教育部高等教育司推荐
国外优秀生命科学教学用书

Biochemistry

生物化学

影印版

Second Edition

• Reginald H. Garrett

• Charles M. Grisham

高等教育出版社
Higher Education Press

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University of Virginia

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Biochemistry, Second Edition
Reginald H. Garrett, Charles M. Grisham

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出 版 前 言

随着克隆羊的问世和人类基因组计划的完成，生命科学成为21世纪名副其实的领头学科，生物高新技术产业逐步成为高科技产业的核心。生物科技和生物产业的发展对世界科技、经济、政治和社会发展等方面产生着深刻的影响，这也是我国赶超世界发达国家生产力水平最有前途和希望的领域。生命科学与技术全方位的发展呼唤高等教育培养更多高水平的复合型科技人才。

为此，教育部在《关于加强高等学校本科教学工作　提高教学质量的若干意见》[教高（2001）4号文件]中提出，高等学校要大力提倡编写、引进和使用先进教材，其中信息科学、生命科学等发展迅速、国际通用性强、可比性强的学科和专业可以直接引进先进的、能反映学科发展前沿的原版教材。教育部高等教育司还于2001年11月向全国主要大学和出版社下发了“关于开展‘国外生命科学类优秀教学用书’推荐工作的通知”，有力推动了生命科学类教材的引进工作。

高等教育出版社对国外生命科学教材进行了充分的调研，并委托教育部高等学校生物科学与工程教学指导委员会的专家教授开展了“引进国外优秀生命科学教材及其教学辅助材料专项研究”，并就国内外同类教材进行了比较，提出了具体的引进教材书目。经过版权谈判，目前我社已经购买了 Pearson Education, McGraw-Hill, John Wiley & Sons, Blackwell Science, Thomson Learning, Cambridge University Press, Lippincott Williams & Wilkins 等出版的13种教材的影印权，学科领域涉及生物化学、细胞生物学、遗传学、微生物学、生态学、免疫学、神经科学、发育生物学、解剖学与生理学、分子生物学、普通生物学等。这些教材具有以下特点：（1）所选教材基本是近2年出版的，及时反映了学科发展的最新进展，在国际上使用广泛，具有权威性和时代感；（2）内容简明，篇幅适中，结构合理，兼具一定的深度和广度，适用范围广；（3）插图精美、丰富，既有很强的艺术性，又不失严谨的科学性，图文并茂，与正文相辅相成；（4）语言简练、流畅，十分适合非英语国家的学生阅读。其中9种已入选教育部高等教育司推荐“国外优秀生命科学教学用书”。

考虑到中国国情，为了让学生买得起，同时又能让学生看到原版书彩色精美的插图，我们在引进学生用原版教材时，一方面采用黑白影印，最大限度地降低定价，另一方面随书附赠含有原书彩色插图的光盘，以充分体现原教材的风格、特色，为读者提供方便。

引进国外优秀生命科学教学用书是我社一项长期的重点工作，因此，我们衷心希望广大专家教授和同学提出宝贵的意见和建议，如有更好的教材值得引进，请与高等教育出版社生命科学分社联系，联系电话：010-68344002，E-mail 地址：lifesciences-hep@x263.net。

高等教育出版社

2002年11月

国外优秀生命科学教学用书

（影印教材）

Biochemistry (2nd ed.)	生物化学
Cell and Molecular Biology (3rd ed.)	分子细胞生物学
Essentials of Genetics (4th ed.)	遗传学基础
Microbiology (5th ed.)	微生物学
Ecology: concepts and applications (2nd ed.)	生态学
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Essential Developmental Biology	发育生物学基础
Understanding Human Anatomy and Physiology (4th ed.)	人体解剖生理学
Gene Cloning and DNA Analysis (4th ed.)	基因克隆和 DNA 分析
Principles of Gene Manipulation (6th ed.)	基因操作原理
An Introduction to Genetic Engineering (2nd ed.)	遗传工程导论
Essential Biology	生物学导论

Abbreviations for Amino Acids

Alanine	Ala	A	Leucine	Leu	L
Arginine	Arg	R	Lysine	Lys	K
Asparagine	Asn	N	Methionine	Met	M
Aspartate	Asp	D	Phenylalanine	Phe	F
Cysteine	Cys	C	Proline	Pro	P
Glutamate	Glu	E	Serine	Ser	S
Glutamine	Gln	Q	Threonine	Thr	T
Glycine	Gly	G	Tryptophan	Trp	W
Histidine	His	H	Tyrosine	Tyr	Y
Isoleucine	Ile	I	Valine	Val	V

The Standard Genetic Code

AAA	Lysine	CAA	Glutamine	GAA	Glutamate	UAA	stop
AAC	Asparagine	CAC	Histidine	GAC	Aspartate	UAC	Tyrosine
AAG	Lysine	CAG	Glutamine	GAG	Glutamate	UAG	stop
AAU	Asparagine	CAU	Histidine	GAU	Aspartate	UAU	Tyrosine
ACA	Threonine	CCA	Proline	GCA	Alanine	UCA	Serine
ACC	Threonine	CCC	Proline	GCC	Alanine	UCC	Serine
ACG	Threonine	CCG	Proline	GCG	Alanine	UCG	Serine
ACU	Threonine	CCU	Proline	GCU	Alanine	UCU	Serine
AGA	Arginine	CGA	Arginine	GGA	Glycine	UGA	stop
AGC	Serine	CGC	Arginine	GGC	Glycine	UGC	Cysteine
AGG	Arginine	CGG	Arginine	GGG	Glycine	UGG	Tryptophan
AGU	Serine	CGU	Arginine	GGU	Glycine	UGU	Cysteine
AUA	Isoleucine	CUA	Leucine	GUA	Valine	UUA	Leucine
AUC	Isoleucine	CUC	Leucine	GUC	Valine	UUC	Phenylalanine
AUG	Methionine*	CUG	Leucine	GUG	Valine	UUG	Leucine
AUU	Isoleucine	CUU	Leucine	GUU	Valine	UUU	Phenylalanine

*AUG also serves as the principal initiation codon.

Physical Constants

Name	Symbol	SI Units	cgs Units
Avogadro's number	N	6.022137×10^{23}/mol	6.022137×10^{23}/mol
Boltzmann constant	k	1.38066×10^{-23} J/K	1.38066×10^{-16} erg/K
Curie	Ci	3.7×10^{10} d/s	3.7×10^{10} d/s
Electron charge	e	1.602177×10^{-19} coulomb†	4.80321×10^{-10} esu
Faraday constant	$\mathcal{F}$	96485 J/V · mol	9.6485×10^{11} erg/V · mol
Gas constant*	R	8.31451 J/K · mol	8.31451×10^{7} erg/K · mol
Gravity acceleration	g	9.80665 m/s^2	980.665 cm/s^2
Light speed (vacuum)	c	2.99792×10^{8} m/s	2.99792×10^{10} cm/s
Planck's constant	h	6.626075×10^{-34} J · s	6.626075×10^{-27} erg · s

*Other values of R: 1.9872 cal/K · mol = 0.082 liter · atm/K · mol

†1 coulomb = 1 J/V

Conversion Factors

Energy: 1 Joule = 10^7 ergs = 0.239 cal
1 cal = 4.184 Joule

Length: 1 nm = 10 Å = $1 \times {}^{-7}$ cm

Mass: 1 kg = 1000 g = 2.2 lb
1 lb = 453.6 g

Pressure: 1 atm = 760 torr = 14.696 psi
1 torr = 1 mm Hg

Temperature: K = °C + 273
C = (5/9)(°F − 32)

Volume: 1 liter = 1×10^{-3} m^3 = 1000 cm^3

Useful Equations

The Henderson–Hasselbalch Equation
$pH = pK_a + \log([A^-]/[HA])$

The Michaelis–Menten Equation
$v = V_{max}[S]/(K_m + [S])$

Temperature Dependence of the Equilibrium Constant
$\Delta H° = -Rd(\ln K_{eq})/d(1/T)$

Free Energy Change under Non-Standard-State Conditions
$\Delta G = \Delta G° + RT \ln ([C][D]/[A][B])$

Free Energy Change and Standard Reduction Potential
$\Delta G°' = -n\mathcal{F}\Delta\mathscr{E}'_o$

Reduction Potentials in a Redox Reaction
$\Delta\mathscr{E}'_o = \mathscr{E}'_o(\text{acceptor}) - \mathscr{E}'_o(\text{donor})$

The Proton-Motive Force
$\Delta p = \Delta\Psi - (2.3RT/\mathcal{F})\Delta pH$

Passive Diffusion of a Charged Species
$\Delta G = G_2 - G_1 = RT \ln(C_2/C_1) + Z\mathcal{F}\Delta\Psi$

Synopsis of Icon and Color Use in Illustrations

The following symbols and colors are used in this text to help in illustrating structures, reactions, and biochemical principles.

Elements:

= Oxygen = Nitrogen = Phosphorus = Sulfur = Carbon = Chlorine

Small molecules and groups, which are common reactants or products in many biochemical reactions, are symbolized by the following icons:

Water

Carbon dioxide

Molecular nitrogen

Molecular oxygen

Inorganic phosphate (P_i)

Pyrophosphate (PP_i)

Icon representing adenosinetriphosphate:

Electrons:  or  **Protons (hydrogen ions):** 

Sugars:


Glucose


Galactose


Mannose


Fructose


Ribose

Nucleotides:

= Guanine = Cytosine = Adenine = Thymine = Uracil

Amino acids:

= Non-polar/hydrophobic = Polar/uncharged = Acidic = Basic

Enzymes:

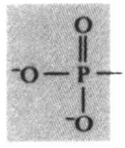
+ = Enzyme activation

⊘ = Enzyme inhibition or inactivation

= Enzyme  = Enzyme Enzyme names are printed in red.

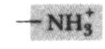
In reactions, blocks of color over parts of molecular structures are used so that discrete parts of the reaction can be easily followed from one intermediate to another and it is easy to see where the reactants originate and how the products are produced.

Some examples:

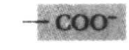


Phosphoryl group

Hydroxyl group



Amino group



Carboxyl group

Red arrows are used to indicate nucleophilic attack. 

These colors are internally consistent within reactions and are generally consistent within the scope of a chapter or treatment of a particular topic.

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

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

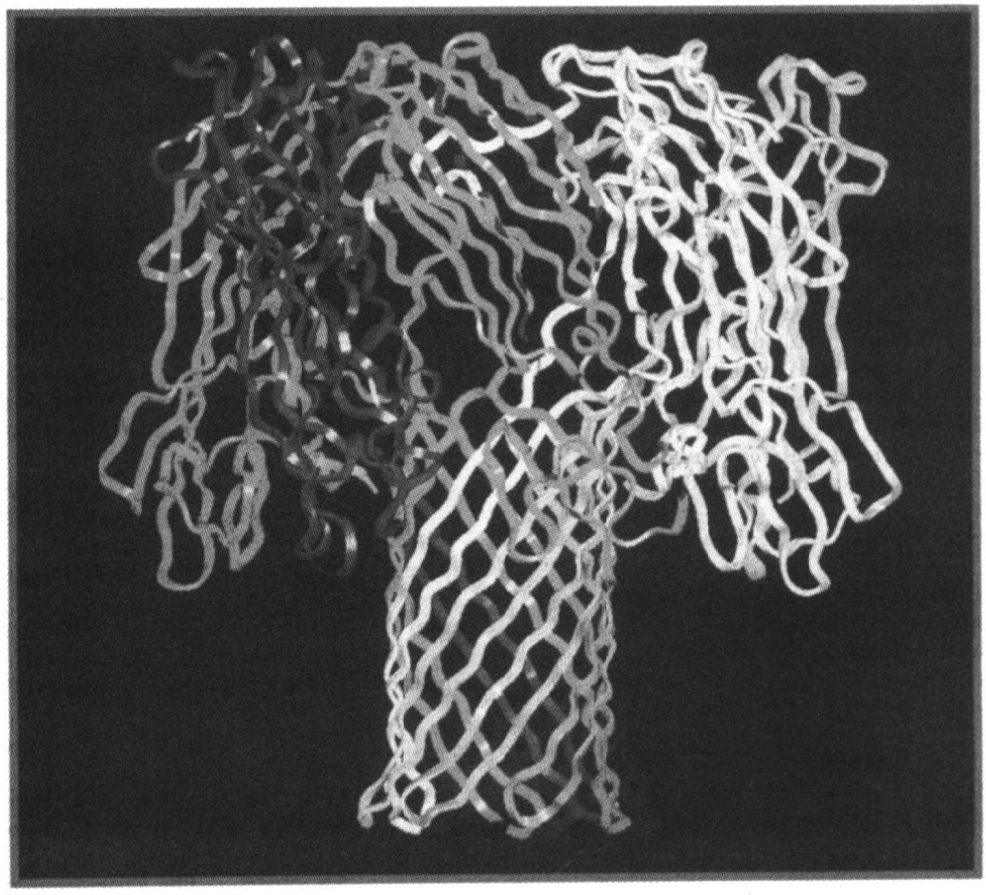
  Chapter 32: Focuses on the conceptual basis for the "second genetic code": the highly specific recognition of the appropriate amino acid and tRNA substrates by aminoacyl-tRNA synthetases

  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.

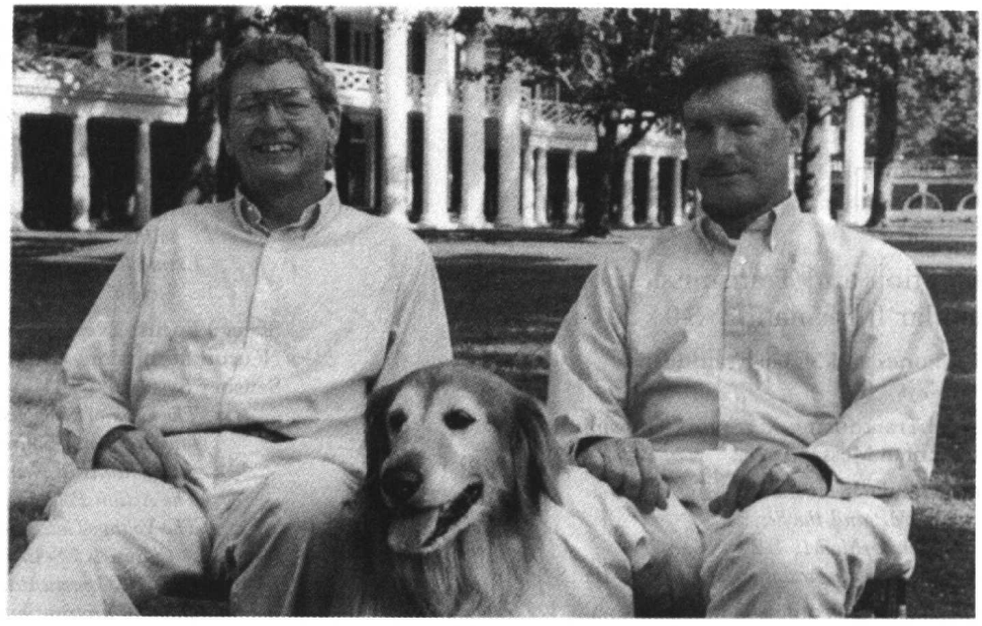
This icon ( ) indicates various subjects throughout the text that are keyed to the CD-ROM.



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.

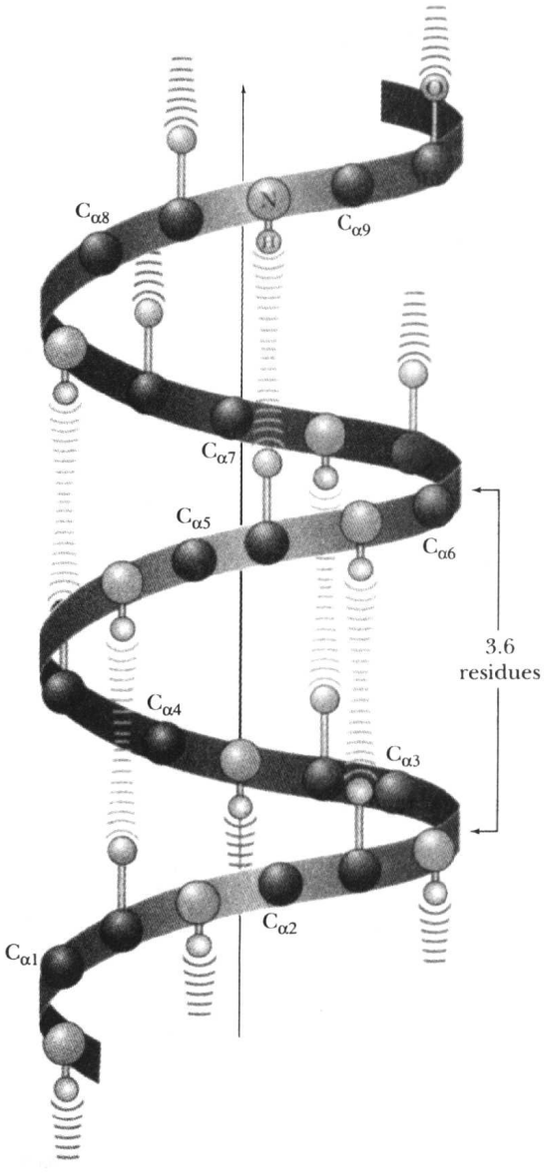
This biochemistry textbook is designed to communicate the fundamental principles governing the structure, function, and interactions of biological molecules to students encountering biochemistry for the first time. We aim to bring an appreciation of the science of biochemistry to a broad audience that 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.

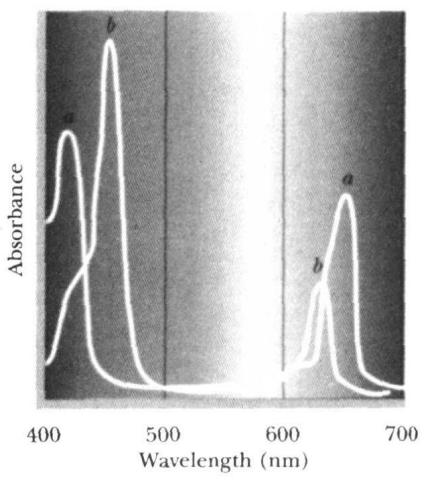
Chapter 11: *Nucleotides and Nucleic Acids* describes the chemistry of nucleotides and the organization of these units into the polymeric macromolecules, ribonucleic acid and deoxyribonucleic acid (RNA and DNA). Chapter 12: *Structure of Nucleic Acids* is highlighted by an explanation of the structural 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.

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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.

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