

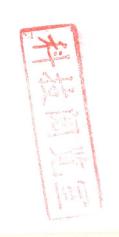
# BIOCHEMISTRY

### J. David Rawn

**Towson State University** 









### NEIL PATTERSON PUBLISHERS

Carolina Biological Supply Company Burlington, North Carolina

### **Biochemistry**

Copyright © 1989 by Carolina Biological Supply Company

All rights reserved. No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or other means, without the prior written permission of the publisher.

Exclusive rights for manufacture and export belong to Neil Patterson Publishers of Carolina Biological Supply Company. The International Edition cannot be exported from the country to which Neil Patterson Publishers has consigned it unless prior written permission is obtained from Neil Patterson Publishers.

Printed in the United States of America: March and June, 1989

Library of Congress Cataloging-in-Publication Data

Rawn, J. David, 1944-

Biochemistry / J. David Rawn.

p. cm.

Includes bibliographies and index.

ISBN 0-89278-400-8—ISBN 0-89278-406-7 (loose-leaf)

ISBN 0-89278-405-9 (International ed.: pbk.)

1. Biochemistry. I. Title.

QP514.2.R39 1989

574.19'2—dc20

89-12206

Color separations for Chapters 1 through 22 and composition are by York Graphic Services, Inc.; balance of separations and printing and binding are by W. A. Krueger Co., Wisconsin Book Division. The text is set in Times Roman; the figure legends are set in Frutiger.

Cover image: Interaction between the DNA-binding domains of cI and the operator site  $O_{R1}$ . (Courtesy of Kim M. Gernert, based on coordinates provided by Carl O. Pabo.)

#### NEIL PATTERSON PUBLISHERS

Carolina Biological Supply Company 1308 Rainey Street Post Office Drawer 2827 Burlington, North Carolina 27216-2827

U. S. A.

Telephone 800 227-1150

919 226-6000

Facsimile 919 222-1926

*Telex* 574354

Cable SQUID

Credits

Publishing Manager:

Neil Patterson

General Manager:

Geoffrey L. Leister

Chief Financial Officer:

Robert L. Saffelle, Jr.

Business Manager:

Robert E. Knauff

Controller:

Charles R. Coté

Editorial Manager:

Sherri Foster

Editors:

Leslie P. Daisy Katherine C. Hodgin Terri L. O'Quin Sue Olsen Judith A. Swan

Editorial Operations Manager:

Kay M. White

Principal Artist:

Lisa A. Shoemaker

Art Production Manager:

Michael S. Webb

Contributing Artists:

Susan C. Averill, Wynne L. Brown, Barbara L. Davison, Tom C. Edgerton, Brian D. Eller, Patricia W. Johnson, Sandy S. Judy, Florence J. Kabir, Sarah Crenshaw McQueen,

Linda LeFevre Murray, Amy B. Wright

Chemistry Design:

George Sauer

Permissions:

Yvonne Taylor Coker

Word Processing:

Donna Stout Curasi

Production Manager:

F. Susan McGehee

Production Staff:

Teresa R. Arrwood, Debra J. Bost, Ann T. S. Imrick,

Ann S. Thompson, Donna Fletcher Young

Administrative Assistant:

Yvette B. King

Sales Manager:

David E. Phanco

International Sales Manager:

Murray L. Douglas

Regional Sales Manager:

Steven A. Dicarlo

Sales Operations Manager:

Christina Quad Faircloth

Sales Information Manager:

Steve Grathwohl

Sales Associate and

Assistant to the President:

C. Douglas Green

Administration: Stewart B. Blanton, Jr., J. Clinton Boggs, D. Tadley DeBerry, Lois S. Luke, Richard L. Shoe, H. Glenn Walker; Permissions Assistant: Simone Couture; Art Consultants: Neil O. Hardy, John Kyrk; Photography: Thomas A. Martin, William R. West; Production Assistants: Virginia S. Ingram, Jane Kelly, Sandra Moore Shoffner; Interns: Susie M. Grimley, Renée M. Martines, Caroline Y. Powell, Cristie A. Sexton; Advertising: J. Gray Amick, Bruce A. Anliker, Sam W. Gaines, Kenneth A. Hardy, Gwen W. Oakley, Harry L. Shoffner; Public Relations: David W. Dupont, James B. MacDonald, Jr., Richard G. Rhyne, Albert E. (Gene) Wolfe, Howard A. Wynne; Exhibits: Chattie P. Byrd, C. Scott Jewell, David A. Middendorf; Staff Reviewers: Jennifer Angyal, Raymond O. Flagg, Brent A. Ford, Ronald E. Hammond, James D. Horne, Daniel E. James, Robert V. Kirchen, Gregg C. Lee, Phillip L. Owens, Frances E. Powell, Thomas E. Register, James C. Scruggs, Daniel F. Thomas, Jr., Clyde S. White; Transportation: Dwayne C. Ayers

To Margie, Max, and Nora

Verweile doch! Du bist so schön! Goethe

此为试读,需要完整PDF请访问: www.ertongbook.com

### **Preface**

Biochemistry is an extraordinary subject. It spans an immense range from thermodynamics, kinetics, and quantum mechanics to cell biology, genetics, and physiology. Chemists, biologists, physicists, psychologists, and even sociologists can find themselves studying problems that are, at least in part, biochemical. (What this means, of course, is that boundaries between disciplines are more semantic than real.) Furthermore, biochemistry is being transformed with astonishing rapidity; the reader (or writer) of a biochemistry textbook can often see the ground slide from beneath his or her feet. But education involves modifying views and discarding concepts that prove to be flawed. If we insist on learning only that which is certifiably and eternally true, we shall have to resign ourselves to learning no science whatsoever. The truth of science is unlike that of art. A Beethoven symphony, for example, is enduring in a way that scientific concepts can never be. Truth in science depends on the integrity of its process—theory tested by experiment—and results in an evolving understanding of the natural world. It is my hope that this text accurately represents current knowledge about the topics covered and that, through future editions, it can evolve with the development of new knowledge.

*Biochemistry* is intended for an introductory course taken by students who have had general and organic chemistry. A knowledge of physical chemistry is not assumed; appropriate physical concepts are reviewed before being applied to biochemical phenomena.

This text is divided into six major parts. Part One consists of two chapters that introduce fundamental aspects of biochemistry. Chapter 1 provides an overview of cell structure and function; it is, in effect, an illustrated tour of the cell. Chapter 2 gives a brief analysis of the chemistry of water and its fundamental role in biochemistry. Part Two deals with protein conformation and function. Topics covered include amino acids and the covalent structure of proteins (Chapter 3), the conformations and functions of fibrous and globular proteins (Chapters 4 and 5, respectively), hemoglobin and myoglobin (Chapter 6), enzyme catalysis and enzyme kinetics (Chapter 7), the activation of digestive enzymes and coagulation factors (Chapter 8), and the structures and properties of biological membranes (Chapter 9).

Part Three covers the generation of metabolic energy through the catabolism of fuel molecules. The general design and regulation of metabolic pathways (Chapter 10) and the principles of bioenergetics (Chapter 11) are presented as a prelude to the discussion of specific metabolic processes. The role of group-transfer reactions and the importance of ATP hydrolysis to these reactions are emphasized. The specific metabolic processes described include glycolysis (Chapter 12); the citric acid cycle (Chapter 13); oxidative phosphorylation (Chapter 14); glycogen metabolism, gluconeogenesis, and the pentose phosphate pathway (Chapter 15); fatty acid metabolism (Chapter 16); amino acid catabolism and the urea cycle (Chapter 17); and photosynthesis (Chapter 18). In each of these chapters, general principles are described first, followed by details of molecular processes. An instructor wishing to skip certain sections will find it easy to do without loss of continuity or sacrifice of major principles. For example, one might choose to cover the basic outlines of a pathway and one or two enzymatic reaction mechanisms, and then move to regulation of the pathway. Part Four describes the biosynthesis of lipids (Chapter 19), amino acids (Chapter 20), and nucleotides (Chapter 21). Each of these chapters contains an overview followed by detailed descriptions of numerous pathways. Thus, an instructor can cover the general principles of biosynthesis and select a few specific examples to illustrate these principles. Students can use the comprehensive coverage for reference in later courses.

Part Five deals with the flow of biological information and the regulation of gene expression. Topics covered include the structures and functions of nucleic acids (Chapter 22), DNA replication (Chapter 23), transcription (Chapter 24), RNA processing (Chapter 25), the genetic code and transfer RNA (Chapter 26), protein synthesis and transport (Chapter 27), regulation of gene expression (Chapters 28 and 29), and recombinant DNA technology (Chapter 30). Part Six focuses on particular topics in molecular and cell biology, including biological membrane transport (Chapter 31), transmission of nerve impulses and signal transduction in sensory systems (Chapter 32), and contractile proteins and the cytoskeleton (Chapter 33).

It has been said that one person can no longer write a biochemistry text; the subject is too vast and the explosion of information is nearly overwhelming. I have found this to be true. Gaps in my knowledge have been filled by comments from the reviewers and advisors who are listed following the preface. These teachers and researchers have contributed their special knowledge and insights; I am greatly in their debt.

Several persons served as advisors for large sections of the text. David Dress-ler gave helpful advice at the inception of the project. Richard Dickerson reviewed chapters dealing with protein and nucleic acid structure and function; Evan Jones, Steven Clarke, and Milton Saier provided skillful assistance in the chapters dealing with intermediary metabolism; and Willy Kalt-Torres, Marvin Salin, and Douglas Youvan contributed significantly to the construction of the chapter on photosynthesis. Deborah Adams and Richard Ogden wrote the chapter on recombinant DNA technology; John Challice, Larry Moran, and Judy Swan provided substantial assistance in the authorship of the remaining molecular biology chapters; and Jim Bamburg, Ching-hsien Huang, Sue Kinnamon, and George Witman provided specialty reviews for the cell biology chapters. Bob Horton, Frank Church, and Evan Jones checked the accuracy of many of the chemical structures, and Gray Scrimgeour reviewed most of the chapters in their nearly final form and helped to construct the index.

The majority of the stereo images in this text were contributed by Richard Feldmann, a computer scientist at the National Institutes of Health and artist par excellence. Other researchers have also provided the results of their work in a stereo format so that students can appreciate the subtle structures of the molecules of the cell.

I am deeply indebted to Keith Porter for his generous gift of time and electron micrographs. I would also like to thank George Palade and John Heuser for their electron micrographs and for their help in obtaining others.

All these people and many others have made a considerable contribution to this text and have, in fact, seen it undergo an immense metamorphosis. Any defects are the sole responsibility of the author.

The publication of this book marks the establishment of a new publishing imprint. In the spring of 1986, Neil Patterson took my rough draft to Carolina Biological Supply Company. The president of that company, Thomas E. Powell, III, bravely chose to publish this manuscript as the foundation for a new science textbook publishing program. Without Ed Powell's commitment to education, a tradition spanning six decades at his company, and without his guidance and support, those pages might have remained a rough draft. I would like to thank Neil Patterson, who shared my vision of crafting a first quality, full-color, introductory biochemistry text and who mustered the resources to bring that vision to reality. Throughout the development of this text, Neil has demonstrated an uncanny ability to see through the knotty and often frustrating problems of the moment and to provide solutions that have kept us all on track. In addition, I would like to thank Sherri Foster, Bob Knauff, and Geoff Leister, who stepped forward at the outset to organize publishing operations, and Dan James, who kept our eyes on the final goal—a good book published on time.

The diverse talents of many persons, working in concert toward the same end, were required to produce the finished book. Sherri Foster directed the editorial process from start to finish. As Editorial Manager, she negotiated the myriad interactions among author, reviewers, advisors, artists, editors, and production staff. As a manuscript editor, she imposed order on an often disordered text. The editors, in fact, played such an integral part in weaving the fabric of this text that one can no longer separate their work from my own. Special thanks to Sherri, Leslie Daisy, Kathy Hodgin, Terri O'Quin, and Sue Olsen for their enhancement of the clarity of this text. Thanks also to Kay White, who kept the editorial department running smoothly with her cheerful efficiency. Recognition should also be accorded to George Sauer for the presentation of chemical structures, reactions, and pathways that are coordinated with the text. The skillful typographic designs created by George and by Donna Young have enhanced the didactic value and the aesthetic appeal of the hundreds of chemical structures. Developing a well-conceived art program for a text of this size is a phenomenal undertaking and one that Lisa Shoemaker has mastered beautifully. Without the fine illustrations devised by Lisa and other artists, this book would have been a lesser object. Thanks also to Mike Webb, who coordinated the efforts of the various artists and who ensured that the art program remained on schedule, and to Yvonne Coker, who obtained the electron micrographs and their requisite permissions. I would also like to thank the talented production staff managed by Susan McGehee, whose technical knowledge of type and four-color printing ensured that the final product would be of top quality. Teresa Arrwood, D. J. Bost, Ann Imrick, Ann Thompson, and Donna Young all contributed significantly to the production of this text. As with all elaborate productions, many critical tasks were performed by workers behind the scenes. Many thanks to Andrew Angyal, John Cooper, Chuck Coté, Donna Curasi, Tad DeBerry, Deborah Hill, Shane Jones, Yvette King, Sharon Luck, Glenda Newcomb, Cris Sexton, and others who supported the publication of this text in large and small ways.

Thus do I commend the book to readers. I welcome any criticism or advice.

#### Reviewers and Advisors

Deborah A. Adams, Agouron Institute

James R. Bamburg, Colorado State University

Robert W. Baughman, Harvard Medical School

Bruce P. Bean, Harvard Medical School

G. Vann Bennett, Duke University School of Medicine

Ludwig Brand, Johns Hopkins University

Greg G. Brown, McGill University

P. Jonathan G. Butler, Medical Research Council, Cambridge, England

Nicholas C. Carpita, Purdue University

John M. Challice, University of Toronto

Frank C. Church, University of North Carolina School of Medicine

Steven G. Clarke, University of California, Los Angeles

James E. Darnell, Jr., The Rockefeller University

Richard E. Dickerson, University of California, Los Angeles

David H. Dressler, Harvard Medical School

Paul T. Englund, Johns Hopkins University School of Medicine

Robert J. Fogelsong, Duke University

Irwin Fridovich, Duke University School of Medicine

Naba K. Gupta, University of Nebraska, Lincoln

James H. Hageman, New Mexico State University

Nancy V. Hamlett, Swarthmore College

Franklin M. Harold, National Jewish Center for Immunology and Respiratory Medicine

Edward D. Harris, Texas A & M University

Kenneth Hellman, Smith College

Robert L. Hill, Duke University School of Medicine

Johns W. Hopkins, III, Washington University

H. Robert Horton, North Carolina State University

Ching-hsien Huang, University of Virginia School of Medicine

Evan E. Jones, North Carolina State University

Mary Ellen Jones, University of North Carolina at Chapel Hill

Willy Kalt-Torres, Duke University

Robert A. B. Keates, University of Guelph

Sue C. Kinnamon, Colorado State University

Aaron Klug, Medical Research Council, Cambridge, England

Arthur Kornberg, Stanford University Medical School

Nicholas A. Kredich, Duke University School of Medicine

James Lake, University of California, Los Angeles

M. Daniel Lane, Johns Hopkins University School of Medicine

Robert N. Lindquist, San Francisco State University

Rose G. Mage, National Institutes of Health

Lynn A. Margulis, University of Massachusetts

James B. Meade, University of North Carolina School of Medicine

William C. Merrick, Case Western Reserve University School of Medicine

Larry A. Moran, University of Toronto

Richard Ogden, Agouron Institute

Marvin R. Paule, Colorado State University

Huntington Potter, Harvard Medical School

Jane H. Potter, University of Maryland

Gary L. Powell, Clemson University

Charlotte W. Pratt, University of North Carolina School of Medicine

Charles C. Richardson, Harvard Medical School

Nadia A. Rosenthal, Children's Hospital/Harvard Medical School

Milton H. Saier, Jr., University of California, San Diego

Marvin L. Salin, Mississippi State University

Vern G. Schirch, Medical College of Virginia

K. Gray Scrimgeour, University of Toronto

B. Trevor Sewell, University of Cape Town, South Africa

Gordon C. Shore, McGill University

James N. Siedow, Duke University

Lewis M. Siegel, Duke University School of Medicine

Gerald R. Smith, Fred Hutchinson Cancer Research Center

Franklin W. Stahl, University of Oregon

Deborah A. Steege, Duke University School of Medicine

Clarence H. Suelter, Michigan State University

Judith A. Swan, Duke University

Keith E. Taylor, University of Windsor

Thomas W. Traut, University of North Carolina at Chapel Hill

Robert W. Wheat, Duke University

George B. Witman, Worcester Foundation for Experimental Biology

Owen N. Witte, University of California, Los Angeles

Charles Yanofsky, Stanford University

Douglas C. Youvan, Massachusetts Institute of Technology

James K. Zimmerman, Clemson University

#### Graduate Student Reviewers:

Jeanie H. Chung, University of North Carolina at Chapel Hill

Sylvia W. Curtis, National Institute of Environmental Health Sciences

Mark J. Feild, North Carolina State University

Kelly Baker Jones, University of North Carolina at Greensboro

Mary A. Lapadat, University of North Carolina at Chapel Hill

Dean M. McCord, University of North Carolina at Chapel Hill

William O. Wilkison, Duke University

## **List of Chapters**

	One	
Intr	oduction	3
1	The World of the Cell	5
2	Water	27
	t Two tein Conformation and Function	49
FIO	tem Comorniation and Function	43
3	Amino Acids and the Primary Structure of Proteins	51
4	Fibrous Proteins	75
5	The Conformations of Globular Proteins	99
6	Hemoglobin and Myoglobin: Oxygen-Binding Proteins	121
7	Enzyme Catalysis and Enzyme Kinetics	149
8	Activation of Digestive Enzymes and Coagulation Factors	195
9	The Structure of Biological Membranes	209
	t Three Generation and Storage of Metabolic Energy	235
10	The Design and Regulation of Metabolic Pathways	237
11	Bioenergetics: The Significance of the Hydrolysis of ATP and Other Energy-Rich Metabolites	265

12	Glycolysis	289
13	The Citric Acid Cycle	329
14	Oxidative Phosphorylation	359
15	Glycogen Metabolism, Gluconeogenesis, and the Pentose Phosphate Pathway	385
16	Fatty Acid Metabolism	421
17	Catabolism of Amino Acids and the Urea Cycle	457
18	Photosynthesis	489
	t Four Biosynthesis of Precursors of Macromolecules	535
19	Biosynthesis and Transport of Membrane Lipids and Formation of Cholesterol Derivatives	537
20	Biosynthesis of Amino Acids and Related Biosynthetic Processes	581
21	Nucleotide Biosynthesis	627
	t Five logical Information Flow	663
22	Nucleic Acids	665
23	DNA Replication	703
24	Transcription	737
25	RNA Processing	781
26	The Genetic Code and Transfer RNA	821
27	Protein Synthesis and Transport	847
28	Regulation of Gene Expression I	887
29	Regulation of Gene Expression II	939
30	Recombinant DNA Technology	975
	t Six lecular Biology of the Cell	1021
31	Biological Membrane Transport	1023
32	Transmission of Nerve Impulses and Signal Transduction in Sensory Systems	1049
33	Contractile Proteins and the Cytoskeleton	1077

### **Contents**

Part One

Intr	oduction	3
	pter 1 World of the Cell	5
1.1	Evolution Introduces Time into Biology	5
1.2	Biological Organisms Can Be Classified by Their Similarities	6
1.3	Viruses Provide Models for Structure and Replication of Living Organisms	6
1.4	Structure and Organization Are Inseparable	8
1.5	All Organisms Are Built from Cells	8
1.6	Escherichia coli Is a Representative Prokaryote	10
1.7	Eukaryotic Cells Contain Many Membrane-Bounded Organelles	12
1.8	Biochemistry Is an Empirical Science	19
1.9	Biochemistry Is a Reductionist Science	22
1.10	Mise-en-Scène	22
Cha	pter 2	
Wat		27
2.1	The Water Molecule Is Polar	27
2.2	Water Readily Forms Hydrogen Bonds	29
2.3	Hydrogen Bonds Are Important in Biological Systems	29
	Box 2·1 Van der Waals Attractions Result from Weak Electrostatic	L-sax
	Interactions	30

2.4	Hydrogen Bonding Is Responsible for the Properties of Liquid Water	32
	Box 2.2 Energy Flow and the Laws of Thermodynamics	34
2.5	Ions Alter the Structure of Liquid Water	35
2.6	Nonpolar Molecules Are Insoluble in Water	36
2.7	Water Undergoes Ionization	37
	<b>Box 2·3</b> Calculation of the $H^{\oplus}$ , $OH^{\ominus}$ , and $Cl^{\ominus}$ Concentrations in Solutions of HCl	38
2.8	Hydrogen Ion Concentrations in Aqueous Solutions Are Measured on the pH Scale	39
	<b>Box 2·4</b> Calculation of Hydrogen Ion Concentrations Given the pH and Calculation of pH Given the Hydrogen Ion Concentration	40
2.9	Weak Acids Dissociate Only Partially in Aqueous Solutions	40
2.10	The pKa Values of Weak Acids Can Be Determined by Titration	41
2.11	Buffer Solutions Resist Changes in pH	44
2.12	Dissolved Bicarbonate and Carbon Dioxide Gas in the Lungs Buffer the pH of Blood	44
Sumn	nary	46
Probl	ems	47
Selec	ted Readings	47
Par	t Two	
Dro	tein Conformation and Function	49
110	tem comormation and runction	43
	pter 3	43
Cha		<b>49</b>
Cha	pter 3	
Cha Am	pter 3 ino Acids and the Primary Structure of Proteins	51
Cha Am	ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among	<b>51</b>
Cha Am	ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains	<b>51</b> 52 53
Cha Am	ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have	51 52 53 55
Cha Am	ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains	51 52 53 55 57
Cha Am	ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains	51 52 53 55 57
Cha Am 3·1 3·2	Ipter 3 ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids	51 52 53 55 57 57 58
Cha Am 3·1 3·2	Ipter 3 ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids Depends on the pH	51 52 53 55 57 57 58 58
Cha Am 3·1 3·2 3·3	Ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids Depends on the pH  Amino Acid Residues in Proteins Are Linked by Peptide Bonds  The Amino Acid Composition of Proteins Can Be Determined	51 52 53 55 57 57 58 58 61
Cha Am 3·1 3·2 3·3 3·4 3·5	Ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids Depends on the pH  Amino Acid Residues in Proteins Are Linked by Peptide Bonds  The Amino Acid Composition of Proteins Can Be Determined Quantitatively  The Edman Degradation Procedure Permits Determination of the	51 52 53 55 57 57 58 58 61
Cha Am 3·1 3·2 3·3 3·4 3·5 3·6	Inpter 3 ino Acids and the Primary Structure of Proteins  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids Depends on the pH  Amino Acid Residues in Proteins Are Linked by Peptide Bonds  The Amino Acid Composition of Proteins Can Be Determined Quantitatively  The Edman Degradation Procedure Permits Determination of the Sequence of Amino Acid Residues in a Protein  Comparisons of the Primary Structures of Some Common Proteins Can Reveal Evolutionary Relationships	51 52 53 55 57 57 58 61 61 66
Cha Am 3·1 3·2 3·3 3·4 3·5 3·6 3·7	proteins Are Made from 20 Amino Acids  Proteins Are Made from 20 Amino Acids  Differences in the Properties of Amino Acids Reflect Differences Among Their Side Chains  A. Several Amino Acids Have Hydrophobic Side Chains  B. Asparagine, Glutamine, Serine, Threonine, and Tyrosine Have Neutral, Hydrophilic Side Chains  C. Lysine, Arginine, and Histidine Have Basic, Hydrophilic Side Chains  D. Aspartate and Glutamate Have Acidic, Hydrophilic Side Chains  The Ionic State of the Acidic and Basic Groups of Amino Acids  Depends on the pH  Amino Acid Residues in Proteins Are Linked by Peptide Bonds  The Amino Acid Composition of Proteins Can Be Determined  Quantitatively  The Edman Degradation Procedure Permits Determination of the Sequence of Amino Acid Residues in a Protein  Comparisons of the Primary Structures of Some Common Proteins Can Reveal Evolutionary Relationships	51 52 53 55 57 57 58 61 61 66

Chapter 4 Fibrous Proteins		
4.1	The Peptide Bond Is Resonance-Stabilized, Polar, and Planar	75
4.2	The $\alpha$ Helix Is a Common Structural Motif in Many Proteins	76
4.3	In $\beta$ -Pleated Sheets, Polypeptide Chains Are Almost Completely Extended	80
4.4	Peptide Chains Can Assume Only a Restricted Number of Conformations	81
4.5	Collagen Is a Mechanically Strong, Fibrous Protein Found in Connective Tissue	84
	A. Tropocollagen Is a Triple Helix	86
	B. Collagen Is Rich in Glycine and Proline	87
	C. Collagen Is a Glycoprotein	88
	D. The Primary Structure of Collagen Is Unusual	88
	E. Covalent Cross-Links Increase the Mechanical Strength of Collagen	89
	F. The Biological Assembly of Collagen Requires Many Steps	90
4.6	Elastin Is a Flexible, Fibrous Protein Also Found in Connective Tissue	94
Sumi	mary	96
Probl	lems	98
Selec	eted Readings	98
	apter 5 e Conformations of Globular Proteins	99
5.1	The Structure of Globular Proteins Is Hierarchical	101
3-1	Box 5·1 Determination of Protein Structure by X-Ray Crystallography	102
5.2	The Structures of Globular Proteins Depend on a Variety of Interactions	106
5 2	A. The Hydrophobic Effect Drives Protein Folding	106
	B. Hydrogen Bonds Stabilize Globular Proteins	106
	C. Ion Pairs Can Form in the Hydrophobic Interiors of Globular Proteins	107
5.3	Denaturing Agents Unfold Globular Proteins	108
5.4	Protein Folding Is a Spontaneous and Sequential Process	109
	Box 5·2 Viruses Illustrate Many Facets of Protein Structure	111
	A. The Structure of Tobacco Mosaic Virus Arises by Spontaneous Self-Assembly	111
	B. The Assembly of Spherical Viruses Depends on Flexible Coat	
	Proteins	115
Sum	mary	117
Prob	lems	118
Selec	eted Readings	119
Hei	apter 6 moglobin and Myoglobin: ygen-Binding Proteins	121
6.1		121
0.1	Myoglobin Is the Oxygen-Storage Protein of Skeletal Muscle A. Myoglobin Contains Extensive Regions of $\alpha$ Helix	121
	B. A Heme Prosthetic Group Binds Oxygen	122
	T C	

	C. A Sterically Hindered Heme Is Essential for the Biological Function of Myoglobin	124
6.2	Myoglobin and Hemoglobin Evolved from a Common Ancestral Protein	125
6.3	Myoglobin and Hemoglobin Have Different Oxygen-Binding Curves	129
0 5	A. The Oxygen-Binding Curve of Myoglobin Is Hyperbolic	129
	B. The Oxygen-Binding Curve of Hemoglobin Is Sigmoidal	131
6.4	Hemoglobin Is an Allosteric Protein	133
0 1	A. The Monod-Wyman-Changeux Model Is a Concerted Model for	100
	Allosteric Interaction	133
	B. The Sequential Model for Allosteric Interaction Allows Intermediate Conformations	135
6.5	Hemoglobin Function Involves Conformational Changes	135
	A. Oxygen Binding Induces a Conformational Change in Hemoglobin	136
	B. 2,3-Bisphosphoglycerate Decreases the Affinity of Hemoglobin for Oxygen	136
	C. The Bohr Effect Influences Oxygen Binding to Hemoglobin	140
6.6	Sickle-Cell Anemia Is a Molecular Disease	141
	A. Normal and Sickle-Cell Hemoglobin Differ by a Single Residue in the $\beta$ Chain	142
	B. The Solubility of Deoxyhemoglobin S Is Abnormally Low	144
	C. Sickle-Cell Trait Is Associated with Increased Resistance to Malaria	144
Sumr		144
Probl		146
	ted Readings	147
Selec	ted Readings	147
	pter 7	
Enz	yme Catalysis and Enzyme Kinetics	149
Part	I: Principles of Enzyme Reactions	149
7.1	Enzymes Decrease the Activation Energy of Reactions	150
7.2	Formation of the Enzyme-Substrate Complex Is Accompanied by a Negative Free-Energy Change	151
7.3	Acid-Base Catalysis Increases the Rates of Many Enzyme-Catalyzed	
	Reactions	154
7.4	A Zinc Ion Functions Catalytically in Carboxypeptidase A	157
7.5	Serine Proteinases Have Similar Reaction Mechanisms	158
	A. A Hydrophobic Pocket Determines the Specificity of Chymotrypsin	158
	B. An Acyl-Enzyme Intermediate Forms in Chymotrypsin-Catalyzed Reactions	159
	C. Serine Residue 195 of Chymotrypsin Is Uniquely Reactive	159
	D. The Active Site of Chymotrypsin Contains Histidine	161
	E. A Charge-Relay Network Enhances the Nucleophilicity of Serine	
	Residue 195	161
	F. Chymotrypsin Catalysis Involves Five Steps	163
7.6	The Conformations of Chymotrypsin, Trypsin, and Elastase Are Similar	163

Part	II: Enzyme Kinetics	166
7.7	Rate Constants Describe Reactions	166
7.8	The Michaelis-Menten Rate Law Governs Enzymatic Reactions	167
	A. The Michaelis-Menten Rate Law Uses Initial Rates	167
	B. In Derivation I, the Enzyme, Substrate, and Enzyme-Substrate	
	Complex Are Assumed to Be in Equilibrium	168
	C. In Derivation II, a Steady State Is Assumed	169
	D. In Derivation III, a Covalent Enzyme-Substrate Intermediate Forms	172
7.9	Enzymes Are Described by Turnover Numbers	173
7.10	pH Affects Rates of Enzymatic Reactions	174
7.11	Temperature Affects Rates of Enzymatic Reactions	174
7.12	$k_{\text{cat}}/K_{\text{M}}$ Is a Measure of Catalytic Efficiency and Enzyme Specificity	174
7.13	Kinetic Isotope Effects Decrease Reaction Rates	176
7.14	Kinetic Data Are Represented by Several Graphical Methods	176
7.15	Enzyme Inhibition Is Described by the Michaelis-Menten Rate Law	178
	A. Competitive Inhibition Increases K <sub>M</sub>	178
	B. Uncompetitive Inhibition Decreases $K_M$ and $V_{\text{max}}$	180
	C. Noncompetitive Inhibition Decreases V <sub>max</sub>	182
7.16	Transition-State Analogs Are Potent Competitive Inhibitors	184
Sumr	nary	185
Probl	ems	186
Selec	ted Readings	193
Cha	pter 8	
Act	ivation of Digestive Enzymes and	
Coa	gulation Factors	195
8.1	The Pancreatic Digestive Enzymes Are Synthesized as Inactive	
0 1	Zymogens and Activated by Proteolytic Enzymes	195
	A. Trypsinogen Is Activated by Enteropeptidase	197
	B. The Pancreas Produces a Trypsin-Inhibitor Protein	197
	C. Chymotrypsin Is Activated in Several Stages	199
	D. Secretion of Pancreatic Zymogens Is Hormonally Regulated	200
8.2	A Cascade of Zymogen Activation Is Responsible for Blood Coagulation	201
	A. Blood Coagulation Results from the Convergence of Two Pathways	202
	B. Blood Clots Are Made of Fibrin	202
	C. Fibrin Is Cross-Linked by Factor XIII <sub>a</sub>	205
	D. Thrombin Is Produced by Activation of Prothrombin	205
	E. Factor X <sub>a</sub> , Thrombin, and Trypsin Have Evolved from a Common	
	Ancestral Proteinase	206
	F. Several Coagulation Factors Contain $\gamma$ -Carboxyglutamate	206
	G. Hemophilia Is a Genetically Transmitted Bleeding Disorder	207
Sumi	nary	208
Problems		208
Selected Readings		208