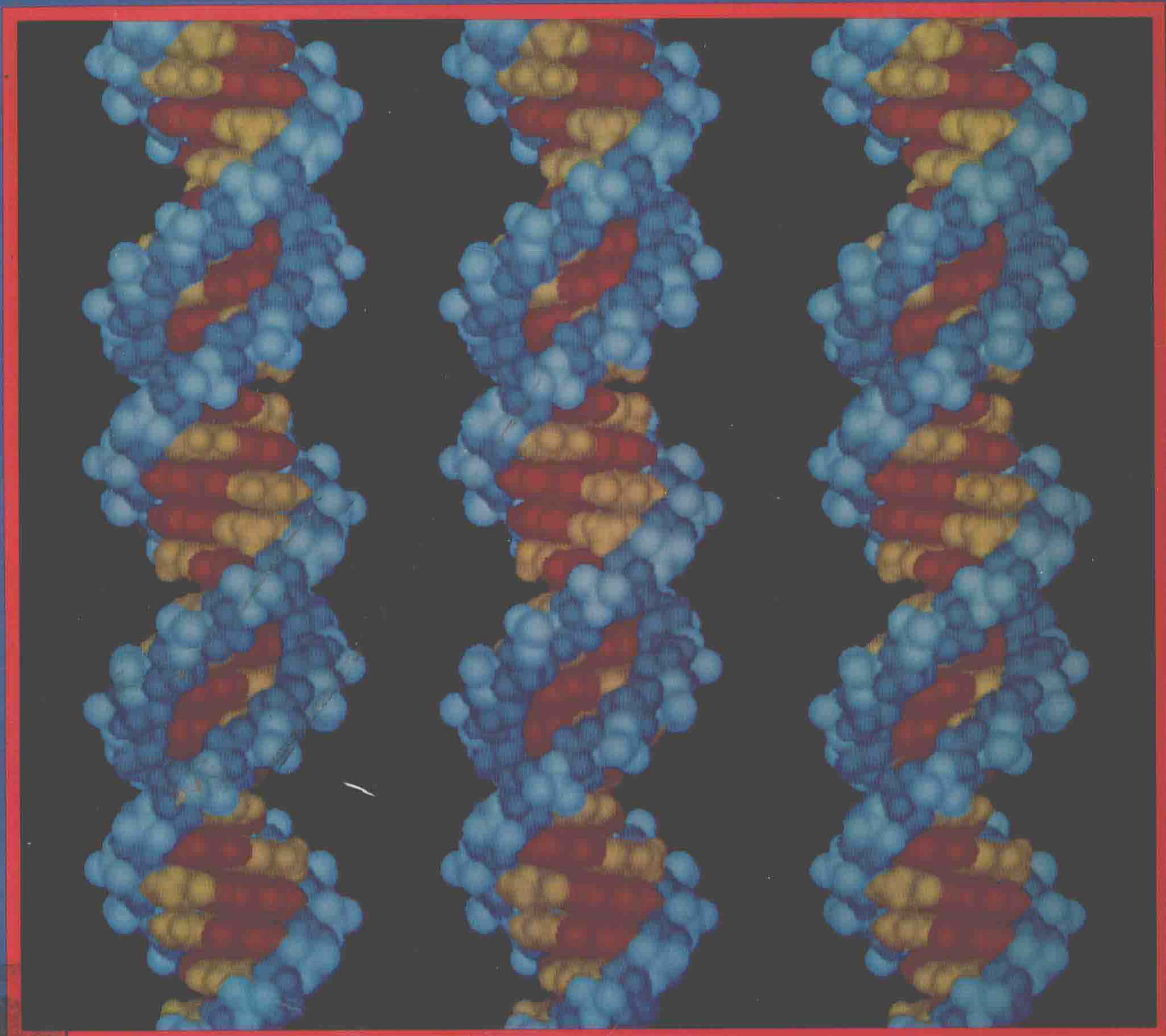
BIOCHEMISTRY

A PROBLEMS APPROACH

SECOND EDITION



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SECOND EDITION

Biochemistry

A Problems Approach

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The cover illustration is a stereo triptych (trip′-tik) showing a DNA double helix. These specially designed three-dimensional graphics are used throughout the book to illustrate a variety of molecular and cellular structures. Techniques for viewing them in stereo are described in the Appendix to Chapter 4. In the cover triptych, phosphate groups are shown in light blue, sugars in blue, purine bases in red, and pyrimidine bases in yellow. (Stereo images courtesy of R. Feldmann, National Institutes of Health.)

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A Problems Approach

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PREFACE

I hear, and I forget,
I see, and I remember,
I do, and I understand.
Ancient Chinese Proverb

This new edition of *Biochemistry, A Problems Approach,* like the first edition, embodies our conviction that the only way to acquire active familiarity with biochemistry is by doing it. Listening to lectures, reading, and memorizing information are important components of learning, but actively analyzing experimental data and solving concrete problems lead to a deeper understanding. This problem-oriented book is intended to help students of biochemistry experience the third line of the proverb as well as the first two.

Scope of the Book

Biochemistry evolved as a descriptive science. The cataloging of biological compounds by natural product chemists and the elucidation of enzymatic pathways by early physiological chemists presented the biochemistry student of the 1950s with a bewildering diversity of chemical structures and reactions. However, subsequent advances in understanding bioenergetics, metabolic control, heredity, evolution, and the origin of life have transformed biochemistry into a more coherent discipline, with its own simplifying principles.

The central challenge of biochemistry in the 1960s and early 1970s was to provide an organized picture of the cell as a functioning chemical system. This challenge has been met successfully, at least for the simplest cells. The challenge of the future is to comprehend, as completely as possible at the molecular level, the more complex systems we call organisms. To do so, we must understand not only the internal chemistry of cells, but also the chemistry of communication between them. This revised edition is intended to help meet that challenge. The book includes new sections on trans-membrane communication, physiology, cytoarchitecture, molecular genetics, and recombinant DNA technology as well as the traditional areas of biochemistry.

Using the Book

This book can be used alone, as the basis for introductory one-semester courses covering macromolecular structure, bioenergetics, metabolism, and gene expression. It also has proven valuable as a complementary text and study aid to more comprehensive biochemistry textbooks in longer courses. The book is designed to encourage self-study and to promote independent exploration, either within or outside a formal course framework.

Each chapter includes presentation of concepts, 15 to 25 problems, and a separate section of answers. The Concepts sections present the material most basic to each topic covered, including all the information necessary to solve the accompanying problems. If the students are encountering this material for the first time, they will benefit from the additional reading suggested in each chapter. At the end of each Concepts section, we provide references to books and articles from the current literature and to four widely used comprehensive biochemistry texts: *Biochemistry* by A. L. Lehninger (second edition); *Biochemistry, The Chemical Reactions of Living Cells,* by D. E. Metzler; *Biochemistry,* by L. Stryer (second edition); and *Principles of Biochemistry,* by A. White, P. Handler, E. Smith, R. Hill, and I. R. Lehman (sixth edition).

The problems relating to each topic are arranged in order of increasing difficulty. The first few are designed to illustrate essential concepts and can be solved by applying the concepts directly. Subsequent problems are more challenging, and may involve analyzing data, designing experiments, or combining basic concepts in a new way. Many important ideas and techniques are presented in the introductions to specific problems in the Problems sections. For reference, these concepts are listed at the end of the corresponding Concepts section.

Solutions to the problems are explained in detail in the Answers sections, wherein lies much of the potential teaching value of the book. Answers to the more challenging problems are written so that the first sentence or two will provide a hint toward the solution, or help steer the student in the right direction. We urge students to work through each answer whether or not they have been able to solve the problem on their own because many ideas not included under Concepts are presented in the Answers sections.

In addition to the answered problems, each chapter includes one to three unanswered problems, marked in the margin with a star (☆). Solutions to these problems are available to instructors on written request from the publisher.

A novel feature of this edition is the expanded use of computer-generated stereo images to illustrate three-dimensional molecular shapes. These striking images, created by Richard Feldmann, are presented as triptychs to allow maximum flexibility in stereo imaging. The triptychs can be used with a conventional stereo viewer, but with a little practice can be viewed in stereo without a viewing aid, as explained in the Appendix to Chapter 4.

Acknowledgments

In preparing this second edition, we have benefited from the experience of many instructors who provided the publishers with suggestions for revisions. We also wish to acknowledge the able assistance of Jim Behnke, sponsoring editor, John Hamburger, production editor, and Gloria Joyce, copy editor, who shepherded the revision through to completion. We are indebted to Cecile Duray-Bito for her knowledgeable rendering of the figures, and to Joan Hargis, Kraig Emmert, Alan Mewbourne, and the staff of the Medical Illustrations Department at Baylor College of Medicine for advice and help in mounting and printing the stereo triptychs. We owe special thanks to Richard J. Feldmann of the Division of Computer Research and Technology, National Institutes of Health, for his patience and generosity in generating and providing the computer images for all the stereo triptychs in the text as well as the color triptych on the cover. Finally, we are grateful to our families and associates for accepting our prolonged involvement with this time-consuming task.

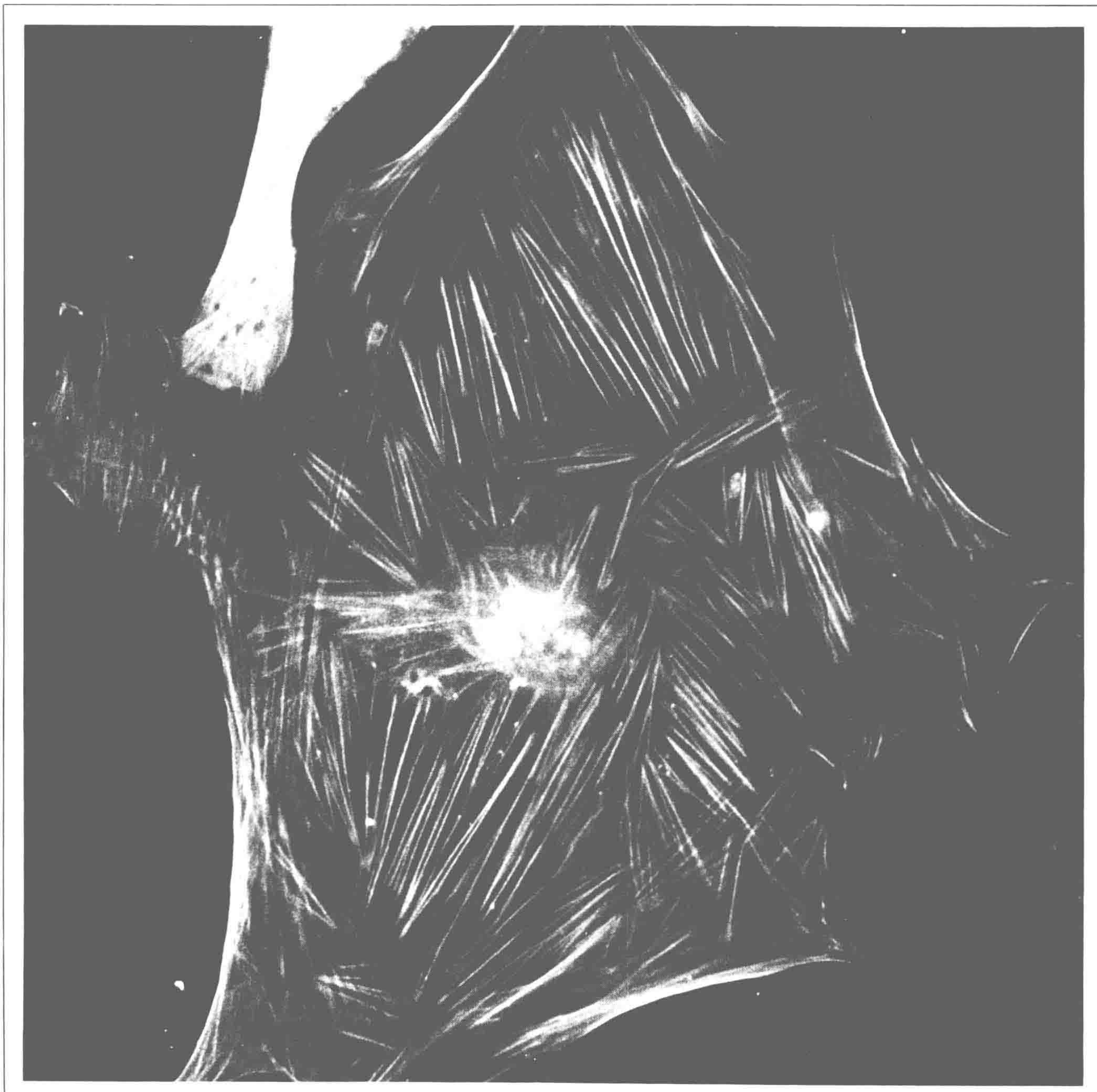
In the course of the revision we have added much new material and have rewritten many sections that required updating. However, we have tried throughout to retain the flavor, format, and general organization of the first edition. We trust that the book will continue to be useful to both students and instructors of biochemistry.

W. B. Wood
J. H. Wilson
R. M. Benbow
L. E. Hood

CONTENTS

PART ONE

Biological Structure and the Chemistry of Proteins



Part One opener photograph: Actin filaments in the cytoskeleton of a mouse fibroblast cell stained with fluorescent anti-actin antibodies and observed with ultraviolet illumination in the light microscope. (Photograph courtesy of E. Lazarides, California Institute of Technology.)

1 Chemical Characteristics of Living Matter

Biochemistry is the study of living organisms at the molecular level. At this level, organisms can be viewed as complex chemical systems that contain all the information necessary to grow and reproduce at the expense of energy and raw materials from the environment. All present-day organisms share common properties in their chemical composition and organization that are the result of natural selection since life began over 3 billion years ago. This chapter considers the chemical makeup of organisms, and the evolutionary rationale for why particular atoms and molecules have been selected over others.

Concepts

1.1 Most organisms are composed of only sixteen chemical elements.

The chemical makeup of organisms appears to have been determined partly by the availability of raw materials in the environment, and partly by the fitness of atoms and molecules for specific roles in life processes. Consequently, the elemental composition of living matter shows both similarities to and distinct differences from the composition of the biosphere—that is, the portion of the earth's crust and atmosphere accessible to organisms. Table 1.1 lists the chemical elements found in organisms, and Table 1.2 compares the elemental composition of living matter to that of the earth's crust. The differences in these compositions can be explained at least partially by the following fitness considerations.

Table 1.1
Elements Found in Organisms

Major covalent-bond-forming elements (all organisms)	Atomic number	Trace elements (all organisms)	Atomic number
H	1	Mn	25
C	6	Fe	26
N	7	Co	27
O	8	Cu	29
P	15	Zn	30
S	16		
Monatomic ions (all organisms)		**Trace elements (some organisms)**	
Na^+	11	B	5
Mg^{2+}	12	Al	13
Cl^-	17	Si	14
K^+	19	V	23
Ca^{2+}	20	Mo	42
		I	53

Table 1.2
Approximate Relative Abundances of Bioelements in All Organisms and in the Earth's Crust (in atoms per 100 atoms)

Element	Organisms[a]	Earth's crust[b]
H	49	0.22
C	25	0.19
O	25	47
N	0.27	<0.1
Ca	0.073	3.5
K	0.046	2.5
Si	0.033	28
Mg	0.031	2.2
P	0.030	<0.1
Na	0.015	2.5
Others	Traces	13.7

[a] From E. S. Deevey, *Scientific American*, September 1970, p. 149.
[b] From E. Frieden, *Scientific American*, July 1972, p. 52.

1. H, O, N, and C, which make up >99% by weight of living matter, are the smallest atoms that can attain stable electronic configurations by sharing 1, 2, 3, and 4 electrons, respectively. They form more stable covalent bonds than any other elements with these valences. Moreover, O, N, and C are the only elements that readily form strong multiple bonds. Carbon, with four valence electrons and the ability to form both C═C and C≡C bonds, has the most versatile combining properties of any element. With H, O, and N, carbon can form a tremendous variety of stable molecules. With O_2 it forms CO_2, a stable gas, soluble in water, that is well suited for circulation of carbon between organisms.

O_2 is also soluble in water and therefore is readily available to nearly all organisms. In addition, it is the third most avid electron acceptor among the elements (behind fluorine and chlorine). Consequently, the transfer of electrons from most other molecules to O_2 yields energy. This process (respiration) provides most of the energy available to nonphotosynthetic organisms.

The chemical properties of carbon contrast markedly with those of silicon, which also has four valence electrons and is more abundant in the biosphere, yet is found in living matter as a trace component only. Because of the larger size of the Si atom, Si—Si bonds are weaker than C—C bonds, and polymers of Si are unstable in the presence of water. In striking contrast to C, Si combines with O to form insoluble silicates or network polymers of silicon dioxide (e.g., quartz) and thus tends to remove itself from circulation in an aerobic environment.

2. Phosphorus and sulfur appear to have been selected for quite different chemical properties. Bonds formed by P and S are often unstable in the presence of water; consequently, considerable energy is required to form them. Because this energy is released when the bonds are hydrolyzed, P- and S-containing molecules such as adenosine triphosphate (ATP) and acetyl coenzyme A are well suited for their roles as the energy carriers of living systems.

3. Monatomic ions (e.g., Na^+, K^+, Ca^{2+}, and Mg^{2+}) play relatively nonspecific roles in organisms, such as the maintenance of osmotic balance, the formation of ionic gradients in nerve conduction and active transport, and the neutralization of charges on macromolecules. The similar ionic compositions of living matter and seawater suggest that the monatomic ions in organisms may have been selected primarily on the basis of their availability.

4. By contrast, at least some of the trace elements undoubtedly were selected for their electronic properties. For example, Fe and Cu, which can exist as stable ions in either of two oxidation states, are well suited to their roles in the active sites of cytochrome proteins, where they serve as acceptors and donors in the electron-transfer reactions of respiration.

1.2 Noncovalent bonds are important in biological structure.

In addition to the familiar covalent bonds that link the atoms in a molecule, four kinds of noncovalent interactions are important in biological systems:

1. **Ionic bonds** result from the electrostatic attraction between two ionized groups of opposite charge, such as carboxyl ($—COO^-$) and amino ($—NH_3^+$) groups in proteins.

2. **Hydrogen bonds (H-bonds)** result from electrostatic attraction between an electronegative atom (usually O or N) and a hydrogen atom that is bonded covalently to a second electronegative atom. The hydrogen atom is thus shared between two electronegative atoms. Three common H-bonds are shown in Figure 1.1.

3. **Van der Waals bonds** are short-range attractive forces between chemical groups in contact. These bonds are much weaker than ionic bonds and H-bonds, but they