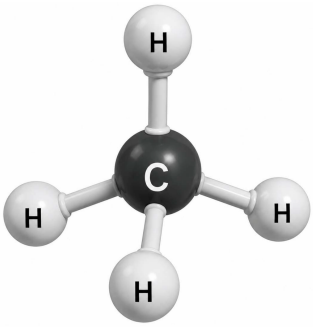
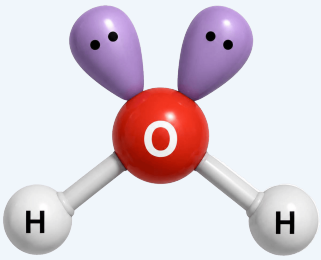
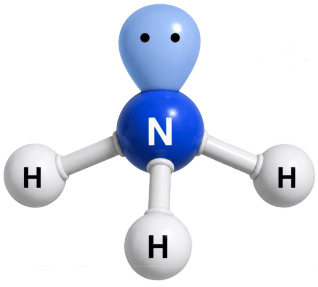
Remember:

Electron geometry includes **all electron domains.**

Molecular geometry includes **only the bonded atoms.**

The difference is illustrated below.

Table 5.2C: Examples of Determining Electronic and Molecular Geometries

Molecule	Visual of Structure	Number of Electron Domains	Number of Lone Pairs	Electron Geometry
CH_4		4	4	Tetrahedral
H_2O		4	2	Tetrahedral
NH_3		4	1	Tetrahedral

Notice that all three molecules contain **four electron domains**. The only difference is the number of lone pairs.

Chemist's Shortcut: AXE Notation

Once you become comfortable predicting molecular geometry, you may find it useful to use **AXE notation** as a shorthand.

- **A** = central atom
- **X** = bonded atoms
- **E** = lone pairs

Table 5.2D: AXE Notation

Molecule	AXE Notation
CO_2	AX_2
BF_3	AX_3
CH_4	AX_4
NH_3	AX_3E
H_2O	AX_2E_2

Notice that the AXE notation simply summarizes the information you already determined using the five-step process. It is not a separate method for predicting molecular geometry.

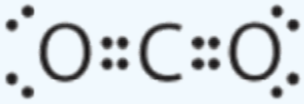
Example 5.2.1

Carbon dioxide is an example of a molecule with **two electron domains** around the central atom. Use the five-step strategy to determine its molecular geometry.

Solution

Step 1: Draw the Lewis Structure

- The Lewis structure for CO_2 is shown below. The central atom, carbon, contributes four valence electrons, and each oxygen atom contributes six. The Lewis electron structure is:



Step 2: Count the Electron Domains

- Around the central carbon atom there are:
  - one carbon–oxygen double bond
  - one carbon–oxygen double bond
- Although each bond is a double bond, each counts as one electron domain.
- Total electron domains = 2

Step 3: Determine the Electron Geometry

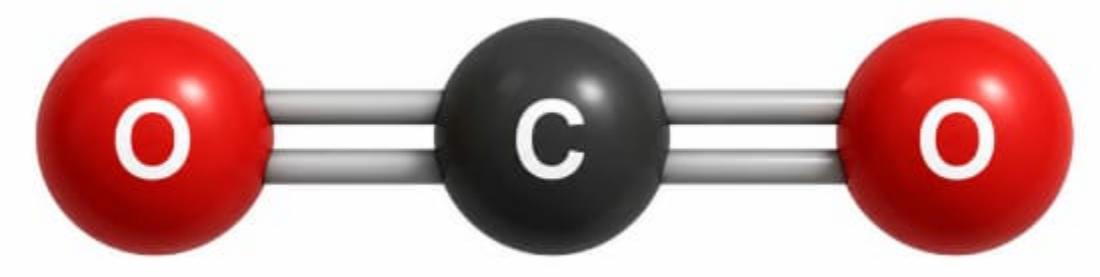
- From Table 5.2A, a central atom with two electron domains has a linear electron geometry.

Step 4: Count the Lone Pairs

- The central carbon atom has no lone pairs.

Step 5: Determine the Molecular Geometry

- Because all electron domains are bonding domains, the molecular geometry is the same as the electron geometry.
- Molecular geometry: Linear



- Carbon dioxide has an ideal bond angle of **180°**.

Key Idea

- Lone pairs on the oxygen atoms do **not** affect the molecular geometry because VSEPR theory considers only the electron domains surrounding the **central atom**.

Exercise 5.2.1

What is the molecular geometry of Boron Trichloride?

Answer available at the end of this section.

Key Idea

- Boron in BCl_3 is an **exception** to the octet rule. It is stable with only six electrons surrounding the central atom.

Exercise 5.2.3

What is the molecular geometry of phosphorous pentachloride?

Answer available at the end of this section.

Key Idea

- Phosphorus is another exception to the octet rule. In PCl_5, the phosphorus atom is surrounded by **10 electrons**, forming an **expanded octet**. Thus, phosphorous can share a total of 3 or 5 bonds
- Sulfur can also support an expanded octet. The normal octet bonding has a total of 2 bonds. Expanded potential for 4 or 6 bonds is also possible.

Molecules Without a Single Central Atom

The five-step VSEPR strategy works best for molecules and polyatomic ions that contain **one central atom**. However, many important molecules—including biological molecules, polymers, and many organic compounds—contain **multiple central atoms** connected together.

Fortunately, VSEPR theory can still be applied to these larger molecules. Instead of analyzing the entire molecule at once, each central atom is considered separately. The local arrangement of atoms around each central atom can be predicted using the same five-step strategy introduced in this chapter.

For example, in ethanol (CH_3CH_2OH), both carbon atoms can be analyzed individually. Each carbon atom has four electron domains, giving each a **tetrahedral electron geometry**. The oxygen atom also has four electron domains but contains two lone pairs, resulting in a **bent molecular geometry** around the oxygen atom.

As molecules become larger and more complex, however, the overall three-dimensional shape depends on more than just the local geometry around each atom. Different parts of the molecule may rotate around single bonds or interact with one another through attractive and repulsive forces. These interactions can change the overall shape of the molecule in ways that VSEPR theory alone cannot predict.

For this reason, VSEPR theory is best viewed as a tool for predicting the **local geometry** around individual atoms. More advanced experimental techniques, such as X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, or computational methods are often used to determine the complete three-dimensional structures of large molecules.

Looking Ahead

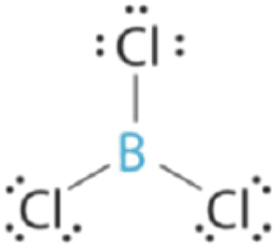
In the next section, we'll build on what you've learned in this chapter by using molecular geometry to determine whether a molecule is **polar or nonpolar**. We'll see that knowing the shape of a molecule is the key to understanding how molecules interact with one another and why substances have different physical properties.

Answers

Exercise 5.2.1

Step 1: Draw the Lewis Structure

- The Lewis structure for BCl_3 is shown below. The central atom, boron, contributes three valence electrons, and each chlorine atom contributes seven valence electrons. The Lewis electron structure is:



Step 2: Count the Electron Domains

- Around the central boron atom there are
  - three boron–chlorine single bonds

Step 3: Determine the Electron Geometry

- According to Table 5.2A, three electron domains produce a trigonal planar electron geometry.

Step 4: Count the Lone Pairs

- The central boron atom has no lone pairs.

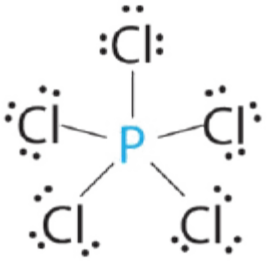
Step 5: Determine the Molecular Geometry

- Because all three electron domains are bonding domains, the molecular geometry is also trigonal planar.
- The ideal bond angle is 120°.
- Each single bond counts as one electron domain.
  - Total electron domains = 3

Exercise 5.2.3

Step 1: Draw the Lewis Structure

- The Lewis structure for PCl_5 is shown below. Phosphorus has five valence electrons, and can form an expanded bonding formation that exceeds the octet rule. Thus, it can form single bonds to each of the five chlorine atoms. Note that each chlorine has seven valence electrons. So, the Lewis electron structure of PCl5 is:



Step 2: Count the Electron Domains

- Around the phosphorus atom there are five phosphorus–chlorine single bonds three equatorial positions, separated by 120° two axial positions, located 90° above and below the equatorial plane

Step 3: Determine the Electron Geometry

- According to Table 5.2A, five electron domains adopt a trigonal bipyramidal electron geometry.

Step 4: Count the Lone Pairs

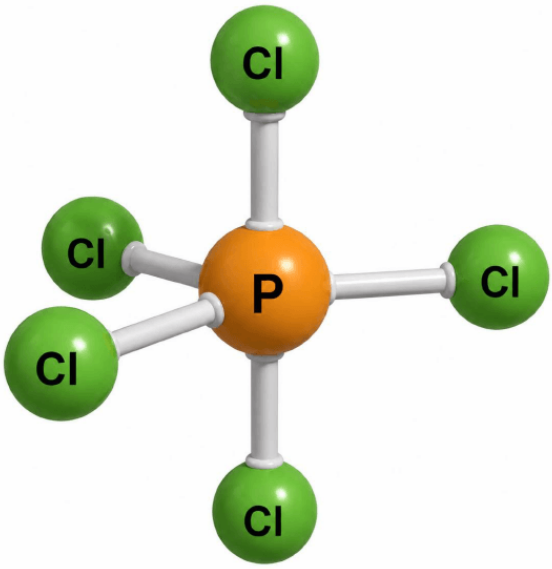
- The phosphorus atom has no lone pairs.

Step 5: Determine the Molecular Geometry

- Because all five electron domains are bonding domains, the molecular geometry is also **trigonal bipyramidal.**

This geometry contains:

- Each bond counts as one electron domain.
- Total electron domains = 5



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5.3: Molecular Polarity

Learning Objectives

After completing this section, you should be able to:

- Distinguish between **bond polarity** and **molecular polarity**.
- Draw bond dipoles for polar covalent bonds.
- Predict whether a molecule is **polar** or **nonpolar** based on its molecular geometry.
- Explain how molecular shape affects the overall distribution of charge.

5.3.1 From Bond Polarity to Molecular Polarity

In Chapter 4, we learned that some covalent bonds are **polar** because electrons are shared unequally between atoms with different electronegativities. The more electronegative atom attracts the shared electrons more strongly, creating a partial negative charge (δ–), while the less electronegative atom develops a partial positive charge (δ+).

However, knowing that a bond is polar does **not** necessarily tell us whether the **entire molecule** is polar.

To determine molecular polarity, we must consider **two factors**:

1. Are the individual bonds polar?
2. How are those bonds arranged in three-dimensional space?

Now that we can predict molecular geometry using VSEPR theory, we have all of the information needed to determine whether an entire molecule is polar or nonpolar.

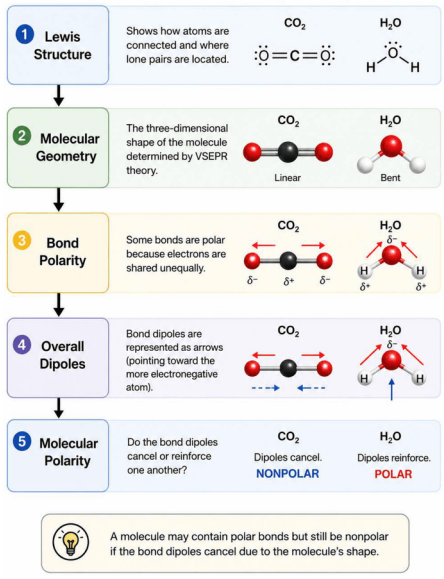


Figure 5.3.1**: Predicting Molecular Polarity from Bond Polarity and Molecular Geometry.** Flowchart illustrating why bond polarity alone does not determine molecular polarity. The diagram presents a five-step process for predicting molecular polarity using carbon dioxide (CO_2) and water (H_2O) as examples. Step 1 begins with drawing the Lewis structure. Step 2 determines the molecular geometry, showing that CO_2 is linear while H_2O is bent. Step 3 identifies the polar bonds in each molecule, with bond dipole arrows pointing toward the more electronegative oxygen atoms.

Step 4 combines the individual bond dipoles to determine the overall molecular dipole. In CO_2, the two bond dipoles are equal in magnitude and point in opposite directions, so they cancel. In H_2O, the bent geometry causes the bond dipoles to reinforce one another, producing a net dipole. Step 5 concludes that CO_2 is a nonpolar molecule, while H_2O is a polar molecule. The figure emphasizes that molecular polarity depends on both bond polarity and molecular geometry.

Key Point: Predicting molecular polarity requires both bond polarity and molecular geometry.

5.3.2 Bond Dipoles

A **bond dipole** forms whenever two atoms with different electronegativities share electrons unequally.

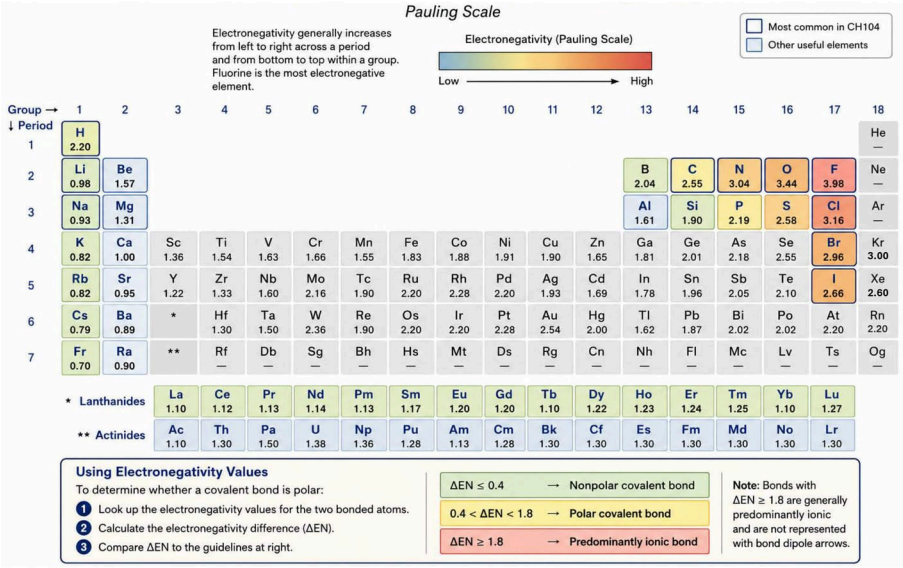
Because the electrons spend more time near the more electronegative atom, one end of the bond becomes slightly negative (δ–) while the other becomes slightly positive (δ+).

Bond dipoles are represented by an arrow that points **toward the more electronegative atom**. The small cross (+) at the tail of the arrow marks the partially positive end of the bond.

Nonpolar covalent bonds do not have bond dipoles because the electrons are shared equally.

As discussed in **Chapter 4**, to determine if a bond is polar or nonpolar, we will use the following Electronegativity Difference (ΔEN) guidelines throughout this textbook:

- ΔEN ≤ 0.4 → nonpolar covalent bond
- 0.4 < ΔEN < 1.8 → polar covalent bond
- ΔEN ≥ 1.8 → predominantly ionic bond



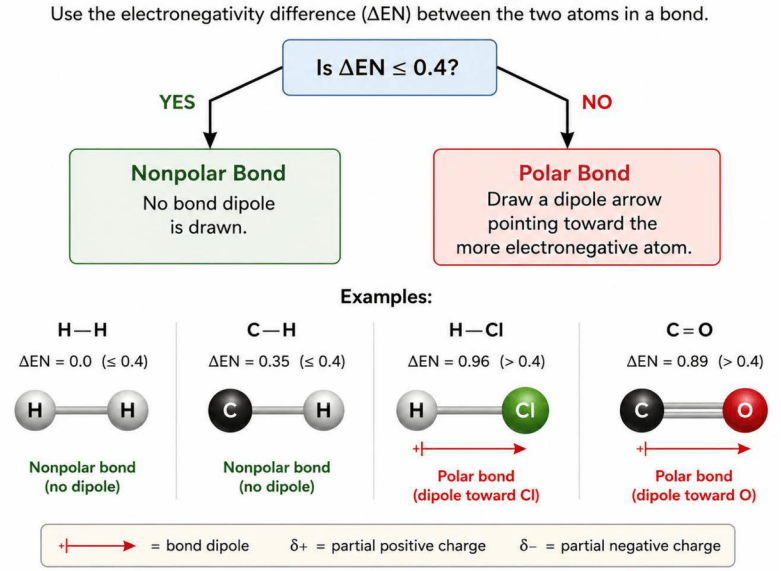


Figure 5.3.2:Determining Whether a Covalent Bond Is Polar. Upper Panel: Periodic table displaying elemental electronegativity values based on the Pauling scale. Each element is labeled with its chemical symbol and electronegativity value and is color-coded to indicate relative electronegativity, with lighter colors representing lower values and darker orange-red colors representing higher values. Electronegativity generally increases from left to right across a period and from bottom to top within a group, with fluorine (3.98) having the highest electronegativity. The table includes the lanthanide and actinide series below the main periodic table. A reference box explains how to use electronegativity values to determine bond polarity by calculating the electronegativity difference (ΔEN) between two bonded atoms. The guidelines indicate that bonds with ΔEN ≤ 0.4 are classified as nonpolar covalent, bonds with 0.4 < ΔEN < 1.8 are classified as polar covalent, and bonds with ΔEN ≥ 1.8 are generally classified as predominantly ionic. A note reminds readers that predominantly ionic bonds are not represented using bond dipole arrows in this chapter. **Lower Panel:** Decision tree for determining whether a covalent bond is polar and whether a bond dipole should be drawn. The process begins by calculating the electronegativity difference (ΔEN) between the two bonded atoms. If ΔEN is **0.4 or less**, the bond is classified as a **nonpolar covalent bond**, and no bond dipole is drawn. If ΔEN is **greater than 0.4**, the bond is classified as a **polar covalent bond**, and a bond dipole arrow is drawn pointing toward the more electronegative atom. Four examples are provided: H–H (ΔEN = 0.0) and C–H (ΔEN = 0.35) are classified as nonpolar covalent bonds with no bond dipoles. H–Cl (ΔEN = 0.96) and C=O (ΔEN = 0.89) are classified as polar covalent bonds, with bond dipole arrows pointing toward chlorine and oxygen, respectively. A legend identifies the bond dipole arrow and the symbols δ⊕ and δ⊖ for partial positive and partial negative charges.

Note: This figure is used to determine **bond dipoles in covalent bonds**. Bonds with an electronegativity difference greater than about **1.8** are generally classified as **ionic** and are not represented using bond dipole arrows.

5.2.3 Five-Step Strategy for Determining Molecular Polarity

Once the molecular geometry has been determined, predicting molecular polarity becomes a straightforward process.

Step 1

Draw the Lewis structure.

Step 2

Determine the molecular geometry using VSEPR theory.

Step 3

Identify the polar bonds.

- Only bonds between atoms with electronegativity differences greater than 0.4 have bond dipoles.

Step 4

Draw the bond dipoles.

- Each dipole points toward the more electronegative atom.

Step 5

Determine whether the bond dipoles cancel.

- If the dipoles cancel completely, the molecule is **nonpolar**.
- If they do not cancel, the molecule is **polar**.

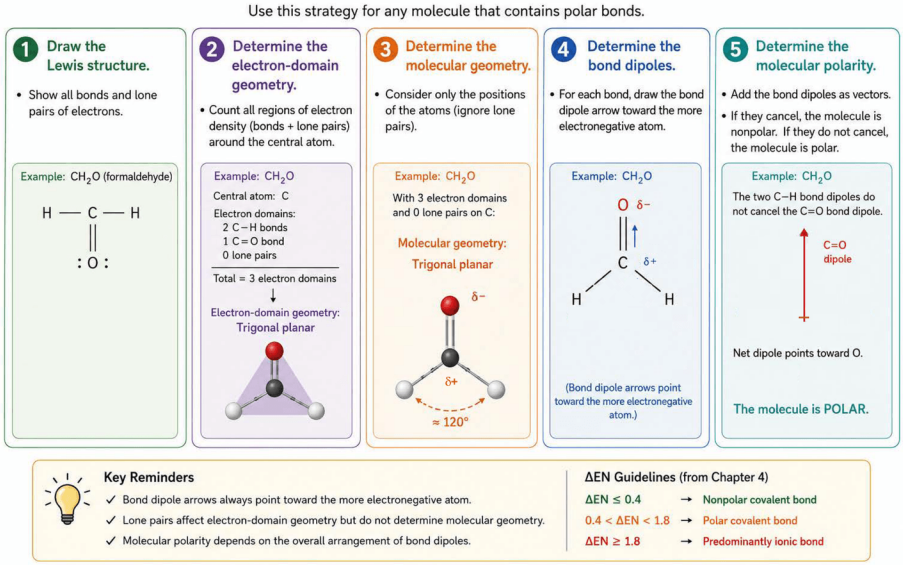


Figure 5.3.3: Five-Step Strategy for Determining Molecular Polarity. Infographic illustrating a five-step strategy for determining molecular polarity using formaldehyde (CH_2O) as an example. Step 1 shows the Lewis structure with carbon as the central atom bonded to two hydrogen atoms by single bonds and to one oxygen atom by a double bond. Step 2 counts the electron domains around the central carbon atom, identifying three bonding domains and no lone pairs, resulting in three electron domains and a trigonal planar electron geometry. Step 3 determines the molecular geometry as trigonal planar with bond angles of approximately 120°. Step 4 identifies the polar bonds and draws bond dipole arrows pointing toward the more electronegative oxygen atom; the carbon–hydrogen bonds are treated as nonpolar and do not have bond dipoles. Step 5 evaluates the overall molecular polarity by combining the bond dipoles. Because the carbon–oxygen bond dipole is not canceled by the surrounding bonds, the molecule has a net dipole directed toward the oxygen atom and is classified as polar. A reminder box notes that bond dipole arrows always point toward the more electronegative atom, lone pairs affect molecular geometry, and molecular polarity depends on the overall arrangement of bond dipoles. A summary box reviews the electronegativity difference guidelines used in the textbook: $\Delta EN \leq 0.4$ indicates a nonpolar covalent bond, $0.4 < \Delta EN < 1.8$ indicates a polar covalent bond, and $\Delta EN \geq 1.8$ indicates a predominantly ionic bond.

5.2.4 Molecular Geometry Determines Molecular Polarity

The three-dimensional arrangement of atoms determines whether the bond dipoles cancel or reinforce one another.

Think of each bond dipole as a small arrow pulling in a particular direction.

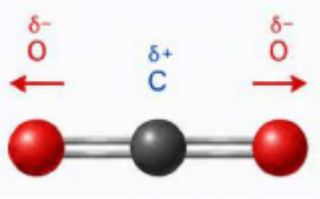
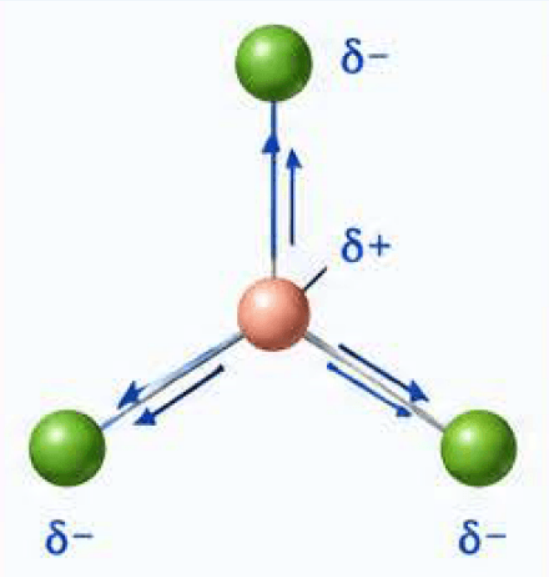
- If the arrows pull equally in opposite directions, they cancel and **the overall molecule is nonpolar**, even if it contains polar bonds within the molecule.
- If one direction is favored, the molecule has a **net dipole** and is polar.

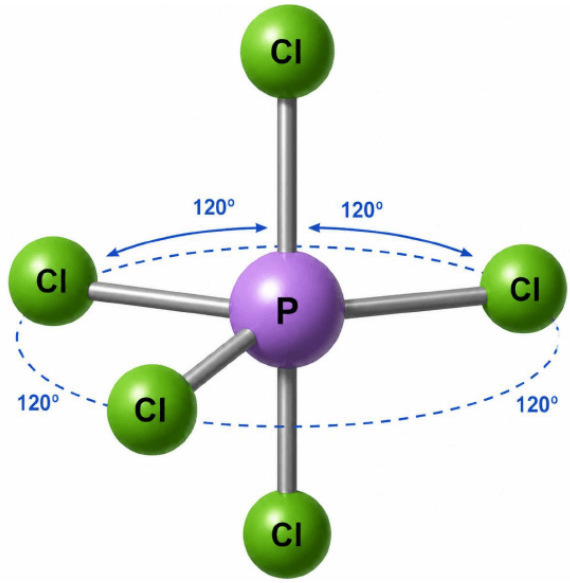
Unlike individual bond dipoles, the **molecular dipole** describes the polarity of the molecule as a whole.

5.2.5 Symmetry Matters

Many molecules can be classified quickly by examining their symmetry. Symmetrical molecules are often nonpolar.

Table 5.3A: Determining Symmetry in Molecules

Chemical Formula	Molecular Geometry	Overall Polarity: Polar? Nonpolar?
CO_2	Linear 	**Nonpolar** - the two carbon-oxygen dipoles are equal in magnitude and opposite in direction, so they cancel.
BCl_3	Trigonal Planar 	**Nonpolar** - the three dipoles are equal in magnitude and each at 120^o from one another. This symmetry causes the forces to cancel out

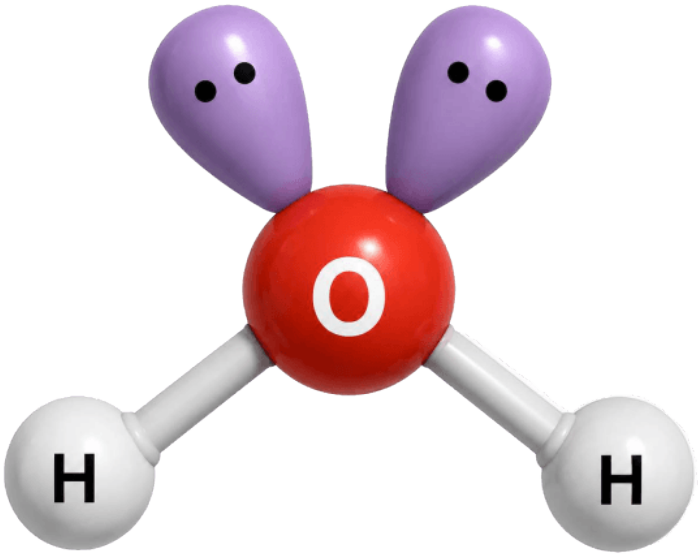
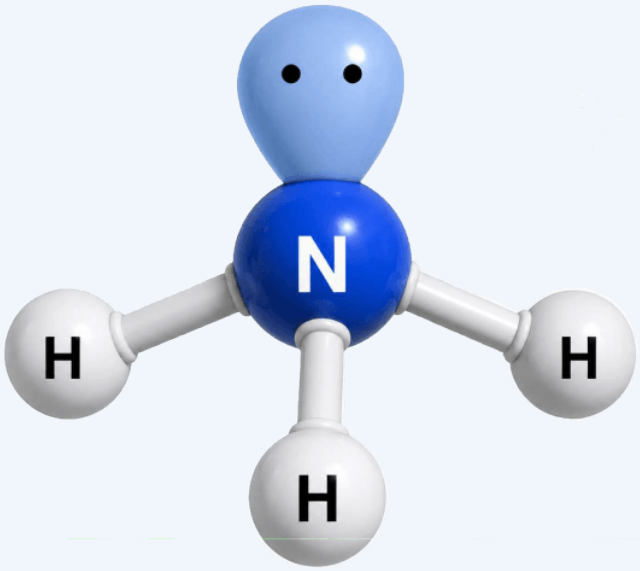
Chemical Formula	Molecular Geometry	Overall Polarity: Polar? Nonpolar?
PCl_5	Trigonal Bipyramidal 	**Nonpolar** - the two axial dipoles are equal in magnitude and are in opposite direction (180^o apart). The three equatorial bond dipoles are also the same magnitude and are at 120^o symmetry. Thus, they also cancel out.

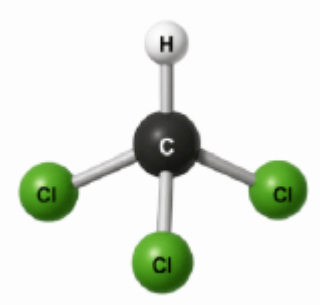
Although these molecules contain polar bonds, their **symmetrical arrangements** cause the **bond dipoles to cancel** completely.

Asymmetrical molecules are often polar. This commonly occurs when:

- lone pairs create an asymmetric shape, or
- the atoms surrounding the central atom are different.

Table 5.3B: Analysis of Assymmetric Molecules

Chemical Formula	Molecular Geometry	Overall Polarity: Polar? Nonpolar?
H_2O	Bent 	**Polar -** The two **O–H bonds** are polar because oxygen is more electronegative than hydrogen. The oxygen atom carries a partial negative charge (δ–), while each hydrogen atom carries a partial positive charge (δ+). The two O–H bond dipoles are equal in magnitude, but because water has a **bent** molecular geometry, they are not arranged directly opposite one another and therefore do not cancel. The two lone pairs of electrons on the oxygen atom contribute to the bent shape of the molecule. As a result, the bond dipoles combine to produce a **net molecular dipole directed toward the oxygen atom**. Consequently, **H_2O is a polar molecule.**
NH_3	Trigonal Pyramidal 	Polar - The three **N–H bonds** are polar because nitrogen is more electronegative than hydrogen. The nitrogen atom carries a partial negative charge (δ–), while each hydrogen atom carries a partial positive charge (δ+). The three N–H bond dipoles are equal in magnitude, but because ammonia has a **trigonal pyramidal** molecular geometry, they are not arranged directly opposite one another and therefore do not cancel. The lone pair of electrons on the nitrogen atom contributes to the asymmetrical shape of the molecule. As a result, the bond dipoles combine to produce a **net molecular dipole directed toward the nitrogen atom**. Consequently, **NH_3 is a polar molecule.**

Chemical Formula	Molecular Geometry	Overall Polarity: Polar? Nonpolar?
$CHCl_3$	Tetrahedral 	**Polar** - The three **C–Cl bonds** are polar because chlorine is more electronegative than carbon. Each chlorine atom carries a partial negative charge (δ–), while the carbon atom carries a corresponding partial positive charge (δ+). The three C–Cl bond dipoles are equal in magnitude. The **C–H bond** is considered **nonpolar** in this textbook because the electronegativity difference between carbon and hydrogen is very small (ΔEN = 0.35). As a result, there is no bond dipole to oppose the three C–Cl bond dipoles. Therefore, the bond dipoles do not cancel, producing a **net molecular dipole directed toward the chlorine atoms**. Consequently, **$CHCl_3$ is a polar molecule.**

In these molecules, the bond dipoles do not cancel, producing a net molecular dipole.

Chemistry in Everyday Life

The polarity of molecules has a tremendous influence on their physical properties. Polar molecules are generally more soluble in water and often have higher boiling points because they experience stronger intermolecular attractions. Nonpolar molecules tend to dissolve in nonpolar substances such as oils and fats.

In the next section, we'll explore how molecular polarity determines the **intermolecular forces** between molecules and how those forces affect melting points, boiling points, solubility, and many other physical properties.

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5.4: Intermolecular Forces and Electrostatic Attractions

Learning Objectives

After completing this section, you should be able to:

- Distinguish between **intramolecular bonds** and **electrostatic attractions between particles**.
- Identify the major types of electrostatic attractions found in introductory chemistry.
- Predict the dominant electrostatic attraction present in a substance.
- Compare the relative strengths of different electrostatic attractions.
- Explain how electrostatic attractions influence physical properties such as melting point, boiling point, solubility, and viscosity.

5.4.1 From Molecules to Materials

So far in this chapter, we have focused on the structure of **individual molecules**. We first learned how to determine molecular geometry using VSEPR theory and then used molecular geometry to predict whether a molecule is polar or nonpolar.

But molecules rarely exist in isolation. Instead, they interact with neighboring particles through a variety of attractive forces. These attractions help explain why some substances are gases at room temperature, while others are liquids or solids. They also influence many familiar physical properties, including melting point, boiling point, viscosity, surface tension, and solubility.

All of these attractions arise from the same fundamental principle:

Opposite charges attract, and like charges repel.

The difference between the various types of attractions lies in **what kinds of particles are interacting** and **whether the charges are full charges or partial charges**.

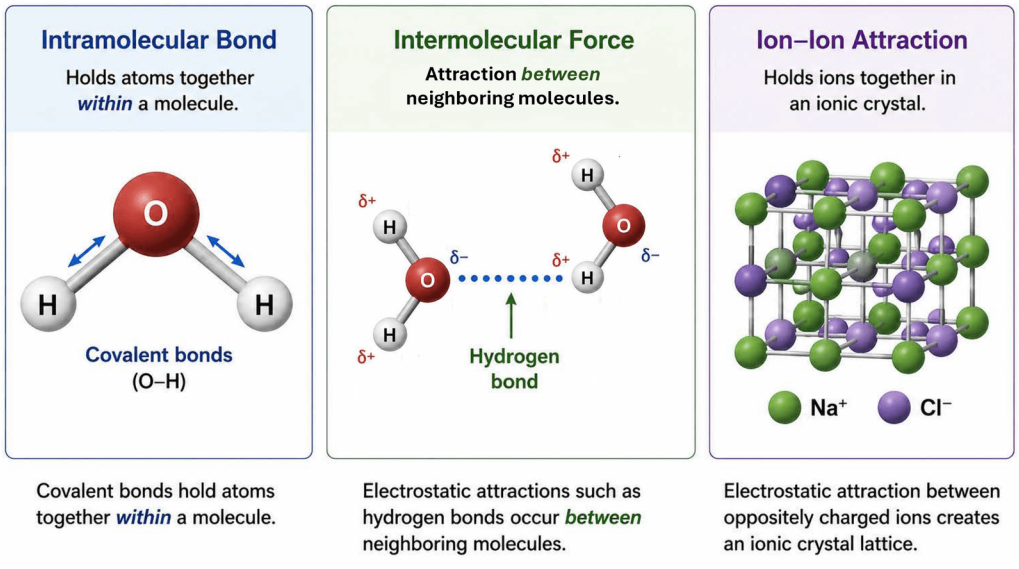


Figure 5.4.1**: Chemical Bonds and Electrostatic Attractions.** Three-panel diagram comparing the types of attractive forces discussed in this chapter. The left panel illustrates an **intramolecular covalent bond** within a single water molecule, showing oxygen covalently bonded to two hydrogen atoms. The panel explains that covalent bonds hold atoms together **within** a molecule. The center panel shows **two neighboring water molecules** connected by a dotted

hydrogen bond between the partially negative oxygen atom of one molecule and the partially positive hydrogen atom of the other. The panel explains that intermolecular forces are electrostatic attractions **between** neighboring molecules. The right panel shows a three-dimensional sodium chloride crystal lattice composed of alternating sodium ions (Na^+) and chloride ions (Cl^-). The panel explains that ion-ion attractions are electrostatic attractions between oppositely charged ions that hold ionic compounds together in an ionic crystal lattice. Together, the three panels distinguish between covalent bonds within molecules, intermolecular forces between molecules, and electrostatic attractions between ions in ionic solids.\

Covalent bonds hold atoms together **within** a molecule and are therefore called **intramolecular bonds**. Electrostatic attractions occur **between** neighboring particles. These attractions include intermolecular forces between molecules, ion-ion attractions between oppositely charged ions, and ion-dipole attractions between ions and polar molecules.

Although electrostatic attractions are generally weaker than covalent bonds, they have a profound effect on the physical properties of matter.

5.4.2 Types of Electrostatic Attractions

Electrostatic attractions can be grouped according to the types of particles involved.

1. Attractions Involving Ions

These attractions occur between positively charged cations and negatively charged anions.

Ion-ion attractions

- Occur between cations and anions.
- Hold ionic compounds together in a repeating three-dimensional crystal lattice.
- Generally represent the strongest type of electrostatic attractions.

Ion-ion attractions occur between **positively charged cations** and **negatively charged anions**. Because ions carry **full positive and negative charges**, the electrostatic attraction between them is much stronger than the attractions that occur between neutral molecules.

Unlike covalent compounds, ionic compounds do **not** exist as individual molecules. Instead, each ion is surrounded by multiple ions of the opposite charge, forming a repeating three-dimensional arrangement called an **ionic crystal lattice** (Figure 5.xx). The crystal lattice extends throughout the entire solid and is responsible for many of the characteristic properties of ionic compounds.

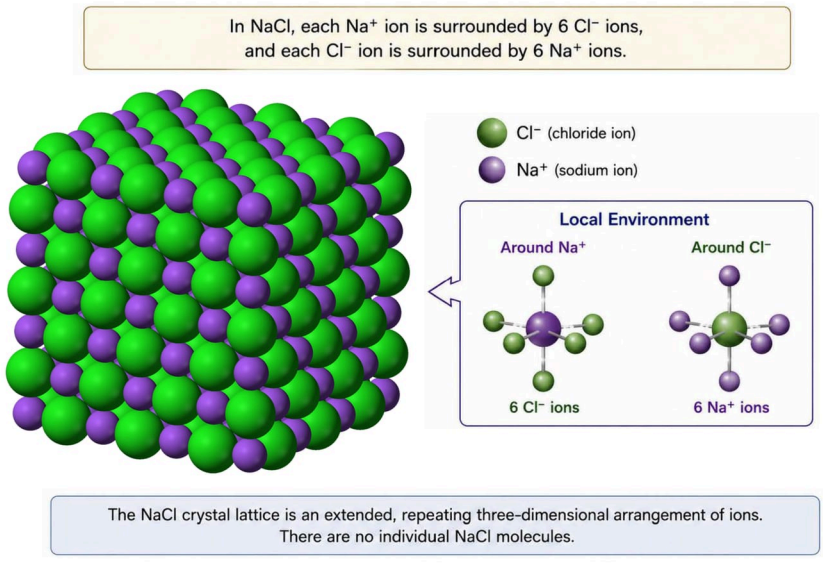


Figure 5.4.2: Sodium Chloride Crystal Lattice. Three-dimensional illustration of the sodium chloride crystal lattice. Purple spheres represent sodium ions (Na^+) and green spheres represent chloride ions (Cl^-) arranged in an alternating, repeating pattern. An inset shows the local coordination environment: each sodium ion is surrounded by six chloride ions, and each chloride ion is surrounded by six sodium ions. The figure emphasizes that solid NaCl is an extended crystal lattice rather than individual NaCl molecules. The formula **NaCl** represents the simplest whole-number ratio of ions in the crystal (a **formula unit**), not an individual molecule.

In sodium chloride (NaCl), each sodium ion (Na^+) is surrounded by chloride ions (Cl^-), and each chloride ion is surrounded by sodium ions. This repeating arrangement maximizes the attractive forces between oppositely charged ions while minimizing repulsions between ions of the same charge. The chemical formula of an ionic compound, such as **NaCl**, represents the **simplest whole-number ratio** of ions present in the crystal and is called a **formula unit**. A formula unit does not represent a single, isolated particle but rather the repeating ratio of ions throughout the crystal lattice.

Because ion-ion attractions are very strong, ionic compounds typically have:

- **High melting points**
- **High boiling points**
- **Hard, crystalline structures**
- **Poor electrical conductivity as solids**
- **Good electrical conductivity when molten or dissolved in water**, because the ions are free to move.

Table 5.4A: The Utility of Ionic Compounds

Ionic Compound	Cation	Anion	Common Use
NaCl	Na^+	Cl^-	Table salt
MgO	Mg^{2+}	O^{2-}	Refractory ceramics, antacids
CaF_2	Ca^{2+}	F^-	Mineral fluorite; source of fluoride
KBr	K^+	Br^-	Laboratory reagent
$NaNO_3$	Na^+	NO_3^-	Fertilizer

Although these compounds contain different ions, they are all held together by **ion-ion electrostatic attractions**.

Key Term: Formula Unit

A **formula unit** is the simplest whole-number ratio of cations and anions in an ionic compound. Unlike a molecular formula, a formula unit does **not** represent an individual molecule but the repeating composition of the ionic crystal lattice.

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2. Attractions Involving Molecules (Intermolecular Forces)

Unlike ion-ion attractions, **intermolecular forces** are electrostatic attractions that occur between **neighboring neutral or uncharged molecules**. These attractions arise from regions of partial positive and negative charge within molecules. Although intermolecular forces are generally weaker than ion-ion attractions, they have a major influence on the physical properties of substances.

The strength of the intermolecular forces between molecules affects many observable properties, including:

- Melting point
- Boiling point
- Viscosity
- Surface tension
- Vapor pressure
- Solubility

In general, **stronger intermolecular forces require more energy to separate neighboring molecules**. As a result, substances with stronger intermolecular forces generally have higher melting points and boiling points than substances with weaker intermolecular forces.

For example, liquids boil when their molecules absorb enough thermal energy to overcome the attractive forces holding neighboring molecules together. Likewise, solids melt when their particles gain enough thermal energy to overcome the attractive forces that hold them in fixed positions.

There are **three major types of intermolecular forces**:

1. Dipole-dipole interactions
2. Hydrogen bonding
3. London dispersion forces

As you read about each type of intermolecular force, remember that **more than one intermolecular force may be present in a substance**. Chemists often identify all of the intermolecular forces that are present and then determine which interaction has the greatest influence on the substance's physical properties.

Dipole-Dipole Interactions

In the previous section, we learned that some molecules are **polar** because they have an unequal distribution of electrons and their bond dipoles do not cancel. Polar molecules possess **permanent dipoles**, meaning one end of the molecule is partially positive (δ⊕) while the other end is partially negative (δ⊖).

When the partially positive end of one polar molecule is adjacent to the partially negative end of a neighboring molecule, an **attractive dipole-dipole interaction** occurs. If like partial charges are adjacent, a **repulsive electrostatic interaction** results (Figure 5.xx).

This behavior is especially apparent in **liquids**, where molecules are constantly moving, rotating, and colliding with one another. As neighboring molecules continually change orientation, they experience both attractive and repulsive interactions. Because attractive orientations are lower in energy, they are favored overall, allowing dipole-dipole interactions to help hold the liquid together.

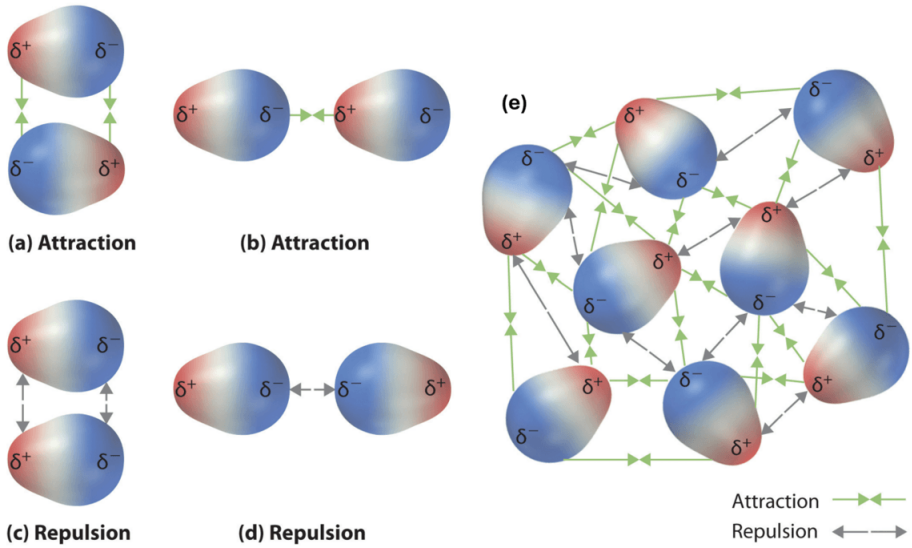


Figure 5.4.3**:Molecular Orientation Determines Dipole-Dipole Interactions (a, b)** When the partially positive end (δ⊕) of one polar molecule is adjacent to the partially negative end (δ⊖) of a neighboring molecule, an **attractive dipole-dipole interaction** occurs. **(c, d)** When like partial charges (δ⊕–δ⊕ or δ⊖–δ⊖) are adjacent, **repulsive electrostatic interactions** occur. **(e)** In a liquid, molecules are in constant motion, continuously rotating, translating,

and colliding with one another. As a result, neighboring molecules continually change orientation, experiencing both attractive and repulsive interactions. Because attractive orientations are lower in energy, they are favored overall, allowing dipole-dipole attractions to help hold the liquid together.

Molecular solids behave differently than liquids. In a molecular solid, intermolecular forces hold neighboring molecules in relatively fixed positions within a crystal. Although the molecules continue to vibrate, they generally cannot translate or rotate freely. As a result, favorable molecular orientations are maintained, producing a stable, ordered arrangement. As the solid is heated, thermal energy eventually overcomes these intermolecular forces, allowing the molecules to move more freely and the solid to melt.

One example of a molecule that exhibits dipole-dipole interactions is **formaldehyde (CH_2O)**. Because formaldehyde is a polar molecule, neighboring molecules align so that the partially negative oxygen atom is attracted to the partially positive carbon atom of a nearby molecule.

Dipole-dipole interactions occur **only between polar molecules**. The strength of the interaction depends on both the magnitude of the molecular dipole and the orientation of neighboring molecules.

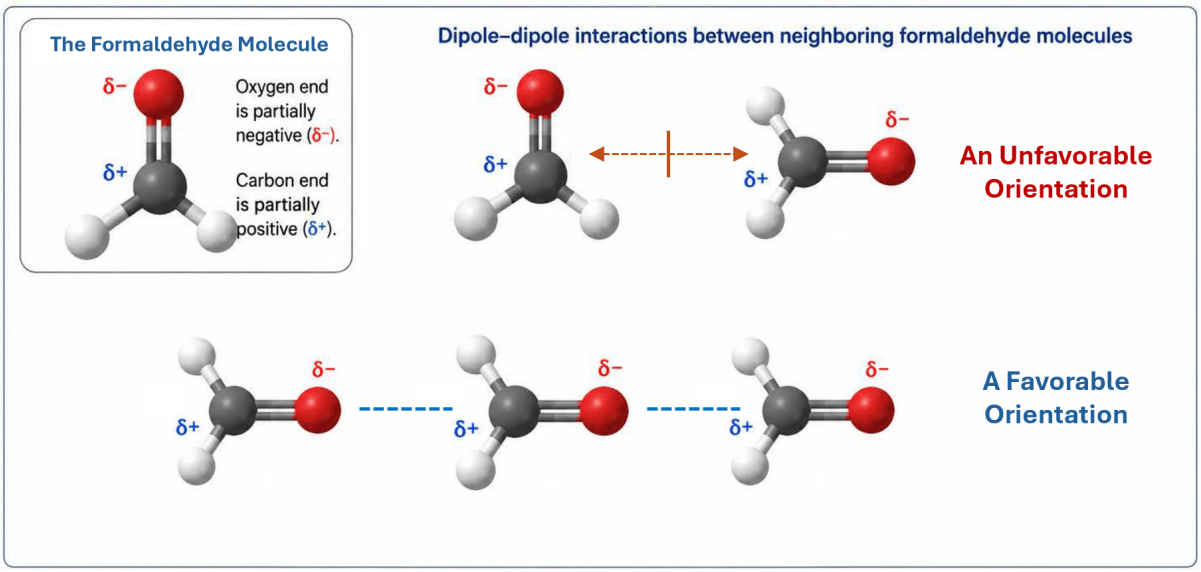


Figure 5.4.4: Dipole-Dipole Interactions Between Formaldehyde Molecules. Diagram illustrating dipole-dipole interactions between formaldehyde (CH_2O) molecules. An inset shows a single formaldehyde molecule with the oxygen atom labeled as partially negative (δ⁻) and the carbon atom labeled as partially positive (δ⁺), indicating the molecule's permanent dipole. The upper example shows an unfavorable orientation in which the partially positive carbon atoms face one another, producing electrostatic repulsion. The lower example shows a favorable orientation in which the partially negative oxygen atom of one molecule is adjacent to the partially positive carbon atom of a neighboring molecule, producing attractive dipole-dipole interactions that can extend throughout the liquid.

Hydrogen Bonding

Hydrogen bonding is a **special type of dipole-dipole interaction** that occurs when a hydrogen atom is covalently bonded to **nitrogen (N), oxygen (O), or fluorine (F).** These highly electronegative atoms pull electron density away from hydrogen, leaving it with a relatively large partial positive charge (δ⁺). A hydrogen bond forms when this partially positive hydrogen is attracted to a **lone pair of electrons on a neighboring nitrogen, oxygen, or fluorine atom** (Figure 5.xx). **Both of these requirements must be present for hydrogen bonding to occur.** Although hydrogen bonds are stronger than ordinary dipole-dipole interactions, they are **still intermolecular forces**, not covalent bonds.

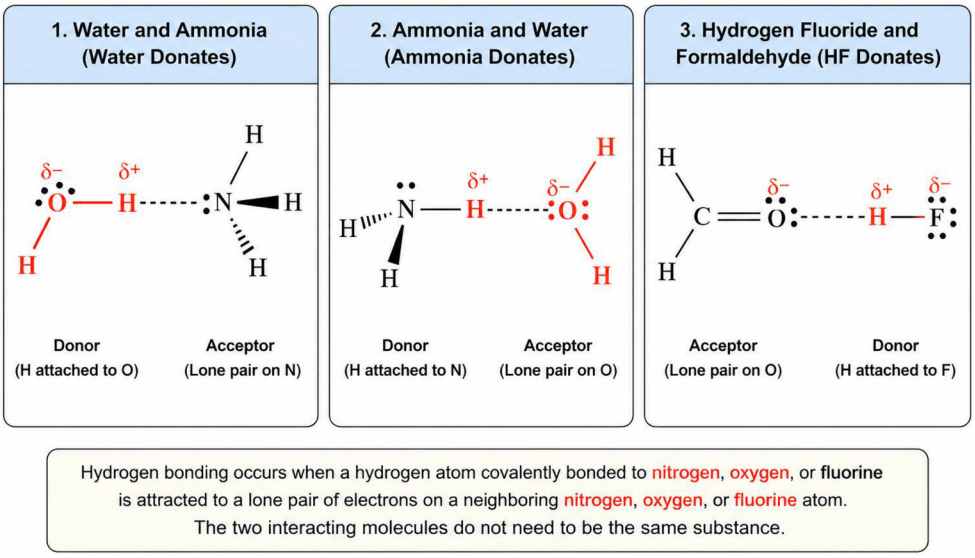


Figure 5.4.5: Requirements for Hydrogen Bonding Between Molecules. Three-panel diagram illustrating the requirements for hydrogen bonding. Hydrogen bonding occurs when a hydrogen atom covalently bonded to **nitrogen (N), oxygen (O), or fluorine (F)** is attracted to a lone pair of electrons on a neighboring nitrogen, oxygen, or fluorine atom. Panel 1 shows a water molecule forming a hydrogen bond to the lone pair on an ammonia molecule. Panel 2 shows an ammonia molecule forming a hydrogen bond to the lone pair on a water molecule. Panel 3 shows hydrogen fluoride forming a hydrogen bond to the carbonyl oxygen of formaldehyde. In each example, the hydrogen bond is represented by a dashed line connecting a hydrogen atom covalently bonded to nitrogen, oxygen, or fluorine with a lone pair of electrons on a neighboring nitrogen, oxygen, or fluorine atom. The figure demonstrates that hydrogen bonding requires both a highly polarized H–N, H–O, or H–F bond and an available lone pair on a neighboring electronegative atom.

Because hydrogen bonding requires a hydrogen atom bonded directly to **N, O, or F**, not all polar molecules are capable of hydrogen bonding. For example, **water (H_2O)**, **ammonia (NH_3)**, and **hydrogen fluoride (HF)** all exhibit hydrogen bonding because they contain hydrogen atoms bonded to highly electronegative atoms. In contrast, **formaldehyde (CH_2O)** is a polar molecule and experiences dipole-dipole interactions, but it cannot form hydrogen bonds with other formaldehyde molecules because its hydrogen atoms are bonded to carbon rather than oxygen (Figure 5.x). However, in mixed solutions, the carbonyl oxygen of formaldehyde can accept hydrogen bonds from neighboring molecules (Figure 5.x.3)

Hydrogen bonding has a profound effect on the physical properties of many substances. Compared with molecules of similar size, substances capable of hydrogen bonding generally have **higher boiling points**, **higher melting points**, and **greater surface tension** because additional energy is required to overcome these stronger intermolecular attractions.

Water (Figure 5.xx) provides one of the best examples of the importance of hydrogen bonding. Each water molecule can form hydrogen bonds with several neighboring water molecules, creating a continuously changing network of intermolecular attractions. Although individual hydrogen bonds continually break and reform as water molecules move, the overall network helps explain many of water's unique properties, including its unusually high boiling point, strong surface tension, and ability to dissolve many ionic and polar substances.

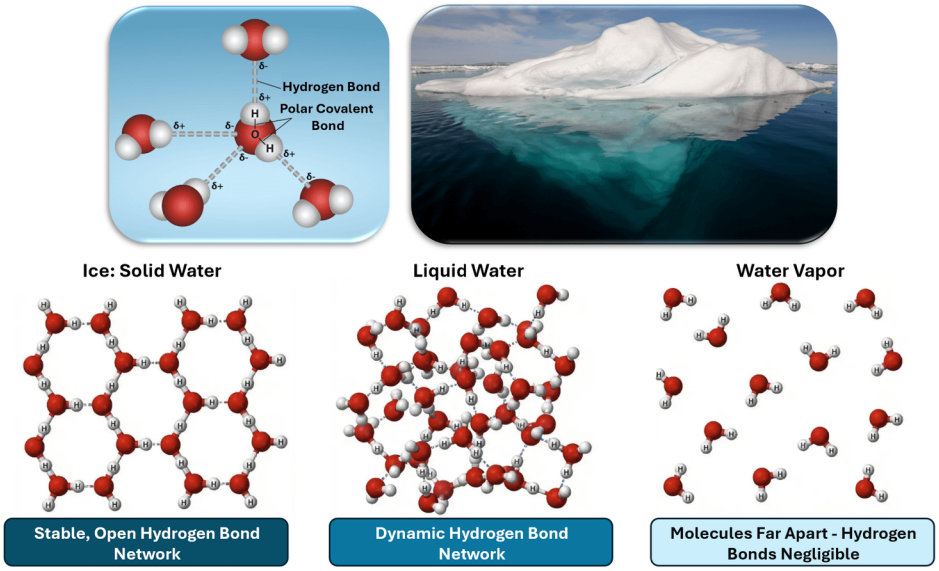


Figure 5.4.6: Hydrogen Bonding Explains the Unique Properties of Water. Composite figure illustrating hydrogen bonding in water across its three phases. The upper left panel shows several water molecules with solid O–H polar covalent bonds within each molecule and dashed hydrogen bonds between neighboring molecules. The upper right panel shows a floating glacier, illustrating that solid ice is less dense than liquid water. The lower panels compare molecular arrangements in the three phases of water. In solid water (ice), hydrogen bonds form a stable, open network that holds molecules in fixed positions. In liquid water, hydrogen bonds continually break and reform as molecules move, creating a dynamic network. In water vapor (gas), molecules are widely separated and hydrogen bonding is negligible.

Photo of Glacial Ice by AWeith - Own work, CC BY-SA 4.0

Chemistry in Action: Why Does Ice Float?

Most substances become **more dense** when they freeze because their particles pack more closely together. Water behaves differently. As water freezes, hydrogen bonds organize the molecules into an open, hexagonal crystal structure that occupies more volume than the liquid. Because the same mass of water now occupies a larger volume, the density decreases, allowing ice to float on liquid water.

This unusual property helps insulate lakes and oceans during the winter, allowing aquatic life to survive beneath the surface.

Connection to Biology

Hydrogen bonding is one of the most important intermolecular forces in living systems. It helps stabilize the three-dimensional structure of proteins, holds the two strands of DNA together, and contributes to the unique properties of water that make life possible

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London Dispersion Forces

Not all molecules are polar. Many molecules have no permanent dipole because their electrons are distributed symmetrically. Yet these substances can still exist as liquids and solids. If no attractive forces existed between their molecules, they would all remain gases under ordinary conditions.

The attraction that allows all atoms and molecules to condense into liquids and solids is called a **London dispersion force**. Unlike dipole-dipole interactions, which arise from permanent molecular dipoles, London dispersion forces arise from **temporary fluctuations in electron density**.

Electrons are constantly moving around the nuclei of atoms. At any instant, the electrons may be distributed slightly unevenly, producing a **temporary (instantaneous) dipole** in an atom or molecule (Figure 5.xx). This temporary dipole can distort the electron cloud of a neighboring atom or molecule, inducing a dipole in that neighbor. The resulting attraction between these temporary, induced dipoles is called a **London dispersion force**.

Video Tutorial on London Dispersion Forces By Bozeman Science.

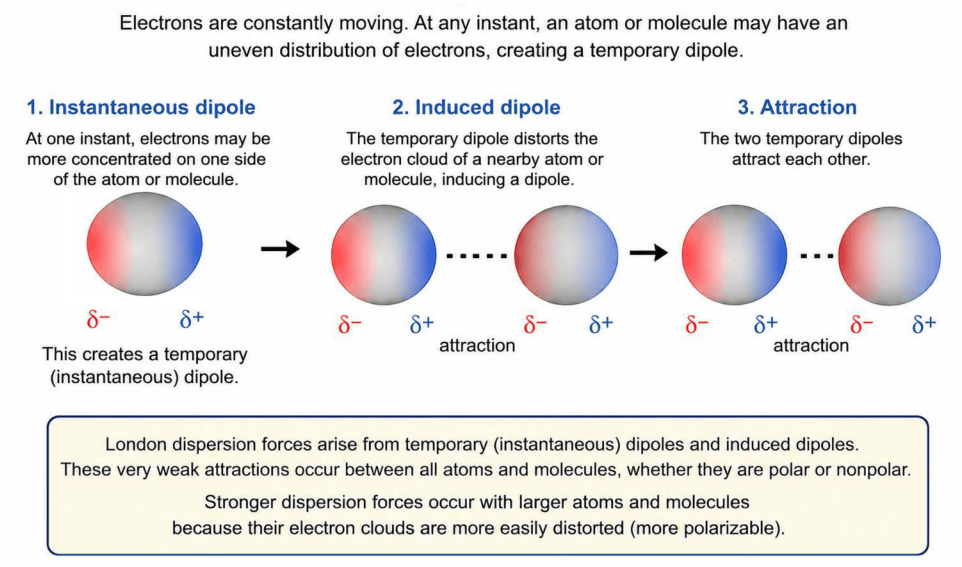


Figure 5.4.7**: Formation of London Dispersion Forces.** Three-panel diagram illustrating the formation of London dispersion forces. Panel 1 shows an atom or molecule developing a temporary (instantaneous) dipole as electrons become unevenly distributed, creating partial negative (δ⁻) and partial positive (δ⁺) regions. Panel 2 shows this temporary dipole inducing an opposite temporary dipole in a neighboring atom or molecule by distorting its electron cloud. Panel 3 shows the two temporary dipoles attracting one another through a London dispersion force. A summary notes that London dispersion forces occur between all atoms and molecules because electrons are always moving, and that these forces become stronger in larger, more polarizable atoms and molecules.

Because electron motion is continuous, these temporary dipoles form and disappear extremely rapidly. Although any single London dispersion force is relatively weak, enormous numbers of these interactions occur simultaneously between neighboring particles. Together, they provide enough attraction to hold many substances together in the liquid and solid phases.

Unlike hydrogen bonding and dipole-dipole interactions, **London dispersion forces occur between all atoms and molecules**, regardless of whether they are polar or nonpolar. Consequently, every molecular substance experiences London dispersion forces. For polar molecules, London dispersion forces act **in addition to** dipole-dipole interactions and hydrogen bonding.

The strength of London dispersion forces depends primarily on **polarizability**, which describes how easily an electron cloud can be distorted. Larger atoms and larger molecules contain more electrons and larger electron clouds, making them more easily polarized. As a result, London dispersion forces generally become stronger as the number of electrons and the size of the molecule increase. As London Dispersion Forces increase due to the increased size of a molecule, the increased binding capacity gives them higher melting and boiling points (Fig 5.xx).

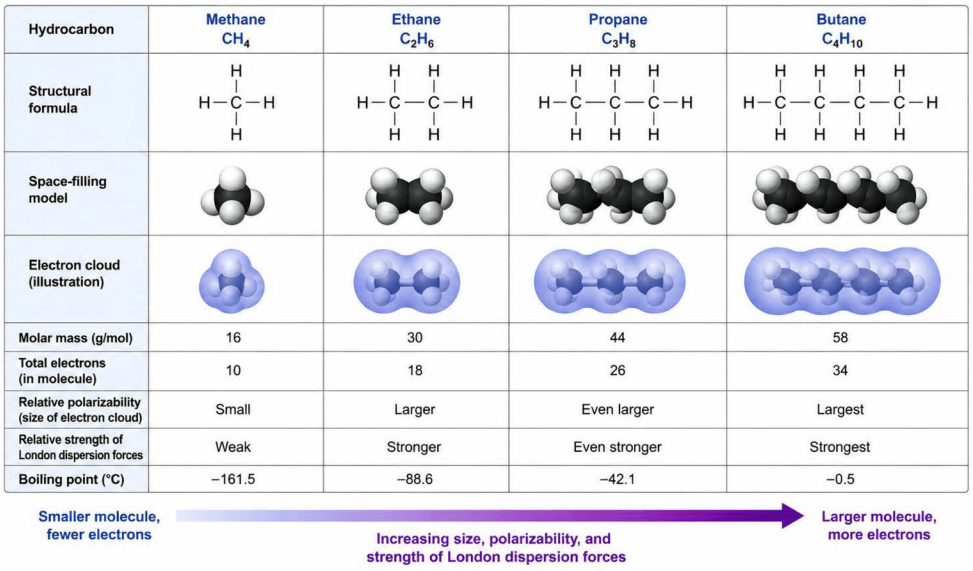


Figure 5.4.8**: Molecular Size, Polarizability, and London Dispersion Forces.** Comparison chart of four hydrocarbons—methane (CH_4), ethane (C_2H_6), propane (C_3H_8), and butane (C_4H_{10}). Each column includes the structural formula, a space-filling model, and an illustration of the electron cloud surrounding the molecule. As molecular size increases from methane to butane, the electron cloud becomes larger, the number of electrons and molar mass increase, polarizability increases, London dispersion forces become stronger, and boiling points increase from –161.5 °C to –0.5 °C. A horizontal arrow emphasizes the overall trend of increasing molecular size, electron cloud size, polarizability, and London dispersion force strength.

Polar Bonds Do Not Always Produce a Polar Molecule

For this section, we will use Carbon dioxide as an example in our analysis of intermolecular forces. Carbon dioxide (CO_2) provides an excellent example of the difference between **polar bonds** and a **polar molecule**. Each carbon-oxygen bond is polar because oxygen is more electronegative than carbon. As a result, each bond has a dipole that points toward the oxygen atom.

However, CO_2 has a **linear molecular geometry** (180°). The two identical bond dipoles point in exactly opposite directions and have equal magnitude. As a result, the bond dipoles cancel one another, and the molecule has **no net dipole moment**.

Because CO_2 is **nonpolar**, it does **not** exhibit dipole-dipole interactions or hydrogen bonding. Like all molecules, however, CO_2 experiences **London dispersion forces**. These dispersion forces are the dominant intermolecular force between neighboring carbon dioxide molecules. Thus, when determining the intermolecular forces within a molecule, it is critical to evaluate the polarity of the overall molecule, not just the individual bonds within the molecule.

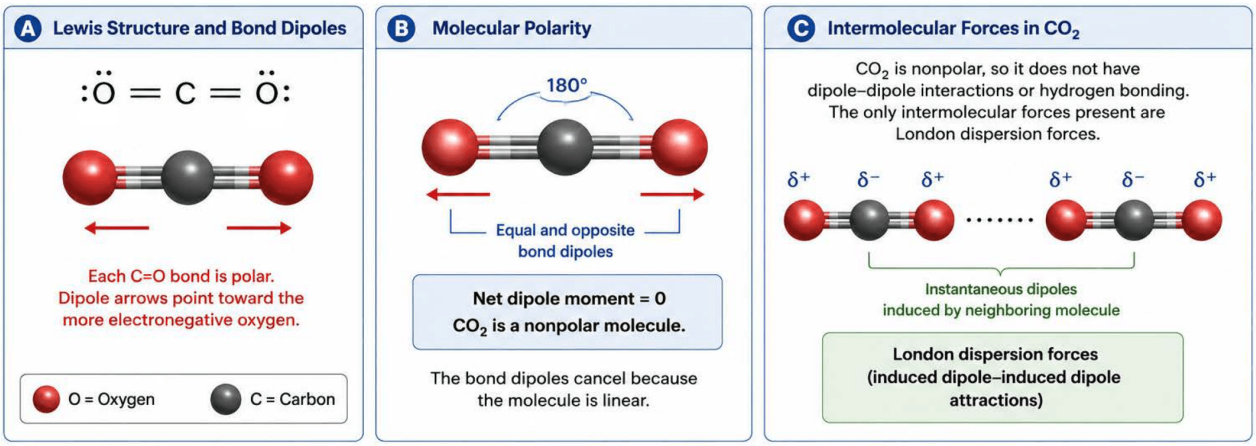


Figure 5.4.9: Carbon Dioxide: Polar Bonds, Nonpolar Molecule. Three-panel diagram illustrating why carbon dioxide is a nonpolar molecule despite containing polar bonds. Panel A shows the Lewis structure and ball-and-stick model of CO_2 with bond dipoles pointing toward each oxygen atom, indicating that each carbon-oxygen bond is polar. Panel B shows the linear (180°) molecular geometry and illustrates that the two equal and opposite bond dipoles cancel, giving the molecule a net dipole moment of zero. Panel C shows two neighboring CO_2 molecules interacting through temporary, induced dipoles, demonstrating that London dispersion forces are the only intermolecular forces present because CO_2 has no permanent molecular dipole.

Polar bonds do not necessarily produce a polar molecule. Molecular geometry determines whether the individual bond dipoles cancel or combine to produce an overall molecular dipole.

Intermolecular forces depend on the polarity of the entire molecule, not the polarity of an individual bond.

Remember

- **London dispersion forces occur between all atoms and molecules.**
- **Intermolecular forces depend on the polarity of the entire molecule, not the polarity of an individual bond.**
- **Polar molecules experience London dispersion forces in addition to dipole-dipole interactions and, when applicable, hydrogen bonding.**
- **Larger atoms and molecules generally exhibit stronger London dispersion forces because their electron clouds are more easily polarized.**

Every atom and every molecule experiences London dispersion forces.

Table 5.4B: Properties of Intermolecular Forces

Property	Dipole-Dipole	Hydrogen Bonding	London Dispersion
Occurs in polar molecules?	✓	✓	✓ (all molecules)
Occurs in nonpolar molecules?	✗	✗	✓
Permanent dipoles required?	✓	✓	✗
Temporary dipoles involved?	✗	✗	✓
Requires H bonded to N, O, or F?	✗	✓	✗
Example	CH_2O	H_2O	I_2

---

3. Attractions Involving Ions and Molecules

After learning about interactions between ions and between molecules, we can now examine what happens when **ions are mixed with polar molecules**.

When an ionic compound dissolves in a polar solvent such as water, the ions separate from the crystal lattice and become surrounded by water molecules. The attractive force between an ion and the partial charges of a polar molecule is called an **ion-dipole interaction**.

Ion-dipole interactions are generally stronger than the intermolecular forces between neutral molecules because they involve the attraction between a full ionic charge and the partial charge of a polar molecule. Although individual ion-dipole interactions are typically weaker than individual ion-ion attractions, many ion-dipole interactions form simultaneously as water molecules

surround each ion during dissolution. These new interactions help stabilize the separated ions in solution and often provide sufficient attraction to overcome the disruption of the crystal lattice and the hydrogen-bonding network of water. As a result, ion-dipole interactions play a critical role in dissolving ionic compounds, transporting ions in biological systems, and many chemical reactions that occur in aqueous solution.

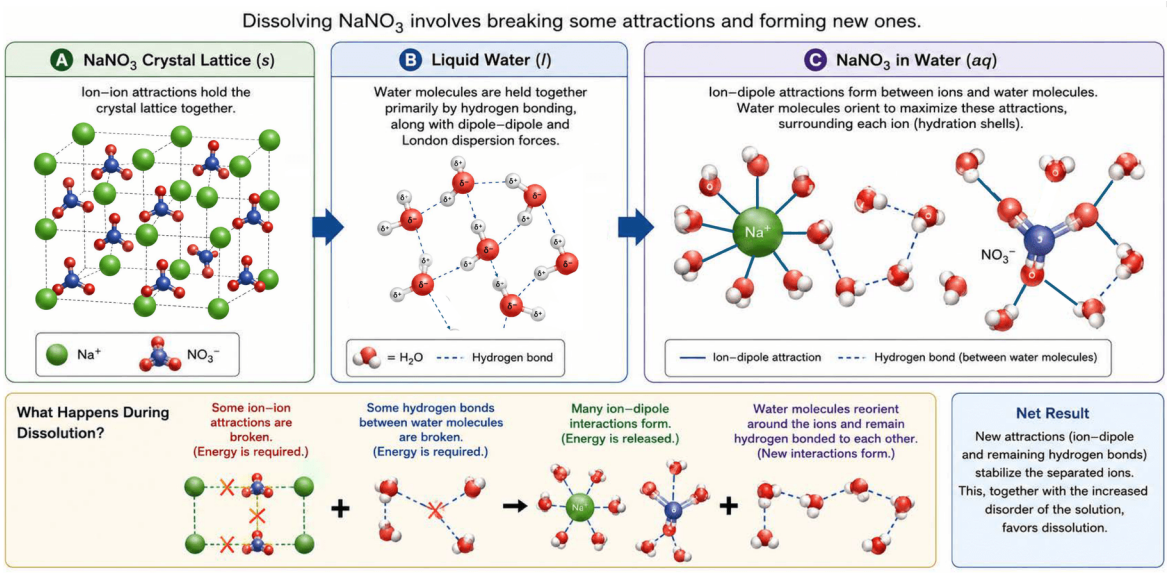


Figure 5.4.10**: Dissolving Sodium Nitrate in Water.** Three-panel diagram illustrating the dissolution of sodium nitrate in water. Panel A shows a solid sodium nitrate crystal lattice held together by ion–ion attractions between sodium ions (Na^+) and nitrate ions (NO_3^-). Panel B shows liquid water in which neighboring water molecules are connected by hydrogen bonds. Panel C shows dissolved sodium nitrate. Water molecules surround each sodium ion with their oxygen atoms directed toward the positive charge and surround each nitrate ion with their hydrogen atoms directed toward the negatively charged oxygen atoms, forming ion–dipole interactions (hydration shells). A summary beneath the panels explains that dissolution involves breaking some ion–ion attractions in the crystal lattice and some hydrogen bonds between water molecules while forming many ion–dipole interactions around the dissolved ions. The combined effect stabilizes the separated ions in solution and favors dissolution.

Ion-dipole attractions replace many of the ion-ion and water-water interactions, allowing the crystal to dissolve.

When sodium nitrate is placed in water, the strong ion-ion attractions that hold the crystal lattice together must first be overcome. At the same time, some of the hydrogen bonds between neighboring water molecules must also be disrupted. Although breaking these attractive forces requires energy, new ion-dipole interactions form as water molecules surround the sodium and nitrate ions.

Water molecules orient themselves according to their partial charges. The partially negative oxygen atoms are attracted to the positively charged sodium ions, while the partially positive hydrogen atoms are attracted to the negatively charged oxygen atoms of the nitrate ion (Figure 5.xx).

When the newly formed ion-dipole interactions are sufficiently favorable, the ions separate from the crystal lattice and become dispersed throughout the solution. Each ion is surrounded by a shell of oriented water molecules called a **hydration shell**.

Table 5.4C: Determining Electrostatic Interactions Between Molecules

Interaction	Present?	Example
Ion-ion	✓	Within $NaNO_3$ crystal
Hydrogen bonding	✓	Between neighboring water molecules

Interaction	Present?	Example
Dipole-dipole	✓	Between water molecules (H-bonding)
London dispersion	✓	Between all molecules
Ion-dipole	✓	Between Na^+/NO_3^- and water

Note

Hydrogen bonding doesn't replace dipole-dipole interactions—it is the strongest, most specific form of dipole-dipole interaction.

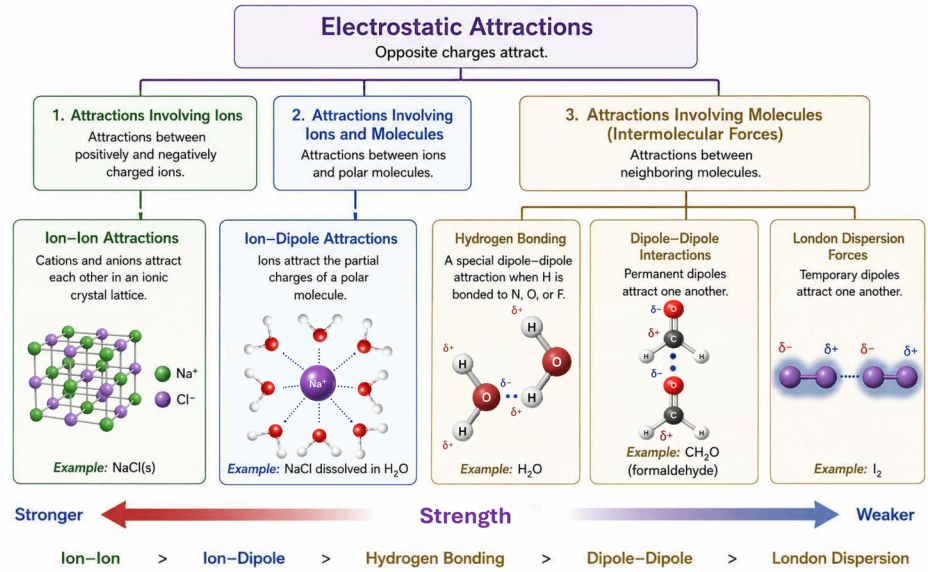


Figure 5.4.11: **Summary of Electrostatic Interactions.** Hierarchy diagram summarizing the major types of electrostatic attractions. Electrostatic attractions are grouped into three categories: **attractions involving ions** (ion-ion attractions in an ionic crystal lattice, illustrated with NaCl), **attractions involving ions and molecules** (ion-dipole attractions between a sodium ion and surrounding water molecules), and **attractions involving molecules** (intermolecular forces), including hydrogen bonding between water molecules, dipole-dipole interactions between formaldehyde (CH_2O) molecules, and London dispersion forces between iodine (I_2) molecules. A strength scale at the bottom indicates the general trend in attraction strength: **ion-ion > ion-dipole > hydrogen bonding > dipole-dipole > London dispersion forces**.

Applying Your Knowledge:

Throughout this section, you have learned how to identify the electrostatic attractions present in different substances.

For each substance below:

1. Determine whether the substance consists of **ions**, **molecules**, or **ions dissolved in molecules**.
2. Identify **all electrostatic attractions** that are present.
3. Identify the **dominant electrostatic attraction**.

(A) SO_2

(B) CH_3Cl

(C) $CaCO_3$

(D) $CoCl_2$ dissolved in water

(E) CH_3OH dissolved in water

(F) CCl_4

Concept Check:

(1) When sodium nitrate dissolves in water, which attraction is responsible for holding the sodium ion inside its hydration shell?

A. Hydrogen bonding

B. Dipole-dipole

C. Ion-dipole

D. London dispersion

(2) Why does carbon dioxide exhibit only London dispersion forces even though each C=O bond is polar?

A. The carbon-oxygen bonds are actually nonpolar.

B. The oxygen atoms cancel each other's electronegativity.

C. The bond dipoles cancel because CO_2 is linear.

D. Carbon dioxide contains too few electrons to be polar.

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5.5: Physical Properties of Intermolecular Forces

Now that we understand **why intermolecular forces exist**, we can use them to explain many of the physical properties of substances. Although molecules differ in size, shape, and polarity, the underlying question is always the same:

How strongly are neighboring particles attracted to one another?

In general, **stronger intermolecular forces require more energy to overcome**. As a result, substances with stronger intermolecular forces tend to have higher boiling points, higher melting points, greater surface tension, and higher viscosity. They also tend to evaporate more slowly and have lower vapor pressures.

Instead of memorizing each property separately, it is often helpful to ask:

What intermolecular force explains this property?

The answer to that question provides the key to understanding the behavior of liquids and molecular solids.

Boiling Point

The **boiling point** is the temperature at which a liquid changes into a gas. During boiling, molecules must completely overcome the intermolecular forces holding them together in the liquid phase. Consequently, substances with stronger intermolecular forces require more energy to separate the molecules and therefore have **higher boiling points**.

For example, methane (CH_4) experiences only London dispersion forces and boils at a much lower temperature than methanol (CH_3OH), which is capable of hydrogen bonding.

Melting Point

The **melting point** is the temperature at which a solid changes into a liquid. Before molecules can move freely in the liquid phase, some of the intermolecular forces that hold neighboring particles in their fixed positions must be overcome.

In general, stronger intermolecular forces produce **higher melting points**, although crystal structure and molecular shape can also influence how efficiently molecules pack together in the solid state.

Vapor Pressure and Evaporation

Even below the boiling point, some molecules at the surface of a liquid possess enough kinetic energy to escape into the gas phase. This process is called **evaporation**.

Liquids with weak intermolecular forces lose molecules more easily and therefore evaporate more rapidly. Because more molecules enter the gas phase, these liquids also develop a **higher vapor pressure**.

In contrast, liquids with strong intermolecular forces retain their molecules more effectively. They evaporate more slowly and have **lower vapor pressures**.

Thus, vapor pressure and intermolecular force strength are **inversely related**:

- **Stronger intermolecular forces → lower vapor pressure**
- **Weaker intermolecular forces → higher vapor pressure**

Surface Tension

Molecules at the surface of a liquid experience fewer attractive interactions than molecules within the interior of the liquid. As a result, the surface behaves like a stretched elastic film, a property known as **surface tension**.

Liquids with stronger intermolecular forces exhibit **higher surface tension** because the molecules attract one another more strongly. Water is a familiar example. Its extensive hydrogen-bonding network produces an unusually high surface tension, allowing small insects to walk across its surface and causing water droplets to bead together.

Viscosity

Viscosity describes a liquid's resistance to flowing. Molecules that strongly attract one another cannot easily slide past their neighbors, producing a more viscous liquid.

Liquids with weaker intermolecular forces flow readily and have **low viscosity**, whereas liquids with stronger intermolecular forces have **higher viscosity**.

For example, glycerol, which contains three hydroxyl (-OH) groups capable of extensive hydrogen bonding, is much more viscous than ethanol.

Connecting Physical Properties to Intermolecular Forces

Rather than memorizing individual trends, remember the following general relationship:

Table 5.5A: How intermolecular forces shape physical properties

Property	Stronger Intermolecular Forces
Boiling point	↑ Higher
Melting point	↑ Higher
Vapor pressure	↓ Lower
Evaporation rate	↓ Slower
Surface tension	↑ Higher
Viscosity	↑ Higher

Challenge Question:

Which intermolecular force best explains each of the following observations?

- Water beads up on a freshly waxed car.
- Rubbing alcohol evaporates quickly from your skin.
- Honey pours much more slowly than water.
- Methanol has a much higher boiling point than methane.
- Carbon dioxide is a gas at room temperature, whereas iodine is a solid.

Worked Examples:

One of the most useful applications of intermolecular forces is predicting physical properties such as boiling point. In general, molecules with stronger intermolecular forces require more energy to separate from one another and therefore have higher boiling points.

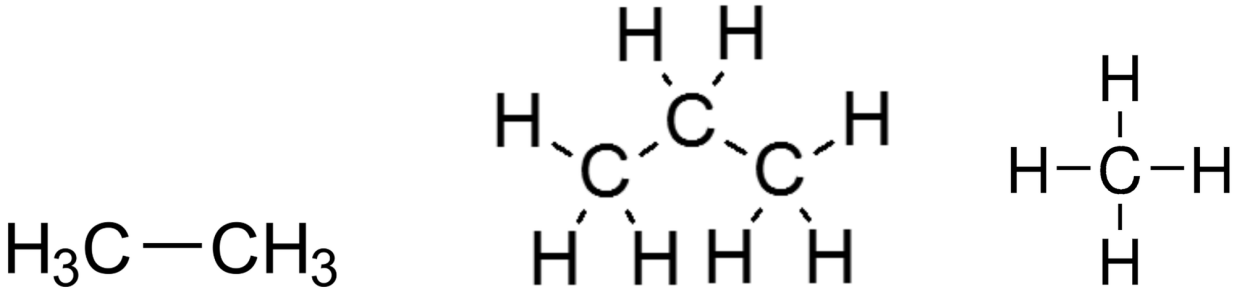
To compare boiling points, first identify the intermolecular forces present in each molecule. Then compare the relative strengths of those forces. If two molecules possess the same dominant intermolecular force, compare their molecular size (molar mass) and shape (surface area), since larger, more polarizable molecules generally exhibit stronger London dispersion forces.

General Guidelines for Comparing Boiling Points

1. All molecules experience London dispersion forces.
2. Polar molecules also experience dipole-dipole interactions.
3. Molecules containing O–H, N–H, or F–H bonds can participate in hydrogen bonding, which generally produces the strongest intermolecular attractions between neutral molecules.
4. If two molecules have the same dominant intermolecular force, the molecule with the larger electron cloud (greater polarizability), higher molar mass, or greater surface area generally has the higher boiling point.

Example 5.5.1

Rank the following molecules from the highest boiling point to the lowest boiling point.



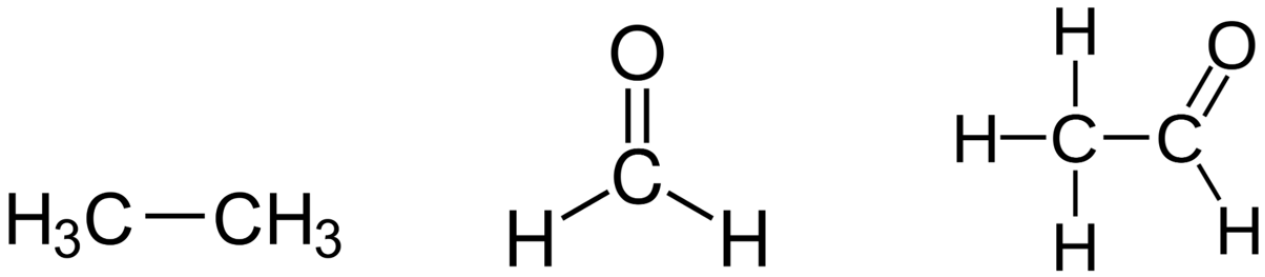
Solution

We can start with the assumption that these molecules each have London dispersion forces. To determine the polarity, we could start by drawing Lewis structures. However, these three molecules are made up of only carbon and hydrogen atoms. We know that carbon-hydrogen bonds are nonpolar. So regardless of the molecular geometry, there will be no net dipole. Because all three molecules are nonpolar, London dispersion forces are the only significant intermolecular force present. The larger molecules contain more electrons and are more polarizable, resulting in progressively stronger London dispersion forces. $CH_3CH_2CH_3$ has the highest molecular weight and will have the highest boiling point. CH_4 has lowest molecular weight and will have the lowest boiling point.

$CH_3CH_2CH_3 > CH_3CH_3 > CH_4$

Exercise 5.5.1

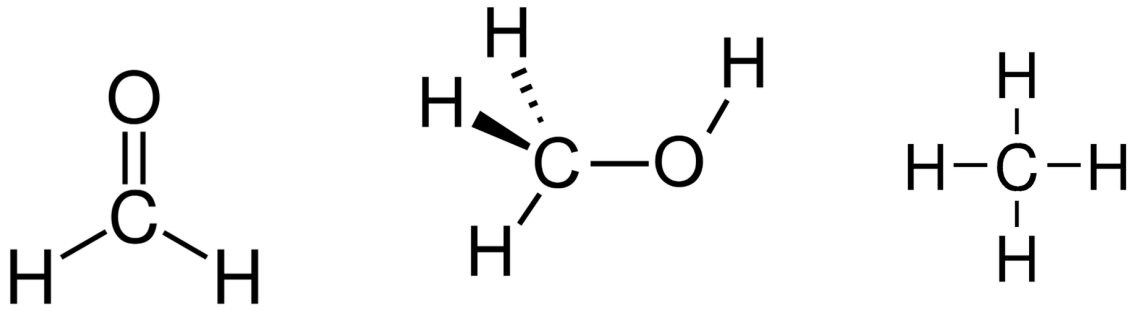
Rank the following molecules from the highest boiling point to the lowest boiling point.



Answer available at the end of this section.

Exercise 5.5.2

Rank the following molecules from the highest boiling point to the lowest boiling point.



Answer available at the end of this section.

Answers

Exercise 5.5.1

Both CH_2O and CH_3CHO contain a polar carbonyl (C=O) bond, making them polar molecules. As a result, they experience both London dispersion forces and dipole-dipole interactions. Neither molecule contains an O–H, N–H, or F–H bond, so neither can hydrogen bond with itself. Since both molecules possess the same dominant intermolecular force (dipole-dipole), the larger molecule, CH_3CHO, has the higher boiling point because it exhibits stronger London dispersion forces. CH_3CH_3 only has London dispersion forces and no permanent dipoles. Thus, it will have the lowest boiling point.

$CH_3CHO > CH_2O > CH_3CH_3$

Exercise 5.5.2

CH_4 only experiences London dispersion forces as it only contains nonpolar C-H bonds. CH_2O experiences London dispersion forces and dipole-dipole interactions, while CH_3OH experiences London dispersion forces, dipole-dipole interactions, and hydrogen bonding. Because hydrogen bonding is the strongest intermolecular force present between these neutral molecules, methanol (CH_3OH) has the highest boiling point.

$CH_3OH > CH_2O > CH_4$

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5.6: Chemistry in the Body- Why Can't Ions Cross the Cell Membrane?

Returning to Our Neuron

At the end of Chapter 4, we encountered an important chemical mystery. Neurons maintain high concentrations of Na⊕ outside the cell and high concentrations of K⊕ inside the cell. Although diffusion favors movement of these ions down their concentration gradients, the **plasma membrane prevents them from freely crossing from one side to the other**.

We now have more chemistry available to help explain why.

Ions Are Surrounded by Polar Water

The fluids inside and outside our cells are composed primarily of water. As we learned in this chapter, water contains polar O—H bonds and has a **bent molecular geometry**. Because the individual bond dipoles do not cancel, water is a **polar molecule**.

This polarity allows water molecules to interact strongly with ions.

When Na⊕ is placed in water, the partially negative oxygen ends of nearby water molecules are attracted to the positively charged ion. Around a negative ion such as Cl⊖, the partially positive hydrogen ends of water molecules point toward the ion.

These attractions between an ion and a polar molecule are called **ion–dipole attractions**.

As a result, dissolved ions do not exist as completely isolated particles in biological fluids. They are surrounded by water molecules, forming a **hydration shell**.

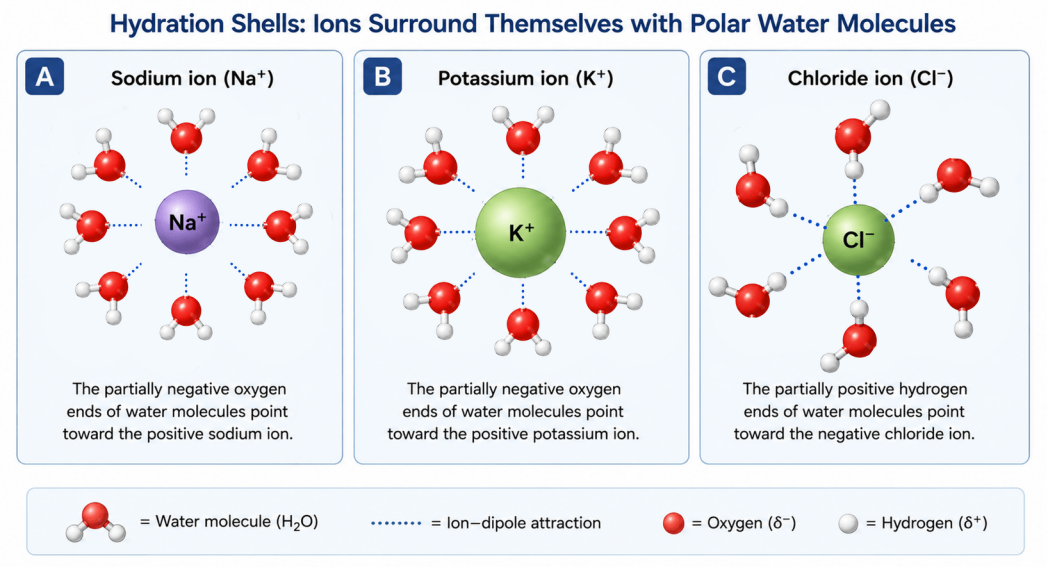


Figure 5.6.1**: Hydration Shells Around Common Biological Ions.** Polar water molecules surround dissolved ions through **ion–dipole attractions**, forming a hydration shell. Around positively charged sodium (Na⊕) and potassium (K⊕) ions (Panels A and B), the partially negative oxygen (δ–) ends of water molecules orient toward the ion. Around a negatively charged chloride (Cl⊖) ion (Panel C), the partially positive hydrogen (δ+) ends of water molecules orient toward the ion. These favorable interactions with polar water help stabilize dissolved ions in the aqueous environments inside and outside of cells.

The Membrane Presents a Very Different Environment

To move from the watery environment on one side of a cell membrane to the watery environment on the other, an ion would have to pass through the **interior of the plasma membrane**.

But the interior of the membrane is largely **nonpolar**.

Charged ions interact very favorably with polar water molecules but very poorly with nonpolar environments. For an ion such as $Na^{\oplus}$ to enter the membrane, it would have to give up many of its favorable ion–dipole interactions with surrounding water molecules and enter an environment that cannot provide equally strong attractions.

This is energetically unfavorable.

Consequently, $Na^{\oplus}$, $K^{\oplus}$, $Ca^{2\oplus}$, $Cl^{\ominus}$, and other ions cannot readily diffuse directly through the nonpolar interior of the plasma membrane.

> **The same intermolecular forces that allow ions to dissolve in water also help prevent those ions from freely crossing cell membranes**.

Ion Pumps and Channels Provide a Different Chemical Pathway

So how can ions cross the membrane at all? Recall from the end of Chapter 4, that we were introduced to the Sodium-Potassium ATPase Pump. To become an excitable cell that can transmit an electric signal, neurons generate a negative resting potential within their cells. This is accomplished by sequestering cations and anions in different concentrations either inside the cell (intracellular) or outside the cell (extracellular). This leaves the inside of the neuron with a resting potential of -70 mV. Thus, the cell is said to be polarized or negatively charged. The neuron is able to generate this negative resting potential largely through the use of the Sodium (Na+)/Potassium (K+) ATPase Protein. This protein is embedded in the plasma membrane of all neurons, where it functions as a pump. **Protein pumps** use energy to physically pump molecules across the plasma membrane against their concentration gradient. The energy being used for this process is Adenosine Triphosphate (ATP). In this case, 3 sodium ions are pumped out of the cell, while 2 potassium ions are pumped inside the cell for each ATP molecule that is broken down into Adenosine Diphosphate (ADP) (Figure 5.6.2). This creates an electrochemical gradient where a high concentration of sodium ions are outside of the cell and a high concentration of potassium ions are inside the cell. Similarly, calcium ions accumulate on the outside of the neuron through a dedicated pump system. The inside of the cell also contains numerous organic anions and phosphate anions causing the large negative resting potential of -70 mV within the cell.

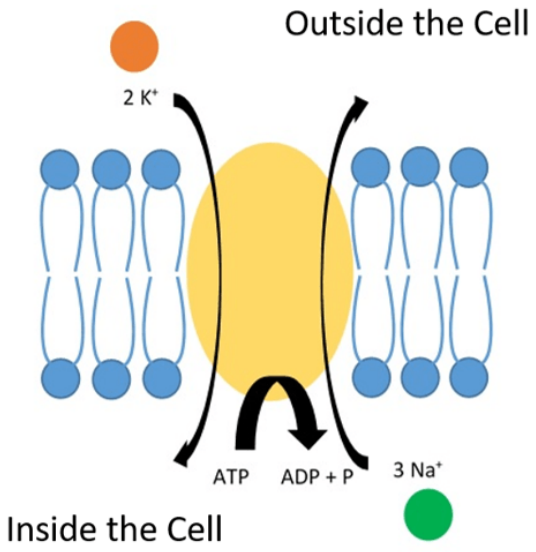


Figure 5.6.2: The Sodium-Potassium ATPase Pump. The Na+/K+ ATPase Pump uses the energy of ATP to pump 3 Na+ out the cell and 2 K+ into the cell. This gradient enables neurons to maintain a resting electrical potential of -70 mV within the neuron.

Image from Wikimedia Commons.

The Na+/K+ ATPase pump is widely expressed in all neurons and is constantly working to maintain this gradient. In fact, this is one of the major uses of energy within the body consuming almost 20% of the body's total energy each day. The formation of this concentration gradient makes it possible for neurons to send electrical impulses down the cell axon and communicate with downstream target cells. This makes it possible to think, move our muscles, and sense the outside world through touch, sight, hearing and smell.

To generate an action potential, a neuron needs a ripple of positive current to flow down the axon. When it reaches the terminal of the axon, this is a signal that neurotransmitters, such as dopamine, serotonin or glutamate should be released into the synaptic cleft (Fig. 5.6.3)

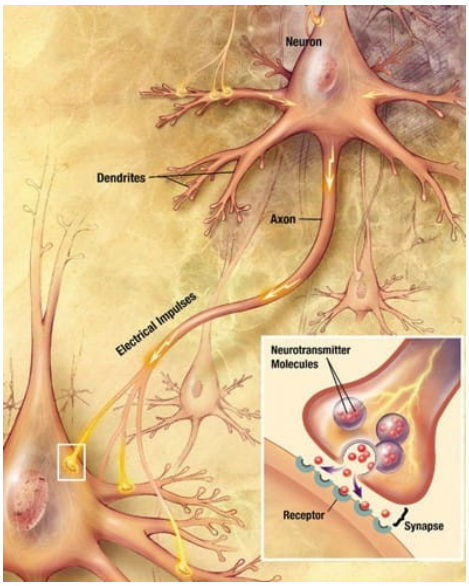


Figure 5.6.3: Neuronal Signaling. This diagram depicts the cell-cell communication between neurons after the firing of an action potential down the axon of a pre-synaptic neuron. At the axon terminal, secretory vesicles containing neurotransmitters such as serotonin and dopamine, are released into the synaptic cleft where they can can interact with receptors on the dendrite or soma of the post-synaptic neuron. Figure provided by Wikimedia.

These small chemical messengers are used to communicate with the downstream neuron or muscle cell. Within the neuron, **ion channels** play an important role in generating the action potential. **Ion channels** are proteins embedded within the plasma membrane of the neuron that form a pore large enough for specific ions to pass through. Because ions are charged particles, their movement through an open channel is influenced by both their **concentration gradient** and the **electrical potential** across the membrane. Together, these forces make up the ion's **electrochemical gradient**.

Two types of ion channels that are important for generating an action potential are **receptor/ligand activated channels** and **voltage-gated channels**. For the receptor/ligand activated channel, a small molecule that is acting as a chemical messenger (also called a **ligand**), binds to the receptor and causes a conformational change that either activates or inhibits the receptor. Usually these types of receptors are found on the dendrite of the receiving neuron, where they will bind to neurotransmitters. Once a neurotransmitter binds, the receptor undergoes a conformational change that opens its ion channel. Depending on the type of receptor, the channel may allow ions such as $Na^{\diamondsuit}$, $K^{\diamondsuit}$, $Ca^{2\diamondsuit}$, or $Cl^{\diamondsuit}$ to cross the membrane. In the example shown in Figure 5.6.4, opening the channel allows $Ca^{2\diamondsuit}$ to move into the cell down its electrochemical gradient, producing a localized depolarization.

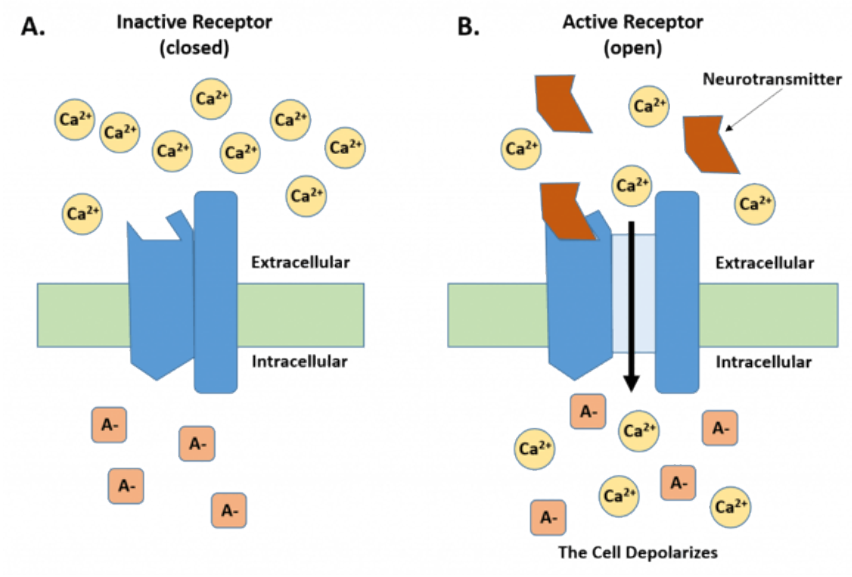


Figure 5.6.4**: Receptor/Ligand Activated Channels.** (A) Shows a receptor in the closed conformation during the resting state of the neuron. Note that calcium ions are in high concentration outside of the cell while increased anion concentrations inside the cell create a -70 mV resting state. (B) When neurotransmitters are released from the axon into the synapse, they will bind with the receptor causing a conformational change in the receptor that opens the calcium ion channel. Ca^{2+} flows into the cell down its concentration gradient causing localized depolarization within the cell.

This localized depolarization event, if strong enough, can activate neighboring voltage-gated sodium channels (Fig. 5.6.5A). These channels are sensitive to the charge state in the neuron and will open when the charge is reduced in the local area. At this time, the voltage-gated sodium channels will undergo a structural change that allows sodium ions to rapidly flow into the cell, down their concentration gradient. This will further cause the neuron to depolarize and cause the opening of other voltage-gated sodium channels that are in close proximity. When the charge state of the neuron surpasses neutral and becomes positive on the inside (approximately +30 mV), the voltage-gated sodium channels undergo another conformational change, closing the channels and stopping the inflow of sodium ions. At this point, the voltage-gated potassium channels are activated allowing potassium ions the flow out of the cell down their concentration gradient (Fig. 5.6.5B).

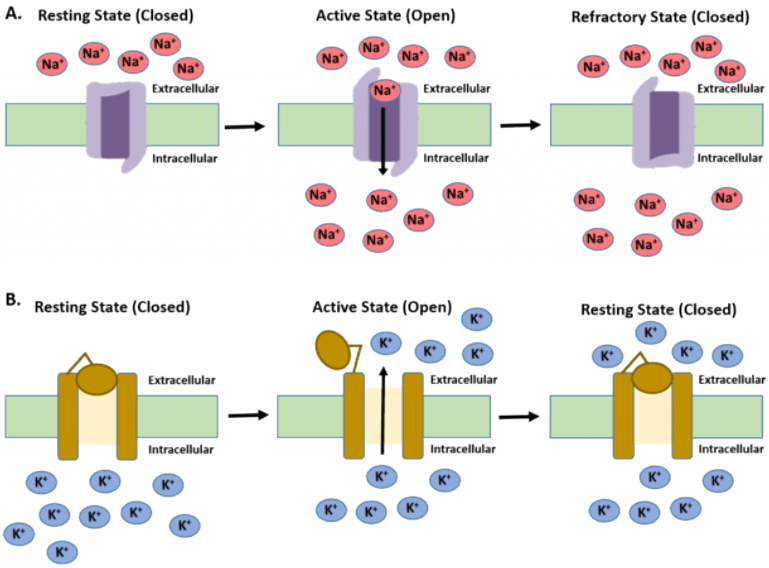


Figure 5.6.5**: Voltage-Gated Ion Channels. (A)** The Voltage-Gated Sodium Channels are closed when the neuron is in the resting state. Following neurotransmitter stimulation, the cellular depolarization causes the voltage-gated sodium channels to undergo

a conformational change, opening the sodium channel and allowing the influx of Na+ into the cell. When the cellular charge becomes positive (approximately +30 mV) the voltage-gated Na+ channels close due to an additional conformation change and enters a refractory period where it cannot be reactivated. The lowering of the charge state within the neuron to -70 mV restores the protein conformation to the resting state. **(B)** The voltage-gated potassium channel is closed during the resting state of the neuron and is not activated until the polarity of the cell shifts to approximately +30 mV. Following activation, potassium ions move out of the cell, down their concentration gradient and restore the resting potential of the neuron to -70 mV.

As voltage-gated Na⋄ channels close, many enter an **inactivated state** in which they cannot immediately reopen. This produces the **absolute refractory period**, during which another action potential cannot be generated in that region of the membrane. As Na⋄ channels recover and voltage-gated K⋄ channels remain open, the membrane may temporarily become more negative than its resting potential. During this **relative refractory period**, another action potential is possible, but a stronger-than-normal stimulus is required.

Only a small fraction of the neuron's Na⋄ and K⋄ ions cross the membrane during a single action potential, so the overall concentration gradients remain largely intact. The Na⋄/K⋄ ATPase continually works to maintain these gradients over time, allowing neurons to remain capable of repeated electrical signaling.

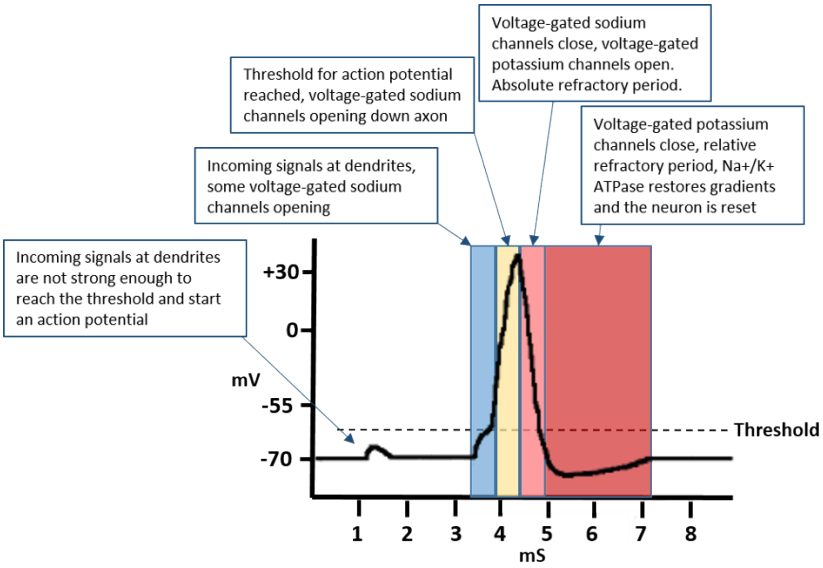


Figure 5.6.6**: Graphic Representation of an Action Potential.** A neuron has a resting membrane potential of approximately –70 mV. When depolarization reaches threshold, voltage-gated Na⋄ channels open, allowing Na⋄ to enter and rapidly depolarize the membrane. Near the peak of the action potential, Na⋄ channels become inactivated and voltage-gated K⋄ channels open. The movement of K⋄ out of the cell repolarizes the membrane and may briefly produce hyperpolarization. As the ion channels return to their resting states, the membrane potential returns toward –70 mV. The Na⋄/K⋄ ATPase continually maintains the Na⋄ and K⋄ concentration gradients required for repeated electrical signaling.

The refractory period in one location in the neuron, also allows the directional movement of the depolarization event from the dendrites of the neuron and through the cell body. If the signal is strong enough to depolarize the neuron to a state of -55 mV when it reaches the axon hillock, this will generate an action potential that will be sent down the axon of the neuron. This is a committed step by the neuron that will cause the release of neurotransmitters into the synaptic cleft, signaling the activation of the downstream neuron or target cell.

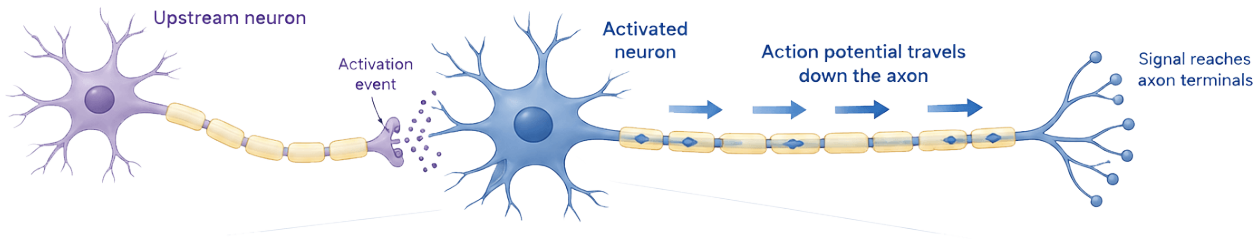


Figure 5.6.7: The Refractory Period Ensures One-Way Propagation of an Action Potential. An action potential travels along an axon as depolarization in one region triggers the opening of voltage-gated Na^+ channels in the next region, allowing Na^+ to enter and continue the electrical signal forward. The region that has just fired then repolarizes as K^+ leaves the cell and enters a brief **refractory period**, during which its voltage-gated Na^+ channels cannot immediately reopen. Because the region behind the advancing signal is temporarily unable to fire again, the action potential cannot propagate backward. This refractory period helps ensure that the electrical signal travels in one direction—from the cell body toward the axon terminals.

Chemistry Makes Electrical Signaling Possible

We can now explain much more of our original neuron story.

The Na^+/K^+ ATPase establishes ion gradients using energy from ATP. The plasma membrane prevents ions from freely dissipating those gradients. Ion channels provide controlled pathways across the membrane. When channels open, ions move down their electrochemical gradients, changing the electrical potential across the membrane and creating an action potential.

But underneath all of this biology is chemistry:

- **Molecular geometry determines molecular polarity**.
- **Molecular polarity influences intermolecular attractions**.
- **Intermolecular attractions determine which chemical environments are favorable for different substances**.
- **Those chemical preferences help determine whether a substance can readily cross a cell membrane**.

The electrical signaling of your nervous system therefore depends, at the molecular level, on the shapes, charges, polarities, and intermolecular attractions of molecules.

But What Makes the Membrane Nonpolar?

> We have now explained **why ions cannot readily enter the nonpolar interior of the plasma membrane**, but we have not yet answered another important question:
>
> **Why does the plasma membrane have a nonpolar interior in the first place**?

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5.7: Chapter Summary

In this chapter, you learned that the **three-dimensional arrangement of atoms within a molecule influences many of its physical and chemical properties**. Beginning with the electronic and molecular geometry and ending with intermolecular forces, the concepts introduced in this chapter demonstrate how molecular structure determines the behavior of matter.

The shape of a molecule can be predicted using **Valence Shell Electron Pair Repulsion (VSEPR) theory**, which states that electron groups around a central atom arrange themselves to minimize repulsion. By counting bonding pairs and lone pairs of electrons, molecular geometries such as linear, bent, trigonal planar, tetrahedral, trigonal pyramidal, and trigonal bipyramidal can be predicted. Lone pairs occupy more space than bonding pairs and often distort bond angles from their ideal values.

Molecular geometry plays a critical role in determining whether a molecule is **polar or nonpolar**. Bond polarity results from differences in electronegativity between bonded atoms, while molecular polarity depends on both the polarity of individual bonds and the overall three-dimensional arrangement of those bonds. In symmetric molecules such as carbon dioxide, bond dipoles cancel, producing a nonpolar molecule. In asymmetric molecules such as sulfur dioxide or water, the bond dipoles do not cancel, resulting in a permanent molecular dipole.

Once molecular polarity is known, the electrostatic attractions between neighboring particles can be predicted. These attractions can be divided into three broad categories.

Attractions Involving Ions

Ionic compounds consist of positively charged cations and negatively charged anions held together by **ion-ion attractions**. These strong electrostatic attractions produce extended crystal lattices rather than individual molecules. As a result, ionic compounds are represented by **formula units** instead of molecular formulas.

Attractions Involving Molecules (Intermolecular Forces)

Neutral molecules are held together by **intermolecular forces**, which influence the physical properties of molecular substances.

Three major intermolecular forces were discussed:

- **Dipole-dipole interactions** occur between neighboring polar molecules.
- **Hydrogen bonding** is a particularly strong type of dipole-dipole interaction that occurs when hydrogen is covalently bonded to nitrogen, oxygen, or fluorine and is attracted to a lone pair on a neighboring nitrogen, oxygen, or fluorine atom.
- **London dispersion forces** arise from temporary fluctuations in electron density and occur between **all atoms and molecules**. Their strength increases as molecular size and polarizability increase.

Because many substances experience more than one intermolecular force, it is important to identify **all** of the interactions that are present before determining which one is **dominant**.

Attractions Involving Ions and Molecules

When ionic compounds dissolve in water, **ion-dipole interactions** form between dissolved ions and surrounding water molecules. These interactions stabilize ions in solution and help explain the dissolution of many ionic compounds, the transport of ions in biological systems, and numerous chemical processes that occur in aqueous solutions.

Molecular Structure Determines Physical Properties

One of the major themes of this chapter is that **molecular structure determines physical properties**.

The type and strength of electrostatic attractions influence many observable properties of substances.

- Stronger attractions generally produce **higher boiling points** and **higher melting points**.
- Stronger attractions produce **higher surface tension** and **greater viscosity**.
- Stronger attractions result in **lower vapor pressures** and **slower rates of evaporation**.

Rather than memorizing these trends individually, ask a single question:

> **What electrostatic attraction best explains this property?**

Chemistry in the Real World

The concepts introduced in this chapter extend far beyond the classroom. Molecular geometry and intermolecular forces help explain why salts dissolve in water, why oil and water do not mix, why carbon dioxide is a gas while water is a liquid at room temperature, and why some environmental contaminants move easily through groundwater while others remain adsorbed to soil. These same principles also help scientists understand the behavior of pharmaceuticals, biological molecules, and persistent pollutants such as PFAS (Forever Chemicals).

Key Takeaways

After completing this chapter, you should be able to:

- Predict molecular geometry using VSEPR theory.
- Distinguish between electron geometry and molecular geometry.
- Explain how lone pairs influence molecular shape and bond angles.
- Determine whether a molecule is polar or nonpolar using bond polarity and molecular geometry.
- Distinguish between ion-ion, dipole-dipole, hydrogen bonding, London dispersion, and ion-dipole interactions.
- Identify all electrostatic attractions present in a substance and determine the dominant interaction.
- Predict how intermolecular forces influence boiling point, melting point, vapor pressure, evaporation, surface tension, and viscosity.
- Explain how molecular structure influences the behavior of substances in biological and environmental systems.

Final Thought

Throughout this chapter, you developed a framework for connecting molecular structure to observable properties. By asking four simple questions, you can explain the behavior of many substances:

1. What is the molecular geometry?
2. Is the molecule polar or nonpolar?
3. What electrostatic attractions are present?
4. How do those attractions influence the physical properties and behavior of the substance?

These four questions provide a logical pathway from the arrangement of atoms in a molecule to the physical and chemical properties observed in the laboratory, in living systems, and in the environment.

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6: INTRODUCTION TO ORGANIC CHEMISTRY

6.1: Carbon- The Framework of Organic Molecules

6.2: Representing Organic Molecules

6.3: Hydrocarbons- Building the Carbon Skeleton

6.4: Isomers and Chirality

6.5: The Importance of Chirality in Biological Systems and Medicine

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6.7: Common Organic Functional Groups

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6.1: Carbon- The Framework of Organic Molecules

Learning Objectives

After completing this section, you should be able to:

- Explain why carbon can form such a large variety of compounds.
- Describe the typical bonding pattern of carbon in organic molecules.
- Recognize carbon chains, branched structures, and rings.
- Distinguish between saturated and unsaturated carbon structures.
- Identify common heteroatoms found in organic molecules.

What Is Organic Chemistry?

Organic chemistry is the study of carbon-containing compounds and their properties and reactions. Carbon is found in an enormous variety of substances, ranging from simple molecules such as methane to complex molecules such as proteins, DNA, hormones, and medications.

Living organisms are particularly dependent on carbon chemistry. Carbohydrates, lipids, proteins, nucleic acids, vitamins, hormones, and many of the molecules used as medications are organic compounds.

What makes carbon capable of forming such an extraordinary variety of molecules?

The answer begins with its ability to form **four covalent bonds**.

Carbon Forms Four Covalent Bonds

Recall that carbon has four valence electrons. To achieve a full valence shell, a carbon atom typically shares electrons with other atoms by forming four covalent bonds.

Carbon can form bonds with many different elements, including hydrogen (H), oxygen (O), nitrogen (N), sulfur (S), phosphorus (P), and the halogens. The simplest organic compounds contain only carbon and hydrogen and are called **hydrocarbons**. Methane (CH_4), for example, is the simplest hydrocarbon.

In many organic molecules, atoms other than carbon and hydrogen are also present. These atoms are collectively called **heteroatoms**. Common heteroatoms include oxygen, nitrogen, sulfur, phosphorus, and the halogens. Heteroatoms are especially important because they often give organic molecules distinctive chemical and physical properties. Later in this chapter, we will see that heteroatoms are frequently found within **functional groups**, the regions of organic molecules that help determine how those molecules behave.

Most importantly, however, **carbon can also form strong covalent bonds with other carbon atoms**. This ability allows carbon atoms to connect repeatedly, forming chains, branches, and rings of many different sizes. These carbon frameworks, or **carbon skeletons**, provide the structural foundation for the enormous diversity of organic molecules found in living organisms.

For example, methane contains a single carbon atom bonded to four hydrogen atoms.

CH_4

Because there are four regions of electron density surrounding the carbon atom, the carbon has a **tetrahedral geometry**, with bond angles of approximately 109.5°. Thus, although methane is often drawn as a flat two-dimensional structure on paper, the actual molecule is three-dimensional.

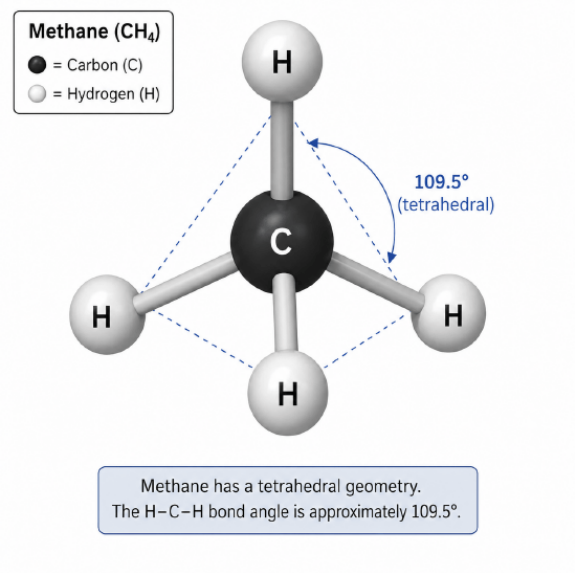


Figure 6.1.1**: Methane (CH4) Ball and Stick Model**. Carbon forms four single covalent bonds with hydrogen. The four bonding pairs around carbon repel each other and arrange themselves as far apart as possible, giving bond angles of 109.5° and forming tetrahedral molecular geometry.

This ability to form four bonds gives carbon tremendous flexibility in constructing larger molecules.

Carbon Can Bond to Carbon

One of the most important characteristics of carbon is its ability to form stable **carbon–carbon bonds**. Carbon atoms can connect repeatedly to produce chains of many different lengths.

For example, compare these simple carbon skeletons:

C–C

C–C–C

C–C–C–C

The carbon atoms can also form **branched chains**, in which one carbon is connected to several other carbon atoms.

Carbon chains can even bend around and connect back to themselves, producing **rings**.

As a result, the carbon skeleton of an organic molecule can be:

- straight or unbranched,
- branched,
- cyclic, or
- a combination of chains and rings.

This carbon framework is sometimes called the **carbon skeleton** of the molecule.

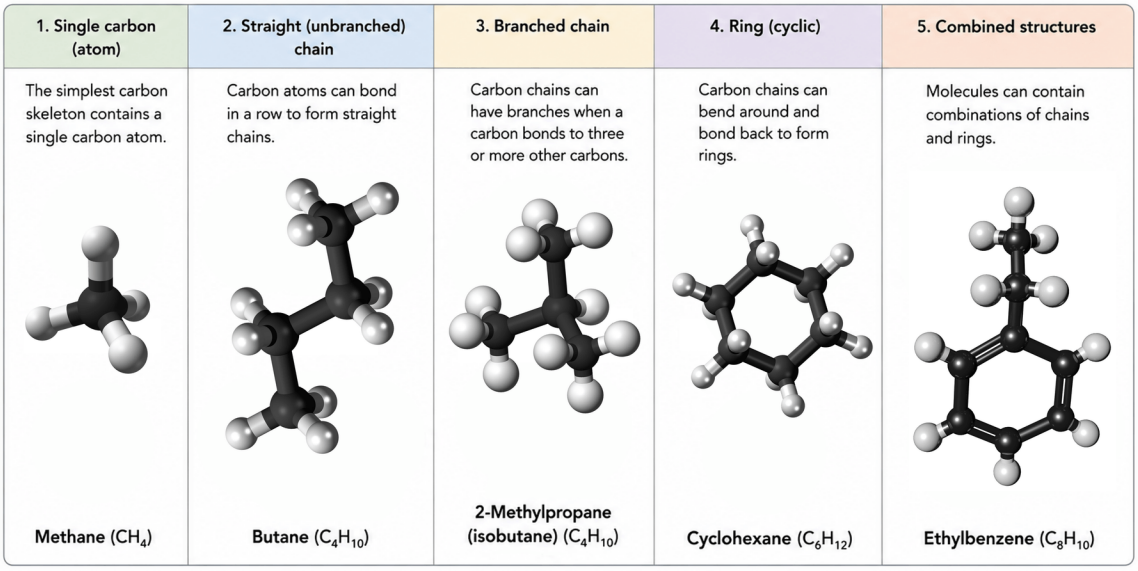


Figure 6.1.2**: Examples of Carbon Skeletons**. Carbon atoms can form a wide variety of skeletons. They may exist as a single atom, form straight chains, create branched chains, form rings, or combine chaings and rings. This structural diversity is the foundation for the vast number of organic molecules found in living organisms.

The size and shape of the carbon skeleton can strongly influence the properties of an organic molecule. Even molecules containing the same kinds and numbers of atoms can behave differently if those atoms are connected in different ways.

We will explore this idea more fully when we discuss **isomers** later in this chapter.

Carbon Can Form Single, Double, and Triple Bonds

Carbon atoms are not limited to forming single bonds with one another. They can share more than one pair of electrons, producing **double** and **triple bonds**.

A carbon–carbon single bond contains one shared pair of electrons:

C–C

A carbon–carbon double bond contains two shared pairs of electrons:

C=C

A carbon–carbon triple bond contains three shared pairs of electrons:

C≡C

These different bonding patterns influence both the **shape** and **reactivity** of organic molecules.

Carbon atoms connected entirely by single bonds have more freedom to rotate around those bonds. Double and triple bonds restrict this rotation and produce different molecular geometries. These structural differences become especially important in biological molecules, where molecular shape can determine how a molecule interacts with enzymes, receptors, membranes, and other molecules.

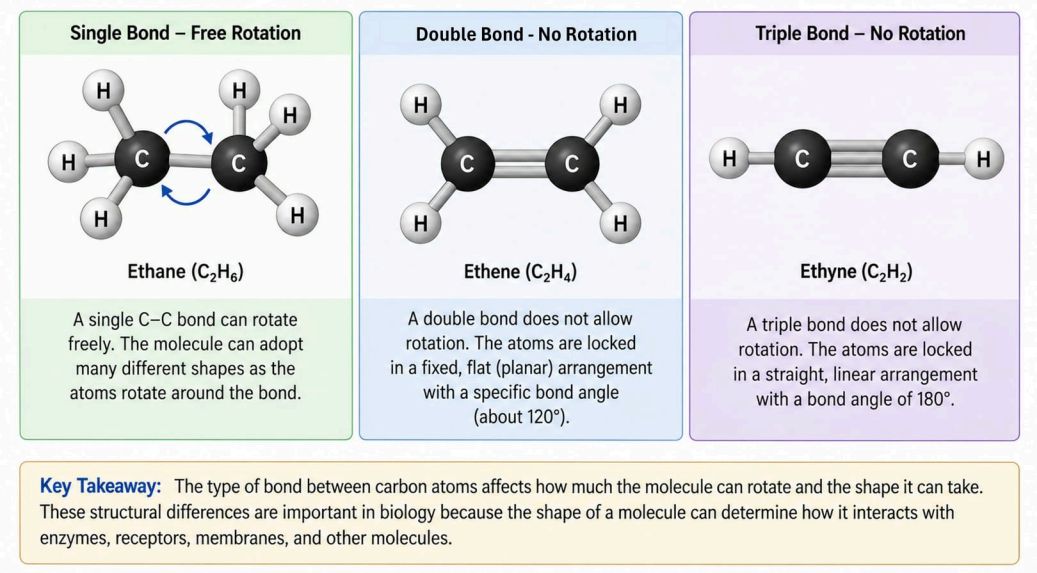


Figure 6.1.3: Rotation and molecular shape in carbon compounds. Carbon atoms connected by single bonds can rotate freely around the bond. Double and triple bonds restrict rotation, creating different molecular geometries.

Saturated and Unsaturated Carbon Skeletons

Organic molecules containing only carbon–carbon single bonds are described as **saturated**. The term *saturated* means that the carbon atoms contain the maximum number of hydrogen atoms possible for that particular carbon skeleton.

Molecules containing one or more carbon–carbon double or triple bonds are described as **unsaturated** because those carbon atoms could potentially bond to additional hydrogen atoms if the multiple bond were replaced by single bonds.

This distinction is especially important in biology and nutrition. For example, the terms **saturated fat** and **unsaturated fat** describe differences in the carbon–carbon bonding within the fatty acid portions of these molecules.

We will examine these types of structures in more detail later in this chapter.

Carbon Rarely Works Alone

Although carbon forms the framework of organic molecules, most biologically important organic molecules contain elements in addition to carbon and hydrogen.

Atoms other than carbon and hydrogen that occur within an organic molecule are commonly called **heteroatoms**.

Some of the most important heteroatoms in biological molecules include:

- **oxygen (O)**
- **nitrogen (N)**
- **sulfur (S)**
- **phosphorus (P)**
- **halogens**, such as fluorine (F), chlorine (Cl), bromine (Br), and iodine (I)

These atoms can dramatically change the properties of a carbon-based molecule.

For example, a region containing only carbon and hydrogen is generally nonpolar. Adding oxygen or nitrogen can introduce polar bonds and allow the molecule to interact more strongly with water. Some groups containing nitrogen, oxygen, phosphorus, or sulfur can even gain or lose hydrogen ions and become electrically charged.

Thus, two organic molecules with similar carbon skeletons can have very different physical, chemical, and biological properties depending on the other atoms attached to them.

From Carbon Skeletons to Biological Molecules

The remarkable diversity of organic chemistry arises from a relatively simple set of possibilities. Carbon can form four covalent bonds, bond repeatedly to itself, form chains and rings, make single, double, or triple bonds, and bond with several other biologically important elements.

From these basic building principles, organisms construct molecules of extraordinary complexity.

A small change in an organic structure can sometimes produce a large change in biological behavior. Changing the location of a double bond, adding an oxygen atom, or rearranging the atoms within a molecule may alter its shape, polarity, water solubility, or ability to interact with a biological receptor.

For this reason, learning organic chemistry begins with learning to **recognize molecular structure**.

Fortunately, chemists have developed several ways to simplify the representation of even very complicated organic molecules. In the next section, we will learn how to read these structures and recognize the carbon skeleton hidden within them.

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6.2: Representing Organic Molecules

Learning Objectives

After completing this section, you should be able to:

- Distinguish among **molecular formulas, displayed formulas, partially condensed formulas, condensed formulas, and skeletal (line) structures** used to represent organic molecules.
- Interpret **ball-and-stick and space-filling models** and explain what each model reveals about molecular structure.
- Convert between common two-dimensional representations of simple organic molecules.
- Interpret **skeletal structures**, including identifying carbon atoms and determining the number of hydrogen atoms attached to each carbon.
- Use **solid wedges and dashed wedges** to represent the three-dimensional orientation of bonds in a molecule.
- Explain how **R groups** are used as abbreviations for portions of organic molecules and recognize R groups in generalized organic structures.

Molecular Formula

A ***molecular formula*** is the simplest way to represent a compound by counting up all of the different types of atoms and listing them in order. For example, the sugar glucose, contains 6 carbons, 12 hydrogens, and 6 oxygens. The molecular formula would then be written as $C_6H_{12}O_6$. By convention, carbon is listed first, hydrogen second, followed by oxygen, nitrogen, sulfur, phosphorus, and finally any halogens.

However, for organic chemistry, molecular formulae don't provide much information. They simply provide the numbers of each type of atom present in the molecule, but they tell you nothing about the way the atoms are joined together in space. For example, two molecules might have the same molecular formula, but a different arrangement of the atoms bonded in space, as is the case for the two sugars glucose and fructose. Both sugars have the molecular formula of $C_6H_{12}O_6$. However, you can see from Figure 6.2.1, that they are different molecules with different properties, because the atoms are linked together in a different order. Molecules that share the same molecular formula but have their atoms bonded in a different order are called ***isomers***. Due to the complexity of isomer structures, molecular formulae not as useful in organic chemistry, because they do not give complete information about the bonding order within the molecule.

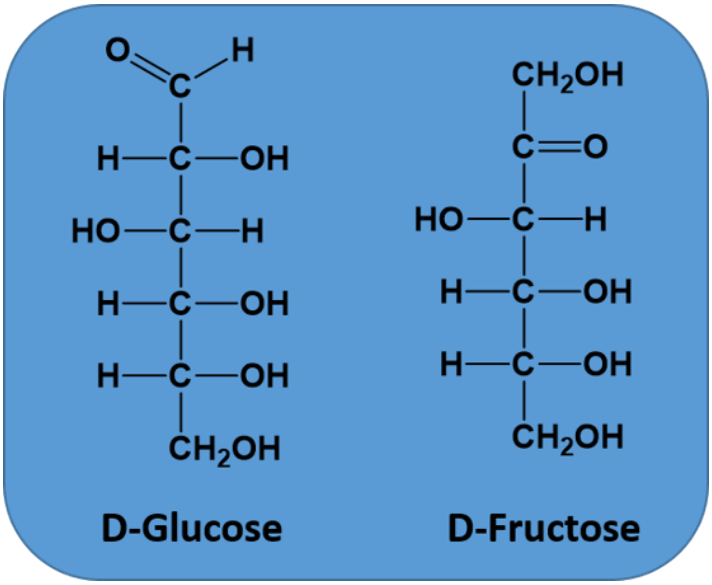


Figure 6.2.1**: Structural Isomers**. When molecules, such as D-Glucose and D-Fructose, share the same molecular formula, but have a different atomic bonding order they are called structural isomers.

Structural formulae and 3-dimensional models

A structural formula shows how the various atoms are bonded, and can be more useful that only writing the molecular formula for a compound. There are various ways of drawing structural formulae and you will need to be familiar with all of them. They include the ***displayed formula, condensed formulas***, and ***line structures***.

Displayed formulae

A ***displayed formula*** shows all the bonds in the molecule as individual lines with each atom written at the end of each line using its elemental abbreviation from the periodic table. The structures of $C_6H_{12}O_6$, above, are all written in ***displayed formulae.*** You need to remember that each line represents a pair of shared electrons. For example, figure 6.2.2 below depicts the displayed formula of methane next to the three-dimensional representations.

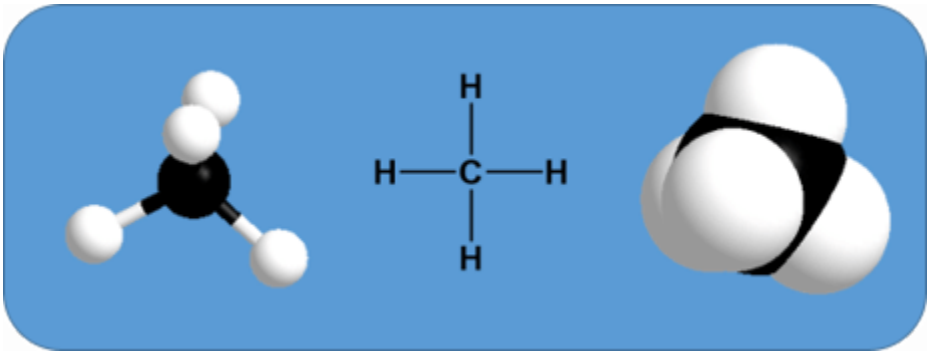
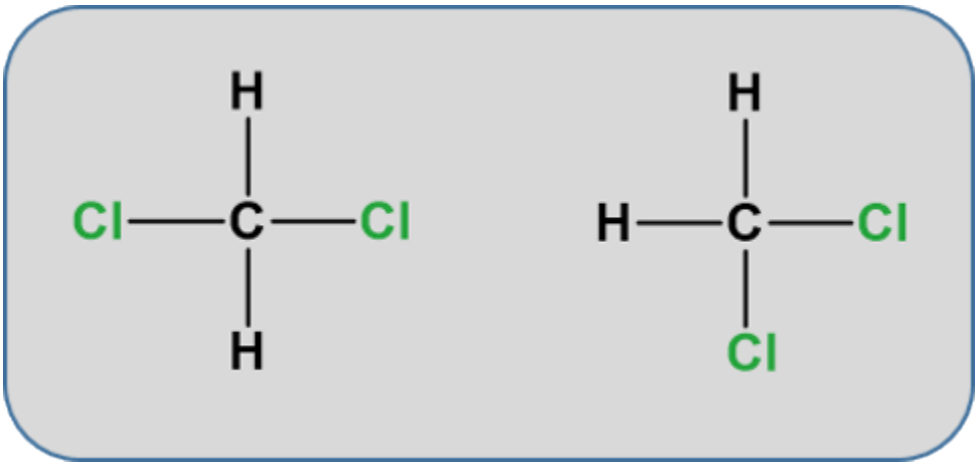


Figure 6.2.2**: Three different representations of CH_4** On the left is the ball and stick model, in the center is the displayed formula, and to the right is the space-filling model.

Notice that the displayed formula of methane does not represent the 3-D shape of the molecule shown in the space-filling diagram on the right. Methane isn't flat with 90° bond angles. This mismatch between what you draw and what the molecule actually looks like can lead to problems if you aren't careful. Thus, for organic chemistry, it is important to begin thinking about the structures in their 3-D form. The more you practice, the more you will be able to visualize and turn the molecule around in your head. For example, consider the simple molecule with the molecular formula CH_2Cl_2. You might think that there were two different ways of arranging these atoms if you drew a displayed formula (Figure 6.2.3 upper panel).



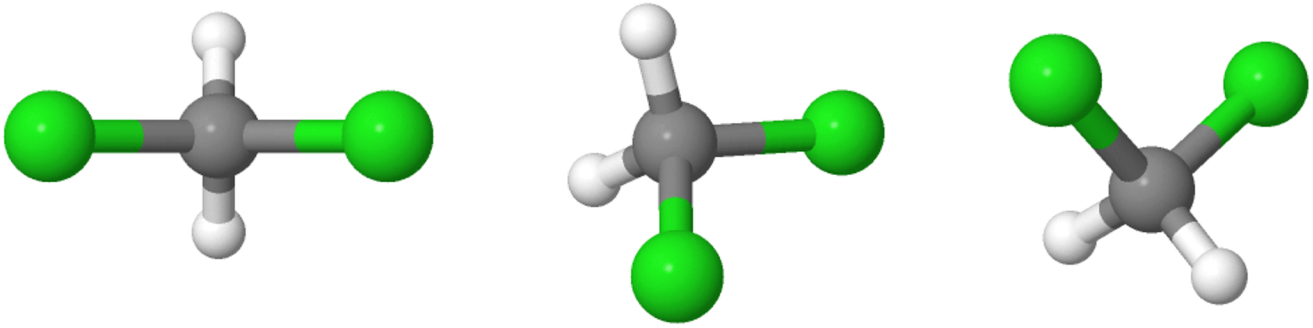


Figure 6.2.3: Displayed formula and 3-D ball and stick model of dichloromethane (CH_2Cl_2). The upper panel shows two drawn versions of the displayed representations of CH_2Cl_2. The lower panel shows the ball and stick model of CH_2Cl_2 in three different rotated views. All representations presented in this diagram are of the same molecule drawn from differing perspectives.

But these two structures are actually exactly the same. When carbon atoms have four bonds, they take on tetrahedral molecular geometry where each bond angle is 109.5°. The molecule is not flat, in the plane of the paper. When the 3-D ball-and-stick model is rotated, it becomes clear that the two displayed formulas simply represent different views of the same molecule.

Consider a slightly more complicated molecule, C_2H_5Cl. The displayed formula is shown in Figure 6.2.4 upper panel. At first glance, they may appear as different molecules. However, closer inspection of the 3-D ball-and-stick models show that they are merely different representations of the same molecule.

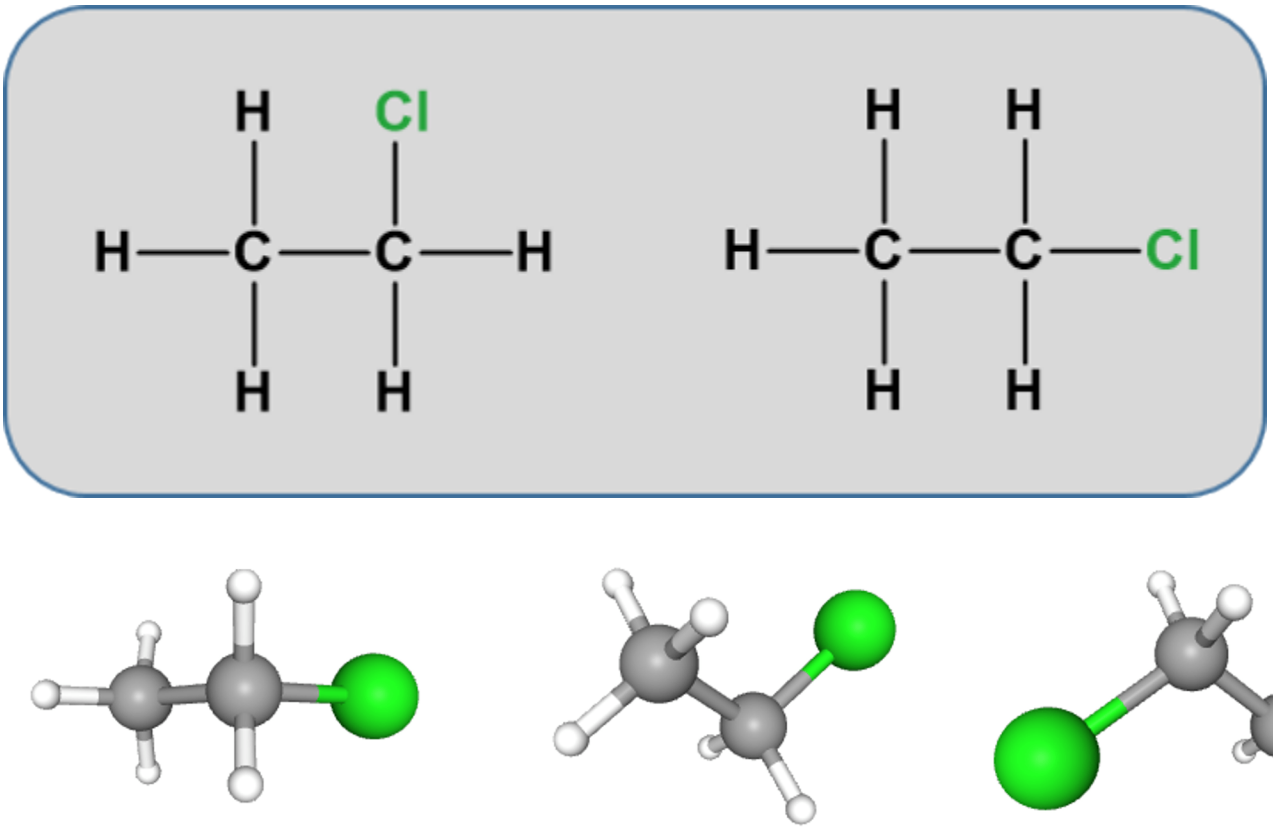


Figure 6.2.4: Displayed formula and 3-D ball and stick model of chloroethane (C_2H_5Cl). The upper panel shows two drawn

versions of the displayed representations of C_2H_5Cl. The lower panel shows the ball and stick model of C_2H_5Cl in three different rotated views. All representations presented in this diagram are of the same molecule drawn from differing perspectives.

As you continue to practice drawing out structural formulae, you will become better at recognizing and distinguishing between isomers that are truly different from one another, and versions of the same molecule written drawn from different 3-dimensional perspectives.

Condensed formulae

For anything other than the most simple molecules, drawing a fully displayed formula can be cumbersome and take up too much space - especially all the carbon-hydrogen bonds. You can simplify - or *condense* - the formula by writing, for example, CH_3 or CH_2 instead of showing all the C-H bonds. For example, ethanoic ($C_2H_4O_2$) acid can be shown in a fully displayed form, a partially condensed form and a fully condensed form (Figure 6.2.5).

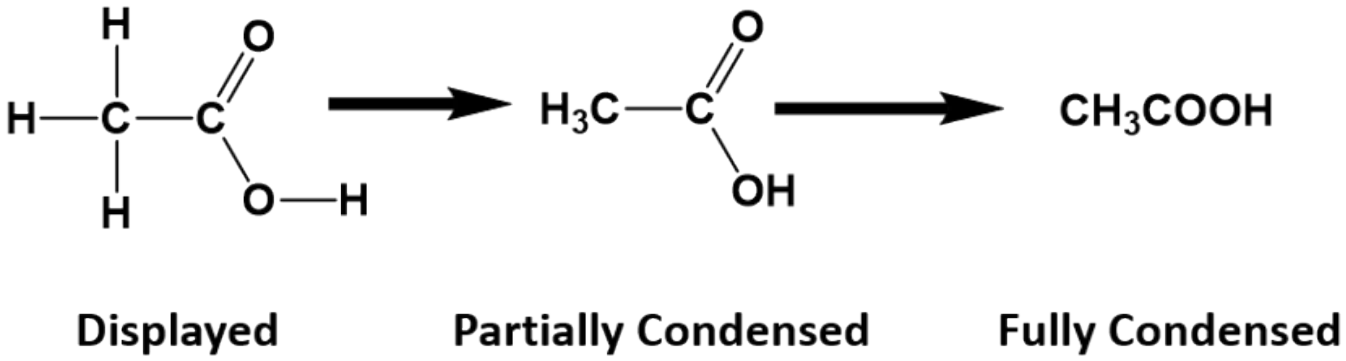
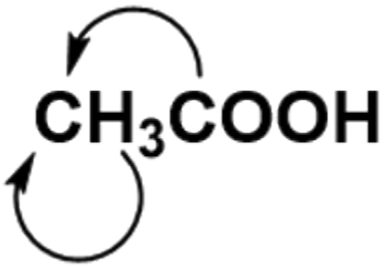


Figure 6.2.5: Organic example of displayed, partially condensed, and fully condensed structures.

Notice that the partially condensed structure still provides a very clear picture of where each of the atoms is bonded in space. However, with the fully condensed structure, it can be challenging to accurately see the bonding patterns. The fully condensed form does contain more information about bonding order than the molecular formula, such that the atoms that are directly bonded to a neighboring atom are placed adjacent to that atom in the condensed form, rather than a simple tallying of the total atom species as in the molecular formula.

By working backwards, we can use the condensed structure of ethanoic acid as an example to recreate the partially condensed structure. When looking at the first carbon position, it is apparent that there are three hydrogens and one carbon bound to the first carbon:



Note that this satisfies the octet rule for the first carbon (four bonds to other atoms). The three hydrogens are also complete with their single bonds to the first carbon. The second carbon has now been assigned one bond to the first carbon. We need to assign the remaining three bonds.

From the condensed formula, it is clear that the first oxygen is attached to the second carbon, however, after that, we become unsure about the position of the second oxygen.



We can clearly deduce that the last hydrogen atom is bound to the second oxygen, as it is placed in that position. However, because oxygen can form two bonds, we can't be sure based on the condensed structure alone, that the second oxygen is bound to the second carbon or to the first oxygen.

When you are unsure of which atom is bonded to which, it is best to draw out the potential structures and evaluate them for their potential correctness.

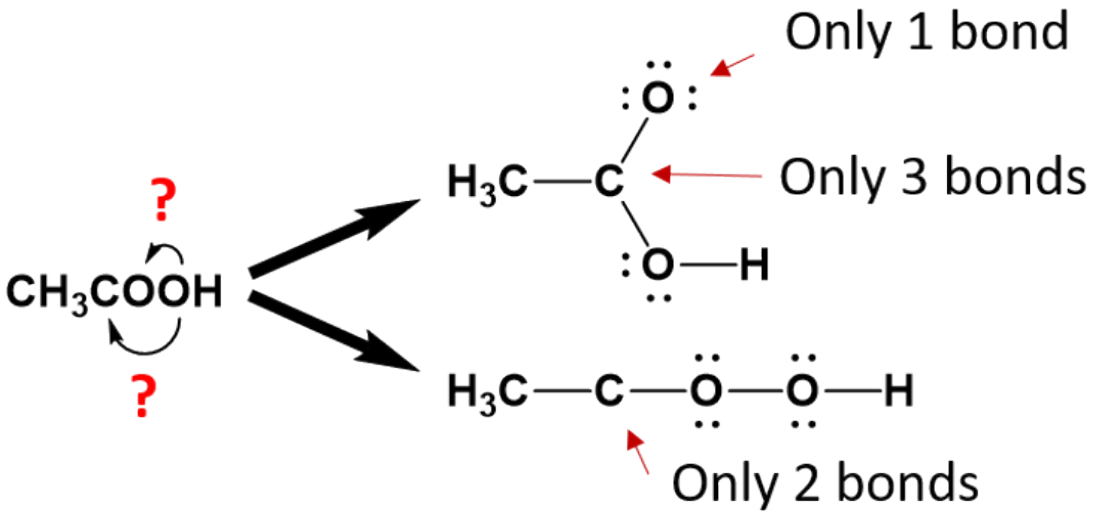
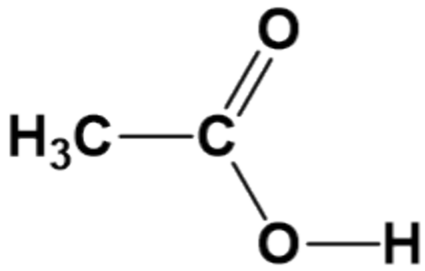


Figure 6.2.6**: Testing Possible Lewis Structures.** When reconstructing the structure of a molecule, more than one arrangement of atoms may initially seem possible. Drawing the different possibilities and applying the octet rule can help determine which arrangement is chemically reasonable. In the upper pathway, the two atoms indicated can complete their octets by forming a double bond, producing a valid Lewis structure. In the lower pathway, the proposed order of bonding does not allow all of the atoms to achieve complete octets. Comparing possible structures in this way can help identify the most reasonable arrangement of atoms in a molecule.

From the analysis of the potential structures above, it is clear that neither structure satisfies the octet rule for one or more atoms within the molecule as currently written. However, the lower structure is less satisfactory than the upper structure, as the second carbon is missing 2 covalent bonds while all of the other atoms have satisfied the octet bonding requirements. In the upper diagram, both the second carbon and the first oxygen atom are lacking one bond. This structure can easily satisfy the octet rule by placing a double bond between carbon 2 and oxygen 1 within the molecule. Whereas, a solution for the missing two carbon bonds for the second carbon in the lower structure is not easily remedied. Thus, the upper structure is a more probable structure than the lower structure with the addition of the double bond between the carbon and the oxygen.



While condensed structures are easier to write than displayed or partially condensed structures they can prove to be a little more challenging to determine the three dimensional bonding pattern of the atoms.

Line or Skeletal Formulae

In a *line or skeletal formula*, all the hydrogen atoms are not shown and all the carbons are not labeled but rather are indicated at the end or bend in every line, leaving just a carbon skeleton with functional groups attached to it. Any *heteroatoms* (any other atom than carbon or hydrogen) and hydrogens attached to heteroatoms are shown in condensed form. For example, the displayed structure, partially condensed structure and the line formula for 2-butanol ($C_4H_{10}O$) look like this:

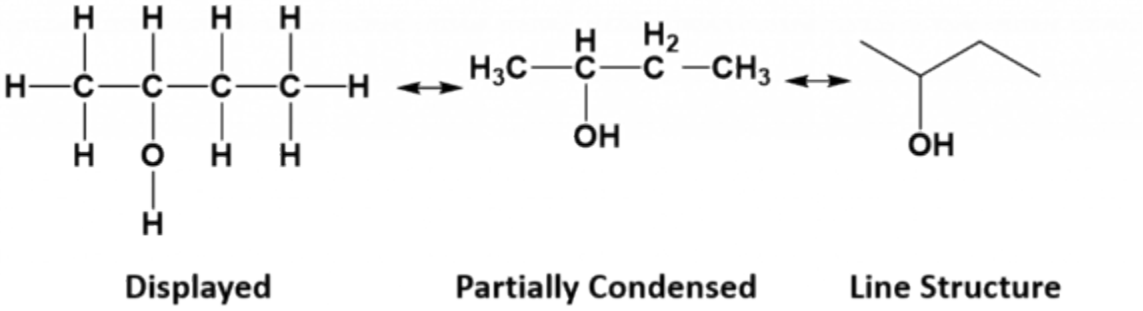


Figure 6.2.7**: Different ways of representing the same molecule**. The far left panel shows the displayed formula for 2-butanol, whereas the middle panel shows the partially condensed structure and the right panel shows the line (or skeletal) structure.

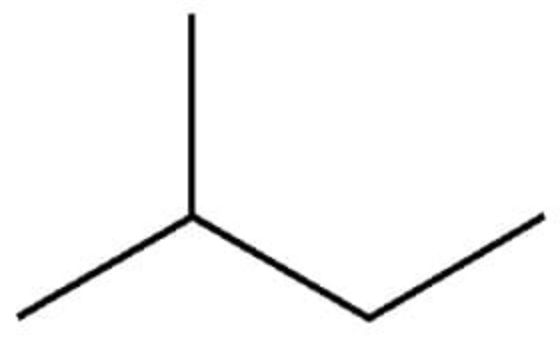
In a line or skeletal diagram, the following assumptions can be made:

- there is a carbon atom at each line junction and at the end of each line.
- there are enough hydrogen atoms attached to each carbon to make the total number of bonds on that carbon equal to 4.
- all heteroatoms (and hydrogens attached to heteroatoms) are shown in condensed format on the skeletal structure.

Within organic chemistry and biochemistry, scientists tend to use a combination of these different formats to represent chemical structures. It is important to become familiar with drawing and interpreting all the different possible representations.

Example 6.2.1

Here is a skeletal structure of an organic molecule:



Determine the molecular formula.

Solution

Step 1: Count the carbon atoms.
Remember that every endpoint and every corner in a skeletal structure represents a carbon atom. There are **5 carbon atoms**.

Step 2: Determine the number of hydrogen atoms attached to each carbon.
Carbon forms four bonds. Count the bonds already shown to each carbon and determine how many additional bonds to hydrogen are needed to give each carbon four bonds.

For this molecule, the carbons contain:

- three terminal carbons with **3 H each**
- one carbon with **1 H**
- one carbon with **2 H**

Step 3: Add the atoms together.

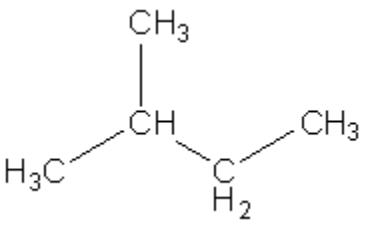
There are 5 carbon atoms and:

3+3+3+1+2=12 hydrogen atoms

Therefore, the molecular formula is:

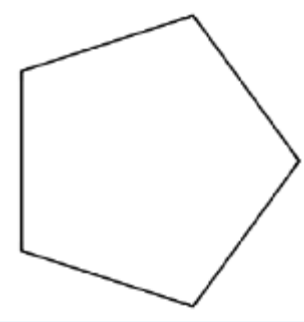
C_5H_{12}

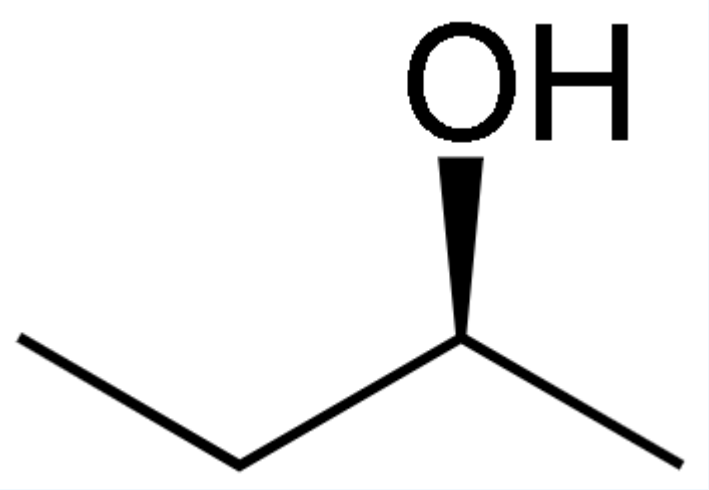
To double check your work, draw the displayed or partially displayed structure:



Exercise 6.2.1

Practice determining the molecular formula of the following compounds:

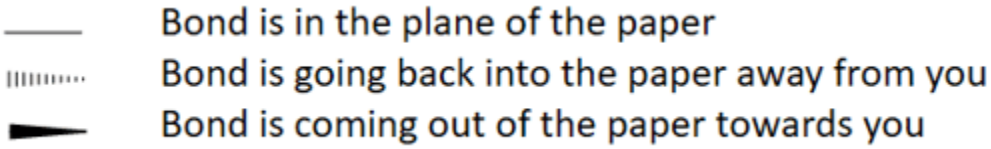
1. 

2. 

Answer available at the end of this section.

How to draw structural formulae in 3-dimensions

There are occasions when it is important to be able to show the precise 3-D arrangement in parts of some molecules when using a structural representation. To do this, the bonds are shown using conventional symbols:



A simple line indicates that the bond is in the plane of the paper, whereas a solid wedge indicated that it is coming out towards you, and a dashed wedge indicates that the bond is going back into the paper away from you.

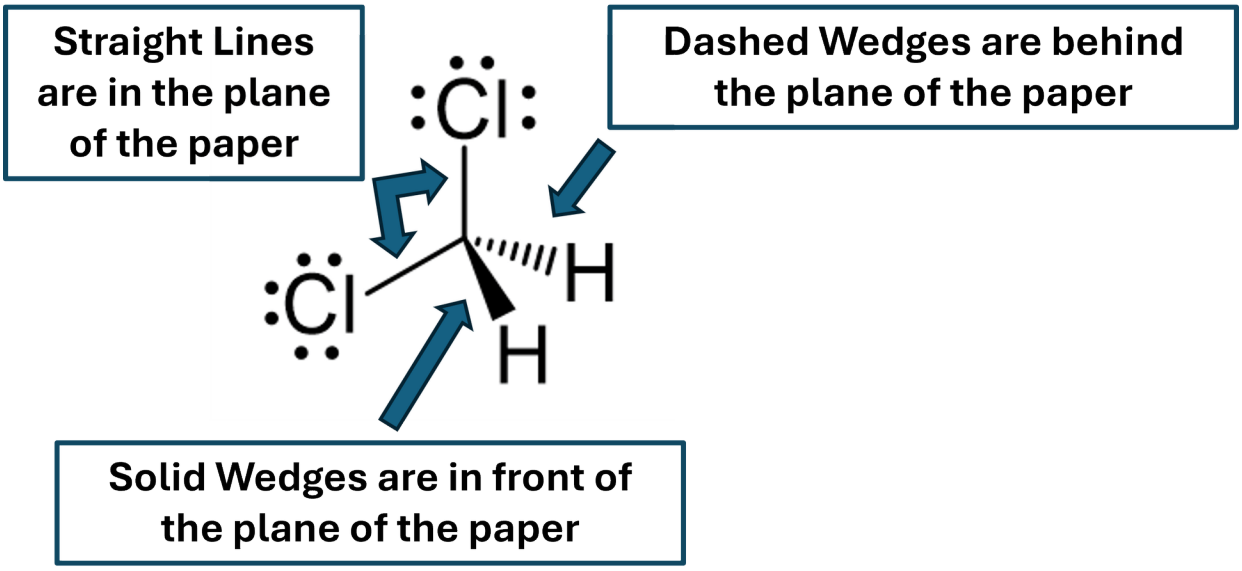


Figure 6.2.8: Using wedges and dashes to indicate 3-dimensional structure. In dash-wedge models, straight lines are in the plane of the paper, dashed wedge lines are behind the plane of the paper, and solid wedge lines are in front of the plane of the paper.

Drawing abbreviated organic structures

Often when drawing organic structures, chemists find it convenient to use the letter **'R'** to designate part of a molecule outside of the region of interest. If we just want to refer in general to a functional group without drawing a specific molecule, for example, we can use **'R groups'** to focus attention on the group of interest as shown in Figure 6.2.9.

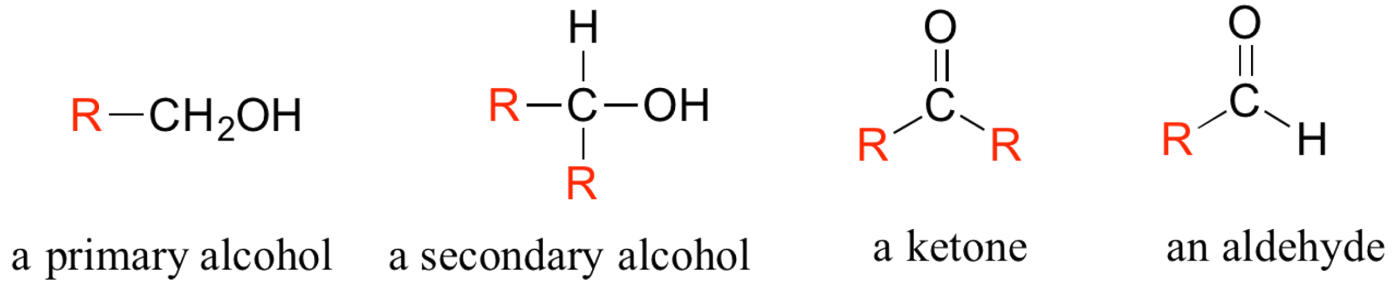


Figure 6.2.9: Using R Groups to Represent Carbon-Containing Structures. The letter **R** is commonly used in organic chemistry as an abbreviation for a carbon-containing portion of a molecule that is not the focus of the structure being shown. An R group may represent a simple carbon group or a much larger and more complex carbon-containing structure. Using R groups allows chemists to emphasize a particular structural feature or functional group without drawing the remainder of the molecule in detail.

The R group is a convenient way to abbreviate the structures of large biological molecules, especially when we are interested in something that is occurring specifically at one location on the molecule. For example, in chapter 15 when we look at biochemical oxidation-reduction reactions involving the flavin molecule, we will abbreviate a large part of the flavin structure (ie. R = FAD) which does not change at all in the reactions of interest.

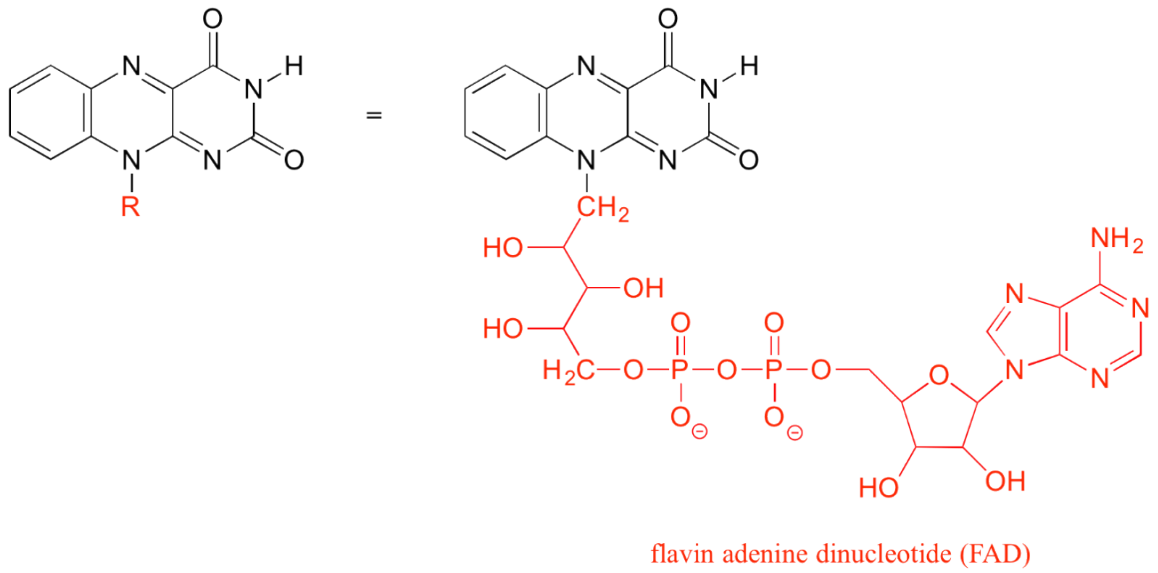


Figure 6.2.10**: Using an R Group to Abbreviate a Large Portion of a Molecule**. An **R group** can represent a large and complex carbon-containing portion of a molecule when that portion is not the focus of the structure or reaction being discussed. In this example, the complex flavin adenine dinucleotide (FAD) structure can be represented simply as **R**, allowing attention to remain focused on the chemically important region of the molecule.

As an alternative to using an R group, chemists sometimes use **continuation marks** to indicate that only a small portion of a much larger molecule is being shown. Short rippled lines at the ends of the structure indicate that the molecule **continues beyond the portion drawn**.

This type of abbreviation is especially useful when focusing on a particular region within a large molecule or polymer. For example, a small portion of a protein or DNA molecule may be drawn while the remainder of the much larger structure is omitted. The continuation marks remind us that the atoms shown are connected to the rest of the molecule.

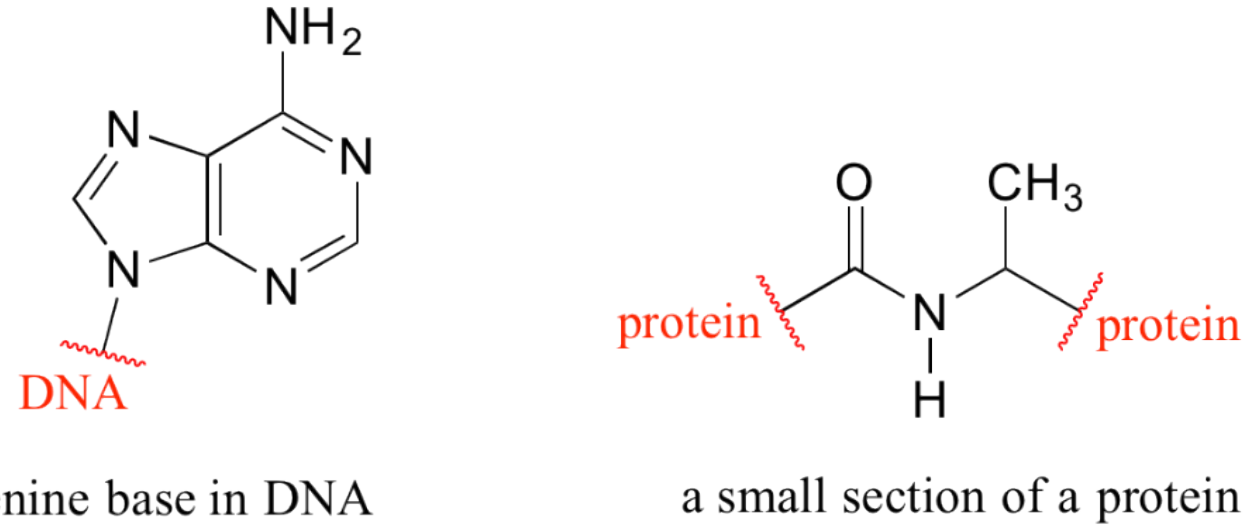


Figure 6.2.10**: Using Continuation Marks to Show Part of a Larger Molecule**. Continuation marks at the ends of a chemical structure indicate that only a portion of a larger molecule is being shown. In these examples, the displayed structures represent small regions within much larger **DNA** or **protein** molecules. The lines extending from the structures indicate that the molecular chain continues beyond the portion shown.

Finally, R groups can be used to concisely illustrate a series of related compounds, such as families of related drug structures that are being tested for biological activity. Figure 6.2.11 shows some common members of penicillin-based antibiotics.

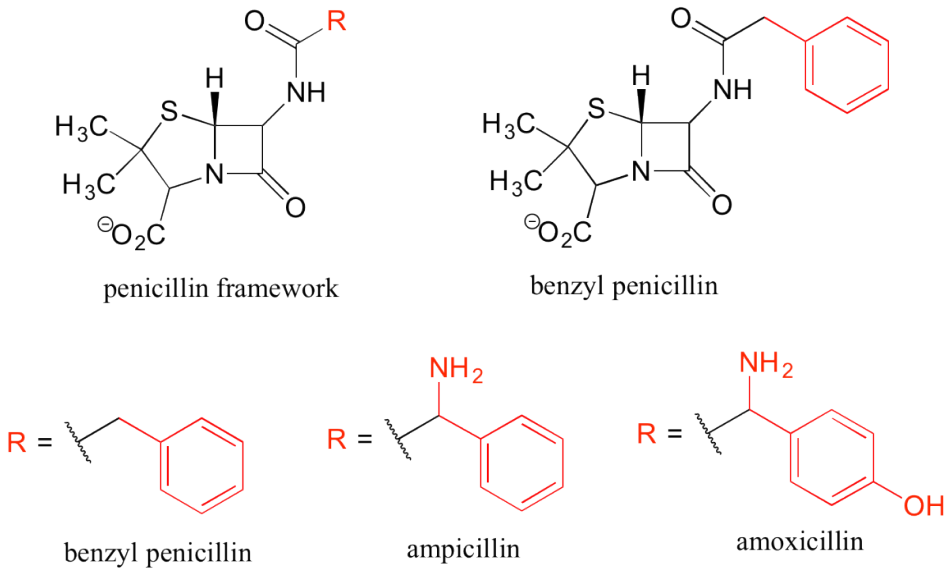


Figure 6.2.11: Using R Groups to Represent Variations within a Family of Related Compounds. R groups can be used to highlight the portion of a molecular structure that varies among a series of related compounds. The common portion of the structure remains the same, while different chemical groups can occupy the position labeled **R**. This notation allows chemists to compare related molecules efficiently and is particularly useful when developing and testing families of related drug compounds.

Using abbreviations appropriately is a very important skill to develop when studying organic chemistry in a biological context, because although many biomolecules are very large and complex (and take forever to draw!), usually we are focusing on just one small part of the molecule where a change is taking place.

As a rule, *you should never abbreviate any atom involved in a bond-breaking or bond-forming event that is being illustrated:* only abbreviate that part of the molecule which is not involved in the reaction of interest.

Key Idea

- **R group** → *"There is some carbon-containing structure attached here, but its identity isn't important right now."*
- **Continuation marks** → *"This is part of a much larger molecule, and the structure continues beyond what we're showing."*

Answers

Exercise 6.2.1

1. C_5H_{10}
2. $C_4H_{10}O$

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6.3: Hydrocarbons- Building the Carbon Skeleton

Learning Objectives

After completing this section, you should be able to:

- Define a **hydrocarbon** and identify structures composed only of carbon and hydrogen.
- Distinguish among **alkanes, alkenes, and alkynes** based on the types of carbon–carbon bonds present.
- Distinguish between **saturated and unsaturated hydrocarbons**.
- Recognize straight-chain, branched, cyclic, and **aromatic** hydrocarbon structures.
- Explain how carbon–carbon double bonds restrict rotation and can produce **cis/trans isomers**.
- Relate differences in hydrocarbon structure to differences in molecular shape and biological properties.

Hydrocarbons Contain Only Carbon and Hydrogen

As we learned earlier in this chapter, **hydrocarbons** are organic compounds composed entirely of carbon and hydrogen. Although this sounds like a very simple combination of elements, carbon atoms can connect in many different ways, producing an enormous variety of structures.

Hydrocarbons may contain straight carbon chains, branched chains, rings, or combinations of these structures. In addition, the carbon atoms may be connected by single, double, or triple covalent bonds.

Hydrocarbons are also useful for understanding more complex biological molecules. Many biologically important molecules are not themselves hydrocarbons because they contain oxygen, nitrogen, phosphorus, sulfur, or other heteroatoms. However, they often contain **hydrocarbon regions** consisting primarily of carbon and hydrogen.

Recall from our discussion of electronegativity that carbon and hydrogen have relatively similar electronegativities. As a result, C–C and C–H bonds are largely nonpolar. Hydrocarbon regions therefore tend to be **nonpolar and hydrophobic**, meaning that they do not interact strongly with water.

This property becomes extremely important in biological systems. The long hydrocarbon chains found in many lipids, for example, help create the hydrophobic interior of cell membranes.

Alkanes: Hydrocarbons with Single Bonds

Hydrocarbons in which all of the carbon atoms are connected by **single bonds** are called **alkanes**.

Methane, which we encountered earlier in this chapter, is the simplest alkane.

CH_4

Additional carbon atoms can be connected to create progressively longer carbon chains:

- methane — 1 carbon
- ethane — 2 carbons
- propane — 3 carbons
- butane — 4 carbons

You do not need to memorize long lists of hydrocarbon names. More importantly, you should be able to **recognize the structural pattern**: an alkane contains only C–C single bonds.

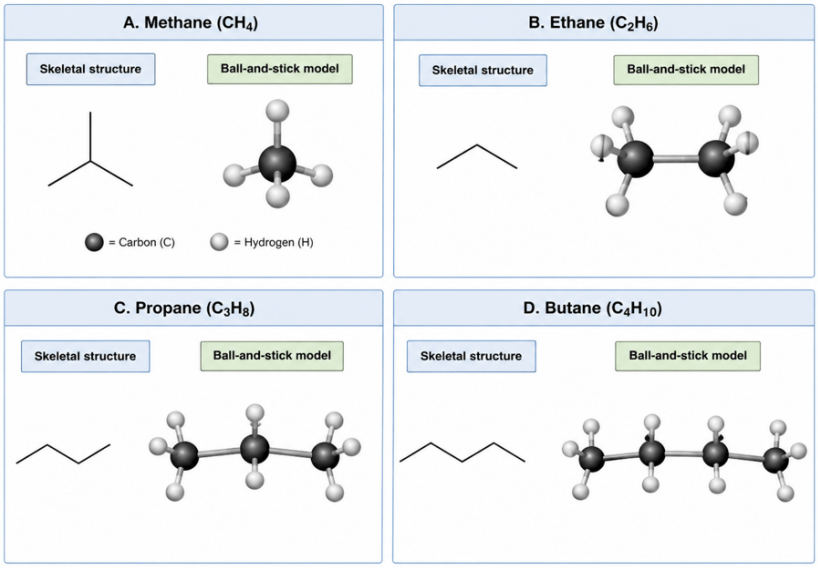


Figure 6.3.1**: Simple alkanes**. Skeletal structures (left) and ball-and-stick models (right) of the first four alkanes: methane (A), ethane (B), propane (C), and butane (D). In skeletal structures, each line end and corner represents a carbon atom, and hydrogen atoms attached to carbons are not shown.

Alkanes are described as **saturated hydrocarbons**. A saturated carbon skeleton contains the maximum number of hydrogen atoms possible for that particular arrangement of carbon atoms.

For example, examine ethane:

$CH_3–CH_3$

Each carbon forms one bond with another carbon and three bonds with hydrogen, giving each carbon a total of four covalent bonds.

Because single carbon–carbon bonds can rotate, alkane chains are also relatively flexible. A long carbon chain should therefore not be imagined as a rigid, straight rod. The molecule can bend and adopt many different three-dimensional shapes as its carbon–carbon single bonds rotate. **Conformers (conformations)** are different three-dimensional arrangements of the **same molecule** that result from rotation around single bonds. No bonds need to be broken for one conformer to change into another, and molecules can rapidly move between many different conformations.

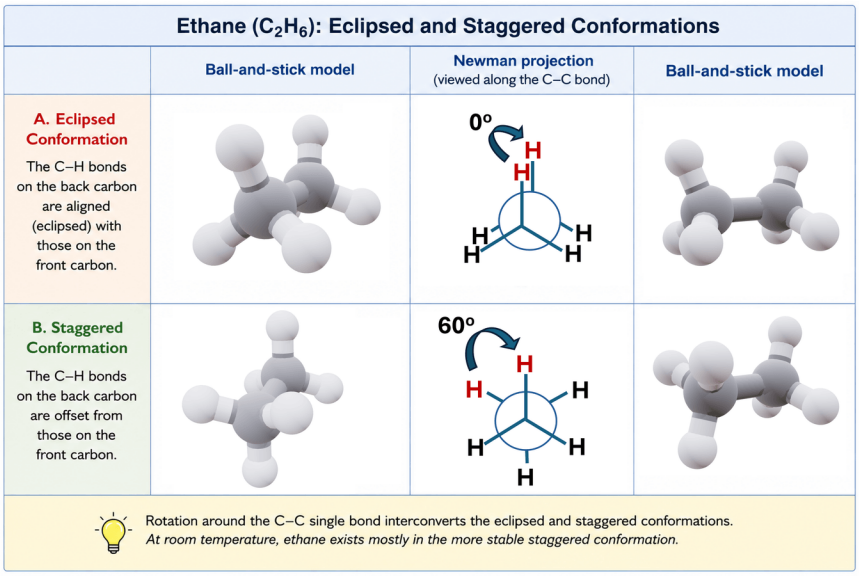


Figure 6.3.2**: Rotation Around the Carbon–Carbon Single Bond in Ethane**. Rotation around the carbon–carbon single bond allows ethane to adopt different three-dimensional arrangements, or **conformations**. The eclipsed and staggered conformations are shown from two different perspectives using ball-and-stick models. The center images use a **Newman projection**, a simplified way of viewing a molecule directly down a carbon–carbon bond: the front carbon is represented by the point where three bonds meet, while the back carbon is represented by the circle. As the C–C bond rotates, the hydrogen atoms move between aligned (**eclipsed**) and offset (**staggered**) positions without breaking any covalent bonds.

Carbon Skeletons Can Be Straight, Branched, or Cyclic

Carbon atoms do not have to form a single unbranched chain. Carbon skeletons can have several different arrangements.

A **straight-chain** or **unbranched** hydrocarbon contains carbon atoms connected in one continuous chain.

A **branched hydrocarbon** contains one or more carbon groups extending away from the main chain.

Carbon chains can also connect back onto themselves to form **rings**. Hydrocarbons containing carbon atoms arranged in rings are called **cyclic hydrocarbons**.

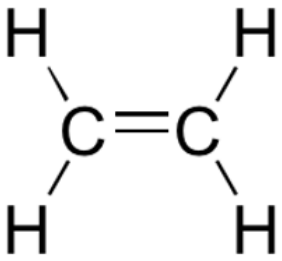
For example, cyclohexane contains six carbon atoms joined together in a ring.

Although a six-membered carbon ring is often represented as a flat hexagon on paper, remember that molecules are three-dimensional. The actual atoms in cyclohexane do not all lie within the same flat plane.

Straight chains, branched chains, and rings occur throughout biological chemistry. The arrangement of the carbon skeleton helps determine the overall **size and shape of a molecule**, which can influence how it interacts with other molecules.

Alkenes and Alkynes:

Alkenes (sometimes called olefins) have carbon-carbon double bonds, and *alkynes* have carbon-carbon triple bonds. Ethene, the simplest alkene example, is a gas that serves as a cellular signal in fruits to stimulate ripening. (If you want bananas to ripen quickly, put them in a paper bag along with an apple - the apple emits ethene gas (also called ethylene), setting off the ripening process in the bananas). Ethyne, commonly called acetylene, is used as a fuel in welding blow torches.



ethene
(an alkene)



ethyne
(an alkyne)

Unlike alkanes, alkenes and alkynes are **unsaturated hydrocarbons**. The carbon atoms participating in the double or triple bond do not contain the maximum possible number of hydrogen atoms. The terms *saturated* and *unsaturated* may already be familiar from nutrition labels. Saturated and unsaturated fats receive their names from the types of carbon–carbon bonds present within their fatty acid chains. We will explore these molecules in greater detail later in this course.

As noted in section 6.1, carbon–carbon double and triple bonds also affects molecular shape. Recall that single bonds allow considerable rotation. A carbon–carbon double or triple bond, however, **restricts rotation**. The atoms attached to the double-bonded carbons are therefore held in more fixed positions relative to one another. This restriction becomes biologically important because it can change the overall shape of a molecule.

Recall that each carbon atom involved in a carbon–carbon double bond has **trigonal planar geometry**, with bond angles of approximately 120°. In alkynes the atoms surrounding the C≡C bond are arranged in a **linear geometry**, producing a bond angle of approximately 180°. Alkynes are less common in the major biological molecules than alkanes and alkenes, but they occur in some natural products and other biologically active compounds. For this course, the most important skill is simply being able to recognize a **C≡C triple bond** and identify the molecule as an alkyne.

Cis and Trans Isomers

Because carbon–carbon double bonds restrict rotation, some alkenes can exist in two different spatial arrangements.

Consider a double bond in which each carbon is attached to two different groups. The groups attached to the double bond cannot simply rotate from one position to another without disrupting the double bond. This makes it possible for two molecules to have the same atoms connected in the same order but differ in how those groups are arranged in space.

These structures are called **geometric isomers**. Two common geometric arrangements are described as **cis** and **trans**. In a **cis isomer**, similar groups are located on the **same side** of the double bond. In a **trans isomer**, similar groups are located on **opposite sides** of the double bond.

For example, 2-butene can exist in both cis and trans forms.

cis-2-butene: the two CH_3 groups are on the same side of the C=C bond and the two Hydrogens are also on the same side of the double bond.

trans-2-butene: the two CH_3 groups are on opposite sides of the C=C bond and the two Hydrogens are also on opposite sides of the double bond.

Importantly, not every carbon–carbon double bond can produce cis and trans isomers. For these two arrangements to be possible, **each carbon of the double bond must be attached to two different groups**. Ethene, shown in the previous section, cannot

form cis-trans isomers because each carbon of the double bond is attached to two identical hydrogen atoms.

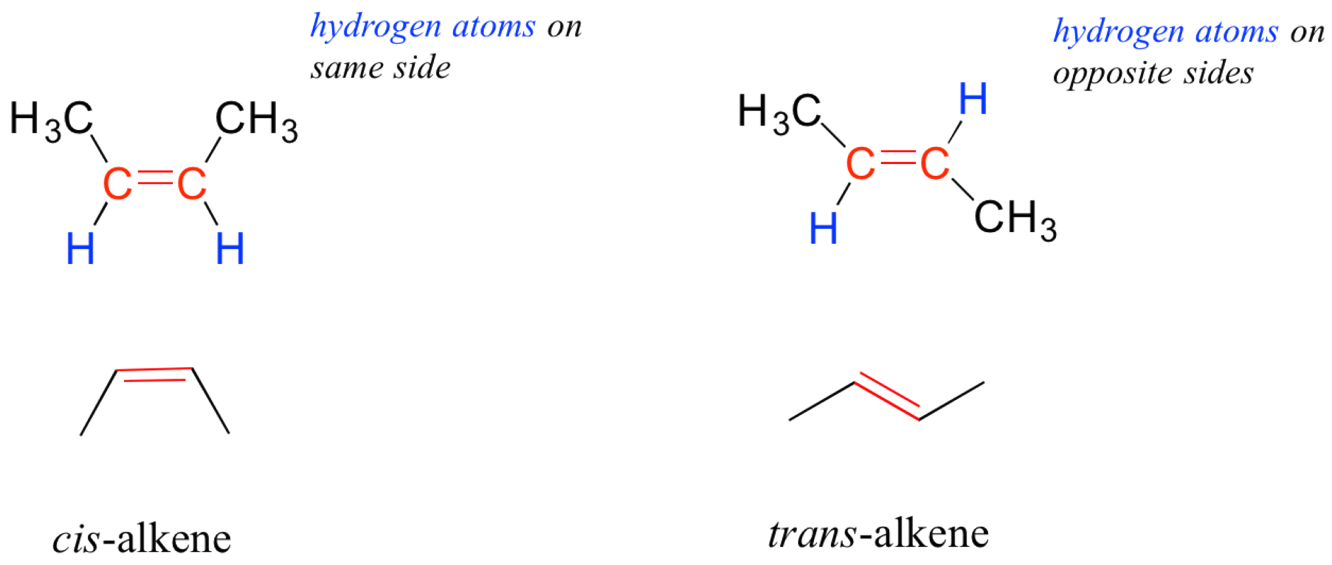


Figure 6.3.3: Cis and Trans Isomers of 2-Butene. The carbon–carbon double bond in 2-butene restricts rotation, allowing two different spatial arrangements. In the **cis isomer**, the hydrogen atoms are located on the same side of the double bond, while in the **trans isomer**, the hydrogen atoms are positioned on opposite sides. Although the two molecules have the same molecular formula and bonding arrangement, their different three-dimensional structures make them distinct stereoisomers.

The difference between cis and trans structures is not merely a difference in how we draw the molecules. The arrangement around a double bond can change the **three-dimensional shape** of a molecule. This is particularly important in fatty acids, which we will review in more detail in chapter 7.

Key Idea

- **Small changes in molecular structure can produce important changes in molecular shape and biological behavior.**

Aromatic Rings: A Special Carbon Skeleton

Another important carbon skeleton is the **aromatic ring**. The **aromatic group** is exemplified by benzene (which was once commonly used as a solvent in organic chemistry laboratories but is now known to be carcinogenic) and naphthalene, a compound with a distinctive "mothball" smell. Aromatic groups are planar (flat) ring structures and are widespread in nature. Benzene is commonly drawn as a six-membered ring with **alternating single and double bonds**. However, the electrons involved in the double bonds are actually **delocalized**, or shared across the entire ring, rather than being confined to specific bonds. The two possible arrangements of the alternating double bonds are called **resonance structures** and represent the same molecule, not two different forms of benzene. For this reason, benzene may also be drawn as a hexagon containing a circle, which represents the delocalized electrons within the ring.

Both representations are used to indicate the same aromatic ring system. The delocalization of electrons across the aromatic ring makes these structures unusually stable compared with other alkene molecules containing localized double bonds. For now, the important skill is to **recognize an aromatic ring when you see one**.

A benzene ring is often called a **phenyl group** when it appears as part of a larger molecule. Aromatic rings are extremely common in biological and medicinal chemistry. They occur within some amino acids, hormones, neurotransmitters, vitamins, natural products, and many medications.

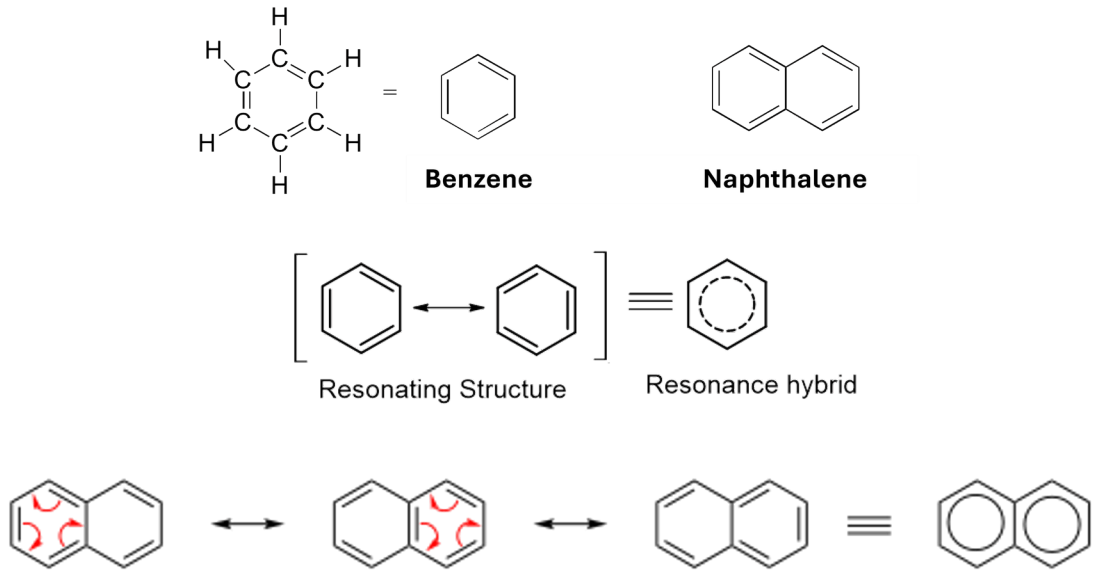


Figure 6.3.4: Aromatic Ring Structures and Resonance. Benzene contains a single six-membered aromatic ring, while naphthalene contains two fused aromatic rings. The two resonance structures of benzene show different possible placements of the alternating double bonds; however, the electrons are actually **delocalized throughout the aromatic ring**. The circle within the benzene ring represents this resonance hybrid and the delocalization of electrons that gives aromatic structures additional stability. The lower diagram shows the delocalization pattern in the double aromatic ring system of naphthalene. Sources: Benzene Resonance and Naphthalene Resonance.

Recognizing the Major Types of Hydrocarbons

Rather than memorizing individual hydrocarbon structures, look first at the **bonds between the carbon atoms** and the overall shape of the carbon skeleton. Hydrocarbons can contain straight chains, branched chains, or rings, and the types of carbon–carbon bonds present help us classify them.

- **Alkanes** contain only carbon–carbon single bonds. Their carbon skeletons may be straight, branched, or cyclic. Because they contain only single bonds, alkanes are described as **saturated hydrocarbons**.
- **Alkenes** contain at least one carbon–carbon double bond (C=C). They are **unsaturated hydrocarbons** and may also contain straight or branched carbon skeletons or occur within ring structures.
- **Alkynes** contain at least one carbon–carbon triple bond (C≡C). Like alkenes, they are **unsaturated hydrocarbons**.
- **Cyclic hydrocarbons** contain carbon atoms joined together to form a ring. Rings can contain carbon–carbon single or double bonds, so a cyclic structure may be saturated or unsaturated.
- **Aromatic hydrocarbons** contain one or more aromatic rings that have alternating carbon-carbon single and double bonds. The electrons within an aromatic ring are delocalized across the ring, giving these structures additional stability.

> When examining an unfamiliar hydrocarbon, begin by asking:
>
> **1. Is the carbon skeleton a chain, a branched chain, or a ring**?
>
> **2. What types of bonds connect the carbon atoms**?

Those two questions will allow you to recognize most of the hydrocarbon structures encountered in this course.

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6.4: Isomers and Chirality

Structural (or Constitutional) Isomers

As seen throughout this chapter, organic chemistry involves infinitely varied structures arising from how the atoms are assembled in 3-dimensional space. Providing only the molecular formula of a compound is often insufficient for defining the compound as many molecular formulas have numerous structural isomers. For example, the molecular formula C_2H_6O, a molecule of only 9 atoms, can refer to dimethyl ether or ethanol, depending on whether the oxygen is in the middle of or at the end of the carbon chain (Figure 6.4.1).

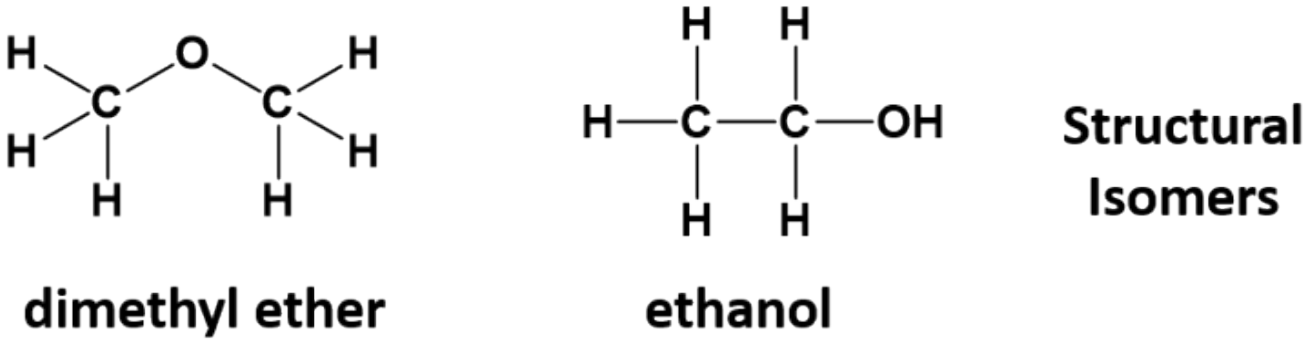


Figure 6.4.1**: Structural isomers of dimethyl ether and ethanol**. Both of these compounds have the same molecular formula of C_2H_6O.

Compounds that have the same molecular formula but differ in the order that the atoms are linked together are called ***structural (or constitutional) isomers***. Structural isomers have different physical and chemical properties. For example, ethanol is liquid at room temperature, whereas diethyl ether is a gas.

Stereoisomers

If the atoms of compounds with the same molecular formula are linked together in the same order, but their 3-dimensional arrangement in space differs, they are considered to be a special type of isomer called a ***stereoisomer***. The sugar molecules glucose and galactose are stereoisomers. This is in comparison to fructose, which is a structural isomer for both of these sugars, as it shares the same molecular formula, but a different arrangement of the bonded atoms (notably the carbon position double bonded to the oxygen is different) Whereas, glucose and galactose only differ in the spatial position of a single -OH group as indicated in the diagram below:

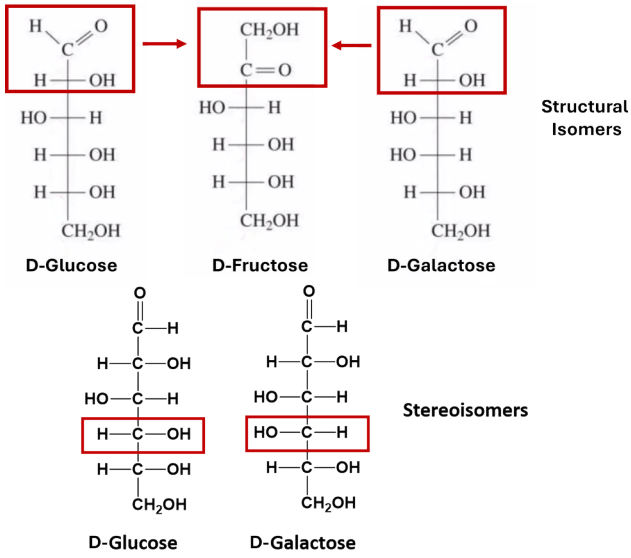


Figure 6.4.2**: Structural Isomers and Stereoisomers of Simple Sugars**. Glucose, fructose, and galactose all have the same molecular formula, $\mathbf{C_6H_{12}O_6}$, but differ in the arrangement of their atoms. *Upper diagram*: Glucose compared with fructose and galactose compared with fructose are **structural isomers** because their atoms are connected differently, including the position of the carbon-oxygen double bond position. *Lower diagram*: Glucose and galactose are **stereoisomers** because their atoms are connected in the same order but differ in the three-dimensional arrangement around one carbon atom, highlighted in the figure. These examples demonstrate that molecules with the same molecular formula can have distinctly different structures.

Enantiomers

There are a special kind of stereoisomers, called ***enantiomers***, that both have the same molecular formula, the same bonding order of atoms, are complete mirror images of each other, but are not superimposable. This means that no matter how you turn them in space that you can never put them on top of one another and recover the same compound. One example is 2-butanol which can be drawn as a pair of enantiomers (Figure 6.4.3)

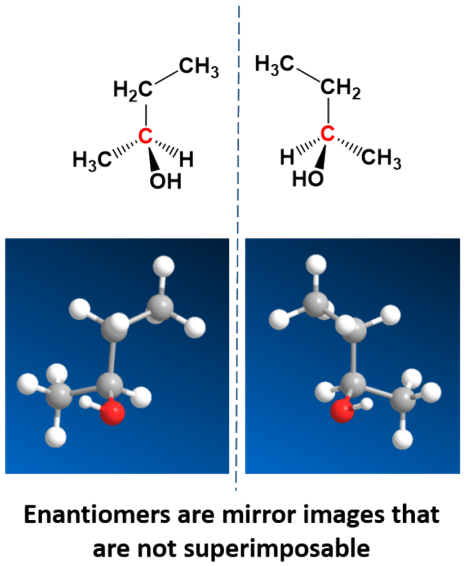


Figure 6.4.3**: The enantiomers of 2-butanol.** The enantiomers are shown in the 3-D structural formula displayed in the top diagram and the ball and stick model in the lower diagram.

Chirality

Enantiomers are said to have the property of ***chirality***. ***Chirality*** is the term that is given to objects that are mirror images but are not superimposable. The term 'chiral' is derived from the Greek word for 'handedness' – ie. right-handedness or left-handedness. Your hands are chiral: your right hand is a mirror image of your left hand, but if you place one hand on top of the other, both palms down, you see that they are not superimposable. (Fig 6.4.4). Thus chiral objects are mirror images of one another, but cannot be superimposed on top of one another. Carbon becomes chiral when it has four different substituents attached to it. You will notice in the example above that the central carbon has four different groups attached to it: an -OH group, an -H, a $-CH_3$, and a $-CH_2CH_3$ group.

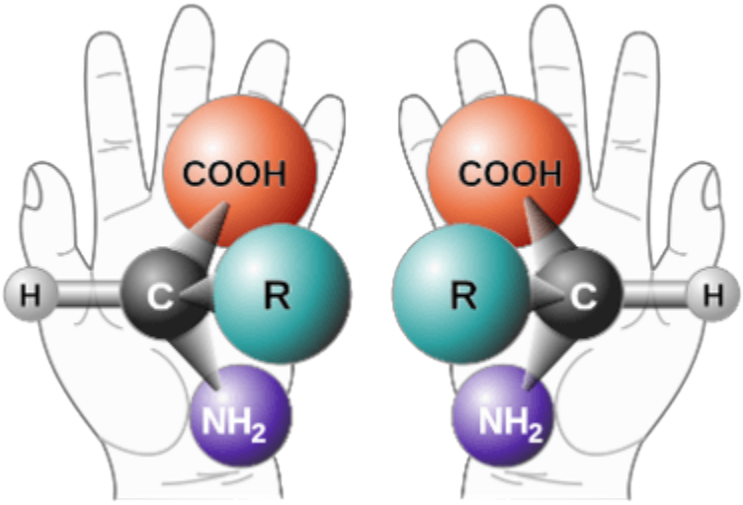


Figure 6.4.4**: The Nature of Chirality**. Carbon becomes chiral when it has four different substituents bonded to it. Any way you rotate the molecule on the left, you cannot superimpose it onto the molecule on the right. Source: Chirality with hands.jpg: Unknown derivative work: -- *περήλιο* Ⓟ - Chirality with hands.jpg.

Stereoisomers that are not enantiomers, such as glucose and galactose shown above, *do* have chiral centers and are not superimposable, but they are not mirror images of one another. Only stereoisomers that are also mirror images and not superimposable are termed *enantiomers*. *Enantiomers* are very hard to separate from one another. They are nearly identical in their physical and chemical properties. They have the same molecular weight, the same polarity, the same melting and boiling points, etc. In fact, enantiomers are so alike that they even share the same name! In Figure 5.14 the two enantiomers of 2-butanol are shown. Both of the molecules are 2-butanol. But they are *not* exactly the same molecule, in the same way that your left shoe is not *exactly* the same as your right. They are non-superimposable mirror images of each other. How do we communicate this difference?

One small difference between enantiomers is the direction that polarized light will rotate when it hits the molecule. One enantiomer will rotate light in the clockwise direction, while the other will rotate it in the counterclockwise direction. The clockwise version is termed 'D' for dextrorotary (or right-handed) and the counterclockwise version is termed 'L' for levorotary (or left-handed). However, light rotation cannot be used in a predictive way to determine the absolute stereo-configuration of a molecule (i.e. you cannot tell which enantiomer is going to rotate the light to the right or to the left until you actually do the experiment).

Thus, another system is needed to describe the absolute configuration. The Cahn-Ingold-Prelog (CIP) priority system was designed to determine the absolute stereo-configuration of enantiomers as either sinister (S) or rectus (R). In this system, the groups that are attached to the chiral carbon are given priority based on their atomic number (*Z*). Atoms with higher atomic number (more protons) are given higher priority (i.e. S > P > O > N > C > H).

For determining the stereochemistry, place the lowest priority group away from you, so that the other three groups are held are facing you. Assign priority to the remaining groups.

The rules for this system of stereochemical nomenclature are, on the surface, fairly simple. We'll use the simple 3-carbon sugar glyceraldehyde as our first example. Try making a model of the stereoisomer of glyceraldehyde shown below. If you don't have a chemistry modeling kit, an easy alternative is to use toothpicks and gumdrops. Be sure that you are making the correct

enantiomer!

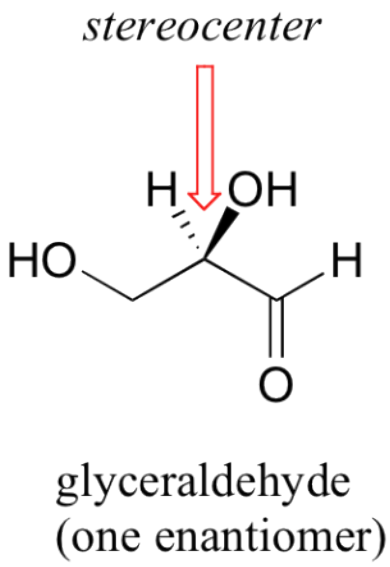


Figure 6.4.5**: One enantiomer of glyceraldehyde**. The chiral center is shown with an arrow.

The first thing that we must do is to assign a **priority** to each of the four substituents bound to the **chiral carbon**. In this nomenclature system, the priorities are based on atomic number, with higher atomic numbers having a higher priority. We first look at the atoms that are directly bonded to the chiral carbon: these are H, O (in the -OH group), C (in the C=O position), and C (in the CH_2OH group).

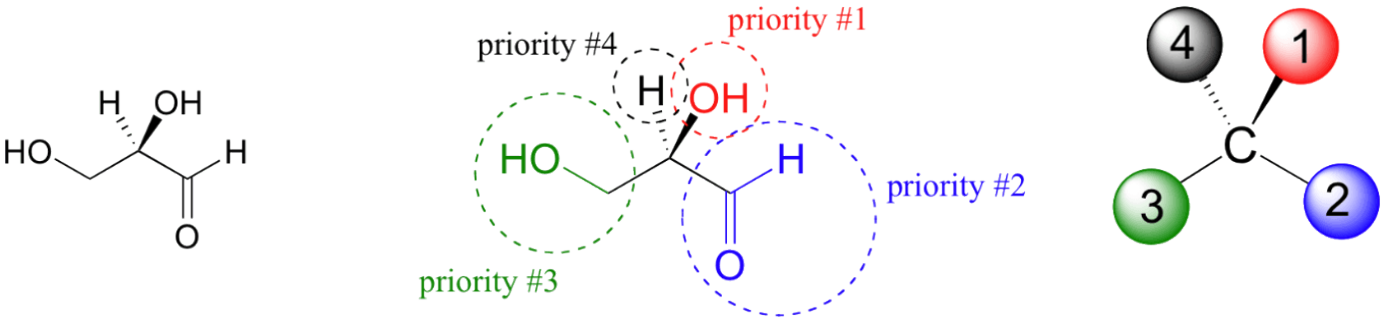


Figure 6.4.6**: Assigning Priority to the Groups Attached to the Chiral Carbon of Glyceraldehyde**. The four groups attached to a chiral carbon are assigned priorities based first on the **atomic number of the atom directly attached to the chiral carbon**. Oxygen has the highest atomic number and receives priority 1, while hydrogen has the lowest and receives priority 4. The remaining two groups both begin with carbon, so we move outward and compare the atoms attached to those carbons. A double bond is treated as though the atom were bonded twice; therefore, the carbon double-bonded to oxygen receives priority 2, while the carbon bonded to oxygen and two hydrogens receives priority 3. With the lowest-priority group pointing away from the viewer, following priorities **1** → **2** → **3** gives a clockwise path, identifying this structure as the **R configuration**.

Two priorities are easy: hydrogen, with an atomic number of 1, is the lowest (#4) priority, and the hydroxyl oxygen, with atomic number 8, is priority #1. Carbon has an atomic number of 6. Which of the two 'C' groups is priority #2, the aldehyde (CHO) or the alcohol (CH_2OH)? To determine this, we move one more bond away from the stereocenter: for the aldehyde we have a *double* bond to an oxygen, while on the CH_2OH group we have a *single* bond to an oxygen. If the atom is the same, double bonds have a higher priority than single bonds. Therefore, the aldehyde group is assigned #2 priority and the CH_2OH group the #3 priority. With our priorities assigned, we next make sure that the #4 priority group (the hydrogen) is pointed back away from ourselves, into the plane of the page (it is already).

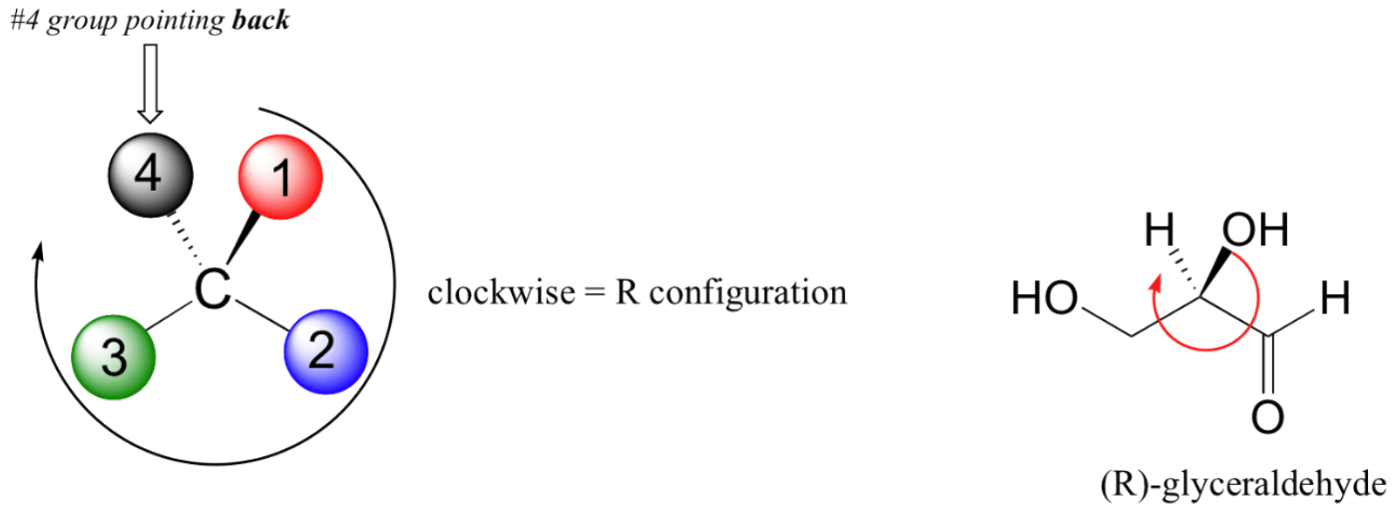


Figure 6.4.7**: Identifying the R Configuration of Glyceraldehyde**. After assigning priorities 1 through 4 to the groups attached to the chiral carbon, orient the molecule so that the **lowest-priority group (4) points away from the viewer**. Trace the remaining groups in order from **1** → **2** → **3**. For this form of glyceraldehyde, the path proceeds **clockwise**, so the chiral carbon has the **R configuration**.

Then, we trace a circle defined by the #1, #2, and #3 priority groups, in increasing order. For our glyceraldehyde example, this circle is clockwise, which tells us that this carbon has the 'R' configuration, and that this molecule is (R)-glyceraldehyde.

For (S)-glyceraldehyde, the circle described by the #1, #2, and #3 priority groups is counter-clockwise. In this example (Figure 6.4.8), we must flip the molecule over so that the H is pointing into the plane of the page. Always be sure that the lowest priority is facing back into the page, before evaluating the other priority groups for clockwise or counterclockwise direction.

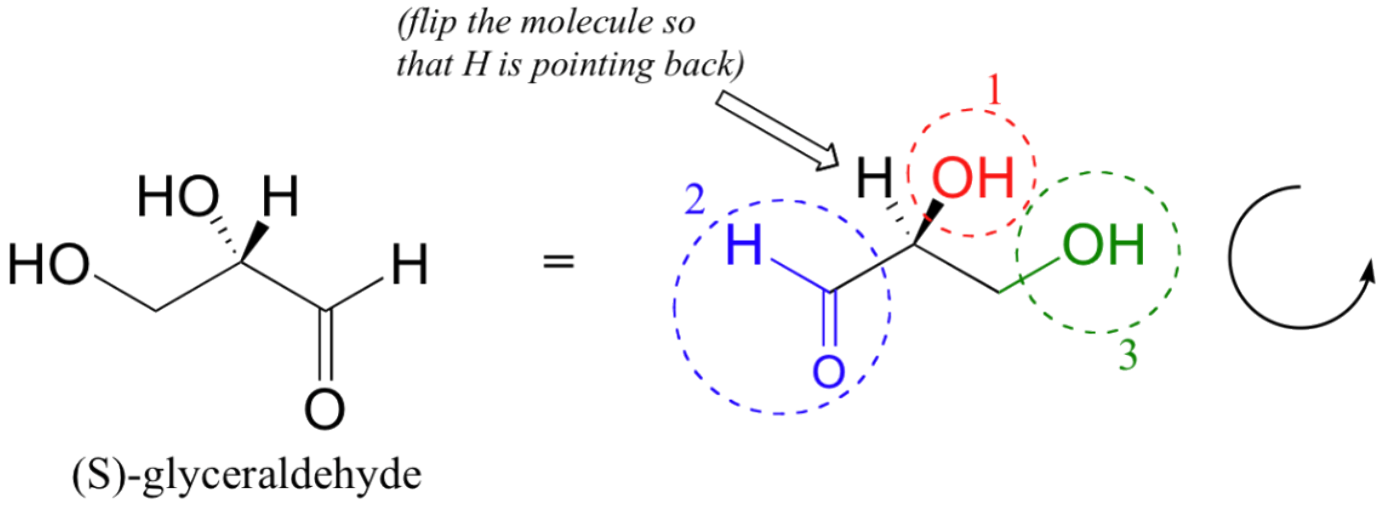


Figure 6.4.8**: Orienting the Lowest-Priority Group Before Assigning R or S Configuration**. After priorities have been assigned to the four groups attached to a chiral carbon, the molecule must be viewed with the **lowest-priority group (priority 4) pointing away from the viewer, into the page**. Only after the molecule is oriented in this way should the direction from **priority 1** → **2** → **3** be evaluated: a clockwise path indicates an **R configuration**, while a counterclockwise path indicates an **S configuration**.

Once all of the groups have been assigned priority and the molecule is positioned with the lowest-priority group pointing back into the paper, you can determine the direction in which the priorities proceed. If the path from priority 1 → 2 → 3 moves in the **clockwise direction**, the chiral center is given the **R designation**. If the path moves in the **counterclockwise direction**, the chiral center is given the **S designation**.

In Figure 6.4.9, the 2-butanol molecule on the left has priorities that proceed in the counterclockwise direction, giving the **S configuration**. The molecule on the right has priorities that proceed in the clockwise direction, giving the **R configuration**.

Notice something important about these two structures: they are **mirror images of one another, but they cannot be superimposed**. They are therefore **enantiomers**. Both molecules are still 2-butanol—they have the same molecular formula and the same connections between their atoms. However, they differ in the three-dimensional arrangement of the groups around the chiral carbon. To distinguish between them, the R or S designation becomes part of the complete name: **(S)-2-butanol** and **(R)-2-butanol**.

This illustrates an important feature of enantiomers: the difference between them is not **what atoms they contain or how those atoms are connected**, but how those atoms are **arranged in three-dimensional space**. As we will see, this seemingly small difference can become extremely important when molecules interact with biological systems.

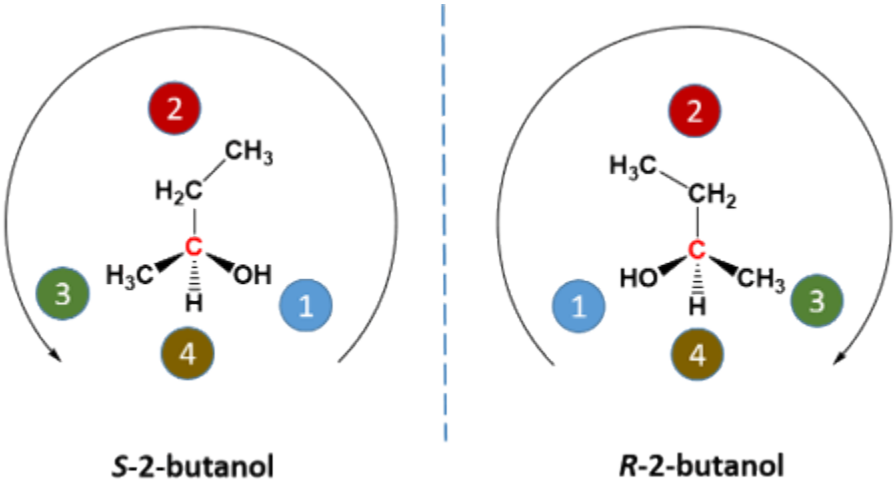


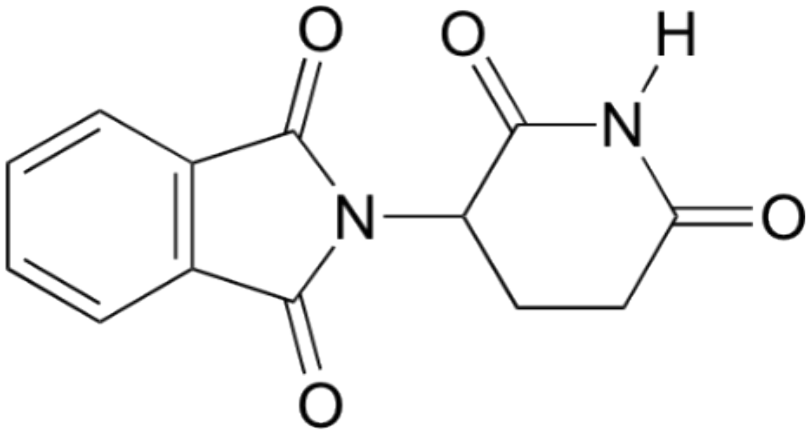
Figure 6.4.9**: Enantiomers Are Nonsuperimposable Mirror Images.** The two forms of 2-butanol have the same atoms connected in the same order but differ in the three-dimensional arrangement around the chiral carbon. **(S)-2-butanol** and **(R)-2-butanol** are mirror images that cannot be superimposed, making them **enantiomers**. When the lowest-priority group (4) is directed away from the viewer, the **1** → **2** → **3** priorities proceed counterclockwise for the S configuration and clockwise for the R configuration.

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6.5: The Importance of Chirality in Biological Systems and Medicine

Thalidomide - A Story of Unintended Consequences

Interestingly, enantiomers have the same physical properties and exactly the same chemical properties, *except* when reacting with other chiral molecules. Thus, chiral molecules have potentially drastic differences in physiology and medicine. For example, in the 1960's, a drug called thalidomide was widely prescribed in Western Europe to alleviate morning sickness in pregnant women.



thalidomide

Thalidomide had previously been used in other countries as an antidepressant, and was believed to be safe and effective. It was not long, however, before doctors realized that something had gone horribly wrong: many babies born to women who had taken thalidomide during pregnancy suffered from severe birth defects.



Figure 6.5.1: Baby born to a mother who had taken thalidomide while pregnant. *(OtisArchives3, CC BY 2.0)*

Researchers later realized that the problem lay in the fact that thalidomide was being provided as a mixture of two different isomeric forms, called a ***racemic mixture***. One of the isomers is associated primarily with the desired therapeutic effects, while the other is associated more strongly with the birth defects observed in babies exposed to the drug *in utero*. A substance that can interfere with embryonic or fetal development and cause birth defects is said to be ***teratogenic***.

Both isomeric forms have the same molecular formula and the same atom-to-atom connectivity, so they are not structural isomers. Instead, they differ in the three-dimensional arrangement of atoms around one tetrahedral chiral carbon. Thus, the two forms of thalidomide are ***enantiomers***.

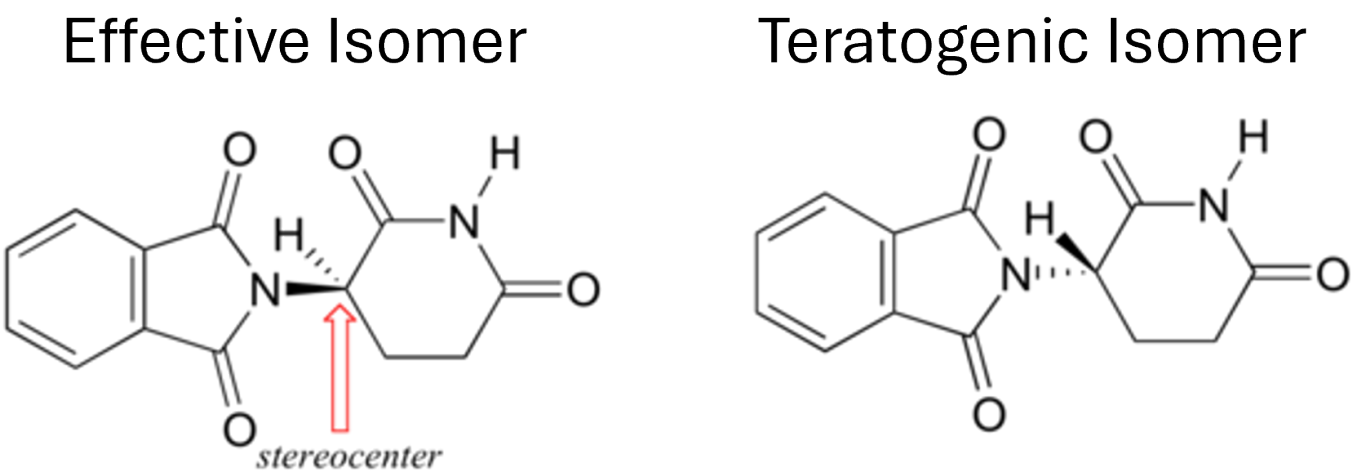


Figure 6.5.2**: Enantiomers of thalidomide**. The enantiomer on the left is the therapeutic version of the drug, whereas the enantiomer on the right is the teratogenic agent. The stereocenter is indicated with a red arrow.

Importantly, simply administering the therapeutically preferred enantiomer would not have solved the problem. Under physiological conditions, the R and S forms of thalidomide can convert into one another. Thus, even a preparation containing only one enantiomer can produce the other form after entering the body.

Let's compare the enantiomers in more depth to show the priority rules and assign the R- and S-configurations. Note that the carbon in question has *four different substituents* (two of these just happen to be connected by a ring structure). Tetrahedral carbons with four different substituent groups are called ***stereocenters***. Looking at the structures of what we are referring to as the two isomers of thalidomide, you may not be entirely convinced that they are actually two different molecules. In order to convince ourselves that they are indeed different, let's create a generalized picture of a tetrahedral carbon stereocenter, with the four substituents designated R_1-R_4. The two stereoisomers of our simplified model are shown in Figure 6.5.3.

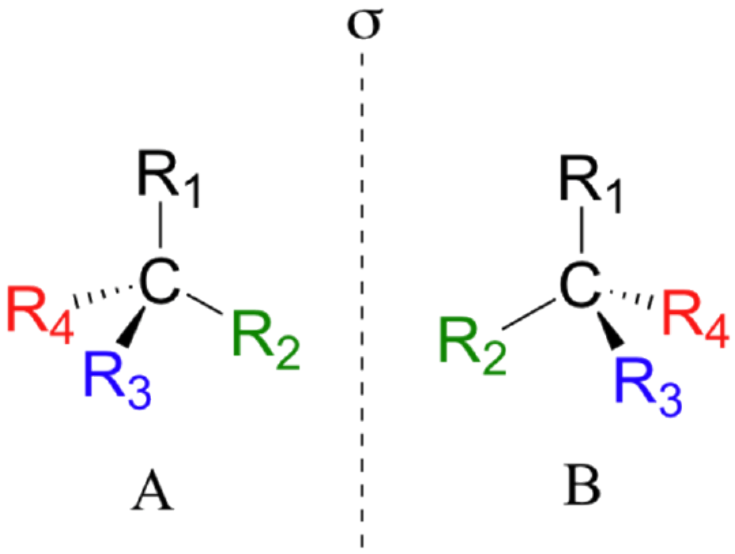


Figure 6.5.3**: Simplified diagram of thalidomide enantiomers**.

If you look carefully at the figure above, you will notice that molecule A and molecule B are mirror images of each other (the line labeled 'σ' represents a mirror plane). Furthermore, *they are not superimposable*: if we pick up molecule A, flip it around, and place it next to molecule B, we see that the two structures cannot be superimposed on each other. They are two different molecules! If you make models of the two stereoisomers of thalidomide and do the same thing, you will see that they too are mirror images, and cannot be superimposed (it will help to look at a color version of the thalidomide enantiomers presented in Figure 6.5.4).

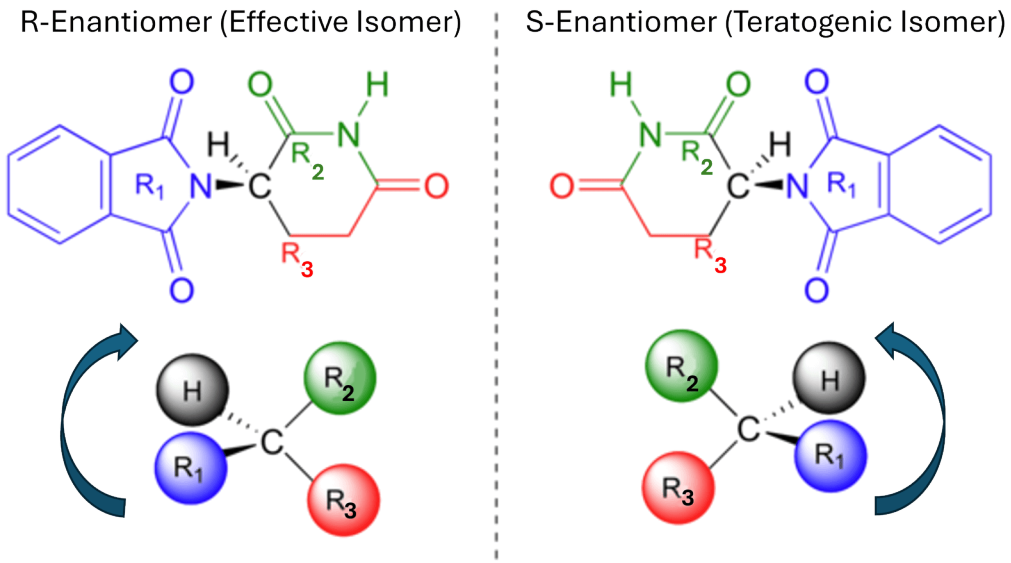


Figure 6.5.4**: Assigning Priorities to the Groups Around the Chiral Carbon in Thalidomide.** The groups surrounding the chiral carbon of thalidomide are color-coded to show their relative priorities. The nitrogen-containing group has **priority 1 (blue)**, the carbonyl-containing pathway has **priority 2 (green)**, the remaining carbon pathway has **priority 3 (red)**, and hydrogen has **priority 4**. The two structures contain the same groups but arrange them differently in three-dimensional space, producing the **R and S enantiomers of thalidomide**.

Thalidomide is a ***chiral*** molecule.

Here are some more examples of chiral molecules that exist as pairs of enantiomers. In each of these examples, there is a single stereocenter, indicated with an arrow. (Many molecules have more than one stereocenter, but we will get to that that a little later!)

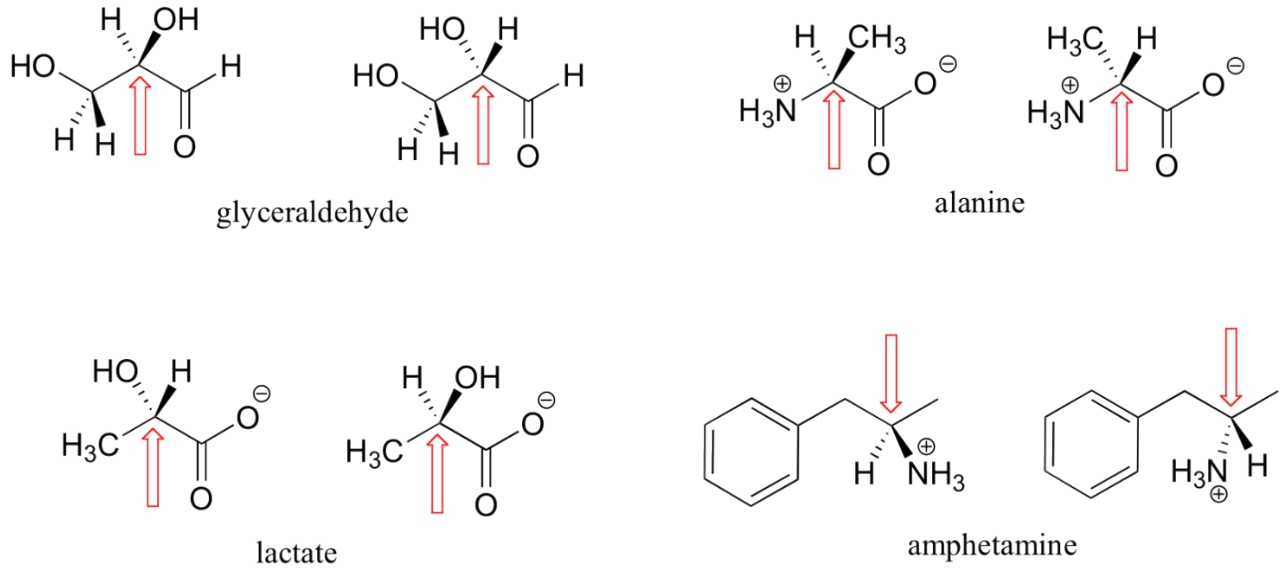


Figure 6.5.5**: Other examples of compounds that contain chiral centers**. Each chiral center is indicated with a red arrow. Note that you can identify chiral carbon centers as they are always bound to four different groups.

Here are some examples of molecules that are ***achiral*** **(not chiral)**. Notice that none of these molecules has a stereocenter (an atom that is bound to four different substituents).

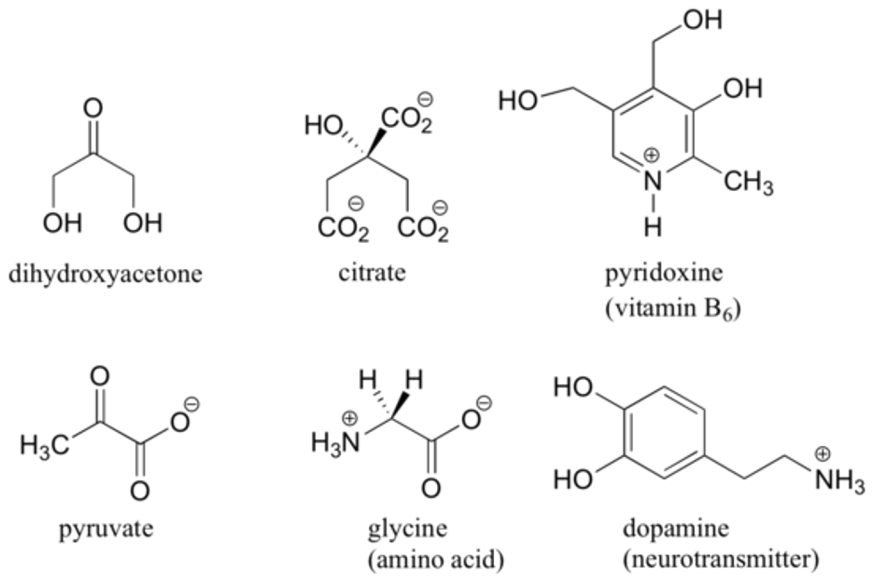


Figure 6.5.6**: Examples of compounds that do NOT contain chiral centers**. Molecules that do not contain chiral centers are ***achiral***.

When evaluating a molecule for chirality, it is important to recognize that the use of the dashed/solid wedge drawing does not necessarily mean that the molecule is chiral. Chiral molecules are sometimes drawn without using wedges. Conversely, wedges may be used on carbons that are not stereocenters – look, for example, at the drawings of glycine and citrate in the figure above. Just because you see dashed and solid wedges in a structure, do not automatically assume that you are looking at a stereocenter.

Here are some guidelines for evaluating chirality:

How to Identify a Chiral Carbon

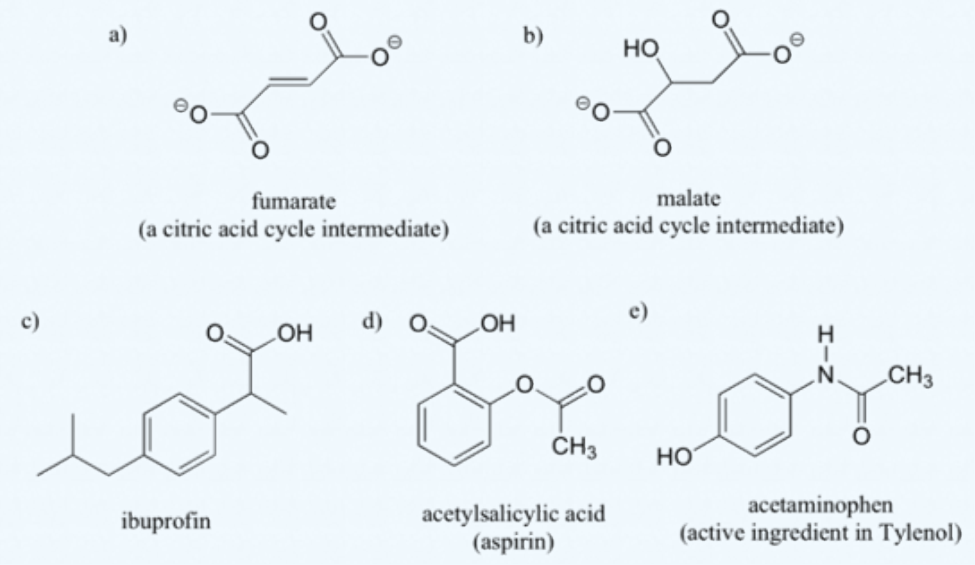
When evaluating a structure for chirality, use the following steps:

1. **Look for tetrahedral carbon atoms with four single bonds.**
   A carbon involved in a double or triple bond cannot be a chiral carbon of the type we are considering here.
2. **Examine the four groups attached to each possible chiral carbon.**
   A **chiral carbon (stereocenter)** must be attached to **four different groups**. Remember that the groups do not have to be single atoms—they may be entire carbon chains or other portions of the molecule.
3. **If two attached groups are the same, the carbon is not chiral.**
   Sometimes this is obvious, such as a carbon bonded to two hydrogen atoms. In a larger molecule, however, you may need to follow the two carbon-containing paths outward from the carbon to determine whether they are actually different.
4. **Do not use wedges and dashes to decide whether a carbon is chiral.**
   Wedges and dashed wedges simply show the **three-dimensional orientation of bonds**. Determine chirality from the identity of the four groups attached to the carbon, not from how the structure happens to be drawn.

Quick Check: Find a tetrahedral carbon and ask, **"Are all four things attached to this carbon different?"** If yes, you have identified a chiral carbon. If any two are identical, that carbon is not a stereocenter.

Exercise 6.5.1

Label the molecules below as chiral or achiral and locate all stereocenters:



Answer available at the end of this section.

Answers

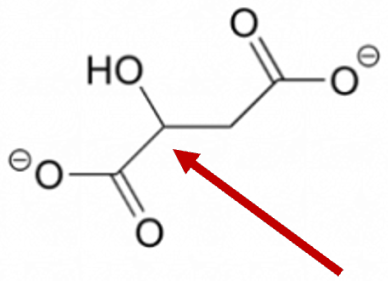
Exercise 6.5.1

Malate: 1 chiral center — the carbon bearing the OH is attached to four different groups.

Ibuprofen: 1 chiral center — the carbon attached to the carboxyl-containing group, methyl group, aromatic-containing group, and H has four different substituents.

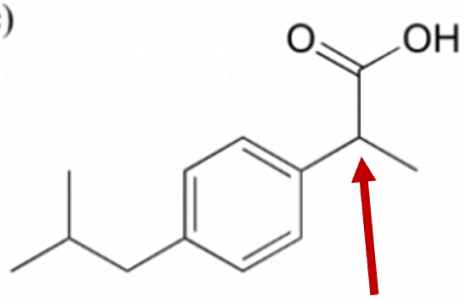
All of the other structures shown are achiral — none contains a tetrahedral carbon attached to four different groups.

b)



malate
(a citric acid cycle intermediate)

c)

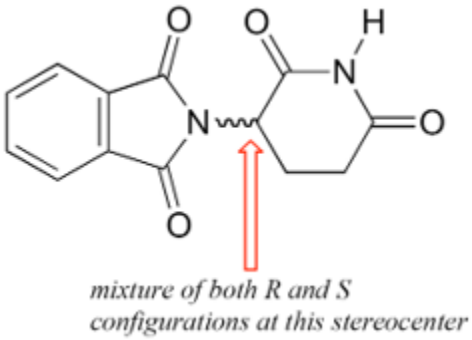


ibuprofin

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6.6: The Importance of Chirality in Protein Interactions

The thalidomide used in the late 1950s and early 1960s was sold as a 50:50 mixture of the R and S enantiomers. An equal mixture of two enantiomers is called a **racemic mixture** or **racemate**. In chemical structures, a **wavy bond** may be used when the stereochemistry at a particular position is unspecified or when both configurations are being represented. Thus, a simplified structure can be used to represent thalidomide without specifying either the R or S configuration.

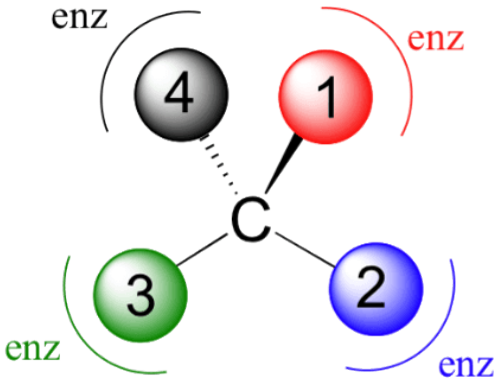


As we learned in the previous section, the two enantiomers of thalidomide do not have identical biological effects. The R enantiomer is associated primarily with the desired therapeutic effects, whereas the S enantiomer is associated more strongly with the **teratogenic effects** of the drug. How can such a seemingly small difference in molecular structure lead to such a dramatic—and, in this case, tragic—difference in biological activity?

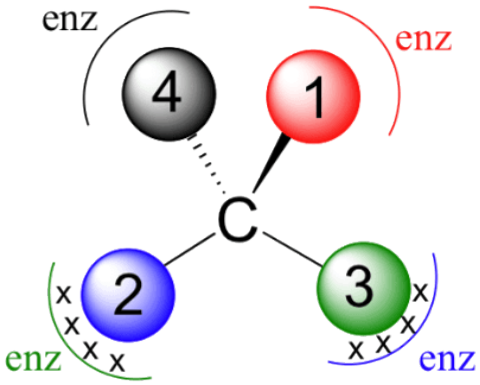
The answer lies in the way drugs interact with biological molecules. Many drugs exert their effects by binding to specific **proteins**, such as receptors or enzymes. For example, a drug might bind to a receptor and alter the signal it produces or bind to an enzyme and change its activity.

Proteins are themselves three-dimensional, chiral molecules, and the regions where other molecules bind have very specific shapes. As a result, a protein can interact differently with two enantiomers of the same drug. Like a right-handed glove fitting a right hand better than a left hand, one enantiomer may fit into a particular binding site much better than its mirror image.

The two enantiomers contain exactly the same atoms and functional connections, but the **three-dimensional positions of those groups are different**. As illustrated in Figure 6.6.1, this can change how well the groups on a drug line up with complementary regions of a protein. One enantiomer may form several favorable interactions, while its mirror image may form fewer interactions or interact with the protein in a different way.



a protein that binds specifically to a chiral molecule . . .



may not bind well at all to a different stereoisomer!

Figure 6.6.1: Enantiomers Can Interact Differently with a Protein Target. The same four groups are present in both molecules, but their different spatial arrangements change which groups can simultaneously align with complementary binding interactions on the protein.

An additional complication with thalidomide is that its R and S enantiomers can convert into one another under physiological conditions. Therefore, even administering only one enantiomer can result in formation of the other after the drug enters the body.

Chirality and Drug–Protein Interactions

The importance of chirality extends far beyond thalidomide. Most drugs produce their effects by interacting with specific **protein targets**, such as receptors, enzymes, ion channels, or transport proteins. These proteins fold into complex three-dimensional shapes, creating binding sites with very specific arrangements of atoms and chemical groups.

Because proteins are themselves **chiral**, their binding sites are also three-dimensional and asymmetric. Consequently, the two enantiomers of a chiral drug may not interact with the same protein in exactly the same way.

As illustrated in Figure 6.6.2, several regions of a drug molecule may need to line up correctly with complementary regions of a protein binding site. One enantiomer may position these groups so that several favorable interactions can occur at the same time. In its mirror-image enantiomer, those same groups are arranged differently in space. Some may no longer line up correctly with the binding site, resulting in weaker binding or perhaps no meaningful binding at all.

Importantly, this does **not** mean that one enantiomer is always active and the other is always inactive. The two enantiomers might bind to the same protein with different strengths, or they may interact with **different proteins altogether**. As a result, enantiomers can differ in their therapeutic effects, side effects, metabolism, or how long they remain in the body.

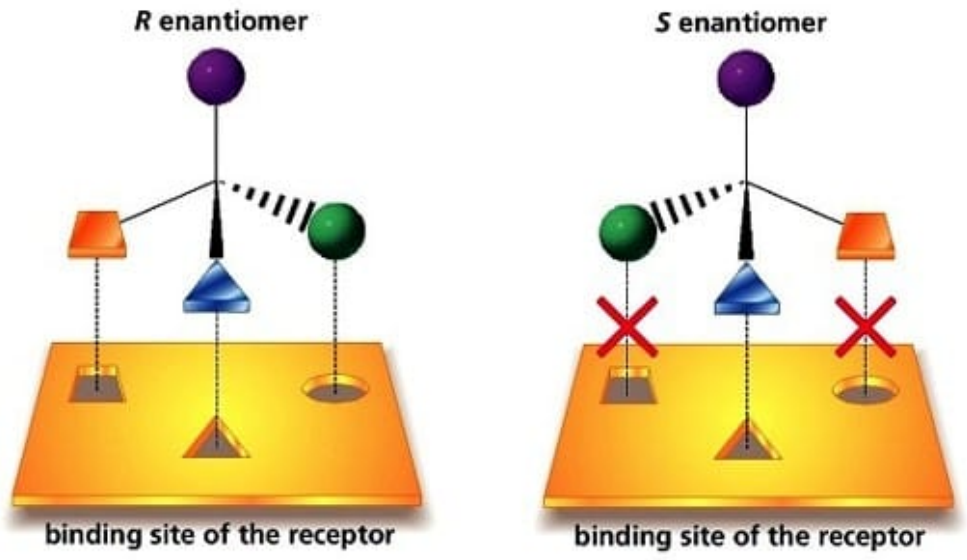


Figure 6.6.2: Protein Binding Sites Can Distinguish Between Enantiomers. Protein binding sites have specific three-dimensional shapes and arrangements of interacting groups. In this simplified model, the groups of one enantiomer align with several complementary regions of the protein binding site, allowing favorable interactions to occur simultaneously. In the mirror-image enantiomer, the same groups are arranged differently in space and cannot all align with the same binding site. Thus, two enantiomers of the same molecule can interact differently with a protein and may produce different biological effects.

Why Chirality Matters in Drug Development

For this reason, stereochemistry is an important consideration during **drug development**. When a potential drug contains one or more chiral centers, researchers must determine whether its different stereoisomers behave differently in the body.

One enantiomer may provide most of the desired therapeutic activity, while another may be less active, inactive, or produce different biological effects. Drug developers therefore study the activity, toxicity, metabolism, and other properties of individual stereoisomers rather than assuming that mirror-image molecules will behave identically.

This brings us back to one of the central ideas of organic chemistry:

> A molecule's biological activity depends not only on which atoms it contains and how they are connected, but also on how those atoms are arranged in three-dimensional space.

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6.7: Common Organic Functional Groups

The number of known organic compounds is a quite large. In fact, there are many times more organic compounds known than all the other (inorganic) compounds discovered so far, about 7 million organic compounds in total. Fortunately, organic chemicals consist of a relatively few similar parts, combined in different ways, that allow us to predict how a compound we have never seen before may react, by comparing how other molecules containing the same types of parts are known to react.

These parts of organic molecules are called *functional groups* and are made up from specific bonding patterns with the atoms most commonly found in organic molecules (C, H, O, N, S, and P). The identification of functional groups and the ability to predict reactivity based on functional group properties is one of the cornerstones of organic chemistry.

Functional groups are specific atoms, ions, or groups of atoms having consistent properties. A functional group makes up part of a larger molecule.

For example, -OH, the hydroxyl group that characterizes alcohols, is an oxygen with a hydrogen attached. It could be found on any number of different molecules.

Just as elements have distinctive properties, functional groups have characteristic chemistries. An -OH functional group on one molecule will tend to react similarly, although perhaps not identically, to an -OH on another molecule.

Organic reactions usually take place at the functional group, so learning about the reactivities of functional groups will prepare you to understand many other things about organic chemistry.

Functional groups are structural units within organic compounds that are defined by specific bonding arrangements between specific atoms. The structure of capsaicin, the fiery compound found in hot peppers, incorporates several functional groups, labeled in the figure below and explained throughout this section.

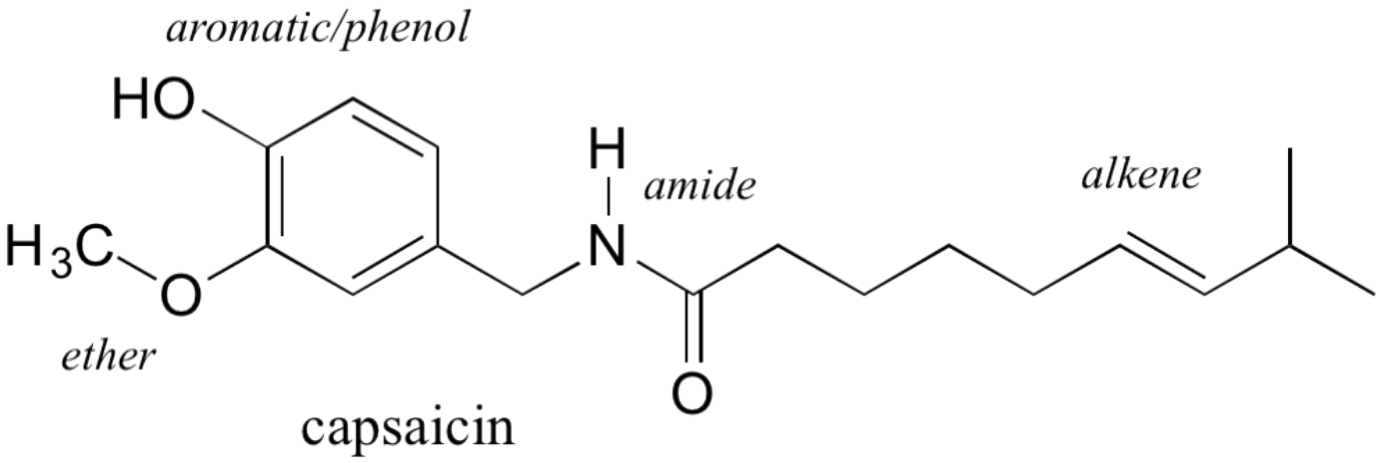


Figure 6.7.1**: Structure of capsaicin**. Capsaicin contains several important functional groups, including an alkene, amide, aromatic ring, and an ether.

As we progress in our study of organic chemistry, it will become extremely important to be able to quickly recognize the most common functional groups, because *they are the key structural elements that define how organic molecules react*. For now, we will only worry about drawing and recognizing each functional group, as depicted by Lewis and line structures. Much of the remainder of your study of organic chemistry will be taken up with learning about how the different functional groups behave in organic reactions. Below is a brief introduction to the major organic functional groups.

A Quick Review: Recognizing the Carbon Skeleton

Before we begin identifying functional groups, let's review the basic **carbon structures** that we have already encountered. Remember that the carbon skeleton forms the underlying framework of an organic molecule. Carbon atoms can connect in several different ways, producing molecules with different shapes and degrees of flexibility.

- **Straight-chain structures** contain carbon atoms connected in one continuous, unbranched chain.
- **Branched-chain structures** contain one or more carbon groups that extend away from the main carbon chain.
- **Cyclic structures** form when carbon atoms connect to create a ring.
- **Alkenes** contain at least one carbon–carbon double bond (**C=C**). The double bond restricts rotation and can influence the shape of the molecule.
- **Alkynes** contain at least one carbon–carbon triple bond (**C≡C**). The atoms surrounding the triple bond have a linear arrangement.
- **Aromatic structures** contain a special, stable ring system. The most familiar example is the six-carbon **benzene ring**, commonly drawn as a hexagon with alternating double bonds or with a circle inside the ring.

A single organic molecule may contain **more than one of these structural features**. For example, a molecule might contain a branched carbon chain, a double bond, and an aromatic ring all within the same structure.

As we move into functional groups, continue to look first at the **carbon skeleton**, but then pay particular attention to the atoms and groups attached to it. These **functional groups** create recognizable regions within an organic molecule and often have a major influence on its chemical and biological properties.

> **Reading Strategy:** First identify the **carbon skeleton**. Then look for the **functional groups** attached to or incorporated within that skeleton.

Alkyl Halides

When the carbon of an alkane is bonded to one or more halogens, the group is referred to as an *alkyl halide or haloalkane*. Chloroform is a useful solvent in the laboratory, and was one of the earlier anesthetic drugs used in surgery. Chlorodifluoromethane was used as a refrigerant and in aerosol sprays until the late twentieth century, but its use was discontinued after it was found to have harmful effects on the ozone layer. Bromoethane is a simple alkyl halide often used in organic synthesis. Alkyl halides groups are quite rare in biomolecules.

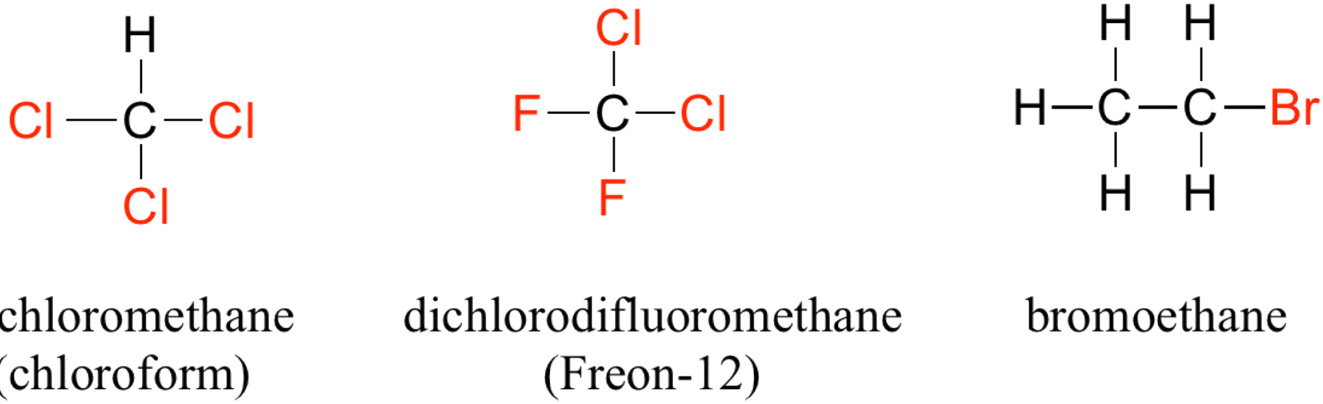


Figure 6.7.1: Examples of Alkyl Halides. **Alkyl halides** contain one or more halogen atoms—fluorine (F), chlorine (Cl), bromine (Br), or iodine (I)—bonded to a carbon atom within an organic molecule. The examples shown illustrate that halogens can occur on carbon skeletons of different sizes and shapes and that a molecule may contain more than one halogen atom. When identifying this functional group, look for a **carbon–halogen (C–X) bond**, where **X represents a halogen**.

Alcohols, Phenols, and Thiols

In the ***alcohol*** functional group, a carbon is single-bonded to an OH group (the OH group, when it is part of a larger molecule, is referred to as a ***hydroxyl group***). Except for methanol, all alcohols can be classified as primary, secondary, or tertiary. In a primary alcohol, the carbon bonded to the OH group is also bonded to only one other carbon. In a secondary alcohol and tertiary alcohol, the carbon is bonded to two or three other carbons, respectively. When the hydroxyl group is *directly* attached to an aromatic ring, the resulting group is called a *phenol*. The sulfur analog of an alcohol is called a thiol (from the Greek *thio*, for sulfur).

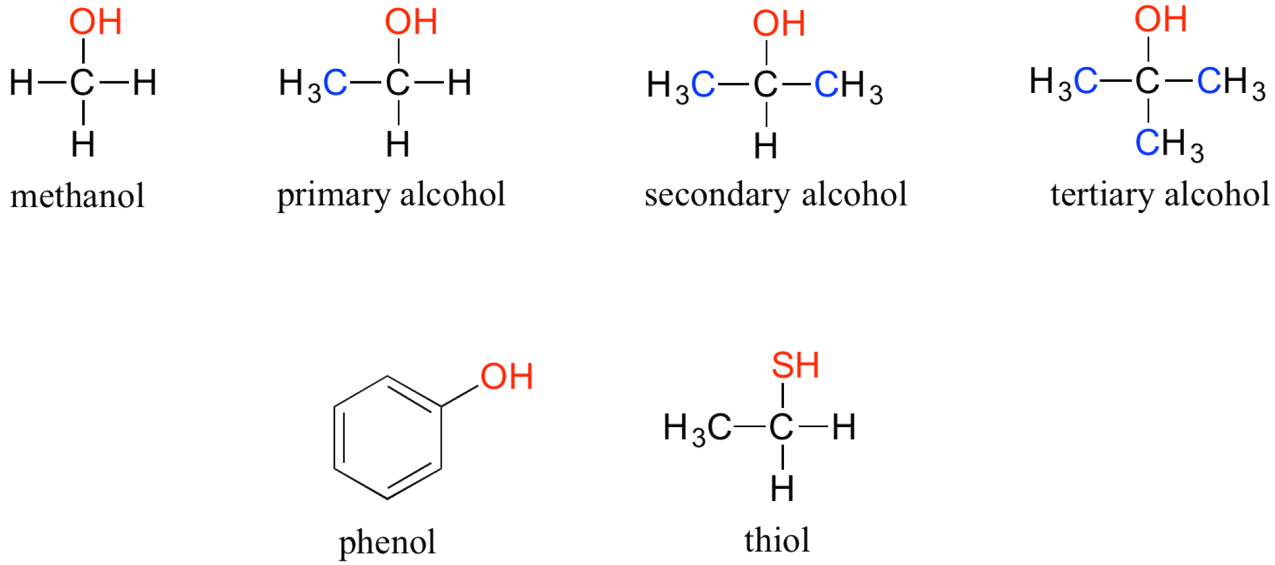
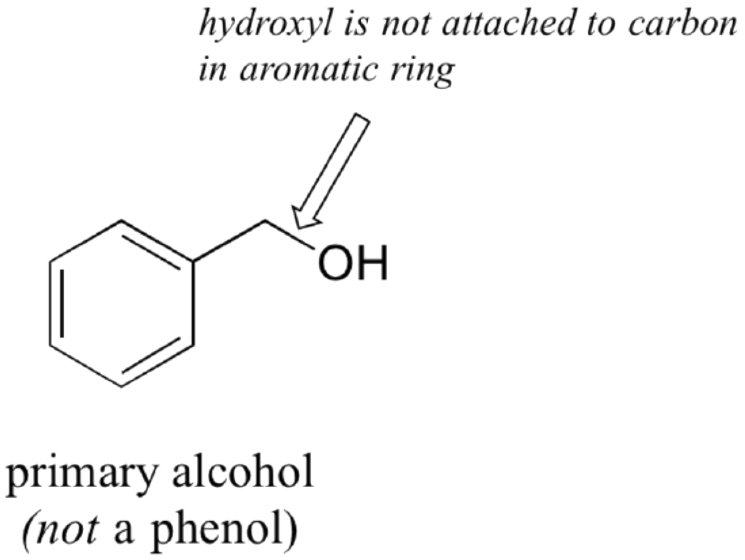


Figure 6.7.2**: Examples of Alcohols, Phenols, and Thiols**. **Alcohols** contain a hydroxyl group (**–OH**) bonded to a carbon atom. Alcohols can be further classified as **primary (1°), secondary (2°), or tertiary (3°)** depending on how many other carbon atoms are attached to the carbon bearing the –OH group. When an –OH group is attached directly to an aromatic ring, the structure is classified as a **phenol**. **Thiols** have a similar structure to alcohols but contain a sulfhydryl group (**–SH**) in place of –OH.

Note that the definition of a phenol states that the hydroxyl oxygen must be *directly* attached to one of the carbons of the aromatic ring. The compound below, therefore, is *not* a phenol - it is a primary alcohol.



The distinction is important, because there is a significant difference in the reactivity of alcohols and phenols

Ethers and Sulfides

In an ***ether*** functional group, an oxygen is bonded to two carbons. Below is the structure of diethyl ether, a common laboratory solvent and also one of the first compounds to be used as an anesthetic during operations. The sulfur analog of an ether is called a ***thioether or sulfide***.

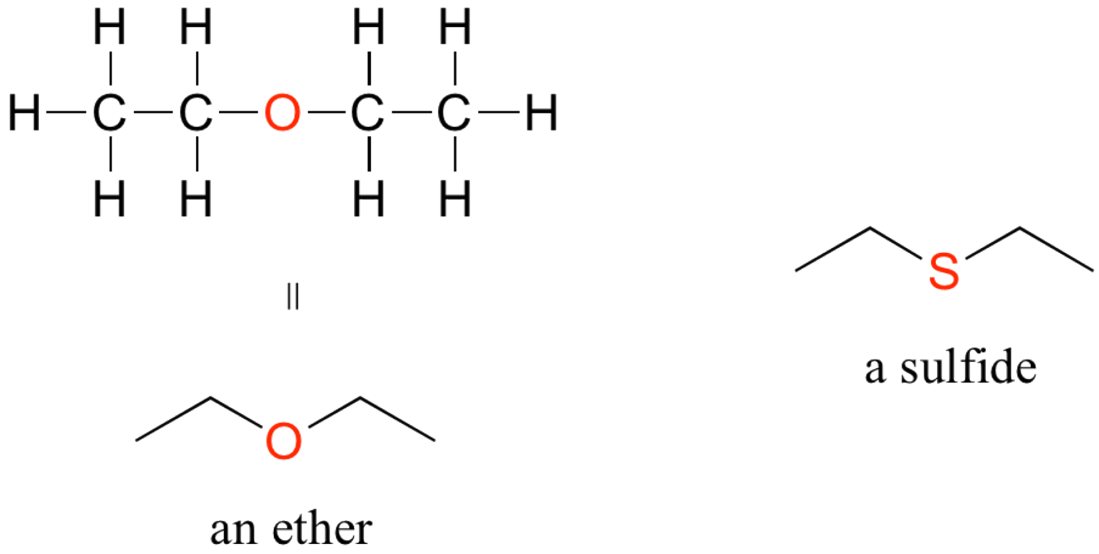


Figure 6.7.3**: Examples of Ethers and Sulfides**. **Ethers** contain an oxygen atom bonded between two carbon-containing groups, giving the general structure **R–O–R′**. **Sulfides** have a similar structure in which sulfur replaces oxygen, giving the general structure **R–S–R'**. In both functional groups, the groups on either side of the oxygen or sulfur may be the same or different.

Amines

*Amine*s are characterized by nitrogen atoms with single bonds to hydrogen and carbon. Just as there are primary, secondary, and tertiary alcohols, there are primary, secondary, and tertiary amines. Ammonia is a special case with no carbon atoms.

One of the most important properties of amines is that they are basic, and are readily protonated to form ammonium cations. In the case where a nitrogen has four bonds to carbon (which is somewhat unusual in biomolecules), it is called a quaternary ammonium ion.

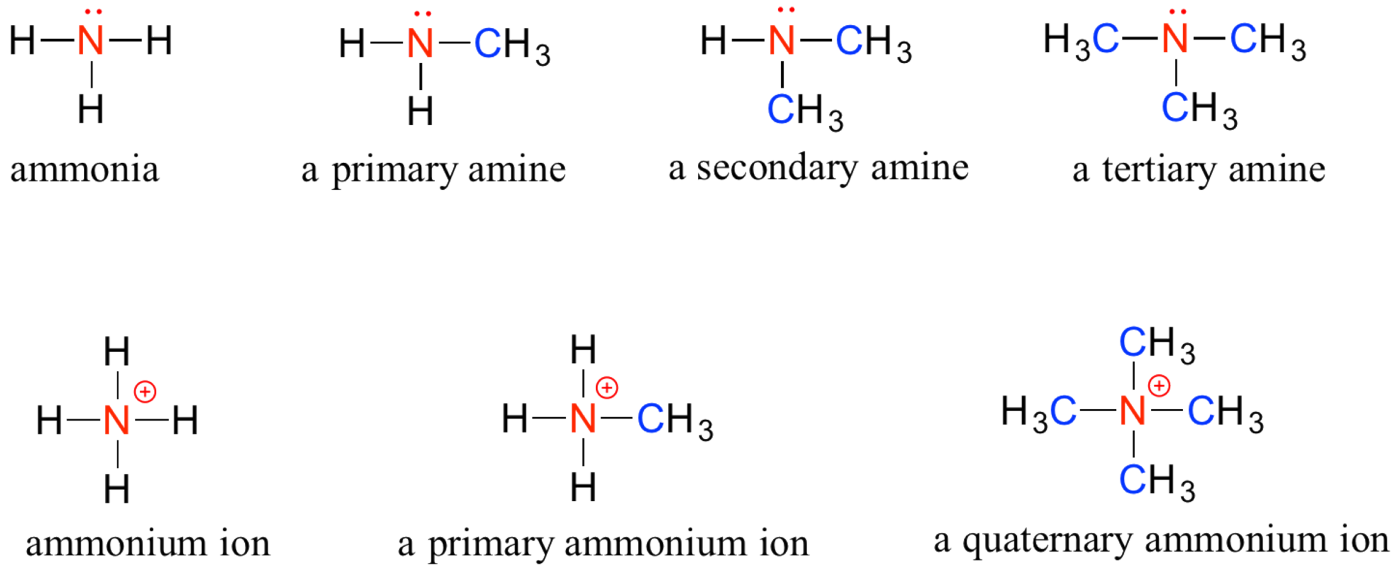


Figure 6.7.4**: Primary, Secondary, and Tertiary Amines and Their Protonated Forms**. **Amines** contain a nitrogen atom bonded to carbon-containing groups and are classified according to the number of carbon groups attached to the nitrogen. A **primary (1°) amine** has one carbon group attached to nitrogen, a **secondary (2°) amine** has two, and a **tertiary (3°) amine** has three. The nitrogen atom also contains a **lone pair of electrons**, which allows an amine to accept an H⊕ ion. When an amine is protonated, the nitrogen gains a fourth bond and carries a **positive charge**, forming an ammonium ion.

Note: Do not be confused by how the terms 'primary', 'secondary', and 'tertiary' are applied to alcohols and amines - the definitions are different. In alcohols, what matters is how many other carbons the alcohol *carbon* is bonded to, while in amines, what matters is how many carbons the *nitrogen* is bonded to.

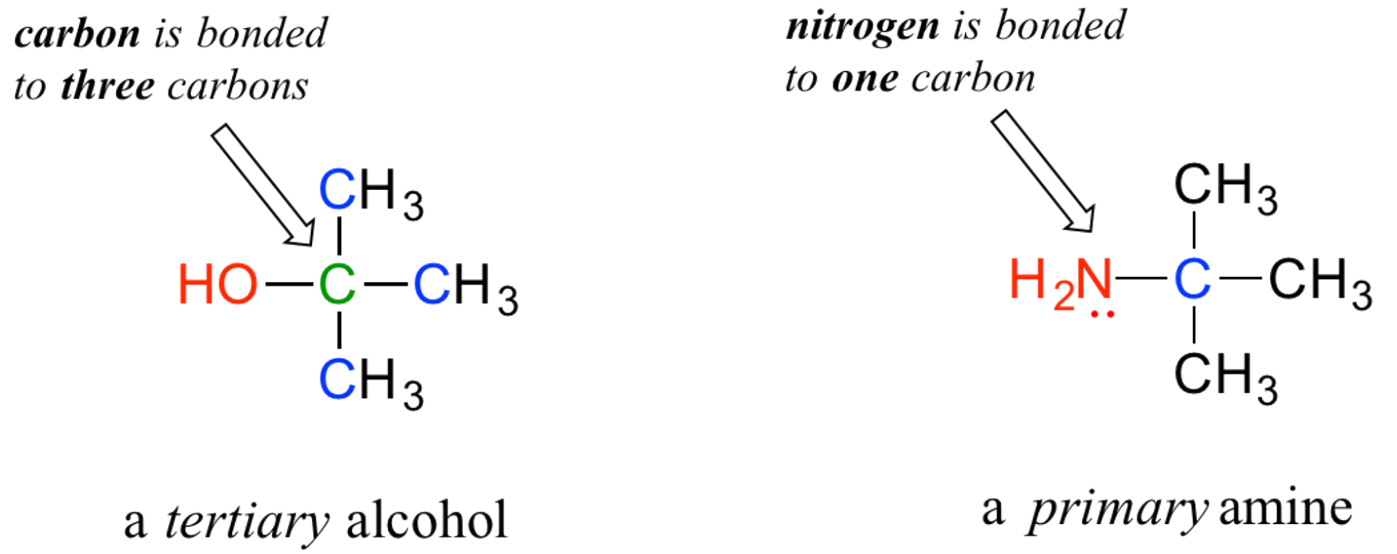


Figure 6.7.5**: Primary, Secondary, and Tertiary Describe Alcohols and Amines Differently**. The terms **primary (1°), secondary (2°), and tertiary (3°)** are used differently for alcohols and amines. For an **alcohol**, classification is based on the number of carbon atoms attached to the **carbon bearing the –OH group**. In the example shown, that carbon is attached to three other carbons, making it a **tertiary (3°) alcohol**. For an **amine**, classification is based instead on the number of carbon-containing groups attached **directly to the nitrogen atom**. In the example shown, nitrogen is attached to only one carbon group, making it a **primary (1°) amine**.

Organic Phosphates

Phosphate and its derivative functional groups are ubiquitous in biomolecules. Phosphate linked to a single organic group is called a ***phosphate ester***; when it has two links to organic groups it is called a phosphate diester. A linkage between two phosphates creates a phosphate anhydride.

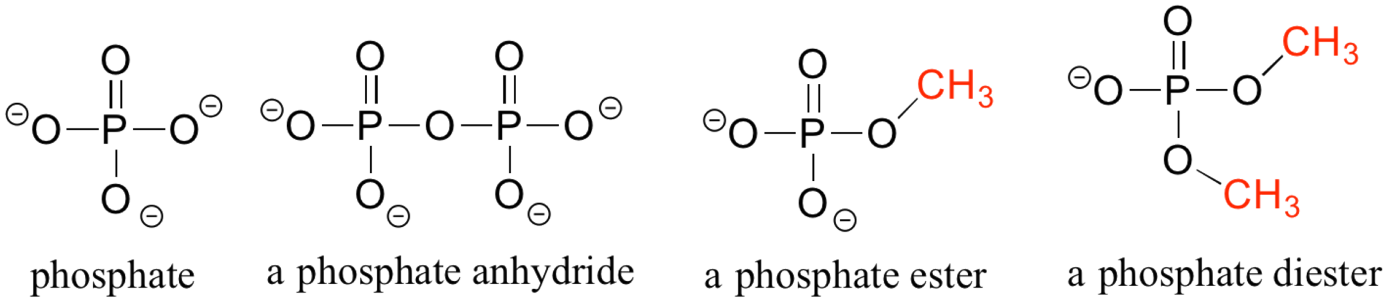


Figure 6.7.6**: Phosphate and Organic Phosphoesters**. **Phosphate** contains a central phosphorus atom bonded to four oxygen atoms. In organic molecules, phosphate can form a **phosphoester** when one of its oxygen atoms is bonded to a carbon-containing group. Phosphate may also form bonds with more than one organic group. These phosphate-containing structures are especially important in biological molecules, where they occur in compounds such as nucleotides, phospholipids, and phosphorylated sugars.

Aldehydes and Ketones

There are a number of functional groups that contain a carbon-oxygen double bond, which is commonly referred to as a *carbonyl***.** Ketones and aldehydes are two closely related carbonyl-based functional groups that react in very similar ways. In a *ketone*, the carbon atom of a carbonyl is bonded to two other carbons. In an ***aldehyde,*** the carbonyl carbon is bonded on one side to a hydrogen, and on the other side to a carbon. The exception to this definition is formaldehyde, in which the carbonyl carbon has bonds to two hydrogens.

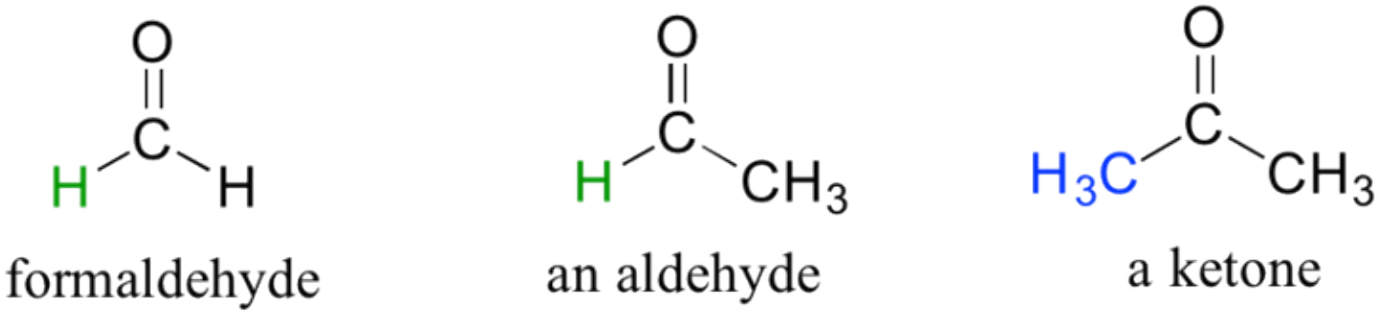


Figure 6.7.7**: Examples of Aldehydes and Ketones**. **Aldehydes** and **ketones** both contain a **carbonyl group (C=O)**. In an aldehyde, the carbonyl carbon is located at the end of a carbon skeleton and is bonded to at least one hydrogen atom. In a ketone, the carbonyl carbon is located within the carbon skeleton and is bonded to carbon atoms on both sides. When identifying these functional groups, first locate the **C=O bond**, then examine what is attached to the carbonyl carbon.

Carboxylic Acids and Their Derivatives

When a carbonyl carbon is bonded on one side to a carbon (or hydrogen) and on the other side to an oxygen, nitrogen, or

sulfur, the functional group is considered to be one of the 'carboxylic acid derivatives', a designation that describes a set of related functional groups. The main member of this family is the ***carboxylic acid*** functional group, in which the carbonyl is bonded to a hydroxyl group. The *carboxylate ion* form has donated the H^+ to the solution. Other derivatives are *carboxylic esters* (usually just called 'esters'), ***thioesters, amides, acyl phosphates, acid chlorides***, and ***acid anhydrides***. With the exception of acid chlorides and acid anhydrides, the carboxylic acid derivatives are very common in biological molecules and/or metabolic pathways and will be discussed in further details in a later chapter.

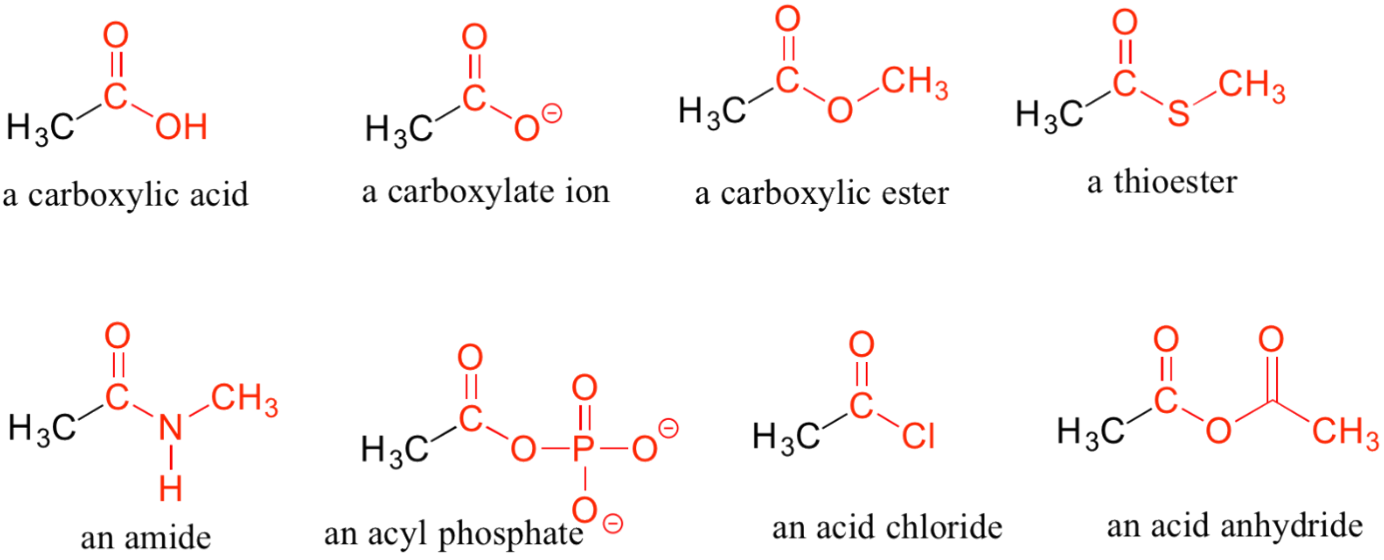
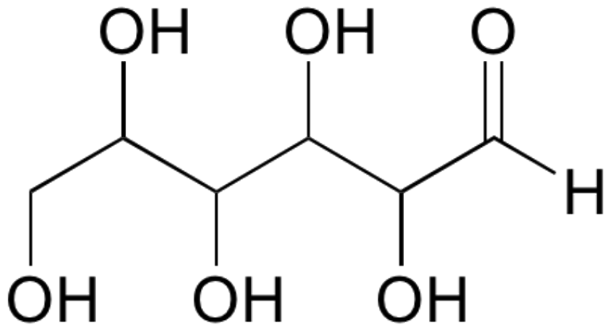


Figure 6.7.8**: Carboxylic Acids and Their Derivatives**. **Carboxylic acids** contain a carbonyl group (C=O) and hydroxyl group (–OH) attached to the same carbon, forming a **carboxyl group (–COOH)**. Related functional groups, called **carboxylic acid derivatives**, retain the carbonyl carbon but replace the –OH with another atom or group. Examples shown include a **carboxylate ion, ester, thioester, amide, acyl phosphate, acyl halide, and acid anhydride**. Although these structures share a common carbonyl-containing framework, differences in the group attached to the carbonyl carbon give each functional group distinct chemical and biological properties.

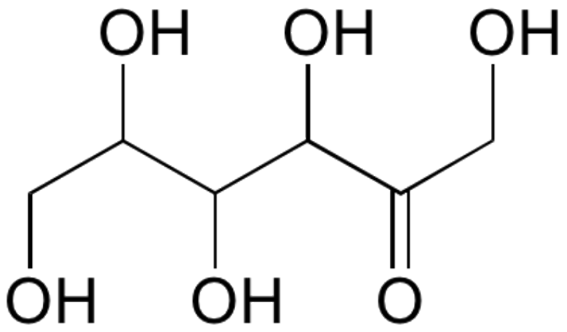
Practice Recognizing Functional Groups in Molecules

Biological molecules often contain **several different functional groups within the same structure**. Rather than memorizing the structure of an entire molecule, practice breaking a complex structure into smaller, recognizable pieces. Look for the characteristic bonding patterns that identify each functional group.

For example, in their **open-chain forms**, the six-carbon sugars glucose and fructose contain an **aldehyde** and a **ketone**, respectively. Both molecules also contain several **alcohol groups**. A molecule containing multiple alcohol groups may be described as a **polyol**.



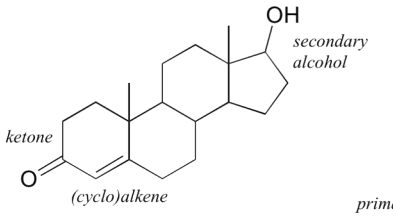
glucose



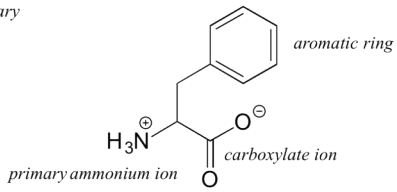
fructose

Figure 6.7.9**: Glucose and Fructose Structures**.

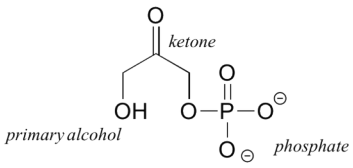
The examples below show several larger biological molecules, including the hormone **testosterone**, the amino acid **phenylalanine**, and the glycolysis intermediate **dihydroxyacetone phosphate**. Each contains more than one structural feature or functional group. As you examine each molecule, try identifying the functional groups yourself **before looking at the labels**.



testosterone



phenylalanine



dihydroxyacetone phosphate
(DHAP)

Figure 6.7.10**: Chemical structures of common biologically relevant molecules**.

When approaching an unfamiliar organic molecule, remember the strategy we have used throughout this chapter:

1. **Identify the carbon skeleton** — look for chains, branches, rings, double or triple bonds, and aromatic rings.
2. **Look for heteroatoms** such as O, N, S, P, or halogens.
3. **Examine how those atoms are bonded** to identify recognizable functional groups.
4. Remember that **one molecule can contain many different functional groups**.

You do not need to memorize the structures of the molecules shown here. The goal is to become comfortable **reading an unfamiliar structure and recognizing features you already know**.

The functional groups introduced in this section represent many of the groups that we will encounter as we study biological molecules and biochemical reactions in later chapters.

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6.8: Chapter Summary

Organic chemistry is the study of **carbon-containing compounds**. Carbon is especially well suited to building complex molecules because it can form four covalent bonds and can form strong bonds with other carbon atoms. Carbon atoms can join together to form straight chains, branched chains, rings, and other complex **carbon skeletons**. Carbon can also bond with heteroatoms such as oxygen, nitrogen, sulfur, phosphorus, and the halogens, greatly expanding the diversity and properties of organic molecules.

Organic molecules can be represented in many different ways. **Molecular formulas** show the numbers and types of atoms present, while **displayed, partially condensed, condensed, and skeletal structures** provide increasing amounts of information about how those atoms are connected. Ball-and-stick and space-filling models help visualize the three-dimensional shapes of molecules. In skeletal structures, carbon atoms and the hydrogen atoms attached to them are largely omitted, allowing even very large organic molecules to be represented efficiently. **Wedges and dashed wedges** can be used to show bonds projecting toward or away from the viewer. Chemists can also simplify structures using **R groups** or continuation marks when portions of a molecule are not the focus of interest.

Hydrocarbons contain only carbon and hydrogen. Alkanes contain only carbon–carbon single bonds and are described as **saturated**, while alkenes and alkynes contain carbon–carbon double and triple bonds, respectively, and are **unsaturated**. Aromatic compounds contain particularly stable ring systems, such as the six-carbon ring found in benzene. Carbon–carbon single bonds can rotate, allowing a molecule to adopt different three-dimensional **conformations** without breaking bonds. Double bonds restrict this rotation and can allow the formation of **cis and trans isomers** when each carbon of the double bond is attached to two different groups.

The same molecular formula does not always describe the same compound. **Structural isomers** contain the same numbers and types of atoms but differ in how those atoms are connected. **Stereoisomers** have the same atom-to-atom connectivity but differ in the three-dimensional arrangement of their atoms. Some stereoisomers are **enantiomers**, which are nonsuperimposable mirror images of one another.

A common source of chirality is a tetrahedral carbon bonded to **four different groups**. Such a carbon is a **chiral carbon or stereocenter**. The four groups surrounding a stereocenter can be assigned priorities and used to designate its configuration as **R or S**. Importantly, wedges and dashed wedges alone do not indicate that a carbon is chiral; the identities of the four groups attached to the carbon must always be examined.

Chirality is especially important in biological systems because proteins and their binding sites are themselves three-dimensional and chiral. Two enantiomers of a molecule may therefore interact differently with enzymes, receptors, ion channels, transport proteins, or other biological targets. Consequently, stereochemistry can influence the therapeutic activity, metabolism, and unwanted effects of medications. The thalidomide example illustrates the potentially profound biological consequences of differences in three-dimensional molecular structure.

Finally, much of the characteristic chemistry of an organic molecule comes from its **functional groups**. Functional groups are recognizable arrangements of atoms that tend to give molecules characteristic chemical and physical properties. This chapter introduced several important functional groups that will appear repeatedly in biological chemistry, including **alkyl halides, alcohols, phenols, thiols, ethers, sulfides, amines, phosphates and phosphoesters, aldehydes, ketones, carboxylic acids, and carboxylic acid derivatives** such as **esters** and **amides**.

Biological molecules commonly contain **several functional groups within the same structure**. Rather than memorizing entire molecular structures, it is more useful to learn how to **read an unfamiliar molecule**: identify its carbon skeleton, locate heteroatoms, recognize familiar functional groups, and consider its three-dimensional structure. Together, these skills provide the foundation needed to understand the larger and more complex molecules encountered in biochemistry and human health.

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7: NATURAL PRODUCTS AND ORGANIC CHEMISTRY

7.1: Natural Products- The Molecules of Life

7.2: Lipids

7.3: Carbohydrates

7.4: Proteins

7.5: Nucleic Acids

7.6: Secondary Metabolites- Chemistry as a Competitive Advantage

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7.1: Natural Products- The Molecules of Life

Learning Objectives

After completing this section, you should be able to:

- Define a **natural product** and explain how natural products are produced.
- Distinguish between **primary metabolites** and **secondary metabolites**.
- Identify the four major classes of biological macromolecules built from primary metabolites.
- Explain why natural products are important in biology, medicine, and drug development.
- Recognize how the organic chemistry concepts introduced in Chapter 6 can be used to understand the structures and properties of natural products.

What Are Natural Products?

Living organisms are remarkable chemists. Plants, animals, fungi, bacteria, and other organisms manufacture an enormous variety of organic molecules. Some of these molecules provide energy or become part of the organism's cellular structures. Others act as hormones or chemical messengers. Still others help organisms defend themselves, attract mates, communicate, or compete with other organisms in their environment.

Organic compounds produced by living organisms are called **natural products**.

Natural products display an extraordinary range of structural diversity. Some are relatively small and simple, while others contain multiple rings, functional groups, stereocenters, and complex carbon skeletons. Many of the structural features introduced in Chapter 6 can be found throughout these molecules.

This is where the organic chemistry you learned in Chapter 6 becomes especially useful.

When you encounter a natural product, you do not need to memorize its entire structure. Instead, you can begin to **read the molecule** using skills you already have:

- What kind of **carbon skeleton** does it contain?
- Is the molecule primarily polar or nonpolar?
- What **functional groups** can you identify?
- Does it contain double bonds, rings, or aromatic structures?
- Are there **chiral carbons**?
- How might these structural features influence the molecule's shape, solubility, intermolecular interactions, or biological activity?

Throughout this chapter, we will continue to practice these skills as we examine the organic molecules produced by living organisms.

Primary and Secondary Metabolites

Natural products can be divided broadly into two groups based on the roles they play in the organisms that produce them: **primary metabolites** and **secondary metabolites**.

Primary Metabolites

Primary metabolites are molecules involved in the fundamental processes required for an organism to live, grow, and reproduce. They participate in essential functions such as obtaining and storing energy, constructing cells and tissues, carrying genetic information, and coordinating cellular activities.

Many primary metabolites serve as the building blocks used to construct the four major classes of biological macromolecules:

- **Lipids**
- **Carbohydrates**
- **Proteins**
- **Nucleic acids**

These molecules will form the major focus of the first part of this chapter.

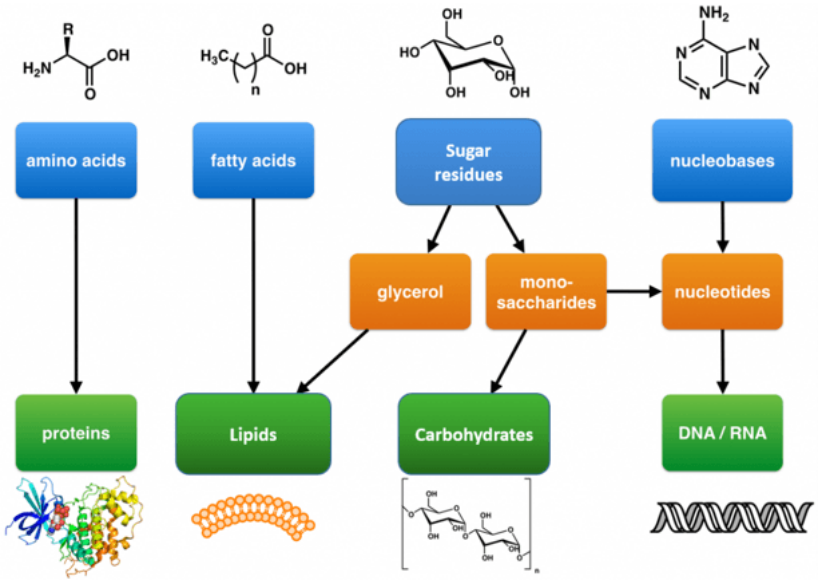


Figure 7.1.1**: The Molecular building blocks of life are made from organic compounds**. Modified from: Boghog.

Although these four classes are often grouped together as biological macromolecules, they are not all constructed in exactly the same way. Proteins and nucleic acids are true polymers assembled from repeating monomer units, and many carbohydrates also form large polymers. Lipids are somewhat different: they include several families of mostly hydrophobic molecules and are not generally considered true polymers.

What these molecules share is their importance to life—and their reliance on the same chemical principles we have already studied.

For example, **fatty acids** contain long hydrocarbon chains and carboxylic acid groups. **Amino acids** contain amine and carboxylic acid groups. **Nucleotides** contain sugars, nitrogen-containing groups, and phosphate groups. Sugars contain multiple hydroxyl groups and often contain several chiral carbons.

Suddenly, those functional groups from Chapter 6 are showing up everywhere!

Secondary Metabolites

Living organisms also produce many organic compounds that are not directly involved in the basic processes required to sustain life. These molecules are called **secondary metabolites**.

Secondary metabolites frequently help an organism interact with its environment. They may:

- discourage predators or herbivores,
- inhibit the growth of competing organisms,
- attract pollinators or mates,
- communicate with other organisms, or
- provide other ecological advantages.

A poisonous compound produced by a plant, an antibiotic produced by a bacterium, or a chemical signal released by an animal can all be examples of secondary metabolites.

Unlike many primary metabolites, which are widely shared among living organisms, particular secondary metabolites may occur only in a species or a relatively small group of organisms. This enormous chemical diversity makes secondary metabolites especially interesting to scientists searching for molecules with useful biological activities.

Natural Products and Medicine

Humans have made use of natural products for thousands of years, often long before the chemical structures of these compounds were understood. Plants, fungi, microorganisms, and animals all produce molecules capable of interacting with biological systems.

Today, natural products continue to provide important starting points for **drug discovery**. Scientists may isolate a biologically active molecule from an organism, determine its chemical structure, investigate how it interacts with its biological target, and then modify its structure to improve properties such as effectiveness, safety, stability, or delivery within the body.

This gives us another important connection to Chapter 6. The biological activity of a natural product depends not simply on the atoms it contains, but on its **functional groups, polarity, molecular shape, and three-dimensional arrangement**. Even relatively small structural changes can alter how strongly a molecule interacts with a receptor, enzyme, ion channel, or other biological target.

Thus, studying natural products provides a bridge between **organic chemistry and biology**.

Two Sides of Natural Product Chemistry

In this chapter, we will examine both major types of natural products, but for different purposes.

We will first focus on the **primary metabolites** and the molecules they form. We will examine lipids, carbohydrates, proteins, and nucleic acids and use the principles of organic chemistry to understand their structures and properties.

Later in the chapter, we will turn to the extraordinary diversity of **secondary metabolites** produced by organisms. Rather than memorizing these structures, we will use them to explore how organisms use chemistry to interact with their environments and how scientists investigate natural products as potential sources of medicines.

> As you work through this chapter, don't try to memorize every molecule you see. Instead, practice reading its structure. Look for carbon skeletons, functional groups, polarity, chirality, and other features you already recognize. The goal is to use the language of organic chemistry to begin understanding the molecules of life.

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7.2: Lipids

Learning Objectives

After completing this section, you should be able to:

- Describe the general properties and major biological functions of **lipids**.
- Identify the structural components of a **fatty acid** and distinguish between saturated and unsaturated fatty acids.
- Explain how **cis and trans double bonds** affect fatty acid shape, intermolecular forces, and melting behavior.
- Describe the general structure of **triacylglycerides (TAGs)** and explain their role in long-term energy storage.
- Identify the major structural features of **phospholipids** and explain why they spontaneously form bilayers in water.
- Explain the meaning of **amphipathic** and identify the hydrophilic and hydrophobic regions of a phospholipid.
- Recognize the characteristic fused-ring structure of **steroids** and describe several biological roles of cholesterol.
- Apply concepts from organic chemistry, including **functional groups, polarity, molecular shape, and intermolecular forces**, to the structures and properties of lipids.

What Are Lipids?

Lipids are a diverse group of organic molecules that include fats, oils, waxes, phospholipids, and steroids. Unlike proteins or nucleic acids, lipids do not all share a single structural pattern and are not generally polymers made from repeating monomers. Instead, they are grouped together largely because of an important physical property: **lipids are primarily hydrophobic and have limited solubility in water**.

Why?

Look back at what you learned about molecular polarity. Many lipids contain large regions made almost entirely of **carbon and hydrogen**. Because C–C and C–H bonds are relatively nonpolar, these hydrocarbon regions cannot form favorable hydrogen-bonding interactions with water. Thus, the hydrophobic behavior of lipids is not a new chemical property to memorize—it is a consequence of the **bonding and intermolecular forces** we have already studied.

Lipids perform many important functions in living organisms. They provide **long-term energy storage**, form much of the structure of **cell membranes**, provide insulation and waterproofing, and can serve as hormones and other signaling molecules. Although the lipid family contains many different types of molecules, we will focus on several particularly important groups: **fatty acids and triacylglycerides, waxes, phospholipids, and steroids**.



Figure 7.2.1: The Importance of Lipids in Nature. Water birds, such as *Larus argentatus* shown here, maintain and waterproof their feathers by smoothing with an oily substance produced by the uropygial gland located near the anus. Photo By Lamiot - Own work, CC BY 2.5.

Fatty Acids: Building Blocks of Many Lipids

A **fatty acid** contains a long hydrocarbon chain with a **carboxylic acid group (–COOH)** at one end. This should already look familiar from Chapter 6!

The long hydrocarbon portion is predominantly **nonpolar and hydrophobic**, whereas the carboxylic acid group is much more **polar**. However, because the hydrocarbon chain can contain many carbon atoms, the nonpolar portion dominates much of the molecule's behavior. Naturally occurring fatty acids commonly contain long carbon chains, often between about 12 and 18 carbon atoms, although shorter and longer fatty acids also occur. Fatty acids can be classified as **saturated** or **unsaturated** depending on the types of carbon–carbon bonds present in the hydrocarbon chain.

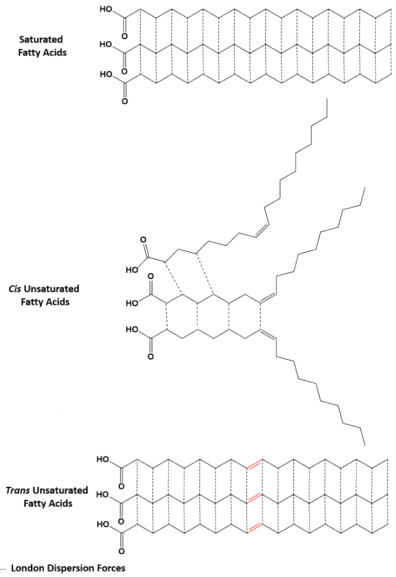


Figure 7.2.2: Saturated and Unsaturated Fatty Acids. Saturated fatty acids only contain carbon-carbon single bonds and thus, can stack on one another forming many London Dispersion intermolecular interactions (dashed lines). Unsaturated fatty acids in the cis conformation have bends in their chains that prevent them from stacking and forming substantial London Dispersion bonds. Thus, they tend to have lower melting temperatures and are liquids at room temperature. Unsaturated fatty acids in the trans conformation, do not have bends and thus, can stack and form London Dispersion interactions similar to that of saturated fatty acids.

Saturated Fatty Acids

A **saturated fatty acid** contains only carbon–carbon single bonds within its hydrocarbon chain. The term *saturated* means that the carbon atoms contain the maximum possible number of hydrogen atoms. Because C–C single bonds can rotate, saturated fatty acid chains are flexible. Overall, however, their relatively straight shapes allow neighboring fatty acid chains to pack closely together.

Close packing allows many **London dispersion forces** to form between the long hydrocarbon chains. Individually these attractions are weak, but when long chains lie next to one another, many interactions can occur simultaneously. As a result, lipids containing large proportions of saturated fatty acids tend to have **higher melting temperatures** and are more likely to be solid at room temperature.

Unsaturated Fatty Acids

An **unsaturated fatty acid** contains one or more carbon–carbon double bonds. A fatty acid containing one C=C double bond is **monounsaturated**, whereas one containing two or more is **polyunsaturated**. Recall from Chapter 6 that a carbon–carbon double bond restricts rotation and can exhibit **cis/trans isomerism**. This seemingly small difference in three-dimensional structure has a major effect on the physical properties of fatty acids.

Most naturally occurring unsaturated fatty acids contain **cis double bonds**. A cis double bond introduces a bend, or *kink*, into the hydrocarbon chain. These bent chains cannot pack together as closely as straighter saturated chains. With less surface-to-surface contact between neighboring molecules, fewer London dispersion interactions can form. Consequently, lipids containing high proportions of cis-unsaturated fatty acids generally have **lower melting temperatures** and are more likely to be liquids at room temperature. This is why many plant oils rich in unsaturated fatty acids are liquids, while fats containing larger proportions of saturated fatty acids are often solids.

What About Trans Fatty Acids?

A **trans double bond** does not introduce the same pronounced bend into a fatty acid chain. Trans-unsaturated fatty acids can therefore pack together more closely than their cis counterparts and tend to have physical properties more similar to saturated fatty acids. Notice how many earlier concepts come together here:

bond type → **molecular geometry** → **molecular packing** → **intermolecular forces** → **physical properties**.

This is an excellent example of one of chemistry's most important ideas: **structure determines properties**.

Triacylglycerides: Fats and Oils

The fats and oils used for long-term energy storage are composed primarily of **triacylglycerides (TAGs)**, also commonly called triglycerides. A triacylglyceride is constructed from two types of molecules:

- one **glycerol** molecule, and
- three **fatty acids**.

Glycerol is a three-carbon alcohol containing three hydroxyl (–OH) groups. Each of these hydroxyl groups can react with the carboxylic acid group of a fatty acid, joining the molecules together.

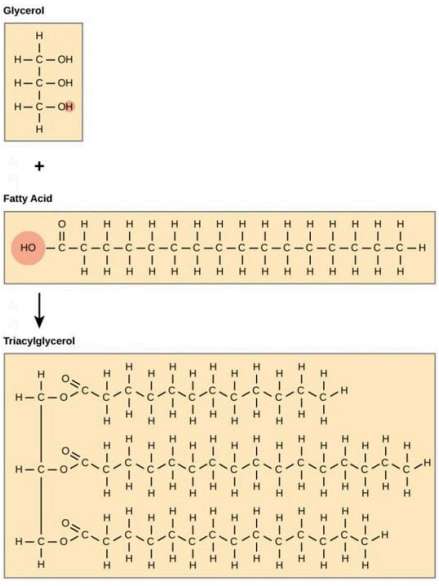


Figure 7.2.3: Formation of Triacylglycerides (TAGS). Triacylglycerides (TAGS) are formed by the joining of three fatty acids

to a glycerol backbone in a dehydration reaction (remember this removes a water molecule and forms a covalent bond). Three molecules of water are released in the process.

Look closely at the resulting structure. The fatty acid is no longer attached to glycerol through a carboxylic acid group. Instead, the reaction creates an **ester functional group**—another structure you learned to recognize in Chapter 6. Three fatty acids become attached to one glycerol molecule, producing a **triacylglyceride**. The formation of these bonds occurs through a type of reaction called **dehydration synthesis**, in which water is removed as a new covalent bond forms. We will examine this reaction in much greater detail in Chapter 8.

Fats Versus Oils

The terms *fat* and *oil* do not describe fundamentally different kinds of molecules. Both consist largely of triacylglycerides. Instead, their physical differences result largely from the fatty acids they contain. Triacylglycerides rich in **saturated fatty acids** can pack relatively tightly and tend to be solids at room temperature. Those rich in **cis-unsaturated fatty acids** pack less efficiently and tend to remain liquid.



Figure 7.2.4**: Fats and Oils**. Fats, like butter and lard contain large quantities of saturated fatty acids within their triacylglyceride structure. Thus, they tend to remain solids at room temperature due to the tighter packing of fatty acids and increased London Disperson Forces. Oils, on the other hand, have elevated levels of unsaturated fatty acids and cannot pack as tightly together. Thus, they have lower melting temperatures and tend to be oils at room temperature. Photo Source: Getty Image

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Thus, once again:

> **A small change in molecular structure can produce a large change in physical properties**.

Triacylglycerides are particularly useful for **long-term energy storage**. Their long hydrocarbon chains contain large amounts of chemical energy, and their hydrophobic nature allows them to be stored without attracting large quantities of water.

Waxes

Waxes are another class of strongly hydrophobic lipids. Many animal waxes contain long-chain fatty acids joined to long-chain alcohols through an **ester linkage**. Because waxes contain extensive nonpolar hydrocarbon regions, they are highly water-repellent. This makes them particularly useful as protective coatings. Plants often produce waxy coatings on the surfaces of leaves and fruits that help reduce water loss and repel external water. Animals also use waxes for protection and other specialized

purposes. Bees, for example, produce beeswax to construct honeycombs.

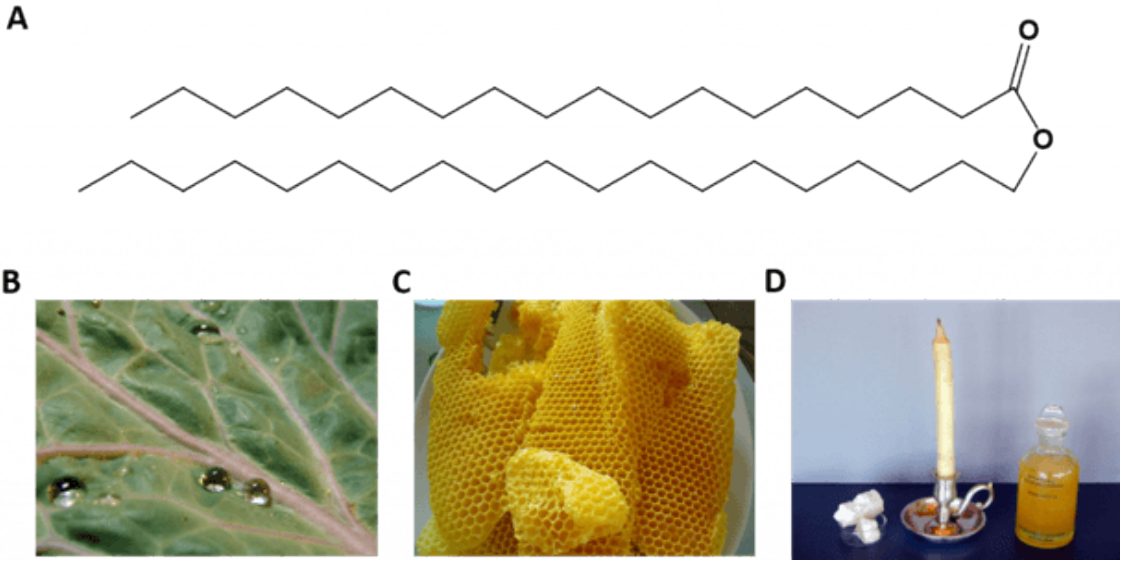


Figure 7.2.5: Examples of Waxes in Nature. (A) A typical wax ester contains two long chain hydrocarbons joined by an ester linkage. (B) Photo of water beading on the waxy cuticle of a kale leaf. (C) honeycomb made of beeswax, and (D) Spermaceti wax sample, a spemaceti candle, and spermaceti oil from the head of a sperm whale. (B) Courtesy of Rei at en.wikipedia, (C) Courtesy of Boutet, E. and (D) Courtesy of Einzelheiten zur Genehmigung.

Phospholipids: Building Cellular Membranes

Phospholipids are among the most important structural molecules in living cells because they form the basic framework of **cellular membranes**. Many phospholipids are structurally related to triacylglycerides. They contain a glycerol backbone, but instead of having three fatty acids attached, they contain:

- **two fatty acid tails**, and
- a **phosphate-containing group**.

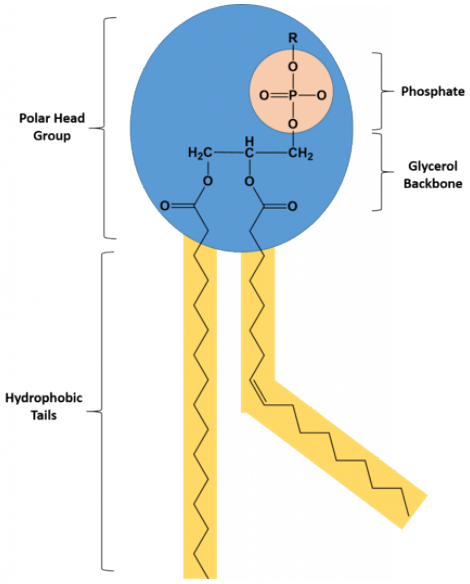


Figure 7.2.6: The Structure of a Phospholipid. A phospholipid is a molecule with two fatty acids and a modified phosphate

group attached to a glycerol backbone. The phosphate may be modified by the addition of charged or polar chemical groups at the position designated with an R.

The difference may appear small, but it dramatically changes the behavior of the molecule. The two fatty acid chains contain long nonpolar hydrocarbon regions and are therefore **hydrophobic**. The phosphate-containing region is polar or charged and interacts readily with water, making it **hydrophilic**. A molecule containing both a hydrophobic region and a hydrophilic region is described as **amphipathic**.

From Molecular Structure to a Membrane

What happens when phospholipids are placed in water? The hydrophilic heads interact favorably with surrounding water molecules, while the hydrophobic tails avoid contact with water. Large numbers of phospholipids therefore spontaneously organize so that their hydrophobic tails cluster together while their hydrophilic heads remain exposed to water. One arrangement produced by this behavior is the **phospholipid bilayer**.

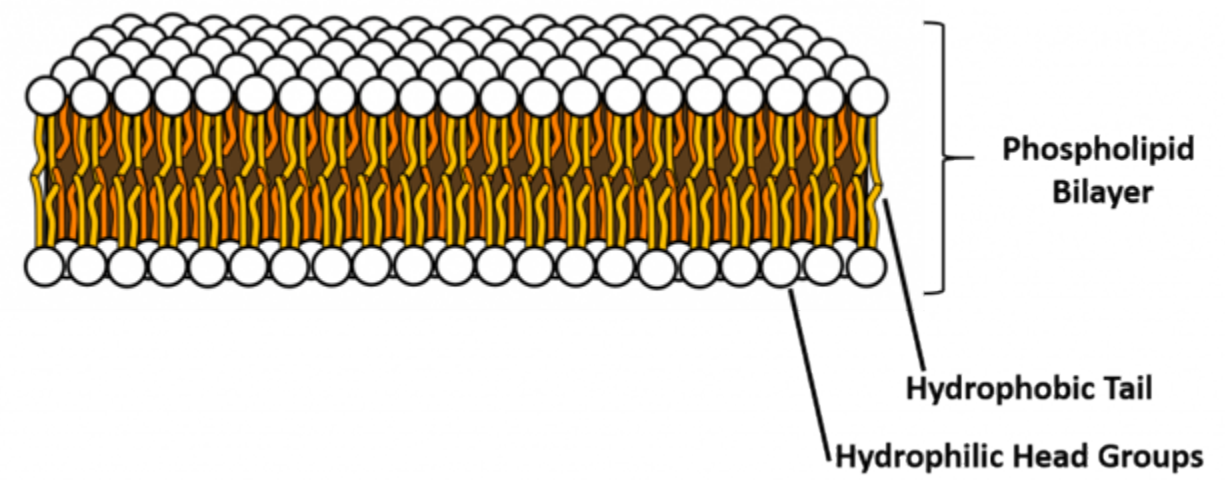


Figure 7.2.7**:The phospholipid bilayer is the major component of all cellular membranes**. The hydrophilic head groups of the phospholipids face the aqueous solution. The hydrophobic tails are sequestered in the middle of the bilayer. Credit AmitWo, Wikimedia.

In a bilayer, two layers of phospholipids arrange with their hydrophobic tails pointing inward toward one another and their hydrophilic heads facing the watery environments on either side. This structure forms the foundation of the **plasma membrane** surrounding every cell.

And now we can connect all the way back to our neuron story from Chapters 4 and 5. The interior of the phospholipid bilayer is **nonpolar and hydrophobic**. Charged ions such as Na^+, K^+, and Cl^- are surrounded by hydration shells in water and cannot easily pass through this hydrophobic interior. Cells must therefore use specialized **membrane proteins**, such as ion channels and pumps, to control the movement of these ions across the membrane. The chemistry of the phospholipid bilayer is therefore directly responsible for one of the fundamental properties of cells: **the ability to control what enters and leaves them.**

The Fluid Mosaic Model

The plasma membrane is not a rigid wall. Phospholipid molecules can move laterally within the bilayer, giving the membrane a flexible, dynamic character. Proteins are embedded within or associated with this phospholipid bilayer. Some span the entire membrane (**Integral membrane proteins**) and can act as channels, transporters, receptors, or pumps. Other proteins associate with only one surface of the membrane and are known as **peripheral membrane proteins**.

Carbohydrates may also be attached to membrane lipids or proteins, where they often participate in cellular recognition and communication. Due to the oily nature of the hydrophobic tails, the plasma membrane retains a fluid nature where the embedded proteins can move laterally from one area to another, much like they are swimming in the membrane. This dynamic arrangement of lipids, proteins, and carbohydrates is known as the **fluid mosaic model** of the plasma membrane.

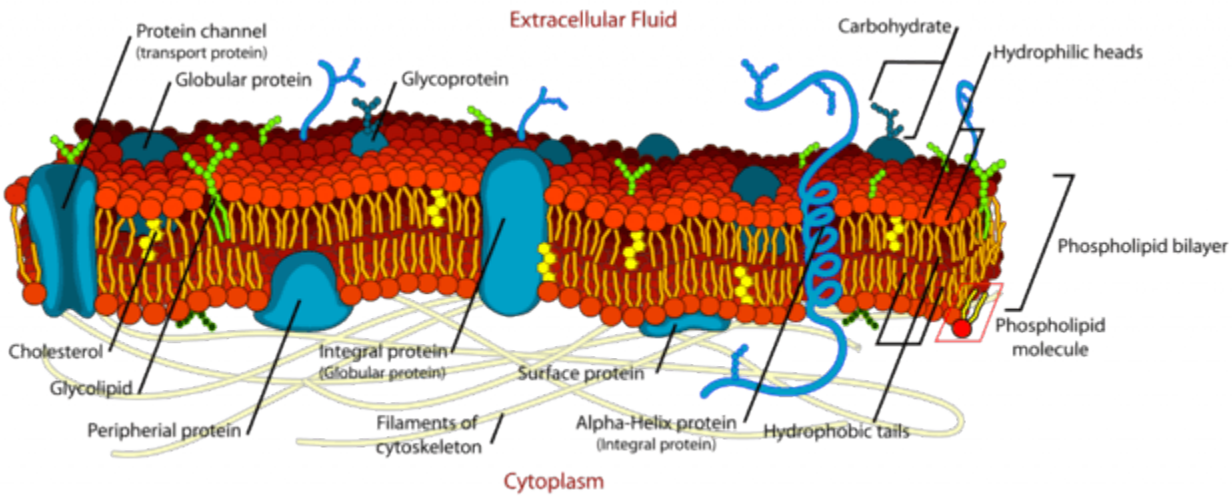
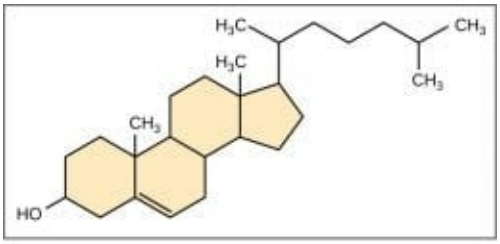


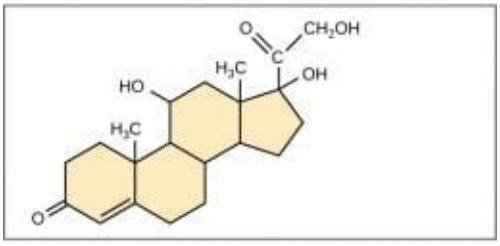
Figure 7.2.8**: The Fluid Mosaic Model of the Plasma Membrane**. The plasma membane core structure is the phospholipid bilayer. Embedded within this core structure are integral and peripheral membrane proteins. The proteins within the plasma membrane can move laterally through the plasma membrane. Carbohydrates are often attached to either lipids or proteins within the plasma membrane where they play a role in cell-to-cell communication.

Steroids: A Different Kind of Lipid

Not all lipids contain fatty acid chains. **Steroids** have a very different carbon skeleton consisting of **four fused carbon rings**. Despite their different structure, steroids are classified as lipids because much of their structure is nonpolar and hydrophobic.



Cholesterol



Cortisol

Figure 7.2.9**: Steroids such as cholesterol and cortisol are composed of four fused hydrocarbon rings**. The core planar ring structure of the steroid backbone is shaded in tan.

Once again, use your Chapter 6 skills when examining a steroid structure. Rather than trying to memorize every carbon, begin by recognizing the **four fused rings** and then look for functional groups attached to them.

One particularly important steroid is **cholesterol**. Cholesterol contains the characteristic four-ring steroid skeleton, a small hydrocarbon tail, and a hydroxyl (–OH) group. Because it contains an alcohol group, cholesterol is more specifically classified as a **sterol**. Cholesterol has several essential biological roles. It is an important component of animal cell membranes and is also used by the body as a starting material for the synthesis of other molecules, including **steroid hormones, bile acids, and vitamin D**. Within cell membranes, cholesterol helps regulate membrane fluidity. Its rigid ring structure fits among the fatty acid tails of phospholipids and helps prevent the membrane from becoming either too fluid or too rigid as conditions change.

Steroid hormones such as **testosterone, estradiol, and cortisol** share the basic four-ring steroid skeleton but differ in the functional groups attached to it.

This provides another powerful example of a principle introduced in Chapter 6:

> **Molecules can share the same basic carbon skeleton yet have very different biological activities because of differences in their functional groups and three-dimensional structures**.

Putting It All Together: Reading Lipid Structures

Lipids may initially look like a collection of very different molecules, but the organic chemistry principles behind them are familiar.

When examining an unfamiliar lipid, ask yourself:

1. **Where are the nonpolar hydrocarbon regions?**
2. **What functional groups can I identify?**
3. **Does the molecule contain saturated or unsaturated carbon chains?**
4. **If double bonds are present, how might their geometry affect molecular shape?**
5. **Is the entire molecule hydrophobic, or does it contain both hydrophobic and hydrophilic regions?**
6. **How might these structural features affect the way the molecule interacts with water or with other molecules?**

You do not need to memorize every lipid structure. Instead, use what you already know about **carbon skeletons, functional groups, polarity, molecular geometry, and intermolecular forces** to understand why different lipids behave the way they do.

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7.3: Carbohydrates

Learning Objectives

After completing this section, you should be able to:

- Describe the general structural features and biological functions of **carbohydrates**.
- Identify **monosaccharides** as the simplest carbohydrate units.
- Apply concepts of **functional groups, structural isomers, and stereoisomers** to carbohydrate structures.
- Recognize the difference between **aldose and ketose sugars**.
- Explain why many monosaccharides form **ring structures** in aqueous environments.
- Distinguish between the **α and β forms** of glucose at a recognition level.
- Describe how monosaccharides are joined by **glycosidic bonds** to form larger carbohydrates.
- Distinguish among **monosaccharides, disaccharides, and polysaccharides**.
- Describe the general structures and biological roles of **starch, glycogen, cellulose, and chitin**.

What Are Carbohydrates?

Carbohydrates are a diverse group of organic molecules composed primarily of carbon, hydrogen, and oxygen. They include simple sugar monomers such as glucose, galactose, fructose and larger disaccharide and polysaccharide structures such as sucrose, starch, and cellulose.

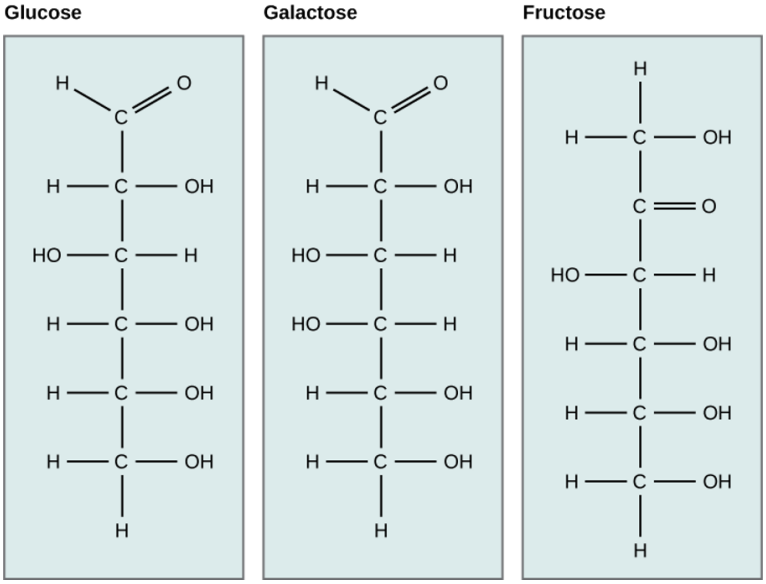


Figure 7.3.1**: Glucose, galactose, and fructose are all hexoses**. They are structural isomers, meaning they have the same chemical formula (C6H12O6) but a different arrangement of atoms. Fructose is a ketose sugar, whereas glucose and galactose are aldoses.

Carbohydrates perform several important functions in living organisms. They can provide an immediate source of **chemical energy**, store energy for later use, contribute to cellular recognition and communication, and provide structural support.

As we examine carbohydrate structures, you will see many familiar features from Chapter 6. Carbohydrates typically contain several **hydroxyl (–OH) groups** and either an **aldehyde or ketone** group in their open-chain forms. Many also contain several **chiral carbons**. Sugar monomers that contain aldehydes are called **aldoses**, whereas sugar monomers that contain ketones, are called **ketoses**. As shown in Figure 7.3.1, glucose and galactose are examples of aldose sugar monomers, whereas fructose is a

ketose.

Rather than memorizing the structure of each carbohydrate, continue practicing the strategy we established in Chapter 6:

> **Look at the structure and identify what you already know**.

Monosaccharides: The Simplest Carbohydrates

The simplest carbohydrates are called **monosaccharides**, or *simple sugars*. Monosaccharides cannot be broken down by hydrolysis into smaller carbohydrate units. Thus, they serve as the building blocks for the larger and more complex sugars.

Carbohydrates can be represented by the stoichiometric formula $(CH_2O)_n$, where n is the number of carbons in the molecule. In other words, the ratio of carbon to hydrogen to oxygen is 1:2:1 in carbohydrate molecules. This formula also explains the origin of the term “carbohydrate”: the components are carbon (“carbo”) and water (hence, “hydrate”). Thus, compared with lipids, carbohydrates are much more polar and many are soluble in water.

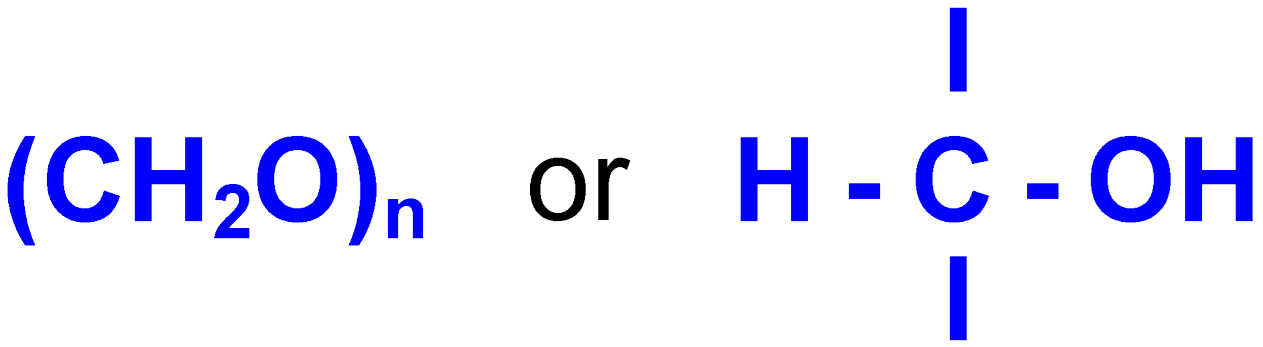


Figure 7.3.2**: Sugars are carbon hydrates**.

One of the most important monosaccharides in human biology is **glucose**, which has the molecular formula:

$C_6H_{12}O_6$

Glucose is an important source of energy for cells and is transported through the bloodstream to tissues throughout the body.

But glucose is not the only molecule with this molecular formula.

Fructose and **galactose** also have the formula $C_6H_{12}O_6$.

You should immediately recognize what this means from Chapter 6:

These molecules are isomers.

And they provide excellent examples of the two different kinds of isomerism we have already encountered. Fructose and glucose are structural (constitutional) isomers, which differ in the bonding order of the atoms, whereas glucose and galactose are stereoisomers that have the same bonded order of the atoms, but differ in their 3-dimensional arrangement in space. Compare galactose with fructose, what type of isomers are these?

Glucose and Fructose: Structural Isomers

Compare the open-chain structures of glucose and fructose. Both contain six carbon atoms, twelve hydrogen atoms, and six oxygen atoms. However, the atoms are not connected in exactly the same way. In its open-chain form, glucose contains an **aldehyde** group, whereas fructose contains a **ketone** group. A monosaccharide containing an aldehyde group is classified as an **aldose**, while a monosaccharide containing a ketone group is classified as a **ketose**.

Thus:

- **Glucose is an aldose.**
- **Fructose is a ketose.**

Because glucose and fructose have the same molecular formula but different atom-to-atom connectivity, they are **structural isomers**. Notice how useful functional-group recognition has suddenly become. You don't need to memorize why one is an aldose and the other is a ketose—you can **look at the structure and figure it out**.

Glucose and Galactose: Stereoisomers

Now compare glucose with another six-carbon sugar, **galactose**. Glucose and galactose have:

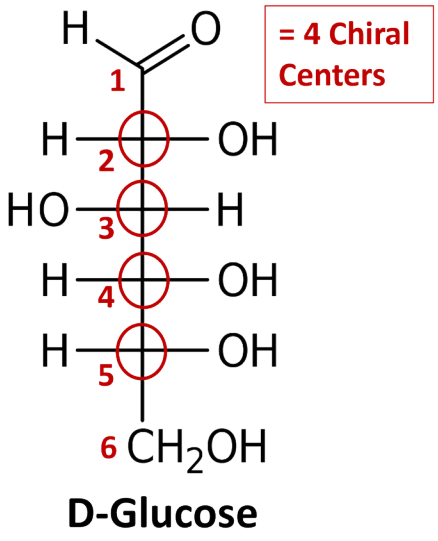
- the same molecular formula,
- the same types of functional groups, and
- the same basic atom-to-atom connectivity.

However, they differ in the three-dimensional arrangement around one of their chiral carbons. They are therefore **stereoisomers**. This is another direct application of Chapter 6. A molecule does not need to have a different molecular formula—or even different atom-to-atom connectivity—to have different chemical and biological properties. Sometimes a change in the three-dimensional orientation around a single carbon atom is enough.

Carbohydrates and Chirality

Many monosaccharides contain **multiple chiral carbons**.

Look at the open-chain structure of glucose. Several carbon atoms are tetrahedral and bonded to four different groups. Each of these is a potential stereocenter.



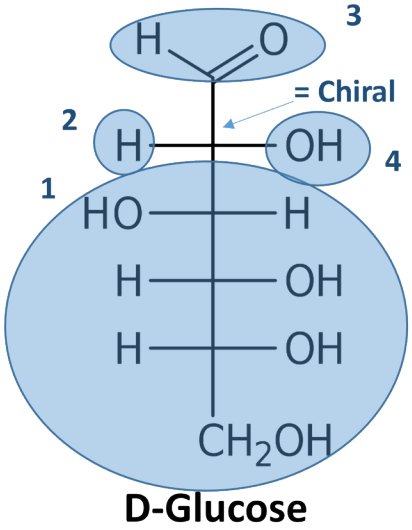


Figure 7.3.3: Identifying the Chiral Carbons in Glucose. Sugars can form many stereoisomers, ie the sugars have the same molecular formula and the same bonded order, but a different 3-dimensional arrangement in space. To determine how many stereoisomers exist for a particular sugar, you need to first determine how many chiral centers the sugar has. If we start with carbon-1 (indicated by the red number 1 in the lefthand figure), we can look at the groups that are attached to it. There are only three different groups. Since the oxygen is double bonded to the carbon, the carbon is found to be achiral and does not generate a stereocenter. Following the examination of the remaining carbons, you can see that there are a total of 4 chiral centers in glucose (carbons 2-5 each have four different groups bonded to the carbon). Carbon-6 has two hydrogens attached to it and is therefore, achiral. The figure on the right shows how to identify bonded groups on a carbon center. For example, carbon-2 (red #2 in lefthand diagram) has four different groups bonded to it (circled in blue in the diagram on the right): the –H, the –OH, and those two larger groups labeled with a blue #1 and #3. Thus, carbon-2 is chiral and ***does*** generate a stereocenter. To determine the number of stereoisomers use the formula, 2^n, where n = the number of chiral carbons in the molecule. For glucose, this would be a total of 16 stereoisomers, created by the 4 chiral carbon centers. Note that this only refers to stereoisomers and not to constitutional isomers.

For glucose, you will see that only the first and the last carbons in the chain are achiral. The first carbon is bonded in the aldehyde functional group and therefore contains two bonds to the same oxygen. Thus, it cannot be chiral. Similarly, the 6th carbon is bonded to two hydrogen atoms and also lacks chirality. The remaining four carbons are each bonded to four different substituents and therefore have chirality.

Due to the high amount of chirality, sugars often have many isomer possibilities. For example, the number of stereoisomers possible for glucose is 2^n, where n = the number of chiral centers. For glucose, n = 4. Thus, there are a total of 2 x 2 x 2 x 2 = 16 possible stereoisomers! Note that we are only listing the stereoisomers, not the vast number of structural isomers that are also possible. Recall that for protein recognition, the shape of the molecule in 3-dimensional space is critical. Thus, since carbohydrates have such a high possibility of isomeric forms, they are ideal components for cell-to-cell recognition, as small changes in the carbohydrate structure can be used for vastly different messages to the surrounding cells.

> **The many stereocenters found in carbohydrates allow molecules with the same molecular formula and connectivity to exist in different three-dimensional forms**.

And, as we learned in Chapter 6, biological molecules such as enzymes and receptors can distinguish between the small differences in stereoisomers, much like a lock and a key.

Sugar Enantiomers:

Note that for every sugar, there will be one other sugar that is exactly opposite at all of the chiral centers of the molecule. This exact opposite is the mirror image of the other sugar, but is not superimposable. This exact opposite is called the enantiomer. Note that enantiomer pairs have all of the same physical properties, except for the direction that they can rotate plain polarized light. Thus, they are very hard to tell apart and to separate from one another. They are in fact, given the same name, with the prefix of D- or L- to designate which way that they rotate plain polarized light. D- is given for sugars that rotate light in the right-handed or dextrorotatory, and L- is given for sugars that rotate light in the left-handed or levorotatory direction.

D-sugars are the ones predominantly produced in nature. To distinguish the D- and the L- conformations from one another, look at the chiral center that is farthest from the ketone or aldehyde functional group. If the hydroxyl (-OH) functional group is on the right hand side, it is the D- conformation, if the hydroxyl (-OH) functional group is on the left hand side, it is the L- conformation. The two enantiomers of glucose and fructose are shown below in Figure 7.3.4 as examples.

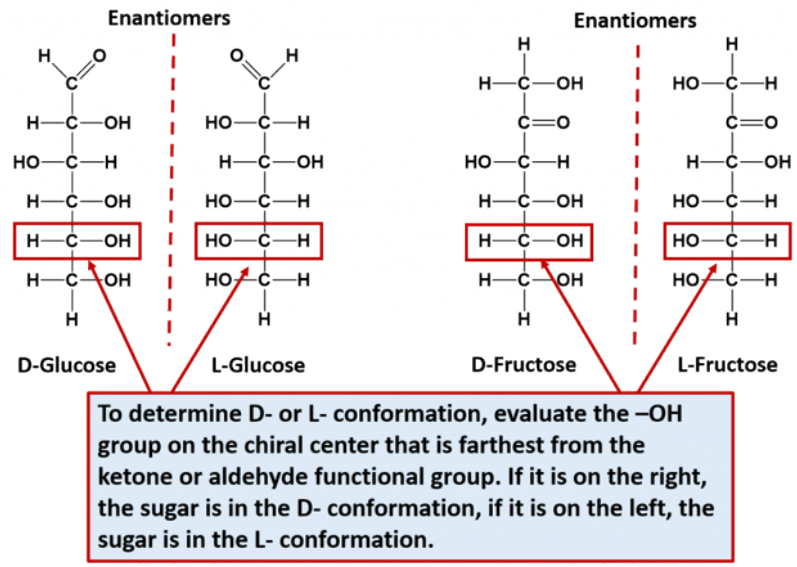


Figure 7.3.4: Enantiomer Pairs. Enantiomers are stereoisomers that are mirror images of one another but are not superimposable. For monosaccharides, each sugar can exist in the D- or L-conformation depending on which direction they rotate plain polarized light. To determine the D- or L- confomation, evaluate the -OH located on the chiral center farthest away from the ketone or aldehyde functional group. If it is on the right hand side, the sugar is the D- conformation. If it is on the left hand side, it is the L- conformation.

Monosaccharides Often Form Rings

So far, we have drawn glucose and other sugars as open chains because these structures make their functional groups and stereocenters easier to see.

In water, however, many monosaccharides—including glucose—exist predominantly in **cyclic, or ring-shaped, forms**.

Ring formation occurs when groups within the same molecule interact and form a new covalent bond. In glucose, this produces a six-membered ring containing five carbon atoms and one oxygen atom.

The ring structure of glucose can exist in two closely related forms called the **α (alpha)** and **β (beta)** forms.

You do **not** need to memorize the detailed mechanism by which these rings form. Instead, recognize that formation of the ring creates a new stereochemical distinction.

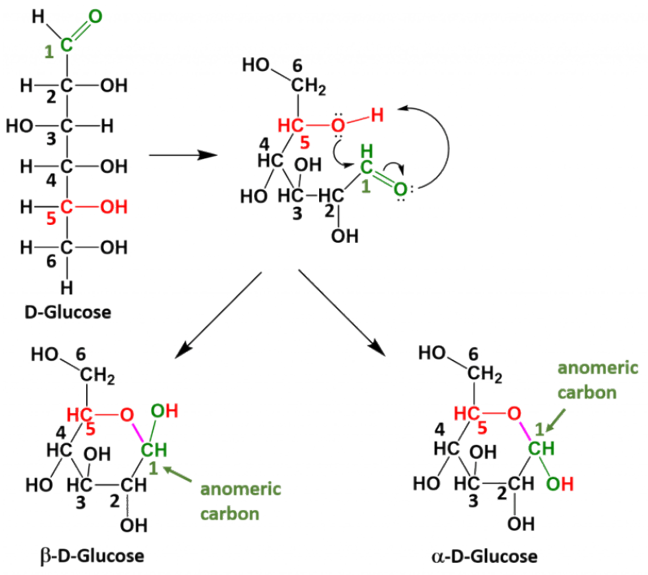


Figure 7.3.5: Cyclization of Glucose. When glucose cylizes the oxygen from the 5th carbon, shown in red, attacks the carbonyl carbon at position 1, shown in green. This pushes the double bond up onto the carbonyl oxygen which enables the carbonyl oxygen to take the hydrogen from the hydroxyl group on position 5. This forms a new bond, shown in purple between the oxygen at position 5 and the carbon at position 1. The carbon at position 1 is then bonded to two oxygen molecules and is known as the anomeric carbon, shown in green.

For glucose, the α and β forms differ in the orientation of the **–OH group attached to carbon 1**, called the **anomeric carbon**.

In the conventional ring structures we will use:

- in **α-glucose**, the –OH on carbon 1 points in the opposite direction from the CH_2OH group;
- in **β-glucose**, the –OH on carbon 1 points in the same direction as the CH_2OH group.

The α and β forms are called **anomers**.

Why bother distinguishing between two structures that differ only in the orientation of a single –OH group?

Because, once again, **three-dimensional structure matters in biology**.

As we will soon see, the α and β forms of glucose can be used to build polysaccharides with dramatically different structures and biological functions.

Building Larger Carbohydrates

Monosaccharides can be covalently joined together to form larger carbohydrates. When two monosaccharides are joined, the resulting molecule is called a **disaccharide**. The covalent bond connecting two sugar molecules is called a **glycosidic bond**. Formation of a glycosidic bond involves the removal of water as a new covalent bond forms—a **dehydration synthesis reaction**.

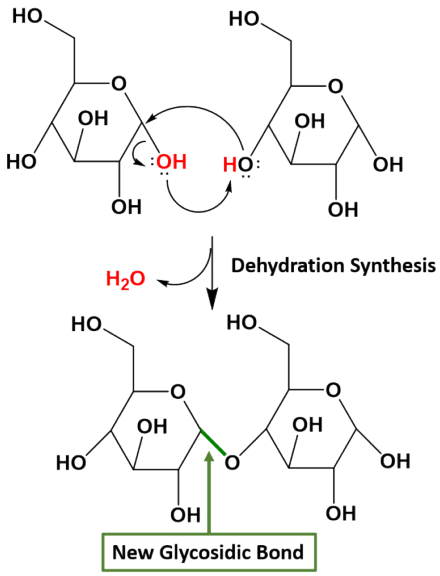


Figure 7.3.6**: Formation of a Glycosidic Bond**. In this example, two α-D-glucose monomers combine to form the disaccharide maltose. Glycosidic bonds, shown in green, are formed when two sugars undergo dehydration synthesis joining the sugar molecules through an oxygen linkage. The hydroxyl from the hemiacetal on one sugar, shown in red, combines with a hydrogen from the hydroxyl of another sugar, shown in red, to form the leaving water molecule, shown in red. The remaining oxygen from the hydroxyl group forms the glycosidic bond, shown in green, with the anomeric carbon atom from the first sugar.

Individual sugar units can be connected by glycosidic bonds to build larger carbohydrates.

Common Disaccharides

Several familiar dietary sugars are disaccharides:

- **Maltose** is composed of two glucose units.
- **Lactose** is composed of glucose and galactose.
- **Sucrose** is composed of glucose and fructose.

Notice that a disaccharide is not simply a mixture of two monosaccharides. The sugar units are **covalently bonded together** to form a new molecule.

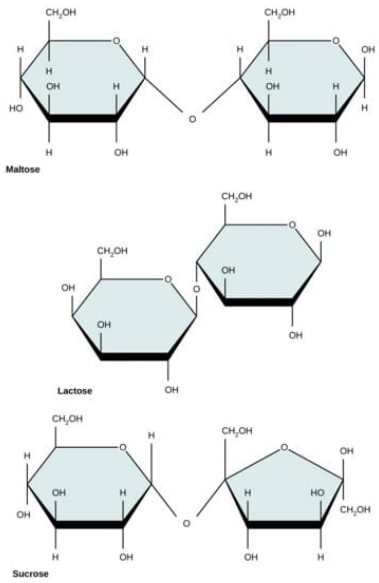


Figure 7.3.7: Common disaccharides include maltose (grain sugar), lactose (milk sugar), and sucrose (table sugar).

Polysaccharides

When many monosaccharide units are connected through glycosidic bonds, they form a **polysaccharide**. Polysaccharides can contain hundreds or thousands of sugar units and may form straight chains, branched chains, or highly organized structural materials. Four particularly important polysaccharides are **starch, glycogen, cellulose, and chitin**.

Starch: Energy Storage in Plants

Starch is a major form of glucose storage in plants. Starch is constructed primarily from **α-glucose** units and includes both relatively unbranched (**amylose**) and branched (**amylopectin**) glucose polymers. Plants store glucose as starch and can break the polymer down when energy is needed. Foods such as potatoes, rice, corn, and grains contain substantial amounts of starch. Humans can digest starch because our digestive enzymes can hydrolyze the types of glycosidic bonds found in it.

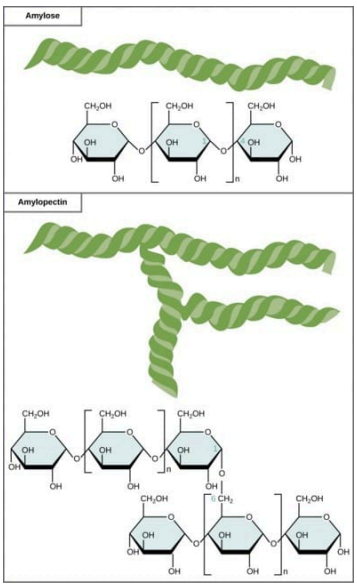


Figure 7.3.8: Amylose and amylopectin are two different forms of starch. Amylose is composed of unbranched chains of

glucose monomers. Amylopectin is composed of branched chains of glucose monomers. Because of the way the subunits are joined, the glucose chains have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more highly branched.

Glycogen: Energy Storage in Animals

Glycogen is the major storage form of glucose in animals. Like starch, glycogen is constructed from α-glucose units. Glycogen, however, is **highly branched**. In humans, glycogen is stored primarily in the **liver and skeletal muscles**. When glucose is needed, glycogen can be broken down rapidly to make stored carbohydrate available for energy metabolism. Thus, starch and glycogen perform similar functions: **starch stores glucose in plants; glycogen stores glucose in animals.** Note that all of the glucose monomers present in both starch and glycogen are in the **α-D-conformation**.

Cellulose: Structural Support in Plants

Cellulose is also composed entirely of glucose—but there is an important difference. Cellulose is constructed from **β-glucose** rather than α-glucose. That seemingly small stereochemical difference changes the shape of the polymer and the way neighboring chains interact. Cellulose chains can align closely and form extensive hydrogen-bonding interactions, producing strong fibers. Cellulose is therefore used primarily for **structural support** rather than energy storage and is a major component of plant cell walls. Humans cannot digest cellulose because our digestive enzymes cannot efficiently break the β-linked glucose chains. Instead, cellulose passes through the digestive system as an important component of **dietary fiber**. This gives us another wonderful example of the importance of stereochemistry:

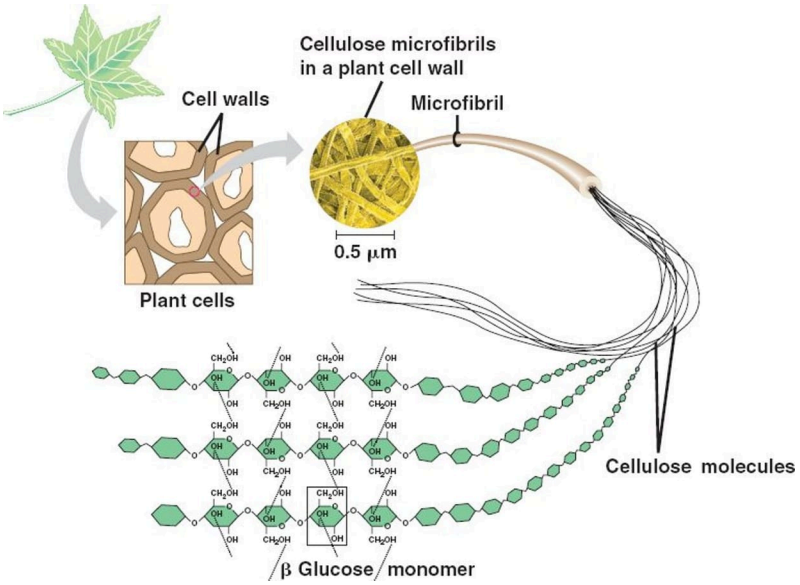


Figure 7.3.9: The Structure of Cellulose. In cellulose, glucose monomers are linked in unbranched chains by **β1,4 linkages**. Because of the way the glucose subunits are joined, every glucose monomer is flipped relative to the next one resulting in a linear structure that can form hydrogen bonds with neighboring strands. The result of the hydrogen bonded strands produces very strong fibrous material.

Starch and cellulose are both made from glucose, but differences in the stereochemistry of their glycosidic bonds produce molecules with very different structures, properties, and biological functions.

N-Acetylglucosamine and Chitin: Structural Support in Animals and Fungi

Chitin is another structural polysaccharide. Its repeating sugar units are modified forms of glucose that contain a **nitrogen-containing group.** The modified glucose monomer is called **N-acetylglucosamine**. Chitin forms strong structural materials and is found in the **exoskeletons of arthropods**, such as insects and crustaceans, and in the **cell walls of fungi**. Look closely

at the structure of chitin and you may recognize something from Chapter 6: the nitrogen-containing group includes an **amide functional group**. Once again, functional-group recognition allows us to begin interpreting a molecule even if we have never seen it before.

Chitin is also a major component of fungal cell walls; fungi are neither animals nor plants and form a kingdom of their own in the domain Eukarya. Polymers containing N-acetyl-β-d-glucosamine also occur in humans where they are present in extracellular matrix and provide cushioning for joints. In fact, N-acetyl-β-D-glucosamine is one of the most prominent dietary supplements sold in the United States, provided to support joint health.

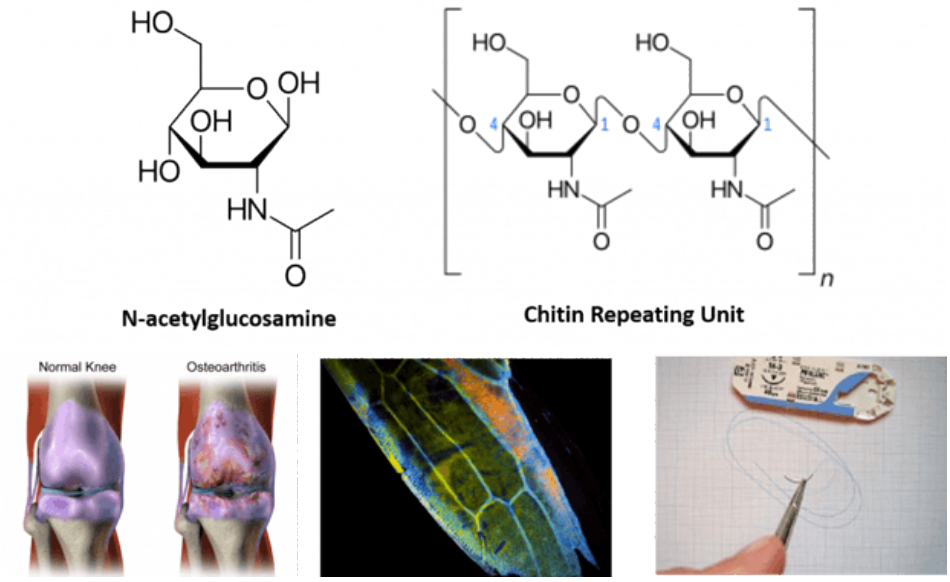


Figure 7.3.10**: N-acetyl-β-d-glucosamine is a common modified sugar in polysaccharides**. N-acetyl-β-d-glucosamine (upper left) is the repeating sugar unit in the polymer, chitin (upper right). N-acetyl-β-d-glucosamine is a component of normal joint cushioning (lower left). Chitin is a primary polysaccharide in the hard exoskeleton of insects as shown in the wing of the leafhopper (middle photo). Chitin has been utilized in medical technology to serve as material for surgical sutures. It provides a self dissolving matrix that will last about two weeks in the body and improves healing speed. Lower left photo provided by BruceBlaus, Middle photo provided by Zituba, and Lower right photo provided by Werneuchen.

Structure Determines Function

Carbohydrates provide some of our best examples of the relationship between molecular structure and biological function. Consider what we have seen:

Glucose and fructose have the same molecular formula but different atom-to-atom connectivity.

Glucose and galactose have the same molecular formula and connectivity but differ in stereochemistry.

α- and β-glucose differ only in the orientation of one group in their cyclic forms.

And polymers constructed from these sugars can have dramatically different properties depending on **which monosaccharides are used, how they are connected, and how the resulting chains interact with one another**. The result can be anything from a small molecule circulating in the bloodstream to a highly branched energy-storage polymer or the rigid structural material of a plant cell wall.

Putting It All Together: Reading Carbohydrate Structures

When you encounter an unfamiliar carbohydrate, don't begin by trying to remember its name. **Read its structure.**

Ask yourself:

1. **How many sugar units are present?** Is it a monosaccharide, disaccharide, or polysaccharide?
2. **What functional groups can you recognize?** Look especially for hydroxyl groups and, in open-chain structures, aldehydes or ketones.
3. **Are chiral carbons present?**
4. **Is the sugar drawn as an open chain or a ring?**
5. **If multiple sugars are present, where are the glycosidic bonds connecting them?**
6. **What intermolecular forces might occur between this molecule and water or between neighboring carbohydrate chains?**

You do not need to memorize the detailed structures of every carbohydrate shown in this section. Instead, use the organic chemistry skills you have developed to understand how **small differences in structure can produce important differences in properties and biological function**.

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7.4: Proteins

Learning Objectives

After completing this section, you should be able to:

- Describe the general structure of an **amino acid** and identify its amino group, carboxylic acid group, and R group.
- Explain how differences in **R groups** give amino acids different chemical properties.
- Describe how amino acids are joined by **peptide bonds** to form peptides and proteins.
- Explain how the **amino acid sequence** of a protein influences its three-dimensional shape.
- Describe how hydrogen bonding, ionic attractions, hydrophobic interactions, and disulfide bonds help stabilize protein structure.
- Describe the relationship between **protein shape and protein function**.
- Distinguish between **protein denaturation** and the breaking of peptide bonds by hydrolysis.
- Apply concepts of functional groups, polarity, intermolecular forces, and molecular shape to protein structure.

Proteins: Structure Creates Function

Proteins are among the most structurally and functionally diverse molecules found in living organisms. They serve as enzymes, receptors, antibodies, transporters, ion channels, hormones, structural materials, and molecular motors, among many other roles.

Despite this enormous variety, proteins are constructed from a relatively small set of building blocks called **amino acids**.

A protein is a polymer composed of amino acids joined together in a specific sequence. The resulting chain does not simply remain stretched out like a string. Instead, it folds into a particular three-dimensional shape.

That shape is critical to what the protein can do.

> **Protein shape determines protein function**.

We have already encountered this idea. In Chapter 6, we saw that the three-dimensional arrangement of a drug molecule can determine how well it fits into a protein binding site. Now we will examine the other side of that interaction: **what gives the protein its three-dimensional shape in the first place?**

Amino Acids: The Building Blocks of Proteins

Proteins are constructed from **20 common amino acids**.

Although their structures differ, all of these amino acids share the same basic framework. Each contains a central carbon, called the **α-carbon**, bonded to:

- an **amino group**,
- a **carboxylic acid group**,
- a hydrogen atom, and
- a variable group called the **R group**, or **side chain**.

The R group is the portion that differs from one amino acid to another.

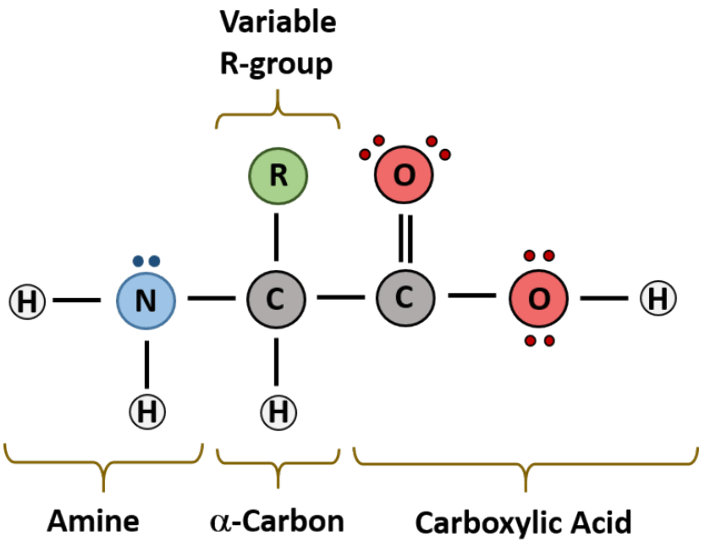


Figure 7.4.1**: General Structure of an Amino Acid**. Amino acids are the building blocks used to construct proteins. Each amino acid contains a central **α-carbon** bonded to four groups: an **amino group**, a **carboxylic acid group**, a **hydrogen atom**, and a variable **R group** (side chain). The R group differs among amino acids and gives each amino acid its characteristic chemical properties. With the exception of glycine, the α-carbon is also a **chiral center** because it is bonded to four different groups.

And now Chapter 6 comes roaring back! Look closely at the structures of the amino acids and you will find many functional groups you already recognize. Depending on the amino acid, an R group may contain hydrocarbon chains, aromatic rings, alcohols, thiols, amines, amides, or carboxylic acids. Your existing chapter already uses these differences in R-group chemistry to explain amino acid behavior.

These structural differences give the amino acids different chemical properties. Some R groups are **nonpolar and hydrophobic**, while others are **polar and hydrophilic**. Some can carry positive (Basic Amino Acids) or negative charges (Acidic Amino Acids).

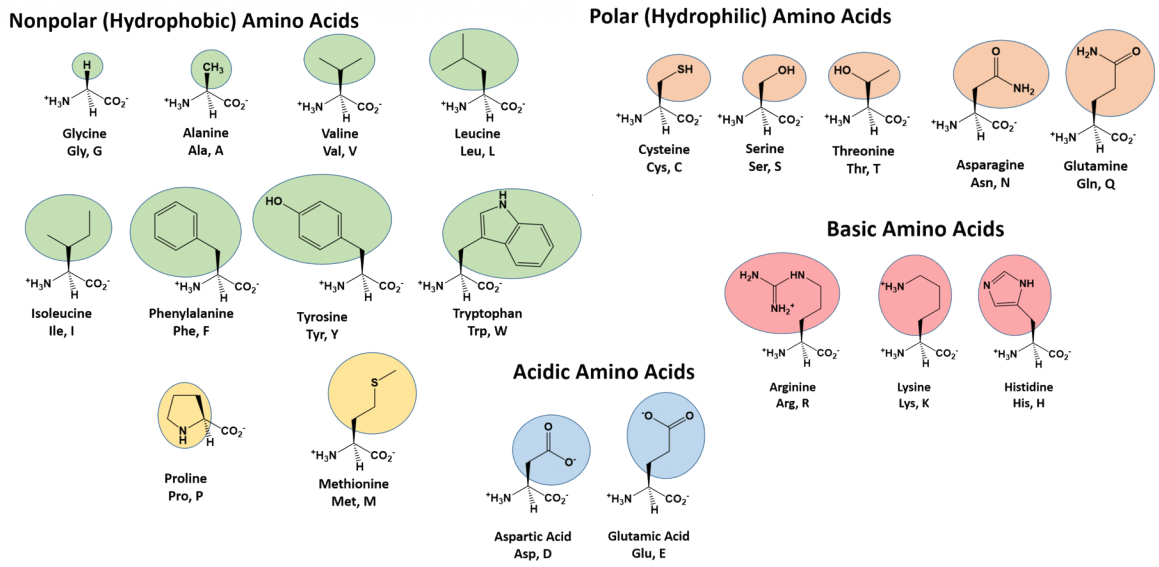


Figure 7.4.2**: The 20 Amino Acids Commonly Found in Proteins**. Proteins are constructed primarily from 20 different amino acids that share the same basic α-amino acid structure but differ in the chemical structure of their **R groups**, or side chains. The amino acids shown here are grouped according to general side-chain properties, including nonpolar, polar, acidic, and basic character. Differences in the size, shape, charge, polarity, and functional groups of the R groups determine how individual amino

acids interact with water and with one another. These interactions ultimately help determine how a protein folds into its three-dimensional structure.

Thus, you do not need to think of the 20 amino acids as 20 completely unrelated structures. Instead, use the organic chemistry you already know to **read their R groups and predict how they might behave**.

A Familiar Example of Chirality

There is another Chapter 6 concept hiding in the amino acid structure.

For most amino acids, the α-carbon is bonded to **four different groups**. What does that tell you?

It is a **chiral carbon**.

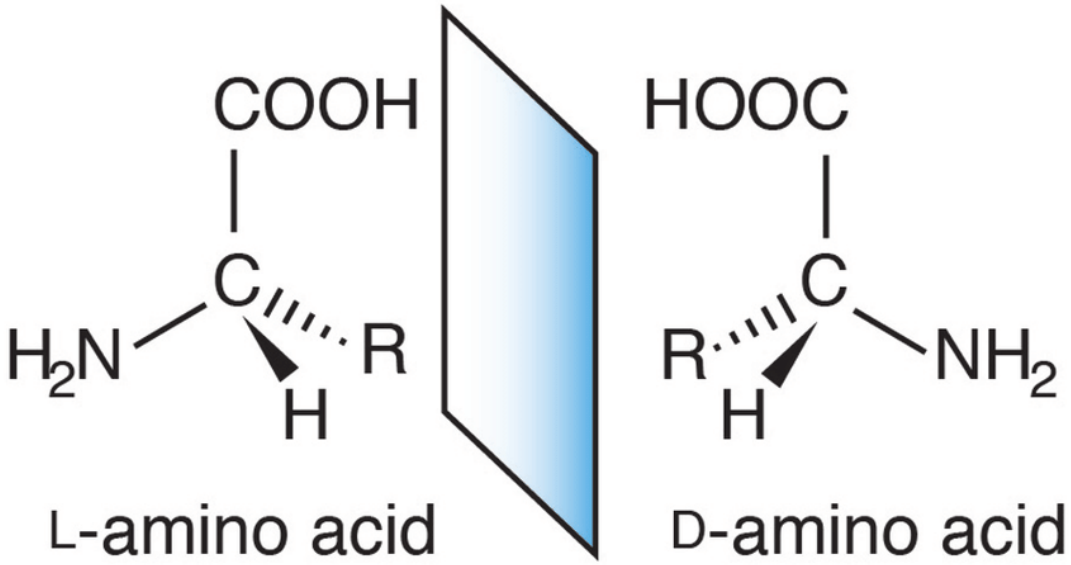


Figure 7.4.3**: Chirality of Amino Acids**. With the exception of glycine, the α-carbon of an amino acid is a **chiral center** because it is bonded to four different groups. Therefore, amino acids can exist as two nonsuperimposable mirror-image forms, designated **D** and **L**. The amino acids incorporated into proteins by cells are overwhelmingly the **L-amino acids**. The mirror-image structures shown here illustrate how the same groups can have different three-dimensional arrangements around a chiral carbon. Figure from: Sasabe and Suzuki.

The major exception is **glycine**, whose R group is simply a hydrogen atom. Glycine therefore has two hydrogen atoms attached to its α-carbon and is **achiral**.

You do not need to assign specific configurations to the amino acids in this chapter. The important point is that chirality is extremely common in biological molecules—and proteins themselves are constructed almost entirely from chiral building blocks. In the case of amino acid building blocks, the L-conformation is most commonly found in nature.

Joining Amino Acids: Peptide Bonds

Amino acids can be covalently joined together to build longer chains.

The carboxylic acid group of one amino acid can react with the amino group of another. During this process, water is removed and a new covalent bond forms between the two amino acids.

The resulting C–N bond is called a **peptide bond**.

Look carefully at the atoms surrounding the peptide bond. You should recognize the resulting functional group from Chapter 6:

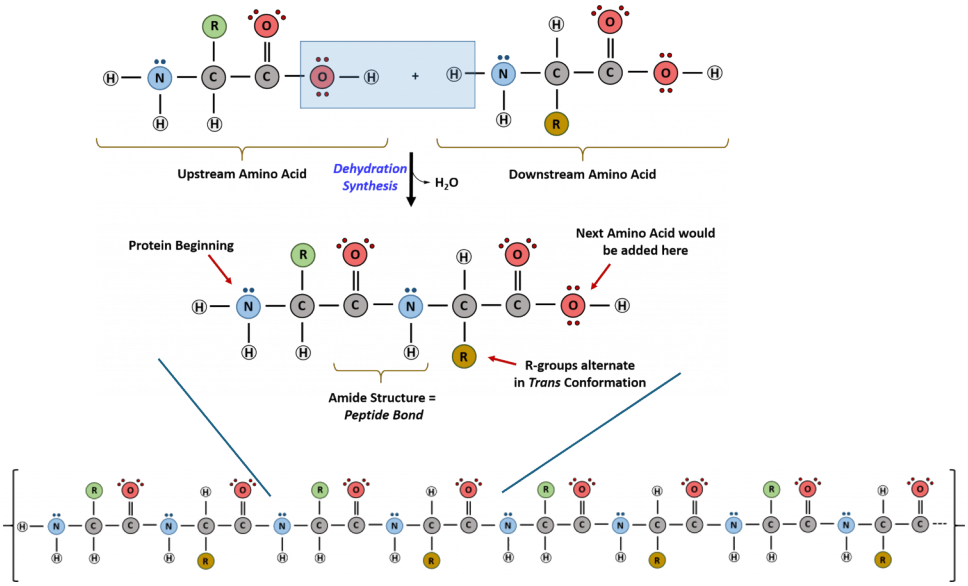


Figure 7.4.4**: Formation of Peptide Bonds and a Polypeptide Chain**. Amino acids are joined together through **dehydration synthesis**. The carboxylic acid group of one amino acid reacts with the amino group of another, releasing a molecule of water and forming a covalent **peptide bond**. Repetition of this reaction links many amino acids together to form a **polypeptide chain**. The resulting chain has a repeating backbone, while the different R groups extend from the backbone and give each amino acid its unique chemical properties. The order of these R groups reflects the amino acid sequence of the protein.

A peptide bond is an amide linkage.

Two amino acids joined together form a **dipeptide**. Adding additional amino acids produces progressively longer chains called **polypeptides**. Proteins consist of one or more polypeptide chains folded into functional three-dimensional structures.

The formation of a peptide bond is another example of a **dehydration synthesis reaction**. We will examine this reaction pattern more closely in Chapter 8.

Amino Acid Sequence: Primary Structure

The amino acids within a protein are not arranged randomly.

The specific order of amino acids in a polypeptide chain is called the protein's **primary structure**.

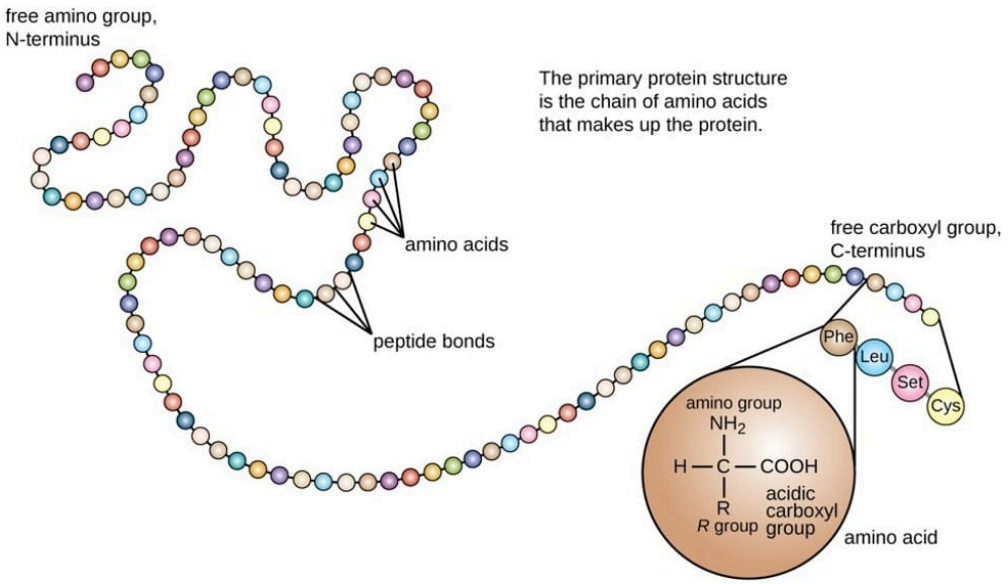


Figure 7.4.5**: Primary Structure of a Protein**. The **primary structure** of a protein is the specific sequence of amino acids joined together by peptide bonds in a polypeptide chain. Each amino acid occupies a particular position in the sequence, and the chain has directionality, extending from the **N-terminus**, which has a free amino group, to the **C-terminus**, which has a free carboxyl group. The identity and order of the amino acids determine the sequence of R groups along the chain and therefore influence the interactions that ultimately cause the protein to fold into its characteristic three-dimensional structure. (credit: modification of work by National Human Genome Research Institute).

For example, imagine two proteins containing exactly the same number and types of amino acids but arranged in different sequences. Their different sequences place different R groups at different positions along the chain. This changes which parts of the molecule can interact with one another as the protein folds.

As a result, different amino acid sequences can produce different three-dimensional structures.

And different structures can produce different functions.

Thus, there is an important progression:

amino acid sequence → interactions → protein folding → three-dimensional shape → protein function.

This is the central idea I would want students to carry away from this section.

Why Do Proteins Fold?

This is where several chapters of chemistry come together.

Remember that every amino acid contributes a different R group to the protein chain. Those R groups can interact with one another and with the environment surrounding the protein.

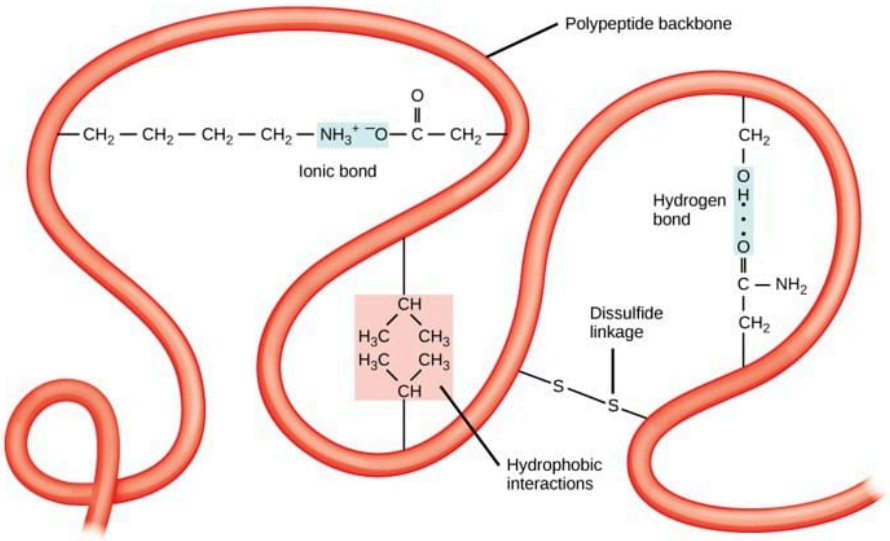


Figure 7.4.6**: Chemical Interactions That Stabilize Protein Structure.** As a polypeptide folds, amino acid R groups located in different regions of the chain can interact with one another. **Hydrogen bonds, ionic attractions, and hydrophobic interactions** help stabilize the folded protein, while **disulfide linkages** can form covalent bonds between sulfur-containing cysteine side chains. Together, these interactions help produce and stabilize the characteristic three-dimensional shape of a protein.

Hydrophobic Interactions

Many proteins function in watery environments such as the cytoplasm or bloodstream.

Nonpolar R groups cannot form favorable interactions with water. As a protein folds, these **hydrophobic groups often become buried within the interior of the protein**, away from surrounding water.

Polar and charged R groups, in contrast, are often found on the protein surface where they can interact with water.

This should sound very familiar from our discussion of lipids and membranes:

> **Nonpolar groups tend to associate with other nonpolar regions, while polar and charged groups interact more favorably with water**.

Interestingly, proteins embedded within a cell membrane face a very different environment. Portions of these proteins that contact the nonpolar fatty acid tails of the phospholipid bilayer often contain many **hydrophobic amino acid side chains**.

Thus, the surrounding environment helps determine which interactions are most favorable.

Hydrogen Bonding

Polar groups within a protein can form **hydrogen bonds** with one another.

Although individual hydrogen bonds are relatively weak, a large protein can form many of them. Together, these interactions can make an important contribution to maintaining protein shape.

Ionic Attractions

Some amino acid R groups can carry full positive or negative charges.

Oppositely charged groups can attract one another, producing **ionic interactions** that help stabilize portions of a folded protein.

London Dispersion Forces

When atoms are packed closely together within a folded protein, **London dispersion forces** also contribute to the overall stability of the structure.

Once again, these are individually weak interactions—but there may be a very large number of them within a protein.

Notice what is happening here:

The same intermolecular forces you learned about in Chapter 5 are now helping create the three-dimensional structure of a protein.

Disulfide Bonds: A Covalent Connection

Most of the interactions that stabilize protein shape are noncovalent, but proteins can also contain additional covalent bonds.

The amino acid **cysteine** contains a **thiol (–SH) group** in its R group. Two cysteine side chains can react to form a covalent **disulfide bond (–S–S–)**.

Disulfide bonds can connect different regions of the same polypeptide chain or help hold different polypeptide chains together.

Because they are covalent bonds, disulfide bonds are considerably stronger than individual hydrogen bonds or other weak interactions and can provide substantial structural stability.

The hormone **insulin**, for example, contains disulfide bonds that help hold its polypeptide chains together. Your current text uses insulin as an example of this structural role.

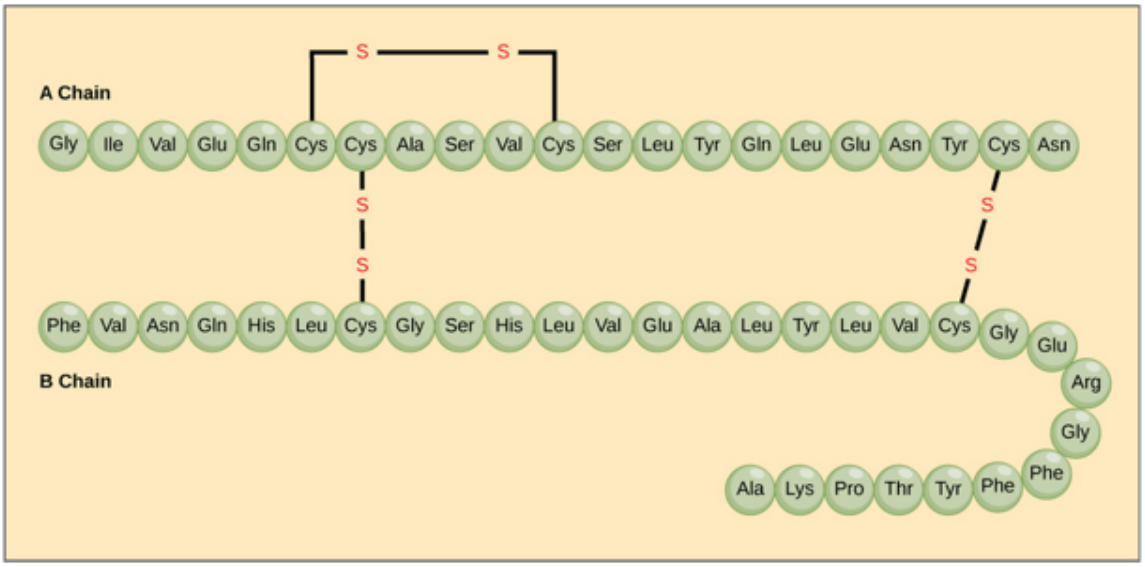


Figure 7.4.7**: Disulfide Bonds**. Disulfide bonds are formed between two cysteine residues within a peptide or protein sequence or between different peptide or protein chains. In the example above the two peptide chains that form the hormone insulin are depicted. Disulfide bridges between the two chains are required for the proper function of this hormone to regulate blood glucose levels.

From a Chain to a Three-Dimensional Protein

Biochemists describe protein organization using several levels of structure.

Primary Structure

The **primary structure** is simply the linear sequence of amino acids in the polypeptide chain.

Secondary Structure

Small regions of the protein backbone can form repeating patterns called **secondary structures**. Two common examples are the:

- **α-helix**, which coils into a spiral, and
- **β-pleated sheet**, in which sections of the protein chain align alongside one another.

Hydrogen bonding between groups in the peptide backbone helps stabilize these structures.

Tertiary Structure

The overall three-dimensional shape of a single polypeptide chain is called its **tertiary structure**. This structure results from the combined effects of hydrophobic interactions, hydrogen bonding, ionic attractions, dispersion forces, and sometimes disulfide bonds. In other words, tertiary structure is where much of the chemistry we've been discussing becomes visible as the **overall shape of the protein**.

Quaternary Structure

Some functional proteins contain more than one polypeptide chain. The way these separate protein subunits associate with one another is called **quaternary structure**. Not every protein has quaternary structure. A protein made from a single polypeptide chain can function perfectly well without it.

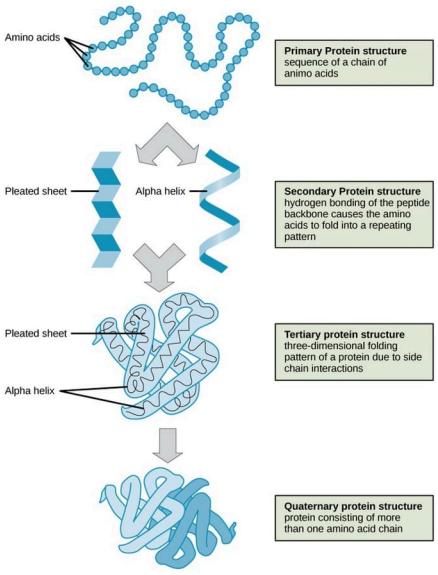


Figure 7.4.8: Levels of Protein Structure. Protein structure can be described at several levels. **Primary structure** is the specific sequence of amino acids in a polypeptide chain. **Secondary structure** results from hydrogen bonding within the peptide backbone and produces repeating structures such as **α-helices** and **β-pleated sheets**. **Tertiary structure** is the overall three-dimensional shape of a single polypeptide produced by interactions among its amino acid side chains and the surrounding environment. Some proteins also have **quaternary structure**, in which two or more polypeptide chains associate to form the functional protein. (credit: modification of work by National Human Genome Research Institute).

Protein Shape Determines Protein Function

Why does all this folding matter?

A protein's function depends on its ability to interact with other molecules. These interactions occur at specific regions of the protein whose shapes and chemical properties allow particular molecules to bind. An enzyme, for example, must have a binding region that can interact with the molecules involved in the reaction it catalyzes. A receptor must recognize particular signaling molecules. An ion channel must have the appropriate structure to span a membrane and allow selected ions to pass through it.

This brings us directly back to Chapter 6.

When we discussed chirality and drug development, we saw that a drug molecule may fit into a protein binding site much like a hand fits into a glove. We can now see that the **shape and chemical character of that glove are created by the amino acid sequence and the interactions that cause the protein to fold**. Change the shape of the protein, and you may change—or completely eliminate—its function.

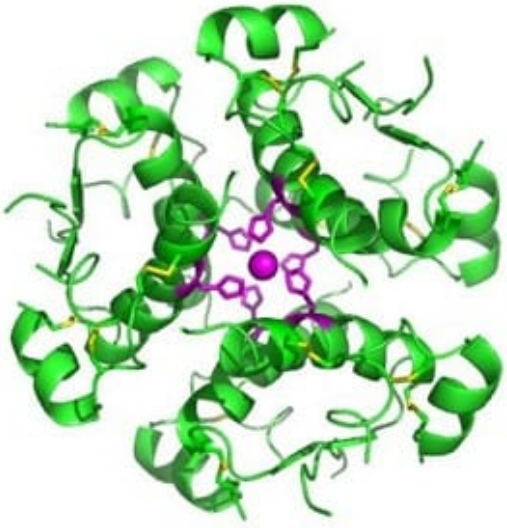


Figure 7.4.9**: Protein Shape and Function—Insulin as an Example**. Insulin illustrates how the organization and shape of a protein are closely connected to its function. Insulin molecules can associate to form a **hexamer**, a quaternary structure containing six insulin molecules that provides a stable form for storage. To carry out its signaling function, however, insulin must dissociate into **individual monomers** that can bind to insulin receptors on target cells. Thus, the same protein can participate in different molecular associations suited to different roles: the assembled hexamer provides stability for storage, while the shape and chemical features of the monomer allow it to interact specifically with its receptor. **For proteins, structure is not simply a physical characteristic—it is fundamental to function**. Figure By: Isaac Yonemoto.

Denaturation: When Proteins Lose Their Shape

Protein folding depends on many chemical interactions, and those interactions can be disrupted.

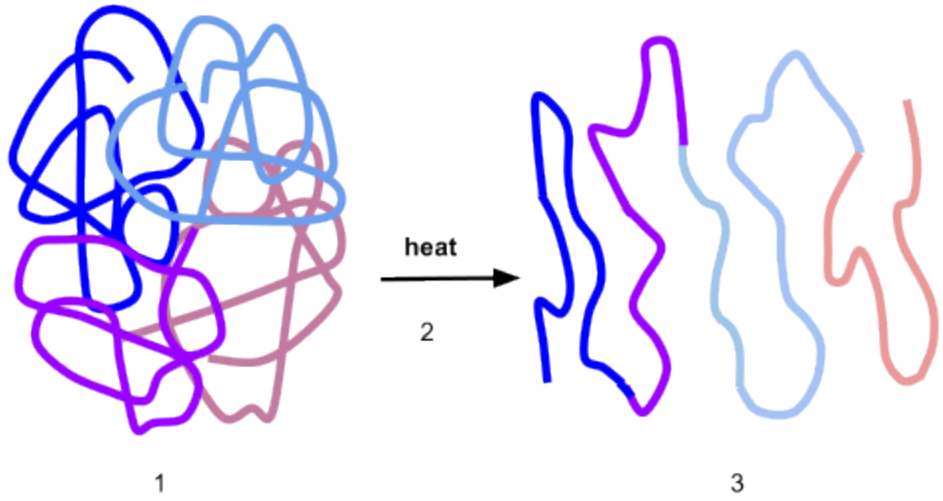


Figure 7.4.10**: Protein Denaturation**. Figure (1) depicts the correctly folded intact protein. Step (2) applies heat to the system that is above the threshold of maintaining the intramolecular protein interactions. Step (3) shows the unfolded or denatured protein. Colored regions in the denatured protein correspond to the colored regions of the natively folded protein shown in (1). Diagram provided by: Scurran15.

Changes in **temperature, pH, or chemical environment** can cause a protein to unfold and lose its normal three-dimensional structure. This process is called **denaturation**. Your existing section uses these same factors and the familiar example of cooking an egg.

Importantly:

> **Denaturation changes protein shape without necessarily breaking the peptide bonds of the primary amino acid sequence**.

For example, when an egg is cooked, heat disrupts many of the interactions maintaining the structures of proteins in the egg white. The proteins unfold and interact with one another in new ways, changing the egg white from a clear liquid into an opaque solid. Depending on the protein and the conditions, denaturation may sometimes be reversible. In other cases, the unfolded proteins form new interactions or aggregate in ways that prevent them from returning to their original structures.

Denaturation Is Not the Same as Hydrolysis

This distinction is important.

During **denaturation**, the protein loses its three-dimensional shape, but its peptide backbone generally remains intact.

During **hydrolysis**, water is used to break covalent peptide bonds. The primary structure itself is therefore broken apart.

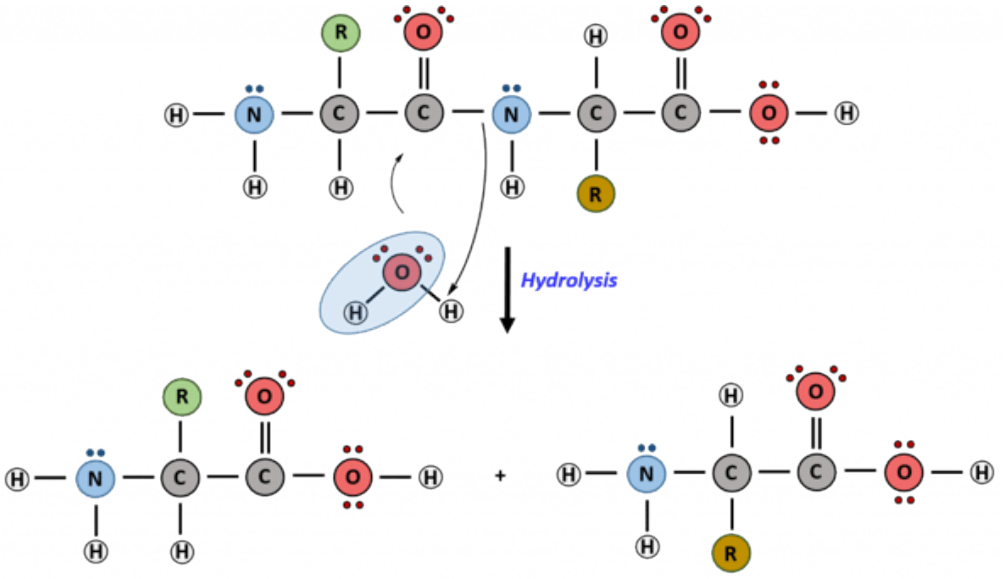


Figure 7.4.11**: Hydrolysis of Proteins**. In the hydrolysis reaction, water is added across the amide bond incorporating the -OH group with the carbonyl carbon and reforming the carboxylic acid. The hydrogen from the water reforms the amine.

We will examine hydrolysis reactions in more detail in Chapter 8. A simple way to remember the distinction is:

Denaturation → changes the folding.

Hydrolysis → breaks the chain.

Putting It All Together: Reading Protein Chemistry

Proteins may be enormous molecules, but you do not need to memorize their complete structures to understand their chemistry.

When examining a protein or peptide, ask:

1. **What are its building blocks?** Proteins are constructed from amino acids.
2. **How are those building blocks connected?** Look for peptide bonds—the **amide linkages** connecting amino acids.
3. **What kinds of R groups are present?** Are they nonpolar, polar, charged, or capable of forming particular interactions?
4. **What interactions might occur?** Look for opportunities for hydrogen bonding, ionic attractions, hydrophobic interactions, and disulfide bonds.
5. **How might the surrounding environment affect the protein?** A protein in water experiences a very different environment from one embedded in a lipid membrane.
6. **What happens if those interactions are disrupted?** Changes in protein folding can alter or destroy protein function.

The enormous diversity of proteins does not come from an enormous number of different building blocks. Instead, it comes from arranging a relatively small collection of amino acids into different sequences and allowing the chemistry of their R groups to guide the resulting chains into different three-dimensional structures.

> **Amino acid sequence influences protein shape, and protein shape determines protein function**.

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7.5: Nucleic Acids

Learning Objectives

After completing this section, you should be able to:

- Identify the three components of a **nucleotide**: a phosphate group, a five-carbon sugar, and a nitrogen-containing base.
- Distinguish between **DNA and RNA** based on their sugars, nitrogenous bases, and general structures.
- Explain how nucleotides are joined by **phosphodiester bonds** to form nucleic acid strands.
- Describe how **hydrogen bonding** produces complementary base pairing between DNA strands.
- Explain how covalent bonds and intermolecular forces play different roles in maintaining DNA structure.
- Describe the relationship between the **sequence of nitrogenous bases** and the storage of genetic information.
- Apply concepts from Chapters 5 and 6, including functional groups, polarity, hydrogen bonding, and molecular structure, to nucleic acids.

Nucleic Acids: Molecules That Store Information

The fourth major class of biological macromolecules is the **nucleic acids**. The two major nucleic acids are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**.

DNA stores the genetic information needed to build and maintain an organism. RNA performs several different roles in using that information, including helping cells produce proteins.

Unlike proteins, which are built from amino acids, nucleic acids are polymers constructed from repeating units called **nucleotides**.

At first glance, nucleic acid structures can look intimidating. However, just as we have done with the other biological molecules in this chapter, we can break them into smaller pieces and identify chemistry that we already recognize.

Nucleotides: The Building Blocks of Nucleic Acids

Every **nucleotide** contains three components:

1. a **five-carbon sugar**,
2. a **phosphate group**, and
3. a **nitrogen-containing base**.

There is quite a lot of Chapter 6 chemistry packed into that small structure!

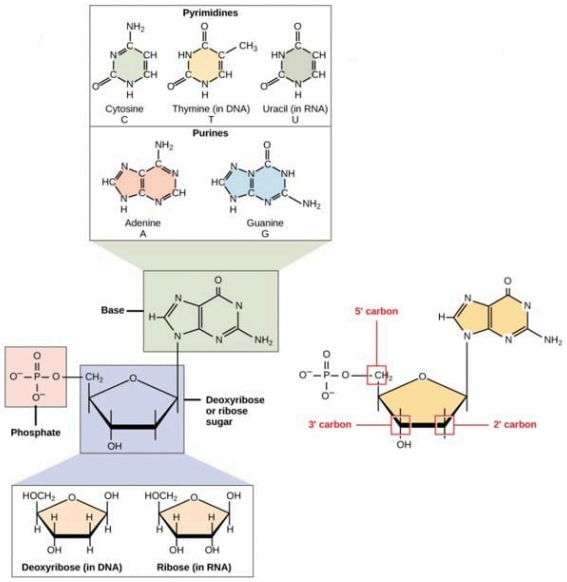


Figure 7.5.1: The Structural Components of DNA and RNA Nucleotides. Nucleotides are composed of three major components: a **phosphate group**, a **five-carbon sugar**, and a **nitrogenous base**. DNA contains the sugar **deoxyribose**, whereas RNA contains **ribose**. The nitrogenous bases are divided into two structural groups: the single-ring **pyrimidines** (cytosine, thymine, and uracil) and the double-ring **purines** (adenine and guanine). DNA uses thymine, whereas RNA uses uracil. The carbon atoms of the sugar are numbered 1′ through 5′; this numbering becomes important when describing how nucleotides are connected to form DNA and RNA strands.

The sugar contains several carbon atoms, oxygen atoms, and hydroxyl groups. The phosphate group is attached to the sugar through a **phosphoester bond**. The nitrogen-containing base contains one or more rings with several nitrogen atoms.

Rather than memorizing every atom in a nucleotide, begin by learning to recognize these **three major regions**.

Nucleosides and Nucleotides

A sugar bonded to a nitrogenous base is called a **nucleoside**.

When one or more phosphate groups are added, the structure becomes a **nucleotide**.

Thus:

sugar + base = nucleoside.

sugar + base + phosphate = nucleotide.

The nucleotides used to build DNA and RNA contain one phosphate group when they become incorporated into the nucleic acid chain. Nucleotides can also occur independently in cells and perform other important functions. **ATP**, for example, is a nucleotide that plays a central role in cellular energy transfer.

DNA and RNA

DNA and RNA are both nucleic acids, but their nucleotides are not identical.

The Sugars

DNA contains the five-carbon sugar **deoxyribose**, whereas RNA contains the closely related sugar **ribose**.

Compare their structures carefully.

Ribose contains an –OH group attached to its 2′ carbon. Deoxyribose has an H in this position instead—hence the name **deoxy**ribose, meaning that it contains one less oxygen.

This small structural difference helps distinguish DNA from RNA.

The Nitrogenous Bases

Five major nitrogenous bases occur in DNA and RNA:

- **adenine (A)**
- **guanine (G)**
- **cytosine (C)**
- **thymine (T)**
- **uracil (U)**

DNA contains **A, G, C, and T**.

RNA contains **A, G, C, and U**.

Thus, RNA uses **uracil in place of thymine**.

You do not need to memorize the complete structures of these bases. However, notice that they contain **nitrogen-containing aromatic rings** and several familiar functional groups. Once again, biological molecules are constructed using the same organic chemistry we learned in Chapter 6.

Building a Nucleic Acid Strand

Individual nucleotides are covalently connected to form a nucleic acid chain.

The phosphate group attached to one sugar forms a bond with the sugar of the neighboring nucleotide. This produces a **phosphodiester bond**.

Why *phosphodiester*?

Recall from Chapter 6 that a phosphate bonded through oxygen to an organic group forms a **phosphoester**. Within the nucleic acid backbone, each phosphate is connected through oxygen atoms to **two different sugars**, producing a **phosphodiester linkage**.

Repeated sugar–phosphate connections create the **sugar-phosphate backbone** of DNA and RNA.

The nitrogenous bases project outward from this backbone.

This gives nucleic acids two very different structural components:

- a repeating **sugar-phosphate backbone**, and
- a variable sequence of **nitrogenous bases**.

The backbone provides the structural framework of the molecule. The sequence of bases carries the information.

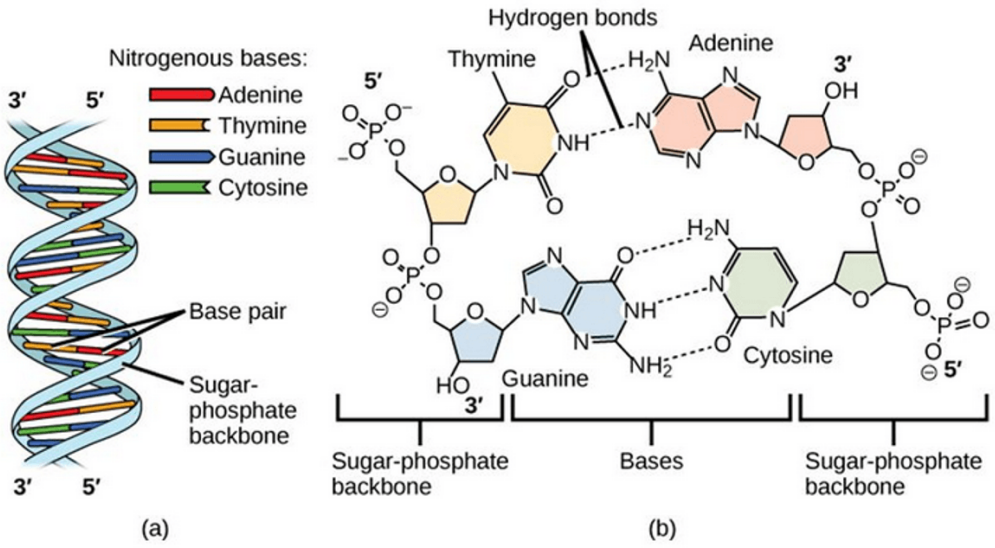


Figure 7.5.2**: Structure and Base Pairing in DNA**. DNA consists of two nucleotide strands arranged in a double helix. Each strand contains a **sugar-phosphate backbone**, while the nitrogenous bases project toward the center of the molecule and form complementary **base pairs** through hydrogen bonding. **Adenine (A) pairs with thymine (T)** through two hydrogen bonds, while **guanine (G) pairs with cytosine (C)** through three hydrogen bonds. The two DNA strands run in opposite directions, or **antiparallel** to one another: one strand runs from 5′ to 3′ while the complementary strand runs from 3′ to 5′. The specific pairing of the bases allows the sequence of one DNA strand to determine the sequence of its complementary strand.

DNA Has Direction

The two ends of a nucleic acid strand are chemically different because the nucleotides are connected in a specific orientation.

One end is called the **5′ (five-prime) end**, and the other is called the **3′ (three-prime) end**. These names refer to numbered carbon atoms in the sugar.

Thus, a DNA or RNA sequence has a direction and is conventionally written:

5′ → 3′ direction.

Students do not need to memorize every numbered carbon in the sugar for our purposes. The important idea is that **nucleic acid strands have directionality because of the way their nucleotides are covalently connected**.

Complementary Base Pairing in DNA

DNA typically consists of **two nucleotide strands** associated with one another.

The sugar-phosphate backbones form the outside of the DNA structure, while the nitrogenous bases point toward the interior.

Bases on opposite strands interact through **hydrogen bonds**.

And here comes Chapter 5 again!

Hydrogen bonds are individually much weaker than covalent bonds. However, DNA contains enormous numbers of these interactions, allowing the two strands to associate strongly while still permitting them to separate when necessary.

The bases do not pair randomly.

In DNA:

- **adenine (A) pairs with thymine (T)**
- **guanine (G) pairs with cytosine (C)**

A and T form **two hydrogen bonds**, whereas G and C form **three hydrogen bonds**.

These are called **complementary base pairs**.

Thus, if the sequence on one DNA strand is known, the sequence of the opposite strand can be predicted.

For example:

5′–A T G C C A–3′

pairs with

3′–T A C G G T–5′

Notice that the two strands run in opposite directions. This arrangement is described as **antiparallel**.

Why Do the Bases Pair Specifically?

Why does adenine pair with thymine rather than cytosine?

The answer comes back to **molecular shape and intermolecular forces**.

The atoms capable of participating in hydrogen bonds occur in specific positions around each nitrogenous base. For favorable hydrogen bonding to occur, the hydrogen-bond donors and acceptors on one base must line up correctly with complementary groups on the other.

Adenine and thymine have the appropriate shapes and arrangement of groups to form their characteristic two hydrogen bonds. Guanine and cytosine have a different—but complementary—arrangement and share three hydrogen bonds (Figure 7.5.2).

This is the same general principle we have encountered repeatedly:

> **Molecular interactions depend on both chemical properties and three-dimensional arrangement**.

Just as a drug must position its functional groups appropriately within a protein binding site, DNA bases must position their hydrogen-bonding groups correctly to form complementary base pairs.

From Base Pairing to the Double Helix

The two complementary DNA strands twist around one another to form the familiar **double helix**.

The sugar-phosphate backbones lie along the outside of the helix, while the paired bases are stacked within the interior.

The structure is stabilized by several types of interactions. **Covalent phosphodiester bonds** hold the nucleotides together within each individual strand, while **hydrogen bonds and other intermolecular attractions** help stabilize interactions between the two strands and among the stacked bases.

This distinction is important:

> **Covalent bonds build each DNA strand; intermolecular forces help organize the strands into the double helix**.

DNA Stores Information in Its Base Sequence

Only four different bases are used to encode the enormous amount of information stored in DNA.

The information does not come from having many different types of nucleotides. Instead, it comes from their **sequence**.

This should remind you of proteins.

Proteins are built from a limited set of amino acids, but changing their sequence can produce proteins with entirely different structures and functions.

Similarly, DNA is built using only four types of nucleotide bases, but their possible sequences are enormous.

> **In proteins, amino acid sequence helps determine protein structure and function. In DNA, nucleotide sequence stores genetic information**.

Cells can use the information stored in DNA to produce RNA, and information in certain RNAs can ultimately direct the production of proteins. We will leave the detailed processes of DNA replication, transcription, and translation to biology courses and focus here on the chemistry that makes the storage and transfer of genetic information possible.

DNA sequence → RNA → Protein.

RNA: Similar Building Blocks, Different Roles

RNA is structurally related to DNA but differs in several important ways.

RNA:

- contains **ribose** instead of deoxyribose,
- contains **uracil (U)** instead of thymine (T), and
- is usually **single-stranded** rather than forming one long, stable double helix.

However, *single-stranded* does not mean *structureless*.

Different regions within an RNA molecule can form complementary base pairs with one another, causing the strand to fold into complex three-dimensional shapes.

Once again:

sequence → molecular interactions → three-dimensional structure → function.

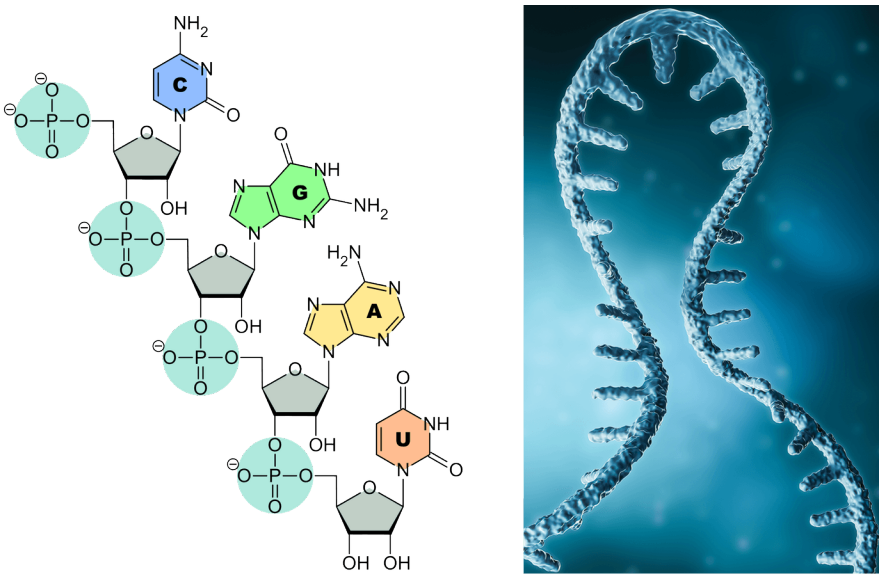


Figure 7.5.3: RNA Structure and Folding. RNA is generally composed of a single strand of nucleotides containing a sugar-phosphate backbone and the nitrogenous bases adenine (A), guanine (G), cytosine (C), and uracil (U). Although RNA is usually single-stranded, complementary regions within the same RNA molecule can interact through base pairing, causing the strand to fold into characteristic three-dimensional structures. The resulting shape of an RNA molecule can be important to its biological function. The RNA illustration is from: MattL Photography/Shutterstock.com.

RNA molecules perform many roles within cells. Some carry genetic information used in protein synthesis, while others participate directly in cellular processes and regulation.

For our purposes, the important point is that DNA and RNA use the same basic chemical strategy: **a sugar-phosphate backbone carries a sequence of nitrogen-containing bases capable of specific molecular interactions.**

Putting It All Together: Reading Nucleic Acid Structures

When examining an unfamiliar nucleic acid structure, don't try to memorize every atom. Instead, look for recognizable features.

Ask yourself:

1. **Can I identify the three parts of a nucleotide?** Look for a sugar, phosphate group, and nitrogen-containing base.
2. **Where is the sugar-phosphate backbone?**
3. **Where are the phosphodiester bonds connecting neighboring nucleotides?**
4. **Which bases are present?** Remember that DNA uses T while RNA uses U.
5. **If two DNA strands are shown, which bases are paired?**
6. **Which interactions are covalent and which are intermolecular?** Phosphodiester bonds hold each strand together, while hydrogen bonding contributes to complementary base pairing.
7. **How does molecular structure contribute to function?** The sequence of bases stores information, while molecular interactions help create and stabilize the three-dimensional structure.

You do not need to memorize the detailed chemical structures of every nucleotide or nitrogenous base. Instead, recognize the **structural patterns** and use the chemistry you already know to understand how nucleic acids are constructed and why they behave as they do.

> **Nucleic acids provide one more example of a central theme running throughout this chapter: biological function emerges from molecular structure, bonding, and intermolecular interactions**.

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7.6: Secondary Metabolites- Chemistry as a Competitive Advantage

Learning Objectives

After completing this section, you should be able to:

- Distinguish between **primary and secondary metabolites**.
- Explain how secondary metabolites can provide an organism with an ecological or competitive advantage.
- Recognize that secondary metabolites occur across many different groups of organisms and exhibit enormous structural diversity.
- Identify **alkaloids, terpenoids, phenylpropanoids, and polyketides** as major classes of secondary metabolites.
- Explain why secondary metabolites are important sources of biologically active compounds and potential medicines.
- Define **bioprospecting** and **pharmacognosy**.
- Apply concepts from organic chemistry to examine the structure of an unfamiliar secondary metabolite.

Beyond the Molecules Required for Life

So far in this chapter, we have focused on **primary metabolites**—molecules involved in the fundamental processes required for life. Sugars provide and store energy, lipids form cellular membranes and store energy, proteins perform an enormous range of cellular functions, and nucleic acids store and transmit genetic information.

But living organisms manufacture many other organic molecules as well.

These molecules may not be directly required for the basic processes of growth and reproduction, yet they can provide important advantages to the organisms that produce them. Such compounds are called **secondary metabolites**.

Secondary metabolites can help organisms interact with the world around them. For example, they may help an organism:

- defend itself against predators or herbivores,
- inhibit the growth of competing organisms,
- attract pollinators or mates,
- communicate with other members of the same species,
- protect itself from environmental stress, or
- capture or immobilize prey.

In this sense, secondary metabolites can be thought of as part of an organism's **chemical toolkit for survival and competition**.

Unlike primary metabolites, which are widely shared among living organisms, particular secondary metabolites may be produced by only one species or by a relatively small group of related organisms. This has resulted in an extraordinary diversity of chemical structures in the natural world.

Why Make a Molecule That Isn't Essential?

At first, it may seem strange that an organism would invest energy and resources in producing a molecule that is not directly required for basic cellular survival.

Imagine two plants growing side by side. Both must make proteins, carbohydrates, lipids, and nucleic acids to survive. But suppose one plant also produces a bitter or toxic compound that discourages insects from eating its leaves.

The plant can survive without that particular molecule—but producing it may increase the plant's chances of **surviving long enough to reproduce**.

Similarly, a microorganism that releases a compound capable of inhibiting nearby bacteria may gain better access to limited nutrients and space. A flower that produces colorful pigments or fragrant molecules may be more successful at attracting pollinators.

Secondary metabolites therefore often influence the interactions **between an organism and its environment or other organisms**.

This distinction gives us a useful way to compare the two major groups of natural products:

Primary metabolites help carry out the fundamental chemistry of life. Secondary metabolites often help an organism compete, communicate, defend itself, or otherwise interact with its environment.

The distinction is useful, although biology does not always fit perfectly into simple categories.

The Chemical Diversity of Secondary Metabolites

Secondary metabolites can be remarkably complex.

Some are small molecules containing only a few carbon atoms. Others contain elaborate ring systems, multiple functional groups, numerous stereocenters, or long carbon skeletons.

But don't let a complicated structure intimidate you.

This is exactly what Chapter 6 prepared you to do.

When you encounter an unfamiliar secondary metabolite, don't try to memorize the entire molecule. Instead, **read the structure**.

Look for:

- straight, branched, cyclic, or aromatic carbon skeletons;
- alkene or alkyne groups;
- oxygen-, nitrogen-, sulfur-, or phosphorus-containing **functional groups**;
- polar and nonpolar regions;
- chiral carbons and other three-dimensional features.

Even when you have never seen a molecule before, these structural features can tell you something about its chemical properties and how it might interact with a biological target.

Major Classes of Secondary Metabolites

Scientists can classify secondary metabolites in several different ways, including their structures and the biochemical pathways organisms use to produce them. Four particularly important groups introduced throughout the next section, include: **alkaloids, terpenoids, phenylpropanoids, and polyketides**.

Below is a brief introduction to features of each of these groups.

Alkaloids

Alkaloids are a diverse group of nitrogen-containing organic compounds.

Many alkaloids have strong biological effects on animals because they can interact with receptors, enzymes, ion channels, and other protein targets.

Familiar natural products belonging to the broad alkaloid family include compounds such as caffeine, nicotine, morphine, and quinine.

When looking at the structure of an alkaloid, one of the first clues is therefore:

Look for nitrogen.

But remember that not every nitrogen-containing organic molecule is automatically classified as an alkaloid. The term describes a broad natural-product family rather than simply a functional group.

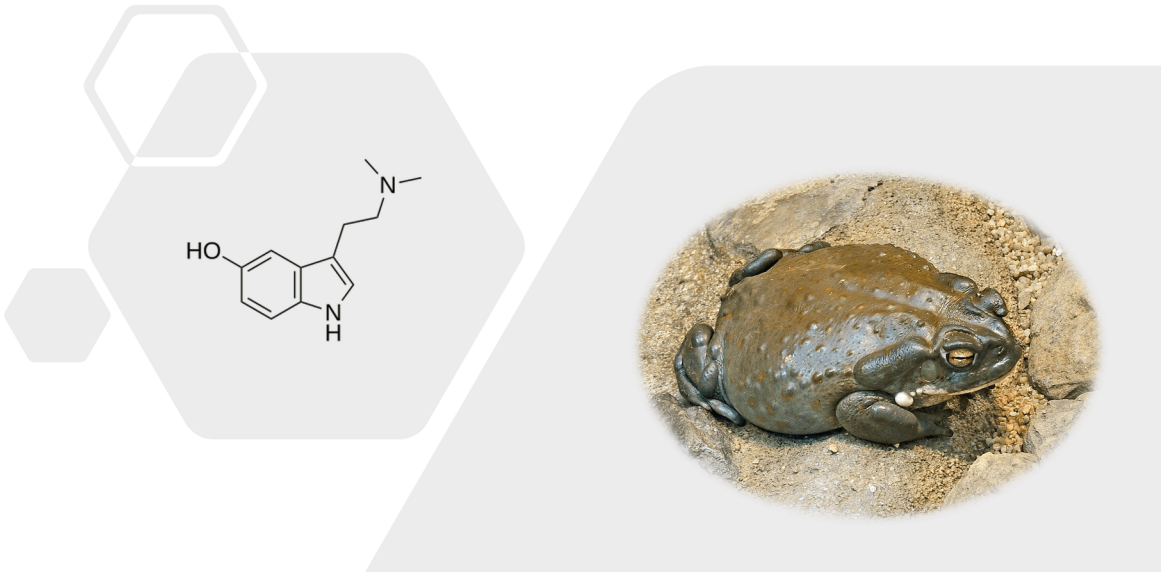


Figure 7.6.1**: Bufotenin—An Alkaloid Found in Toad Secretions**. Bufotenin is a naturally occurring **alkaloid** found in the skin and parotoid gland secretions of several species of toads, as well as in some plants. Like many alkaloids, bufotenin contains nitrogen atoms within its structure and has biological activity. Alkaloids represent a chemically diverse group of secondary metabolites, many of which interact strongly with biological systems and have served as important sources of medicines, toxins, and other pharmacologically active compounds. Photo from: **Wildfeuer**.

Terpenoids

Terpenoids are an enormous family of natural products constructed biologically from small five-carbon building units.

Terpenoids are particularly common in plants and contribute to many of the characteristic **scents, flavors, pigments, and chemical defenses** found in the plant world. Many essential-oil components are terpenoids, and larger members of this family include biologically important molecules such as carotenoid pigments. Structurally, terpenoids often contain extensive hydrocarbon skeletons, rings, branches, and carbon–carbon double bonds—features you should readily recognize from Chapter 6.

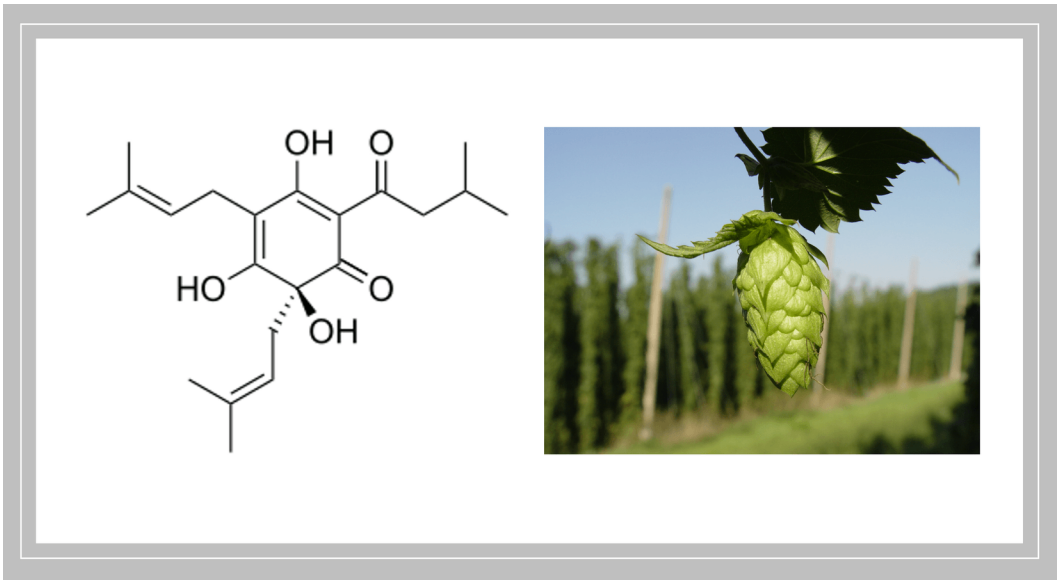


Figure 7.6.2**: Humulone—A Terpenoid from Hops**. Humulone is a naturally occurring **terpenoid** found in the resin of hops (*Humulus lupulus*). It is one of the major **α-acids** produced by the plant and contributes to the characteristic bitter flavor of beer following chemical changes that occur during brewing. Like other terpenoids, humulone is built from smaller **five-carbon isoprene units**, illustrating how relatively simple carbon building blocks can be assembled and modified to produce structurally diverse natural products. Photo from: LuckyStarr.

Phenylpropanoids

Phenylpropanoids are natural products derived biologically from the amino acids phenylalanine or tyrosine. Many contain an **aromatic ring** along with a short carbon-containing side chain. Members of this broad family contribute to plant pigments, structural materials, fragrances, flavors, and chemical defenses. Again, you do not need to memorize the biosynthetic pathway. Instead, notice the structural connection to organic chemistry:

there's that aromatic ring again!



Figure 7.6.3**: Cinnamic Acid—A Simple Phenylpropanoid Found in Cinnamon**. Cinnamic acid is a naturally occurring

phenylpropanoid found in cinnamon and many other plants. Phenylpropanoids are characterized by a basic **six-carbon aromatic ring attached to a three-carbon unit (C_6–C_3)**. Plants modify this basic carbon skeleton in many different ways to produce a remarkably diverse family of secondary metabolites involved in functions such as defense, pigmentation, structural support, and interactions with other organisms.**Photo from:** Simon A. Eugster.

Polyketides

Polyketides are another large and structurally diverse family of secondary metabolites. Organisms construct them through biochemical pathways using small carbon-containing building blocks derived from compounds such as acetate and malonate. The resulting molecules can contain rings, carbonyl groups, alcohols, aromatic regions, and many stereocenters.

Polyketides are especially important in medicine because this family includes natural products with antibacterial, antifungal, and other biological activities. Others may be toxic.

For CH112, the important point isn't learning how organisms synthesize a polyketide. It is recognizing that **living organisms can assemble relatively simple carbon-containing building blocks into extraordinarily complex organic molecules**.

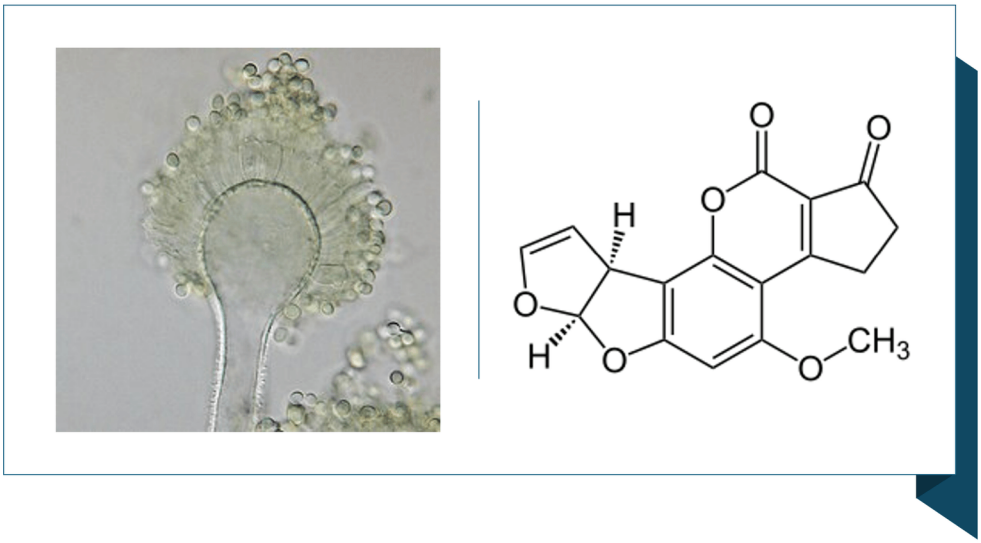


Figure 7.6.4: Aflatoxin B_1—A Toxic Polyketide Produced by Fungi. Aflatoxin B_1 is a secondary metabolite produced by certain species of *Aspergillus* fungi, including *Aspergillus flavus*. These fungi can contaminate agricultural products such as corn, peanuts, and other stored foods. Aflatoxin B_1 is a **polyketide-derived natural product** and is a potent toxin and carcinogen, illustrating that secondary metabolites can have powerful biological effects that may be beneficial, harmful, or even deadly to other organisms. Photo by: Medmyco.

Secondary Metabolites and Biological Activity

Why are chemists and medical researchers so interested in these compounds?

Secondary metabolites often evolved specifically because they **interact with other living organisms**.

Consider what that means chemically.

A molecule that deters an insect, inhibits a competing microorganism, paralyzes prey, or sends a chemical signal must interact somehow with molecules in another organism.

Frequently, those targets are **proteins**.

A secondary metabolite might:

- bind to an enzyme,
- activate or block a receptor,
- interfere with an ion channel,
- disrupt a cellular membrane, or
- interfere with another important cellular process.

This takes us directly back to Chapter 6 and our discussion of drug–protein interactions.

A secondary metabolite's biological activity depends on its **molecular shape, functional groups, polarity, charge, and stereochemistry**. Those features determine whether the molecule can reach a biological target and how effectively it can interact with it.

And this helps explain why natural products have played such an important role in medicine.

From Natural Product to Medicine

Humans have used plants and other natural materials as medicines for thousands of years. Modern chemistry allows us to go much further: scientists can isolate the active compounds, determine their structures, study their biological targets, and evaluate their safety and effectiveness.

A natural product with useful biological activity may sometimes be used directly as a medicine. In other cases, its structure provides a **starting point for drug development**.

Chemists can modify parts of the molecule to try to improve its properties. A modified version might bind more strongly to its target, produce fewer unwanted effects, remain in the body longer, or be easier to manufacture and administer.

Thus, nature does not necessarily hand us a finished drug.

Sometimes it gives us a **chemical starting point**.

Bioprospecting: Searching Nature for Useful Chemistry

The search for biologically useful natural products is often called **bioprospecting**.

Researchers may investigate plants, fungi, bacteria, marine organisms, or other forms of life to discover compounds with interesting biological activities. Your original chapter emphasizes that useful natural products have been discovered throughout the living world—from soil microorganisms to plants, fungi, animals, and marine organisms.

Once a promising compound is discovered, scientists may need to determine:

What molecule is producing the activity? What is its chemical structure? What biological target does it affect? Could it be useful as a medicine?

The field concerned with natural substances and their potential medicinal properties is called **pharmacognosy**. Your original chapter pairs pharmacognosy with bioprospecting as important parts of natural-product discovery.

Modern natural-product research brings together chemistry, biology, pharmacology, ecology, and medicine.

Nature as a Chemical Library

One way to think about secondary metabolites is as an enormous **natural chemical library**.

Over evolutionary time, organisms have produced and modified countless organic molecules. Molecules that provided useful interactions—repelling a predator, killing a competitor, attracting a pollinator, or immobilizing prey—could provide an advantage to the organisms producing them.

Some of those same molecular interactions can be useful to us.

A molecule that inhibits an enzyme in another organism might provide the starting point for an antibiotic. A molecule that alters an ion channel might inspire a medication for pain. A compound that interferes with cell division might provide clues for developing an anticancer drug.

The molecule did not evolve **for humans to use as medicine**. Its biological activity served the organism that produced it. We are learning how to recognize and sometimes harness that chemistry for our own purposes.

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7.7: Exploring Secondary Natural Products

In the remainder of this chapter, we will explore examples of secondary metabolites produced by different organisms and examine how some have contributed to medicine and drug discovery.

You are not expected to memorize the structures of these compounds.

Instead, use them as opportunities to practice the chemistry you have learned:

- Where are the functional groups?
- What portions of the molecule are polar or nonpolar?
- Are aromatic rings present?
- Are there chiral centers?
- What features might allow the molecule to interact with a biological target?
- What advantage might producing this molecule provide to the organism?

These are also the kinds of questions scientists ask when they encounter a newly discovered natural product.

> **Secondary metabolites show us that organic chemistry is not simply something that happens inside a chemistry laboratory. Living organisms have been building, modifying, and using complex organic molecules throughout the history of life**.

Natural products come from every major group of organisms on the planet. Throughout the next sections, we will take examples and highlights from each of the major kingdoms of life and display a small sample of the unique chemistry that they are capable of producing. Living organisms can be broadly divided into **prokaryotic** and **eukaryotic** organisms based on the organization of their cells. **Prokaryotic organisms**, which include the domains **Bacteria and Archaea**, consist of cells that do not contain a membrane-bound nucleus. In contrast, **eukaryotic organisms** have cells containing a nucleus and other membrane-bound organelles. Eukaryotes include the familiar kingdoms **Fungi, Plantae (plants), and Animalia (animals)**, along with a diverse collection of organisms historically grouped together as **Protista**. Modern genetic studies have shown that evolutionary relationships among eukaryotes are considerably more complex than these traditional kingdom groupings suggest, but these categories provide a useful framework for exploring the tremendous diversity of natural products produced throughout the living world.

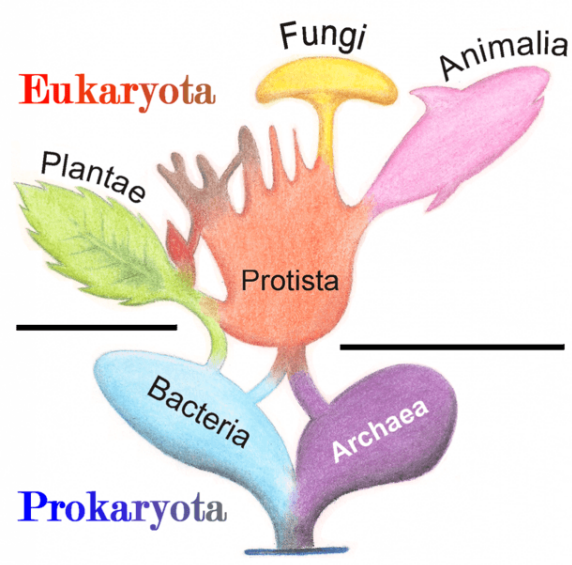


Figure 7.7.1**: Major groups of living organisms**. Life can be broadly divided into organisms with **prokaryotic cells**, represented by Bacteria and Archaea, and organisms with **eukaryotic cells**, including fungi, plants, animals, and the diverse organisms traditionally grouped as protists. Prokaryotic cells lack a membrane-bound nucleus, whereas eukaryotic cells contain a nucleus

and other membrane-bound organelles. Although the traditional kingdom groupings shown here provide a useful introduction to biological diversity, modern classification based on genetic and evolutionary relationships is more complex. Source: Maulucioni y Doridí.

Bacteria: Chemical Warfare on a Microscopic Scale

Bacteria are single-celled prokaryotic organisms found in nearly every environment on Earth. They inhabit soil, water, living organisms, deep ocean sediments, and environments that would be inhospitable to many other forms of life.

These environments can be extraordinarily competitive. A small patch of soil, for example, may contain an enormous community of microorganisms competing for limited nutrients and space.

One way bacteria compete is through **chemistry**.

Many bacteria produce secondary metabolites that inhibit or kill neighboring microorganisms. For the bacterium producing the compound, this can provide a competitive advantage. For humans, some of these same compounds have become extraordinarily useful **antibiotics**.

> **An antibiotic that we use as a medicine may have originated as one microorganism's chemical weapon against another**.

From Soil Bacteria to Antibiotics

The discovery and clinical success of penicillin, a fungal natural product, prompted scientists to begin searching systematically for other microorganisms capable of producing antibacterial compounds.

Soil proved to be an especially rich place to look.

One important discovery was **streptomycin**, isolated from the soil bacterium *Streptomyces griseus*. Streptomycin became particularly important because it was effective against tuberculosis and demonstrated that **bacteria themselves could be an important source of antibacterial natural products**.

That discovery helped launch an intensive search of soil microorganisms for new medicines.

Members of the bacterial genus *Streptomyces* turned out to be remarkably productive natural-product chemists. Compounds originating from *Streptomyces* species include **streptomycin, tetracyclines, erythromycin, chloramphenicol, neomycin, amphotericin B, and daptomycin**.

These molecules do not all have the same structures or mechanisms of action. What they share is **biological activity**—they interact with particular molecular targets strongly enough to inhibit other organisms.

This brings us back once again to Chapter 6:

molecular structure → interaction with a biological target → biological effect.

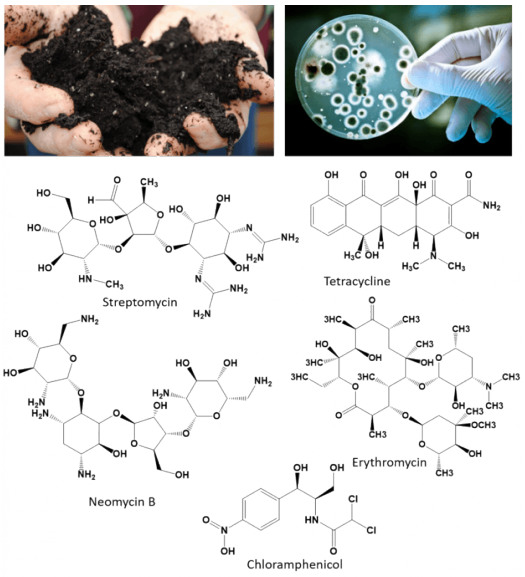


Figure 7.7.2**: Soil Bacteria as a Source of Antibiotics.** Soil contains an extraordinarily diverse community of microorganisms, including bacteria that produce natural products to compete with other organisms in their environment. Screening soil bacteria for these biologically active compounds has led to the discovery of many important antibiotics. Members of the bacterial genus *Streptomyces* have been particularly productive sources, yielding drugs such as streptomycin, tetracycline, erythromycin, and many others.

Bacterial Natural Products Beyond Antibiotics

Not every medically useful bacterial product is an antibiotic.

One particularly dramatic example is **botulinum toxin**, a protein toxin produced by *Clostridium botulinum*. Botulinum toxin interferes with communication between nerves and muscles, producing **muscle paralysis**. Exposure to sufficiently large amounts can cause the potentially fatal illness **botulism**.

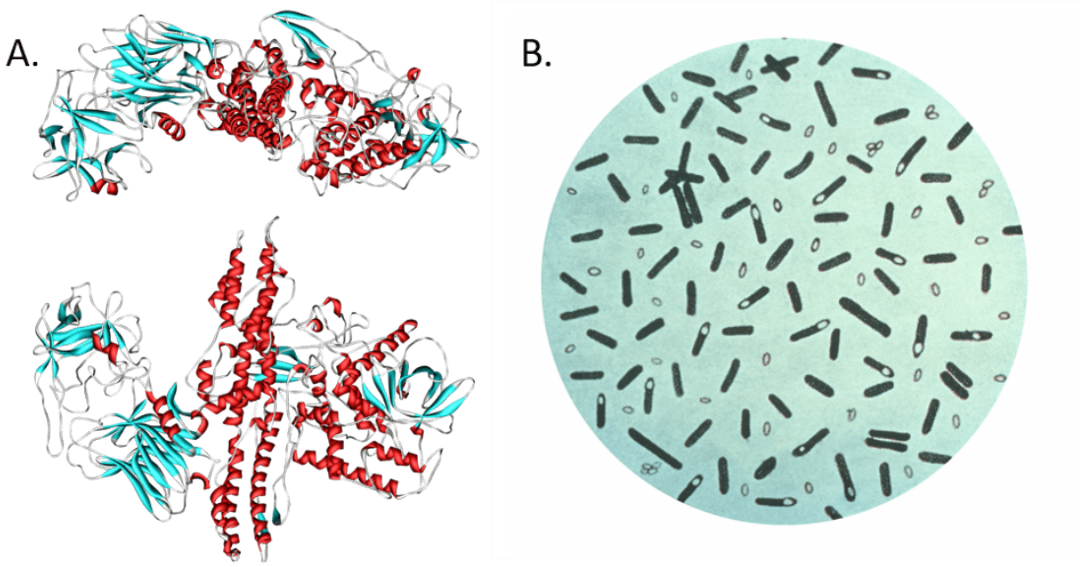


Figure 7.7.3**: Botulinum toxin**. (A) Diagram of botulinum toxin A. Consuming food products tainted with the neurotoxin produced by (B) the bacterium Clostridium botulinum, can cause paralysis and death. Interestingly, the neurotoxin (marketed as Botox, Dysport, Xeomin, and MyoBloc) has been adapted for medicinal use to reduce epileptic seizures and for cosmetic use to reduce

wrinkles and frown lines by paralyzing muscle tissue in the forehead. Diagram (A) provided at Wikipedia. Diagram (B) provided by the CDC Prevention's Public Health Image Library

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That certainly doesn't sound like a promising medicine!

But the same biological activity becomes useful when the toxin is carefully administered in extremely small, controlled doses. Botulinum toxin preparations are now used medically to temporarily reduce excessive muscle activity and for several other conditions. They are also widely known for their cosmetic use in temporarily reducing the appearance of facial wrinkles.

This illustrates an important principle:

> **A biologically active molecule is not inherently a "medicine" or a "poison." Its effects depend on factors including dose, route of exposure, biological target, and how it is used**.

Another bacterial natural product, **bleomycin**, originally isolated from *Streptomyces*, damages DNA and is used as part of the treatment for several types of cancer.

So the biological activities bacteria evolved for their own purposes can sometimes be redirected toward entirely different medical applications.

Searching for the Next Bacterial Natural Product

Scientists continue to search for useful bacterial natural products, but the search has expanded far beyond easily cultured bacteria from ordinary soil samples.

Researchers now investigate microorganisms from **marine environments, deep underground, extreme habitats, and bacteria living in close association with other organisms**.

Some bacteria live as **symbionts**, meaning that they maintain a close association with another organism. Bacteria living within plant tissues without causing disease are known as **endophytes**. These relationships can be especially interesting sources of natural products because microorganisms living in complex ecological communities may use chemical signals or defenses to interact with their hosts and with competing organisms.

Many bacterial species cannot easily be grown using conventional laboratory methods, which means that much of their chemistry remains unexplored.

The search continues because every newly investigated microbial community potentially contains organisms producing molecules that chemists have **never seen before**.

Archaea: An Untapped Source of Natural Products

Archaea are single-celled prokaryotic organisms that form a domain of life distinct from Bacteria. Although archaea occur in many ordinary environments, some species are famous for surviving under extreme conditions, including high temperatures, extreme pH, high salt concentrations, and high pressures.

Compared with bacteria, fungi, and plants, archaea have been **remarkably underexplored as sources of natural products**. To date, archaeal natural products have not provided major pharmaceutical drugs comparable to antibiotics from *Streptomyces*, cyclosporine from fungi, or artemisinin from plants. This does not necessarily mean that archaea lack useful chemistry. Instead, scientists may simply have explored only a small fraction of it.

Archaea are already known to produce antimicrobial peptides called **archaeocins**. Some archaea living in extremely salty environments produce archaeocins called **halocins**, which can inhibit competing microorganisms. These compounds appear to serve a familiar ecological purpose: **chemical competition for limited resources**.

Searching the Archaeome for New Antibiotics

New technologies are now allowing scientists to search for useful natural products without first having to isolate and grow every

organism in the laboratory.

In a recent study, researchers used **artificial intelligence and deep learning** to search the protein sequences of 233 archaeal species for hidden peptides predicted to have antimicrobial activity. The search identified more than **12,000 potential antimicrobial peptides**, which the researchers named **archaeasins**.

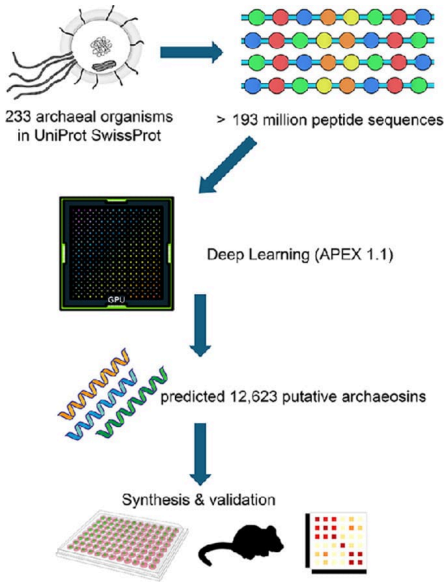


Figure 7.7.4**: Using Deep Learning to Search Archaea for New Antimicrobial Peptides**. Researchers used protein sequence data from 233 archaeal organisms to generate more than 193 million possible peptide sequences. A deep-learning model was then used to identify peptides predicted to have antimicrobial activity, resulting in more than 12,000 candidates called **archaeasins**. Selected candidates were synthesized and experimentally tested for antimicrobial activity. This approach demonstrates how genomic databases and artificial intelligence can help scientists search previously underexplored organisms for potential new medicines. Figure from: 2025 Nature Microbiology archaeasin study.

When 80 of the predicted archaeasins were synthesized and tested, **93% showed antimicrobial activity in laboratory experiments**. One particularly promising molecule, **archaeasin-73**, was subsequently tested in mice with bacterial infections and significantly reduced bacterial levels. Its activity in these early experiments was comparable to that of an established antibiotic, polymyxin B.

Archaeasin-73 is **not an approved antibiotic** and remains at the preclinical stage of research. Nevertheless, the discovery suggests that the archaeal domain may contain a large reservoir of biologically active molecules that has barely been explored.

> **For much of the history of natural-product drug discovery, scientists searched the organisms they could collect, culture, and test in the laboratory. Modern genome sequencing and artificial intelligence now allow researchers to search the chemistry encoded within organisms that have previously been difficult to study**.

Fungi

Fungi are eukaryotic organisms that include yeasts, molds, and mushrooms. Unlike plants, fungi are **heterotrophs** and must obtain organic nutrients from their surroundings. Many fungi act as decomposers, breaking down dead organic material and recycling nutrients through ecosystems.

Fungi also live in environments crowded with bacteria, other fungi, and competing organisms. One strategy for surviving this competition is chemical: fungi produce an extraordinary variety of **secondary metabolites**.

Some of these compounds are toxic. The common names of poisonous mushrooms such as the *death cap* and *destroying angel* provide dramatic reminders that fungal natural products can have powerful biological effects.

But those same kinds of biologically active molecules have also provided humans with some extraordinarily useful medicines.

Fungal Natural Products in Medicine

Perhaps the most famous example is **penicillin**, originally discovered from a *Penicillium* mold. Penicillins interfere with the construction of bacterial cell walls and revolutionized the treatment of bacterial infections.

Fungi have provided other anti-infective compounds as well. **Cephalosporins**, another important family of antibacterial drugs, trace their origins to a fungus, while **griseofulvin**, originally isolated from *Penicillium griseofulvum*, is used to treat fungal infections. Your existing section highlights all three of these examples.

But fungal natural products have uses far beyond treating infections.

Lovastatin, originally isolated from *Aspergillus terreus*, inhibits an enzyme involved in cholesterol synthesis. It became the first FDA-approved statin and helped establish a major class of cholesterol-lowering medications.

Another group of fungal natural products, the **ergot alkaloids**, is produced by fungi in the genus *Claviceps*, which can infect cereal grains such as rye and other grasses. These compounds can strongly affect the nervous and cardiovascular systems. Historically, consumption of heavily contaminated grain caused outbreaks of **ergotism**, which could produce convulsions and severe vasoconstriction. Yet controlled doses of particular ergot-derived compounds have also been useful in medicine.

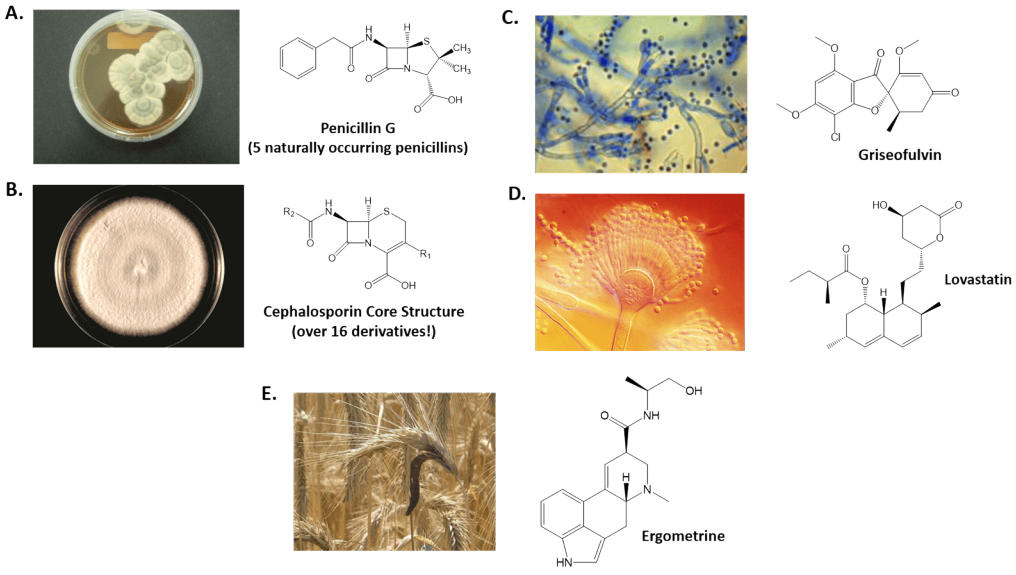


Figure 7.7.5**: Fungi Are Diverse Sources of Natural Products**. Fungi include an enormous diversity of organisms with different growth forms and ecological roles. Shown here are examples of filamentous fungi growing in culture and viewed microscopically, along with a fungal infection of a plant host. Fungi produce a wide variety of **secondary metabolites** that can help them compete with other organisms, defend resources, or interact with their hosts. Many of these compounds have important biological activities, making fungi a rich source of natural products used in medicine, including **antibiotics, cholesterol-lowering drugs, immunosuppressants, and other pharmaceuticals**.

This contrast illustrates an important principle of pharmacology:

> **Whether a biologically active compound acts as a medicine or a poison can depend on its target, its dose, and how it is used**.

And one fungal natural product transformed an entirely different area of medicine.

A Closer Look: Cyclosporine and Organ Transplantation

Cyclosporine is a remarkable secondary metabolite originally isolated from the fungus *Tolypocladium inflatum* in the early 1970s. Unlike penicillin, cyclosporine was not valuable because it killed bacteria.

Instead, researchers discovered that it could **suppress the human immune response**.

That initially might not sound like a desirable property. After all, the immune system protects us from infectious disease.

But consider what happens during an **organ transplant**.

A transplanted kidney, heart, liver, or other organ contains cells that are genetically different from those of the person receiving it. The recipient's immune system can recognize the transplanted tissue as foreign and attack it, producing **organ rejection**.

Doctors therefore need a way to suppress the immune response enough to protect the transplanted organ while still retaining as much immune function as possible.

Cyclosporine provided a powerful new way to do that.

Its introduction into transplantation medicine in the early 1980s dramatically improved the ability to prevent organ rejection and helped make successful transplantation much more widely possible.

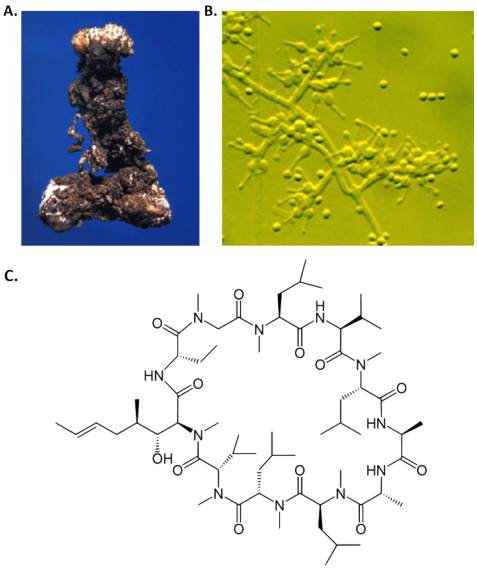


Figure 7.7.6: Fungal Production of Cyclosporin. (A) Multicellular life-stage of the fungus, known as Cordyceps subsessilis, (B) unicellular life-stage of the fungus, known as Tolypocladium inflatum. (C) Structure of cyclosporine. Photos By: Kathie Hodge.

Look at the Chemistry

Cyclosporine is also a wonderful molecule for practicing the structural skills developed in Chapter 6.

At first glance, its structure looks intimidating. Don't try to memorize it.

Instead, look for what you recognize.

Cyclosporine is a **cyclic peptide**, meaning that it is constructed from amino-acid-derived units joined into a ring. Look along its structure and you can identify numerous **amide linkages**—the same type of functional group found in the peptide bonds of proteins.

You can also see:

- a large cyclic carbon skeleton,
- numerous carbonyl groups,
- several nonpolar hydrocarbon regions,
- multiple stereocenters, and
- many different three-dimensional features.

This is exactly the strategy we have been practicing throughout Chapters 6 and 7:

> **A complex molecule becomes less intimidating when you break it into structural features you already recognize**.

From Fungal Defense to Immunosuppressive Drug

Cyclosporine provides another excellent example of why scientists study secondary metabolites.

The fungus did not produce cyclosporine so that humans could perform organ transplants. The molecule evolved because its biological activity provided some advantage to the organism producing it.

Humans discovered that biological activity and found an entirely different use for it.

This is the same broader pattern we saw with chlorotoxin and artemisinin:

organism → biologically active natural product → discovery of its activity → medical application.

And importantly, the medical use is not always obvious from the ecological role of the original compound.

A fungal metabolite can become an antibiotic.

A plant defense molecule can become an antimalarial drug.

A venom peptide can become a tumor-targeting tool.

And a fungal secondary metabolite can help make **organ transplantation** possible.

Plants

Plants are multicellular, eukaryotic organisms capable of producing their own food through **photosynthesis**. Using energy from sunlight, plants convert carbon dioxide and water into energy-rich organic molecules, releasing oxygen as a by-product.

But plants manufacture far more than the primary metabolites required for growth and reproduction. They also produce an extraordinary diversity of **secondary metabolites**.

Why so many?

Unlike animals, plants cannot simply run away from an organism that wants to eat them. Instead, many have evolved chemical defenses that make them toxic, bitter, irritating, or otherwise unattractive to herbivores and pathogens. Other secondary metabolites help plants attract pollinators, compete with neighboring plants, communicate, or protect themselves from environmental stress.

These ecological interactions have produced an enormous library of biologically active molecules.

Only a fraction of plant species and their natural products have been thoroughly investigated, yet plant-derived compounds have already provided many important medicines and starting points for drug development. Examples include **paclitaxel**, originally isolated from the Pacific yew (*Taxus brevifolia*) and used in cancer treatment; **vinblastine**, from the Madagascar periwinkle (*Catharanthus roseus*), also used in cancer therapy; **morphine**, from the opium poppy (*Papaver somniferum*), used for severe pain; **galantamine**, originally obtained from plants in the Amaryllis family and used in the treatment of Alzheimer's disease; and

artemisinin, from sweet wormwood (*Artemisia annua*), which transformed the treatment of malaria.

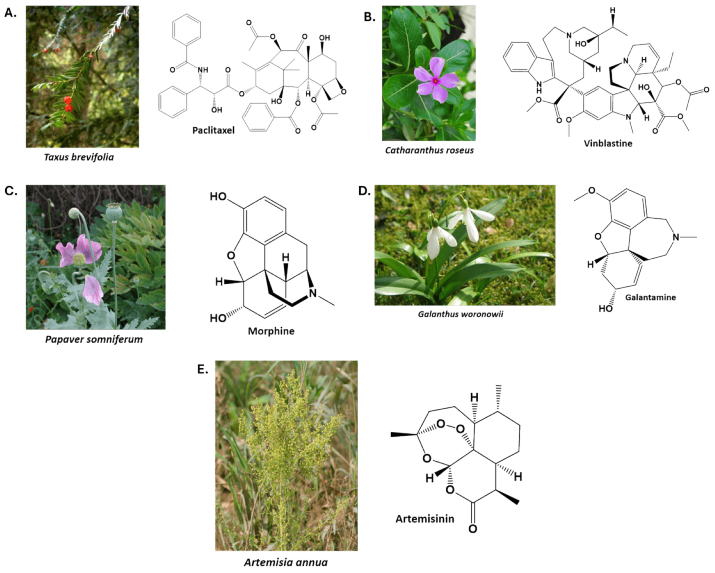


Figure 7.7.7**: Plants as Sources of Medicinal Natural Products.** Plants produce an enormous variety of secondary metabolites, many of which have become important medicines. Examples shown here include plants that produce natural products with **anticancer, pain-relieving, antimalarial, and neurological effects**. These include (A) the Pacific yew (*Taxus brevifolia* - Photo by:Jason Hollinger.), (B) Madagascar periwinkle (*Catharanthus roseus* - Photo by:Joydeep.), opium poppy (*Papaver somniferum* - Photo by:Dinkum.), (D) snowdrop (*Galanthus* spp. - Photo by:Meneerke Bloem and Peter Coxhead.), and (E) sweet wormwood (*Artemisia annua* - Photo by:Kristian Peters.). These are sources of compounds such as **paclitaxel, vinblastine, morphine, galantamine, and artemisinin**, respectively. The tremendous structural and chemical diversity of plant secondary metabolites has made the Plant Kingdom an important source of both traditional medicines and modern pharmaceuticals.

The discovery of artemisinin provides an especially powerful example of how traditional knowledge, careful scientific investigation, and chemistry can come together in the development of modern medicine.

A Closer Look: Tu Youyou and the Discovery of Artemisinin



Figure 7.7.8**: Photo of Youyou Tu from Vaxholm, Sweden in 2015. Photo by:** Bengt Nyman.

Malaria is caused by *Plasmodium* parasites transmitted to humans through the bites of infected mosquitoes. One particularly dangerous species, *Plasmodium falciparum*, can cause severe and potentially fatal disease.

By the 1960s, resistance to existing antimalarial drugs such as chloroquine was becoming an increasingly serious problem. In China, this led to the creation of a large, secret antimalarial research effort in 1967 known as **Project 523**, named for its starting date of May 23.

Among the scientists recruited to the project was **Tu Youyou**, a researcher at the China Academy of Traditional Chinese Medicine.

Tu took an approach that was unusual but remarkably logical: she looked to the accumulated knowledge of **traditional Chinese medicine** for clues about plants that had historically been used to treat fever.

Tu and her research team examined ancient medical texts, consulted traditional practitioners, and investigated hundreds of herbal preparations. Eventually, their attention focused on **qinghao**, the plant *Artemisia annua*, or sweet wormwood, which had been used historically to treat intermittent fevers.

There was a problem.

The extracts did not consistently work.

Rather than simply concluding that the plant was ineffective, Tu returned to the historical literature and reconsidered the extraction process itself.

She found an important clue in a Chinese medical text written by **Ge Hong in the fourth century CE**. The ancient preparation instructed that qinghao be soaked in water and the liquid squeezed from the plant rather than boiled.

Tu realized that this detail might matter chemically.

The Extraction Method Matters

The research team had been using extraction procedures involving heat. What if the biologically active compound was **heat sensitive**?

Tu redesigned the procedure to extract *Artemisia annua* at lower temperatures using **ethyl ether**. In 1971, an extract prepared using this modified method showed striking antimalarial activity in infected rodents, and subsequent experiments showed similar activity in monkeys. In her Nobel lecture, Tu described the low-temperature ether extraction as the critical breakthrough that led to the discovery of artemisinin.

This is an important chemistry lesson in its own right.

> **Isolating a natural product requires more than finding the correct organism. The chemical properties of the molecule determine how it must be extracted, purified, and handled**.

The plant had contained the active compound all along. The experimental procedure had been interfering with the scientists' ability to recover it effectively.

From Plant Extract to Medicine

Once the research team had obtained a promising extract, another question remained:

Was it safe enough to test in humans?

In an extraordinary demonstration of commitment to the project, Tu and several colleagues volunteered to receive the extract themselves before it was administered to malaria patients.

Clinical studies subsequently showed that the preparation could rapidly eliminate malaria parasites. Researchers then worked to

isolate and characterize the active compound, which became known as **artemisinin**.

The findings emerged from a large collaborative Chinese research program, and early reports were published without individual authorship. Tu's particular role in the discovery was therefore not widely recognized internationally for many years.

That eventually changed.

In 2015, **Tu Youyou received one-half of the Nobel Prize in Physiology or Medicine for her discoveries concerning a novel therapy against malaria**, becoming the first Chinese woman to receive a Nobel Prize.

Her Nobel lecture was fittingly titled *Artemisinin—A Gift from Traditional Chinese Medicine to the World*. Tu Youyou's Nobel Prize lecture and biography(opens in new window).

Artemisinin Today

Artemisinin and related compounds remain critically important in modern malaria treatment. Because using artemisinin alone can promote the development of drug resistance, it is generally administered as part of an **artemisinin-based combination therapy (ACT)**. The artemisinin derivative rapidly reduces the number of parasites, while a second antimalarial drug helps eliminate the remaining infection. ACTs remain the best available treatment for uncomplicated *P. falciparum* malaria.

The story is not finished, however. *Plasmodium falciparum* populations with **partial resistance to artemisinin** have emerged in parts of Southeast Asia and Africa. These parasites are cleared from the bloodstream more slowly following treatment. Most patients can still be cured when the partner drug in the ACT remains effective, but the spread of resistance makes continued surveillance and development of new antimalarial therapies extremely important.

Importantly, WHO recommends approved artemisinin-based medicines for malaria treatment and **does not recommend using *Artemisia* teas, plant material, or supplements as substitutes for antimalarial medication**.

The Legacy of Tu Youyou's Discovery

Tu Youyou's discovery is sometimes described simply as the discovery of an antimalarial compound in an ancient medicinal plant. But that description misses much of what makes the story remarkable.

Traditional knowledge provided an important clue—but **scientific investigation was required to turn that clue into a reproducible medicine**.

Tu and her colleagues had to search the historical literature, select promising plants, prepare and test extracts, recognize inconsistent results, reconsider their assumptions, develop a new extraction procedure, evaluate biological activity, test safety, isolate the active compound, and ultimately determine its chemical structure.

Most importantly, when an experiment failed, Tu did not simply discard the original hypothesis.

She asked why it had failed.

By returning to an old preparation method and considering it through the lens of chemistry, she recognized that **temperature during extraction could determine whether the active natural product was successfully recovered**.

Her work provides a powerful example of the persistence and creativity required in scientific research—and of the discoveries that can emerge when knowledge from different traditions is examined using modern scientific methods.

> **A 1,600-year-old observation provided the clue. Chemistry helped reveal why it worked. Persistent scientific investigation transformed that clue into one of the world's most important antimalarial medicines**.

Animals

Animals are multicellular, eukaryotic organisms of the kingdom Animalia. As described earlier, animals are heterotrophic

organisms and are characterized by being mobile at some point in their lifetime. Animals can be divided broadly into vertebrates and invertebrates. Vertebrates have a backbone or spine (vertebral column), and amount to less than five percent of all described animal species. They include fish, amphibians, reptiles, birds and mammals. The remaining animals are the invertebrates, which lack a backbone. These include molluscs (clams, oysters, octopuses, squid, snails); arthropods (millipedes, centipedes, insects, spiders, scorpions, crabs, lobsters, shrimp); annelids (earthworms, leeches), nematodes (filarial worms, hookworms), flatworms (tapeworms, liver flukes), cnidarians (jellyfish, sea anemones, corals), ctenophores (comb jellies), and sponges. The study of animals is called zoology.

Animals also represent a source of bioactive natural products. In particular, venomous animals such as snakes, spiders, scorpions, caterpillars, bees, wasps, centipedes, ants, toads, and frogs have attracted much attention. This is because venom constituents (peptides, enzymes, nucleotides, lipids, biogenic amines etc.) often have very specific interactions with a macromolecular target in the body. As with plant feeding deterrents, this biological activity is attributed to natural selection, organisms capable of killing or paralyzing their prey and/or defending themselves against predators being more likely to survive and reproduce.



Figure 7.7.9: Chlorotoxin from the deathstalker scorpion (Leiurus quinquestriatus). A ribbon diagram of the chlorotoxin protein is shown on the right. Photo of the deathstalker scorpion by: Ester Inbar and Ribbon diagram of chlorotoxin by: Lijealso.

From Scorpion Venom to Tumor Targeting

Venoms provide fascinating examples of **secondary metabolites and other natural products that interact very specifically with biological targets**. Scorpions, snakes, spiders, and other venomous animals produce mixtures of biologically active molecules that help them capture prey or defend themselves. Because these molecules have evolved to interact with receptors, ion channels, enzymes, and other cellular targets, they can also provide unexpected starting points for biomedical research.

One remarkable example is **chlorotoxin**, a small 36-amino-acid peptide originally isolated from the venom of the deathstalker scorpion (*Leiurus quinquestriatus*). Chlorotoxin contributes to the biological activity of the scorpion's venom, but researchers discovered something unexpected: it also binds preferentially to several types of tumor cells, particularly cells from **gliomas**, tumors that arise from cells of the central nervous system.

Early studies of chlorotoxin focused on its effects on chloride channels, which gave the peptide its name. Subsequent research has shown that its interactions with tumor cells are more complicated and appear to involve proteins that are abundant on the surfaces of some tumor cells, including **matrix metalloproteinase-2 (MMP-2)** and **neuropilin-1 (NRP1)**. The precise mechanisms responsible for chlorotoxin's tumor-targeting properties continue to be investigated.

Using Chlorotoxin as a Molecular Delivery System

Once researchers discovered that chlorotoxin could preferentially associate with tumor tissue, an intriguing possibility emerged:

Could chlorotoxin be used to find a tumor—and then carry something useful along with it?

One early approach used a synthetic version of chlorotoxin called **TM-601**. Researchers attached radioactive iodine-131 (^131I) to TM-601 and investigated whether the chlorotoxin-derived peptide could help concentrate radiation within malignant gliomas. Rather than allowing radiation to affect tissues indiscriminately, the goal was to use chlorotoxin's tumor-targeting properties to deliver the radioactive isotope preferentially to tumor tissue. Early clinical studies demonstrated tumor-specific uptake and helped establish chlorotoxin as a potential molecular targeting agent.

Although ^131I-TM-601 did not ultimately become an established treatment for glioma, the concept opened the door to other ways of exploiting chlorotoxin's unusual targeting properties.

Tumor Paint: Making Cancer Glow

Researchers led by Dr. Jim Olson at the Fred Hutchinson Cancer Center developed another ingenious approach. Instead of attaching a radioactive isotope to a chlorotoxin-derived peptide, they attached a **near-infrared fluorescent dye**.

The resulting compound, originally called **BLZ-100** and now known as **tozuleristide**, has sometimes been described as **Tumor Paint®**.

The idea is beautifully simple. The chlorotoxin-derived portion helps target tumor tissue, while the fluorescent dye produces a signal that can be detected using specialized imaging equipment. During surgery, this fluorescence may help distinguish tumor tissue from surrounding healthy tissue and reveal tumor margins that are difficult to see with the naked eye.

Early animal studies produced striking results. In dogs undergoing surgery for naturally occurring cancers, fluorescent imaging revealed tumor tissue that could not readily be distinguished during conventional surgery. These early experiments helped provide the foundation for subsequent human clinical studies.

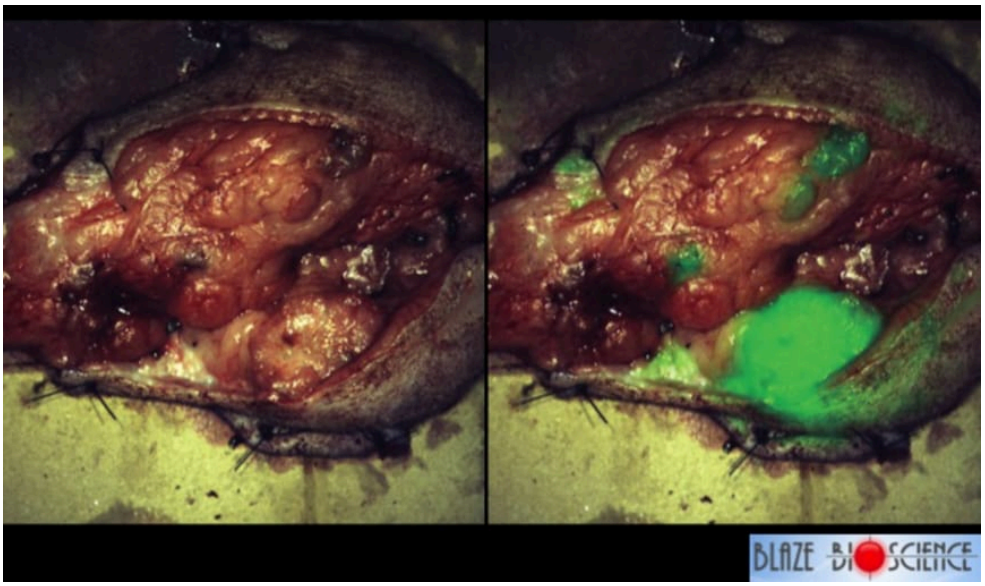


Figure 7.7.10**: Using Tumor Paint to Visualize Cancer During Surgery**. These images show an early demonstration of fluorescence-guided tumor imaging in a dog with naturally occurring mammary carcinoma. **Left:** Under normal visualization, surgeons could identify the primary tumor but could not readily distinguish all of the surrounding cancerous tissue. **Right:** After administration of the chlorotoxin-derived fluorescent imaging agent later developed as **tozuleristide (Tumor Paint®)**, additional areas of tumor tissue produced a fluorescent signal, making cancerous tissue that was difficult to see with the naked eye more visible. Studies such as these helped demonstrate the potential of chlorotoxin-derived molecules to help surgeons identify tumor margins and locate additional cancerous tissue during surgery.

The technology has since progressed into human trials. In a clinical study published in 2025 involving children undergoing surgery for primary central nervous system tumors, tozuleristide was administered in **32 surgical cases involving 29 patients**. Researchers reported no dose-limiting toxicities or allergic reactions and detected fluorescence in multiple types of brain tumors, supporting continued investigation of fluorescence-guided surgery using tozuleristide.

The development of Tumor Paint is described by Dr. Jim Olson in this earlier GeekWire presentation. Although the talk predates the more recent clinical results described above, it provides a fascinating look at the origins of the project and the process of turning a molecule discovered in scorpion venom into a potential biomedical tool.

Jim Olson: How to Defeat Cancer with Help from Nature, Scorpions and Innovative Thinking — GeekWire(opens in new window)

A New Direction: Chlorotoxin and CAR T Cells

More recently, researchers have found yet another potential use for chlorotoxin's tumor-targeting properties.

CAR T-cell therapy uses a patient's immune cells that have been genetically engineered to recognize particular features on cancer cells. Researchers have developed experimental CAR T cells that use chlorotoxin as part of their tumor-recognition system, allowing the engineered immune cells to recognize glioblastoma cells.

Early results from a Phase 1 clinical trial were reported in 2025. In the first four patients with recurrent glioblastoma described in the study, chlorotoxin-directed CAR T cells could be administered without dose-limiting toxicities. Three patients experienced **stable disease** as their best response. These are very early results and do not establish that the treatment is effective, but they demonstrate another remarkable way in which the tumor-targeting properties of chlorotoxin may potentially be adapted for medicine.

From Venom to Medicine

The chlorotoxin story provides a powerful example of the value of studying natural products. The deathstalker scorpion did not evolve chlorotoxin to locate brain tumors or help surgeons treat cancer. The peptide evolved as one component of a venom system that benefits the scorpion.

Scientists discovered that the same molecular features that allow chlorotoxin to interact with biological targets also give it unusual interactions with certain tumor cells. Researchers have subsequently explored those properties in several very different ways:

scorpion venom → chlorotoxin → tumor targeting → radioactive delivery, fluorescent imaging, and engineered immune cells.

This does not mean that chlorotoxin itself has become a cure for cancer. Rather, it illustrates something perhaps even more important about **natural-product drug discovery**: a molecule evolved by another organism can provide a chemical tool or starting point that scientists can adapt for an entirely different purpose.

> **Nature provides an enormous library of biologically active molecules. By understanding how those molecules interact with living systems, scientists can sometimes transform an organism's chemical defense or survival strategy into a new tool for medicine**.

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7.8: Chapter Summary

Natural Products and the Chemistry of Life

Natural products are chemical compounds produced by living organisms. They include an enormous variety of molecules made by plants, animals, fungi, bacteria, and archaea. Natural products can be broadly divided into **primary metabolites** and **secondary metabolites**.

Primary metabolites are molecules directly involved in the fundamental processes required for growth, development, reproduction, and cellular function. The major classes include:

- carbohydrates
- lipids
- proteins
- nucleic acids

Secondary metabolites are not directly required for the basic processes of growth and reproduction but can provide important ecological advantages. They may function in defense, communication, competition, attraction, or interactions with other organisms.

The biological activity of natural products ultimately depends upon their **molecular structure**. The carbon skeletons, functional groups, stereochemistry, polarity, and intermolecular interactions introduced in Chapter 6 determine how these molecules interact with other substances and with biological targets.

Carbohydrates

Carbohydrates are composed primarily of carbon, hydrogen, and oxygen and serve several important biological roles, including energy storage and structural support. The simplest carbohydrates are **monosaccharides**, such as glucose. Monosaccharides can join together to form larger carbohydrates. Two monosaccharides can form a **disaccharide**, while many monosaccharides can be linked together to form **polysaccharides**. Carbohydrates can therefore be organized as:

monosaccharides → disaccharides and oligosaccharides → polysaccharides.

The arrangement of functional groups and stereochemistry within a carbohydrate strongly influences its structure and biological properties. Even molecules with the same molecular formula can behave differently when their atoms are arranged differently in three-dimensional space. Larger carbohydrates are formed by joining sugar units through **glycosidic bonds**. Different bonding arrangements can produce polysaccharides with very different properties and functions. Examples include carbohydrates used for energy storage and carbohydrates that provide structural support.

Lipids

Lipids are a diverse group of molecules characterized largely by their substantial nonpolar character and limited solubility in water. Important biological lipids include **fatty acids, triacylglycerols, phospholipids, and steroids**. Fatty acids contain a long hydrocarbon region and a carboxylic acid functional group. A **saturated fatty acid** contains no carbon-carbon double bonds within its hydrocarbon chain, while an **unsaturated fatty acid** contains one or more carbon-carbon double bonds. The presence and geometry of double bonds influence molecular shape and intermolecular interactions. Cis double bonds commonly introduce bends or "kinks" into fatty acid chains, reducing their ability to pack tightly together.

Triacylglycerols (TAGs) are formed from glycerol and three fatty acids connected through ester bonds. They are important molecules for long-term energy storage.

Phospholipids contain both hydrophilic and hydrophobic regions. This amphipathic structure causes phospholipids to organize spontaneously in water and makes them major components of cellular membranes.

Steroids contain a characteristic structure of four fused carbon rings. Small changes in the functional groups attached to this carbon skeleton can produce molecules with very different biological functions.

Proteins

Proteins are polymers constructed from amino acid building blocks. Each amino acid contains an amino group, a carboxylic acid group, and a variable **R group** attached to a central carbon. The chemical properties of the R group distinguish one amino acid from another. Amino acids are joined through **peptide bonds** to form polypeptide chains. Protein structure can be described at several levels:

Primary structure is the amino acid sequence.

Secondary structure describes localized folding patterns within the polypeptide backbone.

Tertiary structure is the overall three-dimensional shape of a single polypeptide chain.

Quaternary structure occurs when multiple polypeptide chains associate to form a functional protein complex.

The amino acid sequence determines the interactions that can occur as a protein folds. Hydrogen bonding, ionic attractions, hydrophobic interactions, and other molecular forces help stabilize the final three-dimensional structure. Thus:

amino acid sequence → molecular interactions → protein folding → three-dimensional shape → protein function.

Protein shape is especially important because proteins must interact with other molecules to perform their functions. Enzymes, receptors, transport proteins, antibodies, and signaling proteins all depend upon specific molecular interactions.

Changing protein structure can therefore change—or completely eliminate—protein function.

Nucleic Acids

Nucleic acids store, transmit, and help express biological information. The two major nucleic acids are **DNA** and **RNA**. Both are polymers constructed from **nucleotides**. Each nucleotide contains three components:

- a phosphate group
- a five-carbon sugar
- a nitrogenous base

DNA contains the sugar **deoxyribose**, while RNA contains **ribose**.

Nucleotides are joined through **phosphodiester bonds**, producing the sugar-phosphate backbone of a nucleic acid strand. DNA contains four major nitrogenous bases:

adenine (A), thymine (T), guanine (G), and cytosine (C).

Complementary bases interact through hydrogen bonding:

A pairs with T.

G pairs with C.

These interactions allow two complementary DNA strands to associate and form the characteristic **double helix**.

RNA uses **uracil (U)** in place of thymine and performs a variety of roles in the expression and regulation of genetic information. As with proteins, the biological function of nucleic acids depends upon molecular structure and intermolecular interactions.

Primary Metabolites Are Chemically Connected

Although carbohydrates, lipids, proteins, and nucleic acids may initially appear to be very different types of molecules, they are built using the same chemical principles. Their structures depend upon:

- covalent bonding;
- carbon skeletons;
- functional groups;
- molecular geometry;
- stereochemistry;
- polarity;
- hydrogen bonding;
- ionic attractions;
- and hydrophobic interactions.

These molecular properties determine how biological molecules interact with water and with one another. They also determine how larger biological structures form. Phospholipids assemble into membranes. Proteins fold into specific three-dimensional shapes. Complementary DNA strands associate through hydrogen bonding. Thus, structures at the cellular level emerge from interactions occurring between individual atoms and molecules.

Secondary Natural Products

Living organisms also produce a remarkable variety of **secondary natural products**. Unlike primary metabolites, secondary metabolites are not directly involved in the fundamental processes required for growth and reproduction. Instead, they often provide an organism with an advantage within its environment. Plants may produce compounds that discourage herbivores, attract pollinators, inhibit competing organisms, or protect against microorganisms. Animals may produce venoms or toxins used for defense or predation. Fungi and bacteria produce compounds that influence interactions with competing microorganisms and other organisms in their environments.

Because these compounds evolved to interact with biological systems, many secondary natural products have become important sources of **medicines and drug leads**. Natural products have contributed to the development of antibiotics, anticancer agents, pain medications, antiparasitic drugs, and many other therapeutics. The discovery of **artemisinin**, for example, demonstrates how studying traditional medicinal plants and their natural products can lead to powerful modern medicines. Other natural products, such as **chlorotoxin** from deathstalker scorpion venom, demonstrate how molecules originally evolved for one biological purpose can potentially be adapted for very different biomedical applications. Natural products therefore represent an enormous reservoir of chemical diversity.

Structure Determines Biological Function

A central theme connects all of the molecules examined in this chapter:

Structure determines function.

A change in carbon skeleton can change molecular shape. A change in functional group can change polarity or chemical reactivity. A change in stereochemistry can alter the three-dimensional orientation of important functional groups. Changes in intermolecular interactions can alter protein folding, membrane formation, molecular recognition, or DNA structure. At every level, biological behavior emerges from chemistry. The relationship can be summarized as:

atomic composition and bonding.

↓

functional groups and molecular shape.

↓

polarity and intermolecular interactions.

↓

larger molecular structures.

↓

biological function.

The natural products examined in this chapter are therefore more than collections of complicated organic structures. They are examples of how the chemical principles developed throughout this course give rise to the molecules of life.

And these molecules do not simply exist within cells—they are continually being **built, broken down, rearranged, and transformed through chemical reactions**.

Those reactions, and the enzymes that control them, are the focus of **Chapter 8: Chemical Reactions in Biological Systems**.

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8: CHEMICAL REACTIONS IN BIOLOGICAL SYSTEMS

8.1: Metabolism and Biological Reactions

8.2: Oxidation States and Redox Reactions

8.3: Oxidation and Reduction in Biological Systems

8.4: Energy, ATP, and Cellular Respiration

8.5: Reaction Energy- Spontanaeity and Activation Energy

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8.1: Metabolism and Biological Reactions

Your body is constantly carrying out chemical reactions. Some reactions break apart the food you eat. Others use those smaller molecules to build proteins, lipids, carbohydrates, and nucleic acids. Still others release and capture energy, remove waste products, transmit signals between cells, or maintain the chemical conditions necessary for cells to survive. The collection of chemical reactions occurring within a living organism is called **metabolism**.

Metabolism is not a single reaction or even a single process. It is an interconnected network involving thousands of chemical reactions. Together, these reactions allow organisms to obtain and use energy, build and repair cellular structures, maintain internal conditions, and respond to changes in their environment. Although these reactions can become extraordinarily complex when considered together, the individual chemical reactions follow the same principles of bonding, molecular shape, polarity, and intermolecular interactions that we have been developing throughout this book.

Catabolic and Anabolic Reactions

Metabolic reactions can be broadly divided into two categories: **catabolic reactions** and **anabolic reactions**.

Catabolic reactions break larger molecules into smaller molecules. For example, during digestion, proteins can be broken into amino acids, carbohydrates into smaller sugars, and triacylglycerols into fatty acids and glycerol. Catabolic processes often release energy that can be captured and used by the cell.

Anabolic reactions, in contrast, build larger molecules from smaller components. Amino acids can be joined to produce proteins, nucleotides can be joined to produce DNA and RNA, and smaller carbon-containing molecules can be used to build lipids and carbohydrates. Building these larger, more complex structures generally requires an input of energy. Thus, a useful way to think about these two sides of metabolism is:

Catabolism: breaking down molecules, often releasing energy.

Anabolism: building molecules, generally requiring energy.

These processes are closely connected. The smaller molecules and energy produced by catabolic processes can be used to support the anabolic reactions required for cellular growth, maintenance, and repair.

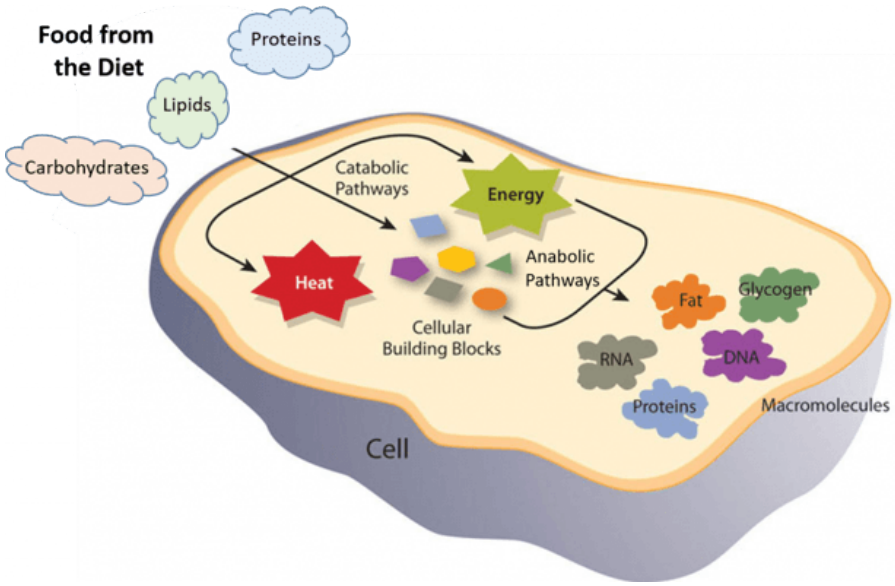


Figure 8.1.1**: Catabolic and Anabolic Reactions.** Catabolic reactions break larger molecules into smaller components and often release energy. Anabolic reactions use smaller molecules to build larger, more complex structures and generally require an input

of energy. Together, catabolic and anabolic reactions form the interconnected processes of metabolism. Figure is modified from Metabolism Overview.

Metabolic Pathways

The conversion of one molecule into another usually does not occur in a single enormous reaction. Instead, biological reactions are organized into **metabolic pathways**. A metabolic pathway is a series of chemical reactions in which the product of one reaction becomes the starting material for the next. For example:

A → **B** → **C** → **D**.

Each arrow represents a separate chemical reaction. Molecule A is converted into molecule B, which is converted into molecule C, and eventually into molecule D.

Why use so many steps?

Breaking a complicated chemical transformation into smaller reactions gives the cell much greater control over the process. Energy can be released or supplied in manageable amounts, useful intermediates can be directed into other pathways, and individual reactions can be turned up, slowed down, or stopped as cellular needs change. This organization is possible largely because individual steps within metabolic pathways are controlled by **enzymes**.

Enzymes Make Biological Chemistry Possible

An **enzyme** is a biological catalyst—a substance that increases the rate of a chemical reaction without being permanently consumed by the reaction.

Most enzymes are proteins. As you learned in Chapter 7, the function of a protein depends strongly on its three-dimensional shape. This relationship between **shape and function** becomes especially important for enzymes.

A region of an enzyme called the **active site** interacts with the molecule or molecules involved in the reaction. A molecule that binds to an enzyme and undergoes a chemical reaction is called a **substrate**.

The shape and chemical properties of the active site—including charge, polarity, hydrogen-bonding ability, and hydrophobic or hydrophilic character—determine which substrates can interact effectively with the enzyme.

Thus, the chemistry we have already studied helps explain enzyme specificity:

amino acid sequence → **protein folding** → **active-site shape and chemistry** → **substrate binding** → **enzyme function**.

Substrate binding is sometimes described using a **lock-and-key model**, in which the substrate and active site already have complementary shapes. However, proteins are flexible molecules. In many cases, substrate binding causes small changes in enzyme shape that improve the interaction between the enzyme and substrate. This is called the **induced-fit model**.

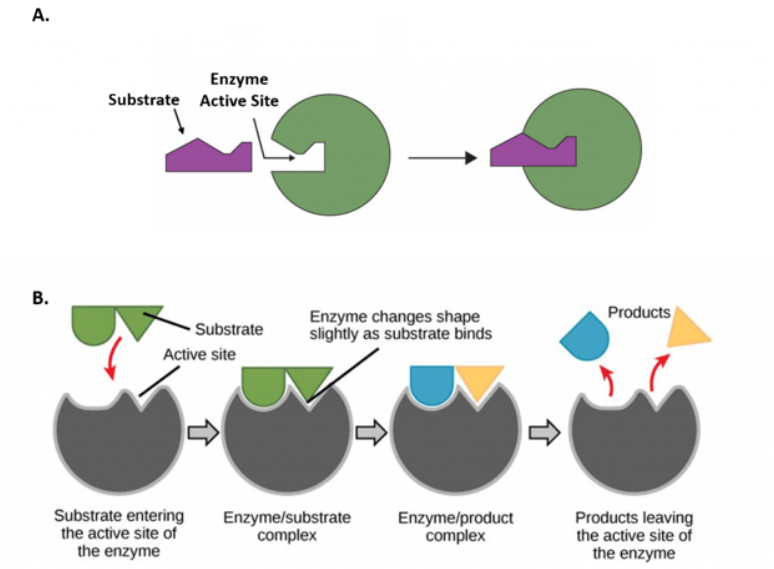


Figure 8.1.2: Enzyme-Substrate Binding. (A) In the lock-and-key model, the substrate has a complementary shape to the enzyme's active site. (B) In the induced-fit model, interactions between the substrate and enzyme cause the enzyme to change shape slightly, creating a better fit. In both cases, the three-dimensional shape and chemical properties of the active site are critical to enzyme function. Figure 7.2A was modified from Socratic and Figure 7.2B was modified from Concepts in Biology.

We will return to enzymes in much greater detail later in this chapter when we examine how they increase reaction rates and how temperature, pH, inhibitors, and drugs can alter their activity.

Biological Reactions Rearrange Atoms and Bonds

Despite the enormous variety of reactions occurring in the body, the fundamental chemistry remains familiar. During a chemical reaction, atoms are **rearranged**. Existing bonds may be broken, new bonds may be formed, or electrons and functional groups may be transferred from one molecule to another. The atoms themselves are conserved.

Several recurring reaction patterns are particularly important in biological systems. These include:

- **Hydrolysis and dehydration synthesis**, which break and form covalent bonds using or producing water.
- **Group-transfer reactions**, in which a functional group is transferred from one molecule to another.
- **Oxidation-reduction reactions**, in which electrons are transferred between chemical species.
- **Rearrangement reactions**, in which atoms within a molecule are reorganized to produce an isomer.

Rather than memorizing a large catalog of reaction names, our goal will be to recognize what is chemically changing and understand why that change matters biologically.

Hydrolysis and Dehydration Synthesis

You have already encountered one of the most important pairs of biological reactions.

In Chapter 7, we saw that smaller building blocks can be joined together to produce larger biological molecules. Amino acids are joined to form proteins, nucleotides are joined to form nucleic acids, and monosaccharides can be joined to form larger carbohydrates.

Many of these bonds are formed through **dehydration synthesis**, a reaction in which molecules are joined together while the components of a water molecule are removed.

The reverse process is **hydrolysis**.

The word *hydrolysis* literally refers to breaking (*lysis*) using water (*hydro*). During a hydrolysis reaction, water participates in breaking a covalent bond, producing smaller molecules.

Thus, these two processes can be viewed as opposites:

Dehydration synthesis: smaller molecules → larger molecule + water.

Hydrolysis: larger molecule + water → smaller molecules.

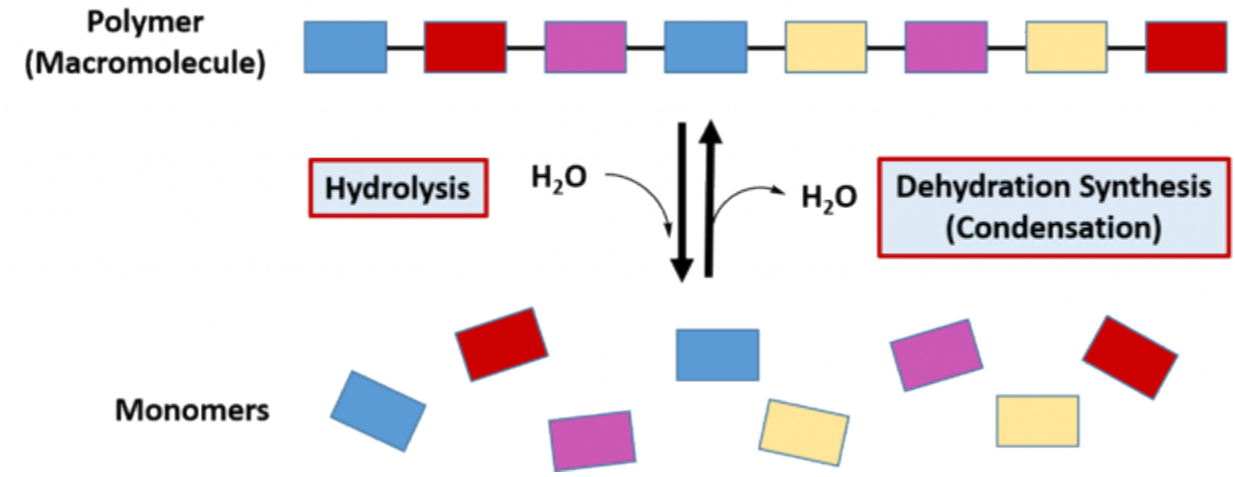


Figure 8.1.3**: Hydrolysis and Dehydration Synthesis**. Dehydration synthesis joins smaller molecules by forming a new covalent bond while producing water. Hydrolysis reverses this process by using water to break a covalent bond. These reaction patterns are important in the formation and breakdown of biological molecules.

This provides an important connection between **structure and metabolism**.

The molecules introduced in Chapter 7 are not static structures. The covalent bonds holding biological molecules together can be formed and broken as molecules are synthesized, digested, stored, transported, and used by cells. Figure 8.1.4 highlights the hydrolysis/dehydration synthesis reactions of the major macromolecules within the body, including lipids, DNA/RNA, proteins, and carbohydrates. When looking at these structures, try to identify the organic functional groups that are changing within the reaction and identify where water is being produced or utilized. For example, during dehydration synthesis, where major macromolecules are being formed, the monomer subunits become dehydrated (or lose water). This results in the formation of the macromolecule and water on the product side of the reaction. Hydrolysis or the breaking down of major macromolecules into their monomer subunits occurs by hydrating (or adding water) to the molecule, causing it to break apart.

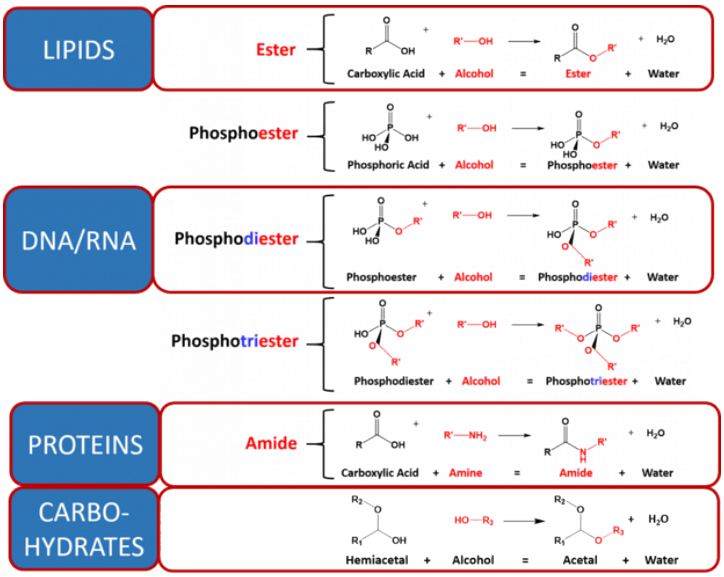


Figure 8.1.4**: Dehydration Synthesis Reactions Involved in Macromolecule Formation.** The major organic reactions required for the biosynthesis of lipids, nucleic acids (DNA/RNA), proteins, and carbohydrates are shown. Note that in all of the reactions, there is a functional group that contains two electron withdrawing groups (the carboxylic acid, phosphoric acid and the hemiacetal each have two oxygen atoms attached to a central carbon or phosphorus atom). This forms a reactive partially positive center atom (carbon in the case of the carboxylic acid and hemiacetal, or phosphorus in the case of the phosphoric acid) that can be attacked by the electronegative oxygen or nitrogen from an alcohol or amine functional group.

The formation of esters and the related compounds, amides, phosphoesters, and acetals are formed by dehydration synthesis, involving the loss of water. The reaction mechanisms for each of these reactions is very similar. Let's take a look at the formation of the ester linkage as an example (Figure 8.1.5).

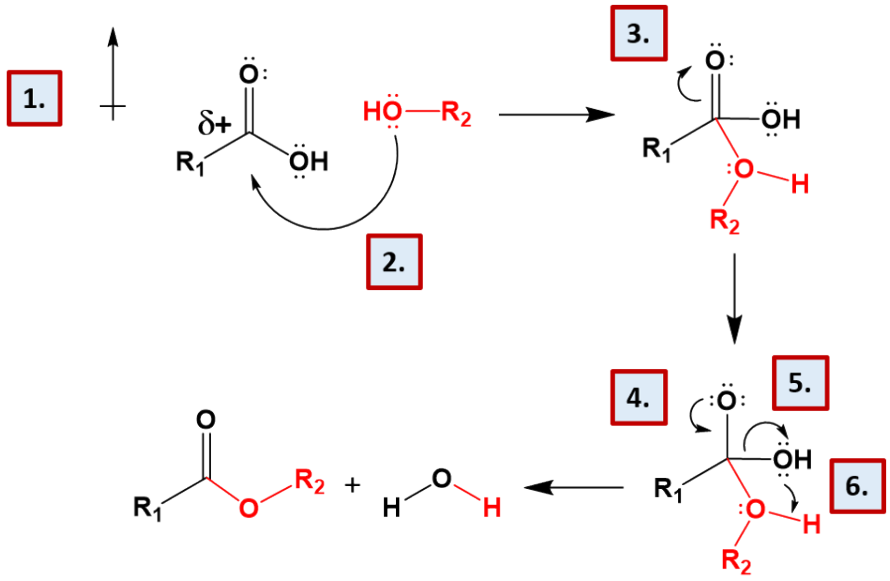


Figure 8.1.5**: Reaction Mechanism of Ester Formation**. (1) This reaction mechanism is set up by the nature of carboxylic acid functional group. The presence of the carbonyl oxygen and the alcohol functional groups create an electron withdrawing situation, where the electronegative oxygen atoms pull the electrons away from the central carbon atom. This creates a very polar situation, where the central carbon has a strong partial positive character. (2) The strong partial positve character of the central carbon atom of the carboxylic acid attracts one of the lone pair electron groups from the alcohol functional group, shown in red. This enables a new covalent bond to form between the alcohol functional group and the carboxylic acid functional group. This creates

an intermediate that has five bonds attached to the central carbon and three bonds attached to the oxygen atom of the incoming alcohol. (3) The intermediate with five bonds to the central carbon is unstable and wouldn't normally form, however the presence of the carbonyl oxygen makes the reaction more favorable. It will be able to temporarily absorb the extra electron potential around the central carbon atom, due to its electronegative character and the double bond will temporarily shift up onto the central oxygen forming a lone pair intermediate. (4) The extra lone pair on the carbonyl oxygen shifts back down to reform the double bond with the central carbon. (5) This causes the shared electron pair between the central carbon atom and the original alcohol functional group to shift over to the alcohol, breaking the covalent bond. (6) The extra lone pair of electrons on the free alcohol group take the proton from the new incoming alcohol group forming a molecule of water and the final ester structure.

All of the dehydration synthesis reactions shown for the major macromolecules have a similar reaction mechanism to that shown for the ester bond formation. Notice that the reverse of the reactions show the hydrolysis of the bond linkage by the addition of the water molecule across the bond. This restores the original functional groups, a carboxylic acid and an alcohol in the case of the ester.

Group-Transfer Reactions

Another common biological reaction involves moving a functional group from one molecule to another. In a **group-transfer reaction**, one molecule acts as a donor and another acts as an acceptor. For example, an amino group can be transferred between molecules during amino acid metabolism. Phosphate groups are also frequently transferred between biological molecules.

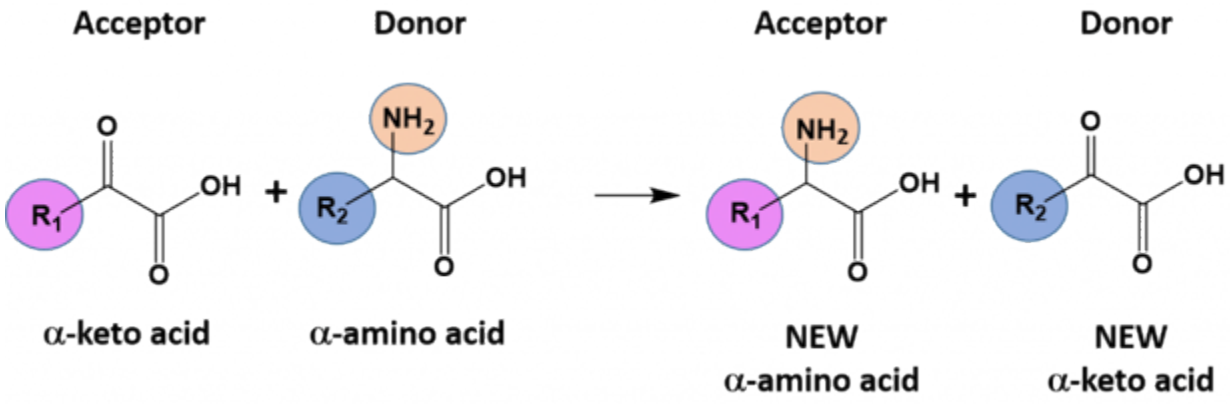


Figure 8.1.5**: Transfer of an Amine Functional Group.** A common group transfer reaction in biological systems is one that is used to produce α-amino acids that can then be used for protein synthesis. In this reaction, one α-amino acid serves as the donor molecule and an α-keto acid (these molecules contain a carboxylic acid functional group and a ketone functional group separated by one α-carbon) serves as the acceptor. In the acceptor molecule, the carbonyl oxygen is replaced with the amine functional group, whereas in the donor molecule, the amine functional group is replaced by an oxygen forming a new ketone functional group.

The identity of the atoms does not change—the functional group is simply transferred from one molecule to another. This provides a useful reminder of the **law of conservation of matter** that was introduced earlier in the course. During a chemical reaction, atoms are not created or destroyed; they are simply rearranged into new combinations. Thus, when a group is transferred from one molecule to another, the atoms that make up that group must come from somewhere and can be followed from the reactants into the products.

In addition, these reactions provide another reason that recognizing the functional groups introduced in Chapter 6 is useful. Functional groups are not merely labels for classifying organic molecules. They often represent the **chemically reactive regions of biological molecules**.

Rearrangement Reactions

Sometimes a biological reaction does not add or remove atoms at all.

In a **rearrangement reaction**, the atoms within a molecule are reorganized to produce an isomer. Because isomers have the same molecular formula but different arrangements of their atoms, a rearrangement can change molecular shape and chemical properties without changing the total number or types of atoms present.

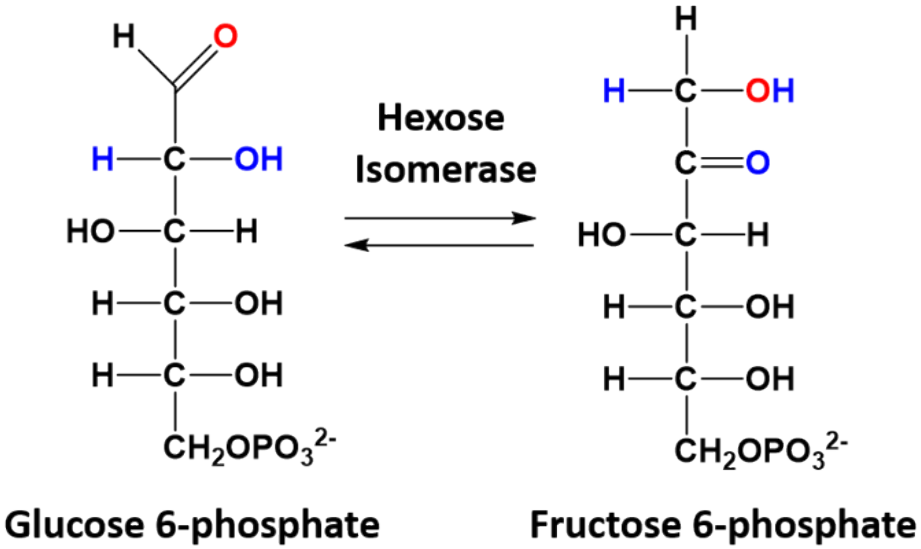


Figure 8.1.6**: Example of a Rearrangement Reaction**. In this reaction, glucose 6-phosphate, an aldose sugar, is converted to fructose 6-phosphate, a ketose sugar. Both molecules are structural isomers and have the molecular formula of $C_6H_{12}O_6$. The enzyme, hexose isomerase, mediates this reaction. Note that the arrows flow in both directions, indicating that this enzyme can shift the molecule in either direction, depending on cellular conditions.

This is another example of an idea we have encountered repeatedly:

Structure influences function.

Changing the arrangement of atoms can change how a molecule interacts with enzymes, receptors, membranes, or other biological molecules.

Oxidation-Reduction Reactions

Finally, some of the most important reactions in metabolism involve the movement of **electrons**. These are called **oxidation-reduction**, or **redox**, reactions. Redox reactions are especially important because electron transfer provides a way for cells to capture and transfer energy. When the molecules obtained from food are metabolized, a series of redox reactions gradually removes high-energy electrons from those molecules.

Rather than releasing all of that energy at once—as occurs when a fuel burns—the cell transfers electrons through a controlled series of reactions. The energy released through this process can ultimately be used to produce **adenosine triphosphate (ATP)**, one of the cell's most important energy-transfer molecules.

This brings us to one of the central chemical stories of life:

How can the chemical energy stored in food be converted into a form that a cell can actually use?

To answer that question, we first need to take a closer look at **oxidation and reduction in biological systems**.

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8.2: Oxidation States and Redox Reactions

An *oxidation-reduction (redox) reaction* is a type of chemical reaction that involves a transfer of electrons between two atoms or compounds. The substance that loses the electrons is said to be oxidized, while the substance that gains the electrons is said to be reduced. The change in electron composition can be evaluated in the change of the *oxidation state (or number)* of an atom. Therefore, an *oxidation-reduction reaction* is any chemical reaction in which the oxidation state (number) of a molecule, atom, or ion changes by gaining or losing an electron. We will learn how to evaluate the oxidation state of a molecule within this section. Overall, redox reactions are common and vital to some of the basic functions of life, including photosynthesis, respiration, combustion, and corrosion or rusting.

As shown in figure 8.2.1, an easy mnemonic for helping you remember which member gains electrons and which member loses electrons is 'LEO the lion says GER', where LEO stands for Lose Electrons = Oxidized and GER stands for Gain Electrons = Reduced.



Figure 8.2.1**:** Mnemonic for Remembering Oxidation and Reduction. LEO the lion says GER is a mnemonic for remembering the if an atom loses electrons it is oxidized, and if an atom gains electrons it is reduced.

Rules for Assigning Oxidation States

The ***oxidation state (or oxidation number)*** of an atom corresponds to the number of electrons an atom loses or gains when forming an ionic compound, or appears to lose or gain when forming covalent compounds. Oxidation states are a bookkeeping tool used to keep track of electron transfer in chemical reactions. In determining the oxidation state of an atom, there are seven guidelines to follow:

1. The oxidation state of an atom in its elemental form is **0**. This includes elements that exist as diatomic molecules. For example, each oxygen atom in $\mathbf{O_2}$ has an oxidation state of **0**.
2. The total oxidation state of all atoms in a *neutral species* is **0** and in an *ion* is equal to the **ion charge**. (For example, the overall oxidation state of NaCl = 0, even though the oxidation state of Na^+ in this bond is +1 and the oxidation state of the chlorine atom, Cl^-, is -1. When you add them together they equal 0. In the case of an ion, the overall charge is always indicated. For example, the overall charge of a OH^- ion is -1, while the oxygen in the OH^- has a -2 oxidation state and the hydrogen has a +1 oxidation state.)
3. Group 1 metals have an oxidation state of **+1**, and Group 2 metals have an oxidation state of **+2** in their compounds.
4. Fluorine always has an oxidation state of **−1** in compounds.

5. Hydrogen generally has an oxidation state of **+1** in compounds
6. Oxygen generally has an oxidation state of **-2** in compounds
7. In binary ionic compounds, Group 17 (7A) elements generally have an oxidation state of –1, Group 16 (6A) elements generally have an oxidation state of –2, and Group 15 (5A) elements generally have an oxidation state of –3.
8. The oxidation states of all other atoms are determined using Rules 1–7.

Rules should be applied in order from top to bottom. If one rule determines the oxidation state of an atom, later rules do not override it.

Table 8.2A: Summary of the Rules for Evaluating Oxidation States

Rule	Oxidation State
Elemental form	0
Neutral compound	Sum = 0
Polyatomic ion	Sum = ion charge
Group 1	+1
Group 2	+2
F	-1
H	Usually +1
O	Usually -2
Halogens	Usually -1

Example 8.2.1

What is the oxidation state of chromium in the chromate anion, CrO_4^{2-}?

Solution

Looking at all the oxidation state rules, we see that the overall oxidation state is equal to the charge of the ion (-2), and that the oxygen usually takes a -2 oxidation state. So we should assign each oxygen atom in the anion an oxidation state of (-2). There are 4 oxygen atoms, thus the overall charge from all of the oxygens is:

$$(-2) \times 4 = -8 \tag{8.2.1}$$

and the total charge on the anion is (-2). Thus, the oxidation state of chromium can be solved using the following equation, where *X* is the overall positive charge:

$$X + (-8) = -2 \tag{8.2.2}$$

$$X = +6 \tag{8.2.3}$$

Since there is only one Chromium ion within the anion, it must be responsible for the entire positive charge on the molecule. Thus, the chromium ion has an oxidation state of +6.

Exercise 8.2.1

More Practice with Oxidation States:

1. What is the oxidation state of chromium in the dichromate anion, $Cr_2O_7^{2-}$?
2. What is the oxidation state of carbon in $H_2C_2O_4$?

3. What is the oxidation state of sulfur in the $Na_2S_2O_3$?
4. What is the oxidation state of carbon in CO? in CO_2?
5. What is the oxidation state of chlorine in ClO_4^-?

Answer available at the end of this section.

Once you have mastered calculating oxidation states, you can start evaluating chemical reactions to determine if they are oxidation-reduction reactions.

Redox reactions are comprised of two parts, a reduced half and an oxidized half, that *always* occur together. The reduced half gains electrons and the oxidation number decreases (or becomes less positive), while the oxidized half loses electrons and the oxidation number increases (becomes more positive). There is no net change in the number of electrons in a redox reaction. Those given off in the oxidation half reaction are taken up by another species in the reduction half reaction.

A good example of a redox reaction is the thermite reaction, in which iron atoms in ferric oxide lose (or give up) O atoms to Al atoms, producing Al_2O_3.

$$\mathbf{Fe_2O_3\,(s) + 2\,Al\,(s) \longrightarrow Al_2O_3\,(s) + 2\,Fe\,(l)} \tag{8.2.4}$$

To recognize redox reactions, begin by determining the oxidation states of each atom in the reaction on both the left and the right sides of the equation. Then determine of the oxidation state of any of the atoms changes from the reactant to the product side. If so, then the reaction is a redox reaction, and you can determine which compound is oxidized (loses electrons) and which is reduced (gains electrons). For example, if we evaluate the thermite reaction above:

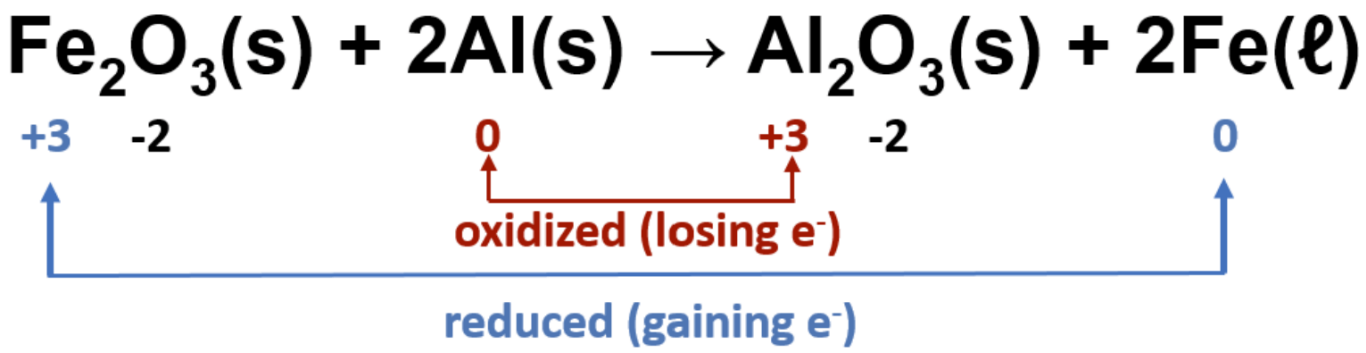
1. First evaluate the reactants side: Start with Fe_2O_3
    - *Table 8.2B: Evaluating the Oxidation States of Atoms in Iron (III) Oxide.*

Fe_2O_3	Fe	O	Overall Charge
Number of Atoms	2	3	
Oxidation State	+3	-2	
Total Charge	+6	-6	0

2. Then evaluate Aluminum (Al). Since aluminum is in its elemental form, the oxidation state is zero = 0.
3. Then evaluate the product side of the reaction. Start with the Al_2O_3
    - *Table 8.2C: Evaluating the Oxidation States of Atoms in Aluminum Oxide.*

Al_2O_3	Al	O	Total Charge
Number of Atoms	2	3	
Oxidation State	+3	-2	
Total Charge	+6	-6	0

4. Then evaluate the iron, Fe. Since iron is in its elemental form, the oxidation state is zero = 0.
5. Finally, write in the values on the equation and evaluate the redox states.



Overall in this reaction, the aluminum is oxidized to aluminum oxide, and the iron in the iron III oxide is reduced to elemental iron. Notice that there is no change to the oxidation state of oxygen.

The two species that exchange electrons in a redox reaction are given special names. The ion or molecule that accepts electrons (or becomes reduced during the reaction) is called the oxidizing agent; by accepting electrons it causes the oxidation of another compound or element. In the thermite reaction above, the iron III oxide is the oxidizing agent. Conversely, the species that donates electrons is called the reducing agent; when the reaction occurs, it reduces the other species. Thus, in the thermite reaction, the aluminum is the reducing agent. In other words, the substance that is oxidized is the reducing agent and the substance that is reduced is the oxidizing agent.

Single replacement reactions are often also redox reactions. A good indicator of a redox reaction is the appearance of an elemental form of a substance on one side that is converted into a compound on the other side. Another common redox reaction is a combustion reaction.

Combustion Reactions

$$\mathrm{CxHy + O_2 \longrightarrow CO_2 + H_2O} \tag{8.2.5}$$

Combustion reactions almost always involve oxygen in the form of O_2, and are almost always ***exothermic***, meaning they produce heat. Chemical reactions that give off light and heat are colloquially referred to as “burning.” Complete combustion of carbon compounds results in the production of carbon dioxide (CO_2) and water (H_2O). Note that carbon can exist in a range of oxidation states, typically from -4 to +4. The burning of fuels that provides the energy to maintain our civilization and the metabolism of foods that furnish the energy that keeps us alive both involve redox reactions.

All combustion reactions are also redox reactions.

$$\mathrm{CxHy + O_2 \longrightarrow CO_2 + H_2O} \tag{8.2.6}$$

One example is the burning of acetylene (C_2H_2) in torches:

$$\mathrm{2\,C_2H_2 + 5\,O_2 \longrightarrow 4\,CO_2 + 2\,H_2O} \tag{8.2.7}$$

Oxygen (in its elemental form) is a crucial reactant in combustion reactions, and it is also present in the products. Combustion reactions can be evaluated for their redox potential, as we did for the thermite reaction above.

1. First evaluate the reactants side: Start with C_2H_2

    - *Table 8.2D: Determining Oxidation States of Atoms in Acetylene (Ethyne).*

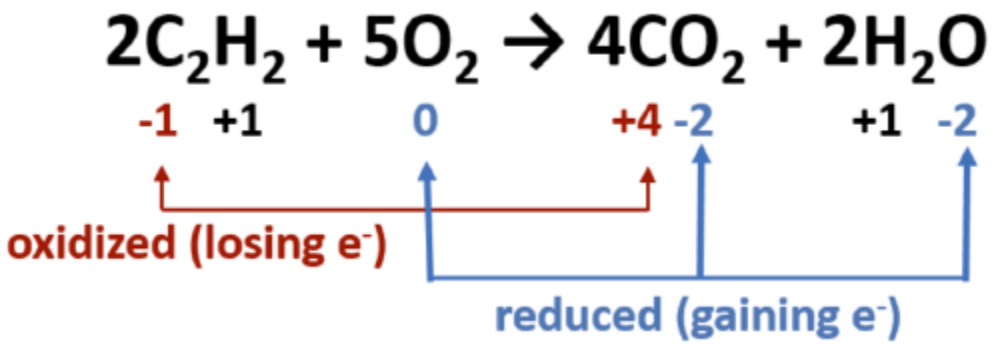
C_2H_2	C	H	Overall Charge
Number of Atoms	2	2	
Oxidation State	-1	+1	
Total Charge	-2	+2	0

2. Then evaluate O_2. Since oxygen is in its elemental form, the oxidation state is zero = 0.
3. Then evaluate the products side: Start with the CO_2

    - *Table 8.2E: Determining the Oxidation States of Atoms in Carbon Dioxide.*

CO_2	C	O	Overall Charge
Number of Atoms	1	2	
Oxidation State	+4	-2	
Total Charge	+4	-4	0

4. Then evaluate H_2O. The Hydrogen takes on the +1 state and the Oxygen takes on the -2 state.
5. Finally, write in the oxidation states on the equation and evaluate the changes.



Overall in combustion reactions, the hydocarbon (in this case, acetylene) is oxidized by molecular oxygen to produce carbon dioxide and water. In the process, oxygen is reduced.

In respiration, the biochemical process by which the oxygen we inhale in air oxidizes foodstuffs to carbon dioxide and water, redox reactions provide energy to living cells. A typical respiratory reaction is the oxidation of glucose ($C_6H_{12}O_6$), a simple sugar. Instead of releasing energy rapidly as heat and light, cells capture the energy from glucose in a controlled series of biochemical reactions to produce ATP.

$$\mathrm{C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O} \tag{8.2.8}$$

A Closer Look at the Importance of Redox Reactions

Organic chemists use a variety of redox reactions. For example, potassium dichromate ($K_2Cr_2O_7$) is a common oxidizing agent that can be used to oxidize alcohols (symbolized by the general formula R-OH, where R can be any group, and the OH represents the alcohol functional group). The product of the reaction depends on the location of the OH functional group in the alcohol molecule, the relative proportions of alcohol and the dichromate ion, and reaction conditions such as temperature. If the OH group is attached to a terminal carbon atom and the product is distilled off as it forms, the product is an aldehyde, which has a terminal carbonyl group (C=O). One example is the reaction used by the Breathalyzer to detect ethyl alcohol (C_2H_5OH) in a person's breath:

$$\mathrm{3\,C_2H_5OH + Cr_2O_7^{2-} + 8\,H^+ \longrightarrow 3\,CH_3CHO + 2\,Cr^{3+} + 7\,H_2O} \tag{8.2.9}$$

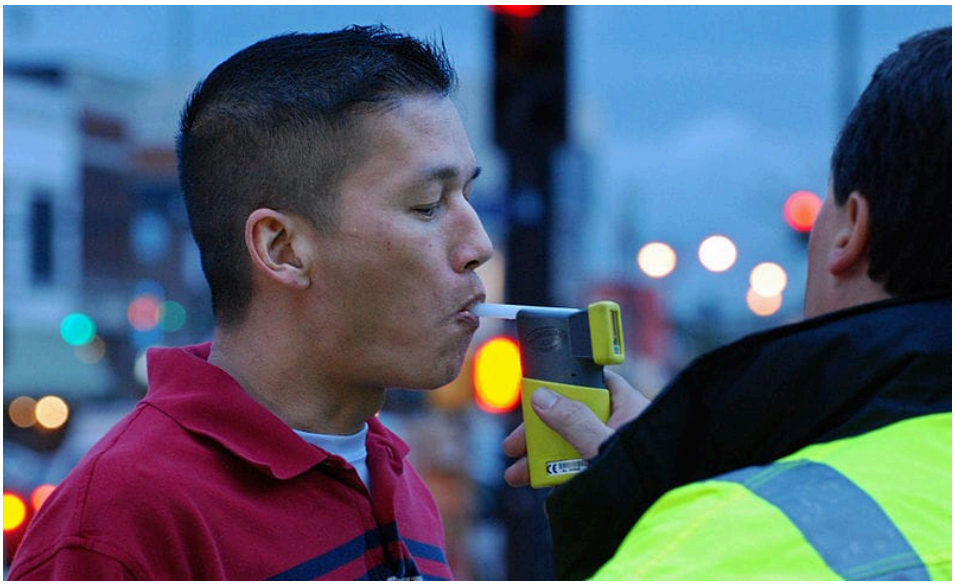
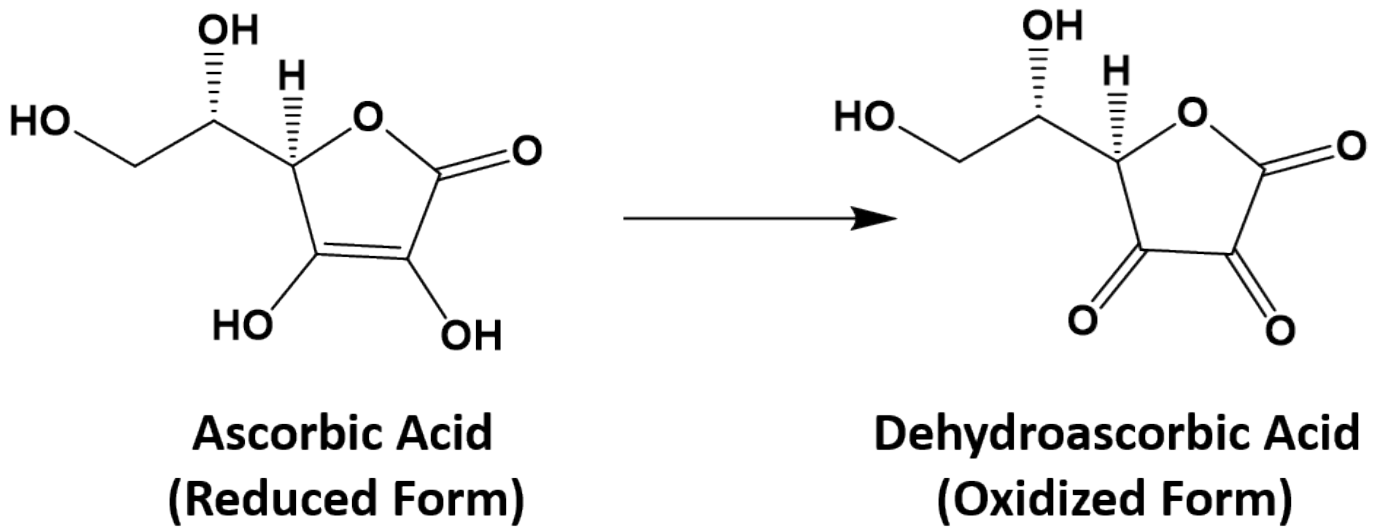


Figure 8.2.2**:** Drinkers Learn Their Limit Using a Standard Breathalyzer Test. Picture from: KOMUnews(opens in new window)

In food chemistry, the substances known as antioxidants are reducing agents. Ascorbic acid (also known as vitamin C; $C_6H_8O_6$) is thought to prevent potentially damaging oxidation of living cells. In the process, it is oxidized to dehydroascorbic acid ($C_6H_6O_6$).

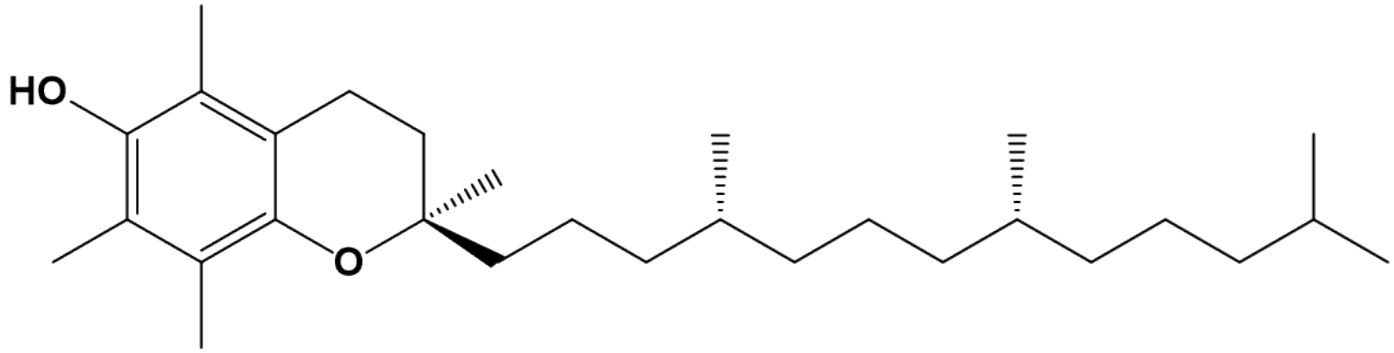


Ascorbic Acid (Reduced Form) **Dehydroascorbic Acid (Oxidized Form)**

In the stomach, ascorbic acid reduces the nitrite ion (NO^{2-}) to nitric oxide (NO):

$$\mathbf{C_6H_8O_6 + 2\,H^+ + 2\,NO_2^- \longrightarrow C_6H_6O_6 + 2\,H_2O + 2\,NO} \tag{8.2.10}$$

If this reaction did not occur, nitrite ions from foods would oxidize the iron in hemoglobin, destroying its ability to carry oxygen.



Vitamin E
(alpha-Tocopherol)

Tocopherol (vitamin E) is also an antioxidant. In the body, vitamin E is thought to act by scavenging harmful by-products of metabolism, such as the highly reactive molecular fragments called free radicals. In foods, vitamin E acts to prevent fats from being oxidized and thus becoming rancid.

Finally, and of greatest importance, green plants carry out the redox reaction that makes possible almost all life on Earth. They do this through a process called photosynthesis, in which carbon dioxide and water are converted to glucose ($C_6H_{12}O_6$). The synthesis of glucose requires a variety of proteins called enzymes and a green pigment called chlorophyll that converts sunlight into chemical energy (Figure 6.4.4). In this reaction, carbon dioxide is reduced to form glucose ($C_6H_{12}O_6$), and water is oxidized to oxygen gas. Other reactions convert the glucose ($C_6H_{12}O_6$) to more complex carbohydrates, plant proteins, and oils. The chemical reaction that occurs is as follows:

$$\mathbf{6\,CO_2 + 6\,H_2O \longrightarrow C_6H_{12}O_6 + 6\,O_2} \tag{8.2.11}$$

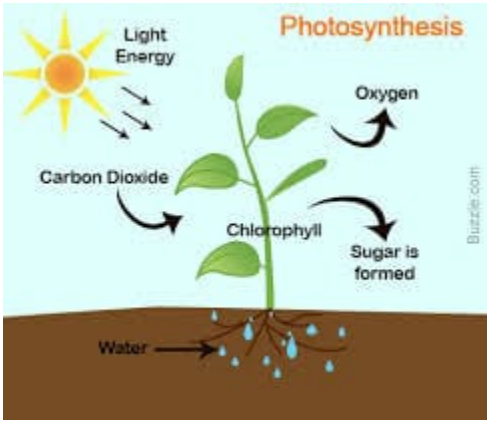


Figure 8.2.3**: Diagram of Photosynthesis**. In photosynthesis, light energy from the sun is harvested by the chlorophyll pigments primarily in the plant leaves where it is used to convert carbon dioxide and water into sugar (glucose). Image provided from: Masroor.nida.ns(opens in new window)

Now that we have a formal method for identifying oxidation and reduction, we can apply these ideas to organic and biological molecules. In large carbon-containing molecules, changes in bonding to hydrogen and oxygen provide a convenient way to recognize many of the same electron-transfer patterns without calculating the oxidation state of every atom.

Answers

Exercise 8.2.1

1. (+6), 2. (+3), 3. (+2), 4. (+2, +4), 5. (+7)

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8.3: Oxidation and Reduction in Biological Systems

In Section 8.2, we learned how **oxidation states** can be used to track changes in electron distribution during a chemical reaction.

Recall that:

Oxidation → loss of electrons → oxidation state increases (becomes more positive).

Reduction → gain of electrons → oxidation state decreases (becomes more negative).

Oxidation states provide a formal method for identifying redox reactions and work particularly well for relatively small molecules and ions.

Biological molecules, however, can be much larger and more complicated. A molecule such as glucose contains six carbon atoms, while a fatty acid may contain 16, 18, or more. Proteins and nucleic acids can contain thousands of atoms.

Calculating the oxidation state of every carbon atom would quickly become cumbersome.

Fortunately, the structures of organic molecules give us another useful way to recognize oxidation and reduction.

Recognizing Oxidation and Reduction in Organic Molecules

In organic and biological chemistry, we can often recognize oxidation and reduction by examining the bonds surrounding carbon atoms.

Two particularly useful patterns are:

Oxidation generally involves the loss of hydrogen and/or an increase in bonding to oxygen.

Reduction generally involves the gain of hydrogen and/or a decrease in bonding to oxygen.

These patterns are not separate from the oxidation-state rules introduced in Section 8.2. They arise from the same underlying redistribution of electrons.

Remember that oxygen is more electronegative than carbon. When carbon forms a bond with oxygen, the bonding electrons are pulled more strongly toward oxygen. Increasing the number of bonds between carbon and oxygen therefore makes the carbon more **oxidized**.

Carbon, however, is more electronegative than hydrogen. In a C–H bond, carbon has greater control over the bonding electrons. Increasing the number of C–H bonds therefore makes carbon more **reduced**.

This gives us a useful structural shortcut:

More C–O bonds / fewer C–H bonds → more oxidized.

More C–H bonds / fewer C–O bonds → more reduced.

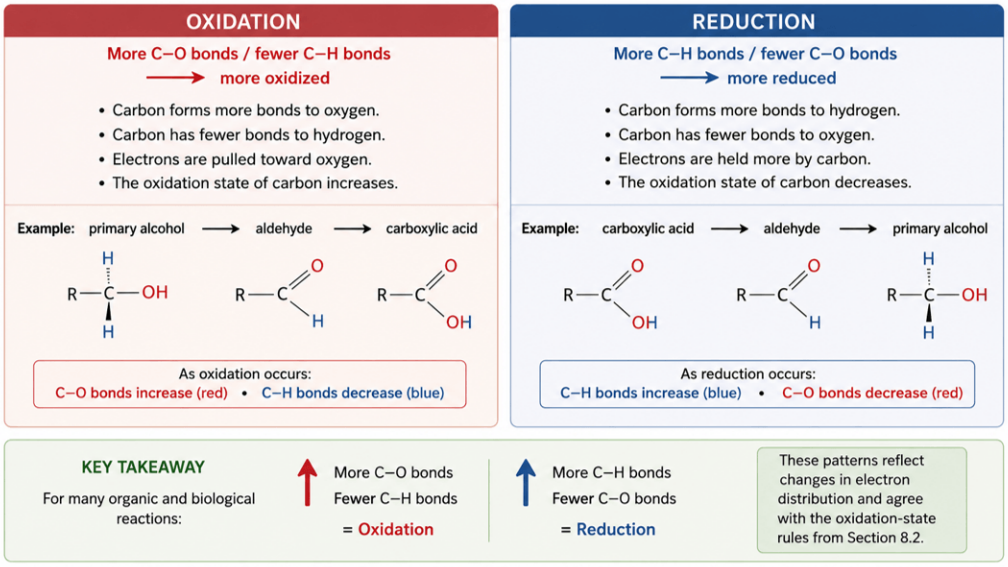


Figure 8.3.1: Recognizing Oxidation and Reduction in Organic Molecules. Organic oxidation generally increases the number of bonds between carbon and oxygen and/or decreases the number of bonds between carbon and hydrogen. Reduction produces the opposite pattern, increasing C–H bonding and/or decreasing C–O bonding. These structural changes provide a convenient way to recognize redox reactions in large biological molecules without calculating the oxidation state of every carbon atom.

Oxidation of Alcohols

The functional groups introduced in Chapter 6 provide an excellent example of how oxidation changes the structure of an organic molecule.

Recall that alcohols contain a hydroxyl (**–OH**) functional group. Alcohols can be classified as **primary, secondary, or tertiary** according to the number of carbon atoms attached to the carbon bearing the –OH group.

A **primary (1°) alcohol** has an –OH-bearing carbon attached to one other carbon.

A **secondary (2°) alcohol** has an –OH-bearing carbon attached to two other carbons.

A **tertiary (3°) alcohol** has an –OH-bearing carbon attached to three other carbons.

These structural differences determine how the alcohol can participate in the oxidation reactions considered in this course.

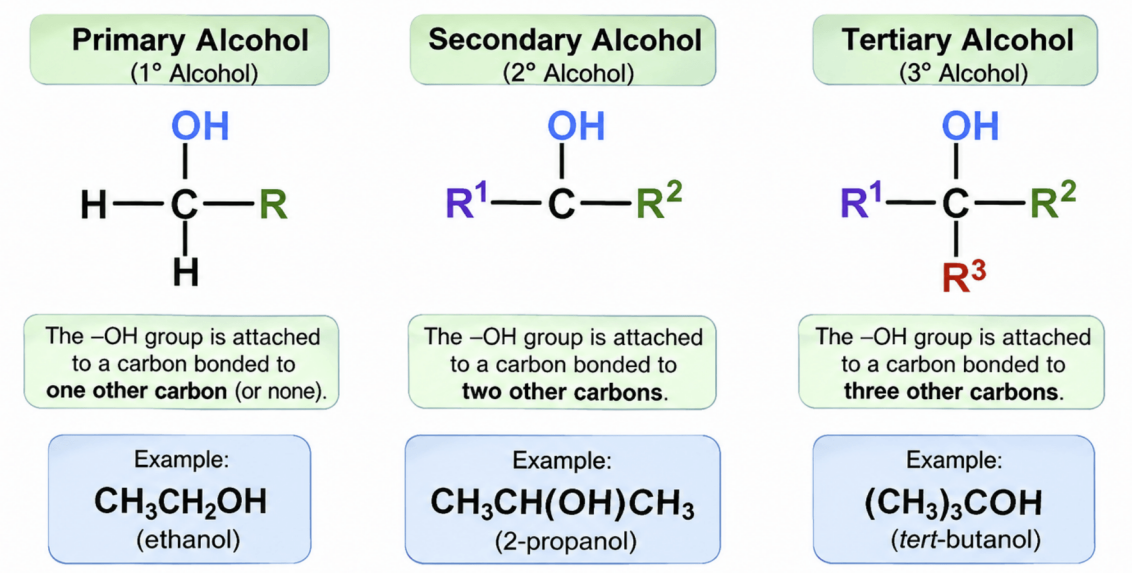


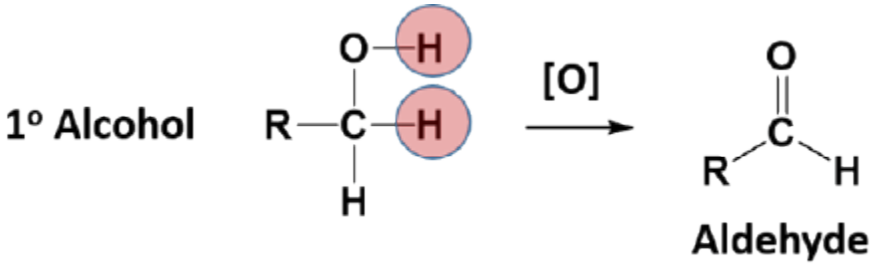
Figure 8.3.2: Classification of Primary, Secondary, and Tertiary Alcohols. Alcohols are classified according to the number of carbon atoms bonded to the carbon bearing the hydroxyl (–OH) group. In a primary (1°) alcohol, this carbon is bonded to one other carbon; in a secondary (2°) alcohol, it is bonded to two other carbons; and in a tertiary (3°) alcohol, it is bonded to three other carbons. Ethanol, isopropanol (2-propanol), and *tert*-butanol are shown as representative examples.

Oxidation of Primary Alcohols

A primary alcohol can be oxidized to form an **aldehyde**.

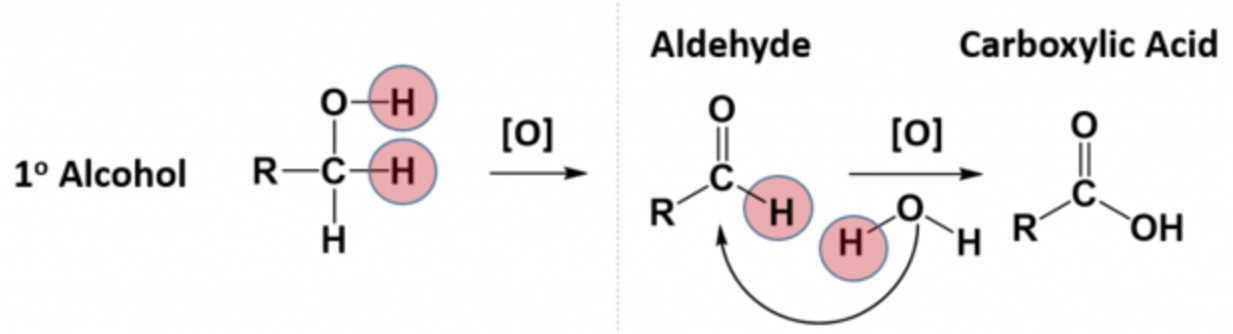
During this process, hydrogen is removed and a carbon-oxygen double bond is formed:

primary alcohol → aldehyde:



An aldehyde can then undergo further oxidation to produce a **carboxylic acid**:

primary alcohol → aldehyde → carboxylic acid:



Notice the structural pattern.

As the carbon becomes progressively oxidized, it has **fewer bonds to hydrogen and more bonding to oxygen**.

Note

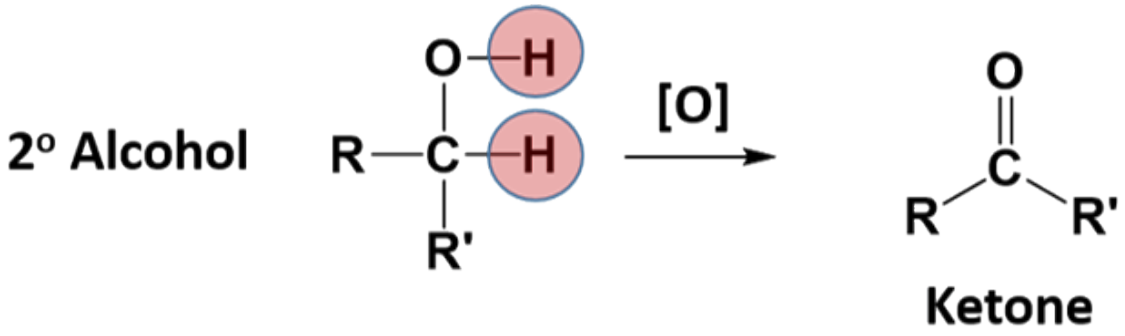
The oxidizing agent shown above the reaction arrow as [O] is also participating in the redox reaction. As the alcohol is **oxidized**, losing hydrogen and electron density, the oxidizing agent **accepts electrons and is reduced**. Remember that oxidation and reduction always occur together—the electrons lost by one chemical species must be accepted by another.

Oxidation of Secondary Alcohols

A secondary alcohol can also undergo oxidation, but it produces a different functional group.

Oxidation of a secondary alcohol produces a **ketone**:

secondary alcohol → ketone:



Again, hydrogen is removed and bonding between carbon and oxygen increases.

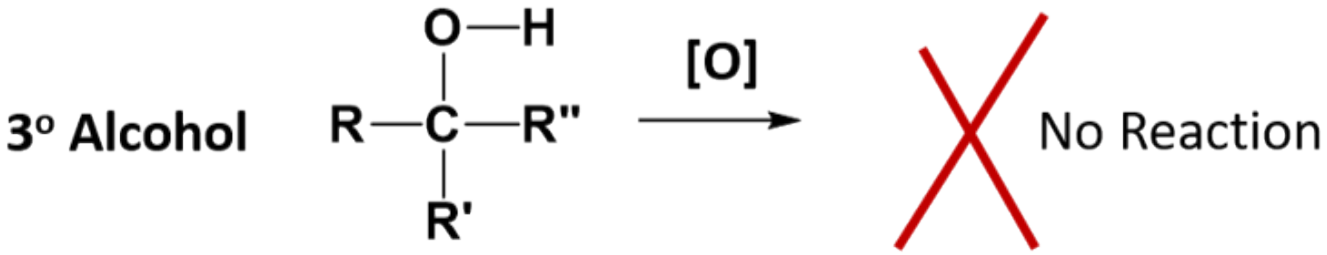
Tertiary Alcohols

Tertiary alcohols behave differently.

The carbon bearing the –OH group in a tertiary alcohol has no hydrogen attached to it. Therefore, the simple oxidation process that occurs with primary and secondary alcohols cannot take place.

For the reactions considered in this course:

tertiary alcohol → no reaction with a typical alcohol oxidizing agent:

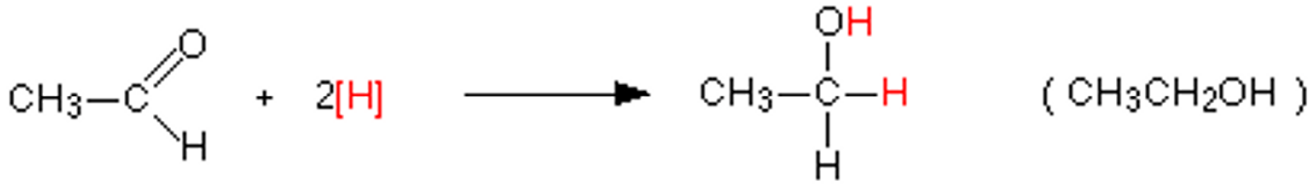


Reduction Reverses the Pattern

Reduction moves organic molecules in the opposite direction.

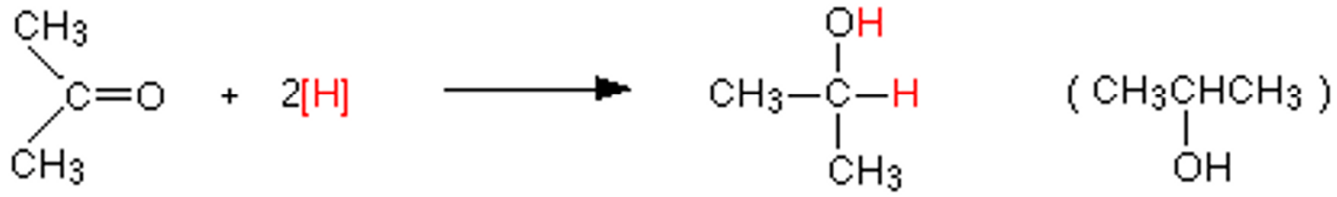
An aldehyde can be **reduced** to a primary alcohol:

aldehyde → primary alcohol:



A ketone can be **reduced** to a secondary alcohol:

ketone → secondary alcohol:



In these reactions, carbon gains hydrogen and decreases its degree of bonding to oxygen.

Thus, rather than memorizing each reaction independently, look for the larger structural pattern:

OXIDATION:

fewer C–H bonds
and/or
more C–O bonds

REDUCTION:

more C–H bonds
and/or
fewer C–O bonds

Oxidation and reduction are therefore complementary processes. Moving in one direction along these structural relationships represents oxidation; moving in the opposite direction represents reduction.

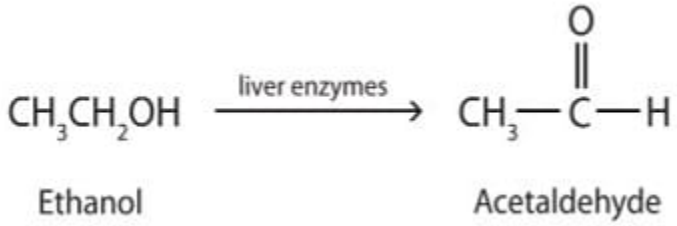
A Biological Example: Metabolism of Ethanol

Alcohol oxidation is not simply a reaction performed in a chemistry laboratory. The same type of chemistry occurs within the human body.

Consider **ethanol**, the alcohol found in alcoholic beverages.

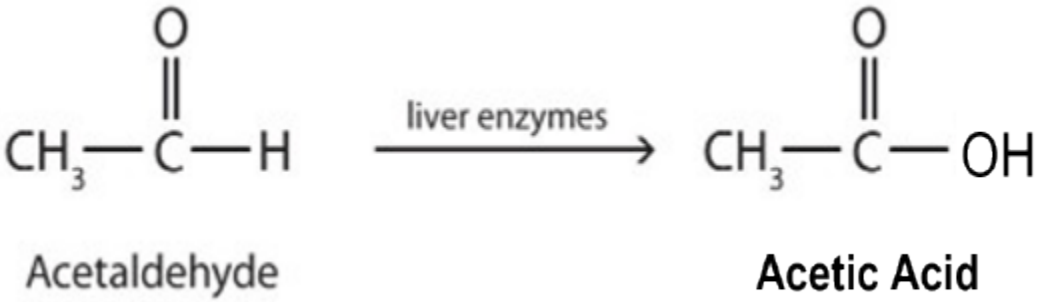
Ethanol is a primary alcohol. In the liver, an enzyme called **alcohol dehydrogenase** catalyzes the oxidation of ethanol to **acetaldehyde**, an aldehyde:

ethanol → **acetaldehyde**:



A second enzyme, **aldehyde dehydrogenase**, then catalyzes the oxidation of acetaldehyde to **acetic acid**, which exists primarily as acetate under physiological conditions:

acetaldehyde → **acetic acid/acetate**:



The overall pathway therefore follows exactly the oxidation pattern we have just learned:

primary alcohol → **aldehyde** → **carboxylic acid**.

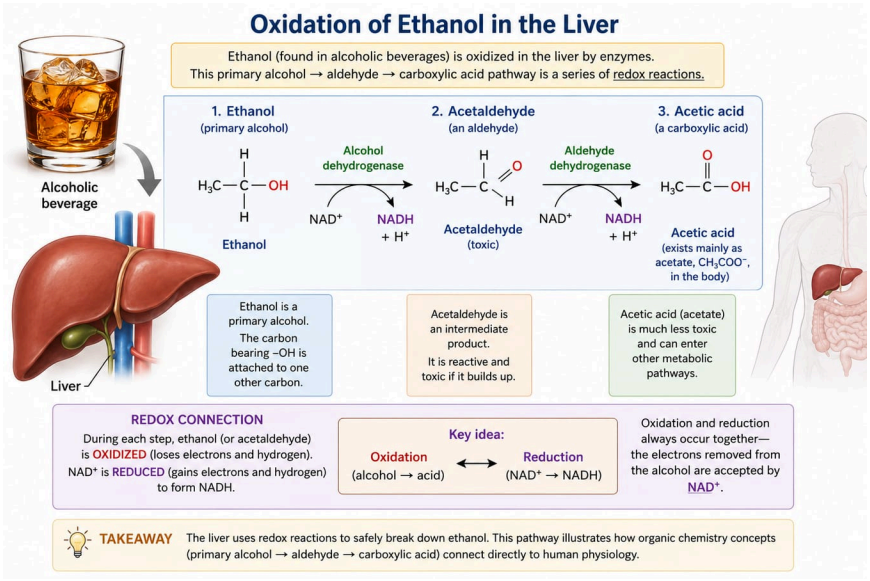


Figure 8.3.3: Oxidation of Ethanol in the Liver. Ethanol is a primary alcohol that is oxidized in the liver to acetaldehyde by alcohol dehydrogenase. Acetaldehyde is then further oxidized by aldehyde dehydrogenase to acetic acid, which exists predominantly as acetate at physiological pH. This metabolic pathway demonstrates the same primary alcohol → aldehyde → carboxylic acid oxidation sequence observed in organic chemistry.

Acetaldehyde is toxic and chemically reactive, so its accumulation can contribute to harmful effects following alcohol consumption. The body normally converts acetaldehyde into acetate, which can then enter additional metabolic pathways.

This provides a direct connection between the organic chemistry of functional groups and human physiology.

Similar Structure, Very Different Consequences: Methanol

The importance of molecular structure becomes even clearer when ethanol is compared with **methanol**.

Methanol differs from ethanol by only one carbon atom:

methanol: CH_3OH.

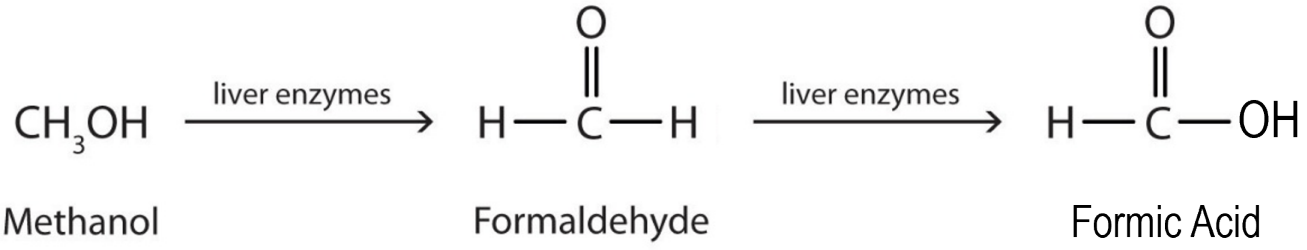
ethanol: CH_3CH_2OH.

Both are primary alcohols, and both can be oxidized by enzymes in the liver.

But their oxidation products are very different.

Methanol is oxidized first to **formaldehyde** and then to **formic acid**, which exists primarily as formate under physiological conditions:

methanol → formaldehyde → formic acid/formate:



These metabolites are highly toxic. Formate can interfere with cellular metabolism and is particularly damaging to the optic nerve. Severe methanol poisoning can result in visual impairment, blindness, metabolic acidosis, and death.

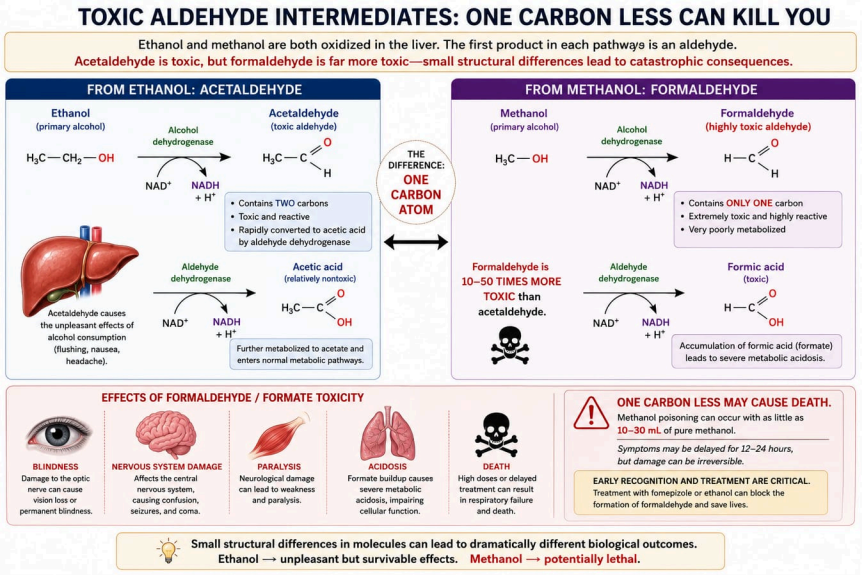


Figure 8.3.4: Similar Alcohols Can Produce Very Different Metabolites. Ethanol and methanol are both primary alcohols and undergo similar types of oxidation reactions in the liver. Ethanol is oxidized to acetaldehyde and then acetate, while methanol is oxidized to formaldehyde and then formate. The very different biological effects of these products illustrate how relatively small differences in molecular structure can lead to dramatically different physiological consequences.

This comparison reinforces one of the central themes of this course:

Key Point

- **Molecular structure influences chemical reactivity, and chemical reactivity influences biological function**.

Oxidation of Food Releases Stored Chemical Energy

We can now apply these ideas to one of the most important redox processes occurring in living organisms: the metabolism of food. Food molecules—particularly carbohydrates and lipids—contain numerous carbon-hydrogen bonds. Carbon atoms with many C–H bonds are relatively **reduced**, which means that they have considerable potential to undergo oxidation. This is especially apparent in fatty acids. Their long hydrocarbon chains contain large numbers of C–H bonds and relatively little oxygen. Fatty acids are therefore highly reduced molecules and contain substantial stored chemical energy.

During metabolism, food molecules are gradually oxidized through a series of enzyme-catalyzed reactions. Carbon atoms lose hydrogen and electrons and generally form increasing numbers of bonds to oxygen. Ultimately, much of the carbon contained in food is converted into **carbon dioxide (CO_2)**. Carbon dioxide represents a highly oxidized form of carbon. At the same time, molecular oxygen (O_2) accepts electrons and hydrogen and is reduced to form **water (H_2O)**.

The overall oxidation of glucose during cellular respiration can be summarized as:

$$\mathrm{C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O} \tag{8.3.1}$$

We can now interpret this reaction using both approaches we have learned. From Section 8.2, oxidation states tell us that oxygen changes from an oxidation state of **0 in O_2 to –2 in H_2O**. Its oxidation state decreases, which means that it has gained electrons (**GER**), so: **O_2 is reduced.** The carbon atoms in glucose ultimately become carbon dioxide. Carbon in CO_2 has an oxidation state of **+4**, representing a highly oxidized state of carbon, indicating that it has lost electrons (**LEO**). Thus, during cellular respiration: **food molecules are oxidized** while **oxygen is reduced**.

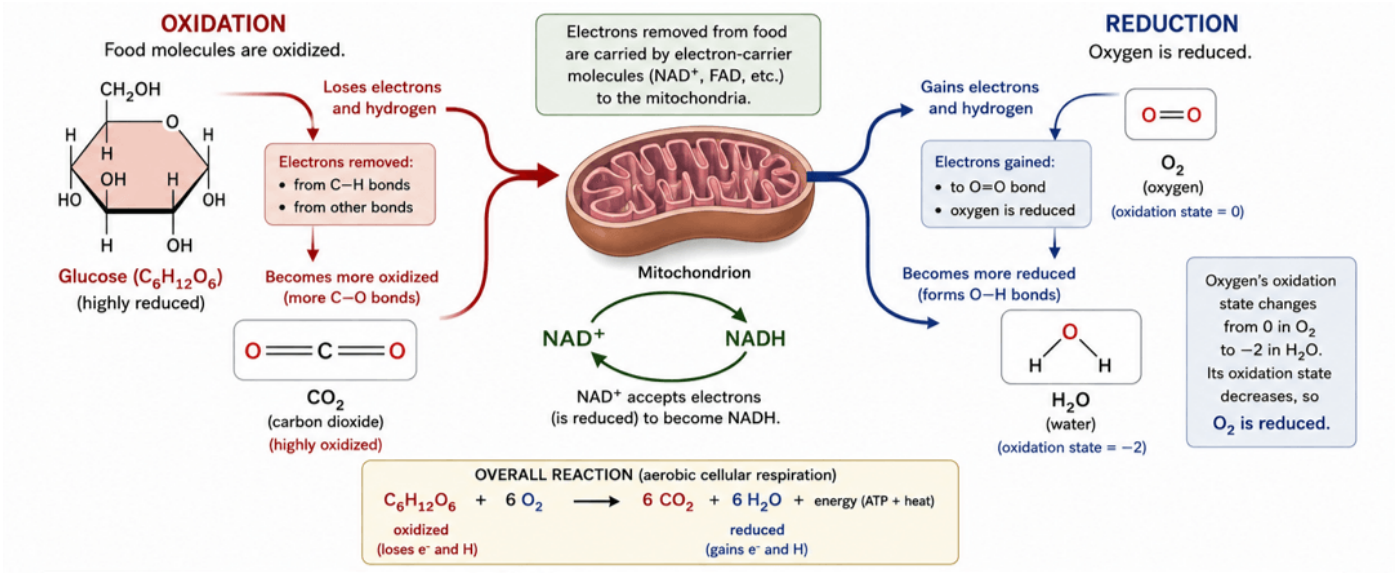


Figure 8.3.5: Oxidation and Reduction During Cellular Respiration. During cellular respiration, carbon-containing food molecules such as glucose are oxidized, ultimately producing carbon dioxide. Molecular oxygen accepts electrons and is reduced to water. This overall reaction connects the formal oxidation-state approach introduced in Section 8.2 with the oxidation of organic molecules examined in this section.

Why Not Just Burn the Glucose?

The overall reaction for cellular respiration resembles the combustion of a fuel. In both processes, a carbon-containing substance reacts with oxygen and ultimately produces carbon dioxide and water.

But there is an important difference. If glucose were simply burned, much of its stored chemical energy would be released rapidly as heat. Cells instead oxidize glucose and other food molecules through a **controlled series of enzyme-catalyzed reactions**. Rather than transferring electrons directly from food molecules to oxygen in a single step, cells remove high-energy electrons gradually and temporarily transfer them to **electron-carrier molecules (like FAD and NAD^+)**. This allows some of the energy released during oxidation to be captured and redirected instead of being lost all at once as heat.

In other words, cells do not merely oxidize food. They **harvest the energy released during oxidation**. Those electrons eventually enter a remarkable series of reactions within the mitochondria. Their energy is used to create a concentration gradient of H⊕ ions across a membrane, and the stored energy in that gradient is then used to produce **ATP**.

So the next question becomes: **How does a cell transform the energy carried by electrons into ATP—the energy-transfer molecule used to power cellular work**? That journey from food to electrons to a proton gradient to ATP is the focus of **Section 8.4**.

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8.4: Energy, ATP, and Cellular Respiration

Every cell requires energy. Muscle cells require energy to contract. Neurons require energy to maintain ion gradients and transmit electrical signals. Cells require energy to build proteins and other biological molecules, transport substances across membranes, repair damaged structures, and carry out the thousands of chemical reactions necessary for life. As we saw in Section 8.3, much of this energy ultimately comes from the **oxidation of food molecules**.

But cells cannot simply plug themselves into a glucose molecule or a fatty acid and use its energy directly. Instead, cells transfer some of the energy released during the oxidation of food into a molecule that can be used to power cellular processes: **adenosine triphosphate (ATP)**.

ATP: An Energy-Transfer Molecule

ATP is composed of the nitrogenous base adenine, the sugar ribose, and three phosphate groups.

If that structure looks familiar, it should.

ATP is a **nucleotide**, one of the same types of molecules introduced in Chapter 7 as the building blocks of RNA. However, ATP has another enormously important role in the cell: it participates in the transfer of energy between chemical reactions.

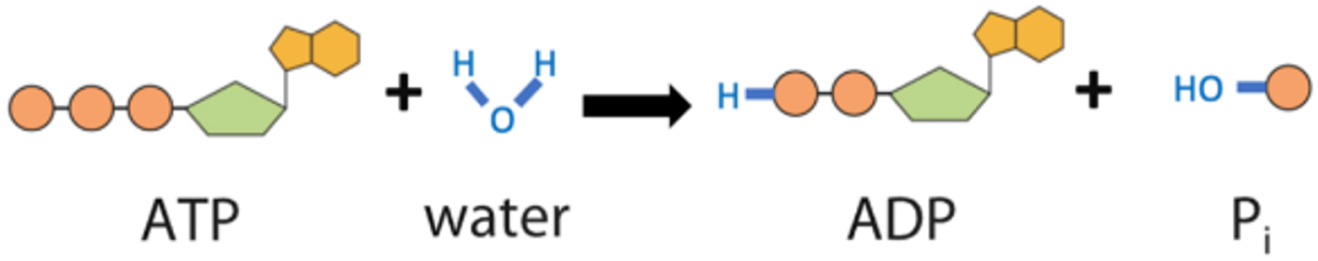


Figure 8.4.1**: ATP and ADP.** Adenosine triphosphate (ATP) contains adenine, ribose, and three phosphate groups. Hydrolysis of ATP removes the terminal phosphate group to produce adenosine diphosphate (ADP) and inorganic phosphate (P_i). The energy released by this process can be coupled to cellular processes that require energy. Figure source: Uminski, C. et al (2025).

ATP can undergo hydrolysis, producing **adenosine diphosphate (ADP)** and inorganic phosphate (**P_i**):

$$\mathbf{ATP + H_2O \longrightarrow ADP + P_i + energy} \tag{8.4.1}$$

This is an **exergonic** process, meaning that overall, **energy is released** as the reaction proceeds. Cells can couple ATP hydrolysis to processes that require energy. In this way, the energy released by ATP hydrolysis can help drive processes such as muscle contraction, active transport of ions across cell membranes, and the synthesis of biological molecules.

You have already encountered an example. Recall the **Na⊕/K⊕ ATPase** discussed earlier in this book. This membrane protein uses energy from ATP hydrolysis to move Na⊕ and K⊕ ions against their concentration gradients. Maintaining those ion gradients is essential for the resting membrane potential and electrical signaling in neurons. Thus, ATP provides a connection between an energy-releasing chemical reaction and cellular work.

ATP Must Be Constantly Recycled

Cells do not maintain an enormous warehouse filled with ATP. Instead, ATP is continually **used and regenerated**. When ATP is hydrolyzed, it produces ADP:

$$\mathbf{ATP \longrightarrow ADP + P_i} \tag{8.4.2}$$

Energy obtained from the metabolism of food can then be used to reverse the process:

$$\mathrm{ADP + P_i + energy \longrightarrow ATP} \tag{8.4.3}$$

The ATP can subsequently be hydrolyzed again to power another cellular process. Thus, ATP and ADP participate in a continuous cycle:

food energy → ATP production → cellular work → ADP → ATP production.

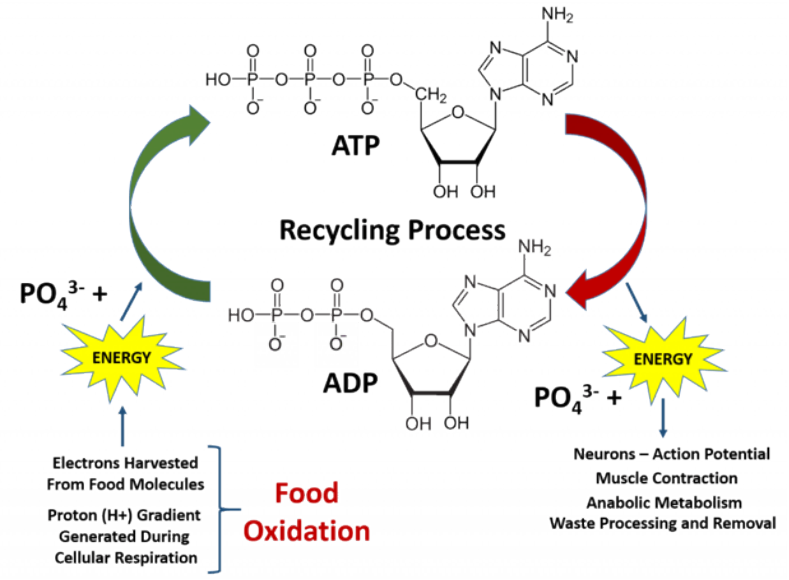


Figure 8.4.2: ATP/ADP Recycling. ATP hydrolysis releases energy that can be coupled to energy-requiring cellular processes. The resulting ADP and inorganic phosphate (P_i) are then recycled to produce ATP using energy harvested during the oxidation of food molecules. ATP therefore acts as an energy-transfer molecule connecting energy-releasing metabolic reactions with energy-requiring cellular processes.

The amount of ATP present in the human body at any one time is relatively small compared with the amount used throughout an entire day. Therefore, individual ATP molecules must be recycled repeatedly. This leads to another important question:

How does the energy released from food actually get transferred into ATP?

For most of the ATP produced under aerobic conditions, the answer can be found inside the **mitochondria**.

Mitochondria and Cellular Energy

Mitochondria are organelles surrounded by two membranes: an **outer mitochondrial membrane** and a highly folded **inner mitochondrial membrane**.

The space enclosed by the inner membrane is called the **mitochondrial matrix**, while the region between the inner and outer membranes is called the **intermembrane space**.

The folds of the inner membrane, called **cristae**, dramatically increase its surface area. This is important because many of the proteins involved in ATP production are embedded within this membrane.

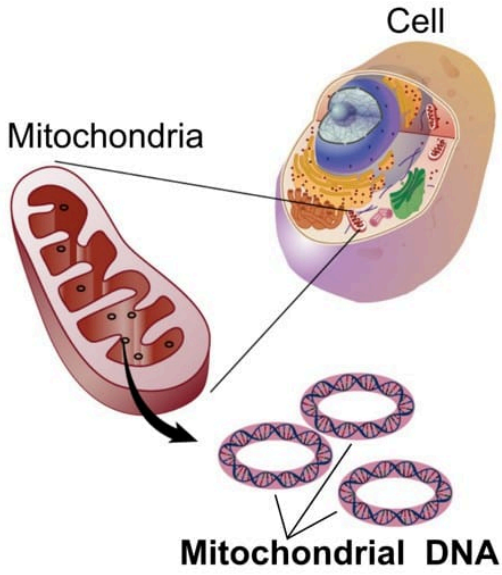


Figure 8.4.3: Mitochondrial Structure and ATP Production. Mitochondria contain an outer membrane and a highly folded inner membrane surrounding the mitochondrial matrix. The region between the two membranes is called the intermembrane space. The folds of the inner membrane, called cristae, provide a large surface area for the proteins involved in electron transport and ATP production. Figure source: National Human Genome Research Institute.

Mitochondria also contain their own small, circular DNA molecules. These and other characteristics support the idea that mitochondria originated from bacteria that entered into a symbiotic relationship with ancestral cells. Today, mitochondria provide the environment in which much of the energy harvested from food is converted into ATP.

From Food to High-Energy Electrons

During digestion, large food molecules are broken into smaller components. Carbohydrates can provide glucose and other monosaccharides. Triacylglycerols can provide fatty acids. Proteins can provide amino acids. These molecules can then enter metabolic pathways in which they are progressively broken down and oxidized. Recall the major pattern from Section 8.2:

Oxidation = loss of electrons.

As food molecules are oxidized, high-energy electrons are removed from them. However, these electrons do not float freely around the cell. Instead, they are transferred to **electron-carrier molecules** that can transport them from one reaction to another. Two important electron carriers in metabolism are **NAD⁺** and **FAD**. When these molecules accept electrons and hydrogen, they become reduced to **NADH** and **$FADH_2$**, respectively. For our purposes, the most important idea is:

Food molecules are oxidized → electron carriers are reduced.

The reduced electron carriers can then transport those high-energy electrons to the inner mitochondrial membrane. They are almost like cellular taxi drivers, shuttling electrons to the appropriate delivery place.

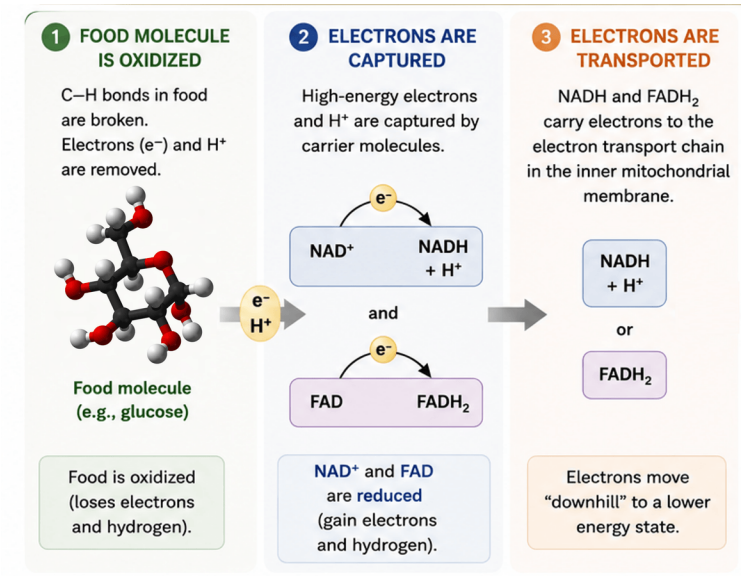


Figure 8.4.4**: Capturing Energy from Food Molecules.** During metabolism, food molecules are progressively oxidized and high-energy electrons are transferred to electron-carrier molecules such as NAD⁺ and FAD. The reduced carriers, NADH and $FADH_2$, transport these electrons to proteins embedded in the inner mitochondrial membrane. In this way, energy from food is transferred through a controlled series of redox reactions rather than released all at once.

The Electron Transport Chain

Embedded within the inner mitochondrial membrane is a series of proteins and other electron carriers collectively called the **electron transport chain**. Reduced electron carriers deliver electrons to this chain. The electrons are then passed from one component of the electron transport chain to another through a series of **redox reactions**. One molecule loses an electron and is oxidized. The next accepts the electron and is reduced. That molecule can then pass the electron to another component, becoming oxidized again. In this way, the electrons move stepwise through the chain.

As the electrons move, they gradually lose energy. Rather than allowing that energy to escape entirely as heat, components of the electron transport chain use some of it to move **H⁺ ions (protons)** from the mitochondrial matrix into the intermembrane space. This is active transport. The H⁺ ions are being moved from an area of lower concentration to an area of higher concentration, so energy is required to move them against their concentration gradient. Where does that energy come from? **From the electrons originally harvested from food.**

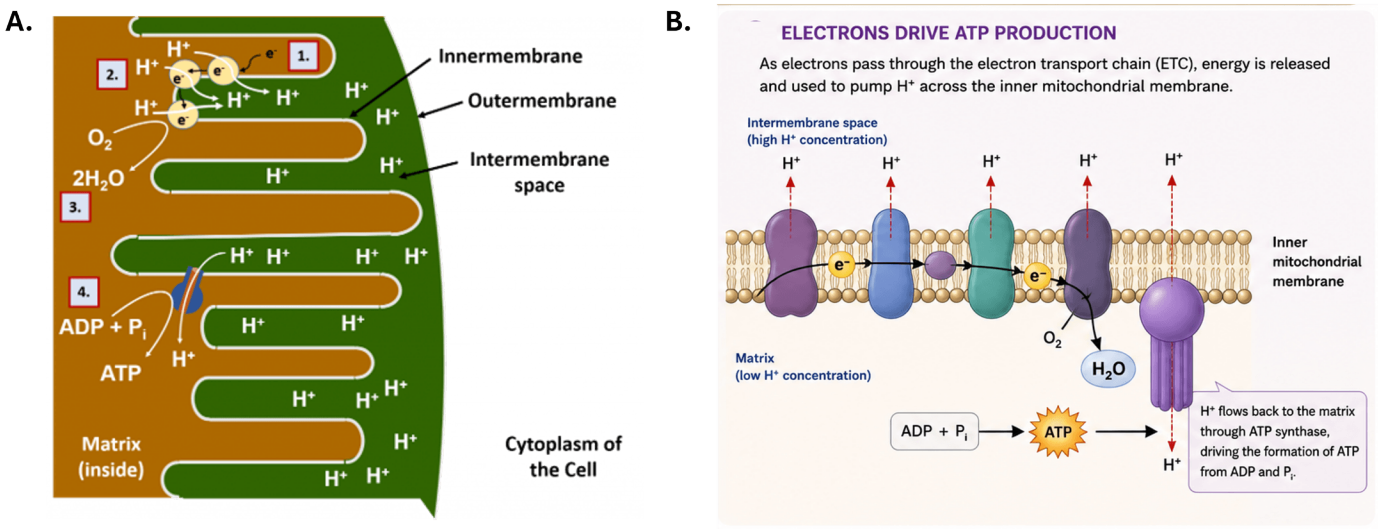


Figure 8.4.5**: Using Electron Energy to Build a Proton Gradient**. ***Diagram A****:* (1) Electrons from food molecules are carried to protein pumps in the innermembrane of the mitochondria. (2) Using the energy of the electrons, the protein pumps move protons (H+) into the intermembrane space, where the protons become concentrated. (Note that the protons also came from the food molecules during the oxidation process - hydrogens and electrons often move together during oxidation!). (3) The electrons are passed through all of the pumps until most of the energy housed in them is spent. Then they are used in combination with protons, to reduce oxygen (O_2) into water (H_2O). (4) The H+ gradient carries energy potential, just like water that has been dammed. When it flows through the ATP synthase protein, the protein turns like a cog wheel and is able to regenerate ATP. ***Diagram B****:* Close up view of the electron transport chain in the inner membrane of the mitochondria. High-energy electrons carried by NADH and $FADH_2$ are transferred through the electron transport chain in the inner mitochondrial membrane. Energy released as the electrons move through the chain is used to pump H⋄ ions from the matrix into the intermembrane space. This creates a region of high H⋄ concentration outside the inner membrane and lower H⋄ concentration within the matrix. Diagram A was adapted from: Geraldine Adele Lewis.

Storing Energy in a Concentration Gradient

As H⋄ ions accumulate in the intermembrane space, a **concentration gradient** develops across the inner mitochondrial membrane. You have encountered concentration gradients before during our discussions of action potentials in neurons. Particles naturally tend to move from regions of higher concentration toward regions of lower concentration. However, because the inner mitochondrial membrane does not allow H⋄ ions to freely cross it, the protons become concentrated on one side. This creates stored potential energy.

A useful analogy is water held behind a dam. Water at a high elevation behind a dam has gravitational potential energy. If the water is allowed to flow downward through a turbine, that stored energy can be converted into another useful form. The mitochondrial proton gradient works in a remarkably similar way. The electron transport chain uses energy to "pump the water uphill" by concentrating H⋄ ions in the intermembrane space. The cell can then recover some of that stored energy by allowing H⋄ to flow back across the membrane through a specialized protein. That protein is **ATP synthase**.

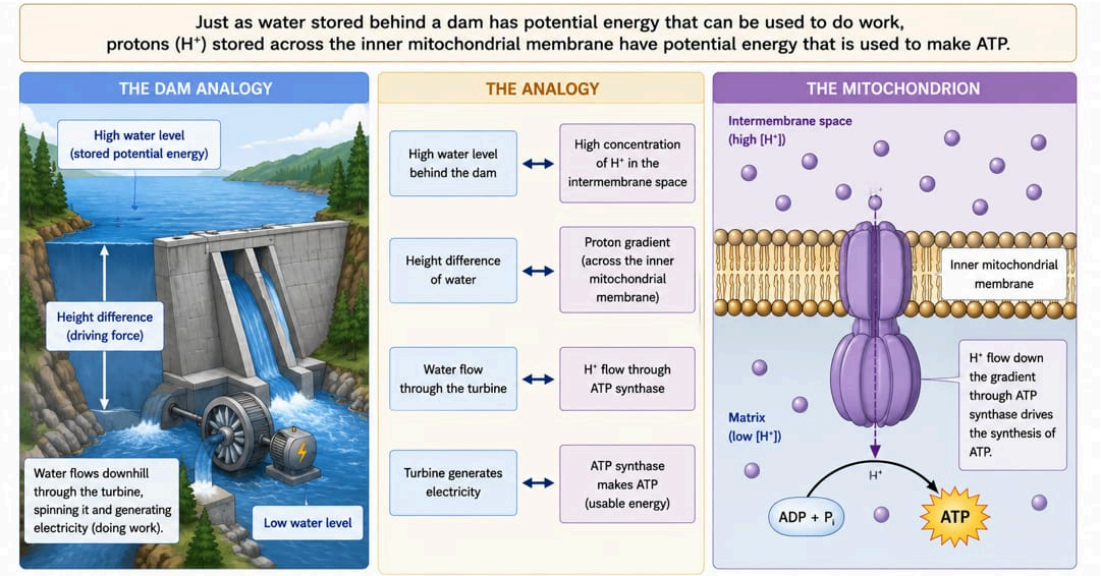


Figure 8.4.6**: Stored Energy in a Gradient.** Water held behind a dam contains potential energy because it is prevented from moving downhill. When released through a turbine, the flow of water can be used to perform work. Similarly, the electron transport chain uses energy to concentrate H⊕ ions in the mitochondrial intermembrane space. When H⊕ flows back down its gradient through ATP synthase, the stored energy of the gradient can be used to produce ATP.

ATP Synthase: A Molecular Turbine

ATP synthase is a large protein complex embedded within the inner mitochondrial membrane. It provides a controlled pathway through which H⊕ ions can move from the intermembrane space back into the matrix. As H⊕ flows through ATP synthase, part of the protein **rotates**. ATP synthase is therefore not merely analogous to a turbine—it actually contains rotating molecular components. This mechanical motion produces changes in the shape of other regions of the protein. Those conformational changes allow ATP synthase to bind ADP and inorganic phosphate and facilitate their conversion into ATP.

$$\mathrm{ADP} + \mathrm{P_i} + \mathrm{energy} \longrightarrow \mathrm{ATP} \tag{8.4.4}$$

Think about how many ideas from earlier chapters come together in this one molecular machine.

The process depends upon:

- ions and electrical charge;
- concentration gradients;
- membrane structure;
- protein folding and shape;
- intermolecular attractions;
- diffusion;
- and chemical reactions involving energy.

Structure determines function at every level.

The inner mitochondrial membrane maintains the H⊕ gradient. The shape of ATP synthase creates a pathway for H⊕. Movement of H⊕ changes the protein's conformation. And those structural changes enable a chemical reaction that produces ATP.

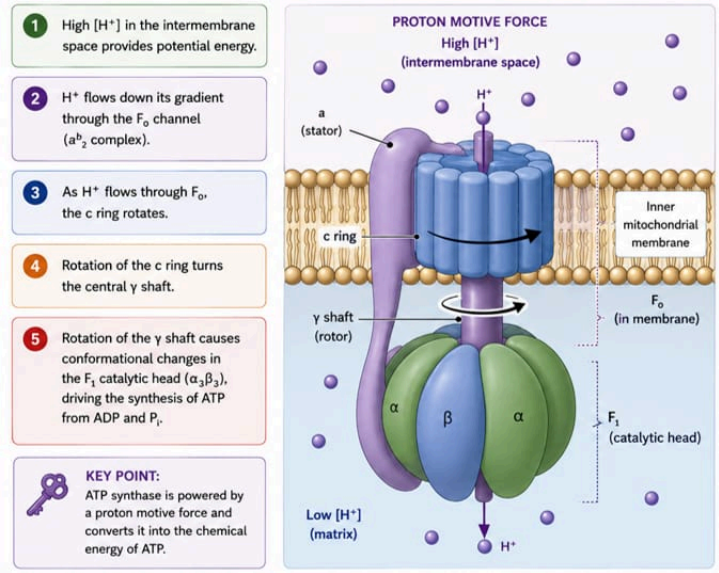


Figure 8.4.7**: ATP Synthase Converts Gradient Energy into Chemical Energy.** H⋄ ions concentrated in the intermembrane space flow down their concentration gradient through ATP synthase. The movement of H⋄ drives rotation within the protein complex, producing conformational changes that facilitate the formation of ATP from ADP and inorganic phosphate. ATP synthase therefore converts energy stored in an ion gradient into chemical energy that can be transferred through ATP.

Why Do We Need Oxygen?

One final problem remains. The electrons moving through the electron transport chain must eventually go somewhere.

At the end of the chain, the electrons are transferred to **molecular oxygen (O_2)**.

Oxygen accepts electrons and combines with H⋄ to form water. In other words:

Oxygen is reduced to water.

This should sound familiar from Section 8.2. In the overall cellular respiration reaction, food molecules such as glucose are oxidized while oxygen is reduced. Oxygen therefore serves as the **final electron acceptor** in the mitochondrial electron transport chain. This explains why a continuous supply of oxygen is so important. Without oxygen, electrons can no longer move efficiently through the electron transport chain. As electron flow stops, proton pumping also stops. Without continued proton pumping, the H⋄ gradient across the inner mitochondrial membrane cannot be maintained. And without the H⋄ gradient, ATP synthase loses its major source of power for ATP production through this pathway.

The consequences can occur rapidly in tissues with high energy demands, particularly the brain. Breathing therefore does much more than simply bring oxygen into the lungs. The oxygen ultimately delivered to our cells provides a destination for the electrons extracted from food.

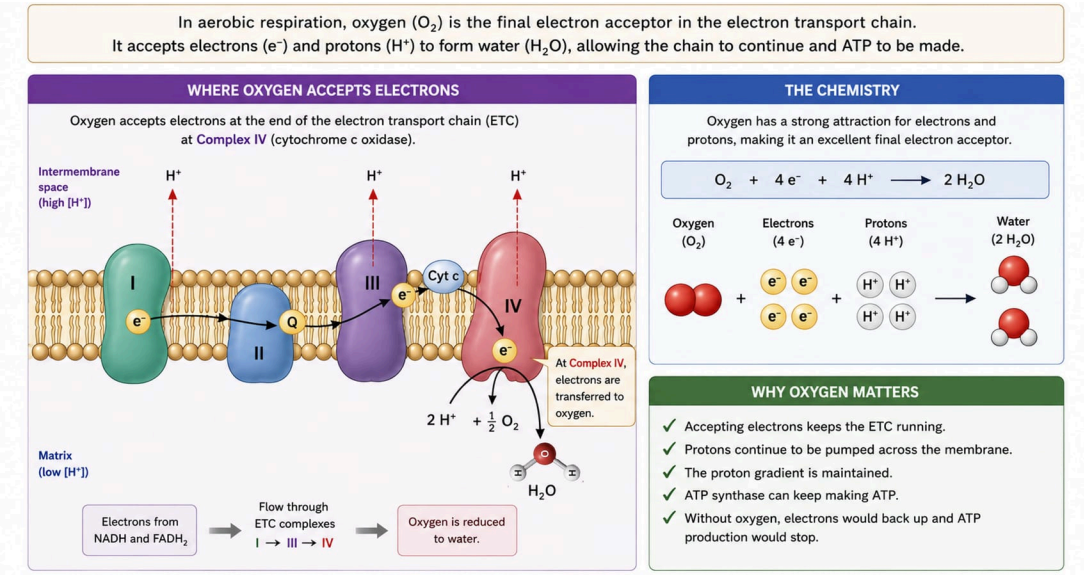


Figure 8.4.8: Oxygen Keeps Electrons Moving Through the Electron Transport Chain. At the end of the mitochondrial electron transport chain, oxygen accepts electrons and H⊕ and is reduced to form water. By continually removing electrons from the end of the chain, oxygen allows continued electron transport, proton pumping, maintenance of the H⊕ gradient, and ATP production.

Putting It All Together: Oxidative Phosphorylation

The overall process in which energy from electron transfer is used to generate a proton gradient that drives ATP production is called **oxidative phosphorylation**.

The name describes the chemistry:

Oxidative refers to the oxidation-reduction reactions that provide the energy.

Phosphorylation refers to the addition of inorganic phosphate to ADP to produce ATP.

We can summarize the process in four major steps:

1. **Food molecules are oxidized.** High-energy electrons are transferred to electron carriers such as NADH and $FADH_2$.
2. **Electrons move through the electron transport chain.** Energy released during electron transfer is used to pump H⊕ into the intermembrane space.
3. **H⊕ flows through ATP synthase.** Movement of H⊕ down its gradient powers the formation of ATP from ADP and P_i.
4. **Oxygen accepts the electrons.** At the end of the electron transport chain, oxygen is reduced to form water.

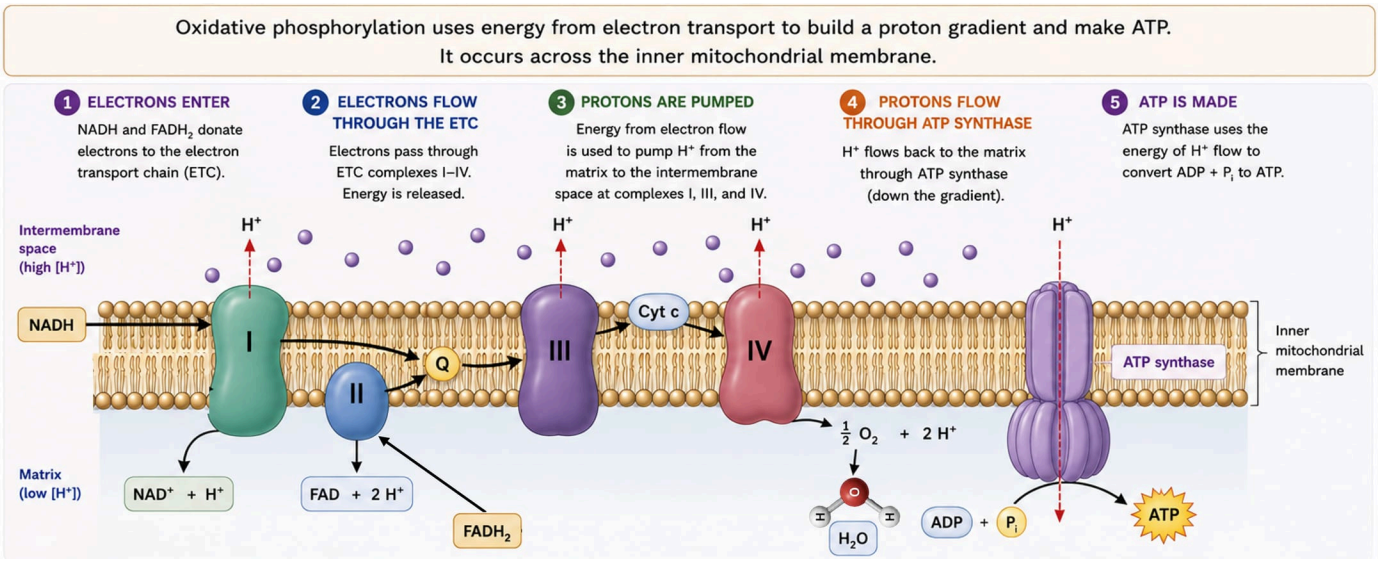


Figure 8.4.9**: Oxidative Phosphorylation Converts Energy from Food into ATP.** (1) Oxidation of food molecules transfers high-energy electrons to electron carriers. (2) These electrons move through the electron transport chain, releasing energy that is used to pump H⊕ into the intermembrane space. (3) H⊕ then flows down its concentration gradient through ATP synthase, providing energy for the formation of ATP from ADP and P_i. (4) At the end of the electron transport chain, oxygen accepts the electrons and is reduced to water. Together, these processes allow cells to capture some of the chemical energy originally stored in food and transfer it into ATP.

Notice the remarkable sequence of energy transformations:

chemical energy in food.

↓

energy carried by electrons.

↓

potential energy stored in an H⊕ gradient.

↓

mechanical motion of ATP synthase.

↓

chemical energy transferred through ATP.

The cell has not created energy from nothing. Instead, it has **transformed energy from one form into another**. And that raises an important chemical question.

Why do some reactions release usable energy while other reactions require an energy input? Why can some reactions proceed spontaneously while others cannot? And if a reaction is energetically favorable, why doesn't it necessarily happen rapidly?

To answer those questions, we need to distinguish between two related—but very different—ideas:

the energy change of a reaction and the rate at which the reaction occurs.

That distinction is the focus of Section 8.5.

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8.5: Reaction Energy- Spontanaeity and Activation Energy

In Section 8.4, we followed energy through a remarkable series of transformations:

chemical energy in food → energy carried by electrons → energy stored in an H⊕ gradient → ATP.

Underlying all of these transformations are **chemical reactions**. Some chemical reactions release energy as they proceed. Others require an input of energy. Some reactions can occur spontaneously but proceed so slowly that we barely notice them. To understand how cells control thousands of chemical reactions at the same time, we need to distinguish between two important questions:

1. Is the reaction energetically favorable?

2. How quickly will the reaction occur?

These may sound like the same question, but they describe two very different properties of a chemical reaction.

The first concerns **thermodynamics**—the overall energy change associated with a reaction.

The second concerns **kinetics**—the rate at which the reaction occurs.

This distinction is particularly important when we begin discussing enzymes.

Energy Changes During Chemical Reactions

Every chemical reaction involves changes in chemical bonding. Some bonds are broken and new bonds are formed as atoms are rearranged from reactants into products.

Recall an important principle:

Breaking chemical bonds requires energy.

Forming chemical bonds releases energy.

Why?

Atoms that are chemically bonded are in a more stable arrangement than those same atoms when separated. Energy must therefore be supplied to overcome the attractive forces holding bonded atoms together. When a new bond forms, the atoms move into a more stable arrangement and energy is released. However, not all chemical bonds have the same strength. The amount of energy required to break a bond depends upon the atoms involved and the chemical environment surrounding that bond. Therefore, the overall energy change of a chemical reaction depends on the combined energetic changes associated with transforming the reactants into the products.

Exergonic and Endergonic Reactions

Chemical reactions can be described according to whether usable energy is released or required as the reaction proceeds. An **exergonic reaction** has an overall release of free energy. The products have less free energy than the reactants, so energy becomes available as the reaction proceeds.

An **endergonic reaction**, in contrast, requires an overall input of free energy. The products have more free energy than the reactants, so energy must be supplied for the reaction to proceed in the forward direction.

These relationships can be summarized as:

Exergonic reaction → releases free energy.

Endergonic reaction → requires free energy.

Cells carry out both types of reactions.

The oxidation of food molecules provides examples of energy-releasing processes. Cells can then use some of that released energy to support energy-requiring processes such as active transport and the synthesis of larger biological molecules. In other words, metabolism connects reactions that **release energy** with reactions that **require energy**.

Gibbs Free Energy and Reaction Spontaneity

The energy available to perform useful work under conditions of constant temperature and pressure can be described using **Gibbs free energy**, represented by the symbol **G**.

For a chemical reaction, we are usually interested in the **change in Gibbs free energy**, written as **ΔG**.

The Greek letter delta (Δ) means "change in," so:

$$\Delta G = G_{\text{products}} - G_{\text{reactants}} \tag{8.5.1}$$

The sign of ΔG tells us whether a reaction is thermodynamically favorable in the forward direction.

When ΔG < 0

If the products have less free energy than the reactants:

$$\Delta G < 0 \tag{8.5.2}$$

The reaction is **exergonic** and thermodynamically favorable in the forward direction.

Such a reaction is described as **spontaneous**.

When ΔG > 0

If the products have more free energy than the reactants:

$$\Delta G > 0 \tag{8.5.3}$$

The reaction is **endergonic** and requires a net input of free energy to proceed in the forward direction.

The forward reaction is **nonspontaneous** under those conditions.

When ΔG = 0

If:

$$\Delta G = 0 \tag{8.5.4}$$

the system is at **equilibrium**.

At equilibrium, the forward and reverse reactions continue to occur, but they occur at equal rates. Therefore, there is no net change in the concentrations of reactants and products.

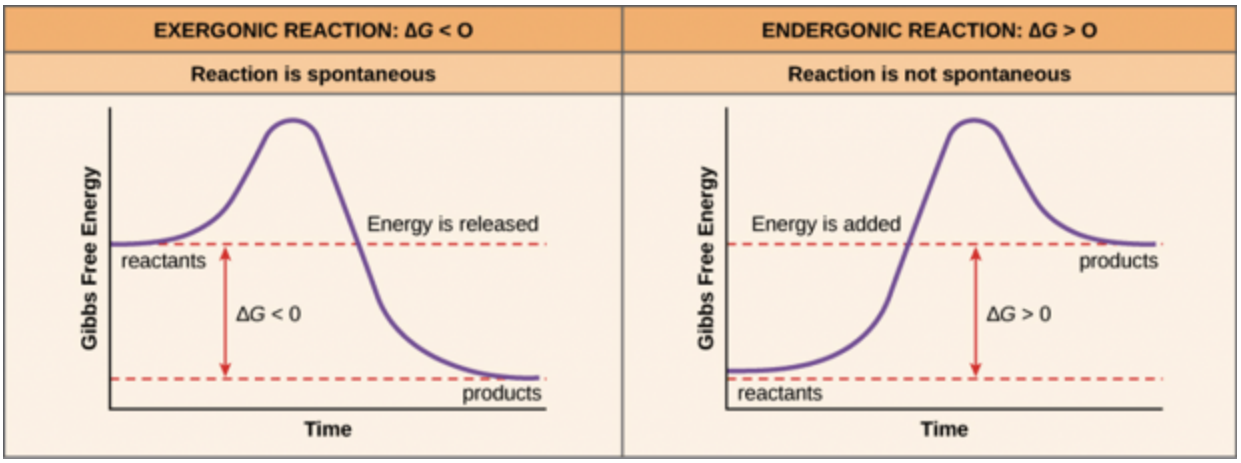


Figure 8.5.1**: Gibbs Free Energy and Reaction Spontaneity.** In an exergonic reaction, the products have lower free energy than the reactants and ΔG is negative. The forward reaction is thermodynamically favorable. In an endergonic reaction, the products have higher free energy than the reactants and ΔG is positive, so an input of free energy is required. At equilibrium, ΔG = 0 and there is no net change in the concentrations of reactants and products. Figure provided by The Khan Academy.

One point is especially important:

Spontaneous does NOT mean fast.

A spontaneous reaction is energetically favorable. It does not tell us how rapidly the reaction will occur.

Spontaneous Does Not Mean Fast

Consider a piece of wood sitting in a room containing oxygen. The molecules in wood can react with oxygen to produce lower-energy products such as carbon dioxide and water. Combustion is an exergonic process. Yet a wooden table does not suddenly burst into flames.

Why not?

Although the overall reaction releases energy, some energy must first be supplied to begin breaking and rearranging bonds in the reactants. A spark or flame can provide that initial energy. Once the reaction begins, the energy released can help additional molecules react, allowing combustion to continue. This illustrates the difference between **reaction spontaneity** and **reaction rate**.

The overall energy difference between reactants and products tells us whether the reaction is thermodynamically favorable.But another energetic barrier determines how readily the reaction can actually occur. That barrier is called the **activation energy**.

Activation Energy: Getting Over the Hill

During a chemical reaction, atoms do not instantaneously transform from reactants into products. Bonds must be distorted and broken, atoms must move into new positions, and new bonds must begin to form. During this process, the reacting molecules pass through a very unstable, high-energy arrangement called the **transition state**.

The energy required for the reactants to reach this transition state is called the **activation energy**. Activation energy is often represented as an energy hill. Imagine pushing a ball over a hill. Even if the valley on the other side is much lower than where the ball started, the ball must first receive enough energy to reach the top of the hill. Once it passes the top, it can roll downhill. Chemical reactions behave similarly.

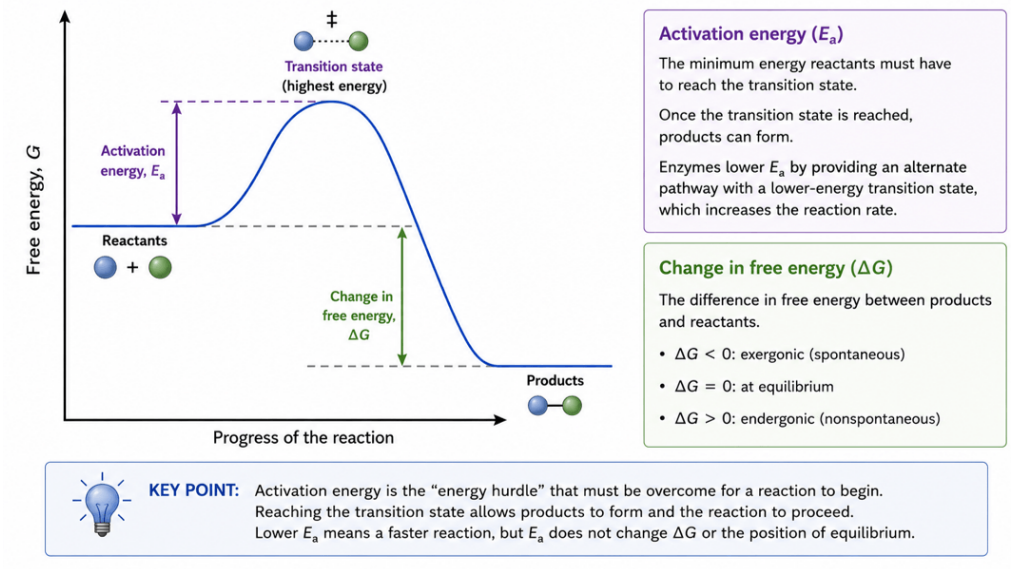


Figure 8.5.2: Activation Energy and the Transition State. Even an exergonic reaction must overcome an initial energy barrier. Reactants must gain enough energy to reach a high-energy transition state before products can form. The difference in energy between the reactants and the transition state is the activation energy. A reaction can therefore be thermodynamically favorable but still occur very slowly if its activation energy is high.

This is why some energetically favorable reactions occur extremely slowly under ordinary conditions. The molecules simply do not reach the transition state often enough for the reaction to proceed at an appreciable rate. For living organisms, this creates a serious problem. A reaction may release energy and be completely favorable from a thermodynamic perspective—but that does little good if the reaction would take years to occur. Cells need many reactions to occur in milliseconds, seconds, or minutes.

This is where **enzymes** become essential.

Enzymes Lower Activation Energy

Enzymes increase the rate of chemical reactions by providing a pathway with a **lower activation energy**.

In other words, an enzyme makes it easier for the reactants to reach the transition state.

The enzyme does **not** provide the net energy released by the reaction, and it does not change the overall free-energy difference between the reactants and products.

Therefore:

Enzymes lower activation energy.

Enzymes increase reaction rate.

But:

Enzymes do NOT change ΔG.

Enzymes do NOT change an endergonic reaction into an exergonic reaction.

Enzymes do NOT determine whether a reaction is thermodynamically spontaneous.

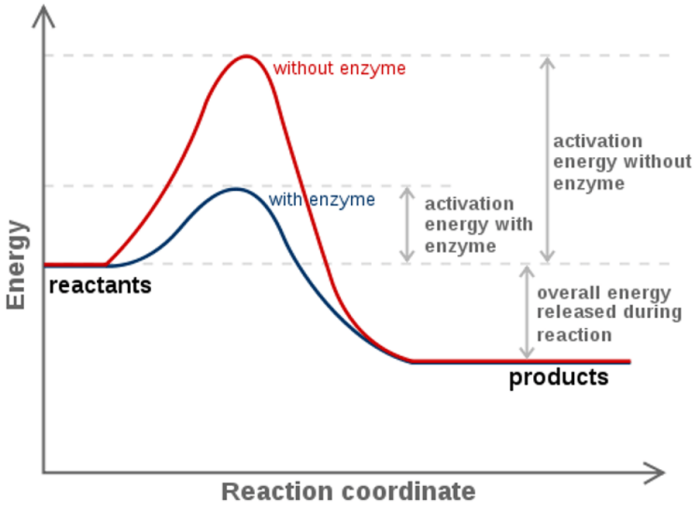


Figure 8.5.3: Effect of an Enzyme on Activation Energy. An uncatalyzed reaction must overcome a relatively large activation-energy barrier to reach the transition state. An enzyme provides an alternative reaction pathway with a lower activation energy, allowing the reaction to proceed more rapidly. Notice that the free energies of the reactants and products—and therefore ΔG—remain unchanged. Enzymes affect reaction rate, not the overall thermodynamic favorability of the reaction. This distinction is one of the most important ideas in biological chemistry. Figure is adapted from Fvasconcellos.

Thermodynamics asks:

Is the reaction energetically favorable?

This is described by **ΔG**.

Kinetics asks:

How rapidly can the reaction occur?

This is strongly influenced by **activation energy**.

An enzyme affects the second question—not the first.

Coupling Reactions: Using One Reaction to Drive Another

If enzymes cannot make an endergonic reaction energetically favorable, how do cells carry out reactions that require energy? They **couple reactions together**.

An energy-requiring reaction can be linked to an energy-releasing reaction so that the overall combined process is energetically favorable. ATP provides one of the most important examples. Recall from Section 8.4 that ATP hydrolysis is exergonic:

$$\textbf{ATP} + \textbf{H}_2\textbf{O} \rightarrow \textbf{ADP} + \textbf{P}_i + \textbf{energy}.$$

Cells can couple this energy-releasing process to reactions or cellular processes that require energy. If enough free energy is released by ATP hydrolysis, the **combined process** can have an overall negative ΔG. This is how ATP can help drive processes that would not otherwise proceed spontaneously.

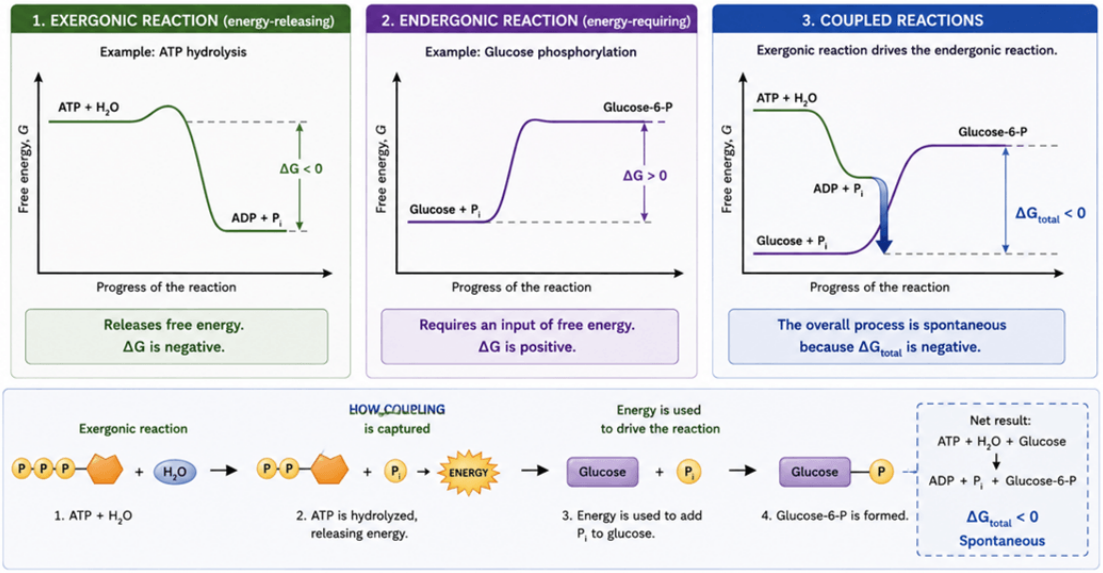


Figure 8.5.4: Energy Coupling with ATP. An endergonic process requires an input of free energy and cannot proceed spontaneously on its own. Cells can couple an energy-requiring process to an exergonic process such as ATP hydrolysis. If the coupled reactions together have an overall negative ΔG, the combined process is thermodynamically favorable.

This gives ATP its central role as an energy-transfer molecule. Energy released during the oxidation of food is used to regenerate ATP. ATP can then be hydrolyzed and coupled to energy-requiring cellular processes. In this way:

food oxidation → ATP production → ATP hydrolysis → cellular work.

Two Different Ways to Control a Reaction

We can now see that cells face two different challenges when carrying out chemical reactions.

First, an energy-requiring process must have an appropriate **energy source**. Cells often solve this problem by coupling the process to an exergonic reaction such as ATP hydrolysis.

Second, even an energetically favorable reaction may occur too slowly to support life. Cells solve this problem using **enzymes**, which lower activation energy and increase reaction rate.

These two ideas should not be confused:

ATP and other energy-coupling processes help make the overall energetics of cellular processes favorable.

Enzymes help those reactions occur rapidly enough to be biologically useful.

Together, energy coupling and enzyme catalysis allow cells to control when, where, and how rapidly metabolic reactions occur.

But enzymes themselves must also be controlled. Their activity depends upon their three-dimensional shape, their interactions with substrates, the concentration of molecules around them, and environmental conditions such as temperature and pH. In the next section, we will examine how these factors influence enzyme activity—and why changing the shape of an enzyme can change the chemistry of an entire metabolic pathway.

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8.6: Enzymes- Controlling Biological Reaction Rates

In Section 8.5, we distinguished between two important properties of a chemical reaction:

Thermodynamics tells us whether a reaction is energetically favorable.

Kinetics tells us how rapidly the reaction occurs.

For living organisms, both are essential. A reaction that is energetically favorable but takes several years to occur is not particularly useful to a cell that needs the product within seconds. Biological reactions must therefore occur at rates that are compatible with life. This is the role of **enzymes**. Enzymes are biological catalysts that increase reaction rates by lowering the activation energy required for a reaction to proceed. They are not permanently consumed during the reaction and can therefore participate in repeated reaction cycles.

But enzyme activity is not constant. Cells can increase, decrease, or stop enzyme activity in response to changing conditions. Temperature, pH, substrate concentration, enzyme concentration, and interactions with other molecules can all affect how rapidly an enzyme-catalyzed reaction occurs. Understanding these effects begins with something we have encountered repeatedly throughout this book:

Molecular shape matters.

Enzyme Shape Determines Enzyme Function

Most enzymes are proteins. As we learned in Chapter 7, the three-dimensional shape of a protein emerges from its amino acid sequence and the interactions that occur as the protein folds. For an enzyme, this folding creates a specific region called the **active site**.

The active site is not simply an empty pocket. It is a three-dimensional chemical environment formed by particular amino acid side chains.

These side chains may provide:

- positive or negative charges;
- polar regions capable of hydrogen bonding;
- nonpolar regions capable of hydrophobic interactions;
- and functional groups that can participate directly in the chemical reaction.

A substrate must therefore have more than an appropriate shape. It must also have chemical properties that allow favorable intermolecular interactions with the active site.

This is the same principle we encountered when considering protein structure in Chapter 7:

Shape and chemical character determine molecular interactions.

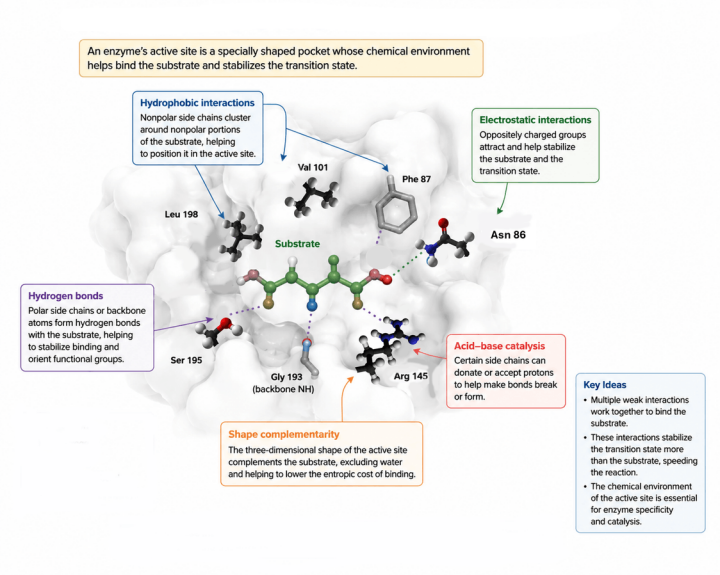


Figure 8.6.1: Enzyme Active Sites Depend on Shape and Chemistry. Protein folding creates an active site with a specific three-dimensional shape and chemical environment. Amino acid side chains within the active site can provide charged, polar, or nonpolar regions that interact with complementary regions of the substrate. These molecular interactions help determine which substrates can bind and which reactions an enzyme can catalyze.

From Substrate Binding to Product Formation

An enzyme-catalyzed reaction can be represented in a simplified form as:

$$\mathbf{E} + \mathbf{S} \rightleftharpoons \mathbf{ES} \longrightarrow \mathbf{E} + \mathbf{P} \tag{8.6.1}$$

where:

E = enzyme.

S = substrate.

ES = enzyme-substrate complex.

P = product.

First, the substrate binds to the enzyme to form an **enzyme-substrate complex**. Interactions between the substrate and active site then help position the reacting atoms appropriately and stabilize the high-energy arrangements that occur as the reaction approaches the transition state. This lowers the activation-energy barrier. The substrate is converted into product, the product is released, and the enzyme is available to bind another substrate molecule.

Because the enzyme is regenerated rather than consumed, a single enzyme molecule can catalyze the same reaction repeatedly.

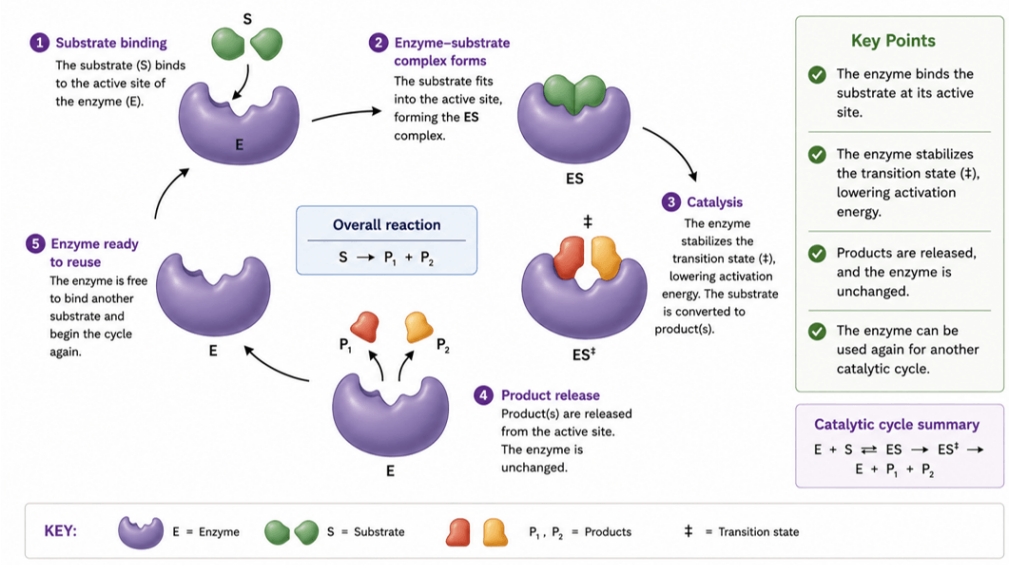


Figure 8.6.2**: The Enzyme Catalytic Cycle.** A substrate binds to the active site of an enzyme to form an enzyme-substrate complex. Interactions within the active site facilitate conversion of the substrate into product by lowering the activation energy of the reaction. The product is then released, leaving the enzyme available to catalyze another reaction.

Induced Fit and Enzyme Function

The simplest model of enzyme binding is the **lock-and-key model**, in which the substrate has a shape that is already complementary to the enzyme's active site. This model is useful, but real proteins are flexible. For many enzymes, substrate binding causes a small change in protein shape. This is called **induced fit**. The interactions that initially form between the substrate and enzyme can pull different parts of the protein into new positions. These changes may bring important amino acid side chains closer to the substrate, orient reacting groups properly, or create an environment that favors the chemical reaction.

Thus, substrate binding is a dynamic process. The substrate affects the shape of the enzyme, and the resulting enzyme shape helps promote the reaction. This also explains why anything that significantly changes protein shape can affect enzyme activity.

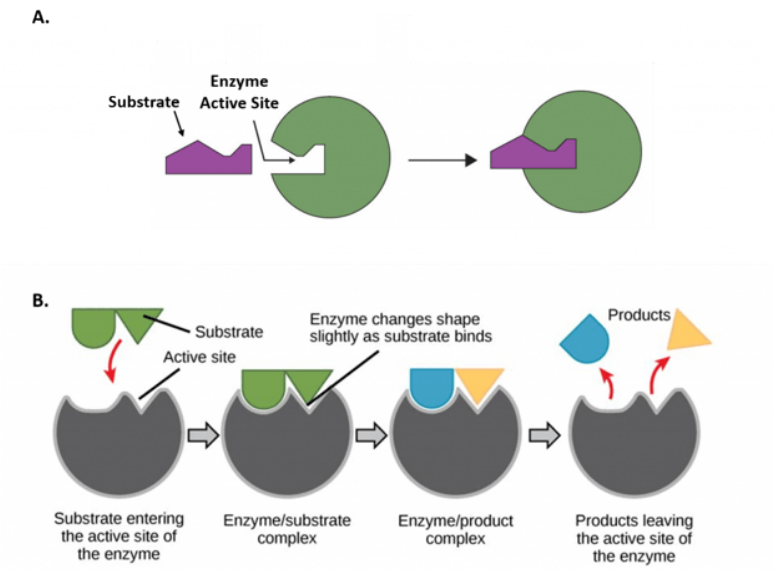


Figure 8.6.3**: Lock and Key, Induced Fit, and Catalysis**. **A**. Enzyme model where the active site is shaped to fit the substrate

model like a key fits into a lock. **B**. Initial interactions between a substrate and enzyme can cause a change in the three-dimensional shape of the enzyme. This induced fit positions the substrate and important amino acid side chains in ways that favor the chemical reaction. After the reaction occurs and the product is released, the enzyme can participate in another catalytic cycle.

Substrate Concentration and Reaction Rate

Imagine a solution containing a fixed number of enzyme molecules but only a few substrate molecules. Many enzyme active sites will remain empty simply because substrate molecules do not encounter them very often. If the substrate concentration increases, enzyme-substrate collisions become more frequent. More active sites become occupied, and the reaction rate increases. However, this increase cannot continue indefinitely.

Eventually, the substrate concentration becomes so high that nearly every enzyme active site is occupied whenever it is available. The enzymes are now operating close to their maximum capacity. This condition is called **enzyme saturation**. Once the enzymes are saturated, adding more substrate produces little additional increase in reaction rate because there are no additional active sites available.

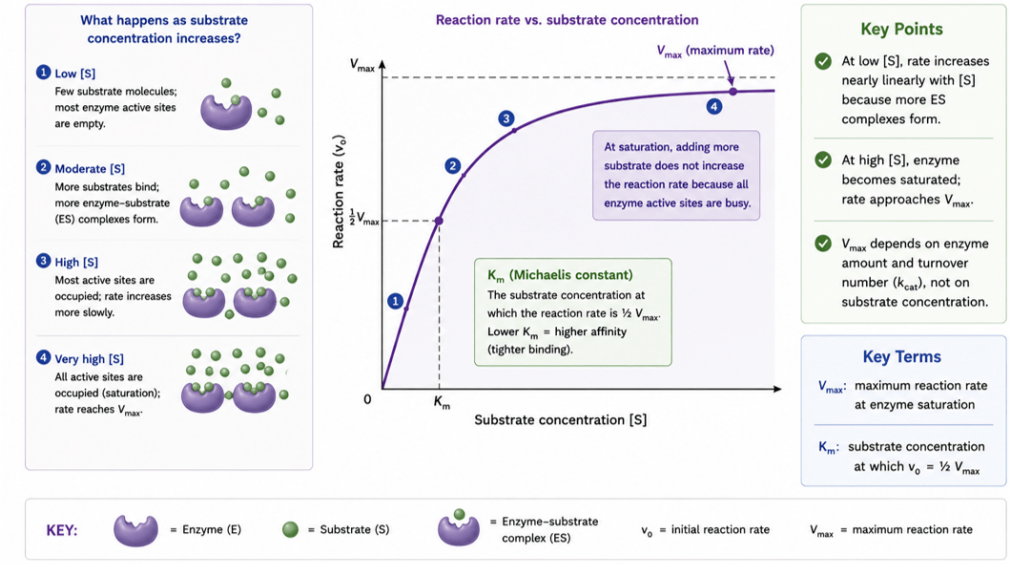


Figure 8.6.4**: Substrate Concentration and Enzyme Saturation.** At low substrate concentrations, increasing the amount of substrate increases the frequency of enzyme-substrate interactions and therefore increases the reaction rate. At high substrate concentrations, most enzyme active sites are occupied. The enzymes become saturated, and adding additional substrate produces little further increase in reaction rate.

A useful analogy is a grocery store with a limited number of checkout lanes. When only a few customers are present, there are empty checkout lanes and customers can be processed immediately. As more customers arrive, more checkout lanes become active and the total number of customers processed per minute increases.

Eventually, every checkout lane is continuously occupied. Adding more customers does not make the cashiers work faster. Instead, the additional customers must wait for an available lane. The system has reached its maximum processing rate unless more checkout lanes—more enzyme molecules—are added.

Enzyme Concentration and Reaction Rate

This brings us to another factor that influences reaction rate: **enzyme concentration**. If plenty of substrate is available, increasing the amount of enzyme provides more active sites where reactions can occur. Thus:

more enzyme → more available active sites → faster reaction rate.

For example, doubling the amount of enzyme can approximately double the reaction rate when sufficient substrate is available. However, enzyme concentration cannot increase reaction rate indefinitely if substrate becomes limiting. Enzymes require substrate molecules to act upon. Thus, enzyme activity depends upon the relationship between both enzyme and substrate concentrations.

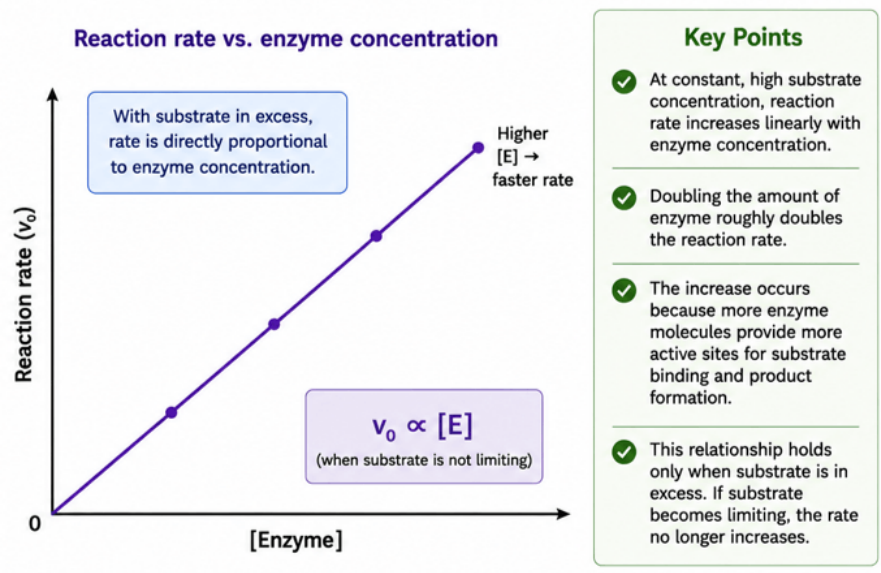


Figure 8.6.5: Enzyme Concentration and Reaction Rate. When sufficient substrate is available, increasing enzyme concentration increases reaction rate because more active sites are available to bind substrate and catalyze the reaction. If substrate becomes limiting, however, adding additional enzyme will no longer produce a proportional increase in reaction rate.

Temperature and Enzyme Activity

Temperature also influences reaction rate. As temperature increases, molecules generally move more rapidly. Faster molecular motion increases the frequency and energy of collisions between molecules. For many chemical reactions, increasing temperature therefore increases reaction rate. Enzyme-catalyzed reactions initially follow this same pattern. But enzymes introduce an additional complication:

enzymes are proteins.

As temperature rises beyond an enzyme's optimal range, the interactions maintaining the protein's three-dimensional structure begin to become disrupted. The protein can begin to unfold or **denature**. When the structure of the enzyme changes, the shape and chemical environment of the active site also change. The substrate may no longer bind properly. Thus, enzyme activity typically increases with temperature until an **optimum temperature** is reached. Beyond this point, activity falls as the enzyme begins to lose its functional structure.

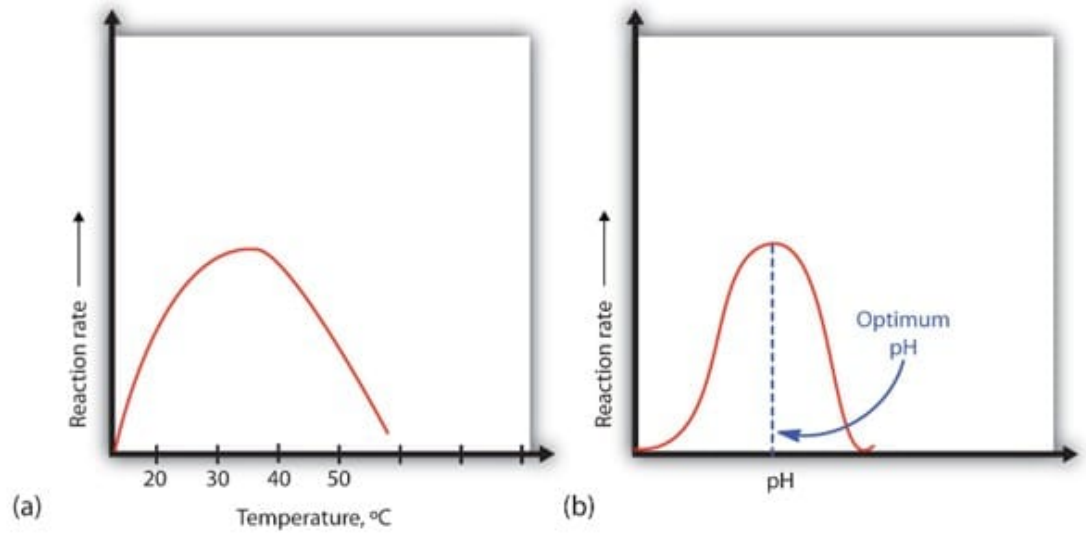


Figure 8.6.6**: Effect of Temperature and pH on Enzyme Activity**. ***Lefthand image***: At low temperatures, reduced molecular motion results in fewer productive enzyme-substrate interactions and a slower reaction rate. As temperature increases, enzyme activity generally increases until an optimum temperature is reached. At higher temperatures, disruption of the interactions maintaining protein structure can cause denaturation, altering the active site and decreasing enzyme activity. ***Righthand image***: Changes in pH can alter the charges of amino acid side chains within a protein. These changes can disrupt interactions that maintain protein structure or alter the chemical properties of the active site. Enzymes therefore have characteristic pH ranges over which they function most effectively.

The optimum temperature of an enzyme reflects the environment in which that enzyme normally functions. Many human enzymes function effectively near normal body temperature, approximately **37°C**. But this is not a universal optimum for all enzymes.

Organisms that live in very different environments have proteins adapted to those conditions. Microorganisms living near deep-sea hydrothermal vents, for example, can possess enzymes that remain folded and functional at temperatures that would denature many human proteins. Temperature therefore affects enzyme activity through **both molecular motion and protein structure**.

Why Refrigeration Preserves Food

The effect of temperature on reaction rate has an everyday application: food preservation. Refrigeration lowers temperature and slows molecular motion. This decreases the rates of many enzyme-catalyzed reactions, including reactions carried out by microorganisms that contribute to food spoilage. Freezing slows these processes even further. Importantly, low temperature does not necessarily destroy enzymes. In many cases, enzyme activity can increase again when the temperature rises.

High temperatures act differently. Sufficient heating can permanently disrupt protein structure and denature enzymes. This is one reason heating and cooking can be effective in reducing microbial activity in food.

pH and Enzyme Activity

Temperature is not the only environmental condition that can change protein structure and function. Enzymes are also sensitive to **pH**. Recall that pH reflects the concentration of H$^+$ ions in a solution. Changes in pH can alter the protonation and electrical charges of functional groups within amino acid side chains.

This can influence an enzyme in at least two important ways. First, changing the charges on amino acid side chains can disrupt ionic attractions and hydrogen-bonding interactions that help maintain the protein's three-dimensional shape. Second, amino acids within the active site may need particular charges to interact with the substrate or participate in the chemical reaction. Changing pH can therefore change both **protein folding** and **active-site chemistry**.

Each enzyme consequently has a range of pH values over which it functions effectively, with maximum activity occurring near its **optimum pH** (Figure 8.6.6).

Different Enzymes Have Different pH Optima

Most regions of the human body are maintained relatively close to neutral pH, and many human enzymes function best within this range. But not all parts of the body have the same chemical environment. The stomach, for example, is highly acidic. **Pepsin**, an enzyme involved in protein digestion in the stomach, functions effectively under these acidic conditions and has an optimum pH near 2. An enzyme adapted to the environment of another tissue might lose activity at such a low pH.

This demonstrates an important principle:

There is no single set of conditions that is optimal for every enzyme.

The structure of an enzyme is adapted to the chemical environment in which it normally functions.

Enzyme Activity Can Be Regulated

So far, we have considered environmental factors that influence enzyme activity. But cells also need ways to deliberately control their enzymes.

Consider a metabolic pathway:

A → **B** → **C** → **D**.

If the cell already has plenty of molecule D, continuing to convert A into D would waste both starting materials and energy. The cell needs a way to slow or stop the pathway.

One way to accomplish this is to alter the activity of one of the enzymes involved. Small molecules can bind to enzymes and increase or decrease their activity. Some bind directly within the active site. Others bind at a different location and change the enzyme's shape. Because **shape determines function**, a molecule does not necessarily need to occupy the active site itself to change enzyme activity. A molecule binding elsewhere on the protein may alter the shape of the active site from a distance. Such regulatory interactions allow cells to rapidly adjust metabolic pathways in response to changing conditions.

The same principle can also be exploited by **drug molecules**. A drug that binds to an enzyme can prevent a substrate from entering the active site, alter the shape of the enzyme, or in some cases permanently modify the protein. In other words, many drugs work not by creating entirely new biological processes, but by **changing the activity of molecular machinery that is already present**. That brings us directly to our next topic:

How can molecules inhibit enzymes—and how can we use that chemistry to alter biological processes?

In Section 8.7, we will examine **competitive, noncompetitive, and irreversible inhibition** and see how these interactions provide an important chemical foundation for understanding drug action.

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8.7: Enzyme Inhibition and Drugs

In Section 8.6, we saw that enzyme activity depends on molecular interactions between a substrate and the three-dimensional active site of an enzyme. This gives cells an important way to regulate metabolism. If another molecule interacts with an enzyme, it may increase or decrease the enzyme's activity. Molecules that decrease enzyme activity are called ***inhibitors***. Enzyme inhibition is an important part of normal cellular regulation. It is also medically important because many **drugs work by inhibiting enzymes**. Drugs that inhibit normal cellular processes are known as ***antagonists***. Other drugs can act as ***agonists*** and activate their cellular target.

Pharmacology is the branch of medicine concerned with the uses, modes and mechanisms of action of drug molecules. The term ***mechanism of action (MoA)*** refers to the specific biochemical interaction through which a drug substance produces its pharmacological effect. A mechanism of action usually includes mention of the specific molecular targets to which the drug binds, such as an enzyme or receptor.

To understand how these drugs work, we can return to a principle that has appeared throughout this book:

Molecular structure determines molecular interactions, and molecular interactions determine biological function.

Drugs Interact with Molecular Targets

A **drug** is a chemical substance that alters a biological process. For a drug to produce an effect, it must interact with something in the body. The molecule with which a drug interacts is often called its **molecular target**. Drug targets can include many different types of biological molecules, including enzymes, receptors, ion channels, transport proteins, and nucleic acids. The particular MoA through which a drug produces its effect may include:

- binding to the active site of an enzyme and prevent substrate binding;
- binding somewhere else on an enzyme and change its shape;
- interacting with a receptor and activate or block cellular signaling;
- blocking an ion channel;
- or interfering with the synthesis or function of DNA or RNA.

Despite this diversity, all of these mechanisms depend upon molecular interactions.

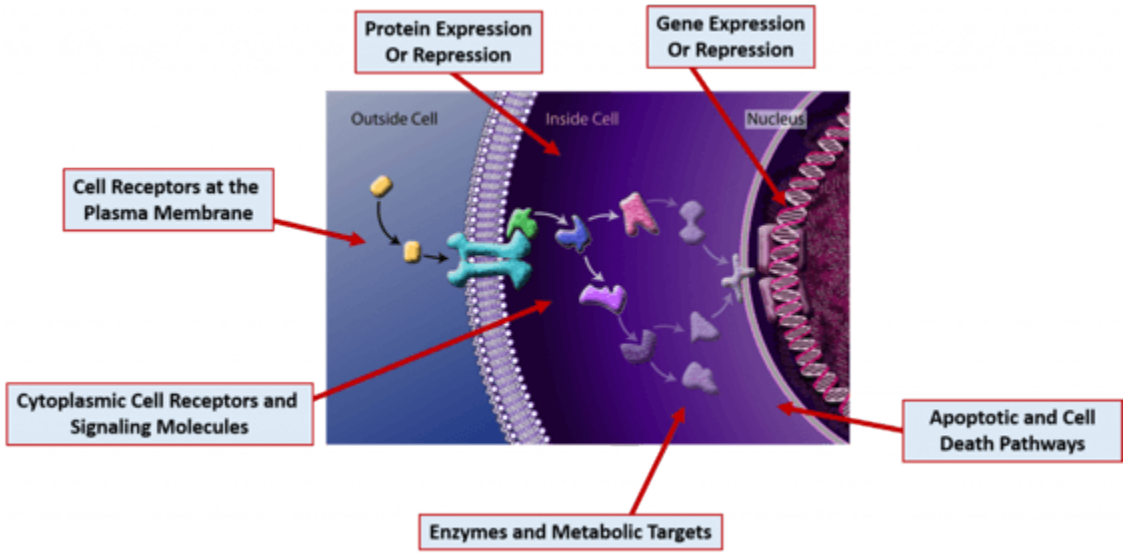


Figure 8.7.1**: Drugs Act by Interacting with Molecular Targets.** Drug molecules can interact with many different cellular targets, including enzymes, receptors, ion channels, transport proteins, and nucleic acids. The biological effect of a drug depends on the identity of its target and how drug binding changes the normal activity of that target. The figure is adapted from: The National

Molecular Shape and Drug Binding

Think back to our discussion of chirality and drug development in Chapter 6. A drug molecule must interact with its molecular target in three dimensions. Its size and shape matter. So do the locations of its functional groups, its charge distribution, polarity, hydrogen-bonding ability, and nonpolar regions. The target protein also has a three-dimensional binding site with its own chemical properties. Effective binding occurs when these features are sufficiently complementary.

This is why even relatively small changes in molecular structure can dramatically alter the biological activity of a drug. Changing a functional group may eliminate an important hydrogen bond. Changing molecular shape may prevent the molecule from fitting into the binding site. Changing stereochemistry can reposition functional groups in three-dimensional space. Thus, two molecules with very similar formulas—or even two enantiomers of the same compound—may interact differently with a biological target.

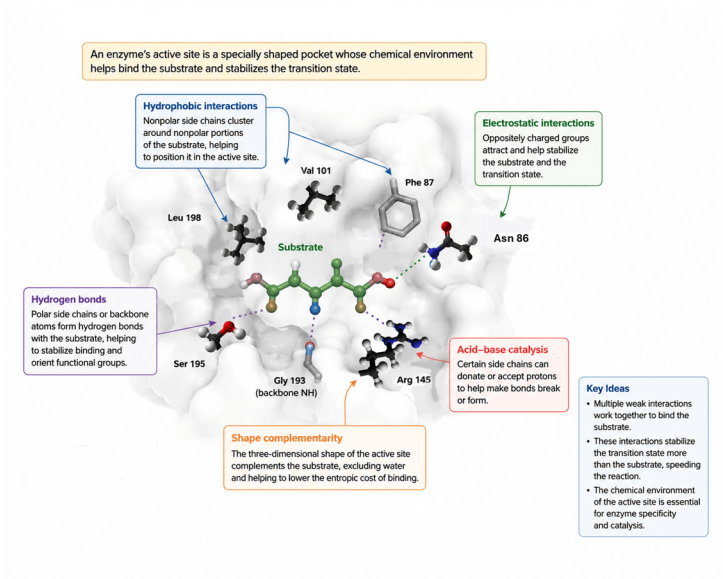


Figure 8.7.2: Molecular Structure Determines Drug-Target Interactions. Drug binding depends on complementary three-dimensional shape and chemical interactions between the drug and its molecular target. Charge, polarity, hydrogen bonding, hydrophobic interactions, functional-group placement, and stereochemistry can all influence binding. Small changes in molecular structure can therefore produce large changes in biological activity.

Enzyme Inhibitors

An **enzyme inhibitor** is a molecule that decreases the activity of an enzyme. Inhibitors can act in several ways. For this course, we will focus on three important types:

competitive inhibition.

noncompetitive inhibition.

irreversible inhibition.

The differences between these mechanisms depend primarily on **where the inhibitor binds and what happens to the enzyme after binding**.

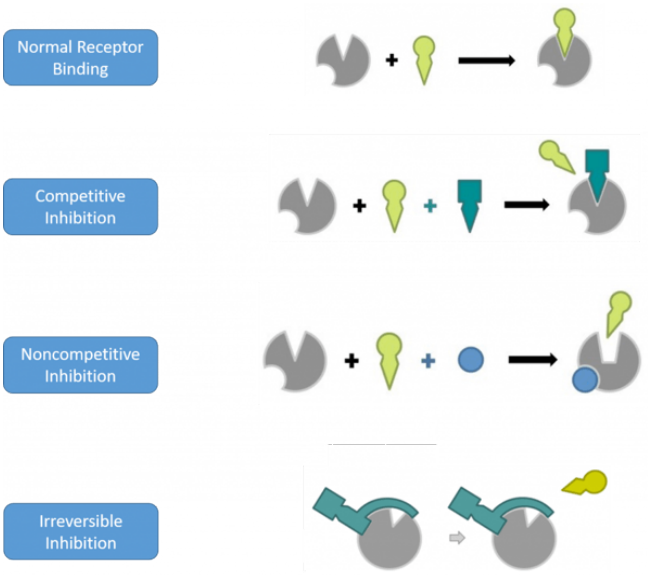


Figure 8.7.3: Mechanisms of Drug Target Inhibition. In competitive inhibition, the antagonist binds to the active site of the drug target and reversibly inhibits the binding of the normal substrate. In noncompetitive inhibition, the antagonist binds at an allosteric site on the drug target where it causes a conformational change in the shape of the drug target and prevents the normal substrate either from binding to the drug target (as shown above) or it effects the efficacy of the normal substrate by decreasing the drug target activation by the normal substrate. Noncompetitive inhibitors bind reversibly to the drug target and do not permanently alter the drug target. Irreversible inhibitors bind covalently to the drug target and permanently alter its activity. This figure was adapted from BioNinja.

Competitive Inhibition

A **competitive inhibitor** binds reversibly to the **active site** of an enzyme. Because the inhibitor occupies the same site normally used by the substrate, the substrate and inhibitor compete for access to the enzyme. When the inhibitor is bound, the substrate cannot bind. When the inhibitor leaves, the active site becomes available again.

Competitive inhibitors often resemble the normal substrate sufficiently in shape and chemical properties to interact with the active site. However, binding of the inhibitor does not result in the normal enzyme-catalyzed reaction. Competitive inhibition provides a direct application of our discussion of substrate concentration in Section 8.6.

Suppose both substrate and competitive inhibitor molecules are moving through the same solution. If relatively little substrate is present, the inhibitor has a greater opportunity to occupy enzyme active sites. But if the substrate concentration becomes very high, substrate molecules encounter the active sites more frequently and can outcompete the inhibitor. Thus, an important characteristic of competitive inhibition is:

Competitive inhibition can be reduced by increasing substrate concentration.

The inhibitor has not permanently altered the enzyme. It is simply competing with the substrate for the same binding location.

Noncompetitive Inhibition

Not all inhibitors bind to the active site. A **noncompetitive inhibitor** binds to a different region of the enzyme. A regulatory binding location away from the active site is called an **allosteric site**. When an inhibitor binds to an allosteric site, interactions between the inhibitor and protein can change the enzyme's three-dimensional shape. That conformational change can alter the active site. The substrate may no longer fit properly, or the active site may no longer position the substrate correctly for the reaction to occur efficiently. This is another direct application of the relationship between protein shape and function:

Binding at one location on a protein can change the shape and activity of another location.

This leads to an important difference between competitive and noncompetitive inhibition:

Competitive inhibitor → active site → can be overcome by increasing substrate.

Noncompetitive inhibitor → allosteric site → cannot be overcome simply by increasing substrate.

Both interactions are **reversible** in the simplified models considered here.

When the inhibitor dissociates from the protein, the enzyme can return to its functional conformation and resume normal activity.

Allosteric Regulation Is Also Used by Cells

Allosteric binding is not limited to drugs or harmful inhibitors. Cells use allosteric interactions to regulate their own metabolic pathways. Imagine again a metabolic pathway:

S → A → B → P.

If the cell already has an abundant supply of P, continuing to produce more P may waste both resources and energy. In some metabolic pathways, the final product can bind to an enzyme involved near the beginning of the pathway and reduce its activity. As the concentration of the product increases, the pathway slows.

When the product concentration decreases, inhibition decreases and the pathway can become more active again. This type of regulation allows metabolic pathways to respond dynamically to the needs of the cell.

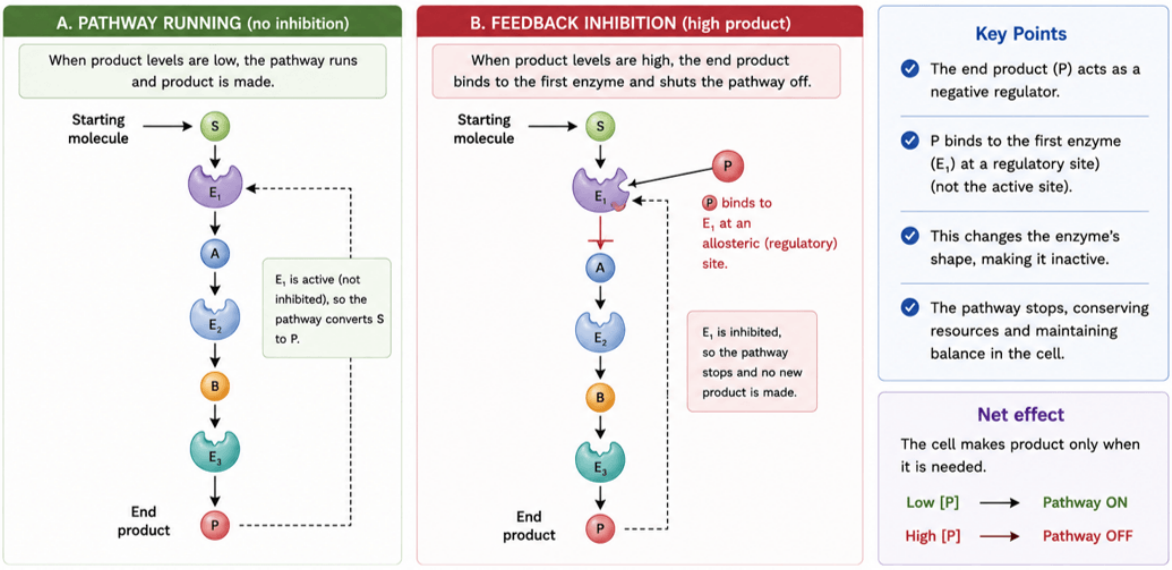


Figure 8.7.4: Allosteric Feedback Inhibition. In a metabolic pathway, the product of one reaction becomes the substrate for the next. When sufficient final product has accumulated, that product can inhibit an enzyme earlier in the pathway through allosteric binding. This feedback mechanism slows production when the cell already has an adequate supply of the product.

Irreversible Inhibition

Competitive and noncompetitive inhibitors interact **reversibly** with their enzyme targets. An **irreversible inhibitor**, in contrast, permanently inactivates an enzyme molecule. This commonly occurs when the inhibitor forms a **covalent bond** with the enzyme. If that covalent modification occurs within the active site, it may physically block substrate binding or modify an amino acid required for catalysis. An irreversible inhibitor can also bind elsewhere and permanently alter the protein in a way that destroys its activity.

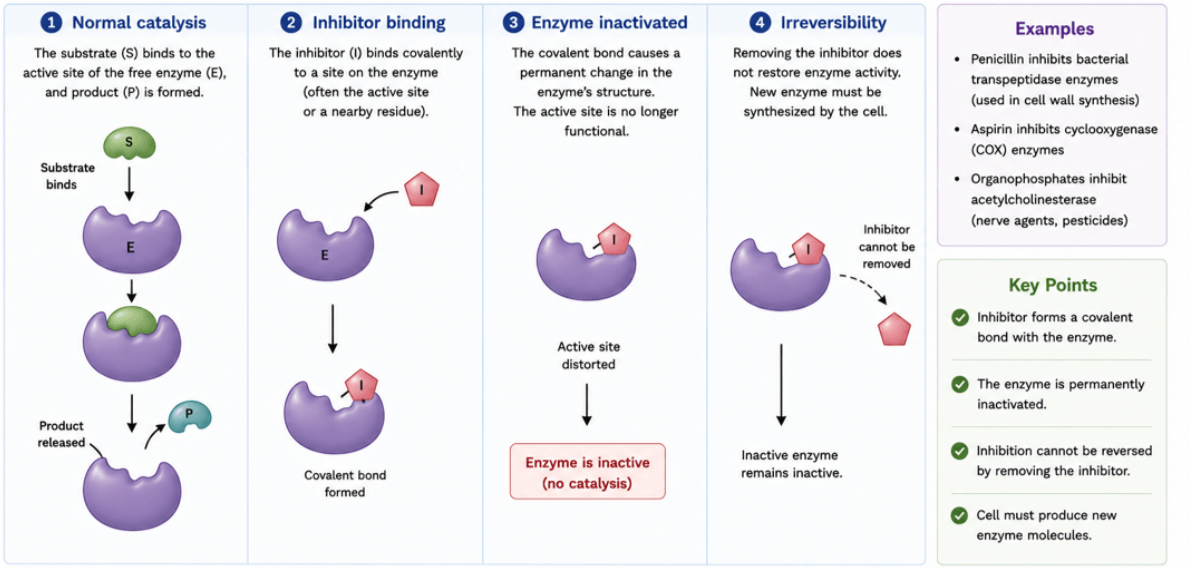


Figure 8.7.5**: Irreversible Inhibition.** An irreversible inhibitor forms a stable interaction, often a covalent bond, with an enzyme. This permanently alters that enzyme molecule and prevents normal catalytic activity. Restoring activity generally requires the cell to produce new functional enzyme molecules.

This is fundamentally different from reversible inhibition. Adding additional substrate cannot remove a covalently attached inhibitor. Nor does enzyme activity simply return when the concentration of free inhibitor decreases. The affected enzyme molecule has been chemically modified. The cell may need to synthesize new enzyme molecules to restore activity.

Comparing the Three Types of Inhibition

The three mechanisms can be summarized by asking three questions:

Table 8.7A: Common Mechanisms of Enzyme Inhibition.

Type of inhibition	**Where does the inhibitor bind?**	**Is binding reversible?**	**Can more substrate overcome the inhibition?**
Competitive	Active site	Yes	Yes
Noncompetitive	Allosteric site	Yes	No
Irreversible	Active site or another critical region	No; often covalent	No

Competitive inhibitors bind reversibly to the active site and compete directly with substrate. Noncompetitive inhibitors bind reversibly at an allosteric site and alter enzyme activity through a change in protein conformation. Irreversible inhibitors permanently modify the enzyme, often through covalent bonding. These different molecular interactions produce different effects on enzyme activity.

Inhibition Can Become Medicine

The word *inhibitor* can sound inherently harmful, but inhibition is neither good nor bad by itself. Its effect depends upon **what is being inhibited**. Suppose an enzyme produces a molecule that contributes to pain or inflammation. Reducing the activity of that enzyme may be beneficial. Suppose a microorganism requires a particular enzyme to survive or reproduce. Inhibiting that enzyme may help treat an infection. Suppose an abnormal signaling pathway causes cells to divide uncontrollably. Inhibiting a protein in that pathway may help slow the growth of cancer cells.

This is one of the fundamental strategies of pharmacology:

Identify a biological process that contributes to disease and find a molecule that can selectively modify an important molecular target within that process.

Selectivity is critical. A drug that interacts strongly with its intended target but also binds many unrelated proteins may produce unwanted effects. Drug development therefore involves finding molecules whose structures favor useful interactions with the desired target while minimizing interactions with other molecules in the body.

Once again, **molecular structure determines biological function**.

Agonists and Antagonists

Not every drug acts by inhibiting an enzyme. Many drugs interact with **receptors**, proteins that normally respond to signaling molecules produced by the body. A drug that binds to a receptor and activates it is called an **agonist**. An agonist mimics or enhances the effect of the normal signaling molecule. A drug that binds to a receptor and blocks its activation is called an **antagonist**. An antagonist prevents or reduces the effect of the normal signaling molecule.

Thus:

Agonist → binds and activates.

Antagonist → binds and blocks activation.

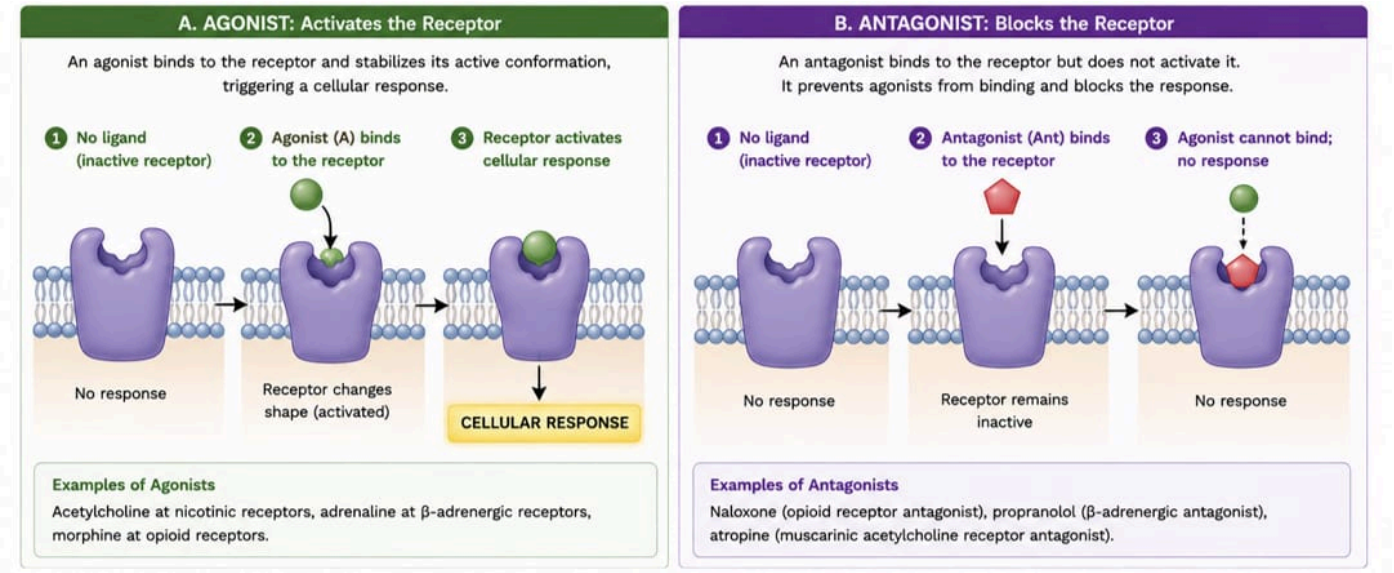


Figure 8.7.6**: Agonists and Antagonists.** A normal signaling molecule binds to its receptor and activates a cellular response. An agonist binds to the receptor and produces activation, mimicking or enhancing the action of the normal signaling molecule. An antagonist binds without producing normal receptor activation and blocks or reduces the action of the signaling molecule.

Although receptor activation differs from enzyme catalysis, the underlying chemistry is remarkably similar. In both cases, biological activity begins with **molecular recognition and binding**. Shape matters. Charge matters. Functional groups matter. Intermolecular attractions matter. And changing the structure of either the small molecule or the protein can change the biological response.

Chemistry Connects Molecular Structure to Medicine

We can now connect ideas from throughout this course.

- Atoms determine bonding.
- Bonding determines molecular structure and polarity.
- Molecular structure determines intermolecular interactions.
- Those interactions help determine how proteins fold and how molecules bind to proteins.
- Protein shape and molecular binding determine biological activity.
- And changing those interactions can change physiology.

This gives us a chemical pathway from the molecular scale all the way to medicine:

atomic structure.

↓

chemical bonding.

↓

molecular shape and polarity.

↓

intermolecular interactions.

↓

protein structure and molecular recognition.

↓

enzyme and receptor activity.

↓

cellular response.

↓

physiological effect.

A drug may be tiny compared with a cell or a human body, but its effects begin with interactions occurring at the scale of individual atoms and molecules. That is why chemistry is so important to the health sciences. Understanding the chemistry of biological molecules helps us understand not only **how life works**, but also how medicines can alter biological processes when those processes go wrong.

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8.8: Chapter Summary

Metabolism and Biological Reactions

Metabolism is the collection of chemical reactions that occur within a living organism. These reactions allow cells to obtain and use energy, build and repair cellular structures, eliminate wastes, and respond to changes in their environment. Metabolic reactions can be broadly divided into two categories:

- **Catabolic reactions** break larger molecules into smaller molecules and often release energy.
- **Anabolic reactions** build larger molecules from smaller components and generally require an input of energy.

Metabolic reactions are organized into **metabolic pathways**, in which the product of one reaction becomes the starting material for another. Individual steps within these pathways are usually controlled by **enzymes**.

Several recurring types of reactions are important in biological systems. **Hydrolysis** uses water to break covalent bonds, while **dehydration synthesis** forms bonds while producing water. **Group-transfer reactions** move functional groups between molecules, while **rearrangement reactions** reorganize atoms within a molecule. **Oxidation-reduction reactions** involve changes in electron distribution and play a particularly important role in cellular energy production.

Chemical reactions rearrange atoms but do not create or destroy them. Thus, all of these reactions obey the **Law of Conservation of Matter**: the same number of atoms of each element must be present before and after a chemical reaction.

Oxidation States, Oxidation, and Reduction

An **oxidation-reduction (redox) reaction** involves the transfer or redistribution of electrons between chemical species. Oxidation and reduction always occur together because electrons lost by one chemical species must be accepted by another.

Recall:

LEO: Lose Electrons = Oxidized.

GER: Gain Electrons = Reduced.

Oxidation States

An **oxidation state**, or **oxidation number**, is a bookkeeping tool that helps us track how electrons are distributed in compounds and how that distribution changes during a reaction. Several basic rules are useful for assigning oxidation states:

- An element in its uncombined form has an oxidation state of **0**.
- A monatomic ion has an oxidation state equal to its **ionic charge**.
- Oxygen usually has an oxidation state of **−2**.
- Hydrogen usually has an oxidation state of **+1** when bonded to nonmetals.
- The sum of the oxidation states in a neutral compound is **0**.
- The sum of the oxidation states in a polyatomic ion equals the **overall charge of the ion**.

Changes in oxidation state allow us to identify oxidation and reduction:

Oxidation → oxidation state increases (becomes more positive, due to loss of electrons).

Reduction → oxidation state decreases (becomes more negative, due to gain of electrons).

The species that causes another substance to be oxidized is the **oxidizing agent**. Because it accepts electrons, the oxidizing agent is itself **reduced**. The species that causes another substance to be reduced is the **reducing agent**. Because it supplies electrons, the reducing agent is itself **oxidized**. Thus, redox reactions always involve a paired process:

One species is oxidized while another species is reduced.

Recognizing Redox in Organic Molecules

For large organic and biological molecules, assigning oxidation states to individual carbon atoms can become cumbersome. Fortunately, changes in molecular structure provide a useful shortcut. In general:

Oxidation → fewer C–H bonds and/or more C–O bonds.

Reduction → more C–H bonds and/or fewer C–O bonds.

These structural patterns reflect the same changes in electron distribution described by oxidation states. They are not a different kind of oxidation and reduction—they are simply a convenient way to recognize redox chemistry in organic molecules.

Primary alcohols can be oxidized to **aldehydes**, which can undergo further oxidation to **carboxylic acids**:

primary alcohol → aldehyde → carboxylic acid.

Secondary alcohols can be oxidized to **ketones**:

secondary alcohol → ketone.

For the reactions considered in this course, tertiary alcohols do not undergo this type of oxidation. Reduction reverses these patterns. Aldehydes can be reduced to primary alcohols, while ketones can be reduced to secondary alcohols. These same reaction patterns occur in biological systems. For example, ethanol is oxidized in the liver first to acetaldehyde and then to acetic acid/acetate.

Food Molecules Provide High-Energy Electrons

Food molecules contain chemical energy that can be harvested through oxidation. Molecules containing many C–H bonds are relatively **reduced** and therefore have considerable potential to undergo oxidation. Fatty acids contain long hydrocarbon chains with many C–H bonds, helping explain their high energy content.

During metabolism, food molecules are progressively oxidized and high-energy electrons are transferred to electron-carrier molecules such as **NAD⁺** and **FAD**, producing their reduced forms, **NADH** and **$FADH_2$**.

Ultimately, much of the carbon from food is oxidized to **CO_2**, while molecular oxygen is reduced to **H_2O**.

For glucose, the overall reaction can be represented as:

$$\mathrm{C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O} \tag{8.8.1}$$

Rather than releasing the energy from this reaction all at once, cells use a controlled series of enzyme-mediated redox reactions to capture and transfer some of the energy.

ATP Transfers Energy Within Cells

Adenosine triphosphate (ATP) is an important energy-transfer molecule within cells.

ATP can undergo hydrolysis to produce ADP and inorganic phosphate:

$$\mathrm{ATP + H_2O \longrightarrow ADP + P_i + energy} \tag{8.8.2}$$

The energy released by ATP hydrolysis can be coupled to energy-requiring cellular processes such as active transport, muscle contraction, and the synthesis of biological molecules.

ATP is continually recycled:

$$\mathrm{ATP} \longrightarrow \text{cellular work} \longrightarrow \mathrm{ADP} + \mathrm{P_i} \longrightarrow \mathrm{ATP} \tag{8.8.3}$$

Energy obtained from the oxidation of food is used to regenerate ATP from ADP and P_i.

Oxidative Phosphorylation Produces ATP

Much of the ATP produced under aerobic conditions is generated in the **mitochondria** through **oxidative phosphorylation**.

During this process:

1. Food molecules are oxidized, and high-energy electrons are transferred to electron carriers.
2. Electrons are delivered to the **electron transport chain** in the inner mitochondrial membrane.
3. As electrons move through the chain, released energy is used to pump **H⊕ ions** from the matrix into the intermembrane space.
4. This creates an H⊕ concentration gradient that stores potential energy.
5. H⊕ flows down its gradient through **ATP synthase**.
6. Movement of H⊕ through ATP synthase drives molecular rotation and conformational changes that facilitate the formation of ATP from ADP and P_i.
7. At the end of the electron transport chain, **oxygen accepts electrons and is reduced to water**.

The energy transformations can be summarized as:

chemical energy in food.

↓

energy carried by electrons.

↓

potential energy of an H⊕ gradient.

↓

mechanical motion of ATP synthase.

↓

chemical energy transferred through ATP.

Reaction Spontaneity and Gibbs Free Energy

Chemical reactions involve changes in chemical bonds.

Breaking bonds requires energy.

Forming bonds releases energy.

The overall energetic favorability of a reaction can be described by the **change in Gibbs free energy (ΔG)**.

ΔG < 0 → exergonic and thermodynamically favorable.

ΔG > 0 → endergonic and requires a net input of free energy.

ΔG = 0 → equilibrium.

A spontaneous reaction is thermodynamically favorable, but **spontaneous does not mean fast**.

Cells can carry out energy-requiring processes by **coupling** them to energy-releasing reactions. ATP hydrolysis is commonly used

for this purpose.

Activation Energy and Enzymes

Before reactants can become products, they must pass through an unstable, high-energy **transition state**. The energy required to reach this state is the **activation energy**. Enzymes increase reaction rates by providing a reaction pathway with a lower activation energy. Importantly:

Enzymes lower activation energy and increase reaction rate.

But:

Enzymes do NOT change ΔG or determine whether a reaction is thermodynamically favorable.

This distinction separates two important chemical ideas:

Thermodynamics → Is the reaction energetically favorable?

Kinetics → How rapidly does the reaction occur?

Enzyme Shape Determines Enzyme Function

Most enzymes are proteins, and their function depends upon their three-dimensional structure. The **active site** contains amino acid side chains arranged to provide a particular shape and chemical environment. Charge, polarity, hydrogen bonding, hydrophobic interactions, and molecular shape all contribute to substrate binding.

An enzyme-catalyzed reaction can be represented as:

$$\mathbf{E} + \mathbf{S} \rightleftharpoons \mathbf{ES} \longrightarrow \mathbf{E} + \mathbf{P} \tag{8.8.4}$$

The substrate binds to the enzyme, forming an enzyme-substrate complex. Interactions within the active site facilitate the reaction, the product is released, and the enzyme can participate in another catalytic cycle. In the **lock and key model**, an enzyme is permanently shaped to receive the substrate. In the **induced-fit model**, substrate binding causes changes in enzyme shape that help position the substrate and active-site groups appropriately for the reaction.

Thus:

amino acid sequence → protein folding → active-site shape and chemistry → substrate binding → enzyme function.

Factors Affecting Enzyme Activity

Several factors influence the rate of enzyme-catalyzed reactions.

- **Substrate concentration:** Increasing substrate concentration initially increases reaction rate. Eventually, most active sites become occupied and the enzyme becomes **saturated**, so additional substrate has little effect on reaction rate.
- **Enzyme concentration:** When sufficient substrate is available, increasing enzyme concentration increases reaction rate by providing more active sites.
- **Temperature:** Increasing temperature initially increases molecular motion and reaction rate. At sufficiently high temperatures, disruption of protein structure can cause enzyme denaturation and loss of activity.
- **pH:** Changes in pH alter the protonation and charge of amino acid side chains. This can affect protein folding, substrate binding, and active-site chemistry. Enzymes therefore have characteristic optimum pH ranges.

Because enzyme activity depends upon protein structure:

Change the shape or chemistry of an enzyme, and you may change its function.

Enzyme Inhibition and Drug Action

An **enzyme inhibitor** decreases enzyme activity. Three important types of inhibition are:

- **Competitive inhibition:** The inhibitor binds reversibly to the active site and competes directly with substrate. Increasing substrate concentration can reduce the effect of the inhibitor.
- **Noncompetitive inhibition:** The inhibitor binds reversibly at an **allosteric site**, changing enzyme conformation and reducing activity. Increasing substrate concentration does not overcome this inhibition.
- **Irreversible inhibition:** The inhibitor permanently modifies an enzyme, often through formation of a covalent bond. The affected enzyme molecule can no longer function normally.

Cells can also use allosteric interactions to regulate their own metabolic pathways. In **feedback inhibition**, accumulation of the final product of a pathway decreases the activity of an enzyme earlier in the pathway.

Many drugs take advantage of these same molecular principles. Drug molecules act by interacting with specific **molecular targets**, including enzymes, receptors, ion channels, transport proteins, and nucleic acids. Drug-target interactions depend upon molecular shape and chemical properties such as charge, polarity, functional-group placement, hydrogen-bonding ability, hydrophobic interactions, and stereochemistry. Some drugs interact with receptors as **agonists**, which activate the receptor, or **antagonists**, which block receptor activation. Ultimately, the biological effects of drugs arise from the same chemical principles that govern all of the molecular interactions discussed throughout this course:

atomic structure.

↓

chemical bonding.

↓

molecular shape and polarity.

↓

intermolecular interactions.

↓

protein structure and molecular recognition.

↓

enzyme and receptor activity.

↓

cellular response.

↓

physiological effect.

The chemistry occurring at the scale of atoms and molecules ultimately shapes the function of cells, tissues, and the entire human body.

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9: SOLUTIONS AND HOMEOSTASIS

9.1: The Chemistry of Solutions

9.2: Solubility and "Like Dissolves Like"

9.3: Measuring Solution Concentration

9.4: Dilution of Solutions

9.5: Osmosis and Tonicity

9.6: Acids, Bases and pH

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9.1: The Chemistry of Solutions

Much of the chemistry of life takes place in **solution**. The blood flowing through your body, the fluid surrounding your cells, and the cytoplasm inside each cell all contain water mixed with dissolved ions and molecules. Nutrients such as glucose must dissolve in body fluids before they can be transported to cells, ions such as Na^+ and K^+ must remain at carefully controlled concentrations, and many of the chemical reactions that keep cells alive occur in an aqueous environment.

For this reason, understanding solutions is essential for understanding how chemistry operates within the human body.

Solutions Are Homogeneous Mixtures

Recall that a **mixture** contains two or more substances that are physically combined but are not chemically bonded to one another. A **solution** is a homogeneous mixture in which the components are distributed uniformly throughout the mixture. A solution contains at least two components:

- The **solvent** is the substance present in the greatest amount and is the substance in which other materials dissolve.
- A **solute** is a substance dissolved in the solvent.

For example, when sodium chloride (NaCl) is dissolved in water, water is the solvent and sodium chloride is the solute.

Solutions are not limited to solids dissolved in liquids. The components of a solution can exist as solids, liquids, or gases. Air, for example, is a gaseous solution composed primarily of nitrogen and oxygen along with smaller amounts of other gases. Brass is a solid solution containing primarily copper and zinc. In biological and healthcare applications, however, many of the most important solutions are **aqueous solutions**, meaning that **water is the solvent**.

Water as a Biological Solvent

Water is an especially effective solvent because of its **polarity**. Recall from Chapter 5 that oxygen is more electronegative than hydrogen. As a result, electrons within the O–H bonds of water are shared unequally. The oxygen end of the molecule carries a partial negative charge (δ–), while the hydrogen ends carry partial positive charges (δ+). These partial charges allow water molecules to interact strongly with ions and other polar molecules. Consider what happens when sodium chloride dissolves in water. Solid sodium chloride consists of Na^+ and Cl^- ions held together by electrostatic attractions in a crystal lattice. When the crystal is placed in water, the polar water molecules interact with the ions. The partially negative oxygen atoms of water are attracted to Na^+ ions, while the partially positive hydrogen atoms are attracted to Cl^- ions. Water molecules surround the ions and help separate them from the crystal.

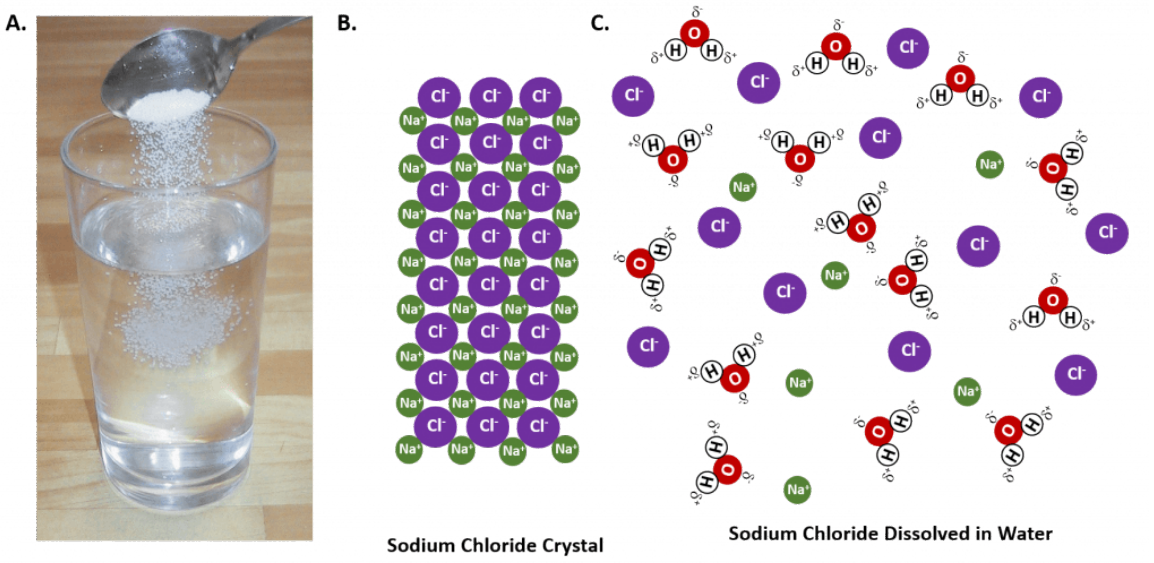


Figure 9.1.1: The Process of Dissolving. When an ionic salt, such as sodium chloride, shown in (A), comes into contact with water, the water molecules dissociate the ion molecules of the sodium chloride into their ionic state, shown as a molecular model in (B) the solid crystalline lattice of sodium chloride, and (C) the sodium chloride dissolved in the water solvent. Water molecules interact with the ions in a sodium chloride crystal. The partially negative oxygen atoms of water orient toward $Na^{\oplus}$ ions, while the partially positive hydrogen atoms orient toward $Cl^{\ominus}$ ions. These interactions help separate the ions from the crystal and stabilize them in solution. (Photo of sodium chloride provided by Chris 73(opens in new window)).

The process in which solvent molecules surround dissolved solute particles is called **solvation**. When water is specifically the solvent, this process is called **hydration**. Thus, when sodium chloride dissolves in water, the ions separate and become surrounded by hydration shells of water molecules:

$$\mathrm{NaCl\,(s)} \longrightarrow \mathrm{Na^+\,(aq) + Cl^-\,(aq)} \tag{9.1.1}$$

The notation **(aq)** means *aqueous* and indicates that the ion or molecule is dissolved in water. Importantly, dissolving a substance does not cause the matter to disappear. The $Na^{\oplus}$ and $Cl^{\ominus}$ ions are still present; they have simply become dispersed throughout the solution. This is another example of the **law of conservation of matter** that we have encountered throughout this text.

Molecular Solutes Can Also Dissolve in Water

Not every substance that dissolves in water separates into ions. Many covalent molecules dissolve as intact molecules. For example, glucose ($C_6H_{12}O_6$) contains several polar O–H bonds. These regions can form hydrogen bonds with surrounding water molecules. When glucose dissolves, individual glucose molecules separate from one another and become surrounded by water molecules, but the glucose molecules themselves remain intact.

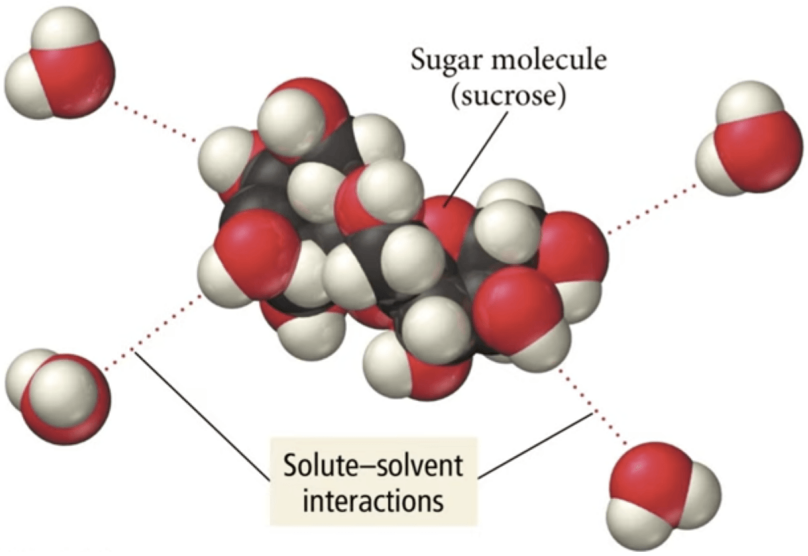


Figure 9.1.2: The Interaction of Glucose with Water. Glucose is a polar covalent molecule that can form hydrogen bonds with water. When glucose dissolves, individual glucose molecules become surrounded by water molecules but do not separate into ions. Figure source: Asih, F., et al. (2021).

This distinction—whether a substance forms ions when it dissolves—has important consequences for the properties of the resulting solution.

Electrolytes and Nonelectrolytes

A solution can conduct electricity when it contains freely moving ions. Substances that produce ions when dissolved in water are called **electrolytes**.

Sodium chloride is an electrolyte because it dissociates into Na⊕ and Cl⊕ ions:

$$\mathrm{NaCl\,(s)} \longrightarrow \mathrm{Na^+\,(aq)} + \mathrm{Cl^-\,(aq)} \tag{9.1.2}$$

Many soluble ionic compounds are **strong electrolytes** because they dissociate essentially completely into ions when they dissolve.

Some molecular compounds can also produce ions in water. If only a portion of the dissolved substance forms ions, the substance is called a **weak electrolyte**. Acetic acid (CH_3COOH), the acid found in vinegar, is one example. We will return to this distinction when we discuss acids and bases later in this chapter.

Other substances dissolve without producing ions and are called **nonelectrolytes**. Glucose and sucrose are examples. Although these molecules dissolve readily in water, they remain neutral molecules and therefore do not contribute significant electrical conductivity to the solution.

Table 9.1A Comparison of Electrolytes and Nonelectrolytes

Type of Solute	What Happens in Water?	Example
Strong electrolyte	Forms ions essentially completely	NaCl
Weak electrolyte	Only some dissolved molecules form ions	CH_3COOH
Nonelectrolyte	Dissolves as neutral molecules	$C_6H_{12}O_6$

Electrolytes in the Human Body

In healthcare, the word **electrolyte** is commonly used to describe physiologically important ions dissolved in body fluids. Some of the major electrolytes include:

Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, and HCO_3^-

These ions participate in many processes necessary for life. They help regulate the movement of water, contribute to electrical signaling in nerves and muscles, participate in muscle contraction, and help maintain acid–base balance.

The concentrations of these ions cannot vary without limit. Cells function properly only when the chemical composition of their surrounding environment remains within an appropriate range.

This brings us to one of the major themes of this chapter: **homeostasis**.

Homeostasis is the maintenance of a relatively stable internal environment despite changes occurring inside or outside the body. From a chemical perspective, homeostasis requires the body to regulate the concentrations of many substances dissolved in its fluids—including water, ions, nutrients, acids, and bases.

Before we can understand how the body maintains these concentrations, however, we first need to understand **why some substances dissolve readily in water while others do not**.

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9.2: Solubility and "Like Dissolves Like"

In Section 9.1, we saw that water molecules can surround ions and polar molecules, allowing many substances to dissolve in water. But not everything dissolves equally well. Table salt and sugar dissolve readily in water, while cooking oil does not.

Why?

Whether a substance dissolves depends largely on the **intermolecular attractions** among the solute particles, among the solvent molecules, and between the solute and solvent.

Solubility

The **solubility** of a substance describes the maximum amount of solute that can dissolve in a given amount of solvent under specified conditions. A substance that dissolves appreciably in a particular solvent is described as **soluble**, while a substance that does not dissolve to an appreciable extent is described as **insoluble**.

Solubility is not an all-or-nothing property. Some substances are highly soluble, others dissolve only slightly, and others have such low solubility that we commonly describe them as insoluble. For a solute to dissolve, the interactions between the solute and solvent must be strong enough to replace at least some of the attractions that previously existed among the solute particles and among the solvent molecules.

This leads to one of the most useful generalizations for predicting solubility:

Like dissolves like.

In general:

- **polar and ionic substances tend to dissolve in polar solvents**.
- **nonpolar substances tend to dissolve in nonpolar solvents**.

This pattern makes sense when we consider intermolecular forces.

Polar Solutes and Polar Solvents

Water is a highly **polar solvent**. As we saw in Section 9.1, the partial charges on water molecules allow them to interact strongly with ions through **ion–dipole attractions**. For example, when NaCl dissolves, the partially negative oxygen atoms of water interact with $Na^{\oplus}$, while the partially positive hydrogen atoms interact with $Cl^{\ominus}$. These attractions help pull the ions away from the ionic crystal and stabilize them in solution.

Polar molecular substances can also dissolve readily in water. Glucose, for example, contains several O–H groups. These groups can form **hydrogen bonds** with water molecules. When glucose dissolves, water molecules replace many of the intermolecular attractions that previously existed between neighboring glucose molecules.

Thus, both sodium chloride and glucose dissolve in water, although they do so in different ways:

- **NaCl separates into ions.**
- **Glucose separates into individual neutral molecules.**

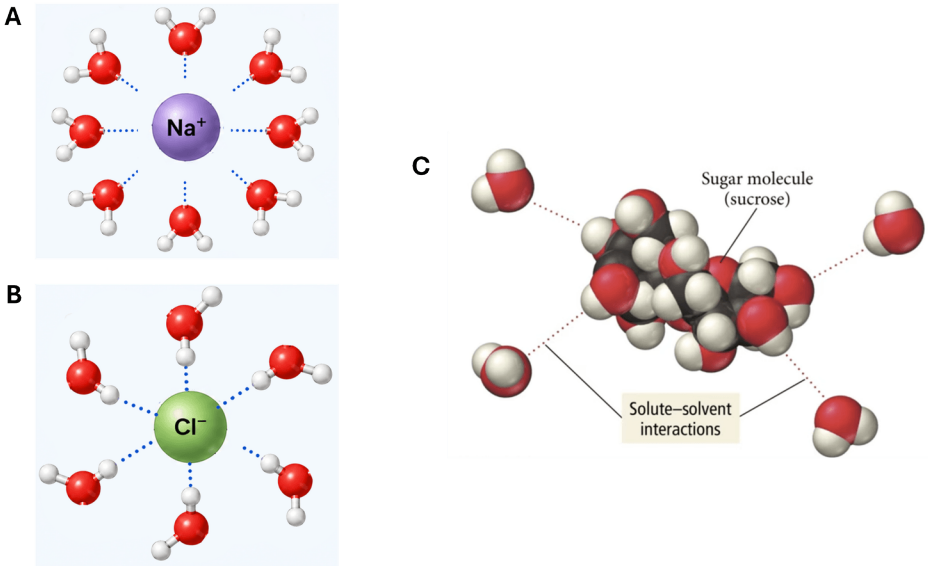


Figure 9.2.1: Interaction of Ions and Polar Covalent Molecules with Water. Both sodium chloride and glucose dissolve in water because they can form favorable interactions with polar water molecules. Sodium chloride dissociates into hydrated Na⊕ and Cl⊖ ions (A and B, respectively), while glucose (C) remains as intact molecules that form hydrogen bonds with the surrounding water. Source of Figure C: Asih, F., et al. (2021)(opens in new window).

Why Oil and Water Do Not Mix

Now consider what happens when oil is added to water.

Most oils consist primarily of molecules containing long regions of nonpolar carbon–carbon and carbon–hydrogen bonds. These molecules cannot form strong hydrogen bonds or ion–dipole attractions with water.

Water molecules are strongly attracted to one another through hydrogen bonding. Mixing oil into water would require disrupting some of these water–water interactions without replacing them with equally favorable water–oil interactions.

As a result, the oil molecules tend to remain together rather than becoming dispersed throughout the water.

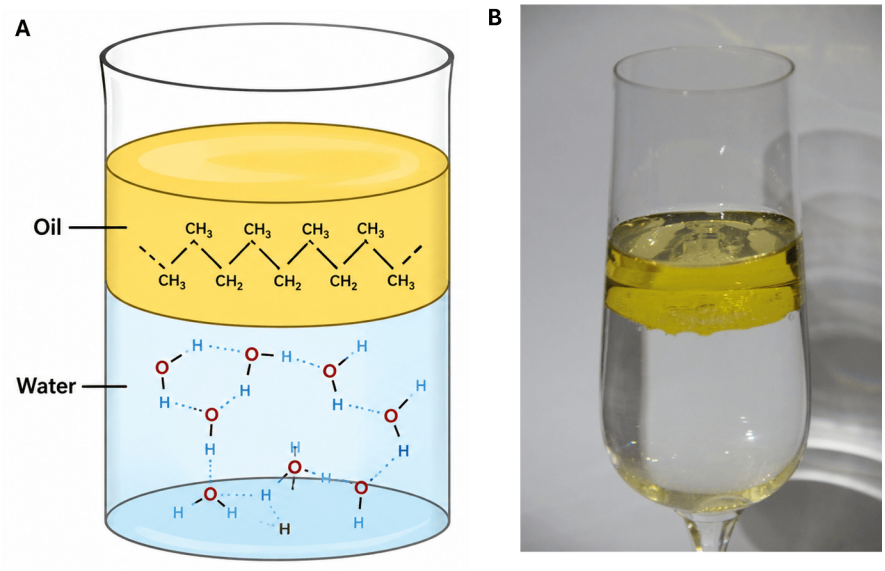


Figure 9.2.2: Oil and Water Do Not Mix. Polar water molecules form strong hydrogen-bonding interactions with one another. Nonpolar oil molecules cannot form comparable interactions with water, so the two liquids separate into distinct layers. (A) Cartoon representation and (B) Photo of oil and water. Source: Bitjungle.

When two liquids mix completely with one another, they are described as **miscible**. When they do not mix and instead form separate layers, they are **immiscible**.

Ethanol and water, for example, are miscible. The –OH group of ethanol can participate in hydrogen bonding with water molecules.

Oil and water are immiscible because their intermolecular properties are very different.

A Molecule Can Have Both Polar and Nonpolar Regions

The phrase *like dissolves like* is useful, but real molecules are not always simply “polar” or “nonpolar.”

Many biological molecules contain **both polar and nonpolar regions**. For example, a fatty acid contains a polar carboxylic acid group attached to a long nonpolar hydrocarbon chain. Phospholipids contain highly polar or charged head groups attached to nonpolar hydrocarbon tails.

Molecules containing both hydrophilic and hydrophobic regions are described as **amphipathic**.

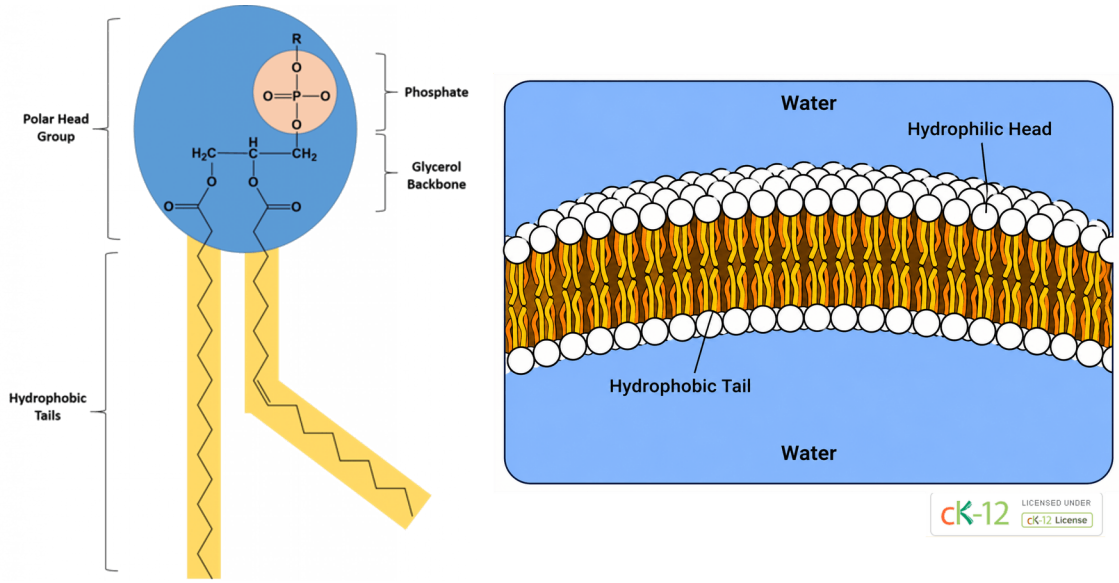


Figure 9.2.3**: Phospholipids are Amphipathic Molecules**. Amphipathic molecules contain both hydrophilic regions that interact favorably with water and hydrophobic regions that do not. ***Lefthand Diagram****:* Phospholipids are important biological examples of amphipathic molecules. ***Righthand Diagram****:* When placed in an aqueous environment, phospholipids will spontaneously form a lipid bilayer, positioning their polar head groups next to the water and their nonpolar hydrocarbon tails inward. Lipid Bilayer Image modified from CK-12.

This property has enormous biological importance. When phospholipids are placed in water, their polar heads interact with the aqueous environment while their nonpolar tails associate with one another away from the water. This behavior contributes to the spontaneous formation of the phospholipid bilayer that makes up cell membranes.

Thus, the structure of the cell membrane itself can be understood in large part through the same intermolecular forces that govern solubility.

Saturated and Unsaturated Solutions

Solubility also has a limit. Suppose sodium chloride is gradually added to a container of water. At first, the added salt dissolves. As more salt is added, the concentration of dissolved ions increases until eventually the solution reaches the maximum amount of solute that can remain dissolved under those conditions.

A solution containing less than the maximum amount of dissolved solute is an **unsaturated solution**. More solute can still dissolve. A solution containing the maximum amount of dissolved solute is a **saturated solution**. If additional solute is added, it will generally remain undissolved. A saturated solution may appear unchanged, but at the molecular level it is dynamic. Solute particles can continue to leave the solid and enter the solution while dissolved particles return to the solid. When these processes occur at equal rates, the system has reached **dynamic equilibrium**.

We will encounter the concept of equilibrium again later in this chapter when we examine acids, bases, and buffers.

Temperature and Solubility

Solubility can also depend on environmental conditions, particularly **temperature**. For many solid solutes dissolved in water, solubility increases as temperature increases. This is why heating a solvent can sometimes allow more solid solute to dissolve. Under special conditions, a hot saturated solution can be cooled without immediately causing the excess dissolved solute to crystallize. The resulting solution contains more dissolved solute than would normally be stable at the lower temperature and is called a **supersaturated solution**. Supersaturated solutions are unstable. Adding a small crystal or otherwise disturbing the solution can cause rapid crystallization. Reusable sodium acetate hand warmers take advantage of this process; crystallization releases energy to the surroundings as heat.

Gases often show the opposite behavior: their solubility in liquids generally decreases as temperature increases. This is one reason a warm carbonated beverage loses dissolved carbon dioxide more readily than a cold one.

Solubility in the Human Body

Solubility has important consequences in biological systems. Body fluids must transport a remarkable variety of substances. Ions, glucose, amino acids, gases, lipids, hormones, metabolic wastes, and medications must all move through environments that are predominantly aqueous. Water-soluble substances can often travel directly within these fluids. Strongly nonpolar substances may require specialized transport mechanisms. For example, many nonpolar molecules are carried through the bloodstream by proteins or within lipid-containing particles that provide a more favorable chemical environment.

Solubility can also become medically important when substances that are normally dissolved begin to precipitate. Kidney stones, for example, can form when certain dissolved substances become sufficiently concentrated that solid crystals begin to form.

Whether a substance *can* dissolve, however, tells us only part of the story. To understand biological solutions, we also need to know **how much of a substance is present**. That quantity is described by **solution concentration**, the focus of the next section.

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9.3: Measuring Solution Concentration

Knowing that a substance dissolves in water does not tell us how much of that substance is present. A glass of lightly sweetened tea and a glass of very sweet tea may both contain sugar dissolved in water, but the amount of sugar relative to the volume of solution is very different.

The **concentration** of a solution describes the amount of solute present in a given amount of solution.

Concentration is especially important in biological and healthcare settings. The concentrations of glucose, Na^+, K^+, Ca^{2+}, medications, and many other substances must often be measured precisely. A solution containing too little of a substance may be ineffective, while one containing too much can be harmful.

There are several ways to express solution concentration. In this section, we will focus on three commonly encountered forms:

- **molarity**
- **percent concentration**
- **parts per million (ppm) and parts per billion (ppb)**

Molarity

One of the most common concentration units used in chemistry is **molarity**. Molarity describes the number of **moles of solute per liter of solution** and is abbreviated with a capital **M**.

$$M = \frac{\text{moles of solute}}{\text{liters of solution}} \tag{9.3.1}$$

Thus, a solution with a concentration of 1.00 M NaCl contains 1.00 mole of NaCl for every liter of solution.

Notice that molarity uses the **total volume of the solution**, not simply the volume of solvent that was added.

For example, to prepare 1.00 L of a 1.00 M NaCl solution, we would not add 1.00 mol of NaCl to 1.00 L of water. Instead, the NaCl would be dissolved in some water and then additional water would be added until the **final volume of the entire solution** reached 1.00 L.

This distinction is important because the solute itself contributes to the final volume.

Using Molarity as a Conversion Factor

Molarity can also be thought of as a conversion factor between **moles of solute** and **volume of solution**.

Consider a 0.100 M NaOH solution:

$$0.100\ \text{M} = \frac{0.100\ \text{mol NaOH}}{1.00\ \text{L}} \tag{9.3.2}$$

This tells us that every liter of this solution contains 0.100 mol of NaOH.

Finding Moles from Molarity

Example 9.3.1

How many moles of NaOH are present in 2.50 L of a 0.100 M NaOH solution?

Solution

Given:

Volume = 2.50 L
Concentration = 0.100 mol/L

Find:

Moles of NaOH

Using molarity as a conversion factor:

$$2.50\ \text{L}\left(\frac{0.100\ \text{mol NaOH}}{1\ \text{L}}\right) = 0.250\ \text{mol NaOH} \tag{9.3.3}$$

Notice how the liter units cancel, leaving the desired unit of moles.

Calculating Molarity from Mass

In the laboratory, solutes are usually measured by **mass**, not by moles. Therefore, calculating the molarity of a solution often requires an additional step.

Example 9.3.2

Suppose 5.85 g of NaCl is dissolved to make 500.0 mL of solution. What is the molarity?

Solution

We need:

$$M = \frac{\text{moles}}{\text{liters}} \tag{9.3.4}$$

But the problem gives us **grams** and **milliliters**.

Therefore, we first convert:

grams → **moles**.

and

milliliters → **liters**.

The molar mass of NaCl is 58.44 g/mol.

$$5.85\ \text{g NaCl}\left(\frac{1\ \text{mol NaCl}}{58.44\ \text{g NaCl}}\right) = 0.100\ \text{mol NaCl} \tag{9.3.5}$$

Next, convert the solution volume:

$$500.0\ \text{mL}\left(\frac{1\ \text{L}}{1000\ \text{mL}}\right) = 0.5000\ \text{L} \tag{9.3.6}$$

Now calculate the molarity:

$$M = \frac{0.100\ \text{mol}}{0.5000\ \text{L}} \tag{9.3.7}$$

Final Answer:

$$M = 0.200\ \text{M} \tag{9.3.8}$$

This type of calculation brings together several skills that you have used throughout this course: dimensional analysis, molar mass, unit conversion, and solution concentration.

Preparing a Solution of Known Molarity

Suppose we wanted to prepare the 0.200 M NaCl solution from the previous example in the laboratory.

We could:

1. Weigh 5.85 g of NaCl.
2. Place the NaCl into an appropriate container.
3. Add some water and mix until the NaCl has completely dissolved.
4. Add additional water until the **total solution volume** reaches exactly 500.0 mL.

The final step is important. Adding 5.85 g of NaCl directly to 500.0 mL of water would produce a final solution volume slightly greater than 500.0 mL and therefore would not produce exactly the concentration intended.



(a) An amount of solute is weighed out on an analytical balance and then

(b) A portion of the solvent is added to the volumetric flask.

(c) The mixture is swirled until *all* of the solute is dissolved.

(d) Additional solvent is added up to the mark on the volumetric flask.

Figure 9.3.1: Preparing a Solution Using a Volumetric Flask. To prepare a solution of known molarity from a solid solute, the required mass of solute is measured and dissolved in less than the final volume of solvent. Additional solvent is then added until the desired total solution volume is reached.

Percent Concentration

Molarity is especially useful in chemistry because it expresses concentration in terms of moles. However, concentrations encountered in healthcare, consumer products, and everyday life are also commonly expressed as **percent concentrations**.

Percent means **parts per hundred**.

The general relationship is:

$$\%\ \text{concentration} = \frac{\text{amount of solute}}{\text{amount of solution}} \times 100 \tag{9.3.9}$$

The units used for the solute and solution determine the type of percent concentration.

Three common forms are:

Table 9.3A: Types of Percent Solutions.

Concentration	Meaning
mass/mass (m/m)%	grams of solute per 100 g of solution
mass/volume (m/v)%	grams of solute per 100 mL of solution
volume/volume (v/v)%	mL of solute per 100 mL of solution

It is important to specify which type of percent concentration is being used.

For example, a **0.9% (m/v) NaCl solution** contains:

$$\mathbf{0.9\ g\ NaCl} \tag{9.3.10}$$

for every:

$$\mathbf{100\ mL\ solution} \tag{9.3.11}$$

or:

$$\mathbf{0.9\%\ (\mathit{m}/\mathit{v})\ NaCl} = \frac{\mathbf{0.9\ g\ NaCl}}{\mathbf{100\ mL\ solution}} \tag{9.3.12}$$

This concentration is commonly encountered in healthcare as **normal saline**. Notice again that the denominator refers to the **final solution**, not simply the amount of solvent.

Example 9.3.3

What is the mass/volume percent concentration of a solution containing 24.0 g of sucrose in a total volume of 243 mL?

Solution

$$\frac{\mathbf{24.0\ g}}{\mathbf{243\ mL}} \times \mathbf{100} \tag{9.3.13}$$

Final Answer:

$$\mathbf{9.88\%\ (\mathit{m}/\mathit{v})} \tag{9.3.14}$$

Thus, approximately 9.88 g of sucrose are present for every 100 mL of solution.

Example 9.3.4

How many grams of NaCl are required to prepare 625 mL of a 13.5% (m/v) NaCl solution?

Solution

A 13.5% (m/v) solution contains:

$$\frac{\mathbf{13.5\ g\ NaCl}}{\mathbf{100\ mL\ solution}} \tag{9.3.15}$$

Using this relationship as a conversion factor:

$$625\ \text{mL}\left(\frac{13.5\ \text{g NaCl}}{100\ \text{mL}}\right) = 84.4\ \text{g NaCl} \tag{9.3.16}$$

Therefore:

$$84.4\ \text{g NaCl} \tag{9.3.17}$$

are required.

Very Small Concentrations: ppm and ppb

Percent concentration works well when relatively large amounts of solute are present. However, sometimes the amount of solute is extremely small. For these solutions, concentration may be expressed as **parts per million (ppm)** or **parts per billion (ppb)**.

$$1\ \text{ppm} = 1\ \text{part solute per } 10^6\ \text{parts solution} \tag{9.3.18}$$

$$1\ \text{ppb} = 1\ \text{part solute per } 10^9\ \text{parts solution} \tag{9.3.19}$$

These units are particularly useful for describing trace quantities of substances such as environmental contaminants.

For dilute aqueous solutions, the density of water allows a particularly useful approximation:

$$1\ \text{ppm} \approx 1\ \text{mg/L} \tag{9.3.20}$$

and

$$1\ \text{ppb} \approx 1\ \mu\text{g/L} \tag{9.3.21}$$

Thus, a water sample containing 5 mg of a contaminant per liter of solution has a concentration of approximately 5 ppm.

Amount and Concentration Are Not the Same Thing

One important distinction is that the **amount of solute** and the **concentration of a solution** are not the same thing.

Imagine two containers:

- Container A contains 1.0 mol of glucose dissolved in 1.0 L of solution.
- Container B contains 1.0 mol of glucose dissolved in 2.0 L of solution.

Both containers contain exactly the **same amount of glucose**.

However:

$$\text{Container A} = 1.0\ \text{M} \tag{9.3.22}$$

while:

$$\text{Container B} = 0.50\ \text{M} \tag{9.3.23}$$

The glucose in Container B is spread throughout a larger volume, so its concentration is lower.

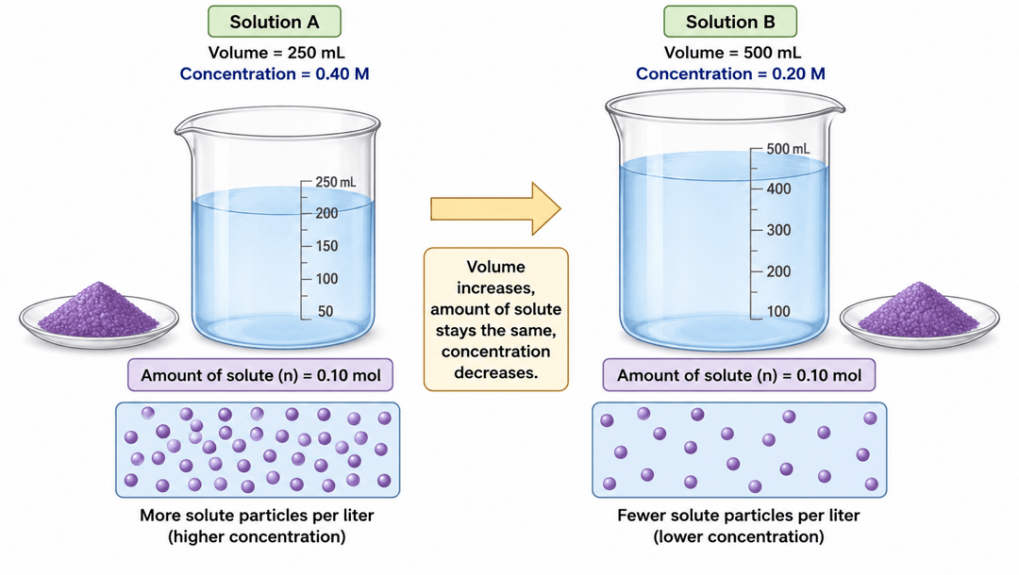


Figure 9.3.2: Solute Amount and Solution Concentration are Different. Two solutions can contain the same amount of solute but have different concentrations. Increasing the volume while keeping the amount of solute constant decreases the concentration.

This relationship is extremely useful. In the laboratory and in healthcare, concentrated solutions are frequently mixed with additional solvent to produce solutions with lower concentrations.

This process is called **dilution**, and it is the focus of the next section.

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9.4: Dilution of Solutions

Many solutions used in laboratories, healthcare settings, and everyday life are prepared by starting with a concentrated solution and adding additional solvent. This process is called **dilution**. The original concentrated solution is often called a **stock solution**. A measured amount of the stock solution is transferred to a new container, and additional solvent is added until the desired final volume and concentration are reached.

During a dilution, two things change:

- the **volume of the solution increases**.
- the **concentration of the solution decreases**.

However, one very important thing does **not** change:

The amount of solute remains constant.

Imagine that 100 mL of a solution contains 0.10 mol of glucose. If we add enough water to increase the total volume to 200 mL, there are still 0.10 mol of glucose present. The glucose molecules have simply become dispersed throughout a larger volume.

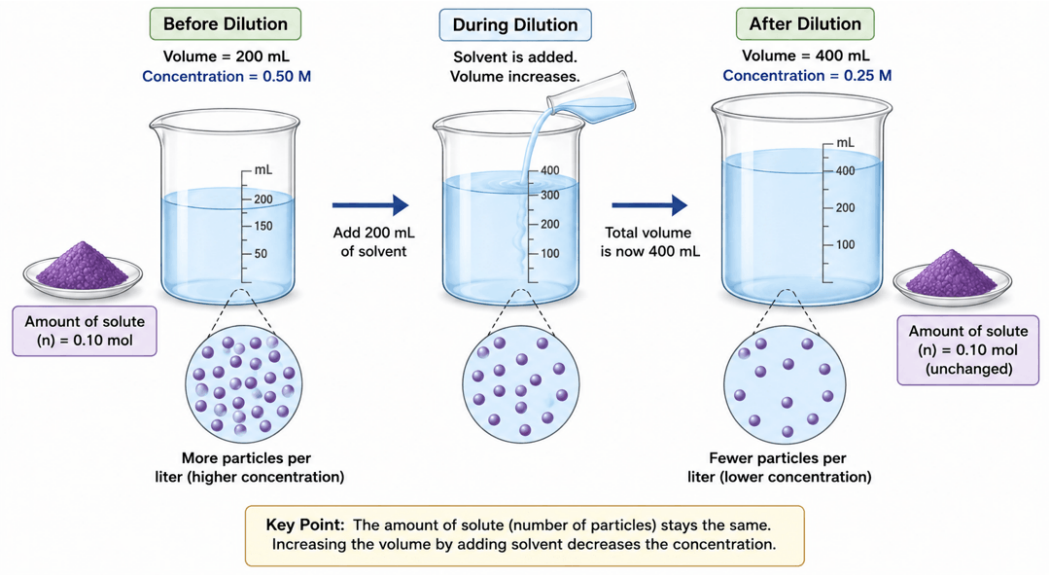


Figure 1: What Changes Occur During a Dilution? During dilution, additional solvent increases the total volume of a solution. The number of solute particles remains unchanged, but the particles become dispersed throughout a larger volume. As a result, the concentration decreases.

The Dilution Equation

Recall from Section 9.3 that molarity is defined as:

$$M = \frac{\text{moles of solute}}{\text{liters of solution}} \tag{9.4.1}$$

We can rearrange this relationship to determine the number of moles of solute present:

$$\text{moles of solute} = M \times V \tag{9.4.2}$$

Before dilution, the amount of solute in the stock solution is therefore:

$$\text{moles of solute} = M_1V_1 \tag{9.4.3}$$

After dilution, the amount of solute is:

$$\text{moles of solute} = M_2V_2 \tag{9.4.4}$$

Because adding solvent does not add or remove solute, the amount of solute before dilution must equal the amount of solute after dilution:

$$M_1V_1 = M_2V_2 \tag{9.4.5}$$

This relationship is known as the **dilution equation**.

In this equation:

- (M_1) = concentration of the initial or stock solution
- (V_1) = volume of stock solution used
- (M_2) = concentration of the final diluted solution
- (V_2) = total volume of the final diluted solution

The subscripts 1 and 2 simply represent the solution **before** and **after** dilution.

Example 9.4.1

Using the Dilution Equation

A concentrated glucose solution has a concentration of 3.00 M. What volume of this stock solution is needed to prepare 2500 mL of a 0.400 M glucose solution?

Solution

Given:

$$M_1 = 3.00\ \text{M} \tag{9.4.6}$$

$$M_2 = 0.400\ \text{M} \tag{9.4.7}$$

$$V_2 = 2500\ \text{mL} \tag{9.4.8}$$

Find:

V_1, the volume of stock solution needed.

Begin with the dilution equation:

$$M_1V_1 = M_2V_2 \tag{9.4.9}$$

Rearrange the equation to solve for V_1:

$$V_1 = \frac{M_2V_2}{M_1} \tag{9.4.10}$$

Substitute the known values:

$$V_1 = \frac{(0.400\ \text{M})(2500\ \text{mL})}{3.00\ \text{M}} \tag{9.4.11}$$

The molarity units cancel:

$$V_1 = 333\ \text{mL} \tag{9.4.12}$$

Therefore, **333 mL of the 3.00 M glucose stock solution** is needed.

To prepare the solution, the 333 mL of stock solution would be measured and then diluted with water until the **total solution volume reaches 2500 mL**.

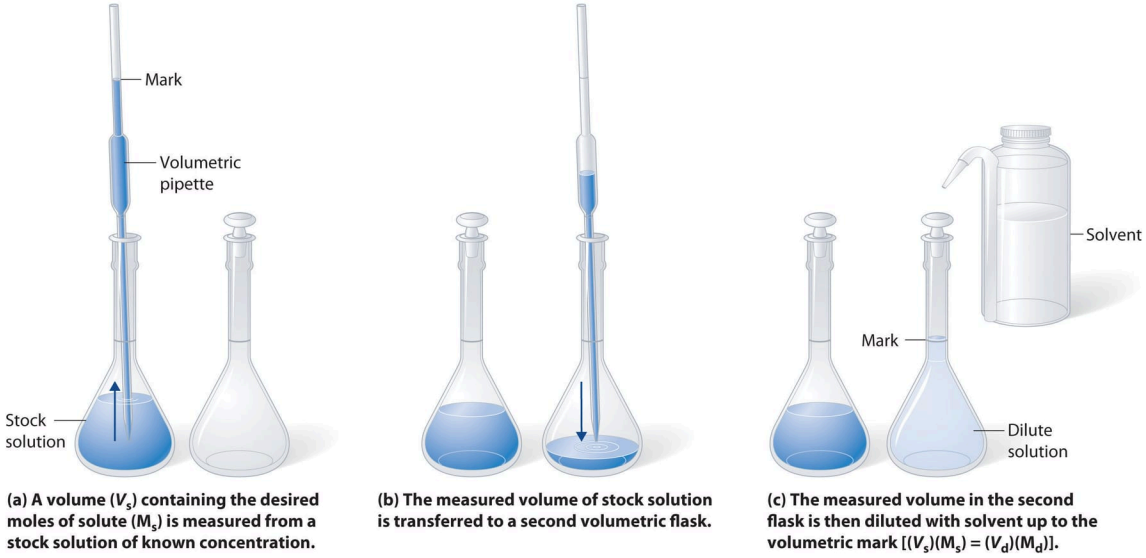


Figure 2: Preparation of a Solution of Known Concentration by Dilution. (a) A measured volume (V_1) of a stock solution with concentration (M_1) is transferred to a volumetric flask. (b) Additional solvent is added until the desired final volume (V_2) is reached. (c) The resulting solution has a lower concentration (M_2), while containing the same number of moles of solute as the original stock solution.

The Volume of Solvent Added Is Not V_2

One common mistake in dilution calculations is to interpret V_2 as the amount of water that should be added. It is not. V_2 represents the **total final volume of the diluted solution**. In our previous example:

$$V_1 = 333\ \text{mL} \tag{9.4.13}$$

and:

$$V_2 = 2500\ \text{mL} \tag{9.4.14}$$

This does **not** mean that 2500 mL of water should be added to the stock solution. Instead, water is added until the **total solution volume** reaches 2500 mL. If we approximate the amount of water required by subtraction:

$$2500\ \text{mL} - 333\ \text{mL} = 2167\ \text{mL} \tag{9.4.15}$$

approximately 2167 mL of water would be added. For accurate laboratory preparation, however, the solution would normally be brought directly to the desired **final volume** rather than measuring the solvent separately.

Concentration and Volume Change in Opposite Directions

The dilution equation also reveals an important relationship between concentration and volume. If the amount of solute remains constant:

increasing the volume decreases the concentration.

For example, suppose the volume of a solution is doubled:

$$V_2 = 2V_1 \tag{9.4.16}$$

Using the dilution equation:

$$M_1V_1 = M_2(2V_1) \tag{9.4.17}$$

the V_1 terms cancel, giving:

$$M_2 = \frac{M_1}{2} \tag{9.4.18}$$

Thus, doubling the volume by dilution cuts the concentration in half.

Similarly, increasing the volume by a factor of ten decreases the concentration by a factor of ten.

This inverse relationship provides a useful way to check whether an answer to a dilution problem makes sense. If solvent is added, the final concentration **must be lower** than the initial concentration.

Dilutions in Healthcare

Dilution calculations are particularly important in healthcare because many medications and other solutions are supplied in concentrated forms.

Suppose a medication is available as a 20.0 mg/mL stock solution, but a 5.00 mg/mL solution is needed. What volume of stock solution is required to prepare 100.0 mL of the diluted medication?

The dilution relationship can be used with concentration units other than molarity, as long as the concentration units on both sides of the equation are the same.

$$C_1V_1 = C_2V_2 \tag{9.4.19}$$

where C represents concentration.

For this problem:

$$(20.0\ \text{mg/mL})(V_1) = (5.00\ \text{mg/mL})(100.0\ \text{mL}) \tag{9.4.20}$$

Solving for V_1:

$$V_1 = \frac{(5.00\ \text{mg/mL})(100.0\ \text{mL})}{20.0\ \text{mg/mL}} \tag{9.4.21}$$

$$V_1 = 25.0\ \text{mL} \tag{9.4.22}$$

Thus, 25.0 mL of the stock solution is required. Additional solvent would then be added until the **total volume reaches 100.0 mL**.

The same basic principle applies whether we are diluting a laboratory reagent, preparing a medication, or changing the concentration of a biological solution:

the amount of solute remains constant while the volume increases and the concentration decreases.

The concentration of a solution also affects how water moves across biological membranes. When solutions with different concentrations are separated by a selectively permeable membrane, water can move from one side to the other through **osmosis**.

This movement of water—and its relationship to **isotonic, hypotonic, and hypertonic solutions**—is the focus of the next section.

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9.5: Osmosis and Tonicity

The concentration of a solution does more than tell us how much solute is present. Differences in concentration can also drive the movement of molecules—and especially water—within biological systems.

Every cell is surrounded by a **cell membrane**, also called a plasma membrane, that separates the contents of the cell from the extracellular fluid surrounding it. Recall that the membrane is composed primarily of a phospholipid bilayer. Because of its structure, the cell membrane is **selectively permeable**, meaning that some substances can cross the membrane more readily than others.

This selective permeability makes differences in concentration across the membrane extremely important.

Concentration Gradients and Diffusion

A **concentration gradient** exists whenever the concentration of a substance differs from one location to another. Particles in liquids and gases are in constant random motion. When a concentration gradient exists, this random movement results in a net movement of particles from an area of **higher concentration toward an area of lower concentration**. This process is called **diffusion**.

For example, if a drop of food coloring is added to a glass of water, the dye molecules initially have a very high concentration in one small region. Over time, the molecules diffuse throughout the water until they are distributed more evenly.

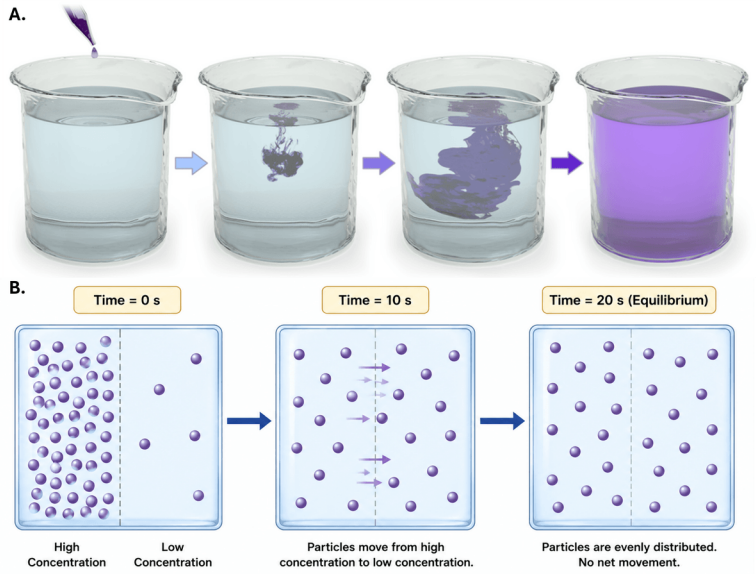


Figure 1: The Process of Diffusion. Particles naturally diffuse from regions of higher concentration toward regions of lower concentration. Over time, the particles become more evenly distributed throughout the available space. (A) Image cascade of a drop of blue dye in a beaker of water over time. Early images show the concentrated drop of dye in the liquid. By the last time point, the dye has fully diffused creating a uniform color in the water. Photo source: BruceBlaus. (B) Molecular representation of the diffusion process showing the movement of molecules down their concentration gradient over time, until dynamic equilibrium is achieved.

Diffusion is a **passive process**. It does not require the cell to expend ATP. Instead, it results from the natural molecular motion of particles. A similar process occurs when water moves across a selectively permeable membrane.

Osmosis Is the Diffusion of Water

Osmosis is the net movement of water across a selectively permeable membrane in response to differences in solute concentration. Consider two solutions separated by a membrane that allows water to cross but does not allow the dissolved solute to cross. If one side contains more dissolved solute, that side contains proportionally **less water**. The side containing less solute contains proportionally **more water**.

Water therefore moves:

from the side with lower solute concentration toward the side with higher solute concentration.

Another way to remember this relationship is:

Water moves toward the region containing more dissolved solute.

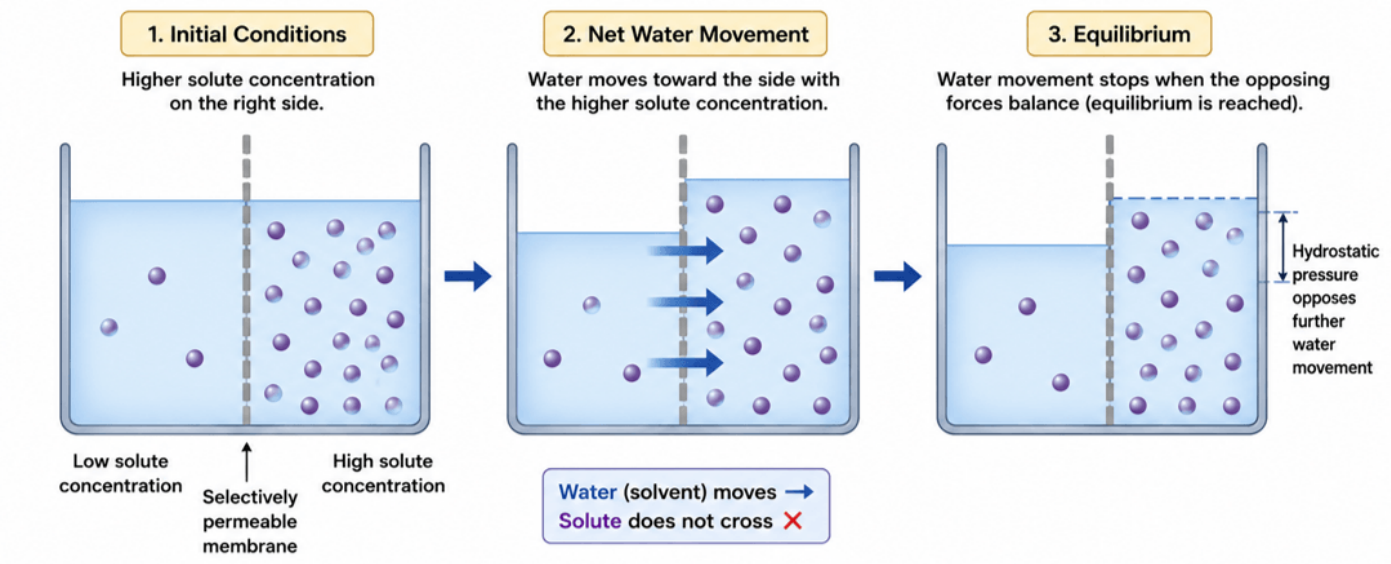


Figure 2: The Process of Osmosis. When two solutions of different solute concentrations are separated by a membrane that allows water—but not the solute—to cross, water moves toward the solution with the higher solute concentration. Net water movement continues until the system reaches equilibrium or another force opposes further movement.

Importantly, individual water molecules actually move across the membrane in **both directions**. The term *net movement* describes the overall result: more water molecules move toward the side with the higher concentration of nonpenetrating solute than move in the opposite direction.

Tonicity Describes the Effect of a Solution on a Cell

The movement of water across cell membranes can dramatically affect cell volume.

Tonicity describes how a surrounding solution affects the movement of water into or out of a cell and therefore affects the cell's volume.

Tonicity is always a **comparison** between two solutions—typically the solution outside the cell and the solution inside the cell.

The extracellular solution can be described as:

- **isotonic**
- **hypotonic**
- **hypertonic**

relative to the cell.

Isotonic Solutions

An **isotonic solution** has an effective concentration of dissolved solutes that produces no net movement of water into or out of the cell.

Water molecules continue to cross the membrane in both directions, but the rates of movement are balanced.

As a result, the cell maintains approximately the same volume.

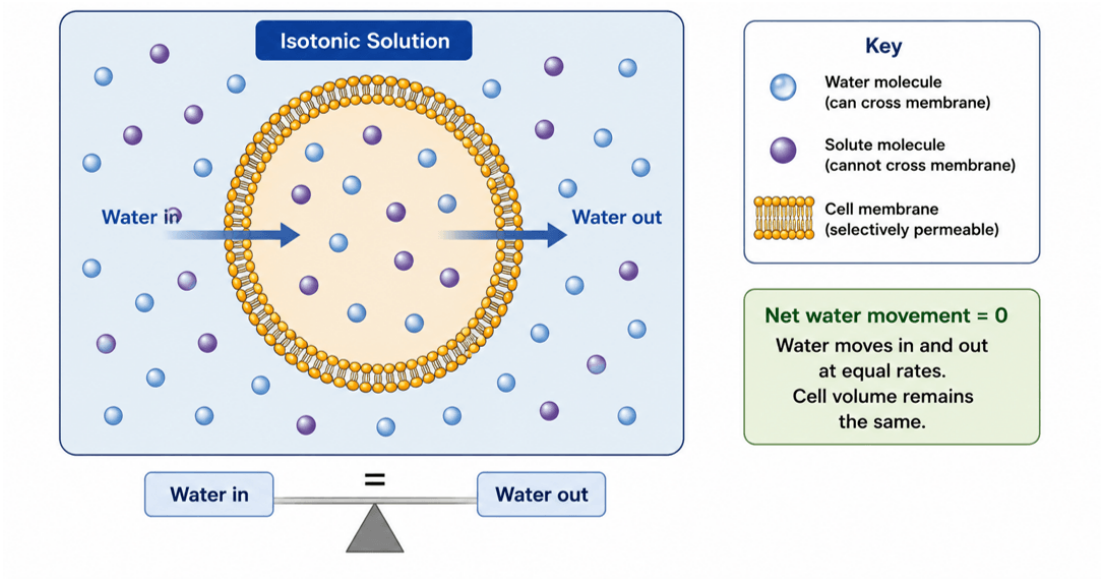


Figure 3: A Cell in an Isotonic Solution. In an isotonic environment, there is no net movement of water into or out of the cell. Water continues to move across the membrane in both directions, but the cell maintains its normal volume.

This is especially important for cells that lack a rigid cell wall, such as human red blood cells. A familiar healthcare example is **0.9% (m/v) NaCl**, commonly called **normal saline**. This solution is approximately isotonic with human blood plasma and is therefore widely used as an intravenous fluid.

Hypotonic Solutions

A **hypotonic solution** has a lower effective solute concentration than the fluid inside the cell. Because the solution outside the cell contains proportionally more water, there is a net movement of water **into the cell** by osmosis. The cell therefore swells. If an animal cell takes in enough water, its membrane may rupture. This process is called **lysis**. When a red blood cell ruptures due to excessive water uptake, the process is specifically called **hemolysis**.

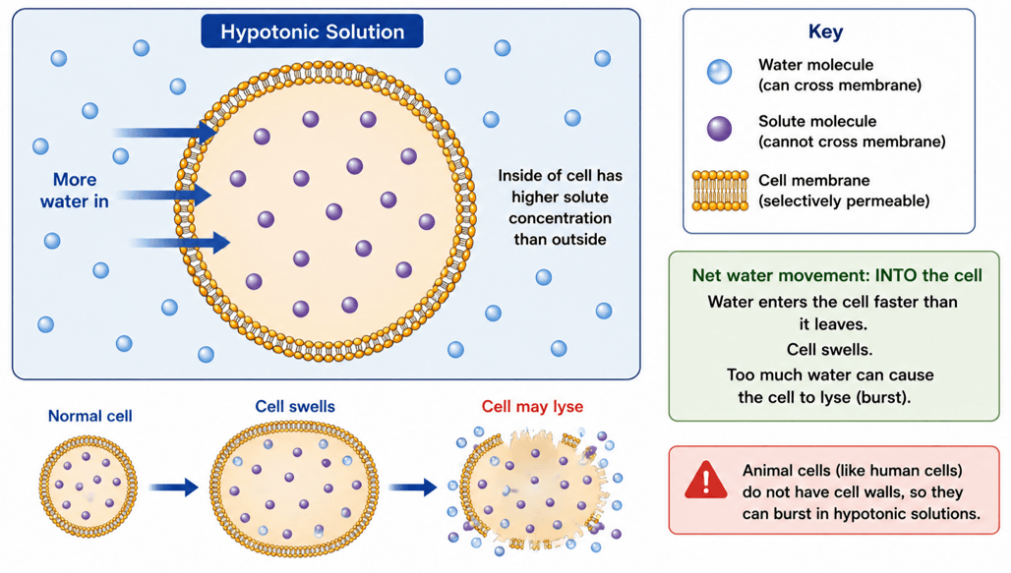


Figure 4: A Cell in a Hypotonic Solution. In a hypotonic environment, the surrounding solution has a lower effective solute concentration than the cell. Water moves into the cell by osmosis, causing the cell to swell. Excessive water uptake can cause an animal cell to lyse.

Hypertonic Solutions

A **hypertonic solution** has a higher effective solute concentration than the fluid inside the cell.

Water therefore undergoes net movement **out of the cell** toward the solution containing the greater concentration of solute.

As the cell loses water, its volume decreases.

In red blood cells, this shrinking produces a characteristic wrinkled appearance called **crenation**.

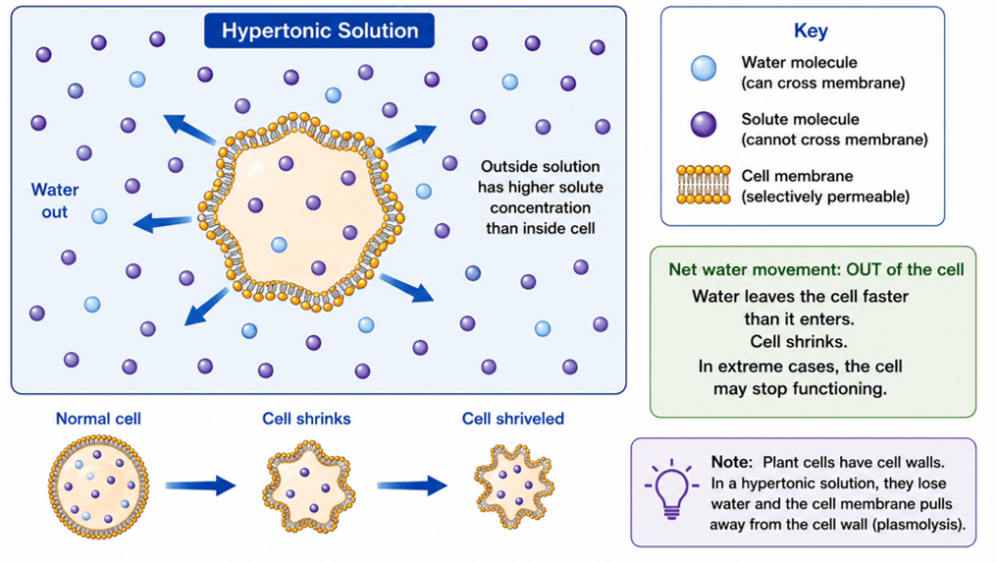


Figure 5: A Cell in a Hyptertonic Solution. In a hypertonic environment, the surrounding solution has a higher effective solute concentration than the cell. Water moves out of the cell by osmosis, causing the cell to shrink.

Comparing Tonicity

The effects of the three types of solutions can be summarized as follows:

Table 9.5A: Characteristics of Tonicity

Surrounding Solution	Relative Effective Solute Concentration	Net Movement of Water	Effect on an Animal Cell
Hypotonic	Lower than inside the cell	Into the cell	Cell swells; may lyse
Isotonic	Produces equal water movement	No net movement	Cell maintains normal volume
Hypertonic	Higher than inside the cell	Out of the cell	Cell shrinks

The concentration of dissolved solutes surrounding a red blood cell affects the direction of net water movement. In a hypotonic solution, water enters the cell and causes it to swell. In an isotonic solution, there is no net movement of water and the cell maintains its normal shape. In a hypertonic solution, water leaves the cell and the cell shrinks.

Why the Number of Dissolved Particles Matters

When considering osmosis, it is important to think about the **number of dissolved particles** in a solution—not simply the concentration of the original compound.

Recall from Section 9.1 that ionic compounds dissociate when they dissolve.

For example:

$$\mathrm{NaCl\,(s)} \longrightarrow \mathrm{Na^+\,(aq)} + \mathrm{Cl^-\,(aq)} \tag{9.5.1}$$

Each formula unit of NaCl produces **two dissolved ions**.

Glucose, in contrast, is a nonelectrolyte. It dissolves as intact molecules:

$$\mathrm{C_6H_{12}O_6\,(s)} \longrightarrow \mathrm{C_6H_{12}O_6\,(aq)} \tag{9.5.2}$$

Thus, one mole of glucose produces approximately one mole of dissolved particles, while one mole of NaCl produces approximately two moles of dissolved particles.

This means that two solutions with the same molarity do not necessarily contain the same total concentration of dissolved particles. This distinction becomes important when predicting how solutions will affect the movement of water across biological membranes.

Osmosis and Homeostasis

Cells can function properly only when their surrounding chemical environment is maintained within an appropriate range. A large change in the concentration of dissolved substances in extracellular fluid can cause water to enter or leave cells, changing their volume and potentially interfering with cellular function.

The body therefore carefully regulates both **water balance and solute concentrations**.

The kidneys play a major role in this regulation by controlling the amount of water and electrolytes retained in or eliminated from the body. Hormones such as **antidiuretic hormone (ADH)** and **aldosterone** help regulate these processes. This regulation is an example of **homeostasis**—the maintenance of a relatively stable internal environment. Maintaining appropriate solute concentrations is only one part of this challenge. The body must also carefully regulate the concentration of hydrogen ions, because even relatively small changes can alter **pH** and affect the structure and function of biological molecules. To understand how the body maintains pH, we first need to examine the chemistry of **acids and bases**.

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9.6: Acids, Bases and pH

The human body must regulate more than the concentrations of water, ions, and nutrients. It must also carefully control the concentration of **hydrogen ions (H⊕)** in its fluids.

Even relatively small changes in hydrogen ion concentration can affect the charge, shape, and function of biological molecules. Proteins are particularly sensitive to changes in pH because many amino acid side chains can gain or lose hydrogen ions. As we saw in Chapter 8, changes in the chemical environment surrounding an enzyme can alter its structure and activity.

Understanding this aspect of homeostasis requires us to examine the chemistry of **acids, bases, and pH**.

Acids and Bases

There are several useful ways to define acids and bases. An **acid** is a substance that can donate a hydrogen ion, H⊕, while a **base** is a substance that can accept a hydrogen ion. This definition is known as the **Brønsted-Lowry definition** of acids and bases. For example, hydrochloric acid (HCl) can transfer H⊕ to a water molecule:

$$\mathrm{HCl} + \mathrm{H_2O} \longrightarrow \mathrm{H_3O^+} + \mathrm{Cl^-} \tag{9.6.1}$$

In this reaction, HCl donates H⊕ and therefore acts as an **acid**. Water accepts H⊕ and therefore acts as a **base**. Notice that a free H⊕ ion does not normally exist by itself in an aqueous solution. Instead, it associates with a water molecule to form the **hydronium ion, H_3O⊕**. For this reason, acid concentrations in water are more accurately described in terms of H_3O⊕. However, H⊕ is frequently used as a convenient shorthand, particularly in biological chemistry.

Bases and Hydroxide Ions

Some bases directly release hydroxide ions (OH⊖) when they dissolve in water.

Sodium hydroxide, for example, dissociates completely:

$$\mathrm{NaOH\,(s)} \longrightarrow \mathrm{Na^+\,(aq)} + \mathrm{OH^-\,(aq)} \tag{9.6.2}$$

do not contain OH⊖ but instead produce OH⊖ by accepting H⊕ from water. Ammonia (NH_3), for example, acts as a base by accepting H⊕ from a water molecule:

$$\mathrm{NH_3} + \mathrm{H_2O} \rightleftharpoons \mathrm{NH_4^+} + \mathrm{OH^-} \tag{9.6.3}$$

Thus, bases can increase the concentration of OH⊖ in water either directly or indirectly.

Conjugate Acid-Base Pairs

When an acid donates H⊕, the substance that remains is called its **conjugate base**.

Likewise, when a base accepts H⊕, the resulting substance is called its **conjugate acid**.

Consider the reaction of acetic acid with water:

$$\mathrm{CH_3COOH} + \mathrm{H_2O} \rightleftharpoons \mathrm{H_3O^+} + \mathrm{CH_3COO^-} \tag{9.6.4}$$

Acetic acid, CH_3COOH, donates H⊕ and becomes acetate, CH_3COO⊖.

Therefore:

CH_3COOH / CH_3COO^- form a conjugate acid-base pair.

Water accepts H^+ and becomes H_3O^+, so:

H_2O / H_3O^+ form another conjugate acid-base pair.

Members of a conjugate acid-base pair differ by **one H^+**.

This relationship will become especially important when we examine **buffers** in the next section.

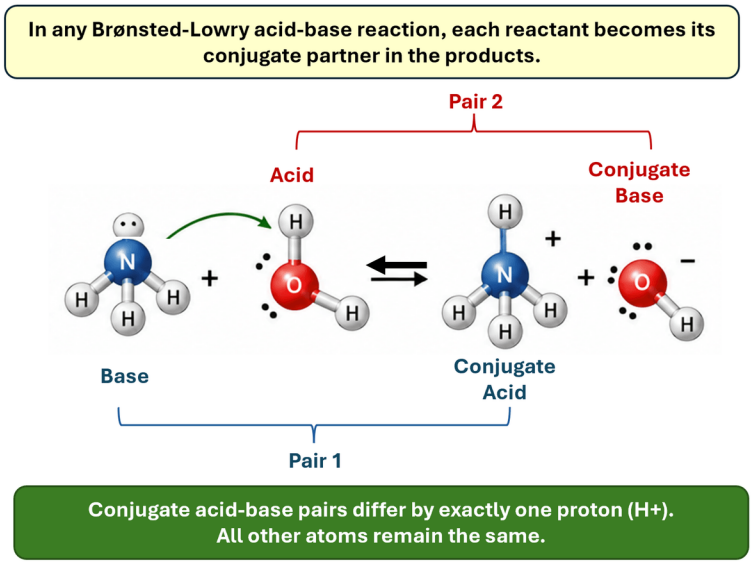


Figure 1: Conjugate Acid/Base Pairs differ by one H^+. In the reaction between ammonia and water, the lone pair of electrons on the nitrogen atom of ammonia is attracted to the partially positive hydrogen of a water molecule. Ammonia accepts H^+ from water to form the ammonium ion, NH_4^+, while water loses H^+ to form the hydroxide ion, OH^-. Thus, NH_3/NH_4^+ and H_2O/OH^- are conjugate acid-base pairs; the members of each pair differ by exactly one H^+. Because ammonia is a weak base, this reaction reaches an equilibrium in which only a small fraction of the ammonia molecules have accepted H^+ at any given time.

Strong and Weak Acids

Acids differ in the extent to which they transfer H^+ to water. A **strong acid** ionizes essentially completely in aqueous solution.

Hydrochloric acid is an example:

$$\mathrm{HCl + H_2O \longrightarrow H_3O^+ + Cl^-} \tag{9.6.5}$$

Because the reaction proceeds essentially completely, a single arrow is used.

A **weak acid**, in contrast, ionizes only partially.

Acetic acid is a weak acid:

$$\mathrm{CH_3COOH + H_2O \rightleftharpoons H_3O^+ + CH_3COO^-} \tag{9.6.6}$$

At any given time, most of the acetic acid molecules remain in their original molecular form, while only a fraction have donated H^+.

The double arrow indicates that the reaction is **reversible** and establishes an equilibrium.

Strong and Weak Bases

Bases can also be classified as strong or weak. **Strong bases** such as NaOH dissociate essentially completely in water, producing OH^- ions.

Weak bases react only partially with water. Ammonia is a common example:

$$\mathbf{NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-} \tag{9.6.7}$$

The distinction between **strong and weak** describes the extent of ionization or reaction with water. It does **not** describe how concentrated the solution is. A dilute solution of a strong acid may contain less acid overall than a concentrated solution of a weak acid. Thus:

strength and concentration are different properties.

Water Can Act as Both an Acid and a Base

Water is unusual because it can act as either an acid or a base depending on what it reacts with.

Water molecules can even react with one another. In this process, one water molecule donates H^+ while another accepts it:

$$\mathbf{2\,H_2O \rightleftharpoons H_3O^+ + OH^-} \tag{9.6.8}$$

This process is called the **autoionization of water**.

In pure water at approximately 25°C, the concentrations of H_3O^+ and OH^- are equal:

$$\mathbf{[H_3O^+] = [OH^-] = 1.0 \times 10^{-7}\ M} \tag{9.6.9}$$

A solution in which these concentrations are equal is **neutral**.

If:

$$\mathbf{[H_3O^+] > [OH^-]} \tag{9.6.10}$$

the solution is **acidic**.

If:

$$\mathbf{[OH^-] > [H_3O^+]} \tag{9.6.11}$$

the solution is **basic**.

The pH Scale

Hydrogen ion concentrations in aqueous solutions can vary over many orders of magnitude. Writing these concentrations repeatedly in scientific notation would be cumbersome, so chemists use the **pH scale**.

pH is related to the hydronium ion concentration by:

$$\mathbf{pH = -\log[H_3O^+]} \tag{9.6.12}$$

At approximately 25°C:

- a solution with **pH < 7** is acidic
- a solution with **pH = 7** is neutral
- a solution with **pH > 7** is basic

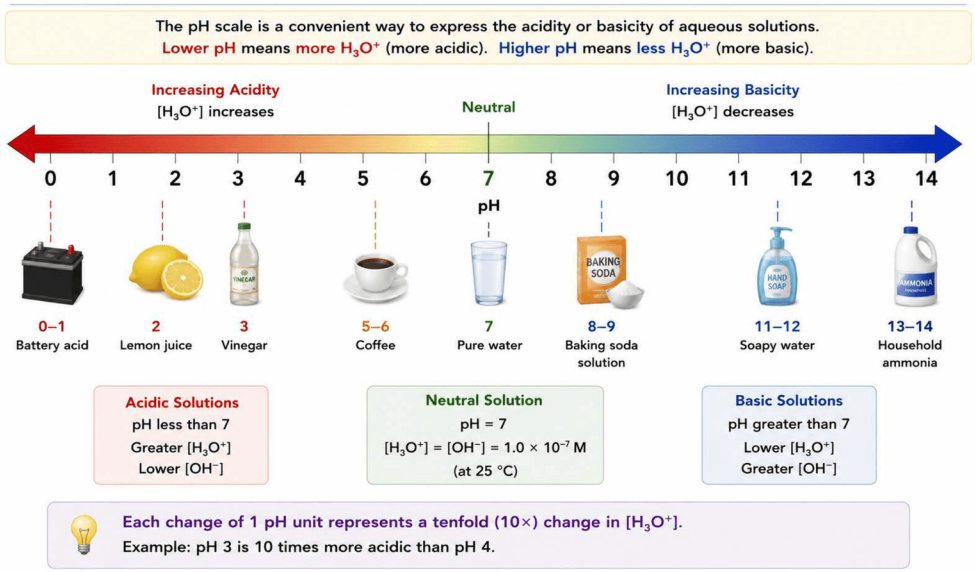


Figure 2: The pH Scale. The pH scale describes the acidity or basicity of an aqueous solution. Lower pH values correspond to higher concentrations of H_3O^+, while higher pH values correspond to lower concentrations of H_3O^+. At approximately 25°C, pure water has a pH of 7 and is neutral.

Calculating pH

Suppose a solution has a hydronium ion concentration of:

$$[\mathbf{H_3O^+}] = \mathbf{1.0 \times 10^{-3}\ M} \tag{9.6.13}$$

The pH is:

$$\mathbf{pH} = -\mathbf{log}(\mathbf{1.0 \times 10^{-3}}) \tag{9.6.14}$$

Therefore:

$$\mathbf{pH = 3.00} \tag{9.6.15}$$

The solution is acidic.

If instead:

$$[\mathbf{H_3O^+}] = \mathbf{1.0 \times 10^{-9}\ M} \tag{9.6.16}$$

then:

$$\mathbf{pH = 9.00} \tag{9.6.17}$$

and the solution is basic.

The pH Scale Is Logarithmic

An important feature of the pH scale is that it is **logarithmic**, not linear.

A change of one pH unit represents a **tenfold change in H_3O^+ concentration**.

For example:

$$\mathrm{pH\ 3} \rightarrow \mathrm{pH\ 2} \tag{9.6.18}$$

represents a tenfold **increase** in H_3O^+ concentration.

A change from pH 3 to pH 1 represents a hundredfold increase:

$$10 \times 10 = 100 \tag{9.6.19}$$

This is why seemingly small numerical changes in pH can represent substantial changes in the chemical environment.

Acids and Bases Neutralize One Another

When an acid and a base react, H_3O^+ and OH^- can combine to form water.

The net ionic reaction can be represented as:

$$\mathrm{H_3O^+ + OH^- \longrightarrow 2\,H_2O} \tag{9.6.20}$$

This type of reaction is called an **acid-base neutralization reaction**.

For example, hydrochloric acid and sodium hydroxide react to form sodium chloride and water:

$$\mathrm{HCl\,(aq) + NaOH\,(aq) \longrightarrow NaCl\,(aq) + H_2O\,(l)} \tag{9.6.21}$$

Neutralization reactions are important not only in the laboratory but also in biological systems, where acids and bases are constantly being produced through metabolism.

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pH in the Human Body

Different regions of the human body operate at very different pH values. The stomach, for example, contains highly acidic gastric fluid that assists in digestion. In contrast, blood must remain within a much narrower range near neutral pH.

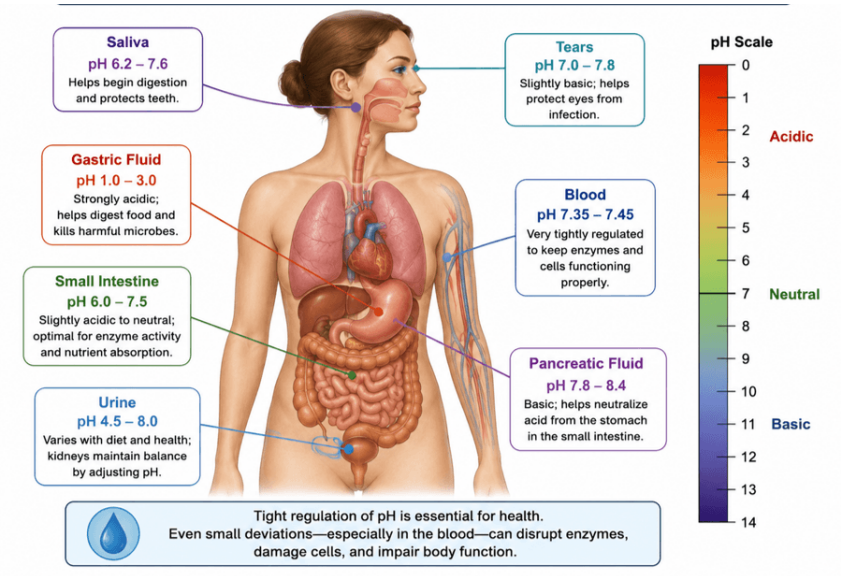


Figure 3: pH in the Human Body. Different regions of the human body maintain different chemical environments. Gastric fluid is strongly acidic, while blood is maintained within a narrow range near pH 7.4. These differences reflect the specialized chemical functions of each environment.

Maintaining an appropriate pH is essential because changes in hydrogen ion concentration can alter intermolecular interactions, protein structure, enzyme activity, membrane function, and many other biological processes. The challenge is that metabolism continually produces substances that can increase or decrease H_3O^+ concentration. If every small addition of acid or base caused a large change in pH, maintaining a stable internal environment would be extremely difficult. Fortunately, biological fluids contain chemical systems that resist sudden changes in pH.

These systems are called **buffers**.

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9.7: Buffers and the Maintenance of pH

Living cells continually carry out chemical reactions that can produce acids or bases. Yet many biological processes can function properly only within a relatively narrow range of pH. How does the body prevent every small addition of acid or base from causing a dramatic change in pH?

One important part of the answer is the use of **buffers**. A **buffer** is a solution that resists large changes in pH when relatively small amounts of acid or base are added. Buffers do not prevent pH from changing completely. Instead, they reduce the magnitude of the change. Buffers are especially important in biological systems because changes in pH can alter protein structure, enzyme activity, membrane function, and many other cellular processes.

What Is in a Buffer?

A buffer generally contains appreciable amounts of a **weak acid and its conjugate base** or a **weak base and its conjugate acid**.

For example, a buffer could contain the weak acid acetic acid, CH_3COOH, together with its conjugate base, acetate, CH_3COO^-.

Recall from Section 9.6 that these two substances differ by one H^+:

$$\mathbf{CH_3COOH \rightleftharpoons H^+ + CH_3COO^-} \tag{9.7.1}$$

The weak acid can donate H^+, while its conjugate base can accept H^+.

Having both members of the conjugate pair present allows the solution to respond to the addition of either an acid or a base.

How a Buffer Responds to Added Acid

Suppose a small amount of acid is added to an acetate buffer. The added acid increases the amount of H_3O^+ in the solution. The conjugate base component of the buffer, CH_3COO^-, can accept the added H^+.

The reaction can be represented as:

$$\mathbf{CH_3COO^- + H_3O^+ \longrightarrow CH_3COOH + H_2O} \tag{9.7.2}$$

Instead of allowing all of the added H_3O^+ to remain free in solution, the acetate ions convert much of it into the weak acid CH_3COOH.

As a result, the H_3O^+ concentration increases much less than it would in an unbuffered solution.

The pH therefore decreases only slightly.

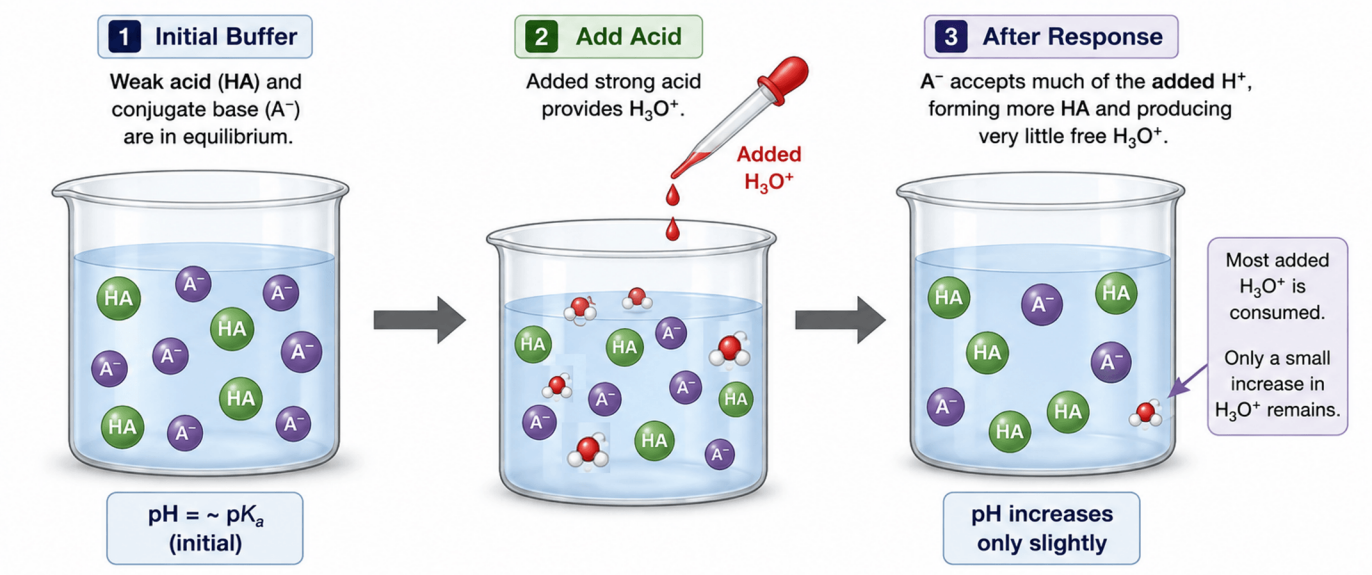


Figure 9.7.1**: How a Buffer Responds to Added Acid**. When acid is added to a buffer, the conjugate base component accepts much of the added H⃝. This converts the conjugate base into the weak acid and limits the increase in H_3O⃝ concentration. Thus, only a small change in pH occurs.

How a Buffer Responds to Added Base

Now suppose a small amount of base is added to the same buffer.

The added OH⃝ can remove H⃝ from the weak acid component of the buffer. Acetic acid therefore donates H⃝, converting the added OH⃝ into water:

$$\mathbf{CH_3COOH + OH^- \longrightarrow CH_3COO^- + H_2O} \tag{9.7.3}$$

The added OH⃝ is therefore largely consumed rather than remaining free in solution.

As a result, the pH increases only slightly.

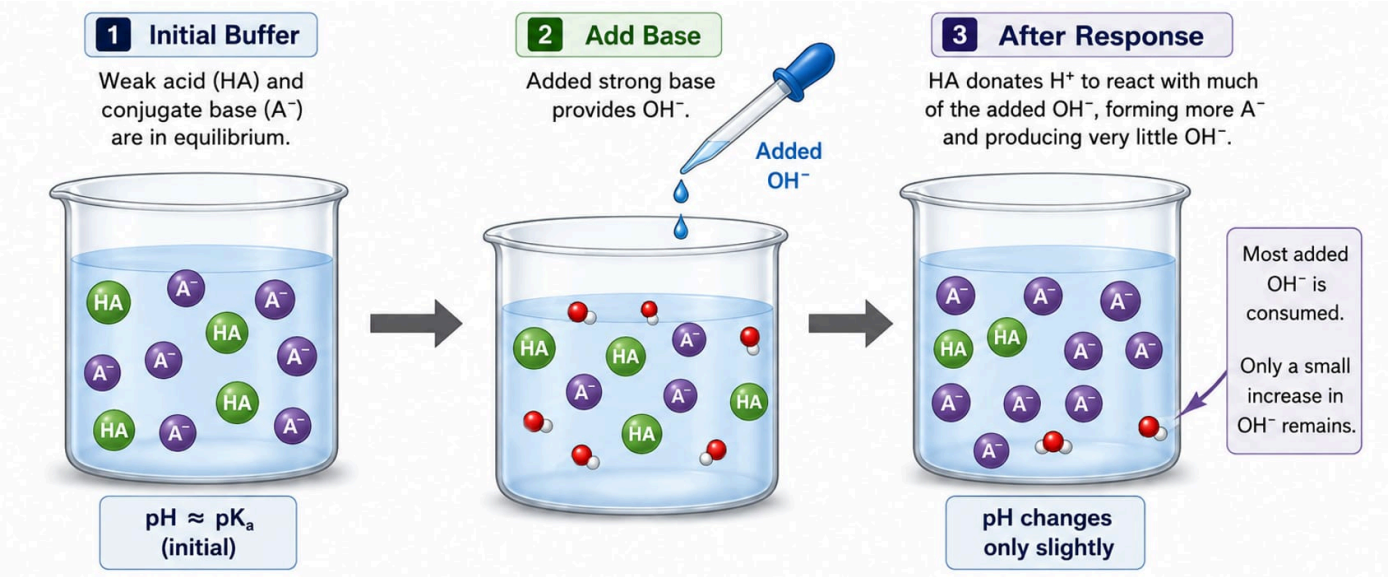


Figure 9.7.2: How a Buffer Responds to Added Base. When base is added to a buffer, the weak acid component donates H⊕ to react with much of the added OH⊕. The weak acid is converted into its conjugate base, limiting the change in pH.

The two components of the buffer therefore work together:

The conjugate base responds to added acid.

The weak acid responds to added base.

Buffers Do Not Keep pH Constant

It is important to recognize that a buffer does **not** maintain an absolutely constant pH. Adding acid to a buffer still lowers the pH, and adding base still raises the pH. The difference is that the change is **much smaller** than it would be without the buffer.

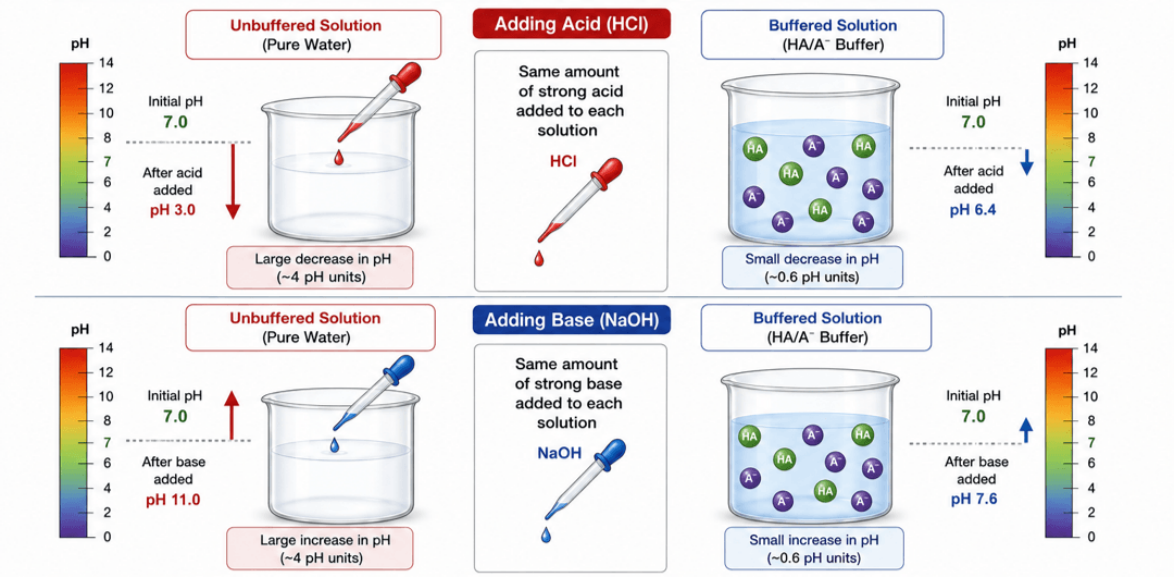


Figure 9.7.3: Buffered vs Unbuffered Solutions. When the same amount of acid or base is added to buffered and unbuffered solutions, the buffered solution undergoes a much smaller change in pH. Buffers resist changes in pH; they do not prevent them completely.

Buffers Have a Limited Capacity

A buffer can neutralize only a limited amount of added acid or base. As acid is added, the conjugate base component of the buffer is gradually consumed. If enough acid is added, too little conjugate base remains to absorb additional H⊕ effectively.

Likewise, continued addition of base eventually consumes the weak acid component of the buffer.

Once a buffer has exceeded its ability to absorb additional acid or base, the pH can begin to change rapidly. This limit is called the **buffer capacity**. A buffer therefore works best when appreciable amounts of **both members of the conjugate acid-base pair** are present.

The Bicarbonate Buffer System

One of the most important buffer systems in the human body involves **carbonic acid (H_2CO_3)** and **bicarbonate ($HCO_3^⊕$)**.

These substances form a conjugate acid-base pair:

$$\mathbf{H_2CO_3 \rightleftharpoons H^+ + HCO_3^-} \tag{9.7.4}$$

The bicarbonate buffer system is particularly important in the blood.

If excess acid is added, bicarbonate can accept H⃝:

$$\mathbf{HCO_3^- + H^+ \longrightarrow H_2CO_3} \tag{9.7.5}$$

If excess base is added, carbonic acid can donate H⃝:

$$\mathbf{H_2CO_3 + OH^- \longrightarrow HCO_3^- + H_2O} \tag{9.7.6}$$

In this way, the carbonic acid/bicarbonate pair helps reduce sudden changes in blood pH.

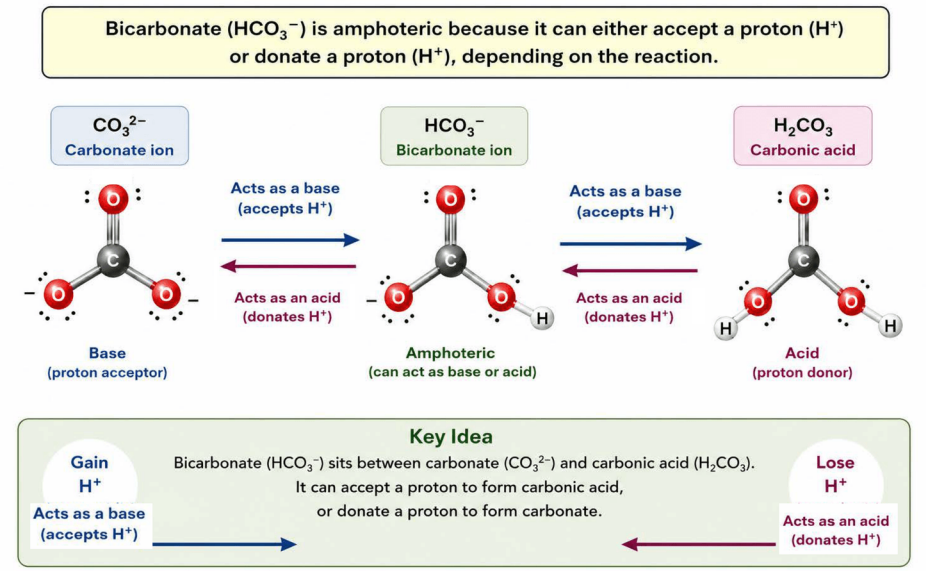


Figure 9.7.4: Bicarbonate Can Act as Either an Acid or a Base. The bicarbonate ion (HCO_3⃝) is **amphoteric**, meaning that it can act as either a Brønsted–Lowry acid or base depending on its chemical environment. Bicarbonate can accept H⃝ to form carbonic acid (H_2CO_3), acting as a base, or donate H⃝ to form carbonate (CO_3^{2-}⃝), acting as an acid. This ability to accept or donate H⃝ contributes to the important role of bicarbonate in acid-base balance and biological buffer systems.

Carbon Dioxide Connects the Buffer to Respiration

The bicarbonate buffer system has another important feature: carbonic acid is chemically connected to carbon dioxide and water.

$$\mathbf{CO_2 + H_2O \rightleftharpoons H_2CO_3} \tag{9.7.7}$$

Carbonic acid can then transfer H⃝ to water:

$$\mathbf{H_2CO_3 + H_2O \rightleftharpoons H_3O^+ + HCO_3^-} \tag{9.7.8}$$

These reactions connect **carbon dioxide concentration directly to acid-base chemistry**.

Recall from Chapter 8 that carbon dioxide is produced during the oxidation of carbon-containing molecules in cellular respiration. CO_2 enters the blood and can participate in the bicarbonate buffer system.

Because carbon dioxide can also be removed from the body through the lungs, breathing provides one mechanism for helping regulate acid-base balance.

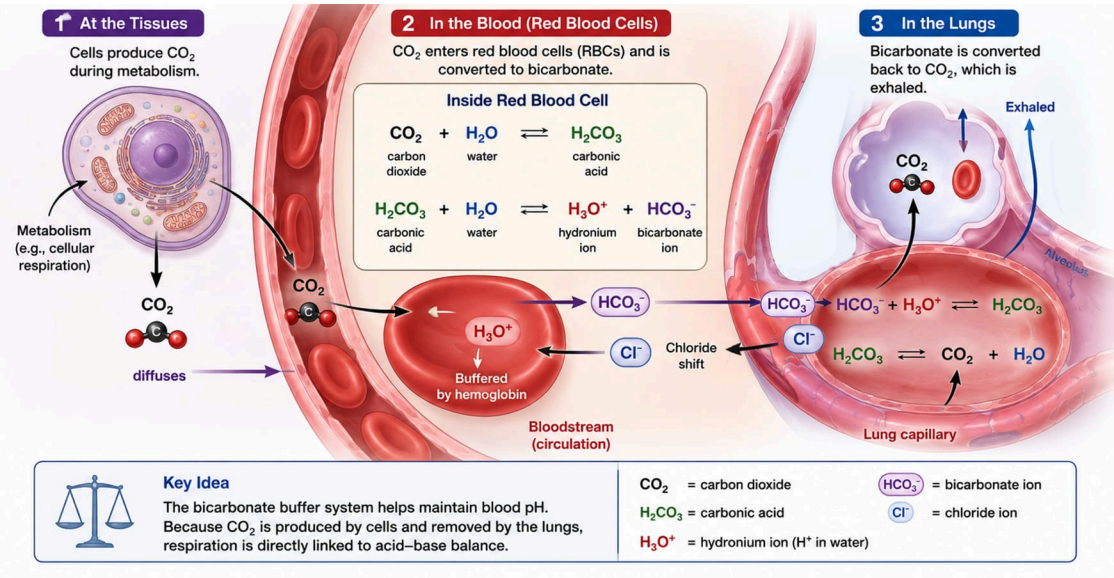


Figure 9.7.5: Carbon Dioxide and the Bicarbonate Buffer System. Carbon dioxide produced by cellular metabolism can enter the blood and react with water to form carbonic acid. Carbonic acid can then form hydronium and bicarbonate ions. Because CO_2 can be removed through the lungs, respiration is directly connected to the regulation of blood pH.

Blood pH Is Carefully Regulated

Normal arterial blood is maintained within a narrow pH range of approximately **7.35–7.45**. Although this range may appear small, recall that the pH scale is logarithmic. Even modest changes in pH represent substantial changes in $H_3O^⊕$ concentration and can alter the function of proteins, enzymes, and cells. A blood pH below the normal range is described as **acidemia**, while a blood pH above the normal range is described as **alkalemia**.

The bicarbonate buffer system provides an immediate chemical defense against changes in pH, but buffers alone cannot maintain blood pH indefinitely. The body must also regulate the substances involved in the buffer system.

Two organ systems are particularly important:

- The **lungs** regulate the removal of CO_2.
- The **kidneys** regulate the removal of $H^⊕$ and the conservation or production of $HCO_3^⊕$.

Together, chemical buffers, the respiratory system, and the kidneys maintain acid-base homeostasis.

Buffers Are an Example of Chemical Homeostasis

The bicarbonate buffer system illustrates an important principle that extends throughout this chapter.

Homeostasis does not mean that the internal environment of the body never changes. Instead, biological systems continually respond to change in ways that keep important chemical conditions within acceptable ranges. Water moves across membranes in response to differences in solute concentration. The kidneys adjust water and electrolyte balance. Buffers respond to acids and bases. The lungs alter CO_2 removal. Hormones regulate the concentration of nutrients such as glucose.

All of these processes help maintain the chemical environment required for cells to function. In the final section of this chapter, we will bring these ideas together and examine **homeostasis as the regulation of the body's internal chemical environment**.

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9.8: Homeostasis- Maintaining the Chemical Environment of the Body

Throughout this chapter, we have examined several properties of aqueous solutions that are essential for life. Cells require appropriate concentrations of water and dissolved substances. Differences in solute concentration influence the movement of water across cell membranes. Hydrogen ion concentration determines pH, and buffers help resist sudden changes in pH. These concepts are connected by one central biological challenge:

Cells can function properly only when their chemical environment remains within an appropriate range.

The processes that maintain this relatively stable internal environment are collectively known as **homeostasis**.

Homeostasis Is a Dynamic Process

Homeostasis does not mean that conditions inside the body remain perfectly constant. The internal environment changes continuously. When you drink water, the amount of water entering the body increases. When you eat a meal, concentrations of glucose, amino acids, and other nutrients in the blood change. Cellular metabolism consumes nutrients and oxygen while producing carbon dioxide, water, acids, and other metabolic products. Exercise increases energy demand, heat production, and carbon dioxide production.

The body must continually respond to these changes. Homeostasis is therefore better described as a **dynamic balance** in which physiological systems detect changes and respond in ways that keep important variables within acceptable ranges.

Examples of regulated variables include:

- body temperature
- blood glucose concentration
- water balance
- electrolyte concentrations
- blood pressure
- blood pH

From a chemical perspective, many of these variables ultimately involve controlling the **concentration of substances in aqueous solution**.

Negative Feedback Maintains Homeostasis

Most homeostatic systems operate through **negative feedback**. In a negative feedback system, a change in a regulated variable triggers responses that **oppose the original change**.

A simplified negative feedback system contains three basic components:

1. A **sensor** detects a change.
2. A **control center** interprets the information and initiates a response.
3. An **effector** produces a response that moves the regulated variable back toward its normal range.

A household thermostat provides a useful analogy. If room temperature falls below the thermostat setting, the heating system turns on. As the room warms, the original change is reversed. Once the desired temperature is reached, the heating system turns off.

The human body uses similar feedback principles to regulate its internal chemical environment.

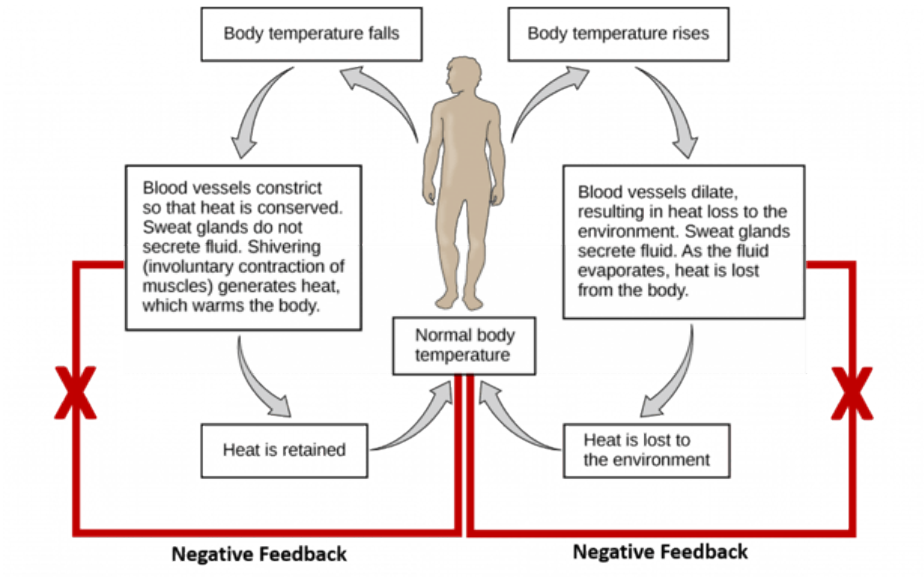


Figure 1: Negative Feedback and Homeostasis. Negative feedback opposes changes in a regulated variable. When a variable moves away from its normal range, the body detects the change and activates responses that move the variable back toward that range. In the example above, if the core temperature rises above (right hand side) or drops below (left hand side) the setpoint, internal biological responses are initiated to return the core temperature back to the setpoint range. Once this is achieved, negative feedback loops are initiated to down regulate the internal biological responses so that the core temperature doesn't overshoot the required change. This Figure is adapted from: The Kahn Academy.

Maintaining Water and Electrolyte Balance

Water and electrolyte concentrations provide one example of chemical homeostasis.

As we saw in Section 9.5, differences in effective solute concentration can cause water to move into or out of cells by osmosis. Large changes in extracellular solute concentration could therefore cause cells to swell or shrink. The body limits these changes by regulating both **water and dissolved ions**.

The kidneys continually filter the blood and adjust how much water and various ions are returned to the bloodstream or eliminated in urine. Hormones help coordinate these responses.

For example, **antidiuretic hormone (ADH)** promotes water conservation by the kidneys when the body needs to retain water. **Aldosterone** promotes Na^+ retention and K^+ excretion by the kidneys, helping regulate electrolyte and fluid balance. These processes help maintain an extracellular environment in which cells can function normally.

Maintaining Acid-Base Balance

The concentration of H_3O^+ must also be carefully controlled. As we saw in Sections 9.6 and 9.7, blood pH is maintained within a narrow range near pH 7.4. Changes in pH can alter the charge and interactions of biological molecules and interfere with protein and enzyme function. Acid-base homeostasis depends on several systems working together.

Chemical buffers respond rapidly to added acids and bases. For example:

- The **lungs** regulate the removal of CO_2, which is chemically connected to the bicarbonate buffer system.
- The **kidneys** regulate the elimination of H^+ and the conservation or production of HCO_3^-.

These mechanisms operate on different timescales but work together to maintain the chemical environment of the blood.

Homeostasis therefore often depends not on a single reaction or organ, but on the coordination of multiple chemical and physiological processes.

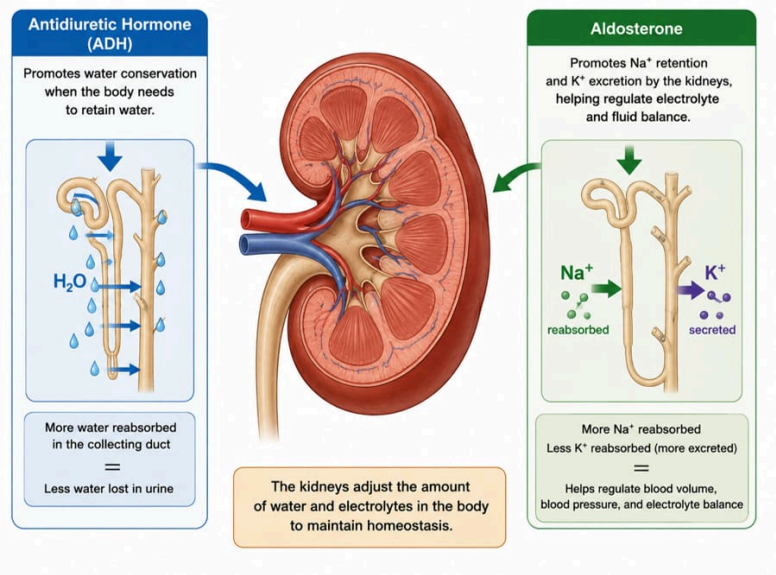


Figure 2: Hormonal Regulation of Water and Electrolyte Balance by the Kidneys. The kidneys help maintain homeostasis by adjusting the amount of water and dissolved ions retained by the body. **Antidiuretic hormone (ADH)** increases water reabsorption by the kidneys, reducing the amount of water lost in urine. **Aldosterone** increases Na^+ reabsorption while promoting K^+ secretion and excretion. Together, these hormonal responses help regulate fluid volume, electrolyte concentrations, and the chemical environment of the body.

Maintaining Blood Glucose Concentration

Blood glucose provides another excellent example of homeostasis. Glucose is an important fuel for cellular metabolism. Recall from Chapter 8 that glucose can be oxidized during cellular respiration, transferring energy that can ultimately be captured in ATP. However, glucose must first be transported through the bloodstream to tissues throughout the body. This requires glucose to be maintained within an appropriate concentration range.

After a carbohydrate-containing meal, digestion and absorption cause the concentration of glucose in the blood to rise. This change triggers a negative-feedback response involving the hormone **insulin**. Insulin is released from **beta cells of the pancreas** in response to elevated blood glucose. Insulin binds to receptors on target cells and promotes processes that lower blood glucose concentration. These responses include increased glucose uptake by many cells and increased storage of glucose as **glycogen**, particularly in the liver and skeletal muscle. As glucose is removed from the bloodstream, blood glucose concentration falls back toward its regulated range.

What Happens When Blood Glucose Falls?

The body must also respond when blood glucose concentration becomes too low. During fasting or between meals, blood glucose concentration begins to decrease. In response, **alpha cells of the pancreas** release the hormone **glucagon**. Glucagon signals the liver to increase the release of glucose into the bloodstream, including through the breakdown of stored glycogen. Blood glucose concentration therefore rises back toward its regulated range.

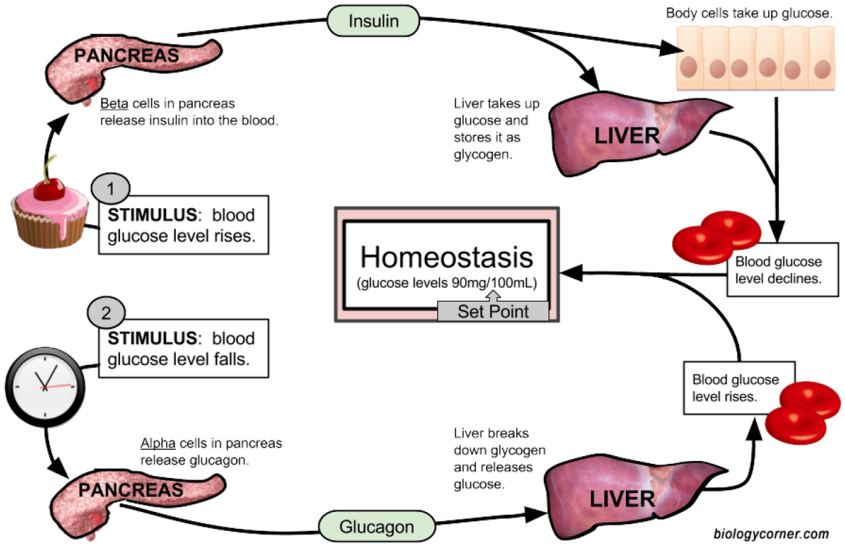


Figure 3: Insulin and Glucagon as Opposing Signals. Insulin and glucagon participate in a negative-feedback system that helps regulate blood glucose concentration. (1) Insulin is released when blood glucose rises and promotes glucose uptake and storage. (2) Glucagon is released when blood glucose falls and promotes the release of glucose into the bloodstream. Figure is by: Shannan Muskopf from Biologycorner.com.

Notice the pattern:

High blood glucose → insulin → blood glucose decreases.

Low blood glucose → glucagon → blood glucose increases.

The two responses oppose the original change and help maintain glucose homeostasis. Over the course of a day, blood glucose levels will fluctuate modestly around the homeostatic set point (Figure 9.8.4). As meals are eaten, this triggers a rise in blood glucose that is counteracted by the secretion of insulin. In between meals, blood glucose levels fall, and glucagon is released by the pancreas to signal to the liver to release glucose back into the blood stream.

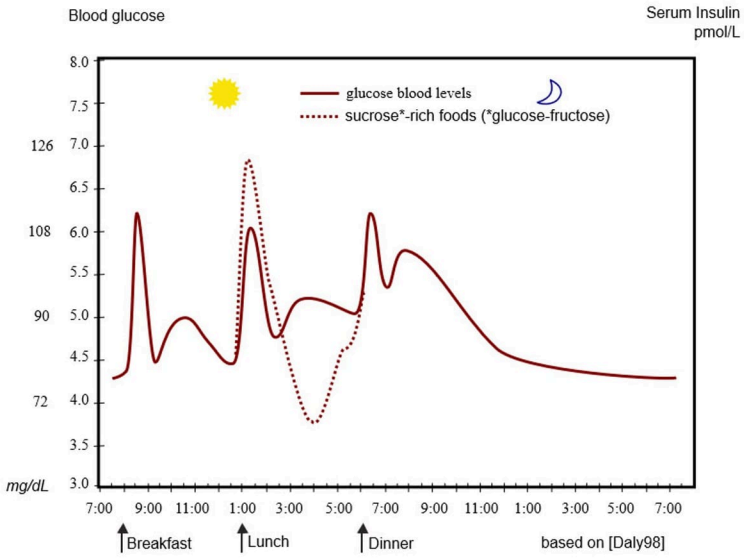


Figure 4: Homeostasis of Glucose Metabolism. This image illustrates glucose metabolism over the course of a day. Homeostasis may become imbalanced if the pancreas is overly stressed, making it unable to balance glucose metabolism. This

can lead to diabetes.

Diabetes: When Glucose Homeostasis Is Disrupted

Diabetes mellitus is a group of metabolic disorders characterized by persistent elevation of blood glucose. The two most common forms are **type 1 diabetes** and **type 2 diabetes**.

In **type 1 diabetes**, the insulin-producing beta cells of the pancreas are destroyed through an autoimmune process. As a result, the body produces little or no insulin. Without sufficient insulin signaling, blood glucose cannot be regulated normally.

In **type 2 diabetes**, insulin is generally still produced, particularly early in the disease, but target tissues become less responsive to its signal. This reduced responsiveness is called **insulin resistance**. Over time, the pancreas may also become less able to produce sufficient insulin to compensate.

Although the underlying mechanisms differ, both conditions interfere with the negative-feedback system that normally regulates blood glucose concentration. The result is **hyperglycemia**, an abnormally high concentration of glucose in the blood.

Concentration Connects Diabetes Back to Solution Chemistry

It is worth recognizing that the phrase **high blood glucose** describes a solution property. Blood plasma is an aqueous solution, and glucose is one of its dissolved solutes. Hyperglycemia therefore literally means that the **concentration of glucose in the blood is too high**. This brings us directly back to the chemistry introduced earlier in this chapter.

If glucose concentration becomes sufficiently high, the kidneys cannot completely recover all of the filtered glucose. Glucose then remains in the urine. The increased concentration of dissolved solute in the forming urine affects the movement of water by **osmosis**, causing more water to remain in the urine and be eliminated from the body.

This helps explain two classic signs associated with uncontrolled diabetes:

- **polyuria** — increased urination
- **polydipsia** — increased thirst

Thus, a disruption in glucose regulation can also disrupt water balance.

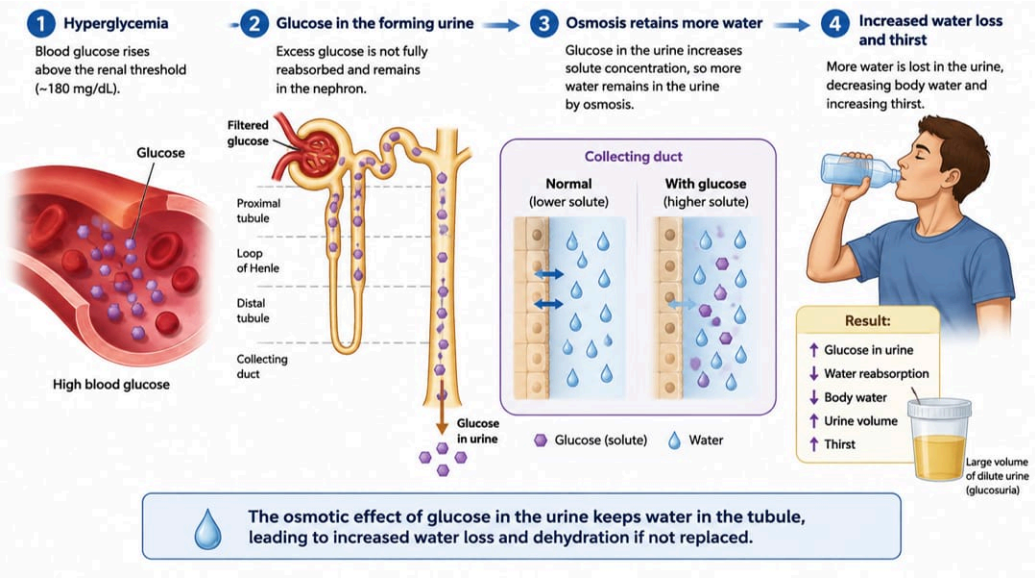


Figure 5: Hyperglycemia, Osmosis, and Water Loss. When blood glucose becomes sufficiently elevated, glucose can remain in

the forming urine. The increased solute concentration retains more water in the urine through osmotic effects, increasing water loss from the body and contributing to increased thirst.

This is a powerful example of how the chemical concepts in this chapter are interconnected:

concentration → osmosis → water balance → homeostasis.

Homeostasis Requires Energy and Communication

Maintaining a stable internal environment is not a passive process. Cells and organs must continually communicate, transport substances, regulate chemical reactions, and move materials against concentration gradients.

Many of these processes require energy. The ATP produced through the metabolic pathways discussed in Chapter 8 helps power the cellular processes required to maintain ion gradients, transport molecules, synthesize and release signaling molecules, and carry out other forms of cellular work.

Homeostasis therefore depends on the connection between **energy, chemical reactions, molecular interactions, and solution chemistry**.

Chemistry and the Maintenance of Life

Throughout this textbook, we have examined matter from increasingly complex perspectives.

Atoms combine through chemical bonds to form molecules. Molecular shape, polarity, and intermolecular forces determine how those molecules interact. Organic functional groups influence the properties and reactions of carbon-containing compounds. Biological molecules participate in enzyme-catalyzed reactions that transfer matter and energy. Those reactions occur within aqueous environments whose composition must be carefully controlled.

The human body is therefore not a static collection of molecules. It is a dynamic chemical system. Every moment, substances dissolve, diffuse, react, bind, separate, transfer electrons, gain or lose hydrogen ions, and move between compartments. Homeostasis coordinates these processes so that the chemical environment required for life remains within workable limits.

In this sense, homeostasis is not separate from chemistry.

Homeostasis is chemistry under continuous regulation.

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9.9: Chapter Summary

The human body is an aqueous chemical system. Cells depend on carefully regulated concentrations of water, ions, nutrients, acids, bases, and other dissolved substances. The maintenance of this internal chemical environment, known as **homeostasis**, provides the conditions necessary for cellular reactions and biological processes to occur.

9.1 The Chemistry of Solutions

A **solution** is a homogeneous mixture containing one or more solutes dissolved in a solvent. The **solvent** is the component present in the greatest amount, while a **solute** is a substance dissolved in the solvent.

Many biological solutions are **aqueous solutions**, meaning that water is the solvent. Because water is polar, it interacts strongly with ions and polar molecules.

When ionic compounds such as NaCl dissolve, the ions separate and become surrounded by water molecules in a process called **hydration**. Polar molecular compounds such as glucose can also dissolve in water but remain as intact molecules.

Substances that produce ions in solution are **electrolytes**. Strong electrolytes produce ions essentially completely, while weak electrolytes produce ions only partially. **Nonelectrolytes**, such as glucose, dissolve without forming ions.

Important biological electrolytes include Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, and HCO_3^-.

9.2 Solubility and “Like Dissolves Like”

Solubility describes the maximum amount of a solute that can dissolve in a particular solvent under specified conditions.

Solubility depends largely on intermolecular attractions between solute and solvent particles.

The general principle **“like dissolves like”** predicts that:

- polar and ionic substances tend to dissolve in polar solvents
- nonpolar substances tend to dissolve in nonpolar solvents

Water can dissolve many ionic and polar substances because it can form ion–dipole interactions, hydrogen bonds, and other favorable intermolecular attractions.

Liquids that mix completely are **miscible**, while liquids that separate into distinct phases are **immiscible**.

Amphipathic molecules contain both hydrophilic and hydrophobic regions. Phospholipids are biologically important amphipathic molecules whose behavior in water contributes to the formation of cell membranes.

An **unsaturated solution** can dissolve additional solute, while a **saturated solution** contains the maximum amount of dissolved solute under the existing conditions.

9.3 Measuring Solution Concentration

Concentration describes the amount of solute present in a given amount of solution.

Molarity (M) expresses concentration as moles of solute per liter of solution.

$$M = \frac{\text{moles of solute}}{\text{liters of solution}} \tag{9.9.1}$$

Percent concentration expresses the amount of solute per 100 parts of solution.

$$\% \text{ concentration} = \frac{\text{amount of solute}}{\text{amount of solution}} \times 100 \tag{9.9.2}$$

Common forms include:

- **mass/mass (m/m)%** = grams solute per 100 g solution
- **mass/volume (m/v)%** = grams solute per 100 mL solution
- **volume/volume (v/v)%** = mL solute per 100 mL solution

Very small concentrations may be expressed in **parts per million (ppm)** or **parts per billion (ppb)**.

The amount of solute and the concentration of a solution are not the same. The same amount of solute can have different concentrations depending on the total volume of solution.

9.4 Dilution of Solutions

A **dilution** decreases the concentration of a solution by adding additional solvent.

During dilution:

- the amount of solute remains constant
- the solution volume increases
- the solute concentration decreases

This relationship gives the dilution equation:

$$M_1V_1 = M_2V_2 \tag{9.9.3}$$

where M_1 and V_1 describe the initial solution and M_2 and V_2 describe the final diluted solution.

More generally:

$$C_1V_1 = C_2V_2 \tag{9.9.4}$$

can be used with other concentration units as long as the concentration units are consistent.

Importantly, V_2 represents the **total final volume**, not the amount of solvent added.

9.5 Osmosis and Tonicity

A **concentration gradient** exists when the concentration of a substance differs between two regions.

Diffusion is the net movement of particles from a region of higher concentration toward a region of lower concentration.

Osmosis is the net movement of water across a selectively permeable membrane in response to differences in effective solute concentration.

Water undergoes net movement toward the region containing the greater concentration of nonpenetrating solute.

Tonicity describes how a surrounding solution affects water movement and cell volume.

- In a **hypotonic solution**, water undergoes net movement into the cell. An animal cell swells and may lyse.
- In an **isotonic solution**, there is no net movement of water and the cell maintains approximately the same volume.
- In a **hypertonic solution**, water undergoes net movement out of the cell and the cell shrinks.

A 0.9% (m/v) NaCl solution, commonly called **normal saline**, is approximately isotonic with human blood plasma.

The number of dissolved particles is important in osmosis. NaCl dissociates into Na^+ and Cl^-, while glucose remains as intact molecules in solution.

9.6 Acids, Bases, and pH

A **Brønsted-Lowry acid** donates H^+, while a **Brønsted-Lowry base** accepts H^+.

In aqueous solutions, H^+ associates with water to form the **hydronium ion, H_3O^+**.

When an acid loses H^+, it forms its **conjugate base**. When a base accepts H^+, it forms its **conjugate acid**. Members of a conjugate acid-base pair differ by one H^+.

Strong acids and bases ionize or dissociate essentially completely in water, while **weak acids and bases** react only partially.

Strength and concentration are different properties. **Strength** describes the extent of ionization, while **concentration** describes how much solute is present in a given amount of solution.

The pH scale describes the concentration of H_3O^+ in an aqueous solution:

$$\mathbf{pH} = -\log[\mathbf{H_3O^+}] \tag{9.9.5}$$

At approximately 25°C:

- pH < 7 is acidic
- pH = 7 is neutral
- pH > 7 is basic

The pH scale is **logarithmic**. A difference of one pH unit represents a tenfold difference in H_3O^+ concentration.

Acids and bases can react in **neutralization reactions**, in which H_3O^+ and OH^- combine to form water.

9.7 Buffers and the Maintenance of pH

A **buffer** is a solution that resists large changes in pH when relatively small amounts of acid or base are added. Buffers generally contain appreciable amounts of a **weak acid and its conjugate base** or a **weak base and its conjugate acid**. When acid is added, the conjugate base component of the buffer accepts H^+. When base is added, the weak acid component donates H^+.

Buffers do not prevent changes in pH completely, and every buffer has a limited **buffer capacity**.

The **carbonic acid/bicarbonate buffer system** is an important buffer in blood.

$$\mathbf{H_2CO_3} \rightleftharpoons \mathbf{H^+ + HCO_3^-} \tag{9.9.6}$$

Carbon dioxide is chemically connected to this buffer system:

$$\mathbf{CO_2 + H_2O} \rightleftharpoons \mathbf{H_2CO_3} \tag{9.9.7}$$

Blood pH is maintained through the combined actions of chemical buffers, the lungs, and the kidneys. The lungs regulate CO_2 removal, while the kidneys regulate H^+ and HCO_3^-.

9.8 Homeostasis—Maintaining the Chemical Environment of the Body

Homeostasis is the maintenance of a relatively stable internal environment despite continuous change. Many homeostatic systems operate through **negative feedback**, in which a change triggers responses that oppose the original change. The body regulates water, electrolytes, pH, nutrients, and many other chemical variables.

Blood glucose regulation provides an important example. When blood glucose rises, pancreatic beta cells release **insulin**, which promotes glucose uptake and storage. When blood glucose falls, pancreatic alpha cells release **glucagon**, which promotes the release of glucose into the bloodstream.

Diabetes mellitus occurs when normal glucose regulation is disrupted. Type 1 diabetes results from autoimmune destruction of insulin-producing beta cells, while type 2 diabetes involves insulin resistance and, often over time, insufficient insulin production.

Persistent **hyperglycemia** illustrates how the concepts in this chapter are connected. Glucose is a dissolved solute, so elevated blood glucose is fundamentally a concentration problem. When excess glucose remains in the forming urine, it alters osmotic water movement and increases water loss.

The chemical concepts explored throughout this chapter—**solutions, concentration, dilution, osmosis, acids, bases, pH, and buffers—are all essential to maintaining the internal environment required for life**.

Homeostasis is chemistry under continuous regulation.

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9.10: Practice Questions

Conceptual Problems

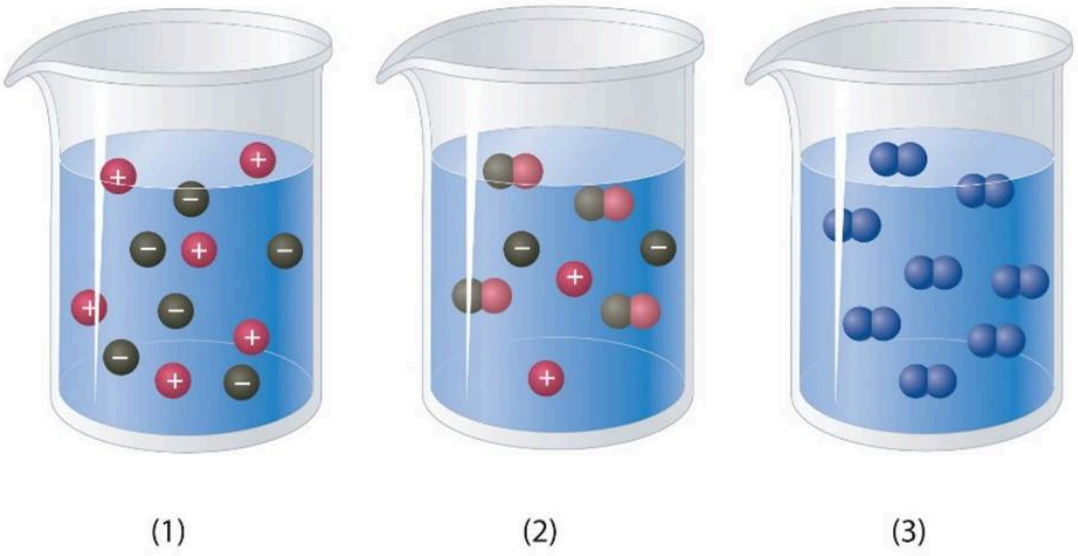
1. Which of the representations best corresponds to a 1 M aqueous solution of each compound? Justify your answers.

A. NH_3

B. HF

C. $CH_3CH_2CH_2OH$

D. Na_2SO_4



2. Which of the representations shown in Problem 1 best corresponds to a 1 M aqueous solution of each compound? Justify your answers.

A. CH_3CO_2H

B. NaCl

C. Na_2S

D. Na_3PO_4

E. acetaldehyde

3. Would you expect a 1.0 M solution of $CaCl_2$ to be a better conductor of electricity than a 1.0 M solution of NaCl? Why or why not?

4. An alternative way to define the concentration of a solution is molality, abbreviated m. Molality is defined as the number of moles of solute in 1 kg of solvent. How is this different from molarity? Would you expect a 1 M solution of sucrose to be more or less concentrated than a 1 m solution of sucrose? Explain your answer.

5. What are the advantages of using solutions for quantitative calculations?

Odd Answers to Conceptual Problems:

1. a) NH_3 is a weak base, which means that some of the molecules will accept a proton from water molecules causing them to dissociate into H+ and -OH ions. The H+ ion will associate with the NH_3 to form NH_4^+. Thus this would look the most like beaker #2. b) HF is a weak acid even though F is strongly electronegative. This is because the H-F molecule can form strong hydrogen bonds with the water molecules and remain in a covalent bond that is harder to dissociate. Thus, beaker #2 is also a good choice for this molecule, as only some of the H-F will dissociate to H3O+ and F- ions. c) $CH_3CH_2CH_2OH$ is a covalent compound and will not dissociate to any appreciable extent, thus, beaker #3 is the correct choice. d) Na_2SO_4 is a soluble ionic compound and will fully dissociate into ions looking most like beaker #1.

3. Yes, because when CaCl2 dissociates it will form 3 ions (1 Ca2+ and 2 Cl- ions) whereas NaCl will only dissociate into 2 ions (Na+ and a Cl-) for each molecule. Thus, CaCl2 will generate more ions per mole than 1 mole of NaCl and be a better conductor of electricity.

5. If the amount of a substance required for a reaction is too small to be weighed accurately, the use of a solution of the substance, in which the solute is dispersed in a much larger mass of solvent, allows chemists to measure the quantity of the substance more accurately.

Numerical Problems

1. Calculate the number of grams of solute in 1.000 L of each solution.

    A. 0.2593 M $NaBrO_3$

    B. 1.592 M KNO_3

    C. 1.559 M acetic acid

    D. 0.943 M potassium iodate

2. Calculate the number of grams of solute in 1.000 L of each solution.

    A. 0.1065 M BaI_2

    B. 1.135 M Na_2SO_4

    C. 1.428 M NH_4Br

    D. 0.889 M sodium acetate

3. If all solutions contain the same solute, which solution contains the greater mass of solute?

    A. 1.40 L of a 0.334 M solution or 1.10 L of a 0.420 M solution

    B. 25.0 mL of a 0.134 M solution or 10.0 mL of a 0.295 M solution

    C. 250 mL of a 0.489 M solution or 150 mL of a 0.769 M solution

4. Complete the following table for 500 mL of solution.

Practicing Conversions

Compound	Mass (g)	Moles	Concentration (M)
calcium sulfate	4.86		
acetic acid		3.62	
hydrogen iodide dihydrate			1.273
barium bromide	3.92		
glucose			0.983
sodium acetate		2.42	

5. What is the concentration of each species present in the following aqueous solutions?

   A. 0.489 mol of NiSO4 in 600 mL of solution

   B. 1.045 mol of magnesium bromide in 500 mL of solution

   C. 0.146 mol of glucose in 800 mL of solution

   D. 0.479 mol of CeCl3 in 700 mL of solution

6. What is the concentration of each species present in the following aqueous solutions?

   A. 0.324 mol of K2MoO4 in 250 mL of solution

   B. 0.528 mol of potassium formate in 300 mL of solution

   C. 0.477 mol of KClO3 in 900 mL of solution

   D. 0.378 mol of potassium iodide in 750 mL of solution

7. What is the molar concentration of each solution?

   A. 8.7 g of calcium bromide in 250 mL of solution

   B. 9.8 g of lithium sulfate in 300 mL of solution

   C. 12.4 g of sucrose (C12H22O11) in 750 mL of solution

   D. 14.2 g of iron(III) nitrate hexahydrate in 300 mL of solution

8. What is the molar concentration of each solution?

   A. 12.8 g of sodium hydrogen sulfate in 400 mL of solution

B. 7.5 g of potassium hydrogen phosphate in 250 mL of solution

C. 11.4 g of barium chloride in 350 mL of solution

D. 4.3 g of tartaric acid (C4H6O6) in 250 mL of solution

Odd Numerical Answers

1. Calculate the number of grams of solute in 1.000 L of each solution.

A. 39.13 g $NaBrO_3$
B. **161.0 g KNO_3**
C. **93.62 g acetic acid**
D. **201.8 g KIO_3**

3. If all solutions contain the same solute, which solution contains the greater mass of solute?

Because the solute is the same in each comparison, the solution containing the greater number of moles also contains the greater mass.

A. **1.40 L of the 0.334 M solution**

B. **25.0 mL of the 0.134 M solution**

C. **250 mL of the 0.489 M solution**

5. What is the concentration of each species present in the following aqueous solutions?

A. 0.489 mol $NiSO_4$ in 600 mL:

- **$[Ni^{2+}] = 0.815$ M**
- **$[SO_4^{2-}] = 0.815$ M**

B. 1.045 mol $MgBr_2$ in 500 mL:

- **$[Mg^{2+}] = 2.09$ M**
- **$[Br^-] = 4.18$ M**

C. 0.146 mol glucose in 800 mL:

- **$[C_6H_{12}O_6] = 0.183$ M**

D. 0.479 mol $CeCl_3$ in 700 mL:

- **$[Ce^{3+}] = 0.684$ M**
- **$[Cl^-] = 2.05$ M**

7. What is the molar concentration of each solution?

A. 8.7 g $CaBr_2$ in 250 mL:

0.17 M $CaBr_2$

B. 9.8 g Li_2SO_4 in 300 mL:

0.30 M Li_2SO_4

C. 12.4 g sucrose in 750 mL:

0.0483 M $C_{12}H_{22}O_{11}$

D. 14.2 g $Fe(NO_3)_3 \cdot 6H_2O$ in 300 mL:

0.135 M $Fe(NO_3)_3 \cdot 6H_2O$.

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