Biochemistry

for the Pharmaceutical Sciences

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Preface

This text is based on my course for first-year students in our PharmD curriculum. These students have taken organic chemistry and are taking physiology concurrently, and they need to gain a background in enzymology and in primary metabolism for their upcoming courses in drug therapy. At the University of Illinois at Chicago, we only spend about one semester on classical biochemical topics. Keeping in mind that we are not preparing students for a career in biochemical research, we therefore need a shorter, less detailed, and less expensive alternative to the available large biochemistry textbooks.

This text follows a traditional organization for a course in biochemistry. There are four main divisions in the text. The first five chapters are largely reviews of topics from organic and basic physical chemistry; then two chapters on enzymes; then eight chapters on primary metabolism; and lastly a chapter on topics at the level of molecular biology: DNA replication and repair, and transcription and translation of genetic messages.

Chapter 1 starts with basic thermodynamic concepts, just enough to help in later explanations of metabolic strategies. Then comes a series of chapters that introduce (or review) the chemistry of the fundamental building blocks of biochemistry: carbohydrates, amino acids, nucleic acids, and lipids. These chapters go from the level of the monomer up to the level of the polymer (or in the case of the lipids, to the level of the biomembrane). Material at the beginning of these chapters may be skipped by students who are well-prepared from their organic chemistry course, though I do recommend that some time be taken with the latter half of each of these chapters, as the topics here are generally not covered in organic chemistry courses.

Next there are two chapters on enzymology. Chapter 6 is on enzyme mechanisms, while Chapter 7 deals with mathematical aspects of enzyme kinetics and inhibition. I believe this approach keeps students interested by making their first contact with enzymology close to their previous study of reaction mechanisms in organic chemistry. The discussion of enzyme mechanisms starts with those we can regard as "classical": ribonuclease A and chymotrypsin. Then carbonic anhydrase introduces the use of metal ion cofactors; cofactor use is elaborated upon in later chapters, for example in discussions of the transaminases, of pyruvate dehydrogenase, and of phenylalanine hydroxylase. Cooperativity and allosterism are introduced via hemoglobin and aspartate transcarbamoylase.

In the second of these chapters on enzymology, the presentation of the mathematics of enzyme kinetics is deliberately kept simple, with little derivation of equations (not a useful exercise for future pharmacists, in my opinion). The Michaelis-Menten model is emphasized, as is competitive inhibition. There is a very brief introduction to drug design of enzyme inhibitors as well.

The main meat of the text comes after we finish with enzymology. Chapter 8 discusses the conventions and basic concepts in metabolic biochemistry: pathways, feedback, and other unifying ideas. Then we move into sugar metabolism and energy generation for the cell (Chapter 9). Glycolysis is first, then gluconeogenesis and glycogen metabolism. After working through the tricarboxylic acid cycle and the notion of anaplerosis, we get to respiratory complexes and the coupling of ATP synthesis in the mitochondrion to proton pumping. This is followed by a short chapter on the pentose phosphate pathway and the generation of reducing power for biosynthesis and protection against oxidative agents.

After this, it is time to deal with energy production from lipids; we also need to treat lipid biosynthesis (Chapter 13). Next comes the metabolism of amino acids (Chapter 14). I have deliberately emphasized their use as a fuel for the cell over their biosynthesis, to maintain an emphasis on energy generation for the cell. I wrap up the presentation of primary metabolism with the synthesis and breakdown of the building blocks of DNA and RNA.

The last chapter is an altogether too brief treatment of cellular transactions with DNA and RNA. This material is typically the subject of multiple chapters in the large encyclopedic textbooks of biochemistry, and I have compressed all of this into one chapter. Necessarily I have left out much; my excuse is that I wished to keep the book to a reasonable length, and my hope is that most, if not all, of the students using this book will have taken a course in modern cell biology, where these topics have received their due attention.

The Questions for Discussion at the end of each chapter are intended to spur in-class review and elaboration of the topics in that chapter. Acquiring the proper specialized vocabulary is necessary in the study of any scientific subject. Toward this end, I have included a short glossary of terms used in this text.

Through this organization and approach, and these helpful features, *Biochemistry for the Pharmaceutical Sciences* makes this important topic accessible to students.

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I also wish to thank the reviewers whose detailed criticisms greatly improved the text.

In preparing several of the figures of proteins and nucleic acids, I have used the Swiss-PdbViewer (also known as DeepView) to visualize structures from the Protein Data Bank. Those wishing to learn more about this highly useful program should visit the web site at http://www.expasy.org/spdbv. The authors of the program have requested that I cite their publication as well: N. Guex and M.C. Peitsch (1997) *Electrophoresis* 18:2714–2723.

Finally, I must thank the many students who have patiently pored over my lecture notes (the precursor to this text), and just as patiently inquired why I had misspelled this, contradicted myself there, and mis-drew that structure or diagram. Their critiques contributed very substantially to this book.

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