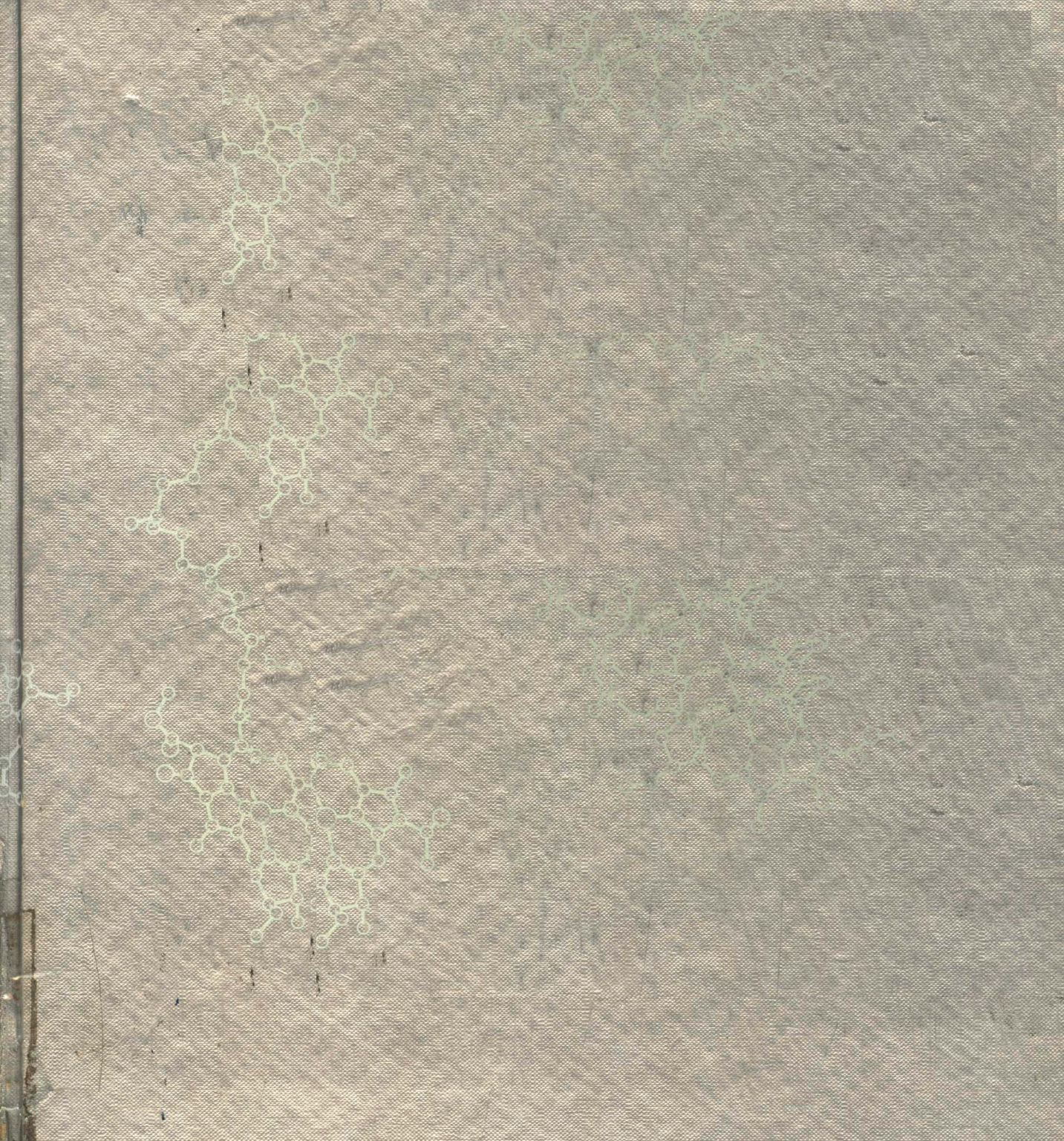


BIOCHEMISTRY

J. David Rawn



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TOWSON STATE UNIVERSITY



HARPER & ROW, PUBLISHERS, New York
Cambridge, Philadelphia, San Francisco,
London, Mexico City, São Paulo, Sydney

Sponsoring Editor: Malvina Wasserman
Project Editor: David Nickol
Designer: Helen Iranyi
Production Assistant: Jacqui Brownstein
Compositor: Progressive Typographers
Printer and Binder: The Murray Printing Company
Art Studio: J&R Art Services, Inc.
Stereo Art: Richard J. Feldmann

The cover shows seven bacteriochlorophyll molecules in the configuration in which they are bound to the bacteriochlorophyll protein (see page 710). The cover design is by Richard J. Feldmann of the National Institutes of Health and is based upon x-ray crystallographic studies of B. W. Matthews and his co-workers.

Biochemistry

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Library of Congress Cataloging in Publication Data

Rawn, J. David, 1944—
Biochemistry.

Includes index.

1. Biological chemistry. I. Title.

QP514.2.R39 1983

574.19'2

82-15454

ISBN 0-06-045335-4

Preface

This text has been written to meet the needs of a full-year, comprehensive, introductory course in biochemistry. The application of chemical principles—especially of organic chemistry—to biochemical phenomena forms the foundation upon which the text has been constructed. A full-year course in organic chemistry is therefore assumed as a prerequisite. Physical chemistry has not, however, been assumed as part of the background of students taking the course for which this text is intended. A biochemistry text based firmly in chemical principles possesses the twofold advantage of using the chemical background of the students and of reflecting the state of the art in biochemistry, where nearly every process is actively investigated in chemical terms and by chemical methods.

Careful attention to the logical development of topics reflects the structure of the text as a whole as well as the individual chapters. The text is divided into three parts.

PART I: THE CONFORMATION AND FUNCTION OF BIOLOGICAL MACROMOLECULES

The Introduction provides a brief overview of biochemistry, a short survey of cell structure, and some generalizations that apply to all of biochemistry. Chapter 1 provides a review of basic concepts of thermodynamics and some examples of their biochemical applications. Chapters 2–4 present a systematic discussion of protein structure. Chapter 5 treats methods for the isolation, purification, and characterization of biological macromolecules. The following two chapters discuss enzyme catalysis (Chapter 6) and enzyme kinetics (Chapter 7). Chemical principles form the heart of the discussion of enzyme-catalyzed reactions in terms of reaction mechanisms familiar to all students who have taken a full-year course in organic chemistry. The principles developed in these chapters recur throughout the text. A discussion of enzyme kinetics can rapidly escalate in mathematical rigor. The level of this presentation, however, is appropriate for students who have not studied physical chemistry. The chapter on enzyme kinetics further develops the principles introduced in the preceding chapter, and the combination of the two chapters provides a thorough introduction to enzymology. Carbohydrates are discussed in Chapter 8 with the conformations of cyclic sugars and the relationship between conformation and biochemical function receiving particular emphasis. The structures, physical properties, and chemistry of nucleosides, nucleotides, and nucleic acids are discussed in Chapter 9, one of the longest chapters in the text. Among the most current topics in this chapter are methods for determining the primary structures of nucleic acids and methods for chemical synthesis of nucleic acids, both of steadily increasing importance. Having discussed the nucleotides, we turn to coen-

zymes in Chapter 10. The mechanisms of the major classes of reactions in which coenzymes participate are discussed in detail in this chapter, and stereochemistry is a central topic. The RS system of configurational nomenclature, familiar to all students who have studied introductory organic chemistry, is reviewed, and the concept of prochirality, perhaps new to many students, is introduced. Part I concludes with a discussion of lipids, biological membranes, and the lipid-soluble vitamins in Chapter 11.

PART II: METABOLISM

The pathways for the degradation and biosynthesis of the major classes of biological molecules are discussed in detail in Part II. This part opens with a discussion of bioenergetics in Chapter 12. Coupled reactions, the structural basis of "energy-rich" metabolites, and the enzymology of phosphoryl group transfer reactions are among the topics discussed in this chapter. Chapter 13 considers the design and regulation of metabolic pathways. The many ways by which allosteric enzymes control the rates of metabolic pathways and the covalent modification of proteins in "cascades" of enzymatic activity are discussed. With the fundamental principles in place, the details of glycolysis (Chapter 14), the citric acid cycle (Chapter 15), oxidative phosphorylation (Chapter 16), carbohydrate metabolism (Chapter 17), photosynthesis (Chapter 18), lipid catabolism and biosynthesis (Chapters 19–20), amino acid catabolism and biosynthesis (Chapters 21–22), and nucleotide biosynthesis (Chapter 23) are each treated in turn. These chapters have similar structures: Each pathway is considered as a whole, and then the individual enzymatic reactions of the pathways are discussed. The bioenergetic aspects of the pathways are considered within the context of the individual reactions as well as from the perspective of the entire pathway. The regulation of each pathway is discussed. Metabolism is thus discussed within a unified perspective and is not treated merely as a list of metabolic steps to be memorized.

PART III: MOLECULAR BIOLOGY

The extraordinarily rapidly advancing field of molecular biology occupies center stage in the final chapters of the book as DNA replication (Chapter 24), transcription of DNA (Chapter 25), protein synthesis (Chapter 26), and regulation of gene expression (Chapter 27) are considered. These chapters are as contemporary as possible within the limits of publishing schedules and they have been carefully constructed for a logical development of the subject. Considered are such important topics as DNA repair, split genes and RNA processing, regulation of protein synthesis at the translational level, and the marvelously baroque process by which antibody diversity is generated. Molecular biology has a highly specialized vocabulary, but jargon has been minimized, and the phenomena discussed in Part III are considered in relation to all that has preceded. The chemical basis of molecular biology is explored to the extent that current knowledge makes possible.

To a significant extent, biochemistry consists of processes that involve interactions of macromolecules with one another or with the small molecules to which they bind. Many of the macromolecules whose three-dimensional structures have been determined are drawn in computer-generated stereo pairs provided through the courtesy (and considerable labor) of Richard J. Feldmann of the National Institutes of Health. A deeper understanding of macromolecular structure can be obtained by viewing these images than is attainable in any other way short of a computer data base of one's own. This aspect of the text is absolutely unique and ought to be of great value to both students and instructors. A stereo viewer is provided inside the back cover of the text. To view the stereo images it is necessary only to center the

viewer over the stereo pair and focus each eye upon a separate image. (About 13 percent of the population is unable to visualize objects in three dimensions by this method).

Problem solving is a fundamental component of biochemistry courses, and many problems have been provided. A solutions manual with completely worked-out solutions to the problems is available. Dr. Robert N. Lindquist (San Francisco State University) is the co-author of the solutions manual.

Each chapter of the text follows a similar pattern. A brief introduction to the topic at hand is followed by a systematic and logical development in which various topics are separated under their own numbered and lettered headings for ease of cross-reference. A concise summary of the essential points is provided at the end of each chapter. A list of leading references and a set of problems are also included at the end of each chapter.

ACKNOWLEDGMENTS

Many persons have labored for many hours to review carefully the contents of the draft manuscript over the years in which it evolved. A critical reviewer, just but unsparing, and intolerant of errors, is the best friend an author ever had. I would like to acknowledge the generous assistance and helpful suggestions of Drs. John N. Aronson (State University of New York at Albany), Nordulf G. W. Debye (Towson State University), Nancy Hamlett (Towson State University), John H. Harrison (University of North Carolina), H. Robert Horton (North Carolina State University), Paul M. Horowitz (The University of Texas, Health Science Center at San Antonio), Robert N. Lindquist (San Francisco State University), and Clarence H. Suelter (Michigan State University). I am also indebted to Floyd A. Blankenship and Alan S. Wingrove who wrote and edited the computer program for preparing the exhaustive index.

I would also like to thank the staff of Harper & Row for their continuous and patient assistance. I am especially indebted to Chemistry Editor Malvina Wasserman, David Nickol, Project Editor, and Helen Iranyi, Designer.

J. DAVID RAWN
Towson, Md.
October, 1982

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