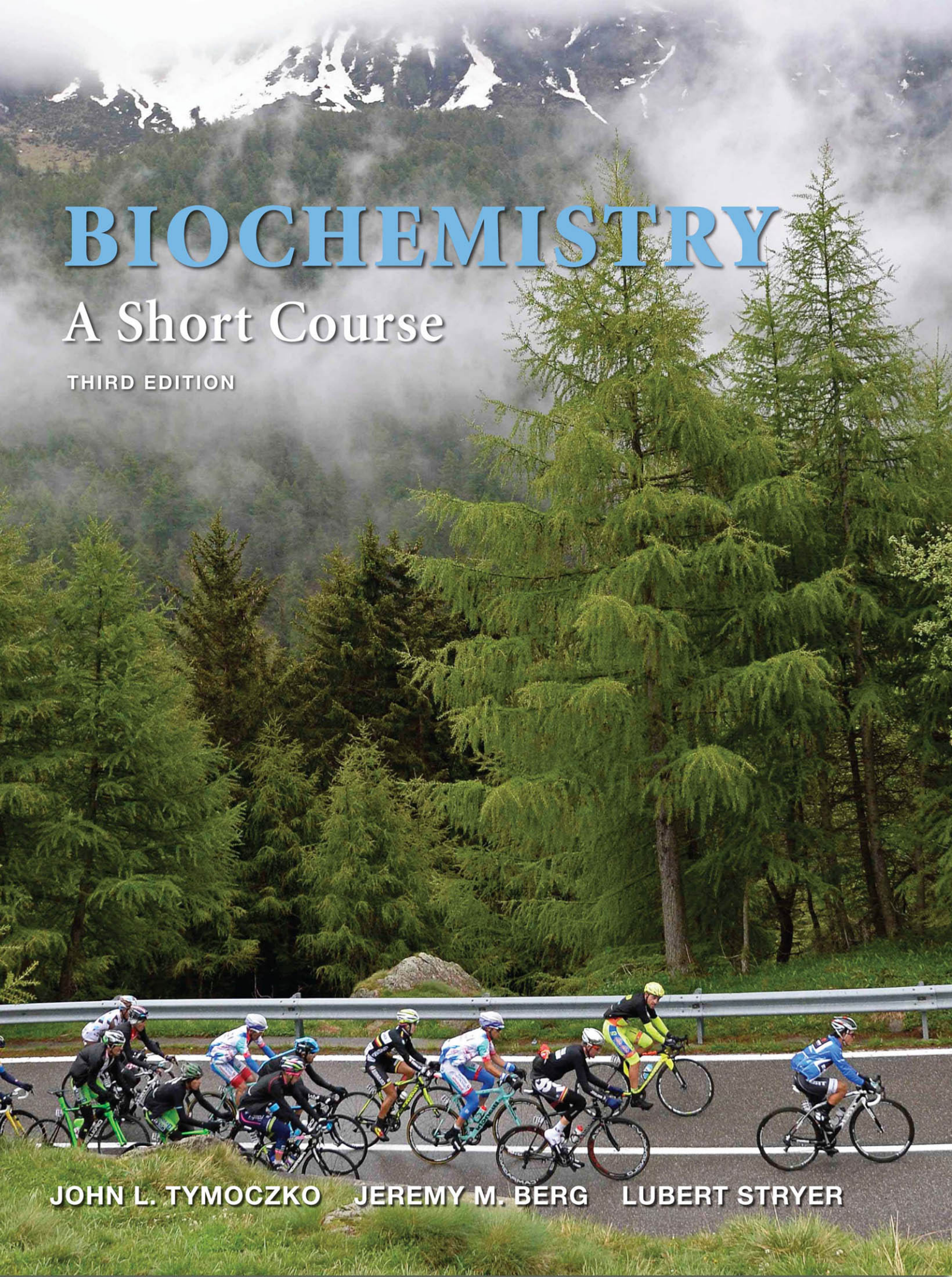
BIOCHEMISTRY
A Short Course
THIRD EDITION
JOHN L. TYMOCZKO JEREMY M. BERG LUBERT STRYER

# Biochemistry

## A Short Course

Third Edition

John L. Tymoczko
Jeremy M. Berg
Lubert Stryer

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To our teachers
and students

# About the Authors

**John L. Tymoczko** is Towsley Professor of Biology at Carleton College, where he has taught since 1976. He currently teaches Biochemistry, Biochemistry Laboratory, Oncogenes and the Molecular Biology of Cancer, and Exercise Biochemistry and co-teaches an introductory course, Energy Flow in Biological Systems. Professor Tymoczko received his B.A. from the University of Chicago in 1970 and his Ph.D. in Biochemistry from the University of Chicago with Shutsung Liao at the Ben May Institute for Cancer Research. He then had a postdoctoral position with Hewson Swift of the Department of Biology at the University of Chicago. The focus of his research has been on steroid receptors, ribonucleoprotein particles, and proteolytic processing enzymes.

**Jeremy M. Berg** received his B.S. and M.S degrees in Chemistry from Stanford (where he did research with Keith Hodgson and Lubert Stryer) and his Ph.D. in Chemistry from Harvard with Richard Holm. He then completed a postdoctoral fellowship with Carl Pabo in Biophysics at Johns Hopkins University School of Medicine. He was an Assistant Professor in the Department of Chemistry at Johns Hopkins from 1986 to 1990. He then moved to Johns Hopkins University School of Medicine as Professor and Director of the Department of Biophysics and Biophysical Chemistry, where he remained until 2003. From 2003 to 2011, he served as Director of the National Institute of General Medical Sciences at the National Institutes of Health. In 2011, he moved to the University of Pittsburgh, where he is now Professor of Computational and Systems Biology and Pittsburgh Foundation Professor and Director of the Institute for Personalized Medicine. He served as President of the American Society for Biochemistry and Molecular Biology from 2011 to 2013. He is a Fellow of the American Association for the Advancement of Science and a member of the Institute of Medicine of the National Academy of Sciences. He is a recipient of the American Chemical Society Award in Pure Chemistry (1994), the Eli Lilly Award for Fundamental Research in Biological Chemistry (1995), the Harrison Howe Award (1997), and the Howard Schachman Public Service Award (2011), was named Maryland Outstanding Young Scientist of the Year (1995), and received public service awards from the Biophysical Society, the American Society for Biochemistry and Molecular Biology, the American Chemical Society, and the American Society for Cell Biology. He also received numerous teaching awards, including the W. Barry Wood Teaching Award (selected by medical students), the Graduate Student Teaching Award, and the Professor's Teaching Award for the Preclinical Sciences. He is coauthor, with Stephen J. Lippard, of the textbook *Principles of Bioinorganic Chemistry*.

**Lubert Stryer** is Winzer Professor of Cell Biology, Emeritus, in the School of Medicine and Professor of Neurobiology, Emeritus, at Stanford University, where he has been on the faculty since 1976. He received his M.D. from Harvard Medical School. Professor Stryer has received many awards for his research on the interplay of light and life, including the Eli Lilly Award for Fundamental Research in Biological Chemistry, the Distinguished Inventors Award of the Intellectual Property Owners' Association, and election to the National Academy of Sciences and the American Philosophical Society. He was awarded the National Medal of Science in 2006. The publication of his first edition of *Biochemistry* in 1975 transformed the teaching of biochemistry.

# Preface

As humans, we are adept learning machines. Long before a baby learns that she can change a sheet of paper by crumpling it, she is absorbing vast amounts of information. This learning continues throughout life in myriad ways: learning to ride a bike and to take social cues from friends; learning to drive a car and balance a checkbook; learning to solve a quadratic equation and to interpret a work of art.

Of course, much of learning is necessary for survival, and even the simplest organisms learn to avoid danger and recognize food. However, humans are especially gifted in that we also acquire skills and knowledge to make our lives richer and more meaningful. Many students would agree that reading novels and watching movies enhance the quality of our lives because we can expand our horizons by vicariously being in situations we would never experience, reacting sympathetically or unsympathetically to characters who remind us of ourselves or are very different from anyone we have ever known. Strangely, at least to us as science professors, science courses are rarely thought of as being enriching or insightful into the human condition. Larry Gould, a former president of Carleton College, was also a geologist and an Arctic explorer. As a scientist, teacher, and administrator, he was very interested in science education especially as it related to other disciplines. In his inaugural address when he became president he said, "Science is a part of the same whole as philosophy and the other fields of learning. They are not mutually exclusive disciplines but they are independent and overlapping." Our goal was to write a book that encourages students to appreciate biochemistry in this broader sense, as a way to enrich their understanding of the world.

## New to this Edition

This third edition takes into account recent discoveries and advances that have changed how we think about the fundamental concepts in biochemistry and human health. To meet the needs of instructors and students alike, particular attention has been paid to the topics outlined below.

### Expanded Physiological Focus

A hallmark feature of *Biochemistry: A Short Course* is its physiological perspective on biochemical processes and its integration of clinical examples to apply and reinforce concepts. In the third edition, we build on this aspect of the book with:

- A **NEW** section: "Mutations in Genes Encoding Hemoglobin Subunits Can Result in Disease" (Chapter 9)
- 17 new Clinical Insights, demonstrating the relevance of biochemistry to human health and disease.

Features highlighting the physiological aspect of biochemistry have been expanded, and include the following:

CLINICAL INSIGHT

**Premature Aging Can Result from the Improper Attachment of a Hydrophobic Group to a Protein**

Farnesyl is a hydrophobic group that is often attached to proteins, usually so that the protein is able to associate with a membrane (Figure 11.10). Inappropriate farnesylation has been shown to result in Hutchinson–Gilford progeria syndrome (HGPS), a rare disease of premature aging. Early postnatal development is normal, but the children fail to thrive, develop bone abnormalities, and have a small beaked nose, a receding jaw, and a complete loss of hair (Figure 11.11). Affected children usually die at an average age of 13 years of severe atherosclerosis, a cause of death more commonly seen in the elderly.

The cause of HGPS appears to be a mutation in the gene for the nuclear protein *lamin*, a protein that forms a scaffold for the nucleus and may take part in the regulation of gene expression. The folded polypeptide that will eventually become lamin is modified and processed many times before the mature protein is produced. One key processing event is the removal of a farnesyl group that had been added to the nascent protein earlier in processing. In HGPS patients, the farnesyl group is not removed, owing to a mutation in the lamin. The incorrectly processed lamin results in a deformed nucleus (Figure 11.11) and aberrant nuclear function that results in HGPS. Much research remains to determine precisely how the failure to remove the farnesyl group leads to such dramatic consequences.

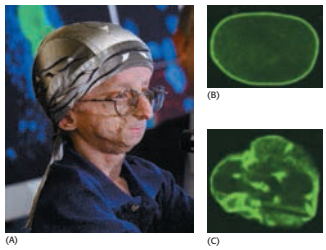



**Figure 11.11** Hutchinson–Gilford progeria syndrome (HGPS). (A) A 15-year-old boy suffering from HGPS. (B) A normal nucleus. (C) A nucleus from a HGPS patient. [(A) AP Photo/Gerald Herbert; (B and C) Scaffidi, P., Gordon, L. and Misteli, T. (2005). The call nucleus and aging: Tantalizing clues and hopeful promises. *PLoS Biol* 3 (11): e395. Courtesy of Paola Scaffidi.]

BIOLOGICAL INSIGHT

**The Dead Zone: Too Much Respiration**

Some marine organisms perform so much cellular respiration, and therefore consume so much molecular oxygen, that the oxygen concentration in the water is decreased to a level that is too low to sustain other organisms. One such hypoxic (low levels of oxygen) zone is in the northern Gulf of Mexico, off the coast of Louisiana where the Mississippi River flows into the Gulf (Figure 20.16). The Mississippi is extremely nutrient rich due to agricultural runoff; so plant microorganisms, called phytoplankton, proliferate so robustly that they exceed the amount that can be consumed by other members of the food chain. When the phytoplankton die, they sink to the bottom and are consumed by aerobic bacteria. The aerobic bacteria thrive to such a degree that other bottom-dwelling organisms, such as shrimp and crabs, cannot obtain enough $O_2$ to survive. The term "dead zone" refers to the inability of this area to support fisheries.

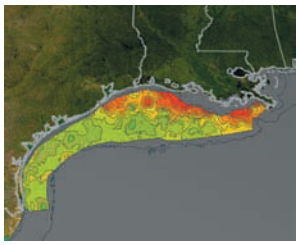


**Figure 20.16** The Gulf of Mexico dead zone. The size of the dead zone in the Gulf of Mexico off Louisiana varies annually but may extend from the Louisiana and Alabama coasts to the westernmost coast of Texas. Reds and oranges represent high concentrations of phytoplankton and river sediment. [NASA/Goddard Space Flight Center/Scientific Visualization Studio.]

### CLINICAL INSIGHTS

In the Clinical Insights, students see how the concepts most recently considered affect an aspect of a disease or its cure. By exploring biochemical concepts in the context of a disease, students learn how these concepts are relevant to human life and what happens when biochemistry goes awry.

### BIOLOGICAL INSIGHTS

Biochemistry affects every aspect of our world, sometimes in strange and amazing ways. Like Clinical Insights, Biological Insights bolster students' understanding of biochemical concepts as they learn how simple changes in biochemical processes can have dramatic effects.

For a complete list of clinical and biological insights see pages xi–xii.

### NUTRITIONAL EXAMPLES

Examples of the underlying relationship between nutrition and biochemistry abound.

### Increased Coverage of the Fundamentals

The third edition features a greater emphasis on the fundamentals of biochemistry, specifically where metabolism is concerned (Chapters 14 and 15). In an effort to explain metabolism more fully, we've expanded on the following areas within Chapters 14 and 15:

- Digestive enzymes
- Protein digestion
- Celiac disease
- Energy
- Phosphates in biochemical processes

## Teaching and Learning Tools

In addition to providing an engaging contextual framework for the biochemistry throughout the book, we have created several opportunities for students to check their understanding, reinforce connections across the book, and practice what they have learned. These opportunities present themselves both in features throughout the text and in the many resources offered in LaunchPad.

### ACTIVE LEARNING RESOURCES

In this new edition, we've responded to instructor requests to provide resources that aid in creating an active classroom environment. All of the new media resources for *Biochemistry: A Short Course* will be available in our new LaunchPad system. For more information on LaunchPad see page ix. To help students adapt to an interactive course, we've added the following resources:

NEW **Case Studies** are a series of online biochemistry case studies that are assignable and assessable. Authored by Justin Hines, Assistant Professor of Chemistry at Lafayette College, each case study gives students practice in working with data, developing critical thinking skills, connecting topics, and applying knowledge to real scenarios. We also provide instructional guidance with each case study (with suggestions on how to use the case in the classroom) and aligned assessment questions for quizzes and exams.

NEW **Clicker Questions** are aligned with key concepts and misconceptions in each chapter so instructors can assess student understanding in real time during lectures.

### END-OF-CHAPTER PROBLEMS

Each chapter includes a robust set of practice problems. We have revised and added to the total number of questions in the third edition.

- **Data Interpretation Problems** train students to analyze data and reach scientific conclusions.
- **Chapter Integration Problems** draw connections between concepts across chapters.
- **Challenge Problems** require calculations, understanding of chemical structures, and other concepts that are challenging for most students.

Brief solutions to all the end-of-chapter problems are provided in the "Answers to Problems" section in the back of the textbook. We are also pleased to offer expanded solutions in the accompanying *Student Companion*, by Frank Deis, Nancy Counts Gerber, Richard Gumport, and Roger Koeppe. (For more details on this supplement see page x.)

### MARGIN FEATURES

We use the margin features in the textbook in several ways to help engage students, emphasize the relevance of biochemistry to their lives, and make it more accessible. We have given these features a new look to make them clearer and more easily identifiable.

- **Learning Objectives** are used in many different ways in the classroom. To help reinforce key concepts while the student is reading the chapter we have indicated them with a ✓ and number and integrated them on a chapter level as well as in the section introductions. They are also tied to the end-of-chapter problems to assist students in developing problem-solving skills and instructors in assessing students' understanding of some of the key concepts in each chapter.

**6.4 Enzymes Facilitate the Formation of the Transition State**

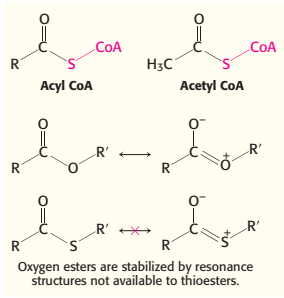
✓ 2 Explain the relation between the transition state and the active site of an enzyme, and list the characteristics of active sites.

The free-energy difference between reactants and products accounts for the equilibrium of a reaction, but enzymes accelerate how quickly this equilibrium is attained. How can we explain the rate enhancement in terms of thermodynamics? To do so, we have to consider not the end points of the reaction but the chemical pathway between the end points.

A chemical reaction of substrate S to form product P goes through a *transition state* $X^{\ddagger}$ that has a higher free energy than does either S or P. The double dagger denotes the transition state. The transition state is a fleeting molecular structure that is no longer the substrate but is not yet the product. The transition state is the least-stable and most-seldom-occurring species along the reaction pathway because it is the one with the highest free energy.

- **Quick Quizzes** emulate that moment in a lecture when a professor asks, "Do you get it?" These questions allow students to check their understanding of the material as they read it so they can immediately gauge whether they need to review a discussion or can advance to the next topic. Answers are given at the end of each chapter.

**?** **QUICK QUIZ** Explain why a person who has a trypsinogen deficiency will suffer from more digestion difficulties than will a person lacking most other zymogens.




Oxygen esters are stabilized by resonance structures not available to thioesters.

- **Margin Structures** provide a quick reminder of a molecule or group that students may have seen earlier in the book or in another course. This allows students to understand the topic at hand without needing to look up a basic structure or organic chemistry principle elsewhere.

- **Did You Know?** features are short asides to the biochemical topic being discussed. They put a personal face on science, or, in the vein of Biological Insights, provide glimpses of how we use biochemistry in everyday life.

**DID YOU KNOW?**

Interestingly, digitalis was used effectively long before the discovery of the $Na^+$–$K^+$ ATPase. In 1785, William Withering, a British physician, heard tales of an elderly woman, known as "the old woman of Shropshire," who cured people of "dropsy" (which today would be recognized as congestive heart failure) with an extract of foxglove. Withering conducted the first scientific study of the effects of foxglove on congestive heart failure and documented its effectiveness.

**NUTRITION FACTS**

**Niacin** Also called vitamin $B_3$, niacin is a component of coenzymes $NAD^+$ and $NADP^+$ (pp. 268–270), which are used in electron-transfer reactions. There are many sources of niacin, including chicken breast. Niacin deficiency results in the potentially fatal disease pellagra, a condition characterized by dermatitis, dementia, and diarrhea. [Brand X Pictures]

- **Nutrition Facts** highlight essential vitamins in the margin next to where they are discussed as part of an enzyme mechanism or metabolic pathway. In these boxes, students will discover how we obtain vitamins from our diets and what happens if we do not have enough of them. These important molecules and their structures are listed in table form in the appendix of the book as well, to help students easily find where each vitamin is discussed in the book.

## Media and Supplements

All of the new media resources for *Biochemistry: A Short Course* are available in our new LaunchPad system.

**www.macmillanhighered.com/launchpad/tymoczko3e**

**LaunchPad** is a dynamic, fully integrated learning environment that brings together all of our teaching and learning resources in one place. It includes easy-to-use, powerful assessment tracking and grading tools, a personalized calendar, an announcement center, and communication tools to help you manage your course. This learning system also contains the fully interactive **e-Book** and other newly updated resources for students and instructors, including the following:

### For Students

- **Case Studies** are a series of online biochemistry case studies that are assignable and assessable. Authored by Justin Hines, Assistant Professor of Chemistry at Lafayette College, each case study gives students practice in working with data, developing critical thinking skills, connecting topics, and applying knowledge to real scenarios.
- **e-Book** allows students to read the online version of the textbook, which combines the contents of the printed book, electronic study tools, and a full complement of student media specifically created to support the text.
- **Hundreds of Self-Graded Practice Problems** allow students to test their understanding of concepts explained in the text, with immediate feedback.
- **Metabolic Map** helps students understand the principles and applications of the core metabolic pathways. Students can work through guided tutorials with embedded assessment questions, or explore the Metabolic Map on their own using the dragging and zooming functionality of the map.
- **Problem-Solving Videos**, created by Scott Ensign of Utah State University, provide 24/7 online problem-solving help to students. Through a two-part approach, each 10-minute video covers a key textbook problem representing a topic that students traditionally struggle to master. Dr. Ensign first describes a proven problem-solving strategy and then applies the strategy to the problem at hand in clear, concise steps. Students can easily pause, rewind, and review any steps they wish until they firmly grasp not just the solution but also the reasoning behind it. Working through the problems in this way is designed to make students better and more confident at applying key strategies as they solve other textbook and exam problems.
- **Living Figures** allow students to view textbook illustrations of protein structures online in interactive 3-D using Jmol. Students can zoom and rotate 54 "live" structures to get a better understanding of their three-dimensional nature and can experiment with different display styles (space-filling, ball-and-stick, ribbon, backbone) by means of a user-friendly interface.
- **Self-Assessment Tool** allows students to test their understanding by taking an online multiple-choice quiz provided for each chapter, as well as a general chemistry review.
- **Animated Techniques** illustrate laboratory techniques described in the text.


- **Learning Curve** is a self-assessment tool that helps students evaluate their progress. Students can test their understanding by taking an online multiple-choice quiz provided for each chapter, as well as a general chemistry review.

### For Instructors

All the features listed above for students plus:

- **e-Book** Instructors teaching from the e-Book can assign either the entire textbook or a custom version that includes only the chapters that correspond to their syllabi. They can choose to add notes to any page of the e-Book and share these notes with their students. These notes may include text, animations, or photographs.
- **Clicker Questions** are aligned with key concepts and misconceptions in each chapter so instructors can assess student understanding in real time during lectures.
- **Newly Updated Lecture PowerPoint Files** have been developed to minimize preparation time for new users of the book. These files offer suggested lectures including key illustrations and summaries that instructors can adapt to their teaching styles.
- **Updated Textbook Images and Tables** are offered as high-resolution JPEG files. The JPEGs are also offered in separate PowerPoint files.
- **Test Bank**, by Harvey Nikkel of Grand Valley State University, Susan Knock of Texas A&M University at Galveston, and Joseph Provost of Minnesota State University Moorhead, offers more than 1500 questions in editable Word format.

### Student Companion

(1-319-03295-8)

For each chapter of the textbook, the *Student Companion* includes:

- Chapter Learning Objectives and Summary
- Self-Assessment Problems, including multiple-choice, short-answer, matching questions, and challenge problems, and their answers
- Expanded Solutions to the end-of-chapter problems in the textbook

## CLINICAL INSIGHTS

*This icon signals the beginning of a Clinical Insight in the text.*

## BIOLOGICAL INSIGHTS

*This icon signals the beginning of a Biological Insight in the text.*

## Acknowledgments

Our thanks go to the instructors and professors who have reviewed the chapters of this book. Their sharp eyes and keen insights strongly influenced us as we wrote and shaped the various drafts of each chapter to create this completed work.

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The German scientist, writer, and statesman Johann Wolfgang von Goethe once remarked, "Thinking is easy, acting is difficult, and to put one's thoughts into action is the most difficult thing in the world." While we may disagree with Goethe's assertion that thinking is easy, we emphatically agree with the rest of the quotation. Thinking about biochemistry and then putting those thoughts into a book that is clear, welcoming, stimulating, and challenging is, if not the most difficult thing in the world, still very demanding. This task would be utterly impossible without our wonderful colleagues at W. H. Freeman. They are intelligent, dedicated, caring people who have taught us much about how to present science to students and, in the process, brought out the best in us. Although we have had the pleasure of working with our collaborators at W. H. Freeman on a number of projects, our appreciation of and gratefulness for their efforts and guidance are as sincere now as they were when we were inexperienced authors. Our experiences with this edition have been as delightful and rewarding as our past projects. We have many people to thank for this experience, some of whom we have worked with previously and some new to the effort. First, we would like to acknowledge the encouragement, patience, excellent advice, and good humor of our Publisher, Kate Ahr Parker. Kate can suggest difficult challenges with such grace and equanimity that we readily accept the challenge. New to our book team is our Senior Acquisitions Editor, Lauren Schultz. Her unfailing enthusiasm was a source of support and energy for the author team. New to our book team for this edition is Heidi Bamatter, our Developmental Editor. Heidi is another in a line of outstanding development editors that we have had the pleasure to work with at Freeman. Her insight, patience, and guidance made this effort successful and enjoyable. Elizabeth Geller, Senior Project Editor, managed the flow of the project with admirable efficiency. Teresa Wilson, our Manuscript Editor, enhanced the literary consistency and clarity of the text. Vicki Tomaselli, Design Manager, produced a design and layout that made the book welcoming and accessible. Christine Buese and Jacquelyn Wong, Photo Editor and Photo Researcher, respectively, found the photographs that helped to achieve one of our main goals—linking biochemistry to the everyday world of the student while making the text a visual treat. Janice Donnola, Illustration Coordinator, deftly directed the rendering of new illustrations. Paul Rohloff, Production Manager, made sure the difficulties of scheduling, composition, and manufacturing were readily overcome. We are more appreciative of the sales staff at W. H. Freeman for their enthusiastic support than we can put into words. Without the efforts of the sales force to persuade professors to examine our book, all of our own excitement and enthusiasm for this text would be meaningless. We also thank Susan Winslow. Her vision for science textbooks and her skill at gathering exceptional personnel make working with W. H. Freeman a true pleasure.

Thanks also to our many colleagues at our own institutions as well as throughout the country who patiently answered our questions and encouraged us on our quest. Finally, we owe a debt of gratitude to our families. Without their support, comfort, and understanding, this project could never have been undertaken, let alone successfully completed.

# Brief Contents

# Contents

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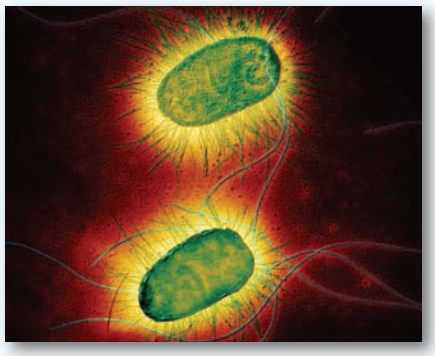






# Biochemistry Helps Us to Understand Our World

The ultimate goal of all scientific endeavors is to develop a deeper, richer understanding of ourselves and the world in which we live. Biochemistry has had and will continue to have an extensive role in helping us to develop this understanding. *Biochemistry*, the study of living organisms at the molecular level, has shown us many of the details of the most fundamental processes of life. For instance, biochemistry has shown us how information flows from genes to molecules that have functional capabilities. In recent years, biochemistry has also unraveled some of the mysteries of the molecular generators that provide the energy that powers living organisms. The realization that we can understand such essential life processes has significant philosophical implications. What does it mean, biochemically, to be human? What are the biochemical differences between a human being, a chimpanzee, a mouse, and a fruit fly? Are we more similar than we are different?

The understanding achieved through biochemistry is greatly influencing medicine and other fields. Although we may not be accustomed to thinking of illness in relation to molecules, illness is ultimately some sort of malfunction at the molecular level. The molecular lesions causing sickle-cell anemia, cystic fibrosis, hemophilia, and many other genetic diseases have been elucidated at the biochemical level. Biochemistry is also contributing richly to clinical diagnostics. For example, elevated levels of heart enzymes in the blood reveal whether a patient has recently had a myocardial infarction (heart attack). Agriculture, too, is employing biochemistry to develop more effective, environmentally safer herbicides and pesticides and to create genetically engineered plants that are, for example, more resistant to insects.

In this section, we will learn some of the key concepts that structure the study of biochemistry. We begin with an introduction to the molecules of biochemistry, followed by an overview of the fundamental unit of biochemistry and life itself—the cell. Finally, we examine the weak reversible bonds that enable the formation of biological structures and permit the interplay between molecules that makes life possible.

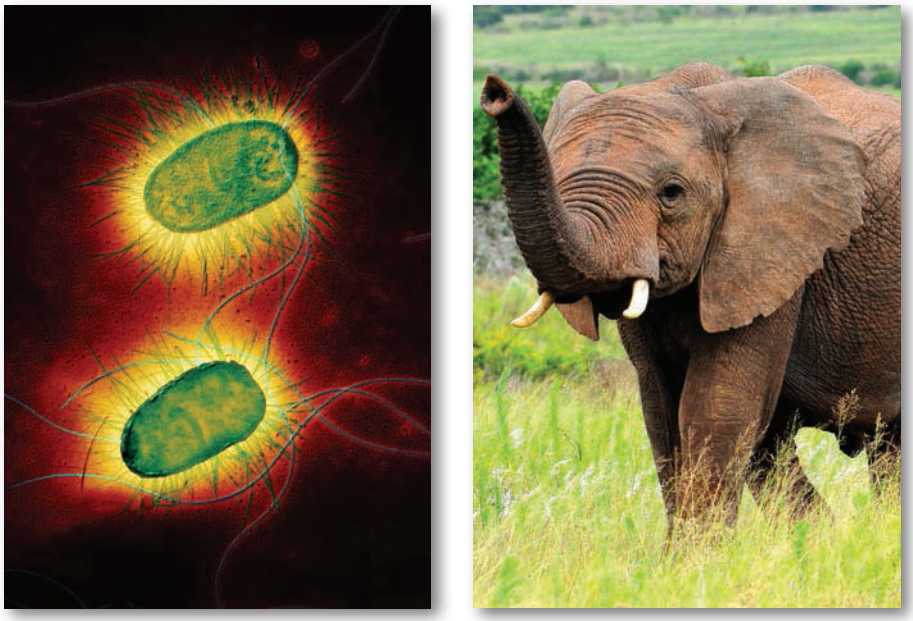
## ✓ By the end of this section, you should be able to:

- ✓ 1 **Describe the key classes of biomolecules and differentiate between them.**
- ✓ 2 **List the steps of the central dogma.**
- ✓ 3 **Identify the key features that differentiate eukaryotic cells from prokaryotic cells.**
- ✓ 4 **Describe the chemical properties of water and explain how water affects biochemical interactions.**
- ✓ 5 **Describe the types of noncovalent, reversible interactions and explain why reversible interactions are important in biochemistry.**
- ✓ 6 **Define pH and explain why changes in pH may affect biochemical systems.**

CHAPTER 1

# Biochemistry and the Unity of Life





Despite their vast differences in mass—the African elephant has a mass $3 \times 10^{18}$ times as great as that of the bacterium *E. coli*—and complexity, the biochemical workings of these two organisms are remarkably similar. [*E. coli*: Eye of Science/Science Source. Elephant: John Michael Evan Potter/Shutterstock.]

A key goal of biochemistry, one that has been met with striking success, is to understand what it means to be alive at the molecular level. Another goal is to extend this understanding to the organismic level—that is, to understand the effects of molecular manipulations on the life that an organism leads. For instance, understanding how the hormone insulin works at the molecular level illuminates how the organism controls the levels of common fuels—glucose and fats—in its blood. Often, such understanding facilitates an understanding of disease states, such as diabetes, which results when insulin signaling goes awry. In turn, this knowledge can be a source of insight into how the disease can be treated.

Biochemistry has been an active area of research for more than a century. Much knowledge has been gained about how a variety of organisms manipulate energy and information. However, one of the most exciting outcomes of biochemical research has been the realization that all organisms have much in common biochemically. *Organisms are remarkably uniform at the molecular level.* This observation is frequently referred to as the *unity of biochemistry,* but, in reality, it illustrates the unity of life. French biochemist Jacques Monod encapsulated this idea in 1954 with the phrase "Anything found to be true of [the bacterium] *E. coli* must also be true of elephants." This uniformity reveals that all organisms on Earth have arisen from a common ancestor. A core of essential biochemical processes, common to all organisms, appeared early in the evolution of life. The

diversity of life in the modern world has been generated by evolutionary processes acting on these core processes through millions or even billions of years.

We begin our study of biochemistry by looking at commonalities. We will examine the molecules and molecular constituents that are used by all life forms and will then consider the rules that govern how biochemical information is accessed and how it is passed from one generation to the next. Finally, we will take an overview of the fundamental unit of life—the cell. This is just the beginning. All of the molecules and structures that we see in this chapter we will meet again and again as we explore the chemical basis of life.

## 1.1 Living Systems Require a Limited Variety of Atoms and Molecules

Ninety naturally occurring elements have been identified, yet only three—oxygen, hydrogen, and carbon—make up 98% of the atoms in an organism. Moreover, the abundance of these three elements in life is vastly different from their abundance in Earth's crust (**Table 1.1**). What can account for the disparity between what is available and what organisms are made of?

One reason that oxygen and hydrogen are so common is the ubiquity of water, or "the matrix of life," as biochemist Albert Szent-Györgi called it. This tiny molecule—consisting of only three atoms—makes life on Earth possible. Indeed, current belief is that all life requires water, which is why so much effort has been made in recent decades to determine whether Mars had water in the past and whether it still does. The importance of water for life is so crucial that its presence is tantamount to saying that life could be present. We will consider the properties of water and how these properties facilitate biochemistry in Chapter 2.

After oxygen and hydrogen, the next most-common element in living organisms is carbon. Most large molecules in living systems are made up predominantly of carbon. Fuel molecules are made entirely of carbon, hydrogen,

**Table 1.1** Chemical compositions as percentage of total number of atoms

| Element | Composition in | | |
|---|---|---|---|
| | Human beings (%) | Seawater (%) | Earth's crust (%) |
| Hydrogen | 63 | 66 | 0.22 |
| Oxygen | 25.5 | 33 | 47 |
| Carbon | 9.5 | 0.0014 | 0.19 |
| Nitrogen | 1.4 | <0.1 | <0.1 |
| Calcium | 0.31 | 0.006 | 3.5 |
| Phosphorus | 0.22 | <0.1 | <0.1 |
| Chloride | 0.03 | 0.33 | <0.1 |
| Potassium | 0.06 | 0.006 | 2.5 |
| Sulfur | 0.05 | 0.017 | <0.1 |
| Sodium | 0.03 | 0.28 | 2.5 |
| Magnesium | 0.01 | 0.003 | 2.2 |
| Silicon | <0.1 | <0.1 | 28 |
| Aluminum | <0.1 | <0.1 | 7.9 |
| Iron | <0.1 | <0.1 | 4.5 |
| Titanium | <0.1 | <0.1 | 0.46 |
| All others | <0.1 | <0.1 | <0.1 |

Note: Because of rounding, total percentages do not equal 100%.
Source: Data from E. Frieden, The chemical elements of life, *Sci. Am.* 227(1), 1972, p. 54.

and oxygen. Biological fuels, like the fuels that power machinery, react with oxygen to produce carbon dioxide and water. In regard to biological fuels, this reaction, called combustion, provides the energy to power the cell. As a means of seeing why carbon is uniquely suited for life, let us compare it with silicon, its nearest elemental relative. Silicon is much more plentiful than carbon in Earth's crust (Table 1.1), and, like carbon, can form four covalent bonds—a property crucial to the construction of large molecules. However, carbon-to-carbon bonds are stronger than silicon-to-silicon bonds. This difference in bond strength has two important consequences. First, large molecules can be built with the use of carbon–carbon bonds as the backbone because of the stability of these bonds. Second, more energy is released when carbon–carbon bonds undergo combustion than when silicon reacts with oxygen. Thus, carbon-based molecules are stronger construction materials and are better fuels than silicon-based molecules. Carbon even has an advantage over silicon after it has undergone combustion. Carbon dioxide is readily soluble in water and can exist as a gas; thus, it remains in biochemical circulation, given off by one tissue or organism to be used by another tissue or organism. In contrast, silicon is essentially insoluble after reaction with oxygen. After it has combined with oxygen, it is permanently out of circulation. Quartz is a common form of silicon dioxide.

Other elements have essential roles in living systems—notably, nitrogen, phosphorus, and sulfur. Moreover, some of the trace elements, although present in tiny amounts compared with oxygen, hydrogen, and carbon, are absolutely vital to a number of life processes. We will see specific uses of these elements as we proceed with our study of biochemistry.

## 1.2 There Are Four Major Classes of Biomolecules

✓ 1 Describe the key classes of biomolecules and differentiate between them.

Living systems contain a dizzying array of biomolecules. However, these biomolecules can be divided into just four classes: proteins, nucleic acids, lipids, and carbohydrates.

### Proteins Are Highly Versatile Biomolecules

Much of our study of biochemistry will revolve around proteins. *Proteins* are constructed from 20 building blocks, called amino acids, linked by peptide bonds to form long unbranched polymers (**Figure 1.1**). These polymers fold into precise three-dimensional structures that facilitate a vast array of biochemical functions. Proteins serve as signal molecules (e.g., the hormone insulin signals that fuel is in the blood) and as receptors for signal molecules. Receptors convey to the cell that a signal has been received and initiates the cellular response. Thus, for example, insulin binds to its particular receptor, called the insulin receptor, and initiates the biological response to the presence of fuel in the blood. Proteins also play structural roles, allow mobility, and provide defenses against environmental

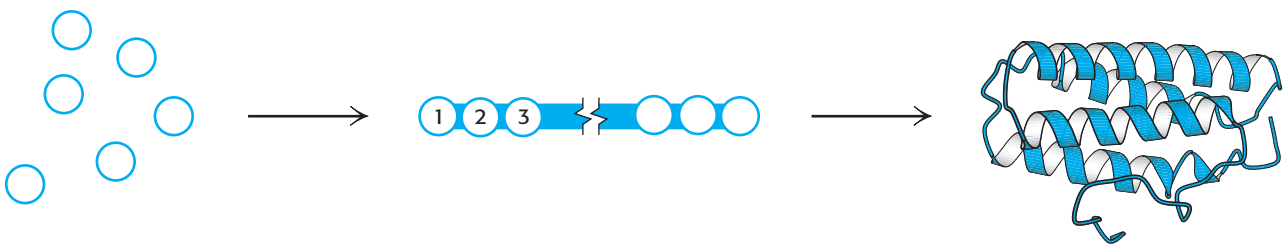
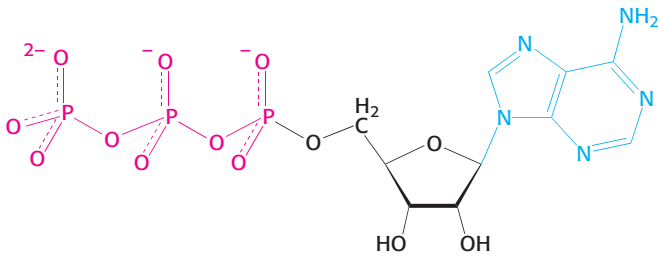



**Figure 1.1 Protein folding.** The three-dimensional structure of a protein is dictated by the sequence of amino acids that constitute the protein.




**Adenosine triphosphate (ATP)**

**Figure 1.2 The structure of a nucleotide.** A nucleotide (in this case, adenosine triphosphate) consists of a base (shown in blue), a five-carbon sugar (black), and at least one phosphoryl group (red).

dangers. Perhaps the most prominent role of proteins is that of *catalysts*—agents that enhance the rate of a chemical reaction without being permanently affected themselves. Protein catalysts are called *enzymes*. Every process that takes place in living systems depends on enzymes.

### Nucleic Acids Are the Information Molecules of the Cell

As information keepers of the cell, the primary function of *nucleic acids* is to store and transfer information. They contain the instructions for all cellular functions and interactions. Like proteins, nucleic acids are linear molecules. However, nucleic acids are constructed from only four building blocks called *nucleotides*. A nucleotide is made up of a five-carbon sugar, either a deoxyribose or a ribose, attached to a heterocyclic ring structure called a base and at least one phosphoryl group (**Figure 1.2**).

There are two types of nucleic acid: *deoxyribonucleic acid* (DNA) and *ribonucleic acid* (RNA). Genetic information is stored in DNA—the "parts list" that determines the nature of an organism. DNA is constructed from four deoxyribonucleotides, differing from one another only in the ring structure of the bases—adenine (A), cytosine (C), guanine (G), and thymine (T). The information content of DNA is the sequence of nucleotides linked together by phosphodiester linkages. DNA in all higher organisms exists as a double-stranded helix (**Figure 1.3**). In the double helix, the bases interact with one another—A with T and C with G.

**Figure 1.3 The double helix.** Two individual chains of DNA interact to form a double helix. The sugar–phosphate backbone of one of the two chains is shown in red; the other is shown in blue. The bases are shown in green, purple, orange, and yellow.

RNA is a single-stranded form of nucleic acid. Some regions of DNA are copied as a special class of RNA molecules called messenger RNA (mRNA). mRNA is a template for the synthesis of proteins. Unlike DNA, mRNA is frequently broken down after use. RNA is similar to DNA in composition with two exceptions: the base thymine (T) is replaced by the base uracil (U), and the sugar component of the ribonucleotides contains an additional hydroxyl (—OH) group.

### Lipids Are a Storage Form of Fuel and Serve as a Barrier

Among the key biomolecules, *lipids* are much smaller than proteins or nucleic acids. Whereas proteins and nucleic acids can have molecular weights of thousands to millions, a typical lipid has a molecular weight of 1300 g $mol^{-1}$. Moreover, lipids are not polymers made of repeating units, as are proteins and nucleic acids. A key characteristic of many biochemically important lipids is their dual chemical nature: part of the molecule is *hydrophilic,* meaning that it can dissolve in water, whereas the other part, made up of one or more hydrocarbon chains, is *hydrophobic* and cannot dissolve in water (**Figure 1.4**). This dual nature allows lipids to form barriers that delineate the cell from its environment and to establish intracellular compartments. In other words, lipids allow the development of "inside" and "outside" at a biochemical level. The hydrocarbon chains cannot interact with water and, instead, interact with those of other lipids to form a barrier, or membrane, whereas the water-soluble components interact with the aqueous environment on either side of the membrane. Lipids are also an important storage form of energy. As we will see, the hydrophobic component of lipids can undergo combustion to provide large amounts of cellular energy. Lipids are crucial signal molecules as well.

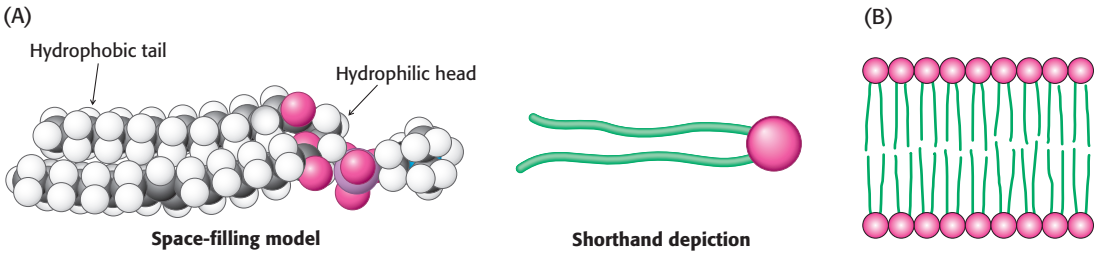
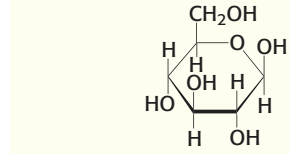



**Figure 1.4 The dual properties of lipids.** (A) One part of a lipid molecule is hydrophilic; the other part is hydrophobic. (B) In water, lipids can form a bilayer, constituting a barrier that separates two aqueous compartments.

### Carbohydrates Are Fuels and Informational Molecules

Most of us already know that *carbohydrates* are an important fuel source for most living creatures. The most-common carbohydrate fuel is the simple sugar glucose. Glucose is stored in animals as *glycogen*, which consists of many glucose molecules linked end-to-end and has occasional branches (**Figure 1.5**). In plants, the storage form of glucose is starch, which is similar to glycogen in molecular composition.

There are thousands of different carbohydrates. They can be linked together in chains, and these chains can be highly branched, much more so than in glycogen or starch. Such chains of carbohydrates play important roles in helping cells to recognize one another. Many of the components of the cell exterior are decorated with various carbohydrates that can be identified by other cells and serve as sites of cell-to-cell interactions.




**?** **QUICK QUIZ 1** Name the four classes of biomolecules, and state an important function of each class.

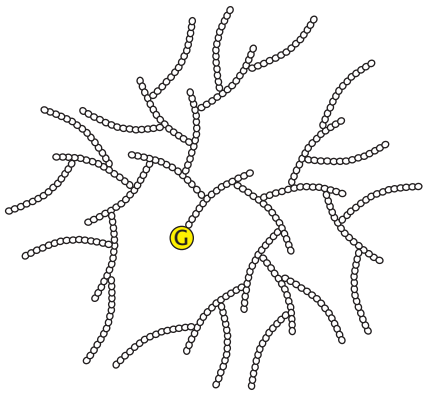
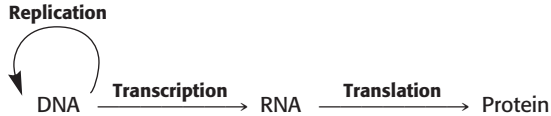



**Figure 1.5 The structure of glycogen.** Glycogen is a branched polymer composed of glucose molecules. The protein identified by the letter G at the center of the glycogen molecule is required for glycogen synthesis (Chapter 25).

## 1.3 The Central Dogma Describes the Basic Principles of Biological Information Transfer

✓ 2 List the steps of the central dogma.

Information processing in all cells is quite complex. It increases in complexity as cells become parts of tissues and as tissues become components of organisms. The scheme that underlies information processing at the level of gene expression was first proposed by Francis Crick in 1958.




Crick called this scheme the *central dogma:* information flows from DNA to RNA and then to protein. Moreover, DNA can be replicated. The basic tenets of this dogma are true, but, as we will see later, this scheme is not as simple as depicted.

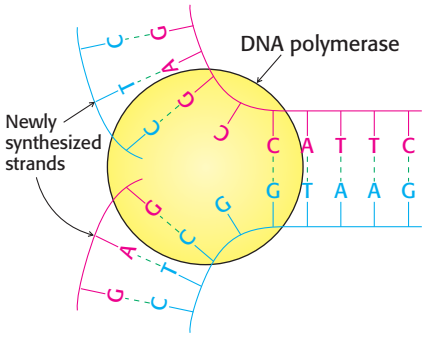



**Figure 1.6 DNA replication.** When the two strands of a DNA molecule are separated, each strand can serve as a template for the synthesis of a new partner strand. DNA polymerase catalyzes replication.

**DID YOU KNOW?**

As defined in the Oxford English Dictionary, to transcribe means to make a copy of (something) in writing; to copy out from an original; to write (a copy).

DNA constitutes the heritable information—the *genome*. This information is packaged into discrete units called *genes*. It is this collection of genes that determines the physical nature of the organism. When a cell duplicates, DNA is copied and identical genomes are then present in the newly formed daughter cells. The process of copying the genome is called *replication*. A group of enzymes, collectively called *DNA polymerase*, catalyze the replication process (**Figure 1.6**).

Genes are useless in and of themselves. The information must be rendered accessible. This accessibility is achieved in the process of *transcription* through which one form of nucleic acid, DNA, is transcribed into another form, RNA. The enzyme *RNA polymerase* catalyzes this process (**Figure 1.7**). Which genes are transcribed, as well as when and where they are transcribed, is crucial to the fate of the cell. For instance, although each cell in a human body has the DNA information that encodes the instructions to make all tissues, this information is parceled out. The genes expressed in the liver are different from those expressed in the muscles and brain. *Indeed, it is this selective expression that defines the function of a cell or tissue.*

A key aspect of the selective expression of genetic information is the transcription of genes into mRNA. The information encoded in mRNA is realized in the process of *translation* because information is literally translated from one chemical form (nucleic acid) into another (protein). Proteins have been described as the workhorses of the cell, and *translation renders the genetic information into a functional form*. Translation takes place on large macromolecular complexes called *ribosomes*, consisting of RNA and protein (**Figure 1.8**).

Now that you have been introduced to the key biomolecules and have briefly examined the central dogma of information transfer, let us look at the platform—the cell—that contains and coordinates the biochemistry required for life.

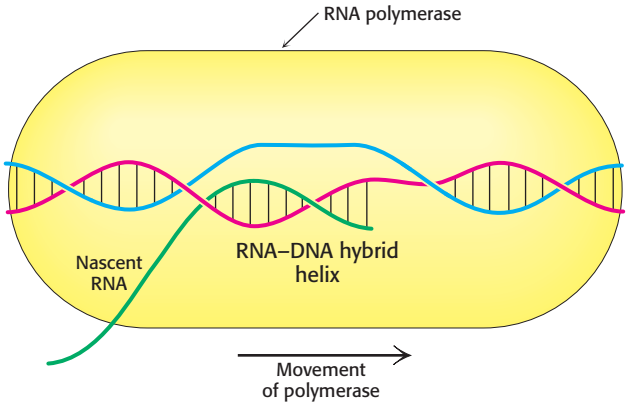



**Figure 1.7 The transcription of RNA.** Transcription, catalyzed by RNA polymerase, makes an RNA copy of one of the strands of DNA.

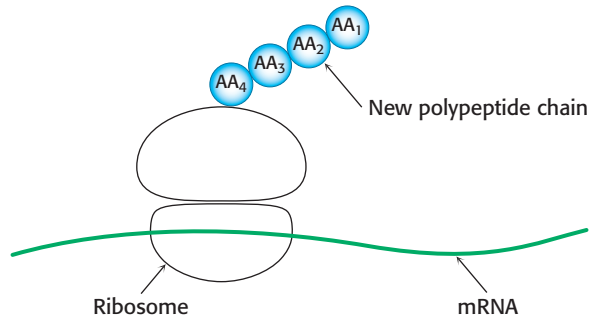



**Figure 1.8 Translation takes place on ribosomes.** A ribosome decodes the information in mRNA and translates it into the amino acid sequence of a protein.

✓ 3 Identify the key features that differentiate eukaryotic cells from prokaryotic cells.

## 1.4 Membranes Define the Cell and Carry Out Cellular Functions

The cell is the basic unit of life. Cells grow, replicate, and interact with their environment. Living organisms can be as simple as a single cell or as complex as a human body, which is composed of approximately 100 trillion cells. Every cell is delineated by a membrane that separates the inside of the cell from its environment. A *membrane* is a *lipid bilayer:* two layers of lipids organized with their hydrophobic chains interacting with one another and the hydrophilic head groups

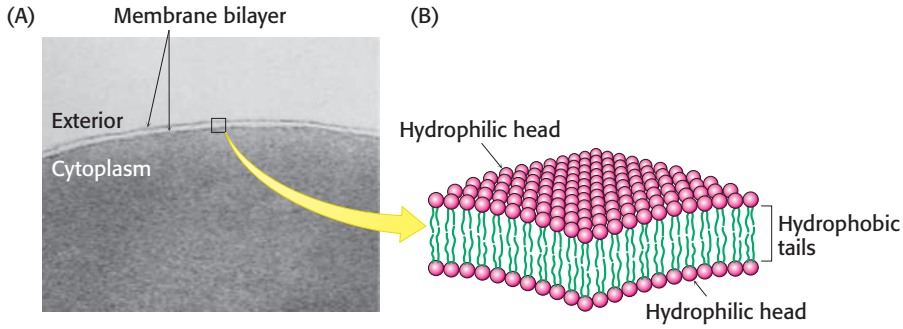



**Figure 1.9 The bilayer structure of a membrane.** (A) Membranes are composed of two layers or sheets. (B) The hydrophobic parts of the layers interact with each other, and the hydrophilic parts interact with the environment. [J. D. Robertson. "Discovery in Cell Biology: Membrane Structure." *Journal of Cell Biology* 91(1981): 189s–204s. Courtesy of J.D. Robertson.]

interacting with the environment (**Figure 1.9**).

There are two basic types of cells: eukaryotic cells and prokaryotic cells (**Figure 1.10**). The main difference between the two is the existence of membrane-enclosed compartments in *eukaryotes* and the absence of such compartments in *prokaryotes*. Prokaryotic cells, exemplified by the human gut

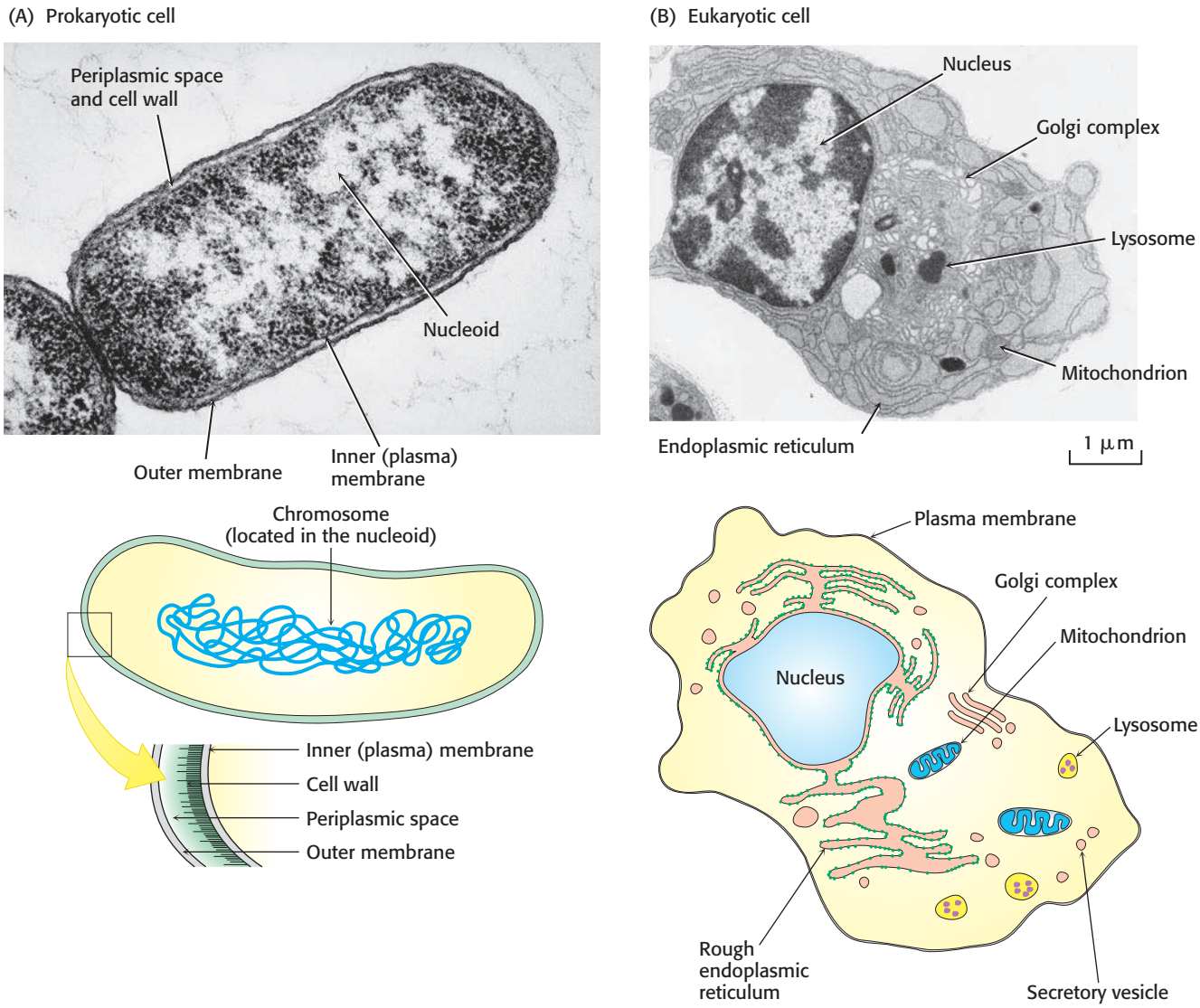



**Figure 1.10 Prokaryotic and eukaryotic cells.** Eukaryotic cells display more internal structure than do prokaryotic cells. Components within the interior of a eukaryotic cell, most notably the nucleus, are defined by membranes. [Micrographs: (A) ©Biology Pics/Science Source; (B) from P. C. Cross and K. L. Mercer, *Cell Tissue Ultrastructure: A Functional Perspective* (W. H. Freeman and Company, 1993), p. 199. Diagrams: (A and B) Information from H. Lodish et al., *Molecular Cell Biology*, 6th ed. (W. H. Freeman and Company, 2008), p. 3.]