The Chemical Basis of Life

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The chemical reactions of living systems take place across a wide range of conditions. Although many microbial species can tolerate extreme heat, multicellular organisms require much more temperate habitats. One exception is *Alvinella pompejana*, the Pompeii worm, which lives near deep-sea hydrothermal vents and thrives at 42°C (107°F). Hair-like colonies of symbiotic bacteria may help insulate its body.

This first chapter offers a preview of the study of biochemistry, broken down into three sections that reflect how topics in this book are organized. First come brief descriptions of the four major types of small biological molecules and their polymeric forms. Next is a summary of the thermodynamics that apply to metabolic reactions. Finally, there is a discussion of the origin of self-replicating life-forms and their evolution into modern cells. These short discussions introduce some of the key players and major themes of biochemistry and provide a foundation for the topics that will be encountered in subsequent chapters.

1.1 What Is Biochemistry?

LEARNING OBJECTIVE

Recognize the main themes of biochemistry.

Biochemistry is the scientific discipline that seeks to explain life at the molecular level. It uses the tools and terminology of chemistry to describe the various attributes of living organisms. Biochemistry offers answers to such fundamental questions as "What are we made of?" and "How do we work?" Biochemistry is also a practical science: It generates powerful techniques that underlie advances in other fields, such as genetics, cell biology, and immunology; it offers insights into the treatment of diseases such as cancer and diabetes; and it improves the efficiency of industries such as wastewater treatment, food production, and drug manufacturing.

Some aspects of biochemistry can be approached by studying individual molecules isolated from cells. A thorough understanding of each molecule's physical structure and chemical reactivity helps lead to an understanding of how molecules cooperate and combine to form larger functional units and, ultimately, the intact organism (**Fig. 1.1**). However, just as a clock completely disassembled no longer resembles a clock, information about a multitude of biological molecules does not necessarily reveal how an organism lives. Biochemists therefore investigate how organisms behave under different conditions or when a particular molecule is modified or absent. In addition, they collect vast amounts of information about molecular structures and functions—information that is stored and analyzed by computer, a field of study known as **bioinformatics.** A biochemist's laboratory is as likely to hold racks of test tubes as flasks of bacteria or computers.

Chapters 3 through 22 of this book are divided into three groups that roughly correspond to three major themes of biochemistry:

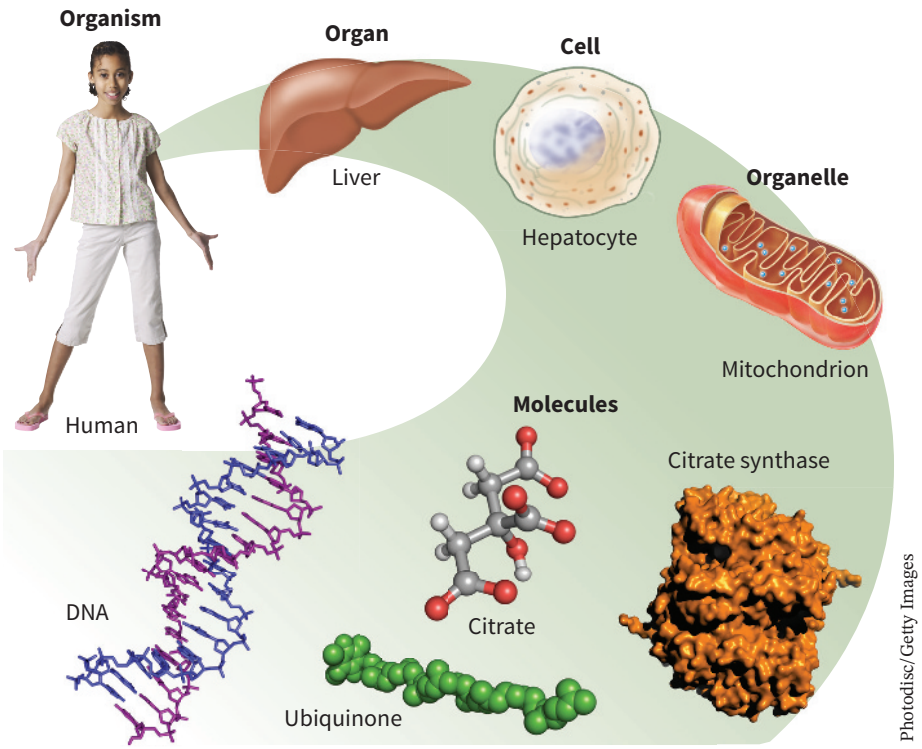


FIGURE 1.1 Levels of organization in a living organism. Biochemistry focuses on the structures and functions of molecules. Interactions between molecules give rise to higher-order structures (for example, organelles), which may themselves be components of larger entities, leading ultimately to the entire organism.

1. *Living organisms are made of macromolecules*. Some molecules are responsible for the physical shapes of cells. Others carry out various activities in the cell. (For convenience, we often use *cell* interchangeably with *organism* since the simplest living entity is a single cell.) In all cases, the structure of a molecule is intimately linked to its function. Understanding a molecule's structural characteristics is therefore an important key to understanding its functional significance.
2. *Organisms acquire, transform, store, and use energy.* The ability of a cell to carry out metabolic reactions—to synthesize its constituents and to move, grow, and reproduce—requires the input of energy. A cell must extract this energy from the environment and spend it or store it in a manageable form.
3. *Biological information is transmitted from generation to generation.* Modern human beings look much like they did 100,000 years ago. Certain bacteria have persisted for millions, if not billions, of years. In all organisms, the genetic information that specifies a cell's structural composition and functional capacity must be safely maintained and transmitted each time the cell divides.

Several other themes run throughout biochemistry and we will highlight these where appropriate.

4. *Cells maintain a state of homeostasis.* Even within its own lifetime, a cell may dramatically alter its shape or metabolic activities, but it does so within certain limits. In order to remain in a steady, nonequilibrium state—**homeostasis**—the cell must recognize changing internal and external conditions and regulate its activities.
5. *Organisms evolve.* Over long periods of time, the genetic composition of a population of organisms changes. Examining the molecular makeup of living organisms allows biochemists to identify the genetic features that distinguish groups of organisms and to trace their evolutionary history.
6. *Diseases can be explained at the biochemical level.* Identifying the molecular defects that underlie human diseases, or investigating the pathways that allow one organism to infect another, is the first step in diagnosing, treating, preventing, or curing a host of ailments.

1.2 Biological Molecules

LEARNING OBJECTIVES

Identify the major classes of biological molecules.

- List the elements found in biological molecules.
- Draw and name the common functional groups in biological molecules.
- Draw and name the common linkages in biological molecules.
- Distinguish the main structural features of amino acids, carbohydrates, nucleotides, and lipids.
- Identify the monomers and linkages in polypeptides, polysaccharides, and nucleic acids.
- Summarize the biological functions of the major classes of biological molecules.

Even the simplest organisms contain a staggering number of different molecules, yet this number represents only an infinitesimal portion of all the molecules that are chemically possible. For one thing, *only a small subset of the known elements are found in living systems* (**Fig. 1.2**). The most abundant of these are C, N, O, and H, followed by Ca, P, K, S, Cl, Na, and Mg. Certain **trace elements** are also present in very small quantities.

Virtually all the molecules in a living organism contain carbon, so biochemistry can be considered to be a branch of organic chemistry. In addition, nearly all biological molecules are constructed from H, N, O, P, and S. Most of these molecules belong to one of a few structural classes, which are described below.

Similarly, *the chemical reactivity of biomolecules is limited relative to the reactivity of all chemical compounds.* A few of the functional groups and intramolecular linkages that are common in biochemistry are listed in **Table 1.1**. Familiarity with these functional groups is essential for understanding the behavior of the different types of biological molecules we will encounter throughout this book.

Cells contain four major types of biomolecules

Most of the cell's small molecules can be divided into four classes. Although each class contains many members, *they are united under a single structural or functional definition*. Identifying a particular molecule's class may help predict its chemical properties and possibly its role in the cell.

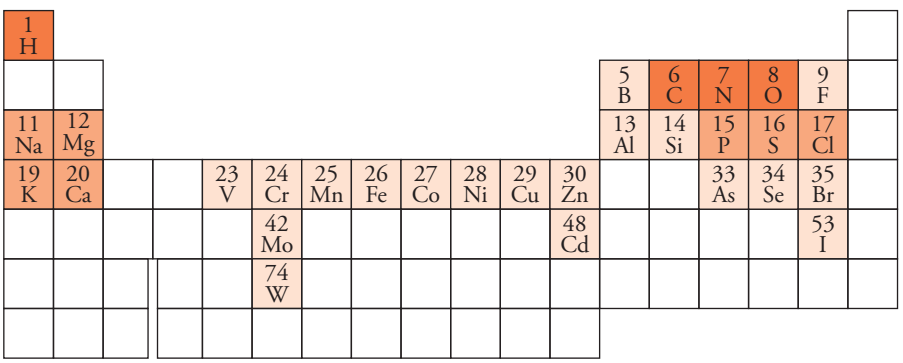


FIGURE 1.2 **Elements found in biological systems.** The most abundant elements are most darkly shaded; trace elements are most lightly shaded. Not every organism contains every trace element. Biological molecules primarily contain H, C, N, O, P, and S.

TABLE 1.1 Common Functional Groups and Linkages in Biochemistry

Compound name	Structure[a]	Functional group
Amine[b]	RNH_2 or RNH_3^+ R_2NH or $R_2NH_2^+$ R_3N or R_3NH^+	—N< or —$\overset{+}{\text{N}}$— (amino group)
Alcohol	ROH	—OH (hydroxyl group)
Thiol	RSH	—SH (sulfhydryl group)
Ether	ROR	—O— (ether linkage)
Aldehyde	R—C(=O)—H	—C(=O)— (carbonyl group), R—C(=O)— (acyl group)
Ketone	R—C(=O)—R	—C(=O)— (carbonyl group), R—C(=O)— (acyl group)
Carboxylic acid[b] (Carboxylate)	R—C(=O)—OH or R—C(=O)—O^-	—C(=O)—OH (carboxyl group) or —C(=O)—O^- (carboxylate group)
Ester	R—C(=O)—OR	—C(=O)—O— (ester linkage)
Thioester	R—C(=S)—OR	—C(=S)—O— (thioester linkage)
Amide	R—C(=O)—NH_2 R—C(=O)—NHR R—C(=O)—NR_2	—C(=O)—N< (amido group)
Imine[b]	R=NH or $R=NH_2^+$ R=NR or $R=NHR^+$	>C=N— or >C=$\overset{+}{\text{N}}$(H)— (imino group)
Phosphoric acid ester[b, c]	R—O—P(=O)(OH)—OH or R—O—P(=O)(O^-)—O^-	—O—P(=O)(OH)—O— (phosphoester linkage) —P(=O)(OH)—OH or —P(=O)(O^-)—O^- (phosphoryl group)
Diphosphoric acid ester[b, d]	R—O—P(=O)(OH)—O—P(=O)(OH)—OH or R—O—P(=O)(O^-)—O—P(=O)(O^-)—O^-	—O—P(=O)(OH)—O—P(=O)(OH)—O— (phosphoanhydride linkage) —P(=O)(OH)—O—P(=O)(OH)—OH or —P(=O)(O^-)—O—P(=O)(O^-)—O^- (diphosphoryl group, pyrophosphoryl group)

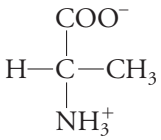
[a] R represents any carbon-containing group. In a molecule with more than one R group, the groups may be the same or different.

[b] Under physiological conditions, these groups are ionized and hence bear a positive or negative charge.

[c] When R = H, the molecule is inorganic phosphate (abbreviated P_i), usually $H_2PO_4^-$ or HPO_4^{2-}.

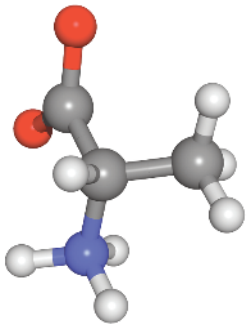
[d] When R = H, the molecule is pyrophosphate (abbreviated PP_i).

Question Cover the structure column and draw the structure for each compound listed on the left. Do the same for each functional group.



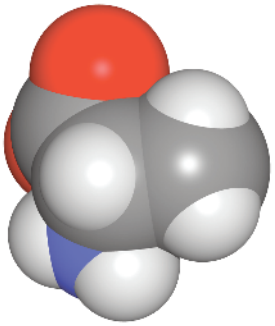
a.

A structural formula includes all the atoms and the major bonds. Some bonds, such as the C—O and N—H bonds, are implied. The central carbon has tetrahedral geometry. The horizontal bonds extend slightly above the plane of the page and the vertical bonds extend slightly behind it.



b.

A ball-and-stick representation more accurately reveals the arrangement of atoms in space, although it does not show their relative sizes or electrical charges. The atoms are color-coded by convention: C gray, N blue, O red, and H white.



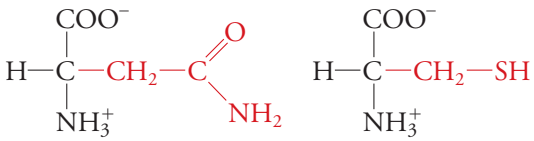
c.

The space-filling model best represents the actual shape of the molecule but may obscure some of its atoms and linkages. Each atom is shown as a sphere whose radius (the van der Waals radius) corresponds to the distance of closest approach by another atom.

FIGURE 1.3 **Representations of alanine.** **a.** Structural formula, **b.** ball-and-stick model, and **c.** space-filling model.

1. Amino Acids

Among the simplest compounds are the **amino acids,** so named because they contain an amino group (—NH_2) and a carboxylic acid group (—COOH). Under physiological conditions, these groups are actually ionized to —NH_3^+ and —COO^-. The common amino acid alanine—like other small molecules—can be depicted in different ways, for example, by a structural formula, a ball-and-stick model, or a space-filling model (**Fig. 1.3**). Other amino acids resemble alanine in basic structure, but instead of a methyl group (—CH_3), they have another group—called a side chain or R group—that may also contain N, O, or S; for example,

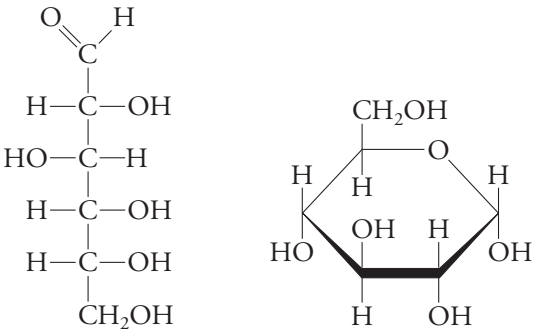


Asparagine

Cysteine

2. Carbohydrates

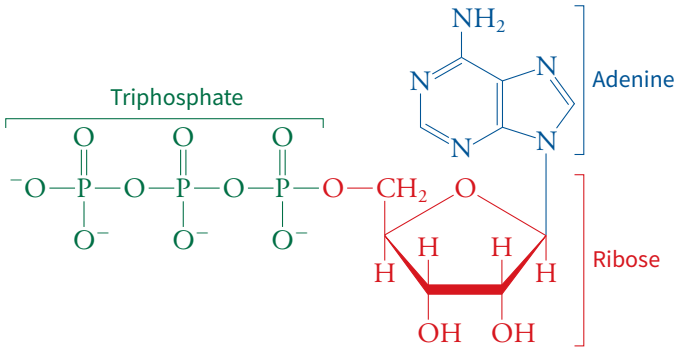
Simple **carbohydrates** (also called **monosaccharides** or just sugars) have the formula $(CH_2O)_n$, where n is ≥ 3. Glucose, a monosaccharide with six carbon atoms, has the formula $C_6H_{12}O_6$. It is sometimes convenient to draw it as a ladder-like chain (*left*); however, glucose forms a cyclic structure in solution (*right*):



Glucose

In the representation of the cyclic structure, the darker bonds project in front of the page and the lighter bonds project behind it. In many monosaccharides, one or more hydroxyl groups are replaced by other groups, but the ring structure and multiple —OH groups of these molecules allow them to be easily recognized as carbohydrates.

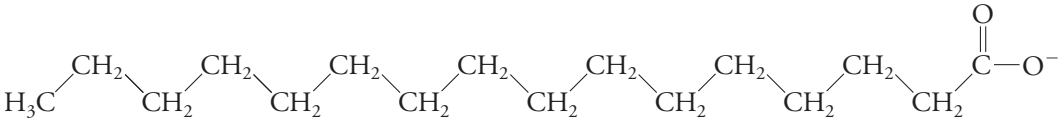
3. Nucleotides A five-carbon sugar, a nitrogen-containing ring, and one or more phosphate groups are the components of **nucleotides.** For example, adenosine triphosphate (ATP) contains the nitrogenous group adenine linked to the monosaccharide ribose, to which a triphosphate group is also attached:



Adenosine triphosphate (ATP)

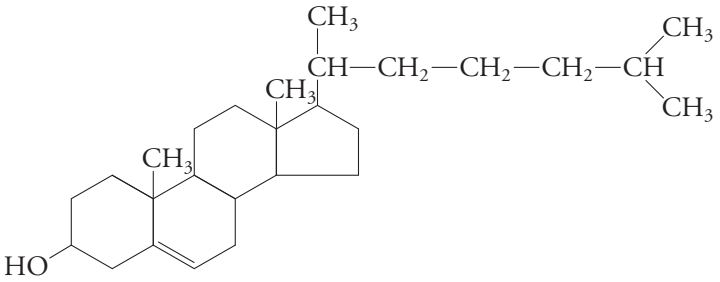
The most common nucleotides are mono-, di-, and triphosphates containing the nitrogenous ring compounds (or "bases") adenine, cytosine, guanine, thymine, or uracil (abbreviated A, C, G, T, and U).

4. Lipids The fourth major group of biomolecules consists of the **lipids.** These compounds cannot be described by a single structural formula since they are a diverse collection of molecules. However, they all tend to be poorly soluble in water because the bulk of their structure is hydrocarbon-like. For example, palmitic acid consists of a highly insoluble chain of 15 carbons attached to a carboxylic acid group, which is ionized under physiological conditions. The anionic lipid is therefore called palmitate.



Palmitate

Cholesterol, although it differs significantly in structure from palmitate, is also poorly soluble in water because of its hydrocarbon-like composition.



Cholesterol

Cells also contain a few other small molecules that cannot be easily classified into the groups above or that are constructed from molecules belonging to more than one group.

There are three major kinds of biological polymers

In addition to small molecules consisting of relatively few atoms, organisms contain macromolecules that may consist of thousands of atoms. Such huge molecules are not synthesized in one piece but are built from smaller units. This is a universal feature of nature: *A few kinds*

Box 1.A Units Used in Biochemistry

Biochemists follow certain conventions when quantifying objects on a molecular scale. For example, the mass of a molecule can be expressed in atomic mass units; however, the masses of biological molecules—especially very large ones—are typically given without units. Here it is understood that the mass is expressed relative to one-twelfth the mass of an atom of the common carbon isotope ^{12}C (12.011 atomic mass units). Occasionally, units of daltons (D) are used (1 dalton = 1 atomic mass unit), often with the prefix kilo, k (kD). This is useful for macromolecules such as proteins, many of which have masses in the range from 20,000 (20 kD) to over 1,000,000 (1000 kD).

The standard metric prefixes are also necessary for expressing the minute concentrations of biomolecules in living cells. Concentrations are usually given as moles per liter (mol · L^{-1} or M), with the appropriate prefix, such as m, μ, or n:

mega (M)	10^6	nano (n)	10^{-9}
kilo (k)	10^3	pico (p)	10^{-12}
milli (m)	10^{-3}	femto (f)	10^{-15}
micro (μ)	10^{-6}		

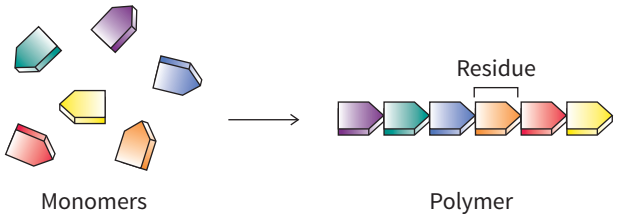
For example, the concentration of the sugar glucose in human blood is about 5 mM, but many intracellular molecules are present at concentrations of μM or less.

Distances are customarily expressed in angstroms, Å (1 Å = 10^{-10} m) or in nanometers, nm (1 nm = 10^{-9} m). For example, the distance between the centers of carbon atoms in a C—C bond is about 1.5 Å and the diameter of a DNA molecule is about 20 Å.

Question **The diameter of a typical spherical bacterial cell is about 1 μm. What is the cell's volume?**

of building blocks can be combined in different ways to produce a wide variety of larger structures. This is advantageous for a cell, which can get by with a limited array of raw materials. In addition, the very act of chemically linking individual units **(monomers)** into longer strings **(polymers)** is a way of encoding information (the sequence of the monomeric units) in a stable form. Biochemists use certain units of measure to describe both large and small molecules (**Box 1.A**).

Amino acids, monosaccharides, and nucleotides each form polymeric structures with widely varying properties. In most cases, the individual monomers become covalently linked in head-to-tail fashion:



The linkage between monomeric units is characteristic of each type of polymer. The monomers are called **residues** after they have been incorporated into the polymer. Strictly speaking, lipids do not form polymers, although they do tend to aggregate to form larger structures such as cell membranes. Most of the mass of a cell consists of polymers, with proteins accounting for the greatest share (**Fig. 1.4**).

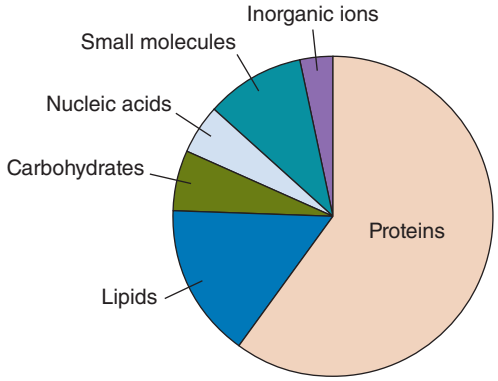
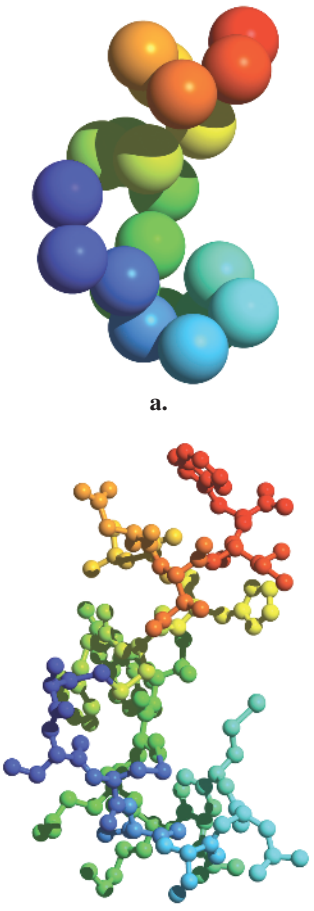


FIGURE 1.4 **Mass of a mammalian cell.** Proteins and lipids account for about 75% of the dry mass of a typical mammalian cell.



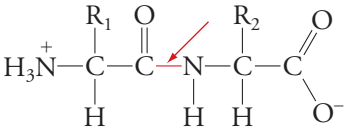
a.

b.

FIGURE 1.5 Structure of human endothelin. The 21 amino acid residues of this polypeptide, shaded from blue to red, form a compact structure. In **a**, each amino acid residue is represented by a sphere. The ball-and-stick model **b** shows all the atoms except hydrogen.

1. Proteins

Polymers of amino acids are called **polypeptides** or **proteins.** Twenty different amino acids serve as building blocks for proteins, which may contain many hundreds of amino acid residues. The amino acid residues are linked to each other by amide bonds called **peptide bonds.** A peptide bond (*arrow*) links the two residues in a dipeptide (the side chains of the amino acids are represented by R_1 and R_2).

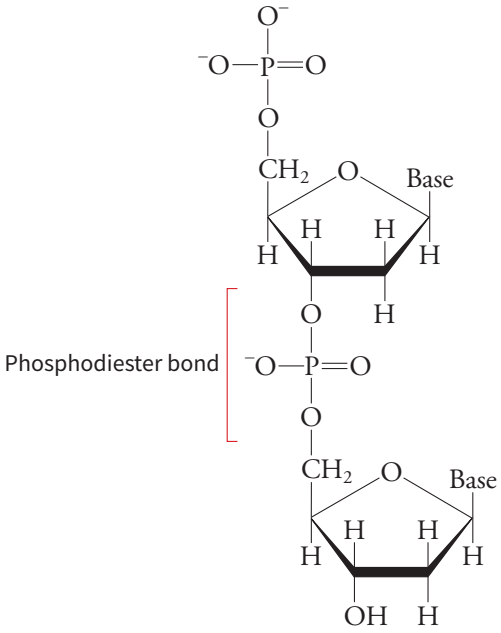


Because the side chains of the 20 amino acids have different sizes, shapes, and chemical properties, the exact **conformation** (three-dimensional shape) of the polypeptide chain depends on its amino acid composition and sequence. For example, the small polypeptide endothelin, with 21 residues, assumes a compact shape in which the polymer bends and folds to accommodate the functional groups of its amino acid residues (**Fig. 1.5**).

The 20 different amino acids can be combined in almost any order and in almost any proportion to produce myriad polypeptides, all of which have unique three-dimensional shapes. This property makes proteins as a class the most structurally variable and therefore the most functionally versatile of all the biopolymers. Accordingly, *proteins perform a wide variety of tasks in the cell, such as mediating chemical reactions and providing structural support.*

2. Nucleic Acids

Polymers of nucleotides are termed **polynucleotides** or **nucleic acids,** better known as DNA and RNA. Unlike polypeptides, with 20 different amino acids available for polymerization, each nucleic acid is made from just four different nucleotides. For example, the residues in RNA contain the bases adenine, cytosine, guanine, and uracil, whereas the residues in DNA contain adenine, cytosine, guanine, and thymine. Polymerization involves the phosphate and sugar groups of the nucleotides, which become linked by **phosphodiester bonds.**

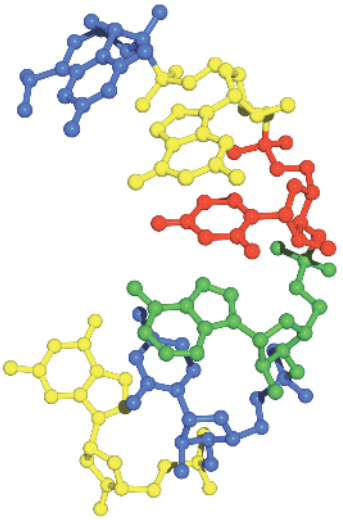


In part because nucleotides are much less variable in structure and chemistry than amino acids, nucleic acids tend to have more regular structures than proteins. *This is in keeping with their primary role as carriers of genetic information, which is contained in their sequence of*

nucleotide residues rather than in their three-dimensional shape (Fig. 1.6). Nevertheless, many nucleic acids do bend and fold into compact globular shapes, as proteins do.

CGUACG

a.

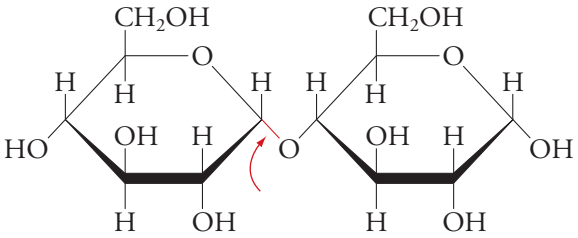


b.

FIGURE 1.6 Structure of a nucleic acid. **a.** Sequence of nucleotide residues, using one-letter abbreviations. **b.** Ball-and-stick model of the polynucleotide, showing all atoms except hydrogen (this structure is a six-residue segment of RNA).

3. Polysaccharides

Polysaccharides usually contain only one or a few different types of monosaccharide residues, so even though a cell may synthesize dozens of different kinds of monosaccharides, most of its polysaccharides are homogeneous polymers. This tends to limit their potential for carrying genetic information in the sequence of their residues (as nucleic acids do) or for adopting a large variety of shapes and mediating chemical reactions (as proteins do). On the other hand, *polysaccharides perform essential cell functions by serving as fuel-storage molecules and by providing structural support.* For example, plants link the monosaccharide glucose, which is a fuel for virtually all cells, into the polysaccharide starch for long-term storage. The glucose residues are linked by **glycosidic bonds** (the bond is shown in red in this disaccharide):



Glucose monomers are also the building blocks for cellulose, the extended polymer that helps make plant cell walls rigid (Fig. 1.7). The starch and cellulose polymers differ in the arrangement of the glycosidic bonds between glucose residues.

The brief descriptions of biological polymers given above are generalizations, meant to convey some appreciation for the possible structures and functions of these macromolecules. *Exceptions to the generalizations abound.* For example, some small polysaccharides encode information that allows cells bearing the molecules on their surfaces to recognize each other. Likewise, some nucleic acids perform structural roles, for example, by serving as scaffolding in ribosomes, the small machines where protein synthesis takes place. Under certain conditions, proteins are called on as fuel-storage molecules. A summary of the major and minor functions of proteins, polysaccharides, and nucleic acids is presented in Table 1.2.

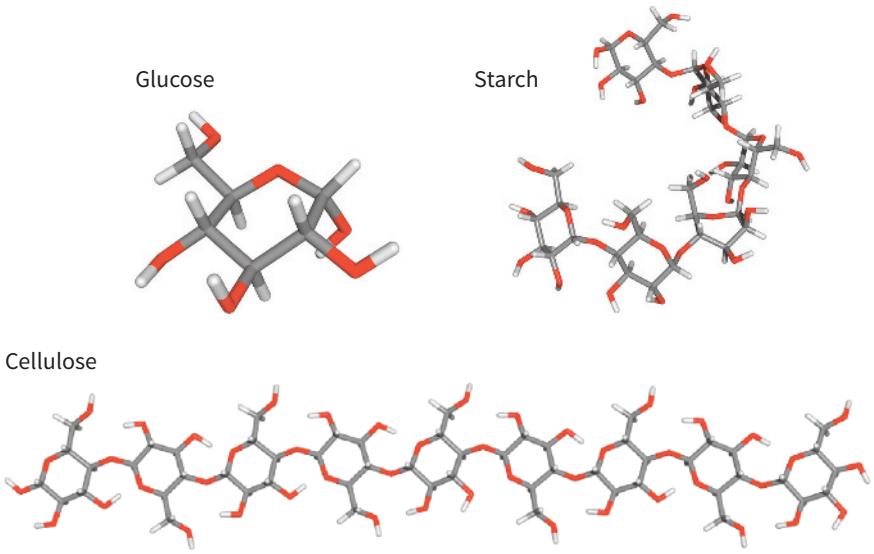


FIGURE 1.7 Glucose and its polymers. Both starch and cellulose are polysaccharides containing glucose residues. They differ in the type of chemical linkage between the monosaccharide units. Starch molecules have a loose helical conformation, whereas cellulose molecules are extended and relatively stiff.

TABLE 1.2 Functions of Biopolymers

Biopolymer	Encode information	Carry out metabolic reactions	Store energy	Support cellular structures
Proteins	—	✔	✓	✔
Nucleic acids	✔	✓	—	✓
Polysaccharides	✓	—	✔	✔

✔ major function
✓ minor function

Before Going On

- List the six most abundant elements in biological molecules.
- Name the common functional groups and linkages shown in Table 1.1.
- Give the structural or functional definitions for amino acids, monosaccharides, nucleotides, and lipids.
- Describe the advantage of building a polymer from monomers.
- Give the structural definitions and major functions of proteins, polysaccharides, and nucleic acids.
- Name the linkage in each type of polymer.
- List the major functions of proteins, polysaccharides, and nucleic acids.

1.3 Energy and Metabolism

LEARNING OBJECTIVES

Explain how enthalpy, entropy, and free energy apply to biological systems.

- Define enthalpy, entropy, and free energy.
- Write the equation that links changes in enthalpy, entropy, and free energy.
- Relate changes in enthalpy and entropy to the spontaneity of a process.
- Describe the energy flow that makes living systems thermodynamically possible.

Assembling small molecules into polymeric macromolecules requires energy. And unless the monomeric units are readily available, a cell must synthesize the monomers, which also requires energy. In fact, *cells require energy for all the functions of living, growing, and reproducing.*

It is useful to describe the energy in biological systems using the terminology of thermodynamics (the study of heat and power). An organism, like any chemical system, is subject to the laws of thermodynamics. According to the first law of thermodynamics, energy cannot be created or destroyed. However, it can be transformed. For example, the energy of a river flowing over a dam can be harnessed as electricity, which can then be used to produce heat or perform mechanical work. Cells can be considered to be very small machines that use chemical energy to drive metabolic reactions, which may also produce heat or carry out mechanical work.

Enthalpy and entropy are components of free energy

The energy relevant to biochemical systems is called the Gibbs free energy (after the scientist who defined it) or just **free energy.** It is abbreviated ***G*** and has units of joules per mol ($J \cdot mol^{-1}$). Free energy has two components: enthalpy and entropy. ***Enthalpy*** (abbreviated ***H***, with units of $J \cdot mol^{-1}$) *is taken to be equivalent to the heat content of the system.* ***Entropy*** (abbreviated ***S***, with units of $J \cdot K^{-1} \cdot mol^{-1}$) *is a measure of how the energy is dispersed within that system.* Entropy can therefore be considered to be a measure of the system's disorder or randomness, because the more ways a system's components can be arranged, the more dispersed its energy. For example, consider a pool table at the start of a game when all 15 balls are arranged in one neat triangle (a state of high order or low entropy). After play has begun, the balls are scattered across the table, which is now in a state of disorder and high entropy (**Fig. 1.8**).

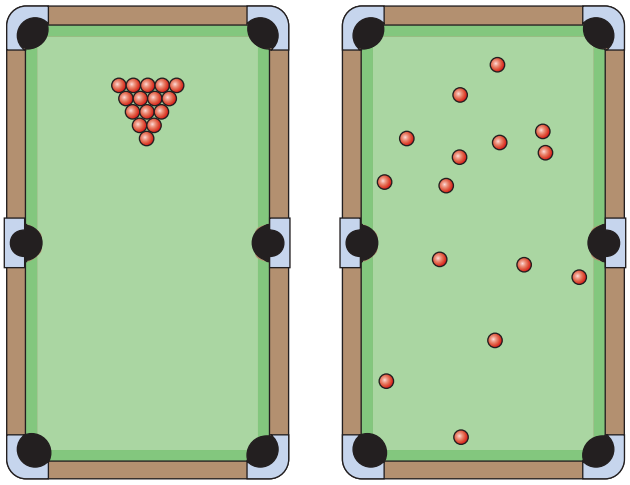
Free energy, enthalpy, and entropy are related by the equation

$$G = H - TS \tag{1.1}$$

where T represents temperature in Kelvin (equivalent to degrees Celsius plus 273). Temperature is a coefficient of the entropy term because entropy varies with temperature; the entropy of a substance increases when it is warmed because more thermal energy has been dispersed within it. The enthalpy of a chemical system can be measured, although with some difficulty, but it is next to impossible to measure a system's entropy because this would require counting all the possible arrangements of its components or all the ways its energy could be spread out among them. Therefore, it is more practical to deal with *changes* in these quantities (change is indicated by the Greek letter delta, Δ) so that

$$\Delta G = \Delta H - T\Delta S \tag{1.2}$$

Biochemists can measure how the free energy, enthalpy, and entropy of a system differ before and after a chemical reaction. For example, **exothermic reactions** are accompanied by the release of heat to the surroundings ($H_{final} - H_{initial} = \Delta H < 0$), whereas **endothermic reactions** absorb heat from the surroundings ($\Delta H > 0$). Similarly, the entropy change, $S_{final} - S_{initial} = \Delta S$, can be positive or negative. When ΔH and ΔS for a process are known, Equation 1.2 can be used to calculate the value of ΔG at a given temperature (see Sample Calculation 1.1).



a. **b.**

FIGURE 1.8 **Illustration of entropy.** Entropy is a measure of the dispersal of energy in a system, so it reflects the system's randomness or disorder. **a.** Entropy is low when all the balls are arranged in a single area of the pool table. **b.** Entropy is high after the balls have been scattered, because there are now a large number of different possible arrangements of the balls on the table.

Question **Compare the entropy of a ball of yarn before and after a cat has played with it.**

SAMPLE CALCULATION 1.1

Problem Use the information below to calculate the change in enthalpy and the change in entropy for the reaction A → B.

	Enthalpy ($kJ \cdot mol^{-1}$)	Entropy ($J \cdot K^{-1} \cdot mol^{-1}$)
A	60	22
B	75	97

Solution

$$\Delta H = H_B - H_A$$
$$= 75\ kJ \cdot mol^{-1} - 60\ kJ \cdot mol^{-1}$$
$$= 15\ kJ \cdot mol^{-1}$$
$$= 15{,}000\ J \cdot mol^{-1}$$

$$\Delta S = S_B - S_A$$
$$= 97\ J \cdot K^{-1} \cdot mol^{-1}$$
$$- 22\ J \cdot K^{-1} \cdot mol^{-1}$$
$$= 75\ J \cdot K^{-1} \cdot mol^{-1}$$

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ΔG is less than zero for a spontaneous process

A china cup dropped from a great height will break, but the pieces will never reassemble themselves to restore the cup. The thermodynamic explanation is that the broken pieces have less free energy than the intact cup. *In order for a process to occur, the overall change in free energy (**ΔG**) must be negative.* For a chemical reaction, this means that the free energy of the products must be less than the free energy of the reactants:

$$\Delta G = G_{products} - G_{reactants} < 0 \qquad \textbf{(1.3)}$$

When ΔG is less than zero, the reaction is said to be **spontaneous** or **exergonic.** A **nonspontaneous** or **endergonic** reaction has a free energy change greater than zero; in this case, the reverse reaction is spontaneous:

$A \rightarrow B$	$B \rightarrow A$
$\Delta G > 0$	$\Delta G < 0$
Nonspontaneous	Spontaneous

Note that thermodynamic spontaneity does not indicate how *fast* a reaction occurs, only whether it will occur as written. (The rate of a reaction depends on other factors, such as the concentrations of the reacting molecules, the temperature, and the presence of a catalyst.) When a reaction, such as A → B, is at equilibrium, the rate of the forward reaction is equal to the rate of the reverse reaction, so there is no net change in the system. In this situation, $\Delta G = 0$.

A quick examination of Equation 1.2 reveals that *a reaction that occurs with a decrease in enthalpy and an increase in entropy is spontaneous at all temperatures because ΔG is always less than zero.* These results are consistent with everyday experience. For example, heat moves spontaneously from a hot object to a cool object, and items that are neatly arranged tend to become disordered, never the other way around. (This is a manifestation of the second law of thermodynamics, which states that energy tends to spread out.) Accordingly, reactions in which the enthalpy increases and entropy decreases do not occur. If enthalpy and entropy both increase or both decrease during a reaction, the value of ΔG then depends on the temperature, which governs whether the $T\Delta S$ term of Equation 1.2 is greater than or less than the ΔH term. This means that a large increase in entropy can offset an unfavorable (positive) change in enthalpy. Conversely, the release of a large amount of heat ($\Delta H < 0$) during a reaction can offset an unfavorable decrease in entropy (see Sample Calculation 1.2).

Life is thermodynamically possible

In order to exist, life must be thermodynamically spontaneous. Does this hold at the molecular level? When analyzed in a test tube (***in vitro,*** literally "in glass"), many of a cell's metabolic reactions have free energy changes that are less than zero, but some reactions do not. Nevertheless, the nonspontaneous reactions are able to proceed ***in vivo*** (in a living organism) because they occur in concert with other reactions that are thermodynamically favorable. Consider two reactions *in vitro,* one nonspontaneous ($\Delta G > 0$) and one spontaneous ($\Delta G < 0$):

$A \rightarrow B \qquad \Delta G = +15\ kJ \cdot mol^{-1}$ (nonspontaneous)

$B \rightarrow C \qquad \Delta G = -20\ kJ \cdot mol^{-1}$ (spontaneous)

SAMPLE CALCULATION 1.2

Problem Use the information given in Sample Calculation 1.1 to determine whether the reaction A → B is spontaneous at 25°C.

Solution Substitute the values for ΔH and ΔS, calculated in Sample Calculation 1.1, into Equation 1.2. To express the temperature in Kelvin, add 273 to the temperature in degrees Celsius: 273 + 25 = 298 K.

$$\Delta G = \Delta H - T\Delta S$$
$$= 15{,}000\ \text{J} \cdot \text{mol}^{-1} - 298\ \text{K}\ (75\ \text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1})$$
$$= 15{,}000 - 22{,}400\ \text{J} \cdot \text{mol}^{-1}$$
$$= -7400\ \text{J} \cdot \text{mol}^{-1}$$
$$= -7.4\ \text{kJ} \cdot \text{mol}^{-1}$$

Because ΔG is less than zero, the reaction is spontaneous. Even though the change in enthalpy is unfavorable, the large increase in entropy makes ΔG favorable.

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When the reactions are combined, their ΔG values are added, so the overall process has a negative change in free energy:

$$\text{A} + \text{B} \rightarrow \text{B} + \text{C} \qquad \Delta G = (15\ \text{kJ} \cdot \text{mol}^{-1}) + (-20\ \text{kJ} \cdot \text{mol}^{-1})$$
$$\text{A} \rightarrow \text{C} \qquad \Delta G = -5\ \text{kJ} \cdot \text{mol}^{-1}$$

This phenomenon is shown graphically in **Figure 1.9**. In effect, the unfavorable "uphill" reaction A → B is pulled along by the more favorable "downhill" reaction B → C.

Cells couple unfavorable metabolic processes with favorable ones so that the net change in free energy is negative. Note that it is permissible to add ΔG values because the free energy, G, depends only on the initial and final states of the system, without regard to the specific chemical or mechanical work that occurred in going from one state to the other.

Most macroscopic life on earth today is sustained by the energy of the sun (this was not always the case, nor is it true of all organisms). In photosynthetic organisms, such as green plants, light energy excites certain molecules so that their subsequent chemical reactions occur with a net negative change in free energy. These thermodynamically favorable (spontaneous) reactions are coupled to the unfavorable synthesis of monosaccharides from atmospheric CO_2 (**Fig. 1.10**). In this process, the carbon is **reduced.** Reduction, the gain of electrons, is accomplished by the addition of hydrogen or the removal of oxygen (the oxidation states of carbon are reviewed in **Table 1.3**). The plant—or an animal that eats the plant—can then break down the monosaccharide to use it as a fuel to power other metabolic activities. In the process, the carbon is **oxidized**—it loses electrons through the addition of oxygen or the removal of hydrogen—and ultimately becomes CO_2. The oxidation of carbon is thermodynamically favorable, so it can be coupled to energy-requiring processes such as the synthesis of building blocks and their polymerization to form macromolecules.

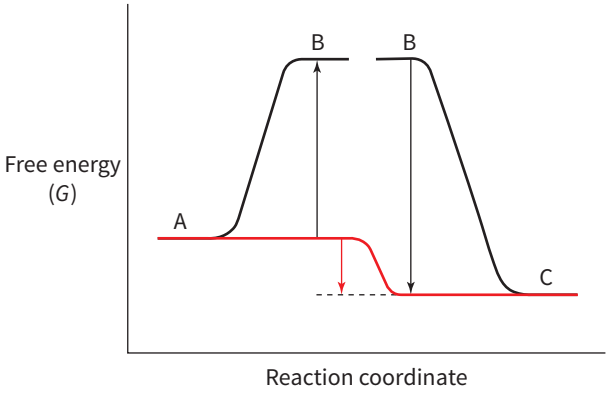


FIGURE 1.9 **Free energy changes in coupled reactions.** A nonspontaneous reaction, such as A → B, which has a positive value of ΔG, can be coupled to another reaction, B → C, which has a negative value of ΔG and is therefore spontaneous. The reactions are coupled because the product of the first reaction, B, is a reactant for the second reaction.

Question **Which reaction occurs spontaneously in reverse: C → B, B → A, or C → A?**

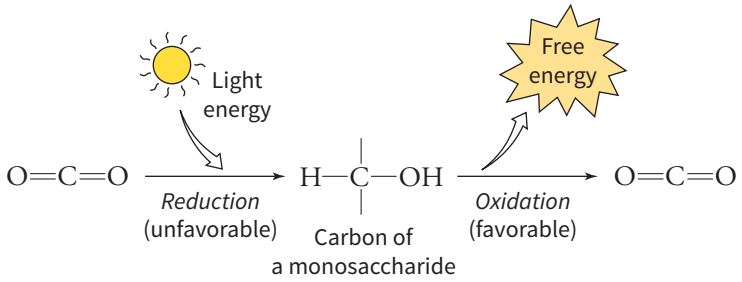
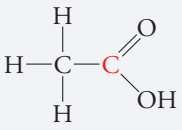
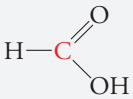
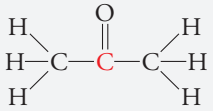
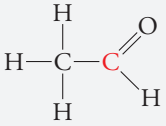
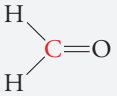
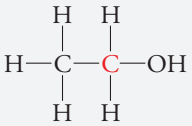
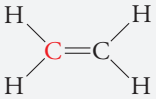
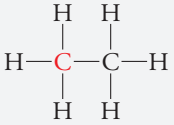
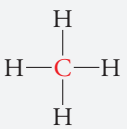


FIGURE 1.10 **Reduction and reoxidation of carbon compounds.** The sun provides the free energy to convert CO_2 to reduced compounds such as monosaccharides. The reoxidation of these compounds to CO_2 is thermodynamically spontaneous, so free energy can be made available for other metabolic processes. Note that free energy is not actually a substance that is physically released from a molecule.

TABLE 1.3 **Oxidation States of Carbon**

Compound[a]	Formula
Carbon dioxide *most oxidized* (*least reduced*)	O=C=O
Acetic acid	
Carbon monoxide	C≡O
Formic acid	
Acetone	
Acetaldehyde	
Formaldehyde	
Acetylene	H—C≡C—H
Ethanol	
Ethene	
Ethane	
Methane *least oxidized* (*most reduced*)	

[a]Compounds are listed in order of decreasing oxidation state of the red carbon atom.

Virtually all metabolic processes occur with the aid of catalysts called **enzymes,** most of which are proteins (a catalyst greatly increases the rate of a reaction without itself undergoing any net change). For example, specific enzymes catalyze the formation of peptide, phosphodiester, and glycosidic linkages during polymer synthesis. Other enzymes catalyze cleavage of these bonds to break the polymers into their monomeric units.

A living organism—with its high level of organization of atoms, molecules, and larger structures—represents a state of low entropy relative to its surroundings. Yet the organism can maintain this thermodynamically unfavorable state as long as it continually obtains free energy from its food. Thus, living organisms do indeed obey the laws of thermodynamics. When the organism ceases to obtain a source of free energy from its surroundings or exhausts its stored food, the chemical reactions in its cells reach equilibrium ($\Delta G = 0$), which results in death.

Before Going On

- Make up values for ΔH and ΔS to generate ΔG values corresponding to a spontaneous and a nonspontaneous reaction.
- Show how increasing temperature affects ΔG when ΔH and ΔS are constant.
- Explain how thermodynamically unfavorable reactions proceed *in vivo*.
- Explain why an organism must have a steady supply of food.
- Describe the cycle of carbon reduction and oxidation in photosynthesis and in the breakdown of a compound such as a monosaccharide.

1.4 The Origin of Cells

LEARNING OBJECTIVES

Summarize the evolutionary history of cells.

- List the events that must have occurred during prebiotic evolution.
- Name the three domains of life.
- Distinguish prokaryotic and eukaryotic cells.
- Summarize the importance of the human microbiota.

Every living cell originates from the division of a parental cell. Thus, the ability to **replicate** (make a replica or copy of itself) is one of the universal characteristics of living organisms. *In order to leave descendants that closely resemble itself, a cell must contain a set of instructions—and the means for carrying them out—that can be transmitted from generation to generation.* Over time, the instructions change gradually, so that species also change, or **evolve.** By carefully examining an organism's genetic information and the cellular machinery that supports it, biochemists can draw some conclusions about the organism's relationship to more ancient life-forms. The history of evolution is therefore contained not just within the fossil record but also in the molecular makeup of all living cells. For example, nucleic acids participate in the storage and transmission of genetic information in all organisms, and the oxidation of glucose is an almost universal means for generating metabolic free energy. Consequently, DNA, RNA, and glucose must have been present in the ancestor of all cells.

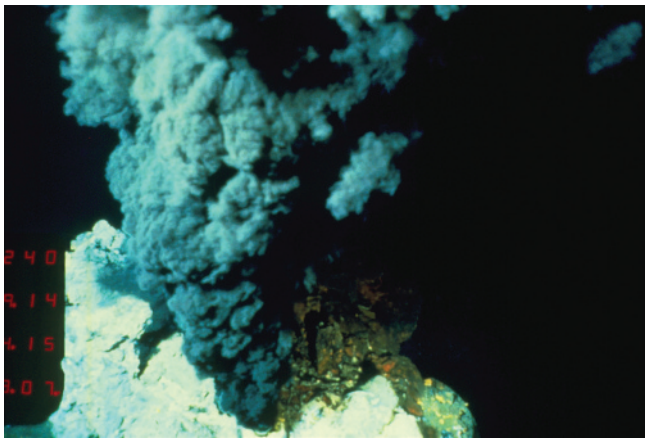


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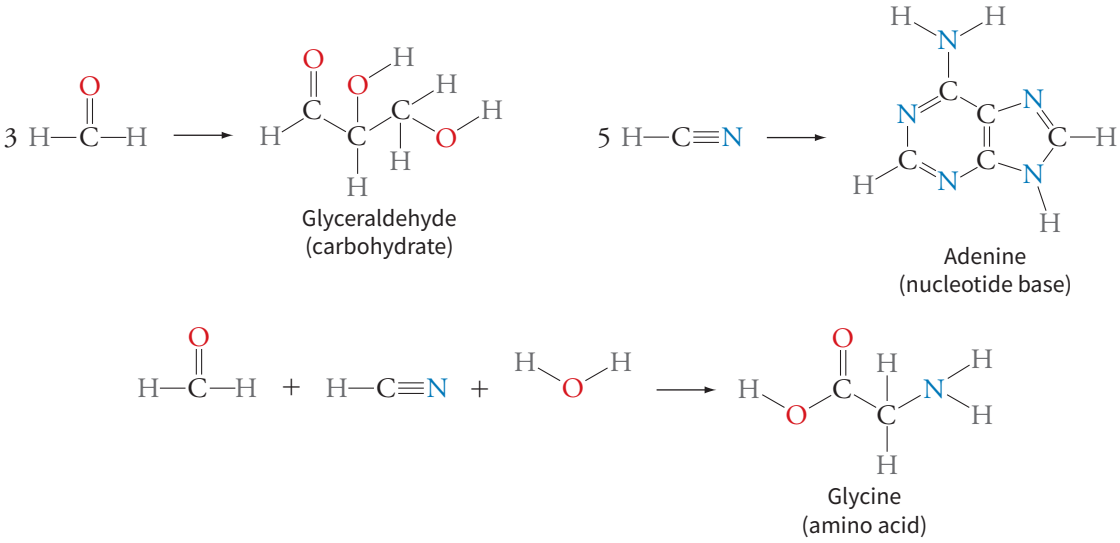
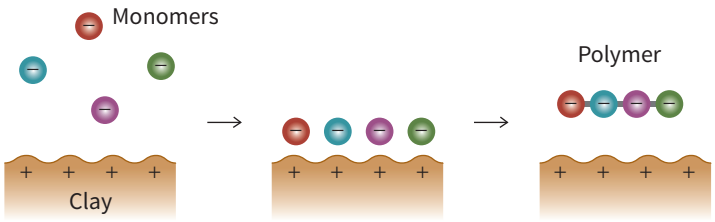
FIGURE 1.11 **A hydrothermal vent.** Life may have originated at these "black smokers," where high temperatures, H_2S, and metal sulfides might have stimulated the formation of biological molecules.

Prebiotic evolution led to cells

Experimental evidence strongly supports the hypothesis that early in the earth's history, small biological molecules such as amino acids and monosaccharides—and even the more elaborate nucleotides—arose spontaneously from inorganic (prebiotic) materials like H_2O, CH_4, and HCN. Such reactions, which need an energy source, might have occurred near hydrothermal vents, where water as hot as 350°C emerges from the sea floor (**Fig. 1.11**), or in terrestrial ponds exposed to lighting and ultraviolet radiation. A less-popular hypothesis is that organic molecules were delivered to the earth by meteorites, although the origin of those molecules also needs an explanation. Researchers have recovered amino acids and other biological molecules from hydrothermal vents and from laboratory experiments designed to mimic conditions on the early earth. Even with some uncertainty about the exact temperatures, reactant concentrations, and the involvement of catalysts like iron or nickel, organic molecules could have formed through hypothetical processes such as these:



Regardless of how they formed, the first biological building blocks must have accumulated, acquired reactive phosphate or thioester groups, and reached concentrations that allowed the formation of polymers. Polymerization might have been stimulated when the organic molecules—often bearing anionic (negatively charged) groups—aligned themselves on a cationic (positively charged) mineral surface:



In fact, in the laboratory, common clay promotes the polymerization of nucleotides into RNA. *Primitive polymers would have had to gain the capacity for self-replication*. Otherwise, no matter how stable or chemically versatile, such molecules would never have given rise to anything larger or more complicated: The probability of assembling a fully functional cell from a solution of thousands of separate small molecules is practically nil. Because RNA in modern cells represents a form of genetic information and participates in all aspects of expressing that information, it may be similar to the first self-replicating biopolymer. It might have made a copy of itself by first making a **complement,** a sort of mirror image, that could then make a complement of *itself,* which would be identical to the original molecule (**Fig. 1.12**).

A replicating molecule's chances of increasing in number depend on **natural selection,** the phenomenon whereby the entities best suited to the prevailing conditions are the likeliest to survive and multiply (**Box 1.B**). This would have favored a replicator that was chemically stable and had a ready supply of building blocks and free energy for making copies of itself. Accordingly, it would have been advantageous to become enclosed in some sort of membrane that could prevent valuable small molecules from diffusing away. Natural selection would also have favored replicating systems that developed the means for synthesizing their own building blocks and for more efficiently harnessing sources of free energy. Fossil evidence for microscopic life dates to about 3.5 billion years ago, about a billion years after the earth formed from interstellar dust.

The first cells were probably able to "fix" CO_2—that is, convert it to reduced organic compounds—using the free energy released in the oxidation of readily available inorganic compounds such as H_2S or Fe^{2+}. Vestiges of these processes can be seen in modern metabolic reactions that involve sulfur and iron.

Later, photosynthetic organisms similar to present-day cyanobacteria (also called blue-green algae) used the sun's energy to fix CO_2:

$$CO_2 + H_2O \rightarrow (CH_2O) + O_2$$

The concomitant oxidation of H_2O to O_2 dramatically increased the concentration of atmospheric O_2, about 2.5 billion years ago, and made it possible for **aerobic**

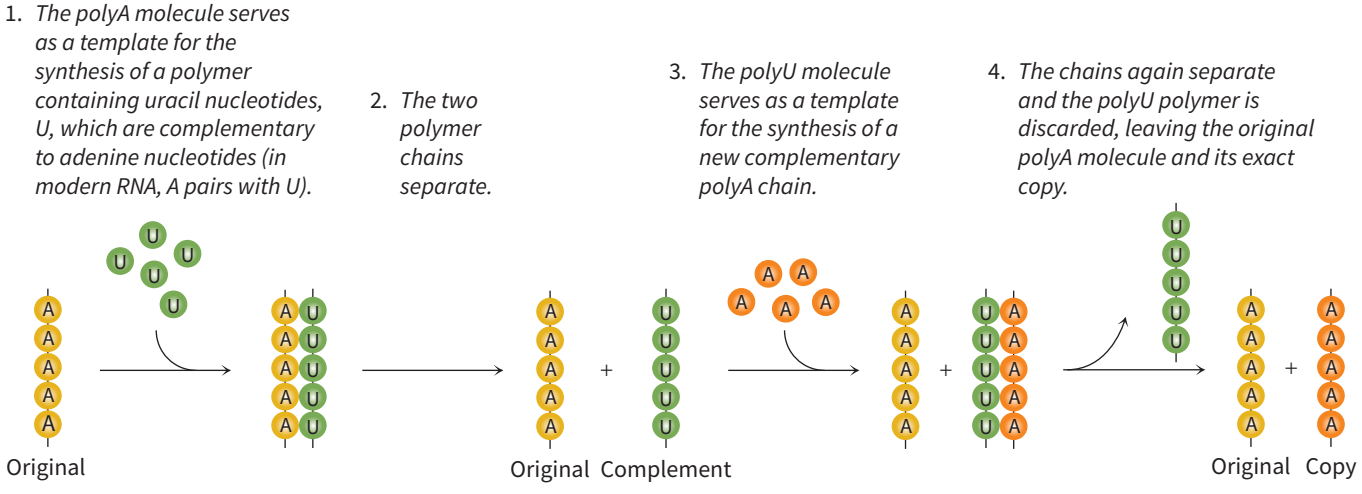


FIGURE 1.12 **Possible mechanism for the self-replication of a primitive RNA molecule.** For simplicity, the RNA molecule is shown as a polymer of adenine nucleotides, A.

Question **Draw a diagram showing how polyU would be replicated.**

Box 1.B How Does Evolution Work?

Documenting evolutionary change is relatively straightforward, but the mechanisms whereby evolution occurs are prone to misunderstanding. Populations change over time, and new species arise as a result of natural selection. Selection operates on individuals, but its effects can be seen in a population only over a period of time. Most populations are collections of individuals that share an overall genetic makeup but also exhibit small variations due to random alterations (mutations) in their genetic material as it is passed from parent to offspring. In general, the survival of an individual depends on how well suited it is to the particular conditions under which it lives.

Individuals whose genetic makeup grants them the greatest rate of survival have more opportunities to leave offspring with the same genetic makeup. Consequently, their characteristics become widespread in a population and, over time, the population appears to adapt to its environment. A species that is well suited to its environment tends to persist; a poorly adapted species fails to reproduce and therefore dies out.

Because evolution is the result of random variations and changing probabilities for successful reproduction, it is inherently random and unpredictable. Furthermore, natural selection acts on the raw materials at hand. It cannot create something out of nothing but must operate in increments. For example, the insect wing did not suddenly appear in the offspring of a wingless parent but most likely developed bit by bit, over many generations, by modification of a heat-exchange appendage. Each step of the wing's development would have been subject to natural selection, eventually making an individual that bore the appendage more likely to survive, perhaps by being able to first glide and then actually fly in pursuit of food or to evade predators.

Although we tend to think of evolution as an imperceptibly slow process, occurring on a geological time scale, it can be observed. For example, under optimal conditions, the bacterium *Escherichia coli* requires only about 20 minutes to produce a new generation. In the laboratory, a culture of *E. coli* cells can progress through about 2500 generations in a year (in contrast, 2500 human generations would require about 60,000 years). Hence, it is possible to subject a population of cultured bacterial cells to some "artificial" selection—for example, by making an essential nutrient scarce—and observe how the genetic composition of the population changes over time.

Experiments such as these have revealed that even after an initial period of rapid adaptation to the new conditions, the population continues to change, suggesting that evolution is an ongoing process with no fixed end point. In addition, so-called neutral mutations, which do not significantly affect an organism's fitness, randomly accumulate. For this reason, it is impossible to explain all genetic changes in terms of adaptations to specific conditions.

Question **Why can't acquired (rather than genetic) characteristics serve as the raw material for evolution?**

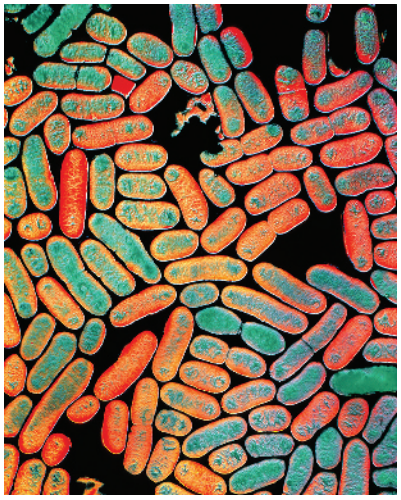
(oxygen-using) organisms to take advantage of this powerful oxidizing agent. The **anaerobic** origins of life are still visible in the most basic metabolic reactions of modern organisms; these reactions proceed in the absence of oxygen. Now that the earth's atmosphere contains about 20% oxygen, anaerobic organisms have not disappeared, but they have been restricted to microenvironments where O_2 is scarce, such as the digestive systems of animals or underwater sediments.

Eukaryotes are more complex than prokaryotes

The earth's present-day life-forms are of two types, which are distinguished by their cellular architecture:

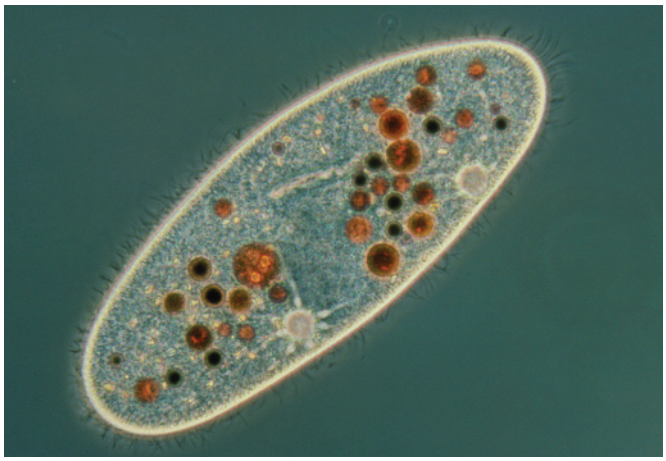
1. ***Prokaryotes*** *are small unicellular organisms that lack a discrete nucleus and usually contain no internal membrane systems.* This group comprises two subgroups that are remarkably different metabolically, although they are similar in appearance: the eubacteria (usually just called **bacteria**), exemplified by *E. coli,* and the **archaea** (or archaebacteria), best known as organisms that inhabit extreme environments, although they are actually found almost everywhere (**Fig. 1.13**).
2. ***Eukaryotic*** *cells are usually larger than prokaryotic cells and contain a nucleus and other membrane-bounded cellular compartments* (such as mitochondria, chloroplasts, and endoplasmic reticulum). Eukaryotes may be unicellular or multicellular. This group (also called the **eukarya**) includes microscopic organisms as well as familiar macroscopic plants and animals (**Fig. 1.14**).

By analyzing the sequences of nucleotides in certain genes that are present in all species, it is possible to construct a diagram that indicates how the bacteria, archaea, and eukarya are related. *The number of sequence differences between two groups of organisms indicates how long ago they diverged from a common ancestor.* Species with similar sequences have a longer shared evolutionary history than species with dissimilar sequences. This sort of analysis has produced the evolutionary tree shown in **Figure 1.15**.



E. Gray/Science Source

FIGURE 1.13 Prokaryotic cells. These single-celled *Escherichia coli* bacteria lack a nucleus and internal membrane systems.



Dr. David J. Patterson/Science Source

FIGURE 1.14 A eukaryotic cell. The paramecium, a one-celled organism, contains a nucleus and other membrane-bounded compartments.

Question Describe the visible differences between prokaryotic and eukaryotic cells (Figures 1.13 and 1.14).

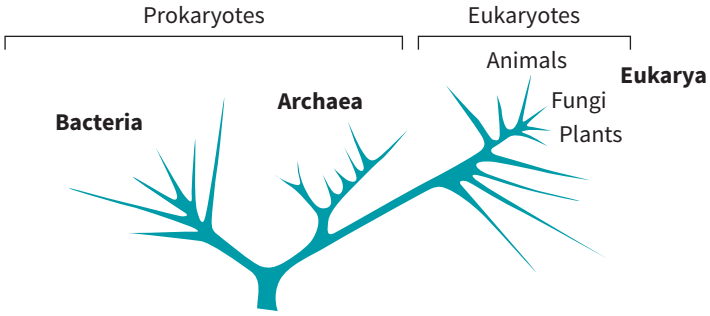


FIGURE 1.15 Evolutionary tree based on nucleotide sequences. This diagram reveals that the ancestors of archaea and bacteria separated before the eukarya emerged from an archaea-like ancestor. Note that the closely spaced fungi, plants, and animals are actually more similar to each other than are many groups of prokaryotes.

Eukaryotic cells are likely to have evolved from a mixed population of prokaryotic cells about 1.8 billion years ago. Over many generations of living in close proximity and sharing each other's metabolic products, some of the bacterial cells became stably incorporated inside archaeal cells, which accounts for the mosaic character of modern eukaryotic cells (**Fig. 1.16**).

The descendants of the once free-living bacteria became mitochondria, which carry out most of the eukaryote's oxidative metabolism, or chloroplasts, which carry out photosynthesis in plants and closely resemble the photosynthetic cyanobacteria. In fact, both mitochondria and chloroplasts contain their own genetic material and protein-synthesizing machinery and can grow and divide independently of the rest of the cell. Remnants of the archaeal ancestor of eukaryotes are found in the eukaryotic cytoskeleton and DNA-replication enzymes.

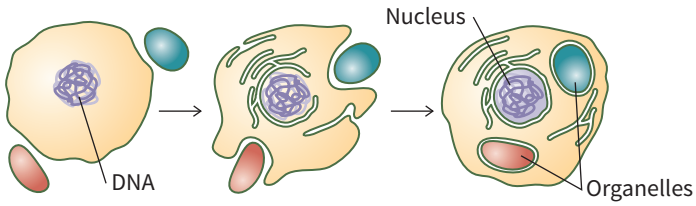


FIGURE 1.16 Possible origin of eukaryotic cells. The close association of different kinds of free-living cells gradually led to the modern eukaryotic cell, which appears to be a mosaic of bacterial and archaeal features and contains organelles that resemble whole bacterial cells.

The evolution of eukaryotes included the development of extensive intracellular membranes, many of which enclose discrete compartments, or **organelles,** with specialized functions, such as lysosomes (for the degradation of macromolecules), peroxisomes (for some oxidative reactions), and vacuoles (for storage). Like mitochondria and chloroplasts, the nucleus is surrounded by a double membrane; the outer nuclear membrane bends and folds extensively to form the endoplasmic reticulum. Some key features of eukaryotic cell structure are shown in **Figure 1.17**. A few types of prokaryotic cells also contain membrane-enclosed compartments devoted to storage or to chemical processes that could potentially damage the rest of the cell, but these cells lack a nucleus and the variety of organelles that characterize eukaryotic cells.

Many types of prokaryotic and eukaryotic cells live in colonies, which may increase metabolic efficiency through the cooperation of individual cells. However, a true multicellular lifestyle, which entails the division of labor and specialization among different types of cells, occurs only in eukaryotes. Multicellular organisms first appeared in the fossil record about 600 million years ago.

The earth currently sustains about 10 million different species (although estimates vary widely). Perhaps some 500 million species have appeared and vanished over the course of evolutionary history. It is unlikely that the earth harbors more than a few mammals that have yet to be discovered, but new microbial species are routinely described. Although the number of known prokaryotes (about 10,000) is much less than the number of known eukaryotes (for example, there are about 900,000 known species of insect), prokaryotic metabolic lifestyles are amazingly varied.

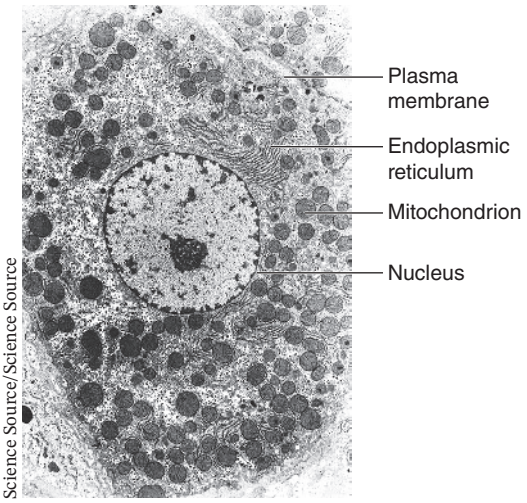


FIGURE 1.17 Eukaryotic cell structure. Key components of an animal cell are labeled in this electron micrograph. A typical plant cell also contains chloroplasts and is surrounded by a cell wall.

The human body includes microorganisms

The human body consists of an estimated 10 trillion (10^{13}) cells, and there may be as many as 40 to 100 trillion microorganisms living in and on the body, including bacteria, archaea, and fungi (viruses are also present but are molecular parasites rather than true cells). The "foreign" cells, mostly living in the intestine, form an integrated community called the **microbiota.** Very few of these cells are pathogens that cause disease; in fact, a diverse and stable microbiota actually helps to prevent the growth of harmful species.

Analysis of microbial DNA has allowed characterization of the **microbiome,** the genetic information contributed by the organisms that make up the microbiota. The microbiome reveals that the human species hosts several thousand different species of microorganisms. Many have not yet been identified, and relatively few have been cultured. However, an individual person typically harbors only a few hundred species of microorganisms. Establishing this community of cells begins at birth and is mostly complete after about a year. The mix of species remains fairly constant throughout the person's lifetime, although the proportions may fluctuate somewhat. The microbiota can vary markedly among individuals, even in the same household. However, the overall metabolic capabilities of the microbial community seem to matter more than which species are actually present. Contrary to expectations, there is no core microbiota that is common to all individuals.

The gut microbiota in particular plays a large role in digestion, providing nutrients to the host and regulating metabolic functions. However, byproducts of microbial metabolism can act as hormones and neurotransmitters with possible links to anxiety and depression. In turn, antibiotics, other types of drugs, and even some personal care products can alter the community of microorganisms and the chemicals they produce. All the while, the human immune system must ignore—or "tolerate"—the microbiota. If this balance is disrupted, the immune system may react to the microorganisms, generating inflammatory responses that can lead to diabetes or inflammatory bowel disease. Untangling these complicated relationships is the goal of the Integrated Human Microbiome Project (https://hmpdacc.org/ihmp/), which organizes data describing the species that inhabit the human body and contribute to human health and disease.

Before Going On

- Describe how simple prebiotic compounds could give rise to biological monomers and polymers.
- Explain why anaerobic organisms arose before aerobic organisms.
- Describe the differences between prokaryotes and eukaryotes.
- Explain why eukaryotic cells appear to be mosaics.
- List some functions of the human microbiota.

Summary

1.2 Biological Molecules

- The most abundant elements in biological molecules are H, C, N, O, P, and S, but a variety of other elements are also present in living systems.
- The major classes of small molecules in cells are amino acids, monosaccharides, nucleotides, and lipids. The major types of biological polymers are proteins, nucleic acids, and polysaccharides.

1.3 Energy and Metabolism

- Free energy has two components: enthalpy (heat content) and entropy (disorder). Free energy decreases in a spontaneous process.
- Life is thermodynamically possible because unfavorable endergonic processes are coupled to favorable exergonic processes.

1.4 The Origin of Cells

- The earliest cells may have evolved in concentrated solutions of molecules or near hydrothermal vents.
- Eukaryotic cells contain membrane-bounded organelles. Prokaryotic cells, which are smaller and simpler, include the bacteria and the archaea.

Key Terms

bioinformatics
homeostasis
trace element
amino acid
carbohydrate
monosaccharide
nucleotide
lipid
monomer
polymer
residue
polypeptide
protein
peptide bond
conformation
polynucleotide
nucleic acid
phosphodiester bond
polysaccharide
glycosidic bond
free energy (G)
enthalpy (H)
entropy (S)
exothermic reaction
endothermic reaction
ΔG
spontaneous process
exergonic reaction
nonspontaneous process
endergonic reaction
in vitro
in vivo
reduction
oxidation
enzyme
replication
evolution
complement
natural selection
aerobic
anaerobic
prokaryote
bacteria
archaea
eukaryote
eukarya
organelle
microbiota
microbiome

Bioinformatics

Brief Bioinformatics Exercises

1.1 The Periodic Table of the Elements and Domains of Life

1.2 Organic Functional Groups and the Three-Dimensional Structure of Vitamin C

Problems

1.2 Biological Molecules

1. Use Table 1.1 to assign the appropriate compound name to each molecule.

a. $H_3C—(CH_2)_{14}—\overset{\overset{O}{\|}}{C}—OH$

b. $H_3C—CH_2—NH_2$

c. $H_3C—\overset{\overset{O}{\|}}{C}—O—CH_2—CH_3$

d. $H_3C—CH_2—OH$

2. Use Table 1.1 to assign the appropriate compound name to each molecule.

a. $H_3C—O—CH_3$

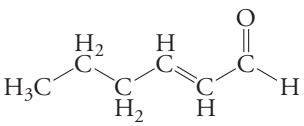
b. $H_3C—O—\overset{\overset{OH}{|}}{\underset{\underset{O}{\|}}{P}}—O—CH_3$

c. $H_3C—CH_2—SH$

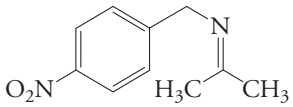
d. $H_3C—\overset{\overset{O}{\|}}{C}—CH_3$

3. Use Table 1.1 to assign the appropriate compound name to each molecule.

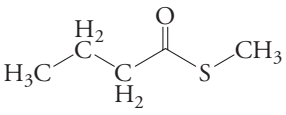
a.



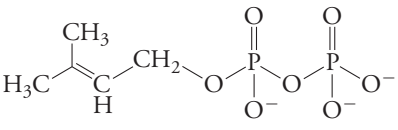
b.



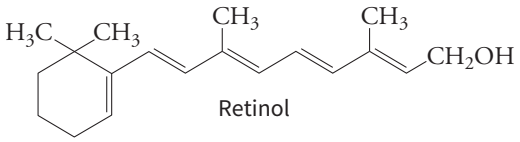
c.

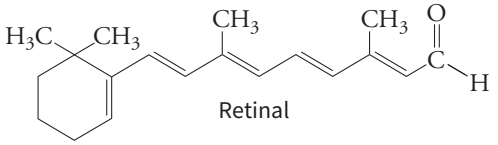


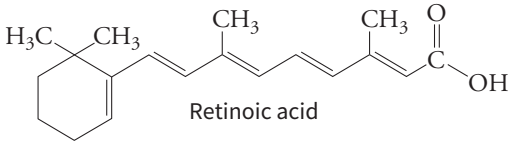
d.



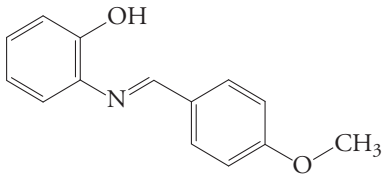
4. The structures of three forms of vitamin A are shown. Use Table 1.1 to assign the appropriate compound name to each molecule.



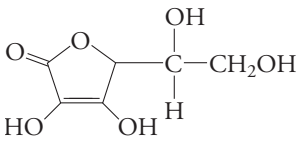


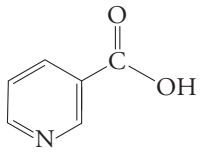


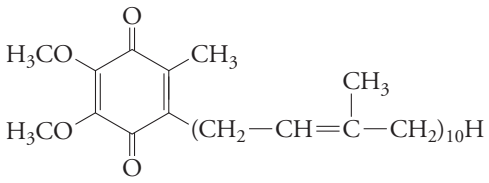
5. Investigators synthesized a series of compounds that showed promise as drugs for the treatment of Alzheimer's disease. The structure of one of the compounds is shown below. Use Table 1.1 to identify the functional groups in this compound.



6. The structures of several molecules are shown below. Use Table 1.1 to identify the functional groups in each structure.







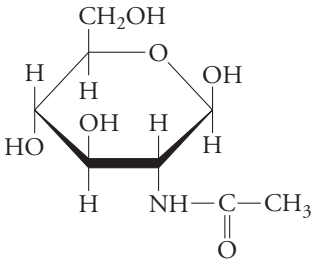
7. Coenzyme A is an important carrier of acetyl groups in metabolism. Its structure is shown in Figure 3.2. Use Table 1.1 to identify the functional groups in this molecule.

8. If an acetyl group is attached to the sulfhydryl group of coenzyme A (see Solution 1.7), what new functional group is formed?

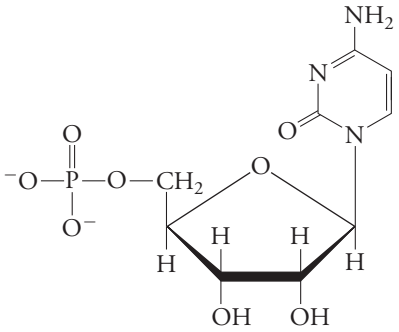
9. Name the four types of small biological molecules. Which three are capable of forming polymeric structures? What are the names of the polymeric structures that are formed?

10. To which of the four classes of biomolecules do the following compounds belong?

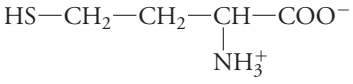
a.



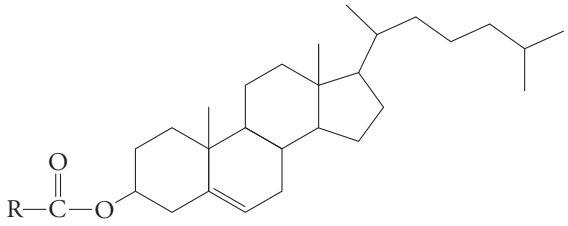
b.



c.

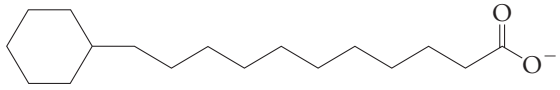


d.

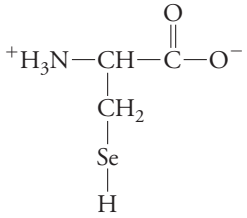


11. To which of the four classes of biomolecules do the following compounds belong?

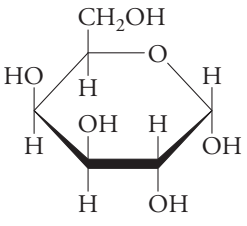
a.



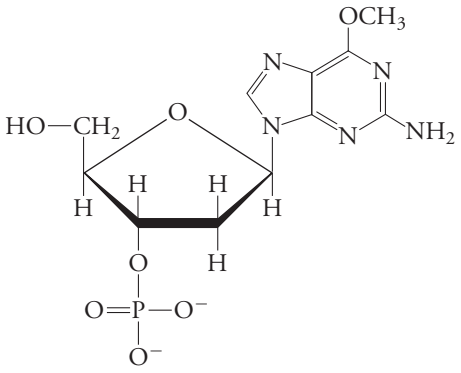
b.



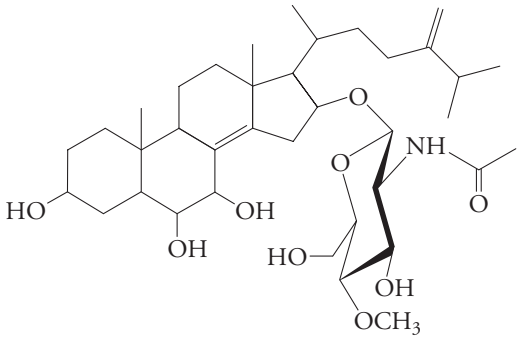
c.



d.



12. The compound shown below was isolated from the starfish *Anthenea aspera*. What two types of biomolecules are found in this compound?

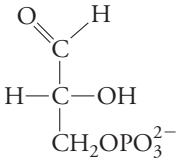


13. The nutritive quality of food can be analyzed by measuring the amounts of the chemical elements it contains. Most foods are mixtures of the three major types of molecules: **a.** fats (lipids), **b.** carbohydrates, and **c.** proteins. What elements are present in each of these types of molecules?

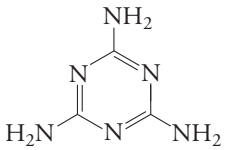
14. A compound present in many foods has the formula $C_{44}H_{86}O_8NP$. To which class of molecules does this compound belong? Explain your answer.

15. A healthy diet must include some protein. Assuming you had a way to measure the amount of each element in a sample of food, which element would you measure in order to tell whether the food contained protein?

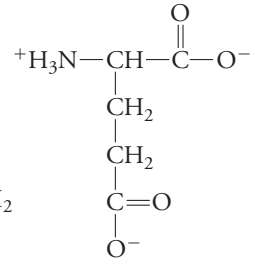
16. The structures of three compounds are shown below. Based on your answer to Problem 15, which of the three compounds would you add to a food sample so that it would appear to contain more protein? Which of the three compounds would already be present in a food sample that actually did contain protein? Explain.



A

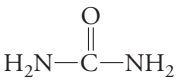


B



C

17. The structure of the compound urea is shown. Urea is a waste product of metabolism excreted by the kidneys into the urine. Why do doctors tell patients with kidney damage that they should consume a low-protein diet?



Urea

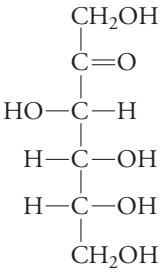
18. The structures of the amino acids asparagine (Asn) and cysteine (Cys) are shown in Section 1.2. What functional group does Asn have that Cys does not? What functional group does Cys have that Asn does not?

19. Consult Table 4.1 for the structures of the amino acids serine and lysine. What functional group does serine have that lysine does not?

20. Many amino acid side chains are modified after translation. Use the structures of serine and lysine from Problem 19 to draw the structures of the following modified amino acids: **a.** phosphoserine, **b.** hydroxylysine, and **c.** acetyllysine.

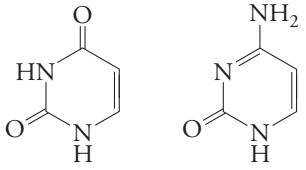
21. The "straight-chain" structure of glucose is shown in Section 1.2. What functional groups are present in the glucose molecule?

22. Consider the monosaccharide fructose. **a.** How does its molecular formula differ from that of glucose? **b.** How does its structure differ from the structure of glucose?



Fructose

23. The structures of the nitrogenous bases uracil and cytosine are shown below. How do their functional groups differ?

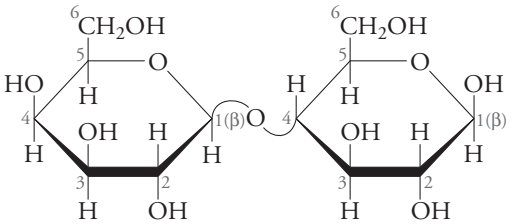


Uracil Cytosine

24. What are the structural components of the biological molecules called nucleotides?

25. What types of linkages are found in the following compounds?

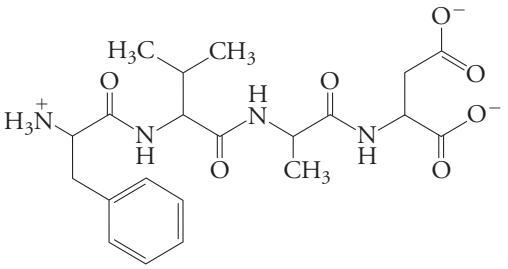
a.



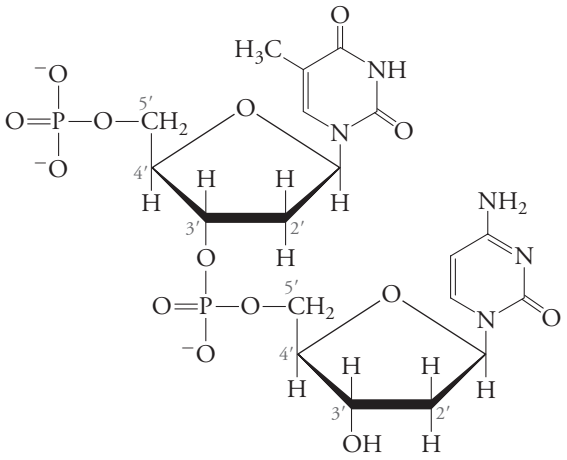
Galactose Glucose

Lactose

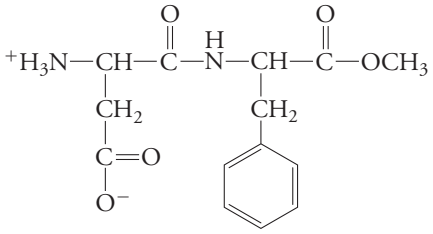
b.



c.



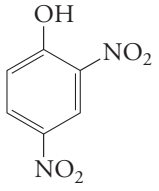
26. The structure of the artificial sweetener aspartame is shown below. What type of linkage is found in this compound?



Aspartame

27. Compare the solubilities in water of alanine, glucose, palmitate, and cholesterol, and explain your reasoning.

28. Cell membranes are largely hydrophobic structures. Which compound will pass through a membrane more easily, glucose or 2,4-dinitrophenol? Explain.



2,4-Dinitrophenol

29. What polymeric molecule forms a more regular structure, DNA or protein? Explain this observation in terms of the cellular roles of the two different molecules.

30. What are the two major biological roles of polysaccharides?

31. Pancreatic amylase digests the glycosidic bonds that link glucose residues together in starch. Would you expect this enzyme to digest the glycosidic bonds in cellulose as well? Explain why or why not.

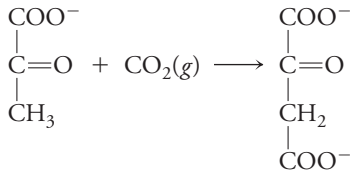
32. The complete digestion of starch in mammals yields 4 kilocalories per gram (see Problem 31). What is the energy yield for cellulose?

1.3 Energy and Metabolism

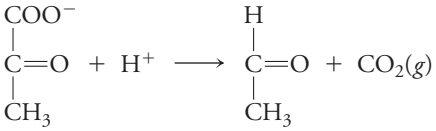
33. What is the sign of the entropy change for each of the following processes? **a.** Water freezes. **b.** Water evaporates. **c.** Dry ice sublimes. **d.** Sodium chloride dissolves in water. **e.** Several different types of lipid molecules assemble to form a membrane.

34. Does entropy increase or decrease in the following reactions in aqueous solution?

a.



b.



35. Which has the greater entropy, a polymeric molecule or a mixture of its constituent monomers?

36. How does the entropy change when glucose undergoes combustion?

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$

37. A soccer coach keeps a couple of instant cold packs in her bag in case one of her players suffers a muscle injury. Instant cold packs are composed of a plastic bag containing a smaller water bag and solid ammonium nitrate. In order to activate the cold pack, the bag is kneaded until the smaller water bag breaks, which allows the released water to dissolve the ammonium nitrate. The equation for the dissolution of ammonium nitrate in water is shown below. How does the cold pack work?

$$NH_4NO_3(s) \xrightarrow{H_2O} NH_4^+(aq) + NO_3^-(aq) \qquad \Delta H = 26.4\ kJ \cdot mol^{-1}$$

38. Campers carry hot packs with them, especially when camping during the winter months or at high altitudes. The design is similar to that described in Problem 37, except that calcium chloride is used in place of the ammonium nitrate. The equation for the dissolution of calcium chloride in water is shown below. How does the hot pack work?

$$CaCl_2(s) \xrightarrow{H_2O} Ca^{2+}(aq) + 2\ Cl^-(aq) \qquad \Delta H = -81\ kJ \cdot mol^{-1}$$

39. Urea (NH_2CONH_2) dissolves readily in water; i.e., this is a spontaneous process. A beaker containing the dissolved compound is cold to the touch. What conclusions can you make about the sign of the **a.** enthalpy change and **b.** entropy change for this process?

40. Would you expect the reaction shown in Problem 36 to be endergonic or exergonic? Explain.

41. Calculate ΔH and ΔS, as described in Sample Calculation 1.1, for the reaction in which reactant A is converted to product B.

	H (kJ · mol^{-1})	S (J · K^{-1} · mol^{-1})
A	54	22
B	60	43

42. Is the reaction described in Problem 41 favorable at **a.** 4°C and **b.** 37°C?

43. For a given reaction, the value of ΔH is 15 kJ · mol^{-1} and the value of ΔS is 51 J · K^{-1} · mol^{-1}. Above what temperature will this reaction be spontaneous?

44. Which of the following processes are spontaneous? **a.** A reaction that occurs with any size decrease in enthalpy and any size increase in entropy. **b.** A reaction that occurs with a small increase in enthalpy and a large increase in entropy. **c.** A reaction that occurs with a large decrease in enthalpy and a small decrease in entropy. **d.** A reaction that occurs with any size increase in enthalpy and any size decrease in entropy.

45. Given that the process described in Problem 37 is spontaneous, what are the signs of ΔS and ΔG? Confirm your answer by using the enthalpy change provided to calculate the sign and magnitude of ΔS. Assume a temperature of 25°C.

46. Given that the process described in Problem 38 is spontaneous, what are the signs of ΔS and ΔG? Confirm your answer by using the enthalpy change provided to calculate the sign and magnitude of ΔS. Assume a temperature of 25°C.

47. The hydrolysis of pyrophosphate at 25°C is spontaneous. The enthalpy change for this reaction is −14.3 kJ · mol^{-1}. What is the sign and the magnitude of ΔS for this reaction?

48. Phosphoenolpyruvate donates a phosphate group to ADP to produce pyruvate and ATP. The ΔG value for this reaction at 25°C is −63 kJ · mol^{-1} and the value of ΔS is 190 J · K^{-1} · mol^{-1}. What is the value of ΔH? Is heat absorbed from or released to the surroundings?

49. A monoclonal antibody binds to the protein cytochrome *c*. The ΔH value for binding at 25°C is −87.9 kJ · mol^{-1} and the ΔS is −118 J · K^{-1} · mol^{-1}. **a.** Does entropy increase or decrease when the antibody binds to the protein? **b.** Calculate ΔG for the formation of the antibody–protein complex. Does the complex form spontaneously? **c.** The ΔG value for the binding of a second monoclonal antibody to cytochrome *c* is −58.2 kJ · mol^{-1}. Which antibody binds more readily to the protein?

50. Phosphofructokinase catalyzes the transfer of a phosphate group (from ATP) to fructose-6-phosphate to produce fructose-1,6-bisphosphate. The ΔH value for this reaction is −9.5 kJ · mol^{-1} and the ΔG is −17.2 kJ · mol^{-1} at 37°C. **a.** Is heat absorbed from or released to the surroundings? **b.** What is the value of ΔS for the reaction? Does this reaction proceed with an increase or decrease in entropy? **c.** Which component makes a greater contribution to the free energy change: the ΔH or ΔS value? Comment on the significance of this observation.

51. Glucose can be converted to glucose-6-phosphate:

$$\text{glucose} + \text{phosphate} \rightarrow \text{glucose-6-phosphate} + H_2O$$
$$\Delta G \text{ is } 13.8\ kJ \cdot mol^{-1}$$

a. Is this reaction favorable? Explain.

b. Suppose the synthesis of glucose-6-phosphate is coupled with the hydrolysis of ATP. Write the overall equation for the coupled process and calculate the ΔG for the coupled reaction. Is the conversion of glucose to glucose-6-phosphate favorable under these conditions? Explain.

$$ATP + H_2O \rightarrow ADP + \text{phosphate} \qquad \Delta G = -30.5\ kJ \cdot mol^{-1}$$

52. Glyceraldehyde-3-phosphate (GAP) is converted to 1,3-bisphosphoglycerate (1,3BPG) as shown.

$$GAP + P_i + NAD^+ \rightarrow 1{,}3BPG + NADH \qquad \Delta G = 6.7\ kJ \cdot mol^{-1}$$

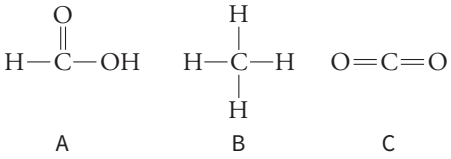
a. Is this reaction spontaneous?

b. The reaction shown above is coupled to the following reaction in which 1,3BPG is converted to 3-phosphoglycerate (3PG):

$$\text{1,3BPG} + \text{ADP} \rightarrow \text{3PG} + \text{ATP} \qquad \Delta G = -18.8 \text{ kJ} \cdot \text{mol}^{-1}$$

Write the equation for the overall conversion of GAP to 3PG. Is the coupled reaction favorable?

53. Place these molecules in order from the most oxidized to the most reduced.



A B C

54. Identify the process described in the following statements as an oxidation or reduction process.

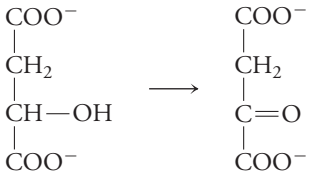
a. Monosaccharides are synthesized from carbon dioxide by plants during photosynthesis.

b. An animal eats the plant and breaks down the monosaccharide in order to obtain energy for cellular processes.

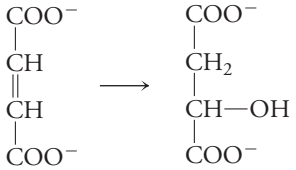
55. Given the following reactions, tell whether the reactant is being oxidized or reduced. Reactions may not be balanced.

a.

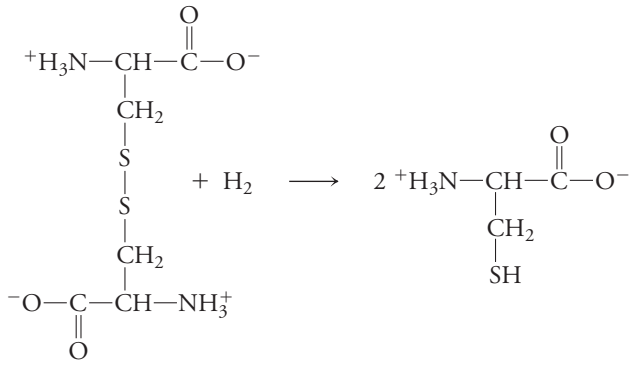
b.



c.



d.



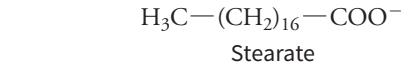
56. For each of the reactions in Problem 55, tell whether an oxidizing agent or a reducing agent is needed to accomplish the reaction.

57. Rank the forms of vitamin A (see Problem 4) in order from most oxidized to most reduced.

58. The reaction shown in Problem 52 requires the coenzyme NAD^+, which is reduced to NADH during the reaction. Which is more oxidized, GAP or 1,3BPG?

59. In some cells, lipids such as palmitate (shown in Section 1.2), rather than monosaccharides, serve as the primary metabolic fuel. **a.** Consider the oxidation state of palmitate's carbon atoms and explain how it fits into a scheme such as the one shown in Figure 1.10. **b.** On a per-carbon basis, which would make more energy available for metabolic reactions: palmitate or glucose?

60. Which yields more free energy when completely oxidized, stearate or α-linolenate?



Stearate

α-Linolenate

61. A protein folds from a random coil into a highly ordered structure. How does this process, which proceeds with a loss of entropy, obey the laws of thermodynamics?

62. An enzyme binds to a substrate, forming an enzyme–substrate complex. Explain how this process obeys the laws of thermodynamics.

1.4 The Origin of Cells

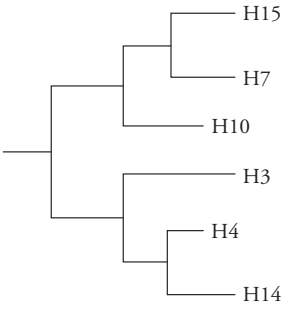
63. Why is molecular information so important for classifying and tracing the evolutionary relatedness of bacterial species but less important for vertebrate species?

64. The first theories to explain the similarities between bacteria and mitochondria or chloroplasts suggested that an early eukaryotic cell engulfed but failed to fully digest a free-living prokaryotic cell. Why is such an event unlikely to account for the origin of mitochondria or chloroplasts?

65. Draw a simple evolutionary tree that shows the relationships between species A, B, and C based on the DNA sequences given here.

Species A	T C G T C G A G T C
Species B	T G G A C T A G C C
Species C	T G G A C C A G C C

66. A portion of the evolutionary tree for a flu virus is shown here. Different strains are identified by an H followed by a number. **a.** Identify two pairs of closely related flu strains. **b.** Which strain(s) is(are) most closely related to strain H3?



67. Propose an explanation why taking antibiotics sometimes leads to illness caused by the intestinal bacterium *Clostridium difficile*.

68. Clinicians know that a drug may be ineffective as an antibiotic when tested with pure cultures of bacteria in the laboratory. Yet when the drug is orally administered to a patient, it has the desired antibacterial effect against the same bacteria. Explain.

Selected Readings

Archibald, J.M., Endosymbiosis and eukaryotic cell evolution, *Current Biol.* 25, R911–R921, doi: 10.1016/j.cub.2015.07.055 (2015). [An extensive review of hypotheses about the origins of mitochondria and chloroplasts in eukaryotic cells.]

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Chapter 1 Credits

Figure 1.4 Adapted from Palm, W. and Thompson, C.B., *Nature* 546, 234–242 (2017).

Figure 1.5 Image based on 1EDN. Janes, R.W., Peapus, D.H., Wallace, B.A., The crystal structure of human endothelin, *Nat. Struct. Biol.* 1, 311–319 (1994).

Figure 1.6 Image based on Nucleic Acids Database ARF0108. Biswas, R., Mitra, S.N., Sundaralingam, M., 1.76 A structure of a pyrimidine start alternating A-RNA hexamer r(CGUAC)dG, *Acta Crystallogr., Sect. D* 54, 570–576 (1998).

Figure 1.15 Adapted from Wheelis, M.L., Kandler, O., and Woese, C.R., *Proc. Natl. Acad. Sci. USA* 89, 2930–2934 (1992).