PREFACE

Biochemistry is a field of enormous fascination and utility, arising, no doubt, from our own self-interest. Human welfare, particularly its medical and nutritional aspects, has been vastly improved by our rapidly growing understanding of biochemistry. Indeed, scarcely a day passes without the report of a biomedical discovery that benefits a significant portion of humanity. Further advances in this expanding field of knowledge will no doubt lead to even more spectacular gains in our ability to understand nature and to control our destinies. It is therefore of utmost importance that individuals embarking on a career in biomedical sciences be well versed in biochemistry.

This textbook is a distillation of our experiences in teaching undergraduate and graduate students at the University of Pennsylvania and Swarthmore College and is intended to provide such students with a thorough grounding in biochemistry. In writing this text we have emphasized several themes. First, biochemistry is a body of knowledge compiled by people through experimentation. In presenting what is known, we therefore stress how we have come to know it. The extra effort the student must make in following such a treatment, we believe, is handsomely repaid, since it engenders the critical attitudes required for success in any scientific endeavor. Although science is widely portrayed as an impersonal subject, it is, in fact, a discipline shaped through the often idiosyncratic efforts of individual scientists. We therefore identify some of the major contributors to biochemistry (the majority of whom are still professionally active) and, in many instances, consider the approaches they have taken to solve particular biochemical puzzles. The student should realize, however, that most of the work described could not have been done without the dedicated and often indispensable efforts of numerous co-workers.

The unity of life and its variation through evolution is a second dominant theme running through the book. Certainly one of the most striking characteristics of life on earth is its enormous variety and adaptability. Yet, biochemical research has amply demonstrated that all living things are closely related at the molecular level. As a consequence, the molecular differences among the various species have provided intriguing insights into how organisms have evolved from one another and have helped to delineate the functionally significant portions of their molecular machinery.

A third major theme is that biological processes are organized into elaborate and interdependent control networks. Such systems permit organisms to maintain relatively constant internal environments, to respond rapidly to external stimuli, and to grow and to differentiate. A fourth theme is that biochemistry has important medical consequences. We therefore frequently illustrate biochemical principles by examples of normal and abnormal human physiology.

We assume that students who use this text have had the equivalent of one year of college chemistry and at least one semester of organic chemistry (perhaps being taken concurrently) so that they are familiar with both general chemistry and the basic principles and nomenclature of organic chemistry. We also assume that students have taken a one-year college course in general biology in which elementary biochemical concepts were discussed. Students who lack these prerequisites are advised to consult the appropriate introductory textbooks in these subjects.

This book is organized into five parts:

I. **Introduction and Background:** An introductory chapter followed by chapters that review the properties of aqueous solutions and the elements of thermodynamics.

II. **Biomolecules:** A description of the structures and functions of proteins, carbohydrates, and lipids.

III. **Mechanisms of Enzyme Action:** An introduction to the properties, reaction kinetics, and catalytic mechanisms of enzymes.

IV. **Metabolism:** A discussion of how living things synthesize and degrade carbohydrates, lipids, amino acids, and nucleotides with emphasis on energy generation and consumption.

V. **The Expression and Transmission of Genetic Information:** An exposition of nucleic acid structures and both prokaryotic and eukaryotic molecular biology.

This organization permits us to cover the major areas of biochemistry in a logical and coherent fashion. Yet, modern biochemistry is a subject of such enormous scope that to maintain a relatively even depth of coverage throughout the text, we include more material than most one-year biochemistry courses will cover in detail. This depth of coverage, we believe, is one of the strengths of this book; it permits the instructor to teach a course of his/her own design and still provide the student with a resource on biochemical subjects not emphasized in the course.

The order in which the subject matter of the book is presented more or less parallels that of most biochemistry courses. However, several aspects of the book's organization deserve comment:

1. We present nucleic acid structures (Chapter 28) as part of molecular biology (Part V) rather than in our discussions of structural biochemistry (Part II) because nucleic acids are not mentioned in any substantive way until Part V. Instructors who, nevertheless, prefer to consider nucleic acid structures in a sequence different from that in the text can easily do so because Chapter 28 requires no familiarity with enzymology or metabolism.

2. We have split our presentation of thermodynamics between two chapters. Basic thermodynamic principles—enthalpy, entropy, free energy, and equilibrium—are discussed in Chapter 3 because these subjects are prerequisite for understanding structural biochemistry, enzyme mechanisms, and kinetics. Metabolic aspects of thermodynamics—the thermodynamics of phosphate compounds and oxidation–reduction reactions—are presented in Chapter 15, since knowledge of these subjects is not required until the chapters that follow.

3. Techniques of protein purification are described in a separate chapter (Chapter 5) that precedes the discussion of protein structure and function. We have chosen this order so that students will not feel that proteins are somehow "pulled out of a hat." Nevertheless, Chapter 5 has been written as a resource chapter to be consulted repeatedly as the need arises.

4. Chapter 9 describes the properties of hemoglobin in detail so as to illustrate concretely the preceding discussions of protein structure and function. This chapter introduces allosteric theory to explain the cooperative nature of hemoglobin oxygen binding. The subsequent extension of allosteric theory to enzymology (Chapter 12) is a relatively simple matter.

5. Concepts of metabolic control are presented in the chapters on glycolysis (Chapter 16) and glycogen metabolism (Chapter 17) through discussions of flux generation, allosteric regulation, substrate cycles, covalent enzyme modification, and cyclic cascades. We believe that these concepts are best understood when they are studied in metabolic context rather than as independent topics.

6. There is no separate chapter on coenzymes. These substances, we feel, are more logically studied in the context of the enzymatic reactions in which they participate.

7. Glycolysis (Chapter 16), glycogen metabolism (Chapter 17), the citric acid cycle (Chapter 19), and oxidative phosphorylation (Chapter 20) are detailed as models of general metabolic pathways with the emphasis placed on many of the catalytic and control mechanisms of the enzymes involved. The principles illustrated in these chapters are reiterated in somewhat less detail in the other chapters of Part IV.

8. Consideration of membrane transport (Chapter 18) precedes that of mitochondrially based metabolic pathways, including the citric acid cycle and oxidative phosphorylation. In this manner, the idea of the compartmentalization of biological processes can be easily assimilated.

9. Discussions of both the synthesis and the degradation of lipids have been placed in a single chapter (Chapter 23) as have the analogous discussions of amino acids (Chapter 24) and nucleotides (Chapter 26).

10. Energy metabolism is summarized and integrated in terms of organ specialization in Chapter 25, followng the descriptions of carbohydrate, lipid, and amino acid metabolism.

11. The basic principles of both prokaryotic and eukaryotic molecular biology are introduced in sequential chapters on transcription (Chapter 29), translation (Chapter 30), and DNA replication, repair and recombination (Chapter 31). Viruses (Chapter 32) are the considered as paradigms of more complex cellular functions followed by discussions of newly emerging concepts of eukaryotic gene expression (Chapter 33).

12. Chapter 34, the final chapter, is a series of minichapters that describe the biochemistry of a variety

of well-characterized human physiological processes: blood clotting, the immune response, muscle contraction, hormonal communication, and neurotransmission.

The old adage that you learn a subject best by teaching it simply indicates that learning is an active rather than a passive process. The problems we provide at the end of each chapter are therefore designed to make students think rather than to merely regurgitate poorly assimilated and rapidly forgotten information. Few of the problems are trivial and some of them (particularly those marked with an asterisk) are quite difficult. Yet, successfully working out such problems can be one of the most rewarding aspects of the learning process. Only by thinking long and hard for themselves can students make a body of knowledge truly their own. The answers to the problems are worked out in detail in the Solutions Manual that accompanies this text. This manual, however, can only be an effective learning tool if the student makes a serious effort to solve a problem before looking up its answer.

We have included lists of references at the end of every chapter to provide students with starting points for independent biochemical explorations. The enormity of the biochemical research literature precludes us from giving all but a few of the most important research reports. Hence, we list what we have found to be the most useful reviews and monographs on the various subjects covered in each chapter.

Biomedical research is advancing at such an astonishing pace that a seminal discovery often leads to the development of a mature subdiscipline within the period of a year or so. Consequently, a textbook on biochemistry can never be truly up to date. To alleviate this problem, we shall periodically bring out supplements to this textbook that review the recent biochemical literature and list some of its most important reviews and research reports. Nevertheless, students should be encouraged to peruse the current biochemical literature for only then will they acquire a feeling for the scope and excitement of modern biochemistry.

Finally, although we have made every effort to make this text error free, we are under no illusions that we have done so. We therefore request that readers provide us with their comments and criticisms.

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