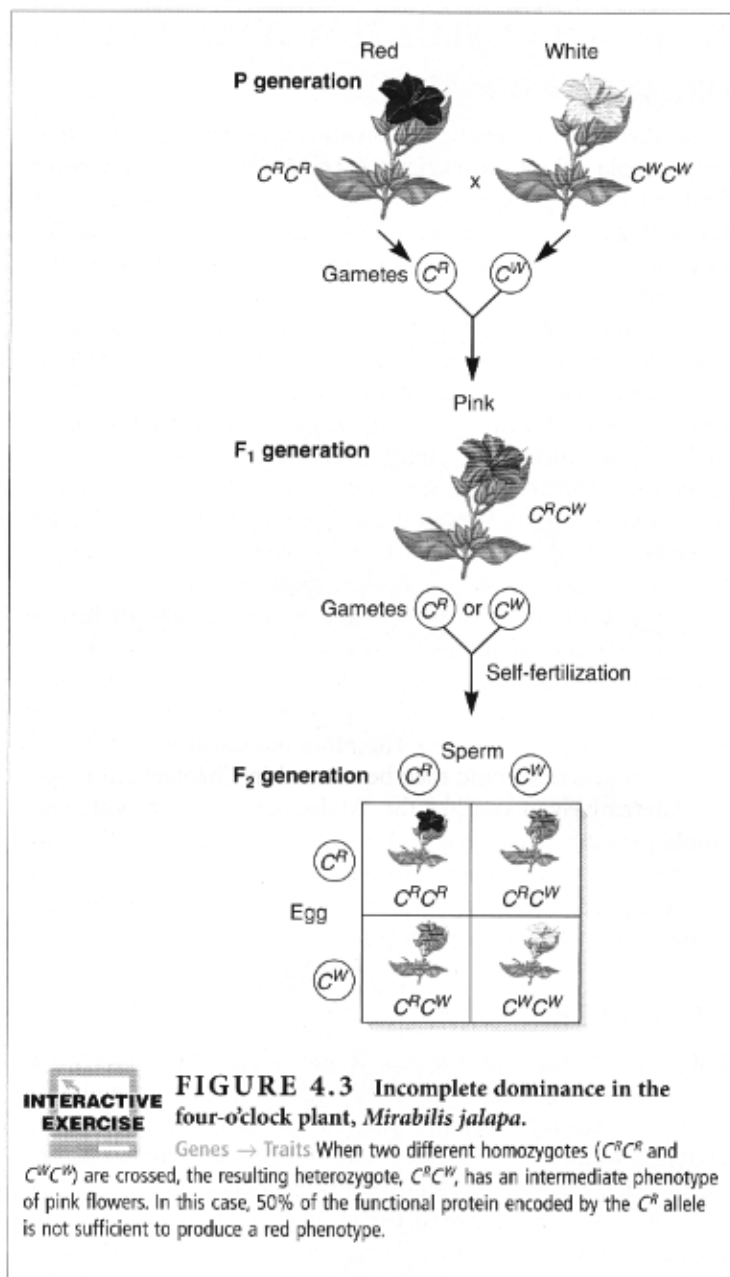


PREFACE



In the fourth edition of *Genetics: Analysis & Principles*, the content has been updated to reflect current trends in the field. In addition, the presentation of the content has been improved in a way that fosters active learning. As an author, researcher, and teacher, I want a textbook that gets students actively involved in learning genetics. To achieve this goal, I have worked with a talented team of editors, illustrators, and media specialists who have helped me to make the fourth edition of *Genetics: Analysis & Principles* a fun learning tool. The features that we feel are most appealing to students, and which have been added to or improved on in the fourth edition, are the following.

- **Interactive exercises** Education specialists have crafted interactive exercises in which the students can make their own choices in problem-solving activities and predict what the outcomes will be. Previously, these exercises focused on inheritance patterns and human genetic diseases. (For example, see Chapters 4 and 22.) For the fourth edition, we have also added many new interactive exercises for the molecular chapters.
- **Animations** Our media specialists have created over 50 animations for a variety of genetic processes. These animations were made specifically for this textbook and use the art from the textbook. The animations make many of the figures in the textbook “come to life.”
- **Experiments** As in the previous editions, 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. 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 discovered using this approach. For students, I hope this textbook helps you to see the fundamental connection between scientific analysis and principles. For both students and instructors, I expect that this strategy makes genetics much more fun to explore.
- **Art** The art has been further refined for clarity and completeness. This makes it easier and more fun for students to study the illustrations without having to go back and forth between the art and the text.
- **Engaging text** As in previous editions, a strong effort has been made in the fourth edition to pepper the text with questions. Sometimes these are questions that scientists considered when they were conducting their research.



Sometimes they are questions that the students might ask themselves when they are learning about genetics.

Overall, an effective textbook needs to accomplish three goals. First, it needs to provide comprehensive, accurate, and up-to-date content in its field. Second, it needs to expose students to the techniques and skills they will need to become successful in

that field. And finally, it should inspire students so they want to pursue that field as a career. The hard work that has gone into the fourth edition of *Genetics: Analysis & Principles* has been aimed at achieving all three of these goals.

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. As a teaching tool, this textbook has been written with these different teaching strategies in mind. The organization and content lend themselves to various teaching formats.

Chapters 2 through 8 are largely inheritance chapters, whereas Chapters 24 through 26 examine population and quantitative 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 through 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 through 8 first, and then possibly 24 through 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 through 23, then return to Chapters 2 through 8, and then cover Chapters 24 through 26 at the end of the course. This textbook was written in such a way that either strategy works well.

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 very hard to catch and correct errors during each phase of development and production.

Each chapter has been reviewed by a minimum of seven people. At least five of these people were faculty members who teach the course or conduct research in genetics or both. In addition, a development editor has gone through the material to check for accuracy in art and consistency between the text and art. With regard to the problem sets, the author personally checked every question and answer when the chapters were completed.

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 (i.e., 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 (e.g., see Figure 4.3).

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, a great amount of effort in improving the fourth edition has gone into the illustrations. The illustrations are created 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 Figure 11.16). 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 fourth 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 on 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 goal of this and previous editions is to make each figure as realistic as possible. When drawing macroscopic elements (e.g., fruit flies, pea plants), the illustrations are based on real images, not on cartoonlike simplifications. Our most challenging goal, and one that we feel has been achieved most successfully, is the realism of our molecular drawings. Whenever possible, we have tried to depict 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, for example proofreading DNA, DNA polymerase is depicted in a way that is as realistic as possible (e.g., see Figure 11.16).

WRITING STYLE

Motivation in learning often stems from enjoyment. If you enjoy what you're reading, you are more likely to spend longer amounts of time with it and focus your 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 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 on 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 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 affect their everyday lives. Because we frequently

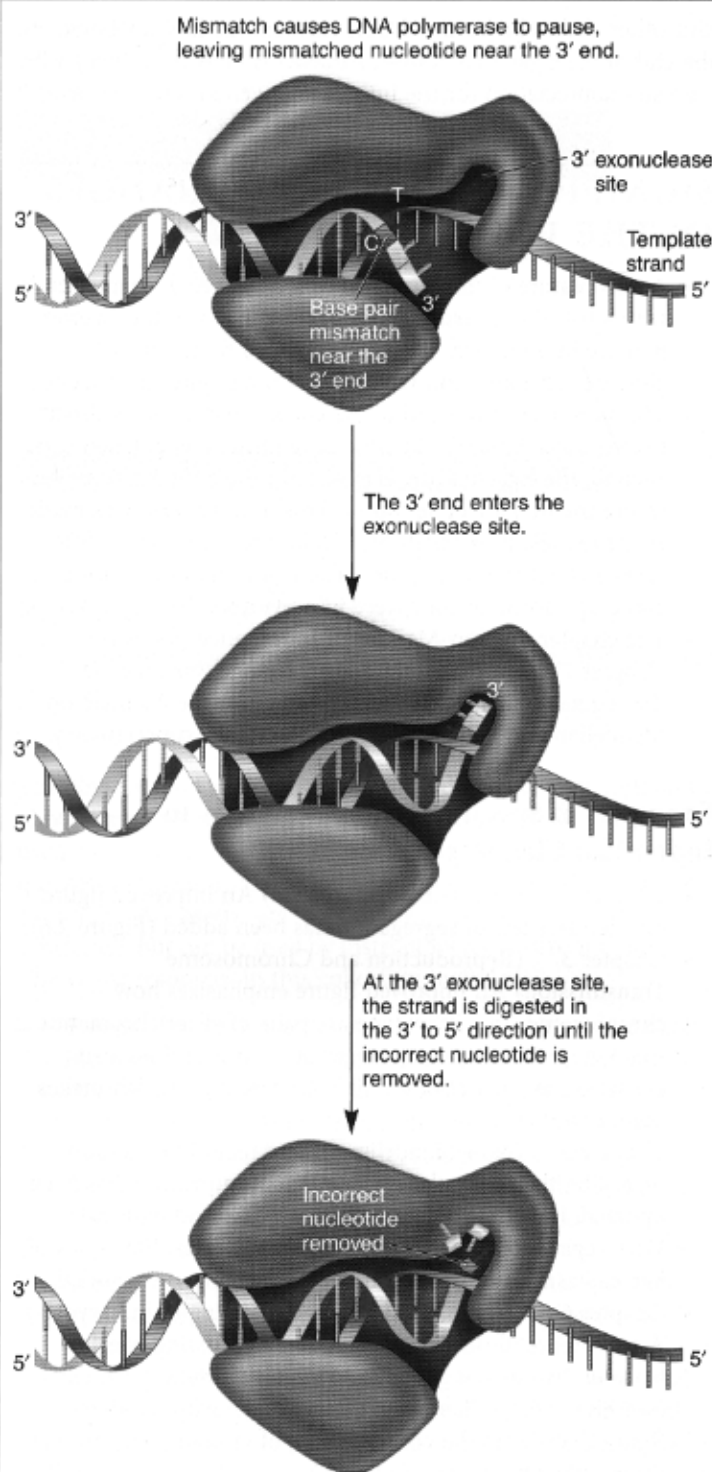


FIGURE 11.16 The proofreading function of DNA polymerase. When a base pair mismatch is found, the end of the newly made strand is shifted into the 3' exonuclease site. The DNA is digested in the 3' to 5' direction to release the incorrect nucleotide.

hear about genetics in the news, 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 these

and other technologies are found throughout this textbook. By the end of their genetics course, students should come away with a greater appreciation for the influence of genetics in their lives.

SIGNIFICANT CONTENT CHANGES IN THE FOURTH EDITION

- A new feature of the fourth edition is that each chapter ends with a list of key terms. These are the terms in the chapter that are in bold face. The terms are also found in the glossary. This addition was made at the request of students.
- The summary at the end of the chapter has been modified in two ways. First, the key points are found as bulleted lists. Second, the bulleted lists also refer to the figures and tables where the topics can be found. This modification was made at the request of students, who said that it was difficult to easily extract the main points from summaries that were in paragraph form, as they were in previous editions.
- The chapter on Non-Mendelian Inheritance (formerly Chapter 7) is now Chapter 5. This change was made at the request of instructors who often cover the chapters on Mendelian and Non-Mendelian inheritance consecutively.

Examples of Specific Content Changes to Individual Chapters

- Chapter 2 (Mendelian Inheritance) An improved figure on Mendel's law of segregation has been added (Figure 2.6).
- Chapter 3 (Reproduction and Chromosome Transmission) An improved figure emphasizes how chromosomes in a karyotype are pairs of sister chromatids (see Figure 3.6). Also, the stages of mitosis and meiosis are set off as subsections with bold headings, which makes them easier to follow.
- Chapter 5 (Non-Mendelian Inheritance) Information regarding the molecular mechanism of imprinting has been updated, including a description of CTC-binding factor. With regard to human mitochondrial diseases, the topics of heteroplasmy and somatic mutation have been expanded.
- Chapter 6 (Genetic and Linkage Mapping in Eukaryotes) A new figure illustrates the outcome of crossing over between two linked genes in Morgan's classic experiments (see Figure 6.4). This is then followed up with another figure that shows the consequences of crossing over among three linked genes (see Figure 6.5).
- Chapter 7 (Genetic Transfer and Mapping in Bacteria and Bacteriophages) A new figure depicts how F' factors arise by the imprecise excision of F factors from a chromosome (see Figure 7.5b).
- Chapter 8 (Variation in Chromosome Structure and Number) New information and figures have been added regarding nonallelic homologous recombination and copy number variation in populations (see Figures 8.5 and 8.8).
- Chapter 10 (Chromosome Organization and Molecular Structure) New figures have been added on the action of DNA gyrase and the relative amounts of unique and

repetitive sequences in the human genome (see Figures 10.9 and 10.12).

- Chapter 11 (DNA Replication) A new figure illustrates DNA replication from a single origin (see Figure 11.11). Also, the topic of how RNA primers are removed by flap endonuclease in eukaryotic cells has been added, which includes a new figure (see Figure 11.23).
- Chapter 12 (Gene Transcription and RNA Modification) The mechanism of transcriptional termination in eukaryotes via the allosteric or torpedo models has been added (see Figure 12.15). Also, RNA editing has been moved to this chapter.
- Chapter 13 (Translation of mRNA) A new figure describes Beadle and Tatum's study of methionine biosynthesis (see Figure 13.2). The topic of the incorporation of selenocysteine and pyrrolysine during translation has been added (see Table 13.3).
- Chapter 14 (Gene Regulation in Bacteria and Bacteriophages) This chapter has a new section on riboswitches (see pp. 377–378).
- Chapter 15 (Gene Regulation in Eukaryotes) A new section has been added on chromatin remodeling, histone variation, and histone modification (see pp. 397–403). A new figure describes the technique of chromatin immunoprecipitation sequencing (see Figure 15.11). A new section has been added on insulators (see pp. 406–407).
- Chapter 16 (Gene Mutation and DNA Repair) The topic of oxidative stress and oxidative DNA damage has been greatly expanded (see pp. 435–437). A new figure depicts the probable mechanism of trinucleotide repeat expansion (see Figure 16.12).
- Chapter 17 (Recombination and Transposition at the Molecular Level) A new figure describes the transposition of non-LTR retrotransposons (see Figure 17.18).
- Chapter 18 (Recombinant DNA Technology) The topic of polymerase chain reaction (PCR) is now expanded to an entire section, which includes several new figures that describe the steps of the PCR cycle, reverse transcriptase PCR, real-time PCR, and the classic experiment that demonstrated the feasibility of real-time PCR (see pp. 491–499).
- Chapter 19 (Biotechnology) A new feature experiment describes the method of gene therapy (see Figure 19.20).
- Chapter 20 (Genomics I: Analysis of DNA) A new subsection has been added on next-generation DNA sequencing methods, including a new figure on pyrosequencing (see pp. 564–566).
- Chapter 21 (Genomics II: Functional Genomics, Proteomics, and Bioinformatics) A new subsection has been added that discusses gene knockout collections.
- Chapter 22 (Medical Genetics and Cancer) Two new subsections have been added on haplotypes and haplotype association studies (see pp. 609–610, Figures 22.5–22.6). The topic of preimplantation genetic diagnosis has also been added. With regard to inherited forms of cancer, a new figure describes how the "loss of heterozygosity" leads to cancer (see Figure 22.22).

- Chapter 23 (Developmental Genetics) A new section has been added at the beginning of the chapter that provides a general overview of animal development (see pp. 638–641). This precedes the two sections on Invertebrate and Vertebrate Development.
- Chapter 24 (Population Genetics) A new figure shows the output from automated DNA fingerprinting (see Figure 24.22).
- Chapter 26 (Evolutionary Genetics) The topic of species concepts is more focused on the factors that are used to distinguish species; the general lineage concept is described (see pp. 734–736). A new example illustrates the concept of a molecular clock (see Figure 26.14).

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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FOR THE STUDENT:

Student Study Guide/Solutions Manual

The solutions to the end-of-chapter problems and questions 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.

Companion Website

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The *Brooker Genetics: Analysis & Principles* companion website offers an extensive array of learning tools, including a variety of quizzes for each chapter, interactive genetics problems, animations and more.



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ACKNOWLEDGMENTS

The production of a textbook is truly a collaborative effort, and I am greatly indebted to a variety of people. All four editions of this textbook went through multiple rounds of rigorous revision that involved the input of faculty, students, editors, and educational and media specialists. Their collective contributions are reflected in the final outcome.

Let me begin by acknowledging the many people at McGraw-Hill whose efforts are amazing. My highest praise goes to Lisa Brufordt and Mandy Clark (Senior Developmental Editors), who managed and scheduled nearly every aspect of this project. I also would like to thank Janice Roerig-Blong (Publisher) for her patience in overseeing this project. She has the unenviable job of managing the budget for the book and that is not an easy task. Other people at McGraw-Hill have played key roles in producing an actual book and the supplements that go along with it. In particular, Jayne Klein (Project Manager) has done a superb job of managing the components that need to be assembled to produce a book, along with Sherry Kane (Buyer). I would also like to thank John Leland (Photo Research Coordinator), who acted as an interface between me and the photo company. In addition, my gratitude goes to David Hash (Designer), who provided much input into the internal design of the book as well as creating an awesome cover. Finally, I would like to thank Patrick Reidy (Marketing Manager), whose major efforts begin when the fourth edition comes out! I would also like to thank Linda Davoli (Freelance Copy Editor) for making grammatical improvements throughout the text and art, which has significantly improved the text's clarity.

I would also like to extend my thanks to Bonnie Briggie and everyone at Lachina Publishing Services, including the many artists who have played important roles in developing the art for the third and fourth editions. Also, folks at Lachina Publishing Services worked with great care in the paging of the book, making sure that the figures and relevant text are as close to each other as possible. Likewise, the people at Pronk & Associates

have done a great job of locating many of the photographs that have been used in the fourth 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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