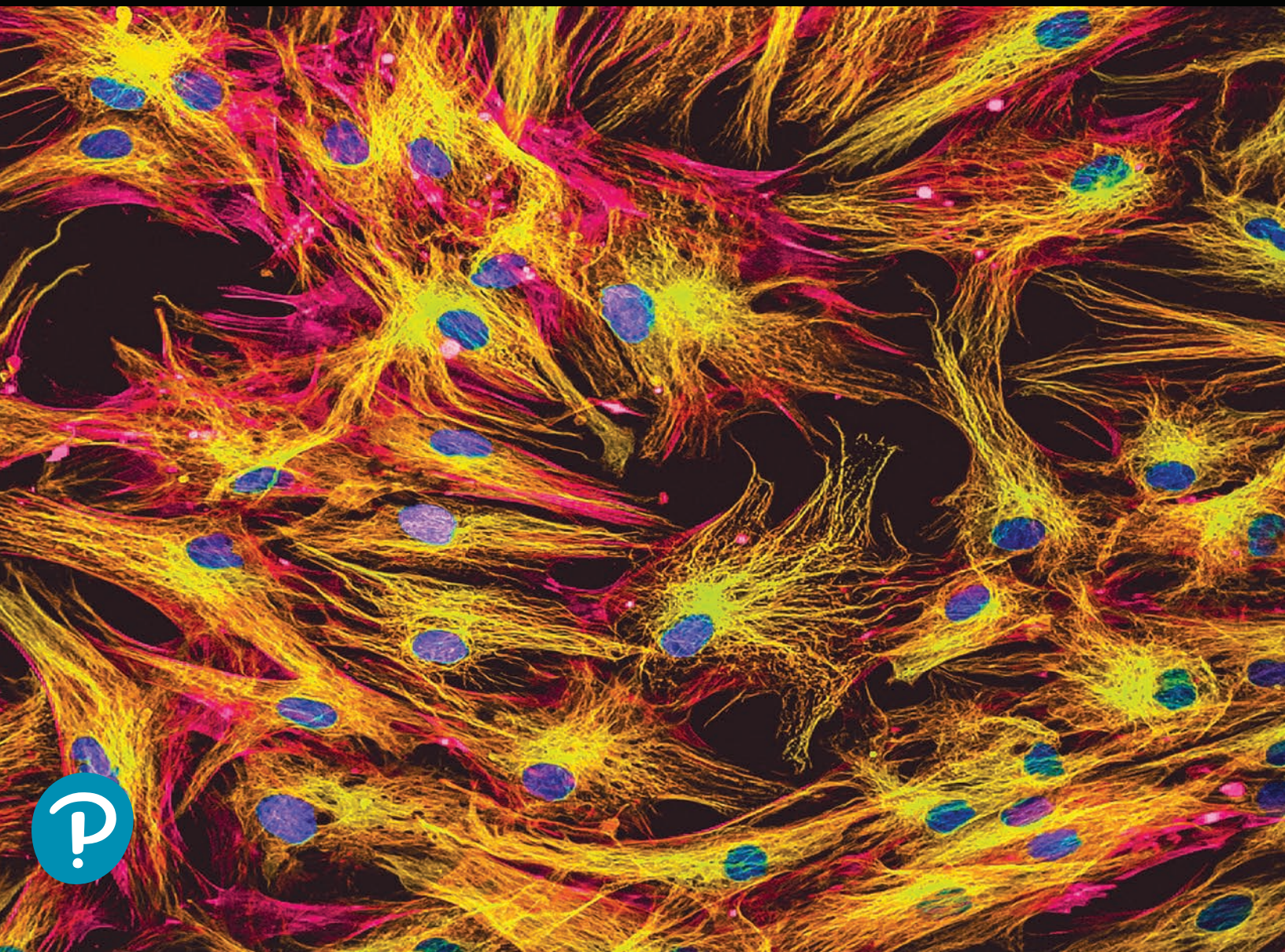
GLOBAL EDITION

Becker's WORLD OF THE CELL

TENTH EDITION

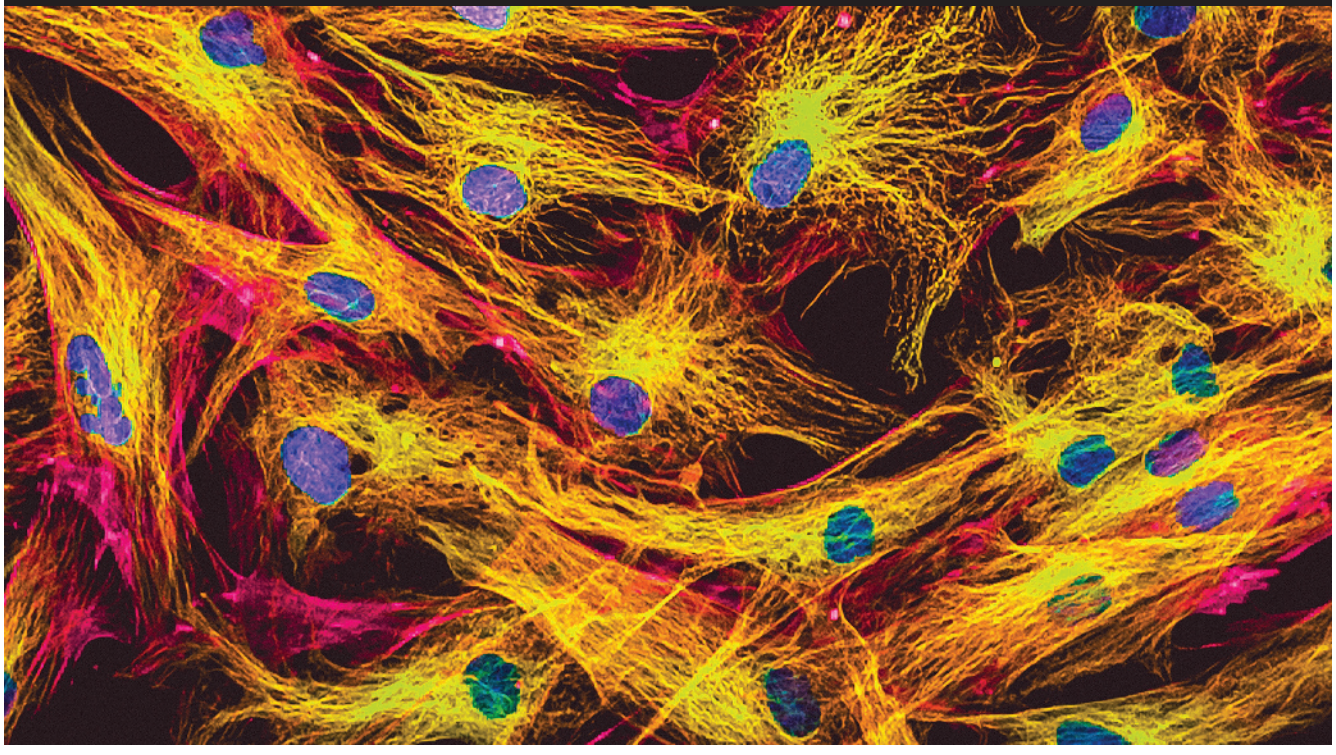
Jeff Hardin
James P. Lodolce



Becker's

10th Edition
Global Edition

WORLD OF THE CELL



JEFF HARDIN
University of Wisconsin–Madison

JAMES P. LODOLCE
Loyola University Chicago

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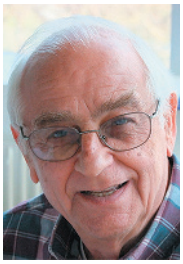
ABOUT THE AUTHORS

JEFF HARDIN received his Ph.D. in Biophysics from the University of California–Berkeley. He is the Raymond E. Keller Professor and Chair of the Department of Integrative Biology at the University of Wisconsin–Madison, where he has been since 1991. For 18 years he was Faculty Director of the Biology Core Curriculum, a four-semester honors biology sequence for undergraduates at Wisconsin known for its teaching innovations. Jeff's research focuses on how cells migrate and adhere to one another during early embryonic development. Jeff's teaching is enhanced by his extensive use of digital microscopy and his web-based teaching materials, which are used on many campuses in the United States and in other countries. Jeff was a founding member of the UW Teaching Academy, and has received several teaching awards, including a Lily Teaching Fellowship, a National Science Foundation Young Investigator Award, and a Chancellor's Distinguished Teaching Award.

JAMES P. LODOLCE earned his Ph.D. in Immunology from the University of Chicago in 2002. His thesis examined the signals that promote the survival of memory lymphocytes. As a postdoctoral fellow in the laboratory of Dr. David Boone, he studied the genetics and regulation of inflammation in autoimmunity. Cell biology was the first class that James taught when he arrived at Loyola University Chicago in 2010. He currently holds the title of Senior Lecturer and teaches a variety of courses ranging from molecular biology to virology. James is an active member of the Department of Biology and was appointed Co-Chairperson of Loyola's 2021 Pre-Health Professions Advisory Committee. In his career at Loyola, James has received several teaching honors, including a nomination for the 2014 Ignatius Loyola Award for Excellence in Teaching, the 2016 Master Teacher Award in the College of Arts and Sciences, and the 2020 Edwin T. and Vivijeanne F. Sujack Award for Teaching Excellence.



WAYNE M. BECKER taught cell biology at the University of Wisconsin–Madison for 30 years until his retirement. His interest in textbook writing grew out of notes, outlines, and problem sets that he assembled for his students, culminating in *Energy and the Living Cell,* a paperback text on bioenergetics published in 1977, and *The World of the Cell,* the first edition of which appeared in 1986. All his degrees are in biochemistry from the University of Wisconsin–Madison, an orientation that is readily discernible in his writing. His research interests were in plant molecular biology, focused on the expression of genes that encode enzymes of the photorespiratory pathway. Later in his career he focused on teaching, especially students from underrepresented groups. His honors include a Chancellor's Award for Distinguished Teaching, Guggenheim and Fulbright Fellowships, and a Visiting Scholar Award from the Royal Society of London. This text builds on his foundation and is inspired by his legacy.

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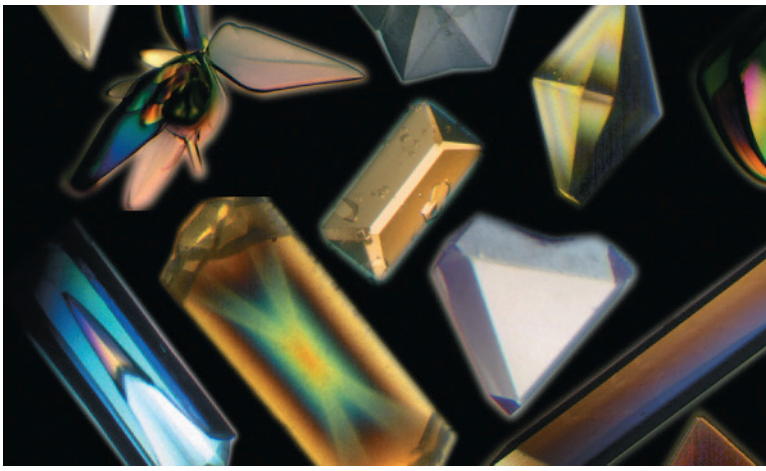

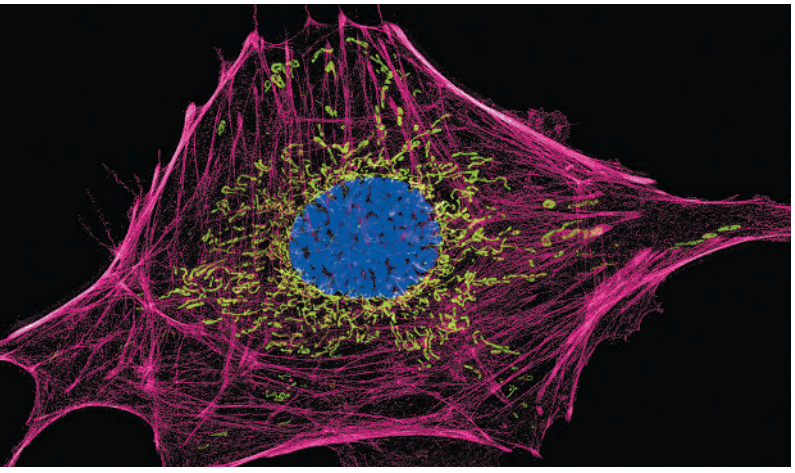

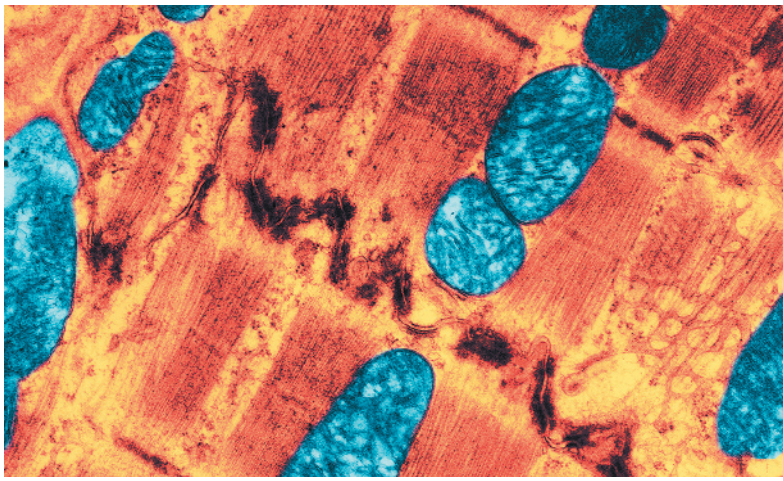

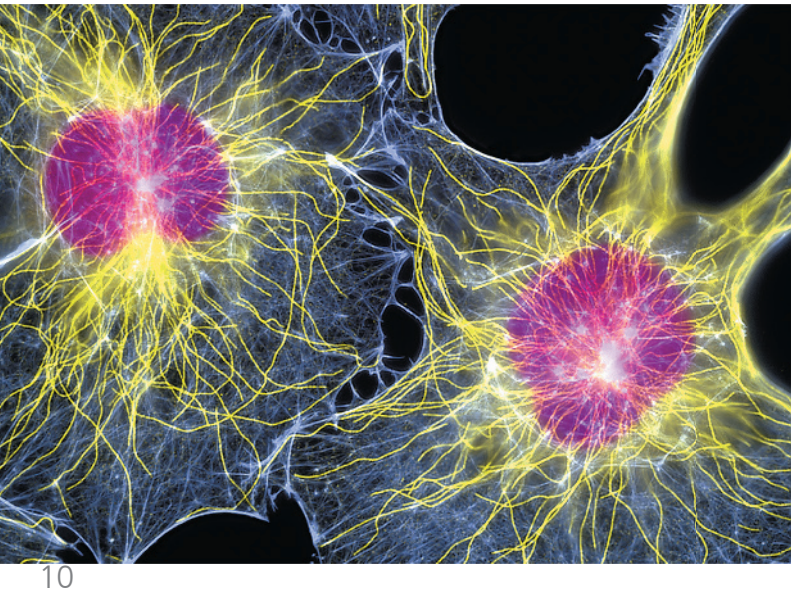

13 Cytoskeletal Systems *380*

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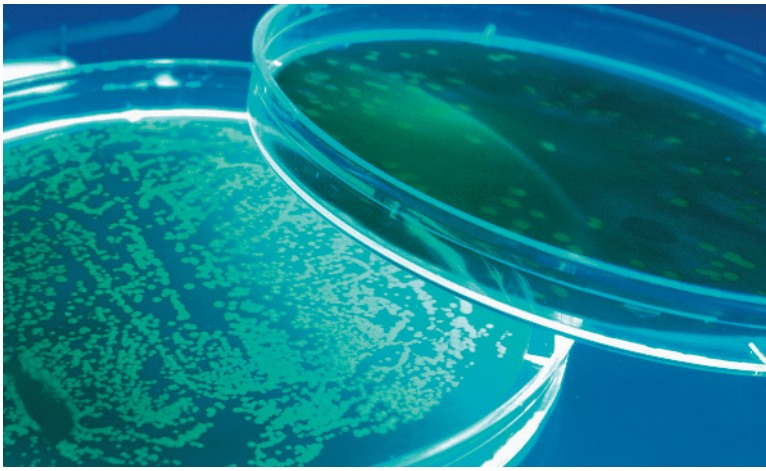
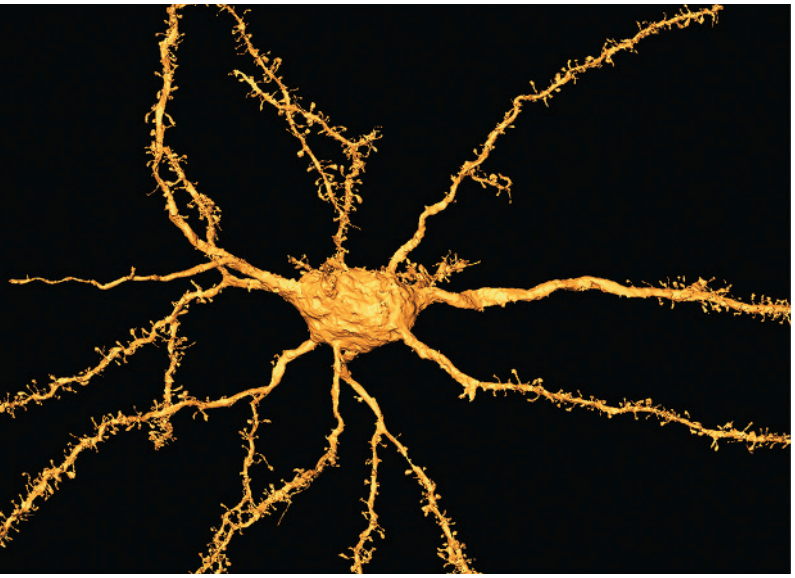
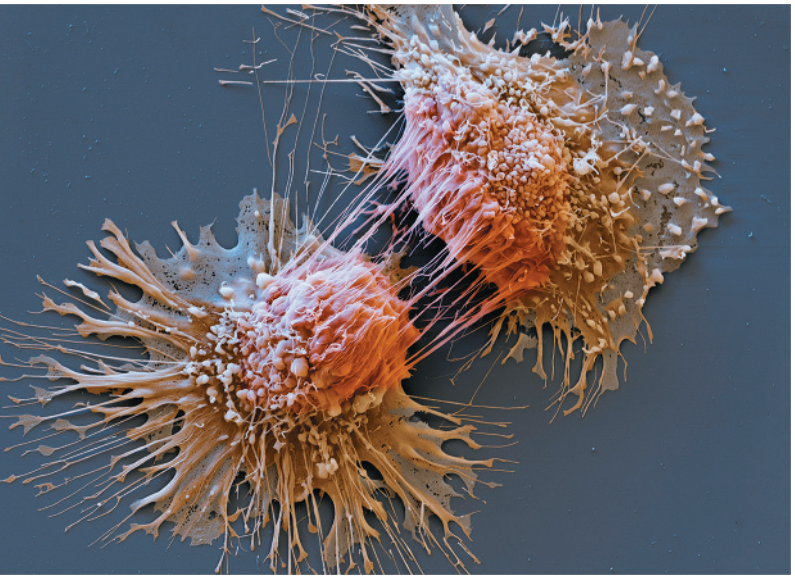






Cells are the fundamental building blocks of life on this planet. Despite their tiny size, they are wonders of intricacy. Moment by moment, the cells of our bodies are engaged in a dazzling repertoire of biochemical events, including signaling processes, transmission of genetic information, and delicately choreographed movements. Understanding the basic functions of cells also gives us insight when something goes wrong, as in the case of a disease, or when the cell is highjacked, as in the case of a viral infection. Helping our students to appreciate the complexities of this amazing cellular world lies at the heart of our goals as authors of *Becker's World of the Cell*. The motivations that drove our colleague, Wayne Becker, to write the first edition of this book continue to drive us today. We believe that our students should have biology textbooks that are clearly written, make the subject matter relevant, and help them to appreciate not only how much we already know about cell biology but also the exciting journey of continued discovery that lies ahead. We, as authors, have an extensive history of teaching undergraduate courses in cell biology and related areas, and we treasure our contact with students as one of the most rewarding aspects of being faculty members.

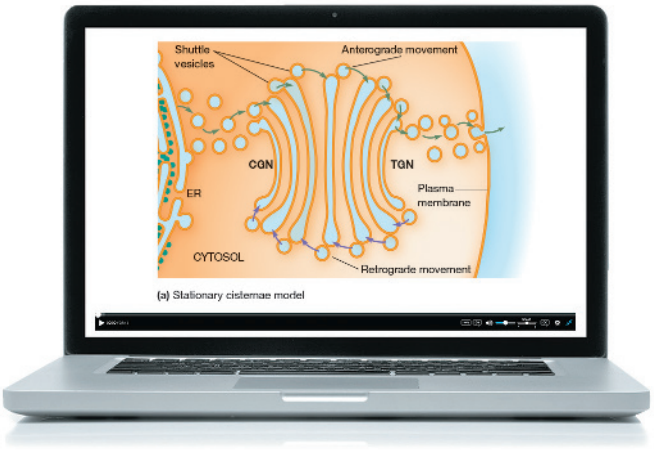
The amazing success of modern cell biology creates both exciting opportunities and central challenges in our teaching. How can we capture the core elements of modern cell biology in a way that draws our students in without overwhelming them? The enormous profusion of information challenges us to keep *Becker's World of the Cell* up to date while ensuring that it remains both manageable in length and readily comprehensible to students studying cell and molecular biology for the first time.

This tenth edition engages students with new innovative features in each chapter and an exciting, fresh look. In addition, a major goal of this edition has been to reorganize the presentation of several key topics. We hope that the often-requested consolidation of translation of secreted and plasma membrane-associated proteins with the larger discussion of the endomembrane system has led to an even more compelling presentation of these important topics. We also hope students and instructors will find that the continued emphasis on molecular biology throughout the tenth edition reinforces how indispensable these techniques are in the everyday work of modern cell biologists.

As with the previous editions, we remain committed to three central goals. First, our primary goal is to introduce students to the fundamental principles that guide cellular organization and function. Second, we want students to understand some of the key scientific evidence that has helped us formulate these central concepts. And third, we have sought to accomplish these goals in a book of manageable length that is easily read and understood by beginning cell biology students—and that still fits in their backpacks! We have therefore been necessarily selective both in the examples chosen to illustrate key concepts and in the quantity of scientific evidence included. The result is an update that we hope students and instructors will be as excited about as we are.

What's New in This Edition

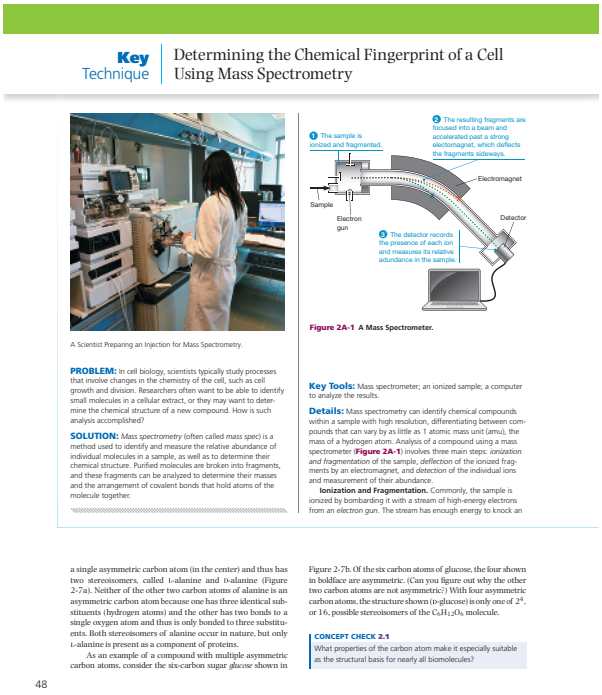
- **Make Connection questions:** Two new questions in every chapter ask students to make connections across concepts and chapters in the text. By reinforcing fundamental conceptual connections throughout cell biology, these features help overcome students' tendencies to compartmentalize information. These questions are also assignable and automatically graded in **Mastering Biology.**
- **Data Analysis questions:** Every chapter of *World of the Cell* now has a Data Analysis question for students to practice their ability to interpret data. Students must be able to analyze data in order to make informed decisions, generate well-formed, testable hypotheses, design follow-up experiments, and provide compelling evidence for results. These questions are also assignable and automatically graded in **Mastering Biology.**
- **Figure Walkthroughs:** In the *World of the Cell* e-text, Figure Walkthroughs guide students through key figures with narrated explanations and figure mark-ups that reinforce important points. All walkthroughs are also assignable in **Mastering Biology** and paired with several auto-gradable questions for student assessment.



- **Reorganization of material on translation and intracellular trafficking:** Because the molecular genetics material comes earlier in the book, topics that relate to translation of secreted and plasma membrane-associated proteins are now more naturally integrated into the discussion of intracellular trafficking. These topics are now combined in Chapter 12, which focuses on the endomembrane system, including cotranslational import into the endoplasmic reticulum of proteins destined for secretion or insertion into the plasma membrane.

Hallmark Features

- **Key Technique boxes in every chapter:** Twenty-six Key Technique boxes are integrated throughout the text, demonstrating how cutting-edge technologies can be used to answer key questions in cell biology.



Key Technique | Determining the Chemical Fingerprint of a Cell Using Mass Spectrometry

A Scientist Preparing an Injection for Mass Spectrometry.

PROBLEM: In cell biology, scientists typically study processes that involve changes in the chemistry of the cell, such as cell growth and division. Researchers often want to be able to identify small molecules in a cellular extract, or they may want to determine the chemical structure of a new compound. How is such analysis accomplished?

SOLUTION: *Mass spectrometry* (often called *mass spec*) is a method used to identify and measure the relative abundance of individual molecules in a sample, as well as to determine their chemical structure. Purified molecules are broken into fragments, and these fragments can be analyzed to determine their masses and the arrangement of covalent bonds that hold atoms of the molecule together.

Figure 2A-1 A Mass Spectrometer.

Key Tools: Mass spectrometer; an ionized sample; a computer to analyze the results.

Details: Mass spectrometry can identify chemical compounds within a sample with high resolution, differentiating between compounds that can vary by as little as 1 atomic mass unit (amu), the mass of a hydrogen atom. Analysis of a compound using a mass spectrometer (**Figure 2A-1**) involves three main steps: *ionization and fragmentation* of the sample, *deflection* of the ionized fragments by an electromagnet, and *detection* of the individual ions and measurement of their abundance.

Ionization and Fragmentation. Commonly, the sample is ionized by bombarding it with a stream of high-energy electrons from an electron gun. The stream has enough energy to knock an

a single asymmetric carbon atom (in the center) and thus has two stereoisomers, called L-alanine and D-alanine (Figure 2-7a). Neither of the other two carbon atoms of alanine is an asymmetric carbon atom because one has three identical substituents (hydrogen atoms) and the other has two bonds to a single oxygen atom and thus is only bonded to three substituents. Both stereoisomers of alanine occur in nature, but only L-alanine is present as a component of proteins.

As an example of a compound with multiple asymmetric carbon atoms, consider the six-carbon sugar *glucose* shown in Figure 2-7b. Of the six carbon atoms of glucose, the four shown in boldface are asymmetric. (Can you figure out why the other two carbon atoms are not asymmetric?) With four asymmetric carbon atoms, the structure shown (D-glucose) is only one of 2^4, or 16, possible stereoisomers of the $C_6H_{12}O_6$ molecule.

CONCEPT CHECK 2.1
What properties of the carbon atom make it especially suitable as the structural basis for nearly all biomolecules?

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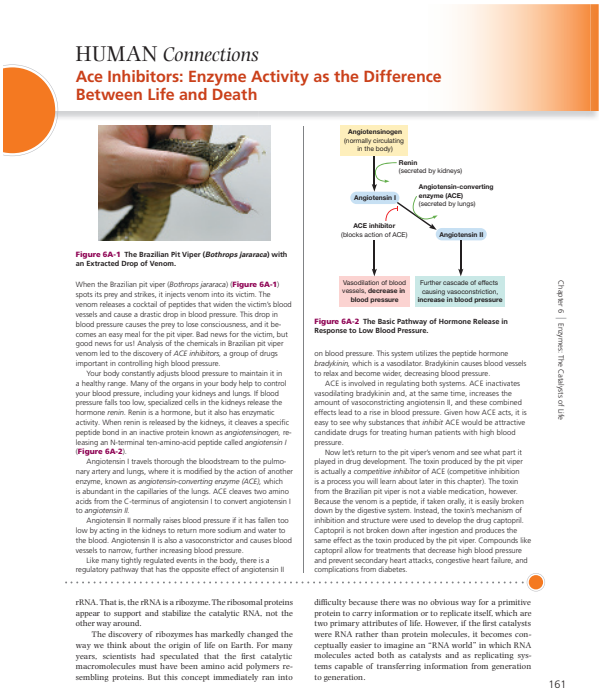
- **Human Connections boxes in every chapter:** Twenty-six Human Connections boxes emphasize the relevance of cell biology to human health and society, from the story of Henrietta Lacks and the HeLa cell line to the relevance of biochemical pathways to our diet, to the many cases in which cell biology helps us diagnose and treat human disease.



HUMAN *Connections*
Ace Inhibitors: Enzyme Activity as the Difference Between Life and Death

Figure 6A-1 The Brazilian Pit Viper (*Bothrops jararaca*) with an Extracted Drop of Venom.

When the Brazilian pit viper (*Bothrops jararaca*) (**Figure 6A-1**) spots its prey and strikes, it injects venom into its victim. The venom releases a cocktail of peptides that widen the victim's blood vessels and cause a drastic drop in blood pressure. This drop in blood pressure causes the prey to lose consciousness, and it becomes an easy meal for the pit viper. Bad news for the victim, but good news for us! Analysis of the chemicals in Brazilian pit viper venom led to the discovery of *ACE inhibitors*, a group of drugs important in controlling high blood pressure.

Your body constantly adjusts blood pressure to maintain it in a healthy range. Many of the organs in your body help to control your blood pressure, including your kidneys and lungs. If blood pressure falls too low, specialized cells in the kidneys release the hormone *renin*. Renin is a hormone, but it also has enzymatic activity. When renin is released by the kidneys, it cleaves a specific peptide bond in an inactive protein known as *angiotensinogen*, releasing an N-terminal ten-amino-acid peptide *called angiotensin I* (**Figure 6A-2**).

Angiotensin I travels thorough the bloodstream to the pulmonary artery and lungs, where it is modified by the action of another enzyme, known as *angiotensin-converting enzyme (ACE)*, which is abundant in the capillaries of the lungs. ACE cleaves two amino acids from the C-terminus of angiotensin I to convert angiotensin I to *angiotensin II*.

Angiotensin II normally raises blood pressure if it has fallen too low by acting in the kidneys to return more sodium and water to the blood. Angiotensin II is also a vasoconstrictor and causes blood vessels to narrow, further increasing blood pressure.

Like many tightly regulated events in the body, there is a regulatory pathway that has the opposite effect of angiotensin II

Figure 6A-2 The Basic Pathway of Hormone Release in Response to Low Blood Pressure.

on blood pressure. This system utilizes the peptide hormone *bradykinin*, which is a vasodilator. Bradykinin causes blood vessels to relax and become wider, decreasing blood pressure.

ACE is involved in regulating both systems. ACE inactivates vasodilating bradykinin and, at the same time, increases the amount of vasoconstricting angiotensin II, and these combined effects lead to a rise in blood pressure. Given how ACE acts, it is easy to see why substances that *inhibit* ACE would be attractive candidate drugs for treating human patients with high blood pressure.

Now let's return to the pit viper's venom and see what part it played in drug development. The toxin produced by the pit viper is actually a *competitive inhibitor* of ACE (competitive inhibition is a process you will learn about later in this chapter). The toxin from the Brazilian pit viper is not a viable medication, however. Because the venom is a peptide, if taken orally, it is easily broken down by the digestive system. Instead, the toxin's mechanism of inhibition and structure were used to develop the drug captopril. Captopril is not broken down after ingestion and produces the same effect as the toxin produced by the pit viper. Compounds like captopril allow for treatments that decrease high blood pressure and prevent secondary heart attacks, congestive heart failure, and complications from diabetes.

rRNA. That is, the rRNA is a ribozyme. The ribosomal proteins appear to support and stabilize the catalytic RNA, not the other way around.

The discovery of ribozymes has markedly changed the way we think about the origin of life on Earth. For many years, scientists had speculated that the first catalytic macromolecules must have been amino acid polymers resembling proteins. But this concept immediately ran into difficulty because there was no obvious way for a primitive protein to carry information or to replicate itself, which are two primary attributes of life. However, if the first catalysts were RNA rather than protein molecules, it becomes conceptually easier to imagine an "RNA world" in which RNA molecules acted both as catalysts and as replicating systems capable of transferring information from generation to generation.

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- **Concept Check questions:** Each main section of a chapter ends with a Concept Check question. These questions provide students with numerous opportunities to assess their understanding as they read. Answers to these questions are available at the back of the book.
- **Quantitative questions in every end-of-chapter Problem Set:** New and existing quantitative questions are flagged at the end of each chapter to encourage students to work on developing their ability to perform calculations or to interpret quantitative information. Most of these questions are assignable through **Mastering Biology.**
- **Content updates:** Updated information highlighting the most recent advances in cell and molecular biology has been added throughout the book (see Content Highlights of the Tenth Edition).

Mastering Biology is an innovative online homework, tutorial, and assessment system that delivers self-paced tutorials with individualized coaching, hints, and feedback. The Mastering system helps instructors and students with customizable, easy-to-assign, and automatically graded assignments.

Integrated links in every chapter of the textbook point students to a variety of interactive online materials, including the following:

- 52 assignable Make Connection questions help students make connections across chapters and concepts
- 10 figure walkthrough tutorials walk students through key figures and then assess their understanding
- More than 100 tutorials and activities that teach complex cell processes
- More than 100 molecular and microscopy videos, which provide vivid images of cellular processes
- 240 Reading Quiz questions, which encourage students to read before class
- Many end-of-chapter questions and problems that are assignable and automatically gradable
- Test Bank questions for every chapter
- The e-text, also available through **Mastering Biology**, which provides both access to the complete textbook and powerful interactive and customizable functions
- A suite of Instructor Resources, including PowerPoint lecture outlines containing all the figures and photos and five to ten personal response system (PRS) clicker questions per chapter
- Learning Catalytics is a "bring your own device" assessment and active classroom system that expands the possibilities for student engagement beyond standard clickers where instructors can deliver a wide range of auto-gradable or open-ended questions that test content knowledge and build critical thinking skills

Content Highlights of the Tenth Edition

Updated material and new information have been added throughout the book in both the text and art. Major topics that have been altered, updated, or added include the following:

Chapter 1: Created new Figure 1-1 (Hooke's microscope and drawing of cork). Added CRISPR genome editing to Figure 1-3 and added a new subsection on CRISPR to Section 1.2. Condensed the three microscopy subsections (The Light Microscope, Specialized Light Microscopes, and The Electron Microscope) into one large subsection subtitled "Microscopy." Modified Figure 1-8 to better illustrate the central dogma in a cell. Added a new Data Analysis question.

Chapter 2: Added reference to organic carbon discoveries made by Mars rover to Section 2.1 and the importance of water transport to Section 2.2. Added new subsection on prion self-assembly to Section 2.5. Added a new Data Analysis question.

Chapter 3: Added reference to gecko pad and van der Waals interactions. Added information about the Folding @ Home initiative. Added subsection on chaperones in protein folding to Section 3.1. Added a new figure to the Human Connections box on Tau tangle formation. Added a new Data Analysis question.

Chapter 4: Significantly updated the discussion of the endosymbiont theory, including discussion of "inside-out" and "outside-in" proposals in a largely revised figure. Moved three domains of life discussion and figure from 9e Ch. 21 to Ch. 4.

Chapter 5: Added a new Data Analysis question; updated Figure 5-1 to add improved concentration work diagram.

Chapter 6: Majorly revised Figure 6-11 and relevant text to conform to the majority of advanced biochemistry texts regarding inhibitors. Removed sucrase discussion to comport with deletion of the relevant figure in the previous edition and generated a new figure showing the catalytic site of lysozyme accordingly. Shortened the discussion of ACE inhibitors in the Human Connections box. Replaced one Problem Set question on biological relevance with another graphical analysis problem on competitive inhibitors.

Chapter 7: Moved SDS-PAGE material to Ch. 21. Reduced treatment of lipid rafts to reflect ongoing controversy in the field. Added a new Key Technique box on fluorescence recovery after photobleaching (FRAP). Added a Human Connections box, adapted from 9e Ch. 12. Reinstated a more detailed structure diagram in Figure 7-6.

Chapter 8: Improved clarity of Figure 8-7. Added panel to Figure 8-10 to show frog oocytes. Added a new Data Analysis question.

Chapter 9: Shortened discussion of other uses of glycolytic enzymes. Improved several biochemical pathway diagrams for clarity.

Chapter 10: Revised the discussion of ATP yield in aerobic respiration while retaining the theoretical yield discussion as a *via media*. Substantially revised electron transport details in several figures. Substantially revised and improved Q cycle discussion and the relevant figure. Trimmed discussion and figure coverage of cristae and added a light micrograph showing mitochondria. Integrated TIM/TOM discussion into this chapter, moving it out of 9e Ch. 19 to join the discussion of the structure of mitochondria. Added figure on location of ATP synthesis in bacteria to compare to mitochondria. Replaced problem on thermogenin with Data Analysis question.

Chapter 11: Added information and figure about carboxysomes in cyanobacteria. Improved the molecular model presentation of light-harvesting complexes. Improved the treatment of electron flow in the chloroplast, including improving and shortening the discussion of the Q cycle. Updated information on protons per ATP. Improved depiction of the glycolate pathway and C_3/C_4 plant leaf anatomy. Added Quantitative and Data Analysis questions.

Chapter 12: Added an update on the types of models used to explain movement through the Golgi. Provided some rationale for grouping peroxisomes into the endomembrane system. Moved protein trafficking/sorting sections from 9E Ch. 19 to here. Added paragraph on how viruses can co-opt endosomes for infection. Combined 9e Sections 12.7 and 12.8 into one section (since the plant vacuole is a digestive compartment). Authored new Human Connections box on the role of autophagy in human disease.

Chapter 13: Updated *MreB* discussion to match current understanding of MreB function. Changed microtubule figures to show curved protofilaments at plus ends as per recent TEM work. Updated discussion of MT minus-end binding proteins; added information on augmin and branched MTs. Added info on CRWN proteins in higher plants to the IF section.

Chapter 14: Made minor changes to Figure 14A-2. Added a new Data Analysis question.

Chapter 15: Added brief mention of mechanotransduction via α-catenin. Added a new Data Analysis question.

Chapter 16: Added a purines/pyrimidine column in Table 16-1 on Chargaff's rules. Added detail on new studies on how histone H1 interacts with the nucleosome. Included an introduction to epigenetics in the section on chromatin remodeling. Mentioned how mRNA modifications are important in nuclear export of mRNA. Added possibility of NMCPs functioning as lamins in plant cells. Mentioned telomere dysfunction as a potential cause of premature aging in HGPS. Added detail about how charges in the histone tails affect DNA packaging. Moved section and figure on retroviruses from 9e Ch. 18 into this chapter.

Chapter 17: Added oxidation damage to Section 17.2. Authored a new Key Technique box on CRISPR genome modification. Updated the mutagenic mechanism of BrdU. Added a description of heteroduplex DNA to the homologous recombination section. Added a note on most likely mechanism of strand discrimination in eukaryotic mismatch repair. Updated nucleotide excision repair figure with more recent mechanism (Figure 17-27). Added quote from Francis Crick about the importance of DNA repair. Moved section and figure on retrotransposons from 9e Ch. 18 into this chapter. Added a new Data Analysis question.

Chapter 18: Improved the flow and organization of the chapter by moving discussion/figure about retroviruses to Ch. 16, moving retrotransposon discussion/figure to Ch. 17, and moving genetic code discussion/figures to Ch. 19. Authored a new Human Connections box on death cap mushrooms. Modified figure on the central dogma to include advances since Francis Crick's first proposal. Authored a new Concept Check question for Section 18.1. Added a note on the discovery of ribozymes, a subsection on mature mRNA nuclear export to Section 18.3, and a new Data Analysis question.

Chapter 19: Significantly reorganized the chapter flow by moving genetic code section from 9e Ch. 18 into new Section 19.1 and moving 9e Section 19.5 on protein targeting and sorting into Ch. 12. Added a new subsection on codon usage bias to Section 19.1.

Chapter 20: Added reference to temperature-sensitive riboswitches in Section 20.1, a paragraph on histone modifications to epigenetics in Section 20.2, and a new Data Analysis question.

Chapter 21: Moved 9e Figure 21-13 (tree of life) to Ch. 4 (new Figure 4-3) and the Key Technique box from 9e Ch. 17 (PCR) into this chapter. Worked the 9e Key Technique box from this chapter (DNA cloning) into the text in Section 21.1. Updated Southern blotting and Western blotting techniques for modern approach of not using film. Reorganized the techniques in Section 21.1 in a more logical way and moved all sequencing techniques into Section 21.2. Updated the description of next-generation and third-generation sequencing techniques to include state of the art in the field. Added a new subsection on quantitative PCR (qPCR). Expanded RNA-seq with details on single-cell RNAseq. Added description of conditional knockout mice engineering.

Chapter 22: Added a Make Connections question on *shibire* mutants in *Drosophila* that was needed in the synaptic transmission section.

Chapter 23: Changed title of Section 23.3 from Protein Kinase-Associated Receptors to Enzyme-Coupled Receptors. Added a subsection to the end of this section on other enzyme-coupled receptors (phosphatase receptor and guanylyl receptor families).

Chapter 24: Updated some sections with more modern treatment at the molecular level, including kinetochore (including revised Figure 24-4), chromosomal congression, FtsZ/divisome in bacteria, and spindle assembly checkpoint. Altered Figure 24-25 (9e 24-23) to improve clarity and moved to a later position.

Chapter 25: Added a paragraph on the potential role of the double-strand break repair model of homologous recombination in meiotic recombination in Section 25.6.

Chapter 26: Updated smoking statistics in Figure 26-7a through 2015 and added gender-specific data. Improved HPV figure (Figure 26-17). Changed emphasis to reflect replication/repair errors as a major cause of cancer, including discussion of the recent work by the Vogelstein group. Updated hallmarks of cancer discussion to correspond to the revised Weinberg paper from 2011. Added more detail in the immunotherapy section on Nobel Prize-winning work and CAR T cells, including a new small figure on CAR T cells. Added detail on Cdk4/6 therapy in the Key Technique box.

Appendix: Added explicit mention of GCaMP proteins in the calcium imaging section. Added a discussion of serial blockface SEM. Updated the cryoEM example image.

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 numbered *concept statement heading,* which summarizes the material and helps students focus on the main points to study and review.
   - Chapters are written and organized to allow instructors to assign chapters and chapter sections in different sequences, making the book adaptable to a wide variety of course plans.
   - Each chapter ends with a bulleted *Summary of Key Points* that briefly describes the main points covered in each section of the chapter.
2. **The illustrations teach concepts at an appropriate level of detail.**
   - Many of the more complex figures incorporate *mini-captions* to help students grasp concepts more quickly by drawing their focus to 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 showing key cellular structures are accompanied by scale 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.

- *Italic type* is used to identify additional technical terms that are less important than boldfaced terms but significant in their own right. Occasionally, italics is also used to highlight important phrases or sentences.
- The Glossary includes definitions and page references for all boldfaced 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. These include highlighted questions that involve quantitative analysis and data analysis. Many are class-tested, having been selected from problem sets and exams we have used in our own courses.

Supplementary Learning Aids

Instructor Resources Area for *Becker's World of the Cell* (See Instructor Resource Area of Mastering Biology)

- PowerPoint lecture tools, including lecture outlines containing all of the figures, photos, and embedded animations, with five to ten personal response system clicker questions per chapter.
- JPEG images of all textbook figures and photos.
- Videos and animations of key concepts, organized by chapter for ease of use in the classroom.

Test Bank for *Becker's World of the Cell* (See Instructor Resource Area of Mastering Biology)

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

Solutions Manual for *Becker's World of the Cell* (See Instructor Resource Area of Mastering Biology)

Written by the authors, this manual includes complete, detailed answers for all of the end-of-chapter problems.

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 here.

Chapters 1–3, 12, 16–21, 23, 25: James P. Lodolce
Department of Biology
Loyola University Chicago
1032 W. Sheridan Rd.
Chicago, IL 60660
e-mail: jlodolce@luc.edu

Chapters 4–11, 13–15, 22, 24, 26, Appendix, and Glossary: Jeff Hardin
Department of Integrative Biology
University of Wisconsin–Madison
Madison, WI 53706
e-mail: jdhardin@wisc.edu

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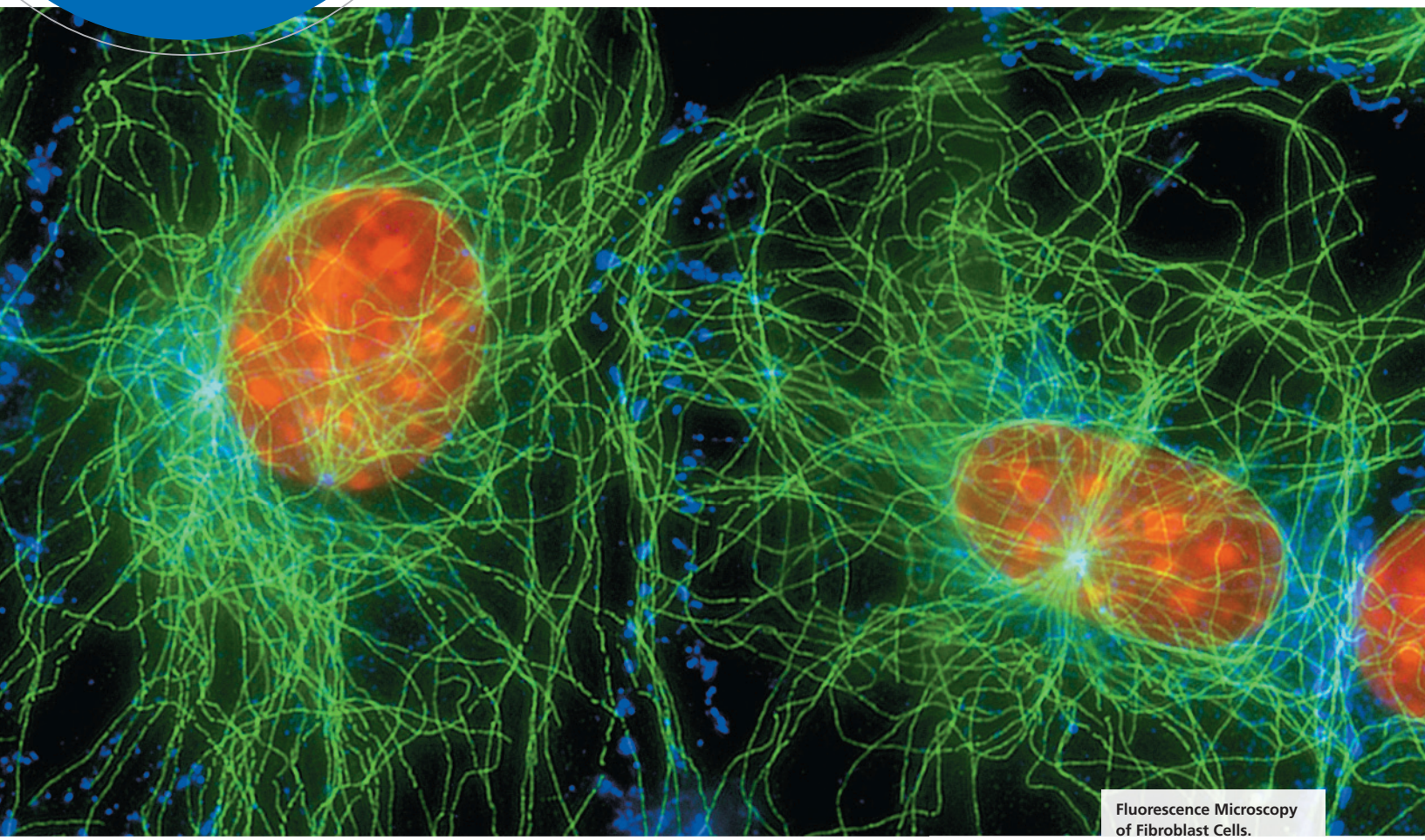
Contributors

Fabrice Caudron, Queen Mary University of London
Håkan Eriksson, Malmo University
Kathryn Ford, University of Bristol
Wendy Ying Ying Liu, Quest International University Perak
Shefali Sabharanjak
Nihal Terzi Çizmecioğlu, Middle East Technical University
Christiane Van den Branden, Vrije Universiteit Brussel

Reviewers

Umut Fahrioğlu, Near East University
Mohammad Farooq, King Saud University
Chris Finlay, University of Glasgow
Juan-Pablo Labrador, Trinity College Dublin
Kiran Paul
Asha Sharma
Christiane Van den Branden, Vrije Universiteit Brussel

1 A Preview of Cell Biology



Fluorescence Microscopy of Fibroblast Cells. This image shows fluorescently labeled cell nuclei (red), microtubules (green), and cell-cell contacts (blue).

The **cell** is the basic unit of biology. Every organism either consists of cells or is itself a single cell. Therefore, it is only by understanding the structure and function of cells that we can appreciate both the capabilities and the limitations of living organisms, whether they are animals, plants, fungi, or microorganisms.

The field of cell biology is rapidly changing as scientists from a variety of related disciplines work together to gain a better understanding of how cells are constructed and how they carry out all the intricate functions necessary for life. Particularly significant is the dynamic nature of the cell. Cells are constantly changing; they have the capacity to grow, reproduce, and become specialized. In addition, once specialized, they have the ability to respond to stimuli and adapt to changes in the environment. The convergence of cytology, genetics, and biochemistry has made modern cell biology one of the most exciting and dynamic disciplines in all of biology. Nowhere is this excitement more evident than in the recent advances being made in our ability to modify genomes. If this text helps you appreciate the marvels and diversity of cellular

functions and allows you to experience the excitement of discovery, then one of our main goals in writing this book for you will have been met.

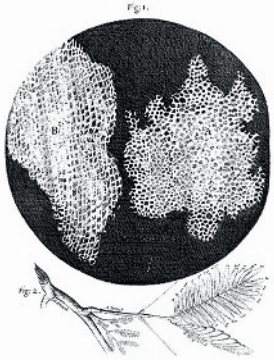
In this introductory chapter, we will look briefly at the origin of cell biology as a discipline. Then we will consider the three main historical strands of cytology, genetics, and biochemistry that have formed our current understanding of what cells are and how they work. The chapter concludes with a brief discussion of the nature of scientific knowledge itself by considering biological facts, the scientific method, experimental design, and the use of some common model organisms to answer important questions in modern cell biology.

1.1 The Cell Theory: A Brief History

The story of cell biology started to unfold more than 300 years ago, as European scientists began to focus their crude microscopes on a variety of biological material ranging from tree bark to bacteria to human sperm. One such scientist was Robert Hooke, Curator of Instruments for the Royal Society of London. In 1665, Hooke built a microscope and examined thin slices of cork (**Figure 1-1**). He observed and sketched a network of tiny boxlike compartments that reminded him of a honeycomb and called these little compartments *cells,* from the Latin word *cellula,* meaning "little room."

What Hooke observed were not cells at all. Those empty boxlike compartments were formed by the cell walls of dead plant tissue, which is what cork is. However, Hooke would not have thought of these cells as dead because he did not understand that they could be alive. Although he noticed that cells in other plant tissues were filled with what he called "juices," he concentrated instead on the more prominent cell walls of the dead cork cells that he had first encountered.

(a) Hooke's microscope



(b) Hooke's drawing of cork

Figure 1-1 The Birth of Microscopy. (a) Pictured is a reconstruction of Robert Hooke's original microscope, which he used to observe cork. **(b)** Hooke then sketched his observations.

Advances in Microscopy Allowed Detailed Studies of Cells

Hooke's observations were limited by the *magnification power* of his microscope, which enlarged objects to only 30 times (30×) their normal size. This made it difficult to learn much about the internal organization of cells. A few years later, Antonie van Leeuwenhoek, a Dutch textile merchant, produced small lenses that could magnify objects to almost 300 times (300×) their size. Using these superior lenses, van Leeuwenhoek became the first to observe living cells, including blood cells, sperm cells, bacteria, and single-celled organisms (algae and protozoa) found in pond water. He reported his observations to the Royal Society of London in a series of letters during the late 1600s. His detailed reports attest to both the high quality of his lenses and his keen powers of observation.

Two factors restricted further understanding of the nature of cells. First, the microscopes of the day had limited *resolution (resolving power)*—the ability to see fine details of structure. Even van Leeuwenhoek's superior instruments could push this limit only so far. The second factor was the descriptive nature of seventeenth-century biology. It was an age of observation, with little thought given to explaining the intriguing architectural details being discovered in biological materials.

More than a century passed before the combination of improved microscopes and more experimentally minded microscopists resulted in a series of developments that led to an understanding of the importance of cells in biological organization. By the 1830s, important optical improvements were made in lens quality and in the *compound microscope,* an instrument in which one lens (the eyepiece) magnifies the image created by a second lens (the objective). This allowed both higher magnification and better resolution. At that point, structures only 1 micrometer (μm) in size could be seen clearly.

The Cell Theory Applies to All Organisms

Aided by such improved lenses, the Scottish botanist Robert Brown found that every plant cell he looked at contained a rounded structure, which he called a *nucleus,* a term derived from the Latin word for "kernel." In 1838, his German colleague Matthias Schleiden came to the important conclusion that all plant tissues are composed of cells and that an embryonic plant always arises from a single cell. A year later, German cytologist Theodor Schwann reported similar conclusions concerning animal tissue, thereby discrediting earlier speculations that plants and animals do not resemble each other structurally. These speculations arose because plant cell walls form conspicuous boundaries between cells that are readily visible even with a crude microscope, whereas individual animal cells, which lack cell walls, are much harder to distinguish in a tissue sample. However, when Schwann examined animal cartilage cells, he saw that they were unlike most other animal cells because they have boundaries that are well defined by thick deposits of collagen fibers. Thus, he became convinced of the fundamental similarity between plant and animal tissue. Based on his astute observations, Schwann

developed a single unified theory of cellular organization. This theory has stood the test of time and continues to be the basis for our own understanding of the importance of cells and cell biology. (The recent discovery of certain giant viruses has led some to speculate that this definition may someday be expanded.)

As originally postulated by Schwann in 1839, the **cell theory** had two basic principles:

1. All organisms consist of one or more cells.
2. The cell is the basic unit of structure for all organisms.

Less than 20 years later, a third principle was added. This grew out of Brown's original description of nuclei, which Swiss botanist Karl Nägeli extended to include observations on the nature of cell division. By 1855 Rudolf Virchow, a German physiologist, concluded that cells arose only by the division of other, preexisting cells. Virchow encapsulated this conclusion in the now-famous Latin phrase *omnis cellula e cellula,* which in translation becomes the third principle of the modern cell theory:

3. All cells arise only from preexisting cells.

Thus, the cell is not only the basic unit of structure for all organisms but also the basic unit of reproduction. No wonder, then, that we must understand cells and their properties to appreciate all other aspects of biology. Because many of you have seen examples of "typical" cells in textbooks that may give the false impression that there are relatively few different types of cells, let's take a look at a few examples of the diversity of cells that exist in our world (**Figure 1-2**).

Cells exist in a wide variety of shapes and sizes, ranging from filamentous fungal cells to spiral-shaped *Treponema* bacteria to the differently shaped cells of the human blood system (Figure 1-2a–c). Other cells have much more exotic shapes,

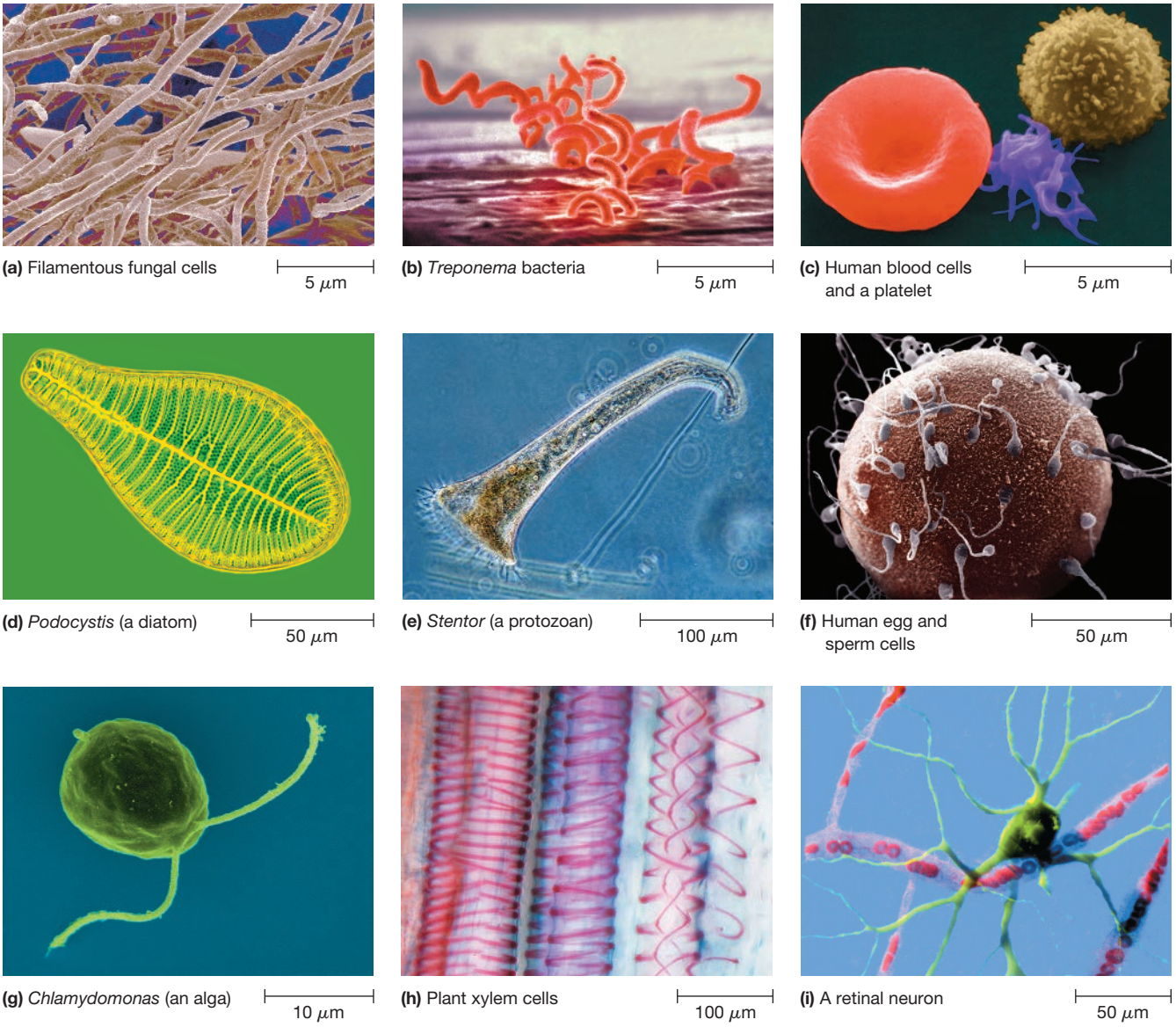


Figure 1-2 The Cells of the World. The diversity of cell types existing all around us includes the examples shown in this figure and thousands upon thousands more.

such as the diatom and the protozoan shown in Figure 1-2d and 1-2e. Note how the two human single-celled gametes, the egg and the sperm, differ greatly in size and shape (Figure 1-2f). As in leaves, the green chlorophyll in a *Chlamydomonas* cell shows that these algae carry out photosynthesis (Figure 1-2g). Often, a cell's shape and structure give clues about its function. For example, the spiral thickenings in the cell walls of plant xylem tissue give strength to these water-conducting vessels in wood (Figure 1-2h), and the highly branched cells of a human neuron allow it to interact with numerous other neurons (Figure 1-2i). In our studies throughout this textbook, we will see many other interesting examples of diversity in cell structure and function. First, though, let's examine the historical roots leading to the development of contemporary cell biology.

CONCEPT CHECK 1.1

What evidence led scientists to develop the basic principles of the cell theory? Note how technology played a role in its development.

1.2 The Emergence of Modern Cell Biology

Modern cell biology results from the weaving together of three different strands of biological inquiry—cytology, biochemistry, and genetics—into a single cord. As the timeline in **Figure 1-3** illustrates, each of the strands had its own historical origins, and each one makes unique and significant contributions to modern cell biology. Contemporary cell biologists must be adequately informed about all three strands, regardless of their own immediate interests.

Historically, the first of the strands to emerge was **cytology**, which is concerned primarily with cellular structure. In biological studies, you will often encounter words containing the Greek prefix *cyto–* or the suffix *–cyte,* both of which mean "hollow vessel" and refer to cells. Cytology had its origins more than three centuries ago and depended heavily on the light microscope for its initial impetus. The advent of electron microscopy and other advanced optical techniques has dramatically increased our understanding of cell structure and function.

The second strand represents the contributions of **biochemistry** to our understanding of cellular structure and function. Most of the developments in this field have occurred over the past 95 years, though the roots go back at least a century earlier. Especially important has been the development of laboratory techniques such as ultracentrifugation, chromatography, radioactive labeling, electrophoresis, and mass spectrometry for separating and identifying cellular components. You will encounter these and other techniques later in your studies as you learn how specific details of cellular structure and function were discovered using these techniques.

The third strand contributing to the development of modern cell biology is **genetics**. Although the timeline for genetics stretches back more than 150 years, most of our present understanding has been gained within the past 75 years. An especially important discovery was the demonstration that, in all organisms, DNA (deoxyribonucleic acid) is the bearer of genetic information. It encodes the tremendous variety of proteins and RNA (ribonucleic acid) molecules responsible for most of the functional and structural features of cells. Recent accomplishments on the genetic strand include the sequencing of the entire **genome** (all of the DNA) of humans and other species, the *cloning* (production of genetically identical organisms) of mammals, including livestock, pets, and primates, and the editing of genomes.

Therefore, an understanding of present-day cell biology requires an appreciation of its diverse roots and the important contributions made by each of its component strands to our current understanding of what a cell is and what it can do. Each of the three historical strands of cell biology is discussed briefly here; a deeper appreciation of these historical strands will come in later chapters as we explore cells in detail. Keep in mind also that in addition to developments in cytology, biochemistry, and genetics, the field of cell biology has benefited greatly from advancements in other fields of study such as chemistry, physics, computer science, and engineering.

The Cytological Strand Deals with Cellular Structure

Strictly speaking, cytology is the study of cells. Historically, however, cytology has dealt primarily with cellular structure, mainly through the use of optical techniques. Here we will describe briefly some of the microscopy that is important in cell biology. (For more detailed discussion of microscopic techniques, see the Appendix.) Microscopy has been invaluable in helping cell biologists overcome a fundamental problem—the problem of small size.

Cellular Dimensions. One challenge involved in understanding cellular structure and organization is the fact that most cells and their organelles are too small to be seen by the unaided eye. The cellular structures that microscopists routinely deal with are measured using units that may not be familiar to you.

The **micrometer** (μm) is the most useful unit for expressing the size of cells and organelles (**Figure 1-4**, on page 28). A micrometer (historically called a *micron*) is one-millionth of a meter (10^{-6} m). One inch equals approximately 25,000 μm. In general, bacterial cells are a few micrometers in diameter, and the cells of plants and animals are 10 to 20 times larger. Organelles such as mitochondria and chloroplasts tend to be a few micrometers in size and are thus comparable in size to whole bacterial cells. In general, if you can see it with a light microscope, you can express its dimensions conveniently in micrometers (Figure 1-4a).

The **nanometer** (nm) is the unit of choice for molecules and subcellular structures that are too small to be seen using the light microscope. A nanometer is one-billionth of a meter (10^{-9} m), so it takes 1000 nanometers to equal 1 micrometer. A ribosome has a diameter of about 25 to 30 nm. Other structures that can be measured conveniently in nanometers are cell membranes, microtubules, microfilaments, and DNA molecules (Figure 1-4b). A slightly smaller unit, the angstrom (Å), is used in cell biology when measuring dimensions within proteins and DNA molecules. An angstrom equals 0.1 nm, which is about the size of a hydrogen atom.

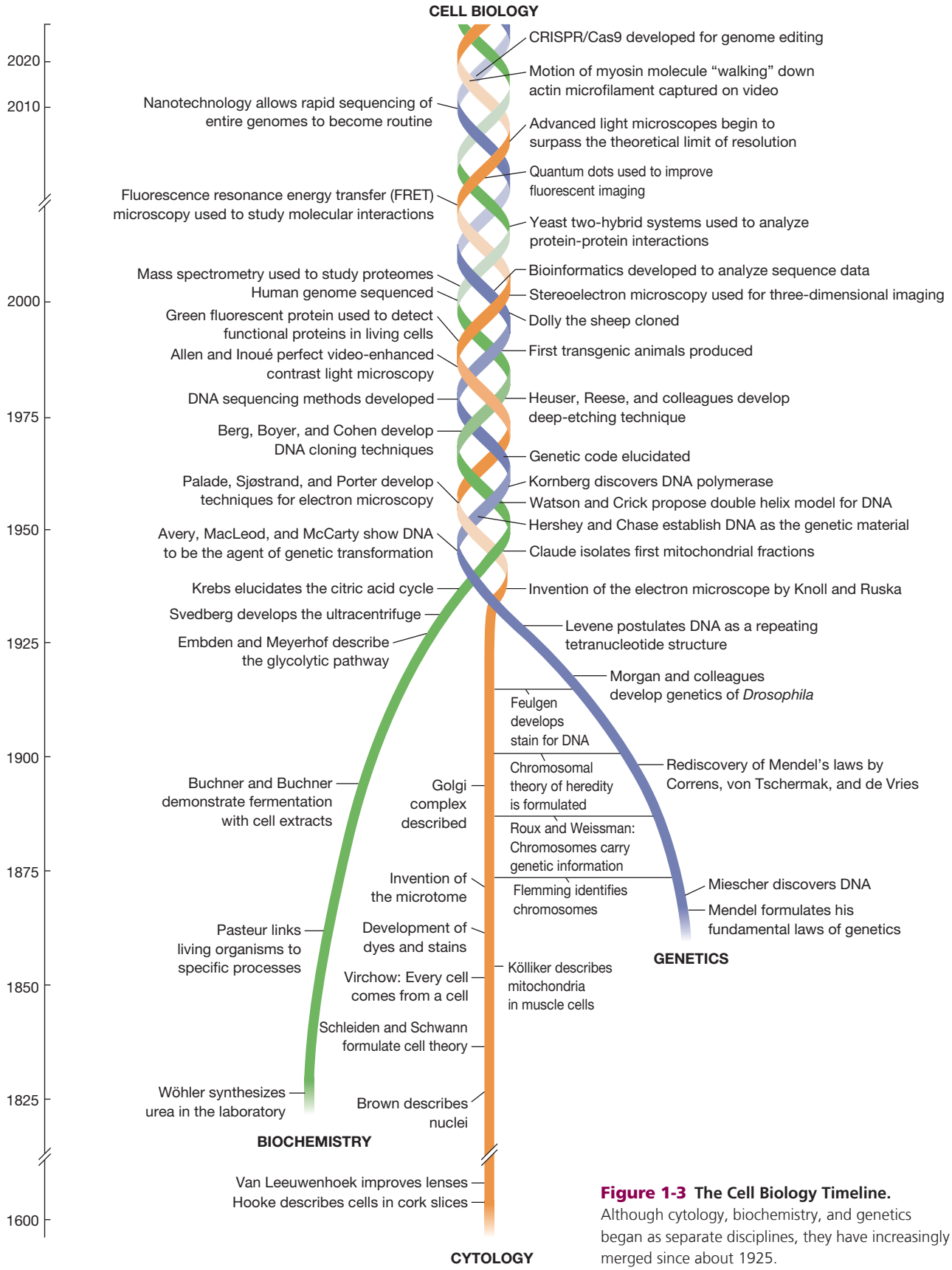


Figure 1-3 The Cell Biology Timeline.
Although cytology, biochemistry, and genetics began as separate disciplines, they have increasingly merged since about 1925.

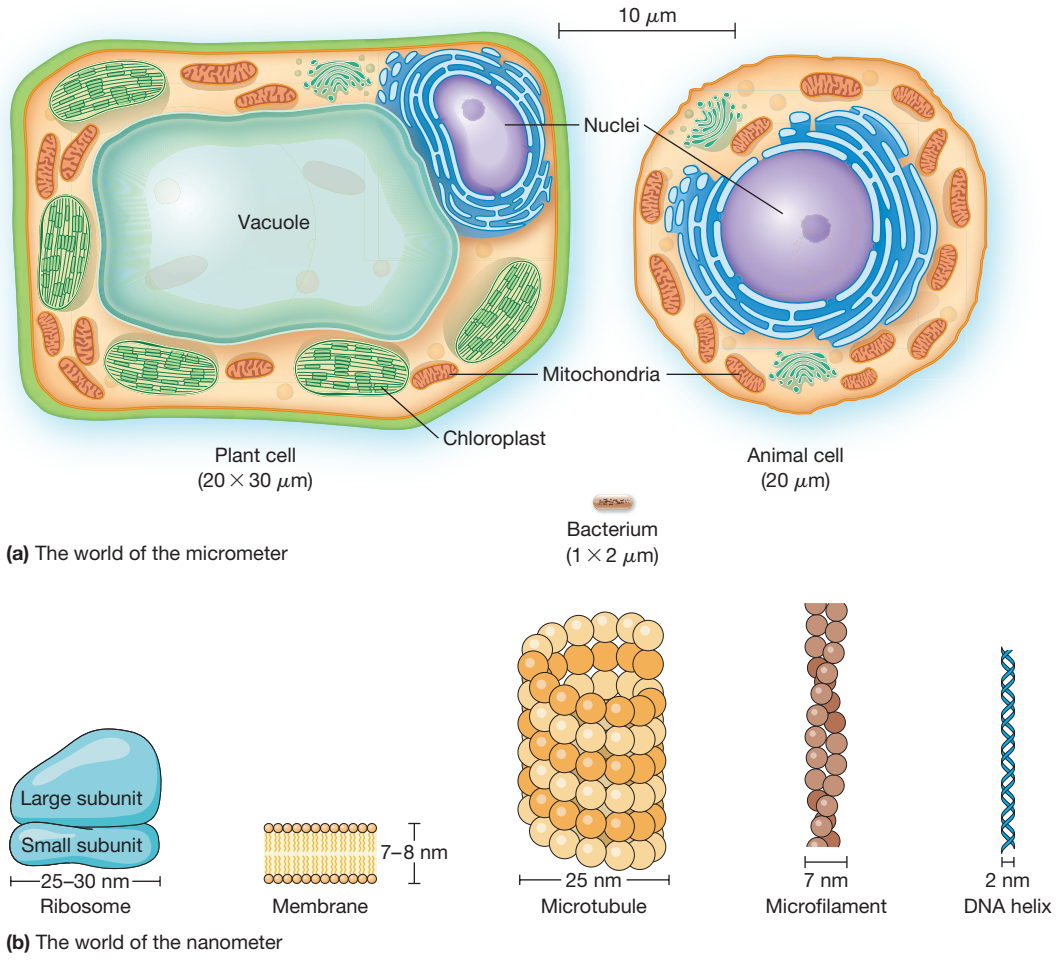


Figure 1-4 The Worlds of the Micrometer and Nanometer. Illustrations show **(a)** typical cells and **(b)** common cellular structures.

Microscopy. The most important technique within the cytological strand is microscopy. This technique allows scientists to visualize cells and cellular components at the previously mentioned cellular dimensions. Depending on the level of resolution required, the two major forms of microscopy used are light microscopy and electron microscopy.

The **light microscope** was the earliest tool of the cytologists and continues to play an important role in our elucidation of cellular structure. Light microscopy allowed cytologists to identify membrane-bounded structures such as *nuclei, mitochondria,* and *chloroplasts* within a variety of cell types. Such structures are called *organelles* ("little organs") and are prominent features of most plant and animal (but not bacterial) cells. (Chapter 4 presents an overview of organelle types, and later chapters investigate their structure and function in more detail.)

The basic type of light microscopy is called *brightfield microscopy* because white light is passed directly through a specimen that is either stained or unstained and the background (the field) is illuminated. A significant limitation of this approach is that specimens often must be chemically fixed (preserved), dehydrated, embedded in paraffin or plastic for slicing into thin sections, and stained to highlight otherwise transparent features. Fixed and stained specimens are no longer alive; therefore, features observed using this method could be distortions caused by slide preparation processes and might not be typical of living cells.

To overcome the limitations of a brightfield microscope, a variety of specialized light microscopes have been developed for observing living cells directly. These techniques include phase-contrast microscopy, differential interference contrast microscopy, fluorescence microscopy, and confocal microscopy. Each of these forms of microscopy is introduced below. (More detail on these techniques, including sample images using them, can be found in the Appendix.)

Phase-contrast and *differential interference contrast* microscopy make it possible to see living cells clearly. Like water waves, light waves have crests and troughs, and the precise positions of these maxima and minima as light travels are known as the *phase* of the light. Both techniques enhance and amplify slight changes in the phase of transmitted light as it passes through a structure having a different density than the surrounding medium.

Fluorescence microscopy is a powerful method that enables researchers to detect specific proteins, DNA sequences, or other molecules that are made fluorescent by coupling them to a fluorescent dye or a fluorescent protein or by binding them to a fluorescently labeled antibody. An **antibody** is a protein molecule produced by the immune system that binds one particular target molecule, known as its antigen.

By simultaneously using two or more such dyes or antibodies, each emitting light of a different color, researchers can follow the distributions of different kinds of molecules in the same cell. Antibody labeling is a powerful method to both visualize and identify specific molecules within cells and is described in more detail (**see Key Technique, pages 30–31**). In recent years, green fluorescent protein (GFP) from the bioluminescent jellyfish *Aequorea victoria* has become an invaluable tool for studying the temporal and spatial distribution of particular proteins in a cell. When a protein of interest is fused with GFP, its synthesis and movement can be followed in living cells using a fluorescence microscope.

An inherent limitation of fluorescence microscopy is that the viewer can focus on only a single plane of the specimen at a time, yet fluorescent light is emitted throughout the specimen, blurring the image. This problem is largely overcome by *confocal microscopy,* which uses a laser beam to illuminate just one plane of the specimen at a time. When used with thick specimens such as whole cells, this approach gives much better resolution.

Another recent development in light microscopy is *digital video microscopy,* which allows researchers to observe cells for extended periods of time using very low levels of light. This image intensification is particularly useful to visualize fluorescent molecules present at low levels in living cells and even to see and identify individual *macromolecules* such as DNA and protein molecules. In fact, extremely powerful *superresolution* light microscopy methods have been developed that use imaging and computational methods so advanced that they can visualize structures 50–100 nm in size, which, until the past few years, were believed impossible to see with any light microscope. However, despite recent significant advances, light microscopy is inevitably subject to the limit of resolution imposed by the wavelength of the light used to view the sample.

As used in microscopy, the **limit of resolution** refers to how far apart adjacent objects must be to appear as separate entities. For example, if the limit of resolution of a microscope is 400 nm, objects must be at least 400 nm apart to be recognizable as separate entities. The smaller the limit of resolution, the greater the **resolving power**, or ability to see fine details of structure, of the microscope. Therefore, a better microscope might have a resolution of 200 nm, meaning that objects only 200 nm apart can be distinguished from each other.

Because of the physical nature of light itself, the theoretical limit of resolution for the light microscope is approximately half the size of the wavelength of light used for illumination, allowing maximum magnifications of about 1000–1400×. For *visible light* (wavelengths of 400–700 nm), the limit of resolution is about 200–350 nm. **Figure 1-5** illustrates the useful range of the light microscope and compares its resolving power with that of the human eye and the electron microscope.

A major breakthrough in resolving power came with the development of the **electron microscope**, which was invented in Germany in 1931 by Max Knoll and Ernst Ruska. In place of visible light and optical lenses, the electron microscope uses a beam of electrons that is deflected and focused by an electromagnetic field. Because the wavelength of electrons is so much shorter than the wavelengths of visible light, the practical limit of resolution for the electron microscope is

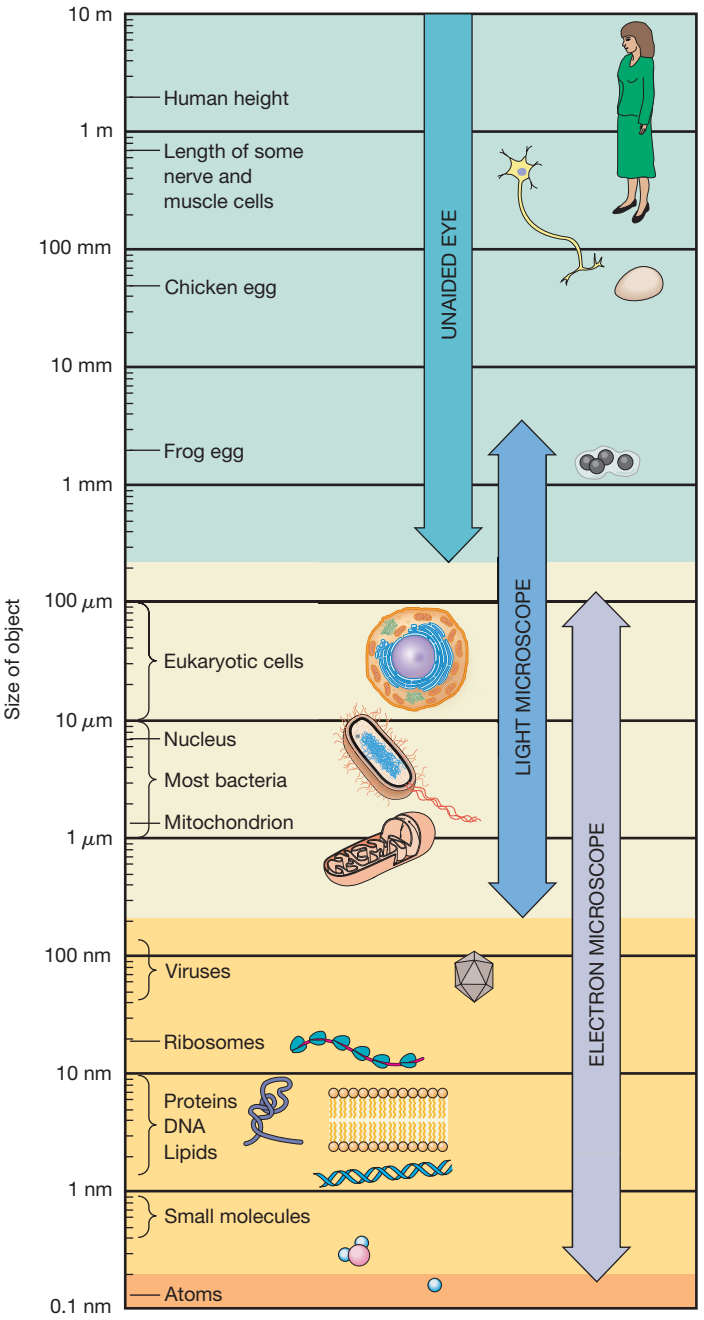


Figure 1-5 Relative Resolving Power of the Human Eye, the Light Microscope, and the Electron Microscope. Notice that the vertical axis is on a logarithmic scale to accommodate the wide range of sizes shown (based on powers of 10).

much better—generally about 100 times better than a light microscope, or 2 nm (see Figure 1-5). As a result, the useful magnification of the electron microscope is also much higher—up to 100,000×.

Electron microscopy continues to revolutionize our understanding of cellular architecture by making detailed ultrastructural investigations possible. Whereas organelles such as nuclei or mitochondria are large enough to be seen with a light microscope, they can be studied in much greater detail with an electron microscope. In addition, electron microscopy has revealed cellular structures that are too small to be seen with a light microscope. These include ribosomes, cell membranes,

Key Technique

Using Immunofluorescence to Identify Specific Cell Components

PROBLEM: Cells are made of thousands of different types of molecules that make up a wide variety of cellular structures. With so many different molecules present, how can researchers determine the presence and location of one specific type of molecule within a cell?

SOLUTION: *Immunofluorescence* is a technique in which a fluorescent molecule is attached to an *antibody,* which recognizes and binds to one specific complementary target molecule, known as its *antigen*. Using a fluorescence or confocal microscope, a researcher can then identify and locate the specific target molecule within the cell.

Key Tools: Fluorescence or confocal microscope; antibodies labeled with a fluorescent dye.

Details: One of the amazing features of animals is the ability of their immune systems to recognize and neutralize a wide variety of potential pathogens. In vertebrates, certain white blood cells, known as *B lymphocytes,* secrete antibodies into the bloodstream, and each different antibody recognizes one specific type of antigen, targeting it for destruction by other white blood cells. An antibody is a protein that has a constant region (C) that is the same for all antibodies of a particular type and variable regions (V) that are identical to each other but unique for each antibody (**Figure 1A-1**). The unique V regions at the tips of the Y contain a binding pocket into which only one specific antigen will fit.

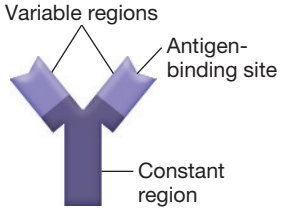


Figure 1A-1 Antibody Structure.

Immunofluorescence exploits the specificity of antibodies for their antigen targets. Rather than targeting antigens for destruction, however, immunofluorescence is used to detect where the antigen is located within a cell. Antibodies can be generated in the laboratory by injecting a foreign protein or other macromolecule into an animal host, such as a rabbit or mouse, producing antibodies that will bind selectively to virtually any protein that a scientist wishes to study. Using *primary* (or *direct*) *immunofluorescence,* antibody molecules are labeled with a fluorescent dye, known as a *fluorophore,* that is covalently linked to the C region of each antibody molecule (**Figure 1A-2**). The antibody recognizes and binds to the target molecule, which can then be detected using fluorescence or confocal microscopy.

More commonly, researchers use *secondary* (or *indirect*) *immunofluorescence.* In this case, a tissue or cell is treated with an antibody that is not labeled with dye (**Figure 1A-3**). This antibody, called the *primary antibody,* attaches to specific antigenic sites within the tissue or cell. A second type of antibody, called the *secondary antibody,* is labeled with a fluorescent dye and then added to the sample, where it attaches to the primary antibody. Because more than one primary antibody molecule can attach to an antigen and more than one secondary antibody molecule can

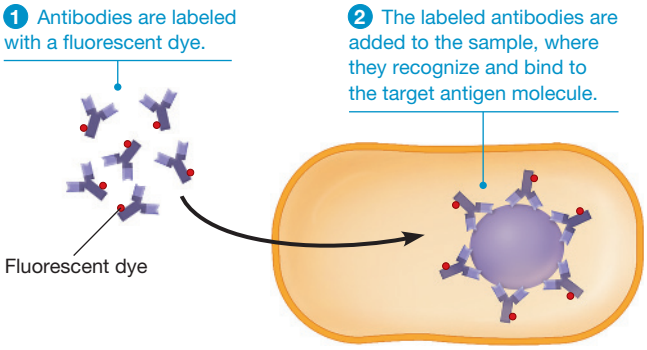


Figure 1A-2 Primary Immunofluorescence. In primary immunofluorescence, an antibody that binds to a specific antigen in a tissue or cell is labeled with a fluorescent dye. The labeled antibody is then added to the sample, where it binds to its target molecule. The pattern of fluorescence that results is visualized using fluorescence or confocal microscopy.

microtubules, and microfilaments (see Figure 1-4b), as well as some *macromolecules* such as DNA and protein molecules.

Most electron microscopes have one of two basic designs: the **transmission electron microscope (TEM)** and the **scanning electron microscope (SEM)**. Images from each are shown in **Figure 1-6** on page 32. Transmission and scanning electron microscopes are similar in that each employs a beam of electrons, but they use quite different mechanisms to form the image. As the name implies, a TEM forms an image from electrons that are transmitted through the specimen. An SEM, on the other hand, scans the surface of the specimen and forms an image by detecting electrons that are deflected from its outer surface. Scanning electron microscopy is an especially spectacular technique because of the sense of depth it gives to biological structures.

Electron microscopy is constantly evolving. Several specialized techniques for electron microscopy allow visualization of specimens in three dimensions and can determine structures of some macromolecules such as proteins. Still other techniques combine some of the principles of TEM and SEM and even allow visualization of cells in liquid without the need for a vacuum. (All of these microscopy techniques are described in detail in the Appendix.)

The Biochemical Strand Concerns the Chemistry of Biological Structure and Function

At about the same time that cytologists started exploring cellular structure with their microscopes, other scientists were making observations that began to explain and clarify cellular function. Using techniques derived from classical chemistry,