

CHAPTER

1



The most pressing and widespread medical problems in the world today are caused by malnutrition, defined as inadequate or improper nourishment. Malnutrition comes in many forms and is present in both poor and rich nations. In less affluent, developing countries, the most significant nutritional problem among young children is the scarcity of proper foods, which leads to the development of marasmus, also called “wasting disease” (caused by starvation), and the disease kwashiorkor (protein inadequacy). In affluent, developed countries, the nutritional problem is the opposite extreme, with excess food consumption leading to obesity and its related diseases (see Biochemistry in the Clinic 1). Biochemists for many years have been busy studying the molecular consequences of all forms of malnutrition in their search for medical treatments and agricultural remedies for relief of the problem.

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Biochemistry: From Atoms to Molecules to Cells

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Welcome to biochemistry! This subject is not entirely new because you have gained some biochemical understanding in prerequisite biology and chemistry classes. But here you will encounter many more details of the complex, but always interesting and practical, concepts in biochemistry. Even though the term *biochemistry*, after about 100 years of use, has become commonplace in our language, a precise definition is difficult and depends on who you ask. Most scientists will agree with the straightforward definition, *the study of life at the molecular level*. The word “biochemistry” has two components, biology and chemistry, and students of the discipline must be well versed in the fundamentals of both subjects.

What Is Biochemistry?

All living organisms participate in certain processes that we define as the important characteristics of life:

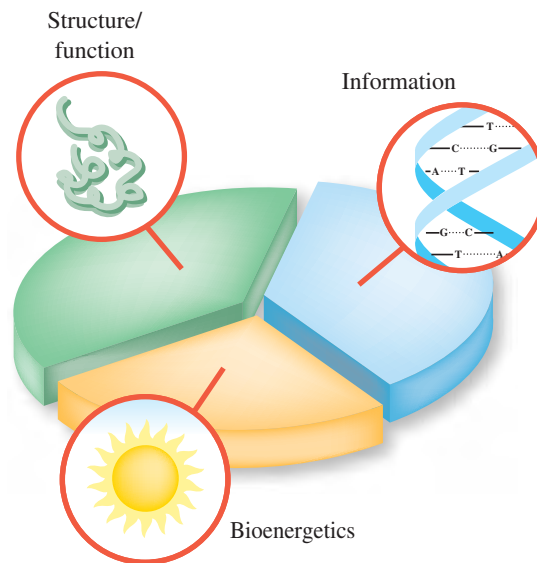
- Organisms are able to extract energy from molecules called nutrients.
- Organisms display the attributes of growth, differentiation, and reproduction.
- Organisms have the ability to respond to changes in their environments.

The overall goal of biochemistry is to describe life’s processes using the language of molecules, that is, applying the principles and methods of chemistry to determine molecular structure from which it is often possible to explain biological function. Even the smallest living cell contains thousands of organic and inorganic chemicals, many of them large molecules called **macromolecules**. All biological processes—including vision, thinking, digestion, immunity, motion, and disease conditions—result from how molecules act and, sometimes, misbehave. Because most biological processes occur within the confines of the fundamental biological unit called the cell, one must know the details of cellular structure. The respective roles and importance of both chemistry and biology in achieving the goals of biochemistry are readily apparent.

To better understand how biochemistry works to describe biological processes, the discipline is often organized into three primary areas (Figure 1.1):

1. **Structural and functional biochemistry** focuses initially on discovering the chemical structures and three-dimensional arrangements of biomolecules, those chemicals that are found in living matter. To describe biological processes, one must have a knowledge of the molecular structures of the participating biomolecules, which then often leads to an understanding of the function or purpose of the cellular molecules.

Figure 1.1 The nature of biochemistry showing the three important areas of study.



2. **Informational biochemistry** defines the language(s) for storing biological data and for transmitting that data in cells and organisms. This area includes molecular genetics, which describes the molecular processes in heredity and expression of genetic information and also processes that communicate molecular signals to regulate cellular activities (i.e., hormone action). An organism is indeed a complex, information-processing system.
3. **Bioenergetics** describes the flow of energy in living organisms and how it may be transferred from one process to another. Some molecular events of cells and organisms such as muscle contraction, synthesis of molecules, and membrane transport require the input of energy (are **endergonic**), whereas others, like metabolic degradation of food and absorption of light from the sun, release energy (are **exergonic**). How organisms use biochemical reactions and biomolecules to transfer energy from exergonic to endergonic events will be pivotal in our understanding of life processes. The transfer of energy usually means the transformation of one type of energy to another. For example, the foods that we eat contain potential molecular energy that is used to maintain body temperature, regulate the flow of ions in nerve transmission, and to provide energy for the contraction of muscle.

Why Should We Study Biochemistry?

Learning biochemical principles is not just important for those who will become biochemists and use the concepts daily. Many aspects of everyday life are related directly to the subject matter of biochemistry. Here are some of the ways that biochemistry impacts and enriches our lives:

1. Biochemical studies lead us to a fundamental understanding of life. All of us have a natural curiosity about how our bodies work. What are the biochemical similarities and differences among the many forms of life? How do organisms store and transfer information necessary to reproduce themselves? What primary molecules and processes were involved in the origin of life? How is food digested to provide cellular energy? How does a brain cell store mathematical and chemical formulas? Research in biochemistry is providing answers to these and other important questions.
2. Biochemistry has a profound impact on our understanding of medicine, health, nutrition, and the environment. Results from biochemical studies have already led to a molecular understanding of diseases such as diabetes, sickle-cell anemia, phenylketonuria, cystic fibrosis, hypercholesterolemia, and some forms of cancer. The recent sequencing of the human genome will help in our search for cures for AIDS, Alzheimer's disease, West Nile virus, depression, influenza, and other disease conditions. For example, we need to understand why people respond quite differently to drug treatments. Recombinant DNA technology and its ability to probe chromosomal regions for genetic mutations will play a major role in the diagnosis and treatment of diseases (gene therapy). Recombinant DNA will also aid in the design of new plants for agricultural purposes, which should alleviate some of the world's food and nutrition problems. The study of enzymes (biological catalysts) and metabolism provides a foundation for the rational design of drugs and for the detailed understanding of nutrition.
3. Biotechnology, the application of biological materials such as cells and macromolecules to technically useful operations, will also advance from biochemical studies. Already enzymes are used in the pharmaceutical industry to synthesize complex drugs. Various strains of microorganisms have been selected and altered for producing therapeutic proteins, for manufacturing fuel alcohol from corn and other plant materials, for cleaning up oil and other toxic spills, and for mining metals from natural ores.



A running person uses energy derived from metabolism of carbohydrates, fats, and proteins. (© David Madison/Allsport/Getty Image.)

Before You Go On . .

1. Your text gave a simple, straightforward definition for biochemistry, “the study of life at the molecular level.” Write a more detailed definition of the field of biochemistry using at least 40–50 words.
2. Consider the following statement: “Biochemistry is a unique discipline because it uses the principles and methods of one science to explain another science.” Name the two science disciplines referred to here, and explain the meaning of the statement.

1.1**The Roots of Biochemistry***Learning Objective*

Have an appreciation for the historical roots of biochemistry in biology, chemistry, and physics. Recognize the scope of topics within the realm of biochemistry, and the impact of the discipline on medicine, health, technology, and everyday life.

Early History of Biochemistry

People of early civilizations in Mesopotamia, Egypt, China, India, Rome, and Greece did not understand the biochemical principles underlying the baking of leavened bread, the fermentation of fruit juices, or the treatment of maladies with plant and animal materials. However, the lack of knowledge did not prevent their enjoyment of the results of these biochemical processes. Early studies in biology, which concentrated on the treatment of illness and the attainment of good health, were firmly rooted in and combined with philosophy and religion.

The Chinese in the fourth century B.C. believed that humans contained five elements: water, fire, wood, metal, and earth. When all elements were present in proper balance, good health resulted. An imbalance in the elements caused illness. Chinese physicians discovered in the seventh century A.D. that night blindness could be treated with pig and sheep livers. Modern biochemists and physicians know that night blindness is caused by a deficiency of vitamin A, a biochemical abundant in liver.

The early Greeks, including Plato (428–348 B.C.), attempted to explain the body in terms of cosmological theories and stressed diet for treatment of disease. The Greek term for digestion, *pepsis*, a word indicating inner heat, is the origin of the word *pepsin*, a digestive enzyme. The Greek physician Galen (A.D. 129–199) campaigned for a pharmacological approach to good health using plant and animal products for disease treatment.

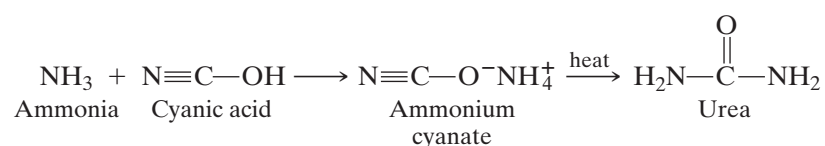
Arabic biology, which flourished after the founding of Baghdad in A.D. 762, was greatly influenced by early Greek scientific knowledge. However, the Arabs were not content with the abstract nature of Greek science so they advanced the use of Greek pharmaceutical recipes by determining and classifying the strength and chemical nature of natural drugs. The Greek and Arabic scientific literature did not arrive in western Europe until the 11th century A.D. During the next several centuries, medical schools, which followed the teachings of the Greeks, were established at Bologna (Italy), Paris (France), and Toledo (Spain). A key figure in European science, Paracelsus (A.D. 1493–1541), began a move away from the ancient medical doctrines of Aristotle, Galen, and the Arab scientist Avicenna (980–1037). Paracelsus studied medicine at several European universities, but it is doubtful whether he ever completed requirements for a medical degree. He spent his life writing and traveling from city to city expounding on his revolutionary ideas about medicine and biology. His concepts of biochemistry have been described by Pachter: “As a biochemist, he [Paracelsus] asserted that man is made out of the same material as the rest of creation, feeds on the substances that make up the universe, and is subject to the laws



Biochemists study the molecular characteristics of living organisms on land and in water. (© NASA.)

which govern their growth and decay. At the same time, each living being is unique, individually constituted, and follows his own destiny.”¹ Even now, over 460 years after Paracelsus’ death, we are impressed with the correctness of his views.

Influenced by Paracelsus, biologists in the 17th and 18th centuries began in earnest a more scientific approach to the study of biological materials and processes. A favorite theme for study was the digestive process, for many scientists began to recognize that this could be explained by chemical principles. During the 19th century, any biological process that could not be understood in chemical terms was explained by the doctrine of **vitalism**. Vitalists argued that it was the presence of a vital force (life force or spirit) that distinguished the living organic world from the inanimate inorganic world. The experiment that destroyed the ideas of vitalism was the synthesis of urea, an organic chemical found in natural cells. In 1828, using only the inorganic and therefore “lifeless” chemicals ammonia and cyanic acid, the German chemist Friedrich Wöhler synthesized urea:



It is difficult to pinpoint a specific time or event that marked the start of modern biochemistry. Many science historians usually select the above in vitro (without biological cells) synthesis of urea by Wöhler as the starting point.

The Road to Modern Biochemistry

There is more than a single path from these historical beginnings to present-day biochemistry. Two separate and distinct avenues of scientific inquiry have led to our current state of biochemical knowledge (Figure 1.2). One avenue can be traced through the physical sciences and emphasizes structural characteristics of biomolecules. This

¹H. Pachter, *Paracelsus. Magic into Science* (New York, 1951), Henry Schuman.

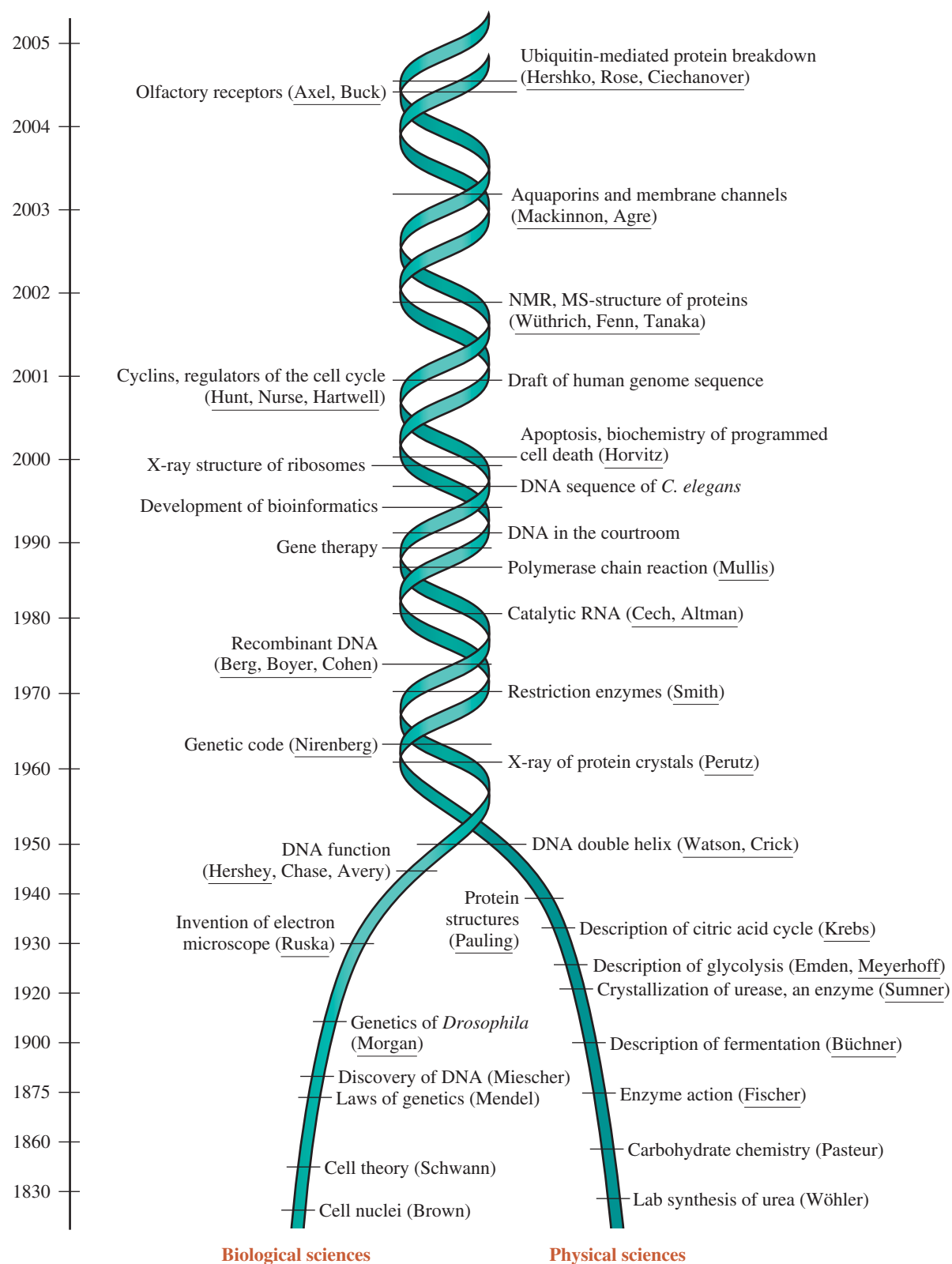


Figure 1.2 The origins of biochemistry from two perspectives, the physical sciences and the biological sciences. The dates of Nobel prizes and of selected important events in the development of biochemistry are noted in the scale on the left. Names of Nobel Prize winners are underlined.



Grape harvest and wine production as depicted in an early Egyptian wall painting. Fermentation of carbohydrates in grape juice to ethanol is carried out by yeast. (© George Holton/Photo Researchers.)

approach has applied the basic laws of physics and chemistry to explain the processes of the living cell. For example, Linus Pauling in the 20th century used the tool of X-ray crystallography to study the structure of amides and peptides. The other avenue traveled by the biologists, especially microbiologists, cell biologists, physiologists, and geneticists, is characterized mainly by a study of cell organization and function. The first use of the term *biochemistry* is unclear (perhaps around 1900); however, early scientists who considered themselves biochemists traveled on the physical sciences pathway. The two avenues of study converged in 1952 with the announcement by James Watson and Francis Crick of the double helix structure for DNA. Here the application of physics (crystallography), chemistry (structure and bonding), and biology (storage and transfer of genetic information) all came together to help solve what was the most exciting and complex biological problem at that time: the structure of the genetic material, DNA. The growth of knowledge in biochemistry since that time has been explosive. Some of the major events are noted in Figure 1.2.

The term **molecular biology** is often used to describe studies at the interface of chemistry and biology. The term was first coined in 1938 by officials at the Rockefeller Foundation to describe a new funding program that provided financial support for the application of the tools of the physical sciences to biology, biochemistry, cell biology, and genetics. Biochemistry and molecular biology have similar goals; however, their approaches to solving problems have been different in the past. Molecular biologists emphasized the study of genetic material (RNA and DNA), especially its role in biological information transfer, and they used more biological experimental approaches involving organisms, recombinant DNA, and molecular genetics. As described earlier, biochemists focused on the structure and function of all biomolecules and energy relationships among them. Biochemists often used tools designed for chemical and physical measurements but are now increasingly using techniques of molecular biology. The boundaries between biochemistry and molecular biology are rapidly disappearing and, in fact, most scientists consider the fields to be the same. It is now important for biochemists to know both the cycle of cell development and the citric acid cycle of metabolism. It is essential for molecular biologists to know and understand the chemical structures of biomolecules. Biochemistry and molecular biology are becoming indistinguishable because they seek answers to the same question: What is life?



James Watson (*left*) and Francis Crick discuss an early model of the DNA double helix. (© A. Barrington Brown/Science Source/Photo Researchers.)



1.2

All Living Matter Contains C, H, O, N, P, and S

Learning Objective

Have a general knowledge of the elemental composition of biomolecules.

Chemical Elements in Biomolecules

Of the 100 plus chemical elements, only about 31 (28%) occur naturally in plants and animals. As shown in Figure 1.3 the elements present in biological material can be divided into three categories:

1. Elements *found in bulk form and essential for life*: Carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur make up about 92% of the dry weight of living things.
2. Elements *in trace quantities in most organisms and very likely essential for life*, such as calcium, manganese, iron, and iodine.
3. Trace elements that *are present in some organisms and may be essential for life*, such as arsenic, bromine, molybdenum, and vanadium.

We do not understand exactly how these elements were selected by primitive life-forms during the early stages of evolutionary development. The elements found in biomolecules do not have similar properties and characteristics. Nearly all groups of the periodic table of elements are represented in biological materials. Both metals and nonmetals are present. One of two hypotheses may explain the selection: There was a deliberate choice because of an element's favorable characteristics or there was a random selection from the alphabet soup of elements present in the earth's crust, atmosphere, and universe. If the latter were true, then we would expect to find approximately the same ratios of elements in biological organisms as we find in the universe. A comparison of the elemental composition of the earth's crust and the universe with that of living matter shown in Figure 1.4 refutes the latter hypothesis.

1.2 All Living Matter Contains C, H, O, N, P, and S

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	Group IA	Group IIA											Group IIIB	Group IVB	Group VB	Group VIB	Group VIIB	Group 0
Period 1	1 H hydrogen																	2
Period 2	3	4											5 B boron	6 C carbon	7 N nitrogen	8 O oxygen	9 F fluorine	10
Period 3	11 Na sodium	12 Mg magnesium	TRANSITION METALS										13 Al aluminum	14 Si silicon	15 P phosphorus	16 S sulfur	17 Cl chlorine	18
Period 4	19 K potassium	20 Ca calcium	21	22	23 V vanadium	24 Cr chromium	25 Mn manganese	26 Fe iron	27 Co cobalt	28 Ni nickel	29 Cu copper	30 Zn zinc	31 Ga gallium	32	33 As arsenic	34 Se selenium	35 Br bromine	36
Period 5					42 Mo molybdenum							48 Cd cadmium					53 I iodine	
Period 6					74 W tungsten													
Period 7																		

Figure 1.3 The biochemist's periodic table. Elements in red are present in bulk form in living cells and are essential for life. Those in yellow are trace elements that are very likely essential. Those elements in blue are present in some organisms and may be essential.

We must conclude that elements were selected according to their abilities to perform certain structural functions or to provide specific reactivities. For example, carbon forms multiple covalent bonds with other carbon atoms as well as with other elements such as nitrogen, hydrogen, oxygen, or sulfur. This feature allows the construction of long carbon chains and rings with the presence of reactive functional

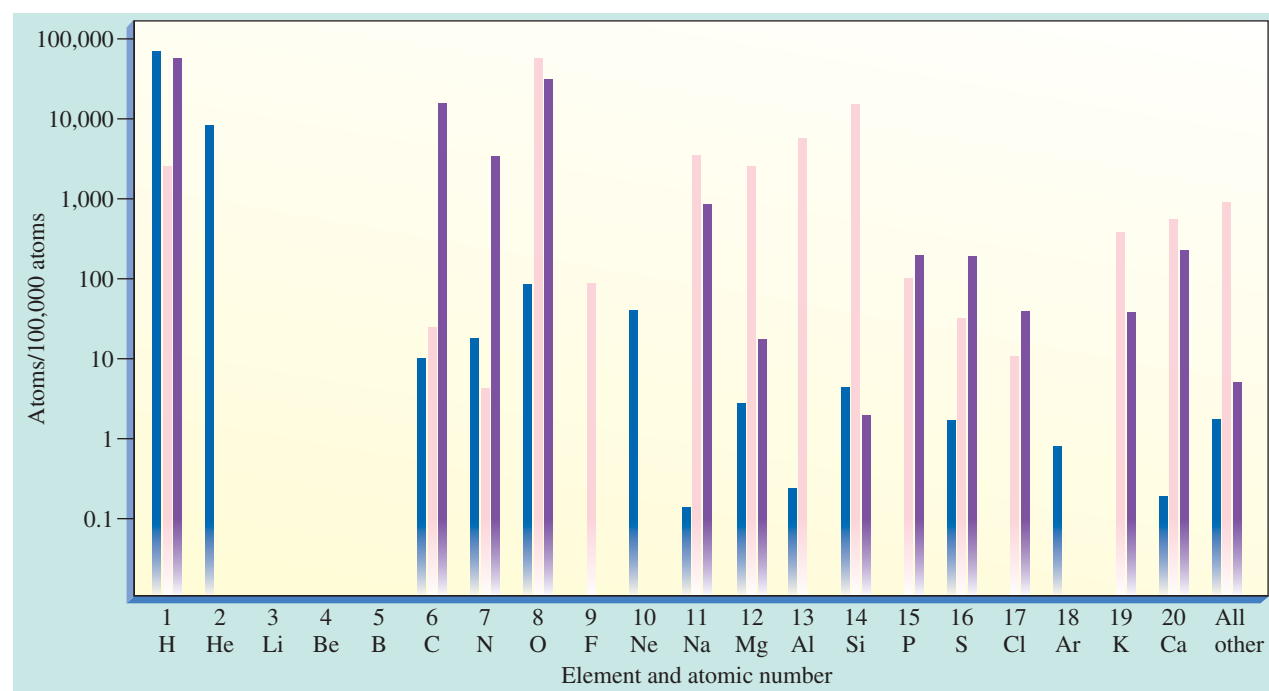


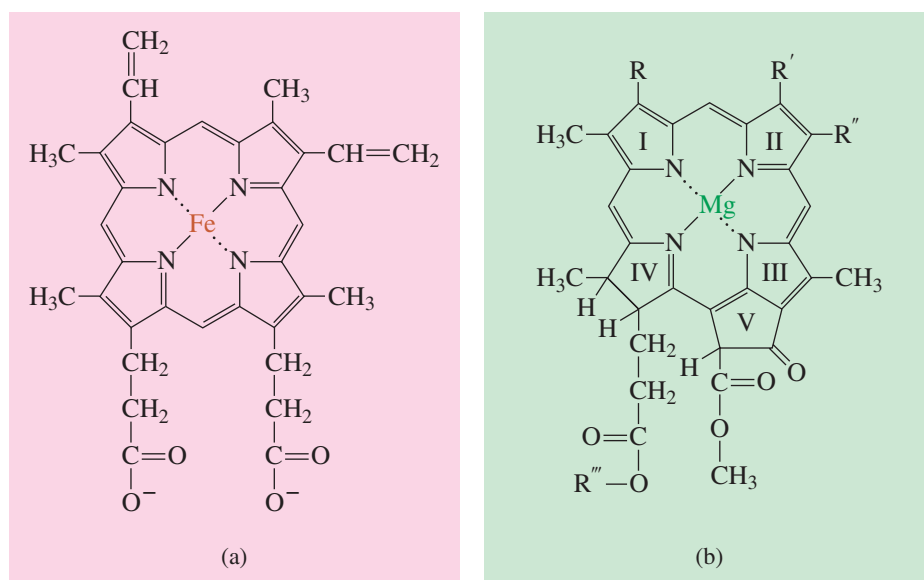
Figure 1.4 Elemental composition of the universe (blue), the earth's crust (pink), and the human body (purple).

groups containing nitrogen, oxygen, and sulfur as in proteins, nucleic acids, lipids, and carbohydrates. Iron was selected by evolutionary forces because it is able to bind the oxygen molecule in a reversible fashion. Elements found in the earth and atmosphere may have been tested by trial and error in living organisms during millions of years. Those elements that most effectively performed the necessary tasks and, most importantly, allowed the plant or animal to thrive were retained.

Combining Elements into Compounds

The combination of chemical elements into biomolecules provides for great variety in chemical structure and reactivity. Biomolecules contain functional groups that are common in organic chemistry (see Just in Time Review 1-1). Compounds representing all three states of matter (gases, liquids, and solids) are present in living cells. One of the most recent advances in biochemistry is the discovery of an enzyme that catalyzes the synthesis of the gas nitric oxide (NO) in the brain and other organs where it serves to regulate biological processes. Nature's molecules include examples of cations, anions, covalent compounds, ionic compounds, metal ions, coordination complexes, and polymers. Several well-known examples illustrate the diverse array of organic and organometallic chemicals that perform a variety of cellular roles. The **amino acids** are building blocks for protein structure. The **carbohydrates** are involved as nutrients in energy metabolism and play roles in cell structure and molecular recognition as well. **Lipids** are a diverse collection of organic compounds that display low water solubility. The lipids have primary functions as energy molecules in metabolism, as components for the construction of cell membranes, and as hormones. The **vitamins**, a broad assortment of organic compounds, ensure proper growth and development by functioning in major biochemical processes. Prominent among the natural organometallic compounds are **heme** and **chlorophyll**. Both consist of a substituted porphyrin ring coordinated with a metal ion. Heme, a porphyrin ring with iron (Figure 1.5a), is found in the oxygen transport proteins myoglobin and hemoglobin, in respiratory proteins such as cytochrome *c*, and in enzymes such as catalase. Chlorophyll, a magnesium-porphyrin complex (Figure 1.5b), is abundant in green plants and algae, where it functions as a receptor of light energy.

Figure 1.5 Two natural organometallic compounds: (a) heme, containing a porphyrin ring and iron; and (b) chlorophyll, containing a porphyrin ring and magnesium.



JUST IN TIME REVIEW

1.1

Important Functional Groups in Biochemistry

The properties and reactions of cellular molecules are best described using the concept of **functional groups** that you learned in organic chemistry. Functional groups are formed by the combination of elements into specific structural units. The important functional groups present in biomolecules are shown below. These units are important in our studies because they are the sites of chemical reactions in biomolecules. A particular kind of functional group, no matter what type of molecule it is in, undergoes the same kinds of chemical reactions. The reactions of the functional groups found in biomolecules are described in Just in Time Review 13-1.

Class of Compound	General Structure ^a	Functional Group Structure	Functional Group Name	Example
Alkane	$\text{RCH}_2\text{—CH}_3$	$\begin{array}{c} & \\ \text{—C—C—} \\ & \\ \text{H} & \text{H} \end{array}$	Carbon-carbon and carbon-hydrogen single bonds	$\text{H}_3\text{C—CH}_3$
Alkene	RCH=CH_2	$\begin{array}{c} \diagup & \diagdown \\ \text{C}=\text{C} \\ \diagdown & \diagup \end{array}$	Carbon-carbon double bond	$\text{H}_2\text{C=CH}_2$
Alcohol	ROH	—OH	Hydroxyl group	CH_3OH
Thiol	RSH	—SH	Thiol or sulfhydryl group	CH_3SH
Ether	R—O—R	—O—	Ether group	$\text{CH}_3\text{—O—CH}_3$
Amine ^b	$\begin{array}{l} \text{RNH}_2 \\ \text{R}_2\text{NH} \\ \text{R}_3\text{N} \end{array}$	$\begin{array}{c} \\ \text{—N—} \\ \end{array}$	Amino group	$\text{H}_3\text{C—NH}_2$
Imine ^b	R=NH	$\begin{array}{c} \diagup & \diagdown \\ \text{C}=\text{N—H} \\ \diagdown & \diagup \end{array}$	Imino group	$\begin{array}{c} \text{H}_3\text{C} \\ \\ \text{C=NH} \\ \\ \text{H}_3\text{C} \end{array}$
Aldehyde	$\begin{array}{c} \text{O} \\ \\ \text{R—C—H} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{—C—H} \end{array}$	Carbonyl group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{C—} \\ \\ \text{H} \end{array}$
Ketone	$\begin{array}{c} \text{O} \\ \\ \text{R—C—R} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{—C—} \end{array}$	Carbonyl group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{CCH}_3 \end{array}$
Carboxylic acid ^b	R—COOH	$\begin{array}{c} \text{O} \\ \\ \text{—C—OH} \end{array}$	Carboxyl group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{C—} \\ \\ \text{OH} \end{array}$
Ester	$\begin{array}{c} \text{O} \\ \\ \text{R—C—OR} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{—C—OR} \end{array}$	Ester group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{C—OCH}_3 \end{array}$
Amide	$\begin{array}{c} \text{O} \\ \\ \text{R—C—NH}_2 \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{—C—N—} \\ \\ \text{H} \end{array}$	Amide group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{C—NH}_2 \end{array}$
Phosphoric acid ^b	$\begin{array}{c} \text{O} \\ \\ \text{HO—P—OH} \\ \\ \text{OH} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{HO—P—OH} \\ \\ \text{OH} \end{array}$	Phosphoric acid group	$\begin{array}{c} \text{O} \\ \\ \text{HO—P—OH} \\ \\ \text{OH} \end{array}$
Phosphoric acid ester ^b	$\begin{array}{c} \text{O} \\ \\ \text{R—O—P—OH} \\ \\ \text{OH} \end{array}$	$\begin{array}{c} \text{O} \\ \\ \text{—O—P—OH} \\ \\ \text{OH} \end{array}$	Phosphoester group or phosphoryl group	$\begin{array}{c} \text{O} \\ \\ \text{CH}_3\text{OP—OH} \\ \\ \text{OH} \end{array}$
Phosphoric acid anhydride ^b	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{R—O—P—O—P—OH} \\ & \\ \text{OH} & \text{OH} \end{array}$	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{—O—P—O—P—OH} \\ & \\ \text{OH} & \text{OH} \end{array}$	Phosphoric anhydride group	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{CH}_3\text{O—P—O—P—OH} \\ & \\ \text{OH} & \text{OH} \end{array}$
Carboxylic acid-phosphoric acid mixed anhydride ^b	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{R—C—O—P—OH} \\ & \\ & \text{OH} \end{array}$	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{—C—O—P—OH} \\ & \\ & \text{OH} \end{array}$	Acyl-phosphoryl anhydride	$\begin{array}{c} \text{O} & \text{O} \\ & \\ \text{CH}_3\text{C—O—P—OH} \\ & \\ & \text{OH} \end{array}$

^aR refers to any carbon-containing group.

^bThese molecules are acids or bases and are able to donate or accept protons under physiological conditions. They may be positively or negatively charged.

1.3

Biological Macromolecules

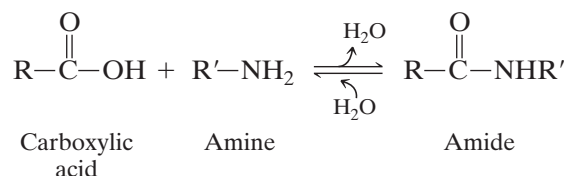
Learning Objective

Identify the major classes of molecules found in living matter and understand their polymeric nature.

Many molecules present in biological cells are very large by the standards of inorganic and organic chemistry. Three major classes of natural polymeric macromolecules are found in biological cells: the **nucleic acids**, **proteins**, and **polysaccharides**. (Lipids are also considered a major class of biomolecules, but because they are not polymeric macromolecules, they are not described in this section but in the previous paragraph.) The major classes of macromolecules participate in a complex array of biological processes, such as storing and transferring genetic information (nucleic acids), catalyzing biochemical reactions (proteins called enzymes), holding cells and organisms together (structural proteins and polysaccharides), transporting small molecules across cell membranes or from one location in an organism to another location (transport proteins), and protecting an organism against disease agents (protein antibodies). Although their structures and functions are quite different, all natural macromolecules have one common characteristic; they are polymers constructed by combining together hundreds, thousands, and sometimes millions of smaller, pre-fabricated molecules called monomers (Figure 1.6).

Cellular Reactions

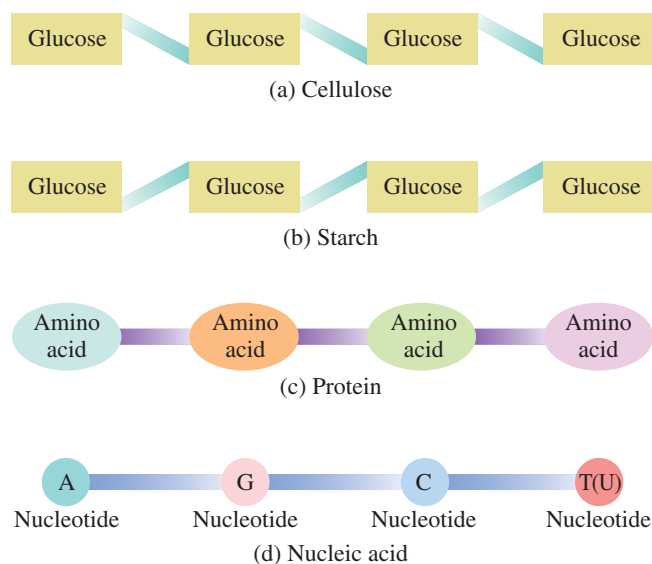
The reaction process that connects monomer units is called **condensation**, a chemical combining that results in the loss of a small molecule, usually water:



In the example given here, a carboxylic acid is condensed with an amine to form a new compound with an amide bond. This represents the chemistry for combining amino acids to make proteins. During metabolic turnover in the living cell, the reverse process, called **cleavage** or **hydrolysis** (if water is used), also becomes important.

The product formed by condensation or polymerization of thousands of glucose monomers is either **starch** or **cellulose**, depending on the type of chemical linkage

Figure 1.6 Types of natural polymers. (a) Cellulose, a homopolymer formed by joining many identical glucose units. (b) Starch, a homopolymer formed by joining many identical glucose molecules. Note that different types of bonding are used in starch and in cellulose. (c) Protein, a heteropolymer formed by linking together amino acids. (d) Nucleic acid, a heteropolymer formed by combining different nucleotides, A, G, C, and T or U.



between the glucose units. These macromolecules are called polysaccharides because they are composed of many saccharide (sugar) molecules. Because the monomeric units comprising these polysaccharides are chemically identical, they are, in general, termed **homopolymers**.

Proteins are the products of joining together amino acids by amide bonds. Because 20 different amino acids are available as monomeric building blocks, the resulting proteins are **heteropolymers**. By combining many different amino acids in proteins, a level of molecular complexity and structural diversity results that is not possible for starch or cellulose. Different proteins are formed by changing the order (sequence) and number of amino acid monomers. This allows the construction of a vast array of different protein molecules, each with its own physical, chemical, and biological characteristics. All molecules of a specific protein (e.g., hemoglobin) within a species of organism, however, normally have an identical sequence of amino acids.

The nucleic acids are heteropolymers of monomeric units called **nucleotides**. **Deoxyribonucleic acid (DNA)**, the chemical storage form of genetic information, is composed of the monomers deoxyadenosine 5'-monophosphate (dAMP), deoxyguanosine 5'-monophosphate (dGMP), deoxycytidine 5'-monophosphate (dCMP), and deoxythymidine 5'-monophosphate (dTMP). Each DNA molecule in the human chromosome contains millions of nucleotides. **Ribonucleic acid (RNA)**, which is involved in the transfer of genetic information and in biological catalysis, is a heteropolymer of adenosine 5'-monophosphate (AMP), guanosine 5'-monophosphate (GMP), cytidine 5'-monophosphate (CMP), and uridine 5'-monophosphate (UMP). The genetic information present in nucleic acids is coded by the sequence of nucleotides.

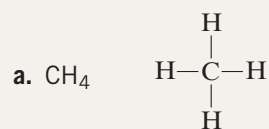
In the last part of this book, we will focus on the important processes of **metabolism**. This refers to the thousands of biochemical reactions that define the synthesis (anabolism) and breakdown (catabolism) of all biomolecules including the macromolecules. The metabolic turnover of proteins, nucleic acids, polysaccharides, and lipids requires complex cellular machinery, strict control to assure reproducibility, the presence of reaction catalysts called enzymes (usually proteins), and complicated processes for exchange of chemical energy. Catabolism (exergonic) and anabolism (endergonic) are linked through the transfer of energy in the molecular form of **adenosine triphosphate (ATP)**. All the information necessary to direct cellular tasks resides in the DNA of the organism, but the message in the form of nucleotide sequence must first be decoded and made into functional proteins before biochemical reactions can occur.

Before You Go On . . .

1. Draw stable structures for each of the following molecular formulas. All of the structures are of compounds that are naturally occurring. Remember from your organic chemistry class that the usual number of covalent bonds formed by each of the elements is:

C	4	O	2	S	2
H	1	N	3	P	5

Note that the first problem is worked.



b. CO_2

c. NH_3

d. H_2S

e. $\text{C}_2\text{H}_6\text{O}$

f. C_2H_4

g. CH_4S

h. CH_2O_2

i. N_2

2. Convert the following molecular formulas to chemical structures. Name the functional group or groups present in each. Choose from alkene, alcohol, aldehyde, ketone, ester, amine, and acid.
- | | |
|--------------------------------------|--------------------------------|
| a. Part e in question 1 | f. CH_3COCH_3 |
| b. Part f in question 1 | g. $\text{CH}_3\text{COOCH}_3$ |
| c. Part h in question 1 | h. CH_3NH_2 |
| d. $\text{CH}_3\text{CH}_2\text{OH}$ | i. H_3PO_4 |
| e. CH_3CHO | |
3. Three of the major classes of biomolecules are polymers composed of units called monomers. The three important biopolymer classes are nucleic acids, proteins, and polysaccharides. Select from the list below the one set of monomeric units that are used to make the three types of polymers.
- RNA, amino acids, and monosaccharides
 - Nucleotides, amino acids, and fatty acids
 - DNA, amino acids, and cellulose
 - Amino acids, adenine, and sucrose
 - Nucleotides, amino acids, and monosaccharides

1.4

Organelles, Cells, and Organisms

Learning Objective

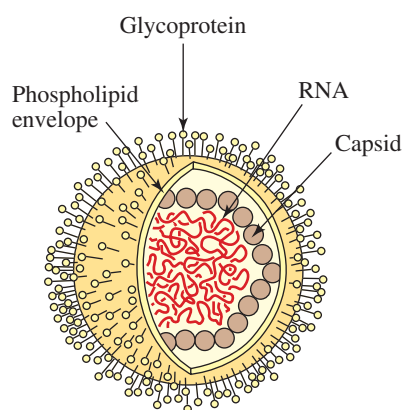
Understand the basic role of the cell as the fundamental unit of life. Know the structural features of and the differences between prokaryotic and eukaryotic cells.

The complexity of biomolecule synthesis and degradation is overshadowed by the next stage of organization—the self-assembly of macromolecules into higher levels of order. Our discussion about biomolecules has proceeded in a stepwise fashion beginning with the chemical elements and continuing with the precise combining of atoms to make small molecules and the joining together of these monomers to make functional polymeric biomolecules.

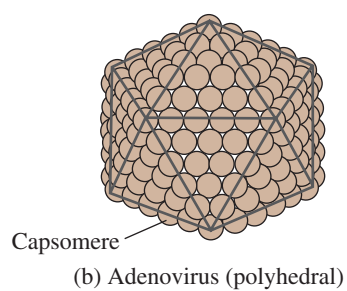
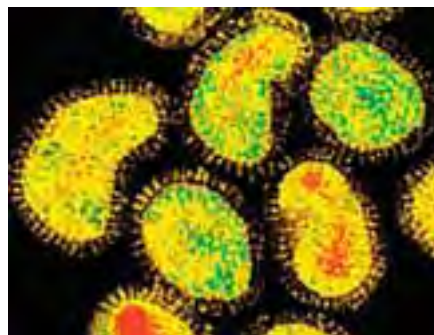
Let us continue in this hierarchical ascent from atoms to higher levels of organization. After the stage of biological macromolecules, we encounter **supramolecular assemblies**, organized clusters of macromolecules. Prominent examples are **cell membranes** (complexes of proteins and lipids), **chromatin** (complexes of DNA and proteins), **ribosomes** (complexes of RNA and proteins), and materials of a fibrous nature, such as the protein-containing **cytoskeleton**. The extensive presence and biological significance of supramolecular assemblies in cells and organisms illustrate the ability of biomolecules to recognize and interact with one another in a specific way. **Molecular recognition** is the result of an exact fit between the surfaces of two molecules. Molecules that are complementary diffuse together to form a complex that displays some biological activity. The molecules are held together by weak and reversible chemical forces. These chemical forces will be described further in later chapters.

Viruses

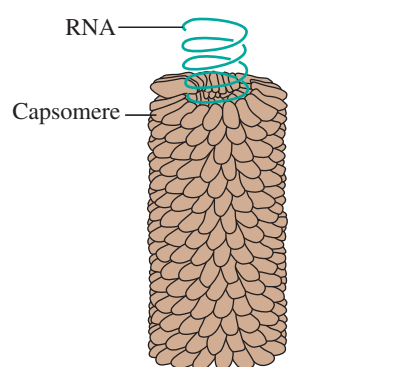
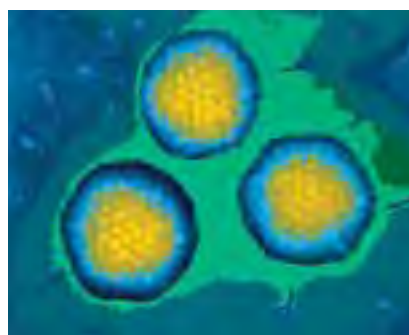
Viruses (Figure 1.7) are another example of supramolecular assemblages. Biochemically, most viruses consist of a single DNA or RNA molecule wrapped in a protein package. Viruses cannot exist independently and are usually not considered a life-form. Instead, they are deemed parasites since they are unable to carry out metabolism or reproduction without the assistance of a host cell. When viruses infect a cell, they take control of the cell's metabolic machinery and force it to synthesize nucleic



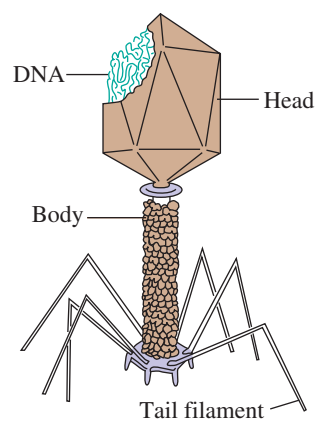
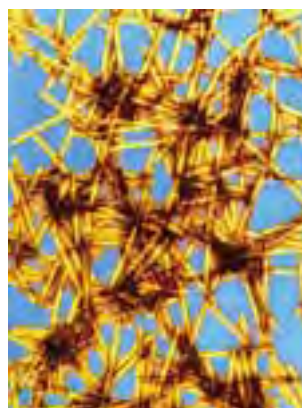
(a) Influenza virus (globular)



(b) Adenovirus (polyhedral)



(c) Tobacco mosaic virus (cylindrical)



(d) Bacteriophage (complex shape)

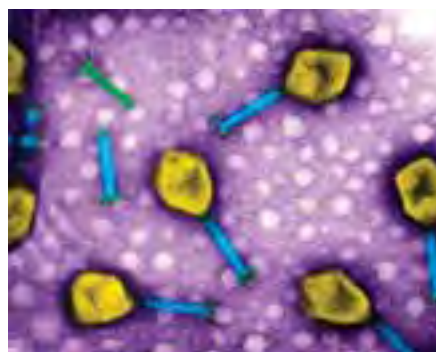


Figure 1.7 Viruses are nonliving packages of nucleic acid and protein. On the left are schematic diagrams of four types of viruses and on the right an electron micrograph of each. ((a, b) Dr. Linda Stannard, UCT/Photo Researchers, Inc.; (c) Dr. Jeremy Burgess/Photo Researchers, Inc.; (d) Dr. Dennis Kunkel/Visuals Unlimited.)



Archaeobacteria usually thrive in extreme environments like these Yellowstone hot springs. (© Jim Sternberg/Photo Researchers.)

acids and proteins for new virus particles. Viruses are the cause of many plant and animal maladies and their presence in the world has resulted in much human suffering; however, an enormous amount of biochemistry has been learned from studies of their actions (see Section 10.5).

Living Cells

After supramolecular assemblies, the next higher level of organization is the fundamental unit of life, the cell. Scientists have long recognized two basic classifications of organisms: (1) the **eukaryotes**, organisms, including plants and animals, whose cells have a distinct membrane-enclosed nucleus and well-defined internal compartmentation, and (2) the **prokaryotes**, simple, unicellular organisms, mainly bacteria and blue-green algae, with neither a distinct cell nucleus nor an internal cellular compartmentation. This classification was achieved primarily by microscopic observation and, hence, is based on morphological cell structure and anatomy. However, if cells are classified by genetic analysis (DNA and RNA sequences), then three distinct types are recognized.

In 1977, Carl Woese, now at the University of Colorado, discovered through genetic analysis of ribosomal RNA that **archaeobacteria** or **archaea** (ancient bacteria) are different from prokaryotes and eukaryotes. The archaeobacteria are also distinctive when their living conditions are examined; many are able to thrive in an environment of high acidity, high salt, high temperature, and absence of oxygen. They can be found in abundance in the hot springs of Yellowstone National Park or in volcanic areas on land and sea. The ability to grow at high temperatures (some bacteria grow at temperatures up to 120°C) is of special interest because nucleic acids and proteins normally become unraveled at temperatures above 60°C to 70°C. Chemists and biochemists are eager to find how archaeobacteria stabilize their macromolecules of DNA and protein under these extreme conditions. (See Window on Biochemistry 1.1.) In our consideration of the biochemical characteristics of all organisms, we will use the new classification into archaea. The archaeobacteria, when classified according to morphological observation, more closely resemble the prokaryotes.

Prokaryotic Cells

The prokaryotic organisms, although the least developed, are the most abundant and widespread of organisms. The structural features of this simple type of cell are illustrated in Figure 1.8 and biochemically characterized in Table 1.1. Several characteristics of prokaryotic cells can be generalized:

1. The size may range from 1 to 10 μm in diameter. Bacteria, an abundant prokaryotic organism, have three basic shapes: *spheroidal* (cocci), *rodlike* (bacilli), and *helically coiled* (spirilla).
2. The cellular components are encapsulated within a cell membrane and rigid cell wall. Occasionally the membrane may infold to form multilayered structures called



Figure 1.8 Schematic diagram of a typical prokaryotic cell.

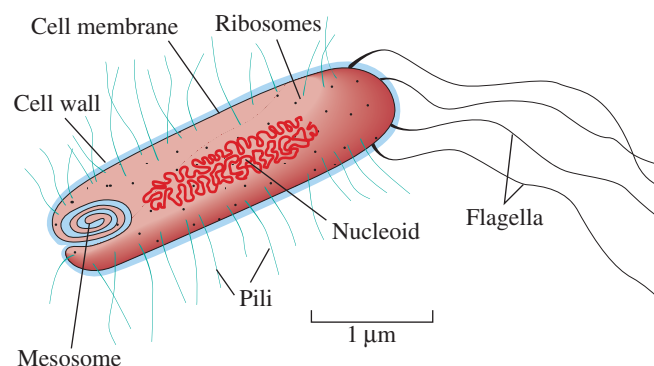


Table 1.1
Molecular composition and biological function of prokaryotic cell components

Structural Feature	Molecular Composition	Biological Function
Cell wall, pili, and flagella	Polysaccharide chains cross-linked by proteins; coated with lipopolysaccharide; pili and flagella are extensions of the cell wall	Protection against mechanical and hypertonic stress; flagella assist in movement; pili assist in sexual conjugation
Cell membrane, mesosome	Bilayer of 40% lipid, 60% protein, perhaps some carbohydrate; mesosome is infolded membrane	Permeable boundary that allows for entry and exit of nutrients, waste; mesosome may play role in DNA replication
Nucleoid region	Contains chromatin, a complex of chromosomal DNA and histone proteins	The genome; storage of genetic information; site of DNA replication
Ribosomes	Complexes of RNA (65%) and protein (35%)	Sites of protein synthesis
Vacuoles	Nutrients stored as small molecules or polymers	Storage of fuel molecules for energy metabolism
Cytoplasm	Small molecules, soluble proteins, enzymes, nutrients, inorganic salts; dissolved in aqueous solution	Region where many metabolic reactions occur

mesosomes. The outside surface is often covered by **flagella**, which are appendages for locomotion, and **pili**, which are structural features responsible for the transfer of DNA during sexual conjugation and for attachment to surfaces.

3. The interior of the cell, called the **cytoplasm**, is a gel-like, heterogeneous suspension of biomolecules including small molecules, soluble enzymes, **ribosomes** (supramolecular particles of RNA and protein), and coiled DNA in the nucleoid region.
4. Each cell has one chromosome, a single copy of DNA (the **genome**). Several copies may be present in a rapidly growing cell that replicates by simple division.

The prokaryotic organism that has been the object of most biochemical studies is the *Escherichia coli* (*E. coli*) bacterium. Indeed, we know more biochemistry about this organism that lives in our gut than any other, including humans. Because so much is understood about this bacterium, it has recently been possible to prepare pictures of the interior of a living cell. Dr. David Goodsell at the University of California, Los Angeles, has combined molecular composition data with structural information to provide the first true-to-life pictures of a living cell. These pictures show the relative distribution of molecules at the proper scale. A typical rodlike *E. coli* cell has dimensions of $2.95\ \mu\text{m}$ by $0.64\ \mu\text{m}$. A cell weighs in at $2 \times 10^{-12}\ \text{g}$ and has a volume of $0.88\ \mu\text{m}^3$. There are between 4000 and 6000 different kinds of molecules in a given cell, of which about 3000 are proteins (only about 1000 have been characterized). The information to make these proteins is stored in a single copy of DNA, which has a molecular mass of 2.5×10^9 kilodaltons (one dalton = one atomic mass unit).

An *E. coli* cell magnified to 50,000 times is shown in Figure 1.9. Three regions are indicated by small lettered squares: (a) the cytoplasm, (b) the cell wall, and (c) the

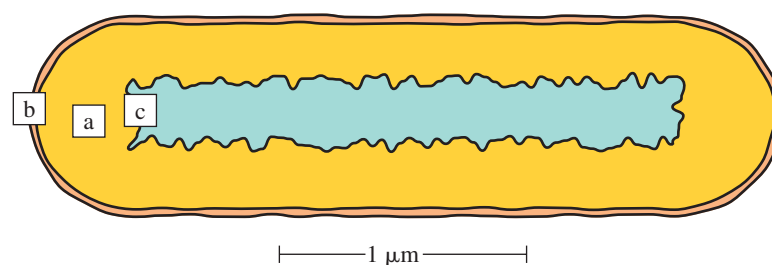
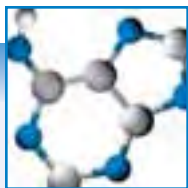


Figure 1.9 A schematic of an *E. coli* cell magnified 50,000 times. Region *a* is cytoplasm, region *b* is the cell wall, and region *c* is the nucleoid with DNA.



1 - 1

Window on Biochemistry

Extremophiles—Living Life on the Edge

As humans venture to regions of the earth that have extreme and inhospitable environments, we are discovering that other life-forms arrived there first. Scientists exploring harsh regions (hot, rocky, subterranean earth; ocean hydrothermal vents; hot-water geysers; salt waters; alkali deserts; glacial ice; and permafrost) are finding evidence for the presence of living organisms. Although most **extremophiles**, organisms that love harsh environments, are microorganisms, bacteria and archaea, some invertebrates like nematode worms are also present. By studying the biochemistry and genetics of these primitive organisms, it is possible to ponder questions about conditions for the origin of life and about how the molecules of life have changed over millions of years. In addition, these organisms provide a treasure chest of ancient enzymes, proteins, and nucleic acids that may have value in modern biotechnology, pharmaceutical development, and industrial products. The discovery of life in harsh environments on the earth has also raised hopes for finding life on other planets and solar systems. Here is a survey of life-forms found in unusual environmental conditions that once were thought to be incompatible with life:

- **Heat:** Viable cultures of *Pyrolobus fumarii*, *Pyrococcus furiosus*, and other microbes have been isolated from regions of Vulcano Island, Italy, and other hydrothermal vents with temperatures up to 120°C (about 250°F). *Thermus aquaticus*, found in the 110°C mineral hot springs of Yellowstone National Park, is the source of *Taq* DNA polymerase, an enzyme used in the polymerase chain reaction (PCR, Section 13.3).
- **Cold:** Scientists at the Astrobiology Institute at NASA are studying microorganisms found in permafrost, polar ice caps, and glaciers of the Arctic and Antarctica. Cold-tolerant organisms include bacteria, archaea, cyanobacteria, and even eukaryotic life such as yeasts and moss. Many life-forms at –10°C, 3.6 km (2.3 miles) below the surface, are cryopreserved but resume metabolic activities when thawed in the laboratory. Cultures of microbes

are also found growing on powdered rock formed by moving glaciers. The rock surfaces contain water, iron–sulfur minerals, and other essential nutrients. The extreme conditions existing at the polar regions of Earth may be similar to ice caps on Mars and the icy moons of Saturn. Bacteria growing in very cold environments have higher than normal levels of polyunsaturated fatty acids. These acids in the human diet have been shown to lower blood cholesterol levels (Biochemistry in the Clinic 8).

- **Extreme pH:** Japanese scientists have recently discovered a crenarchaeote, *Sulfolobus* sp. strain 7, in an 80°C hot spring with a pH between 2.5 and 3. Chinese investigators isolated a *Marinospirillum alkaliphilium* sp. nov. from a lake in Inner Mongolia, where the pH was 9.5. Enzymes from the alkaliophile may be used in laundry detergents that encounter pH environments between 8 and 12.
- **Salt:** *Halobacterium halobium* thrives in sunny, salt lakes or brine ponds where the sodium chloride concentrations may reach 3 *M* (see Section 4.5).
- **High pressure:** Scientists investigating ocean hydrothermal vents near the Juan de Fuca Ridge off the Oregon–Washington coast of the United States and in the Marianas Trench of the Pacific have found an abundance of **methanogens**, strict anaerobes that use hydrogen gas to reduce carbon dioxide to methane. At 5–7 miles below the surface, pressures can reach several hundred atmospheres.
- **Radioactivity:** A recombinant strain of *Deinococcus radiodurans* has been engineered that can withstand not only high levels of radiation, but also environments containing the organic pollutants chlorobenzene and toluene. This organism's growth is only slowed when it is exposed to radiation levels of 1.5 million rads. A human exposed to 1000 rads of radiation energy will die in 1–2 weeks. The key to this organism's survival is its ability to repair up to 500 DNA breaks at a time compared to *E. coli*, which can repair only 2–3 breaks at a time.

nucleoid region. Each of these regions is magnified another 20 times in Figures 1.10a,b,c so that the actual drawings show a cell with a total magnification of 1 million times. To put these figures in perspective, it would require 600 of the cubes shown in Figure 1.10a to represent the entire volume of cytoplasm in a single cell. One almost gets the urge to walk through the cell and take a closer look. This may be more difficult than it seems. The pictures are snapshots of an instant in time; they do

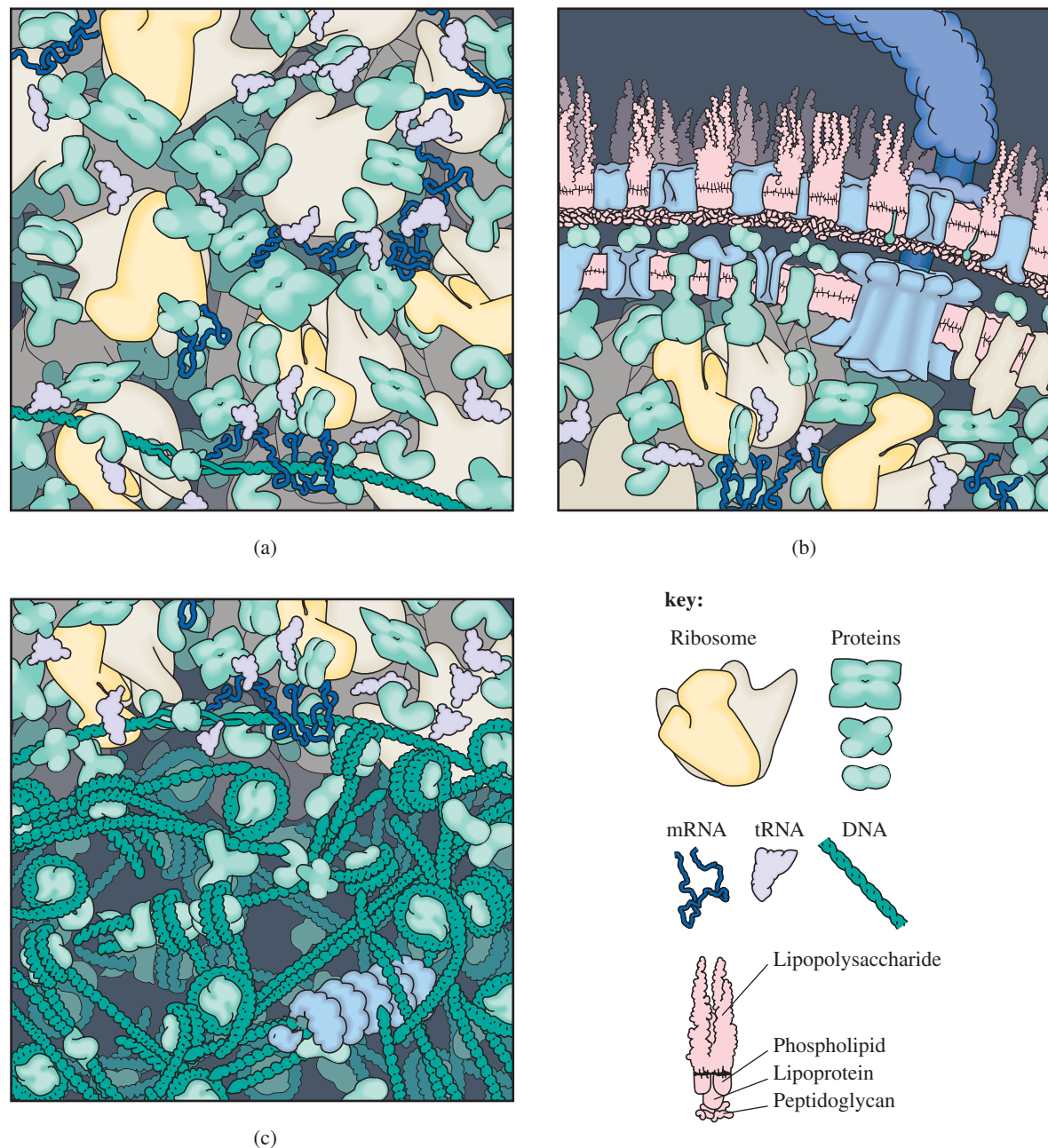


Figure 1.10 The shapes of biomolecules are shown in the key. From Figure 1.9: (a) Region a is the cytoplasm magnified 20 times. (b) Region b is the cell wall magnified 20 times. (c) Region c is the nucleoid region magnified 20 times. (Adapted from Goodsell, 1991.)

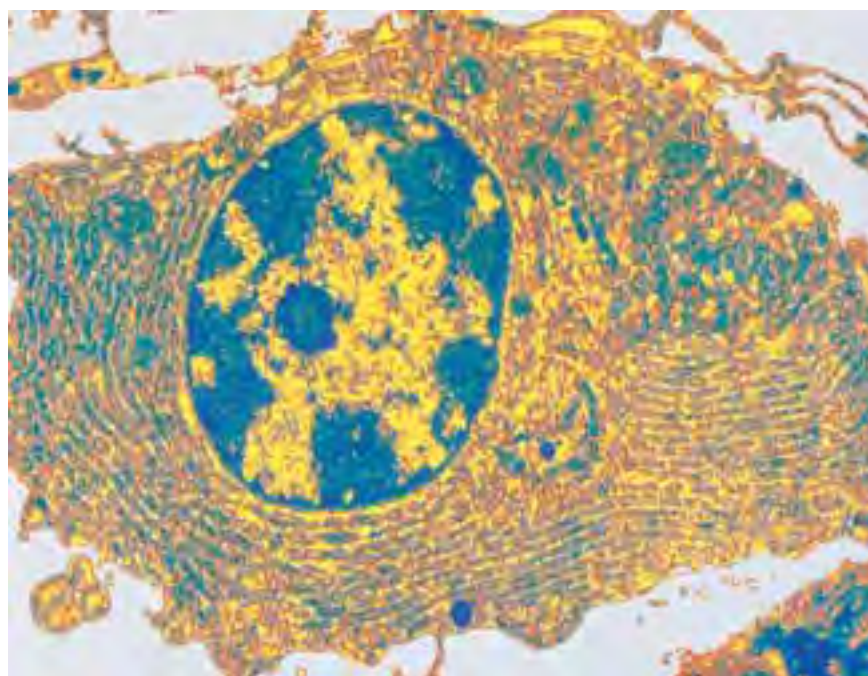
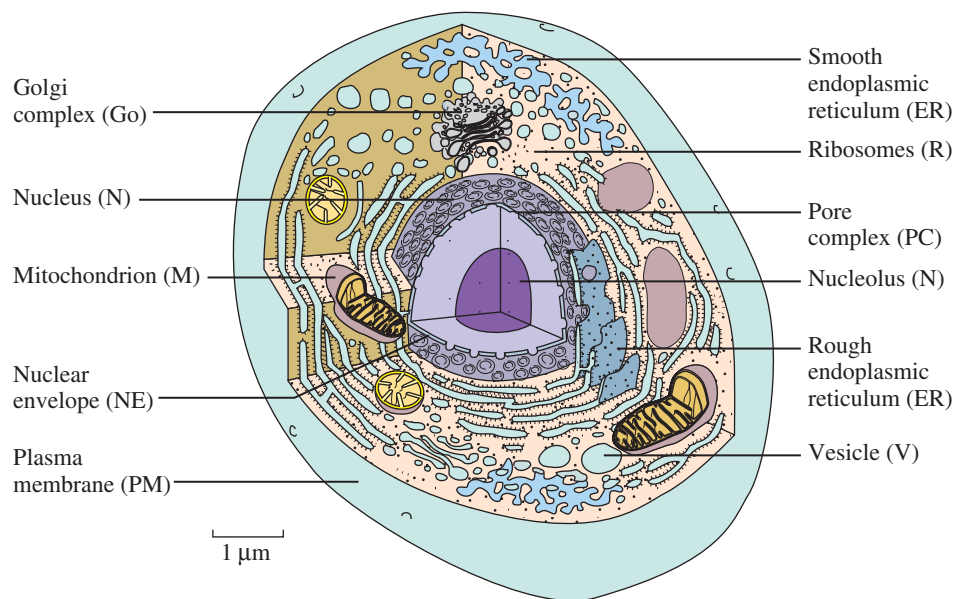
not show the actual movement of molecules in the gel-like cytoplasm. Dr. Goodsell has estimated that the average speed of a 160,000-dalton molecular mass protein is 500 cm/s. At this rate, the protein molecule would cover a distance of 10 nanometers (nm, its approximate size) in about 2 nanoseconds (ns). Even this small movement would result in much pushing and shoving because of the tight quarters inside the cell. The relative sizes of biomolecules, organelles, and organisms are compared in the Just in Time Review 1-2.

Before You Go On . .

1. Which structural feature and biological function are correctly matched below? Correct those that are wrong.

Structural Feature	Biological Function
a. Cell wall	Soluble cellular region where many metabolic reactions occur
b. Ribosome	Permeable boundary that allows entry of nutrients and exit of wastes
c. Nucleoid region	Storage of genetic information and site of DNA replication
d. Cell membrane	Site of protein synthesis
e. Cytoplasm	Protection against mechanical and hypertonic stress

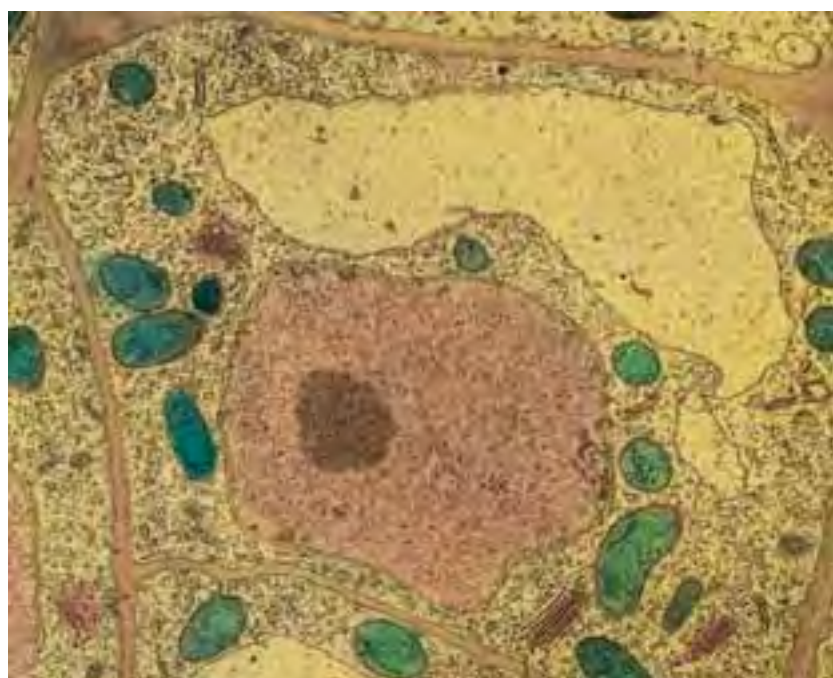
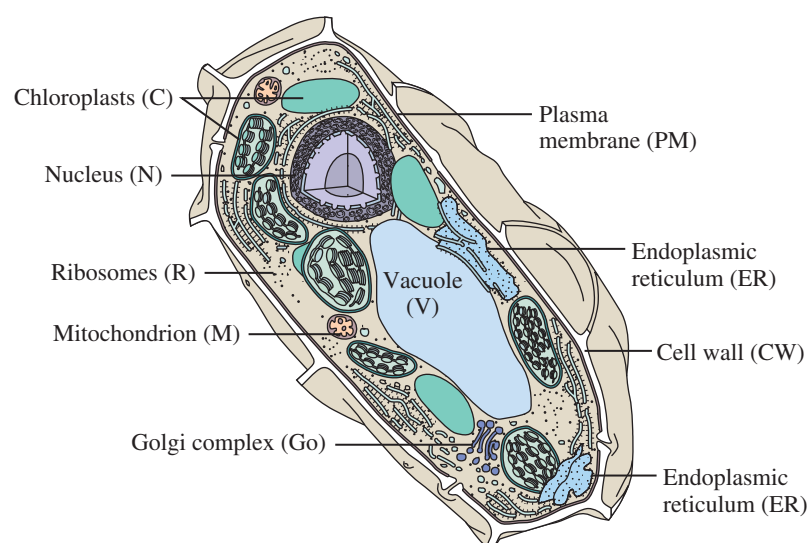
Figure 1.11 Typical eukaryotic cells showing a schematic drawing (*above*) and an electron micrograph (*below*): (a) An animal cell. (© Biophoto Associates/Photo Researchers (b, on opposite page), A plant cell. © Alfred Pasiceka/Science Photo Library/Photo Source: Based on Wolfe, 1993.)



(a)

Eukaryotic Cells

The class of eukaryotes includes plants, animals, fungi, protozoans, yeasts, and some algae. The cells found in these organisms have little in common with the prokaryotes. The complex eukaryotic cells are much larger, with diameters ranging from 10 to 100 μm . They are surrounded by a plasma membrane made up of protein and lipid (see Figure 1.11). This is a chemical barrier through which all molecules that enter or exit the cell must pass. A unique feature of the eukaryotic cell is the compartmentation of cellular components and, therefore, the compartmentation of biological function. These compartments, called **organelles**, are actually membrane-enclosed packages of organized macromolecules that perform a specialized function for the cell. A listing of organelles along with their constituent biomolecules and biological function is found in Table 1.2. The organelles found in all eukaryotic cells are the **nucleus**; the **endoplasmic reticulum**, which contains **ribosomes**; the Golgi apparatus; and the **mitochondria**. In addition to these, animal cells have specialized organelles, the **lysosomes** and **peroxisomes**, whereas plant cells have **chloroplasts** and



(b)

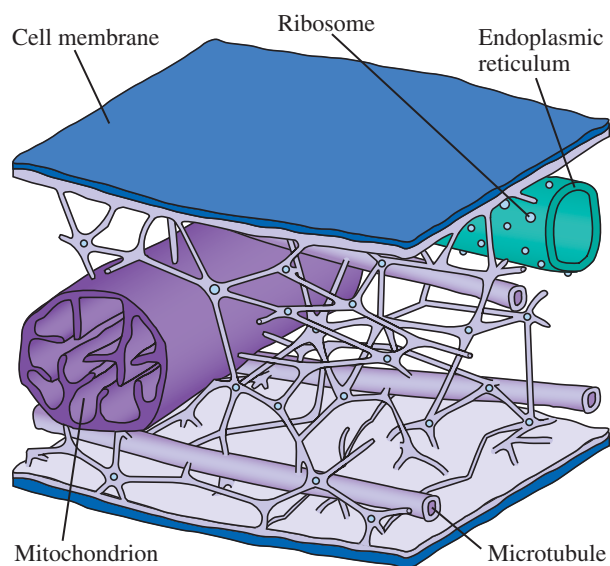
Table 1.2
Eukaryotic organelles, their constituent biomolecules, and biological function

Structural Feature	Molecular Composition	Biological Function
Cell membrane	Bilayer of proteins (50%) and lipids (50%) and some carbohydrate	Selectively permeable boundary for entry and exit of nutrients and waste; some important enzyme activities; location of receptors for signaling
Nucleus	Contains genomic DNA, and histone proteins as chromatin; RNA	Storage of genetic information; site of DNA replication and transcription to RNA
Endoplasmic reticulum with ribosomes	Flat, single-membraned vesicles of lipid and protein; ribosomes consist of RNA and proteins	Surfaces on which ribosomes bind for protein synthesis
Golgi apparatus	Flattened vesicles of lipid, protein, and polysaccharide	Secretion of cell waste products; site of protein processing
Mitochondria	Double-membraned with protein and lipids; interior (matrix) contains soluble and insoluble enzymes, RNA, and DNA	Site of energy metabolism and synthesis of high-energy ATP
Lysosomes (animal)	Single-membraned vesicles containing enzymes for hydrolysis	Metabolism of materials ingested by endocytosis
Peroxisomes (animal) or glyoxysomes (plant)	Single-membraned vesicles containing catalase and other oxidative enzymes	Oxidative metabolism of nutrients using O_2 to generate H_2O_2
Chloroplasts (plant)	Double-membraned organelles containing protein, lipid, chlorophyll, RNA, DNA, and ribosomes	Sites of photosynthesis; convert light energy into chemical energy (ATP)
Cytoplasm	Cytoskeleton made of proteins; small molecules, soluble proteins, enzymes, nutrients, and salts in aqueous solution	Provides shape to cell; region where many metabolic reactions occur

glyoxysomes, a modification of the peroxisomes. Plant cells are surrounded by a plasma membrane and a rigid cell wall composed primarily of the polysaccharide cellulose. Both plant and animal cells contain **vacuoles** for storage of nutrients and wastes, although these are more prominent in plant cells.

The organelles of a eukaryotic cell are not floating freely in a cytoplasmic sea. Rather, their movement and location are limited by the **cytoskeleton**, the three-dimensional fibrous matrix extended throughout the inside of the cell (see Figure 1.12). The function of the cytoskeleton is to give the cell shape, to allow it to move, and to guide internal movement of organelles. The fibers are composed primarily of protein. The prominent

Figure 1.12 The interior of a cell showing the cytoskeleton. Microtubules and other filaments form an extended network in the cytoplasm.



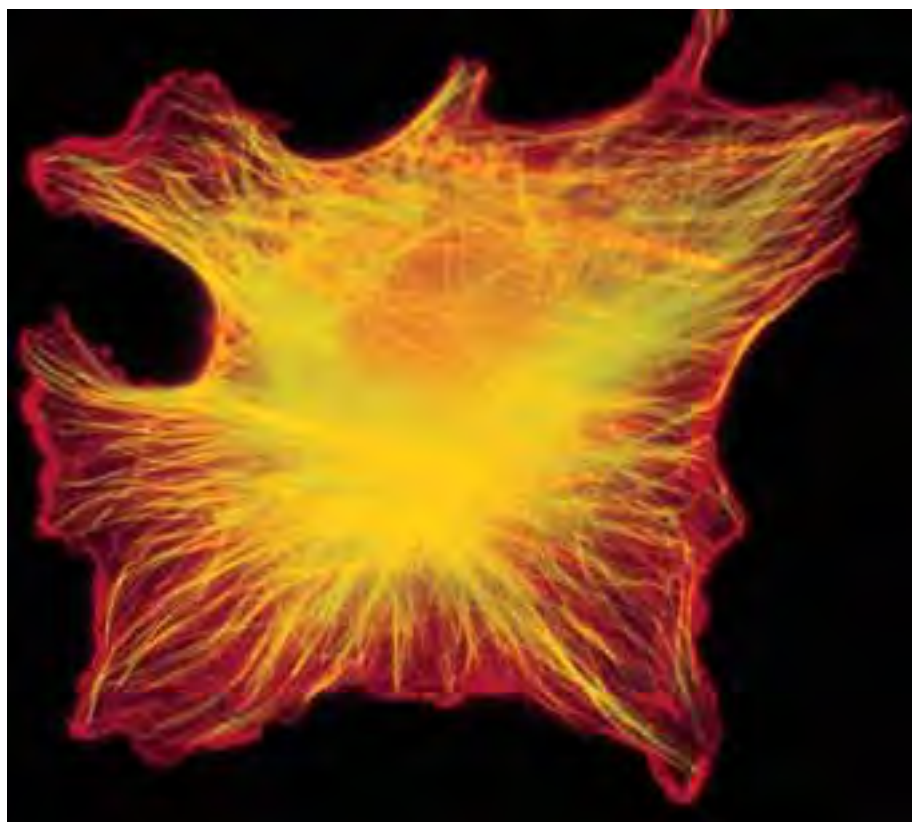


Figure 1.13 Micrograph of part of the cytoskeleton within a hamster kidney cell. Actin is shown in red, and tubulin is shown in green. (© M. Schliwa/Visuals Unlimited.)

fiber types are (1) the microtubules (diameter 22 nm) composed of the protein tubulin, (2) the microfilaments (diameter 6 nm) composed of actin, and (3) the intermediate filaments (diameter 7–11 nm) (Figure 1.13). The major constituent protein in the intermediate filaments varies from cell to cell; for example, skin cells have an extensive array of intermediate fibers made of keratin.

1.5

Storage and Transfer of Biological Information— A Preview

Learning Objective

Have a general understanding of the roles of DNA and RNA in the molecular processes of storage, retrieval, and transfer of biological (genetic) information.

Biochemistry is much more than just a study of molecules and chemical reactions in the cell. As we learned in the introduction to this chapter, biochemistry has three major themes: structure and function of molecules, information processing, and energy transfer. Of these three, biological information is a predominant theme because in order for cells to grow and divide, and for species to remain viable, secure and faithful processes for storage and transfer of genetic information must be available. If a cell is unable to store and pass on important directions to progeny, then it makes no difference if a macromolecule has the correct structure or if the cell is able to obtain energy. A brief introduction to informational biochemistry will be given here since it is a prerequisite for understanding most future topics in the book.

Biological Information

Biochemists and molecular biologists have for many years been interested in learning how biological information is transferred from one generation to another. What has been discovered is that the flow of information can be described using the basic principles of chemistry. DNA, RNA, proteins, and even some carbohydrates are

1.2 JUST IN TIME REVIEW

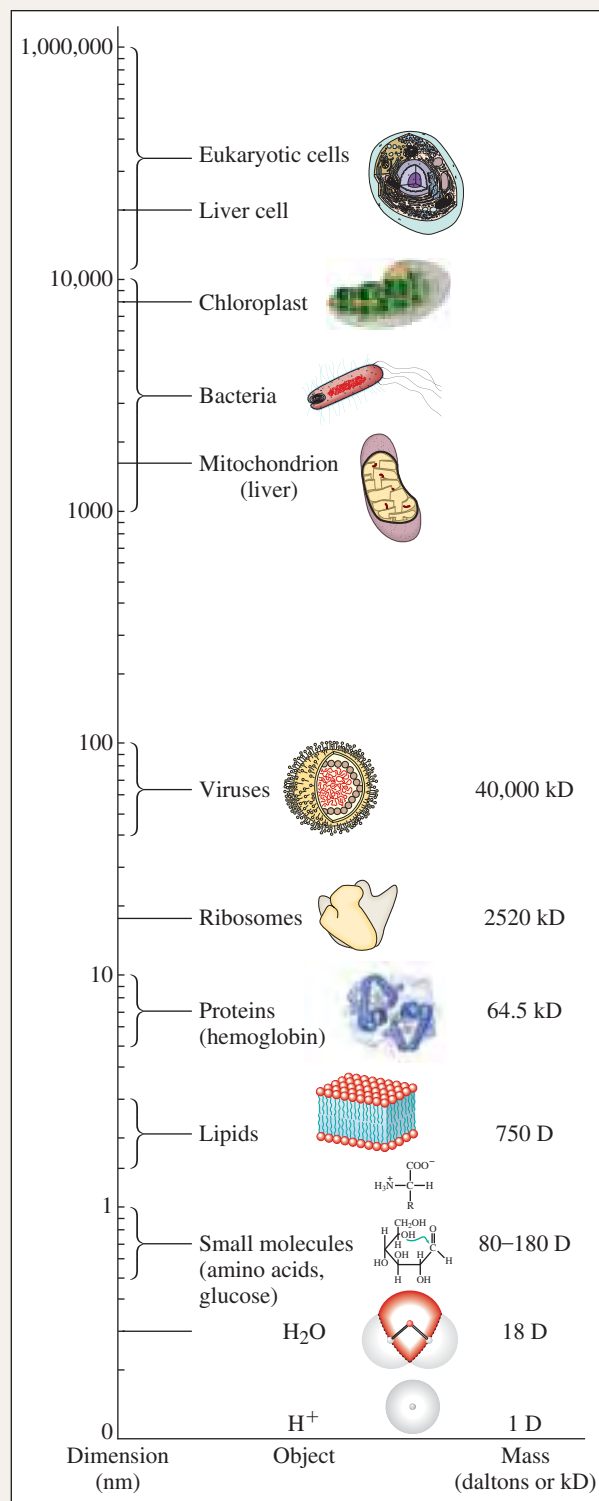
Biochemistry Comes in All Sizes, S, M, L, and XL

The molecules, cell components, and cells that biochemists work with come in a wide range of sizes. We will concern ourselves here with two perspectives of size: (1) the **dimensions** of biochemical objects in terms of length and width or diameter and (2) the **molecular mass**, which is a measure of the quantity of material in an object. The dimensions for biochemical entities (molecules, particles, cells) are usually expressed in units of **nanometers** (nm, 1×10^{-9} meter or 10 angstroms, Å). A molecule of water has a diameter of about 0.3 nm; the amino acid alanine, a diameter of 0.5 nm; the oxygen-carrying protein hemoglobin, a diameter of about 5.5 nm; and a liver mitochondrion, a length of about 1500 nm (see graphic).

The standard, biochemical units for molecular mass are **daltons (D)** or **kilodaltons (kD, 1000 daltons)**. One dalton is equal to the mass of a hydrogen atom. (You may also be familiar with the term *molecular weight* or *molar mass* of a substance, which is the mass of one mole of that substance, expressed in grams.) The mass of a water molecule is 18 D; alanine, 89 D; and hemoglobin, 64,500 D (64.5 kD). (Is it realistic to think of the mass of the mitochondrion in terms of daltons?)

Perhaps the smallest entity studied routinely by biochemists is the proton, H^+ , which is approximately 0.1 nm in diameter. This tiny cation is of interest to scientists measuring the pH (negative log of the $[H^+]$) of a solution and to someone studying the mechanism of acid-catalyzed reactions. A biochemist wishing to work with larger items of biological interest could use bacterial cells (2000–3000 nm long \times 600 nm wide) or animal cells (at least 10–20 times larger than bacterial cells). For example, a liver cell has, on average, a length of 20,000 nm. Unfortunately, none of these objects from protons to animal cells is visible to the unaided eye, which has a minimal viewing limit of about 0.2–0.3 mm. Therefore, these particles may be observed best with the help of molecular computer graphics programs linked to light microscopy, electron microscopy, nuclear magnetic resonance spectroscopy, and X-ray diffraction. Some animal cells are much larger; for example, vertebrate nervous system cells (like in the eel) are up to one meter long and are quite visible to the naked eye.

The size range we will be mostly concerned with in biochemistry has a lower limit of the proton and an upper limit of an average eukaryotic cell, which represents a total range of about one million. If the proton is represented in size by a shelled peanut, then a typical eukaryotic cell would have the size of volume enclosed by a sports stadium such as the Houston Astrodome. Reviewing the graphic reveals the enormous range of sizes and masses represented by biomolecules and other particles. Note that the scale is logarithmic so that differences are much greater than they appear.



information-rich molecules that carry instructions for cellular processes. These groups of biopolymers are composed of monomeric units held together by covalent bonds that are stable enough to store important data for relatively long periods of time. The informational content of these molecules is utilized by “reading” the sequence of the monomeric units. The sequential information is based on the formation of weak, non-covalent interactions between biomolecules. There are four types of noncovalent interactions that are of importance: van der Waals forces, ionic bonds, hydrogen bonds, and hydrophobic interactions (Section 2.1).

The total genetic information content of each cell, referred to as the **genome**, resides in the long, coiled, macromolecules of DNA. Thus, DNA is the major molecular repository for genetic information. The informational message is expressed or processed in two important ways: (1) exact duplication of the DNA so it can be transferred during cell division to a daughter cell and (2) expression of stored information to first produce RNA and then manufacture proteins, the molecular tools that carry out the activities of the cell. In this indirect way, DNA exerts its primary effects by storing the information for synthesis of proteins that direct the thousands of chemical reactions that occur in a cell. It is the protein molecules that are responsible for building cellular components and for maintaining the proper functioning of the cell. A schematic outline showing the storage and transfer of genetic information is given in Figure 1.14. Details of information transfer processes are described in Chapters 10–12.

The DNA Molecule

The chemistry of the DNA molecule seems rather simple in view of the enormous amount of information stored and its fundamental role in the cell. The DNA chain is a long, unbranched heteropolymer, constructed from just four types of monomeric nucleotide units. Each monomer unit consists of three parts: an organic base containing nitrogen, a carbohydrate, and a phosphate. In 1952, Watson and Crick, using

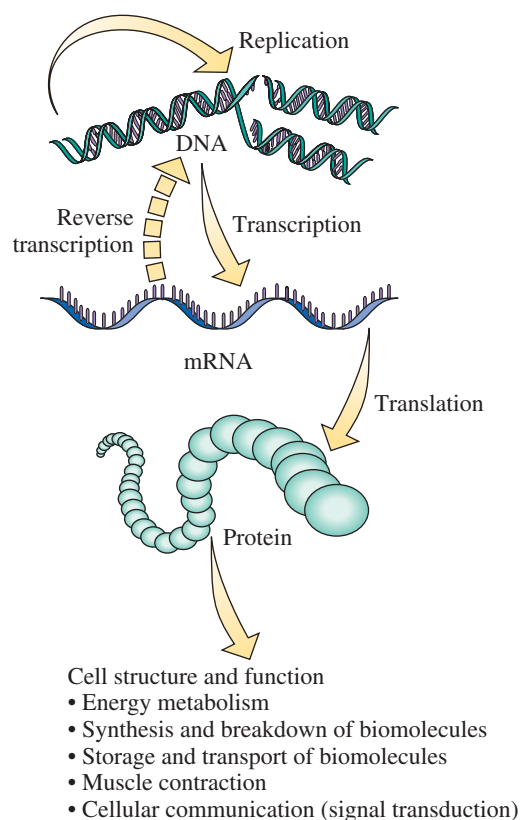


Figure 1.14 The storage and replication of biological information in DNA and its transfer via RNA to synthesize proteins that direct cellular structure and function.

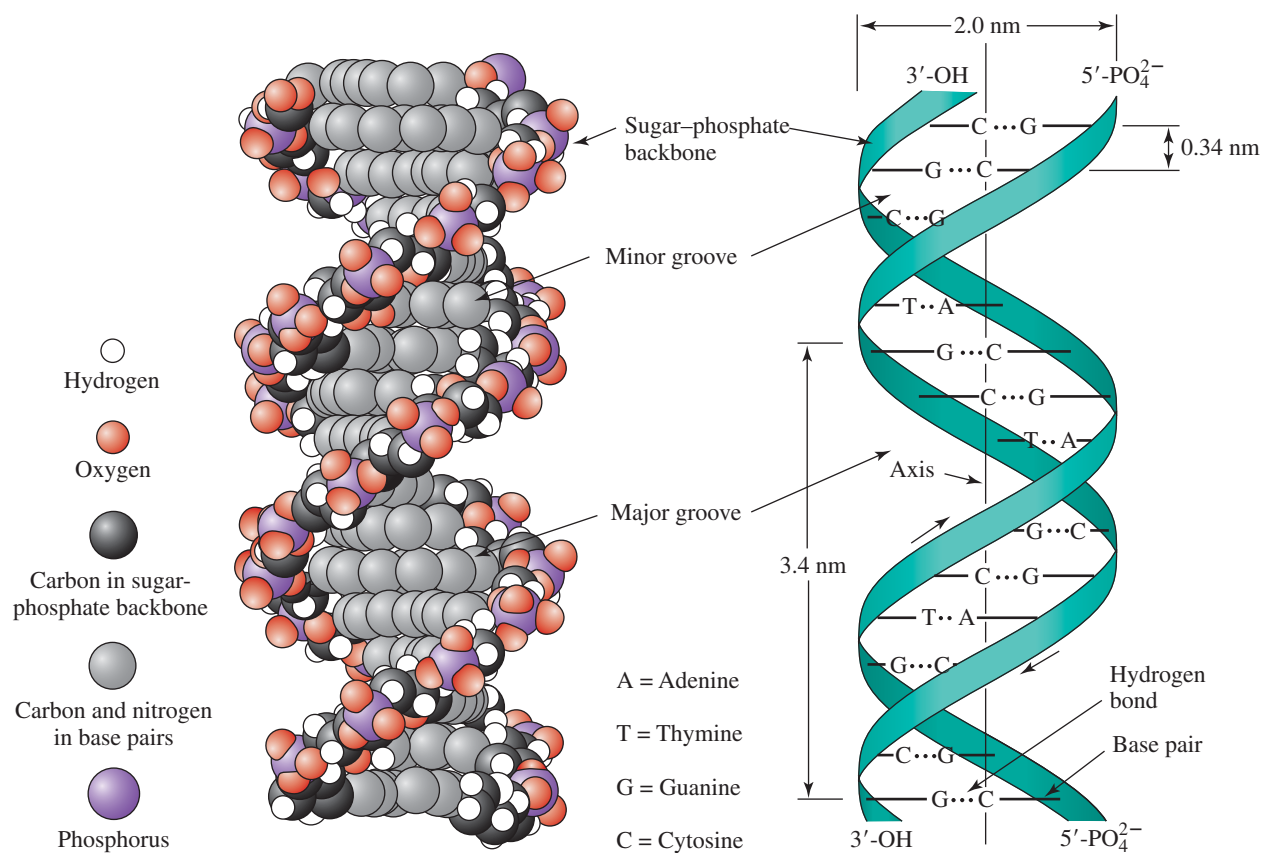


Figure 1.15 The Watson and Crick double helix model for DNA showing the stacking of nucleotide bases on the same strand and the hydrogen bonds between complementary nucleotide bases on opposite strands.

X-ray diffraction data and models, discovered that the DNA molecule is constructed of two strands interwoven into a three-dimensional helical structure (double helix; see Figure 1.15). The structural backbone of each strand, which makes up the outside of the molecule, is formed by covalent phosphodiester bonds, using the carbohydrate and phosphate groups of the nucleotide subunits. This arrangement brings the organic bases to the inside of the double helix. Neighboring bases on the same strand are stacked on top of each other (arranged like steps on a spiral staircase), which allows the formation of noncovalent interactions. Bases on opposite strands are also close neighbors, allowing the formation of **complementary base pairs** by specific hydrogen bonding. The optimal arrangement is adenine (A) in combination with thymine (T) and guanine (G) with cytosine (C). The format for storage is a linear sequence of the nucleotides in DNA that vary in size and sequence with each species. The entire human genome, for example, is about 1 m long and contains an estimated 3 billion nucleotide base pairs. A DNA molecule from *E. coli* is about 2 mm long and contains about 4 million nucleotide pairs. We will return to details of DNA structure and function in Chapters 10 through 13.



The goal of the **Human Genome Project (HGP)** was to map and sequence the estimated 3 billion nucleotide base pairs of the human genome by the year 2005. The collaborative effort is sponsored by five governments (United States, United Kingdom, Japan, Germany, and France) and by the privately funded corporation, Celera Genomics. An initial stage of the project, which is now completed, was to sequence the genomes of other species including *Saccharomyces cerevisiae* (yeast) and *Caenorhabditis elegans* (nematode worm) (Table 1.3). A “rough draft” of the human genome sequence was announced in June 2000, five years ahead of the deadline. Results from the HGP are already having an impact on medicine and science. We

Table 1.3
Sequenced genomes

Organism	Genome Size (kb)	Number of Chromosomes*
<i>Borrelia burgdorferi</i> (agent of Lyme disease)	1444	1
<i>Haemophilus influenzae</i> (human pathogenic bacterium)	1830	1
<i>Mycobacterium tuberculosis</i> (cause of tuberculosis)	4412	1
<i>Escherichia coli</i> (bacterium)	4639	1
<i>Saccharomyces cerevisiae</i> (yeast)	11,700	16 [†]
<i>Caenorhabditis elegans</i> (nematode worm)	97,000	6 [‡]
<i>Drosophila melanogaster</i> (fruit fly)	137,000	4
<i>Arabidopsis thaliana</i> (flowering plant)	117,000	5
<i>Oryza sativa</i> (rice)	430,000	12
<i>Mus musculus</i> (mouse)	2,500,000	20
<i>Homo sapiens</i> (human)	3,200,000	23

*The diploid chromosome number is shown for all eukaryotes except yeast.

[†]The haploid chromosome number.

[‡]Number of chromosomes for females; males have 11 chromosomes.

now know the chromosomal positions of genes that are defective in many diseases including cystic fibrosis, muscular dystrophy, some forms of breast cancer, colon cancer, and Huntington's disease. The next step is to apply techniques of gene therapy to treat these diseases (see Chapter 13). New branches of science are being created to deal with the flood of data coming from the HGP. It is estimated that there are between 20,000 and 25,000 genes in the human genome that are expected to code for a large number of proteins (the proteome). **Proteomics** is the name given to the broad field investigating the thousands of protein products made from the genome. Scientists trained in this area will attempt to classify and characterize the proteins, study their interactions with other proteins, and identify their functional roles. Those specializing in the subfield of **bioinformatics** will apply computers to organizing the mass of nucleic acid sequence data and studying relationships between protein sequence and structure.

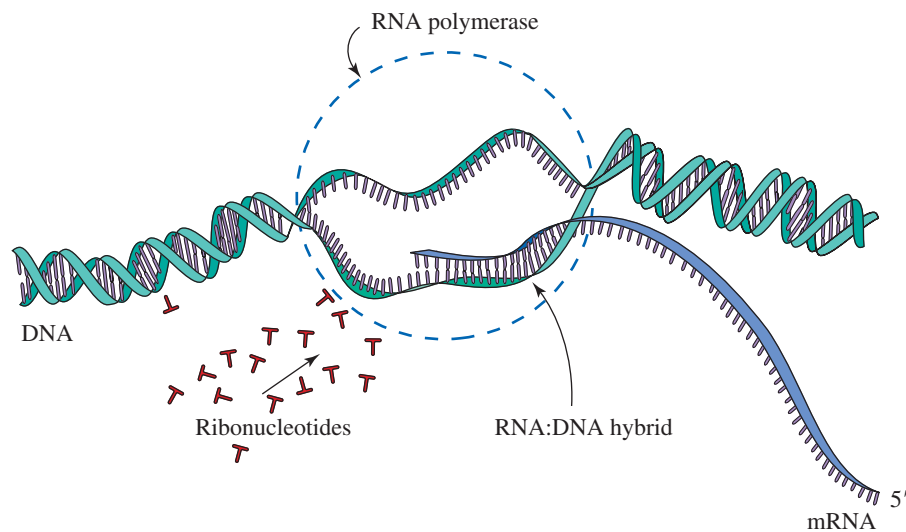
DNA → DNA

The duplication of DNA is a self-directed process. The DNA in concert with many accessory proteins dictates and directs the construction of identical DNA for progeny cells. The process of DNA copying, called **replication**, begins with the unwinding of a short segment of the two complementary strands (see Figure 10.11). Each strand is then used as a **template** (pattern) for production of a new complementary partner strand. A new nucleotide unit brought into the process must first be held in position by hydrogen bonds and van der Waals forces to a complementary base on the template. Then it is covalently linked to the growing DNA chain by an enzyme called **DNA polymerase**. The chemical details of DNA **replication** are discussed in Chapter 11. The entire DNA molecule is duplicated, resulting in two identical molecules, one remaining in the parent cell and one for the daughter cell.

DNA → RNA

In the previous paragraph, we discovered how parental DNA is duplicated for genetic transfer to progeny cells. Here we review the transformation of the message of DNA into the form of RNA. The word **transcription** is used to describe this process. A significant fraction, but not all, of the information in DNA is expressed into RNA. The early hereditary studies of Mendel and others, showing transfer of characteristic traits

Figure 1.16 Transcription of DNA to produce mRNA.



to offspring, are best explained by dividing the genome into specific coding regions called **genes**. In prokaryotic cells, the sequence of bases in a gene is read in a continuous fashion with no gaps or interruptions. A gene in prokaryotic DNA can be defined as a region of DNA that codes for a specific RNA or protein product.

The process of transcription to produce RNA is similar to DNA replication except that (1) ribonucleotides rather than deoxyribonucleotides are the monomeric building blocks, (2) the base thymine, which forms complementary base pairs with adenine, is replaced with uracil (U), which pairs with adenine, and (3) the enzyme linking the nucleotides in the new RNA is **RNA polymerase** (see Figure 1.16). Details of the transcription process are discussed in Chapter 11.

Many viruses, including those causing polio, influenza, and AIDS, and retroviruses that cause tumors, have a genome that consists of single-stranded RNA rather than DNA. Two different strategies are used by these viruses to assure multiplication. The retroviruses rely on a special enzyme, the structure of which is coded in their RNA and produced by the synthetic machinery of the infected cell. This enzyme, **reverse transcriptase** (RT), converts the RNA genome of the virus into the DNA form that is incorporated into the host cell genome. Viral genetic information in this form can persist in the host cell in a latent and noninfectious state for years until stressful environmental conditions induce infection. Other RNA viruses affect multiplication by dictating the production of **replicase**, an enzyme that catalyzes the duplication of viral genomic RNA in a process similar to DNA replication.

The transcription of cellular DNA leads to a heterogeneous mixture of three different kinds of RNA: ribosomal, transfer, and messenger. The most abundant, **ribosomal RNA**, is found in combination with proteins in the ribonucleoprotein complexes called ribosomes. **Transfer RNA**, which is the smallest of the three types, combines with an amino acid and incorporates it into a growing protein chain. **Messenger RNA** carries the message found in a single gene or group of genes. The sequence of nucleotide bases in the mRNA is complementary to the sequence of bases in the template DNA. Messenger RNA is an unstable, short-lived product in the cell, so its message for protein synthesis must be immediately decoded and is done so several times by the ribosomes to make several copies of the protein from each copy of mRNA (Figure 1.17).

mRNA → Proteins

The ultimate products of DNA expression in the cell are proteins. The full array of proteins made from the genomic DNA of an organism is called the **proteome**. Information residing in DNA is used to make single-stranded mRNA (transcription),

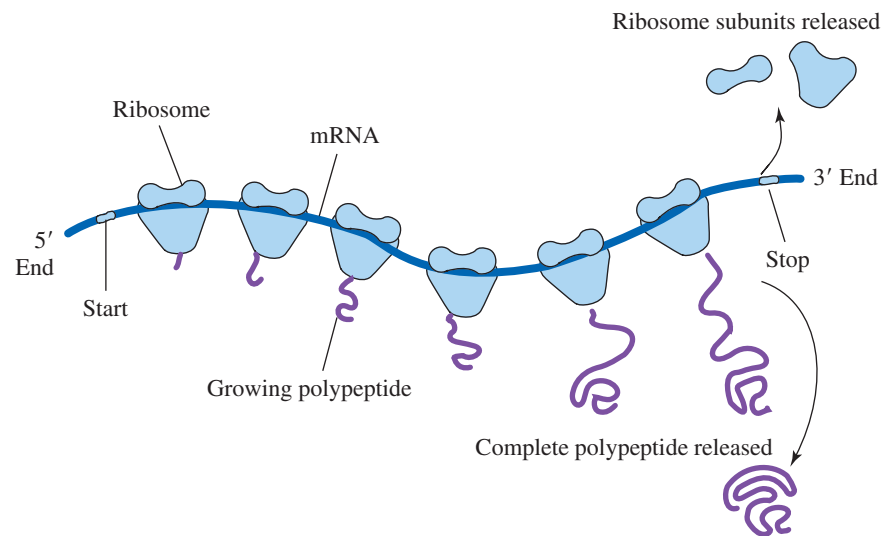


Figure 1.17 Schematic diagram of the synthesis of proteins on ribosomes. Each copy of mRNA may have several ribosomes moving along its length, each synthesizing a molecule of the protein. Each ribosome starts near the 5' end of an mRNA molecule and moves toward the 3' end.

which then relays the message to the cellular machinery designed for protein synthesis. Thus, mRNA serves as an intermediate carrier of the information in DNA. The message in the form of DNA is in the form of a linear sequence of nucleotide bases (A, T, G, C); the message in mRNA is a slightly different set of bases (A, U, G, C). Protein molecules, however, are linear sequences of structurally different molecules: amino acids. Two different “languages” are involved in the transformation from DNA to proteins; therefore, a **translation** process is required.

The Genetic Code

By studying the nucleotide base sequence of hundreds of genes and correlating them with the linear arrangement of amino acids in protein products of those genes, biochemists have noted a direct relationship. The sequence of bases in a gene is arranged in an order corresponding to the order of amino acids in the protein. A set of coding rules, called the **genetic code**, has been deciphered: The coding ratio is a set of three nucleotides per amino acid incorporated into the protein. Therefore, a triplet code is in effect (Figure 1.18).

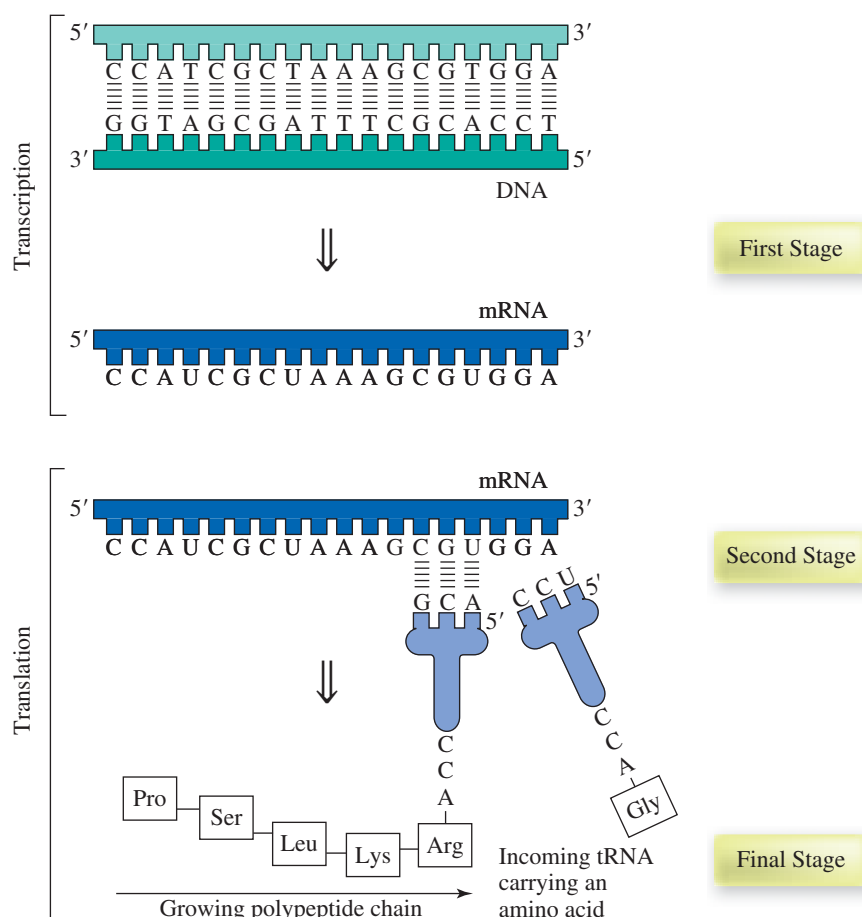
Eukaryotic DNA: Exons and Introns

DNA expression in eukaryotic cells is a bit more complicated than in prokaryotic cells. It was discovered in 1977 that coding regions on eukaryotic DNA are often interrupted by noncoding regions; hence, it was said that such genes are split. The coding regions are called **exons**; the noncoding regions, intervening sequences or **introns**. The reasons for the presence of introns in eukaryotic DNA are not completely understood. On one hand, some believe that they contain “junk DNA” that serves no useful purpose and will eventually disappear as evolutionary forces continue to work. More likely, introns serve some purpose to more efficiently produce diverse arrays of proteins. The discovery of noncoding regions in DNA raises important questions about protein synthesis: Is the intron message in DNA coded into RNA, and if so, at what level is it removed, before or after protein synthesis? These questions will be answered in Chapters 6 and 11.

DNA Mutations

We have described DNA expression (replication, transcription, translation) as events that are carried out in a precise, accurate, and reproducible manner. All of the steps are dependent on weak noncovalent interactions for molecular recognition and binding. No mention was made regarding the possibility of errors in these processes or the

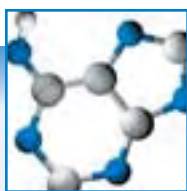
Figure 1.18 The collinear relationship between the nucleotide base sequence of a gene and the linear arrangement of amino acids in a protein. First, mRNA is formed as a complementary copy of one strand of the DNA. Sets of three nucleotides on the mRNA are then read by tRNA molecules. This involves the formation of hydrogen bonds between complementary bases. The amino acid attached to the tRNA is incorporated into the growing polypeptide.



result of chemical or physical changes to DNA. Throughout millions of years of development, organisms have evolved mechanisms that faithfully transfer genetic information; however, they have also developed repair processes to detect and correct errors. Occasionally an error does occur; the wrong nucleotide may be incorporated, a nucleotide may be deleted, or an extra one may be added. Changes of these kinds, called **mutations**, have consequences for that cell as well as for future cells since those genetic changes will be continued. Repair systems to correct such errors will be discussed in Chapter 11.

Before You Go On . . .

- Determine whether each of the following statements about DNA is true or false. Rewrite each false statement so it is true.
 - DNA is a polymer composed of many nucleotide monomers.
 - The Watson-Crick helix consists of a single strand of polymeric DNA.
 - In double-stranded DNA, the base A on one strand is complementary to the base T on the other strand.
 - The nucleotide bases in DNA include A, T, G, and U.
- Write the RNA nucleotide sequence that is complementary to the strands of RNA shown below:
 - 5' UACCG
 - 5' CCCUUU
- Why is the information transfer process mRNA → protein called translation?



1 - 2

Window on Biochemistry

Capturing and Handling Cell Components

Biochemistry is an experimental science. Our understanding of biological processes at the molecular level comes from the laboratory observation of cells and cell constituents, especially cell organelles and biomolecules. Before one can do experimental biochemistry, the desired object of study must be separated from its natural surroundings. One tool useful for isolating cells, cell organelles, and biomolecules is the centrifuge. Using this instrument, scientists take advantage of the fact that biochemical entities have different physical characteristics: weights, sizes, densities, and shapes. Subjecting a biological sample to an extreme gravitational force, by spinning the sample at high speed, causes sedimentation of sample components at a rate that depends on their physical characteristics. Bacterial cells in a fermentation medium and erythrocytes (red blood cells) in blood plasma can be isolated by spinning a tube containing them at a rate of about 1000–2000 rpm (develops a gravitational field of about 1000g, 1000 times gravity). Whole cells sediment to the bottom of the tube, leaving a liquid supernatant above them that can be decanted away from the cells.

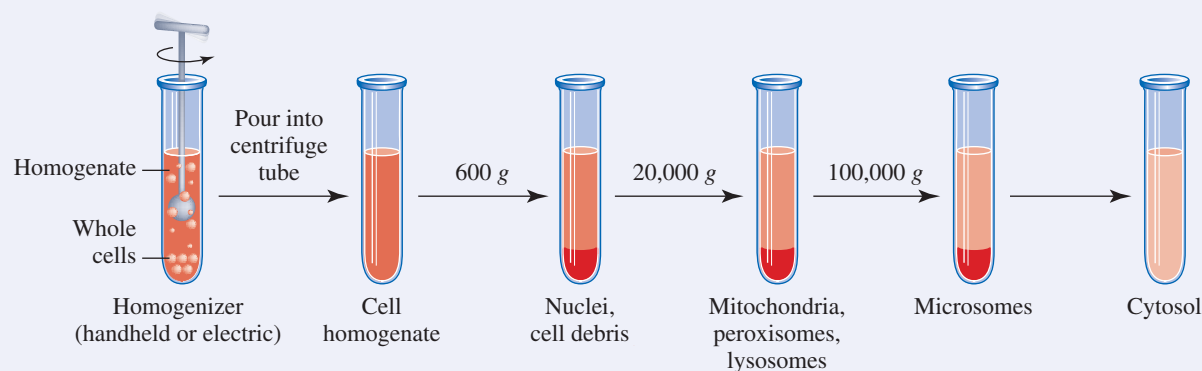
Biochemists rarely work with whole cells, using **cell homogenates** instead. Whole prokaryotic or eukaryotic cells are homogenized or sonicated in an aqueous, buffered solution, a process that breaks open the plasma membrane and cell wall (if present) and allows all the cell's internal components to be released into the solution. Homogenization is accomplished by one of several methods: grinding in a mortar with pestle and an abrasive substance, like sand; breaking the cells under high pressure; or using an electric homogenizer consisting of a rotating Teflon pestle in a glass tube. In **sonication**, cells are broken using sound waves.

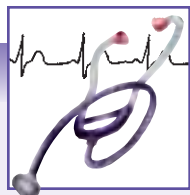
Now that the cell components are freed and suspended in solution, organelles may be isolated by the technique of **fractional centrifugation**. The cell homogenate is subjected to successive centrifugations at increasing speeds (see figure).

The supernatant from each run is decanted into another tube and centrifuged at a higher speed. Each type of cell organelle has a unique size, shape, and weight and can be isolated from the rest because it sediments at a different gravitational force. For example, mitochondria sediment in a tube spinning at a force of about 20,000g. After this spin, the biochemist can decant the supernatant leaving behind mitochondria for further study. The final centrifugation at 100,000g requires a high-speed ultracentrifuge and leaves a supernatant representing the cytoplasm and its soluble proteins and other molecules. Many of the enzymes of metabolism are present in the soluble cytoplasm (cytosol). Now that the basic cell components are separated, the biomolecules present in each may be isolated on an individual basis (called “purification”) using techniques of **chromatography** (see Section 3.5).



A centrifuge used to separate cell components and fractions. (Courtesy of Eppendorf North America, Inc.)





1 - 1

Biochemistry in the Clinic**Obesity**

Obesity, the accumulation of excessive body fat, is a growing worldwide health problem, especially in the United States where it is considered to be at epidemic levels. Health officials estimate that over one-half of the U.S. adult population are overweight (defined as up to 20% over the ideal standard weight based on height and build) and about one-third are obese, clinically defined as having a body weight more than 20% their ideal body weight. (See Biochemistry in the Clinic 20-1 for calculation of body mass index, a measure of ideal weight.) Obesity is a major risk factor for many disease conditions, including diabetes, heart disease, high blood pressure, and stroke, and some kinds of cancers. New biochemical research is showing that obesity is not just a consequence of overeating but is often linked to malfunctions in the hormone-controlled systems that regulate energy consumption and body weight.

The direct causes of most obesity cases are not known, but genetic (and perhaps environmental) factors are of central importance. Eighty percent of children of two obese parents become obese, while only 14% of children with normal-weight parents become obese. Genetic studies have discovered that obese mice decrease their food intake, show increased activity, and lose weight when injected with **leptin**, a fat-tissue-derived, protein hormone. Similar studies using human-derived leptin on obese humans have not been as encouraging as with mice. Unfortunately, leptin's role in human weight regulation appears to be much more complicated than in mice, so a daily injection of leptin will not be the much sought after "magic bullet" treatment for human obesity. One problem is that humans display a decreased sensitivity to leptin or become "leptin resistant," a condition that may result from malfunctioning receptors or from a limited number of them. Biochemical research continues to confirm that leptin plays an important, but unknown, role in the pathogenesis of human obesity. Its actions may not be direct, however, but effected through messenger molecules such as neuropeptide Y, a hypothalamic hormone, and other regulatory proteins. Leptin research, though, is greatly broadening our understanding of body weight control and may lead to new drug therapy for obese patients. On another front, research on muscle mitochondrial uncoupling proteins (UCP), respiratory factors that stimulate heat generation and energy use, may also lead to new drugs for treatment of obesity. More details on the biochemistry of obesity are covered in Section 20.5.



(© Mauro Fermariello/Photo Researchers, Inc.)

Study Questions

1. The hormone leptin is involved in the control of body weight. To what major class of biomolecules does it belong, carbohydrate, nucleic acid, or protein? Describe the general structure of leptin and name the type of monomeric units that are used to synthesize the hormone.
2. The U.S. Food and Drug Administration (FDA) suggests that no more than 30% of our dietary calories should come from fats. Describe your present diet and explain why you think it is appropriate and healthy for you. Do you believe it complies with the FDA suggestion?

References

- Friedman, J. and Halaas, J., 1998. Leptin and the regulation of body weight in mammals. *Nature* 395:763–770.
- Marx, J., 2003. Cellular warriors at the battle of the bulge. *Science* 299:846–849.

SUMMARY

- Biochemistry is the discipline of experimental science that studies the molecules of the living cell.
- Biochemistry has many impacts on our lives: It attempts to explain the origin and cures for diseases; it improves nutrition; it develops methods to solve technological problems; it provides basic molecular understanding of life's processes.
- The principles of biochemistry have been used by humans for thousands of years to ferment juices and bake bread. The discipline originated by a combination of biology, chemistry, and physics.
- The important classes of biomolecules include carbohydrates, lipids, proteins, and nucleic acids.
- Scientists have recognized two main types of organisms: **eukaryotes**, organisms that have membrane-enclosed organelles, and **prokaryotes**, simple, unicellular organisms. The prokaryotes are sometimes divided into two groups, eubacteria and archaea.
- DNA, RNA, proteins, and some carbohydrates serve as informational molecules in that they carry instructions for the direction and control of biological processes. The chemical information in molecules is read by the formation of weak, noncovalent interactions.
- The genetic information in DNA flows through the sequence DNA → RNA → proteins → cellular processes.
- Eukaryotic genes are discontinuous, consisting of coding regions called **exons** and noncoding regions called **introns**.

STUDY EXERCISES

Understanding Terms

1.1 Define or explain the following important biochemical terms in 25 words or less.

- | | |
|------------------------------|--------------------------|
| a. Prokaryotic cells | t. Daltons |
| b. Eukaryotic cells | u. Cell homogenate |
| c. Cell plasma membrane | v. Condensation |
| d. Mitochondria | w. Biotechnology |
| e. Nucleus | x. Hydrolysis reactions |
| f. Bioenergetics | y. Thermophilic bacteria |
| g. Nucleic acids | z. Molecular biology |
| h. Viruses | aa. Replication of DNA |
| i. Fractional centrifugation | bb. Template |
| j. DNA | cc. Intron |
| k. Biomolecules | dd. tRNA |
| l. Hemoglobin | ee. Exon |
| m. Cell organelle | ff. Mutation |
| n. Biochemistry | gg. Genetic code |
| o. Macromolecules | hh. Proteome |
| p. Vitalism | ii. Genome |
| q. Ribosomes | jj. Human Genome Project |
| r. Starch | kk. Transcription |
| s. Metabolism | ll. Translation |

Reviewing Concepts

1.2 Describe the special structural features and some biological functions of the lipid class of biomolecules.

1.3 Draw stable structural molecules with the following molecular formulas.

- | | | |
|-----------------|------------------|----------------|
| a. $C_2H_5NO_2$ | d. C_2H_4OS | g. $C_2H_4O_3$ |
| b. CH_4N_2O | e. $C_3H_4N_2$ | h. H_2O_2 |
| c. $C_2H_4O_2$ | f. $C_3H_7NO_2S$ | i. H_3PO_4 |

Indicate the structures you drew that represent naturally occurring compounds.

Hint: The number of covalent bonds formed by each element is:

Carbon	4	Hydrogen	1
Oxygen	2	Sulfur	2
Nitrogen	3	Phosphorus	5

1.4 List five chemical elements present in biomolecules.

1.5 Name four gases that are essential for life.

1.6 List four metal ions present in living organisms.

Hint: Begin with Na^+ .

1.7 List the major classes of biomolecules.

1.8 Without referring to figures in this book, draw the structure of a bacterial cell and an animal cell. Draw and label internal components of each type of cell.

1.9 Describe the differences between molecular biology and biochemistry.

1.10 Name at least one biological function for each of the following biomolecules.

- | | | |
|----------------|------------------|-------------|
| a. DNA | d. Lipids | g. Proteins |
| b. RNA | e. Carbohydrates | h. Water |
| c. Amino acids | f. Vitamins | |

1.11 Describe the major differences between prokaryotic and eukaryotic cells.

1.12 Which of the following are biopolymers (large-molecular-weight compounds made up of monomers)?

- | | | |
|--------------|----------------|----------|
| a. Glucose | e. Amino acids | i. Water |
| b. Cellulose | f. Hemoglobin | j. O_2 |
| c. DNA | g. Nucleotides | |
| d. Urea | h. Proteins | |

1.13 For each cell organelle listed below, tell whether it is present in plant cells, animal cells, or both.

- | | |
|----------------|-----------------|
| a. Nucleus | e. Chloroplasts |
| b. Ribosomes | f. Mitochondria |
| c. Lysosomes | g. Glyoxysomes |
| d. Peroxisomes | |

1.14 Biopolymers are composed of smaller monomeric units. Match the monomers used to synthesize each of the naturally occurring polymers.

Polymers	Monomers
___ 1. Nucleic acids	a. Glucose
___ 2. Polysaccharides	b. Amino acids
___ 3. Proteins	c. Nucleotides
___ 4. Cellulose	d. Monosaccharides
___ 5. Starch	

1.15 Describe how you would centrifuge a homogenate of heart muscle cells in order to isolate mitochondria.

Hint: See Window on Biochemistry 1-2.

1.16 What metal ions are present in each of the following biomolecules?

- | | |
|----------------|------------------------|
| a. Hemoglobin | c. Cytochrome <i>c</i> |
| b. Chlorophyll | d. Catalase |

1.17 Briefly describe how you would prepare a cell extract of bean plant leaves.

1.18 Put the following biochemical entities in order according to size. Begin with the largest and proceed to the smallest.

- | | |
|-------------------|-------------------|
| a. Mitochondria | e. Glucose |
| b. Red blood cell | f. O ₂ |
| c. DNA | g. Bacterial cell |
| d. Hemoglobin | h. Ethanol |

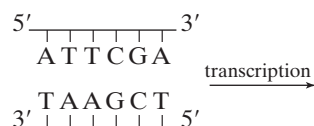
1.19 Describe two ways in which DNA and RNA differ in terms of chemical structure.

1.20 Write the nucleotide sequence that is complementary to the single strands of DNA shown below.

- a. 5'ATTTGACC b. 5'CTAAGCCC

1.21 Draw a complementary, double-stranded polynucleotide that consists of one DNA strand and one RNA strand. Each strand should contain ten nucleotides and the two strands must be antiparallel, that is, one running 5' → 3', the other 3' → 5'.

1.22 Assume that the short stretch of DNA drawn below is transcribed into RNA. Write out the base sequence of the RNA product.



Solving Problems

1.23 Predict in what cell organelle or region of the cell the following biochemical reactions or processes occur.

- $2 \text{H}_2\text{O}_2 \longrightarrow 2 \text{H}_2\text{O} + \text{O}_2$ (animal cells)
- DNA replication (animal and bacterial cells)
- Hydrolysis of RNA ingested by endocytosis
- Protein biosynthesis
- $\text{CO}_2 + \text{H}_2\text{O} \xrightarrow{h\nu} (\text{CH}_2\text{O}) + \text{O}_2$ (synthesis of carbohydrates by photosynthesis)
- $\text{NADH} + \text{H}^+ + \frac{1}{2}\text{O}_2 + \text{ADP} + \text{P}_i \longrightarrow \text{NAD}^+ + \text{H}_2\text{O} + \text{ATP}$ (P_i = phosphate)

1.24 The enzyme hexokinase is required for the metabolism of the carbohydrate glucose. It is a soluble enzyme found in the cytoplasm. Describe how you could use centrifugation to prepare a cell fraction containing the enzyme separated from cell organelles.

1.25 The protein cytochrome *c* is necessary for converting energy from electron transport to the form of chemical bond energy in ATP. In which organelle would you expect to find the most cytochrome *c*?

1.26 Why was Wöhler's synthesis of urea from ammonium cyanate an important achievement in biochemistry?

1.27 Describe the contributions of chemists, biologists, and physicists to the origin of biochemistry.

1.28 What centrifuge fraction would you use to study the molecules involved in DNA function?

1.29 Speculate on why so many of the molecules in nature are based on the element carbon.

1.30 It is often said that in order for life to reproduce, develop, and thrive, there are three basic requirements: (1) a blueprint (directions), (2) materials, and (3) energy. What specific biomolecules or biological processes provide each of these needs?

1.31 Some scientists have argued that biochemical data obtained from cellular extracts (prepared by breaking open cells and thus killing them) are artifactual and that biochemistry should only be studied using living cells. Comment on the pros and cons of this statement.

1.32 Although you have not yet studied the biochemistry of metabolism, describe in your own words how food is converted to energy for muscle contraction.

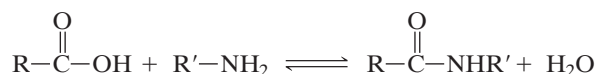
1.33 Describe in general terms how energy from the sun is used by plants to make carbohydrates.

1.34 Use chemical structures to write condensation reactions of acetic acid, CH_3COOH , with each of the following molecules.

- $\text{CH}_3\text{CH}_2\text{OH}$, ethyl alcohol
- NH_3 , ammonia
- CH_3COOH , acetic acid
- CH_3SH , methylthiol
- $\begin{array}{c} \text{CH}_2\text{---CH---CH}_2 \\ | \quad | \quad | \\ \text{OH} \quad \text{OH} \quad \text{OH} \end{array}$, glycerol

1.35 DNA is more stable to hydrolysis reactions than RNA or protein. Is this consistent with the role of DNA in cells? Explain.

1.36 Consider a typical condensation/hydrolysis reaction:



In a living cell, would you expect the equilibrium to lie toward the condensation products or the hydrolysis products? Explain.

1.37 Speculate on how proteins and other biomolecules in thermophilic organisms may be made to be more stable than the same molecules in organisms living under temperate conditions.

1.38 Which of the following statements are distinctive characteristics of living organisms?

- Capable of self-replication
- Complex and highly organized
- Most of their functional biomolecules are small monomeric chemicals
- Extract and use energy from their environment

1.39 Why are the elements C, H, O, and N especially suitable for life's molecules?

- Because they are so abundant and all are present as gases in the environment.

- b. Because they are able to form strong covalent bonds with each other and in some cases with themselves.
- c. Because they came into the environment from the degradation of organisms that were once alive.

1.40 Which of the following biomolecules are made in cells by the polymerization of simple molecules?

- a. Proteins
- b. Nucleic acids
- c. Lipids
- d. Vitamins
- e. Polysaccharides

1.41 Some biomolecules (nucleic acids, proteins, polysaccharides) have the ability to carry biological information. How is the information in biomolecules “read”?

- a. By counting the number of monomer units.
- b. By noting the specific sequence of monomer units used as building blocks.
- c. By noting the number of glucose units.
- d. By analyzing the number of carbon atoms in a monomer unit.

1.42 Identify the organelle that is involved in each of the following biological functions. Choose from these organelles: mitochondria, Golgi apparatus, peroxisomes, or lysosomes.

- a. Oxidation of carbohydrates, fats, and amino acids with the consumption of oxygen and production of ATP.
- b. Oxidation of nutrients to generate hydrogen peroxide.
- c. Metabolism of materials ingested by endocytosis.
- d. Site of protein processing and secretion of cell waste products.

Writing Biochemistry

1.43 Find an article in a current newspaper or newsmagazine that is based on biochemistry or biomedicine. The topic should be related to concepts present in this chapter. Write a 50-word summary of the article emphasizing the importance of biomolecules or biological processes. Discuss ethical implications if appropriate.

1.44 The Sixty-Second Paper. Immediately after reading this chapter, allow yourself just one minute to write down your answers to the following two questions: (1) What were the central concepts introduced in this chapter? and (2) What are the ideas introduced in this chapter that you found confusing or hard to understand?

1.45 Find a current article describing the Human Genome Project (HGP) in a popular science magazine like *Scientific American*. In 100 words, summarize the article by describing the HGP, its current status, and ethical implications of using the results for treatment of a disease.

1.46 In cell structure, the concept of “compartmentation” is an important one. This characteristic of cells is first obvious when

we note that all living cells have some kind of boundary in the form of cell walls and/or membranes. The idea of compartmentation continues inside the cell in the form of vesicles and organelles. What special advantages does compartmentation provide for a living cell?



FURTHER READING

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