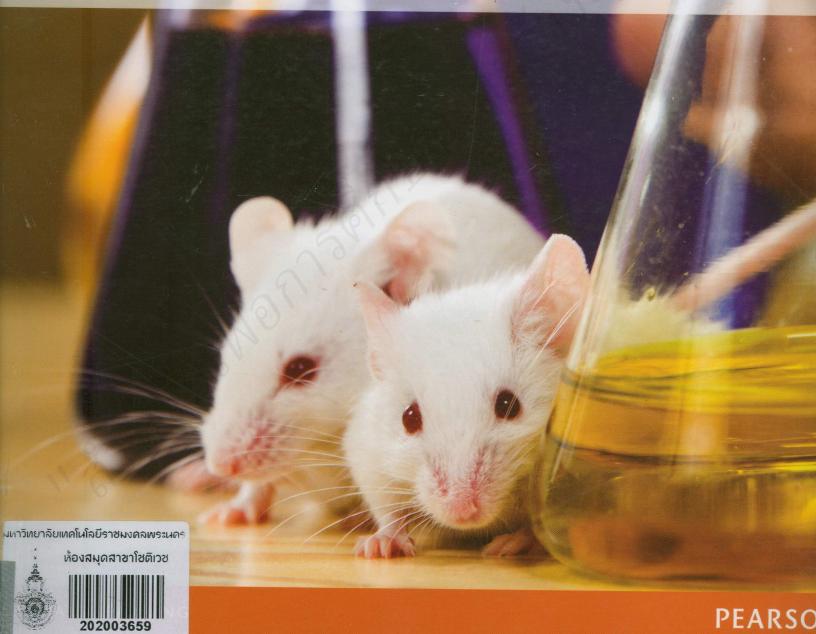


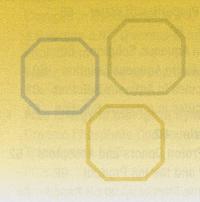
Biochemistry

Concepts and Connections

Dean R. Appling • Spencer J. Anthony-Cahill • Christopher K. Mathews



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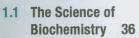
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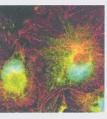
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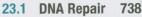
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Biochemistry: Concepts and Connections

As genomics and informatics revolutionize biomedical science and health care, we must prepare students for the challenges of the twenty-first century and ensure their ability to apply quantitative reasoning skills to the science most fundamental to medicine: biochemistry.

We have written *Biochemistry: Concepts and Connections* to provide students with a clear understanding of the chemical logic underlying the mechanisms, pathways, and processes in living cells. The title reinforces our vision for this book—twin emphases upon fundamental *concepts* at the expense of lengthy descriptive information, and upon *connections*, showing how biochemistry relates to all other life sciences and to practical applications in medicine, agricultural sciences, environmental sciences, and forensics.

Inspired by our experience as authors of the biochemistry majors' text, *Biochemistry, Fourth Edition*, and as teachers of biochemistry majors' and mixed-science-majors' courses, we believe there are several requirements that a textbook for the mixed-majors' course must address:

- The need for students to understand the structure and function of biological molecules before moving into metabolism and dynamic aspects of biochemistry.
- The need for students to understand that biochemical concepts derive from experimental evidence, meaning that the principles of biochemical techniques must be presented to the greatest extent possible.
- The need for students to encounter many and diverse real-world applications of biochemical concepts.
- The need for students to understand the quantitative basis for biochemical concepts. The Henderson–Hasselbalch equation, the quantitative expressions of thermodynamic laws, and the Michaelis–Menten equation, for example, are not equations to be memorized and forgotten when the course moves on. The basis for these and other quantitative statements must be understood and constantly repeated as biochemical concepts, such as mechanisms of enzyme action, are developed. They are essential to help students grasp the concepts.

In designing *Biochemistry: Concepts and Connections*, we have stayed with the organization that serves us well in our own classroom experience. The first 10 chapters cover structure and function of biological molecules, the next 10 deal with intermediary metabolism, and the final 6 with genetic biochemistry. Our emphasis on biochemistry as a quantitative science can be seen in Chapters 2 and 3, where we focus on water, the matrix of life, and bioenergetics. Chapter 4 introduces nucleic acid structure, with a brief introduction to nucleic acid and protein synthesis—topics covered in much more detail at the end of the book.

Chapters 11 through 20 deal primarily with intermediary metabolism. We cover the major topics in carbohydrate metabolism, lipid metabolism, and amino acid metabolism in one chapter each (12, 16, and 18, respectively). Our treatment of cell signaling is a bit unconventional, since it appears in Chapter 20, well after we present hormonal control of carbohydrate and lipid metabolism. However, this treatment allows more extended presentation of receptors, G proteins, oncogenes, and neurotransmission. In addition, because cancer often results from aberrant signaling processes, our placement of the signaling chapter leads fairly naturally into genetic biochemistry, which follows, beginning in Chapter 21.

With assistance from talented artists, we have built a compelling visual narrative from the ground up, composed of a wide range of graphic representations, from macromolecules to cellular structures as well as reaction mechanisms and metabolic pathways that highlights and reinforces overarching themes (chemical logic, regulation, interface between chemistry and biology). In addition, novel **Foundation Figures** integrate core chemical and biological connections visually, providing a way to organize the complex and detailed material intellectually, thus making relationships among key concepts clear and easier to study. "Concept" and "Connection" statements within the narrative highlight fundamental concepts and real-world applications of biochemistry.

In *Biochemistry: Concepts and Connections*, we emphasize our field as an experimental science by including 15 separate sections, called **Tools of Biochemistry**, that highlight the most important research techniques. We also provide students with end-of-chapter references (about 12 per chapter), choosing those that would be most appropriate for our target audience, such as links to Nobel Prize lectures.

We consider end-of-chapter problems to be an indispensable learning tool and have provided 15 to 25 problems for each chapter. About half of the problems have brief answers at the end of the book, with complete answers provided in a separate solutions manual. Additional tutorials in MasteringChemistry* will help students with some of the most basic concepts and operations.

Producing a book of this magnitude involves the efforts of dedicated editorial and production teams. We have not had the pleasure of meeting all of these talented individuals, but we consider them close friends nonetheless. First, of course, is Jeanne Zalesky, our sponsoring editor, now Editor-in-Chief, Physical Sciences, who always found a way to keep us focused on our goal. Coleen Morrison, Program Manager, kept us organized and on schedule, juggling disparate elements in this complex project. Jay McElroy, Art Development Editor, was our intermediary with the talented artists at Imagineering, Inc., and displayed considerable artistic and editorial gifts in his own right. Over the course of the project, we worked with three experienced development editors—Dan Schiller, John Murdzek, and Erica Pantages

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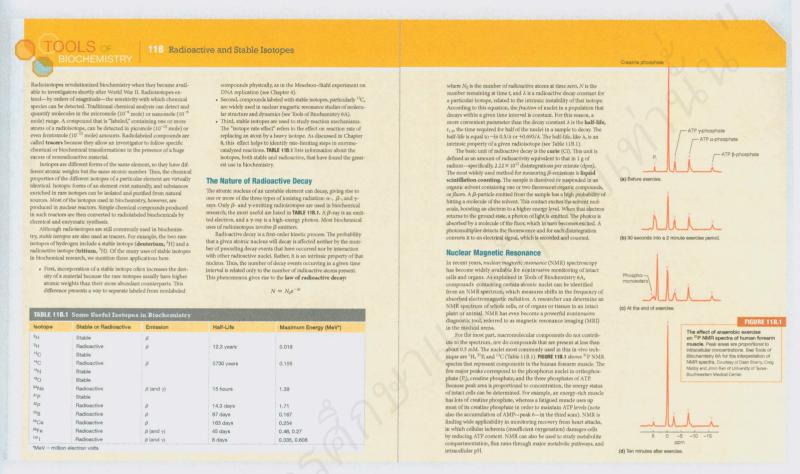


Christopher K. Mathews is Distinguished Professor Emeritus of Biochemistry at Oregon State University. He earned his B.A. in chemistry from Reed College (1958) and Ph.D. in biochemistry from the University of Washington (1962). He served on the faculties of Yale University and the University of Arizona from 1963 until 1978, when he moved to Oregon State University as Chair of the

Department of Biochemistry and Biophysics, a position he held until 2002. His major research interest is the enzymology and regulation of DNA precursor metabolism and the intracellular coordination between deoxyribonucleotide synthesis and DNA replication. From 1984 to 1985, Dr. Mathews was an Eleanor Roosevelt International Cancer Fellow at the Karolinska Institute in Stockholm, and in 1994-1995 he held the Tage Erlander Guest Professorship at Stockholm University. Dr. Mathews has published about 185 research papers, book chapters, and reviews dealing with molecular virology, metabolic regulation, nucleotide enzymology, and biochemical genetics. From 1964 until 2012 he was principal investigator on grants from the National Institutes of Health, National Science Foundation, and the Army Research Office. He is the author of Bacteriophage Biochemistry (1971) and coeditor of Bacteriophage T4 (1983) and Structural and Organizational Aspects of Metabolic Regulation (1990). He was lead author of four editions of Biochemistry, a textbook for majors and graduate students. His teaching experience includes undergraduate, graduate, and medical school biochemistry courses.

He has backpacked and floated the mountains and rivers, respectively, of Oregon and the Northwest. As an enthusiastic birder he has served as President of the Audubon Society of Corvallis and is President of the Great Basin Society, which operates the Malheur Field Station in eastern Oregon.



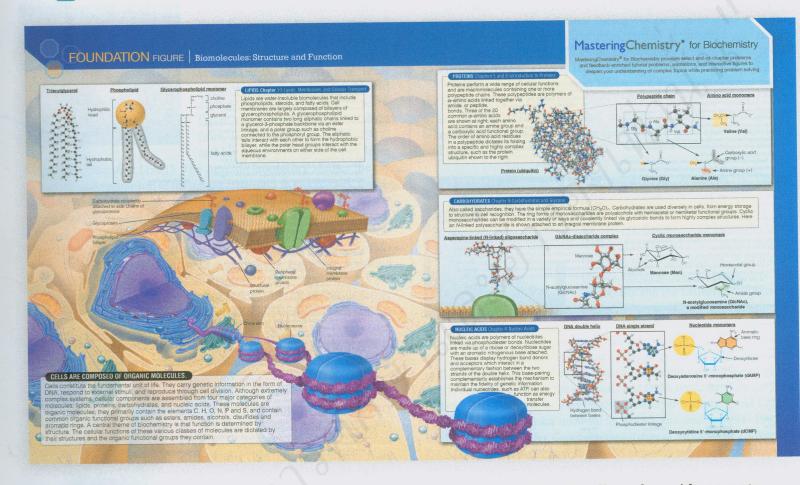


Tools of Biochemistry emphasize our field as an experimental science and highlight the most important research techniques relevant to students today.

- 2A Electrophoresis and Isoelectric Focusing 76
- 4A Manipulating DNA 131
- 4B An Introduction to X-Ray Diffraction 136
- 5A Protein Expression and Purification 163
- **5B** Mass, Sequence, and Amino Acid Analyses of Purified Proteins 170
- **6A** Spectroscopic Methods for Studying Macromolecular Conformation in Solution 210
- 6B Determining Molecular Masses and the Number of Subunits in a Protein Molecule 217
- 7A Immunological Methods 262

- **8A** How to Measure the Rates of Enzyme-Catalyzed Reactions 301
- 9A The Emerging Field of Glycomics 331
- 11A Metabolomics 393
- 11B Radioactive and Stable Isotopes 396
- 13A Detecting and Analyzing Protein–Protein Interactions 474
- 21A Polymerase Chain Reaction 706
- 24A DNA Microarrays 785
- 24B Chromatin Immunoprecipitation 786

FOUNDATION FIGURES

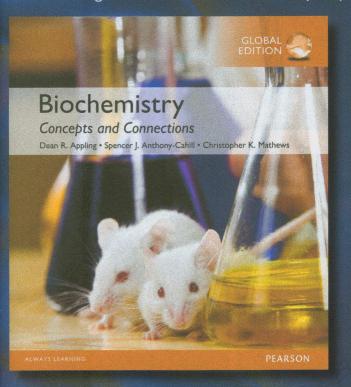


Foundation Figures integrate core chemical and biological connections visually and provide a way to organize the complex and detailed material intellectually, thus making relationships among key concepts clear and easier to study.

- 1 Biomolecules: Structure and Function 78
- 2 Protein Structure and Function 220
- 3 Regulation of Enzyme Activity 304
- 4 Enzyme Kinetics and Drug Action 398
- 5 Intermediary Metabolism 510
- 6 Cell Signaling and Protein Regulation 682
- 7 Antibody Diversity and Use as Therapeutics 760
- 8 Information Flow in Biological Systems 844

Making Connections

BIOCHEMISTRY: CONCEPTS AND CONNECTIONS engages students in the rapidly evolving field of biochemistry, better preparing them for the challenges of 21st century science through quantitative reasoning skills and a rich, chemical perspective on biological processes.



This concise first edition teaches mixed-science majors the chemical logic underlying the mechanisms, pathways, and processes in living cells through ground-breaking biochemical art and a clear narrative which illustrates biochemistry's relation to all other life sciences. Integration of biochemistry's experimental underpinnings alongside modern techniques, encourages students to consider how their understanding of biochemistry can, and will, contribute to solving problems in medicine, agricultural sciences, environmental sciences, and forensics.

The text is fully integrated with MasteringChemistry® to provide support for students before, during, and after class. Highlights include interactive animations and tutorials based on the textbook's biochemical art program.

Visually compelling chapter openers show the relevancy of the material to draw students into biochemistry at every turn.



Groundbreaking Biochemical Art

AN INNOVATIVE VISUAL NARRATIVE TEACHES BIOCHEMICAL

DETAILS while reinforcing over-arching themes of chemical logic, regulation, and the interface between chemistry and biology to help students see the bigger picture.

Figure 3.10: Bioenergetic calculations mapped to three-dimensional structures create a visual and mathematical overview of selected cellular processes. Integrated text explains specifics of how the

equations are linked to physical elements Newly synthesized protein spontaneously folds into its within a cell. Newly synthesized protein active structure (hexokinase is shown here). Protein folding $\Delta G = \Delta H - T \Delta S$ Messenger RNA Metabolic reactions)P) + G6P Ribosomal synthesis $\Delta G = \Delta G^{\circ'} + RT \ln Q$ of a typical protein CO₂ + (NADH) ATP synthase At lower values of pH proteins in At higher values of pH proteins will carry more positive charge. Electron transport $\Delta G = -nF\Delta F^{\circ} + RT \ln \Omega$ NAD. NADH is oxidized in mitochondria in a multistep electron transport process that produces a proton chemical gradient. Isoelectric point (pl) = 6.8

Figure 2.18: Several layers of information (surface charge, pH, and how the charges are distributed across a three-dimensional protein) are combined in an easy to follow format to explain the effect of pH on overall surface charge. Annotations reinforce the major concepts.

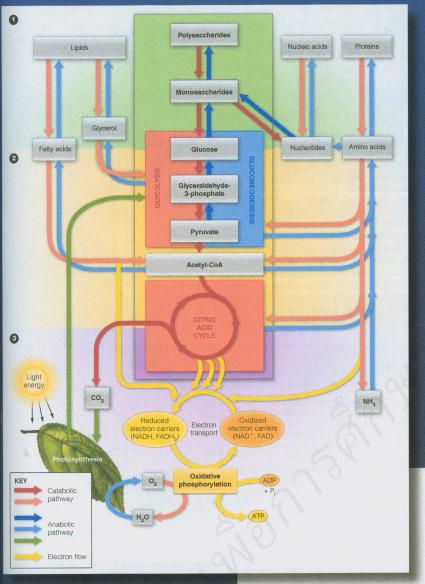
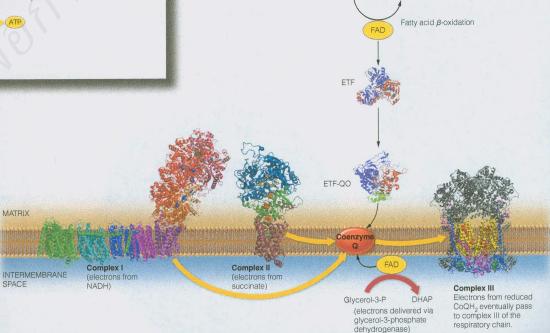


Figure 11.2: Major biochemical themes such as intermediary metabolism are presented as carefully designed reference charts connecting relevant concepts from multiple chapters. These flow charts enable students to visualize the big picture and think about relationships while referring to chapter text for detailed descriptions.

Figure 14.12: Detailed molecular models lend interest and realism to microscopic processes. Here, proteins in the inner mitochondrial membrane give context to electron flow in a portion of the respiratory chain. Vibrant color-coded arrows make multiple pathways clear and understandable.

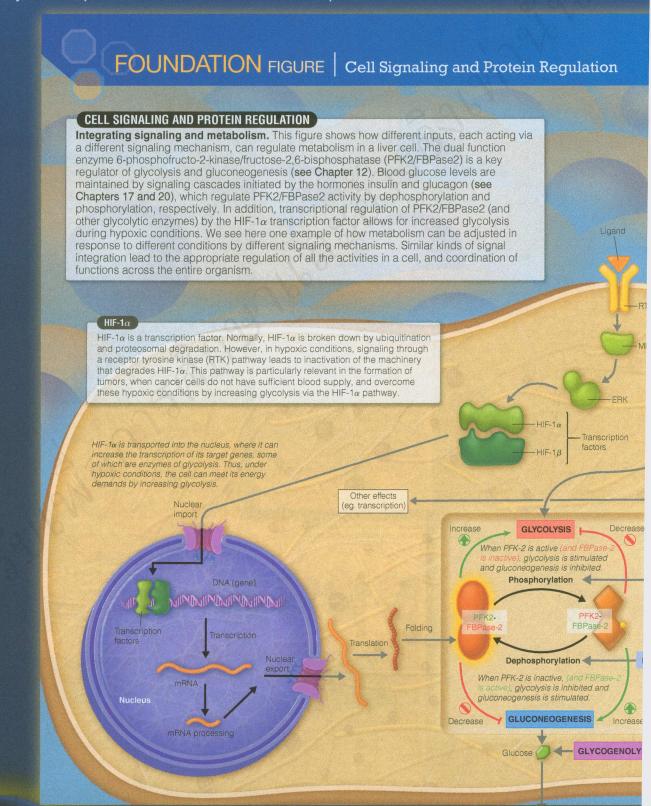
Fatty acyl

Fatty enoyl



Interactive Foundation Figures

INTERACTIVE FOUNDATION FIGURES integrate core chemical and biological connections visually and provide a way to organize highly complex and detailed material, making biochemistry more manageable, understandable, and easier to synthesize. These figures will have dedicated questions for use in class via Learning Catalytics™ and will also be assignable in MasteringChemistry® as step-wise animations with follow-up assessment.

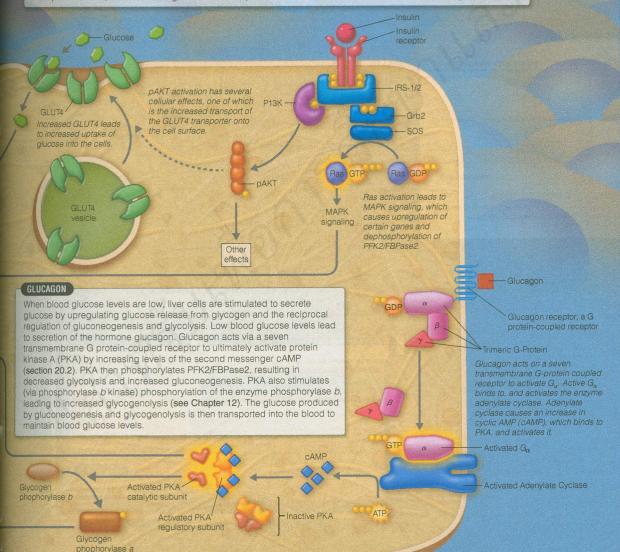




MasteringChemistry® for Biochemistry provides select end-of-chapter problems and feedback-enriched tutorial problems, animations, and interactive figures to deepen your understanding of complex topics while practicing problem solving.

INSULIN

Under conditions of high blood glucose, the pancreatic β-cells secrete the hormone insulin. Insulin binds to its receptor on the liver cell, causing autophosphorylation and activation of the receptor. Activation of the insulin signaling pathway (section 20.3) leads to activation of two main proteins– pAKT, and Ras. Dephosphorylated PFK2/FBPase2 increases glycolysis while decreasing gluconeogenesis (see Chapter 12). These two activities of insulin (increased glucose transport into cells, and increased glucose utilization) result in an overall decrease in the levels of blood glucose.



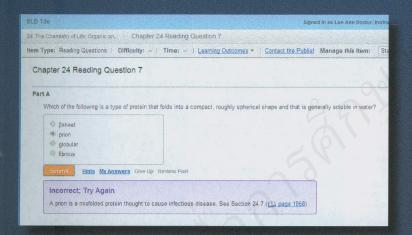
MasteringChemistry®

New MasteringChemistry for Biochemistry provides interactive animations and tutorials based on the textbook's biochemical art program and Foundation Figures helping students visualize complex processes, test conceptual understanding, apply what they have learned to novel scenarios, and practice quantitative reasoning.

Ensure students arrive ready to learn by assigning educationally effective content before class, and encourage critical thinking and retention with in-class resources such as Learning Catalytics. Students can further master concepts after class through traditional homework assignments that provide hints and answer-specific feedback. The Mastering gradebook records scores for all automatically graded assignments while diagnostic tools give instructors access to rich data to assess student understanding and misconceptions.

Mastering brings learning full circle by continuously adapting to each student and making learning more personal than ever—before, during, and after class.

BEFORE CLASS



READING QUIZZES

READING QUIZZES give instructors the opportunity to assign reading and test students on their comprehension of chapter content.

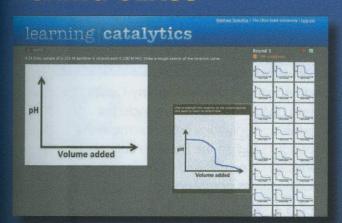
DYNAMIC STUDY MODULES

DYNAMIC STUDY MODULES (DSMs) enable your students to study the required organic chemistry and fundamental biochemistry concepts effectively on their own in order to be better prepared for higher-order learning in class. These modules can be completed on smartphones, tablets, or computers and assignments will automatically be synced to the MasteringChemistry Gradebook.



for Biochemistry

DURING CLASS



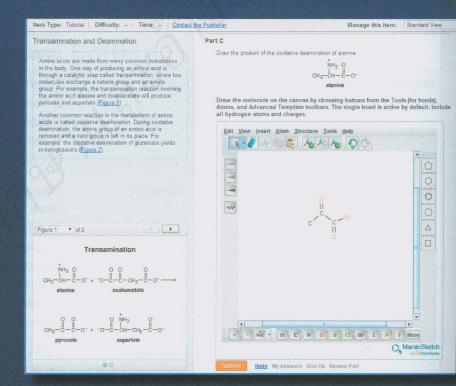
LEARNING CATALYTICS

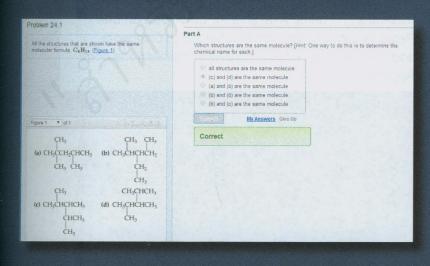
NEW! Learning Catalytics™ is a student engagement, assessment, and classroom intelligence system allowing students to use their smartphones, tablets, or laptops to respond to questions in class. Questions focused on the eight Foundation Figures, as well as key biochemistry concepts throughout the text help students visualize and analyze complex biochemical processes in the classroom.

AFTER CLASS

STUDENT TUTORIALS

MasteringChemistry® for Biochemistry provides feedback-enriched tutorial problems, animations, and interactive figures to deepen your understanding of complex topics while practicing problem solving.





END-OF-CHAPTER PROBLEMS FROM THE TEXTBOOK

Selected end of chapter problems within the textbook are available within **MasteringChemistry®** and can be automatically graded and assigned for homework or practice.

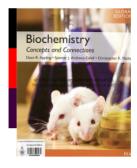
Instructor and Student Resources

BIOCHEMISTRY: CONCEPTS AND CONNECTIONS provides an integrated teaching and learning package of support material for both students and professors.

Resource	Instructor or Student Resource	Description
Solutions Manual	Instructor	Prepared by Dean Appling, Spencer Anthony-Cahill, and Chris Mathews, the solutions manual includes worked-out answers and solutions for problems in the text. Available for download on the Pearson catalog page for <i>Biochemistry: Concepts and Connections</i> at www.pearsonglobaleditions.com/Appling
MasteringChemistry® www.masteringchemistry.com	Student & Instructor	MasteringChemistry from Pearson is the leading online teaching and learning system designed to improve results by engaging students before, during, and after class with powerful content.
Pearson eText within MasteringChemistry®	Student	Biochemistry: Concepts and Connections features a Pearson eText within MasteringChemistry. The Pearson eText offers students the power to create notes, highlight text in different colors, create bookmarks, zoom, and view single or multiple pages.
TestGen Test Bank	Instructor	Prepared by Kathryn Stowell, this resource includes more than 550 questions in multiple-choice, matching, true/false, and short answer format. Test bank problems are linked to textbook-specific learning outcomes as well as MCAT-associated outcomes. Available for download on the Pearson catalog page for <i>Biochemistry: Concepts and Connections</i> at www.pearsonglobaleditions.com/Appling
Instructor Resource Materials	Instructor	Includes all the art, photos, and tables from the book in JPEG format, as well as Lecture powerpoints, for use in classroom projection or when creating study materials and tests. Available for download on the Pearson catalog page for <i>Biochemistry: Concepts and Connections</i> at www.pearsonglobaleditions.com/Appling

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