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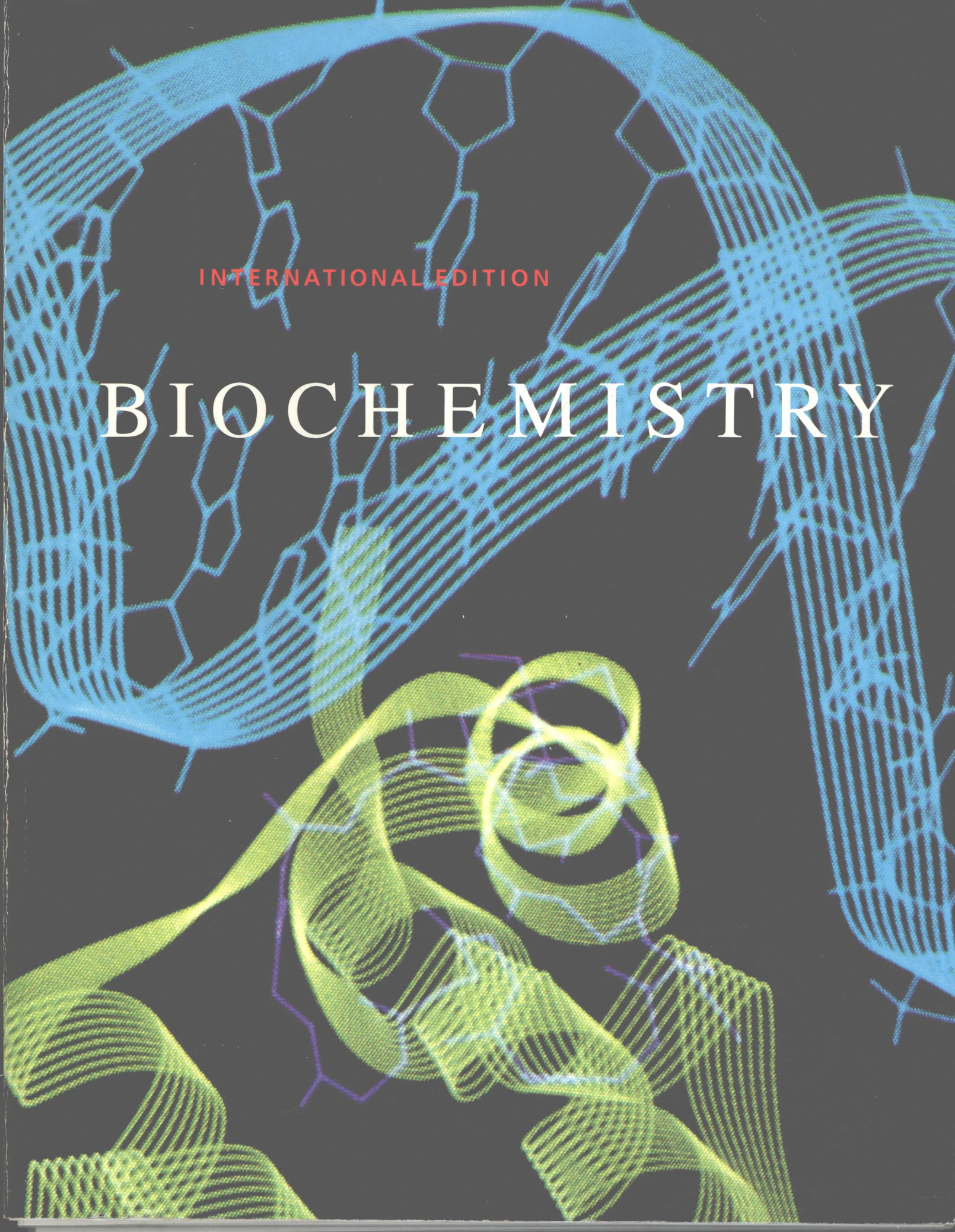

BIOCHEMISTRY

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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.)

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To Margie, Max, and Nora

Verweile doch! Du bist so schön! Goethe

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 Dressler 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.

J. David Rawn

January, 1989

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