PREFACE

Several years ago, we set out to write a short biochemistry textbook that combined succinct, clear chapters with extensive problem sets. We believed that students would benefit from a modern approach involving broad but not overwhelming coverage of biochemical facts, focusing on the chemistry behind biology, and providing students with practical knowledge and problem-solving opportunities. Our experience in the classroom tells us that effective learning also requires students to become as fully engaged with the material as possible. To that end, we have embraced a strategy of posing questions in different ways throughout each chapter, so that students will not simply read and memorize but will explore and discover on their own—a truer reflection of how biochemists approach their work in the laboratory or clinic.

As always, we view our textbook as a guidebook for students, providing a solid foundation in biochemistry, presenting complete, up-to-date information, and showing the practical aspects of biochemistry as it applies to human health, nutrition, and disease. We hope that students will develop a sense of familiarity and comfort as they encounter new material, explore it, and test their understanding through problem solving.

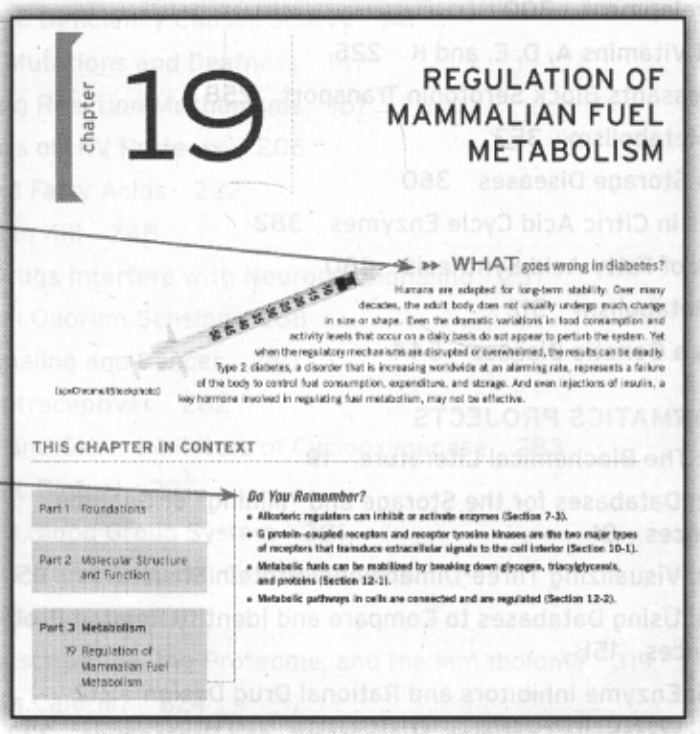
New to This Edition

Learning is an active rather than passive activity, and one of the most powerful mechanisms for encouraging students to assume responsibility for their learning is to prompt them to examine the material in different ways. This edition includes a variety of questions that require students to review what they already know, to take a closer look at diagrams, to derive their own explanations, and to apply their skills to novel situations. Some features of this question-based approach are outlined here.

Chapter opening "Do you Remember?" sections. Students often have difficulty recalling previously learned material and relating it to the new topics they encounter. New chapter openers provide context with a set of 4 to 6 *Do You Remember* questions to remind students about relevant, foundational material they have seen in previous chapters.

Chapter opening questions are answered within that chapter

Do You Remember? reminds students about relevant material from previous chapters.



Art program. Revisions to the art program have been made with students in mind. Our goal has been to maximize the clarity and improve the pedagogical value of the illustrations that accompany the text.

- In this edition, we focused on adding visual impact in illustrations by providing more accurate three-dimensional depictions of proteins and membranes.
- **Figure Questions** are now included in many captions to prompt students to inspect the diagram more closely, compare it to similar figures, or draw connections to other topics.

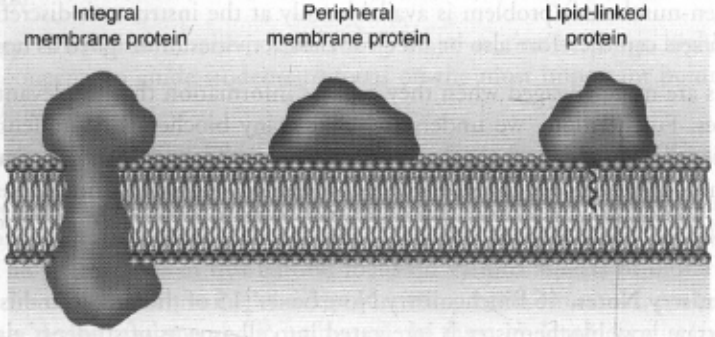


Figure 8-6 Types of membrane proteins. This schematic cross-section of a membrane shows an integral protein spanning the width of the membrane, a peripheral membrane protein associated with the membrane surface, and a lipid-linked protein whose attached hydrophobic tail is incorporated into the lipid bilayer.

? Which type of membrane protein would be easiest to separate from the lipid bilayer?

Figure Questions encourage students to more fully engage the material.

- Many of the molecular graphics were re-rendered at higher resolution and to show newly discovered structural features. A number of illustrations were provided by the researchers themselves, providing students a glimpse of how biochemists create models to communicate their new discoveries.

Sample Calculations with Practice Problems. Students need to develop their quantitative skills to understand particular aspects of biochemistry. This edition includes 6 new Sample Calculations, for a total of 24. In addition, each Sample Calculation now includes a set of Practice Problems to provide additional opportunities for students to master quantitative skills. Students can quickly check their answers in the Appendix before moving on.

SAMPLE CALCULATION 10-1 ●●●

PROBLEM

A sample of cells has a total receptor concentration of 10 mM. Twenty-five percent of the receptors are occupied with ligand, and the concentration of free ligand is 15 mM. Calculate K_d for the receptor–ligand interaction.

SOLUTION

Because 25% of the receptors are occupied, $[R \cdot L] = 2.5$ mM and $[R] = 7.5$ mM. Use Equation 10-1 to calculate K_d:

$$K_d = \frac{[R][L]}{[R \cdot L]} = \frac{(0.0075)(0.015)}{(0.0025)} = 0.045\ M = 45\ mM$$

PRACTICE PROBLEMS ●●●

1. A sample of cells has a total receptor concentration of 24 μM, and 40% of the receptors are occupied with ligand. The concentration of free ligand is 10 μM. Calculate K_d.
2. K_d for a receptor–ligand interaction is 3 mM. When the concentration of free ligand is 18 mM and the concentration of free receptor is 5 mM, what is the concentration of receptor that is occupied by ligand?
3. The total concentration of receptors in a sample is 20 mM. The concentration of free ligand is 5 mM, and K_d is 10 mM. Calculate the percentage of receptors that are occupied by ligand.

Sample Calculation models the application of key equations to real data.

Practice Problems provide opportunities to check progress.

End-of-chapter problems. Students need ample opportunities to practice and apply their knowledge. This edition includes 36% more problems than the previous edition, bringing the total number of end-of-chapter problems to 1380. The problems, encompassing a variety of types, are grouped by section and are designed to prompt students to recall information, apply it to novel situations, draw connections between different topics, and relate new material to material learned previously or in other courses. Many problems are case studies based on data from research publications and clinical reports. To promote students' independence and to build confidence in their problem-solving skills, virtually all problems are arranged as successive pairs that address the same or related topics. The solution to the first (odd-numbered) problem is included in an appendix, while the solution to the second (even-numbered) problem is available only at the instructor's discretion. The problem sets can therefore also be used for class activities or assigned as homework.

Students are more engaged when they process information that is relevant to their own lives. Furthermore, we understand that many biochemistry students pursue careers in related fields and want to better understand how the subject matter they are learning in biochemistry relates to their intended study of nutrition, pharmacology, biotechnology, exercise science, and so on. Students also need an introduction to what is new and exciting in the field of biochemistry.

Biochemistry Notes. 46 Biochemistry Note boxes (15 of them new to this edition) demonstrate how biochemistry is integrated into all aspects of students' daily lives, addressing a wide range to topics including carbon monoxide poisoning, antifungal drugs, cellulosic biofuels, dietary guidelines, and antibiotics. Each box includes at least one question for students to consider.

Clinical Connections. A total of 15 Clinical Connection boxes, most of them new to this edition, explore the biochemical causes of diseases, their symptoms, and their treatment. Topics include diseases related to protein misfolding, vitamin deficiencies, antidepressants, alcohol toxicity, and metabolism of cancer cells. Questions at the end of each Clinical Connection box help students develop their analytical skills. Answers are provided in an appendix, so students can easily check their understanding as they proceed.

Up-to-date topics. New material for this edition focuses on developments in genomic analyses (Chapter 3), quantitative PCR (Chapter 3), mass spectrometry for protein analysis (Chapter 4), receptor protein structure (Chapter 10), the ATP synthase mechanism (Chapter 15), the role of probiotic organisms (Chapter 19), treatments for diabetes (Chapter 19), the histone code (Chapter 20), and eukaryotic ribosome structure (Chapter 22).

Traditional Pedagogical Strengths

Key Concepts. The information conveyed in biochemistry can be overwhelming to students. Key Concepts at the beginning of each section prompt students to recognize the important takeaways or concepts in each section, providing the scaffolding for understanding by better defining these important points.

Concept Review. Students need to "keep up" in biochemistry. Concept Review questions appear at the end of every section and are designed for students to check their mastery of the section's key concepts.

Key sentences summarizing main points are printed in italics to assist with quick visual identification.

Tools and Techniques Sections. These portions of text, appearing at the end of Chapters 2, 3, and 4, showcase some practical aspects of biochemistry and provide an overview of some key experimental techniques that students are likely to

encounter in their reading or laboratory experience, such as preparation of buffers, techniques for manipulating nucleic acids (DNA sequencing, PCR, recombinant DNA, genetically modified organisms, and gene therapy), and protein analysis (chromatographic separations, protein sequencing, and techniques for determining protein three-dimensional structure).

Metabolism overview figures. Metabolism is a challenging subject for students. An overview figure outlining the major metabolic pathways is introduced in Chapter 12 and revisited in subsequent chapters on metabolism in order to help students place individual metabolic pathways into a broader context. Chapters 13 and 17, which focus heavily on multiple pathways, include an additional summary figure as a study aid.

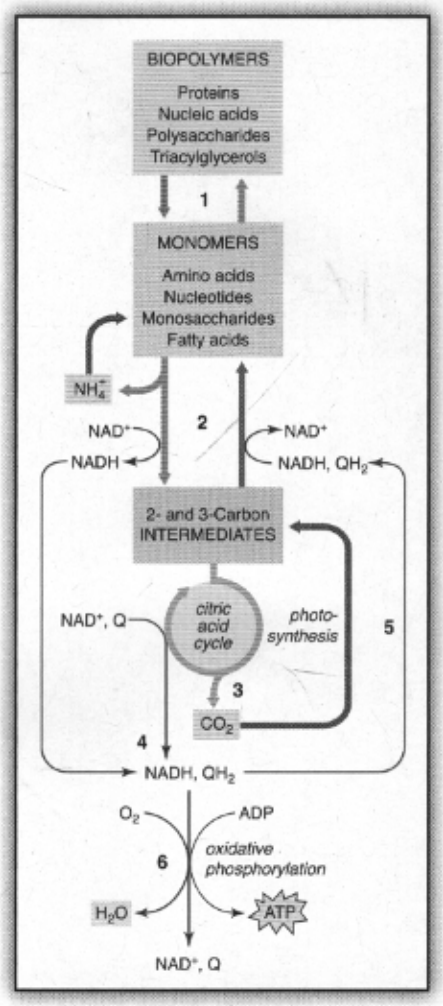
Summary. Chapter summaries, organized by major section headings, highlight important concepts to guide students to focus on the most important points within each section.

Key terms are in boldface. Their definitions are also included in the **Glossary**.

Bioinformatics Projects. A great deal of biochemistry can be done outside the laboratory, using databases and programs available to researchers as well as students. The six exercises in this edition focus on various aspects of bioinformatics (the biochemical literature, nucleotide sequences, protein structures, protein evolution, drug design, and metabolic pathways), In these in-depth exercises, designed to introduce students to the online databases and software tools of bioinformatics, students are given detailed instructions for accessing and manipulating different types of information as well as specific questions to answer and suggestions for further exploration.

An annotated list of **Selected Readings** following each chapter includes recent short papers, mostly reviews, that students are likely to find useful as sources of additional information.

Metabolic Overview Figures provide "big picture" context.



Organization

We have chosen to focus on aspects of biochemistry that tend to receive little coverage in other courses or present a challenge to many students. Thus, in this textbook, we devote proportionately more space to topics such as acid–base chemistry, enzyme mechanisms, enzyme kinetics, oxidation–reduction reactions, oxidative phosphorylation, photosynthesis, and the enzymology of DNA replication, transcription, and translation. At the same time, we appreciate that students can become overwhelmed with information. To counteract this tendency, we have intentionally left out some details, particularly in the chapters on metabolic pathways, in order to emphasize some general themes, such as the stepwise nature of pathways, their evolution, and their regulation.

In keeping with our guidebook approach to biochemistry, we have attempted to place some information in its broader biological context by telling a story. For example, in Chapter 9, the generation of a nerve impulse ties together information about membrane permeability, transport, and fusion. In Chapter 17, different aspects of lipid metabolism are linked to atherosclerosis.

The 22 chapters of *Essential Biochemistry* are relatively short so that students can spend less time reading and more time extending their learning through active problem-solving. Most of the problems require some analysis rather than simple recall of facts. Many problems based on research data provide students a glimpse of the "real world" of science and medicine.

Although each chapter of *Essential Biochemistry, Third Edition* is designed to be self-contained so that it can be covered at any point in the syllabus, the 22 chapters are organized into four parts that span the major themes of biochemistry, including

some chemistry background, structure–function relationships, the transformation of matter and energy, and how genetic information is stored and made accessible.

Part 1 of the textbook includes an introductory chapter and a chapter on water. Students with extensive exposure to chemistry can use this material for review. For students with little previous experience, these two chapters provide the chemistry background they will need to appreciate the molecular structures and metabolic reactions they will encounter later.

Part 2 begins with a chapter on the genetic basis of macromolecular structure and function (Chapter 3, From Genes to Proteins). This is followed by chapters on protein structure (Chapter 4) and protein function (Chapter 5), with coverage of myoglobin and hemoglobin, and cytoskeletal and motor proteins. An explanation of how enzymes work (Chapter 6) precedes a discussion of enzyme kinetics (Chapter 7), an arrangement that allows students to grasp the importance of enzymes and to focus on the chemistry of enzyme-catalyzed reactions before delving into the more quantitative aspects of enzyme kinetics. A chapter on lipid chemistry (Chapter 8, Lipids and Membranes) is followed by two chapters that discuss critical biological functions of membranes (Chapter 9, Membrane Transport, and Chapter 10, Signaling). The section ends with a chapter on carbohydrate chemistry (Chapter 11), completing the survey of molecular structure and function.

Part 3 begins with an introduction to metabolism that provides an overview of fuel acquisition, storage, and mobilization as well as the thermodynamics of metabolic reactions (Chapter 12). This is followed, in traditional fashion, by chapters on glucose and glycogen metabolism (Chapter 13); the citric acid cycle (Chapter 14); electron transport and oxidative phosphorylation (Chapter 15); the light and dark reactions of photosynthesis (Chapter 16); lipid catabolism and biosynthesis (Chapter 17); and pathways involving nitrogen-containing compounds, including the synthesis and degradation of amino acids, the synthesis and degradation of nucleotides, and the nitrogen cycle (Chapter 18). The final chapter of Part 2 explores the integration of mammalian metabolism, with extensive discussions of hormonal control of metabolic pathways and disorders of fuel metabolism (Chapter 19).

Part 4, the management of genetic information, includes three chapters, covering DNA replication and repair (Chapter 20), transcription (Chapter 21), and protein synthesis (Chapter 22). Because these topics are typically also covered in other courses, Chapters 20–22 emphasize the relevant biochemical details, such as topoisomerase action, nucleosome structure, mechanisms of polymerases and other enzymes, structures of accessory proteins, proofreading strategies, and chaperone-assisted protein folding.