

PREFACE

Biochemistry is no longer a specialty subject but is part of the core of knowledge for modern biologists and chemists. In addition, familiarity with biochemical principles has become an increasingly valuable component of medical education. In revising this textbook, we asked, "Can we provide students with a solid foundation in biochemistry, along with the problem-solving skills to use what they know? We concluded that it is more important than ever to meet the expectations of a standard biochemistry curriculum, to connect biological chemistry to its chemical roots, and to explore the ways that biochemistry can explain human health and disease. We also wanted to provide students with opportunities to develop the practical skills that they will need to meet the scientific and clinical challenges of the future. This Global edition of *Principles of Biochemistry* continues to focus on basic principles while taking advantage of new tools for fostering student understanding. Because we believe that students learn through constant questioning, this edition features expanded problem sets, additional questions within the text, and extensive online resources for assessment. We have strived to provide our students with a textbook that is complete, clearly written, and relevant.

New for the Global Edition

The global edition of *Principles of Biochemistry* includes significant changes and updates to the contents. In recognition of the tremendous advances in biochemistry, we have added new information about prion diseases, trans fats, membrane transporters, signal transduction pathways, mitochondrial respiratory complexes, photosynthesis, nitrogen fixation, nucleotide synthesis, chromatin structure, and the machinery of DNA replication, transcription, and protein synthesis. New experimental approaches for studying complex systems are introduced, including next generation DNA sequencing techniques, cryo-electron microscopy, metabolomics, genome editing with the CRISPR-Cas9 system, and the role of noncoding RNAs in gene regulation. Notes on a variety of human diseases and pharmacological effectors have been expanded to reflect recent research findings.

Pedagogy

As in the previous editions of *Principles of Biochemistry*, we have given significant thought to the pedagogy within the text and have concentrated on fine-tuning and adding new elements to promote student learning. Pedagogical enhancements in this global edition include the following:

- **Gateway Concepts.** Short statements placed in the margin to summarize some of the general concepts that underpin modern biochemistry, such as Evolution, Macromolecular Structure/Function, Matter/Energy Transformation, and Homeostasis. These reminders help students develop a richer understanding as they place new information in the context of what they have encountered in other coursework.

GATEWAY CONCEPT

Free Energy Change

You can think of the free energy change (ΔG) for a reaction in terms of an urge or a force pushing the reactants toward equilibrium. The larger the free energy change, the farther the reaction is from equilibrium and the stronger is the tendency for the reaction to proceed. At equilibrium, of course, the reactants undergo no net change and $\Delta G = 0$.

GATEWAY CONCEPT

The Steady State

Although many reactions are near equilibrium, an entire metabolic pathway—and the cell's metabolism as a whole—never reaches equilibrium. This is because materials and energy are constantly entering and leaving the system, which is in a steady state. Metabolic pathways proceed, as if trying to reach equilibrium (Le Châtelier's principle), but they cannot get there because new reactants keep arriving and products do not accumulate.

- **Focus on evolution.** An evolutionary tree icon marks passages in the text that illuminate examples of evolution at the biochemical level.
- **Reorganized and Expanded Problem Sets.** End-of-chapter problems are now divided into two categories so that students and instructors can better assess lower- and higher-order engagement: **Exercises** allow students to check their basic understanding of concepts and apply them in straightforward problem solving. **Challenge Questions** require more advanced skills and/or the ability to make connections between topics. The global edition contains nearly 1000 problems, an increase of 26% over the previous edition. Most of the 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. (www.wiley.com/college/voet). Complete solutions to both odd- and even-numbered problems are available in the *Instructor resources on book companion site of Principles of Biochemistry, Global Edition*.

Artwork

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. In addition to designing new illustrations and redesigning existing figures to enhance clarity, we have continued to address the needs of visual learners by using several unique features to help students use the visuals in concert with the text:

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

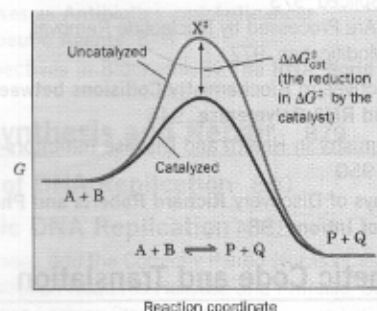


FIG. 11-7 Effect of a catalyst on the transition state diagram of a reaction. Here $\Delta\Delta G_{\text{cat}}^{\ddagger} = \Delta G_{\text{uncat}}^{\ddagger} - \Delta G_{\text{cat}}^{\ddagger}$.

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

- **Molecular Graphics.** Numerous 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.

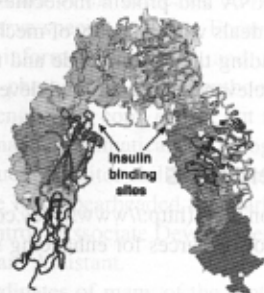


FIG. 13-4 X-Ray structure of the insulin receptor ectodomain. One of its $\alpha\beta$ protomers is shown in ribbon form with its six domains successively colored in rainbow order with the N-terminal domain blue and the C-terminal domain red. The other protomer is represented by its identically colored surface diagram. The β subunits consist of most of the orange and all of the red domains. The protein is viewed with the plasma membrane below and its twofold axis vertical. In the intact receptor, a single transmembrane helix connects each β subunit to its C-terminal cytoplasmic PTK domain. [Based on an X-ray structure by Michael Weiss, Case Western Reserve University; and Michael Lawrence, Walter and Eliza Hall Institute of Medical Research, Victoria, Australia. PDBid 3LOH.]

Traditional Pedagogical Strengths

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

- **Learning Objectives** 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.
- **Review 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.
- **Key sentences** printed in italics to assist with quick visual identification.
- **Overview figures** for many metabolic processes.
- **Detailed enzyme mechanism figures** throughout 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.

PROCESS DIAGRAM

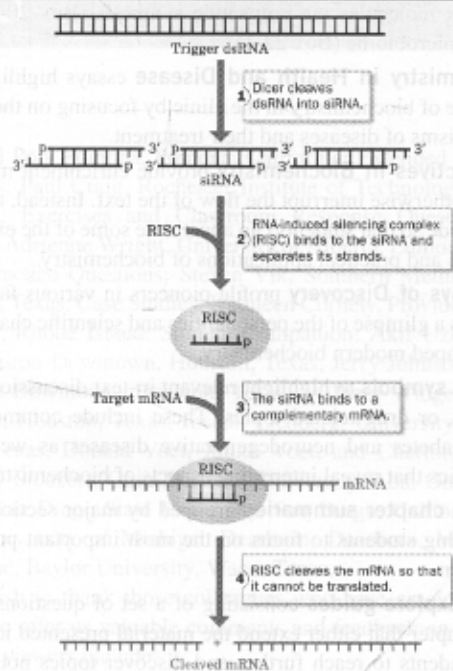


FIG. 28-37 A mechanism of RNA interference. ATP is required for Dicer-catalyzed cleavage of RNA and for RISC-associated helicase unwinding of double-stranded RNA. Depending on the species, the mRNA may not be completely degraded.

? Explain why RNAi is a mechanism for “silencing” genes.

- **PDB identification codes** in the figure legend for each molecular structure so that students can easily access the structures online and explore them on their own.
- **Reviews of chemical principles** that underlie biochemical phenomena, including thermodynamics and equilibria, chemical kinetics, and oxidation–reduction reactions.
- **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 $[\text{Ca}^{2+}] = 1 \text{ mM}$) to the cytosol (where $[\text{Ca}^{2+}] = 0.1 \mu\text{M}$). Assume $\Delta\Psi = 0$.

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

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

Hence, ΔG is negative.

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

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.

- **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.
- **More to Explore guides** consisting of a set of questions at the end of each chapter that either extend the material presented in the text or prompt students to reach further and discover topics not covered in the textbook.
- **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.**
- List of **references** for each chapter, selected for their relevance and user-friendliness.

Organization

As in the earlier 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 (Saccharide Chemistry), Chapter 9 (Lipids, Bilayer and Membranes), and Chapter 10 (Passive and Active 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 (Mitochondrial ATP synthesis) 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 en-

zymatic 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 DNA 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.

Online Supplements

The book's companion site (<http://www.wiley.com/college/voet>) contains an extensive set of resources for enhancing student understanding of biochemistry.

Student Resources

Bioinformatics Projects: A set of 12 newly updated exercises by Paul Craig, Rochester Institute of Technology, covering the contents and uses of databases related to nucleic acids, protein sequences, protein structures, enzyme inhibition, and other topics. The exercises use real data sets, pose specific questions, and prompt students to obtain information from online databases and to access the software tools for analyzing such data.

Case Studies: A set of 33 case studies by Kathleen Cornely, Providence College, using problem-based learning to promote understanding of biochemical concepts. Each case presents data from the literature and asks questions that require students to apply principles to novel situations, often involving topics from multiple chapters in the textbook.

Instructor Resources

PowerPoint Slides contain all images and tables in the text, optimized for viewing onscreen. The figures are optimized for classroom projection, with bold leader lines and large labels.

Test Bank with over 1400 questions in a variety of question types (multiple choice, matching, fill in the blank, and short answer) by Marilee Benore, University of Michigan-Dearborn and Robert Kane, Baylor University, and revised by Amy Stockert, Ohio Northern University and Peter van der Geer, San Diego State University. Each question is keyed to the relevant section in the text and is rated by difficulty level. (Tests can be created and administered online or with test-generator software.)

Classroom Response Questions (“Clicker Questions”), by Rachel Milner and Adrienne Wright, University of Alberta, are interactive questions designed for classroom response systems to facilitate classroom participation and discussion. These questions can also be used by instructors as prelecture questions that help gauge students' knowledge of overall concepts, while addressing common misconceptions.

Solutions to all problems are available.

Instructor resources are password protected.

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