GENETIC ANALYSIS

AN INTEGRATED APPROACH

THIRD EDITION

Mark F. Sanders
John L. Bowman

Brief Table of Contents

Table A The Genetic Code

Second Position

First Position (5′ end)	U	C	A	G	Third Position (3′ end)
U	UUU, UUC — Phe (F) UUA, UUG — Leu (L)	UCU, UCC, UCA, UCG — Ser (S)	UAU, UAC — Tyr (Y) UAA — stop UAG — stop	UGU, UGC — Cys (C) UGA — stop UGG — Trp (W)	U C A G
C	CUU, CUC, CUA, CUG — Leu (L)	CCU, CCC, CCA, CCG — Pro (P)	CAU, CAC — His (H) CAA, CAG — Gln (Q)	CGU, CGC, CGA, CGG — Arg (R)	U C A G
A	AUU, AUC, AUA — Ile (I) AUG — Met (M)	ACU, ACC, ACA, ACG — Thr (T)	AAU, AAC — Asn (N) AAA, AAG — Lys (K)	AGU, AGC — Ser (S) AGA, AGG — Arg (R)	U C A G
G	GUU, GUC, GUA, GUG — Val (V)	GCU, GCC, GCA, GCG — Ala (A)	GAU, GAC — Asp (D) GAA, GAG — Glu (E)	GGU, GGC, GGA, GGG — Gly (G)	U C A G

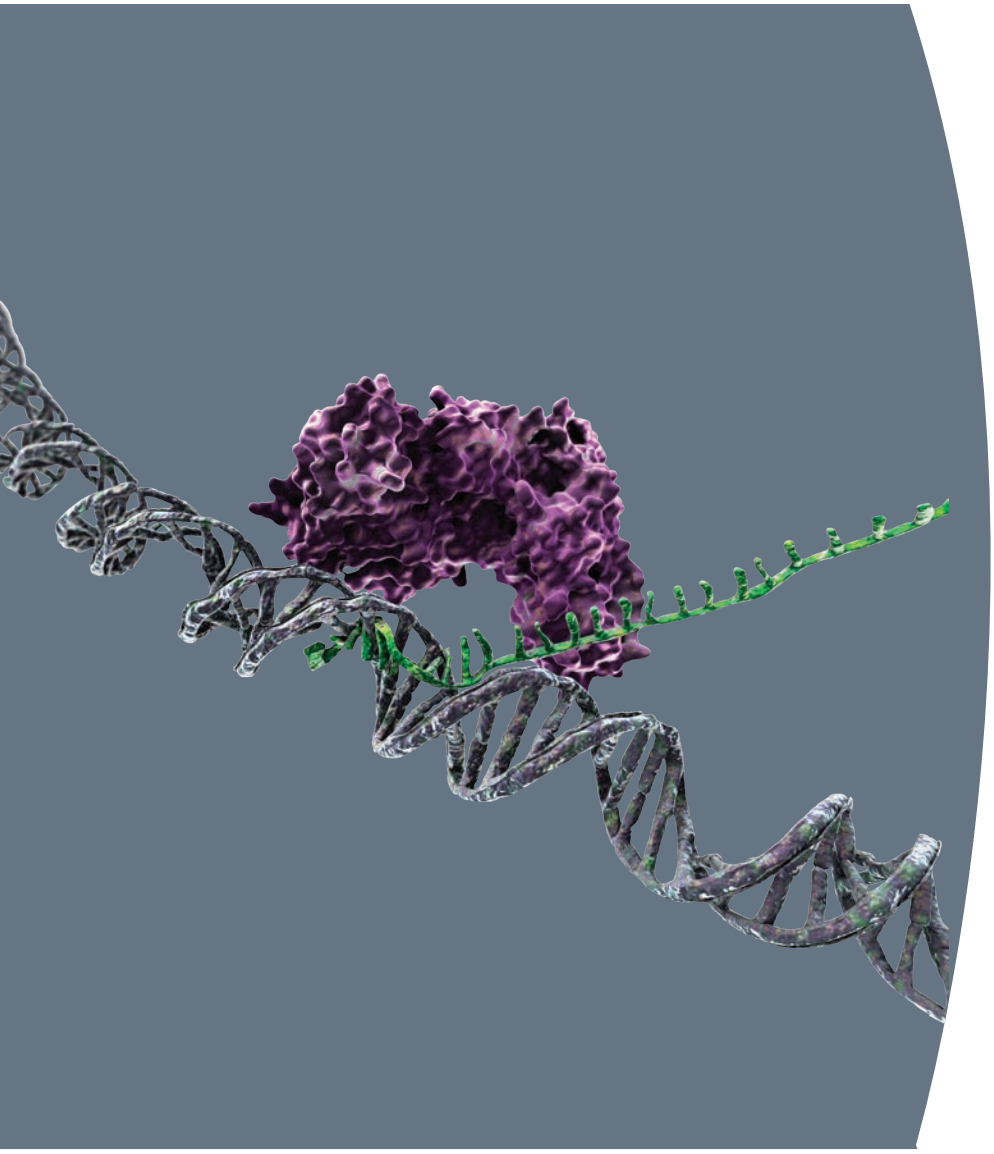
Table B Redundancy of the Genetic Code

Amino Acid	Abbreviation		Codons
	3-letter	1-letter	
Alanine	Ala	A	GCA, GCC, GCG, GCU
Arginine	Arg	R	AGA, AGG, CGA, CGC, CGG, CGU
Asparagine	Asn	N	AAC, AAU
Aspartic acid	Asp	D	GAC, GAU
Cysteine	Cys	C	UGC, UGU
Glutamic acid	Glu	E	GAA, GAG
Glutamine	Gln	Q	CAA, CAG
Glycine	Gly	G	GGA, GGC, GGG, GGU
Histidine	His	H	CAC, CAU
Isoleucine	Ile	I	AUA, AUC, AUU
Leucine	Leu	L	UUA, UUG, CUA, CUC, CUG, CUU
Lysine	Lys	K	AAA, AAG
Methionine	Met	M	AUG
Phenylalanine	Phe	F	UUC, UUU
Proline	Pro	P	CCA, CCC, CCG, CCU
Serine	Ser	S	AGC, AGU, UCA, UCC, UCG, UCU
Threonine	Thr	T	ACA, ACC, ACG, ACU
Tryptophan	Trp	W	UGG
Tyrosine	Tyr	Y	UAC, UAU
Valine	Val	V	GUA, GUC, GUG, GUU

Genetic Analysis

AN INTEGRATED APPROACH

Third Edition



Mark F. Sanders
University of California at Davis

John L. Bowman
Monash University,
Melbourne, Australia
University of California at Davis

Pearson

330 Hudson Street, NY NY 10013

Director, Courseware Portfolio Manager: *Beth Wilbur*
Courseware Portfolio Manager: *Michael Gillespie*
Content Producer: *Melanie Field*
Development Editor: *Moira Lerner*
Courseware Sr. Analysts, Content Development: *Margot Otway, Barbara Price*
Courseware Editorial Assistant: *Summer Giles*
Courseware Director, Content Development: *Ginnie Simione Jutson*
Managing Producer: *Michael Early*
Full Service Project Manager: *Thomas Russell*
Full Service Vendor: *SPi Global*
Design Manager: *Mark Ong*
Interior and Cover Design: *Cadence*
Rights and Permissions Project Manager: *Linda DeMasi*
Photo Researcher: *Maureen Spuhler*
Rich Media Content Producer: *Chloé Veylit*
Manufacturing Buyer: *Stacey Weinberger*
Product Marketing Manager: *Christa Pelaez*
Field Marketing Manager: *Kelly Galli*
Cover Photo Credit: *Gunilla Elam/Science Photo Library*
Illustrator: *Lachina*

Library of Congress Cataloging-in-Publication Data

Names: Sanders, Mark Frederick, author. | Bowman, John L., author.
Title: Genetic analysis : an integrated approach / Mark F. Sanders, John L. Bowman.
Description: Third edition. | New York : Pearson Education, Inc., [2019] | Includes bibliographical references and index.
Identifiers: LCCN 2017052380 | ISBN 9780134605173 | ISBN 0134605179
Subjects: | MESH: Genetic Phenomena | Genetic Techniques
Classification: LCC QH430 | NLM QU 500 | DDC 616/.042--dc23
LC record available at https://lccn.loc.gov/2017052380

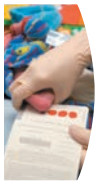
1 17

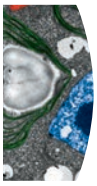
ISBN-10: 0134605179
ISBN-13: 9780134605173

Pearson

www.pearsonhighered.com

Table of Contents





19 Genetic Analysis of Quantitative Traits 696

20 Population Genetics and Evolution at the Population, Species, and Molecular Levels 725

About the Authors

Mark F. Sanders has been a faculty member in the Department of Molecular and Cellular Biology at the University of California, Davis, since 1985. In that time, he has taught more than 150 genetics courses to nearly 35,000 undergraduate students. Although he specializes in teaching the genetics course for which this book is written, his genetics teaching experience also includes a genetics laboratory course, an advanced human genetics course for biology majors, and a human heredity course for nonscience majors, as well as introductory biology and courses in population genetics and evolution. He has also served as an advisor to undergraduate students and in undergraduate education administration, and he has directed several undergraduate education programs.

Dr. Sanders received his B.A. degree in Anthropology from San Francisco State University, his M.A. and Ph.D. degrees in Biological Anthropology from the University of California, Los Angeles, and 4 years of training as a postdoctoral researcher studying inherited susceptibility to human breast and ovarian cancer at the University of California, Berkeley.

John L. Bowman is a professor in the School of Biological Sciences at Monash University in Melbourne, Australia, and an adjunct professor in the Department of Plant Biology at the University of California, Davis, in the United States. He received a B.S. in Biochemistry at the University of Illinois at Urbana-Champaign in 1986 and a Ph.D. in Biology from the California Institute of Technology in Pasadena, California. His Ph.D. research focused on how the identities of floral organs are specified in *Arabidopsis* (described in Chapter 18), and he conducted postdoctoral research at Monash University on the regulation of floral development. From 1996 to 2006, his laboratory at UC Davis investigated developmental genetics of plants, focusing on how leaves are patterned. From 2006 to 2011, he was a Federation Fellow at Monash University, where his laboratory is studying land plant evolution using a developmental genetics approach. He was elected a Fellow of the Australian Academy of Science in 2014. At UC Davis he taught genetics, "from Mendel to cancer," to undergraduate students, and he continues to teach genetics courses at Monash University.

Dedication

To my extraordinary wife and partner Ita. She is a treasure whose support, patience, and encouragement throughout this ongoing project make me very fortunate. To my wonderful children Jana and Nick, to their spouses John and Molly, to my grandson Lincoln, and to all my students, from whom I have learned as much as I have taught.

Mark F. Sanders

For my parents, Lois and Noel, who taught me to love and revere nature, and Tizita, my partner in our personal genetics experiments. And to all my genetics students who have inspired me over the years, I hope that the inspiration was mutual.

John L. Bowman

We dedicate this third edition of *Genetic Analysis: An Integrated Approach* to our friend and colleague Mel Green, who passed away in October 2017 at the age of 101. Mel was a stellar geneticist and was engaged in genetics until the end. Over his long career, he made numerous important contributions to genetics, inspiring scores of geneticists including the authors of this textbook.

Preface

We are now almost two decades into the second century of modern genetics, and the expansion of knowledge in this rapidly progressing field continues at a dizzying pace. Topics that seemed impenetrable just a few years ago are coming into focus. Novel approaches to old problems are providing profound insights into the genomics, development, and evolution of organisms in all three domains of life. CRISPR–Cas9, which was discovered in basic research on bacterial immunity, has been developed into a genome-editing system that has revolutionized the manipulation of genomic sequences in living cells. Advancements in genomics, proteomics, transcriptomics, and other enterprises of the "omic" world have opened avenues for research that were unimaginable in years past. And the resulting advancements in knowledge are quickly being turned into new applications. These are great times to be a geneticist or a student studying genetics!

In keeping with these exciting times of revolutionary change in our field, our textbooks too must undergo change. This third edition of *Genetic Analysis: An Integrated Approach* contains some significant changes that have been made with students foremost in our minds. As authors and instructors of genetics, we have had front row seats in the discipline and in the classroom. Between the two of us, we have more than 50 years' experience and experimentation in teaching genetics. We have used that experience to produce this new edition. We hope that it conveys the excitement we feel about genetics and the dynamism at work in the field, and that it offers students new and interesting examples of and insights into our favorite scientific discipline. As teachers and student mentors, our highest goal is to see students succeed. To accomplish this we seek to motivate students to pursue and explore genetics more fully and to incorporate what they learn into their thinking and plans for their future. We hope teachers and students alike will find motivation and encouragement in the subject matter and examples in this book.

Our Integrated Approach

This third edition, like its predecessors, carries the unique subtitle *An Integrated Approach*. The phrase embodies our pedagogical approach, consisting of three principles: (1) to integrate problem solving throughout the text—not relegating it to the ends of chapters—and consistently to model a powerful, three-step problem-solving approach (Evaluate, Deduce, and Solve) in every worked example; (2) to integrate an evolutionary perspective throughout the book; and (3) to integrate descriptions of Mendelian genetics with molecular genetics and genomics so as to demonstrate the value of each of these different approaches for investigating the same basic sets of observations. In this edition, we adhere to and strengthen the integration that has resonated strongly with instructors and students.

New to This Edition

As was the case in our previous editions, our aim above all is to assist the student by making the learning of genetics easier, more interesting, and more effective. Thus, three specific goals have driven this revision, and each is supported by new features that help accomplish it. Goal 1 is to provide more interesting, real-world applications of genetics. We have addressed this goal by writing five "Application Chapters" that each highlight a particular applied topic in human genetics. Goal 2 is to make the job of learning the details of genetics easier. We have addressed this goal by writing "Caption Queries" to accompany chapter figures and by providing a new feature, titled "Preparing for Problem Solving," at the end of each chapter. Goal 3 is to facilitate group work and discussion of genetics problems and concepts among classmates. We have addressed this goal in part through the Caption Queries and in part by providing a new category of chapter problems, called "Collaboration and Discussion," that are specifically designed to be tackled in groups. Along with these important pedagogical changes, this revision is also important for incorporating new genetic information that is defining the future of the field. The following descriptions highlight key new features and information designed to accomplish our revision goals.

Application Chapters

Many students come to genetics curious about human heredity and about how genetic principles are applied in real-world activities. This edition, like the previous ones, features numerous human examples to help illustrate the operation of genetic principles, and it features five new Application Chapters—short chapters focused on specific applied topics in human genetics and evolutionary genetics. The Application Chapters are written to give students information on topics of particular interest and to illustrate some of the practical uses of genetics and genetic analysis. Each of these special chapters is about half the length of a typical textbook chapter, and each has a specific applied focus. They are spaced periodically throughout the book in such a way that each of them comes just after the key prerequisite material has been presented. Importantly, these new Application Chapters do not add to the length of the book. We have made reorganization and revision decisions that have maintained the depth of

coverage while allowing for the addition of the Application Chapters in a space-neutral way.

Every Application Chapter opens with a story that exemplifies why the topic of the chapter is important, and each contains several end-of-chapter problems to guide student learning and discussion. The five Application Chapters are:

- **Application Chapter A – Human Hereditary Disease and Genetic Counseling** This chapter describes the role of genetic counselors and the genetic information and analysis they employ in medical decision-making. Students interested in human hereditary transmission, as well as those potentially interested in careers in medical genetics or genetic counseling, will find satisfying discussions of these topics in this chapter.
- **Application Chapter B – Human Genetic Screening** Numerous invasive and non-invasive methods of screening for inherited conditions are described in this chapter, and their results are discussed. Topics include carrier screening; pre-natal, newborn, and pre-symptomatic genetic testing; and amniocentesis and chorionic villus sampling.
- **Application Chapter C – The Genetics of Cancer** This chapter discusses cancer from two perspectives. The first is an overview of the major hallmarks of cancer that have been articulated over the last decade or so. The second is a discussion of cancers that have a simpler genetic basis and cancers for which inherited susceptibility has been identified. New, immune system–based approaches to cancer treatment are also discussed.
- **Application Chapter D – Human Evolutionary Genetics** This chapter presents the current interpretation of human evolution from a genomic perspective and describes the relationship of modern humans to their archaic predecessors. The discussion includes up-to-date information on Neandertal and Denisovan genome sequencing, along with recent evidence on interbreeding among archaic human populations.
- **Application Chapter E – Forensic Genetics** This chapter focuses on the uses and analysis of DNA in the contexts of crime scene analysis, paternity testing, and direct-to-consumer genealogy, genetic ancestry testing, and genetic health risk assessment. Examples of genetic analysis using the Combined DNA Index System (CODIS) and of genetic analysis to determine the paternity index and combined paternity index are given. Descriptions of the direct-to-consumer genetic analyses provided by AncestryDNA and 23andMe are part of the chapter as well.

Caption Queries

Textbook figures are an integral part of the pedagogical apparatus of a textbook, but they are only effective if the reader takes the time to look at and understand them. How does one help students examine a figure attentively enough to derive the critical content and meaning? One way is by asking questions about the figure. In this revision, we have written Caption Queries for virtually every figure in the book to help students dissect the illustrated content and more fully understand its meaning and importance. Several Caption Queries have been printed below their corresponding figure in the chapter itself, and all Caption Queries are available as clicker questions for classroom use and in Mastering Genetics as assignable homework. Some Caption Queries require the student to solve a problem using information from the figure, some require an explanation be provided, and others ask students to expand on the information or idea in the figure. All Caption Queries, whatever their form, will help students focus on the figures and derive a better understanding of their content.

Caption Queries serve a second purpose as well. Genetics instructors are becoming increasingly interested in the pedagogical approach known as "flipping the classroom." This approach has students do their textbook reading and review of lecture, PowerPoint®, and other course materials outside of class, leaving class time open for discussion, problem solving, and inquiry-based learning. In our own classrooms, we have found that asking questions about chapter figures is an effective way to stimulate discussion and jumpstart problem solving and inquiry-based learning. The clicker versions of Caption Queries can be the first line of interactive questions in this approach.

Preparing for Problem Solving

Building on the strong problem-solving guidance of our Genetic Analysis worked examples (the three-step problem-solving approach described momentarily), we have added a new chapter feature titled Preparing for Problem Solving, located between the Chapter Summary and the end-of-chapter problems. This feature is a list identifying the specific knowledge and skills required to answer chapter problems. The listed items draw students' attention back to the major ideas described in the chapter and to the practical skills that were modeled there, before the students begin working on end-of-chapter problems.

Collaboration and Discussion Problems

Having students work in groups to solve problems is an increasingly popular and productive way to encourage participation in, and to enhance, active learning. In this revision, each end-of-chapter problem set has been expanded to include several new problems in a section titled Collaboration and Discussion. As the name implies, these problems are designed to be evaluated and solved by small groups of students working together. Whether assigned as homework or as part of flipped classroom activities, these exercises offer an array of opportunities for comprehensive and hands-on problem solving.

Redesigned Chapter Content

The content and coverage of all chapters has been reworked in this revision to keep up with changes in the field and keep all discussions timely. Several chapter revisions reflect changes in approaches to genetic analysis. In Chapter 5 ("Genetic Linkage and Mapping in Eukaryotes"), for example, the discussion of mapping of molecular genetic markers has been substantially expanded. To make way for this expansion, discussion of tetrad analysis in yeast has been dropped. Chapter 13 ("Regulation of Gene Expression in Eukaryotes") has undergone revision to feature more discussion of epigenetic regulation and the roles of epigenetic readers, writers, and erasers. Chapters 14 ("Analysis of Gene Function by Forward Genetics and Reverse Genetics") and 15 ("Recombinant DNA Technology and Its Application") have a greatly expanded descriptions of the CRISPR–Cas9 system and its applications in gene editing and gene drive systems. Chapter 16 ("Genomics: Genetics from a Whole-Genome Perspective") has undergone substantial revision to feature new genomic approaches.

Several chapters include important new information that became available just as writing was being completed. Among numerous examples are the discussion in Chapter 7 ("DNA Structure and Replication") of the apparently stochastic pattern of DNA replication initiation in *E. coli* that was described in mid-2017; and the description in Application Chapter C (Genetics of Cancer) of the CAR-T cell method for treating certain cancers that was recommended for approval by a panel of the U.S. Food and Drug Administration in mid-2017.

A chapter from the first two editions, "The Integration of Genetic Approaches: Understanding Sickle Cell Disease," has been removed in this edition to help make room for the inclusion of the Application Chapters. We know many professors are fond of this chapter, and they can access it in Mastering Genetics or in custom versions of this text.

Maintaining What Works

While making numerous pedagogical and content changes in this third edition of *Genetic Analysis: An Integrated Approach*, we have maintained all of the features that made previous editions of the book so popular and effective. These include the systematic problem-solving approach, the pervasive evolutionary perspective, and the consistent cross connections drawn throughout between transmission and molecular genetics.

A Problem-Solving Approach

To help train students to become more effective problem solvers, we employ a unique problem-solving feature called Genetic Analysis that gives students a consistent, repeatable method to help them learn and practice problem solving. Genetic Analysis teaches how to start thinking about a problem, what the end goal is, and what kind of analysis is required to get there. The three steps of this problem-solving framework are *Evaluate*, *Deduce*, and *Solve*.

Evaluate: Students learn to identify the topic of the problem, specify the nature or format of the requested answer, and identify critical information given in the problem.

Deduce: Students learn how to use conceptual knowledge to analyze data, make connections, and infer additional information or next steps.

Solve: Students learn how to accurately apply analytical tools and to execute their plan to solve a given problem.

Irrespective of the type of problem presented to them, this framework guides students through the stages of solving it and gives them the confidence to undertake new problems.

Each Genetic Analysis worked example is laid out in a two-column format to help students easily follow the steps of the Solution Strategy that are enumerated in the left-hand column and executed in the right-hand column. "Break It Down" comments point to key elements in the problem statement of each example, as an aid to students, who often struggle to identify the concepts and information that are critical to starting the problem-solving process. We also include problem-solving Tips to help with critical steps, as well as warnings of common Pitfalls to avoid; these suggestions and admonitions are gathered from our teaching experience. It is also important to note that the Genetic Analysis examples are integrated into the chapters, right after discussions of important content, to help students immediately apply the concepts they are learning. Each chapter includes two or three Genetic Analysis problems, and the book contains nearly 50 in all.

Complementing the Genetic Analysis problems are strong end-of-chapter problems that are divided into three groups. Chapter Concept problems come first and review the critical information, principles, and analytical tools discussed in the chapter. These are followed by Application and Integration problems that are more challenging and broader in scope. Last come the chapter's Collaboration and Discussion questions, a new addition described above. All solutions to the end-of-chapter problems in the *Study Guide and Solutions Manual* use the evaluate–deduce–solve model to reinforce the book's problem-solving approach.

An Evolutionary Perspective

Geneticists are acutely aware of evolutionary relationships between genes, genomes, and organisms. Evolutionary processes at the organismal level, discovered through comparative biology, can shed light on the function of genes and organization of genomes at the molecular level.

Likewise, the function of genes and organization of genomes informs the evolutionary model. The integration of evolution and of the evolutionary perspective remains a central organizing theme of this third edition, greatly strengthened through enhanced coverage of molecular genetic evolution. For example, Chapter 20 includes updated discussion of the molecular genetic evolution of Darwin's finches, and Application Chapter D includes extensive discussion of the role of interbreeding between Neandertals and archaic humans in forming the modern human genome.

Connecting Transmission and Molecular Genetics

Experiments that shed light on principles of transmission genetics preceded by several decades the discovery of the structure and function of DNA and its role in inherited molecular variation. Yet biologists already recognized that DNA variation is the basis of inherited morphological variation observed in transmission genetics. Understanding how these two approaches to genetics are connected is vital to thinking like a geneticist. We have retained the integration of transmission genetics and molecular genetics in the text and have enhanced this feature in two ways: first, through additional discussion of the molecular basis of hereditary variation, including the mutations that underlie the four identified genes examined by Mendel, and second, with a much more robust genomic approach.

Pathways through the Book

This book is written with a Mendel-first approach that many instructors find to be the most effective pedagogical approach for teaching genetics. We are cognizant, however, that the scope of information covered in genetics courses varies and that instructor preferences differ. We have kept such differences and alternative approaches in mind while writing the book. Thus, we provide *four pathways* through the book that instructors can use to meet their varying course goals and objectives. Each pathway features integration of problem solving through the inclusion of Genetic Analysis worked examples in each chapter.

1. Mendel-First Approach

Ch 1–20

This pathway provides a traditional approach that begins with Mendelian genetics but integrates that material with evolutionary concepts and connects it solidly to molecular genetics. This approach is exemplified by the discussion in Chapter 2 of genes responsible for four of Mendel's traits, followed in Chapters 10 and 11 by a description of the molecular basis of mutations of those genes.

2. Molecular-First Approach

Ch 1 → Ch 7–9 → Ch 2–6 → Ch 10–20

This pathway provides a molecular-first approach, to develop a clear understanding of the molecular basis of heredity and variation before delving into the analysis of hereditary transmission.

3. Quantitative Genetics Focus

Ch 1, 2, 4 → Ch 19 → Ch 3, 4–18 → Ch 20

This pathway incorporates quantitative genetics early in the course by introducing polygenic inheritance (Chapter 4) and following it up with a comprehensive discussion of quantitative genetics (Chapter 19).

4. Population Genetics Focus

Ch 1–2 → Ch 20 → Ch 3–19

This pathway incorporates population genetics early in the course. Instructors can use the introduction to evolutionary principles and processes (Chapter 1) and the role of genes and alleles in transmission (Chapter 2) and then address evolution at the population level and at higher levels (Chapter 20).

Chapter Features

A principal goal of our writing style, chapter format, and design and illustration program is to engage the reader intellectually and to invite continuous reading, all the while explaining complex and difficult ideas with maximum clarity. Our conversational tone encourages student reading and comprehension, and our attractive design and realistic art program visually engage students and put them at ease. Experienced instructors of genetics know that students are more engaged when they can relate concepts to the real world. To that end, we use real experimental data to illustrate genetic principles and analyses as well as to familiarize students with exciting research and creative researchers in the field. We also discuss a broad array of organisms—such as humans, bacteria, yeast, plants, fruit flies, nematodes, vertebrates, and viruses—to exemplify genetic principles.

Careful thought has been given to our chapter features; each of them serves to improve student learning. The following list illustrates how we highlight central ideas, problems, and methods that are important for understanding genetics.

- **Essential Ideas:** Each chapter begins with a short list of concepts that embody the principal ideas of the chapter.
- **Genetic Analysis:** Our key problem-solving feature that guides students through the problem-solving process by using the *evaluate–deduce–solve* framework.
- **Foundation Figures:** Highly detailed illustrations of pivotal concepts in genetics.

- **Caption Queries:** Questions that help students dissect the illustrated content of book figures and more fully understand their meaning and importance.
- **Experimental Insights:** Discussions of critical or illustrative experiments, including the observed results of the experiments and the conclusions drawn from their analysis.
- **Research Techniques:** Explorations of important research methods, illustrating the results and interpretations.
- **Case Studies:** Short, real-world examples, at the end of every chapter, that highlight central ideas or concepts of the chapter while reminding students of some practical applications of genetics.
- **Preparing for Problem Solving:** Immediately preceding the end-of-chapter problems, this list of approaches and suggestions briefly highlights the tools and concepts students will use most often in answering chapter problems.

Mastering Genetics

http://www.masteringgenetics.com

A key reviewing and testing tool offered with this textbook is Mastering Genetics, the most powerful online homework and assessment system available. Tutorials follow the Socratic method, coaching students to the correct answer by providing feedback specific to a student's misconceptions as well as proffering hints students can access if they get stuck. The interactive approach of the tutorials provides a unique way for students to learn genetics concepts while developing and honing their problem-solving skills. In addition to tutorials, Mastering Genetics includes animations, quizzes, and end-of-chapter problems from the textbook. This exclusive product of Pearson greatly enhances the learning of genetics. Its features include:

- New tutorials on topics like CRISPR–Cas, to help students master important and challenging concepts.
- New Dynamic Study Modules. These interactive flashcards present multiple sets of questions and provide extensive feedback so students can test, learn, and retest until they achieve mastery of the textbook material. Whether assigned for credit or used for self-study, they are powerful pre-class activities that help prepare students for more involved content coverage or problem solving in class.
- eText 2.0, a dynamic digital version of the textbook, adapts to the size of the screen being used, includes embedded videos and hotlinked glossary, and allows student and instructor note-taking, highlighting, bookmarking, and searches.
- Practice Problems, similar to end-of-chapter questions in scope and level of difficulty, are found only in Mastering Genetics. Solutions are not available in the *Study Guide and Solutions Manual*, and the bank of questions extends your options for assigning challenging problems. Each problem includes specific wrong-answer feedback to help students learn from their mistakes and to guide them toward the correct answer.
- Inclusion of nearly 90% of the end-of-chapter questions among the assignment possibilities in the item library. The broad range of answer types the questions require, in addition to multiple choice, includes sorting, labeling, numerical, and ranking.
- Learning Catalytics is a "bring your own device" (smartphone, tablet, or laptop) assessment and active classroom system that expands the possibilities for student engagement. Instructors can create their own questions, draw from community content shared by colleagues, or access Pearson's library of question clusters that explore challenging topics through two- to five-question series that focus on a single scenario or data set, build in difficulty, and require higher-level thinking.

Student Supplements

Mastering Genetics

http://www.masteringgenetics.com

Used by over one million science students, the Mastering platform is the most effective and widely employed online tutorial, homework, and assessment system for the sciences; it helps students perform better on homework and exams. As an instructor-assigned homework system, Mastering Genetics is designed to provide students with a variety of assessment tools to help them understand key topics and concepts and to build problem-solving skills. Mastering Genetics tutorials guide students through the toughest topics in genetics with self-paced tutorials that provide individualized coaching offering hints and feedback specific to a student's individual misconceptions. Students can also explore the Mastering Genetics Study Area, which includes animations, chapter quizzes, the eText, and other study aids. The interactive eText 2.0 allows students to highlight text, add study notes, and watch embedded videos.

Study Guide and Solutions Manual

ISBN: 0134832256 / 9780134832258

Heavily updated and accuracy-checked by Peter Mirabito from the University of Kentucky, the *Study Guide and Solutions Manual* is divided into four sections: Genetics Problem-Solving Toolkit, Types of Genetics Problems, Solutions to End-of-Chapter Problems, and Test Yourself. In the "toolkit" section, students are reminded of key terms and concepts and key relationships they need to know to solve the problems in each chapter. This material is followed, in the second section of the manual, by a breakdown of the types of problems students will encounter in the end-of-chapter problems, the key strategies for solving each problem type, variations on the problem type that may also be encountered, and a worked

example modeled after the Genetic Analysis feature of the main textbook. The solutions provided in the third section of the manual also reflect the *evaluate–deduce–solve* strategy of the Genetic Analysis feature. Finally, for more practice, we've included five to ten Test Yourself problems and accompanying solutions for each chapter in the textbook.

Instructor Supplements

Mastering Genetics

Mastering Genetics engages and motivates students to learn and allows you to easily assign automatically graded activities. Tutorials provide students with personalized coaching and feedback. Using the gradebook, you can quickly monitor and display student results. Mastering Genetics easily captures data to demonstrate assessment outcomes. Resources include:

- In-depth tutorials that coach students with hints and feedback specific to their misconceptions.
- An item library of thousands of assignable questions, including reading quizzes and end-of-chapter problems. You can use publisher-created prebuilt assignments to get started quickly. Each question can be easily edited to precisely match the language you use.
- A gradebook that provides you with quick results and easy-to-interpret insights into student performance.

TestGen Test Bank

ISBN: 0134872762 / 9780134872766

Test questions are available as part of the TestGen EQ Testing Software, a text-specific testing program that is networkable for administering tests. It also allows instructors to view and edit questions, export the questions as tests, and print them out in a variety of formats.

Instructor Resources

A robust suite of instructor resources offers adopters of the text a comprehensive and innovative selection of lecture presentation and teaching tools. Developed to meet the needs of veteran and newer instructors alike, these resources include:

- The JPEG files of all tables and line drawings from the text. Drawings have labels individually enhanced for optimal projection results and also are provided in unlabeled versions.
- Most of the text photos, including all photos with pedagogical significance, as JPEG files.
- A set of PowerPoint® presentations consisting of a thorough lecture outline for each chapter augmented by key text illustrations and animations.
- PowerPoint® presentations containing a comprehensive set of in-class Classroom Response System (CRS) questions for each chapter.
- PowerPoint® presentations containing clicker-based Caption Query questions for all figures in the text.
- In Word and PDF files, a complete set of the assessment materials and study questions and answers from the test bank. Files are also available in TestGen format.

We Welcome Your Comments and Suggestions

Genetics is continuously changing, and textbooks must also change continuously to keep pace with the field and to meet the needs of instructors and students. Communication with our talented and dedicated users is a critical driver of change. We welcome all suggestions and comments and invite you to contact us directly. Please send comments or questions about the book to us at **mfsanders@ucdavis.edu** or **john.bowman@monash.edu**.

Acknowledgments

In our first edition, we described the adage that begins with the words "It takes a village . . . " as aptly applying to the development and assembly of our textbook. This new edition too has been a true team effort, and we are grateful to all of our teammates. We particularly wish to thank our editorial team led by our senior editor Michael Gillespie, our developmental editor Moira Lerner Nelson, and our content producer Melanie Field for their guidance and assistance in bringing this new edition to life. Margot Otway and Barbara Price also brought their developmental editing expertise to improving the art and page layouts. Our thanks to proofreader Pete Shanks for his keen attention to detail. We also thank our compatriot Peter Mirabito, author of the *Study Guide and Solutions Manual*, for his work assembling an exceptionally useful supplement. Beth Wilbur, Adam Jaworski, and Ginnie Simione Jutson have also been essential supporters who have made this new edition a reality.

On the production side, we thank the fine artists at Lachina who have managed to turn our rudimentary cartoons into instructive pieces of art. We thank the production team at SPi Global led by Thomas Russell.

The Pearson Education marketing team led by Kelly Galli and Christa Pelaez have provided expert guidance in bringing our textbook to the attention of genetics instructors throughout North America and indeed around the world.

Finally, and perhaps most importantly, we thank the scores of gifted genetics instructors and the thousands of genetics students who used the previous editions of our book and the many reviewers and accuracy checkers whose contributions have been invaluable. Many of our users and all of our reviewers have provided comments and feedback that have immeasurably improved this third edition. We particularly want to thank Ben Harrison at the University of Alaska, Anchorage; Pamela Sandstrom at the University of

Nevada, Reno; Christopher Halweg at North Carolina State University; and Nancy Staub at Gonzaga University for their more than generous expert advice.

Reviewers

Jade Atallah, *University of Toronto*
Michelle Boissiere, *Xavier University of Louisiana*
Sarah Chavez, *Washington University*
Claire Cronmiller, *University of Virginia*
Robert Dotson, *Tulane University*
Steven Finkel, *University of Southern California*
Benjamin Harrison, *University of Alaska Anchorage*
Laura Hill, *University of Vermont*
Adam Hrincevich, *Louisiana State University*
Steven Karpowicz, *University of Central Oklahoma*
Kirkwood Land, *University of the Pacific*
Craig Miller, *University of California at Berkeley*
Jessica Muhlin, *Maine Maritime Academy*
Anna Newman, *University of Houston*
Joanne Odden, *Pacific University Oregon*
Matthew Skerritt, *Corning Community College*
Nancy Staub, *Gonzaga University*
David Waddell, *University of North Florida*
Cynthia Wagner, *University of Maryland Baltimore County*
Rahul Warrior, *University of California at Irvine*

Supplements and Media Contributors

Laura Hill Bermingham, *University of Vermont*
Pat Calie, *Eastern Kentucky University*
Christy Fillman, *University of Colorado–Boulder*
Kathleen Fitzpatrick, *Simon Fraser University*
Michelle Gaudette, *Tufts University*
Christopher Halweg, *North Carolina State University*
Jutta Heller, *Loyola University*
Steven Karpowicz, *University of Central Oklahoma*
David Kass, *Eastern Michigan University*
Fordyce Lux III, *Metropolitan State College*
Peter Mirabito, *University of Kentucky*
Pam Osenkowski, *Loyola University*
Jennifer Osterhage, *University of Kentucky*
Louise Paquin, *McDaniel College*
Fiona Rawle, *University of Toronto Mississauga*
Pamela Sandstrom, *University of Nevada, Reno*
Tara Stoulig, *Southeastern Louisiana State*
Kevin Thornton, *University of California at Irvine*
Douglas Thrower, *University of California, Santa Barbara*
Sarah Van Vickle-Chavez, *Washington University in St. Louis*
Dennis Venema, *Trinity Western University*
Andrew J. Wood, *Southern Illinois University*

Unparalleled Problem-Solving Support

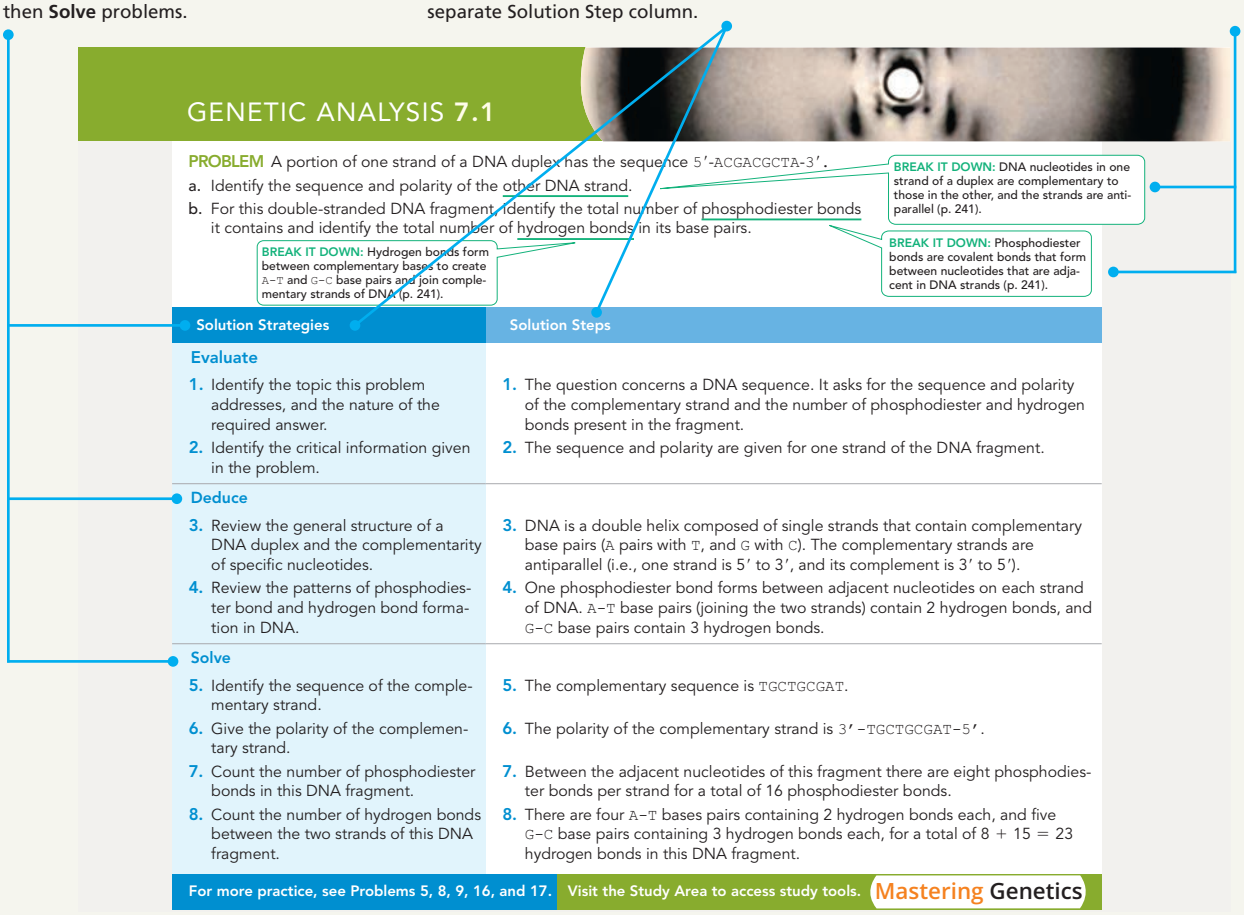
Genetic Analysis expertly guides students through the core ideas of genetics while introducing them to real-world applications and supporting them with unparalleled problem-solving guidance.

A consistent approach to problem solving is used in every **Genetic Analysis** worked example to help students understand the logic and purpose of each step in the problem-solving process.

Each example guides students with a unique, consistent, three-step approach that trains them to **Evaluate, Deduce,** and then **Solve** problems.

Every example is presented in a clear, **two-column format** that helps students see the Solution Strategy in one column and its corresponding execution in a separate Solution Step column.

"Break It Down" prompts help students get started with formulating an approach to solving a problem.



GENETIC ANALYSIS 7.1

PROBLEM A portion of one strand of a DNA duplex has the sequence 5′-ACGACGCTA-3′.

a. Identify the sequence and polarity of the other DNA strand.

b. For this double-stranded DNA fragment, identify the total number of phosphodiester bonds it contains and identify the total number of hydrogen bonds in its base pairs.

BREAK IT DOWN: DNA nucleotides in one strand of a duplex are complementary to those in the other, and the strands are antiparallel (p. 241).

BREAK IT DOWN: Hydrogen bonds form between complementary bases to create A–T and G–C base pairs and join complementary strands of DNA (p. 241).

BREAK IT DOWN: Phosphodiester bonds are covalent bonds that form between nucleotides that are adjacent in DNA strands (p. 241).

Solution Strategies	Solution Steps
Evaluate	
1. Identify the topic this problem addresses, and the nature of the required answer.	1. The question concerns a DNA sequence. It asks for the sequence and polarity of the complementary strand and the number of phosphodiester and hydrogen bonds present in the fragment.
2. Identify the critical information given in the problem.	2. The sequence and polarity are given for one strand of the DNA fragment.
Deduce	
3. Review the general structure of a DNA duplex and the complementarity of specific nucleotides.	3. DNA is a double helix composed of single strands that contain complementary base pairs (A pairs with T, and G with C). The complementary strands are antiparallel (i.e., one strand is 5′ to 3′, and its complement is 3′ to 5′).
4. Review the patterns of phosphodiester bond and hydrogen bond formation in DNA.	4. One phosphodiester bond forms between adjacent nucleotides on each strand of DNA. A–T base pairs (joining the two strands) contain 2 hydrogen bonds, and G–C base pairs contain 3 hydrogen bonds.
Solve	
5. Identify the sequence of the complementary strand.	5. The complementary sequence is TGCTGCGAT.
6. Give the polarity of the complementary strand.	6. The polarity of the complementary strand is 3′-TGCTGCGAT-5′.
7. Count the number of phosphodiester bonds in this DNA fragment.	7. Between the adjacent nucleotides of this fragment there are eight phosphodiester bonds per strand for a total of 16 phosphodiester bonds.
8. Count the number of hydrogen bonds between the two strands of this DNA fragment.	8. There are four A–T bases pairs containing 2 hydrogen bonds each, and five G–C base pairs containing 3 hydrogen bonds each, for a total of 8 + 15 = 23 hydrogen bonds in this DNA fragment.

For more practice, see Problems 5, 8, 9, 16, and 17. Visit the Study Area to access study tools. Mastering Genetics

PREPARING FOR PROBLEM SOLVING

In addition to the list of problem-solving tips and suggestions given here, you can go to the Study Guide and Solutions Manual that accompanies this book for help at solving problems.

1. Be familiar with and able to describe the structure of DNA.
2. Know the four DNA nucleotide bases and be able to describe complementary base pairing and the antiparallel alignment of strands. If required by your instructor, know the structure of the DNA bases.
3. Be able to describe the evidence that identified DNA as the hereditary material.
4. Understand the overall process of DNA replication and be able to diagram the general structure of a replication bubble.
5. Be able to identify the major enzymatic activities during DNA replication.
6. Be prepared to use an understanding of DNA replication processes and biochemical activities to analyze and predict the results of experiments involving DNA replication.
7. Understand the polymerase chain reaction (PCR) process and results.
8. Be able to describe dideoxy DNA sequencing and to analyze DNA sequencing results.

NEW! Preparing for Problem Solving feature in every chapter identifies specific knowledge and skills students need to answer end of chapter problems.

Applications of Genetics

This edition introduces five Application Chapters—brief chapters focused on specific applied topics in human genetics. Each topic is highly relevant and engaging, and the Application Chapters illustrate some of the practical uses of genetics and genetic analysis.

The Application Chapters are integrated into the book, each following relevant prerequisite material (see table of contents). The five Application Chapters are:

- A: Human Hereditary Disease and Genetic Counseling (pp. 223–234)
- B: Human Genetic Screening (pp. 346–360)
- C: The Genetics of Cancer (pp. 538–551)
- D: Human Evolutionary Genetics (pp. 758–777)
- E: Forensic Genetics (pp. 778–791)

APPLICATION B

Human Genetic Screening

A heel stick is a minimally invasive procedure, being used here to collect a small amount of blood from a newborn infant. The blood is used to screen for disorders on the Recommended Uniform Screening Panel (RUSP) list of human hereditary diseases, as discussed in this chapter.

Kristen Powers is not the most famous graduate of Stanford University, but she is one of the bravest. In 2003, when Kristen was 9 years old, her mother Nicola was diagnosed with the autosomal dominant neurological disorder Huntington disease (HD). HD is a devastating and fatal disease. It usually strikes people in their thirties or forties, with initial symptoms that include a loss of balance and coordination. Over the next few years the symptoms progress. People with the disease move with increasing jerkiness, lose the ability to walk and perform daily tasks, experience behavioral changes, and ultimately develop dementia and require full-time care. Nicola Powers was 37 years of age when she was diagnosed, and she died in 2011 at the age of 45.

Nicola had not known that HD ran in her family. She had lost touch with her biological father after her parents' divorce and did not find out he had HD until after her own diagnosis. By then, Kristen and her younger brother Nate had been born, and they each had a 50% chance of having the disease.

APPLICATION A

Human Hereditary Disease and Genetic Counseling

Genetic counseling, a central activity in medical genetics, seeks to provide individuals, couples, and families with medical and genetic information they can use to make informed decisions about genetic testing and medical treatment, in person-to-person meetings involving physicians, genetic counselors, and consultants.

When B.K. was born in San Francisco, California, in July 2015, he appeared to be a healthy baby boy. Among the myriad forms B.K.'s parents signed at the hospital was one informing them that B.K. would undergo mandated newborn genetic testing for almost four dozen different hereditary conditions within 24 hours of his birth. All the conditions tested are rare, but each can be treated to eliminate or substantially reduce the symptoms and complications of the disease. California, like all U.S. states and many other countries, mandates tests for several dozen rare genetic diseases of all newborns. We discuss this testing again later in the chapter and more fully in Application Chapter B: Human Genetic Screening.

Parents almost never hear about the results of these newborn genetic tests because a positive result is rare. But B.K.'s parents were told of a result indicating that B.K. had argininemia, commonly abbreviated ARG. B.K.'s parents had

NEW! Each Application Chapter includes problems, many of which are assignable in Mastering Genetics.

New Questions Support Active Learning

New types of questions help engage students while they read the book and when they are in the classroom. Questions related to key figures and problems for group work help support instructor efforts to build students' critical thinking and problem solving skills.

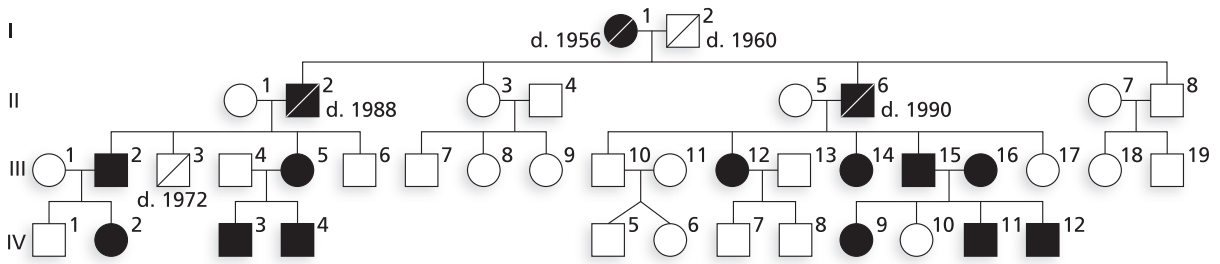


Figure 2.17 Autosomal dominant inheritance. Table 2.6 summarizes common observations in families with this pattern of inheritance.

Using *D* for the dominant allele and *d* for the recessive allele, give the genotypes for III-15, III-16, IV-9, IV-10, IV-11, and IV-12. (Hint: Look at the cross-producing III-15.)

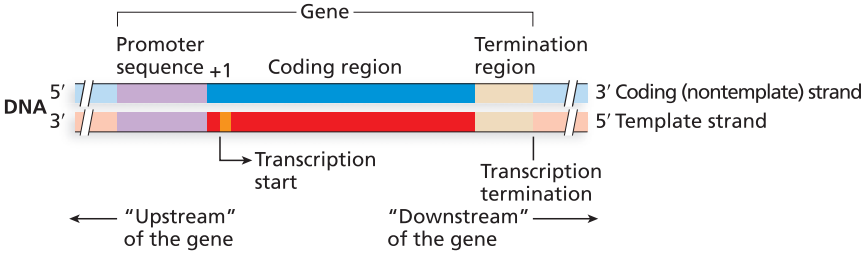


Figure 8.3 Gene structure and associated nomenclature.

If a consensus DNA sequence occurs upstream of the start of transcription, is it part of the coding sequence of a gene?

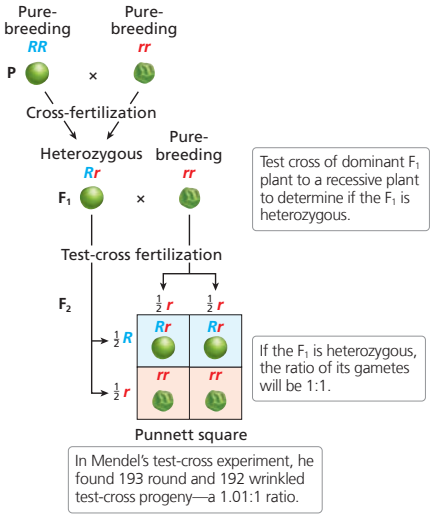


Figure 2.6 Test-cross analysis of F_1 plants. A test cross between an F_1 plant and one that is homozygous recessive produces progeny with a 1:1 ratio of the dominant to the recessive phenotype if the F_1 plant is heterozygous.

If a test-cross experiment identical to the one shown here produces 826 progeny plants, how many plants are expected in each phenotype category?

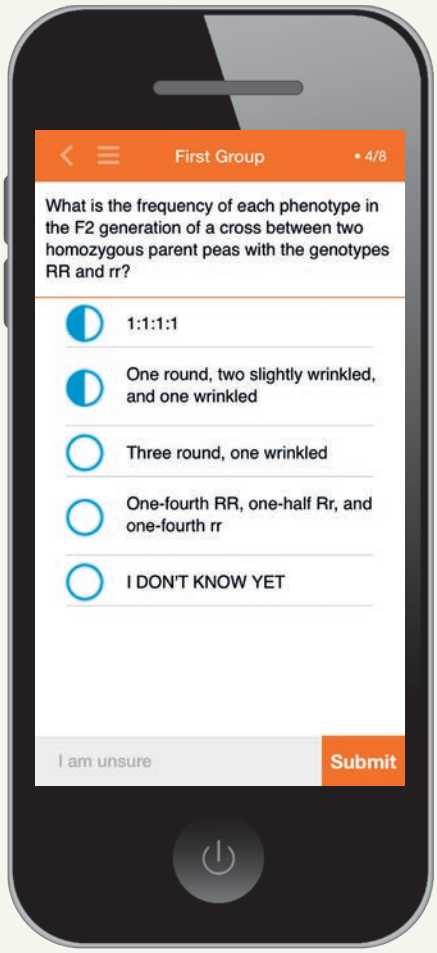
NEW! Caption Queries accompany many figures in the book, helping students focus on the illustrations and more fully understand the content. Some questions ask students to solve a problem using information from the figure, some require an explanation, and others ask students to expand on the information or idea in the figure. As an instructor resource, we provide Caption Queries for all book figures as clicker questions for in-class use.

Collaboration and Discussion

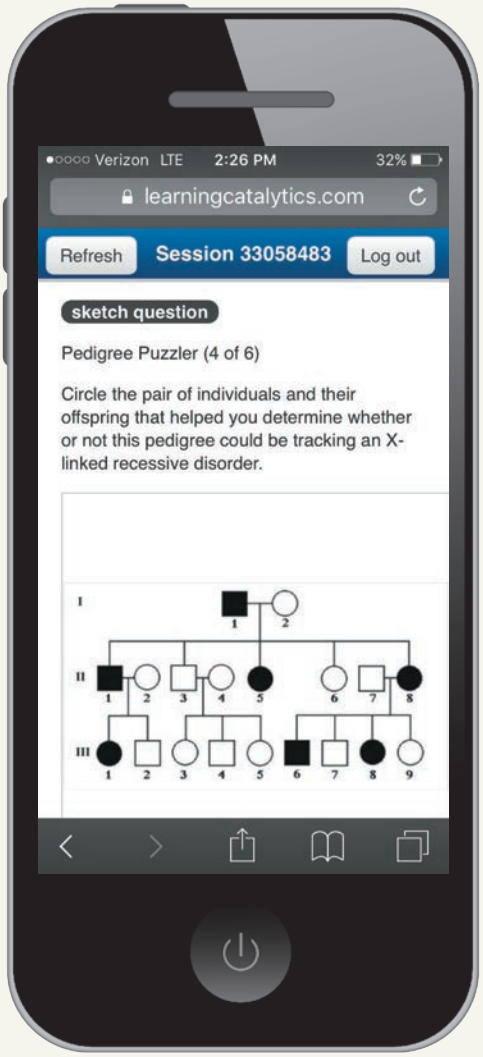
NEW! Collaboration and Discussion Problems have been added to every end of chapter question set to facilitate group work and hands-on problem solving in class.

Learn Genetics Concepts and Problem Solving

Mastering™ Genetics is an online homework, tutorial, and assessment platform designed to improve results by helping students quickly master concepts. Students benefit from self-paced tutorials that feature personalized wrong-answer feedback and hints that emulate the office-hour experience and help keep students on track. Learn more at www.pearson.com/mastering/genetics



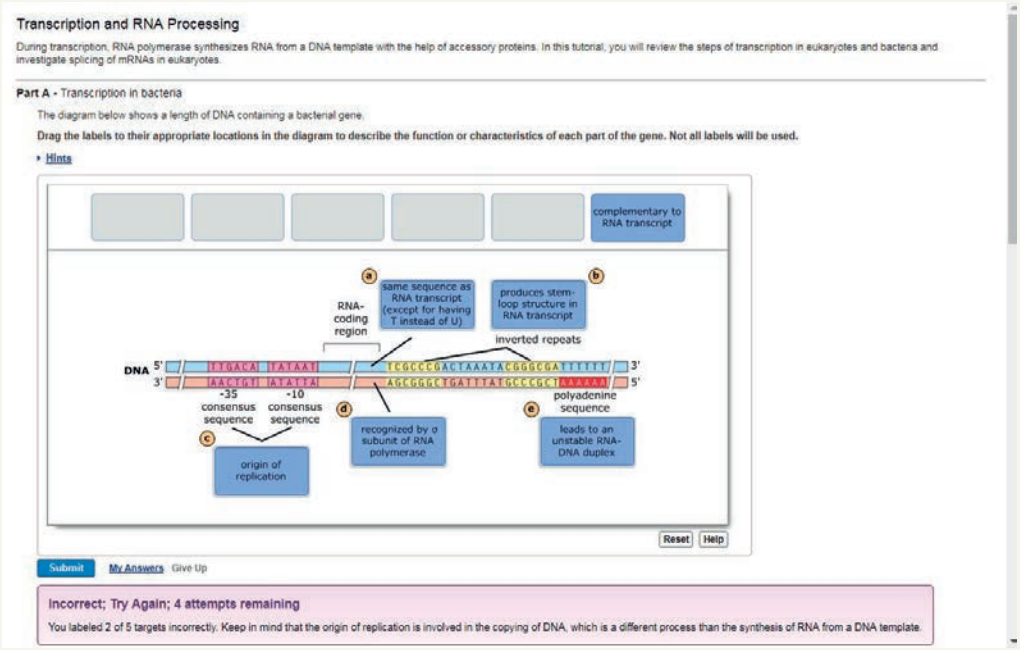
NEW! Dynamic Study Modules personalize each student's learning experience. Available for assignments or for self-study, these chapter-based modules help prepare students for class so they'll be ready for discussions or problem solving. These modules are accessible on smartphones, tablets, and computers.



Learning Catalytics™ helps generate class discussion, customize lectures, and promote peer-to-peer learning with real-time analytics. Learning Catalytics is a student response tool that uses students' smartphones, tablets, or laptops to engage them in more interactive tasks and thinking.

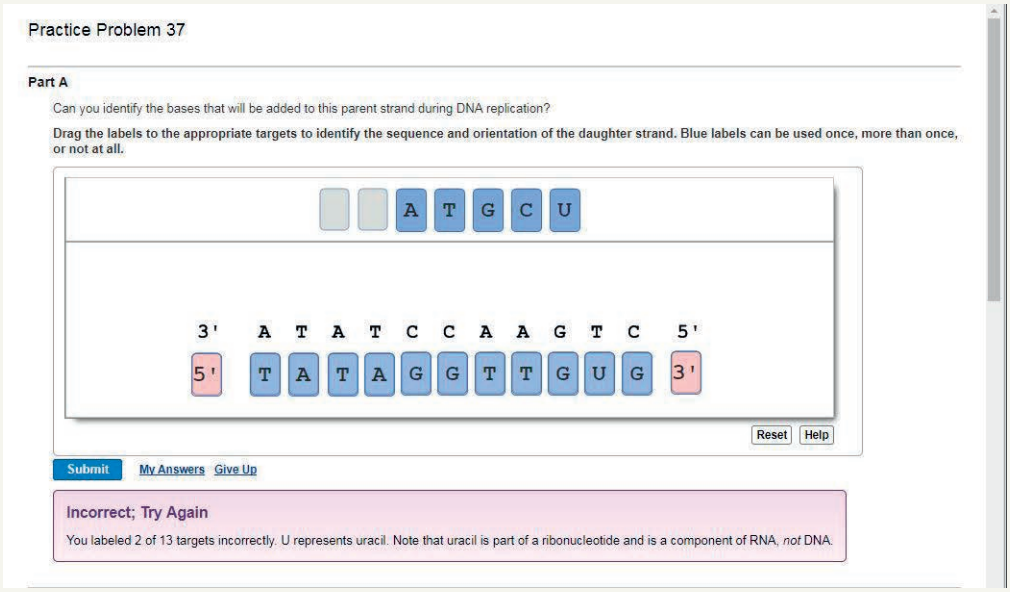
- Help your students develop critical thinking skills
- Monitor responses to find out where your students are struggling
- Rely on real-time data to adjust your teaching strategy

With Mastering Genetics



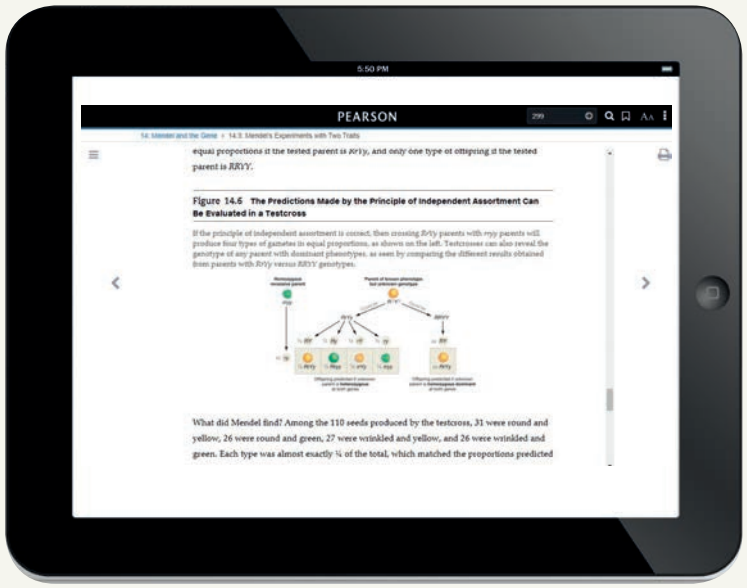
Activities feature personalized wrong-answer feedback and hints that emulate the office-hour experience to guide student learning. New tutorials include coverage of topics like CRISPR-Cas.

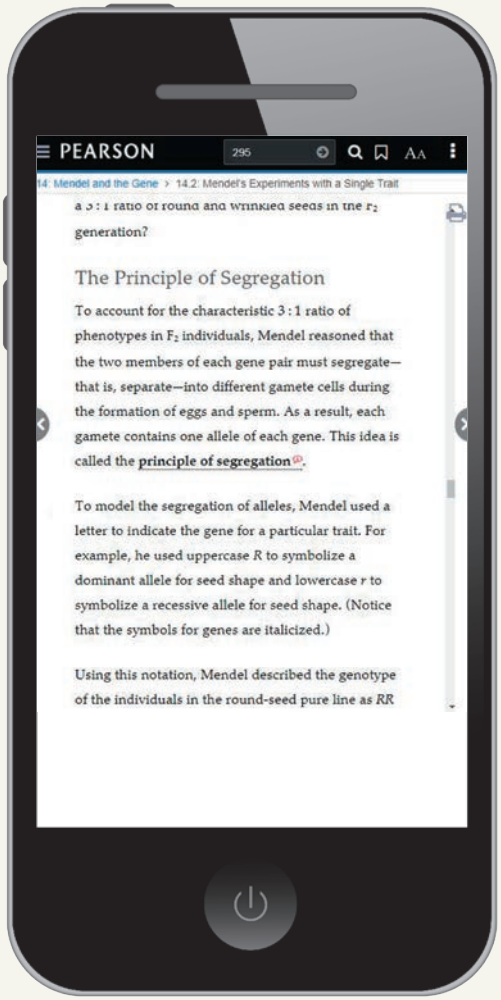
140 Practice Problems offer more opportunities to develop problem-solving skills. These questions appear only in Mastering Genetics and include targeted wrong answer feedback to guide students to the correct answer.



Access the text anytime, anywhere with Pearson eText

NEW! Pearson eText is built to adapt to the device readers are using—smartphone, tablet, or computer.





Pearson eText Mobile App offers offline access and can be downloaded for most iOS and Android phones/tablets from the Apple App Store or Google Play.

- Seamlessly integrated videos
- Accessible (screen-reader ready)
- Configurable reading settings, including resizable type and night reading mode
- Instructor and student note-taking, highlighting, bookmark-ing, and search

Unparalleled Problem-Solving Support

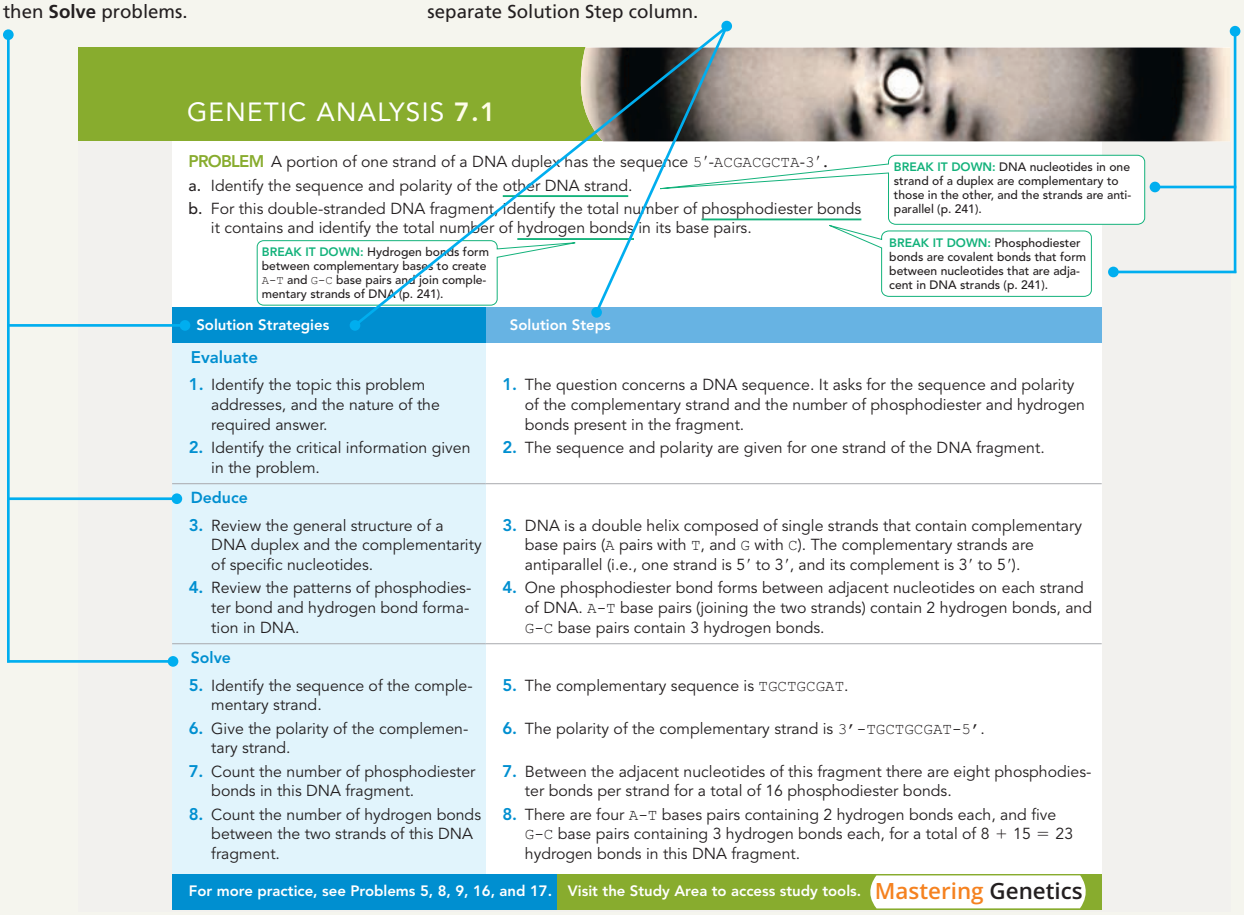
Genetic Analysis expertly guides students through the core ideas of genetics while introducing them to real-world applications and supporting them with unparalleled problem-solving guidance.

A consistent approach to problem solving is used in every **Genetic Analysis** worked example to help students understand the logic and purpose of each step in the problem-solving process.

Each example guides students with a unique, consistent, three-step approach that trains them to **Evaluate, Deduce,** and then **Solve** problems.

Every example is presented in a clear, **two-column format** that helps students see the Solution Strategy in one column and its corresponding execution in a separate Solution Step column.

"Break It Down" prompts help students get started with formulating an approach to solving a problem.



GENETIC ANALYSIS **7.1**

PROBLEM A portion of one strand of a DNA duplex has the sequence 5′-ACGACGCTA-3′.

a. Identify the sequence and polarity of the other DNA strand.

b. For this double-stranded DNA fragment, identify the total number of phosphodiester bonds it contains and identify the total number of hydrogen bonds in its base pairs.

BREAK IT DOWN: DNA nucleotides in one strand of a duplex are complementary to those in the other, and the strands are antiparallel (p. 241).

BREAK IT DOWN: Hydrogen bonds form between complementary bases to create A–T and G–C base pairs and join complementary strands of DNA (p. 241).

BREAK IT DOWN: Phosphodiester bonds are covalent bonds that form between nucleotides that are adjacent in DNA strands (p. 241).

Solution Strategies	Solution Steps
Evaluate	
1. Identify the topic this problem addresses, and the nature of the required answer.	1. The question concerns a DNA sequence. It asks for the sequence and polarity of the complementary strand and the number of phosphodiester and hydrogen bonds present in the fragment.
2. Identify the critical information given in the problem.	2. The sequence and polarity are given for one strand of the DNA fragment.
Deduce	
3. Review the general structure of a DNA duplex and the complementarity of specific nucleotides.	3. DNA is a double helix composed of single strands that contain complementary base pairs (A pairs with T, and G with C). The complementary strands are antiparallel (i.e., one strand is 5′ to 3′, and its complement is 3′ to 5′).
4. Review the patterns of phosphodiester bond and hydrogen bond formation in DNA.	4. One phosphodiester bond forms between adjacent nucleotides on each strand of DNA. A–T base pairs (joining the two strands) contain 2 hydrogen bonds, and G–C base pairs contain 3 hydrogen bonds.
Solve	
5. Identify the sequence of the complementary strand.	5. The complementary sequence is TGCTGCGAT.
6. Give the polarity of the complementary strand.	6. The polarity of the complementary strand is 3′-TGCTGCGAT-5′.
7. Count the number of phosphodiester bonds in this DNA fragment.	7. Between the adjacent nucleotides of this fragment there are eight phosphodiester bonds per strand for a total of 16 phosphodiester bonds.
8. Count the number of hydrogen bonds between the two strands of this DNA fragment.	8. There are four A–T bases pairs containing 2 hydrogen bonds each, and five G–C base pairs containing 3 hydrogen bonds each, for a total of 8 + 15 = 23 hydrogen bonds in this DNA fragment.

For more practice, see Problems 5, 8, 9, 16, and 17. Visit the Study Area to access study tools. Mastering Genetics

PREPARING FOR PROBLEM SOLVING

In addition to the list of problem-solving tips and suggestions given here, you can go to the Study Guide and Solutions Manual that accompanies this book for help at solving problems.

1. Be familiar with and able to describe the structure of DNA.
2. Know the four DNA nucleotide bases and be able to describe complementary base pairing and the antiparallel alignment of strands. If required by your instructor, know the structure of the DNA bases.
3. Be able to describe the evidence that identified DNA as the hereditary material.
4. Understand the overall process of DNA replication and be able to diagram the general structure of a replication bubble.
5. Be able to identify the major enzymatic activities during DNA replication.
6. Be prepared to use an understanding of DNA replication processes and biochemical activities to analyze and predict the results of experiments involving DNA replication.
7. Understand the polymerase chain reaction (PCR) process and results.
8. Be able to describe dideoxy DNA sequencing and to analyze DNA sequencing results.

NEW! Preparing for Problem Solving feature in every chapter identifies specific knowledge and skills students need to answer end of chapter problems.

Applications of Genetics

This edition introduces five Application Chapters—brief chapters focused on specific applied topics in human genetics. Each topic is highly relevant and engaging, and the Application Chapters illustrate some of the practical uses of genetics and genetic analysis.

The Application Chapters are integrated into the book, each following relevant prerequisite material (see table of contents). The five Application Chapters are:

- A: Human Hereditary Disease and Genetic Counseling (pp. 223–234)
- B: Human Genetic Screening (pp. 346–360)
- C: The Genetics of Cancer (pp. 538–551)
- D: Human Evolutionary Genetics (pp. 758–777)
- E: Forensic Genetics (pp. 778–791)

APPLICATION B

Human Genetic Screening

A heel stick is a minimally invasive procedure, being used here to collect a small amount of blood from a newborn infant. The blood is used to screen for disorders on the Recommended Uniform Screening Panel (RUSP) list of human hereditary diseases, as discussed in this chapter.

Kristen Powers is not the most famous graduate of Stanford University, but she is one of the bravest. In 2003, when Kristen was 9 years old, her mother Nicola was diagnosed with the autosomal dominant neurological disorder Huntington disease (HD). HD is a devastating and fatal disease. It usually strikes people in their thirties or forties, with initial symptoms that include a loss of balance and coordination. Over the next few years the symptoms progress. People with the disease move with increasing jerkiness, lose the ability to walk and perform daily tasks, experience behavioral changes, and ultimately develop dementia and require full-time care. Nicola Powers was 37 years of age when she was diagnosed, and she died in 2011 at the age of 45.

Nicola had not known that HD ran in her family. She had lost touch with her biological father after her parents' divorce and did not find out he had HD until after her own diagnosis. By then, Kristen and her younger brother Nate had been born, and they each had a 50% chance of having the disease.

APPLICATION A

Human Hereditary Disease and Genetic Counseling

Genetic counseling, a central activity in medical genetics, seeks to provide individuals, couples, and families with medical and genetic information they can use to make informed decisions about genetic testing and medical treatment, in person-to-person meetings involving physicians, genetic counselors, and consultants.

When B.K. was born in San Francisco, California, in July 2015, he appeared to be a healthy baby boy. Among the myriad forms B.K.'s parents signed at the hospital was one informing them that B.K. would undergo mandated newborn genetic testing for almost four dozen different hereditary conditions within 24 hours of his birth. All the conditions tested are rare, but each can be treated to eliminate or substantially reduce the symptoms and complications of the disease. California, like all U.S. states and many other countries, mandates tests for several dozen rare genetic diseases of all newborns. We discuss this testing again later in the chapter and more fully in Application Chapter B: Human Genetic Screening.

Parents almost never hear about the results of these newborn genetic tests because a positive result is rare. But B.K.'s parents were told of a result indicating that B.K. had argininemia, commonly abbreviated ARG. B.K.'s parents had

NEW! Each Application Chapter includes problems, many of which are assignable in Mastering Genetics.

New Questions Support Active Learning

New types of questions help engage students while they read the book and when they are in the classroom. Questions related to key figures and problems for group work help support instructor efforts to build students' critical thinking and problem solving skills.

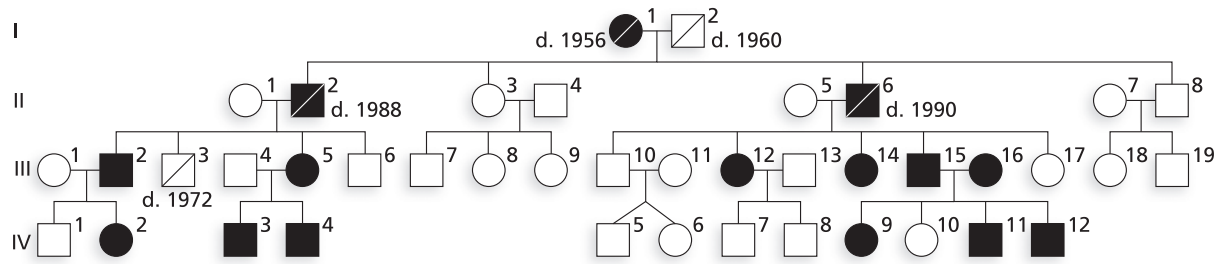


Figure 2.17 **Autosomal dominant inheritance.** Table 2.6 summarizes common observations in families with this pattern of inheritance.

Using *D* for the dominant allele and *d* for the recessive allele, give the genotypes for III-15, III-16, IV-9, IV-10, IV-11, and IV-12. (Hint: Look at the cross-producing III-15.)

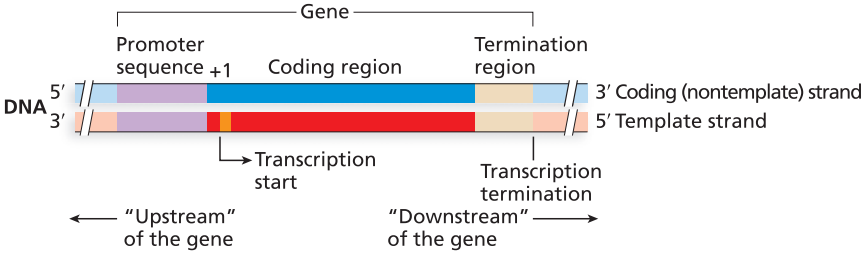


Figure 8.3 **Gene structure and associated nomenclature.**

If a consensus DNA sequence occurs upstream of the start of transcription, is it part of the coding sequence of a gene?

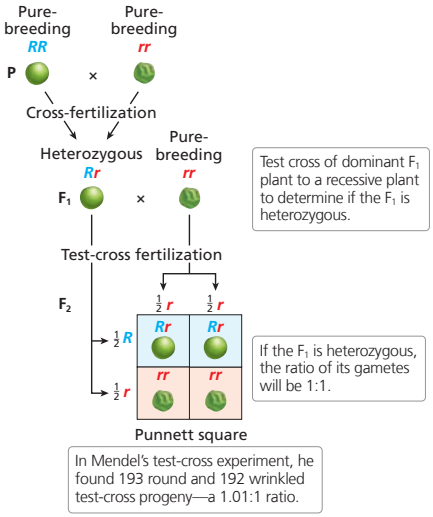


Figure 2.6 **Test-cross analysis of F_1 plants.** A test cross between an F_1 plant and one that is homozygous recessive produces progeny with a 1:1 ratio of the dominant to the recessive phenotype if the F_1 plant is heterozygous.

If a test-cross experiment identical to the one shown here produces 826 progeny plants, how many plants are expected in each phenotype category?

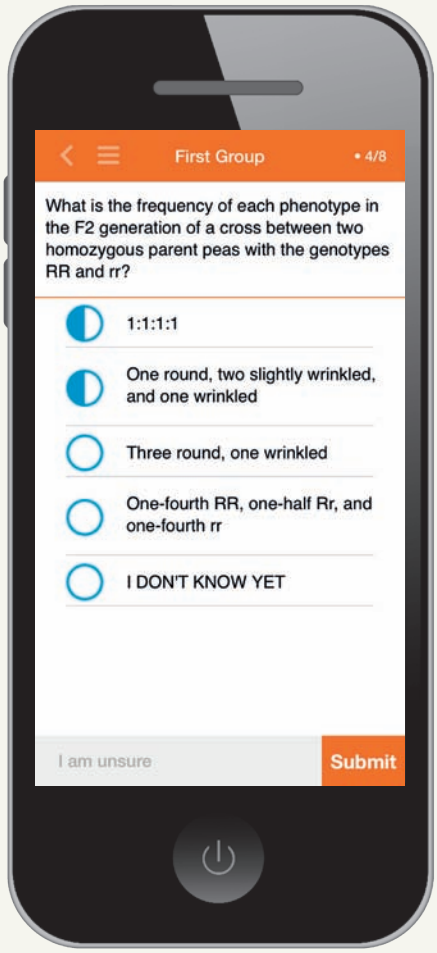
NEW! Caption Queries accompany many figures in the book, helping students focus on the illustrations and more fully understand the content. Some questions ask students to solve a problem using information from the figure, some require an explanation, and others ask students to expand on the information or idea in the figure. As an instructor resource, we provide Caption Queries for all book figures as clicker questions for in-class use.

Collaboration and Discussion

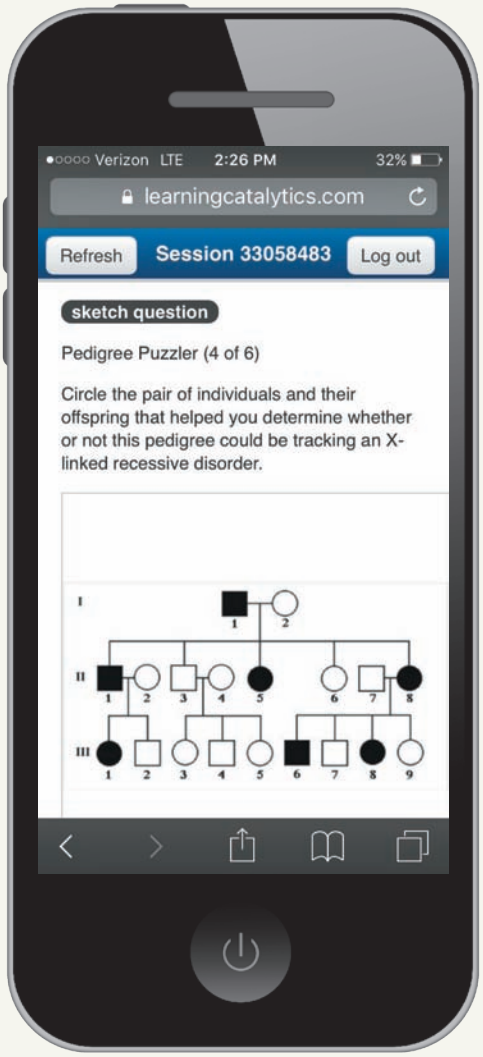
NEW! Collaboration and Discussion Problems have been added to every end of chapter question set to facilitate group work and hands-on problem solving in class.

Learn Genetics Concepts and Problem Solving

Mastering™ Genetics is an online homework, tutorial, and assessment platform designed to improve results by helping students quickly master concepts. Students benefit from self-paced tutorials that feature personalized wrong-answer feedback and hints that emulate the office-hour experience and help keep students on track. Learn more at www.pearson.com/mastering/genetics



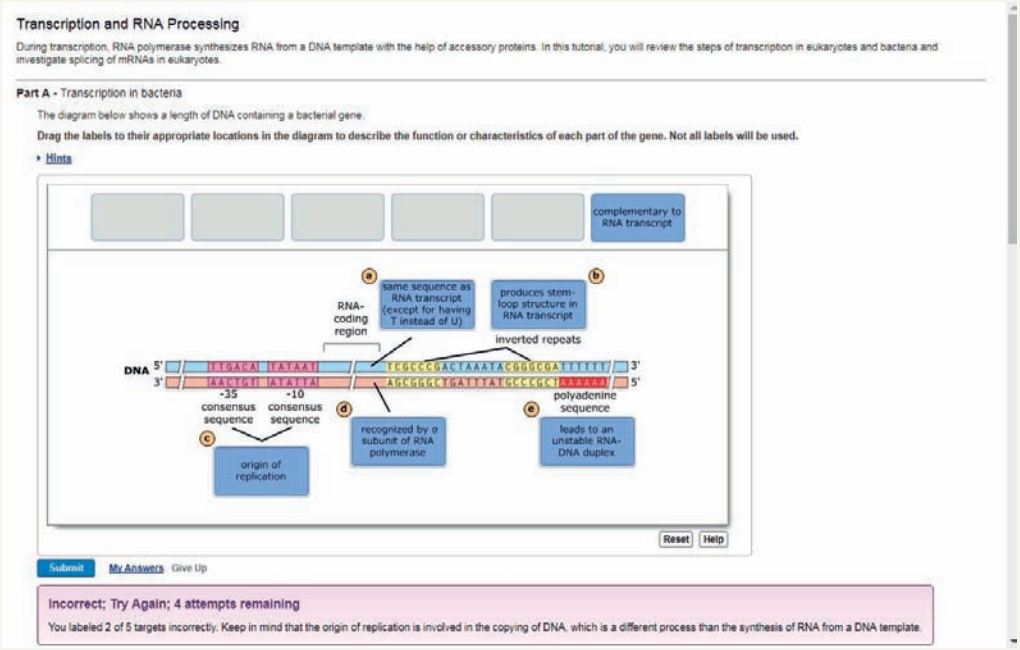
NEW! Dynamic Study Modules personalize each student's learning experience. Available for assignments or for self-study, these chapter-based modules help prepare students for class so they'll be ready for discussions or problem solving. These modules are accessible on smartphones, tablets, and computers.



Learning Catalytics™ helps generate class discussion, customize lectures, and promote peer-to-peer learning with real-time analytics. Learning Catalytics is a student response tool that uses students' smartphones, tablets, or laptops to engage them in more interactive tasks and thinking.

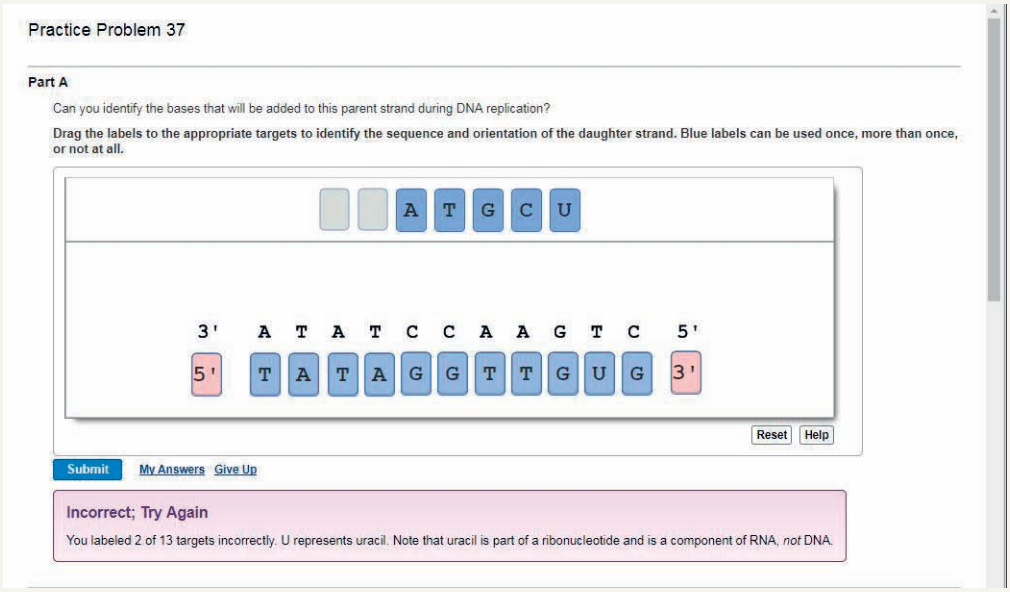
- Help your students develop critical thinking skills
- Monitor responses to find out where your students are struggling
- Rely on real-time data to adjust your teaching strategy

With Mastering Genetics



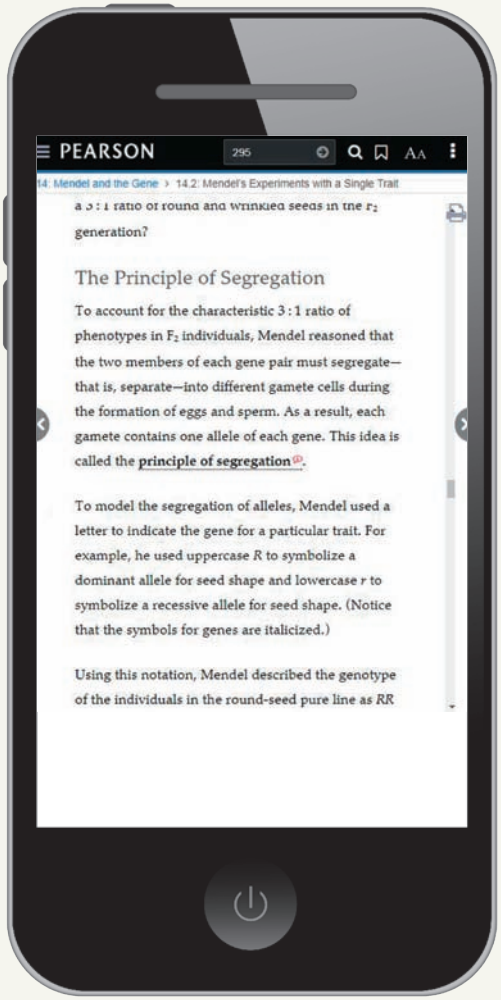
Activities feature personalized wrong-answer feedback and hints that emulate the office-hour experience to guide student learning. New tutorials include coverage of topics like CRISPR-Cas.

140 Practice Problems offer more opportunities to develop problem-solving skills. These questions appear only in Mastering Genetics and include targeted wrong answer feedback to guide students to the correct answer.



Access the text anytime, anywhere with Pearson eText

NEW! Pearson eText is built to adapt to the device readers are using—smartphone, tablet, or computer.



Pearson eText Mobile App offers offline access and can be downloaded for most iOS and Android phones/tablets from the Apple App Store or Google Play.

- Seamlessly integrated videos
- Accessible (screen-reader ready)
- Configurable reading settings, including resizable type and night reading mode
- Instructor and student note-taking, highlighting, bookmarking, and search

The Molecular Basis of Heredity, Variation, and Evolution

1

The Helix Bridge is a 280-meter pedestrian bridge spanning the marina in downtown Singapore. The bridge design is inspired by the structure of DNA and features two twisting helices with colored lights representing the A–T and G–C base pairs.

CHAPTER OUTLINE

ESSENTIAL IDEAS

- Modern genetics developed during the 20th century and is a prominent discipline of the biological sciences.
- DNA replication produces exact copies of the original molecule.
- The "central dogma of biology" describing the relationship between DNA, RNA, and protein is a foundation of molecular biology.
- Gene expression is a two-step process that first produces an RNA transcript of a gene and then synthesizes an amino acid string by translation of RNA.
- Inherited variation can be detected by laboratory methods that examine DNA, RNA, and proteins.
- Evolution is a foundation of modern genetics that occurs through four processes.

Life is astounding, both in the richness of its history and in its diversity. From the single-celled organisms that evolved billions of years ago have descended millions of species of microorganisms, plants, and animals. These species are connected by a shared evolutionary past that is revealed by the study of genetics, the science that explores genome composition and organization and the transmission, expression, variation, and evolution of hereditary characteristics of organisms.

Genetics is a dynamic discipline that finds applications everywhere humans interact with one another and with other organisms. In research laboratories, on farms, in grocery stores, in medical offices, in courtrooms, and in other settings, genetics

plays a prominent and expanding role in our lives. Modern genetics is an increasingly genome- and gene-based discipline—that is, it is increasingly focused on the entirety of the hereditary information carried by organisms and on the molecular processes that control and regulate the expression of genes. Despite its increasingly gene-focused emphasis, however, genetics retains a strong interest in traditional areas of inquiry and investigation—heredity, variation, and evolution. The fascinating discipline of genetics explores the basis of life—past and present—and its study will provide you with an exciting and rewarding journey.

In this chapter, we survey the scope of modern genetics and reacquaint you with some basic information about deoxyribonucleic acid—DNA, the carrier of genetic information. We begin with a brief overview of the origins and contemporary range of genetic science. Next we retrace some of the fundamentals of *DNA replication,* and of *transcription* and *translation* (the two main components of gene expression), by reviewing what you learned about these processes in previous biology courses. We also look at some research techniques that are indispensable for studying genetic variation in the laboratory; and we meet the most prominent of the modern-day "-omic" avenues of research and investigation in genetics. The chapter's final section describes the central position of evolution in genetics and discusses the roles of heredity and variation in evolution.

1.1 Modern Genetics Is in Its Second Century

Humans have been implicitly aware of genetics for more than 10,000 years (**Figure 1.1**). From the time of the domestication of rice in Asia, maize in Central America, and wheat in the Middle East, humans have recognized that desirable traits found in plants and animals can be reproduced and enhanced in succeeding generations through selective mating. On the other hand, explicit exploration and understanding of the hereditary principles of genetics—what we might think of as the science of modern genetics—is a much more recent development.

The Development of Modern Genetics

In a sense, modern genetics can trace its early roots back to the invention of the compound microscope in the 1590s by a father and son team of Dutch eyeglass makers, Hans and Zacharias Jansen. The genesis of ideas about cells—their origins, structure, contents—was made possible by the Jansen's invention, and by numerous improvements in microscope technology over the centuries. Collectively, these developments paved the way for theories like the cell theory and the germ plasm theory that are foundational to modern genetics.

In 1665, Robert Hooke first described cells he observed in thin sections of cork. In the 1670s and 1680s, Anton van Leeuwenhoek, often called the father of microbiology, described the abundance of tiny single-celled organisms in pond water and made numerous observations of bacteria. In the 1830s, Matthias Schleiden and Theodor Schwann described cells in plants and in animals, respectively, and are credited with proposing the cell theory that states all life is composed of cells and that cells are the basic building blocks of organisms. Rudolph Virchow expanded and extended the ideas of the cell theory in 1855, declaring that "every cell stems from another cell." Virchow's contribution was important for giving the cell theory an evolutionary basis. In 1831, Robert Brown provided the first description of the nucleus of a cell; and after descriptions by others of the contents of the nucleus—including chromosomes—Walter Fleming, Theodor Boveri, and Walter Sutton in the 1880s described chromosome separation during cell division, cementing the importance of the cell theory and giving rise to the germ plasm theory.

It was August Weismann who proposed the germ plasm theory, in 1889, bringing together multiple threads of evidence linking chromosomes and heredity. The germ plasm theory posits that reproductive organs (ovaries and testes, for example) carry full sets of genetic information and that the sperm and egg cells they produce carry the genetic information brought together in fertilization. This was followed by the proposal of Edmund Beecher Wilson in 1895 that DNA, known at the time as "nuclein," was the hereditary molecule and a component of chromosomes (whose separation during cell division was observed, as noted above, by Fleming, Boveri, and Sutton). Just a few years later, a British physician-scientist named Archibald Garrod identified the first human hereditary condition, an autosomal recessive disorder called alkaptonuria, by examining several generations of British families with the condition.

The ideas embodied in the cell theory, the germ plasm theory, and Wilson's proposal that DNA was the hereditary molecule took shape against a backdrop of other developments in 19th century biology. The most important of these was Charles Darwin's theory of evolution by natural selection in 1859. Darwin recognized the importance of heredity in his theory of evolution, but despite his attempts to decipher a mechanism, he was never able to describe how organisms transmitted their hereditary traits. Little did Darwin know that the explanation for hereditary transmission was already available. In 1866, Gregor Mendel published the descriptions and analysis of his experiments of the inheritance of seven traits in pea plants. Although Mendel's work would lie in obscurity for nearly 35 years—until more than a decade after his death—his experiments and analysis form the foundation of modern genetics.

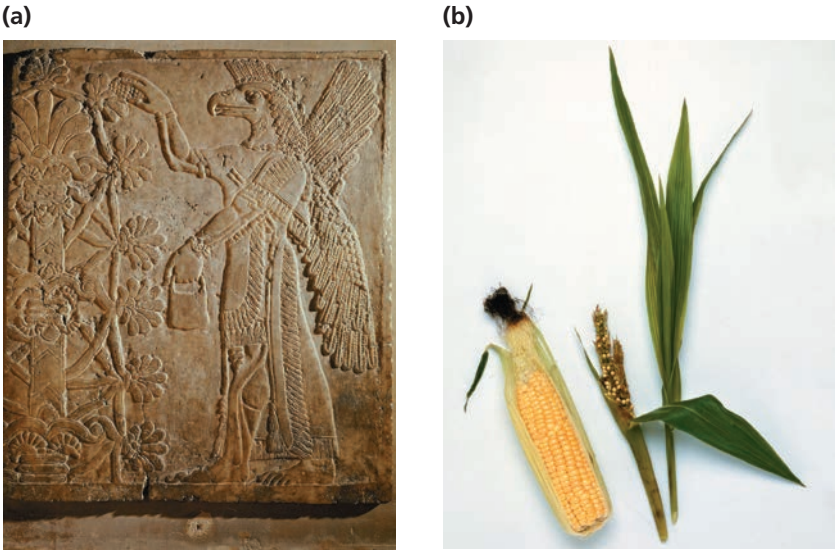


Figure 1.1 Ancient applications of genetics. **(a)** An early record of human genetic manipulation is this Assyrian relief (882–859 BCE) showing priests in bird masks artificially pollinating date palms. **(b)** Modern maize (left) developed through human domestication of its wild ancestor teosinte (right).

The Four Phases of Modern Genetics

In 1900, three botanists working independently of one another—Carl Correns in Germany, Hugo de Vries in Holland, and Erich von Tschermak in Austria—reached strikingly similar conclusions about the pattern of transmission of hereditary traits in plants. Each reported that his results mirrored those published in 1866 by an obscure amateur botanist and Augustinian monk named Gregor Mendel. (Mendel's work is discussed in Chapter 2.) Although Correns, de Vries, and Tschermak had actually *rediscovered* an explanation of hereditary transmission that Mendel had published 34 years earlier, their announcement of the identification of principles of hereditary transmission gave modern genetics its start.

Biologists immediately began testing, verifying, and expanding on the newly appreciated explanation of heredity. In 1901, during a train ride from Cambridge to London, William Bateson read the publication by Archibald Garrod describing the pattern of occurrence of alkaptonuria and immediately realized that Garrod's description depicted "exactly the conditions most likely to enable a rare, usually recessive character to show itself." According to his own retelling, Bateson was converted into a firm believer in Mendelism during that train ride. Garrod—with Bateson's interpretive assistance—having produced the first documented example of a human hereditary disorder, continued to study alkaptonuria for decades, eventually devising the designation "inborn error of metabolism," a phrase still used today to describe many recessive genetic conditions.

From that starting point in the first years of the 20th century, modern genetics has moved through four phases that we discuss below and then explore in greater detail as we advance through the book. The first phase was the identification of the cellular and chromosomal basis of heredity. The second phase was the identification of DNA as the hereditary material. Phase three was the description of the informational and regulatory processes of heredity, that is, the encoding of information in genes and the processes of transcription and translation. The current and fourth phase of modern genetics can be described as the genomic era. This phase began in the 1980s with the completion of the first genome sequences, but it reached popular recognition in 2001 when the complete human genome was produced.

Location of the Genetic Material Fleming, Sutton, and Boveri independently used microscopy to observe chromosome movement during cell division in reproductive cells. They each noted that the patterns of chromosome movement mirrored the transmission of the newly rediscovered Mendelian hereditary units. This finding implied that the hereditary units, or *genes,* posited by Mendel are located on *chromosomes.* We now know that **genes**—the physical units of heredity—are composed of defined DNA sequences that collectively control gene *transcription* (described later in the chapter) and contain the information to produce RNA molecules, one category of which is called messenger RNA, or mRNA, and is used to produce proteins by *translation* (described later in the chapter). **Chromosomes** consist of single long molecules of double-stranded DNA that in plants and animals are bound by many different kinds of protein that give chromosomes their structure and can affect the transcription of genes the chromosomes carry. The chromosomes of sexually reproducing organisms typically occur in pairs known as **homologous pairs,** or, more simply, as **homologs.** Each chromosome carries many genes, and homologs carry genes for the same traits in the same order on each member of the pair.

Bacteria and archaea are single-celled organisms that do not have a true nucleus. In almost all cases, species of bacteria and archaea have a single, usually circular chromosome. As a consequence, in the genome of these organisms, there is just one copy of each gene, a condition described as **haploid**. Bacterial and archaeal chromosomes are bound by a

relatively small amount of protein. Limited amounts of other proteins help localize bacterial chromosomes to a region of the cell known as the **nucleoid**. Some archaeal species have chromosomes and associated proteins that in appearance resemble those in bacteria, but other species appear to have a more eukaryote-like chromosome organization.

In contrast to bacteria and archaea, the cells of eukaryotes—a classification that includes all single-celled and multicellular plants and animals—contain a true nucleus holding multiple sets of chromosomes. Almost all eukaryotes have haploid and **diploid** stages in their life cycles. For example, sperm and eggs produced in animals are haploid, having one copy of each chromosome pair in the genome. In the diploid state, the eukaryotic genome contains two copies—a homologous pair—of each gene. (Even in a diploid cell, genes located on eukaryotic sex chromosomes might not be present in two copies, as we see in Chapter 4.) Numerous eukaryotic genomes, particularly those of plants, contain more than two copies of each chromosome—a genome composition known as **polyploidy**.

In addition to the chromosomes carried in their nuclei—the so-called nuclear chromosomes—plant and animal cells also contain genetic material in specialized organelles called **mitochondria** (singular: *mitochondrion*), and plant cells contain a third type of gene-containing organelle called **chloroplasts.** Many of these organelles are present by the dozens in each cell, and each mitochondrion or chloroplast carries one or more copies of its own chromosome. Mitochondrial and chloroplast genes produce proteins that work with proteins produced by nuclear genes to perform essential functions in cells—mitochondria are essential for the production of adenosine triphosphate (ATP) that is the principal source of cellular energy, and chloroplasts are necessary for photosynthesis. Mitochondria and chloroplasts are transmitted in the cytoplasm during cell division, and the term **cytoplasmic inheritance** is used to refer to the random distribution of mitochondria and chloroplasts among daughter cells.

Mitochondria and chloroplasts have an evolutionary history, having descended from ancient parasitic bacterial invasion of eukaryotic cells. Since the time of their acquisition by eukaryotes, mitochondria and chloroplasts have evolved an endosymbiotic relationship with their eukaryotic hosts, and the precise genetic content of mitochondria and chloroplasts varies by eukaryotic host species (see Chapter 17).

A complete set of nuclear chromosomes are transmitted during the cell-division process called **mitosis**, to produce genetically identical daughter cells. In contrast, sexual reproduction to produce offspring occurs by the cell-division process called **meiosis**, that produces reproductive or sex cells, often identified as **gametes**—sperm and egg in animals and pollen and egg in plants. The gametes of a diploid species are haploid and contain one chromosome from each of the homologous pairs of chromosomes in the genome. The union of haploid gametes at fertilization produces a diploid fertilized egg that begins mitotic division to produce the zygote.

Predictable patterns of gene transmission during sexual reproduction are a focus of later chapters that discuss hereditary transmission and the analysis of transmission ratios (Chapter 2), cell division and chromosome heredity (Chapter 3), gene action and interaction of genes in producing variation of physical characteristics (Chapter 4), and the analysis of genetic linkage between genes (Chapter 5).

Genetic experiments taking place in roughly the first half of the 20th century developed the concept of the gene as the physical unit of heredity and revealed the relationship between **phenotype**, meaning the observable traits of an organism, and **genotype**, meaning the genetic constitution of an organism. Biologists also described how hereditary variation is attributable to alternative forms of a gene, called **alleles.** The alleles of a gene have differences in DNA sequence that alter the product of the gene.

During the early decades of the 20th century, the study of gene transmission was established as a central focus of genetics. The concepts of gene action and gene interaction in producing phenotype variation were described, as was the concept of mapping genes along chromosomes. It was also during this period that evolutionary biologists developed gene-based models of evolution. These, too, are integral to genetic analysis, and their use continues to the present day.

Identifying the Genetic Material An experiment conducted in 1944 by Oswald Avery, Colin MacLeod, and Maclyn McCarty identified *deoxyribonucleic acid (DNA)* as the hereditary material and is commonly credited with inaugurating the "molecular era" in genetics (see Chapter 7). This new era, which spanned the second half of the 20th century and continues to the present day, began an effort to discover the molecular structure of DNA. Molecular genetic research reached a milestone in 1953, when the experimental work of many biologists, including, most famously, James Watson, Francis Crick, Maurice Wilkins, and Rosalind Franklin, led to the identification of the double-helical structure of DNA. A few years later, in 1958, the general mechanism of DNA replication was ascertained. We examine details of this work in Chapter 7.

Describing the Nature and Processing of Genetic Information By the mid-1960s, the basic mechanisms of DNA transcription and messenger RNA (mRNA) translation were laid out, and the genetic code by which mRNA is translated into proteins was deciphered. This period also saw the first descriptions of mechanisms that regulate transcription in cells of different types or in response to a wide variety of stimuli from outside and inside cells. Chapters 8 and 9 are devoted to discussions of transcription and translation, and Chapters 12 and 13 describe processes that regulate gene expression in bacteria and in eukaryotes.

The Genomics Era Gene cloning and the development of recombinant DNA technologies developed and progressed rapidly during the 1970s. By the early 1980s, biologists realized that to properly understand the unity and complexity

of life, they would have to study and compare the **genomes** of species—the complete sets of DNA sequences, including all genes and regions controlling genes. This realization launched the "genomics era" in genetics, which continues to expand rapidly today.

Since the inception of genome sequencing, biologists have deciphered thousands of genomes that range in size from a few tens of thousands of DNA base pairs in the simplest viral genomes to tens of billions of base pairs in the largest plant and animal genomes. Fittingly, in 2001, a century after Garrod and Bateson's historic identification of alkaptonuria as a human hereditary disease, collaborative scientific groups from around the world published the completed "first draft" of the human genome. Collective efforts like the Human Genome Project and the other genome sequencing projects that have been and will be undertaken promise to provide databases that will make the second century of genetics every bit as remarkable as its first century. Chapters 14, 15, and 16 are primarily devoted to descriptions of the analysis and functions of genomes.

Genetics—Central to Modern Biology

One of the foundations of modern biology is the demonstration that all life on Earth shares a common origin in the form of the "*l*ast *u*niversal *c*ommon *a*ncestor," or **LUCA** (Figure 1.2). All life is descended from this common ancestor and is most commonly divided into three major domains. These three domains of life are **Eukarya**, **Bacteria**, and **Archaea**.

The three-domain model of life is originally derived from the research of Carl Woese and colleagues in the mid-1970s. In contrast to earlier models, which were based on morphology alone, Woese used molecular sequences to determine phylogenetic relationships between existing organisms and thus to trace the evolution of life. Woese used the sequence of ribosomal RNA (rRNA), a small molecule produced directly from DNA in all organisms, as his basis for comparison. His premise was simple—evolutionary theory predicts that closely related species will have more similarity in their rRNA sequences than will species that are less closely related. Furthermore, species that are members of the same evolutionary lineage will share certain rRNA sequence changes that are not shared with species outside the lineage. Since Woese's work, many researchers have used other molecules to refine and propose additional details to the three-domain model. The tree of life remains a work in progress, but the three-domain model is well established. We use this model in subsequent chapters to compare and contrast molecular features, activities, and processes that shed additional light on the evolutionary relationships between the three domains.

A second foundation of biology is the recognition that the hereditary material—the molecular substance that

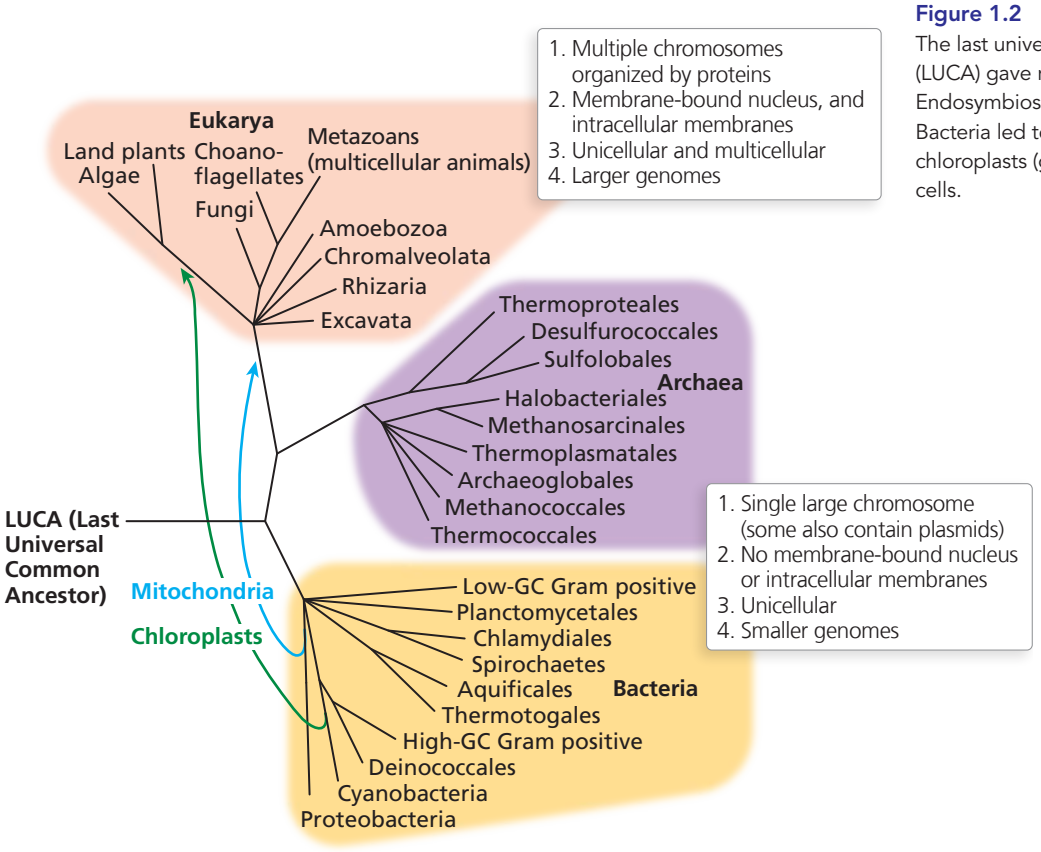


Figure 1.2 The three domains of life. The last universal common ancestor (LUCA) gave rise to three domains of life. Endosymbiosis between Eukarya and Bacteria led to mitochondria (blue) and chloroplasts (green) populating eukaryotic cells.

conveys and stores genetic information—is **deoxyribonucleic acid (DNA)** in all organisms. Certain viruses use **ribonucleic acid (RNA)** as their hereditary material. Most biologists argue that viruses are not alive. Rather, they are obligate intracellular parasites that are noncellular and must invade host cells to reproduce, at the expense of the host cell. In living organisms, DNA has a double-stranded structure described as a **DNA double helix**, or as a **DNA duplex**, consisting of two strands joined together in accordance with specific biochemical rules. Certain viral genomes consist of a small single-stranded DNA molecule that replicates to form a DNA duplex in a host cell.

Eukarya, Bacteria, and Archaea share general mechanisms of **DNA replication**, the process that precisely duplicates the DNA duplex prior to cell division, and they also share general mechanisms of gene expression, the processes through which the genetic information guides development and functioning of an organism. All organisms express their genetic information by a two-step process that begins with **transcription**, a process in which one strand of DNA is used to direct the synthesis of a single strand of RNA. Transcription produces various forms of RNA, including **messenger RNA (mRNA),** which in all organisms undergoes **translation** to produce proteins at structures called **ribosomes**.

As the biological discipline devoted to the examination of all aspects of heredity and variation, between generations and through evolutionary time, genetics is central to modern biology. Modern genetics has three major branches. **Transmission genetics,** also known as **Mendelian genetics**, is the study of the transmission of traits and characteristics in successive generations. **Evolutionary genetics** studies the origins of and genetic relationships between organisms and examines the evolution of genes and genomes. **Molecular genetics** studies inheritance and variation in nucleic acids (DNA and RNA), proteins, and genomes and tries to connect them to inherited variation and evolution in organisms.

These branches of genetics are not rigidly differentiated. There is substantial cross-communication among them, and it is rare to find a geneticist today who doesn't use analytical approaches from all three. Similarly, not only are most biological scientists, to a greater or lesser extent, also geneticists, but in addition many of the methods and techniques of genetic experimentation and analysis are shared by all biological scientists. After all, genetic analysis interprets the common language of life by integrating information from all three branches.

1.2 The Structure of DNA Suggests a Mechanism for Replication

At its core, hereditary transmission is the process of dispersing genetic information from parents to offspring. In sexually reproducing organisms, this process is accomplished by the generation of reproductive sex cells in males (the sperm or pollen) and females (the egg), followed by the union of egg and sperm (animals) or pollen (plants) or spores (yeast) at fertilization, with the subsequent development of an organism. DNA is the hereditary molecule in reproductive cells. Similarly, in somatic (body) cells of plants and animals and in organisms that reproduce by asexual processes, DNA is the hereditary molecule that ensures that successive generations of cells are identical. Clearly, then, discovering the molecular structure of DNA would be the key that opened the door to two fundamental areas of inquiry: (1) how DNA could carry the diverse array of genetic information present in the various genomes of animals and plants; and (2) how the molecule replicated. In this section, we review basic concepts of DNA structure and DNA replication.The molecular details of DNA structure and replication are provided in Chapter 7.

The Discovery of DNA Structure

In the early 1950s, James Watson, an American in his mid-20s who had recently completed a doctoral degree, and Francis Crick, a British biochemist in his mid-30s, began working together at the University of Cambridge, England, to solve the puzzle of DNA structure. Their now-legendary collaboration culminated in a 1953 publication that ignited the molecular era in genetics.

Watson and Crick's paper accurately described the molecular structure of DNA as a double helix composed of two strands of DNA, with an invariant sugar-phosphate backbone on the outside and nucleotide bases—adenine, thymine, guanine, and cytosine—forming complementary base pairs within the center of the molecule. This discovery was of enormous importance, because with the structure of DNA unveiled, the "gene" had a known physical form and was no longer just a conceptual entity. This physical form of a gene could be examined and sequenced, compared with other genes in the genome, and compared with similar genes in other species.

Watson and Crick's description of DNA structure was not the product of their work exclusively. In fact, unlike others who made significant contributions to the discovery of DNA structure, Watson and Crick were not actively engaged in laboratory research. Outside of their salaries, they had very little financial support available to conduct research. In lieu of laboratory research, Watson and Crick put their efforts into DNA-model building, basing their interpretations on experimental data gathered by others.

Rosalind Franklin, a biophysicist working in a laboratory with Maurice Wilkins at King's College in London, was one of the principal sources of information used by Watson and Crick (Figure 1.3). Franklin used an early form of X-ray diffraction imagery to examine the crystal structure of DNA. In Franklin's method, X-rays bombarding crystalline preparations of DNA were diffracted as they encountered the atoms in the crystals. The pattern of diffracted X-rays was recorded on X-ray film, and the structure of the molecules in the crystal was deduced from that pattern. Franklin's most famous X-ray diffraction photograph, Photo 51, clearly showed (to the well-trained eye) that DNA is a duplex, consisting of two strands

Figure 1.3 Rosalind Franklin, shown here on holiday, used X-ray diffraction to investigate the structure of DNA.

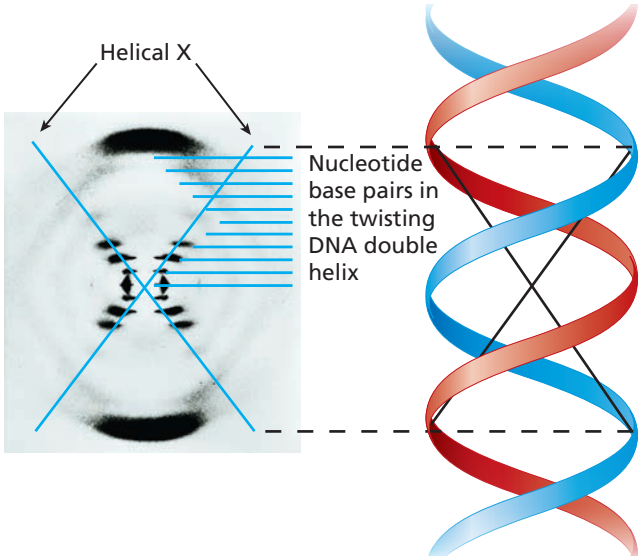


Figure 1.4 Rosalind Franklin's Photo 51, revealing DNA to be a double helix. The photo is an image of DNA viewed down the center of the helix from the top. The "rungs" of the twisting helix are base pairs, and the "X" superimposed on the photo identifies the helical shape of the molecule.

twisted around one another in a double helix. Figure 1.4 shows Photo 51 and provides a schematic interpretation of its distinctive image. The photo captures a DNA double helix from the top. The "X" superimposed on the photo traces the spiral of nucleotide base pairs as it recedes from the focal plane.

There is considerable controversy surrounding the use of Franklin's Photo 51 by Watson and Crick. The essential story is that Wilkins, who did not get along with Franklin, took Photo 51 from a drawer in Franklin's laboratory space and showed it to Watson without Franklin's consent or knowledge. Watson and Wilkins have both admitted in later years that the story is true and that Watson's knowledge of the photo's contents violated scientific ethics. When Watson and Crick published their paper describing DNA structure in the British science periodical *Nature* in 1953, the article following theirs in the same volume was authored by Franklin and Wilkins and provided supporting evidence, including Photo 51. Watson, Crick, and Wilkins were awarded the Nobel Prize in Physiology or Medicine in 1962 for their work on DNA structure. Franklin did not share in the award since she died in 1958, at the age of 38, of ovarian cancer. The Nobel Prize is not awarded posthumously.

In devising their DNA model, Watson and Crick combined Franklin's X-ray diffraction data with information published a few years earlier by Erwin Chargaff. Chargaff had determined the percentages of the four DNA nucleotide bases in the genomes of a wide array of organisms and had concluded that (allowing for experimental error) the percentages of adenine and thymine are approximately equal to one another and that the percentages of cytosine and guanine are equal to one another as well (Table 1.1). Known as **Chargaff's rule**, this information helped Watson and Crick formulate the hypothesis that DNA nucleotides are arranged in **complementary base pairs**. Adenine, on one strand of the double helix, pairs only with thymine on the other DNA strand, and cytosine pairs only with guanine to form the other base pair. With these data, their own knowledge of biochemistry, and their analysis of incorrect models of DNA structure, Watson and Crick built a table-top model of DNA out of implements and materials scattered around their largely inactive research laboratory space—wire, tin, tape, and paper, supported by ring stands and clamps (Figure 1.5).

DNA Nucleotides

Each strand of the double helix is composed of **DNA nucleotides** that have three principal components: a five-carbon deoxyribose sugar, a phosphate group, and one of four nitrogen-containing nucleotide bases, designated **adenine** (A), **guanine** (G), **thymine** (T), and **cytosine** (C) (Figure 1.6). The nucleotides forming a strand are linked together by a covalent **phosphodiester bond** between the 5′ phosphate group of one nucleotide and the 3′ hydroxyl (OH) group of the adjacent nucleotide. Phosphodiester bonding leads to alternation of deoxyribose sugars and phosphate groups along the strand and gives the molecule a sugar-phosphate backbone.

Table 1.1 Nucleotide-Base Composition of Various Genomes

Source Genome	Percentage of Each Nucleotide Base				Ratios	
	Adenine (A)	Guanine (G)	Cytosine (C)	Thymine (T)	G+C	G/C
Bacteria						
E. coli (B)	23.8	26.8	26.3	23.1	53.1	1.02
Yeast						
S. cerevisiae	31.3	18.7	17.1	32.9	35.8	1.09
Fungi						
N. crassa	23.0	27.1	26.6	23.3	53.7	1.02
Invertebrate						
C. elegans	31.2	19.3	20.5	29.1	39.8	0.94
D. melanogaster	27.3	22.5	22.5	27.6	45.0	1.00
Plant						
A. thaliana	29.1	20.5	20.7	29.7	41.2	0.99
Vertebrate						
M. musculus	29.2	21.7	19.7	29.4	41.4	1.10
H. sapiens	30.6	19.7	19.8	30.3	39.5	0.99

The nucleotide bases are hydrophobic (water-avoiding) and naturally orient toward the water-free interior of the duplex. The bases can occur in any order along one strand of the molecule, but DNA is most stable as a duplex of two strands that have complementary base sequences, so that an A on one strand faces a T on the second strand and a G on one strand faces a C on the other. This complementary base pairing is the basis of Chargaff's rule and produces equal percentages of A and T and of C and G in double-stranded DNA molecules. **Hydrogen bonds**, noncovalent bonds consisting of weak electrostatic attractions, form between complementary base pairs to join the two DNA strands into a double helix. Two hydrogen bonds form between each A–T base pair and three hydrogen bonds are formed between each G–C base pair. Each strand of DNA has a 5′ end and a 3′ end. These designations refer to the phosphate group (5′) and hydroxyl group (3′) at the opposite ends of each strand of DNA and establish **strand polarity**, that is, the 5′-to-3′ orientation of each strand. The differences at each end of a strand allow the ends to be readily distinguished from one another. (Complementary strands of DNA are **antiparallel**, meaning that the polarities of the complementary strands run in opposite directions—one strand is oriented 5′ to 3′ and the complementary strand is oriented 3′ to 5′. Genetic Analysis 1.1 guides you through a problem that tests your understanding of base-pair complementation and complementary strand polarity.

Figure 1.5 James Watson and Francis Crick's metal-and-wire model of DNA constructed in 1953.

Notice that the A-T base pairs and the G-C base pairs in this model are each connected by two wires. If the wires represent hydrogen bonds, what is wrong with the model? (See also Figure 1.6)

If you are like many biology students, you have probably wondered from time to time what DNA actually looks like, both on the macroscopic and microscopic level. Even today's best microscopes have difficulty capturing high-resolution images of DNA, although computer-aided techniques for analyzing molecular structure can produce an interpretation of its microscopic appearance, as you'll see, for example, in Chapters 7, 8, and 9. However, you do not need sophisticated instrumentation to produce a sample of DNA that you can hold in your hand. Experimental Insight 1.1 presents a

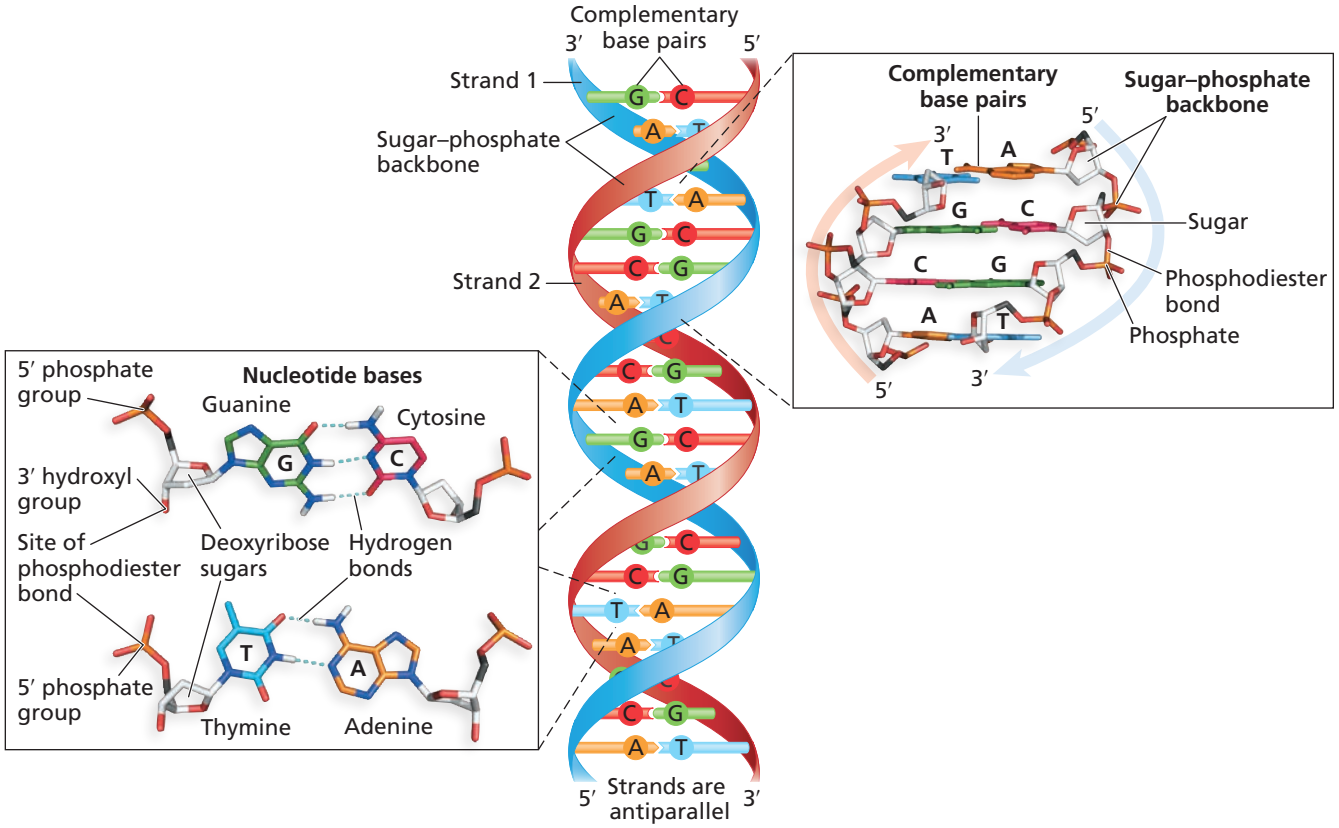


Figure 1.6 DNA composition and structure. DNA nucleotides contain a deoxyribose sugar, a phosphate group, and a nucleotide base (A, T, G, or C). Phosphodiester bonds join adjacent nucleotides in each strand, and hydrogen bonds join complementary nucleotides of strands that have antiparallel orientation.

simple recipe for DNA isolation you can do at home with common and safe household compounds.

DNA Replication

The identification of the double-helical structure of DNA established a starting point for a new set of questions about heredity. The first of these questions concerned how DNA replicates. After correctly describing DNA structure in their 1953 paper, Watson and Crick closed with a directive for future research on the question of DNA replication: "It has not escaped our notice that the specific base-pairing we have proposed immediately suggests a possible copying mechanism for the genetic material."

Indeed, as a consequence of the A-T and G-C complementary base-pairing rules, it was evident that each single strand of DNA contains the information necessary to generate the second strand of DNA and that DNA replication generates two identical DNA duplexes from the original parental duplex during each replication cycle. At the time Watson and Crick described the structure of DNA, however, the mechanism of replication was not known. It would take another 5 years for Matthew Meselson and Franklin Stahl, in an ingenious experiment of simple design, to prove that DNA replicates by a *semiconservative* mechanism (see Chapter 7).

In **semiconservative replication,** the mechanism by which DNA usually replicates, the two complementary strands of original DNA separate from one another, and each strand acts as a template to direct the synthesis of a new, complementary strand of DNA with antiparallel polarity. The mechanism is termed "semiconservative" because after the completion of DNA replication, each new duplex is composed of one **parental strand** (conserved from the original DNA) and one newly synthesized **daughter strand** (Figure 1.7).

DNA replication begins at an origin of replication, with the breaking of hydrogen bonds that hold the strands together. (This process is much like what happens when a zipper comes undone.) DNA polymerases are the enzymes active in DNA replication. Using each parental DNA strand as a template, these enzymes identify the nucleotide that is complementary to the first unpaired nucleotide on the parental strand and then catalyze formation of a phosphodiester bond to join the new nucleotide to the previous nucleotide in the nascent (growing) daughter strand.

The biochemistry of nucleic acids and DNA polymerases dictates that DNA strands elongate only in the 5′-to-3′ direction. In other words, nucleotides are added exclusively to the 3′ end of the nascent strand, leading to 5′-to-3′ growth. Like the parental duplex, each new DNA duplex contains antiparallel strands. Each parental strand–daughter strand combination forms a new double helix of DNA that is an exact replica of the original parental duplex.