GARRETT & GRISHAM

# BIOCHEMISTRY

SECOND EDITION

# Biochemistry

SECOND EDITION

**Reginald H. Garrett**
**Charles M. Grisham**
*University of Virginia*



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*On the Cover:* The structure of UQ-cyt*c* reductase, also known as the cytochrome $bc_1$ complex. Image provided by Johann Deisenhofer and Di Xia, reprinted with permission from *Proceedings of the National Academy of Sciences* **95:** 8028, © 1998 National Academy of Sciences, U.S.A.

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*What Your Colleagues Are Saying About*

# *Garrett & Grisham's BIOCHEMISTRY*

SECOND EDITION

*"I have been partial towards Garrett and Grisham ever since I first looked through it. My opinion is that it is an excellent textbook, that is, overall, extremely well-written. The single-most strength of the book is its ability to serve as a textbook in a two-semester comprehensive course in biochemistry, as well as for a one-semester course that serves mostly pre-professional students."*

MIKE REDDY, University of Wisconsin, Milwaukee

*"The strengths of this book are its readability and lots of illustrations. Overall, I think this is an excellent text."*

JUDY CALLIS, University of California, Davis

*"I use Garrett and Grisham and have used it since its introduction. I look for a high level of coverage of the major topics in biochemistry and the book fills that requirement."*

WILLIAM M. SCOVELL, Bowling Green State University

*"Based on the chapters that I have read, I would say that the overall quality of this book is high. It would seem appropriate for use in either an upper level undergraduate course or a entry level graduate course."*

SIDNEY R. KUSHNER, University of Georgia

*"Well organized and clear. The illustrations are good, providing relevance to humans in addition to useful information. The special topics (the akee tree, migratory birds, desert animals) are interesting and entertaining.*

MARY LUCKEY, San Francisco State University

*The examples of enzyme mechanisms of aspartic proteases, in Chapter 16, specifically HIV-1 protease, and the corresponding protease inhibitors [are] extremely current. Also, the mention of TPA as an agent to promote the breakdown of clots in heart-attack patients is an interesting human application.*

LEIGH A. PLESNIAK, University of San Diego

*"The chapter on enzyme mechanisms is outstanding. The authors are to be congratulated for a superb job with a difficult subject. . . . HIV protease and aspartic protease examples are outstanding! The use of current, interesting, and relevant examples throughout the text is great."*

CHARLES B. GRISSOM, University of Utah

*"My overall impression of this book is extremely positive, and I am quite impressed with the efforts of Garrett and Grisham. The text provides students with an in-depth look into the traditional areas of biochemistry in a very readable format with outstanding illustrations and graphics."*

RUSSELL KERR, Florida Atlantic University

*"I found the book to be very readable and pitched at the level of understanding that I ask from my students. I appreciated the inclusion of a chapter on molecular motors and cytoskeletal fundamentals, as I have used this topic in my class."*

STEVEN M. THEG, University of California, Davis

*"Biochemistry, second edition, by Garrett and Grisham is a very thorough, extremely well illustrated presentation of the essentials of biochemistry. It is appropriate for upper-level undergraduate courses and contains many examples that students will find both interesting and illuminating."*

CHARLES E. MATZ, University of Illinois, Urbana-Champaign

*"Chapter 30 on DNA replication and repair . . . is very current and talks about some of the most important questions that are currently being resolved by scientists studying DNA replication.*

MARC S. WOLD, University of Iowa College of Medicine

*"The manuscript contains timely revisions. . . . [A] good combination of descriptive factorology and atomic structures, interspersed with some quantitative aspects."*

GARY R. KUNKEL, Texas A&M University

# *New To This Edition*

We are grateful to the many users of the first edition and our panel of reviewers for their positive comments and recommendations. Various changes incorporated into this second edition stem from their enthusiasm for this book.

- The complete text is incorporated into a single volume. We accomplished this economy by selective editing and distillation of the material. Chapter 34 includes many essential elements of molecular cell biology.
- A whole new category of *Human Biochemistry* boxes has been added to emphasize the biomedical basis of various diseases and clinical disorders. Students pursuing careers in the biomedical sciences will find these of particular interest.
- We have also added many new *A Deeper Look* and *Critical Development* boxes. These boxes—124 in all—bring biochemistry home to students, deepening and enriching their understanding of the subject.
- Much of the artwork has been modified to reflect recent advances.
- New molecular graphics prepared by Michael Sabat at the University of Virginia have been added to help students better understand protein structure.
- Individual chapters have been modified as follows:

  **Chapter 3:** Covers thermodynamics (formerly covered in Chapter 15) and "energy-rich" compounds

  **Chapter 6:** Describes Rose and Srinivasan's computer algorithm to predict the tertiary structure of proteins from their amino acid sequences. Protein folding and tertiary structure prediction remain a major intellectual frontier in molecular biology

  **Chapters 9 and 10:** Present membranes and cell surfaces and the new paradigms for the structures of pore-forming toxins and transport proteins

  **Chapter 12:** Includes the recently solved atomic structure of nuclesomes complexed with DNA

  **Chapter 13:** Describes experimental protocols for functional genomics and the construction and screening of combinatorial libraries

  **Chapter 15:** Presents glycogen phosphorylase as a paradigm for the major concepts in enzyme regulation: allosteric control and covalent modification through reversible phorphorylation

  **Chapter 17:** A brand-new chapter, *Molecular Motors* describes protein assemblies involved in movements at the cellular and subcellular levels

  **Chapter 18:** Now covers human nutrition as well as an introduction to metabolism

  **Chapter 20:** Considers the intriguing possibility that, early in biological evolution, the citric acid cycle ran in reverse to drive reductive $CO_2$ fixation

  **Chapter 21:** Presents the newly revealed atomic structures of Complex III (the cytochrome $bc_1$ complex) and Complex IV (cytochrome oxidase)

  **Chapter 22:** Covers the newly solved crystal structure of Photosystem I

  **Chapter 26:** Features the crystal structure of the $N_2$-fixing enzyme nitrogenase

  **Chapter 28:** Placed appropriately at the end of the section on metabolism, this chapter includes an integrated systems analysis view of metabolism

  **Chapter 29:** Highlights the molecular model for recombination at the Holliday junction

  **Chapter 30:** Offers the latest insights into the replisome, the molecular machine that replicates DNA

  **Chapter 31:** Reveals our enhanced understanding of the assembly of RNA polymerase and reviews the properties of DNA-binding proteins that serve as transcription regulators

  **Chapter 32:** Focuses on the conceptual basis for the "second genetic code": the highly specific recognition of the appropriate amino acid and tRNA substrates by aminoacyl-tRNA synthetases

  **Chapter 33:** Graphically depicts ribosome structure and function, the role of chaperones as participants in protein folding, the importance of proteolysis in protein level regulation, and the role of ubiquitination and the 26S proteasome degradation

  **Chapter 34:** This Special Topic chapter (highlighted by separate pagination) reviews the mechanisms by which cells interpret and respond to hormones, neurotransmitters and light. The role of scaffold proteins in the assembly of heteromeric signaling complexes is also thoroughly introduced.

**Our Interactive Biochemistry CD-ROM** (available packaged with the text), developed by Charles Grisham, includes many 3-D protein graphics, virtual reality animations, and interactive exercises.

This icon (  ) indicates various subjects throughout the text that are keyed to the CD-ROM.

# About the Authors

**Reginald H. Garrett** was educated in the Baltimore city public schools and at the Johns Hopkins University, where he received his Ph.D. in biology in 1968. Since that time, he has been at the University of Virginia, where he is currently professor of biology. He is the author of numerous papers and review articles on biochemical, genetic, and molecular biological aspects of inorganic nitrogen metabolism. Since 1964, his research interests have centered on the pathway of nitrate assimilation in filamentous fungi. His investigations have contributed substantially to our understanding of the enzymology, genetics, and regulation of this major pathway of biological nitrogen acquisition. His research has been supported by grants from the National Institutes of Health, the National Science Foundation, and private industry. He is a former Fulbright Scholar and has been a Visiting Scholar at the University of Cambridge on two sabbatical occasions. He has taught biochemistry at the University of Virginia for 30 years. He is a member of the American Society for Biochemistry and Molecular Biology.

**Charles M. Grisham** was born and raised in Minneapolis, Minnesota, and educated at Benilde High School. He received his B.S. in chemistry from the Illinois Institute of Technology in 1969 and his Ph.D. in chemistry from the University of Minnesota in 1973. Following a postdoctoral appointment at the Institute for Cancer Research in Philadelphia, he joined the faculty of the University of Virginia, where he is professor of chemistry. He has authored numerous papers and review articles on active transport of sodium, potassium, and calcium in mammalian systems, on protein kinase C, and on the applications of NMR and EPR spectroscopy to the study of biological systems. His work has been supported by the National Institutes of Health, the National Science Foundation, the Muscular Dystrophy Association of America, the Research Corporation, the American Heart Association and the American Chemical Society. He is a Research Career Development Awardee of the National Institutes of Health, and in 1983 and 1984 he was a Visiting Scientist at the Aarhus University Institute of Physiology, Aarhus, Denmark. He has taught biochemistry and physical chemistry at the University of Virginia for 24 years. He is a member of the American Society for Biochemistry and Molecular Biology.

*Left to right:* Reginald Garrett, Clancy, Charles Grisham
*(Rosemary Jurbala Grisham)*

# Preface

Scientific understanding of the molecular nature of life is growing at an astounding rate. Significantly, society is the prime beneficiary of this increased understanding. Cures for diseases, better public health, remediations for environmental pollution, and the development of cheaper and safer natural products are just a few practical benefits of this knowledge.

In addition, this expansion of information fuels, in the words of Thomas Jefferson, *"the illimitable freedom of the human mind."* Scientists can use the tools of biochemistry and molecular biology to explore all aspects of an organism—from basic questions about its chemical composition, through inquiries into the complexities of its metabolism, its differentiation and development, to analysis of its evolution and even its behavior. Biochemistry is a science whose boundaries now encompass all aspects of biology, from molecules to cells, to organisms, to medicine, and to ecology.

As the explication of natural phenomena rests more and more on biochemistry, its inclusion in undergraduate and graduate curricula in biology, chemistry, and the health sciences becomes imperative. And the challenge to authors and instructors is a formidable one: how to familiarize students with the essential features of modern biochemistry in an introductory course or textbook.

Fortunately, the increased scope of knowledge allows scientists to make generalizations connecting the biochemical properties of living systems with the character of their constituent molecules. As a consequence, these generalizations, validated by repetitive examples, emerge in time as principles of biochemistry, principles that are useful in discerning and describing new relationships between diverse biomolecular functions and in predicting the mechanisms underlying newly discovered biomolecular processes.

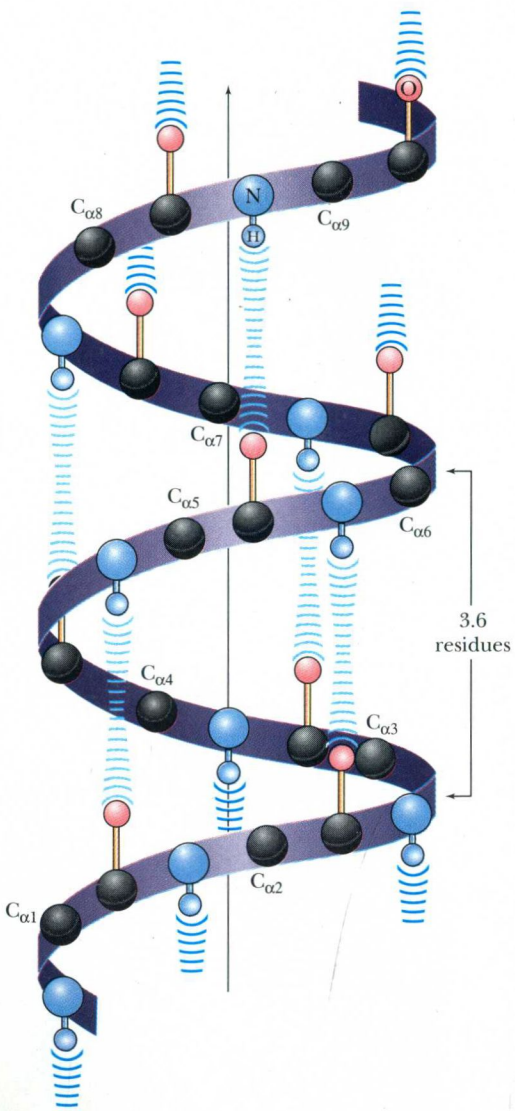
This biochemistry textbook is designed to communicate the fundamental principles governing the structure, function, and interactions of biological molecules to students encountering biochemistry for the first time. We aim to bring an appreciation of the science of biochemistry to a broad audience that includes undergraduates majoring in biology, chemistry, or premedical programs, as well as medical students and graduate students in the various health sciences for whom biochemistry is an important route to understanding human physiology.

We are both biochemists, but one of us is in a biology department, and the other is in a chemistry department. Undoubtedly, our approaches to biochemistry are influenced by the academic perspectives of our respective disciplines. We believe, however, that our collaboration on this textbook represents a melding of our perspectives that will provide new dimensions of appreciation and understanding for all students.

## Features and Organization

The organizational approach we have taken in this textbook is traditional in that it builds from the simple to the complex. Part I, **Molecular Components of Cells,** creates a continuum between biochemistry and the prerequisite course in organic chemistry that should precede it. This section starts with the basics—the structure and hierarchical organization of biomolecular structures in cells (Chapter 1) and the central role of water as the solvent of life (Chapter 2). Chapter 3, *Thermodynamics of Biological Systems* presents fundamental thermodynamic relationships useful for understanding the energetics of cellular metabolism. The thermodynamics of protein folding is illustrated as an apt example for the relative contributions of enthalpy and entropy changes to free energy changes in biological systems. This chapter also discusses the particular chemical features of ATP and other biomolecules that make these substances effective as cellular energy carriers.

Chapter 4: *Amino Acids* begins our survey of biomolecules by describing the structure and chemistry of these substances that serve as the monomeric units of proteins. Chapters 5 and 6: *Proteins—Their Biological Functions and Primary Structure* and *Proteins—Secondary, Tertiary, and Quaternary Structure* are devoted to a fresh and comprehensive description of the molecular anatomy of proteins, illustrated by a gallery of ribbon diagrams and space-filling computer graphics that capture the diversity of these structurally most sophisticated of all the biological macromolecules.




Chapter 7: *Carbohydrates* and Chapter 8: *Lipids* describe the structure and chemistry of these great classes of biomolecules, allowing an in-depth exploration of the structure, chemistry, and function of the architectural features that define cellular boundaries in Chapter 9: *Membranes and Cell Surfaces.* Highlights of Chapter 9 include the structural chemistry of lipid-anchored membrane proteins and the complex proteoglycan structures that adorn cell surfaces. Chapter 10: *Membrane Transport* then addresses the intriguing question of how cells acquire nutrients and dispose of waste despite their enclosure within otherwise impermeable envelopes.

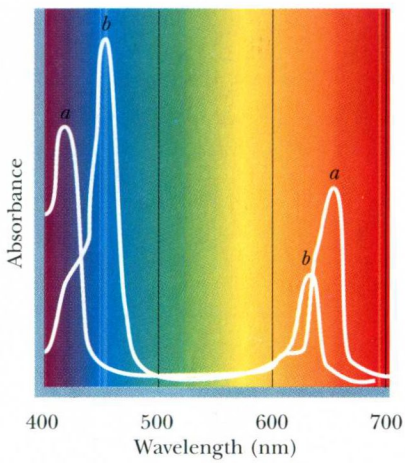
Chapter 11: *Nucleotides and Nucleic Acids* describes the chemistry of nucleotides and the organization of these units into the polymeric macromolecules, ribonucleic acid and deoxyribonucleic acid (RNA and DNA). Chapter 12: *Structure of Nucleic Acids* is highlighted by an explanation of the structural order in the various forms of the DNA double helix (the ABZs of DNA structure). A chapter on recombinant DNA technology (Chapter 13: *Recombinant DNA: Cloning and Creation of Chimeric Genes*) is provided at this point in the text to familiarize students with the basic concepts and applications of this methodology. This technology is one of the newest tools available to biochemical research, and its enormous success in illuminating the relationships between genetic information, biomolecular structure, and biomolecular function is unparalleled. Some instructors might prefer to present lipids and carbohydrates after a discussion of nucleotides and nucleic acids, and these chapters have been written so that this alternative sequence of presentation will go smoothly. The chapters of Part I, like all the chapters in this text, feature **Text Boxes** of three kinds: **Human Biochemistry, A Deeper Look,** and **Critical Developments in Biochemistry.** These text boxes focus on aspects of medical biochemistry or delve a little deeper into selected topics or experimental observations, drawing the student into a greater appreciation for the relevance, logic, and historical context of significant biochemical advances.

Part II, **Protein Dynamics,** begins with a quantitative but easily grasped discussion of the kinetics of enzyme-catalyzed reactions (Chapter 14). Also described are the exciting new discoveries of catalytic roles for certain RNA

molecules (so-called *ribozymes*) and the purposeful design of antibodies with catalytic properties (dubbed *abzymes*). Chapter 15: *Enzyme Specificity and Regulation* reviews mechanisms by which enzymes—and hence metabolic processes—are regulated. Highlights of this chapter include a close scrutiny of structure-function relationships in glycogen phosphorylase and its regulation by allosteric mechanisms and reversible phosphorylation. The atomic structure of this paradigm of allosteric enzymes has been solved by x-ray crystallography, and the details of its structure provide fundamental insights into the catalytic and regulatory properties of enzymes. This chapter concludes with a special focus on hemoglobin and its allosteric properties.

Chapter 16: *Mechanisms of Enzyme Action* presents the basic physicochemical principles of transition-state stabilization that underlie the catalytic power of enzymes. It also examines a gallery of enzyme mechanisms, including the well-studied serine proteases and aspartic proteases. This latter class includes the clinically important HIV aspartic protease (HIV is the causative agent in AIDS). Chapter 17: *Molecular Motors* collects in one chapter a discussion of molecular motors—protein complexes that transduce chemical energy into the mechanics of movement. Included here is a discussion of the structure and function of muscle, as well as other systems of movement, such as the movement of cilia, vesicle and organelle transport within cells by kinesin and dynein, and the novel rotating mechanism by which flagella impart motion to cells.

Part III, **Metabolism and Its Regulation,** encompassing Chapters 18 through 28, describes the metabolic pathways that orchestrate the synthetic and degradative chemistry of life. Emphasis is placed on the chemical logic of intermediary metabolism. Chapter 18: *Metabolism: An Overview* points out the basic similarities in metabolism that unite all forms of life and gives a survey of nutrition and the underlying principles of metabolism, with particular emphasis on the role of vitamins as coenzymes. The fundamental aspects of catabolic metabolism are described in Chapter 19: *Glycolysis,* Chapter 20: *The Tricarboxylic Acid Cycle,* and Chapter 21: *Electron Transport and Oxidative Phosphorylation.* The contemporary view that energy coupling in mitochondria is probably nonstoichiometric, yielding a P/O ratio of 2.5 rather than the traditionally held value of 3.0, is a pertinent feature of Chapter 21.




The photosynthetic processes that provide the energy and fundamental carbohydrate synthesis upon which virtually all life depends are described in Chapter 22: *Photosynthesis.* Focal points of this chapter include the exciting new descriptions of the molecular structure of photosynthetic reaction centers and the mechanism and regulation of ribulose bisphosphate carboxylase. Chapter 23: *Gluconeogenesis, Glycogen Metabolism, and the Pentose Phosphate Pathway* includes a detailed discussion of carbohydrate metabolism beyond glycolysis and stresses the interconnections and interrelationships between the different pathways of carbohydrate conversion. A two-chapter discussion of lipid metabolism follows. Chapter 24: *Fatty Acid Catabolism* describes the pathways of fatty acid oxidation, whereas Chapter 25: *Lipid Biosynthesis* details the novel properties of acetyl-CoA carboxylase, which catalyzes the principal regulated step in fatty acid biosynthesis, and lays out the metabolic pathways for synthesis of cholesterol and the biologically active lipids (eicosanoids and steroid hormones).

Chapter 26: *Nitrogen Acquisition and Amino Acid Metabolism* gives greater emphasis than similar chapters in other textbooks to the biological acquisition of inorganic nitrogen from the inanimate environment and examines the pathways for degradation and biosynthesis of amino acids. Chapter 27: *The Synthesis and Degradation of Nucleotides* profiles purine and pyrimidine metabolism and spotlights the biochemical basis of genetic defects in these pathways and the potential for pharmacological intervention to control unwanted cell proliferation, such as occurs in cancer or microbial infections. Chapter 28: *Metabolic Integration and the Unidirectionality of Pathways* is unique among textbook chapters

in defining the essentially unidirectional nature of metabolic pathways and the stoichiometric role of ATP in driving vital processes that are thermodynamically unfavorable. This chapter also reveals the interlocking logic of metabolic pathways and the metabolic relationships between the various major organs of the human body.

Part IV, **Information Transfer,** addresses the storage and transmission of genetic information in organisms, as well as mechanisms by which organisms interpret and respond to chemical and physical information coming from the environment. The historical documentation of DNA molecules as the repository of inheritable information is presented in Chapter 29: *DNA: Genetic Information, Recombination, and Mutation,* along with the latest discoveries unraveling the molecular mechanisms underlying genetic recombination. Chapter 30: *DNA Replication and Repair* treats the biochemistry involved in the maintenance and the replication of genetic information for transmission to daughter cells, accenting exciting new information on the complex enzymatic choreography of DNA replication. Chapter 31: *Transcription and the Regulation of Gene Expression* then characterizes the means by which DNA-encoded information is expressed through synthesis of RNA and how expression of this information is regulated. Highlights of this chapter include the molecular structure and mechanism of RNA polymerase and the DNA-binding transcription factors that modulate its activity.

Chapter 32: *The Genetic Code* recounts the biochemical approaches that "cracked" the genetic code and describes the molecular events that underlie the "second" genetic code—how aminoacyl-tRNA synthetases uniquely recognize their specific tRNA acceptors. Chapter 33: *Protein Synthesis and Degradation* presents the structure and function of ribosomes, with emphasis on the interesting new realization that 23S rRNA is the peptidyl transferase enzyme responsible for peptide bond formation. This chapter also discusses the new appreciation of heat-shock proteins as molecular chaperones in the proper folding of proteins, and the emerging importance of protein degradation as a means to regulate cellular levels of specific proteins.

Chapter 34: *The Reception and Transmission of Extracellular Information* pulls together an up-to-date perspective on the rapidly changing field of cellular signaling and stresses the information transfer aspects involved in the interpretation of environmental information, with coverage of hormone action, signal transduction cascades, membrane receptors, oncogenes, tumor suppressor genes, sensory transduction and neurotransmission, and the biochemistry of neurological disorders.

## Acknowledgments

We are indebted to the many experts in biochemistry and molecular biology who carefully reviewed the manuscript at several stages for their outstanding and invaluable advice on how to construct an effective textbook. Their names are cited in the *List of Reviewers* at the end of this Preface.

We wish to warmly and gratefully acknowledge many other people who assisted and encouraged us in this endeavor. These include the highly skilled and dedicated professionals at Saunders College Publishing. Prominent among them are our publisher John Vondeling, who recruited us to this monumental task and who relentlessly urged us to its completion, and Sandi Kiselica,, our Developmental Editor. Sandi's singular purpose brought this project to fruition by keeping us focused on the matters at hand, the urgencies of the schedule, and limits of scale in a textbook's dimensions. We also applaud the unsung but absolutely indispensable contributions by those colleagues whose efforts trans-

formed a rough manuscript into this final product: Charlene Squibb, the Senior Production Manager, Carol Bleistine, the Art Director, and our Project Editors, Linda Boyle Riley, Beth Ahrens, and especially Sarah Fitz-Hugh. Sarah has been the loyal steward of this text through all its incarnations; we appreciate her work and cherish our friendship with her. We also credit Pauline Mula, who is more than the Marketing Director, she is our friend. If this book has visual appeal and editorial grace, it is due to them. The beautiful illustrations that not only decorate this text but explain its contents are a testament to the creative and tasteful work of the team at Dartmouth Graphics and to the legacy of John Woolsey and Patrick Lane at J/B Woolsey Associates. We are thankful to our many colleagues who provided original art and graphic images for this work, particularly Professor Jane Richardson of Duke University, who gave us numerous original line drawings of the protein ribbon structures. Michael Sabat and Mindy Whaley prepared the molecular graphics displayed herein. Flora Lackner cheerfully accomplished the tedious but essential task of compiling the index. Peter T. Gates contributed to the proofreading of this manuscript. We owe a very special thank-you to our spouses, especially to Rosemary Jurbala Grisham whose tireless work as our photograph acquisitions specialist was but a small measure of her forbearance and dedication. Also to be acknowledged with love and appreciation are our children Jeffrey, Randal, and Robert Garrett, and David, Emily, and Andrew Grisham, and finally Clancy, a Golden retriever of epic patience and perspicuity. With the publication of this second edition, we celebrate and commemorate the role of our mentors in bringing biochemistry to life for us—Alvin Nason, Kenneth R. Schug, William D. McElroy, Ronald E. Barnett, Maurice J. Bessman, Albert S. Mildvan, Ludwig Brand, and Rufus Lumry.

**Reginald H. Garrett**
**Advance Mills, VA**

**Charles M. Grisham**
**Ivy, VA**
*September 1998*

# List of Reviewers

*We are very grateful to these reviewers for their careful reading of the manuscript. Their suggestions have proven invaluable.*

Michael Behe, *Lehigh University*
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Scott Champney, *East Tennessee State University, School of Medicine*
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Gail Willsky, *State University of New York, Buffalo*
Marc Wold, *University of Iowa, College of Medicine*

# Support Package

**Study Guide** by David Jemiolo (Vassar College) and Steven Theg (University of California, Davis) contains chapter summaries, **detailed solutions** to all end-of-chapter problems, chapter objectives, additional problems with answers, self-tests, important definitions, and illustrations of major metabolic pathways.

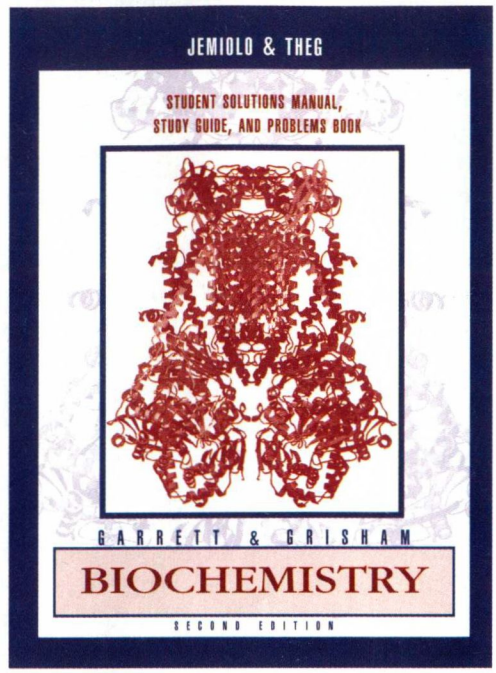
**Interactive Biochemistry CD-ROM,** developed by Charles Grisham at the University of Virginia, includes three-dimensional protein graphics, virtual reality animations, and hundreds of interactive Java-based exercises. The presence of the blue icon (shown at left) throughout the text indicates links to the CD-ROM.

**Saunders Web site** for Biochemistry can be accessed through the following address, www.saunderscollege.com. It includes PowerPoint lecture images to accompany this text.

**Overhead Transparency Acetates** include 200 of the pedagogically important figures from the text.

**Instructor's Resource CD-ROM** is a teacher tool containing the images from the text.

**Test Bank** by Charles Matz (University of Illinois) includes over 1000 multiple-choice questions for professors to use as tests, quizzes, and homework assignments. The bank of questions is available in printed form, and in computerized form for Macintosh and Windows users.

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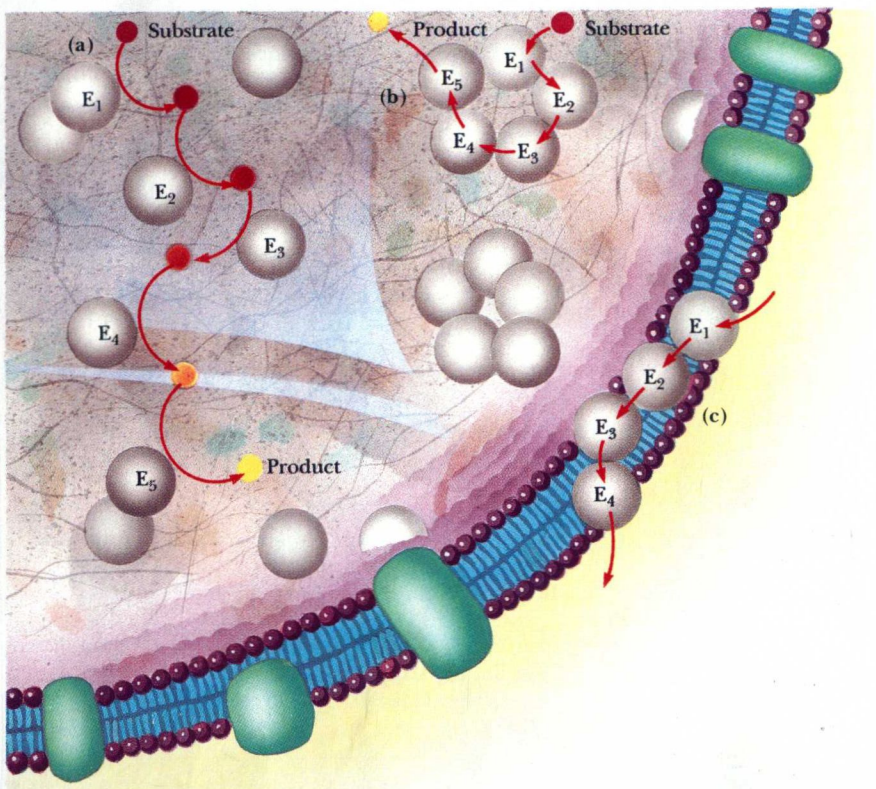
# Dedication

*We dedicate this book to those whose parental influences kindled our curiosity and unerringly, though unintentionally, led us to explore science and questions about the nature of life:*

Cora Blankenship
William W. Garrett
Marjorie K. Garrett
Lelia B. Bosley
Mary Charlotte Markell Grisham
Ernest M. Grisham

# Contents in Brief





# List of Boxes

## HUMAN BIOCHEMISTRY



## CRITICAL DEVELOPMENTS IN BIOCHEMISTRY



## A DEEPER LOOK