PREFACE

My desire to write this genetics textbook actually stemmed from a cell biology course that I introduced at the University of Minnesota many years ago. Our department decided to offer an intermediate-level cell biology course to bridge the gap between our basic undergraduate cell biology course and a more advanced graduate course, and I was asked to create it. I developed and taught this course for many years. It was a particularly fun experience, but I must admit that it got off to a rocky start. Let me explain.

The goal was to develop an intermediate cell biology course that used an undergraduate level of explanation but incorporated experiments from actual research papers. For each class session, the students were expected to read one or two research papers and understand them enough to discuss them in class. As a young, naive yet enthusiastic assistant professor, I thought this was a good plan. During the first few weeks of this course, however, I would walk into the classroom each day and say to the class, "So, tell me about the first experiment in the paper you were supposed to read for today." I was hoping that lots of volunteers would go to the blackboard and explain the experiment. But instead, I received the "deer in the headlights" response. Obviously something was wrong.

I knew that the problem wasn't the students in the course, because many of our brightest and hardest working students were enrolled. Hoping that I wasn't the problem, I sought another cause. Over time, the students and I uncovered the problem. Their previous coursework had not trained them to analyze experiments according to the scientific method. Sure, they had learned many "facts" and bits and pieces of experiments, but they hadn't been exposed, in a systematic and rigorous way, to the scientific process. We needed to fix that.

To transform the intermediate cell biology course into a success, the students and I had to develop a systematic way to dissect the parts of each research experiment. Looking back on it, the solution seems obvious: we needed to follow the scientific method. To integrate this process into our class discussions, I would ask the class the same series of questions for each experiment:

1. **Why was this experiment done?** The students' answers would have two parts. First, they would need to consider the background work that led to the experiment. And second, the students would have to explicitly state the hypothesis that the researchers were trying to test.
2. **How was the experiment done?** As a class, we would generate a flow diagram that described the experimental methods.
3. **What are the results?** We would look at the raw data and quantitatively analyze it.
4. **What do the results mean?** We would discuss our interpretations of the data. The goal of such interpretations was to derive conceptual ideas that underlie the experimental data. Sometimes, our interpretations were quite different from the researchers who had actually done the experiments. The occasional conflict between our interpretations and those of the researchers provided the most meaningful moments in the classroom. It caused many students to realize that the scientific concepts and principles they had learned about in previous courses are the product of scientific interpretations of research data. And maybe, they aren't always right!

I have to say that the intermediate cell biology course has been my most inspiring teaching experience. What I mean is that the students were inspiring to me. (I hope that I was inspiring to them as well.) On the positive side, it was impressive to see how the students' abilities to analyze experiments improved as the course progressed. The course turned out to be really fun for the students because it was the first time that many of them had taken a college course that allowed them to unleash their curiosity and use their critical thinking skills. It was also fun for me because I could witness this happening. On the negative side, however, it left me with a deeply disappointing sense that most college-level science courses do not provide students with an adequate exposure

to the scientific process. To some extent, I felt that textbooks were to blame. In an effort to include too much information, science textbooks had largely deleted the essence of science, namely, the scientific method. At that point, I decided to write a textbook that would incorporate the scientific method into each chapter. Since my primary background is in genetics rather than cell biology, it was logical for me to write a genetics textbook, although I strongly feel that all scientific disciplines would benefit from this approach.

As you will see when you use this textbook, each chapter (beginning with chapter 2) incorporates one or two experiments that are presented according to the scientific method. These experiments are not "boxed off" from the rest of the chapter for you to read in your spare time. Rather, they are integrated within the chapters and flow with the rest of the text. As you are reading the experiments, you will simultaneously explore the scientific method and the genetic principles that have been learned from this approach. For students, I hope this textbook will help you to see the fundamental connection between scientific analysis and principles. For both students and instructors, I expect that this strategy will make genetics much more fun to explore.

HOW WE EVALUATED YOUR NEEDS

ORGANIZATION

In surveying many genetics instructors, it became apparent that most people fall into two camps: **Mendel first** versus **Molecular first.** I have taught genetics both ways on many occasions. As a teaching tool, this textbook has been written with these different teaching strategies in mind. The organization and content lend themselves to such different formats of teaching.

Chapters 2 through 8 are largely inheritance chapters, while chapters 24 to 26 examine quantitative and population genetics. The bulk of the molecular genetics is found in chapters 9 through 23, although I have tried to weave a fair amount of molecular genetics into chapters 2 through 8 as well. The information in chapters 9 to 23 *does not assume* that a student has already covered chapters 2 through 8. Actually, each chapter is written with the perspective that instructors may want to vary the order of their chapters to fit their students' needs.

For those who like to discuss inheritance patterns first, a common strategy would be to cover chapters 1 to 8 first, and then possibly 24 to 26. (However, many instructors like to cover quantitative and population genetics at the end. Either way works fine.) The more molecular and technical aspects of genetics would then be covered in chapters 9 through 23. Alternatively, if you like the "Molecular first" approach, you would probably cover chapter 1, then skip to chapters 9 to 23, then return to chapters 2 to 8, and then cover chapters 24 to 26 at the end of the course. This textbook was written in such a way that either strategy works just fine.

ACCURACY

Both the publisher and I acknowledge the fact that inaccuracies can be a source of frustration for both the instructor and students. Therefore, throughout the writing and production of this textbook we have worked diligently to catch and correct errors during each phase of development and production.

A team of seven instructors worked as an accuracy consultant panel and checked every chapter, illustration, and problem in the textbook. I also had a team of students work through all the problems sets.

The page proofs were double-proofread against the manuscript to ensure the correction of any errors introduced when the manuscript was typeset. The textual examples, practice problems and solutions, end-of-chapter questions and problems, and problem answers were accuracy checked by reviewers and students again at page proof stage after the manuscript was typeset. This last round of corrections was then cross-checked against the solution manuals.

PEDAGOGY

Based on our discussions with instructors from many institutions, some common goals have emerged. Instructors want a broad textbook that clearly explains concepts in a way that is interesting, accurate, concise, and up-to-date. Likewise, most instructors want students to understand the experimentation that revealed these genetic concepts. In this textbook, concepts and experimentation are woven together to provide a story that enables students to learn the important genetic concepts that they will need in their future careers, and also to be able to explain the types of experiments that allowed researchers to derive such concepts. The end-of-chapter problem sets are categorized according to their main focus, either conceptual or experimental, although some problems contain a little of both. The problems are meant to strengthen students' abilities in a wide variety of ways.

- By bolstering their understanding of genetic principles.
- By enabling students to apply genetic concepts to new situations.
- By analyzing scientific data.
- By organizing their thoughts regarding a genetic topic.
- By improving their writing skills.

Finally, since genetics is such a broad discipline ranging from the molecular to the populational levels, many instructors have told us that it is a challenge for students to see both "the forest and the trees." It is commonly mentioned that students often have trouble connecting the concepts they have learned in molecular genetics with the traits that occur at the level of a whole organism. For example, What does transcription have to do with blue eyes? To try to make this connection more meaningful, certain figure legends in each chapter, designated **Genes → Traits,** remind students that molecular and cellular phenomena ultimately lead to the traits that are observed in each species (see fig. 4.13).

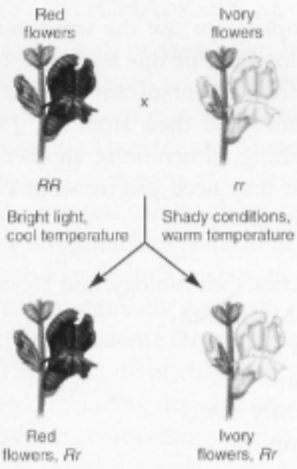

FIGURE 4.13 Variation in the expression of a trait due to environmental effects.

GENES→TRAITS In this example, snapdragon flower color in the heterozygote, *Rr*, is affected by the amount of light and temperature in the plant's environment. Presumably, the protein encoded by this gene is sensitive to changes in temperature and light intensity.

ILLUSTRATIONS

In surveying students whom I teach, I often hear it said that most of their learning comes from studying the figures. Likewise, instructors frequently use the illustrations from a textbook as a central teaching tool. For these reasons, the greatest amount of effort in improving the second edition has gone into the illustrations. Every illustration of the second edition has been redrawn with four goals in mind:

1. **Completeness** For most figures, it should be possible to understand an experiment or genetic concept by looking at the illustration alone. Students have complained that it is difficult to understand the content of an illustration if they have to keep switching back and forth between the figure and text. In cases where an illustration shows the steps in a scientific process, the steps are described in brief statements that allow the students to understand the whole process (e.g., see fig. 12.9). Likewise, such illustrations should make it easier for instructors to explain these processes in the classroom.
2. **Clarity** The figures have been extensively reviewed by students and instructors. This has helped us to avoid drawing things that may be confusing or unclear. I hope that no one looks at an element in any figure and wonders, "What is that thing?" Aside from being unmistakably drawn, all new elements within each figure are clearly labeled.
3. **Consistency** Before we began to draw the figures for the second edition, we generated a style sheet that contained recurring elements that are found in many places in the textbook. Examples include the DNA double helix, DNA polymerase, and fruit flies. We agreed upon the best way(s) to draw these elements and also what colors they should be. Therefore, as students and instructors progress through this textbook, they become accustomed to the way things should look.
4. **Realism** An important, albeit tiring, goal of this second edition was to make each figure as realistic as possible. When drawing macroscopic elements (e.g., fruit flies, pea plants), the illustrations were based on real images, not on cartoon-like simplifications. Our most challenging goal, and one that we feel has been the most successful in this second edition, was the realism of our molecular drawings. Whenever possible, we tried to draw molecular elements according to their actual structures, if such structures are known. For example, the ways we have drawn RNA polymerase, DNA polymerase, DNA helicase, and ribosomes are based on their crystal structures. When a student sees a figure in this textbook that illustrates an event in transcription, RNA polymerase is depicted in a way that is as realistic as possible (e.g., see fig. 12.9).

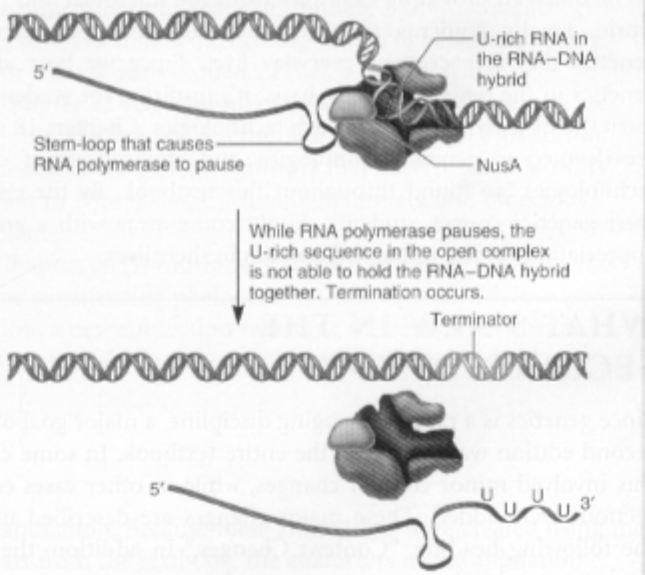

FIGURE 12.9 ρ-independent or intrinsic termination. When RNA polymerase reaches the end of the gene, it transcribes a uracil-rich sequence. Soon after this uracil-rich sequence is transcribed, a stem-loop forms just upstream from the open complex. The formation of this stem-loop causes RNA polymerase to pause in its synthesis of the transcript. This pausing is stabilized by NusA, which binds near the region where RNA exits the open complex. While it is pausing, the RNA-DNA hybrid region is a uracil-rich sequence. Since UA hydrogen bonds are relatively weak interactions, the transcript and RNA polymerase dissociate from the DNA.

WRITING STYLE

Motivation in learning often stems from enjoyment. If someone enjoys what they're reading, they are more likely to spend longer amounts of time with it and focus their attention more crisply. The writing style of this book is meant to be interesting, down to earth, and easy to follow. Each section of every chapter begins with an overview of the contents of that section, usually with a table or figure that summarizes the broad points. The section then unfolds as a story that examines how those broad points were discovered experimentally, as well as explaining many of the finer scientific details. Important terms are introduced in a boldface font. These terms are also found in the glossary.

There are various ways to make a genetics book interesting and inspiring. The subject matter itself is pretty amazing, so it's not difficult to build on that. In addition to describing the concepts and experiments in ways that motivate students, it is important to draw upon examples that bring the concepts to life. In a genetics book, many of these examples come from the medical realm. This textbook contains lots of examples of human diseases that exemplify some of the underlying principles of genetics. Students often say that they remember certain genetic concepts because they remember how defects in certain genes can cause disease. For example, defects in DNA repair genes cause a higher predisposition to develop cancer. In addition, I have tried to be evenhanded in providing examples from the microbial and plant world. Finally, students are often interested in applications of genetics that impact their everyday lives. Since we hear about genetics in the news on a daily basis, it's inspiring for students to learn the underlying basis for such technologies. Chapters 18 to 21 are devoted to genetic technologies, and applications of other technologies are found throughout this textbook. By the end of their genetics course, students should come away with a greater appreciation for the impact of genetics in their lives.

WHAT'S NEW IN THE SECOND EDITION?

Since genetics is a rapidly changing discipline, a major goal of the second edition was to update the entire textbook. In some cases, this involved minor content changes, while in other cases entire sections were added. These major changes are described under the following heading, "Content Changes." In addition, the following general improvements were made:

- **Illustrations** As mentioned earlier in the Preface, all of the illustrations in the second edition were newly drawn using state-of-the-art technology. These illustrations were drawn with an eye toward completeness, clarity, consistency, and realism.
- **Problem sets** A large number of new and challenging problems were added to the problem sets of every chapter.
- **Animations** The student and instructor CD-ROM contains over 40 animations.
- **Website (Online Learning Center)** As described later in this Preface, the website for the instructor and students contains a much wider variety of resources and activities.

SUGGESTIONS WELCOME!

It seems very appropriate to use the word *evolution* to describe the continued development of this textbook. I welcome any and all comments. The refinement of any science textbook requires input from instructors and their students. These include comments regarding writing, illustrations, supplements, factual content, and topics that may need greater or less emphasis. You are invited to contact me at:

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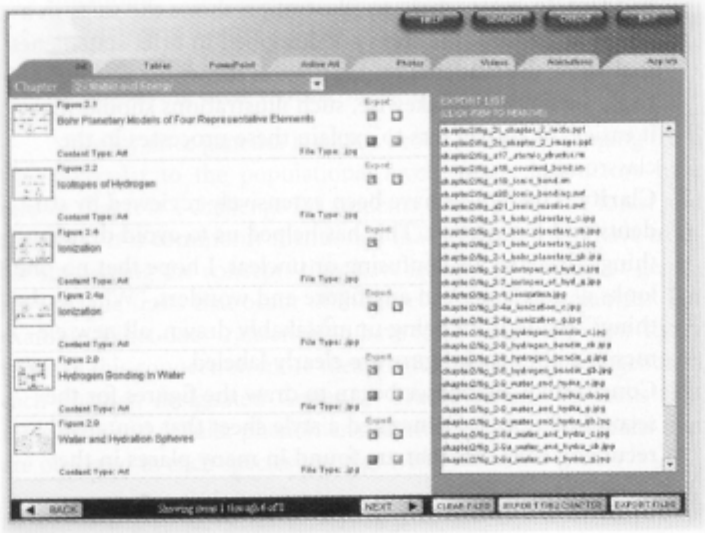
TEACHING AND LEARNING SUPPLEMENTS

McGraw-Hill offers various tools and technology products to support the second edition of *Genetics: Analysis and Principles.* Students can order supplemental study materials via their bookstore. Instructors can obtain teaching supplements by calling the Customer Service Department at 800-338-3987, by visiting our textbook website at www.mhhe.com/brooker, or by contacting their local McGraw-Hill sales representative.

FOR THE INSTRUCTOR:

Digital Content Manager CD-ROM
This multimedia collection of visual resources allows instructors to use artwork from the textbook in multiple formats to create customized classroom presentations, visually based tests and quizzes, dynamic course website content, or attractive printed support material. The digital assets on this cross-platform CD-ROM are grouped by chapter within the following easy-to-use folders:



MAJOR CONTENT CHANGES

- **Chapter 4 (Extensions of Mendelian Inheritance)** A greater emphasis is placed on the molecular mechanisms that underlie the various patterns of inheritance.
- **Chapter 6 (Genetic Transfer and Mapping in Bacteria and Bacteriophages)** The process of bacterial conjugation is updated and more realistically illustrated.
- **Chapter 7 (Non-Mendelian Inheritance)** The molecular mechanisms that underlie X inactivation and genomic imprinting are substantially updated.
- **Chapter 10 (Chromosome Organization and Molecular Structure)** The structure of eukaryotic chromosomes is greatly updated including descriptions of the nuclear matrix, chromatin remodeling proteins, and two multiprotein complexes called condensin and cohesin, which play a critical role in chromosomal condensation and sister chromatid alignment.
- **Chapter 11 (DNA Replication)** Descriptions are presented of newly discovered DNA polymerases, such as lesion-replicating polymerases, along with updates regarding the molecular mechanisms of the DNA polymerases that play a major role in DNA replication.
- **Chapter 12 (Gene Transcription and RNA Modification)** This chapter contains updated information regarding the structure of RNA polymerase, the functions of general transcription factors, and the role of chromatin remodeling during transcription.
- **Chapter 15 (Gene Regulation in Eukaryotes)** This area has changed considerably since the first edition. New information regarding the roles of TFIID and mediator, which communicate the effects of regulatory transcription factors, was added, along with the importance of chromatin remodeling for transcriptional activation and silencing. A new subsection on RNA interference also was added.
- **Chapter 16 (Gene Mutation and DNA Repair)** A new subsection was added that explains some of the chemical changes that underlie spontaneous mutations. Also, a subsection was added that concerns the roles of translesion DNA polymerases in the replication of damaged DNA.
- **Chapter 19 (Biotechnology)** The topic of stem cells has received considerable attention in the news lately. In a new subsection, which contains three figures and one table, the genetic issues that underlie the proliferative capacities of stem cells are discussed, along with their potential applications and societal concerns.
- **Chapter 20 (Structural Genomics)** Since the first edition, the area of genomics has expanded to the point where it needs to be divided into two chapters. Chapter 20 contains the updated methods that are used to dissect genomes and sequence them.
- **Chapter 21 (Functional Genomics, Proteomics, and Bioinformatics)** The first two sections of this chapter are new to the second edition. Functional genomics includes updates to topics such as EST libraries, subtractive libraries, and the applications of DNA microarrays. The proteomics section explains the techniques of two-dimensional gel electrophoresis, mass spectrometry, and protein microarrays. The bioinformatics section is supplemented with tools at our Online Learning Center, where students can actually run programs to analyze sequence files. These include programs that can translate a DNA sequence, generate a multiple sequence alignment, or search databases for homologous sequences (i.e., a BLAST search).
- **Chapter 23 (Developmental Genetics)** An entire new section regarding sex determination was added. This section describes the genetic pathways that govern sex determination in *Drosophila*, *C. elegans*, mammals, and dioecious plants.
- **Chapter 26 (Evolutionary Genetics)** The UPGMA method for constructing phylogenetic trees is described. In addition, a new subsection regarding the role of horizontal gene transfer in the evolution of species was added.

Art Library Full-color digital files of all illustrations in the textbook, plus the same art saved in gray-scale versions, can be readily incorporated into lecture presentations, exams, or custom-made classroom materials.

TextEdit Art Library Every art piece is placed into a PowerPoint presentation that allows the user to revise, move, or delete labels as desired for creation of customized presentations and/or for testing purposes.

Active Art Library Active Art consists of art files that have been converted to a format that allows the artwork to be edited inside PowerPoint. Each piece can be broken down to its core elements, grouped or ungrouped, and edited to create customized illustrations.

Animations Library Full-color presentations involving key figures in the textbook have been brought to life via animation. Because these animations were created using the art from the textbook, the characters in the animation match those found in the textbook.

Photo Library Like the Art Library, digital files of all photographs from the textbook are available.

Table Library Every table that appears in the textbook is provided in electronic form.

PowerPoint Lecture Outlines Based on the information in the Instructor's Manual (described next), it is possible to create ready-made presentations that combine art and lecture notes for each of the 26 chapters of the textbook. Written by Johnny El-Rady, University of South Florida, these lectures can be used as they are or customized to reflect your preferred lecture topics and sequences.

Instructor's Testing and Resource CD-ROM This cross-platform CD-ROM contains the Instructor's Manual, Test Item File, and Solutions Manual/Study Guide, all written by Michael Windelspecht, Appalachian State University. The manual follows the order of sections and subsections in the textbook and summarizes the main points in the text, figures, and tables. The Instructor's Manual also includes links to relevant websites, answers to the problem sets at the end of each chapter, and a Test Bank of additional questions that can be used for homework assignments and/or the preparation of exams. These additional questions are found in a computerized test bank using Brownstone Diploma testing software to quickly create customized exams. This user-friendly program allows instructors to search questions by topic, format, or difficulty level; edit existing questions or add new ones; and scramble questions and answer keys for multiple versions of the same test.

Transparencies A set of 600 transparency overheads includes nearly every piece of line art and all the tables from the textbook. The images are printed with better visibility and contrast than ever before, and labels are large and bold for clear projection.

eInstruction This Classroom Performance System (CPS) brings interactivity into the classroom/lecture hall. It is a wireless response system that gives the instructor and students immediate feedback from the entire class. The wireless response pads are essentially remotes that are easy to use and engage students. CPS allows you to motivate student preparation, interactivity, and active learning so you can receive immediate feedback and know what students understand.

Course Delivery Systems With help from our partners, WebCT, Blackboard, TopClass, eCollege, and other course management systems, instructors can take complete control over their course content. These course cartridges also provide online testing and powerful student tracking features. The Brooker Online Learning Center is available within all of these platforms.

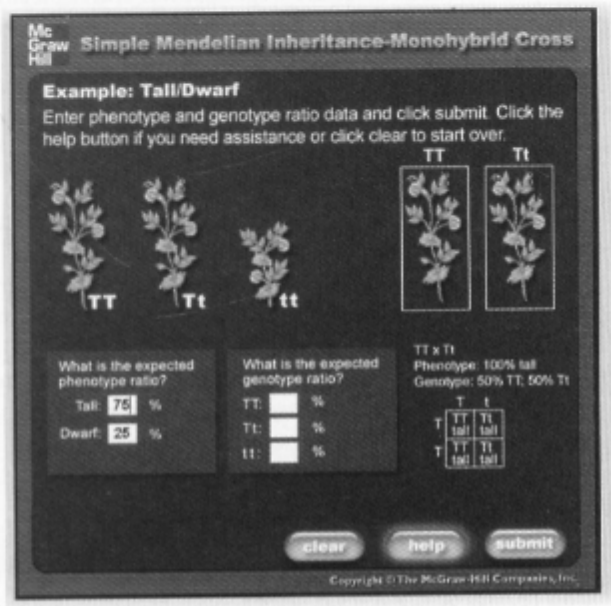
FOR THE STUDENT:

Solutions Manual/Study Guide The solutions to the end-of-chapter problems and questions will aid the students in developing their problem-solving skills by providing the steps for each solution. The Study Guide follows the order of sections and subsections in the textbook and summarizes the main points in the text, figures, and tables. It also contains concept-building exercises, self-help quizzes, and practice exams.

Brooker Interactive CD-ROM Set up in an easy to use tabular format, this dual-platform CD-ROM is a fully interactive learning tool. The CD is organized chapter-by-chapter and provides a link directly to the text's Online Learning Center. Standard features include chapter-based quizzes, animations of complex processes, and PowerPoints of all the images found in the textbook. Brooker Interactive CD-ROM offers an indispensable resource for enhancing topics covered within the text.

Online Learning Center Our website, which is organized according to the chapters in the textbook, has a variety of activities and resources that include the following:

Interactive Genetic Problems For chapters involving inheritance patterns and other quantitative problems (chapters 2, 3, 4, 5, 7, 24, and 25), students can set up crosses and attempt to predict the outcome according to genetic principles. Students have the freedom to alter parameters to see how such changes affect the outcome.



Computer Programs to Analyze Genetic Data For chapter 21, which involves issues of genomics and bioinformatics, students can access files that contain genetic data and run various types of computer programs. For example, students can use a DNA sequence file and run a program that translates it to an amino acid sequence according to the genetic code.

Tweaking the Experiment For the in-depth experiments that are found in each chapter, a self-help quiz is provided. The questions ask students to predict how changes in the experimental parameters may affect the outcome of the experiment. These quizzes should help students to improve their skills of designing experiments and predicting their outcome according to genetic hypotheses.

Answers to Problem Sets The answers to all of the problems in the textbook are given.

References Classic and modern references to the literature are provided for each chapter.

Links Internet links to a variety of websites related to the course material are available according to the relevant chapter.

ACKNOWLEDGMENTS

The production of a textbook is truly a collaborative effort. I am greatly indebted to a variety of people. The first and second editions went through multiple rounds of rigorous revisions that involved the input of scientists, students, and editors. The collective contributions of all these people are reflected in the final outcome.

There are many people at McGraw-Hill whom I deeply respect and whose efforts are amazing. Since the McGraw-Hill people work as a well-greased and integrated team, it's sometimes difficult to sort out their relative contributions, but I'll do my best. Patrick Reidy, Senior Sponsoring Editor, and Marty Lange, Publisher, have been committed to the second edition since the very beginning. They provided important pedagogical input and maintained a level of financial commitment that was vital to the outcome of this project. Of course, Kris Tibbetts gets my highest amount of praise for her dedicated role of Director of Development. Her ability to organize the various components of this project is pretty incredible. Grinding through the process of writing a second edition can be unnerving at times, and it's really great to have someone you know you can count on. Other people at McGraw-Hill have played key roles in producing an actual book and the supplements that go along with it. In particular, Peggy Selle, Project Manager, was an important interface between me and the art and editorial staff. The input of Designer Wayne Harms was important with regard to the layout and design of the chapters and cover.

Outside of McGraw-Hill, several people/groups were involved with the production of this textbook. My copy editor, Laura Beaudoin, did an exceptional job of strengthening the writing with regard to clarity and consistency. I am deeply grateful. Chris Hammond should be acknowledged for his tireless work at locating photographs for the textbook. I would also like to extend a special thanks to the folks at Imagineering, the art house that produced the illustrations in this second edition. Though we initially considered several art houses, when I saw how Imagineering could draw RNA polymerase, it was clear who the winner was. Their ability to draw three-dimensional molecular structures is just plain outstanding. I particularly want to thank Kierstan Hong at Imagineering, who played a key role in communicating my vision to the art team.

I am also deeply indebted to my wife, Deborah, and kids, Dan, Nate, and Sarah, for keeping me grounded and for being excited about the first edition when it came out. I would also like to acknowledge that my wife, Deb, and my colleague Peter Franco have been my "super proofreaders." They tenaciously read the page proofs for all 26 chapters and provided critical input during the final stages of the second edition.

Finally, I want to thank the many scientists who reviewed the chapters of this textbook. Their broad insights and constructive suggestions were an important factor that shaped its final content and organization. I am truly grateful for their time and effort.

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