

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

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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 Simone 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

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