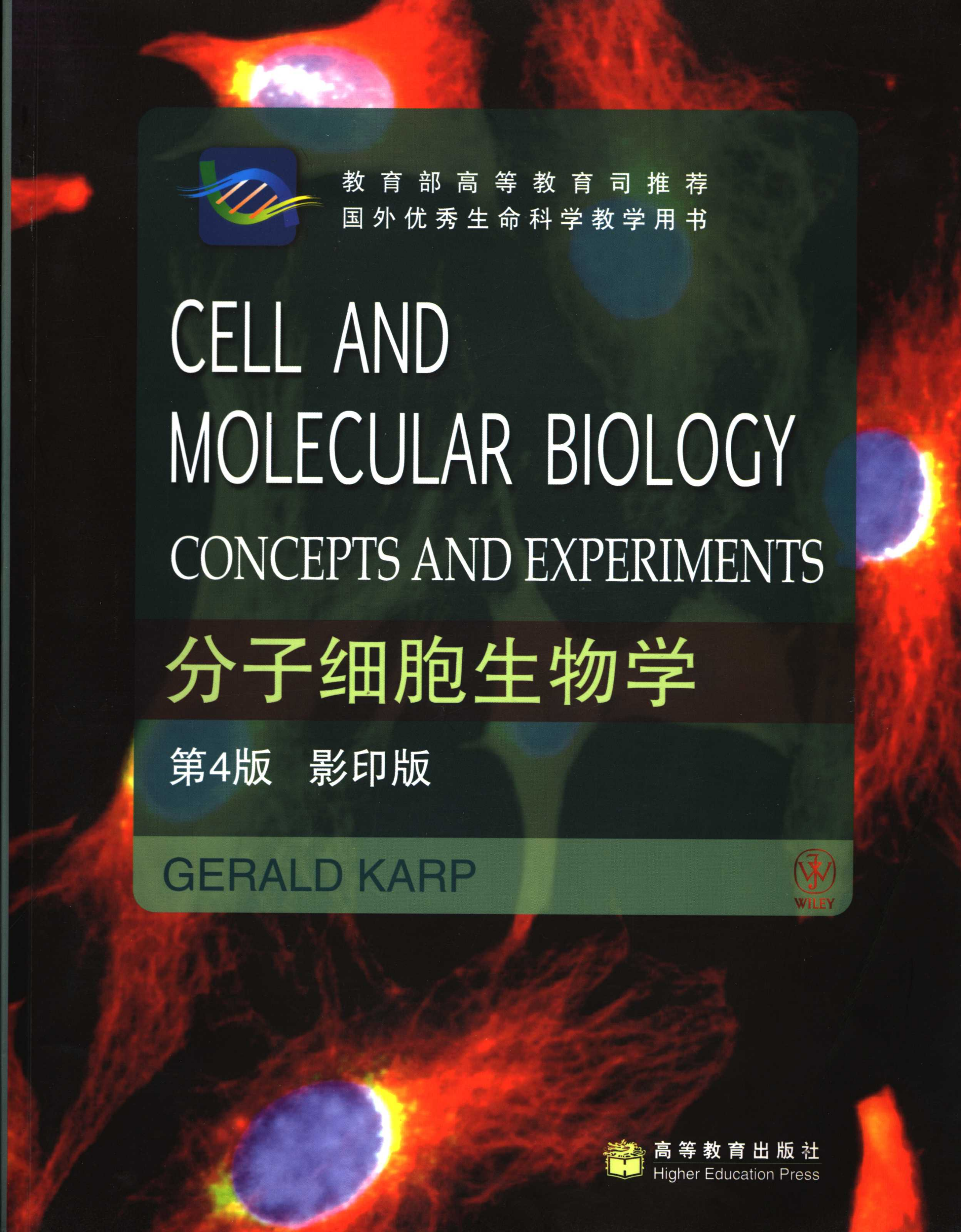

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国外优秀生命科学教学用书

CELL AND MOLECULAR BIOLOGY

CONCEPTS AND EXPERIMENTS

分子细胞生物学

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About the Author

Gerald C. Karp received a bachelor's degree from UCLA and a Ph.D. from the University of Washington. He conducted postdoctoral research at the University of Colorado Medical Center before joining the faculty at the University of Florida. Gerry is the author of numerous research articles on the cell and molecular biology of early development. His interests have included the synthesis of RNA in early embryos, the movement of mesenchyme cells during gastrulation, and cell determination in slime molds. For 13 years, he taught courses in molecular, cellular, and developmental biology at the University of Florida. During this period, Gerry co-authored a text in developmental biology with N. John Berrill and authored a text in cell and molecular biology. Finding it impossible to carry on life as both full-time professor and author, Gerry gave up his faculty position to concentrate on writing. He hopes to revise this text every three years.

About the Cover

Humans fall victim to many disorders that lead to the deterioration and death of specialized cells within an organ. Parkinson's disease, Alzheimer's disease, and Huntington's disease, for example, lead to the death of nerve cells in different parts of the brain. What if it were possible to give new life to such patients by transplanting healthy nerve cells into their brains? Recent studies suggest that the brains of adult mammals, including humans, contain cells that could provide the source of such transplants. These cells are referred to as adult neural stem cells, and they possess two remarkable properties. Not only can these cells divide indefinitely, but they can give rise to any type of brain cell that might be needed. The bright green cell in the cover photograph is a nerve cell that has developed recently from a neural stem cell in the brain of an adult mouse. The cell exhibits this color because its cytoplasm contains the green fluorescent protein (GFP), a protein that occurs naturally only in certain jellyfish. This mouse brain cell is able to manufacture GFP because the animal had been infected four weeks earlier with a virus that had been genetically engineered by researchers to carry the gene for this fluorescent protein. The virus used in this experiment is only able to infect cells that are capable of dividing, which means that this brain cell must have undergone division in the weeks following introduction of the virus and prior to preparation of the brain tissue. The potential role of adult stem cells in cell transplantation is discussed on page 18. (*From Henriette van Praag, et al,, courtesy of Fred H. Gage. Reprinted with permission from* Nature 415*:1031, 2002. © Copyright 2002, Macmillan Magazines Ltd.)*

Preface for the Fourth Edition

Before I began work on the *first* edition of this text, I drew up a number of basic guidelines regarding the type of book I planned to write.

- I wanted a text suited for a course that ran either a single semester or 1–2 quarters that would be taken in the sophomore or junior year. I set out to draft a text of about 800 pages that would not overwhelm or discourage students at this level.
- I wanted a text that elaborated on fundamental concepts, such as the relationship between molecular structure and function, the dynamic character of cellular organelles, the use of chemical energy in running cellular activities and ensuring accurate macromolecular biosynthesis, unity and diversity at the macromolecular and cellular levels, and the mechanisms that regulate cellular activities.
- I wanted a text that was grounded in the experimental approach. Cell and molecular biology is an experimental science and, like most instructors, I believe students should gain some knowledge of how we know what we know. With this in mind, I decided to approach the experimental nature of the subject in two ways. As I wrote each chapter, I included enough experimental evidence to justify many of the conclusions that were being made. Along the way, I described the salient features of key experimental techniques and referred the reader to a more detailed discussion in the last chapter on methodologies. Chapters 8 and 9, for example, contain introductory sections on techniques that have proven most important in the analysis of cytomembranes and the cytoskeleton, respectively. I included brief discussions of selected experiments of major importance in the body of the chapters to reinforce the experimental basis of our knowledge. I placed the more detailed aspects of methodologies in the final chapter because (1) I did not want to interrupt the flow of discussion of a subject with a large tangential section on technology and (2) I realized that different instructors prefer to discuss a particular technology in connection with different subjects.

  For students and instructors who wanted to explore the experimental approach in greater depth, I included the "Experimental Pathways" at the end of each chapter. Each of these narratives describes some of the key experimental findings that have led to our current understanding of a particular subject that is relevant to the chapter at hand. Because the scope of the narrative is limited, the design of the experiments can be considered in some detail. The figures and tables provided in these sections are often those that appeared in the original research article, which provides the reader an opportunity to examine original data and to realize that its analysis is not beyond their means. The Experimental Pathways also illustrate the stepwise nature of scientific discovery, showing how the result of one study raises questions that provide the basis for subsequent studies.
- I wanted a text that was interesting and readable. To make the text more relevant to undergraduate readers, particularly premedical students, I included The Human Perspective. These sections illustrate that virtually all human disorders can be traced to disruption of activities at the cellular and molecular level. Furthermore, they reveal the importance of basic research as the pathway to understanding and eventually treating most disorders. In Chapter 11, for example, The Human Perspective describes how small synthetic siRNAs may prove to be an important new tool in the treatment of cancer and viral diseases, including AIDS. In this same chapter, the reader will learn how the action of such RNAs were revealed in studies on nematodes. It becomes evident that one can never predict the practical importance of basic research in cell and molecular biology. I have also tried to include relevant information about human biology and clinical applications throughout the body of the text.
- I wanted a high-quality illustration program that helped students visualize complex cellular and molecular processes. To meet this goal, many of the illustrations have been "stepped-out" so that information can be more easily broken down into manageable parts. Events occurring at each step are described in the figure legend and/or in the corresponding text. I also sought to include a large number of micrographs to enable students to see actual representations of most subjects being discussed.

Included among the photographs are many fluorescence micrographs that illustrate either the dynamic properties of cells or provide a means to localize a specific protein or nucleic acid sequence. Wherever possible, I have tried to pair line art drawings with micrographs to help students compare idealized and actual versions of a structure.

I have been gratified by the mail I have received from teachers and students containing both praise and criticism of the first three editions. These communications, together with numerous fine reviews of the current manuscript, have guided the preparation of the fourth edition. The most important changes in the fourth edition can be delineated as follows:

- The body of information in cell and molecular biology is continually changing, which provides much of the excitement we all feel about our selected field. Even though only three years have passed since the publication of the third edition, nearly every discussion in the text has been modified to a greater or lesser degree. This has been done without allowing the chapters to increase in length.
- Several of the Experimental Pathways from the first edition have been removed from the text and placed on the World Wide Web. Of the 17 original Experimental Pathways, 9 have been retained in the text (Chapters 1, 2, 4, 8, 10, 11, 14, 16, and 17), whereas 7 others can be found on the web at www.wiley.com/college/karp. The latter Experimental Pathways are indicated by a mouse icon where they are referred to in the text. Experimental Pathways have been updated where appropriate. The Experimental Pathway from Chapter 3 on the mechanism of lysozyme catalysis has been deleted in the light of new findings that appear to have invalidated much of its content.
- Two of the Human Perspectives from the third edition have been replaced. The Human Perspective on muscular dystrophy in Chapter 9 has been replaced by a discussion of diseases that result from abnormal ciliary function, and the Human Perspective on the use of ribozymes and antisense oligonucleotides in Chapter 11 has been replaced with a discussion of the potential use of siRNAs in the treatment of disease.
- Every illustration in the third edition has been scrutinized and many of those that were reutilized in the fourth edition have been modified to some extent. Many of the drawings from the third edition have been deleted to make room for approximately 65 new pieces. Instructors have expressed particular approval for figures that juxtapose line art and micrographs, and this style of illustration has been expanded in the fourth edition. Altogether, the fourth edition contains approximately 90 new micrographs and computer-derived images, all of which were provided by the original source.

Supplements

New Web Site (www.wiley.com/college/karp)
This text-specific web site provides students with additional resources and extends the chapters of the text to the resources of the World Wide Web.

Resources include:

- Animations of key concepts based on illustrations in the text.
- Weblinks to some of the best cell biology sites currently available, updated every semester.
- Answers to the end-of-chapter analytic questions for students to check their understanding of the material.
- Instructor ancillaries are also available for download.

Student Study Guide
Written by Nancy L. Pruitt of Colgate University, the study guide offers students a great way to review materials from the text and test their knowledge. The following six tools have been included to help students master the material: Learning Objectives, Key Terms and Phrases, Reviewing the Chapter, Key Figures, Questions for Thought, Review Problems.

Take Note!
An art notebook that contains noteworthy figures from the text, allowing students to take notes directly on the page during class or lecture. This is a perfect student companion to presentations using PowerPoint slides or Transparencies.

Laboratory Investigations in Cell and Molecular Biology, Fourth Edition, by Allyn Bregman, State University of New York, New Paltz. This lab manual contains over 20 projects that cover key concepts in cell and molecular biology, such as, biochemistry and cytochemistry; organelles and their physiology; and more advanced molecular topics, including restriction mapping strategies.

Instructor's Image Manager
New to this edition is a comprehensive dual platform CD-ROM. An essential resource for classroom presentations, this CD contains every piece of line art, photograph and table from the text. Animations from the student website are also included on the image manager. The figures have been broken into consecutive steps where appropriate, to simplify complex processes. Leader lines and labels have been enlarged for clear viewing in large classrooms. The figures are offered both as preloaded PowerPoint™ presentations as well as JPEG files.

Instructor's Manual and Test Bank
Written by Joel Piperberg of Millersville University, these tools make class preparation time more efficient. Instructor's manual includes objectives, lecture outlines, and lecture hints. Test bank includes critical thinking questions, Experimental Pathway questions, Human Perspective questions, and art questions. For this edition, we've also added a new section of multiple-choice questions to make grading large classes easier.

Full Color Transparencies
Full-color acetates for key illustrations are provided for classroom presentation. The images have been enlarged and fonts bolded for better projection and clarity in the classroom.

To the Student

At the time I began college, biology would have been at the bottom of a list of potential majors. I enrolled in a physical anthropology course to fulfill the life science requirement by the easiest possible route. During that course, I learned for the first time about chromosomes, mitosis, and genetic recombination, and I became fascinated by the intricate activities that could take place in such a small volume of cellular space. The next semester, I took Introductory Biology and began to seriously consider becoming a cell biologist. I am burdening you with this personal trivia so you will understand why I wrote this book and to warn you of possible repercussions.

Even though many years have passed, I still find cell biology the most fascinating subject to explore, and I still love spending the day reading about the latest findings by colleagues in the field. Thus, for me, writing a text in cell biology provides a reason and an opportunity to keep abreast with what is going on throughout the field. My primary goal in writing this text is to help generate an appreciation in students for the activities in which the giant molecules and minuscule structures that inhabit the cellular world of life are engaged. Another goal is to provide the reader with an insight into the types of questions that cell and molecular biologists ask and the experimental approaches they use to seek answers. As you read the text, think like a researcher; consider the evidence that is presented, think of alternate explanations, plan experiments that could lead to new hypotheses.

You might begin this approach by looking at one of the many electron micrographs that fill the pages of this text. To take this photograph, you would be sitting in a small, pitch-black room in front of a large metallic instrument whose column rises several meters above your head. You are looking through a pair of binoculars at a vivid, bright green screen. The parts of the cell you are examining appear dark and colorless against the bright green background. They are dark because they've been stained with heavy metal atoms that deflect a fraction of the electrons within a beam that is being focused on the viewing screen by large electromagnetic lenses in the wall of the column. The electrons that strike the screen are accelerated through the evacuated space of the column by a force of tens of thousands of volts. One of your hands may be gripping a knob that controls the magnifying power of the lenses. A simple turn of this knob can switch the image in front of your eyes from that of a whole field of cells to a tiny part of a cell, such as a few ribosomes or a small portion of a single membrane. By turning other knobs, you can watch different parts of the specimen glide across the screen, giving you the sensation that you're driving around inside a cell. Once you have found a structure of interest, you can turn a handle that lifts the screen out of view, allowing the electron beam to strike a piece of film and produce a photographic image of the specimen.

Because the study of cell function generally requires the use of considerable instrumentation, such as the electron microscope just described, the investigator is physically removed from the subject being studied. To a large degree, cells are like tiny black boxes. We have developed many ways to probe the boxes, but we are always groping in an area that cannot be fully illuminated. A discovery is made or a new technique is developed and a new thin beam of light penetrates the box. With further work, our understanding of the structure or process is broadened, but we are always left with additional questions. We generate more complete and sophisticated constructions, but we can never be sure how closely our views approach reality. In this regard, the study of cell and molecular biology can be compared to the study of an elephant as conducted by six blind men in an old Indian fable. The six travel to a nearby palace to learn about the nature of elephants. When they arrive, each approaches the elephant and begins to touch it. The first blind man touches the side of the elephant and concludes that an elephant is smooth like a wall. The second touches the trunk and decides that an elephant is round like a snake. The other members of the group touch the tusk, leg, ear, and tail of the elephant, and each forms his impression of the animal based on his own limited experiences. Cell biologists are limited in a similar manner to what they can learn by using a particular technique or experimental approach. Although each new piece of information adds to the preexisting body of knowledge to provide a better concept of the activity being studied, the total picture remains uncertain.

Before closing these introductory comments, let me take the liberty of offering the reader some advice: Don't accept everything you read as being true. There are several reasons for urging such skepticism. Undoubtedly, there are errors in this text that reflect the author's ignorance or misinterpretation of some aspect of the scientific literature. But, more importantly, we should consider the nature of biological research. Biology is an empirical science; nothing is ever proved. We compile data concerning a particular cell organelle, metabolic reaction, intracellular movement, etc., and draw some type of conclusion. Some conclusions rest on more solid evidence than others. Even if there is a consensus of agreement concerning the "facts" regarding a particular phenomenon, there are often several possible interpretations of the data. Hypotheses are put forth and generally stimulate further research, thereby leading to a reevaluation of the original proposal. Most hypotheses that remain valid undergo a sort of evolution and, when presented in the text, should not be considered wholly correct or incorrect.

Cell biology is a rapidly moving field and some of the best hypotheses often generate considerable controversy. Even though this is a textbook where one expects to find material that is well tested, there are many places where new ideas are presented. These ideas are often described as models. I've included such models because they convey the current thinking in the field, even if they are speculative. Moreover, they reinforce the idea that cell biologists operate at the frontier of science, an area between the known and unknown. Remain skeptical.

Acknowledgments

Many people contributed to the development of this book. I would first like to acknowledge Peter van der Geer of the Department of Chemistry and Biochemistry at the University of California, San Diego. Peter was gracious enough to take on the primary responsibility for revision of Chapter 15 on cell communication. I am grateful to Geraldine Osnato who served as an outstanding editor on the project. Together, we plotted the course for this revision and I was always able to count on her sound judgment. Thanks, Geraldine, for your help and advice. I am particularly indebted to the production staff at John Wiley & Sons, who are simply the best. Barbara Russiello, the Production Editor, has truly been a guiding force for the last three editions. Barbara is dedicated to producing the best possible text, regardless of the time and energy she has to expend to achieve this goal. Hilary Newman and Anna Melhorn were responsible for the photo and line-art programs, respectively. It has been my good fortune to work with Hilary on all four editions of this text. Hilary is skillful and perseverant, and I have utmost confidence in her ability to obtain any image requested. It was also a great pleasure working with Anna for the second time. The book has a complex illustration program and Anna did a superb job in coordinating all of the many facets required to guide it to completion. I was fortunate, once again, to have Harry Nolan as the senior designer. Harry has directed a vibrant style for the chapters and an elegant design for the cover. Clay Stone has been a terrific marketing manager for the past edition, which gives me confidence he will be successful in the effort that lies ahead. I would also like to thank the artists at Imagineering for creating all of the new illustrations and Kierstan Hong, in particular, for playing such an important role in coordinating the art program. I have been very pleased with the high quality of the artwork that the studio has rendered. Thanks also to Professors David Asai and Ken Robinson of Purdue University for providing a number of interesting analytic questions in Chapters 2–5. A special thanks to Dana Kasowitz, who handled most of the editorial communications and was always so helpful. I would also like to thank Brian Rose, who copy edited the manuscript; Adriane Ruggiero, who proofread the pages; Steve Ingle, who prepared the index; and Dr. Elizabeth Coolidge-Stolz, who wrote the original glossary for the first edition.

I am especially grateful to the many biologists who have contributed micrographs for use in this book; more than any other element, these images bring the study of cell biology to life on a printed page. Finally, I would like to apologize, in advance, for any errors that may occur in the text, and express my heartfelt embarrassment. Any comments or criticisms from readers would be greatly appreciated. They can be directed to: Biology Editor, John Wiley & Sons, 111 River Street, Hoboken, NJ 07030.

In preparing the final version of the manuscript for the third edition, I sought the advice of numerous scientists whose work I have admired. I asked these individuals to review a chapter or two, and most were very gracious in agreeing to help with the project. I am grateful for the constructive criticism and sound advice from the following reviewers:

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