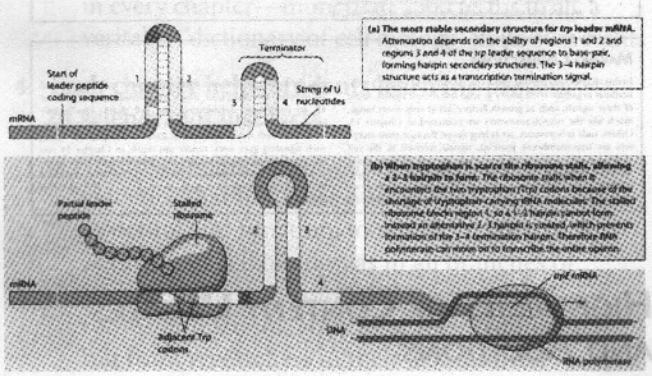
Preface

"Because we enjoy interacting with biology undergrads and think that they should have biology textbooks that are clearly written, make the subject matter relevant to the reader, and help them appreciate not only how much we already know about biology—cell biology, in our case—but also how much more remains to be investigated and discovered." That's how any of the authors of this text would likely respond if asked why we've invested so much time in writing and revising *The World of the Cell*. Each of us has an extensive history of teaching undergraduate courses in cell biology and related areas, and each of us treasures our contact with students as one of the most rewarding aspects of being a faculty member.

As we reflect on the changes we've seen in our courses over the years, we realize that the past several decades have seen an explosive growth in our understanding of the properties and functions of living cells. This enormous profusion of information presents us with a daunting challenge as we confront the task of keeping *The World of the Cell* up to date while simultaneously ensuring that it remains both manageable in length and readily comprehensible to students encountering the field of cell and molecular biology for the first time. This seventh edition represents our most recent attempt to rise to that challenge. As with the previous editions, each of us has brought our own teaching and writing experience to the venture in ways that we have found mutually beneficial—a view that we hope our readers will share.

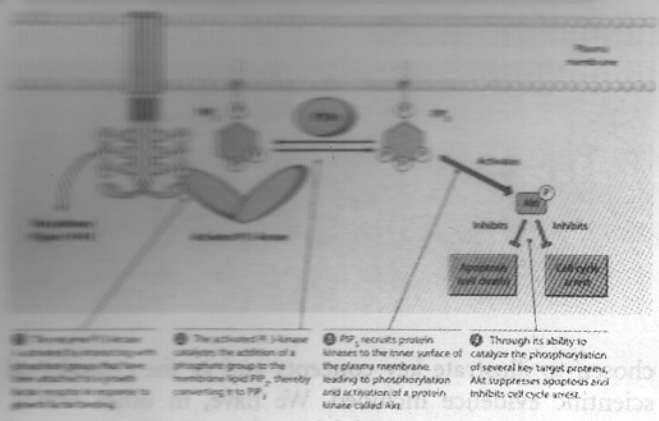
One major objective for this edition has been to update the content of the text, especially in areas where the pace of research is especially brisk and recent findings are particularly significant. At the same time, we have remained committed to the three central goals that have characterized each preceding edition. As always, our primary goal is to introduce students to the fundamental principles that guide cellular organization and function. Second, we think it is important for students to understand some of the critical scientific evidence that has led to the formulation of these central concepts. And finally, we have sought to accomplish these goals in a book of manageable length that can be easily read and understood by beginning cell biology students—and that still fits in their backpacks! To accomplish this third goal, we have necessarily been selective both in the types of examples chosen to illustrate key concepts and in the quantity of scientific evidence included. We have, in other words, attempted to remain faithful to the overall purpose of each previous edition: to present the essential principles, processes, and methodology of molecular and cell biology as lucidly as possible. We have also given careful attention to accuracy, consistency, vocabulary, and readability to minimize confusion and maximize understanding for our readers.

Another objective for the seventh edition has been to enhance the effectiveness of the art program through the widespread introduction of *minicaptions* to help students understand technically complex diagrams. A minicaption is a pedagogical tool that takes detailed textual descriptions previously found in lengthy figure legends and incorporates the information directly into the illustration itself. With diagrams that use minicaptions, students no longer need to look back and forth between the figure legend and the illustration to understand what is taking place. Two types of minicaptions have been widely introduced into this edition of *The World of the Cell*: **Text Box Minicaptions** are colored text boxes that describe events taking place in various locations within a diagram.

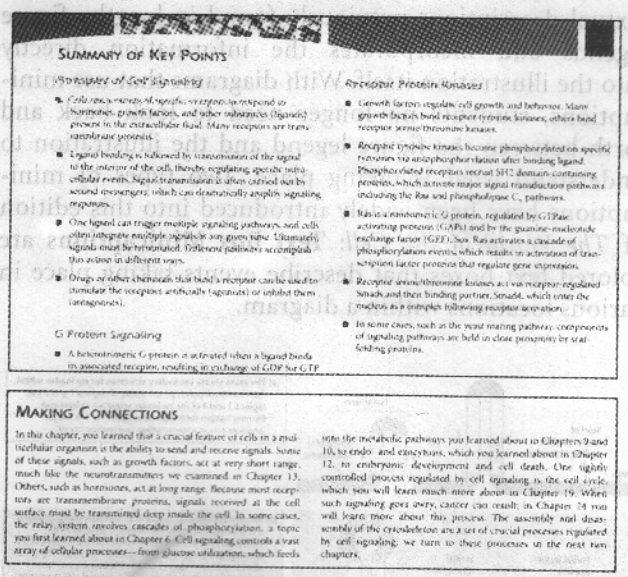


Step Circle Minicaptions are consecutively numbered, brief blocks of colored text that point to various steps within a sequential pathway and describe the events occurring at each step. These devices are designed to help students grasp concepts more quickly by drawing their focus into the body of an illustration rather than

depending solely on a separate figure legend to describe what is taking place.



Two other features new to the seventh edition provide an overview of the key points covered in each chapter and highlight connections between material covered in different chapters. These two pedagogical tools, which appear at the end of each chapter, are a bulleted **Summary of Key Points** that briefly describes the main points covered in each section of the chapter and a **Making Connections** paragraph that highlights connections between the content of the current chapter and topics covered elsewhere in the book.



SUMMARY OF KEY POINTS

Overview of Cell Signaling

- Cells receive a variety of signals; receptors respond to hormones, growth factors, and other substances (ligands) present in the extracellular fluid. Many receptors are transmembrane proteins.
- Ligand binding is followed by transmission of the signal to the interior of the cell, thereby regulating specific intracellular events. Signal transduction is often carried out by second messengers, which can dramatically amplify signaling responses.
- One ligand can trigger multiple signaling pathways, and cells often integrate multiple signals at any given time. Ultimately, signals must be terminated. Different pathways accomplish this at one in different ways.
- Drugs or other chemicals that bind a receptor can be used to stimulate the receptor's activity (agonists) or inhibit them (antagonists).

G Protein Signaling

- A heterotrimeric G protein is activated when a ligand binds its associated receptor, resulting in exchange of GDP for GTP

Receptor Protein Kinases

- Growth factors regulate cell growth and behavior. Many growth factors bind receptor tyrosine kinases; others bind receptor serine/threonine kinases.
- Receptor tyrosine kinases become phosphorylated on specific tyrosines via autophosphorylation after binding ligand. Phosphorylated receptors recruit SH2 domain-containing proteins, which activate major signal transduction pathways including the Ras and phospholipase C_γ pathways.
- Ras is a monomeric G protein, regulated by GTPase-activating proteins (GAPs) and by the guanine-nucleotide exchange factor (GEF) Sos. Ras activates a cascade of phosphorylation events, which results in activation of transcription factor proteins that regulate gene expression.
- Receptor serine/threonine kinases act via receptor-regulated Smads and their binding partner, Smad4, which enter the nucleus as a complex following receptor activation.
- In some cases, such as the yeast mating pathway, components of signaling pathways are held in close proximity by scaffolding proteins.

MAKING CONNECTIONS

In this chapter, you learned that a crucial feature of cells in a multicellular organism is the ability to send and receive signals. Some of these signals, such as growth factors, act at very short range; much like the neurotransmitters we examined in Chapter 13. Others, such as hormones, act at long range. Because most receptors are transmembrane proteins, signals received at the cell surface must be transmitted deep inside the cell. In some cases, the relay system involves cascades of phosphorylation, a topic you first learned about in Chapter 6. Cell signaling controls a vast array of cellular processes—from glucose utilization, which feeds into the metabolic pathways you learned about in Chapters 9 and 10, to endo- and exocytosis, which you learned about in Chapter 12, to embryonic development and cell death. One tightly controlled process regulated by cell signaling is the cell cycle, which you will learn much more about in Chapter 19. When such signaling goes awry, cancer can result; in Chapter 24 you will learn more about this process. The assembly and disassembly of the cytoskeleton are a set of crucial processes regulated by cell signaling; we turn to these processes in the next two chapters.

HIGHLIGHTS OF CONTENT UPDATES AND ADDITIONS

Updated material and new information has been added throughout the book. Topics that have been altered, updated, or added include the following:

CHAPTER 1: diversity of cell types, cell biology timeline, deconvolution microscopy, green fluorescent protein

CHAPTER 3: *trans* fats and health, hair structure

CHAPTER 4: relationship between archaea, bacteria, and eukaryotes, actin-like and tubulin-like cytoskeletal proteins in bacteria, bacterial cell wall composition

CHAPTER 5: oxidation-reduction, autotrophs and heterotrophs, coupled reactions

CHAPTER 6: quantum tunneling mechanism of certain enzymes, relationship of enzyme cofactors to dietary needs for vitamins and metals, use of substrate analogs to fight diseases such as AIDS

CHAPTER 7: involvement of adhesive surface proteins and glycocalyx in bacterial pathogenesis, effect of dietary *trans* fats on membrane structure, two-dimensional electrophoresis, Western blotting, antifungal antibiotics

CHAPTER 8: antibiotic resistance arising from mutations in porins or from acquisition of multiple drug resistance proteins, effect of cellular pH on transport of oxygen by hemoglobin

CHAPTER 9: novel roles of glycolytic enzymes, entropy contribution to the exergonic nature of ATP hydrolysis

CHAPTER 10: mitochondrial structure and cristae junctions, ATP synthase structure and mechanism of action, Q cycle, respirasomes

CHAPTER 11: mobility of light harvesting complexes, chloroplast Q cycle, similarities between chloroplast and mitochondrial electron transport, chloroplast ATP synthase, overview of Calvin cycle

CHAPTER 12: endomembrane trafficking of proteins and lipids, pharmacogenetics, steroid biosynthesis, ER retention tags on NMDA receptor, autophagy and cancer, desensitization and tumor formation, tolerance to barbiturates, caveolae and cholesterol uptake, phagocytosis by white blood cells to educate the immune system

CHAPTER 13: Goldman equation relationship to the Nernst equation, direct (ionotropic) and indirect (metabotropic) mechanism of neurotransmitter action, nicotinic acetylcholine receptors

CHAPTER 14: signal integration, opioid receptors, G protein-linked receptor kinases, β-arrestin, protein kinase A, regulators of G protein signaling, $G_{\beta\gamma}$ subunit signaling, metabotropic neurotransmitter receptors, yeast mating pathway and scaffolding complexes, insulin signaling

CHAPTER 15: bacterial cytoskeletal proteins, molecular models for tubulin and actin, microtubule-interacting proteins and actin-binding proteins, cytoskeletal inhibitors overview of cytoskeletal systems in eukaryotes, dynamic instability of microtubules

CHAPTER 16: kinesin and myosin families, primary ("9 + 0") cilia, cell crawling and focal adhesions, cyclosis

CHAPTER 17: tissue organization, human disorders linked to the extracellular matrix, cell-cell adhesion, or junctions

CHAPTER 18: bioinformatics, transcriptomes, BLAST searching, haplotypes, copy number variants, transposable elements (LINEs and SINEs), plasmid functions, nuclear substructures

CHAPTER 19: flow cytometry, bacterial cell division, telomere shortening and aging, spindle assembly in cells lacking centrosomes, role of Ran-GTP in spindle assembly, Rho and the contractile ring, TOR signaling and cell growth

CHAPTER 20: parthenogenesis in Komodo dragons, cytostatic factor (CSF), pairing sites in synapsis, knockout mice, use of PCR for gene cloning, epitope and polyhistidine tagging

CHAPTER 21: RNA proofreading, transcription factories, archaeal promoters, exon-junction complex, alternative splicing, the "one gene–many polypeptides" concept

CHAPTER 22: initiation factors for eukaryotic translation, hybrid states during translocation step of protein synthesis, peptide anticodons, similarities between archaeal and eukaryotic translation, unfolded protein response, ER-associated degradation (ERAD)

CHAPTER 23: regulons and stimulons, cloning of carrot plants, genomic imprinting, DNA methylation, histone methylation, DNA insulators, translational control by eIF2 and eIF4F, pulse-chase technique, mRNA degradation, P bodies, RNA interference-based disease treatments, developmental role of microRNAs

CHAPTER 24: epigenetic changes in cancer cells, cancer stem cells, immune surveillance, BRCA genes, HPV vaccine, microRNAs in cancer, genetic basis of aneuploidy

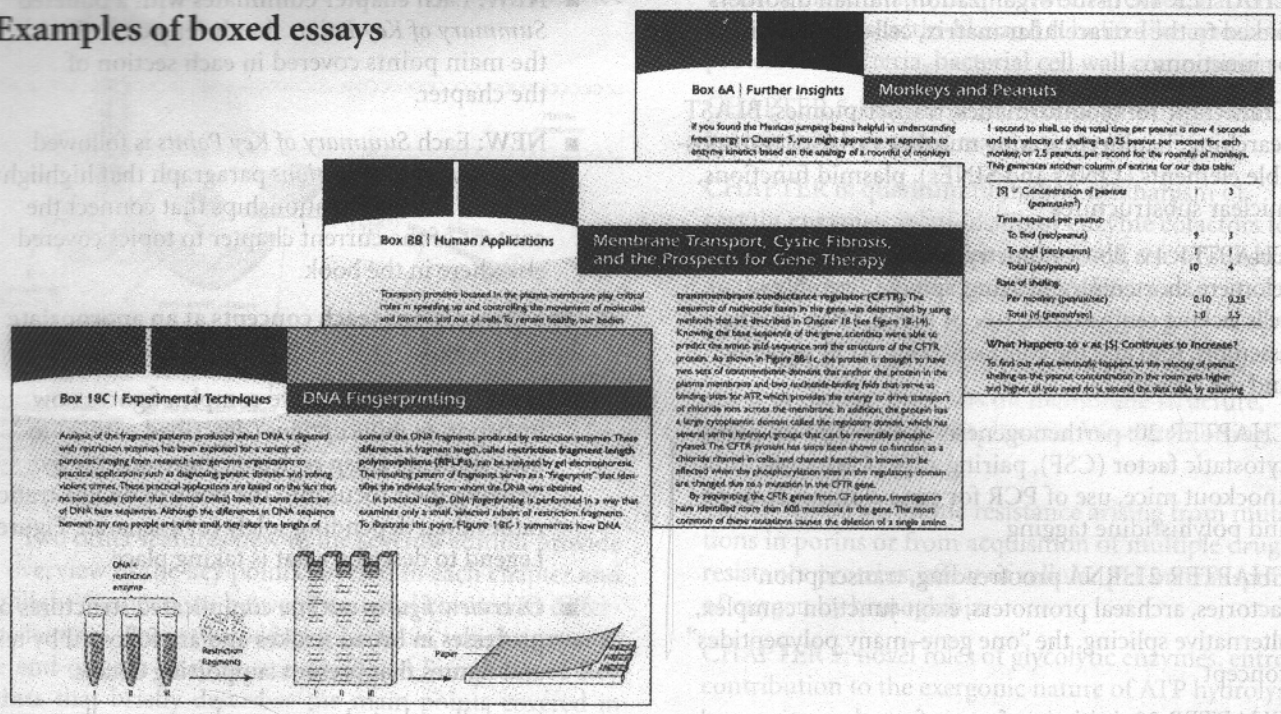
APPENDIX: 3-D electron tomography, multichannel fluorescent imaging

Building on the Strengths of Previous Editions

We have retained and built upon the strengths of prior editions in four key areas:

1. **The chapter organization focuses on main concepts.**
   - Each chapter is divided into sections that begin with a *concept statement heading*, which summarizes the material and helps students focus on the main points to study and review.
   - Chapters are written and organized in ways that allow instructors to assign the chapters and chapter sections in different sequences to make the book adaptable to a wide variety of course plans.
   - **NEW:** Each chapter culminates with a bulleted *Summary of Key Points* that briefly describes the main points covered in each section of the chapter.
   - **NEW**: Each *Summary of Key Points* is followed by a *Making Connections* paragraph that highlights some of the interrelationships that connect the content of the current chapter to topics covered elsewhere in the book.
2. **The illustrations teach concepts at an appropriate level of detail.**
   - **NEW**: Many of the more complex figures now incorporate *minicaptions* (described earlier) to help students grasp concepts more quickly by drawing their focus into the body of an illustration rather than depending solely on a separate Figure Legend to describe what is taking place.
   - *Overview figures* outline complicated structures or processes in broad strokes and are followed by text and figures that present supporting details.
   - Carefully-selected micrographs are usually accompanied by size bars to indicate magnification.
3. **Important terminology is highlighted and defined in several ways.**
   - **Boldface type** is used to highlight the most important terms in each chapter, all of which are defined in the Glossary.
   - *Italics* are employed to identify additional technical terms that are less important than boldfaced terms but significant in their own right. Occasionally, italics are also used to highlight important phrases or sentences.
   - The Glossary includes definitions and page references for all bold-faced key terms and acronyms in every chapter—more than 1500 terms in all, a veritable "dictionary of cell biology" in its own right.
4. **Each chapter helps students learn the process of science, not just facts.**
   - Text discussions emphasize the experimental evidence that underlies our understanding of cell structure and function, to remind readers that advances in cell biology, as in all branches of science, come not from lecturers in their classrooms or textbook authors at their computers but from researchers in their laboratories.
   - The inclusion of a *Problem Set* at the end of each chapter reflects our conviction that we learn science not just by reading or hearing about it, but by working with it. The problems are designed to emphasize understanding and application, rather than rote recall. Many of the problems are class-tested, having been selected from problem sets

Examples of boxed essays



and exams we have used in our own courses. To maximize the usefulness of the problem sets, detailed answers for all problems are available for students in a *Solutions Manual* that is available for purchase separately.

- Each chapter contains one or more *Boxed Essays* to aid students in their understanding of particularly important or intriguing aspects of cell biology (see samples at top of page). Some of the essays provide Further Insights into potentially difficult principles, such as the essay that uses the analogy of monkeys shelling peanuts to explain enzyme kinetics (Box 6A). Other essays describe some of the important Experimental Techniques used by cell biologists, as exemplified by the description of DNA fingerprinting in Box 18C. And yet another role of the boxed essays is to describe Human Applications of research findings in cell biology, as illustrated by the discussion of cystic fibrosis and the prospects for gene therapy in Box 8B.
- A *Suggested Reading* list is included at the end of each chapter, with an emphasis on review articles and carefully selected research publications that motivated students are likely to understand. We have tried to avoid overwhelming readers with lengthy bibliographies of the original literature but have referenced articles that are especially relevant to the topics of the chapter. In most chapters, we have included a few citations of especially important historical publications, which are marked with blue dots to alert the reader to their historical significance.

Techniques and Methods

Throughout the text, we have tried to explain not only *what* we know about cells but also *how* we know what we know. Toward that end, we have included descriptions of experimental techniques and findings in every chapter, almost always in the context of the questions they address and in anticipation of the answers they provide. For example, polyacrylamide gel electrophoresis is introduced not in a chapter that simply catalogues a variety of methods for studying cells but in Chapter 7, where it becomes important to our understanding of how membrane proteins can be separated from one another. Similarly, equilibrium density centrifugation is described in Chapter 12, where it is essential to our understanding of how lysosomes were originally distinguished from mitochondria and subsequently from peroxisomes as well.

To help readers locate techniques out of context, an alphabetical Guide to Techniques and Methods appears on the inside of the front cover, with references to chapters, pages, tables, figures, and boxed essays, as appropriate. To enhance its usefulness, the Guide to Techniques and Methods includes references not just to laboratory techniques but also to the mathematical determination of values such as ΔG (free energy change) and $\Delta E_0'$ (standard reduction potential), bioinformatics techniques such as BLAST searching, and even to clinical procedures such as the treatment of methanol poisoning.

Microscopy is the only exception to our general approach of introducing techniques in context. The techniques of light and electron microscopy are so pervasively relevant to contemporary cell biology that they warrant special consideration as a self-contained unit, which is

included as an Appendix entitled *Visualizing Cells and Molecules*. This Appendix gives students ready access to detailed information on a variety of microscopy techniques, including cutting-edge uses of light microscopy for imaging and manipulating molecular processes.

Supplementary Learning Aids

1. Supplements That Connect Instructors to Students

Printed Test Bank for *The World of the Cell* • 0-321-52746-1

Computerized Test Bank for *The World of the Cell* • 0-321-52742-9

The test bank provides over 1000 multiple-choice, short-answer, and inquiry/activity questions.

Instructor Resource CD-ROM for *The World of the Cell* • 0-321-52743-7

Available to adopters, this CD-ROM includes all illustrations from the text in high resolution JPG and PowerPoint® formats. Also included are videos and animations of key concepts, organized by chapter for ease of use in the classroom.

Transparency Acetates for *The World of the Cell* • 0-321-52745-3

Includes 200 full-color acetates with large, clear labels for easy viewing.

2. Additional Resources for Students

Solutions Manual for *The World of the Cell* • 0-321-52747-X

Written by the authors, this is a collection of complete, detailed answers for all of the end-of-chapter questions and problems.

The Cell Place for *The World of the Cell* • 0-321-52744-5

The book's companion website, *www.thecellplace.com*, helps students explore a variety of cell biology topics in depth, and includes interactive tutorials, simulations, animations, and step-by-step problems. Practice quizzes contain 20 multiple-choice questions for each chapter, with instant feedback for correct and incorrect answers.

We Welcome Your Comments and Suggestions

The ultimate test of any textbook is how effectively it helps instructors teach and students learn. We welcome feedback and suggestions from readers and will try to acknowledge all correspondence. Please send your comments, criticisms, and suggestions to the appropriate authors listed below.

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