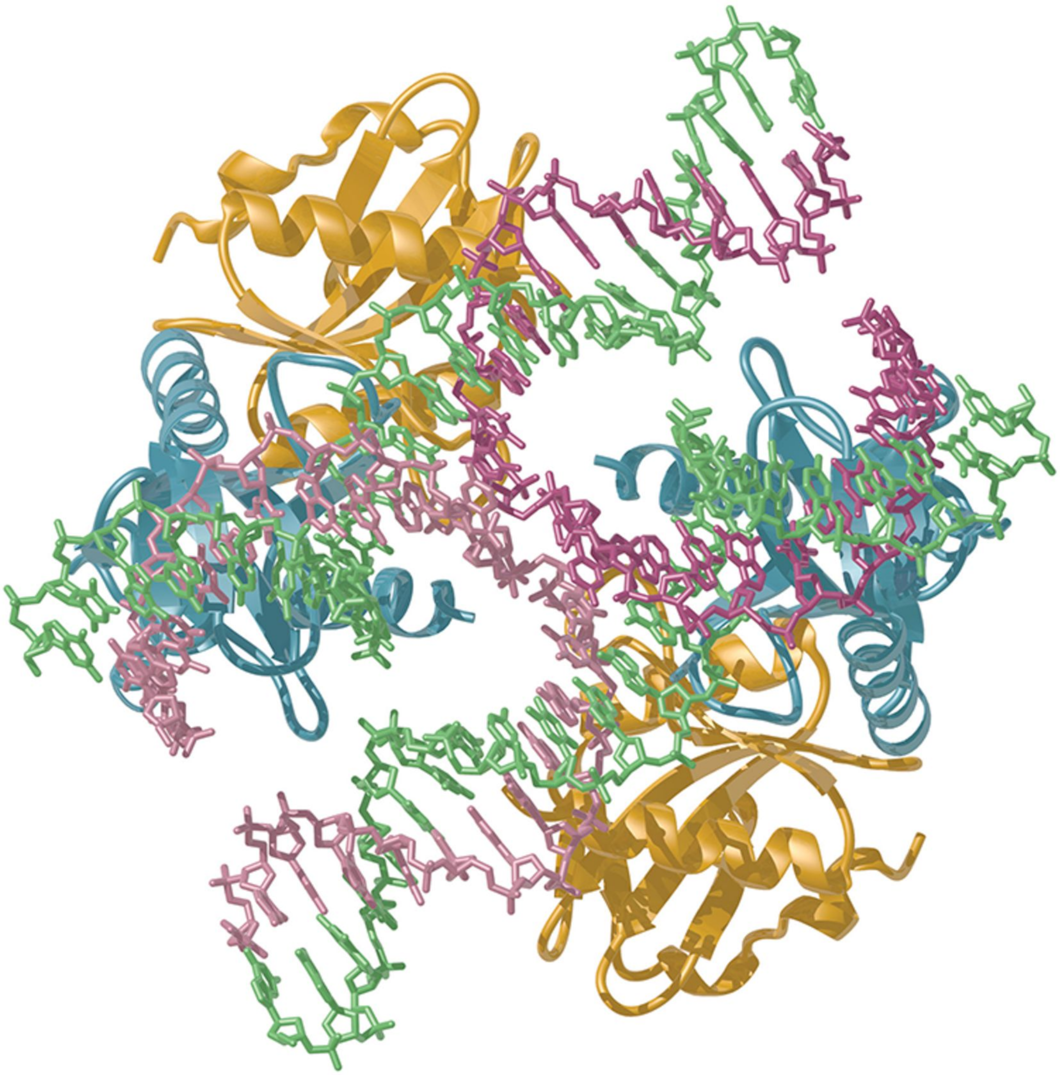
BIOCHEMISTRY

THE MOLECULAR BASIS OF LIFE

SIXTH EDITION



TRUDY McKEE | JAMES R. McKEE

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Trudy McKee
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Only the educated are free.
—Epictetus (Greek philosopher, 55–135 AD)

True freedom requires an education that begins with literacy and then evolves into compassion for all humans and respect for the natural world.

This book is dedicated to those individuals around the world who struggle to educate all children.

Brief Contents

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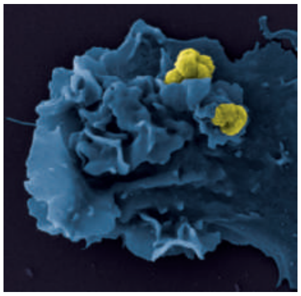

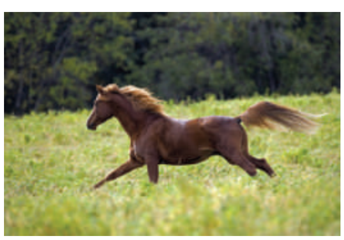

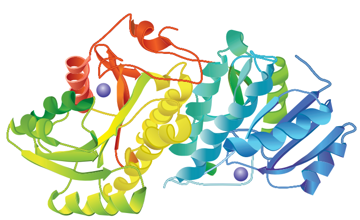

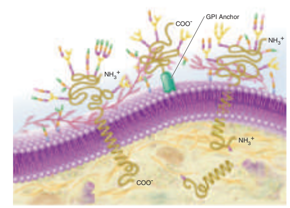
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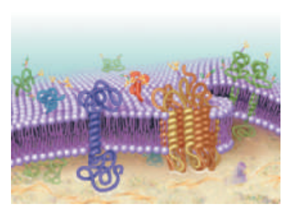

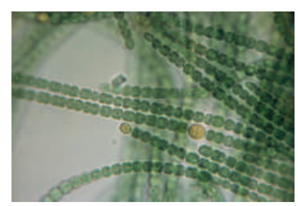

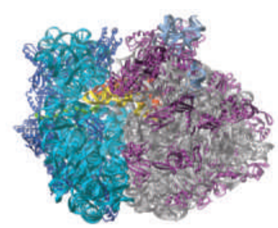

Chapter Opening Vignettes

Biochemistry in Perspective Essays

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Chapter 9 NEW! **Carcinogenesis: The Warburg Effect and Metabolic Reprogramming**	What is aerobic glycolysis and how does it impact cancerous cells?	Aerobic glycolysis is a process in tumor cells in which there is rapid glycolysis-generated ATP synthesis that occurs even when O_2 is present. Loss of glycolyisis regulation is one facet of carcinogenesis, the set of mechanisms whereby normal cells gradually transform into cancerous cells that are no longer responsive to the body's regulatory signals.	343
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Biochemistry in Perspective Essays

Biochemistry in Perspective Essays

	Questions for Students	Key Points	Page No.
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Chapter 18 **Carcinogenesis**	What is cancer, and what are the biochemical processes that facilitate the transformation of normal cells into those with cancerous properties?	Carcinogenesis is the process whereby cells with a growth advantage over their neighbors are transformed by mutations in the genes that control cell division into cells that no longer respond to regulatory signals.	720
Chapter 19 **Trapped Ribosomes: RNA to the Rescue!**	How are ribosomes bound to damaged mRNAs retrieved so they can be recycled?	Living organisms, faced with the high metabolic cost of protein synthesis, have evolved the means of ensuring the efficiency of the process. Both prokaryotes and eukaryotes have methods for rescuing ribosomes trapped by association with damaged mRNAs.	746
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Biochemistry in the Lab Boxes

Don't forget your favorite Biochemistry in Perspective essays from past editions, now available on the companion website at www.oup.com/us/mckee:

Organelles and Human Disease (Chapter 2)
Water, Abiotic Stress, and Compatible Solutes (Chapter 3)
The Extremophiles: Organisms That Make a Living in Hostile Environments (Chapter 4)
Protein Poisons (Chapter 5)
Protein Folding and Human Disease (Chapter 5)
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Your favorite Biochemistry in the Lab boxes from past editions are also available on the companion website at www.oup.com/us/mckee:

Dialysis (Chapter 3)
Protein Sequence Analysis: The Edman Degradation (Chapter 5)
Glycomics (Chapter 7)
Photosynthetic Studies (Chapter 13)

Preface

Welcome to the sixth edition of *Biochemistry: The Molecular Basis of Life*. Although this textbook has been revised and updated to reflect the latest research in biochemistry, our original mission remains unchanged. We continue to believe that the cornerstone of an education in the life sciences is a coherent understanding of the basic principles of biochemistry. Once biochemical concepts have been mastered, students are then prepared to tackle the complexities of their chosen science fields. To that end, we have sought comprehensive coverage of biochemical systems, structures, and reactions, but within the context of the organism. We have thus sought a unique balance between chemistry, biology, and their applications to medicine and human health.

ORGANIZATION AND APPROACH

CHEMICAL AND BIOLOGICAL PRINCIPLES IN BALANCE. As with previous editions, the sixth edition is designed for both life science students and chemistry majors. We provide thorough coverage of biochemical principles, structures, and reactions, but within a biological context that emphasizes their relevance.

A REVIEW OF BASIC PRINCIPLES. Few assumptions have been made about a student's chemistry and biology background. To ensure that all students are sufficiently prepared for acquiring a meaningful understanding of biochemistry, the first four chapters review the principles of such topics as organic functional groups, noncovalent bonding, thermodynamics, and cell structure. These chapters can either be covered in class or assigned for self-study.

Several topics are introduced in these early chapters and then continued throughout the book. Examples include cell volume changes triggered by metabolic processes that alter osmotic balance across membranes, the self-assembly of biopolymers such as proteins into supermolecular structures, and the nature and function of molecular machines. New in this edition is coverage of proteostasis, the mechanism whereby cells protect their proteins. Other important concepts that are emphasized include the relationship between biomolecular structure and function and the dynamic, unceasing, and self-regulating nature of living processes. Students are also provided with overviews of the major physical and chemical techniques that biochemists have used to explore life at the molecular level.

REAL-WORLD RELEVANCE. Because students who take the one-semester biochemistry course come from a range of backgrounds and have diverse career goals, the sixth edition consistently demonstrates the fascinating connections between biochemical principles and the worlds of medicine, nutrition, agriculture, bioengineering, and forensics. Features such as the Biochemistry in Perspective essays and chapter opening vignettes, as well as dozens of examples integrated into the body of the text, help students see the relevance of biochemistry to their chosen fields of study.

SUPERIOR PROBLEM-SOLVING PROGRAM. Analytical thinking is at the core of the scientific enterprise, and mastery of biochemical principles requires consistent and sustained engagement with a wide range of problems. The sixth edition continues to present students with a complete problem-solving system. This includes the effective in-chapter worked problems, which illustrate how quantitative problems are solved, as well as dozens of practice questions throughout, when new concepts and high-interest topics are introduced. There is also a large set of end-of-chapter questions, 285 of which are new. These include review, fill-in-the-blank, short-answer, and thought questions, which will allow students to test their knowledge. Sapling Learning's Online Homework System provides a powerful and effective tool for teaching and learning.

SIMPLE, CLEAR ILLUSTRATIONS. Biochemical concepts often require a high degree of visualization, and we have crafted an art program that brings complex processes to life. More than 720 full-color figures fill the pages of the sixth edition, many newly enhanced for a more vivid presentation in three dimensions and consistent scale and color of chemical structures.

CURRENCY. The sixth edition has been updated to present recent developments in the field, while remaining focused on the "big-picture" principles that are the cornerstone of the one-term biochemistry course. These changes again reflect the goal of balanced and thorough coverage of chemistry within a biological context. A detailed list of updated material follows in the next section.

NEW IN THIS EDITION

As a result of the rapid pace of discovery in the life sciences and our commitment to provide students with the highest-quality learning system available in any biochemistry textbook, we have revised the sixth edition in the following ways:

- **Enhanced Supplements Program.** Adding to the already robust ancillary program, an all-new video and animation guide provides links to dozens of freely available and high-quality online resources. In addition, an expanded and enriched test-item file written completely by the textbook authors accompanies the sixth edition.
- **General and Organic Chemistry Review Primer.** This edition includes a helpful in-text review of foundational general chemistry and organic chemistry topics to help students refresh their memories and begin to apply their knowledge in new biochemical contexts.
- **New and Updated Applications.** The sixth edition includes two new Biochemistry in Perspective essays, "Carcinogenesis: The Warburg Effect and Metabolic Reprogramming" and "The Artificial Leaf: Biomimetic Photosynthesis," which will capture student interest. In addition, several essays have been updated to reflect recent research. These include "Myocardial Infarct: Ischemia and Reperfusion," "Atherosclerosis," "Diabetes Mellitus," and "HIV Infection."
- **Expanded Problem-Solving Program.** The sixth edition includes a total of 285 additional questions at the end of the chapters. The expanded problem sets span a range of difficulty, from basic practice problems to more challenging integrative exercises.
- **Brand-New Illustrations.** With 28 new figures, the sixth edition incorporates a superior and expanded art program designed to help students develop a strong visual grasp of biochemical processes. Many figures have been enhanced for vivid, clear, and consistent presentation in color and three dimensions.
- **Important Themes.** We have retained and strengthened the themes of macromolecular crowding and systems biology, introduced in the fourth edition, and introduced a new theme, referred to as proteostasis.

    - Macromolecular crowding, the dense packing of vast numbers of proteins and other molecules within cells, has a profound effect on a wide variety of living processes. The concept of macromolecular crowding provides students with a more realistic view of cell structure and function.
    - The relatively new field of systems biology is an approach to biochemical processes that is based on engineering principles. Developed in response to the overwhelmingly vast amounts of information now available to life scientists, systems biology is the computer-assisted investigation of the complex interactions among biomolecules. Our accessible introduction to systems biological principles provides students with newly revised and expanded insights into the basic patterns of biomolecular processes.
    - We offer new coverage of proteostasis, a diverse set of mechanisms whereby cells control the folding of the proteome, has a crucial impact on cellular processes such as gene expression and signaling pathways. It protects against the toxic effects of protein aggregation.

- **Increased Attention to Reaction Mechanisms.** Catalytic mechanisms provide students with an enhanced understanding of the means by which biochemical reactions occur. Examples include the rubisco and proline residue hydroxylation mechanisms. We have retained a description of the roles of amino acid side chains in the catalytic mechanisms of enzymes and the mechanisms of the nucleic acid polymerases and ribosome-catalyzed peptide bond formation. Here, too, we have sought to enhance the text's unique balance between chemistry and biology.
- **Current Topics.** The following is a list of some, but not all, of the updated content that has been introduced in the sixth edition:
    - **Chapter 1** contains a revision of the section devoted to systems biology. Explanations of the terms *network*, *module*, and *motif* facilitate students' efforts to understand biochemical principles. Building on the discussions of organic reaction mechanisms introduced in the Chemistry Primer, the revised description of biochemical reactions relates each reaction type to its basic organic mechanism.
    - **Chapter 2** contains an expanded basic themes section. The signal transduction section includes overviews of the role of calcium ions in signaling and the relationship between signaling, metabolism, and gene expression. A new basic theme, proteostasis, provides an introduction to the strategies that cells use to protect the integrity of their proteins. A newly revised discussion of the endomembrane system in eukaryotic cells provides insight into the relationship between cell architecture and biochemical functions such as signaling, protein processing, and gene expression. A revised section concerned with mitochondria includes descriptions of the effects of the ER-mitochondrial interactions on cell signaling and phospholipid synthesis. The Biochemistry in Perspective essay on primary cilia has been updated. The Biochemistry in the Lab reading now includes a brief description of live cell imaging.
    - In **Chapter 5** the section devoted to unstructured proteins has been expanded to include p53, a major tumor suppressor protein with an unstructured domain. The discussion of molecular chaperones, proteins that have a central role in proteostasis, has been expanded and updated. The description of hemoglobin allostery has been revised to improve clarity. The Biochemistry in the Lab reading on protein technology has been expanded to include the use of affinity chromatography in the purification of recombinant proteins and the use of top-down mass spectrometry and NMR spectroscopy in protein structure analysis.

- The discussion of transition state stabilization in **Chapter 6** has been revised using triose phosphate isomerase as an example.
- The section in **Chapter 8** devoted to glycolysis regulation has been expanded with a description of glucose-induced gene expression.
- **Chapter 9** has a new Biochemistry in Perspective reading that describes the relationship between aerobic glycolysis and carcinogenesis.
- A revised and updated Biochemistry in Perspective reading in **Chapter 10** describes the biochemical consequences of the reintroduction of oxygen to heart cells damaged by clot-induced inadequate blood flow.
- In **Chapter 11** the discussion of the plasma membrane protein CFTR has been updated to include a brief overview of the clinical use of molecules that improve folding and/or function of the receptor in cystic fibrosis patients.
- In **Chapter 12** the section devoted to lipolysis in adipocytes has been revised to reflect recent discoveries concerning the roles of perilipin A and several enzymes. The Biochemistry in Perspective reading on atherosclerosis now includes a description of the consequences of AGE formation in endothelial cells.
- In **Chapter 13** a new Biochemistry in Perspective reading, "The Artificial Leaf," describes the attempts of researchers to imitate natural photosynthesis for fuel synthesis.
- The discussion of nitrogen fixation in **Chapter 14** has been revised to reflect recent discoveries. The transamination reaction mechanism figure has been modified to improve clarity.
- In **Chapter 15** the section devoted to the ubiquitin proteasomal system has been revised to increase clarity.
- The section devoted to cell surface receptor function in **Chapter 16** has been revised and expanded. The Biochemistry in Perspective reading on diabetes mellitus has been updated.
- In **Chapter 17** the section devoted to histones and chromatin structure has been revised to improve clarity and expanded to include recent research. Descriptions of noncoding DNA in the human genome have been updated. In the Biochemistry in the Lab reading devoted to nucleic acid methods, descriptions of Illumina and ion torrent DNA sequencing have been added. The description of ncRNAs has been revised. The Biochemistry in Perspective on HIV infection has been updated.
- In the Biochemistry in the Lab on genomic methods in **Chapter 18**, the description of genome projects has been updated with an introduction to ENCODE (the Encyclopedia of DNA Elements). The discussion of eukaryotic RNA polymerase II now includes a brief description of transcription factories in the nucleus. The section devoted to eukaryotic transcription and posttranscriptional processing has been revised and expanded to reflect recent discoveries.
- A new section of **Chapter 19** describes the proteostasis network, which protects the integrity of proteins from their synthesis through folding, transport, and degradation when they are damaged or obsolete. The discussion includes brief descriptions of the heat shock response and the role of the proteostasis network in several human diseases.

LEARNING PACKAGE

We have created a comprehensive set of additional resources to accompany the sixth edition. These are designed to help students master the subject matter and to assist instructors in meeting this objective.

For Students

STUDENT STUDY GUIDE AND SOLUTIONS MANUAL. Written by the textbook authors, this manual provides the solutions to all of the exercises from the text that are not included in the book itself. Each solution has been independently checked for accuracy by a panel of expert reviewers.

NEW! ANIMATION AND VIDEO GUIDE. New to the sixth edition, the student companion website now includes a curated guide to biochemical animations. This set of more than 200 high-quality and freely available animations help students visualize complex biochemical processes.

WEB QUIZZES. At http://www.oup.com/us/mckee/, students seeking an online resource to test their knowledge of biochemistry can gain access to more than 600 questions written by Dan Sullivan (University of Nebraska at Omaha). Students receive a feedback summary with each graded quiz.

INTERACTIVE 3D MOLECULES. Todd Carlson (Grand Valley State University) has created more than 300 interactive 3D molecules in JMOL format to accompany this text. Students can manipulate and study individual molecules and their structures, take self-guided concept tutorials, and test their molecule-recognition abilities by working through the interactive self-quizzes at http://www.oup.com/us/mckee/.

For Instructors

SAPLING LEARNING ONLINE HOMEWORK SYSTEM. Sapling Learning's online homework system includes algorithmic questions, exercises and guided tutorials for molecule drawing, chemical equation entry, 2D and 3D atom selection, labeling diagrams, and graphing. Automatic homework grading, diagnostic feedback, and dedicated support from chemists provide instructors all the resources they need to finally assign homework their students will actually complete. To schedule a live demonstration of Sapling, go to http://www.oup.com/us/mckee/.

ANCILLARY RESOURCE CENTER. The Ancillary Resource Center (ARC) at **http://www.oup-arc.com** is a convenient, instructor-focused single destination for resources that accompany the text. Accessed online through individual user accounts, the ARC provides instructors with up-to-date ancillaries at any time while guaranteeing the security of grade-significant resources. The following instructor's resources are available on the McKee ARC:

- **All text images in electronic format.** Instructors who adopt the sixth edition gain access to every numbered illustration, photo, figure caption, and table from the text in high-resolution electronic format. Labels have been enlarged and multipart figures have been broken down into separate components for clearer projection in large lecture halls. Images are available on both the Instructor's Resource CD and the sixth edition website, http://www.oup.com/us/mckee/.
- **Computerized test-item file.** Written by the authors and completely revised for the sixth edition, the test-item file includes more than 1,400 questions provided

as editable Word files that can be easily customized. Using the test-authoring and -management tool Diploma, the computerized version of the test bank is designed for both novice and advanced users. Diploma enables instructors to create and edit questions, create randomized quizzes and texts with an easy-to-use drag-and-drop tool, publish quizzes and tests to online courses, and print quizzes and tests for paper-based assessments.

LECTURE NOTES SLIDES. This set of more than 1100 editable lecture notes slides makes preparing lectures faster and easier than ever. Available in PowerPoint format, the lecture notes for the sixth edition now include embedded links from the new curated animations and video guide.

COURSE MANAGEMENT SYSTEMS. All instructor and student resources, including the text images, the test bank files, and the online self-quiz questions, are compatible with a variety of management systems.

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We wish to express our appreciation for the efforts of the dedicated individuals who provided detailed content and accuracy reviews of the text and the supplemental materials of the sixth edition:

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Biochemistry

THE MOLECULAR BASIS OF LIFE

CHAPTER

1 Biochemistry: An Introduction

Life Scientists at Work
A thorough knowledge of biochemistry is a core requirement for life scientists.

OUTLINE

Why Study Biochemistry?

Why study biochemistry? For students embarking on careers in the life sciences, the answer should be obvious: biochemistry, the scientific discipline concerned with chemical processes within living organisms, is the bedrock upon which all of the modern life sciences are built. During the past two decades the influence of biochemistry and the allied field of molecular biology has increased exponentially. Life sciences as diverse as agronomy (the science of soil management and crop production), forensics, marine biology, plant biology, and ecology are now being explored with powerful biotechnological tools. As a result, there is now a vast array of career opportunities in federal or state government agencies and industry (e.g., pharmaceutical, biotechnology, and agribusiness companies) for recent graduates with life science degrees. Examples of such fields include biomedical and clinical research, forensic analysis, plant or animal genetics, environmental protection, and wildlife biology.

Economic conditions often dictate life science career choices. (The Occupational Outlook Handout on the U.S. Bureau of Labor Statistics website offers an unbiased assessment of future employment prospects.) No matter the economic conditions when students graduate, employment opportunities are always better for those who have undergraduate research experience. Developing a network of connections beginning with professors and expanding into the student's field or interests (e.g., by attending science career fairs or professional society conferences) also increases employment opportunities. Furthermore, writing, data analysis, problem solving, and communication are skills that employers always value highly. For students not interested in research careers, there are opportunities in science journalism, education, and software engineering. Other examples of alternate careers where a life science degree will be an asset include public policy (e.g., public health risk assessment and health product regulation), law (e.g., lawyers for pharmaceutical and biotech companies and environmental organizations), and marketing and sales (e.g., drugs and medical devices).

Overview

FROM MODEST BEGINNINGS IN THE LATE NINETEENTH CENTURY, THE SCIENCE OF BIOCHEMISTRY HAS PROVIDED INCREASINGLY MORE sophisticated intellectual and laboratory tools for the investigation of living processes. Today, in the early years of the twenty-first century, we find ourselves in the midst of a previously unimagined biotechnological revolution. Life sciences as diverse as medicine, agriculture, and forensics have generated immense amounts of information. The capacity to understand and appreciate the significance of this phenomenon begins with a thorough knowledge of biochemical principles. This chapter provides an overview of these principles. The chapters that follow focus on the structure and functions of the most important biomolecules and the major biochemical processes that sustain the living state.

This textbook is designed to provide an introduction to the basic principles of biochemistry. The opening chapter provides an overview of the major components of living organisms and the processes that sustain the living state. After a brief description of the nature of the living state, an introduction to the structures and functions of the major biomolecules is provided. This material is followed by an overview of the most important biochemical processes.

The chapter concludes with a brief discussion of the concepts of modern experimental biochemistry and an introduction to *systems biology*, an investigative strategy used to improve our understanding of living organisms as integrated systems rather than collections of isolated components and chemical reactions.

1.1 WHAT IS LIFE?

What is life? Despite the work of life scientists over several centuries, a definitive answer to this deceptively simple question has been elusive. Much of the difficulty in delineating the precise nature of living organisms lies in the overwhelming diversity of the living world and the apparent overlap in several properties of living and nonliving matter. Consequently, life has been viewed as an intangible property and is usually described in operational terms, such as movement, reproduction, adaptation, and responsiveness to external stimuli. The work of life scientists, made possible by the experimental approaches of biochemistry, has revealed that all organisms obey the same chemical and physical laws that rule the universe.

1. **Life is complex and dynamic**. All organisms are composed of the same set of chemical elements, primarily carbon, nitrogen, oxygen, hydrogen, sulfur, and phosphorus. **Biomolecules**, the molecules synthesized by living organisms, are organic (carbon based). Living processes, such as growth and development, involve thousands of chemical reactions in which vast quantities and varieties of vibrating and rotating molecules interact, collide, and rearrange into new molecules.
2. **Life is organized and self-sustaining**. Living organisms are hierarchically organized systems: they consist of patterns of organization from smallest (atom) to largest (organism) (**Figure 1.1**). In biological systems, the functional capacities of each level of organization are derived from the structural and chemical properties of the level below it. Biomolecules are composed of atoms, which in turn are formed from subatomic particles. Certain biomolecules become linked to form polymers called **macromolecules**. Examples include nucleic acids, proteins, and polysaccharides, which are formed from nucleotides, amino acids, and sugars, respectively. Cells are composed of a diversity of biomolecules and macromolecules that form into more complex supermolecular structures. At the molecular level, there are hundreds of biochemical reactions that together sustain the living state. Catalyzed by biomolecular catalysts called **enzymes**, these reactions are organized into pathways. (A *biochemical pathway* is a series of reactions in which a specific molecule is converted into a terminal product.) The sum total of all the reactions in a living organism is referred to as **metabolism**. The capacity of living organisms to regulate metabolic processes despite variability in their internal and external environments is called **homeostasis**. In multicellular organisms there are other levels of organization that include tissues, organs, and organ systems.
3. **Life is cellular**. Cells, the basic units of living organisms, differ widely in structure and function, but each is surrounded by a membrane that controls the transport of substances into and out of the cell. The membrane also mediates the response of the cell to the extracellular environment. If a cell is divided into its component parts, it will cease to function in a life-sustaining way. Cells arise only from the division of existing cells.
4. **Life is information-based**. Organization requires information. Living organisms can be considered information-processing systems because maintenance of their structural integrity and metabolic processes involves

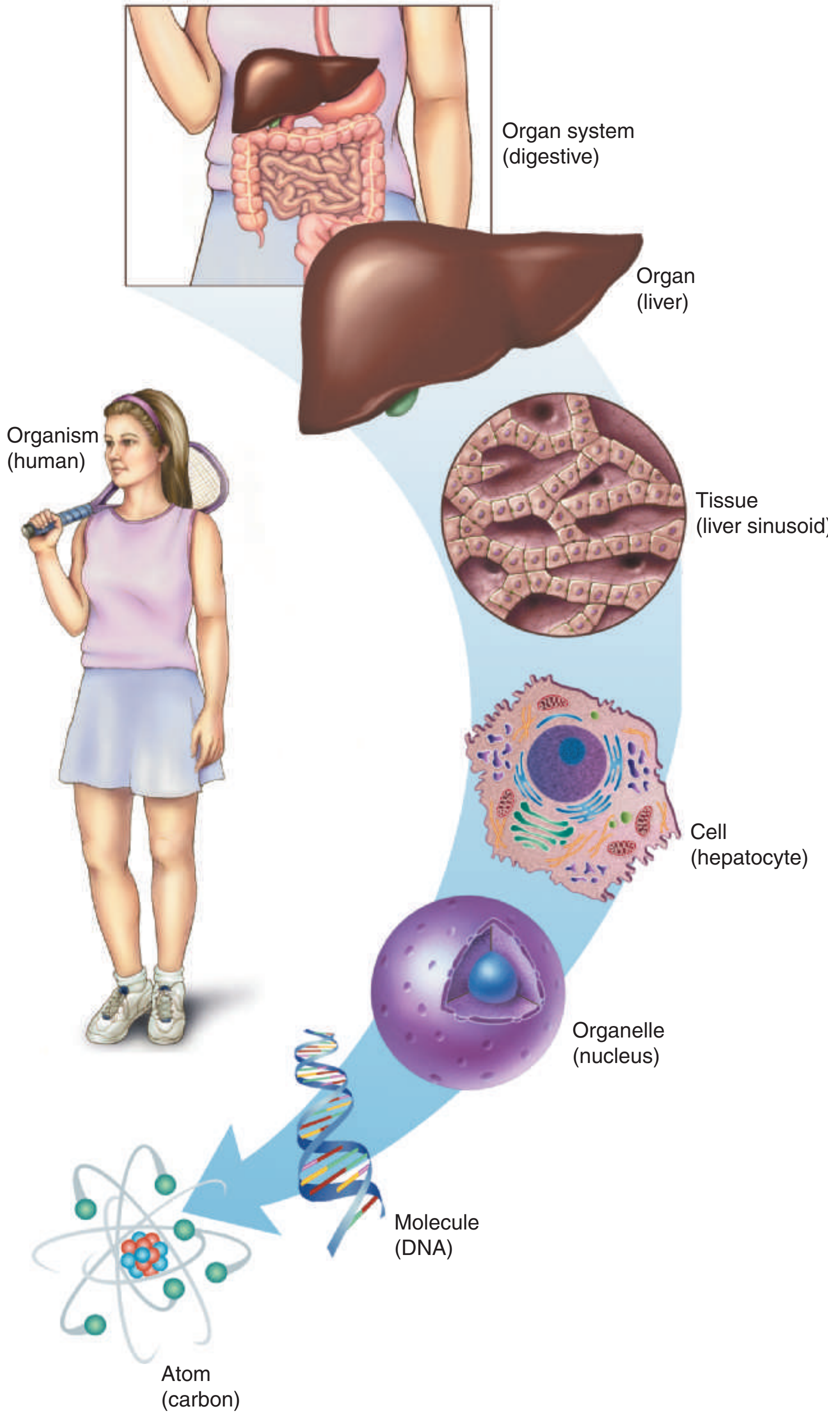


FIGURE 1.1

Hierarchical Organization of a Multicellular Organism: The Human Being

Multicellular organisms have several levels of organization: organ systems, organs, tissues, cells, organelles, molecules, and atoms. The digestive system and one of its component organs (the liver) are shown. The liver is a multifunctional organ that has several digestive functions. For example, it produces bile, which facilitates fat digestion, and it processes and distributes the food molecules absorbed in the small intestine to other parts of the body. DNA, one type of molecule found in cells, contains the genetic information that controls cell function.

interactions among a vast array of molecules within and between cells. Biological information is expressed in the form of coded messages that are inherent in the unique three-dimensional structure of biomolecules. Genetic information, which is stored in **genes**, the linear sequences of nucleotides in deoxyribonucleic acid (DNA), in turn specifies the linear sequence of amino acids in proteins and how and when those proteins are synthesized. Proteins perform their function by interacting with other molecules. The unique three-dimensional structure of each type of protein allows it to bind to, and interact with, a specific type of molecule that has a precise complementary shape. Information is transferred during the binding process. For example, the binding of the protein insulin to insulin receptor molecules on the surface of certain cells is a signal that initiates the uptake of the nutrient molecule glucose.

5. **Life adapts and evolves**. All life on earth has a common origin, with new forms arising from older forms. When an individual organism in a population reproduces itself, stress-induced DNA modifications and errors that occur when DNA molecules are copied can result in **mutations** or sequence changes. Most mutations are silent; that is, they either are repaired or have no effect on the functioning of the organism. Some, however, are harmful, serving to limit the reproductive success of the offspring. On rare occasions mutations may contribute to an increased ability of the organism to survive, to adapt to new circumstances, and to reproduce. A principal driving force in this process is the capacity to exploit energy sources. Individuals possessing traits that allow them to better exploit a specific energy source within their habitat may have a competitive advantage when resources are limited. Over many generations, the interplay of environmental change and genetic variation can lead to the accumulation of favorable traits and eventually to increasingly different forms of life.

KEY CONCEPTS

- All living organisms obey the chemical and physical laws.
- Life is complex, dynamic, organized, and self-sustaining.
- Life is cellular and information-based.
- Life adapts and evolves.

1.2 BIOMOLECULES

Living organisms are composed of thousands of different kinds of inorganic and organic molecules. Water, an inorganic molecule, may constitute 50 to 95% of a cell's content by weight, and ions such as sodium (Na^+), potassium (K^+), magnesium (Mg^{2+}), and calcium (Ca^{2+}) may account for another 1%. Almost all the other kinds of molecules in living organisms are organic. Organic molecules are principally composed of six elements: carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur, and they contain trace amounts of certain metallic and other nonmetallic elements. The atoms of each of the most common elements found in living organisms can readily form stable covalent bonds, the kind that allow the formation of such important molecules as proteins.

The remarkable structural complexity and diversity of organic molecules are made possible by the capacity of carbon atoms to form four strong, single covalent bonds either to other carbon atoms or to atoms of other elements. Organic molecules with many carbon atoms can form complicated shapes such as long, straight structures or branched chains and rings.

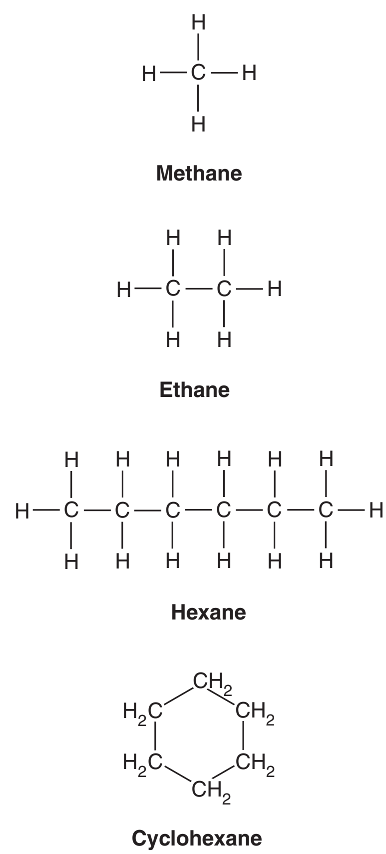


FIGURE 1.2
Structural Formulas of Several Hydrocarbons

Functional Groups of Organic Biomolecules

Most biomolecules can be considered derived from the simplest type of organic molecules, called the **hydrocarbons**. Hydrocarbons (**Figure 1.2**) are carbon- and hydrogen-containing molecules that are **hydrophobic**, or insoluble in water. All other organic molecules are formed by attaching other atoms or groups of atoms to the carbon backbone of the hydrocarbon. The chemical properties of these derivative molecules are determined by the specific arrangement of atoms called **functional groups** (**Table 1.1**). For example, alcohols result when hydrogen atoms are replaced by hydroxyl groups (—OH). Thus methane (CH_4), a component of natural gas, can be converted into methanol (CH_3OH), a toxic liquid that is used as a solvent in many industrial processes.

Most biomolecules contain more than one functional group. For example, many simple sugar molecules have several hydroxyl groups and an aldehyde group. Amino acids, the building-block molecules of proteins, have both an amino group and a carboxyl group. The distinct chemical properties of each functional group contribute to the behavior of any molecule that contains it.

TABLE 1.1 Important Functional Groups in Biomolecules

Family Name	Group Structure	Group Name	Significance
Alcohol	R—OH	Hydroxyl	Polar (and therefore water-soluble), forms hydrogen bonds
Aldehyde	R—C(=O)—H	Carbonyl	Polar, found in some sugars
Ketone	R—C(=O)—R′	Carbonyl	Polar, found in some sugars
Acids	R—C(=O)—OH	Carboxyl	Weakly acidic, bears a negative charge when it donates a proton
Amine	R—NH_2	Amino	Weakly basic, bears a positive charge when it accepts a proton
Amide	R—C(=O)—NH_2	Amido	Polar but does not bear a charge
Thiol	R—SH	Thiol	Easily oxidized; can form —S—S— (disulfide) bonds readily
Ester	R—C(=O)—O—R′	Ester	Found in certain lipid molecules
Alkene	RCH═CHR′	Double bond	Important structural component of many biomolecules (e.g., found in lipid molecules)

Major Classes of Small Biomolecules

Many of the organic compounds found in cells are relatively small, with molecular masses of less than 1000 daltons (Da). (One dalton, 1 atomic mass unit, is equal to 1/12 of the mass of one atom of ^{12}C.) Cells contain four families of small molecules: amino acids, sugars, fatty acids, and nucleotides (**Table 1.2**). Members of each group serve several functions. First, they are used in the synthesis of larger molecules, many of which are polymers. For example, proteins, certain carbohydrates, and nucleic acids are polymers composed of amino acids, sugars, and nucleotides, respectively. Fatty acids are components of lipid (water-insoluble) molecules of several types.

Second, some molecules have special biological functions. For example, the nucleotide adenosine triphosphate (ATP) serves as a cellular reservoir of

TABLE 1.2 Major Classes of Biomolecules

Small Molecule	Polymer	General Functions
Amino acids	Proteins	Catalysts and structural elements
Sugars	Carbohydrates	Energy sources and structural elements
Fatty acids	N.A.	Energy sources and structural elements of complex lipid molecules
Nucleotides	DNA	Genetic information
	RNA	Protein synthesis

chemical energy. Finally, many small organic molecules are involved in complex reaction pathways. Examples of each class of molecule are described next.

AMINO ACIDS AND PROTEINS There are hundreds of naturally occurring **amino acids**, each of which contains an amino group and a carboxyl group. Amino acids are classified α, β, or γ according to the location of the amino group in reference to the carboxyl group. In α-amino acids, the most common type, the amino group is attached to the carbon atom (the α-carbon) immediately adjacent to the carboxyl group (**Figure 1.3**). In β- and γ-amino acids, the amino group is attached to the second and third carbon, respectively, from the carboxyl group. Also attached to the α-carbon is another group, referred to as the side chain or R group. The chemical properties of each amino acid, once incorporated into protein, are determined largely by the properties of its side chain. For example, some side chains are hydrophobic (i.e., low solubility in water), whereas others are **hydrophilic** (i.e., dissolve easily in water). Several examples of α-amino acids are illustrated in **Figure 1.4**.

Twenty standard α-amino acids occur in proteins. Some standard amino acids have unique functions in living organisms. For example, glycine and glutamic acid function in animals as **neurotransmitters**, signal molecules released by nerve cells. Proteins also contain nonstandard amino acids that are modified versions of the standard amino acids. The structure and function of protein molecules are often altered by conversion of certain amino acid residues to derivatives via phosphorylation, hydroxylation, and other chemical modifications. (The term "residue" refers to a small biomolecule that is incorporated in a macromolecule, e.g., amino acid residues in a protein.) For example, many of the residues of proline are hydroxylated in collagen, the connective tissue protein. Many naturally occurring amino acids are not α-amino acids. Prominent examples include β-alanine, a precursor of the vitamin pantothenic acid, and γ-aminobutyric acid (GABA), a neurotransmitter found in the brain (**Figure 1.5**).

Amino acid molecules are used primarily in the synthesis of long, complex polymers known as **polypeptides**. Up to a length of about 50 amino acids, these molecules are called **peptides**. **Proteins** consist of one or more polypeptides. Polypeptides play a variety of roles in living organisms. Examples include transport proteins, structural proteins, and the enzymes (catalytic proteins).

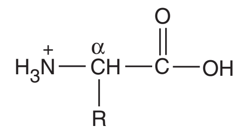


FIGURE 1.3

General Formula for α-Amino Acids

For 19 of the 20 standard amino acids the α-carbon is bonded to a hydrogen atom, a carboxyl group, an amino group, and an R group.

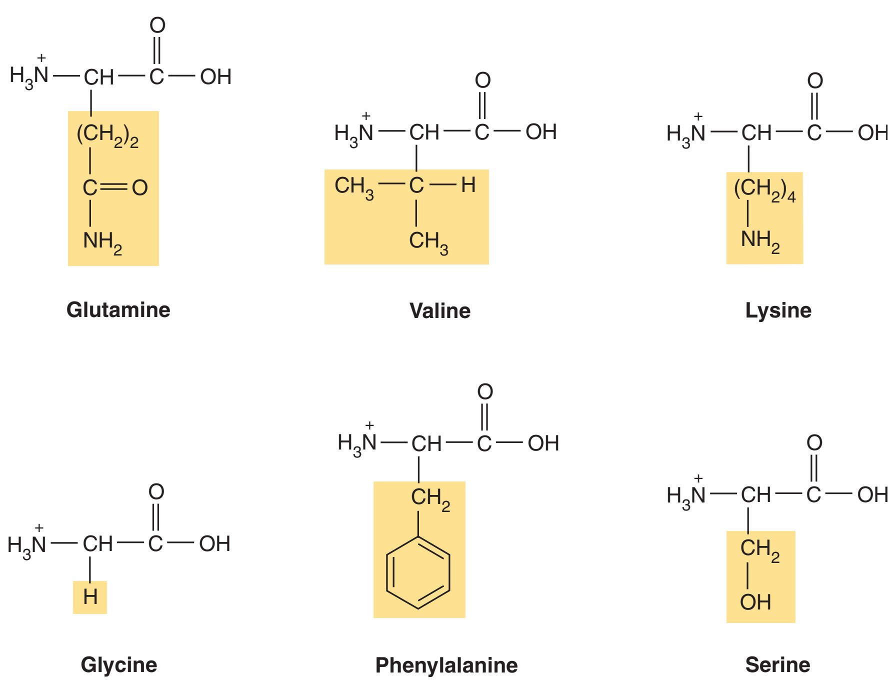


FIGURE 1.4

Structural Formulas for Several α-Amino Acids

An R group (highlighted) in an amino acid structure can be a hydrogen atom (e.g., in glycine), a hydrocarbon group (e.g., the isopropyl group in valine), or a hydrocarbon derivative (e.g., the hydroxymethyl group in serine).

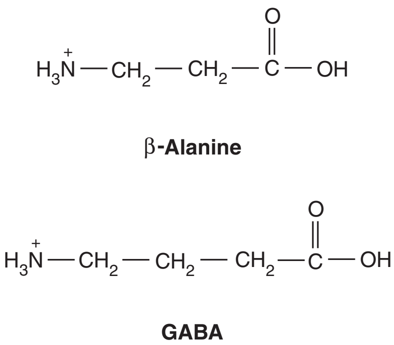


FIGURE 1.5

Selected Examples of Naturally Occurring Amino Acids That Are Not α-Amino Acids: β-Alanine and γ-Aminobutyric Acid (GABA)

The individual amino acids are connected in peptides (**Figure 1.6**) and polypeptides by the peptide bond. **Peptide bonds** are amide linkages that form in a type of nucleophilic substitution reaction (p. 12) in which the amino group nitrogen of one amino acid attacks the carbonyl carbon in the carboxyl group of another. The final three-dimensional structure, and therefore biological function, of polypeptides results largely from interactions among the R groups (**Figure 1.7**).

WORKED PROBLEM 1.1

Living organisms generate a vast number of different biopolymers by linking monomers in different sequences. A set of tripeptides, each containing three amino acid residues, contains only two types of amino acids: A and B. How many possible tripeptides are in this set?

SOLUTION

The number of possible tripeptides is given by the formula $\mathbf{X}^n$, where

$\mathbf{X}$ = the number of types of constituent amino acid residues

and n = length of the peptide.

Substituting these values into the formula yields $2^3 = 8$. The eight tripeptides are as follows: AAA, AAB, ABA, BAA, ABB, BAB, BBA, and BBB. ■

SUGARS AND CARBOHYDRATES **Sugars**, the smallest carbohydrates, contain alcohol and carbonyl functional groups. They are described in terms of both carbon number and the type of carbonyl group they contain. Sugars that possess an aldehyde group are called *aldoses* and those that possess a ketone group are called *ketoses*. For example, the six-carbon sugar glucose (an important energy source in most living organisms) is an aldohexose; fructose (fruit sugar) is a ketohexose (Figure 1.8).

Sugars are the basic units of carbohydrates, the most abundant organic molecules found in nature. Carbohydrates range from the simple sugars, or **monosaccharides**, such as glucose and fructose, to the **polysaccharides**, polymers that contain thousands of sugar units. Examples of the latter include starch and cellulose in plants and glycogen in animals. Carbohydrates serve a variety of functions in living organisms. Certain sugars are important energy sources. Glucose is the principal carbohydrate energy source in animals and plants. Sucrose is used by many plants as an efficient means of transporting energy throughout their tissues. Some carbohydrates serve as structural materials. Cellulose is the major structural component of wood and certain plant fibers. Chitin, another type

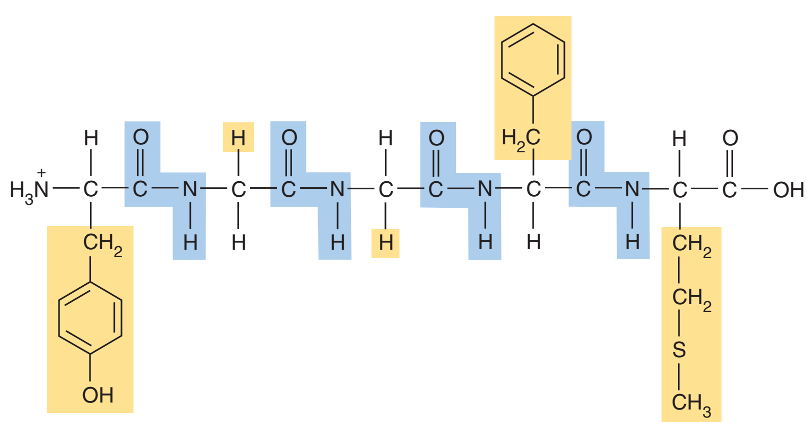


FIGURE 1.6

Structure of Met-Enkephalin, a Pentapeptide

Met-enkephalin is one of a class of molecules that have opiate-like activity. Found in the brain, metenkephalin inhibits pain perception. (The peptide bonds are colored blue. The R groups are highlighted.)

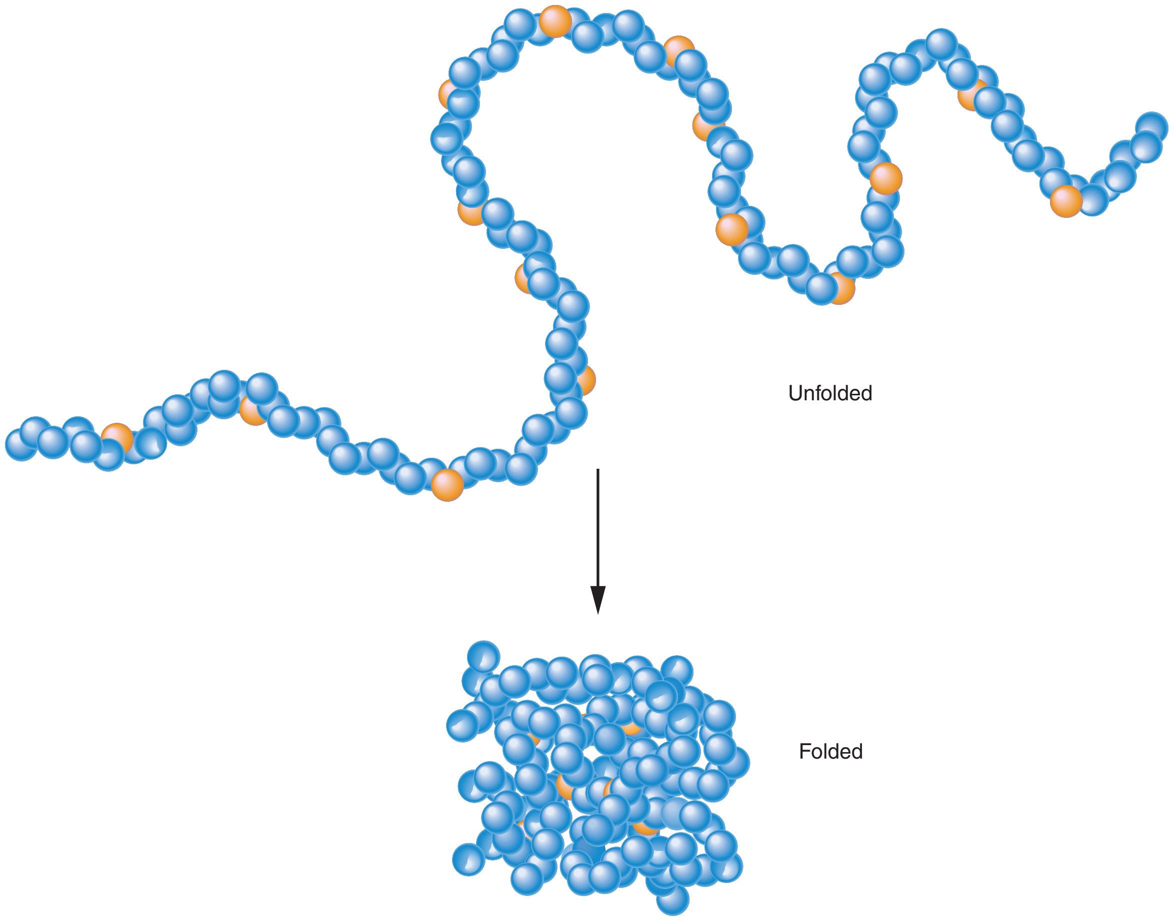
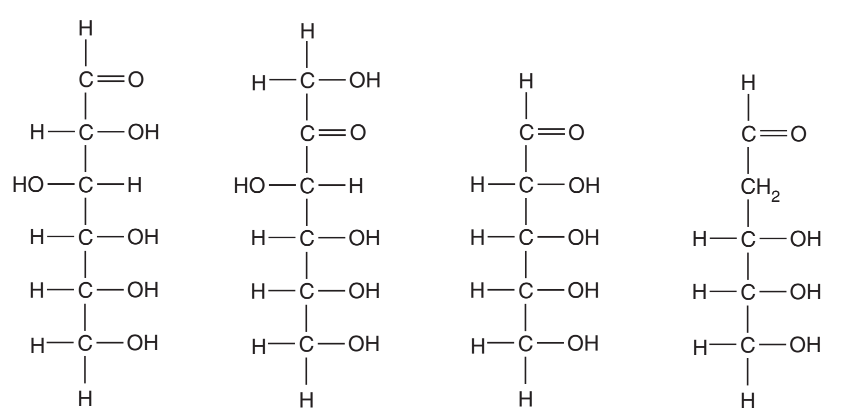


FIGURE 1.7
Polypeptide Structure
As a polypeptide folds into its unique three-dimensional form, at least 50% of the hydrophobic R groups (yellow spheres) become buried in the interior away from water. Hydrophilic groups usually occur on the surface.



Glucose (an aldohexose) | Fructose (a ketohexose) | Ribose (an aldopentose) | 2-Deoxyribose (an aldopentose)

FIGURE 1.8
Some Biologically Important Monosaccharides
Glucose and fructose are important sources of energy in plants and animals. Ribose and deoxyribose are components of nucleic acids. These monosaccharides occur as ring structures in nature.