Preface

This is a wonderful time in biochemistry. Recombinant DNA technology, protein chemistry, and structural biology have come together to reveal the molecular mechanisms of fundamental biological processes. Many of our dreams of only a few years ago have been fulfilled. One of the fruits of this continuing harvest is a deeper understanding of protein form and function. We now see that proteins are highly sophisticated molecular machines that process energy, matter, and information. Their beautiful molecular ballet is coming into view. Indeed, we can even see the steps taken by a single molecular motor and the flow of ions through a single membrane channel.

These profound advances compel a change in how biochemistry is taught. I have expanded Part II, Proteins: Conformation, Dynamics, and Function, to bring our new understanding of proteins into the core of biochemistry. Membrane channels and pumps, signal transduction cascades, antibodies and T-cell receptors, and molecular motors are now presented in Part II rather than in a separate section at the end of the book. The proteins considered in these chapters reveal much about fundamental processes such as free-energy conversion, signal amplification, and molecular recognition. An understanding of proteins as energy-transforming and information-processing devices enriches the study of metabolism. Oxidative phosphorylation and photosynthesis, for example, are more readily understood and appreciated if the proton-pumping mechanism of bacteriorhodopsin is considered first. Likewise, the hormonal control of metabolism is easier to comprehend if G-protein and tyrosine-kinase cascades are presented first. Another noteworthy change is the new chapter on protein folding and design, an exciting area of inquiry that has broad import.

In 1962, the structures of only two proteins—myoglobin and hemoglobin—were known at atomic resolution. I was fortunate to see them at close range while I was a postdoctoral fellow at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England. Max Perutz, John Kendrew, and the young crystallographers in the laboratory instilled in me a deep appreciation of molecular architecture and its importance in understanding the molecular basis of life. Now, three decades later, we see the fruition of structural biology. X-ray crystallography, joined by electron crystallography and nuclear magnetic resonance spectroscopy, have revealed the structures of hundreds of proteins. This wealth of structural information has illuminated and enriched our understanding of how proteins function as enzymes, transporters, motors, signal transducers, and gene regulators. Recurring structural modules have come into view, bringing insight into how proteins evolved. Structural

biology has also contributed greatly to our understanding of how genetic information is replicated and expressed. DNA is now seen as a highly dynamic molecule that can twist, bend, and breathe. The structures of many complexes of DNA and RNA with polymerases, synthetases, transcriptional regulators, and other cognate proteins have been immensely informative. They are presented in depth in Part V, Genes: Replication and Expression. Throughout this edition, as in previous ones, I have sought to vividly depict the beautiful relations between molecular architecture and biological function, inspired by the experiences of my scientific childhood.

I am grateful to Elva Diaz, Richard Gumport, Roger Koeppe, Carl Rhodes, and John Tymoczko for their critical and perceptive review of the entire manuscript, and to Alexander Glazer for his sustained support and wise counsel. Clint Ballou, Ronald Bentley, Stuart Edelstein, Roger Koeppe II, Brian Law, Peter Rubenstein, Alan Sachs, Ihor Skrypka, Ronald Somerville, Mary Waltner, and Derrick Williamson provided valuable comments on major parts of this book. I have also gained much from the advice provided by Robert Baldwin, Jeremy Berg, Nicholas Cozzarelli, Marilyn Farquhar, Michel Goldberg, Peter Kim, Daniel Koshland, Jr., Richard Mathies, David McKay, George Palade, Peter Parham, Suzanne Pfeffer, Alexander Rich, Timothy Ryan, Robert Shulman, Paul Sigler, James Spudich, Thomas Steitz, Nigel Unwin, Max Vasquez, John Wagner, and William Weis. Joanne Tisch carefully scrutinized the proofs and helped in many other ways with the preparation of this edition, as with the last.

I wish to thank Richard Gumport, Ana Jonas, Richard Mintel, Carl Rhodes, and Roger Koeppe for having written a *Student Companion* to this work. This valuable study guide is an outgrowth of their devotion to teaching and the advancement of biochemical knowledge.

The flowering of structural biology has been accompanied and reinforced by rapid advances in molecular graphics. This edition contains hundreds of new drawings of biomolecules that were generated using a host of powerful tools for visualizing molecular architecture. I am indebted to Michael Levitt for introducing me to *MacImdad*, his interactive graphics program for personal computers, and for providing advice on molecular structure and graphics. Most of the new space-filling models shown in this edition were drawn using *MIDAS*, a program developed by Thomas Ferrin and Conrad Huang. Ball-and-stick models and schematic representations were drawn primarily with *MOLSCRIPT*, a program written by Per Kraulis. I have also benefited from *GRASP*, a program devised by Anthony Nicholls. David Hinds, Kevin Flaherty, and Peter David guided me through UNIX and helped me in many ways with both software and hardware on my Silicon Graphics IRIS computer. I am grateful to Paul Haeberli for making it possible to capture in print the striking molecular images seen on the IRIS screen. I have made extensive use of the Protein Data Bank, a rich and highly accessible repository of structural information maintained by Brookhaven National Laboratory. Many crystallographers shared with me the atomic coordinates of their recently solved structures.

Sonia DiVittorio played a key role in developing this edition and in guiding the preparation of new art. Her sensitive appreciation of biochemistry and dedication to excellence in publishing have made their mark. I am grateful to her for her outstanding contributions. Bill O'Neal, Jr., thoughtfully edited the manuscript, which gained much from his care-

ful scrutiny. I am also indebted to Tomo Narashima and Ian Worpole for many fine drawings. Bill Page was the illustration coordinator. John Hatzakis provided an esthetic design, and Stan Hatzakis crafted each page with a fine eye for integrating word and picture. Georgia Lee Hadler expertly guided the flow and convergence of manuscript and thousands of pages of text and art proof. Julia DeRosa ably coordinated a challenging production process. Nancy Brooks provided valuable assistance at crucial times. Her command of the classics enlivened and enriched the preparation of this edition.

The twelve foreign-language editions of this book—Chinese, French, German, Greek, Italian, Japanese, Korean, Polish, Portuguese, Russian, Serbo-Croatian, and Spanish—have given me special pleasure. I am indebted to the translators for their devoted and scholarly contributions. They have made this book accessible to students in many lands and have fostered the universality of biochemistry. I have greatly enjoyed my contact with students and faculty around the world and look forward to continuing this stimulating and rewarding dialogue.

I was invited several years ago by a medical student newsletter to contribute to an issue entitled "Why Teach?" I responded by recounting my earliest recollection of school. During World War II, in the midst of uncertainty and strife, I attended a primary school in Shanghai that was taught by two Danish ladies in their small apartment. Their educational strategy was simple and highly effective: each student both taught and learned. I learned multiplication from a youngster who had mastered it only a week earlier, and in turn, I taught subtraction to a less advanced peer. Teaching remains my best way of learning. I also teach because the sharing of knowledge is joyful. Kindred souls are joined by the inseparable acts of teaching and learning.

Twenty-three years have passed since I embarked on the intellectual journey of writing a textbook of biochemistry. Each edition has been demanding in a different way. I am deeply grateful to my wife, Andrea, for her sustained support of this endeavor from its inception. Her wisdom has made all the difference. I have been nurtured too by our enlarging family. Two wonderful daughters have joined us—Daniel's wife, Stacy, and Michael's wife, Barri. The birth of our granddaughter Leah a few weeks ago has been an added blessing.

Lubert Stryer

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