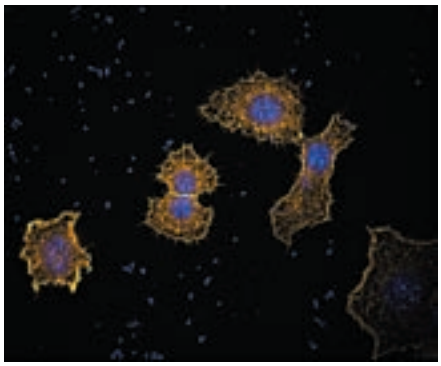
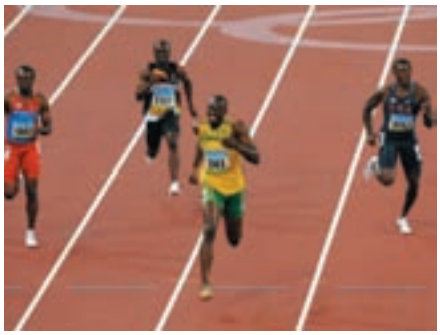
BIOCHEMISTRY A Short Course

SECOND EDITION

JOHN L. TYMOCZKO JEREMY M. BERG LUBERT STRYER





Biochemistry

A SHORT COURSE

Second 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, the Metabolic Basis of Human Disease, 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 in 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 in 1973. He then held 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 University (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 Associate Senior Vice Chancellor for Science Strategy and Planning and a faculty member in the Department of Computational and Systems Biology. 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 Maryland Outstanding Young Scientist of the Year (1995), the Harrison Howe Award from the Rochester Section of the American Chemical Society (1997), the Howard Schachman Public Service Award from the American Society for Biochemistry and Molecular Biology (2011), and the Public Service Award from the American Chemical Society (2011). He is a member of the Institute of Medicine of the National Academy of Sciences and a Fellow of the American Association for the Advancement of Science. While at Johns Hopkins, he received 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.

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 human beings, 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.

Much of learning is necessary for survival, and even the simplest organisms learn to avoid danger and recognize food. However, human beings 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 enhances the quality of our lives because we can expand our horizons by vicariously being in situations that 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 consider biochemistry in this broader sense, as a way to enrich their understanding of the world.

Biochemistry in Context

All of biochemistry, esoteric as it may seem in isolation, can be understood in a context that is relevant to the student. We emphasize these connections throughout the book.

New to this Edition

This second edition takes into account recent discoveries and advances that have changed how we think about the fundamental concepts in biochemistry and human health. Particular attention has been paid to the following topics:

- The **metabolic basis of cancer** and the role of glycolysis in cancer (Chapters 16 and 18)
- The **biochemical roles of glycoproteins** (Chapter 10)
- **Recombination in DNA repair** (Chapter 35)
- **Quantitative PCR** (Chapter 41)

New sections are identified by **NEW** in the detailed table of contents, starting on page xvii.

Experimental Techniques

In this new edition, our coverage of experimental techniques has been updated, expanded, and included in the printed textbook. Chapter 5, Techniques in Protein Biochemistry, and Chapter 41, Immunological and Recombinant DNA Techniques, explore important techniques used by biochemists in the past as well as new technologies with which biochemists make discoveries in present-day laboratories.

Metabolism in Context: Diet and Obesity

New information about the role of leptin in hunger and satiety has greatly influenced how we think about obesity and the growing epidemic of diabetes. In Metabolism in Context sections in this edition, we cover the integration of metabolism in regard to diet and obesity. By showing how the products of one pathway affect or are affected by others, we take students back to the big picture of biochemistry. Students see that the pathways that they are studying at the moment do not exist in isolation; rather, they work in concert with all of the other pathways that they have already studied. With examples of the relation between metabolic control and obesity, cancer, and exercise, the connection between life and biochemistry is made even more readily apparent. Metabolism of all biomolecules is tied together in:

- Insulin Signaling Regulates Metabolism (Chapter 13)
- Cell Signaling Facilitates Caloric Homeostasis (Chapter 14)
- Precursors Formed by Muscle Are Used by Other Organs (Chapter 17)
- Glycogen Breakdown and Synthesis Are Reciprocally Regulated (Chapter 25)
- Fatty Acid Metabolism Is a Source of Insight into Various Physiological States (Chapter 27)
- Ethanol Alters Energy Metabolism in the Liver (Chapter 28)

Clinical Insights

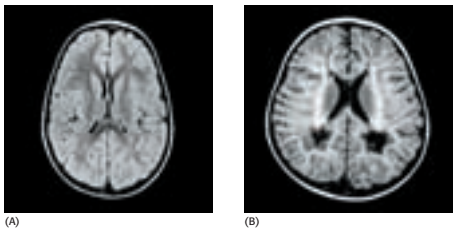
In the Clinical Insights, students see how the concepts most recently considered affect an aspect of a disease or its cure. By exploring biochemical concepts in the context of a disease, students learn how these concepts are relevant to human life and what happens when biochemistry goes awry. Some examples of the questions that we ask about human health throughout the book include:

- Why do some people get stomach aches from drinking milk? (p. 285)
- In what ways are cancer and exercise training biologically similar? (p. 292)
- What happens when nucleotide metabolism is disrupted? (p. 568)
- How do cataracts result from a defect in a simple biochemical pathway? (p. 286)
- How does aspirin work? (p. 201)
- How do certain kinds of cholesterol predict heart attacks? (p. 512)
- What happens when athletes take steroids? (p. 514)
- How can mistakes in the replication of DNA lead to cancer? (p. 619)
- How can inducing more mistakes actually treat cancer? (pp. 592 and 620)

Clinical Insight

Mutations in Initiation Factor 2 Cause a Curious Pathological Condition

Mutations in eukaryotic initiation factor 2 result in a mysterious disease, called vanishing white matter (VWM) disease, in which nerve cells in the brain disappear and are replaced by cerebrospinal fluid (Figure 40.13). The white matter of the brain consists predominately of nerve axons that connect the gray matter of the brain to the rest of the body. Death, resulting from fever or extended coma, is anywhere from a few years to decades after the onset of the disease. An especially puzzling aspect of the disease is its tissue specificity. A mutation in a biochemical process as fundamental to life as protein-synthesis initiation would be predicted to be lethal or to at least affect all tissues of the body. Diseases such as VWM graphically show that, although much progress has been made in biochemistry, much more research will be required to understand the complexities of health and disease. ■



(A) (B)

Figure 40.13 The effects of vanishing white matter disease. (A) In the normal brain, magnetic resonance imaging (MRI) visualizes the white matter as dark gray. (B) In the diseased brain, MRI reveals that white matter is replaced by cerebrospinal fluid, seen as white. [Courtesy of Marjo S. van der Knaap, M.D., Ph.D., VU University Medical Center, The Netherlands.]

Biological Insights

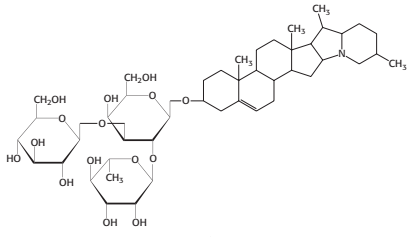
Biochemistry affects every aspect of our world, sometimes in strange and amazing ways. Like Clinical Insights, Biological Insights bolster students' understanding of biochemical concepts as they learn how simple changes in biochemical processes can have dramatic effects. We aim to enrich students' understanding of their world by answering such questions as:

- How do snakes digest food before they eat it? (p. 242)
- What happens when algae breathe too much? (p. 362)
- Why does bread go stale? (p. 413)
- Why is it a bad idea to eat green potato chips? (p. 395)
- How do weed killers work? (p. 403)
- What makes snakes such effective hunters? (p. 206)
- How does a mutation in a mitochondrial protein alter pig behavior? (p. 378)

Biological Insight

Chlorophyll in Potatoes Suggests the Presence of a Toxin

Chlorophyll synthesis is a warning sign when it comes to identifying poisonous potatoes. Light activates a noxious pathway in potatoes that leads to the synthesis of solanine, a toxic alkaloid. Plant alkaloids include such molecules as nicotine, caffeine, morphine, cocaine, and codeine.



Solanine

Solanine is toxic to animals because it inhibits acetylcholinesterase, an enzyme crucial for controlling the transmission of nerve impulses. Plants are thought to synthesize solanine to discourage insects from eating the potato. Light also causes potatoes to synthesize chlorophyll, which causes the tubers to turn green. Potatoes that are green have been exposed to light and are therefore probably also synthesizing solanine (Figure 22.9). For this reason, it is best not to eat green potatoes or potato chips with green edges. ■

Figure 22.9 Toxic potatoes. Potatoes that are exposed to light synthesize chlorophyll, resulting in greenish potatoes. Light also activates a pathway that results in the synthesis of solanine, a toxic alkaloid. Potato chips made from light-exposed potatoes have green edges. [Science Photo Library/Alamy.]

Lists of all Clinical and Biological Insights are included on page x as a quick reference for instructors.

Nutritional Examples

Examples of the underlying relation between nutrition and biochemistry abound. Some examples in this edition answer questions such as:

- Why do we depend on Vitamin C? (p. 55)
- Are CoQ 10 supplements effective? (p. 360)
- How does bread crust become crisp? (p. 414)
- Why is Vitamin D an "honorary steroid?" (p. 513)

For a full list of the nutritional examples in this edition, see page xi.

Vitamin and Coenzyme Appendix

We have included a redesigned appendix of nine key vitamins including important information such as main food sources, diseases that are caused by deficiencies, the recommended daily allowance, and the book page on which each vitamin is discussed in detail. This table appears on pages A6–A15.

Teaching and Learning with this Book

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.

Applied Approach to Difficult Topics

Working with feedback from instructors across North America, we have focused particular attention on topics that students find difficult, resulting in new sections such as:

- Making Buffers Is a Common Laboratory Practice (Chapter 2): takes an applied approach to helping students understand pH.
- There Are Six Major Classes of Enzymes (Chapter 6): helps students recognize the capabilities of enzymes.

End-of-Chapter Problems

Each chapter includes a robust set of practice problems. We have increased the number of end-of-chapter problems by 50% in the second edition.

- A new **Challenge Problems** section requires calculations plus an understanding of chemical structures and of concepts that are challenging for most students.
- **Data Interpretation Problems** train students to analyze data and reach scientific conclusions.
- **Chapter Integration Problems** draw connections between concepts across chapters.

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

Learning Objectives

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 identified these concepts with a ✓and number. These identifiers appear in the Section introductions as well as in the chapters in which the key concepts are presented. 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.

In this chapter, we will examine the properties of the various levels of protein structure. Then, we will investigate how primary structure determines the final three-dimensional structure.

✓ 2 Compare and contrast the different levels of protein structure and how they relate to one another.

4.1 Primary Structure: Amino Acids Are Linked by Peptide Bonds to Form Polypeptide Chains

Proteins are complicated three-dimensional molecules, but their three-dimensional structure depends simply on their *primary structure*—the *linear polymers* formed by linking the α-carboxyl group of one amino acid to the α-amino group of another amino acid. The linkage joining amino acids in a protein is called a *peptide bond* (also called an *amide bond*). The formation of a dipeptide from two amino acids is accompanied by the loss of a water molecule (Figure 4.1). The equilibrium of this reaction lies on the side of hydrolysis rather than synthesis under most conditions. Hence, the biosynthesis of peptide bonds requires an input of free energy. Nonetheless, peptide bonds are quite stable kinetically because the rate of hydrolysis is extremely slow; the lifetime of a peptide bond in aqueous solution in the absence of a catalyst approaches 1000 years.

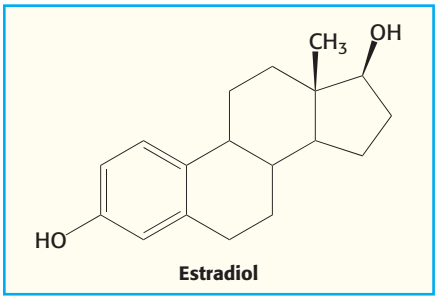
Margin Features

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.

- **Quick Quizzes** allow students to check their understanding of the material as they read it so that they can immediately gauge whether they need to review a topic or advance to the next one. Answers to the Quick Quizzes can be found at the end of each chapter.

? QUICK QUIZ 1 What factors determine the melting point of fatty acids?

- **Margin Structures** enable students to understand the topic at hand without needing to look up a basic structure or functional group that they may have seen earlier in the book or in another course.



Estradiol

- **Margin Facts** are short asides to the biochemical topic under consideration that relate the topic to everyday life or provide glimpses of how scientists think about science.

Vitamin C
Human beings are among the few mammals unable to synthesize vitamin C. Citrus products are the most common source of this vitamin. Vitamin C functions as a general antioxidant to reduce the presence of reactive oxygen species throughout the body. In addition, it serves as a specific antioxidant by maintaining metals, required by certain enzymes such as the enzyme that synthesizes hydroxyproline, in the reduced state. [Photograph from Don Farrell/Digital Vision/Getty Images.]

- **Vitamins and Coenzymes** are featured in the margin next to their inclusion as part of an enzyme mechanism or metabolic pathway. Through these margin features, students will learn how we obtain vitamins from our diets and what happens if we do not have enough of them. These important molecules and their structures can be found in Appendix D to help students easily find where each vitamin is discussed in the book.

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.*

Nutritional Examples

Media and Supplements

A full package of media resources and supplements provides instructors and students with innovative tools to support a variety of teaching and learning approaches. All these resources are fully integrated with the style and goals of the textbook.

eBook

http://ebooks.bfwpub.com/tymoczko2e

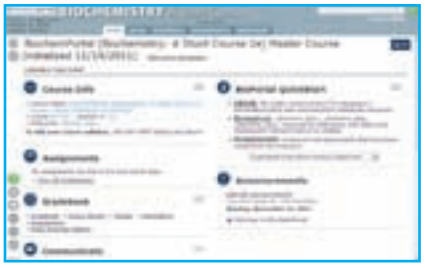
This online version of the textbook combines the contents of the printed book, electronic study tools, and a full complement of student media specifically created to support the textbook. Problems and resources from the printed textbook are incorporated throughout the eBook to ensure that students can easily review specific concepts. The eBook enables students to:

- Access the complete book and its electronic study tools from any Internet-connected computer by using a standard Web browser;
- Navigate quickly to any section or subsection of the book or any page number of the printed book;
- Add their own bookmarks, notes, and highlighting;
- Access all the fully integrated media resources associated with the book;
- Review quizzes and personal notes to help prepare for exams; and
- Search the entire eBook instantly, including the index and glossary.

Instructors teaching from the eBook 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 eBook and share these notes with their students. These notes may include text, Web links, animations, or photographs.

BiochemPortal

http://courses.bfwpub.com/tymockzo2e



BiochemPortal is a dynamic, fully integrated learning environment that brings together all of our teaching and learning resources in one place. This learning system also includes easy-to-use, powerful assessment tracking and grading tools that enable instructors to assign problems for practice, as homework, quizzes, or tests. A personalized calendar, an announcement center, and communication tools help instructors to manage their courses. In addition to all the resources found on the companion Web site, BiochemPortal includes the following resources:

- The **Interactive eBook** integrates the complete text with all relevant media resources.
- **Learning Curve** is a new quizzing engine that adapts to learning needs and tells students just what to study.
- The **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 they can explore the Metabolic Map on their own by using the dragging and zooming function of the map.

Companion Web site at www.whfreeman.com/tymoczko2e

For Students

- **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 on a topic that students traditionally struggle to master. Dr. Ensign first describes a 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 of the steps 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** enable students to view every textbook illustration of a protein structure online in interactive 3-D using Jmol. Students can zoom and rotate 56 "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, or backbone) by means of a user-friendly interface.
- **Self-assessment tool** enables students to test their understanding by taking an online multiple-choice quiz for each chapter, as well as a multiple-choice quiz as a general chemistry review.
- **Web links** connect students with the world of biochemistry beyond the classroom.

For Instructors

All of the features listed for students plus:

- **Optimized JPEGs** of all illustrations, photographs, and tables in the textbook, including structures of common compounds, ensure maximum clarity and visibility in lecture halls and on computer screens. 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 at Moorhead, offers more than 1500 questions in editable Word format.
- **Clicker Questions** include more than 100 questions for classroom use that will work seamlessly with any personal response system.

Instructor's Resource DVD

(1-4641-0976-1)
The DVD includes all instructor resources that are on the Web site.

Student Companion

By Frank Deis, Rutgers University; Nancy Counts Gerber, San Francisco State University; Richard I. Gumport, College of Medicine at Urbana-Champaign, University of Illinois; and Roger E. Koeppe, II, University of Arkansas at Fayetteville.
(1-4641-0934-6)
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

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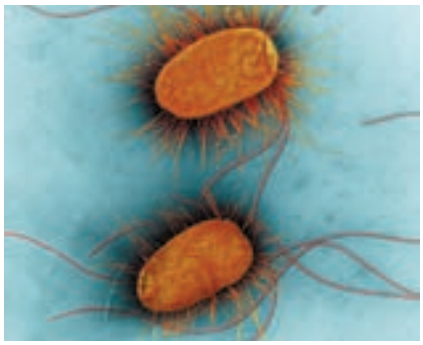
Brief Contents

Contents



Chapter 1: Biochemistry and the Unity of Life

Chapter 2: Water, Weak Bonds, and the Generation of Order Out of Chaos

SECTION 1

Biochemistry Helps Us 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 power 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 telltale 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 created genetically engineered plants that are, for example, more resistant to insects.

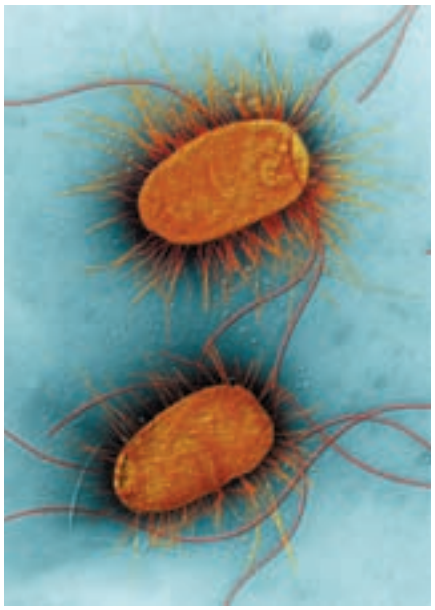
In this section, we will learn some of the key concepts that structure the study of biochemistry. We begin with an introduction to the molecules of biochemistry, followed by an overview of the fundamental unit of biochemistry and life itself—the cell. Finally, we examine the weak reversible bonds that 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 3×10^{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/Photo Researchers. Elephant: Imagebroker/Alamy.]

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 fuels 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 investigation 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, and oxygen.

Table 1.1 Chemical compositions as percentage of total number of atoms

	Composition in		
Element	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: After E. Frieden, The chemical elements of life, *Sci. Am.* 227(1), 1972, p. 54.

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 (see 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 in reactions with oxygen. After it has combined with oxygen, it is permanently out of circulation.

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

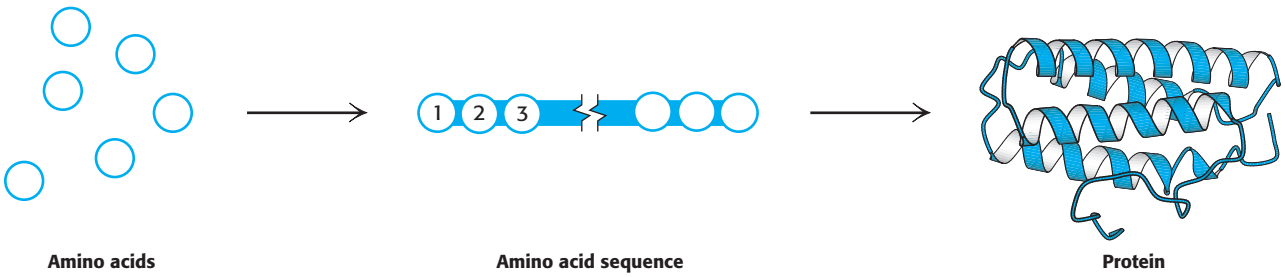
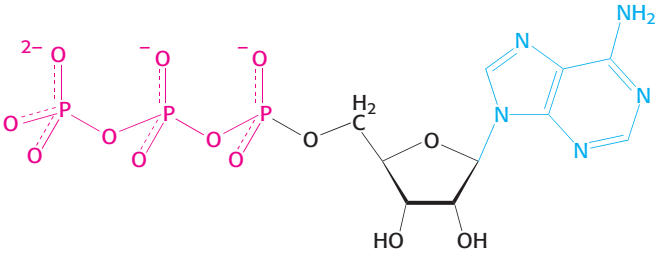


Figure 1.1 Protein folding. The three-dimensional structure of a protein is dictated by the sequence of amino acids that constitute the protein.



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). Messenger RNA 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. 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 and the cellular compartments. 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.

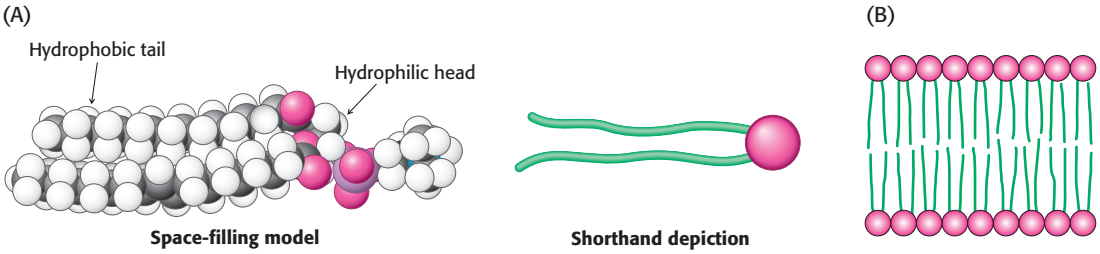
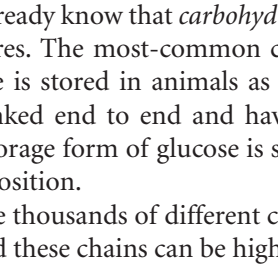


Figure 1.4 The dual properties of lipids. (A) One part of a lipid molecule is hydrophilic; the other part is hydrophobic. (B) In water, lipids can form a bilayer, constituting a barrier that separates two aqueous compartments.

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 having 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 recognized 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.

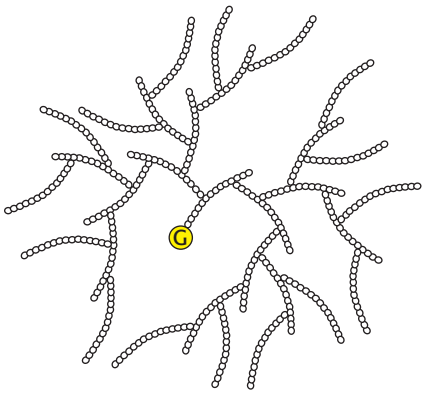
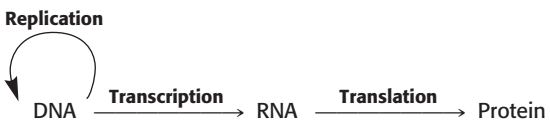


Figure 1.5 The structure of glycogen. Glycogen is a branched polymer composed of glucose molecules. The protein identified by the letter G at the center of the glycogen molecule is required for glycogen synthesis (Chapter 25).

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

Information processing in all cells is quite complex. It increases in complexity as cells become part 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 tenants of this dogma are true, but, as we will see later, this scheme is not as simple as depicted.

✓ 2 List the steps of the central dogma.

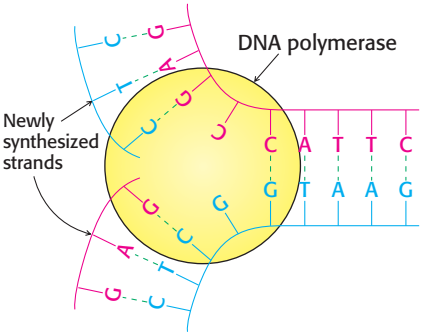


Figure 1.6 DNA replication. When the two strands of a DNA molecule are separated, each strand can serve as a template for the synthesis of a new partner strand. DNA polymerase catalyzes replication.

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.

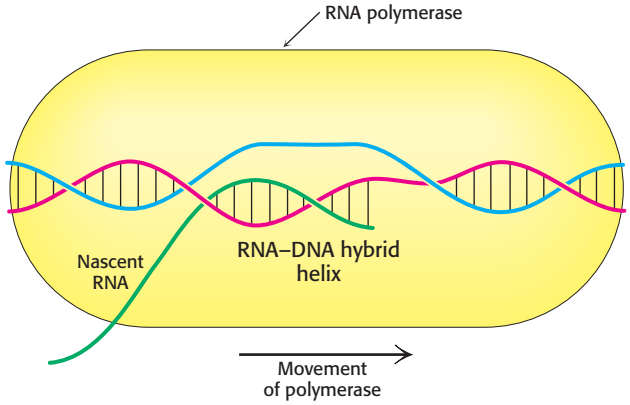


Figure 1.7 The transcription of RNA. Transcription, catalyzed by RNA polymerase, makes an RNA copy of one of the strands of DNA.

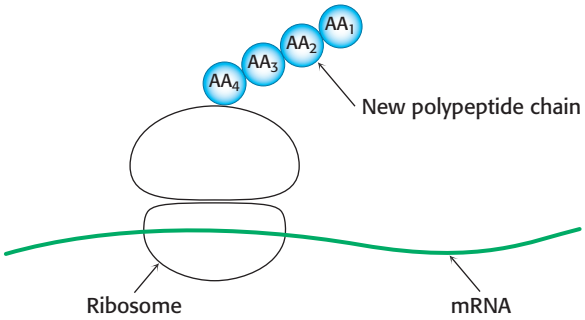


Figure 1.8 Translation takes place on ribosomes. A ribosome decodes the information in mRNA and translates it into the amino acid sequence of a protein.

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

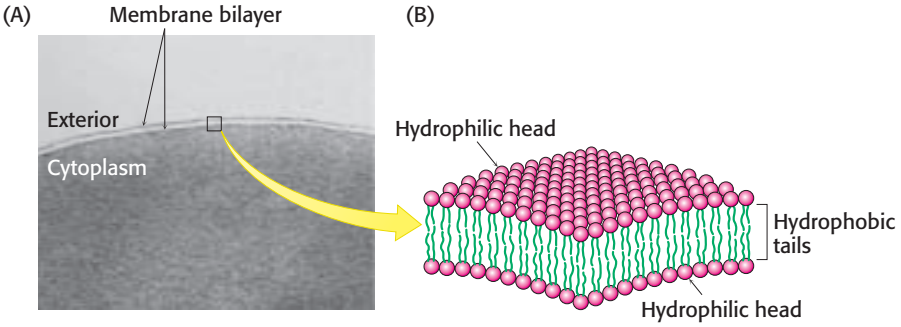


Figure 1.9 The bilayer structure of a membrane. (A) Membranes are composed of two layers or sheets. (B) The hydrophobic parts of the layers interact with each other, and the hydrophilic parts interact with the environment. [Photograph courtesy of J. D. Robertson.]

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 bacterium *Escherichia coli*, have a relatively simple structure. They are surrounded by

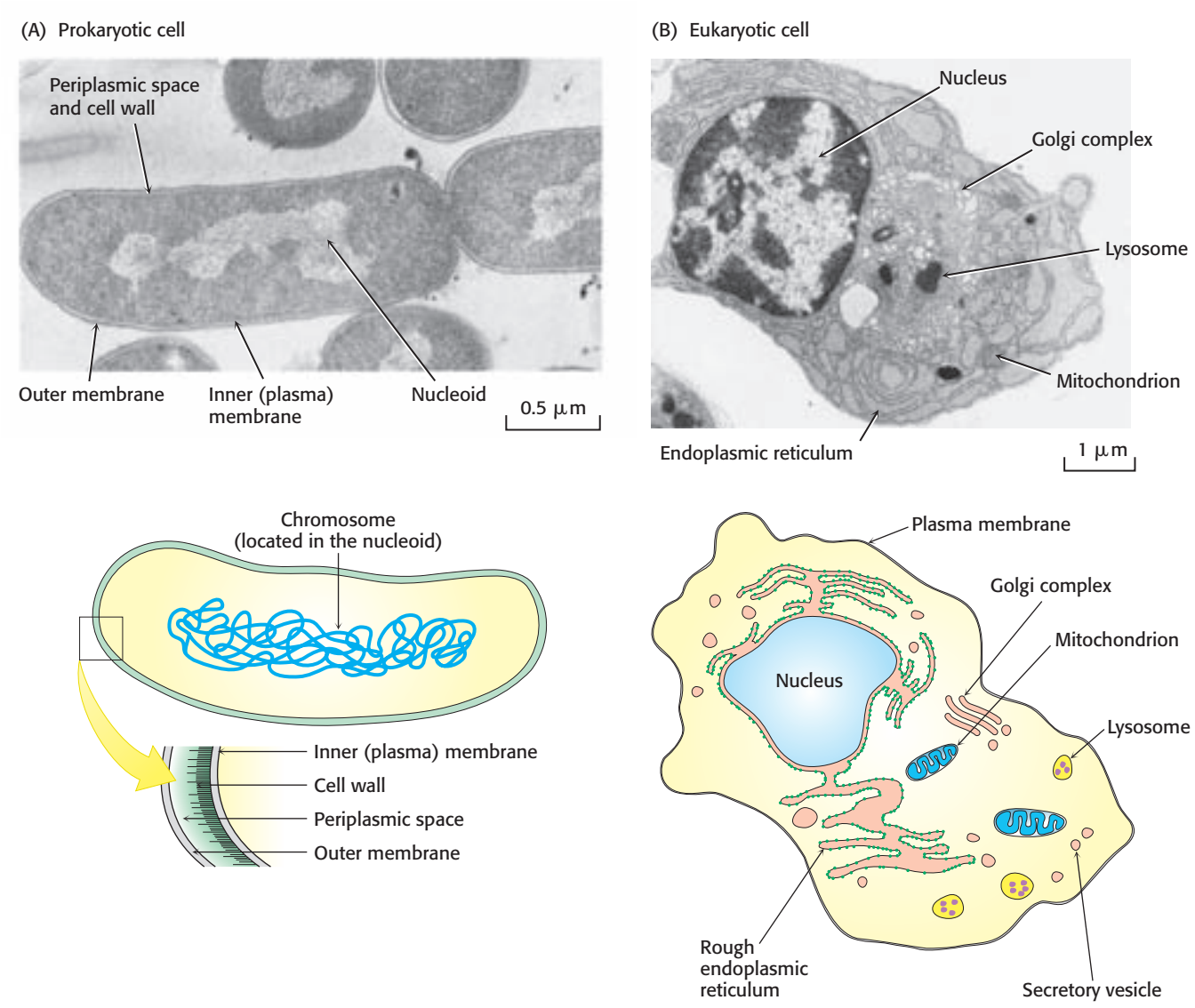


Figure 1.10 Prokaryotic and eukaryotic cells. Eukaryotic cells display more internal structure than do prokaryotic cells. Components within the interior of a eukaryotic cell, most notably the nucleus, are defined by membranes. [Micrographs: (A) Courtesy of I. D. J. Burdett and R. G. E. Murray; (B) from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