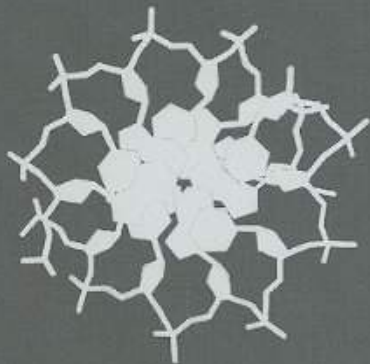


SEVENTH EDITION

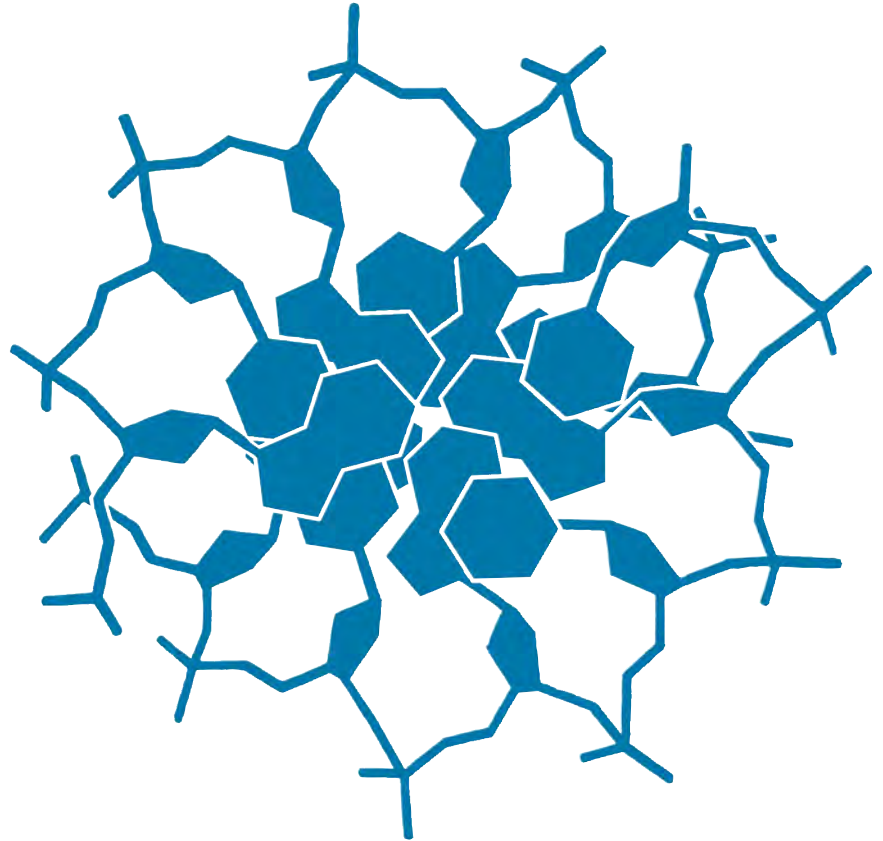
Biochemistry



Jeremy M. Berg
John L. Tymoczko
Lubert Stryer

SEVENTH EDITION

Biochemistry



Jeremy M. Berg

John L. Tymoczko

Lubert Stryer

with
Gregory J. Gatto, Jr.

Publisher: Kate Ahr Parker
Developmental Editor: Lisa Samols
Senior Project Editor: Georgia Lee Hadler
Manuscript Editors: Patricia Zimmerman and Nancy Brooks
Design Manager: Vicki Tomaselli
Page Make Up: Patrice Sheridan
Illustrations: Jeremy Berg with Network Graphics
Illustration Coordinator: Janice Donnola
Photo Editor: Christine Buese
Photo Researcher: Jacalyn Wong
Production Coordinator: Paul Rohloff
Media Editors: Andrea Gawrylewski, Patrick Shriner, Rohit Phillip,
and Marnie Rolfes
Supplements Editor: Amanda Dunning
Associate Director of Marketing: Debbie Clare
Composition: Aptara®, Inc.
Printing and Binding: RR Donnelley

Library of Congress Control Number: 2010937856

Gregory J. Gatto, Jr., is an employee of GlaxoSmithKline (GSK), which has not supported or funded this work in any way. Any views expressed herein do not necessarily represent the views of GSK.

ISBN 13: 9781429229364

ISBN 10: 1429229365

©2012, 2007, 2002 by W. H. Freeman and Company; © 1995, 1988, 1981, 1975 by
Lubert Stryer

All rights reserved

Printed in the United States of America

First printing

W. H. Freeman and Company
41 Madison Avenue
New York, NY 10010

www.whfreeman.com

To our teachers and our students

ABOUT THE AUTHORS

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. He then became Director of the National Institute of General Medical Sciences at the National Institutes of Health. He is an elected Fellow of the American Association for the Advancement of Science and an elected member of the Institute of Medicine of the National Academy of Sciences. He received the American Chemical Society Award in Pure Chemistry (1994) and the Eli Lilly Award for Fundamental Research in Biological Chemistry (1995), was named Maryland Outstanding Young Scientist of the Year (1995), received the Harrison Howe Award (1997), the Distinguished Service Award from the Biophysical Society (2009), and the Howard K. Schachman Public Service Award from the American Society for Biochemistry and Molecular Biology (2011). 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*.

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 coteaches 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.

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.

GREGORY J. GATTO, JR., received his A.B. degree in Chemistry from Princeton University, where he worked with Martin F. Semmelhack and was awarded the Everett S. Wallis Prize in Organic Chemistry. In 2003, he received his M.D. and Ph.D. degrees from the Johns Hopkins University School of Medicine, where he studied the structural biology of peroxisomal targeting signal recognition with Jeremy M. Berg and received the Michael A. Shanoff Young Investigator Research Award. He then completed a postdoctoral fellowship in 2006 with Christopher T. Walsh at Harvard Medical School, where he studied the biosynthesis of the macrolide immunosuppressants. He is currently an Investigator in the Heart Failure Discovery Performance Unit at GlaxoSmithKline Pharmaceuticals.

PREFACE

In writing this seventh edition of *Biochemistry*, we have balanced the desire to present up-to-the minute advances with the need to make biochemistry as clear and engaging as possible for the student approaching the subject for the first time. Instructors and students have long relied on *Biochemistry* for:

- **Clear writing** The language of biochemistry is made as accessible as possible. A straightforward and logical organization leads the reader through processes and helps navigate complex pathways and mechanisms.
- **Single-concept illustrations** Illustrations in this book address one point at a time so that each illustration clearly tells the story of a mechanism, pathway, or process without the distraction of excess detail.
- **Physiological relevance** Biochemistry is the study of life on the smallest scale, and it has always been our goal to help students connect biochemistry to their own lives. Pathways and processes are presented in a physiological context so that the reader can see how biochemistry works in different parts of the body and under different environmental and hormonal conditions.
- **Clinical insights** Wherever appropriate, pathways and mechanisms are applied to health and disease. These applications show students how biochemistry is relevant to them while reinforcing the concepts that they have just learned. (For a full list, see p. xi.)
- **Evolutionary perspective** Evolution is evident in the structures and pathways of biochemistry and is woven into the narrative of the textbook. (For a full list, see p. x.)

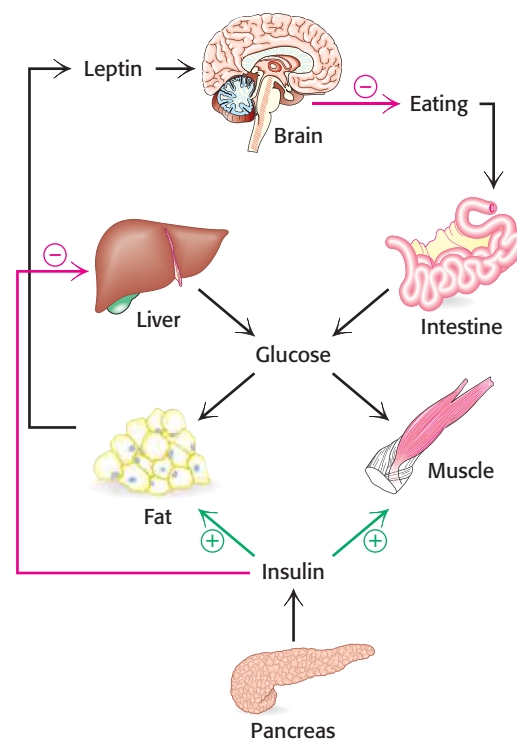
New to This Edition

Researchers are making new discoveries in biochemistry every day. The seventh edition takes into account the discoveries that have changed how we think about the fundamental concepts in biochemistry and human health. New aspects of the book include:

- **Metabolism integrated in a new context** New information about the role of leptins in hunger and satiety has greatly influenced how we think about obesity and the growing epidemic of diabetes. In this edition, we cover the integration of metabolism in the context of diet and obesity.
- **New chapters on gene regulation** To relate to the rapidly growing understanding of the biochemical aspect of eukaryotic gene regulation,

we have greatly expanded our discussion of regulation and have split the chapter in the preceding editions into two: Chapter 31, “The Control of Gene Expression in Prokaryotes,” and Chapter 32, “The Control of Gene Expression in Eukaryotes.” These chapters address recent discoveries such as quorum sensing in prokaryotes, induced pluripotent stem cells, and the role of microRNAs in regulating gene expression.

- **Experimental techniques updated and clarified** We have revised Chapters 3 (“Exploring Proteins and Proteomes”), 5 (“Exploring Genes and Genomes”), and 6 (“Exploring Evolution and Bioinformatics”) to give students a practical understanding of the benefits and limitations of the techniques that they will be using in the laboratory. We have expanded explanations of mass spectrometry and x-ray crystallography, for instance, and made them even clearer for the first-time student. We explain new techniques such as next-generation sequencing and real-time PCR in the context of their importance to modern research in biochemistry. (For a full list, see p. xii.)



Chapter 27 A schematic representation illustrates a few of the many metabolic pathways that must be coordinated to meet the demands of living.

Recent Advances

Some of the exciting advances and new topics that we present in the seventh edition include:

- Osteogenesis imperfecta, or brittle bone disease (Chapter 2)
- Intrinsically unstructured proteins and metamorphic proteins (Chapter 2)
- Recent updates in protein-misfolding diseases (Chapter 2)
- The use of recombinant DNA technology in protein purification (Chapter 3)
- Expanded discussion of mass spectrometry and x-ray crystallography (Chapter 3)
- Next-generation sequencing methods (Chapter 5)
- Real-time PCR (Chapter 5)
- DNA microarrays (Chapter 5)
- Carbon monoxide poisoning (Chapter 7)
- Single-molecule studies of enzyme kinetics (Chapter 8)
- Myosins as a model of a catalytic strategy for ATP hydrolysis (Chapter 9)
- Glycobiology and glycomics (Chapter 11)
- Hurler disease (Chapter 11)
- Avian influenza H5N1 (Chapter 11)
- Lipid rafts (Chapter 12)
- Transferrin as an example of receptor-mediated endocytosis (Chapter 12)
- Long QT syndrome and arrhythmia caused by the inhibition of potassium channels (Chapter 13)
- Defects in the citric acid cycle and the development of cancer (Chapter 17)
- Synthesizing a more efficient rubisco (Chapter 20)
- The structure of mammalian fatty acid synthetase (Chapter 22)
- Pyrimidine salvage pathways (Chapter 25)
- Physical association of enzymes in metabolic pathways (Chapter 25)
- Phosphatidic acid phosphatase in the regulation of lipid metabolism (Chapter 26)
- The regulation of SCAP-SREBP movement in cholesterol metabolism (Chapter 26)
- Mutations in the LDL receptor (Chapter 26)
- The role of HDL in protecting against arteriosclerosis (Chapter 26)

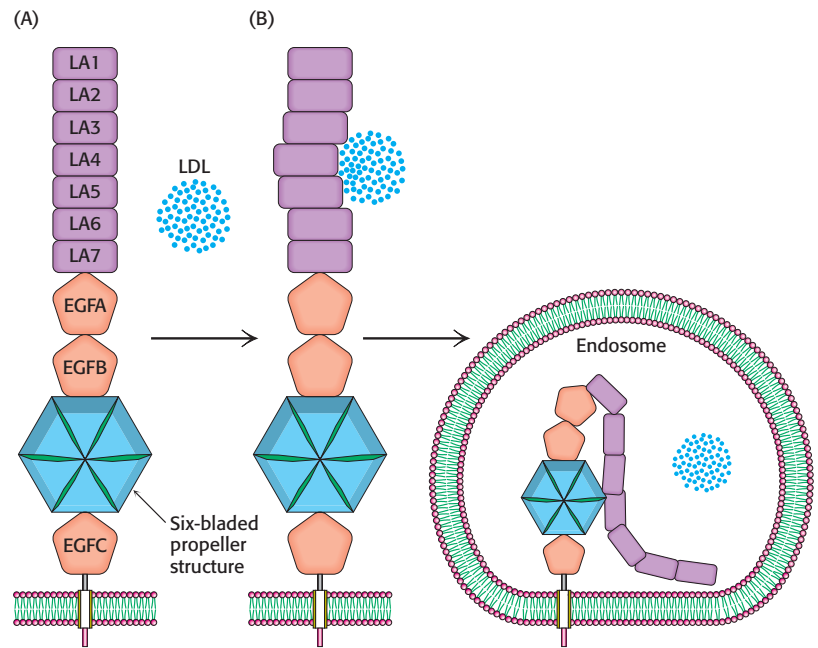


Figure 26.24 LDL receptor releases LDL in the endosomes. [After I. D. Campbell, *Biochem. Soc. Trans.* 31:1107–1114, 2003, Fig 1A.]

- Aromatase inhibitors in the treatment of breast and ovarian cancer (Chapter 26)
- The role of leptin in long-term caloric homeostasis (Chapter 27)
- Obesity and diabetes (Chapter 27)
- Exercise and its effects on cellular biochemistry (Chapter 27)
- Updated detailed mechanism of helicase's action (Chapter 28)
- Updated detailed mechanism of topoisomerase's action (Chapter 28)
- Riboswitches (Chapter 29)
- The production of small regulatory RNAs (Chapter 29)
- Vanishing white matter disease (Chapter 30)
- Quorum sensing (Chapter 31)
- Biofilms (Chapter 31)
- Induced pluripotent stem cells (Chapter 32)
- The role of microRNAs in gene regulation (Chapter 32)
- How vaccines work (Chapter 34)
- The structure of myosin head domains (Chapter 35)

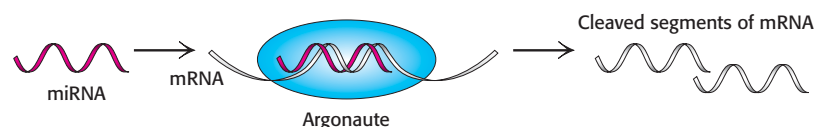


Figure 32.27 MicroRNA action.

New End-of-Chapter Problems

Biochemistry is best learned by practicing it and, to help students practice biochemistry, we have increased the number of end-of-chapter problems by 50%. In addition to many traditional problems that test biochemical knowledge and the ability to use this knowledge, we have three categories of problems to address specific problem-solving skills.

- **Mechanism problems** ask students to suggest or elaborate a chemical mechanism.
- **Data interpretation problems** ask questions about a set of data provided in tabulated or graphic form. These problems give students a sense of how scientific conclusions are reached.
- **Chapter integration problems** require students to use information from several chapters to reach a solution. These problems reinforce a student's awareness of the interconnectedness of the different aspects of biochemistry.

Brief solutions to these problems are presented at the end of the book; expanded solutions are available in the accompanying *Student Companion*.

Visualizing Molecular Structure

All molecular structures have been selected and rendered by Jeremy Berg and Gregory Gatto. To help students read and understand these structures, we include the following tools:

- A **molecular-model “primer”** explains the different types of protein models and examines their strengths and weaknesses (see appendices to Chapters 1 and 2).

- **Figure legends** direct students explicitly to the key features of a model.
- A **great variety of types of molecular structures** are represented, including clearer renderings of membrane proteins.
- For most molecular models, the **PDB number** at the end of the figure legend gives the reader easy access to the file used in generating the structure from the Protein Data Bank Web site (www.pdb.org). At this site, a variety of tools for visualizing and analyzing the structure are available.
- **Living figures** for most molecular structures now appear on the Web site in Jmol to allow students to **rotate three-dimensional molecules** and view alternative renderings online.

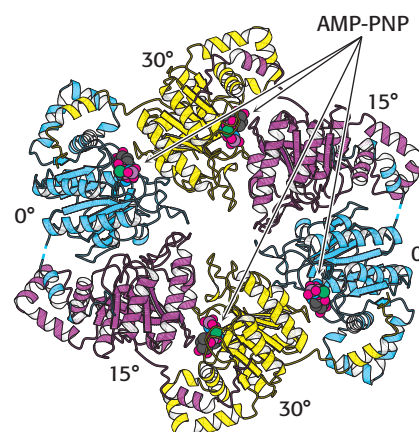


Figure 28.12 Helicase asymmetry. Notice that only four of the subunits, those shown in blue and yellow, bind AMP-PNP. [Drawn from 1EOK.pdb.]

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.

eBook

<http://ebooks.bfwpub.com/berg7e>

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 text. 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 spoken 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.

BIOCHEM PORTAL

<http://courses.bfwpub.com/berg7e>

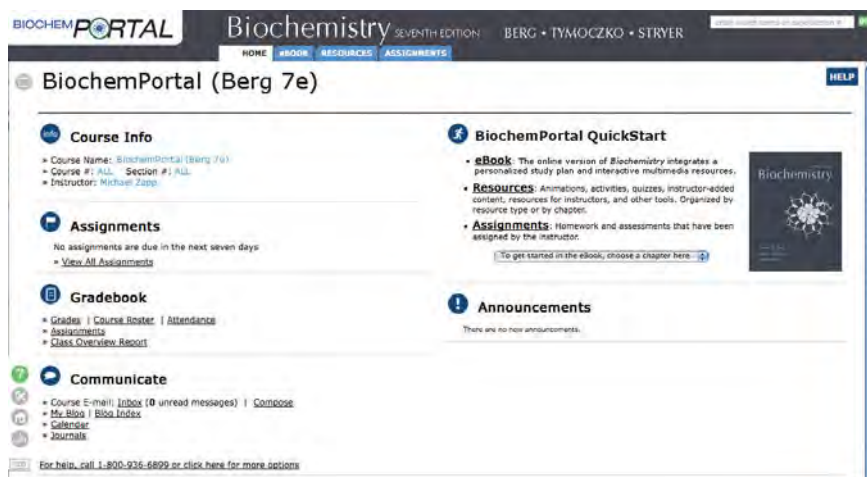
BiochemPortal is a dynamic, fully integrated learning environment that brings together all of our teaching and learning resources in one place. It features easy-to-use assessment tracking and grading tools that enable instructors to assign problems for practice, as homework, quizzes, or tests. A personalized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

- The **interactive eBook** integrates the complete text with all relevant media resources.
- Hundreds of **self-graded practice problems** allow students to test their understanding of concepts explained in the text, with immediate feedback.
- 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 explore the Metabolic Map on their own using the dragging and zooming functionality of the map.
- **Jmol tutorials** by Jeffrey Cohlberg, California State University at Long Beach, teach students how to create models of proteins in Jmol based on data from the Protein Database. By working through the tutorial

and answering assessment questions at the end of each exercise, students learn to use this important database and fully realize the relationship between structure and function of enzymes.

- **Animated techniques** illustrate laboratory techniques described in the text.
- **Concept tutorials** walk students through complex ideas in enzyme kinetics and metabolism.

BiochemPortal.



The screenshot displays the BiochemPortal interface for the seventh edition of Biochemistry by Berg, Tymoczko, and Stryer. The main navigation bar includes 'HOME', 'eBOOK', 'RESOURCES', and 'ASSIGNMENTS'. The page is titled 'BiochemPortal (Berg 7e)' and features several sections: 'Course Info' with details on course name, course number, and instructor; 'Assignments' showing a message about upcoming assignments; 'Gradebook' with links to grades, roster, attendance, assignments, and a class overview report; 'Communicate' with links to email, blog, and journals; and a 'BiochemPortal QuickStart' section with links to the eBook, resources, and assignments. A 'HELP' button is visible in the top right corner.

Companion Web Site

www.whfreeman.com/berg7e

For students

- **Living figures** allow students to explore protein structure in 3-D. Students can zoom and rotate the “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.
- **Concept-based tutorials** by Neil D. Clarke help students build an intuitive understanding of some of the more difficult concepts covered in the textbook.
- **Animated techniques** help students grasp experimental techniques used for exploring genes and proteins.
- The **self-assessment tool** 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.
- The **glossary** of key terms.
- **Web links** connect students with the world of biochemistry beyond the classroom.

For Instructors

All of the student resources plus:

- All **illustrations and tables** from the textbook, in jpeg and PowerPoint formats optimized for classroom projection.
- The **Assessment Bank** offers more than 1500 questions in editable Microsoft Word format.

Instructor's Resource DVD

[1-4292-8411-0]

The CD includes all the instructor's resources from the Web site.

Overhead Transparencies

[1-4292-8412-9]

200 full-color illustrations from the textbook, optimized for classroom projection

Student Companion

[1-4292-3115-7]

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 end-of-chapter problems in the textbook

Molecular Evolution



This icon signals the start of the many discussions that highlight protein commonalities or other molecular evolutionary insights.

- Only L amino acids make up proteins (p. 27)
- Why this set of 20 amino acids? (p. 33)
- Additional human globin genes (p. 211)
- Fetal hemoglobin (p. 213)
- Catalytic triads in hydrolytic enzymes (p. 260)
- Major classes of peptide-cleaving enzymes (p. 263)
- Zinc-based active sites in carbonic anhydrases (p. 271)
- Common catalytic core in type II restriction enzymes (p. 278)
- P-loop NTPase domains (p. 283)
- Conserved catalytic core in protein kinases (p. 302)
- Why might human blood types differ? (p. 335)
- Archaeal membranes (p. 350)
- Ion pumps (p. 374)
- P-type ATPases (p. 378)
- ATP-binding cassettes (p. 378)
- Sequence comparisons of Na⁺ and Ca⁺ channels (p. 386)
- Small G proteins (p. 410)
- Metabolism in the RNA world (p. 447)
- Why is glucose a prominent fuel? (p. 455)
- NAD⁺ binding sites in dehydrogenases (p. 469)
- The major facilitator superfamily of transporters (p. 477)
- Isozymic forms of lactate dehydrogenase (p. 490)
- Evolution of glycolysis and gluconeogenesis (p. 491)
- The α -ketoglutarate dehydrogenase complex (p. 507)
- Domains of succinyl CoA synthase (p. 509)
- Evolution of the citric acid cycle (p. 518)
- Mitochondria evolution (p. 527)
- Conserved structure of cytochrome *c* (p. 543)
- Common features of ATP synthase and G proteins (p. 550)
- Related uncoupling proteins (p. 557)
- Chloroplast evolution (p. 568)
- Evolutionary origins of photosynthesis (p. 584)
- Evolution of the C₄ pathway (p. 600)
- The coordination of the Calvin cycle and the pentose phosphate pathway (p. 609)
- Evolution of glycogen phosphorylase (p. 627)
- Increasing sophistication of glycogen phosphorylase regulation (p. 628)
- The α -amylase family (p. 629)
- A recurring motif in the activation of carboxyl groups (p. 645)
- Prokaryotic counterparts of the ubiquitin pathway and the proteasome (p. 677)
- A family of pyridoxal-dependent enzymes (p. 684)
- Evolution of the urea cycle (p. 688)
- The P-loop NTPase domain in nitrogenase (p. 708)
- Similar transaminases determine amino acid chirality (p. 713)
- Feedback inhibition (p. 724)
- Recurring steps in purine ring synthesis (p. 741)
- Ribonucleotide reductases (p. 747)
- Increase in urate levels during primate evolution (p. 754)
- The cytochrome P450 superfamily (p. 783)
- DNA polymerases (p. 821)
- Thymine and the fidelity of the genetic message (p. 841)
- Sigma factors in bacterial transcription (p. 858)
- Similarities in transcription between archaea and eukaryotes (p. 869)
- Evolution of spliceosome-catalyzed splicing (p. 881)
- Classes of aminoacyl-tRNA synthetases (p. 897)
- Composition of the primordial ribosome (p. 900)
- Homologous G proteins (p. 903)
- A family of proteins with common ligand-binding domains (p. 926)
- The independent evolution of DNA-binding sites of regulatory proteins (p. 927)
- Regulation by attenuator sites (p. 932)
- CpG islands (p. 946)
- Iron-response elements (p. 952)
- miRNAs in gene evolution (p. 954)
- The odorant-receptor family (p. 959)
- Photoreceptor evolution (p. 969)
- The immunoglobulin fold (p. 984)
- Relationship of actin to hexokinase and prokaryotic proteins (p. 1019)

Clinical Applications



This icon signals the start of a clinical application in the text. Additional, briefer clinical correlations appear in the text as appropriate.

- Osteogenesis imperfecta (p. 45)
- Protein-misfolding diseases (p. 55)
- Protein modification and scurvy (p. 55)
- Antigen detection with ELISA (p. 88)
- Synthetic peptides as drugs (p. 96)
- Gene therapy (p. 167)
- Functional magnetic resonance imaging (p. 197)
- Carbon monoxide poisoning (p. 213)
- Sickle-cell anemia (p. 209)
- Thalassemia (p. 210)
- Aldehyde dehydrogenase deficiency (p. 232)
- Action of penicillin (p. 244)
- Protease inhibitors (p. 264)
- Carbonic anhydrase and osteoporosis (p. 266)
- Isozymes as a sign of tissue damage (p. 297)
- Emphysema (p. 306)
- Vitamin K (p. 310)
- Hemophilia (p. 311)
- Tissue-type plasminogen activator (p. 312)
- Monitoring changes in glycosylated hemoglobin (p. 325)
- Erythropoietin (p. 330)
- Hurler disease (p. 331)
- Blood groups (p. 335)
- I-cell disease (p. 336)
- Influenza virus binding (p. 339)
- Clinical applications of liposomes (p. 354)
- Aspirin and ibuprofen (p. 358)
- Digitalis and congenital heart failure (p. 377)
- Multidrug resistance (p. 378)
- Long QT syndrome (p. 392)
- Signal-transduction pathways and cancer (p. 420)
- Monoclonal antibodies as anticancer drugs (p. 421)
- Protein kinase inhibitors as anticancer drugs (p. 421)
- Vitamins (p. 441)
- Lactose intolerance (p. 471)
- Galactosemia (p. 472)
- Exercise and cancer (p. 478)
- Phosphatase deficiency (p. 514)
- Defects in the citric acid cycle and the development of cancer (p. 515)
- Beriberi and mercury poisoning (p. 517)
- Mitochondrial diseases (p. 558)
- Hemolytic anemia (p. 609)
- Glucose 6-phosphate deficiency (p. 611)
- Glycogen-storage diseases (p. 634)
- Carnitine deficiency (p. 646)
- Zellweger syndrome (p. 652)
- Diabetic ketosis (p. 655)
- The use of fatty acid synthase inhibitors as drugs (p. 663)
- Effects of aspirin on signaling pathways (p. 665)
- Diseases resulting from defects in E3 proteins (p. 676)
- Diseases of altered ubiquitination (p. 678)
- Using proteasome inhibitors to treat tuberculosis (p. 679)
- Inherited defects of the urea cycle (hyperammonemia) (p. 688)
- Alcaptonuria, maple syrup urine disease, and phenylketonuria (p. 697)
- High homocysteine levels and vascular disease (p. 719)
- Inherited disorders of porphyrin metabolism (p. 730)
- Anticancer drugs that block the synthesis of thymidylate (p. 749)
- Adenosine deaminase and severe combined immunodeficiency (p. 752)
- Gout (p. 753)
- Lesch–Nyhan syndrome (p. 754)
- Folic acid and spina bifida (p. 755)
- Second messengers derived from sphingolipids and diabetes (p. 765)
- Respiratory distress syndrome and Tay–Sachs disease (p. 765)
- Diagnostic use of blood-cholesterol levels (p. 774)
- Hypercholesterolemia and atherosclerosis (p. 776)
- Mutations in the LDL receptor (p. 777)
- The role of HDL in protecting against arteriosclerosis (p. 778)
- Clinical management of cholesterol levels (p. 779)
- Aromatase inhibitors in the treatment of breast and ovarian cancer (p. 785)
- Rickets and vitamin D (p. 786)
- Antibiotics that target DNA gyrase (p. 831)
- Blocking telomerase to treat cancer (p. 837)
- Huntington disease (p. 842)
- Defective repair of DNA and cancer (p. 842)
- Detection of carcinogens (Ames test) (p. 843)
- Antibiotic inhibitors of transcription (p. 861)
- Burkitt lymphoma and B-cell leukemia (p. 869)
- Diseases of defective RNA splicing (p. 877)
- Vanishing white matter disease (p. 908)
- Antibiotics that inhibit protein synthesis (p. 909)
- Diphtheria (p. 910)
- Ricin, a lethal protein-synthesis inhibitor (p. 911)
- Induced pluripotent stem cells (p. 944)
- Anabolic steroids (p. 948)
- Color blindness (p. 970)
- The use of capsaicin in pain management (p. 974)
- Immune-system suppressants (p. 990)
- MHC and transplantation rejection (p. 998)
- AIDS vaccine (p. 999)
- Autoimmune diseases (p. 1001)
- Immune system and cancer (p. 1001)
- Vaccines (p. 1002)
- Charcot-Marie-Tooth disease (p. 1016)
- Taxol (p. 1019)

Tools and Techniques

The seventh edition of *Biochemistry* offers three chapters that present the tools and techniques of biochemistry: “Exploring Proteins and Proteomes” (Chapter 3), “Exploring Genes and Genomes” (Chapter 5), and “Exploring Evolution and Bioinformatics” (Chapter 6). Additional experimental techniques are presented throughout the book, as appropriate.

Exploring Proteins and Proteomes (Chapter 3)

Protein purification (p. 66)
Differential centrifugation (p. 67)
Salting out (p. 68)
Dialysis (p. 69)
Gel-filtration chromatography (p. 69)
Ion-exchange chromatography (p. 69)
Affinity chromatography (p. 70)
High-pressure liquid chromatography (p. 71)
Gel electrophoresis (p. 71)
Isoelectric focusing (p. 73)
Two-dimensional electrophoresis (p. 74)
Qualitative and quantitative evaluation of protein purification (p. 75)
Ultracentrifugation (p. 76)
Edman degradation (p. 80)
Protein sequencing (p. 82)
Production of polyclonal antibodies (p. 86)
Production of monoclonal antibodies (p. 86)
Enzyme-linked immunoabsorbent assay (ELISA) (p. 88)
Western blotting (p. 89)
Fluorescence microscopy (p. 89)
Green fluorescent protein as a marker (p. 89)
Immunoelectron microscopy (p. 91)
MALDI-TOF mass spectrometry (p. 91)
Tandem mass spectrometry (p. 93)
Proteomic analysis by mass spectrometry (p. 94)
Automated solid-phase peptide synthesis (p. 95)
X-ray crystallography (p. 98)
Nuclear magnetic resonance spectroscopy (p. 101)
NOESY spectroscopy (p. 102)

Exploring Proteins (other chapters)

Basis of fluorescence in green fluorescent protein (p. 58)
Using irreversible inhibitors to map the active site (p. 241)
Enzyme studies with catalytic antibodies (p. 243)
Single-molecule studies (p. 246)

Exploring Genes and Genomes (Chapter 5)

Restriction-enzyme analysis (p. 141)
Southern and northern blotting techniques (p. 142)
Sanger dideoxy method of DNA sequencing (p. 143)
Solid-phase synthesis of nucleic acids (p. 144)
Polymerase chain reaction (PCR) (p. 145)
Recombinant DNA technology (p. 148)
DNA cloning in bacteria (p. 149)
Creating cDNA libraries (p. 154)

Mutagenesis techniques (p. 156)
Next-generation sequencing (p. 160)
Quantitative PCR (p. 161)
Examining expression levels (DNA microarrays) (p. 162)
Introducing genes into eukaryotes (p. 163)
Transgenic animals (p. 164)
Gene disruption (p. 164)
Gene disruption by RNA interference (p. 165)
Tumor-inducing plasmids (p. 166)

Exploring Genes (other chapters)

Density-gradient equilibrium sedimentation (p. 119)
Chromatin immunoprecipitation (ChIP) (p. 945)

Exploring Evolution and Bioinformatics (Chapter 6)

Sequence-comparison methods (p. 174)
Sequence-alignment methods (p. 176)
Estimating the statistical significance of alignments (by shuffling) (p. 177)
Substitution matrices (p. 178)
Performing a BLAST database search (p. 181)
Sequence templates (p. 184)
Detecting repeated motifs (p. 184)
Mapping secondary structures through RNA sequence comparisons (p. 186)
Construction of evolutionary trees (p. 187)
Combinatorial chemistry (p. 188)
Molecular evolution in the laboratory (p. 189)

Other Techniques

Functional magnetic resonance imaging (fMRI) (p. 197)
Sequencing of carbohydrates by using MALDI-TOF mass spectroscopy (p. 336)
The use of liposomes to investigate membrane permeability (p. 353)
The use of hydropathy plots to locate transmembrane helices (p. 360)
Fluorescence recovery after photobleaching (FRAP) for measuring lateral diffusion in membranes (p. 361)
Patch-clamp technique for measuring channel activity (p. 383)
Measurement of redox potential (p. 528)

Animated Techniques

Animated explanations of experimental techniques used for exploring genes and proteins are available at www.whfreeman.com/berg7e.

Acknowledgments

Thanks go first and foremost to our students. Not a word was written or an illustration constructed without the knowledge that bright, engaged students would immediately detect vagueness and ambiguity. We also thank our colleagues who supported, advised, instructed, and simply bore with us during this arduous task. We are also grateful to our colleagues throughout the world who patiently answered our questions and shared their insights into recent developments.

We thank Susan J. Baserga and Erica A. Champion of the Yale University School of Medicine for their outstanding contributions in the sixth edition's revision of Chapter 29. We also especially thank those who served as reviewers for this new edition. Their thoughtful comments, suggestions, and encouragement have been of immense help to us in maintaining the excellence of the preceding editions. These reviewers are:

Fareed Aboul-Ela
Louisiana State University

Paul Adams
University of Arkansas, Fayetteville

Kevin Ahern
Oregon State University

Edward Behrman
Ohio State University

Donald Beitz
Iowa State University

Sanford Bernstein
San Diego State University

Martin Brock
Eastern Kentucky University

W. Malcom Byrnes
Howard University College of Medicine

C. Britt Carlson
Brookdale Community College

Graham Carpenter
Vanderbilt University

Jun Chung
Louisiana State University

Michael Cusanovich
University of Arizona

David Daleke
Indiana University

Margaret Daugherty
Colorado College

Dan Davis
University of Arkansas, Fayetteville

Mary Farwell
East Carolina University

Brent Feske
Armstrong Atlantic University

Wilson Francisco
Arizona State University

Masaya Fujita
University of Houston, University Park

Peter Gegenheimer
University of Kansas

John Goers
California Polytechnic University, San Luis Obispo

Neena Grover
Colorado College

Paul Hager
East Carolina University

Frans Huijing
University of Miami

Nitin Jain
University of Tennessee

Gerwald Jogl
Brown University

Kelly Johanson
Xavier University of Louisiana

Todd Johnson
Weber State University

Michael Kalafatis
Cleveland State University

Mark Kearly
Florida State University

Sung-Kun Kim
Baylor University

Roger Koeppe
University of Arkansas, Fayetteville

Dmitry Kolpashchikov
University of Central Florida

John Koontz
University of Tennessee

Glen Legge
University of Houston, University Park

John Stephen Lodmell
University of Montana

Timothy Logan
Florida State University

Michael Massiah
Oklahoma State University

Diana McGill
Northern Kentucky University

Michael Mendenhall
University of Kentucky

David Merkler
University of South Florida

Gary Merrill
Oregon State University

Debra Moriarity
University of Alabama, Huntsville

Patricia Moroney
Louisiana State University

M. Kazem Mostafapour
University of Michigan, Dearborn

Duarte Mota de Freitas
Loyola University of Chicago

Stephen Munroe
Marquette University

Xiaping Pan
East Carolina University

Scott Pattison
Ball State University

Stefan Paula
Northern Kentucky University

David Pendergrass
University of Kansas

Reuben Peters
Iowa State University

Wendy Pogozeleski
State University of New York, Geneseo

Geraldine Prody
Western Washington University

Greg Raner
University of North Carolina, Greensboro

Joshua Rausch
Elmhurst College

Tanea Reed
Eastern Kentucky University

Lori Robins
California Polytechnic University, San Luis Obispo

Douglas Root
University of North Texas

Theresa Salerno
Minnesota State University, Mankato

Scott Samuels
University of Montana, Missoula

Benjamin Sandler
Oklahoma State University

Joel Schildbach
Johns Hopkins University

Hua Shi
State University of New York, University at Albany

Kerry Smith
Clemson University

Robert Stach
University of Michigan, Flint

Scott Stagg
Florida State University
Wesley Stites
University of Arkansas, Fayetteville
Paul Straight
Texas A&M University
Gerald Stubbs
Vanderbilt University
Takita Felder Sumter
Winthrop University
Jeremy Thorner
University of California, Berkeley

Liang Tong
Columbia University
Kenneth Traxler
Bemidji State University
Peter Van Der Geer
San Diego State University
Nagarajan Vasumathi
Jacksonville State University
Stefan Vetter
Florida Atlantic University
Edward Walker
Weber State University

Xuemin Wang
University of Missouri, St. Louis
Kevin Williams
Western Kentucky University
Warren Williams
University of British Columbia
Shiyong Wu
Ohio University
Laura Zapanta
University of Pittsburgh

Three of us have had the pleasure of working with the folks at W. H. Freeman and Company on a number of projects, whereas one of us is new to the Freeman family. Our experiences have always been delightful and rewarding. Writing and producing the seventh edition of *Biochemistry* was no exception. The Freeman team has a knack for undertaking stressful, but exhilarating, projects and reducing the stress without reducing the exhilaration and a remarkable ability to coax without ever nagging. We have many people to thank for this experience. First, we would like to acknowledge the encouragement, patience, excellent advice, and good humor of Kate Ahr Parker, Publisher. Her enthusiasm is source of energy for all of us. Lisa Samols is our wonderful developmental editor. Her insight, patience, and understanding contributed immensely to the success of this project. Beth Howe and Erica Champion assisted Lisa by developing several chapters, and we are grateful to them for their help. Georgia Lee Hadler, Senior Project Editor, managed the flow of the entire project, from copyediting through bound book, with her usual admirable efficiency. Patricia Zimmerman and Nancy Brooks, our manuscript editors, enhanced the literary consistency and clarity of the text. Vicki Tomaselli, Design Manager, produced a design and layout that makes the book exciting and eye-catching while maintaining the link to past editions. Photo Editor Christine Beuse and Photo Researcher Jacalyn Wong found the photographs that we hope make the text more inviting. Janice Donnola, Illustration

Coordinator, deftly directed the rendering of new illustrations. Paul Rohloff, Production Coordinator, made sure that the significant difficulties of scheduling, composition, and manufacturing were smoothly overcome. Andrea Gawrylewski, Patrick Shriner, Marni Rolfes, and Rohit Phillip did a wonderful job in their management of the media program. Amanda Dunning ably coordinated the print supplement plan. Special thanks also to editorial assistant Anna Bristow. Debbie Clare, Associate Director of Marketing, enthusiastically introduced this newest edition of *Biochemistry* to the academic world. We are deeply appreciative of the sales staff for their enthusiastic support. Without them, all of our excitement and enthusiasm would ultimately come to naught. Finally, we owe a deep debt of gratitude to Elizabeth Widdicombe, President of W. H. Freeman and Company. Her vision for science textbooks and her skill at gathering exceptional personnel make working with W. H. Freeman and Company 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—our wives, Wendie Berg, Alison Unger, and Megan Williams, and our children, Alex, Corey, and Monica Berg, Janina and Nicholas Tymoczko, and Timothy and Mark Gatto. Without their support, comfort, and understanding, this endeavor could never have been undertaken, let alone successfully completed.

BRIEF CONTENTS

Part I THE MOLECULAR DESIGN OF LIFE

- 1 Biochemistry: An Evolving Science 1
- 2 Protein Composition and Structure 25
- 3 Exploring Proteins and Proteomes 65
- 4 DNA, RNA, and the Flow of Genetic Information 109
- 5 Exploring Genes and Genomes 139
- 6 Exploring Evolution and Bioinformatics 173
- 7 Hemoglobin: Portrait of a Protein in Action 195
- 8 Enzymes: Basic Concepts and Kinetics 219
- 9 Catalytic Strategies 253
- 10 Regulatory Strategies 289
- 11 Carbohydrates 319
- 12 Lipids and Cell Membranes 345
- 13 Membrane Channels and Pumps 371
- 14 Signal-Transduction Pathways 401

Part II TRANSDUCING AND STORING ENERGY

- 15 Metabolism: Basic Concepts and Design 427
- 16 Glycolysis and Gluconeogenesis 453
- 17 The Citric Acid Cycle 497
- 18 Oxidative Phosphorylation 525
- 19 The Light Reactions of Photosynthesis 565
- 20 The Calvin Cycle and the Pentose Phosphate Pathway 589
- 21 Glycogen Metabolism 615
- 22 Fatty Acid Metabolism 639
- 23 Protein Turnover and Amino Acid Catabolism 673

Part III SYNTHESIZING THE MOLECULES OF LIFE

- 24 The Biosynthesis of Amino Acids 705
- 25 Nucleotide Biosynthesis 735
- 26 The Biosynthesis of Membrane Lipids and Steroids 759
- 27 The Integration of Metabolism 791
- 28 DNA Replication, Repair, and Recombination 819
- 29 RNA Synthesis and Processing 851
- 30 Protein Synthesis 887
- 31 The Control of Gene Expression in Prokaryotes 921
- 32 The Control of Gene Expression in Eukaryotes 937

Part IV RESPONDING TO ENVIRONMENTAL CHANGES

- 33 Sensory Systems 957
- 34 The Immune System 977
- 35 Molecular Motors 1007
- 36 Drug Development 1029

CONTENTS

- Preface v

Part I THE MOLECULAR DESIGN OF LIFE

Chapter 1 Biochemistry: An Evolving Science 1

1.1 Biochemical Unity Underlies Biological Diversity 1

1.2 DNA Illustrates the Interplay Between Form and Function 4

DNA is constructed from four building blocks 4

Two single strands of DNA combine to form a double helix 5

DNA structure explains heredity and the storage of information 5

1.3 Concepts from Chemistry Explain the Properties of Biological Molecules 6

The double helix can form from its component strands 6

Covalent and noncovalent bonds are important for the structure and stability of biological molecules 7

The double helix is an expression of the rules of chemistry 10

The laws of thermodynamics govern the behavior of biochemical systems 11

Heat is released in the formation of the double helix 12

Acid–base reactions are central in many biochemical processes 13

Acid–base reactions can disrupt the double helix 14

Buffers regulate pH in organisms and in the laboratory 15

1.4 The Genomic Revolution Is Transforming Biochemistry and Medicine 17

The sequencing of the human genome is a landmark in human history 17

Genome sequences encode proteins and patterns of expression 18

Individuality depends on the interplay between genes and environment 19

APPENDIX: Visualizing Molecular Structures I: Small Molecules 21

Chapter 2 Protein Composition and Structure 25

2.1 Proteins Are Built from a Repertoire of 20 Amino Acids 27

2.2 Primary Structure: Amino Acids Are Linked by Peptide Bonds to Form Polypeptide Chains 33

Proteins have unique amino acid sequences specified by genes 35

Polypeptide chains are flexible yet conformationally restricted 36

2.3 Secondary Structure: Polypeptide Chains Can Fold into Regular Structures Such As the Alpha Helix, the Beta Sheet, and Turns and Loops	38	3.2 Amino Acid Sequences of Proteins Can Be Determined Experimentally	79
The alpha helix is a coiled structure stabilized by intrachain hydrogen bonds	38	Peptide sequences can be determined by automated Edman degradation	80
Beta sheets are stabilized by hydrogen bonding between polypeptide strands	40	Proteins can be specifically cleaved into small peptides to facilitate analysis	82
Polypeptide chains can change direction by making reverse turns and loops	42	Genomic and proteomic methods are complementary	84
Fibrous proteins provide structural support for cells and tissues	43	3.3 Immunology Provides Important Techniques with Which to Investigate Proteins	84
2.4 Tertiary Structure: Water-Soluble Proteins Fold into Compact Structures with Nonpolar Cores	45	Antibodies to specific proteins can be generated	84
2.5 Quaternary Structure: Polypeptide Chains Can Assemble into Multisubunit Structures	48	Monoclonal antibodies with virtually any desired specificity can be readily prepared	86
2.6 The Amino Acid Sequence of a Protein Determines Its Three-Dimensional Structure	49	Proteins can be detected and quantified by using an enzyme-linked immunosorbent assay	88
Amino acids have different propensities for forming alpha helices, beta sheets, and beta turns	50	Western blotting permits the detection of proteins separated by gel electrophoresis	89
Protein folding is a highly cooperative process	52	Fluorescent markers make the visualization of proteins in the cell possible	90
Proteins fold by progressive stabilization of intermediates rather than by random search	52	3.4 Mass Spectrometry Is a Powerful Technique for the Identification of Peptides and Proteins	91
Prediction of three-dimensional structure from sequence remains a great challenge	54	The mass of a protein can be precisely determined by mass spectrometry	91
Some proteins are inherently unstructured and can exist in multiple conformations	54	Peptides can be sequenced by mass spectrometry	93
Protein misfolding and aggregation are associated with some neurological diseases	55	Individual proteins can be identified by mass spectrometry	94
Protein modification and cleavage confer new capabilities	57	3.5 Peptides Can Be Synthesized by Automated Solid-Phase Methods	95
APPENDIX: Visualizing Molecular Structures II: Proteins	60	3.6 Three-Dimensional Protein Structure Can Be Determined by X-ray Crystallography and NMR Spectroscopy	98
Chapter 3 Exploring Proteins and Proteomes	65	X-ray crystallography reveals three-dimensional structure in atomic detail	98
The proteome is the functional representation of the genome	66	Nuclear magnetic resonance spectroscopy can reveal the structures of proteins in solution	101
3.1 The Purification of Proteins Is an Essential First Step in Understanding Their Function	66	Chapter 4 DNA, RNA, and the Flow of Information	109
The assay: How do we recognize the protein that we are looking for?	67	4.1 A Nucleic Acid Consists of Four Kinds of Bases Linked to a Sugar–Phosphate Backbone	110
Proteins must be released from the cell to be purified	67	RNA and DNA differ in the sugar component and one of the bases	110
Proteins can be purified according to solubility, size, charge, and binding affinity	68	Nucleotides are the monomeric units of nucleic acids	111
Proteins can be separated by gel electrophoresis and displayed	71	DNA molecules are very long	113
A protein purification scheme can be quantitatively evaluated	75	4.2 A Pair of Nucleic Acid Chains with Complementary Sequences Can Form a Double-Helical Structure	113
Ultracentrifugation is valuable for separating biomolecules and determining their masses	76	The double helix is stabilized by hydrogen bonds and van der Waals interactions	113
Protein purification can be made easier with the use of recombinant DNA technology	78	DNA can assume a variety of structural forms	115
		Z-DNA is a left-handed double helix in which backbone phosphates zigzag	116

Some DNA molecules are circular and supercoiled	117		
Single-stranded nucleic acids can adopt elaborate structures	117		
4.3 The Double Helix Facilitates the Accurate Transmission of Hereditary Information	118		
Differences in DNA density established the validity of the semiconservative-replication hypothesis	119		
The double helix can be reversibly melted	120		
4.4 DNA Is Replicated by Polymerases That Take Instructions from Templates	121		
DNA polymerase catalyzes phosphodiester-bridge formation	121		
The genes of some viruses are made of RNA	122		
4.5 Gene Expression Is the Transformation of DNA Information into Functional Molecules	123		
Several kinds of RNA play key roles in gene expression	123		
All cellular RNA is synthesized by RNA polymerases	124		
RNA polymerases take instructions from DNA templates	126		
Transcription begins near promoter sites and ends at terminator sites	126		
Transfer RNAs are the adaptor molecules in protein synthesis	127		
4.6 Amino Acids Are Encoded by Groups of Three Bases Starting from a Fixed Point	128		
Major features of the genetic code	129		
Messenger RNA contains start and stop signals for protein synthesis	130		
The genetic code is nearly universal	131		
4.7 Most Eukaryotic Genes Are Mosaics of Introns and Exons	131		
RNA processing generates mature RNA	132		
Many exons encode protein domains	133		
<hr/> Chapter 5 Exploring Genes and Genomes	139		
5.1 The Exploration of Genes Relies on Key Tools	140		
Restriction enzymes split DNA into specific fragments	141		
Restriction fragments can be separated by gel electrophoresis and visualized	141		
DNA can be sequenced by controlled termination of replication	143		
DNA probes and genes can be synthesized by automated solid-phase methods	144		
Selected DNA sequences can be greatly amplified by the polymerase chain reaction	145		
PCR is a powerful technique in medical diagnostics, forensics, and studies of molecular evolution	146		
The tools for recombinant DNA technology have been used to identify disease-causing mutations	147		
		5.2 Recombinant DNA Technology Has Revolutionized All Aspects of Biology	148
		Restriction enzymes and DNA ligase are key tools in forming recombinant DNA molecules	148
		Plasmids and lambda phage are choice vectors for DNA cloning in bacteria	149
		Bacterial and yeast artificial chromosomes	151
		Specific genes can be cloned from digests of genomic DNA	151
		Complementary DNA prepared from mRNA can be expressed in host cells	154
		Proteins with new functions can be created through directed changes in DNA	156
		Recombinant methods enable the exploration of the functional effects of disease-causing mutations	157
		5.3 Complete Genomes Have Been Sequenced and Analyzed	157
		The genomes of organisms ranging from bacteria to multicellular eukaryotes have been sequenced	158
		The sequencing of the human genome has been finished	159
		Next-generation sequencing methods enable the rapid determination of a whole genome sequence	160
		Comparative genomics has become a powerful research tool	160
		5.4 Eukaryotic Genes Can Be Quantitated and Manipulated with Considerable Precision	161
		Gene-expression levels can be comprehensively examined	161
		New genes inserted into eukaryotic cells can be efficiently expressed	163
		Transgenic animals harbor and express genes introduced into their germ lines	164
		Gene disruption provides clues to gene function	164
		RNA interference provides an additional tool for disrupting gene expression	165
		Tumor-inducing plasmids can be used to introduce new genes into plant cells	166
		Human gene therapy holds great promise for medicine	167
		<hr/> Chapter 6 Exploring Evolution and Bioinformatics	173
		6.1 Homologs Are Descended from a Common Ancestor	174
		6.2 Statistical Analysis of Sequence Alignments Can Detect Homology	175
		The statistical significance of alignments can be estimated by shuffling	177
		Distant evolutionary relationships can be detected through the use of substitution matrices	178
		Databases can be searched to identify homologous sequences	181

6.3 Examination of Three-Dimensional Structure Enhances Our Understanding of Evolutionary Relationships	182	Additional globins are encoded in the human genome	211
Tertiary structure is more conserved than primary structure	183	APPENDIX: Binding Models Can Be Formulated in Quantitative Terms: the Hill Plot and the Concerted Model	213
Knowledge of three-dimensional structures can aid in the evaluation of sequence alignments	184	Chapter 8 Enzymes: Basic Concepts and Kinetics	219
Repeated motifs can be detected by aligning sequences with themselves	184	8.1 Enzymes Are Powerful and Highly Specific Catalysts	220
Convergent evolution illustrates common solutions to biochemical challenges	185	Many enzymes require cofactors for activity	221
Comparison of RNA sequences can be a source of insight into RNA secondary structures	186	Enzymes can transform energy from one form into another	221
6.4 Evolutionary Trees Can Be Constructed on the Basis of Sequence Information	187	8.2 Free Energy Is a Useful Thermodynamic Function for Understanding Enzymes	222
6.5 Modern Techniques Make the Experimental Exploration of Evolution Possible	188	The free-energy change provides information about the spontaneity but not the rate of a reaction	222
Ancient DNA can sometimes be amplified and sequenced	188	The standard free-energy change of a reaction is related to the equilibrium constant	223
Molecular evolution can be examined experimentally	189	Enzymes alter only the reaction rate and not the reaction equilibrium	224
Chapter 7 Hemoglobin: Portrait of a Protein in Action	195	8.3 Enzymes Accelerate Reactions by Facilitating the Formation of the Transition State	225
7.1 Myoglobin and Hemoglobin Bind Oxygen at Iron Atoms in Heme	196	The formation of an enzyme–substrate complex is the first step in enzymatic catalysis	226
Changes in heme electronic structure upon oxygen binding are the basis for functional imaging studies	197	The active sites of enzymes have some common features	227
The structure of myoglobin prevents the release of reactive oxygen species	198	The binding energy between enzyme and substrate is important for catalysis	229
Human hemoglobin is an assembly of four myoglobin-like subunits	199	8.4 The Michaelis–Menten Equation Describes the Kinetic Properties of Many Enzymes	229
7.2 Hemoglobin Binds Oxygen Cooperatively	199	Kinetics is the study of reaction rates	229
Oxygen binding markedly changes the quaternary structure of hemoglobin	201	The steady-state assumption facilitates a description of enzyme kinetics	230
Hemoglobin cooperativity can be potentially explained by several models	202	Variations in K_M can have physiological consequences	232
Structural changes at the heme groups are transmitted to the $\alpha_1\beta_1$ – $\alpha_2\beta_2$ interface	204	K_M and V_{max} values can be determined by several means	232
2,3-Bisphosphoglycerate in red cells is crucial in determining the oxygen affinity of hemoglobin	204	K_M and V_{max} values are important enzyme characteristics	233
Carbon monoxide can disrupt oxygen transport by hemoglobin	205	k_{cat}/K_M is a measure of catalytic efficiency	234
7.3 Hydrogen Ions and Carbon Dioxide Promote the Release of Oxygen: The Bohr Effect	206	Most biochemical reactions include multiple substrates	235
7.4 Mutations in Genes Encoding Hemoglobin Subunits Can Result in Disease	208	Allosteric enzymes do not obey Michaelis–Menten kinetics	237
Sickle-cell anemia results from the aggregation of mutated deoxyhemoglobin molecules	209	8.5 Enzymes Can Be Inhibited by Specific Molecules	238
Thalassemia is caused by an imbalanced production of hemoglobin chains	210	Reversible inhibitors are kinetically distinguishable	239
The accumulation of free alpha-hemoglobin chains is prevented	211	Irreversible inhibitors can be used to map the active site	241
		Transition-state analogs are potent inhibitors of enzymes	243
		Catalytic antibodies demonstrate the importance of selective binding of the transition state to enzymatic activity	243
		Penicillin irreversibly inactivates a key enzyme in bacterial cell-wall synthesis	244

8.6 Enzymes Can Be Studied One Molecule at a Time	246	The altered conformation of myosin persists for a substantial period of time	282
APPENDIX: Enzymes are Classified on the Basis of the Types of Reactions That They Catalyze	248	Myosins are a family of enzymes containing P-loop structures	283
Chapter 9 Catalytic Strategies	253	Chapter 10 Regulatory Strategies	289
A few basic catalytic principles are used by many enzymes	254	10.1 Aspartate Transcarbamoylase Is Allosterically Inhibited by the End Product of Its Pathway	290
9.1 Proteases Facilitate a Fundamentally Difficult Reaction	255	Allosterically regulated enzymes do not follow Michaelis–Menten kinetics	291
Chymotrypsin possesses a highly reactive serine residue	255	ATCase consists of separable catalytic and regulatory subunits	291
Chymotrypsin action proceeds in two steps linked by a covalently bound intermediate	256	Allosteric interactions in ATCase are mediated by large changes in quaternary structure	292
Serine is part of a catalytic triad that also includes histidine and aspartate	257	Allosteric regulators modulate the T-to-R equilibrium	295
Catalytic triads are found in other hydrolytic enzymes	260	10.2 Isozymes Provide a Means of Regulation Specific to Distinct Tissues and Developmental Stages	296
The catalytic triad has been dissected by site-directed mutagenesis	262	10.3 Covalent Modification Is a Means of Regulating Enzyme Activity	297
Cysteine, aspartyl, and metalloproteases are other major classes of peptide-cleaving enzymes	263	Kinases and phosphatases control the extent of protein phosphorylation	298
Protease inhibitors are important drugs	264	Phosphorylation is a highly effective means of regulating the activities of target proteins	300
9.2 Carbonic Anhydrases Make a Fast Reaction Faster	266	Cyclic AMP activates protein kinase A by altering the quaternary structure	301
Carbonic anhydrase contains a bound zinc ion essential for catalytic activity	267	ATP and the target protein bind to a deep cleft in the catalytic subunit of protein kinase A	302
Catalysis entails zinc activation of a water molecule	268	10.4 Many Enzymes Are Activated by Specific Proteolytic Cleavage	302
A proton shuttle facilitates rapid regeneration of the active form of the enzyme	269	Chymotrypsinogen is activated by specific cleavage of a single peptide bond	303
Convergent evolution has generated zinc-based active sites in different carbonic anhydrases	271	Proteolytic activation of chymotrypsinogen leads to the formation of a substrate-binding site	304
9.3 Restriction Enzymes Catalyze Highly Specific DNA-Cleavage Reactions	271	The generation of trypsin from trypsinogen leads to the activation of other zymogens	305
Cleavage is by in-line displacement of 3'-oxygen from phosphorus by magnesium-activated water	272	Some proteolytic enzymes have specific inhibitors	306
Restriction enzymes require magnesium for catalytic activity	274	Blood clotting is accomplished by a cascade of zymogen activations	307
The complete catalytic apparatus is assembled only within complexes of cognate DNA molecules, ensuring specificity	275	Fibrinogen is converted by thrombin into a fibrin clot	308
Host-cell DNA is protected by the addition of methyl groups to specific bases	277	Prothrombin is readied for activation by a vitamin K-dependent modification	310
Type II restriction enzymes have a catalytic core in common and are probably related by horizontal gene transfer	278	Hemophilia revealed an early step in clotting	311
9.4 Myosins Harness Changes in Enzyme Conformation to Couple ATP Hydrolysis to Mechanical Work	279	The clotting process must be precisely regulated	311
ATP hydrolysis proceeds by the attack of water on the gamma-phosphoryl group	279	Chapter 11 Carbohydrates	319
Formation of the transition state for ATP hydrolysis is associated with a substantial conformational change	280	11.1 Monosaccharides Are the Simplest Carbohydrates	320
		Many common sugars exist in cyclic forms	322
		Pyranose and furanose rings can assume different conformations	324

Glucose is a reducing sugar	325	A membrane lipid is an amphipathic molecule containing a hydrophilic and a hydrophobic moiety	351
Monosaccharides are joined to alcohols and amines through glycosidic bonds	326	12.3 Phospholipids and Glycolipids Readily Form Bimolecular Sheets in Aqueous Media	352
Phosphorylated sugars are key intermediates in energy generation and biosyntheses	326	Lipid vesicles can be formed from phospholipids	353
11.2 Monosaccharides Are Linked to Form Complex Carbohydrates	327	Lipid bilayers are highly impermeable to ions and most polar molecules	354
Sucrose, lactose, and maltose are the common disaccharides	327	12.4 Proteins Carry Out Most Membrane Processes	355
Glycogen and starch are storage forms of glucose	328	Proteins associate with the lipid bilayer in a variety of ways	355
Cellulose, a structural component of plants, is made of chains of glucose	328	Proteins interact with membranes in a variety of ways	356
11.3 Carbohydrates Can Be Linked to Proteins to Form Glycoproteins	329	Some proteins associate with membranes through covalently attached hydrophobic groups	359
Carbohydrates can be linked to proteins through asparagine (<i>N</i> -linked) or through serine or threonine (<i>O</i> -linked) residues	330	Transmembrane helices can be accurately predicted from amino acid sequences	359
The glycoprotein erythropoietin is a vital hormone	330	12.5 Lipids and Many Membrane Proteins Diffuse Rapidly in the Plane of the Membrane	361
Proteoglycans, composed of polysaccharides and protein, have important structural roles	331	The fluid mosaic model allows lateral movement but not rotation through the membrane	362
Proteoglycans are important components of cartilage	332	Membrane fluidity is controlled by fatty acid composition and cholesterol content	362
Mucins are glycoprotein components of mucus	333	Lipid rafts are highly dynamic complexes formed between cholesterol and specific lipids	363
Protein glycosylation takes place in the lumen of the endoplasmic reticulum and in the Golgi complex	333	All biological membranes are asymmetric	363
Specific enzymes are responsible for oligosaccharide assembly	335	12.6 Eukaryotic Cells Contain Compartments Bounded by Internal Membranes	364
Blood groups are based on protein glycosylation patterns	335	<hr/> Chapter 13 Membrane Channels and Pumps	371
Errors in glycosylation can result in pathological conditions	336	The expression of transporters largely defines the metabolic activities of a given cell type	372
Oligosaccharides can be “sequenced”	336	13.1 The Transport of Molecules Across a Membrane May Be Active or Passive	372
11.4 Lectins Are Specific Carbohydrate-Binding Proteins	337	Many molecules require protein transporters to cross membranes	372
Lectins promote interactions between cells	338	Free energy stored in concentration gradients can be quantified	373
Lectins are organized into different classes	338	13.2 Two Families of Membrane Proteins Use ATP Hydrolysis to Pump Ions and Molecules Across Membranes	374
Influenza virus binds to sialic acid residues	339	P-type ATPases couple phosphorylation and conformational changes to pump calcium ions across membranes	374
<hr/> Chapter 12 Lipids and Cell Membranes	345	Digitalis specifically inhibits the Na ⁺ –K ⁺ pump by blocking its dephosphorylation	377
Many common features underlie the diversity of biological membranes	346	P-type ATPases are evolutionarily conserved and play a wide range of roles	378
12.1 Fatty Acids Are Key Constituents of Lipids	346	Multidrug resistance highlights a family of membrane pumps with ATP-binding cassette domains	378
Fatty acid names are based on their parent hydrocarbons	346		
Fatty acids vary in chain length and degree of unsaturation	347		
12.2 There Are Three Common Types of Membrane Lipids	348		
Phospholipids are the major class of membrane lipids	348		
Membrane lipids can include carbohydrate moieties	349		
Cholesterol is a lipid based on a steroid nucleus	350		
Archaeal membranes are built from ether lipids with branched chains	350		

13.3 Lactose Permease Is an Archetype of Secondary Transporters That Use One Concentration Gradient to Power the Formation of Another	380	Insulin binding results in the cross-phosphorylation and activation of the insulin receptor	412
13.4 Specific Channels Can Rapidly Transport Ions Across Membranes	382	The activated insulin-receptor kinase initiates a kinase cascade	412
Action potentials are mediated by transient changes in Na ⁺ and K ⁺ permeability	382	Insulin signaling is terminated by the action of phosphatases	415
Patch-clamp conductance measurements reveal the activities of single channels	383	14.3 EGF Signaling: Signal-Transduction Pathways Are Poised to Respond	415
The structure of a potassium ion channel is an archetype for many ion-channel structures	383	EGF binding results in the dimerization of the EGF receptor	415
The structure of the potassium ion channel reveals the basis of ion specificity	384	The EGF receptor undergoes phosphorylation of its carboxyl-terminal tail	417
The structure of the potassium ion channel explains its rapid rate of transport	387	EGF signaling leads to the activation of Ras, a small G protein	417
Voltage gating requires substantial conformational changes in specific ion-channel domains	387	Activated Ras initiates a protein kinase cascade	418
A channel can be activated by occlusion of the pore: the ball-and-chain model	388	EGF signaling is terminated by protein phosphatases and the intrinsic GTPase activity of Ras	418
The acetylcholine receptor is an archetype for ligand-gated ion channels	389	14.4 Many Elements Recur with Variation in Different Signal-Transduction Pathways	419
Action potentials integrate the activities of several ion channels working in concert	391	14.5 Defects in Signal-Transduction Pathways Can Lead to Cancer and Other Diseases	420
Disruption of ion channels by mutations or chemicals can be potentially life threatening	392	Monoclonal antibodies can be used to inhibit signal-transduction pathways activated in tumors	420
13.5 Gap Junctions Allow Ions and Small Molecules to Flow Between Communicating Cells	393	Protein kinase inhibitors can be effective anticancer drugs	421
13.6 Specific Channels Increase the Permeability of Some Membranes to Water	394	Cholera and whooping cough are due to altered G-protein activity	421
<hr/> Chapter 14 Signal-Transduction Pathways	401	<hr/> Part II TRANSDUCING AND STORING ENERGY	
Signal transduction depends on molecular circuits	402	<hr/> Chapter 15 Metabolism: Basic Concepts and Design	427
14.1 Heterotrimeric G Proteins Transmit Signals and Reset Themselves	403	<hr/> 15.1 Metabolism Is Composed of Many Coupled, Interconnecting Reactions	428
Ligand binding to 7TM receptors leads to the activation of heterotrimeric G proteins	405	Metabolism consists of energy-yielding and energy-requiring reactions	428
Activated G proteins transmit signals by binding to other proteins	406	A thermodynamically unfavorable reaction can be driven by a favorable reaction	429
Cyclic AMP stimulates the phosphorylation of many target proteins by activating protein kinase A	406	15.2 ATP Is the Universal Currency of Free Energy in Biological Systems	430
G proteins spontaneously reset themselves through GTP hydrolysis	407	ATP hydrolysis is exergonic	430
Some 7TM receptors activate the phosphoinositide cascade	408	ATP hydrolysis drives metabolism by shifting the equilibrium of coupled reactions	431
Calcium ion is a widely used second messenger	409	The high phosphoryl potential of ATP results from structural differences between ATP and its hydrolysis products	433
Calcium ion often activates the regulatory protein calmodulin	410	Phosphoryl-transfer potential is an important form of cellular energy transformation	434
14.2 Insulin Signaling: Phosphorylation Cascades Are Central to Many Signal-Transduction Processes	411		
The insulin receptor is a dimer that closes around a bound insulin molecule	412		

15.3 The Oxidation of Carbon Fuels Is an Important Source of Cellular Energy	435		
Compounds with high phosphoryl-transfer potential can couple carbon oxidation to ATP synthesis	436		
Ion gradients across membranes provide an important form of cellular energy that can be coupled to ATP synthesis	437		
Energy from foodstuffs is extracted in three stages	437		
15.4 Metabolic Pathways Contain Many Recurring Motifs	438		
Activated carriers exemplify the modular design and economy of metabolism	438		
Many activated carriers are derived from vitamins	441		
Key reactions are reiterated throughout metabolism	443		
Metabolic processes are regulated in three principal ways	445		
Aspects of metabolism may have evolved from an RNA world	447		
<hr/> Chapter 16 Glycolysis and Gluconeogenesis	453		
Glucose is generated from dietary carbohydrates	454		
Glucose is an important fuel for most organisms	455		
16.1 Glycolysis Is an Energy-Conversion Pathway in Many Organisms	455		
Hexokinase traps glucose in the cell and begins glycolysis	455		
Fructose 1,6-bisphosphate is generated from glucose 6-phosphate	457		
The six-carbon sugar is cleaved into two three-carbon fragments	458		
Mechanism: Triose phosphate isomerase salvages a three-carbon fragment	459		
The oxidation of an aldehyde to an acid powers the formation of a compound with high phosphoryl-transfer potential	460		
Mechanism: Phosphorylation is coupled to the oxidation of glyceraldehyde 3-phosphate by a thioester intermediate	462		
ATP is formed by phosphoryl transfer from 1,3-bisphosphoglycerate	463		
Additional ATP is generated with the formation of pyruvate	464		
Two ATP molecules are formed in the conversion of glucose into pyruvate	465		
NAD ⁺ is regenerated from the metabolism of pyruvate	466		
Fermentations provide usable energy in the absence of oxygen	468		
The binding site for NAD ⁺ is similar in many dehydrogenases	469		
Fructose and galactose are converted into glycolytic intermediates	469		
Many adults are intolerant of milk because they are deficient in lactase	471		
Galactose is highly toxic if the transferase is missing	472		
16.2 The Glycolytic Pathway Is Tightly Controlled	472		
Glycolysis in muscle is regulated to meet the need for ATP	473		
The regulation of glycolysis in the liver illustrates the biochemical versatility of the liver	474		
A family of transporters enables glucose to enter and leave animal cells	477		
Cancer and exercise training affect glycolysis in a similar fashion	478		
16.3 Glucose Can Be Synthesized from Noncarbohydrate Precursors	479		
Gluconeogenesis is not a reversal of glycolysis	481		
The conversion of pyruvate into phosphoenolpyruvate begins with the formation of oxaloacetate	482		
Oxaloacetate is shuttled into the cytoplasm and converted into phosphoenolpyruvate	483		
The conversion of fructose 1,6-bisphosphate into fructose 6-phosphate and orthophosphate is an irreversible step	484		
The generation of free glucose is an important control point	484		
Six high-transfer-potential phosphoryl groups are spent in synthesizing glucose from pyruvate	485		
16.4 Gluconeogenesis and Glycolysis Are Reciprocally Regulated	486		
Energy charge determines whether glycolysis or gluconeogenesis will be most active	486		
The balance between glycolysis and gluconeogenesis in the liver is sensitive to blood-glucose concentration	487		
Substrate cycles amplify metabolic signals and produce heat	489		
Lactate and alanine formed by contracting muscle are used by other organs	489		
Glycolysis and gluconeogenesis are evolutionarily intertwined	491		
<hr/> Chapter 17 The Citric Acid Cycle	497		
The citric acid cycle harvests high-energy electrons	498		
17.1 Pyruvate Dehydrogenase Links Glycolysis to the Citric Acid Cycle	499		
Mechanism: The synthesis of acetyl coenzyme A from pyruvate requires three enzymes and five coenzymes	500		
Flexible linkages allow lipoamide to move between different active sites	502		
17.2 The Citric Acid Cycle Oxidizes Two-Carbon Units	503		
Citrate synthase forms citrate from oxaloacetate and acetyl coenzyme A	504		

Mechanism: The mechanism of citrate synthase prevents undesirable reactions	504	Ubiquinol is the entry point for electrons from FADH ₂ of flavoproteins	535
Citrate is isomerized into isocitrate	506	Electrons flow from ubiquinol to cytochrome <i>c</i> through Q-cytochrome <i>c</i> oxidoreductase	535
Isocitrate is oxidized and decarboxylated to alpha-ketoglutarate	506	The Q cycle funnels electrons from a two-electron carrier to a one-electron carrier and pumps protons	536
Succinyl coenzyme A is formed by the oxidative decarboxylation of alpha-ketoglutarate	507	Cytochrome <i>c</i> oxidase catalyzes the reduction of molecular oxygen to water	537
A compound with high phosphoryl-transfer potential is generated from succinyl coenzyme A	507	Toxic derivatives of molecular oxygen such as superoxide radical are scavenged by protective enzymes	540
Mechanism: Succinyl coenzyme A synthetase transforms types of biochemical energy	508	Electrons can be transferred between groups that are not in contact	542
Oxaloacetate is regenerated by the oxidation of succinate	509	The conformation of cytochrome <i>c</i> has remained essentially constant for more than a billion years	543
The citric acid cycle produces high-transfer-potential electrons, ATP, and CO ₂	510	18.4 A Proton Gradient Powers the Synthesis of ATP	543
17.3 Entry to the Citric Acid Cycle and Metabolism Through It Are Controlled	512	ATP synthase is composed of a proton-conducting unit and a catalytic unit	545
The pyruvate dehydrogenase complex is regulated allosterically and by reversible phosphorylation	513	Proton flow through ATP synthase leads to the release of tightly bound ATP: The binding-change mechanism	546
The citric acid cycle is controlled at several points	514	Rotational catalysis is the world's smallest molecular motor	547
Defects in the citric acid cycle contribute to the development of cancer	515	Proton flow around the <i>c</i> ring powers ATP synthesis	548
17.4 The Citric Acid Cycle Is a Source of Biosynthetic Precursors	516	ATP synthase and G proteins have several common features	550
The citric acid cycle must be capable of being rapidly replenished	516	18.5 Many Shuttles Allow Movement Across Mitochondrial Membranes	550
The disruption of pyruvate metabolism is the cause of beriberi and poisoning by mercury and arsenic	517	Electrons from cytoplasmic NADH enter mitochondria by shuttles	551
The citric acid cycle may have evolved from preexisting pathways	518	The entry of ADP into mitochondria is coupled to the exit of ATP by ATP-ADP translocase	552
17.5 The Glyoxylate Cycle Enables Plants and Bacteria to Grow on Acetate	518	Mitochondrial transporters for metabolites have a common tripartite structure	553
Chapter 18 Oxidative Phosphorylation	525	18.6 The Regulation of Cellular Respiration Is Governed Primarily by the Need for ATP	554
18.1 Eukaryotic Oxidative Phosphorylation Takes Place in Mitochondria	526	The complete oxidation of glucose yields about 30 molecules of ATP	554
Mitochondria are bounded by a double membrane	526	The rate of oxidative phosphorylation is determined by the need for ATP	555
Mitochondria are the result of an endosymbiotic event	527	Regulated uncoupling leads to the generation of heat	556
18.2 Oxidative Phosphorylation Depends on Electron Transfer	528	Oxidative phosphorylation can be inhibited at many stages	558
The electron-transfer potential of an electron is measured as redox potential	528	Mitochondrial diseases are being discovered	558
A 1.14-volt potential difference between NADH and molecular oxygen drives electron transport through the chain and favors the formation of a proton gradient	530	Mitochondria play a key role in apoptosis	559
18.3 The Respiratory Chain Consists of Four Complexes: Three Proton Pumps and a Physical Link to the Citric Acid Cycle	531	Power transmission by proton gradients is a central motif of bioenergetics	559
The high-potential electrons of NADH enter the respiratory chain at NADH-Q oxidoreductase	533	Chapter 19 The Light Reactions of Photosynthesis	565
		Photosynthesis converts light energy into chemical energy	566
		19.1 Photosynthesis Takes Place in Chloroplasts	567
		The primary events of photosynthesis take place in thylakoid membranes	567
		Chloroplasts arose from an endosymbiotic event	568

19.2 Light Absorption by Chlorophyll Induces Electron Transfer	568	20.2 The Activity of the Calvin Cycle Depends on Environmental Conditions	597
A special pair of chlorophylls initiate charge separation	569	Rubisco is activated by light-driven changes in proton and magnesium ion concentrations	598
Cyclic electron flow reduces the cytochrome of the reaction center	572	Thioredoxin plays a key role in regulating the Calvin cycle	598
19.3 Two Photosystems Generate a Proton Gradient and NADPH in Oxygenic Photosynthesis	572	The C ₄ pathway of tropical plants accelerates photosynthesis by concentrating carbon dioxide	599
Photosystem II transfers electrons from water to plastoquinone and generates a proton gradient	572	Crassulacean acid metabolism permits growth in arid ecosystems	600
Cytochrome <i>bf</i> links photosystem II to photosystem I	575	20.3 The Pentose Phosphate Pathway Generates NADPH and Synthesizes Five-Carbon Sugars	601
Photosystem I uses light energy to generate reduced ferredoxin, a powerful reductant	575	Two molecules of NADPH are generated in the conversion of glucose 6-phosphate into ribulose 5-phosphate	601
Ferredoxin–NADP ⁺ reductase converts NADP ⁺ into NADPH	576	The pentose phosphate pathway and glycolysis are linked by transketolase and transaldolase	601
19.4 A Proton Gradient Across the Thylakoid Membrane Drives ATP Synthesis	577	Mechanism: Transketolase and transaldolase stabilize carbanionic intermediates by different mechanisms	604
The ATP synthase of chloroplasts closely resembles those of mitochondria and prokaryotes	578	20.4 The Metabolism of Glucose 6-phosphate by the Pentose Phosphate Pathway Is Coordinated with Glycolysis	606
Cyclic electron flow through photosystem I leads to the production of ATP instead of NADPH	579	The rate of the pentose phosphate pathway is controlled by the level of NADP ⁺	606
The absorption of eight photons yields one O ₂ , two NADPH, and three ATP molecules	580	The flow of glucose 6-phosphate depends on the need for NADPH, ribose 5-phosphate, and ATP	607
19.5 Accessory Pigments Funnel Energy into Reaction Centers	581	Through the looking-glass: The Calvin cycle and the pentose phosphate pathway are mirror images	609
Resonance energy transfer allows energy to move from the site of initial absorbance to the reaction center	581	20.5 Glucose 6-phosphate Dehydrogenase Plays a Key Role in Protection Against Reactive Oxygen Species	609
Light-harvesting complexes contain additional chlorophylls and carotenoids	582	Glucose 6-phosphate dehydrogenase deficiency causes a drug-induced hemolytic anemia	609
The components of photosynthesis are highly organized	583	A deficiency of glucose 6-phosphate dehydrogenase confers an evolutionary advantage in some circumstances	611
Many herbicides inhibit the light reactions of photosynthesis	584	Chapter 21 Glycogen Metabolism	615
19.6 The Ability to Convert Light into Chemical Energy Is Ancient	584	Glycogen metabolism is the regulated release and storage of glucose	616
Chapter 20 The Calvin Cycle and Pentose Phosphate Pathway	589	21.1 Glycogen Breakdown Requires the Interplay of Several Enzymes	617
20.1 The Calvin Cycle Synthesizes Hexoses from Carbon Dioxide and Water	590	Phosphorylase catalyzes the phosphorolytic cleavage of glycogen to release glucose 1-phosphate	617
Carbon dioxide reacts with ribulose 1,5-bisphosphate to form two molecules of 3-phosphoglycerate	591	Mechanism: Pyridoxal phosphate participates in the phosphorolytic cleavage of glycogen	618
Rubisco activity depends on magnesium and carbamate	592	A debranching enzyme also is needed for the breakdown of glycogen	619
Rubisco also catalyzes a wasteful oxygenase reaction: Catalytic imperfection	593	Phosphoglucomutase converts glucose 1-phosphate into glucose 6-phosphate	620
Hexose phosphates are made from phosphoglycerate, and ribulose 1,5-bisphosphate is regenerated	594	The liver contains glucose 6-phosphatase, a hydrolytic enzyme absent from muscle	621
Three ATP and two NADPH molecules are used to bring carbon dioxide to the level of a hexose	597		
Starch and sucrose are the major carbohydrate stores in plants	597		

21.2 Phosphorylase Is Regulated by Allosteric Interactions and Reversible Phosphorylation	621	The complete oxidation of palmitate yields 106 molecules of ATP	647
Muscle phosphorylase is regulated by the intracellular energy charge	621		
Liver phosphorylase produces glucose for use by other tissues	623		
Phosphorylase kinase is activated by phosphorylation and calcium ions	623		
21.3 Epinephrine and Glucagon Signal the Need for Glycogen Breakdown	624	22.3 Unsaturated and Odd-Chain Fatty Acids Require Additional Steps for Degradation	648
G proteins transmit the signal for the initiation of glycogen breakdown	624	An isomerase and a reductase are required for the oxidation of unsaturated fatty acids	648
Glycogen breakdown must be rapidly turned off when necessary	626	Odd-chain fatty acids yield propionyl CoA in the final thiolysis step	649
The regulation of glycogen phosphorylase became more sophisticated as the enzyme evolved	627	Vitamin B ₁₂ contains a corrin ring and a cobalt atom	650
21.4 Glycogen Is Synthesized and Degraded by Different Pathways	627	Mechanism: Methylmalonyl CoA mutase catalyzes a rearrangement to form succinyl CoA	651
UDP-glucose is an activated form of glucose	627	Fatty acids are also oxidized in peroxisomes	652
Glycogen synthase catalyzes the transfer of glucose from UDP-glucose to a growing chain	628	Ketone bodies are formed from acetyl CoA when fat breakdown predominates	653
A branching enzyme forms α -1,6 linkages	629	Ketone bodies are a major fuel in some tissues	654
Glycogen synthase is the key regulatory enzyme in glycogen synthesis	629	Animals cannot convert fatty acids into glucose	656
Glycogen is an efficient storage form of glucose	629	22.4 Fatty Acids Are Synthesized by Fatty Acid Synthase	656
21.5 Glycogen Breakdown and Synthesis Are Reciprocally Regulated	630	Fatty acids are synthesized and degraded by different pathways	656
Protein phosphatase 1 reverses the regulatory effects of kinases on glycogen metabolism	631	The formation of malonyl CoA is the committed step in fatty acid synthesis	657
Insulin stimulates glycogen synthesis by inactivating glycogen synthase kinase	632	Intermediates in fatty acid synthesis are attached to an acyl carrier protein	657
Glycogen metabolism in the liver regulates the blood-glucose level	633	Fatty acid synthesis consists of a series of condensation, reduction, dehydration, and reduction reactions	658
A biochemical understanding of glycogen-storage diseases is possible	634	Fatty acids are synthesized by a multifunctional enzyme complex in animals	659
Chapter 22 Fatty Acid Metabolism	639	The synthesis of palmitate requires 8 molecules of acetyl CoA, 14 molecules of NADPH, and 7 molecules of ATP	661
Fatty acid degradation and synthesis mirror each other in their chemical reactions	640	Citrate carries acetyl groups from mitochondria to the cytoplasm for fatty acid synthesis	662
22.1 Triacylglycerols Are Highly Concentrated Energy Stores	641	Several sources supply NADPH for fatty acid synthesis	662
Dietary lipids are digested by pancreatic lipases	641	Fatty acid synthase inhibitors may be useful drugs	663
Dietary lipids are transported in chylomicrons	642	22.5 The Elongation and Unsaturation of Fatty Acids Are Accomplished by Accessory Enzyme Systems	663
22.2 The Use of Fatty Acids As Fuel Requires Three Stages of Processing	643	Membrane-bound enzymes generate unsaturated fatty acids	664
Triacylglycerols are hydrolyzed by hormone-stimulated lipases	643	Eicosanoid hormones are derived from polyunsaturated fatty acids	664
Fatty acids are linked to coenzyme A before they are oxidized	644	22.6 Acetyl CoA Carboxylase Plays a Key Role in Controlling Fatty Acid Metabolism	666
Carnitine carries long-chain activated fatty acids into the mitochondrial matrix	645	Acetyl CoA carboxylase is regulated by conditions in the cell	666
Acetyl CoA, NADH, and FADH ₂ are generated in each round of fatty acid oxidation	646	Acetyl CoA carboxylase is regulated by a variety of hormones	666
		Chapter 23 Protein Turnover and Amino Acid Catabolism	673
		23.1 Proteins Are Degraded to Amino Acids	674
		The digestion of dietary proteins begins in the stomach and is completed in the intestine	674
		Cellular proteins are degraded at different rates	675

23.2 Protein Turnover Is Tightly Regulated	675	Part III SYNTHESIZING THE MOLECULES OF LIFE	
Ubiquitin tags proteins for destruction	675		
The proteasome digests the ubiquitin-tagged proteins	677	Chapter 24 The Biosynthesis of Amino Acids	705
The ubiquitin pathway and the proteasome have prokaryotic counterparts	677	Amino acid synthesis requires solutions to three key biochemical problems	706
Protein degradation can be used to regulate biological function	678	24.1 Nitrogen Fixation: Microorganisms Use ATP and a Powerful Reductant to Reduce Atmospheric Nitrogen to Ammonia	706
23.3 The First Step in Amino Acid Degradation Is the Removal of Nitrogen	680	The iron–molybdenum cofactor of nitrogenase binds and reduces atmospheric nitrogen	707
Alpha-amino groups are converted into ammonium ions by the oxidative deamination of glutamate	680	Ammonium ion is assimilated into an amino acid through glutamate and glutamine	709
Mechanism: Pyridoxal phosphate forms Schiff-base intermediates in aminotransferases	681	24.2 Amino Acids Are Made from Intermediates of the Citric Acid Cycle and Other Major Pathways	711
Aspartate aminotransferase is an archetypal pyridoxal-dependent transaminase	682	Human beings can synthesize some amino acids but must obtain others from the diet	711
Pyridoxal phosphate enzymes catalyze a wide array of reactions	683	Aspartate, alanine, and glutamate are formed by the addition of an amino group to an alpha-ketoacid	712
Serine and threonine can be directly deaminated	684	A common step determines the chirality of all amino acids	713
Peripheral tissues transport nitrogen to the liver	684	The formation of asparagine from aspartate requires an adenylated intermediate	713
23.4 Ammonium Ion Is Converted into Urea in Most Terrestrial Vertebrates	685	Glutamate is the precursor of glutamine, proline, and arginine	714
The urea cycle begins with the formation of carbamoyl phosphate	685	3-Phosphoglycerate is the precursor of serine, cysteine, and glycine	714
The urea cycle is linked to gluconeogenesis	687	Tetrahydrofolate carries activated one-carbon units at several oxidation levels	715
Urea-cycle enzymes are evolutionarily related to enzymes in other metabolic pathways	688	S-Adenosylmethionine is the major donor of methyl groups	716
Inherited defects of the urea cycle cause hyperammonemia and can lead to brain damage	688	Cysteine is synthesized from serine and homocysteine	718
Urea is not the only means of disposing of excess nitrogen	689	High homocysteine levels correlate with vascular disease	719
23.5 Carbon Atoms of Degraded Amino Acids Emerge As Major Metabolic Intermediates	690	Shikimate and chorismate are intermediates in the biosynthesis of aromatic amino acids	719
Pyruvate is an entry point into metabolism for a number of amino acids	691	Tryptophan synthase illustrates substrate channeling in enzymatic catalysis	722
Oxaloacetate is an entry point into metabolism for aspartate and asparagine	692	24.3 Feedback Inhibition Regulates Amino Acid Biosynthesis	723
Alpha-ketoglutarate is an entry point into metabolism for five-carbon amino acids	692	Branched pathways require sophisticated regulation	723
Succinyl coenzyme A is a point of entry for several nonpolar amino acids	693	An enzymatic cascade modulates the activity of glutamine synthetase	725
Methionine degradation requires the formation of a key methyl donor, S-adenosylmethionine	693	24.4 Amino Acids Are Precursors of Many Biomolecules	726
The branched-chain amino acids yield acetyl CoA, acetoacetate, or propionyl CoA	693	Glutathione, a gamma-glutamyl peptide, serves as a sulfhydryl buffer and an antioxidant	727
Oxygenases are required for the degradation of aromatic amino acids	695	Nitric oxide, a short-lived signal molecule, is formed from arginine	727
23.6 Inborn Errors of Metabolism Can Disrupt Amino Acid Degradation	697		

Porphyrins are synthesized from glycine and succinyl coenzyme A	728	The synthesis of purine nucleotides is controlled by feedback inhibition at several sites	751
Porphyrins accumulate in some inherited disorders of porphyrin metabolism	730	The synthesis of deoxyribonucleotides is controlled by the regulation of ribonucleotide reductase	752
Chapter 25 Nucleotide Biosynthesis	735	25.5 Disruptions in Nucleotide Metabolism Can Cause Pathological Conditions	752
Nucleotides can be synthesized by de novo or salvage pathways	736	The loss of adenosine deaminase activity results in severe combined immunodeficiency	752
25.1 The Pyrimidine Ring Is Assembled de Novo or Recovered by Salvage Pathways	737	Gout is induced by high serum levels of urate	753
Bicarbonate and other oxygenated carbon compounds are activated by phosphorylation	737	Lesch–Nyhan syndrome is a dramatic consequence of mutations in a salvage-pathway enzyme	754
The side chain of glutamine can be hydrolyzed to generate ammonia	737	Folic acid deficiency promotes birth defects such as spina bifida	755
Intermediates can move between active sites by channeling	737		
Orotate acquires a ribose ring from PRPP to form a pyrimidine nucleotide and is converted into uridylate	738	Chapter 26 The Biosynthesis of Membrane Lipids and Steroids	759
Nucleotide mono-, di-, and triphosphates are interconvertible	739	26.1 Phosphatidate Is a Common Intermediate in the Synthesis of Phospholipids and Triacylglycerols	760
CTP is formed by amination of UTP	739	The synthesis of phospholipids requires an activated intermediate	761
Salvage pathways recycle pyrimidine bases	740	Sphingolipids are synthesized from ceramide	763
25.2 Purine Bases Can Be Synthesized de Novo or Recycled by Salvage Pathways	740	Gangliosides are carbohydrate-rich sphingolipids that contain acidic sugars	764
The purine ring system is assembled on ribose phosphate	740	Sphingolipids confer diversity on lipid structure and function	765
The purine ring is assembled by successive steps of activation by phosphorylation followed by displacement	741	Respiratory distress syndrome and Tay–Sachs disease result from the disruption of lipid metabolism	765
AMP and GMP are formed from IMP	743	Phosphatidic acid phosphatase is a key regulatory enzyme in lipid metabolism	766
Enzymes of the purine synthesis pathway associate with one another in vivo	744	26.2 Cholesterol Is Synthesized from Acetyl Coenzyme A in Three Stages	767
Salvage pathways economize intracellular energy expenditure	744	The synthesis of mevalonate, which is activated as isopentenyl pyrophosphate, initiates the synthesis of cholesterol	767
25.3 Deoxyribonucleotides Are Synthesized by the Reduction of Ribonucleotides Through a Radical Mechanism	745	Squalene (C ₃₀) is synthesized from six molecules of isopentenyl pyrophosphate (C ₅)	768
Mechanism: A tyrosyl radical is critical to the action of ribonucleotide reductase	745	Squalene cyclizes to form cholesterol	769
Stable radicals other than tyrosyl radical are employed by other ribonucleotide reductases	747	26.3 The Complex Regulation of Cholesterol Biosynthesis Takes Place at Several Levels	770
Thymidylate is formed by the methylation of deoxyuridylate	748	Lipoproteins transport cholesterol and triacylglycerols throughout the organism	773
Dihydrofolate reductase catalyzes the regeneration of tetrahydrofolate, a one-carbon carrier	749	The blood levels of certain lipoproteins can serve diagnostic purposes	774
Several valuable anticancer drugs block the synthesis of thymidylate	749	Low-density lipoproteins play a central role in cholesterol metabolism	775
25.4 Key Steps in Nucleotide Biosynthesis Are Regulated by Feedback Inhibition	750	The absence of the LDL receptor leads to hypercholesterolemia and atherosclerosis	776
Pyrimidine biosynthesis is regulated by aspartate transcarbamoylase	751	Mutations in the LDL receptor prevent LDL release and result in receptor destruction	777

HDL appears to protect against arteriosclerosis	778	Metabolic adaptations in prolonged starvation minimize protein degradation	808
The clinical management of cholesterol levels can be understood at a biochemical level	779	27.6 Ethanol Alters Energy Metabolism in the Liver	810
26.4 Important Derivatives of Cholesterol Include Bile Salts and Steroid Hormones	779	Ethanol metabolism leads to an excess of NADH	810
Letters identify the steroid rings and numbers identify the carbon atoms	781	Excess ethanol consumption disrupts vitamin metabolism	812
Steroids are hydroxylated by cytochrome P450 monooxygenases that use NADPH and O ₂	781	Chapter 28 DNA Replication, Repair, and Recombination	819
The cytochrome P450 system is widespread and performs a protective function	782	28.1 DNA Replication Proceeds by the Polymerization of Deoxyribonucleoside Triphosphates Along a Template	820
Pregnenolone, a precursor of many other steroids, is formed from cholesterol by cleavage of its side chain	783	DNA polymerases require a template and a primer	820
Progesterone and corticosteroids are synthesized from pregnenolone	783	All DNA polymerases have structural features in common	821
Androgens and estrogens are synthesized from pregnenolone	784	Two bound metal ions participate in the polymerase reaction	821
Vitamin D is derived from cholesterol by the ring-splitting activity of light	785	The specificity of replication is dictated by complementarity of shape between bases	822
Chapter 27 The Integration of Metabolism	791	An RNA primer synthesized by primase enables DNA synthesis to begin	823
27.1 Caloric Homeostasis Is a Means of Regulating Body Weight	792	One strand of DNA is made continuously, whereas the other strand is synthesized in fragments	823
27.2 The Brain Plays a Key Role in Caloric Homeostasis	794	DNA ligase joins ends of DNA in duplex regions	824
Signals from the gastrointestinal tract induce feelings of satiety	794	The separation of DNA strands requires specific helicases and ATP hydrolysis	824
Leptin and insulin regulate long-term control over caloric homeostasis	795	28.2 DNA Unwinding and Supercoiling Are Controlled by Topoisomerases	825
Leptin is one of several hormones secreted by adipose tissue	796	The linking number of DNA, a topological property, determines the degree of supercoiling	826
Leptin resistance may be a contributing factor to obesity	797	Topoisomerases prepare the double helix for unwinding	828
Dieting is used to combat obesity	797	Type I topoisomerases relax supercoiled structures	828
27.3 Diabetes Is a Common Metabolic Disease Often Resulting from Obesity	798	Type II topoisomerases can introduce negative supercoils through coupling to ATP hydrolysis	829
Insulin initiates a complex signal-transduction pathway in muscle	798	28.3 DNA Replication Is Highly Coordinated	831
Metabolic syndrome often precedes type 2 diabetes	800	DNA replication requires highly processive polymerases	831
Excess fatty acids in muscle modify metabolism	800	The leading and lagging strands are synthesized in a coordinated fashion	832
Insulin resistance in muscle facilitates pancreatic failure	801	DNA replication in <i>Escherichia coli</i> begins at a unique site	834
Metabolic derangements in type 1 diabetes result from insulin insufficiency and glucagon excess	802	DNA synthesis in eukaryotes is initiated at multiple sites	835
27.4 Exercise Beneficially Alters the Biochemistry of Cells	803	Telomeres are unique structures at the ends of linear chromosomes	836
Mitochondrial biogenesis is stimulated by muscular activity	804	Telomeres are replicated by telomerase, a specialized polymerase that carries its own RNA template	837
Fuel choice during exercise is determined by the intensity and duration of activity	805	28.4 Many Types of DNA Damage Can Be Repaired	837
27.5 Food Intake and Starvation Induce Metabolic Changes	806	Errors can arise in DNA replication	837
The starved–fed cycle is the physiological response to a fast	807	Bases can be damaged by oxidizing agents, alkylating agents, and light	838

DNA damage can be detected and repaired by a variety of systems	839	Enhancer sequences can stimulate transcription at start sites thousands of bases away	868
The presence of thymine instead of uracil in DNA permits the repair of deaminated cytosine	841	29.3 The Transcription Products of Eukaryotic Polymerases Are Processed	869
Some genetic diseases are caused by the expansion of repeats of three nucleotides	842	RNA polymerase I produces three ribosomal RNAs	869
Many cancers are caused by the defective repair of DNA	842	RNA polymerase III produces transfer RNA	870
Many potential carcinogens can be detected by their mutagenic action on bacteria	843	The product of RNA polymerase II, the pre-mRNA transcript, acquires a 5' cap and a 3' poly(A) tail	870
28.5 DNA Recombination Plays Important Roles in Replication, Repair, and Other Processes	844	Small regulatory RNAs are cleaved from larger precursors	872
RecA can initiate recombination by promoting strand invasion	844	RNA editing changes the proteins encoded by mRNA	872
Some recombination reactions proceed through Holliday-junction intermediates	845	Sequences at the ends of introns specify splice sites in mRNA precursors	873
<hr/> Chapter 29 RNA Synthesis and Processing	851	Splicing consists of two sequential transesterification reactions	874
RNA synthesis comprises three stages: Initiation, elongation, and termination	852	Small nuclear RNAs in spliceosomes catalyze the splicing of mRNA precursors	875
29.1 RNA Polymerases Catalyze Transcription	853	Transcription and processing of mRNA are coupled	877
RNA chains are formed de novo and grow in the 5'-to-3' direction	854	Mutations that affect pre-mRNA splicing cause disease	877
RNA polymerases backtrack and correct errors	856	Most human pre-mRNAs can be spliced in alternative ways to yield different proteins	878
RNA polymerase binds to promoter sites on the DNA template to initiate transcription	856	29.4 The Discovery of Catalytic RNA Was Revealing in Regard to Both Mechanism and Evolution	879
Sigma subunits of RNA polymerase recognize promoter sites	857	<hr/> Chapter 30 Protein Synthesis	887
RNA polymerases must unwind the template double helix for transcription to take place	858	30.1 Protein Synthesis Requires the Translation of Nucleotide Sequences into Amino Acid Sequences	888
Elongation takes place at transcription bubbles that move along the DNA template	858	The synthesis of long proteins requires a low error frequency	888
Sequences within the newly transcribed RNA signal termination	859	Transfer RNA molecules have a common design	889
Some messenger RNAs directly sense metabolite concentrations	860	Some transfer RNA molecules recognize more than one codon because of wobble in base-pairing	891
The <i>rho</i> protein helps to terminate the transcription of some genes	860	30.2 Aminoacyl Transfer RNA Synthetases Read the Genetic Code	893
Some antibiotics inhibit transcription	861	Amino acids are first activated by adenylation	893
Precursors of transfer and ribosomal RNA are cleaved and chemically modified after transcription in prokaryotes	863	Aminoacyl-tRNA synthetases have highly discriminating amino acid activation sites	894
29.2 Transcription in Eukaryotes Is Highly Regulated	864	Proofreading by aminoacyl-tRNA synthetases increases the fidelity of protein synthesis	895
Three types of RNA polymerase synthesize RNA in eukaryotic cells	865	Synthetases recognize various features of transfer RNA molecules	896
Three common elements can be found in the RNA polymerase II promoter region	866	Aminoacyl-tRNA synthetases can be divided into two classes	897
The TFIID protein complex initiates the assembly of the active transcription complex	867	30.3 The Ribosome Is the Site of Protein Synthesis	897
Multiple transcription factors interact with eukaryotic promoters	868	Ribosomal RNAs (5S, 16S, and 23S rRNA) play a central role in protein synthesis	898
		Ribosomes have three tRNA-binding sites that bridge the 30s and 50s subunits	900

The start signal is usually AUG preceded by several bases that pair with 16S rRNA	900	31.3 Regulatory Circuits Can Result in Switching Between Patterns of Gene Expression	928
Bacterial protein synthesis is initiated by formylmethionyl transfer RNA	901	Lambda repressor regulates its own expression	928
Formylmethionyl-tRNA _f is placed in the P site of the ribosome in the formation of the 70S initiation complex	902	A circuit based on lambda repressor and Cro form a genetic switch	929
Elongation factors deliver aminoacyl-tRNA to the ribosome	902	Many prokaryotic cells release chemical signals that regulate gene expression in other cells	929
Peptidyl transferase catalyzes peptide-bond synthesis	903	Biofilms are complex communities of prokaryotes	930
The formation of a peptide bond is followed by the GTP-driven translocation of tRNAs and mRNA	904	31.4 Gene Expression Can Be Controlled at Posttranscriptional Levels	931
Protein synthesis is terminated by release factors that read stop codons	906	Attenuation is a prokaryotic mechanism for regulating transcription through the modulation of nascent RNA secondary structure	931
30.4 Eukaryotic Protein Synthesis Differs from Prokaryotic Protein Synthesis Primarily in Translation Initiation	907	<hr/> Chapter 32 The Control of Gene Expression in Eukaryotes	937
Mutations in initiation factor 2 cause a curious pathological condition	908	<hr/> 32.1 Eukaryotic DNA Is Organized into Chromatin	938
30.5 A Variety of Antibiotics and Toxins Can Inhibit Protein Synthesis	909	Nucleosomes are complexes of DNA and histones	939
Some antibiotics inhibit protein synthesis	909	DNA wraps around histone octamers to form nucleosomes	939
Diphtheria toxin blocks protein synthesis in eukaryotes by inhibiting translocation	910	32.2 Transcription Factors Bind DNA and Regulate Transcription Initiation	941
Ricin fatally modifies 28S ribosomal RNA	911	A range of DNA-binding structures are employed by eukaryotic DNA-binding proteins	941
30.6 Ribosomes Bound to the Endoplasmic Reticulum Manufacture Secretory and Membrane Proteins	911	Activation domains interact with other proteins	942
Signal sequences mark proteins for translocation across the endoplasmic reticulum membrane	911	Multiple transcription factors interact with eukaryotic regulatory regions	943
Transport vesicles carry cargo proteins to their final destination	913	Enhancers can stimulate transcription in specific cell types	943
<hr/> Chapter 31 The Control of Gene Expression in Prokaryotes	921	Induced pluripotent stem cells can be generated by introducing four transcription factors into differentiated cells	944
31.1 Many DNA-Binding Proteins Recognize Specific DNA Sequences	922	32.3 The Control of Gene Expression Can Require Chromatin Remodeling	944
The helix-turn-helix motif is common to many prokaryotic DNA-binding proteins	923	The methylation of DNA can alter patterns of gene expression	945
31.2 Prokaryotic DNA-Binding Proteins Bind Specifically to Regulatory Sites in Operons	923	Steroids and related hydrophobic molecules pass through membranes and bind to DNA-binding receptors	946
An operon consists of regulatory elements and protein-encoding genes	924	Nuclear hormone receptors regulate transcription by recruiting coactivators to the transcription complex	946
The <i>lac</i> repressor protein in the absence of lactose binds to the operator and blocks transcription	925	Steroid-hormone receptors are targets for drugs	948
Ligand binding can induce structural changes in regulatory proteins	926	Chromatin structure is modulated through covalent modifications of histone tails	949
The operon is a common regulatory unit in prokaryotes	926	Histone deacetylases contribute to transcriptional repression	950
Transcription can be stimulated by proteins that contact RNA polymerase	927	32.4 Eukaryotic Gene Expression Can Be Controlled at Posttranscriptional Levels	951
		Genes associated with iron metabolism are translationally regulated in animals	951
		Small RNAs regulate the expression of many eukaryotic genes	953

Part IV RESPONDING TO ENVIRONMENTAL CHANGES

Chapter 33	Sensory Systems	957		
33.1	A Wide Variety of Organic Compounds Are Detected by Olfaction	958		
	Olfaction is mediated by an enormous family of seven-transmembrane-helix receptors	958		
	Odorants are decoded by a combinatorial mechanism	960		
33.2	Taste Is a Combination of Senses That Function by Different Mechanisms	962		
	Sequencing of the human genome led to the discovery of a large family of 7TM bitter receptors	963		
	A heterodimeric 7TM receptor responds to sweet compounds	964		
	Umami, the taste of glutamate and aspartate, is mediated by a heterodimeric receptor related to the sweet receptor	965		
	Salty tastes are detected primarily by the passage of sodium ions through channels	965		
	Sour tastes arise from the effects of hydrogen ions (acids) on channels	965		
33.3	Photoreceptor Molecules in the Eye Detect Visible Light	966		
	Rhodopsin, a specialized 7TM receptor, absorbs visible light	966		
	Light absorption induces a specific isomerization of bound 11- <i>cis</i> -retinal	967		
	Light-induced lowering of the calcium level coordinates recovery	968		
	Color vision is mediated by three cone receptors that are homologs of rhodopsin	969		
	Rearrangements in the genes for the green and red pigments lead to “color blindness”	970		
33.4	Hearing Depends on the Speedy Detection of Mechanical Stimuli	971		
	Hair cells use a connected bundle of stereocilia to detect tiny motions	971		
	Mechanosensory channels have been identified in <i>Drosophila</i> and vertebrates	972		
33.5	Touch Includes the Sensing of Pressure, Temperature, and Other Factors	973		
	Studies of capsaicin reveal a receptor for sensing high temperatures and other painful stimuli	973		
	More sensory systems remain to be studied	974		
Chapter 34	The Immune System	977		
	Innate immunity is an evolutionarily ancient defense system	978		
	The adaptive immune system responds by using the principles of evolution	979		
34.1	Antibodies Possess Distinct Antigen-Binding and Effector Units	981		
34.2	Antibodies Bind Specific Molecules Through Hypervariable Loops	983		
	The immunoglobulin fold consists of a beta-sandwich framework with hypervariable loops	984		
	X-ray analyses have revealed how antibodies bind antigens	984		
	Large antigens bind antibodies with numerous interactions	986		
34.3	Diversity Is Generated by Gene Rearrangements	987		
	J (joining) genes and D (diversity) genes increase antibody diversity	987		
	More than 10 ⁸ antibodies can be formed by combinatorial association and somatic mutation	988		
	The oligomerization of antibodies expressed on the surfaces of immature B cells triggers antibody secretion	989		
	Different classes of antibodies are formed by the hopping of V _H genes	990		
34.4	Major-Histocompatibility-Complex Proteins Present Peptide Antigens on Cell Surfaces for Recognition by T-Cell Receptors	991		
	Peptides presented by MHC proteins occupy a deep groove flanked by alpha helices	992		
	T-cell receptors are antibody-like proteins containing variable and constant regions	994		
	CD8 on cytotoxic T cells acts in concert with T-cell receptors	994		
	Helper T cells stimulate cells that display foreign peptides bound to class II MHC proteins	996		
	Helper T cells rely on the T-cell receptor and CD4 to recognize foreign peptides on antigen-presenting cells	996		
	MHC proteins are highly diverse	998		
	Human immunodeficiency viruses subvert the immune system by destroying helper T cells	999		
34.5	The Immune System Contributes to the Prevention and the Development of Human Diseases	1000		
	T cells are subjected to positive and negative selection in the thymus	1000		
	Autoimmune diseases result from the generation of immune responses against self-antigens	1001		
	The immune system plays a role in cancer prevention	1001		
	Vaccines are a powerful means to prevent and eradicate disease	1002		
Chapter 35	Molecular Motors	1007		
35.1	Most Molecular-Motor Proteins Are Members of the P-Loop NTPase Superfamily	1008		
	Molecular motors are generally oligomeric proteins with an ATPase core and an extended structure	1008		

ATP binding and hydrolysis induce changes in the conformation and binding affinity of motor proteins	1010		
35.2 Myosins Move Along Actin Filaments	1012		
Actin is a polar, self-assembling, dynamic polymer	1012		
Myosin head domains bind to actin filaments	1014		
Motions of single motor proteins can be directly observed	1014		
Phosphate release triggers the myosin power stroke	1015		
Muscle is a complex of myosin and actin	1015		
The length of the lever arm determines motor velocity	1018		
35.3 Kinesin and Dynein Move Along Microtubules	1018		
Microtubules are hollow cylindrical polymers	1018		
Kinesin motion is highly processive	1020		
35.4 A Rotary Motor Drives Bacterial Motion	1022		
Bacteria swim by rotating their flagella	1022		
Proton flow drives bacterial flagellar rotation	1022		
Bacterial chemotaxis depends on reversal of the direction of flagellar rotation	1024		
<hr/> Chapter 36 Drug Development	1029		
36.1 The Development of Drugs Presents Huge Challenges	1030		
Drug candidates must be potent modulators of their targets	1030		
Drugs must have suitable properties to reach their targets	1031		
Toxicity can limit drug effectiveness	1036		
36.2 Drug Candidates Can Be Discovered by Serendipity, Screening, or Design	1037		
Serendipitous observations can drive drug development	1037		
Screening libraries of compounds can yield drugs or drug leads	1039		
Drugs can be designed on the basis of three-dimensional structural information about their targets	1042		
36.3 Analyses of Genomes Hold Great Promise for Drug Discovery	1045		
Potential targets can be identified in the human proteome	1045		
Animal models can be developed to test the validity of potential drug targets	1046		
Potential targets can be identified in the genomes of pathogens	1046		
Genetic differences influence individual responses to drugs	1047		
36.4 The Development of Drugs Proceeds Through Several Stages	1048		
Clinical trials are time consuming and expensive	1048		
The evolution of drug resistance can limit the utility of drugs for infectious agents and cancer	1050		
Answers to Problems			A1
Selected Readings			B1
Index			C1