

Preface

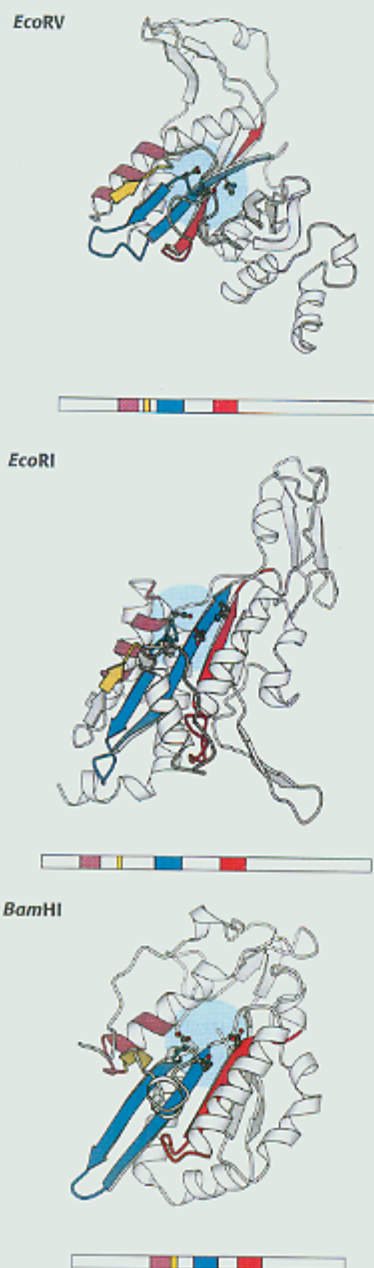


FIGURE 9.44 A conserved structural core in type II restriction enzymes.

For more than 25 years, and through four editions, Stryer's *Biochemistry* has laid out this beautiful subject in an exceptionally appealing and lucid manner. The engaging writing style and attractive design have made the text a pleasure for our students to read and study throughout our years of teaching. Thus, we were delighted to be given the opportunity to participate in the revision of this book. The task has been exciting and somewhat daunting, doubly so because of the dramatic changes that are transforming the field of biochemistry as we move into the twenty-first century. Biochemistry is rapidly progressing from a science performed almost entirely at the laboratory bench to one that may be explored through computers. The recently developed ability to determine entire genomic sequences has provided the data needed to accomplish massive comparisons of derived protein sequences, the results of which may be used to formulate and test hypotheses about biochemical function. The power of these new methods is explained by the impact of evolution: many molecules and biochemical pathways have been generated by duplicating and modifying existing ones. Our challenge in writing the fifth edition of *Biochemistry* has been to introduce this philosophical shift in biochemistry while maintaining the clear and inviting style that has distinguished the preceding four editions.

A New Molecular Evolutionary Perspective

How should these evolution-based insights affect the teaching of biochemistry? Often macromolecules with a common evolutionary origin play diverse biological roles yet have many structural and mechanistic features in common. An example is a protein family containing macromolecules that are crucial to moving muscle, to transmitting the information that adrenaline is present in the bloodstream, and to driving the formation of chains of amino acids. The key features of such a protein family, presented to the student once in detail, become a model that the student can apply each time that a new member of the family is encountered. The student is then able to focus on how these features, observed in a new context, have been adapted to support other biochemical processes. Throughout the text, a stylized tree icon  is positioned at the start of discussions focused primarily on protein homologies and evolutionary origins.

TWO NEW CHAPTERS. To enable students to grasp the power of these insights, two completely new chapters have been added. The first, "Biochemical Evolution" (Chapter 2), is a brief tour from the origin of life to the development of multicellular organisms. On one level, this chapter provides an introduction to biochemical molecules and pathways and their cellular context. On another level, it attempts to

deepen student understanding by examining how these molecules and pathways arose in response to key biological challenges. In addition, the evolutionary perspective of **Chapter 2** makes some apparently peculiar aspects of biochemistry more reasonable to students. For example, the presence of ribonucleotide fragments in biochemical cofactors can be accounted for by the likely occurrence of an early world based largely on RNA. The second new chapter, “Exploring Evolution” (**Chapter 7**), develops the conceptual basis for the comparison of protein and nucleic acid sequences. This chapter parallels “Exploring Proteins” (**Chapter 4**) and “Exploring Genes” (**Chapter 6**), which have thoughtfully examined experimental techniques in earlier editions. Its goal is to enable students to use the vast information available in sequence and structural databases in a critical and effective manner.

ORGANIZATION OF THE TEXT. The evolutionary approach influences the organization of the text, which is divided into four major parts. As it did in the preceding edition, Part I introduces the language of biochemistry and the structures of the most important classes of biological molecules. The remaining three parts correspond to three major evolutionary challenges—namely, the interconversion of different forms of energy, molecular reproduction, and the adaptation of cells and organisms to changing environments. This arrangement parallels the evolutionary path outlined in **Chapter 2** and naturally flows from the simple to the more complex.

PART I, THE MOLECULAR DESIGN OF LIFE, introduces the most important classes of biological macromolecules, including proteins, nucleic acids, carbohydrates, and lipids, and presents the basic concepts of catalysis and enzyme action. Here are two examples of how an evolutionary perspective has shaped the material in these chapters:

- **Chapter 9**, on catalytic strategies, examines four classes of enzymes that have evolved to meet specific challenges: promoting a fundamentally slow chemical reaction, maximizing the absolute rate of a reaction, catalyzing a reaction at one site but not at many alternative sites, and preventing a deleterious side reaction. In each case, the text considers the role of evolution in fine-tuning the key property.

- **Chapter 13**, on membrane channels and pumps, includes the first detailed three-dimensional structures of an ion channel and

an ion pump. Because most other important channels and pumps are evolutionarily related to these proteins, these two structures provide powerful frameworks for examining the molecular basis of the action of these classes of molecules, so important for the functioning of the nervous and other systems.

PART II, TRANSDUCING AND STORING ENERGY, examines pathways for the interconversion of different forms of energy. **Chapter 15**, on signal transduction, looks at how DNA fragments encoding relatively simple protein modules, rather than entire proteins, have been mixed and matched in the course of evolution to generate the wiring that defines signal-transduction pathways. The bulk of Part II discusses pathways for the generation of ATP and other energy-storing molecules. These pathways have been organized into groups that share common enzymes. The component reactions can be examined once and their use in different biological contexts illustrated while these reactions are fresh in the students' minds.

- **Chapter 16** covers both glycolysis and gluconeogenesis. These pathways are, in some ways, the reverse of each other, and a core of enzymes common to both pathways catalyze many of the steps in the center of the pathways. Covering the pathways together makes it easy to illustrate how free energy enters to drive the overall process either in the direction of glucose degradation or in the direction of glucose synthesis.

- **Chapter 17**, on the citric acid cycle, ties together through evolutionary insights the pyruvate dehydrogenase complex, which feeds molecules into the citric acid cycle, and the α -ketoglutarate dehydrogenase complex, which catalyzes one of the key steps in the cycle itself.

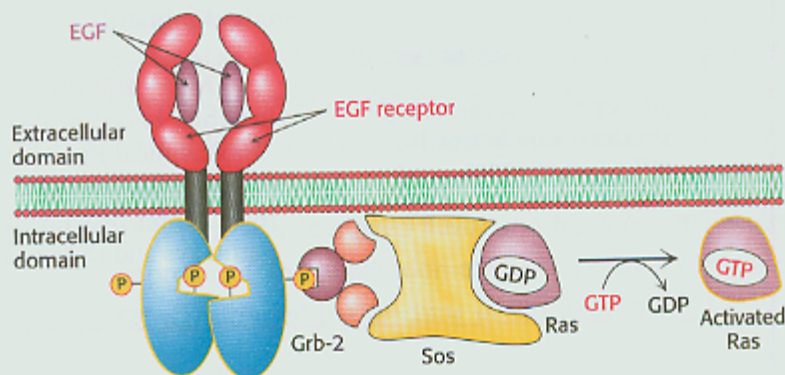


FIGURE 15.34 EGF signaling pathway.

Oxidative phosphorylation, in **Chapter 18**, is immediately followed in **Chapter 19** by the light reactions of photosynthesis to emphasize the many common chemical features of these pathways.

The discussion of the light reactions of photosynthesis in **Chapter 19** leads naturally into a discussion of the dark reactions—that is, the components of the Calvin cycle—in **Chapter 20**. This pathway is naturally linked to the pentose phosphate pathway, also covered in **Chapter 20**, because in both pathways common enzymes interconvert three-, four-, five-, six-, and seven-carbon sugars.

PART III, SYNTHESIZING THE MOLECULES OF LIFE, focuses on the synthesis of biological macromolecules and their components.

Chapter 24, on the biosynthesis of amino acids, is linked to the preceding chapter on amino acid degradation by a family of enzymes that transfer amino groups to and from the carbon frameworks of amino acids.

Chapter 25 covers the biosynthesis of nucleotides, including the role of amino acids as biosynthetic precursors. A key evolutionary insight emphasized here is that many of the enzymes in these pathways are members of the same family and catalyze analogous chemical reactions. The focus on enzymes and reactions common to these biosynthetic pathways allows students to understand the logic of the pathways, rather than having to memorize a set of seemingly unrelated reactions.

Chapters 27, 28, and 29 cover DNA replication, recombination, and repair; RNA synthesis and splicing; and protein synthesis. Evolutionary connections between prokaryotic systems and eukaryotic systems reveal how the basic biochemical processes have been adapted to function in more-complex biological systems. The recently elucidated structure of the ribosome gives students a glimpse into a possible early RNA world, in which nucleic acids, rather than proteins, played almost all the major roles in catalyzing important pathways.

PART IV, RESPONDING TO ENVIRONMENTAL CHANGES, looks at how cells sense and adapt to changes in their environments. Part IV examines, in turn, sensory systems, the immune system, and molecular motors and the cytoskeleton. These chapters illustrate how signaling and

response processes, introduced earlier in the text, are integrated in multicellular organisms to generate powerful biochemical systems for detecting and responding to environmental changes. Again, the adaptation of proteins to new roles is key to these discussions.

Integrated Chemical Concepts

We have attempted to integrate chemical concepts throughout the text. They include the mechanistic basis for the action of selected enzymes, the thermodynamic basis for the folding and assembly of proteins and other macromolecules, and the structures and chemical reactivity of the common cofactors. These fundamental topics underlie our understanding of all biological processes. Our goal is not to provide an encyclopedic examination of enzyme reaction mechanisms. Instead, we have selected for examination at a more detailed chemical level specific topics that will enable students to understand how the chemical features help meet the biological needs.

Chemical insight often depends on a clear understanding of the structures of biochemical molecules. We have taken considerable care in preparing stereochemically accurate depictions of these molecules where appropriate. These structures should make it easier for the student to develop an intuitive feel for the shapes of molecules and comprehension of how these shapes affect reactivity.



Newly Updated to Include Recent Discoveries

Given the breathtaking pace of modern biochemistry, it is not surprising that there have been major developments since the publication of the fourth edition. Foremost among them is the sequencing of the human genome and the genomes of many simpler organisms. The text's evolutionary framework allows us to naturally incorporate information from these historic efforts. The determination of the three-dimensional structures of proteins and macromolecular assemblies also has been occurring at an astounding pace.

As noted earlier, the discussion of excitable membranes in **Chapter 13** incorporates the detailed structures of an ion channel (the prokaryotic potassium channel) and an ion pump (the sarcoplasmic reticulum calcium ATPase).

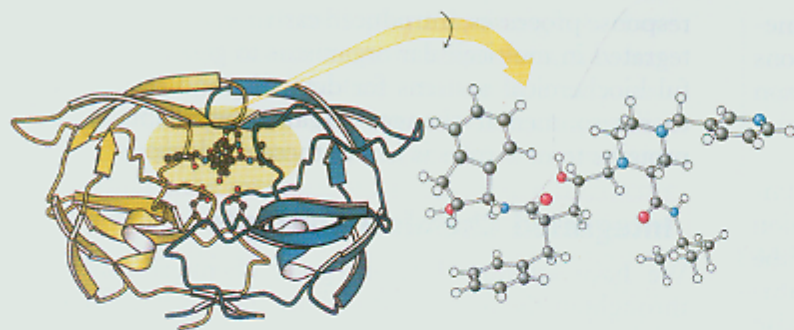


FIGURE 9.21 HIV protease-Crixivan complex.

- Great excitement has been generated in the signal transduction field by the first determination of the structure of a seven-transmembrane-helix receptor—the visual system protein rhodopsin—discussed in **Chapters 15 and 32**.
- The ability to describe the processes of oxidative phosphorylation in **Chapter 18** has been greatly aided by the determination of the structures for two large membrane protein complexes: cytochrome *c* oxidase and cytochrome *bc₁*.
- Recent discoveries regarding the three-dimensional structure of ATP synthase are covered in **Chapter 18**, including the remarkable fact that parts of the enzyme rotate in the course of catalysis.
- The determination of the structure of the ribosome transforms the discussion of protein synthesis in **Chapter 29**.
- The elucidation of the structure of the nucleosome core particle—a large protein–DNA complex—facilitates the description in **Chapter 31** of key processes in eukaryotic gene regulation.

Finally, each of the three chapters in Part IV is based on recent structural conquests.

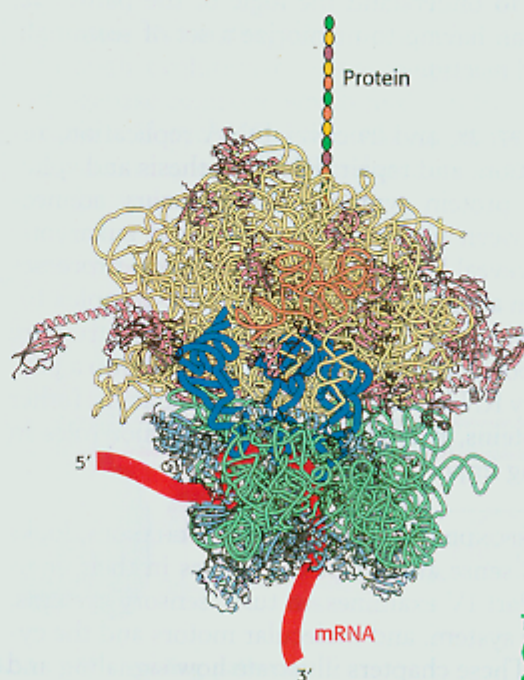
- The ability to grasp key concepts in sensory systems (**Chapter 32**) is aided by the structures of rhodopsin and the aforementioned ion channel.
- **Chapter 33**, on the immune system, now includes the more recently determined structure of the T-cell receptor and its complexes.
- The determination of the structures of the molecular motor proteins myosin and kinesin first revealed the evolutionary connections on which **Chapter 34**, on molecular motors, is based.

New and Improved Illustrations

The relation of structure and function has always been a dominant theme of *Biochemistry*. This relation becomes even clearer to students using the fifth edition through the extensive use of molecular models. These models are superior to those in the fourth edition in several ways.

- All have been designed and rendered by one of us (JMB), with the use of MOLSCRIPT, to emphasize the most important structural features. The philosophy of the authors is that the reader should be able to write the caption from looking at the picture.
- We have chosen ribbon diagrams as the most effective, clearest method of conveying molecular structure. All molecular diagrams are rendered in a consistent style. Thus students are able to compare structures easily and to develop familiarity and facility in interpreting the models. Labels highlight key features of the molecular models.
- Many new molecular models have been added, serving as sources of structural insight into additional molecules and in some cases affording multiple views of the same molecule.

In addition to the molecular models, the fifth edition includes more diagrams providing an overview of pathways and processes and setting processes in their biological context.



The ribosome (Chapter 29 opener).