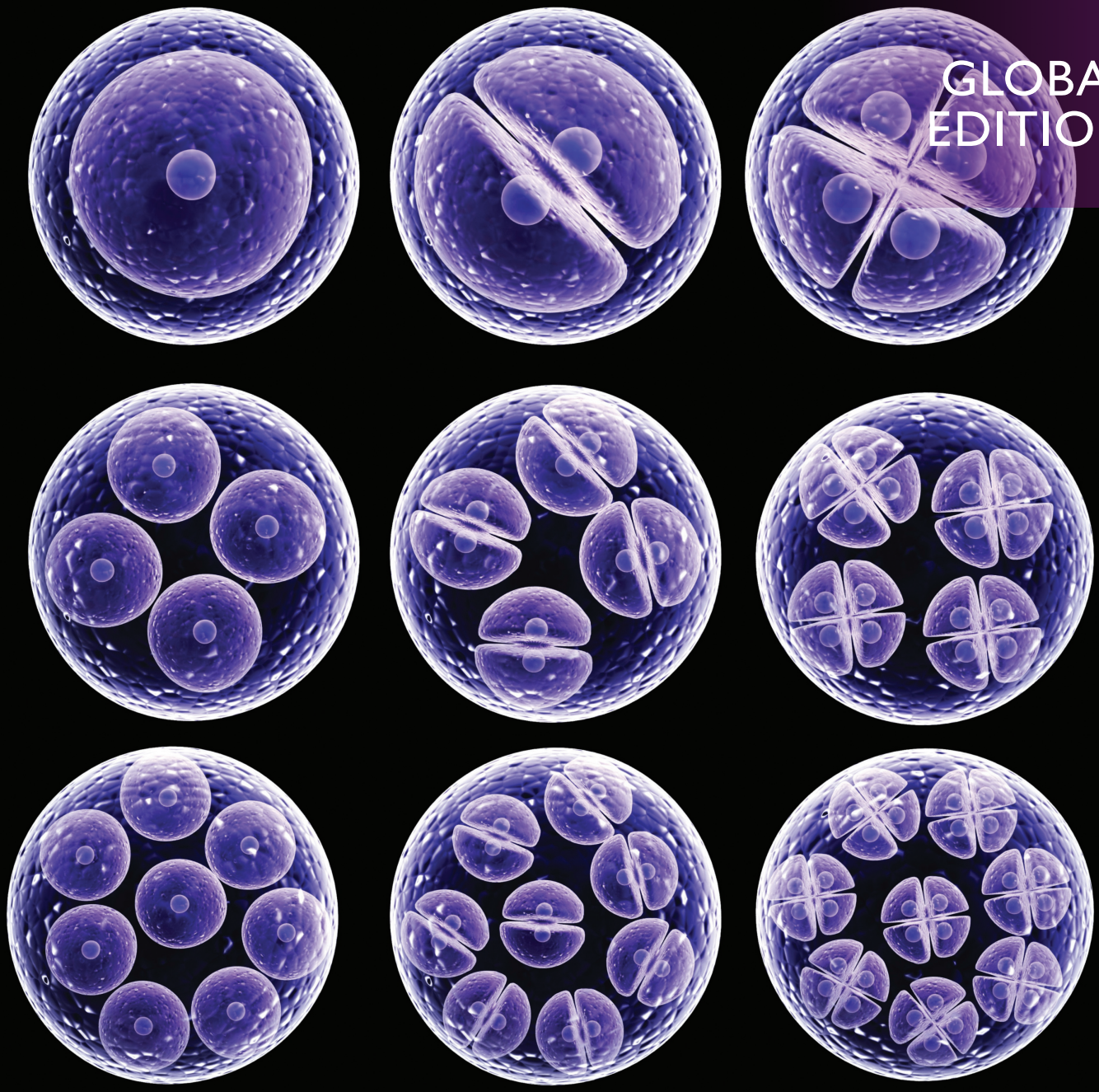


GLOBAL EDITION

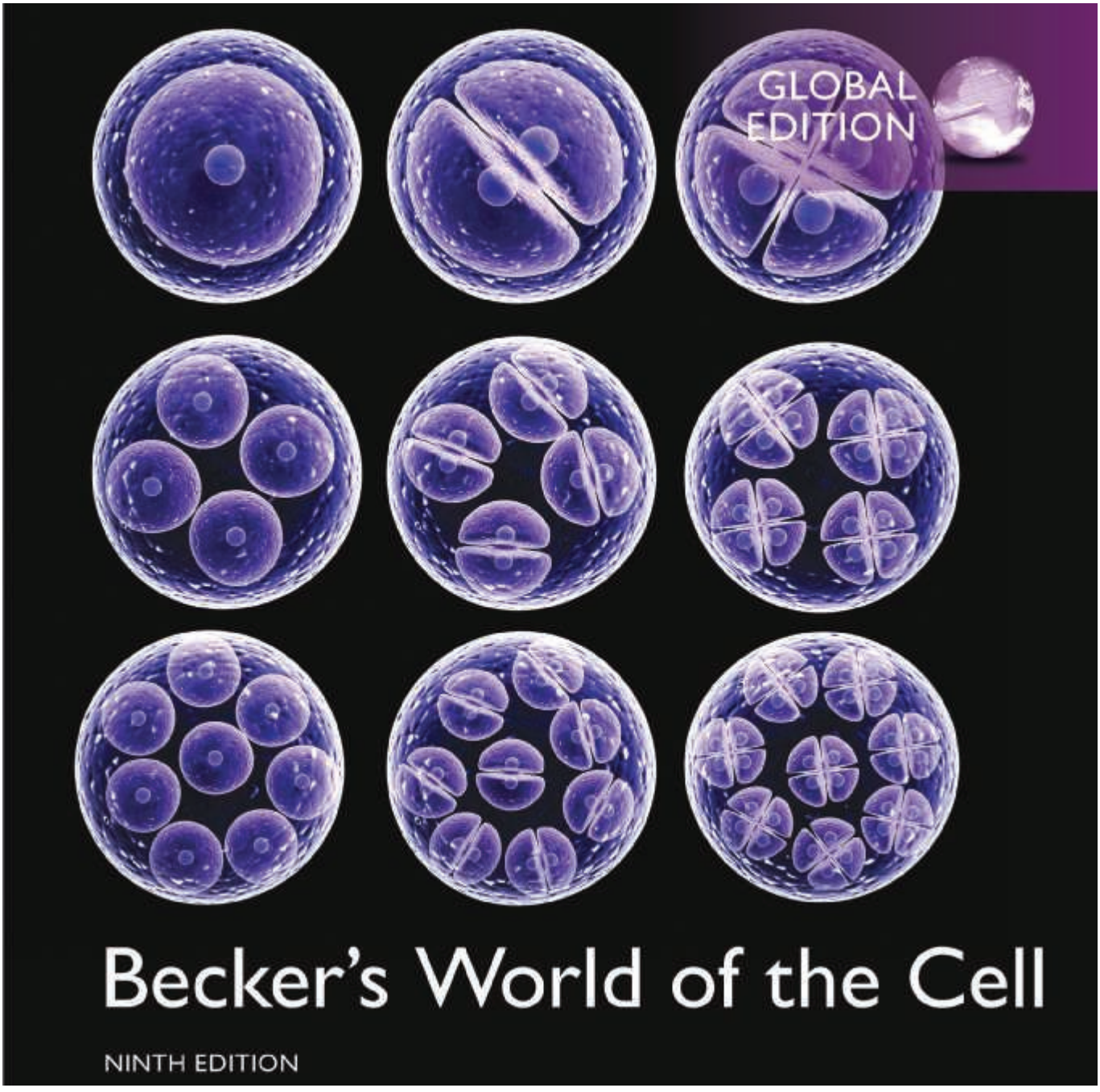
Becker's World of the Cell

NINTH EDITION

Jeff Hardin • Gregory Bertoni

Pearson

BRIEF CONTENTS



JEFF HARDIN
University of Wisconsin–Madison

GREGORY BERTONI
The Plant Cell

Pearson

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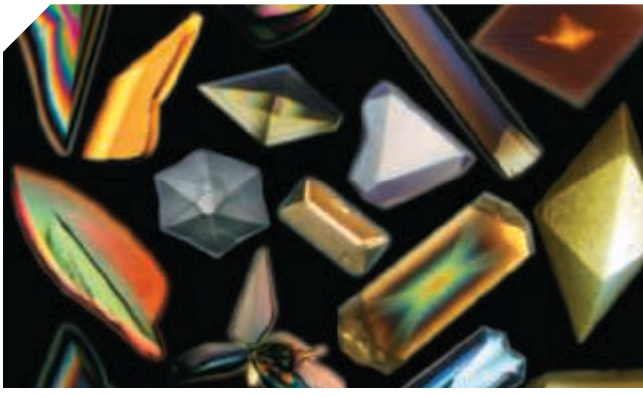
ABOUT THE AUTHORS

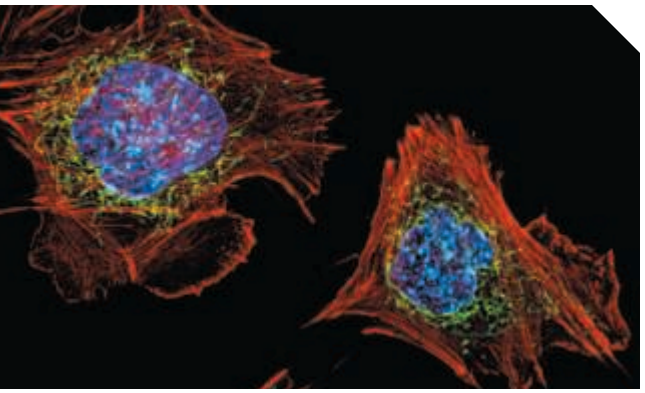
JEFF HARDIN received his Ph.D. in Biophysics from the University of California–Berkeley. He is Professor and Chair of the Zoology Department at the University of Wisconsin–Madison, where he has been since 1991. He is also Faculty Director of the Biology Core Curriculum, a four-semester honors biology 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.

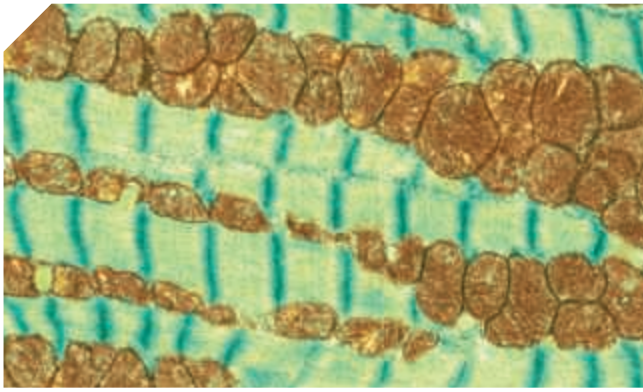
GREGORY BERTONI has been active in teaching, research, and scientific writing for more than 30 years. He earned a Ph.D. in Cell and Molecular Biology from the University of Wisconsin–Madison with Wayne Becker, where his research investigated the effects of light quality and carbon dioxide concentration on photorespiratory gene expression. While in Madison, he and Wayne helped to develop a new course entitled "Ways of Knowing" designed to introduce entering freshmen to the learning process. His published research includes studies in bacterial pathogenesis, plant–microbe interactions, and plant gene expression. Currently, Gregory is a Science Editor for *The Plant Cell,* a leading international research journal in plant cell and molecular biology. For the past 12 years, Gregory has been teaching biology, chemistry, and microbiology part-time at the community college level, and currently teaches at Southern Maine Community College in South Portland, Maine. He is also a freelance scientific writer who contributes to text- and web-based projects in biology, physics, and microbiology. His hobbies include hiking, gardening, and growing certified organic seedlings for A Good Start, a small business he and his wife Marianne Potter founded in 2003.

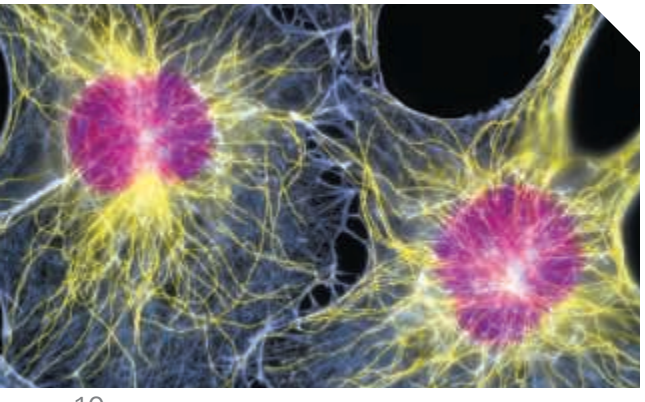
WAYNE M. BECKER taught cell biology at the University of Wisconsin–Madison for 30 years until his retirement. His interest in textbook writing grew out of notes, outlines, and problem sets that he assembled for his students, culminating in *Energy and the Living Cell,* a paperback text on bioenergetics 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.

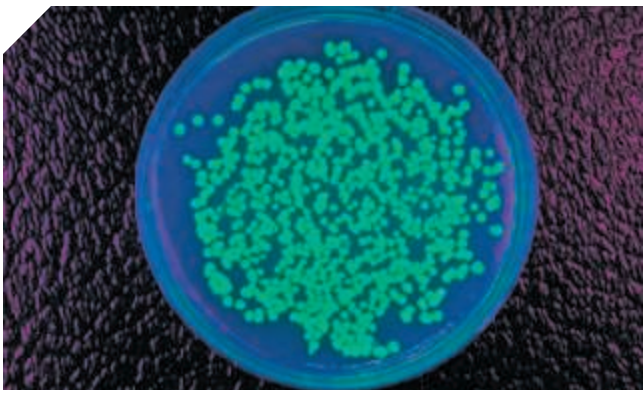
DETAILED CONTENTS

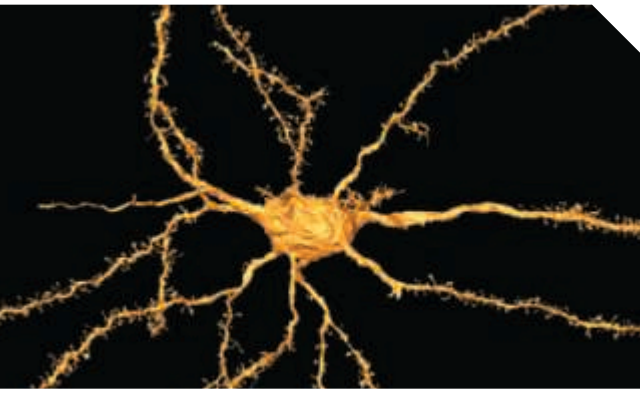












Key Technique

Chapter 1: Using Immunofluorescence to Identify Specific Cell Components

Chapter 2: Determining the Chemical Fingerprint of a Cell Using Mass Spectrometry

Chapter 3: Using X-ray Crystallography to Determine Protein Structure

Chapter 4: Using Centrifugation to Isolate Organelles

Chapter 5: Measuring How Molecules Bind One Another Using Isothermal Titration Calorimetry

Chapter 6: Determining K_m and V_{max} Using Enzyme Assays

Chapter 7: SDS–Polyacrylamide Gel Electrophoresis (SDS-PAGE) of Membrane Proteins

Chapter 8: Expression of Heterologous Membrane Proteins in Frog Oocytes

Chapter 9: Using Isotopic Labeling to Determine the Fate of Atoms in a Metabolic Pathway

Chapter 10: Visualizing Cellular Structures with Three-Dimensional Electron Microscopy

Chapter 11: Determining Absorption and Action Spectra via Spectrophotometry

Chapter 12: Visualizing Vesicles at the Cell Surface Using Total Internal Reflection Microscopy (TIRF)

Chapter 13: Studying the Dynamic Cytoskeleton

Chapter 14: Watching Motors Too Small to See

Chapter 15: Building an ECM from Scratch

Chapter 16: FISHing for Specific Sequences

Chapter 17: The Polymerase Chain Reaction

Chapter 18: Hunting for DNA-Protein Interactions

Chapter 19: Protein Localization Using Fluorescent Fusion Proteins

Chapter 20: Gene Knockdown via RNAi

Chapter 21: DNA Cloning

Chapter 22: Patch Clamping

Chapter 23: Calcium Indicators and Ionophores

Chapter 24: Measuring Cells Millions at a Time (FACS Analysis)

Chapter 25: Using Mendel's Rules to Predict Human Disease

Chapter 26: "Rational" Drugs in the Fight Against Cancer

Human Connections

Chapter 1: The Immortal Cells of Henrietta Lacks (The origin of the first human cultured cell line)

Chapter 2: Taking a Deeper Look—Magnetic Resonance Imaging (MRI) (How an MRI can image human tissues)

Chapter 3: Aggregated Proteins and Alzheimer Disease (Protein misfolding and human disease)

Chapter 4: When Cellular "Breakdown" Breaks Down (Diseases caused by lysosome dysfunction)

Chapter 5: The "Potential" of Food to Provide Energy (Calorie contents of foods)

Chapter 6: ACE Inhibitors: Enzyme Activity as the Difference Between Life and Death (Blood pressure medication based on snake venom)

Chapter 8: Membrane Transport, Cystic Fibrosis, and the Prospects for Gene Therapy

Chapter 9: What Happens to the Sugar? (Dietary food intake and metabolism)

Chapter 10: A Diet Worth Dying For? (The dangers of using uncouplers such as DNP to lose weight)

Chapter 11: How Do Plants Put on Sunscreen? (How the plant xanthophyll cycle dissipates excess solar energy)

Chapter 12: It's All in the Family (LDL receptors, cholesterol uptake, hypercholesterolemia)

Chapter 13: When Actin Kills (*Listeria* infection and actin polymerization)

Chapter 14: Dyneins Help Us Tell Left from Right (Motors and left-right axis specification)

Chapter 15: The Costly Effects of Weak Adhesion (Blistering diseases of the skin)

Chapter 16: Lamins and Premature Aging (Progeria and the nuclear envelope)

Chapter 17: Children of the Moon (Xeroderma pigmentosum and DNA repair)

Chapter 19: To Catch a Killer: The Problem of Antibiotic Resistance in Bacteria

Chapter 20: The Epigenome: Methylation and Disease (Rett syndrome and imprinting disorders)

Chapter 21: More Than Your Fingertips: Identifying Genetic "Fingerprints" (STRs in genetic identification)

Chapter 22: In the Search for the Fountain of Youth, Are People Paying for Poison? (Cosmetic uses of *Botulinum* toxin)

Chapter 23: How to Prevent a Heart Attack (Nitric oxide signaling and vasoconstriction)

Chapter 24: What do Ethnobotany and Cancer Have in Common? (Taxol and cancer treatment)

Chapter 25: When Meiosis Goes Awry (Down syndrome and nondisjunction)

Chapter 26: Molecular Sleuthing in Cancer Diagnosis (Molecular analysis of breast cancer)

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. Helping our students to appreciate the complexities of this amazing cellular world lies at the heart of our goals as authors of *Becker's The 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.

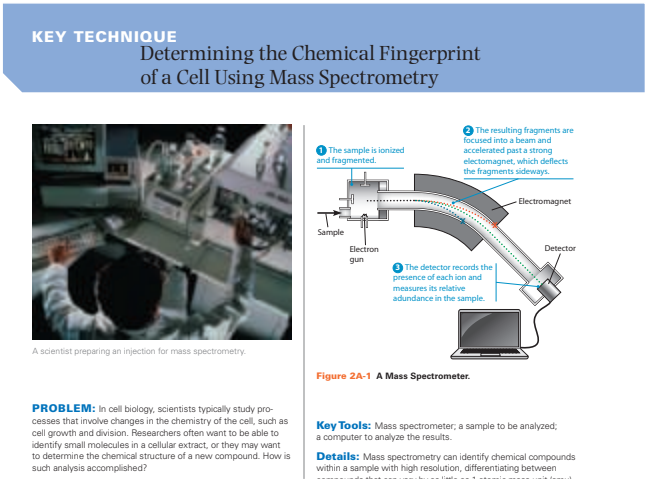
The amazing success of modern cell biology creates both exciting opportunities and central challenges in our teaching. How can we capture the core elements of modern cell biology in a way that draws our students in without overwhelming them? The enormous profusion of information challenges us to keep *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 ninth 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 students and instructors will find that the greater emphasis on molecular biology earlier in the text integrates even better with learning about other aspects of cellular function, just as molecular approaches have become ever more tightly integrated into the everyday work of modern cell biologists.

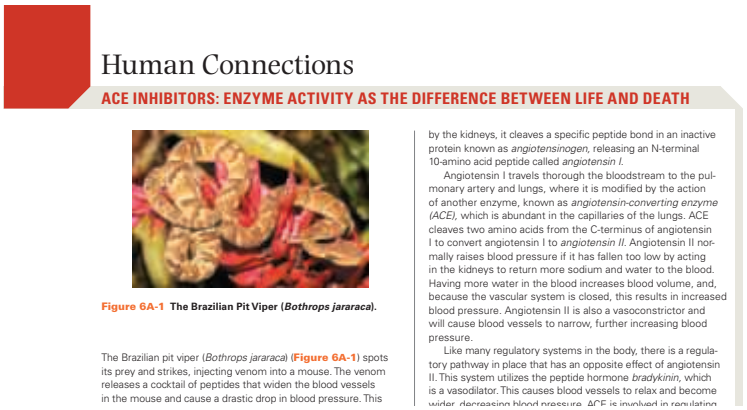
As with the previous editions, we remain committed to three central goals. First, our primary goal is to introduce students to the fundamental principles that guide cellular organization and function. Second, we want students to understand some of the key scientific evidence that has helped us formulate 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

- **New look:** The art program has been updated throughout the book to give drawings a more dynamic and inviting look. Striking new chapter-opening images draw students into the topic of each chapter. In addition, new figures based on molecular structures have been added in several key locations.
- **Reorganization of molecular biology material:** The molecular genetics section of the text has been completely reorganized. These chapters now come earlier in the book and contain substantial new material on chromosomes, mechanisms of DNA mutation and repair, and mobile genetics elements.
- **New chapter on molecular techniques:** This new chapter focuses on the tools that have revolutionized molecular biology and biochemistry—the key technologies cell biologists use to analyze and manipulate DNA, genomes, RNA and proteins, and gene function.
- **Reorganization of materials on cell signaling, cell division, and the cell cycle:** Because the molecular genetics material comes earlier in the book, topics that relate to regulation of gene and protein expression are now more naturally integrated into the discussion of cell signaling and cell cycle control. These topics now come immediately before the chapter on cancer.



- **Key Techniques boxes in every chapter:** Twenty-six Key Techniques boxes are integrated throughout the text, demonstrating how cutting-edge technologies can be used to answer key questions in cell biology. See page 17 for a complete list.



- **Human Connections boxes:** Twenty-four 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. See page 17 for a complete list.
- **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.
- **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 Ninth Edition below).

Pearson Mastering Biology®

Pearson 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:

- 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
- 17 3-D Structure Tutorials that allow students to manipulate molecular structures, with assessment activities
- 240 Reading Quiz questions, which encourage students to read before class
- Many end-of-chapter questions and problems that are now assignable and automatically gradable
- Test Bank questions for every chapter
- The eText, also available through Pearson Mastering Biology, which provides both access to the complete textbook and powerful interactive and customizable functions. In addition, a custom textbook option is available, allowing bundling of selected chapters chosen by the instructor to suit a particular course.
- A suite of Instructor Resources, including PowerPoint lecture outlines containing all the figures and photos.
- Learning Catalytics is a "bring your own device" assessment and active classroom system that expands the possibilities for student engagement beyond standard clickers. Using Learning Catalytics, 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 Ninth Edition

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

Chapter 1: A revised section on expression of genetic information in cells is presented much earlier in the textbook to integrate with other aspects of modern cell biology. New overview figure showing information expression in cells. New figures to introduce chromatography and electrophoresis. Described superresolution microscopy and photoactivatable GFP. Earlier introduction of immunoprecipitation, RNA sequencing, transcriptomics, DNA microarrays. New figure showing a DNA microarray. Revised figure showing importance of model organisms in cell biology research. Expanded discussion on the use on antibodies and immunofluorescence to identify cell components. Large new section describing experimental design, the null hypothesis, and experimental variables. Discussed use of mutants, reverse genetics, biochemical inhibitors in cell biology research.

Chapter 2: Clarified properties of acids and bases with respect to functional groups. Introduced use of mass spectrometry to identify and characterize chemical compounds. Reinforced concepts of valence, the octet rule, and lone electron pairs to explain the shape and polarity of water molecules. Introduced glycobiology sooner. New figure to clarify concept of membrane semipermeability. New figure with updated three-dimensional structure of insulin. Introduced use of MRI to study the chemistry of tissues in the human body.

Chapter 3: Emphasized protein denaturation in the context of human protein-folding diseases. Introduced base stacking in discussion of hydrophobic effects on DNA structure. New figure highlighting β-sheet structure in a fibrous protein. Emphasized differences between storage and structural polysaccharides. Improved description of linear versus Haworth illustrations of monosaccharide structure.

Chapter 4: New showcase figures of animal and plant cells. New section describing proposed origin of cells, the RNA world, liposomes (with accompanying figure), and new figure on Miller's classic 1953 experiments on the abiotic origins of organic molecules. Moved discussion of the endosymbiont theory forward to this chapter to accompany introduction of mitochondria and chloroplasts. Discussion of centrifugation to study organelles also introduced much earlier. New figure showing updated ribosome structure. New figure showing scanning EM of human chromosomes. New figure showing immunofluorescent detection of cytoskeletal elements.

Chapter 5: More emphasis on open versus closed systems. Revised discussion of bioluminescence versus fluorescence. Expanded discussion of aequorin and GFP. Expanded discussion of oxidation and reduction reaction and relevance to cellular metabolism. Improved definition of free energy. Introduction of isothermal titration calorimetry to determine thermodynamic parameters in biological processes.

Chapter 6: New figure to show binding of substrate to specific amino acids in an enzyme active site. Revised explanation of inorganic and organic catalysts and earlier introduction of trans fats. More emphasis on why we study enzyme kinetics. Better explanation of cooperativity using hemoglobin as an example. More emphasis on substrate analogues and inhibitors in treatment of human disease.

Chapter 7: Updated discussion of lipid nomenclature. Added information on ABO blood groups to illustrate membrane glycoproteins in a relevant human example. More emphasis on fungal and bacterial sterols. Introduced common abbreviations for fatty acid chain length and saturation. Noted differential charges on membrane monolayers.

Chapter 8: New figure and updated information on structure and selectivity of the aquaporin water channel. Introduced bacterial aquaglyceroporins. Revised and simplified discussion of electrochemical potential. New paragraph introducing the Na^+/glucose symporter with an explanation of how glucose phosphorylation in the cell keeps the transmembrane free glucose concentration far from equilibrium. Clarified discussion of osmosis and added intravenous phosphate-buffered saline as a relevant example. Noted how cells can have multiple types of glucose transporters using intestinal cells as an example. Simplified the figure showing *Halobacterium* proton pump to highlight essential details. Updated the structure of the CFTR chloride channel.

Chapter 9: New section describing the Warburg effect and aerobic glycolysis in cancer cells, with a new figure describing how PET scans exploit this to visualize tumors in the body. Better explanations of energy-rich bonds in phosphorylated compounds and charge repulsion/resonance stabilization in ATP. Revised figure showing phosphate group transfer reactions. Described experimental use of frog muscle tissue to elucidate steps in glycolysis. More emphasis on how cells use fermentation to ensure a steady supply of NAD^+ in anaerobic conditions. Better description of allosteric effectors of glycolysis.

Chapter 10: Expanded discussion of mitochondrial morphology based on EM tomography and updated figures to show new information on cristae junctions. Expanded discussion of respiratory complexes I to IV, with new figure showing accurate molecular models. New figure panel with a ribbon model showing the molecular structure of the ATP synthase complex. More emphasis on the difference between oxidative and substrate-level phosphorylation. Expanded discussion of experimental evidence that isolated F_1 particles can synthesize ATP. Simplified figure showing the binding change model for ATP synthesis.

Chapter 11: New figure showing autofluorescence of a *Spirogyra* chloroplast. New figure with accurate molecular model of the 16 subunits of the RuBisCO enzyme. Completely updated figure of the structure of the bacterial photosynthetic reaction center. Clarified the meaning of carbon fixation and introduced this concept sooner. Improved figure showing folded membranes in photosynthetic cyanobacteria. Clarified figure showing energy capture by photosynthetic accessory pigments. More emphasis on the difference between cyclic and noncyclic electron flow.

Chapter 12: Simplified the overview figures based on student and instructor feedback. Introduced the dangers of synergistic effects of alcohol and barbiturates. More experimental detail regarding Palade's classic work showing protein synthesis and secretion. Described Rothman's work on vesicle trafficking. Emphasized yeast as a model organism. More emphasis on the differences between rough and smooth ER. New figure contrasting the stationary cisternae with the cisternal maturation models in Golgi transport. New information about lysosomal storage diseases, peroxisome biogenesis, multivesicular endosomes, and newly proposed roles for cellular caveolae.

Chapter 13: Added material on septins to the introductory section and a new EM figure showing the density of cytoskeletal elements. Added new molecular renderings of bacterial cytoskeletal proteins. Significantly improved the coverage of centrioles and γ-tubulin ring complexes/centrosomes, including new figure panels. Updated the schematic of Tau to be more realistic and added panels showing the effects of Tau

overexpression. New material on EB1 and +-TIP proteins, including new figure panels. Updated coverage of Rho family GTPases and their regulation.

Chapter 14: Revised discussion of motors to remove mixed anatomical metaphors. Added a new figure on motors based on molecular structures. Added major new material on dyneins based on new molecular structures, and figures were revised accordingly. Added brief mention of SAS-6/cartwheels in basal bodies. Added an essentially new figure on kinesin movement along microtubules. Added new figure on microtubule sliding in the axoneme and made major improvements to figures dealing with cilia and flagella. Added a new molecular structure panel to the thin filament figure.

Chapter 15: Reorganized and streamlined the first section of the chapter (cell-cell adhesion). Material on the glycocalyx and blood typing was moved to Chapter 7. Figures on cadherins, tight junctions, and desmosomes were upgraded and consolidated. Added a major new figure on the assembled extracellular matrix. Added more images of fibronectin and costameres.

Chapter 16: The molecular genetics sections were completely reorganized. Many elements were moved to the new molecular techniques chapter (Chapter 21). Added extra material on Avery's experiments, RNA as the genetic material in TMV, and more on Watson/Crick/Franklin. Added material on base stacking and DNA double helix structure. Moved some material on chromatin regulation to this chapter. The heterochromatin discussion was reorganized to feature centromeres and telomeres in a more coherent fashion and to better set up the discussion of repeated DNA sequences. Added material on G bands and karyotyping. Revised treatment of variable number tandem repeats (VNTRs), short tandem repeats (STRs), etc.

Chapter 17: Cell cycle material was moved to Chapter 24. Added Taylor's experiments to the semiconservative replication section. Added material and a figure on origins of replication and replication bubbles. Added material on DNA polymerase proofreading. Performed a major upgrade to the replisome section, including a major new figure. Major upgrades to the mutation section to include DNA adducts and intercalating agents, and the DNA error repair section to include photorepair, major upgrades and clarifications to base excision repair, nucleotide excision repair, and SOS repair/translesion synthesis. Major upgrade to the recombination section to include synthesis-dependent strand annealing (SDSA) and modernized treatments of the double-stranded break model for homologous recombination and Holliday junction resolution. Added material on DNA-only transposons.

Chapter 18: Added new comparison of bacterial and eukaryotic transcription. Added new table on types of RNA. Added nucleolus material to this chapter (moved from Chapter 16). Added more detail on phosphorylation of the polymerase II CTD in initiation and coordination of mRNA processing. Added "scrunching" to section on bacterial initiation and updated the section on bacterial elongation with more discussion based on structural data. Added new section clarifying RNA polymerase proofreading.

Chapter 19: Added more material on ribosome biogenesis and ribosome structure. Wobble coverage was expanded, and a new figure added. Added significant new coverage of eukaryotic translational initiation, poly(A)-binding protein, etc. Enhanced coverage of IRESs. Added a section on polyribosomes. Added a significant new section on chaperones. Added new paragraph on posttranslational processing of insulin (with figure). Added discussion on making multipass transmembrane proteins, plus a new figure panel.

Chapter 20: Improved explanation of what "on" and "off" mean for gene expression. Added major new material on CRISPR/Cas. Added discussion of somatic hypermutation to the section on immunoglobulin genes. Yeast mating type switching was moved to the gene silencing discussion. Added new material on X chromosome inactivation. Added material to section on domain swapping of transcription factors. Added new sections on piRNAs and long, noncoding RNAs. Added a new figure on DNA methylation and on the structure of the eukaryotic 26S proteasome.

Chapter 21: This is a new chapter that consolidates many molecular techniques from previous editions in one location, including material on genomes, restriction enzymes, detecting DNA methylation, dideoxy sequencing, nucleic acid blotting, recombinant DNA, cDNA, Ti plasmids, transgenic mice, mouse knockouts, microarrays, and the yeast two-hybrid method. Enhanced treatment of different types of DNA libraries. New nucleic acid material, including genome sequencing, the tree of life, sequence comparisons and databases, Human Genome Project data, systems biology, RFLP/STR analysis, RT-PCR, RNA in situ, transcriptional reporters, genome editing, TILLING, and CRISPR/Cas9. New protein material, including 2D gels, immunoblotting, chromatography, mass spectrometry for peptides, pulldowns, co-immunoprecipitation, and engineering of tagged proteins.

Chapter 22: Improved and streamlined the discussion of electrochemical potential, including a completely revised figure on the resting potential. Added to patch clamping material. Improved the treatment of channel inactivation in the main action potential figure. Added new paragraphs on optogenetics and NMDA receptors.

Chapter 23: More setup using a biological example familiar to students. Wnt receptors and cancer now deferred to Chapter 26. Added an overview of basic pathways to be discussed in detail and added a figure. Signaling crosstalk is now deferred until the end of the growth factor section, and a new figure was added. Added new section on K_d. Molecular structures of a GPCR and EGFR were added. Added to cholera discussion.

Chapter 24: This is a newly organized chapter, with material taken from Chapter 19 of the previous edition (mitosis, cytokinesis, DNA licensing, cell cycle control, apoptosis). Added more material on structure of kinetochores, midbodies, and abscission. Added material on bacterial and chloroplast division and FtsZ. Expanded and revised treatment of regulation of mitotic exit via the APC and spindle assembly checkpoint control which are now split into separate figures. Clarified coverage of checkpoints by segregating the discussion into its own section. Autoradiography problems updated to use BrdU instead.

Chapter 25: This is a new chapter, with material taken from Chapter 20 of the previous edition. Switched to purple/white flower color as main example from Mendel's work. Revised figure on genes, loci, alleles, etc. Updated gamete formation figure to more accurately reflect how polar bodies form in oocytes. Added more material on the synaptonemal complex and DNA repair proteins during recombination. Added new material on control of meiosis in amphibians and moved discussion of Masui's experiments on MPF from the cell cycle chapter (Chapter 24) to this chapter.

Chapter 26: Reorganized the introductory discussion of cancer. Improved discussion of cancer stem cells. Added new figures or part of figures: a colon polyp, chromosomal translocation in BCR-ABL, and genomic instability. Clarified the discussion of the two-hit hypothesis and loss of heterozygosity. Improved discussion of Wnt receptors/coreceptors. Added material on the Cancer Genome Atlas, GWAS, and sequencing of the genome of HeLa cells.

Appendix: Moved TIRF discussion to group it with light sheet and multiphoton microscopy. Removed X-ray crystallography because this is now covered in detail in the main text (Chapter 3). Added discussion of optogenetics.

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 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 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. Many are class-tested, having been selected from problem sets and exams we have used in our own courses.

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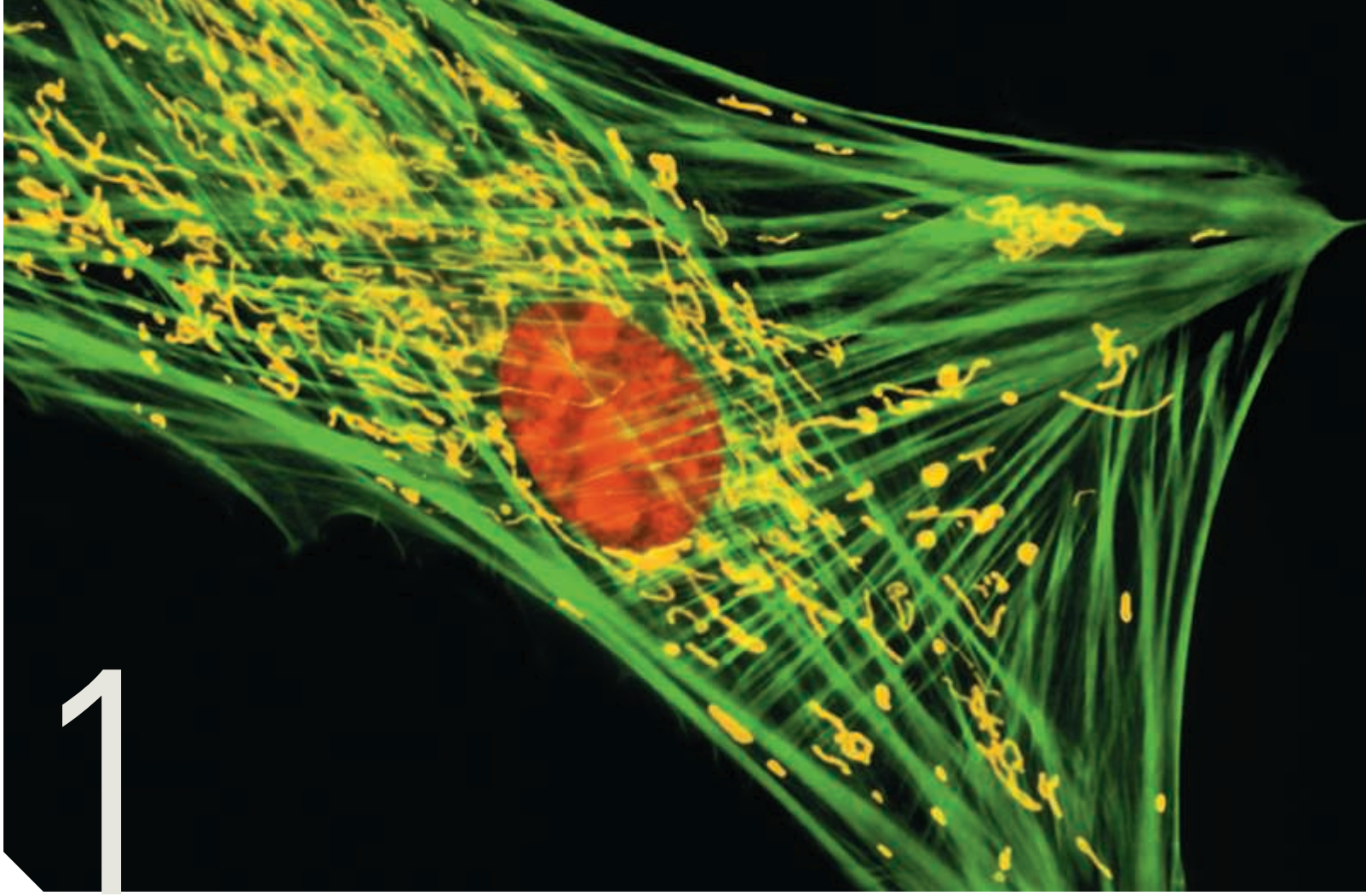

1

A Preview of Cell Biology

Fluorescence Microscopy of a Cultured Lung Cell. This image shows the fluorescently labeled cell nucleus (orange), mitochondria (yellow), and the actin filaments (green)

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. If this text helps you to 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 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. He saw 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.

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 main 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.

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 1-1**).

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 1-1a–c). Other cells have much more exotic shapes, such as the diatom and the protozoan shown in Figure 1-1d and e. Note how the two human single-celled gametes, the egg

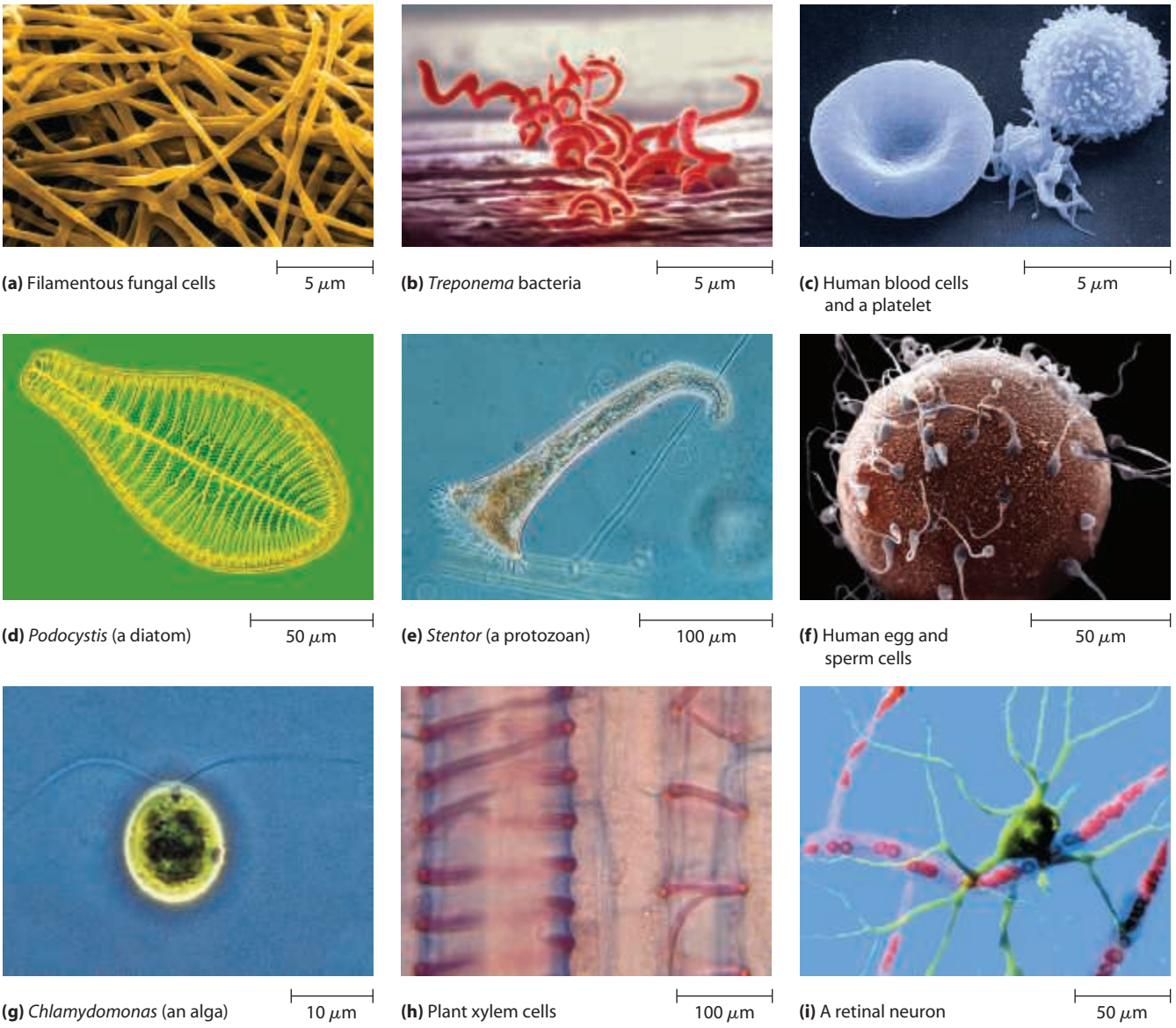

Figure 1-1 Cells of the World. The diversity of cell types existing all around us includes the examples shown in this figure and thousands upon thousands more.

and the sperm, differ greatly in size and shape (Figure 1-1f). As in leaves, the green chlorophyll in a *Chlamydomonas* cell shows that these algae carry out photosynthesis (Figure 1-1g). Often, an appreciation of a cell's shape and structure gives 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 1-1h), and the highly branched cells of a human neuron allow it to interact with numerous other neurons (Figure 1-1i). 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 1-2** 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

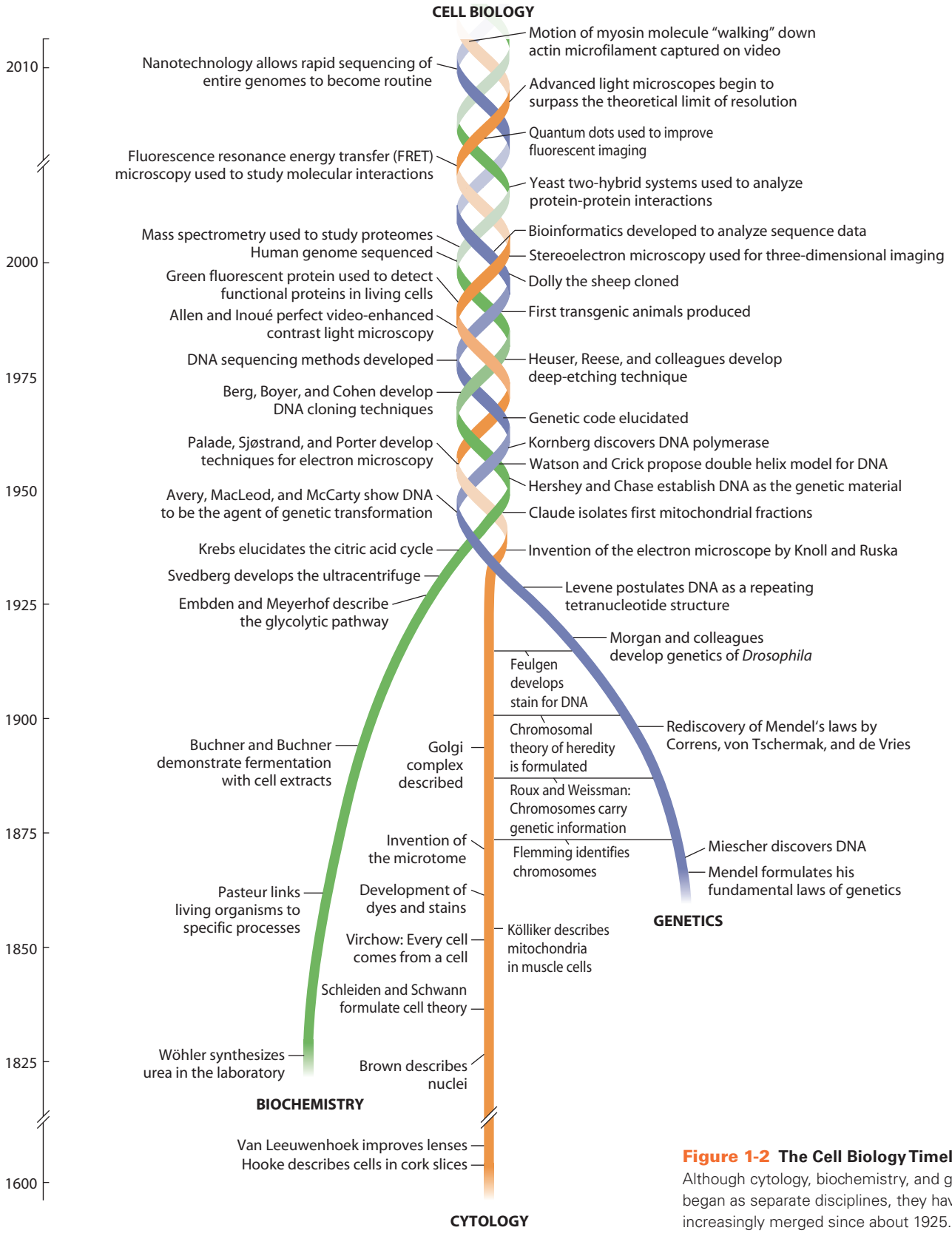

Figure 1-2 The Cell Biology Timeline. Although cytology, biochemistry, and genetics began as separate disciplines, they have increasingly merged since about 1925.

of electron microscopy and other advanced optical techniques has dramatically increased our understanding of cell structure and function.

The second strand represents the many contributions of **biochemistry** to our understanding of cellular structure and function. Most of the developments in this field have occurred over the past 75 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 those of other species and the *cloning* (production of genetically identical organisms) of mammals, including sheep, cattle, and cats.

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. 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 1-3a**).

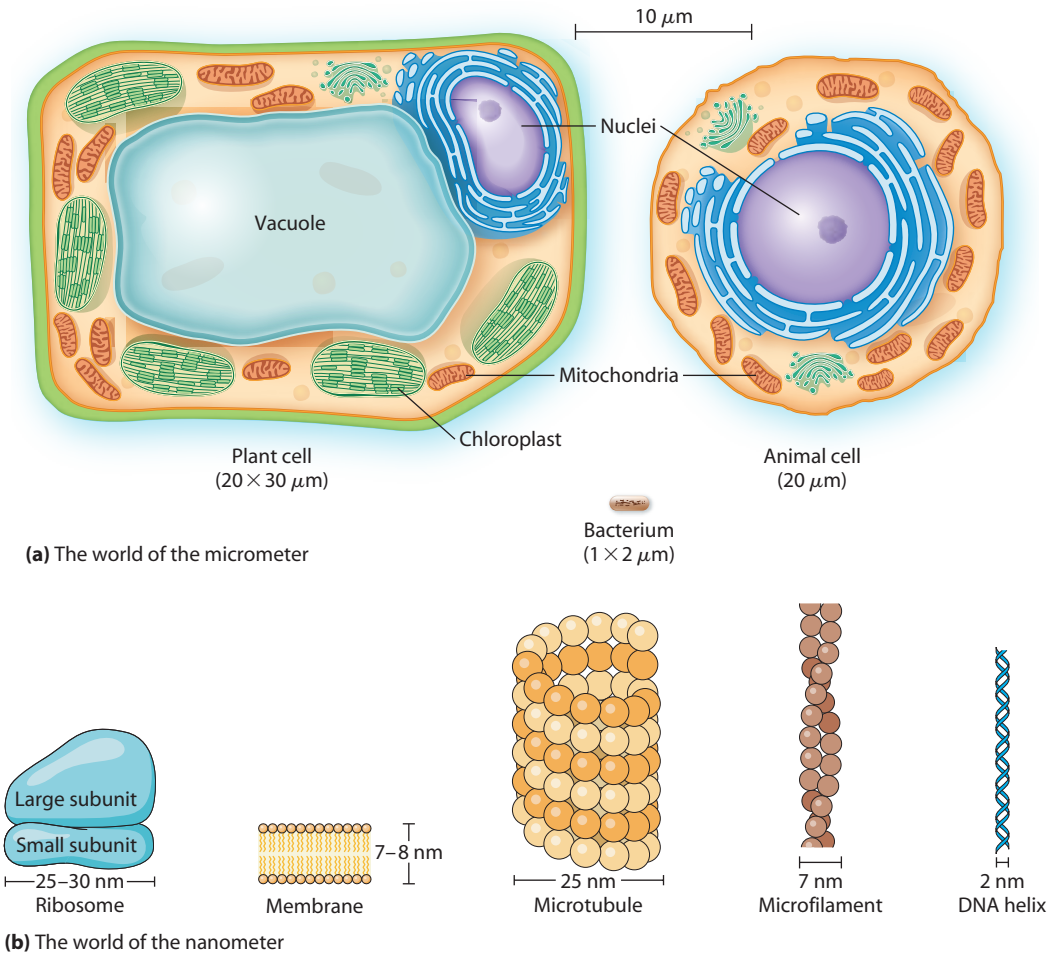

Figure 1-3 The Worlds of the Micrometer and Nanometer. Illustrations show **(a)** typical cells and **(b)** common cellular structures.

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 1-3b). 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.

The Light Microscope. 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.)

Other significant advancements in microscopy include the development of the microtome in the mid-1800s and the availability of various dyes and stains at about the same time. A *microtome* is an instrument developed for rapid and efficient preparation of very thin (several μm) tissue slices of biological samples. Many of the dyes important for staining and identifying subcellular structures were developed in the latter half of the nineteenth century by German industrial chemists working with coal tar derivatives. Together with improved optics and more sophisticated lenses, these developments extended light microscopy to the physical limits of resolution imposed by the size of the wavelengths of visible light.

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 of 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 would be about 200–350 nm. **Figure 1-4** illustrates the useful range of the light microscope and compares its resolving power with that of the human eye and the electron microscope, which is discussed shortly.

The type of microscopy described thus far 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, and therefore features observed by this method could be distortions caused by slide preparation processes that are not typical of the living cells.

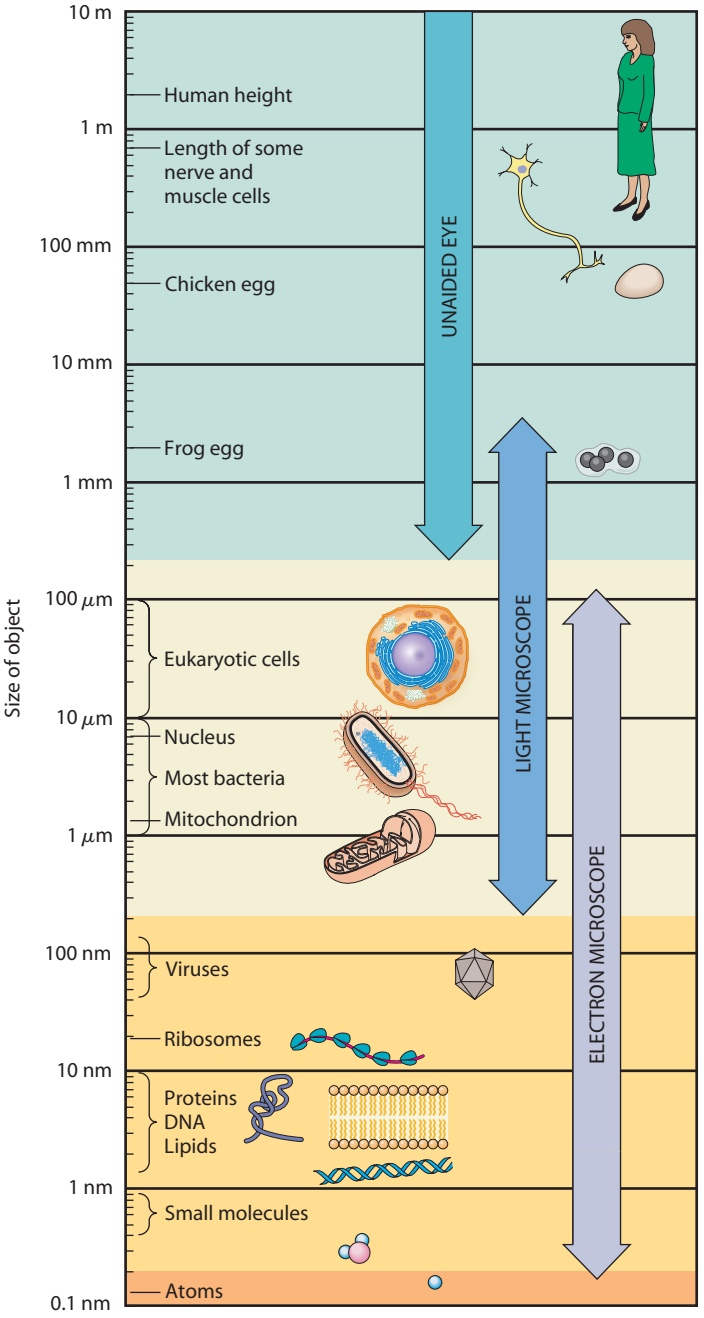

Figure 1-4 Relative Resolving Power of the Human Eye, the Light Microscope, and the Electron Microscope. Notice that the vertical axis is on a logarithmic scale to accommodate the wide range of sizes shown.

MB Use of GFP Fusions for Protein Localization

Specialized Light Microscopes. To overcome the limitations of a brightfield microscope, a variety of special optical techniques have been developed for observing living cells directly. These techniques include phase-contrast microscopy, differential interference contrast microscopy, fluorescence microscopy, and confocal microscopy. In **Table 1-1,** you can see images taken using each of these techniques and compare them with the images seen with brightfield microscopy for both unstained and stained specimens. Because these