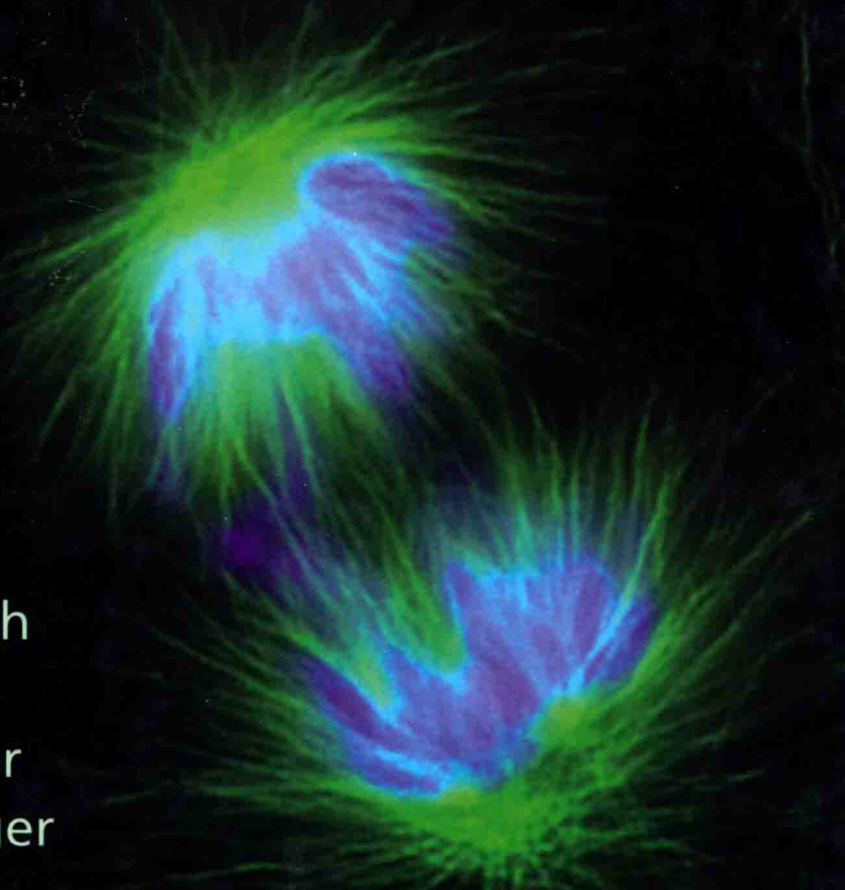
MOLECULAR CELL BIOLOGY

SIXTH EDITION



Lodish
Berk
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Matsudaira

MOLECULAR CELL BIOLOGY

SIXTH EDITION

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MEDIA CONNECTIONS

Below is a chapter-by-chapter list of the media resources available on the Instructor's CD-ROM and Web site www.whfreeman.com/lodish6e. More than 125 animations and videos are available with this textbook, as well as 25 podcasts narrated by the authors.

Animations, now offered for both your MP3 player and personal computer, serve three different purposes:

- Overview Animations (21 total) introduce key processes.
- Focus Animations (38 total) home in on the detail of those processes.
- Technique Animations (13 total) reveal the experimental techniques available to researchers today.

Videos (64 total): Live research videos of key cellular processes show the latest experimental techniques.

Podcasts (25 total): Narrated by the authors, these podcasts give students a deeper understanding of key figures in the text and a sense of the thrill of scientific discovery.

CHAPTER 1 LIFE BEGINS WITH CELLS

Video: Plasmodium *Sporozoite* Entering and Exiting a Liver Cell (Figure 1-4)

Video: Early Embryonic Development (Figure 1-7)

Overview Animation: Biological Energy Interconversions (Figure 1-14)

Overview Animation: Life Cycle of a Cell (Figure 1-17)

Focus Animation: Mitosis (Figure 1-21)

Podcast: Common Experimental Organisms (Figure 1-25)

CHAPTER 2 CHEMICAL FOUNDATIONS

Podcast: Macromolecules Can Bind Multiple Ligands (Figure 2-24)

CHAPTER 3 PROTEIN STRUCTURE AND FUNCTION

Overview Animation: Oil Drop Model of Protein Structure (Figure 3-7)

Focus Animation: Chaperone-Mediated Folding (Figure 3-16)

Video: GroEl ATPase Cycle (Figure 3-17)

Overview Animation: The Proteasome (Figure 3-29)

Overview Animation: Life Cycle of a Protein (Section 3.4)

Technique Animation: SDS Gel Electrophoresis (Figure 3-35)

Technique Animation: Immunoblotting (Figure 3-38)

Podcast: Use of Mass Spectrometry in Cell Biology (Figure 3-43)

CHAPTER 4 BASIC MOLECULAR GENETIC MECHANISMS

Video: Rotating 3-D Model of TATA Box-Binding Protein Bending Double-Stranded DNA (Section 4.1)

Focus Animation: Basic Transcriptional Mechanism (Figure 4-11)

Video: Rotating 3-D Model of Bacterial RNA Polymerase Synthesizing RNA from DNA (Section 4.2)

Overview Animation: Life Cycle of an mRNA (Figure 4-15)

Podcast: Structure of the Ribosome (Figure 4-23)

Video: Rotating 3-D Model of a Bacterial Ribosome (Figure 4-23)

Focus Animation: Protein Synthesis (Figure 4-25)

Focus Animation: Nucleotide Polymerization by DNA Polymerase (Figure 4-30)

Focus Animation: Coordination of Leading- and Lagging-Strand Synthesis (Figure 4-31)

Focus Animation: Bidirectional Replication of DNA (Figure 4-32)

Focus Animation: Coordination of Leading- and Lagging-Strand Synthesis (Figure 4-33)

Overview Animation: Life Cycle of a Retrovirus (Figure 4-49)

Focus Animation: Retroviral Gene Expression (Section 4.7)

Focus Animation: Retroviral Genome Integration (Section 4.7)

CHAPTER 5 MOLECULAR GENETIC TECHNIQUES

Focus Animation: Mitosis (Figure 5-3)

Focus Animation: Meiosis (Figure 5-3)

Technique Animation: Expression Cloning of Receptors (Section 5.2)

Technique Animation: Plasmid Cloning (Figure 5-14)

Technique Animation: Dideoxy Sequencing of DNA (Figure 5-21)

Technique Animation: Polymerase Chain Reaction (Figure 5-23)

Technique Animation: Synthesizing an Oligonucleotide Array (Figure 5-29)

Technique Animation: Screening for Patterns of Gene Expression (Figure 5-29)

Video: Microinjection of ES Cells into a Blastocyst (Figure 5-41)

Technique Animation: Creating a Transgenic Mouse (Figure 5-43)

Video: DNA Injected into a Pronucleus of a Mouse Zygote (Figure 5-43)

Podcast: RNA Interference (Figure 5-45)

CHAPTER 6 GENES, GENOMICS, AND CHROMOSOMES

Podcast: Eukaryotic Transcription Units (Figure 6-3)

Focus Animation: Retroviral Reverse Transcription (Figure 6-14)

Focus Animation: Telomere Replication (Figure 6-48)

Focus Animation: Telomere Replication (Figure 6-49)

CHAPTER 7 TRANSCRIPTIONAL CONTROL OF GENE EXPRESSION

Podcast: Assembly of the Pol II Preinitiation Complex (Figure 7-31)

Video: 3-D Model of an RNA Polymerase II Preinitation Compex (Figure 7-32)

Technique Animation: Yeast Two-Hybrid System (Figure 7-45)

Video: Hormone-Regulated Nuclear Translocation of the Glucocorticoid Receptor (Figure 7-49)

CHAPTER 8 POST-TRANSCRIPTIONAL GENE CONTROL

Overview Animation: Life Cycle of an mRNA (Figure 8-2)

Video: hnRNP A1 Nucleocytoplasmic Shuttling (Figure 8-4)

Podcast: Discovery of Introns (Figure 8-6)

Focus Animation: mRNA Splicing (Figure 8-9)

Focus Animation: mRNA Splicing (Figure 8-11)

Video: Dynamic Nature of Pre-mRNA Splicing Factor Movement in Living Cells (Figure 8-15)

CHAPTER 9 VISUALIZING, FRACTIONATING, AND CULTURING CELLS

Overview Animation: Protein Secretion (Figure 9-5)

Video: Three-Dimensional Model of a Golgi Complex (Figure 9-6)

Video: Three-Dimensional Model of a Mitochondrion (Figure 9-8)

Podcast: Light and Electron Microscopy (Figure 9-14)

Technique Animation: Preparing Monoclonal Antibodies (Figure 9-35)

CHAPTER 10 BIOMEMBRANE STRUCTURE

Podcast: Annular Phospholipids (Figure 10-17)

CHAPTER 11 TRANSMEMBRANE TRANSPORT OF IONS AND SMALL MOLECULES

Video: Frog Oocyte Expressing Aquaporin Bursts in Hypotonic Solution (Figure 11-7)

Overview Animation: Biological Energy Interconversions (Figure 11-12)

Overview Animation: Biological Energy Interconversions (Figure 11-24)

Overview Animation: Biological Energy Interconversions (Figure 11-25)

Podcast: The Two-Na^+/One-Leucine Symporter (Figure 11-26)

CHAPTER 12 CELLULAR ENERGETICS

Video: Mitochondrion Reconstructed by Electron Tomography (Figure 12-6)

Video: Mitochondrial Fusion and Fission (Figure 12-7)

Focus Animation: Electron Transport (Figure 12-16)

Focus Animation: Proton Translocating, Rotary F-ATPase (Figure 12-24)

Focus Animation: ATP Synthesis (Figure 12-25)

Podcast: ATP Synthesis (Figure 12-25)

Video: Rotation of Actin Filament Bound to ATP Synthase (Figure 12-26)

Focus Animation: Photosynthesis (Figure 12-33)

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MOLECULAR CELL BIOLOGY

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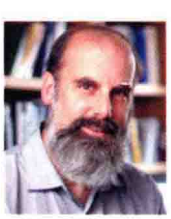

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HIDDE PLOEGH is Professor of Biology at the Massachusetts Institute of Technology and a member of the Whitehead Institute for Biomedical Research. One of the world's leading researchers in immune system behavior, Dr. Ploegh studies the various tactics that viruses employ to evade our immune responses and the ways our immune system distinguishes friend from foe. Dr. Ploegh teaches immunology to undergraduate students at Harvard University and MIT.

To our students and to our teachers,
from whom we continue to learn,
and to our families, for their support,
encouragement, and love

In writing the sixth edition of *Molecular Cell Biology* we have incorporated many of the spectacular advances made over the past four years in biomedical science, driven in part by new experimental technologies that have revolutionized many fields. High-velocity techniques for sequencing DNA, for example, have generated the complete sequence of dozens of eukaryotic genomes; these in turn have led to important discoveries about the organization of the human genome and regulation of gene expression, as well as novel insights into the evolution of life-forms and the functions of individual members of multiprotein families. New imaging techniques have generated profound revelations about cell organization and movement, and new molecular structures have greatly increased our understanding of life processes such as cell-cell signaling, photosynthesis, gene transcription, and chromatin structure.

New Author Team

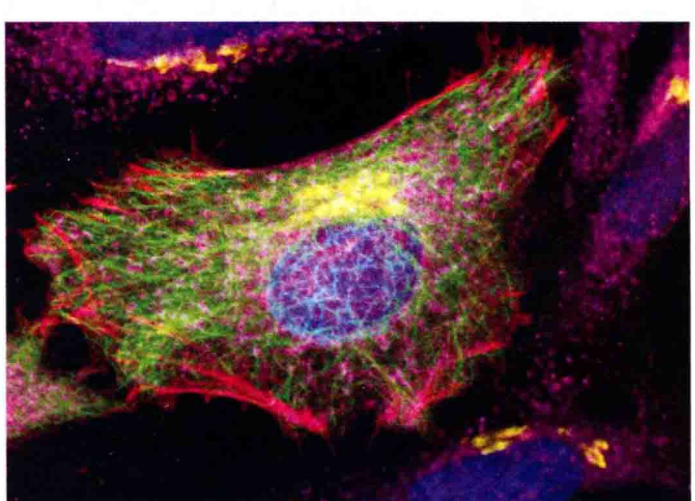
Two new authors have been instrumental in refocusing this book toward these exciting new developments. **Anthony Bretscher** of Cornell University is known for identifying and characterizing new components of the actin cytoskeleton and elucidating their biological functions in relation to cell polarity and membrane traffic. **Hidde Ploegh,** of the Massachusetts Institute of Technology, has made major contributions to our understanding of immune system behavior, particularly in regard to the various tactics that viruses employ to evade our immune responses and the ways our immune system responds. Both authors are widely recognized for their research as well as their classroom teaching abilities.

We are grateful to Paul Matsudaira, Jim Darnell, Larry Zipursky, and David Baltimore for their exceptional contributions to the previous editions of *Molecular Cell Biology*. Much of their vision and insight is apparent at many places in this book.

Experimental Emphasis

The hallmark of *Molecular Cell Biology* has always been the use of experiments to teach students how we have learned what we know. A number of experimental organisms, from yeasts to worms to mice, are used throughout so the student can see how discoveries made with a "lower organism" can lead directly to insights even about human biology and disease. This experimental approach, evident in the text itself, has also been thoroughly integrated into the pedagogical framework. For example:

- Experimental Figures lead students through important experimental results.
- Classic Experiments essays focus on historically important and Nobel Prize–winning experiments.
- New and revised Analyze the Data problems at the end of each chapter require the student to synthesize real experimental data to answer a series of questions.
- Updated Perspectives for the Future essays explore potential applications of future discoveries and unanswered questions that lie ahead in research.



Fluorescence microscopy shows the location of DNA and multiple proteins within the same cell. [From B.N.G. Giepmans et al., 2006, *Science* **312**:217.]

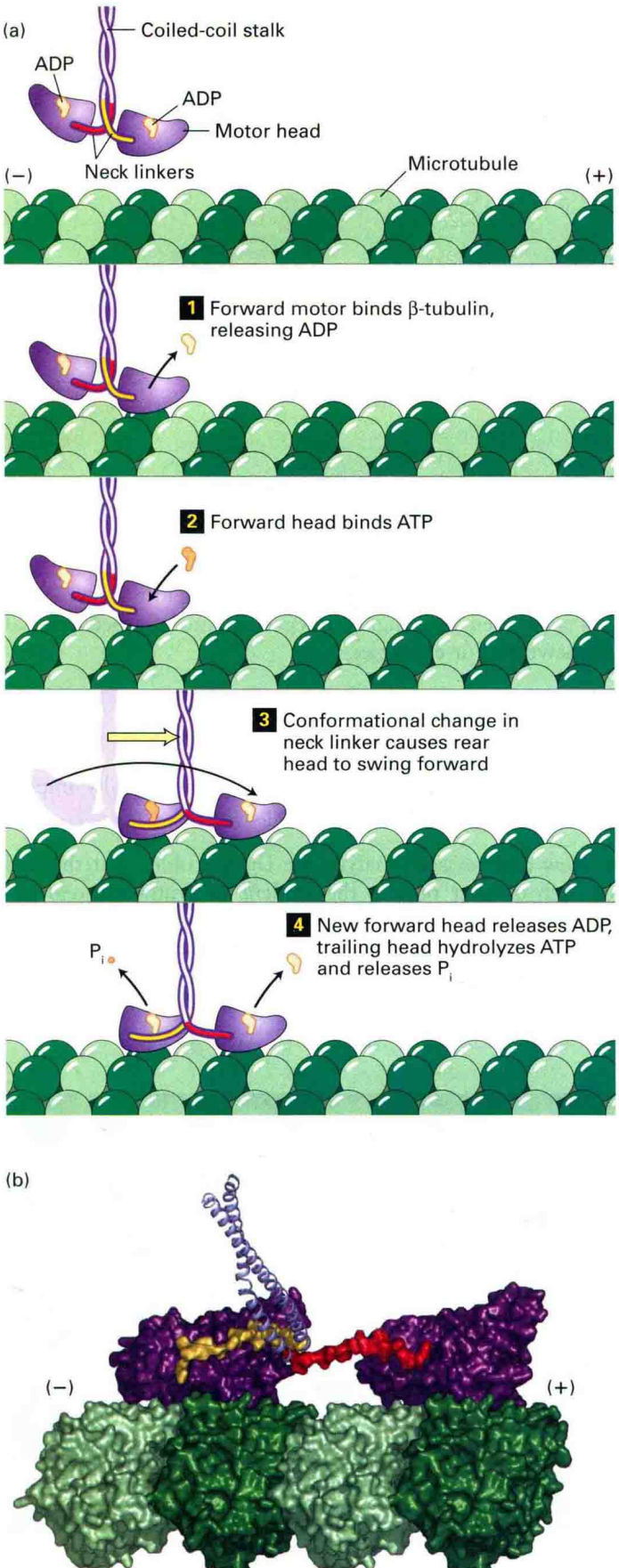


Figure 18-22 Kinesin-1 uses ATP to "walk" down a microtubule.

New Discoveries, New Methodologies

Methodological advances continue to expand and enrich our knowledge of molecular cell biology, and lead to new understanding. Following are just a selection of the new experimental methodologies and cutting-edge science introduced in this edition:

- Expanded coverage of proteomics, including organelle proteome profiling and advances in mass spectroscopy (Chapter 3)
- Expanded coverage of RNAi, including the use of shRNAs to inhibit any gene of interest in a cultured cell or organism (Chapters 5, 8)
- Updated discussions of chromatin, including structure and condensation (Chapter 6), control of gene expression by chromatin remodeling (Chapter 7), and chromatin-remodeling proteins and tumor development (Chapter 25)
- Evolution of chromosomes and the mitochondrion (Chapter 6)
- New molecular models, including pre-initiation complex and mediator complex (Chapter 7); annular phospholipids (Chapter 10); Ca^{2+} ATPase (Chapter 11); rhodopsin, transducin, and protein kinase A (Chapter 15); and myosin ATPase (Chapter 17)
- Latest advances in light and electron microscopy, including cryoelectron tomography (Chapter 9)
- Reactive oxygen species (ROS) (Chapter 12)
- Role of supercomplexes in electron transport (Chapter 12)
- Human epidermal growth factor receptors (HERs) and treatment of cancer (Chapter 16)
- Myosin ATPase cycle (Chapter 17)
- Kinesin-1 ATPase cycle (Chapter 18)
- Use of retrovirus infection for tracing cell lineage (Chapter 21)
- Axon guidance molecules (Chapter 23)
- Somatic gene rearrangement in immune cells (Chapter 24)
- Cancer stem cells (Chapter 25)
- Use of DNA microarray analysis in tumor typing (Chapter 25)

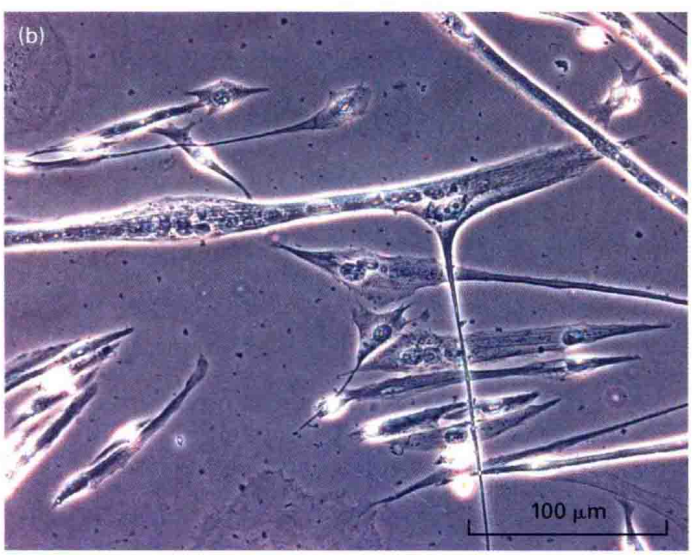
Increased Clarity and Accessibility

In writing the sixth edition we have taken a step back and asked what we, as experienced teachers of both undergraduate and graduate students, can do to make material that can be daunting for students more approachable. We have tried to balance our coverage of the latest scientific developments with students' need for clear explanations of the fundamentals, and we have intensified our commitment to making both the concepts and experiments more accessible.

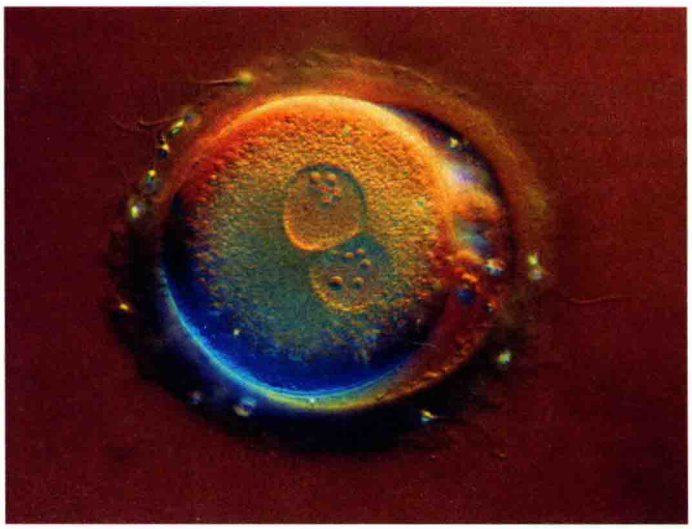
In particular, we have improved the **chapter overviews,** making sure that they give students the big picture and provide a solid foundation for what is to come. We have also simplified the text and headings, removing jargon wherever possible. Clear **concept-oriented headings** now provide an easy-to-read roadmap of each chapter.

New Organization

In consultation with more than 100 professors of cell biology from around the country, we have revised the table of contents to unite related material and mirror the organization of most courses. We also streamlined and focused coverage of many topics by reorganizing several chapters, enabling us to make room for the addition of new material. Each chapter has an up-to-date list of references of landmark studies and comprehensive review articles that direct students and instructors to much additional information.



Experimental Figure 9-30 Differentiation in culture of primary mouse satellite (myoblast) cells into muscle cells. [Courtesy of C. Emerson and J. Chen, Boston Biomedical Research Institute.]



Fertilized human egg cell showing male and female pronuclei. [Courtesy of The Lennart Nilson Award Board.]

New Chapters

The sixth edition of *Molecular Cell Biology* includes three new chapters:

- "The Molecular Cell Biology of Development" (Chapter 22) presents the fundamentals of development from fertilization through pattern formation, with increased focus on mammalian development.
- "Nerve Cells" (Chapter 23) provides unified coverage of the cell biology of these specialized cells, including the latest advances in axonal path finding and sensory reception.
- "Immunology" (Chapter 24) applies principles of molecular cell biology to the vertebrate immune system.

Medical Relevance

Many advances in basic cellular and molecular biology have led to new treatments for cancer and other significant human diseases. These medical examples are woven throughout the chapters where appropriate to give students an appreciation for the clinical applications of the basic science they are learning. Many of these applications hinge on a detailed understanding of multiprotein complexes in cells–complexes that catalyze cell movements, regulate DNA transcription, coordinate metabolism, and connect cells to other cells and to proteins and carbohydrates in their extracellular environment. A complete list of the medical examples in the sixth edition can be found overleaf.

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CLINICAL APPLICATIONS

 This icon signals the start of a clinical application in the text. Additional briefer clinical correlations appear in the text as appropriate:

MEDIA AND SUPPLEMENTS

For Students

Companion Web Site
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- **NEW: Podcasts** narrated by the authors give students a deeper understanding of key figures in the text and a sense of the thrill of discovery.

- **NEW:** Now available for your MP3 player or personal computer, more than 125 **animations and research videos** show the dynamic nature of key cellular processes and important experimental techniques. The animations were storyboarded by the textbook authors in conjunction with BioStudio, Inc., and programmed by Sumanas, Inc.

- **Classic Experiment** essays focus on classic groundbreaking experiments and explore the investigative process.

- **Online Quizzing** is provided, including multiple-choice and short answer questions.

Student Solutions Manual (ISBN:1-4292-0127-4), written by Brian Storrie, Eric A. Wong, Richard Walker, Glenda Gillaspy, and Jill Sible of Virginia Polytechnic Institute and State University and updated by Cindy Klevickis of James Madison University and Greg M. Kelly of the University of Western Ontario, contains complete worked-out solutions to all the end-of-chapter problems in the textbook.

NEW: eBook (ISBN: 1-4292-0955-0) New to the sixth edition, this customizable eBook fully integrates the complete contents of the text and its interactive media in a format that features a variety of helpful study tools, including full-text searching, note-taking, bookmarking, highlighting, and more. Easily accessible on any Internet-connected computer via a standard Web browser, the eBook enables students to take an active approach to their learning in an intuitive, easy-to-use format. Visit **http://ebooks.bfwpub.com** to learn more.

For Instructors

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All the student resources, plus:

- All figures and tables from the book in **jpeg and layered PowerPoint** formats, which instructors can edit or project section by section, allowing students to follow underlying concepts. Optimized for lecture-hall presentation, including enhanced colors, enlarged labels, and boldface type.

- **Test Bank** in editable Microsoft Word format now featuring *new and revised questions* for every chapter. The test bank is written by Brian Storrie of the University of Arkansas for Medical Sciences and Eric A. Wong, Richard Walker, Glenda Gillaspy, and Jill Sible of Virginia Polytechnic Institute and State University and revised by Cindy Klevickis of James Madison University and Greg M. Kelly of the University of Ontario.

- Additional **Analyze the Data** problems are available in PDF format.

- **NEW:** Lecture-ready **Personal Response System "clicker" questions** are available as Microsoft Word files and Microsoft PowerPoint slides.

Instructor's Resource CD-ROM (ISBN: 1-4292-0126-6) includes all the instructor's resources from the Web site, including all the illustrations from the text, animations, videos, test bank files, clicker questions, and the solutions manual files.

Overhead Transparency Set (ISBN: 1-4292-0477-X) contains 250 key illustrations from the text, optimized for lecture-hall presentation.

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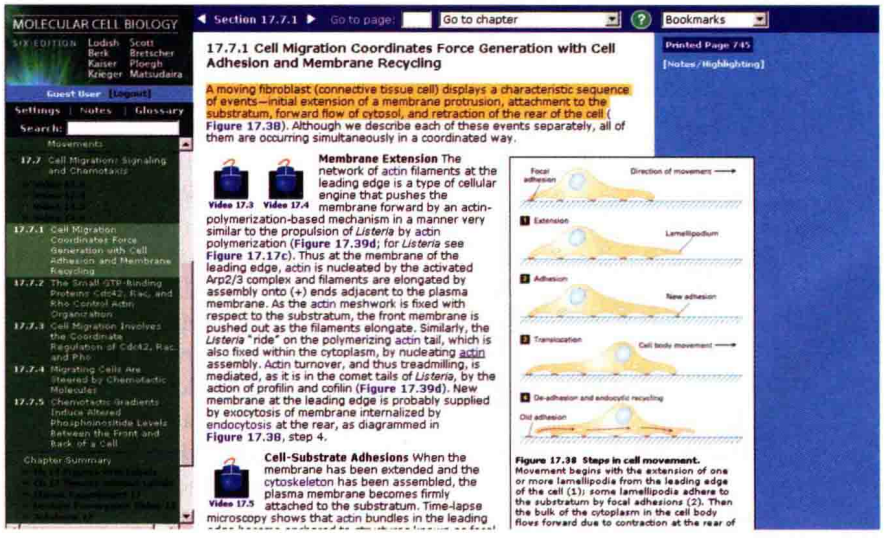

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