PREFACE

The last several years have seen enormous advances in biochemistry, particularly in the areas of macromolecular structure and function and in molecular biology. Against this backdrop, we asked, "*What do students of modern biochemistry really need to know and how can we, as authors, help them appreciate the details without losing sight of the big picture?*" We concluded that it is more important than ever to provide a solid biochemical foundation, rooted in chemistry, to prepare students for the scientific challenges of the future. With that in mind, we reexamined the contents of *Principles of Biochemistry*, focusing on basic principles and striving to polish the text and improve the pedagogy throughout the book so that it is even more accessible to students. We added additional opportunities for students to check their understanding as they read. At the same time, we incorporated new material in a way that links it to the existing content, mindful that students optimally assimilate new information in the proper context. We believe that students are best served by a textbook that is complete, clearly written, and relevant to human health and disease.

New for the Fourth Edition

The fourth edition of *Principles of Biochemistry* includes significant changes and updates to the contents. In recognition of the tremendous advances in structural biochemistry, we have added new information about membrane transporters, signal transduction proteins, mitochondrial respiratory complexes, and the DNA replication and protein synthesis machinery. New experimental approaches for studying complex systems are introduced, including the DNA pyrosequencing technique, metagenomics, atomic force microscopy, genome-wide disease association studies, DNA polymorphisms in genealogy, and the role of microRNAs in gene regulation. Notes on a variety of human diseases and pharmacological effectors have been expanded to reflect recent research findings.

Artwork

In this edition, we have also focused on improving and updating the artwork in the text. Students' ability to understand and interpret biochemical diagrams, illustrations, and processes plays a significant role in their understanding both the big picture and details of biochemistry. We've created several unique features to help students use the visuals in concert with the text:

- **Process Diagrams.** These visually distinct illustrations highlight important biochemical processes and integrate descriptive text into the figure, appealing to visual learners. By following information in the form of a story, students are more likely to grasp the key principles and less likely to simply memorize random details.

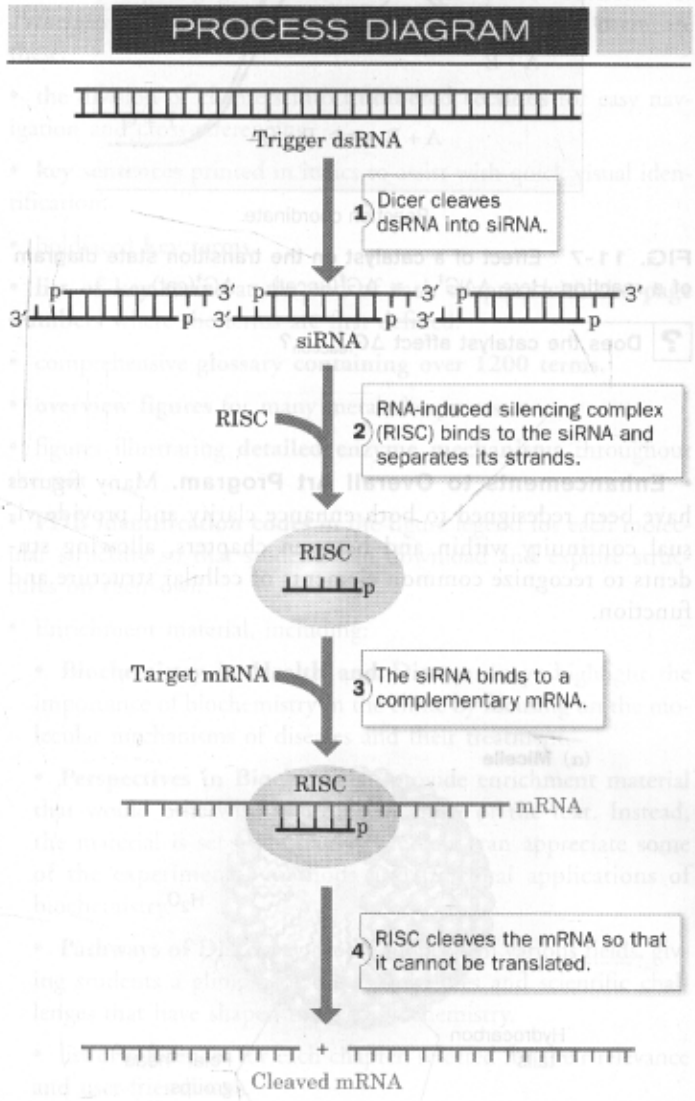

FIG. 28-37 A mechanism of RNA interference. ATP is required for Dicer-catalyzed cleavage of RNA and for RISC-associated helicase unwinding of double-stranded RNA. Depending on the species, the mRNA may not be completely degraded.

- **Figure Questions.** To further underscore the importance of students' ability to interpret various images and data, we've included questions within figure captions that encourage students to more fully engage the material and test their understanding of the process being illustrated.

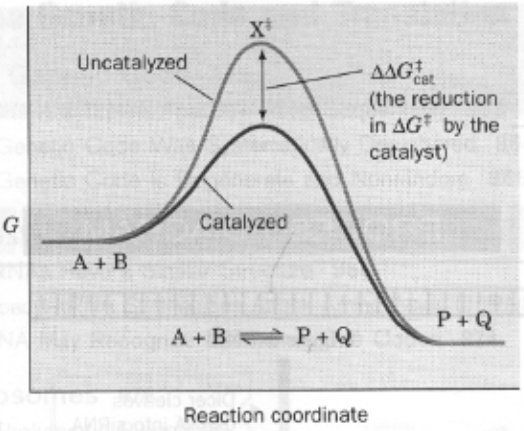

FIG. 11-7 Effect of a catalyst on the transition state diagram of a reaction. Here $\Delta\Delta G^{\ddagger}_{cat} = \Delta G^{\ddagger}(\text{uncat}) - \Delta G^{\ddagger}(\text{cat})$.

? **Does the catalyst affect $\Delta G_{reaction}$?**

• **Enhancements to Overall Art Program.** Many figures have been redesigned to both enhance clarity and provide visual continuity within and between chapters, allowing students to recognize common elements of cellular structure and function.

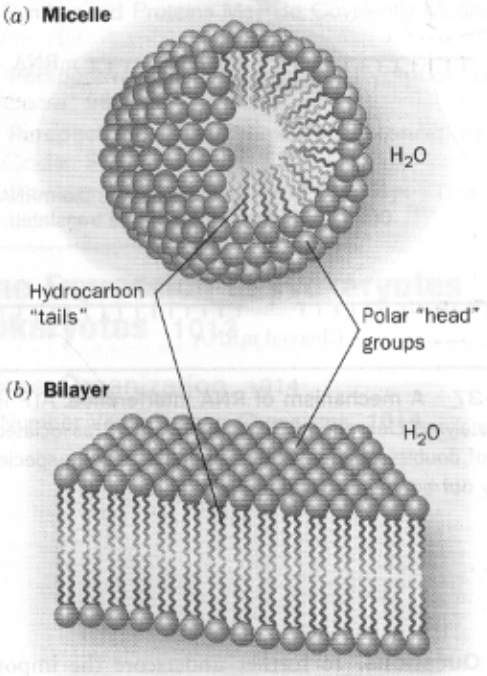

FIG. 2-11 Structures of micelles and bilayers. In aqueous solution, the polar head groups of amphipathic molecules are hydrated while the nonpolar tails aggregate by exclusion from water. (*a*) A micelle is a spheroidal aggregate. (*b*) A bilayer is an extended planar aggregate.

• **Molecular Graphics.** Well over 100 figures have been replaced with state-of-the-art molecular graphics. The new figures are more detailed, clearer, and easier to interpret, and in many cases, reflect recent refinements in molecular visualization technology that have led to higher-resolution macromolecular models or have revealed new mechanistic features.

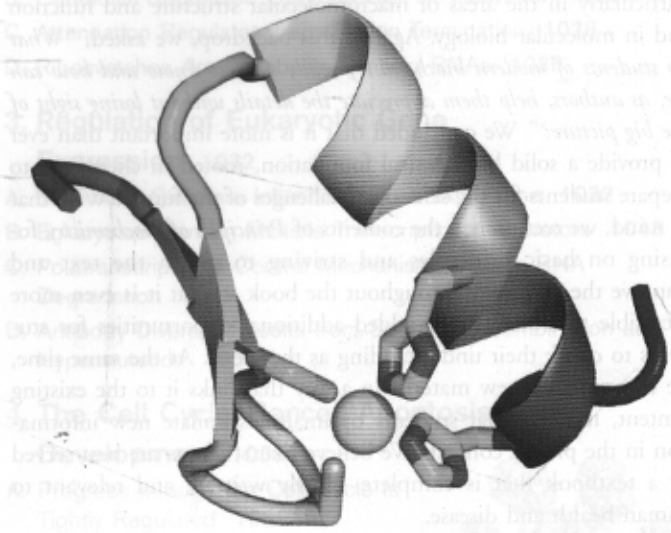

FIG. 6-37 X-Ray structure of a zinc finger motif of the DNA-binding protein Zif268. The polypeptide chain is drawn in ribbon form and colored in rainbow order from its N-terminus (*blue*) to its C-terminus (*red*). The side chains of the Cys and His residues that tetrahedrally ligand a Zn^{2+} ion (*cyan sphere*) are drawn in stick form with C green, N blue, and S yellow. [Based on an X-ray structure by Carl Pabo, MIT. PDBid 1ZAA.]

• **Media Assets.** The dedicated *WileyPLUS* course, our online teaching and learning solution to accompany *Principles of Biochemistry, Fourth Edition,* plays a key role in students' ability to understand and manipulate structural images. The media assets in *WileyPLUS,* such as Guided Explorations, Animated Figures, Interactive Exercises, and Kinemages, employ extensive animations and three-dimensional structures so that students can experience biochemistry beyond the static, two-dimensional page. Users can interact with the materials at their own pace, making them ideal for independent study.

Pedagogy

Throughout the previous three editions of *Principles of Biochemistry,* we have always given significant thought to the pedagogy within the text and have concentrated on fine-tuning and adding some new elements to promote student learning. We have continued to refine the pedagogy in this fourth edition; the enhancements include the following:

• **Key concepts** at the beginning of each section that prompt students to recognize the important "takeaways" or concepts in each section, providing the scaffolding for understanding by better defining these important points.

- **Checkpoint** questions, a robust set of study questions that appear at the end of every section for students to check their mastery of the section's key concepts. Separate answers are not provided, encouraging students to look back over the chapter to reinforce their understanding, a process that helps develop confidence and student-centered learning.

- **Reviews of chemical principles** that underlie biochemical phenomena, including thermodynamics and equilibria, chemical kinetics, and oxidation–reduction reactions. New additions include reviews of Le Châtelier's principle and the curved-arrow convention for reaction mechanisms.

- **Boxes to highlight topics** that link students to areas beyond basic biochemistry. The fourth edition includes discussions of ocean acidification (Box 2-1), production of complex molecules via polyketide synthesis (Box 20-3), and the intestinal microbiome (Box 22-1),

- **Caduceus symbols** to highlight relevant in-text discussions of medical, health, or drug related topics. These include common diseases such as diabetes and neurodegenerative diseases as well as lesser known topics that reveal interesting aspects of biochemistry.

- **Expanded chapter summaries** grouped by major section headings, again guiding students to focus on the most important points within each section.

- **Sample calculations** that demonstrate how students can apply key equations to real data.

SAMPLE CALCULATION 10-1

Show that $\Delta G < 0$ when Ca^{2+} ions move from the endoplasmic reticulum (where $[Ca^{2+}] = 1$ mM) to the cytosol (where $[Ca^{2+}] = 0.1$ μM). Assume $\Delta\Psi = 0$.

The cytosol is *in* and the endoplasmic reticulum is *out*.

$$\Delta G = RT\ln\frac{[Ca^{2+}]_{in}}{[Ca^{2+}]_{out}} = RT\ln\frac{10^{-7}}{10^{-3}}$$
$$= RT(-9.2)$$

Hence, ΔG is negative.

- **New end-of-chapter problems** to provide students with more opportunities to apply their knowledge. Over 60% of the problems are new to this edition. To promote students' independence and to develop their problem-solving skills, virtually all problems are arranged as successive pairs that address the same or related topics. Complete solutions to the odd-numbered problems are included in an appendix for quick feedback.

Finally, we have added a More to Explore feature, a new type of question in each chapter that either extends the material presented in the text or prompts students to reach further and discover topics not covered in the textbook. In addition, WileyPLUS offers over 1,000 conceptually based questions that can be assigned and automatically graded, providing students with additional valuable practice opportunities.

Traditional Pedagogical Strengths

Successful pedagogical elements from prior editions of *Principles of Biochemistry* have been retained. Among them are these:

- the division of chapters into **numbered sections** for easy navigation and cross-referencing.
- **key sentences** printed in italics to assist with quick visual identification.
- boldfaced **key terms.**
- **list of key terms** at the end of each chapter, with the **page numbers** where the terms are first defined.
- comprehensive **glossary containing over 1200 terms.**
- **overview figures** for many metabolic processes.
- figures illustrating **detailed enzyme mechanisms** throughout the text.
- **PDB identification codes** in the figure legend for each molecular structure so that students can download and explore structures on their own.
- Enrichment material, including:
  - **Biochemistry in Health and Disease** essays highlight the importance of biochemistry in the clinic by focusing on the molecular mechanisms of diseases and their treatment.
  - **Perspectives in Biochemistry** provide enrichment material that would otherwise interrupt the flow of the text. Instead, the material is set aside so that students can appreciate some of the experimental methods and practical applications of biochemistry.
  - **Pathways of Discovery** profile pioneers in various fields, giving students a glimpse of the personalities and scientific challenges that have shaped modern biochemistry.
  - list of **references** for each chapter, selected for their relevance and user-friendliness.

Organization

As in the third edition, the text begins with two introductory chapters that discuss the origin of life, evolution, thermodynamics, the properties of water, and acid–base chemistry. Nucleotides and nucleic acids are covered in Chapter 3, since an understanding of the structures and functions of these molecules supports the subsequent study of protein evolution and metabolism.

Four chapters (4 through 7) explore amino acid chemistry, methods for analyzing protein structure and sequence, secondary through quaternary protein structure, protein folding and stability, and structure–function relationships in hemoglobin, muscle proteins, and antibodies. Chapter 8 (Carbohydrates), Chapter 9 (Lipids and Biological Membranes), and Chapter 10 (Membrane Transport) round out the coverage of the basic molecules of life.

The next three chapters examine proteins in action, introducing students first to enzyme mechanisms (Chapter 11), then shepherding them through discussions of enzyme kinetics, the effects of inhibitors, and enzyme regulation (Chapter 12). These themes are continued in Chapter 13, which describes the components of signal transduction pathways.

Metabolism is covered in a series of chapters, beginning with an introductory chapter (Chapter 14) that provides an overview of metabolic pathways, the thermodynamics of "high-energy" compounds, and redox chemistry. Central metabolic pathways are presented in detail (e.g., glycolysis, glycogen metabolism, and the citric acid cycle in Chapters 15–17) so that students can appreciate how individual enzymes catalyze reactions and work in concert to perform complicated biochemical tasks. Chapters 18 (Electron Transport and Oxidative Phosphorylation) and 19 (Photosynthesis) complete a sequence that emphasizes energy-acquiring pathways. Not all pathways are covered in full detail, particularly those related to lipids (Chapter 20), amino acids (Chapter 21), and nucleotides (Chapter 23). Instead, key enzymatic reactions are highlighted for their interesting chemistry or regulatory importance. Chapter 22, on the integration of metabolism, discusses organ specialization and metabolic regulation in mammals.

Six chapters describe the biochemistry of nucleic acids, starting with their metabolism (Chapter 23) and the structure of DNA and its interactions with proteins (Chapter 24). Chapters 25–27 cover the processes of replication, transcription, and translation, highlighting the functions of the RNA and protein molecules that carry out these processes. Chapter 28 deals with a variety of mechanisms for regulating gene expression, including the histone code and the roles of transcription factors and their relevance to cancer and development.

Additional Support

Student Companion to Principles of Biochemistry, 4th Edition

This enhanced study resource by Akif Uzman, University of Houston-Downtown, Jerry Johnson, University of Houston-Downtown, William Widger, University of Houston, Joseph Eichberg, University of Houston, Donald Voet, Judith Voet, and Charlotte Pratt, is designed to help students master basic concepts and hone their analytical skills. Each chapter contains a summary, a review of essential concepts, and additional problems. The fourth edition features new *Behind the Equations* sections and *Calculation Analogies* that provide connections between key equations in the text and their applications. The authors have also included new categories of questions for the student:

- *Graphical analysis questions,* which focus on quantitative principles and challenge students to apply their knowledge.
- *Play It Forward questions* that draw specifically on knowledge obtained in previous chapters.