Preface

This book was conceived more than 15 years ago when W. W. Norton editor Jack Repcheck popped his head into Roger Miesfeld's office one sunny afternoon in Tucson, Arizona. Jack had just seen Roger's new textbook on molecular genetics in the bookstore and had been impressed with the illustrations. He said, "Dr. Miesfeld, how would you like to author a full-color textbook that takes the same visual approach to biochemistry as you did for the topic of molecular genetics?" And with those fateful words began a conversation, and then the creation of a textbook that focuses on how biochemistry relates to the world around us without relying on rote memorization of facts by students. In 2011, Roger's colleague at the University of Arizona and next-door-office neighbor, Megan McEvoy, who is also an instructor of a large biochemistry service course, mentioned that she would be eager to work on a textbook that would improve pedagogy in the field. Thus, this project, which began years ago with a simple question, has resulted in the publication of the first truly new biochemistry textbook in decades.

Meanwhile, we (Roger and Megan) have been teaching biochemistry to undergraduate, graduate, and medical school students for nearly 40 years combined and have loved every minute of it—seriously. During this time, we noticed that many biochemistry textbooks seemed to sidestep a very basic question in the minds of most students: "Why do I need to learn biochemistry?" To answer this question in the classroom, we developed a number of story lines that revolve around a simple premise: how it works and why it matters. We used the assigned textbook to fill in the details for our students but used the in-class lectures to provide the context the students needed to see the big picture. During this same time, the Internet became much more accessible so that it was almost trivial to find the name of an enzyme in a metabolic reaction or the equation required for calculating changes in free energy.

But despite the ease with which "info-bytes" could be obtained, and often simply memorized, what still required thought was integration of these pieces of information to fully understand concepts such as allosteric regulation of an enzyme, rates of metabolic flux, or the importance of weak noncovalent interactions in assembling gene transcription complexes. We challenged the students in our classes to approach each biochemical process—especially those that are conceptually the most difficult—to answer the questions how does it work and why does it matter to me. The "it" could be a cancer drug that inhibits an enzyme, an external stimulus that activates a signaling pathway and controls blood sugar, or a biochemical assay that measures gene expression levels. We told them that to answer the how it works part, they would have to explain the biochemical process in clear and concise language, while the why it matters part required them to make it relevant to their own life experience.

As we collected more and more of these "how and why" examples over the years, it became clear to us that our biochemistry textbook should focus on presenting core concepts in a relatable way centered around three themes: (1) the interdependence of energy conversion processes, (2) the role of signal transduction in metabolic regulation, and (3) biochemical processes affecting human health and disease. The pedagogical foundation for each of these themes is that molecular structure determines chemical function. In developing the outline for the book, we ignored the urge to write it like an automobile owner's manual in which all of the parts are listed first (proteins, lipids, carbohydrates, nucleic acids), and then the function of the car (metabolic pathways) is described by assembling the parts in a systematic way (easy to memorize).

Instead, we chose to organize the book using five core blocks (collections of chapters, or parts) that consist of modules (individual chapters) made up of concept-based submodules (numbered chapter sections) with limited, focused, unnumbered subsections. The five core blocks we chose are "Part 1: Principles of Biochemistry" (Chapters 1–3), "Part 2: Protein Biochemistry" (Chapters 4–8), "Part 3: Energy Conversion Pathways" (Chapters 9–12), "Part 4: Metabolic Regulation" (Chapters 13–19), and "Part 5: Genomic Regulation" (Chapters 20–23). This organization provides the student with an opportunity to work through related concepts before moving on to new ones. For example, what is needed to understand protein structure and function is presented in Part 2, including how proteins function as enzymes or as relay partners in a signal transduction pathway. In Part 4, carbohydrate structure and function (Chapter 13) and carbohydrate metabolism (Chapter 14) are paired together, as are lipid structure and function (Chapter 15) and lipid metabolism (Chapter 16),

Clear Explanations and a Distinctive Chapter Sequence Help Students Make Connections between Concepts

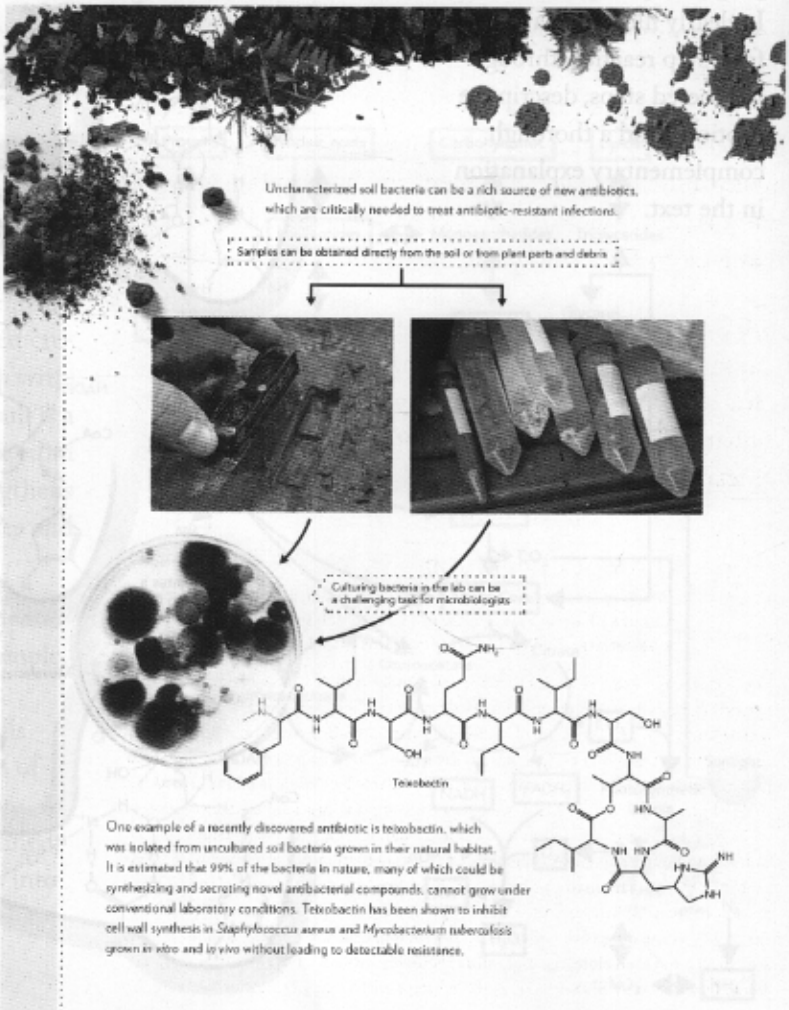
Our distinctive chapter sequence highlights connections between key biochemical processes, encouraging students to move beyond mere memorization to consider *how* biochemistry works.

- In Part 1, we introduce essential, unifying concepts that are interwoven throughout the chapters that follow: hierarchical organization of biochemical complexity; energy conversion in biological systems; the chemical role of water in life processes; the function of cell membranes as hydrophobic barriers; and the central dogma of molecular biology from a biochemical perspective.
- As a capstone to the chapters on protein structure and function (Part 2), we present signal transduction (Chapter 8) as the prototypical example of how proteins work to mediate cellular processes.
- The topical sequence in Parts 3 and 4 underscores the importance of energy conversion as the foundation for all other metabolic pathways, introducing enzyme regulation of metabolic flux as a central theme. In Part 3, we present the pathways involved in energy conversion processes before presenting degradative and biosynthetic pathways in Part 4. This helps students see complex processes and connections between concepts more clearly.
- We present the biomolecular structure and function of carbohydrates, lipids, amino acids, and nucleotides in Part 4 in the context of their metabolic pathways. This integrated approach encourages students to associate biochemical structure with cellular function in a way that promotes deeper understanding.
- Rather than an encyclopedic list of individual reactions that can obscure students' understanding of the important concepts, in Parts 3 and 4 we emphasize the regulation of 10 major (and broadly representative) metabolic pathways, with a special emphasis on the human diseases associated with these pathways.

Unmatched Emphasis on Applications and Biomedical Examples Motivates Learning by Helping Students Connect the Material to both Their Majors and Their Everyday Experience

We know from our teaching that students can be equally engaged by biomedical examples and examples of biochemistry in the world around them. So throughout this book we've reinforced key biochemical concepts with applied examples that show why biochemistry matters.

- Each chapter-opening vignette provides an introduction to a biochemical application connected to the chapter's central topic. Later, we ask students to reexamine the application in light of their newly acquired knowledge of the biochemistry behind it. For example, the opening vignette for Chapter 22 examines how an ingenious laboratory method enabled study of soil bacteria that were previously impossible to culture in the lab, which led to discovery of a new antibiotic. Another example is the opening vignette for Chapter 13, which visually presents the biochemistry behind the commercial product Beano.



- Real-life examples from nature help students understand how structure (of a protein, lipid, carbohydrate, or nucleic acid) affects function, an important takeaway insight we stress in our biochemistry courses. A great example is the discussion in Chapter 2 concerning antifreeze proteins in fish and insects that live in extreme cold. Threonine amino acids in these proteins line up perfectly with ice crystals and thus prevents them from growing within the animals.
- We distributed human health examples, particularly discussions of human disease, throughout the text. These are especially relevant for the many students planning to pursue careers in medicine or other health-related professions. A prominent example occurs in Chapter 21—the description of a degenerative disease of the retina called retinitis pigmentosa, which is caused by defects in the RNA splicing machinery. This is a surprise to students, who expect that most human disease is the result of enzyme defects.

Thoughtful Pedagogy and Assessment Promotes Mastery of Biochemical Concepts

We feel strongly that myriad boxes and sidebars in textbooks distract from the content of the chapters and are rarely read by students. As a result, this book has a design that is clean and uncluttered.

- A Concept Integration question and its answer occurs at the end of each numbered chapter section. This feature prompts students to think critically about what they're reading and to synthesize concepts in a meaningful way.

concept integration 5.1

A frog species was found to contain a cytosolic liver protein that bound a pharmaceutical drug present at high levels in effluent from a wastewater facility. Describe how this protein could be purified.

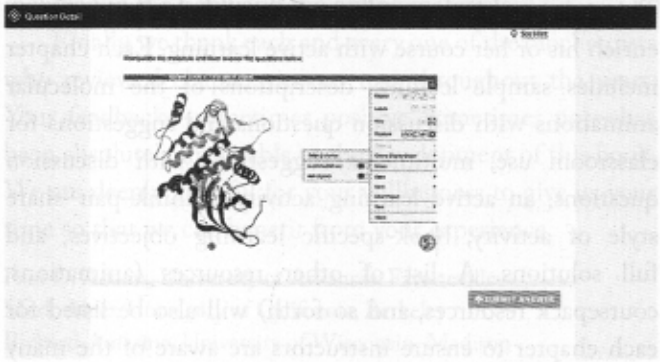
The first step in purifying an uncharacterized protein is to develop a method to detect it specifically, such as an enzyme activity assay or binding assay. In this case, the protein is known to bind to a small molecule (pharmaceutical drug), and this binding activity can be used to develop a protein detection assay. The assay could be based on protein binding to the drug that has been radioactively labeled or it might be possible to develop a fluorescently labeled version of the drug that has an altered absorption or emission spectrum as a function of specific protein binding. The next step would be to use cell fractionation, centrifugation, and a combination of gel filtration and ion-exchange column chromatography to enrich for drug binding activity relative to total protein in the frog liver extract. A final step would be to develop an affinity column that contains the drug covalently linked to a solid matrix and use this column to bind specifically, and then elute, the high-affinity binding protein. The purity of the protein would be assessed by SDS-PAGE at several steps within the purification protocol.

concept integration 14.3

Why does it make physiologic sense for muscle glycogen phosphorylase activity to be regulated by both metabolite allosteric control and hormone-dependent phosphorylation?

Muscle glycogen phosphorylase is allosterically activated by AMP, which signals low energy charge in the cell. High AMP levels also indicate a need for glycogen degradation and release of glucose substrate for ATP generation to support muscle contraction. Both ATP and glucose-6-P are allosteric inhibitors of muscle glycogen phosphorylase activity and signal a ready supply of chemical energy without the need for glycogen degradation. Both types of allosteric regulation occur rapidly on a timescale of seconds in response to sudden changes in AMP, ATP, and glucose-6-P levels. Allosteric control by metabolites provides a highly efficient means to control rates of glycogen degradation in response to the immediate energy needs of muscle cells. In contrast, hormonal regulation of muscle glycogen phosphorylase activity by glucagon and epinephrine is a delayed response (occurring on a timescale of hours), resulting in phosphorylation and activation of the enzyme after neuronal and physiologic inputs at the organismal level. Similarly, insulin signaling, which inhibits muscle glycogen phosphorylase activity through dephosphorylation, is also a delayed response at the organismal level and depends on multiple physiologic inputs. Taken together, allosteric regulation of muscle glycogen phosphorylase activity provides a rapid-response control mechanism to modulate muscle glucose levels, whereas hormonal signaling requires input from multiple stimuli at the organismal level and provides a longer-term effect on enzyme activity through covalent modifications.

- We know the quality and quantity of end-of-chapter problems is an important litmus test for many instructors when reviewing textbooks. Our end-of-chapter material includes a plentiful, balanced mix of basic Chapter Review questions and thought-provoking Challenge Problems.
- Online homework is becoming a more and more powerful learning tool for biochemistry courses. Norton's Smartwork5 online homework platform offers book-specific assessment through a wide array of exercises: art-based interactive questions, critical-thinking questions, application questions, process animation questions, and chemistry drawing questions, as well as all of the book's end-of-chapter questions. We are particularly excited to be the first to offer interactive 3D molecular visualization questions within the homework platform. Everything the student needs to interrogate a molecular structure is embedded in Smartwork5 using Molsoft's ICM Browser application.



Resources for Instructors and Students

Smartwork5

This dynamic and powerful online assessment resource uses answer-specific feedback, a variety of engaging question types, the integration of the stunning book art, 3D molecular animations, and process animations to help students visualize and master the important course concepts. Smartwork5 also integrates easily with your campus learning management system and features a simple, intuitive interface, making it an easy-to-use online homework system for both instructors and students.

3D Molecular Animations

Eleven photorealistic 3D molecular animations based on PDB files were created by renowned molecular animator Dr. Janet Iwasa from the Department of Biochemistry at the University of Utah College of Medicine. Janet brings some of the most difficult concepts in biochemistry to life in stunning detail. These animations are available to students in coursepack assessments and through the ebook and are available with associated assessments for instructors to assign in the Smartwork5 homework system. Links to the animations are available to instructors at wwnorton.com/instructors.

Process Animations

Twenty process animations showcase the complex topics that students find most challenging. The animations are available to students in mobile-compatible format in the coursepack and the ebook, as well as online. Assessments written specifically for the animations are included in Smartwork5. Links to the animations are available to instructors at wwnorton.com/instructors.

Ultimate Guide to Teaching with Biochemistry

This enhanced instructor's manual will help any professor enrich his or her course with active learning. Each chapter includes sample lectures, descriptions of the molecular animations with discussion questions and suggestions for classroom use, multimedia suggestions with discussion questions, an active learning activity, a think–pair–share style of activity, book-specific learning objectives, and full solutions. A list of other resources (animations, coursepack resources, and so forth) will also be listed for each chapter to ensure instructors are aware of the many instructor-provided materials available to them. Activity handouts will be available for download at wwnorton.com/instructors for easy printing and distribution.

Coursepacks

Available at no cost to professors or students, Norton Coursepacks for online or hybrid courses are available in a variety of formats, including Blackboard, Desire2Learn (D2L), and Canvas. With just a simple download from the instructor's website, instructors can bring high-quality Norton digital media into a new or existing online course. Content is fully customizable and includes chapter-based assignments with high-quality visual assessments, perfect for distance learning classes or assignments between classes. The coursepack for *Biochemistry* also features the full suite of animations, vocabulary flashcards, and assignments based on 3D animations as well as art from the book—everything students need for a great out-of-the-classroom experience.

PowerPoint Presentations and Figures

PowerPoint slide options meet the needs of every instructor and include lecture PowerPoint slides providing an overview of each chapter, five clicker questions per chapter, and links to animations. There is also a separate set of art PowerPoint slides featuring every photograph and drawn figure from the text. In addition, the PDB files used as the basis for many of the molecular structures in the book are available for download.

Test Bank

The Test Bank for *Biochemistry* is designed to help instructors prepare exams quickly and effectively. Questions are tagged according to Bloom's taxonomy, and each chapter includes approximately 75 multiple-choice and 25 essay questions. Five to ten questions per chapter use art taken directly from the book. In addition to tagging with Bloom's, each question is tagged with metadata that places it in the context of the chapter and assigns it a difficulty level, enabling instructors to easily construct tests that are meaningful and diagnostic.

Ebook

Available for students to purchase online at any time, the *Biochemistry* ebook offers students a great low price, exceptional functionality, and access to the full suite of accompanying resources.