PREFACE

Today's students are enthusiastic to learn about genetics and genomics. Their curiosity is refreshed by almost daily reports in the media of new discoveries dealing with genetic differences in drug responses, genetic risk factors for disease, and genetic evidence for human origins and history. There are also ethical controversies: Should genetic manipulation be used on patients for the treatment of disease? Should human embryonic stem cells be used in research? Should human beings be cloned? And social controversies: Should there be laws governing genetic privacy? Who should have access to genetic testing records, and for what purpose?

For the teacher of genetics, the challenges are:

- To sustain the students' enthusiasm;
- To help motivate a desire to understand the principles of genetics in a comprehensive and rigorous way;
- To guide students in gaining an understanding that genetics is not only a set of principles but also an experimental approach to solving a wide range of biological problems; and
- To help students learn to think about genetic problems and about the wider social and ethical issues arising from genetics and genomics.

Genetics: Analysis of Genes and Genomes, Seventh Edition, addresses these challenges while also showing the beauty, logical clarity, and unity of the subject. Our pedagogical approach is to treat transmission genetics, molecular genetics, and evolutionary genetics as fully integrated subjects. This appeals to most modern geneticists, who recognize that the distinctions between the subfields are artificial. The chapters have been arranged to match the organization of the overwhelming majority of college courses in genetics, including our own.

Our aim has been to provide a clear, comprehensive, rigorous, and balanced introduction to genetics and genomics at the college level. It is our belief that a good course should maintain the right balance between two important aspects of genetics. The first aspect is that genetics is a body of knowledge pertaining to genetic transmission, function, and mutation; the second is that genetics is an experimental approach, or a kit of "tools," for the study of biological

processes such as development or behavior. The rationale of the book is that any student claiming a knowledge of genetics must:

- Understand the basic processes of gene transmission, mutation, expression, and regulation;
- Be familiar with the principal experimental methods that geneticists and molecular biologists use in their studies, and recognize the advantages and limitations of these approaches;
- Be able to think like a geneticist at the elementary level of being able to formulate genetic hypotheses, work out their consequences, and test the results against observed data;
- Be able to state genetic principles in his or her own words and to recognize the key terms of genetics in context;
- Be able to solve problems of several types, including single-concept exercises that require application of definitions or the basic principles of genetics, problems in genetic analysis in which several concepts must be applied in logical order, and problems in quantitative analysis that call for some numerical calculation;
- Gain some sense of the social and historical context in which genetics and genomics has developed and is continuing to develop; and
- Acquire a basic familiarity with the genetic resources and information that are available through the Internet.

Special Features

We have included many special features to help students achieve these learning goals. The text is clearly and concisely written in a somewhat relaxed prose style without being chummy or excessively familiar. Each chapter contains two or three **Connections** in which the text material is connected to excerpts of classic papers that report key experiments in genetics or raise important social, ethical, or legal issues in genetics. Each Connection has a brief introduction of its own, explaining the importance of the experiment and the historical context in which it was carried out. At the end of each chapter is a **Chapter Summary** in the form of bullet points, a **Review the Basics** feature in which the major concepts are reviewed in the form of questions for discussion, a **Guide to Problem Solving** in which typical types of problems that apply the principles are worked in full, a large number of **Analysis and Applications** problems for solution (with answers to even-numbered problems at the end of the book), and a special set of **Challenge Problems** for students wanting to stretch. The chapter-end material also includes instructions for accessing the book's Web site, where there are complete chapter summaries, key terms, many more problems and exercises of various types, and a feature called **Genetics on the Web** to acquaint students with key Internet sites containing resources in genetics and genomics. At the end of the book are **Answers to Even-Numbered Problems** in which the logic of each answer is explained in full, a list of **Further Reading** for students who want additional depth, a compilation of **Word Roots** to help students master the essential terminology of genetics and genomics, and a **Concise Dictionary of Genetics and Genomics**.

What's New in the Seventh Edition?

This edition has been completely revised and updated. Each chapter has been thoroughly reworked. Nonessential or outdated material has been deleted, new methods and results have been added, and several of the chapters have been reorganized to allow seamless integration of the new material. Several new Connections have been added, and there are more than 70 new or updated illustrations and tables. Hundreds of new, classroom-tested problems have been added, and the Guide to Problem Solving has been expanded.

Chapter Organization

In order to help students keep track of the main issues and avoid being distracted by details, each chapter begins with an Outline showing the road map of the territory ahead. An opening paragraph gives an overview of the chapter, illustrates the subject with some specific examples, and shows how the material is connected to genetics as a whole. The text makes liberal use of

numbered lists and "bullets" in order to help students organize their learning, as well as summary statements set off in special type in order to emphasize important principles.

Contents and Organization

The organization of the chapters is that favored by the majority of instructors who teach genetics. It is the organization we use in our own courses. An important feature is the presence of two introductory chapters providing a broad overview of DNA, genes, and genomes—what they are, how they function, how they change by mutation, and how they evolve through time. Today, most students learn about DNA in grade school or high school; in our teaching, we have found it artificial to pretend that DNA does not exist until the middle of the term. The introductory chapters serve to connect the more advanced concepts that students are about to learn with what they already know. They also serve to provide each student with a solid framework for integrating the material that comes later.

Throughout each chapter, there is a balance between observation and theory, between principle and concrete example, and between challenge and motivation. Molecular, classical, and evolutionary genetics are completely integrated. Throughout the book are frequent references to human genetics. The book is also liberally populated with applications to other animals and plants, including the key model organisms used in genetics and genomics.

A number of points related to organization and coverage should be noted:

- **Chapter 1** is an overview of genetics designed to bring students with disparate backgrounds to a common level of understanding. This chapter enables classical, molecular, and evolutionary genetics to be integrated in the rest of the book. Included in Chapter 1 are the basic concepts of molecular genetics: DNA structure, replication, expression, and mutation. New to this edition is a thorough introduction to genetic analysis, focusing on the classical experiments of Beadle and Tatum but also summarizing applications of genetic analysis that have led to six Nobel Prizes.
- **Chapter 2** emphasizes that the primary tools of the modern geneticist derive from the experimental manipulation of DNA. It includes a more detailed look at DNA structure, and it introduces the principal methods of DNA manipulation including restriction enzymes, electrophoresis, DNA hybridization, Southern blotting, and the polymerase chain reaction. We also introduce single-nucleotide polymorphisms (SNPs) and copy-number polymorphisms (CNPs), and discuss how these types of genetic markers can be assayed on a genome-wide scale using oligonucleotide microarrays (DNA chips).
- **Chapters 3 through 5** are the core of Mendelian genetics, including segregation and independent assortment, the chromosome theory of heredity, mitosis and meiosis, linkage and chromosome mapping, and tetrad analysis in fungi. Also included is the basic probability framework of Mendelian genetics and the testing of genetic models by means of the chi-square test. Unique in Chapter 3 is the integration of molecular genetics with Mendel's experiments. We describe the molecular basis of the wrinkled mutation and show how a modern geneticist would carry out Mendel's study, examining the molecular phenotypes on the one hand and the morphological phenotypes on the other. This pedagogy provides a solid basis for understanding not only Mendel's experiments as he actually performed and interpreted them, but also for understanding how modern molecular approaches are used in genetic analysis. Molecular markers are also integrated into human genetic analysis, which includes a new discussion of the molecular genetics of the taster polymorphism and its relation to one's dislike of broccoli.
- **Chapters 6 and 7** deal with the molecular structure and replication of DNA and the molecular organization of chromosomes. Chapter 6 also covers the molecular mechanisms of recombination, and Chapter 7 includes a discussion of repetitive DNA sequences in eukaryotic genomes and the molecular structures of centromeres and telomeres. New to this edition is an expanded discussion of DNA sequencing, including the newest massively parallel sequencing technologies that can yield a billion base pairs of DNA sequence within a few hours.

- Chapter 8 covers the principles of chromosome mechanics with special reference to human chromosome number and structure and the types of aberrations that are found in human chromosomes. The genetic implications of chromosome abnormalities—duplications, deficiencies, inversions, and translocations—are also discussed. New to this edition are data on the incomplete inactivation of genes in the "inactive" X Chromosome, updated information on the molecular structure of the Y Chromosome, and the evidence from genomic sequencing for ancient polyploidy in a number of key model organisms.
- Chapter 9 deals with the principles of genetics in bacteria, beginning with the genetics of mobile DNA, plasmids, and integrons, and their relationships to the evolution of multiple antibiotic resistance. It examines mechanisms of genetic recombination in microbes including transformation, conjugation, and transduction, as well as temperate and virulent bacteriophages. This edition also includes a discussion of the mosaic structure of bacterial chromosomes as evidenced by genomic and pathogenicity islands of DNA introduced by horizontal transmission.
- Chapters 10 and 11 deal with molecular genetics in the strict sense. These chapters include the classical principles of gene expression and gene regulation. They include broad aspects of gene regulation that are topics of much current research: chromatin remodeling complexes, imprinting and other epigenetic modifications of gene expression, riboswitches, and the mechanisms of gene regulation through siRNA and microRNA. For the first time we examine the eukaryotic transcription complex in detail, and include an expanded discussion of regulation of the classical *GAL* system in yeast.
- Chapter 12 focuses on recombinant DNA and genomics. Included are the use of restriction enzymes and vectors in recombinant DNA, cloning strategies, site-directed mutagenesis, the production of genetically defined transgenic animals and plants, and applications of genetic engineering. We emphasize the extraordinary number and variety of genomes that have been sequenced and summarize the principles that have emerged, while acknowledging that it will probably require decades to fully understand all that the genomic sequences imply. This edition includes an introduction to comparative genomics and computational genomics. Functional genomics is introduced by examining how DNA microarrays are used to study global patterns of coordinated gene expression, and proteomics is exemplified by a discussion of two-hybrid analysis and its application.
- Chapter 13 deals with the genetic control of development, focusing on genetic analysis of development in nematodes (*Caenorhabditis elegans*) and *Drosophila*, and also includes a thorough examination of the genetic basis of floral development in *Arabidopsis thaliana*. For the first time we examine how the principle of epistasis is used in the genetic analysis of developmental mutants to identify the regulatory switches that control developmental processes.
- Chapter 14 deals with the molecular basis of mutation. A thorough discussion of different types of mutation also includes genetically unstable sequences, such as the trinucleotide repeats whose amplification causes the fragile–X syndrome of mental retardation. The molecular action of various types of mutagens is examined, along with the genetic effects of the Chernobyl nuclear accident. Chapter 14 also covers the important field of DNA repair, with updated and expanded discussions of ectopic recombination, nucleotide excision repair, and DNA-damage bypass repair.
- Chapter 15 stresses cancer from the standpoint of the genetic control of cell division, with emphasis on the checkpoints that, in normal cells, result either in inhibition of cell division or in programmed cell death (apoptosis). Cancer results from a series of successive mutations, usually in somatic cells, that overcome the normal checkpoints that control cellular proliferation. In this edition we include an expanded discussion of the characteristics of cancer cells, the role of telomerase, the poison-subunit mutants of p53, and the role of microRNA in cell-cycle regulation.
- Chapter 16 covers organelle genetics, including genetic defects in human mitochondrial DNA. The history of domestication of the dog is elucidated by an examination of

the mitochondrial DNA sequences of domestic breeds of dogs in comparison with their wild relatives.

- **Chapters 17 and 18** deal with population and evolutionary genetics and include an overview of the principles of molecular evolution. The discussion also includes DNA typing in criminal investigations and paternity testing, the effects of inbreeding, and the evolutionary mechanisms that drive changes in allele frequency. How mitochondrial DNA sequences inform us about human history and migration is also examined. The approach to quantitative genetics includes a discussion of how particular genes influencing quantitative traits (QTLs, or quantitative-trait loci) may be identified and mapped by linkage analysis. New in this edition is discussion of the emerging principles from studies of QTLs affecting human traits. There is also a section on the genetic determinants of human behavior with emphasis on a depression-related polymorphism in the human serotonin transporter gene and its relation to the response to "club drugs" such as Ecstasy.

Connections

A unique feature of this book is found in boxes called Connections. Each chapter has two or three of these boxes. They are our way of connecting genetics to the world outside the classroom. All of the Connections include short excerpts from the original literature of genetics, usually papers, each introduced with a short explanatory passage. Many of the Connections are excerpts from classic papers, such as Mendel's paper, but by no means are all "classic" papers old papers. Many of them are very recent.

The pieces are called Connections because each connects the material to something that broadens or enriches implications. Some of the Connections raise issues of ethics in the application of genetic knowledge or social issues that need to addressed. Some of the pieces were published originally in French, others in German. These appear in English translation. In papers that use outmoded or unfamiliar terminology, or that use archaic gene symbols; we have substituted the modern equivalent because the use of a consistent terminology in the text and in the Connections makes the material more accessible to the student.

Genetics on the Web features links that introduce students to the vast repository of information about genetics and genomics that is available on the Internet. Genetics is a dynamic science, and through this venue we can introduce the newest discoveries as soon as they appear to keep the textbook up to date. The Internet sites are accessed through the use of key words that are highlighted in the book's web site. The URLs are maintained as hot links at the publisher's Web site:

http://biology.jbpub.com/book/genetics

and are kept constantly up to date, tracking the address of each site if it should change.

Problems

Each chapter provides about 50 problems, graded in difficulty, for the students to test their understanding of the material. The problems are of several different types:

Review the Basics problems ask for genetic principles to be restated in the student's own words; some are matters of definition or call for the application of elementary principles.

Guide to Problem Solving demonstrates problems worked in full. The concepts needed to solve the problem, and the reasoning behind the answer, are explained in detail. This feature serves as a review of the important concepts used in working problems. It also highlights some of the most common mistakes made by beginning students and gives pointers on how the student can avoid falling into these conceptual traps.

Analysis and Applications problems are more traditional types of genetic problems in which several concepts must be applied in logical order and often require some numerical calculation. The level of mathematics is that of arithmetic and elementary probability as it pertains to genetics. None of the problems uses mathematics beyond elementary algebra.

Challenge Problems are similar to those in Analysis and Applications, but they are a degree more challenging, often because they require a more extensive analysis of data before the question can be answered.

Solutions

The answers to even-numbered *Analysis and Applications* problems are included in the answer section at the end of the book. The answers are complete. They explain the logical foundation of the solution and lay out the methods. The answers to the rest of the *Analysis and Applications* and *Challenge Problems* are available in the *Student Solutions Manual and Supplemental Problems* book.

We find that many of our students, like students everywhere, often sneak a look at the answer before attempting to solve a problem. This is a pity. Working backward from the answer should be a last resort. This is because problems are valuable opportunities to learn. Problems that the student cannot solve are usually more important than the ones that can be solved, because the sticklers usually identify trouble spots, areas of confusion, or gaps in understanding. We therefore urge our students to try answering each question before looking at the answer.

Word Roots and Concise Dictionary

At the end of the book we include a short list of *Word Roots* that are used in many of the technical terms of genetics. The *Word Roots* are useful in helping students to interpret and to remember the meaning of key terms. There is also a *Concise Dictionary of Genetics* for students to check their understanding of the key words or look up any technical terms they may have forgotten. The *Dictionary* includes not only the key words but also genetic terms that students are likely to encounter in exploring the Internet or in their further reading.

Further Reading

This feature includes recommendations for *Further Reading* for the student who either wants more information or who needs an alternative explanation for the material presented in the book. Some additional "classic" papers and historical perspectives are included.

Illustrations

The art program is spectacular and a learning aid itself. Every chapter is richly illustrated with beautiful graphics in which color is used functionally to enhance the value of each illustration. The illustrations are also heavily annotated with explanatory boxes explaining step-by-step what is happening at each level of the illustration. These labels make the art inviting as well as informative. They also allow the illustrations to stand relatively independently of the text, enabling the student to review material without rereading the whole chapter.

The art program is used not only for its visual appeal, but also to increase the pedagogical value of the book:

- Characteristic colors and shapes have been used consistently throughout the book to indicate different types of molecules—DNA, mRNA, tRNA, and so forth. For example, DNA is illustrated in any one of a number of ways, depending on the level of resolution necessary for the illustration, and each time a particular level of resolution is depicted, the DNA is shown in the same way. It avoids a great deal of potential confusion that DNA, RNA, and proteins are represented in the same manner in every chapter.
- There are numerous full-color photographs of molecular models in three dimensions; these give a strong visual reinforcement of the concept of macromolecules as physical entities with defined three-dimensional shapes and charge distributions that serve as the basis of interaction with other macromolecules.
- The page design is clean, crisp, and uncluttered. As a result, the book is pleasant to look at and easy to read.

Flexibility

There is no necessary reason to start at the beginning and proceed straight to the end. Each chapter is a self-contained unit that stands on its own. This feature gives the book the flexibility to be used in a variety of course formats. Throughout the book, we have integrated molecular

and classical principles, so you can begin a course with almost any of the chapters. Most teachers will prefer starting with the overview in Chapter 1 because it brings every student to the same basic level of understanding. Chapter 2 introduces the basic experimental manipulations used in modern genetics and serves to integrate molecular and classical genetics in the discussion of Mendel in Chapter 3. Teachers preferring the Mendel-early format should start with Chapter 1, continue with Chapter 3, then backtrack to Chapter 2. Some teachers are partial to a chromosomes-early format, which would suggest the order chapter 1, 4, 2, 3, and 5. A novel approach would be a genomes-first format, which could be implemented by beginning with chapters 1, 2, and 12. The writing and illustration program was designed to accommodate a variety of formats, and we encourage teachers to take advantage of this flexibility in order to meet their own special needs.

Supplements

Jones and Bartlett Publishers offers a suite of traditional and interactive multimedia supplements to assist instructors and aid students in mastering genetics. Additional information and review copies of any of the following items are available through your Jones and Bartlett Sales Representative.

Instructor's ToolKit CD-ROM includes:

- A Test Bank containing over a thousand questions and complete answers. The questions, authored by Elena Lozovsky of Harvard University and Teri Shors of University of Wisconsin – Oshkosh, are a mix of factual, descriptive, and quantitative types. A typical chapter contains multiple-choice, fill-in-the-blank, and short answer questions. The Test Bank is provided as Rich Text files.
- The PowerPoint® Image Bank is an easy-to-use multimedia tool that provides all of the illustrations and photos from the text (to which Jones and Bartlett holds the rights to reproduce electronically) for use in classroom presentation. You can select images you need or easily generate your own slide shows, print the files for transparency creation. Many images have already been inserted into the PowerPoint Lecture Outline presentations for ease of use.
- A PowerPoint presentation containing the detailed outline for each chapter of *Genetics: Analysis of Genes and Genomes, Seventh Edition* is included. The presentation, designed to mirror the text, is constructed flexibly in order to meet your lecture's organization. The outline is open, allowing you to provide the elements you deem necessary, whether it be new text or more images from the Image Bank.
- Microsoft Word files of the *Student Solutions Manual and Supplemental Problems* are provided. This manual is also available to your students as a printed supplemental text. It provides detailed answers for all of the problems at the end of chapters. It also contains supplemental problems with explanations to help give your students further practice with difficult genetics concepts.

Genetics on the Web
http://biology.jbpub.com/book/genetics

Updated and expanded for this edition, the student Web site Genetics on the Web offers support to students as they further explore course content and the field of genetics. Students will find Animated Flashcards that reinforce important terms and Crossword Puzzles that provide an exciting way to review course material. Research and Reference links point students to valuable information on genetics-related organizations and news outlets. For students' convenience, an Interactive Online Glossary is available for quick reference.

Student Solutions Manual and Supplemental Problems

This completely revised supplemental text, available to all students, is comprised of two parts. First, it contains a complete set of solutions for all of the end-of-chapter problems in the text.

Second, it contains hundreds of supplemental problems with complete solutions, as well as a chapter summary and list of key terms for each chapter of the text. The problems, written by Elena Lozovsky of Harvard University, are a tremendous resource for students seeking an extra self-assessment of understanding. The problems are designed to test their knowledge of each chapter's content, but particularly to practice critical thinking and working through some of the more difficult concepts in genetics.

The Gist of Genetics: Guide to Learning and Review

Written by Rowland H. Davis and Stephen G. Weller of the University of California, Irvine, this study aid uses illustrations, tables, and text outlines to review all of the fundamental elements of genetics. It includes extensive practice problems and review questions with solutions for self-check. *The Gist* helps students formulate appropriate questions and generate hypotheses that can be tested with classical principles and modern genetic techniques.