

# Preface

As teachers of genetics and the authors of *An Introduction to Genetic Analysis*, we are aware of the quiet revolution occurring in the way genetics is being taught to beginning students. Many instructors are finding that a strictly chronological or historical approach no longer fits their method of teaching genetics, nor does it meet their students' needs. More and more, molecular genetics is being introduced earlier in the course and integrated with phenotypic and genotypic analysis.

*Modern Genetic Analysis: Integrating Genes and Genomes*, Second Edition, was written for instructors and students who need a textbook that supports an integrated "DNA early" approach. This departure from the traditional historical unfolding of genetics has had some significant side effects—chief among them, a more streamlined presentation in which genetic principles stand in bolder relief.

Regardless of whether the presentation is traditional or modern, it is essential that students learn to think like geneticists. Thus, as in *An Introduction to Genetic Analysis*, the focus in *Modern Genetic Analysis: Integrating Genes and Genomes*, Second Edition, is on teaching students to analyze data and draw conclusions.

## A Modern Approach

We have divided this edition of *Modern Genetic Analysis* into four parts that reflect the broad divisions of modern genetics. Because of the way this edition is structured, not only is there an opportunity for the vertical integration of concepts at the organismal, cellular, chromosomal, protein, and DNA levels, but "classical genetics" is presented in a less abstract way that can be better grasped by students. We hope that this new approach will enable students to understand how genetics is done in the "real world," where classical and molecular approaches are not segregated but complement each other.

Part 1: Fundamentals of Gene Structure, Function, and Transmission deals with the fundamental themes of genetics. In this part, a student is immediately shown "the forest" before "the trees," a well-established learning method. After an opening chapter that gives an introductory overview of genetics, Chapter 2 introduces the student to gene and genome structure. Chapter 3 presents transcription and translation. Chapter 4 describes the molecular and cellular basis of gene

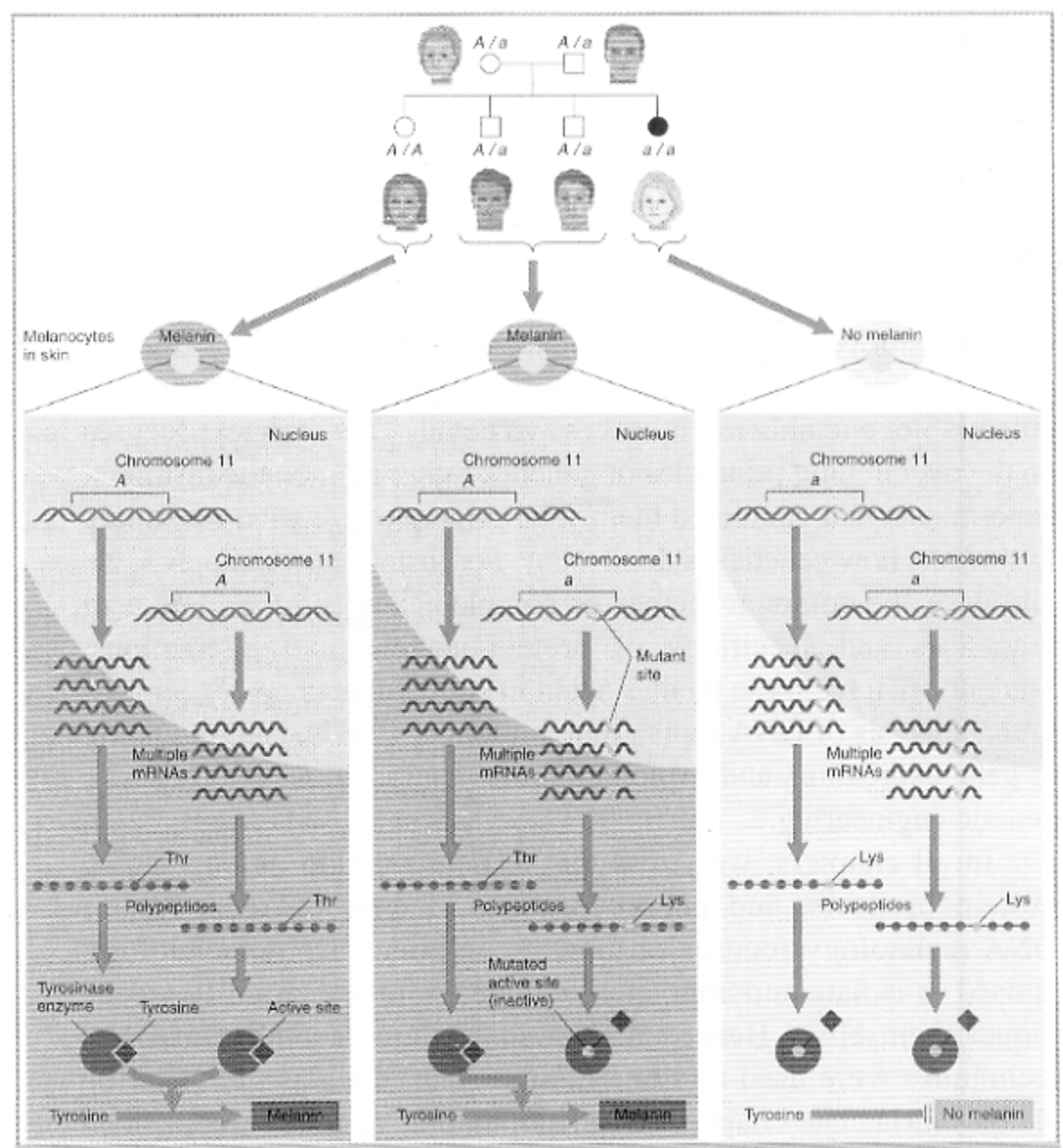


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transmission. Chapters 5 and 6 cover the principles of inheritance and recombination in eukaryotes, and Chapter 7 deals with the corresponding processes in prokaryotes. Thus, in this part, the core principles of inheritance are presented and integrated at the classical and molecular levels.

**Part 2: Methods of Genetic Manipulation** focuses on genetic manipulation. The presentation begins in Chapter 8 with a demonstration of the incisiveness of DNA technology as a means of manipulating individual genes; then Chapter 9 extends these approaches into the analysis of whole genomes—the subject of genomics. This part of the book then takes up the subject of mutation, examining gene mutation and repair in Chapter 10, continuing with chromosome mutation in Chapter 11, and culminating with a description of the power of mutation to manipulate and dissect genetic systems in Chapter 12.

**Part 3: Systems Genetics: From Gene to Phenotype** expands from the simple principles of genetics to the systems of complex interacting genetic components found in living cells. The part begins in Chapter 13 with an exquisite example of complex genetic interactions in the regulation of transcription. The theme of interaction is continued in Chapter 14 with an exploration of the complex relationships between genes and environment in controlling phenotype. Part 3 concludes with two topics that illustrate the wide variety of biological activities that result from gene interaction: cancer in Chapter 15 and development in Chapter 16.

**Part 4: Genetic Analysis of Populations** covers the special approaches used to analyze genes at the population level. Chapter 17 covers formal population genetics, and Chapter 18 lets quantitative genetics lead into evolutionary genetics in Chapter 19, the final chapter.

## Focus on Principles

A primary goal in writing *Modern Genetic Analysis* was that the understanding and application of core genetic principles take priority over historical detail. We hope that students will more readily recognize and grasp fundamental principles and themes if their presentation is not encumbered by excessive detail. Thus, the text focuses on the overarching principles of genetics rather than on the historical experiments that generated them. The principles are used to explain to students how genetics is done today. For instance, in Chapter 3, we introduce the common themes of complementarity of nucleic acid sequences and specificity of protein–nucleic acid interactions. Students then see these themes again in subsequent chapters, applied in the analysis of DNA replication, protein synthesis, and regulation of gene expression, and exploited in the manipulations that underlie genetic engineering.

In all chapters, we stress the vertical relation among DNA, protein products, and phenotype. The chapter on recombinant DNA technology focuses on how recombinant DNA technology is used to isolate and characterize genes, rather than on the techniques themselves. Here students will see how recombinant DNA techniques were used to clone human genes such as the gene for alkaptonuria. The chapter on developmental genetics emphasizes the importance of signal transduction cascades in all aspects of a cell's or an organism's development and the important and varied switch mechanisms that underlie all developmental decisions.

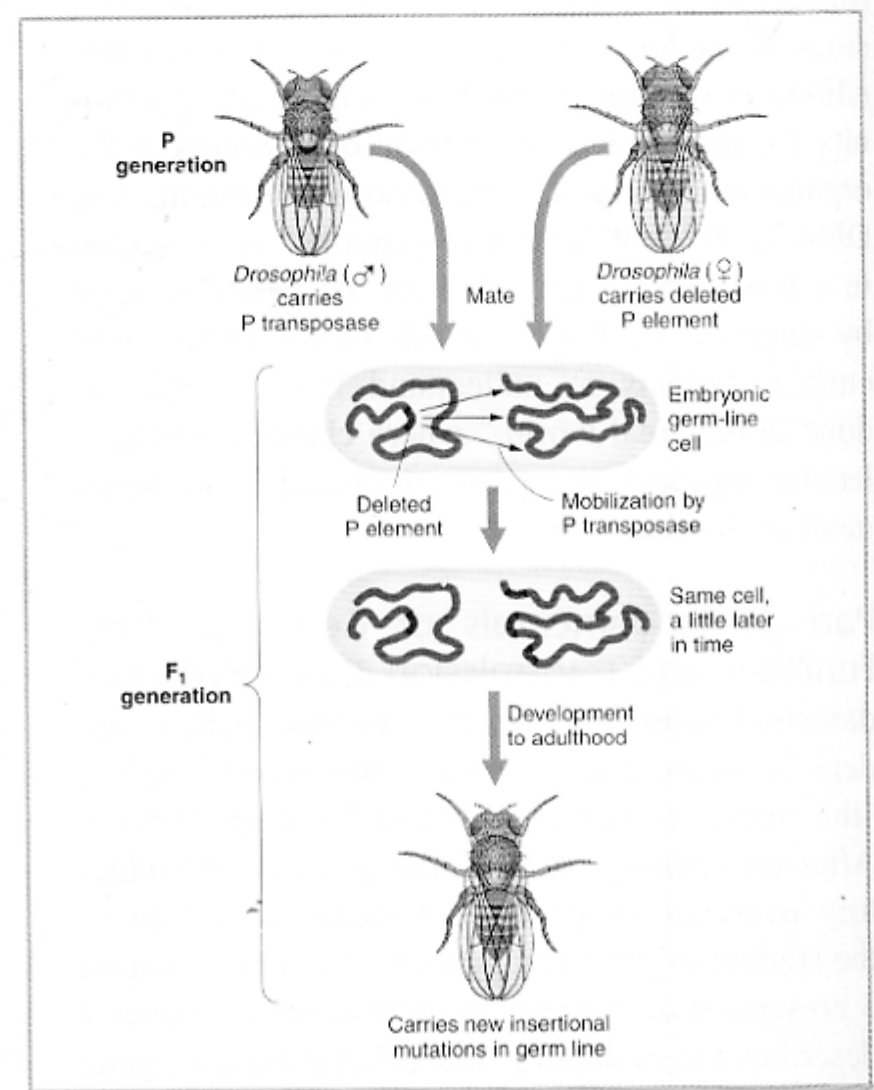


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## Focus on Genetic Analysis

In *Modern Genetic Analysis* we focus on the questions that underlie much of modern genetics, such as, "How may genes affect this phenotypic difference? Are the genes linked? Are the mutations allelic? What is the cellular function of the gene?" In short, the focus is on the modes of inference geneticists use today. A well-rounded study of genetics should also expose students to some of the landmark experiments. These important investigations are set apart from the text in boxes called *FOUNDATIONS OF GENETICS*.

In these Foundations boxes, students will read about how Archibald Garrod inferred the nature of inborn errors of metabolism; the research that led Charles Yanofsky to deduce that gene and protein structure are colinear; Watson and Crick's model for the structure of DNA, including Watson's own description of the first assembly of the metal model; and Luria and Delbrück's method of deducing the random nature of mutation.

Added to this edition are experiments such as that of Hershey and Chase (presented in a solved problem that makes an interesting learning exercise for the student), the development of the Ames test, and Muller's experiment demonstrating that X rays are mutagenic. If your course favors a very heavy emphasis on landmark experiments, please visit Modern Genetics Online for Instructors ([www.whfreeman.com/mga](http://www.whfreeman.com/mga)) to access our Landmark Experiments Resource Library.

**Problems** at the end of each chapter have been created to give students the chance to apply and exercise their analytical skills. Almost all problems have been class tested. Problems begin at the basic level and then proceed to a more challenging level. Included are *Pattern Recognition Problems*, which the authors designed to aid students in recognizing hereditary patterns in data, a key skill in genetic analysis. Most chapters also include a problem titled *Unpacking the Problem*. These exercises, written by Tony Griffiths, reveal the underlying levels of knowledge that must be applied for a problem to be solved constructively. In this edition, we now provide 20 Web-based *INTERACTIVE UNPACKING THE PROBLEM* exercises, which are indicated by the  icon next to each one. These exercises were written by Craig Berezowsky in consultation with Tony Griffiths, both of the University of British Columbia.

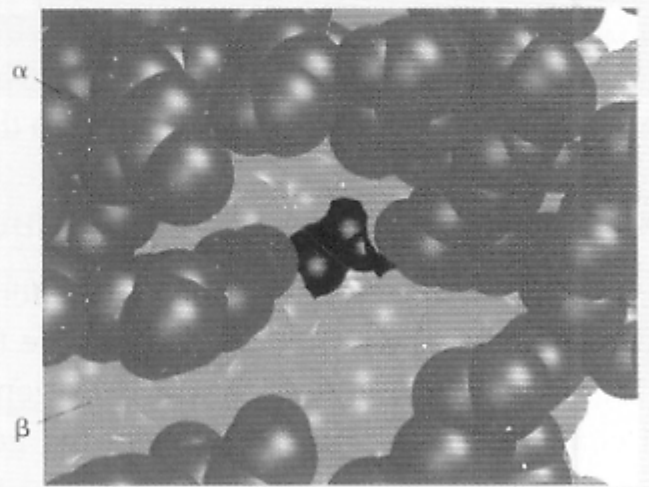
Many chapters also include several *Solved Problems* that walk students through the ways in which geneticists apply principles to experimental data. This type of problem will prepare students for solving problems on their own.

### FOUNDATIONS OF GENETICS 3-2

#### Charles Yanofsky and the Colinearity of Gene and Protein Structure

In 1941, George Beadle and Edward Tatum originated the one-gene-one-enzyme hypothesis. When James Watson and Francis Crick deduced the structure of DNA in 1953, it seemed likely that there must be a linear correspondence between the nucleotide sequence in DNA and the amino acid sequence in protein (such as an enzyme). However, it was not until 1963 that an experimental demonstration of this colinearity was obtained, from two research groups, one of which was led by Charles Yanofsky at Stanford University.

Yanofsky had induced 16 mutant alleles of the *trpA* gene of *Escherichia coli*, whose wild-type allele was known to code for the  $\alpha$  protein subunit of the enzyme tryptophan syn-



Model of tryptophan synthetase, with substrate in red.

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## New to This Edition

### The Latest Approaches

In keeping with the book's title, we continue to emphasize the most current genetic research throughout the book. More specifically, *CHAPTER 9, GENOMICS*, has been updated to show how genetics has migrated from recombination-based maps to

sequence-level maps and to the sequencing of entire genomes. Beyond the acquisition of structural data, this chapter describes how bioinformatic and experimental approaches have been developed for analyzing genes and their products at the genomic level. It sets the stage for an integration of genomic approaches into most of the subsequent chapters, reflecting the fact that genetics and genomics have now become companion disciplines. In addition, through a class of Web-based tutorials new to this edition, entitled *EXPLORING GENOMES*, students can learn how to make use of the many genomic databases that have become an integral part of genetics today. (More on the specifics of these exercises can be found on the front endpapers of this text.)

A new *CHAPTER 19, EVOLUTIONARY GENETICS*, has been added in recognition of the inseparability of genetics and evolution in modern research. Some material from the first edition's Chapter 17, which briefly covered evolution along with population genetics, has been relocated to this chapter.

### Reorganized, Expanded, and Updated

The material on gene inheritance (Chapter 4 in the first edition) has been reorganized into two chapters. In this edition, the first of these chapters, Chapter 4, focuses on the molecular and cellular basis of gene inheritance. Building on this, the second chapter, Chapter 5, then covers the genetic ratios that arise in the progeny of heterozygotes. Splitting this content into two chapters was done partly to shorten each chapter and partly to delineate the two complementary approaches.

The first edition had two chapters on genetic engineering and its applications (Chapters 10 and 11). These have now been streamlined into one chapter, Chapter 8, which has been completely reworked so that the two fundamental processes of base complementarity and sequence-specific interactions between DNA/RNA and proteins form its scaffold. The chapter takes a principles-based approach to genetic engineering.

The chapter on gene mutation in the first edition (Chapter 7) has now been expanded into two chapters: Chapter 10, on mechanisms of gene mutation and repair, as before, and Chapter 12, a new chapter on mutational dissection with a focus on the analytical process. Moving this topic to its new location after the chapters on genetic engineering and genomics allows the newer techniques of site-directed mutagenesis and targeted gene knockouts to be treated as part of the modern arsenal of techniques for mutation research.

Topics from the first edition Chapter 13, *Transposable Genetic Elements*, have here been separated and included in three chapters. Chapter 9, *Genomics*, examines the prominent representation of these mobile genetic elements as repetitive sequences in eukaryotic genomes. Chapter 10, *Gene Mutation*, discusses the mechanisms of transposition in both prokaryotic and eukaryotic systems, as well as the mutagenic potential of these elements. Chapter 12, *Mutational Dissection*, discusses the use of transposable elements as mutagens.

The first edition chapter on gene interaction (Chapter 6) has been redesigned and placed in Part 3 as Chapter 14, *From Gene to Phenotype*.

### New Tools for Learning

Some instructors told us that in our attempt to focus on principles and avoid excessive detail in the first edition, we occasionally streamlined the text too much. In the second edition, we have addressed this feedback by fleshing out the explanations, providing additional background information where necessary, and adding new pedagogical diagrams to facilitate understanding of the more complex processes, such as DNA replication. While still focused on the essential principles, these enhanced explanations should make the material more accessible to students.

We also have taken the opportunity to add a number of new learning tools. Students want to and should learn about the exciting applications happening in genetics today and those that are poised to happen in the future. Each chapter now opens with a *REAL-WORLD STORY* that makes material even more relevant for students. Stories such as the existence of high frequencies of Huntington disease in certain human populations introduce the broader questions introductory students want answered concerning the inheritance and the cellular basis for such genetic diseases. Each chapter-opening story is revisited toward the end of the chapter in light of the principles that have been covered.

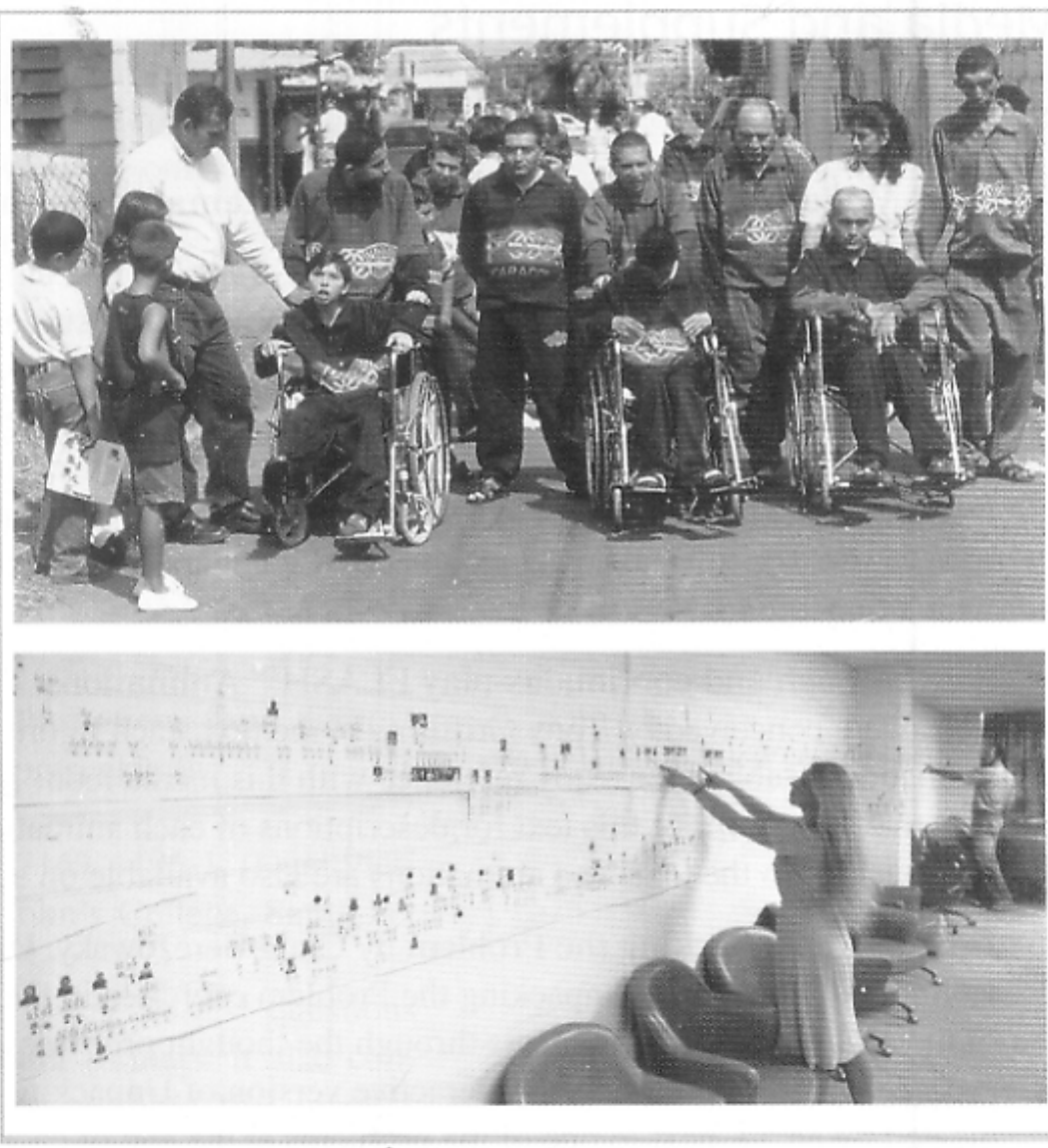
Pedagogically useful, conceptually rich illustrations are invaluable resources to help students develop genetic insight. In the second edition, the illustration program has been thoroughly expanded, updated, and revised with an emphasis on clarity and educational value in support of the text discussion. Over 60 new illustrations have been added with this theme in mind. Each of the remaining text illustrations has been carefully edited to ensure that its message is conveyed clearly. In addition, the colors of the entire art program have been enhanced so that images are more vibrant and will thus project better during lecture hall presentations.

In our commitment to focus on principles, we have developed for each new chapter a *CHAPTER OVERVIEW ILLUSTRATION* that serves as a clear and graphic road map for the chapter. These overviews were regarded by reviewers as an extremely useful learning tool and an innovative approach to presenting complex concepts.

As in the first edition, we continue to use study aids such as *Key Concepts*, *Message boxes*, end-of-chapter *Summaries*, *Concept Maps*, and *Unpacking the Problem* exercises.

As a result of user feedback, the end-of-chapter problem sets have been divided in this edition into a group of *BASIC PROBLEMS* followed by a group of *CHALLENGING PROBLEMS*. Each group of Basic Problems allows students to practice their mastery of the chapter and so gain confidence in their ability to apply principles learned. This arrangement should reduce any frustration some students might feel when dealing with a challenging problem later on.

Students should find two new appendixes very useful. Appendix A, *Genetic Nomenclature*, lists model organisms and their nomenclature. Appendix B, *Bioinformatic Resources for Genetics and Genomics*, builds on the theme of introducing students to the latest genetic research tools by providing valuable starting points for exploring the rapidly expanding universe of online resources for genetics and genomics.



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CHAPTER OVERVIEW figure

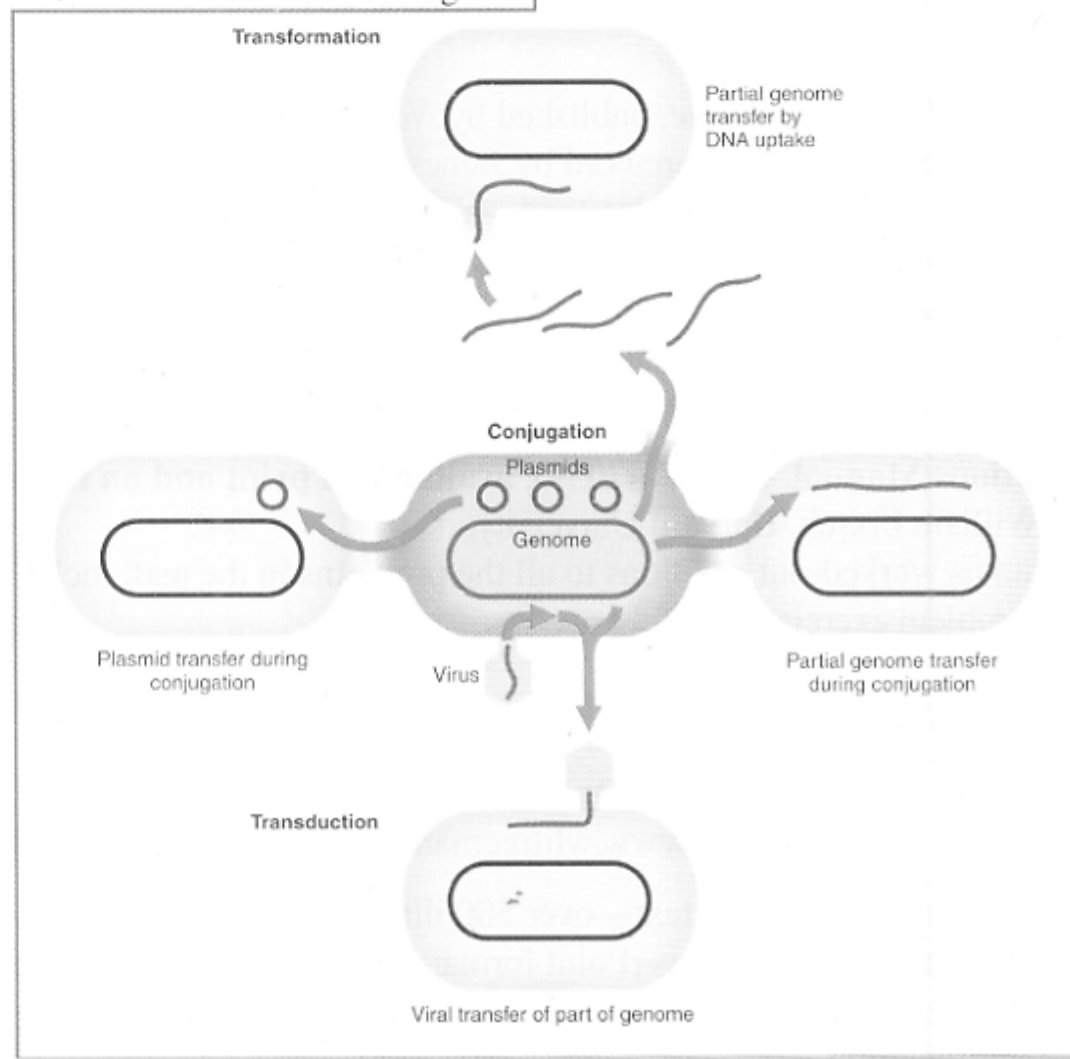


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- PowerPoint lecture outlines
- 45 step-through and continuous-play FLASH™ Animations
- Landmark Experiments Resource Library (available on Web site only)
- Electronic Instructor's Resource Manual, Test Bank, and Student Solutions Manual

**★NEW!** In partnership with NCBI Bookshelf, *Modern Genetic Analysis*, Second Edition, is now available as an online resource to assist instructors, researchers, and students while using PubMed. From a PubMed abstract, click on the "Books" link to view hyperlinked phrases that lead to sections from *Modern Genetic Analysis* for immediate online reference.



**Overhead Transparency Set, 0-7167-4497-X**

The full-color overhead transparency set contains 150 key illustrations from the text with enlarged labels that project more clearly for lecture hall presentation.

**Instructor's Resource Manual and Test Bank**, (printed) 0-7167-4496-1, (Dual Platform CD-ROM) 0-7167-4499-6, by Ewen J. Harrison, St. John's College, Santa Fe, and Sally Lyman Allen, University of Michigan.

The *Instructor's Resource Manual and Test Bank* contains over 700 test questions rated by difficulty in multiple-choice, true-false, and matching formats. It also contains extensive teaching notes, including ideas and tips for teaching the genetics course, learning objectives, vocabulary, teaching strategies, annotated problem solutions, expanded Unpacking the Problem exercises, and ethics/current-events topics. The easy-to-use electronic version of the test bank lets instructors edit and rearrange questions as well as add their own.

## Media and Supplements

### For STUDENTS

**★NEW! Modern Genetics Online:** [www.whfreeman.com/mga](http://www.whfreeman.com/mga)

- **Exploring Genomes: Web-Based Bioinformatics Tutorials** by Paul G. Young of Queen's University. These 10 interactive tutorials teach students to use the vast genomic resources of the Web site of the National Center for Biotechnology Information. As a basis for the tutorials, Young draws from relevant material in the textbook, showing students how to use these bioinformatic resources as well as how to see the potential for their application in modern genetic analysis. For ease of use, the tutorials can be completed independently of the chapters in which they are located.
- **Step-through and continuous-play FLASH™ Animations.** These 45 animations were conceived by Tony Griffiths. In the text, each figure that has a related animation is tabbed for ready reference with this media icon:  See the list inside the front cover of this text for descriptions of each animation and where each is connected to the text. The animations are also available on a student CD-ROM.
- **Interactive Unpacking the Problem** by Craig Berezowsky, University of British Columbia. As with the Unpacking the Problem exercises in the text, each series of these questions steps students through the thought processes needed to solve a problem. This Web-based and interactive version of Unpacking the Problem, indicated by an  next to one of the problems at the end of each chapter, features immediate feedback and grading functions.
- **Online Sample Tests.** In addition to practicing knowledge through the interactive Unpacking the Problem set of exercises, students can also test their fundamental understanding of key concepts and experiments through these online questions. All questions were chosen and often written by the textbook and test bank author teams to ensure that all questions cover what is core to each chapter. Questions are also keyed to the text so that students can easily review material needed for understanding.
- **The Human Genome**, published by Nature  From the frontline of science reporting, and with a foreword by James Watson, here is the one book every student of genetics needs to understand—and to appreciate—one of the great revolutions in science. *The Human Genome* is the first comprehensive report on the Human Genome Project that combines essential background information, clear explanations, and expert analysis. Additionally, this invaluable resource evaluates the impact on science, medicine, and society—both opportunities and risks.

**Solutions Manual**, 0-7167-4703-0, **available in print and on the Web**

by William Fixsen, Harvard University.

Contains worked-out solutions to all the problems in the text, including the Unpacking the Problem exercises.

### For INSTRUCTORS

**★NEW! Modern Genetics Online for Instructors**

Available on the Web at [www.whfreeman.com/mga](http://www.whfreeman.com/mga) or on CD-ROM, 0-7167-4498-8

- All images from the text—over 500 illustrations—in multiple downloadable formats including PowerPoint format. Also available in JPEG and PICT formats. All include enlarged labels that project more clearly for lecture hall presentation.

