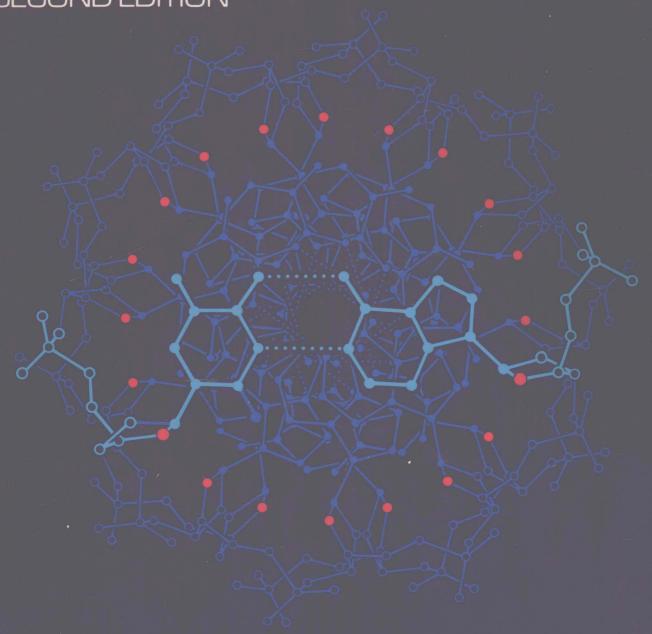
FRANK B. ARMSTRONG

# BIOCHEMISTRY

SECOND EDITION



# BIOCHEMISTRY

SECOND EDITION

FRANK B. ARMSTRONG

North Carolina State University

New York Oxford

Copyright © 1979, 1983 by Oxford University Press, Inc.

Library of Congress Cataloging in Publication Data

Armstrong, Frank Bradley. Biochemistry.

Bibliography: p.

Includes index.

1. Biological chemistry. I. Title.

QP514.2.A73 1983 574.19'2 81-18922

ISBN 0-19-503109-1

AACR2

Outside front cover: Top view of B DNA depicting one complete turn of the helix (ten base pairs). See P. 233.

Illustration (C) by Irving Geis.

Inside front cover: The von Liebig Laboratory in

Giessen, Germany.

(The Bettmann Archive, Inc.)

Cover design by Charles and Ruth Kaplan.

Printing (last digit): 9 8 7 6 5 4 3 2 1 Printed in the United States of America

### PREFACE

The writing of the second edition of Biochemistry was influenced significantly by the constructive critiques and suggestions provided by colleagues, students, reviewers, and users of the first edition. With regard to the changes incorporated into the second edition, two new chapters, Lipid Biosynthesis (Chapter 19) and Recombinant DNA Research (Chapter 26), were added, and presentations in many of the other chapters were revised and/or expanded. Some of these changes include a discussion of glycogen synthesis (Chapter 11), the catalytic mechanism of ribonuclease A (Chapter 13), the glyoxylate cycle (Chapter 16), restriction mapping and the newer systems for DNA sequencing (Chapter 21), the mitochondrial genetic code and attenuation (Chapter 22), intracellular transport of proteins (Chapter 23), recent research findings on prostaglandins (Chapter 24), and the mode of action of vitamins A, D, and K (Chapter 25). Particular attention was also given to an expansion of the presentation on nitrogen metabolism (Chapter 20) by including nitrogen fixation, nitrate reduction, and the synthesis and catabolism of all 11 nonessential amino acids. Also, the discussion on purine metabolism is now complemented by one on pyrimidine metabolism.

The expanded second edition may now contain more material than can be conveniently presented in a one-semester, introductory course in biochemistry. If such is the case, it is hoped that individual instructors will select those topics from the book that best suit their treatment of the discipline in meeting the educational needs of their classes.

In preparing the new edition, I was again fortunate to have the assistance of colleagues who provided critical reviews of individual chapters. For their valuable contributions, my sincere appreciation

is extended to Wendy F. Boss, William E. Donaldson, H. Robert Horton, Daniel W. Israel, William A. Jackson, Bryan H. Johnson, William L. Miller, David W. Niesel, Joanne M. Ravel, and Samuel B. Tove. The useful critiques furnished by the reviewers selected by Oxford University Press are also appreciated. I recognize with gratitude the help provided by Jeanne B. Koger in proofreading the galleys and by Irene Nunes, who carefully and thoroughly copyedited the manuscript. The impeccable typing of Anne Richardson, who prepared the manuscript, is also gratefully acknowledged. I express a special thanks to my editor, Michael R. Cook, whose dedicated efforts assured a smooth transition from the first to the second edition. Finally, I extend my appreciation and love to my family; their contributions of patience, support, and encouragement made the task of revising the text much easier.

Raleigh, North Carolina

F.B.A.

### PREFACE TO FIRST EDITION

Biochemistry is for an introductory course designed to accommodate undergraduates from widely varying curricula. For an instructor, the current broad interest in such offerings in biochemistry poses the challenge of teaching a course that meets the educational needs of majors from preprofessional programs, biological sciences, agricultural sciences, chemisty, engineering, and science education curricula. Such a generalized course has been taught by Frank B. Armstrong at North Carolina State University since 1968 and by Thomas Peter Bennett at the Rockefeller University. It was this mutual interest in teaching introductory biochemistry that prompted us to engage in the collaborative effort that made *Biochemistry* a reality.

The topics covered in the text were selected after seeking the advice of a number of instructors from various campuses who teach courses in biochemistry. A majority of the material, therefore, represents a basic core of instruction that all those consulted considered necessary for an introductory course and that we have found desirable in our own teaching. In the interest of brevity, the text is written in a simple, direct style. Where appropriate, the text is accented with historical notes, definitions, or information pertaining to the relevant aspects of the material being presented; medical anomalies, for example, are tied to inborn errors of metabolism.

Chapters 1 through 5 are introductory in nature and recognize the various backgrounds of students taking their first course in biochemistry. This section includes a brief history of biochemistry, emphasizing the development of molecular biology; a review of the elements needed for life and of biogeochemical cycles; a discussion of water and buffers; chemical topics that are important to the subsequent text; and an overview of cell biology.

Amino acids and proteins are two of the classes of biomolecules discussed in the book's second section, Chapters 6-13. A presentation of the molecular aspects of the structure and biological function of proteins, with emphasis on myoglobin, hemoglobin, and enzymes, precedes a description of other principal types of biomolecules, i.e., carbohydrates, lipids, nucleic acids, and B-vitamins.

The molecular basis of bioenergetics serves as a prelude to the third section (Chapters 14-20), which includes the production of chemical energy by living systems and interrelated topics on intermediary metabolism. The synthesis of ATP is the underlying theme of the chapters on glycolysis, tricarboxylic acid cycle, electron transport, oxidative phosphorylation, and photosynthesis. Carbon metabolism, emphasized in the presentation of the recovery of energy from sugars, is complemented by a discussion of the metabolism of nitrogen-containing biomolecules. This section concludes with a presentation of the molecular aspects of human nutrition.

The last section, Chapters 21–24, returns to some of the key accomplishments attained by molecular studies of biological phenomena. Chapter 21 on hormones includes the impressive strides that have been made toward understanding the molecular basis of hormone action. Chapters 22–24 are devoted to the classes of macromolecules of the Central Dogma, stressing molecular studies on DNA, RNA, and protein synthesis, respectively. A discussion of the coding capacity of the bacteriophage  $\phi$ X174 was selected for the book's closing, since the results of these studies succinctly exemplify the revolutionary impact that molecular biology continues to have on the study of biology.

The authors gratefully acknowledge those who aided in the preparation of *Biochemistry*. The following provided constructive critiques of many of the chapters and contributions of information and materials: Drs. Mary Bonneville, Janice Glenn, Thomas Conway, H. Robert Horton, Evan E. Jones, Joseph S. Kahn, Ian S. Longmuir, A. Russell Main, John F. Roberts, and Harold F. Swaisgood. The reviews and information provided by Mr. Hugh Craft are also acknowledged, and a special acknowledgment goes to Mr. Richard R. Randall, who served as an in-house editor for the manuscript. Thanks are given to the graduate students of the Department of Biochemistry at North Carolina State University for their careful help in proofreading the galleys. Appreciation is also expressed for the critical persistence and guidance of Mr. Robert

J. Tilley and his associates at Oxford University Press and for the thoughtful critiques provided by the reviewers selected by the publisher. The excellent typing of Mrs. Anne Richardson, who prepared the copies of the manuscript, is sincerely appreciated. We save for last our thanks to our families, who endured many months with authors-in-residence and who, in spite of this imposition, provided us with continuous support and encouragement.

FRANK BRADLEY ARMSTRONG

Raleigh, North Carolina

THOMAS PETER BENNETT

Philadelphia, Pennsylvania

December, 1978

But the task of the biochemist is, after all, the study of the physicochemical processes associated with the manifestations of what we call life—not the life of some particular animal or group of animals, but life in its most general sense.

ERNEST BALDWIN, 1937
Preface to *An Introduction*to Comparative Biochemistry

## LIST OF CHAPTERS

An Historical Review 3

2	Chemical Elements and Biogeochemical Cycles 15	
3	Water as the Solvent of Life 25	
4	Some Basic Aspects of the Chemistry of Life 41	
5	Cells: Biological Units of Molecular Organization 51	
6	Proteins I: Amino Acid Components and Structural Features 67	
7	Proteins II: Determination of Amino Acid Sequences 87	
8	Proteins III: Structure and Function 105	
9	Proteins IV: Enzymes 129	
10	B-Vitamins as Coenzymes 163	
11	Carbohydrates 183	

12	Lipids and Membranes 205
13	Nucleic Acids 225
14	Energy and Life 251
15	Anaerobic Synthesis of ATP (Glycolysis) and Pentose Phosphate Pathway 267
16	Aerobic Synthesis of ATP I: Tricarboxylic Acid Cycle 297
17	Aerobic Synthesis of ATP II: Electron Transport and Oxidative Phosphorylation 315
18	Photosynthesis: Sine Qua Non of Life 341
19	Lipid Biosynthesis 367
20	Nitrogen Metabolism 395
21	Molecular Insights into DNA 437
22	Genetic Information: Transcription and Its Control 473
23	Translation of Genetic Information 503
24	Hormones: Intercellular Chemical Messengers 537
25	Basic Aspects of Human Nutrition 567
26	Recombinant DNA Research 597
	Answers 625

Index

635

# CONTENTS

An Historical Review 3

	Introduction 3 Nineteenth Century 3 First Fifty Years of This Century 7 Emergence of Molecular Biology 9
2	Chemical Elements and Biogeochemical Cycles 15
	Introduction 15 The Carbon Cycle 16 The Nitrogen Cycle 18 The Phosphorus Cycle 19 The Oxygen Cycle 19 The Water Cycle 20 Modification of Biogeochemical Cycles 21
3	Water as the Solvent of Life 25
	Introduction 25 Physical Properties of Water 26 Some Biological Importances of Water 28 Water as a Solvent 28 Hydrogen Ion Concentration of Biological Systems 29 Dissociation of Water 29 pH Scale 30 Brönsted-Lowry Acids and Bases 31

*	CC
IV	1 1

Strong and Weak Acids 31 Ionization of Weak Acids 32 Henderson-Hasselbalch Equation 33 Titration of a Weak Acid by a Strong Base 33 35 Dissociable Biological Compounds Physiological Buffer Systems 36

#### Some Basic Aspects of the Chemistry of 4 41 Life

Introduction 41 Bonding Properties of Carbon Asymmetry of Carbon Compounds 42 44 cis-trans Isomerism Noncovalent Interactions 45 Van der Waals Forces 45 Hydrogen Bonds 46 47 Ionic Bonds Hydrophobic Interactions 47

#### Cells: Biological Units of Molecular 5 Organization 51

Introduction 51 Two Basic Types of Cells 52 53 **Diversity Among Cells** Procaryotic Cell 53 Animal Cell 55 Cell membrane 55, Nucleus 56, Mitochondria 56, Rough

62

and smooth endoplasmic reticula 57, Golgi apparatus 59, Lysosomes 59, Microbodies or peroxisomes 60 Plant Cell 60 Cell wall 61, Vacuoles 62, Glyoxysomes 62, Chloroplasts

#### Proteins I: Amino Acid Components 6 and Structural Features 67

Introduction 67 68 Two General Properties of Amino Acids General Bonding Features of Polypeptides 71 Amino Acid Residues of Polypeptides 71
Nonpolar R groups 72, Uncharged polar R groups 73,
Negatively charged (acidic) polar R groups 74, Positively
charged (basic) polar R groups 74, *Allo* forms of amino
acids 74
Some Other Naturally Occurring Amino Acids 75
Structural Levels of Proteins 76
Primary structure 77, Secondary structure 77, Tertiary
structure 79, Quaternary structure 80

Specification of Conformation by Primary Structure 81
Two Major Types of Protein Conformation 82

# Proteins II: Determination of AminoAcid Sequences 87

Introduction 87

Determination of Amino Acid Composition 88

Determination of Amino-Terminal Amino Acid 91

Determination of Carboxyl-Terminal Amino Acid 93

Selective Fragmentation of a Polypeptide 95

Edman Degradation 98

Required Second Fragmentation 100

The Complete Sequence 100

### Proteins III: Structure and Function 105

Introduction 105 Myoglobin 107

General molecular features 107, Tertiary structure 107

Hemoglobins 109

Tertiary and quaternary structure 110, Biological significance of quaternary structure 111, Oxygen dissociation curves 112, Molecular aspects of hemoglobin oxygenation 113, Bisphosphoglycerate as a hemoglobin regulator 115, Physiological importance of hemoglobin regulation 116, Hemoglobin as a H<sup>+</sup> and CO<sub>2</sub> transport protein 117, Binding of H<sup>+</sup> and CO<sub>2</sub> to deoxyhemoglobin 118, N- and C-terminal residues of hemoglobin 119

Medical Aspects of Hemoglobin Abnormalites 119
Sickle-cell anemia 119, History of sickle-cell research
120, Molecular basis of sickle-cell anemia 121, Individual

genetics of sickle-cell anemia 123, Population genetics of sickle-cell anemia 123, An anemia related to sickle-cell anemia 124, Hemoglobin and molecular biology 124

#### Proteins IV: Enzymes 129

Introduction 129

General Catalytic Properties of Enzymes 130

Classification of Enzymes by Catalytic Function 132

Enzyme Assays 134

**Enzyme Reaction Rates** 135

Michaelis-Menten Equation 136

Lineweaver-Burk Plot 138

Enzyme Inhibition 139

Competitive Inhibition 139, Noncompetitive Inhibition

140, Irreversible Inhibition 140

Lineweaver-Burk Plots of Inhibition 141

Active Site and Substrate Binding 142

Quaternary Structure and Isozymes 143

Allosteric Enzymes 145

Catalytic Effectiveness of Enzymes 145

Acid-Base Catalysis 146

Chymotrypsin 147

Activation of chymotrypsinogen 147, Three-dimensional structure of chymotrypsin 147, Substrate specificity of

chymotrypsin 148

Proposed Catalytic Mechanism of Chymotrypsin 150 "Charge relay system" 150, Double-displacement

mechanism for the hydrolysis of peptide bonds 151

**Biochemical Evolution** 153

Enzymology and Industry 156

#### 163 B-Vitamins as Coenzymes 10

Introduction 163

The B-Vitamins 164

> Thiamin 164, Nicotinamide 165, Riboflavin 168, Vitamin B<sub>6</sub> 169, Biotin 171, Pantothenic acid 172, Folic acid 173, Vitamin B<sub>12</sub> 174, Lipoic acid 177

B-Vitamin Supplementation of Foods 178

### 11 Carbohydrates 183

Introduction 183

Monosaccharides 184

Nomenclature and Fischer projections 184, Closed-ring structures 185, Haworth projections 186, Other monosaccharides of importance 187

Oligosaccharides 189

Sugars as reducing agents 191, Sugars and other molecules as sweetners 192

Polysaccharides 192

Starches and glycogen 192, Glycogen synthesis 194, Cellulose 196, Conformations of cellulose and starch 197, Heteroglycans 197, Chemical and functional versatility 199

The Many Uses of Polysaccharides 200

Dextrins 200, Dextrans 200, Additional comments 201

### 12 Lipids and Membranes 205

Introduction 205

Triacylglycerols 206

Structural components 206, Saponification 207

Lipids of Membranes 208

Phosphoglycerides 208, Sphingolipids 210, Glycolipids 210

Abnormal Lipid Metabolism 211

Tay-Sachs disease 212, Fabry disease 213, Gaucher disease 213, Niemann-Pick disease 213, Impaired biosynthesis of lipids 214

Membranes 215

Bilayer lipid membranes 215, Proteins of membranes 218, Fluid mosaic model of membranes 219

### 13 Nucleic Acids 225

Introduction 225

Levels of Nucleic Acid Structure 226
Nitrogenous bases 226, Nucleosides 228, Nucleotides 229, Polynucleotide structure 231

Structure of DNA 232

Molecular Species of RNA 234
Sequencing of tRNAs 236
RNA Hydrolysis 237
Alkaline Hydrolysis 237
Proposed Catalytic Mechanism of Ribonuclease A 239
Structure of tRNAs 242
Nucleic Acids as Hereditary Material 243

### 14 Energy and Life 251

Introduction 251 252 Free Energy Change of a Chemical Reaction Standard Free Energy Changes ATP as an Energy Carrier 254 Hydrolysis of AMP Other Phosphorylated Biomolecules 258 Hydrolytic Reactions Yielding a Large Negative  $\Delta G^{\circ}$ 259 262 Synthesis of Nucleoside Triphosphates 263 Synthesis of ATP from AMP and ADP

# Anaerobic Synthesis of ATP (Glycolysis) and Pentose Phosphate Pathway 267

Introduction 267
Reactions of the Glycolytic Pathway 269
Phosphorylation of glucose 269, Derivation of glucose 6phosphate from glycogen 269, Production of p-fructose
1,6-bisphosphate 272, 6-Phosphofructokinase as a
regulatory enzyme 273, Metabolic production of pglyceraldehyde 3-phosphate 274, sn-Glycerol 3phosphate dehydrogenase 274, Thermodynamics of the
aldolase and triosephosphate isomerase reactions 275,
Oxidation of p-glyceraldehyde 3-phosphate 276, First
synthesis of ATP 277, Second synthesis of ATP 278,
Production of lactate 279

Efficiency of Energy Conservation 279

Alcoholic Fermentation 280

2,3-Bisphosphoglycerate Synthesis and

Degradation 281

Gluconeogenesis from Lactate 282

Physiologically irreversible reactions of glycolysis 282,