

Genetics: Analysis of Genes and Genomes, Sixth Edition, treats transmission genetics, molecular genetics, and evolutionary genetics as fully integrated subjects. This approach 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
- Have some 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 is headed by a list of Principles that are related at numerous points to the larger whole. 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 complete Summary, Key Terms, GeNETics on the Web exercises that guide students in the use of Internet resources in genetics, and several different types and levels of Problems. These features are discussed individually below.

In recent decades, both the amount of genetic knowledge and its rate of growth have exploded. Many of the new discoveries have personal and social relevance through applications of genetics to human affairs in prenatal diagnosis, testing for carriers, and identification of genetic risk factors for complex traits, such as breast cancer and heart disease. There are also ethical controversies: Should genetic manipulation be used on patients for the treatment of disease? Should human fetuses be used in research? Should human beings be cloned? There are also social controversies—for example, should there be laws governing genetic privacy, and how far should they go? Who should have access to genetic testing records, and for what purpose?

Inspired in part by the controversies and the publicity, many of today's students come to a course in genetics with great enthusiasm. The challenges for the teacher are:

- To sustain this 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.

While addressing these challenges, we have also tried to show the beauty, logical clarity, and unity of the subject. Endlessly fascinating, genetics is the material basis of the continuity of life.

Chapter Organization

In order to help the student keep track of the main issues and avoid being distracted by details, each chapter begins with a list of the Principles that provide the main focus of the chapter. There is also an Outline, showing step by step the path along the way. 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. Each chapter ends with a Summary and list of Key Terms as well as the Problems. At the end of the book is a brief list of Word Roots as well as a Concise Dictionary of Genetics.

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. It also serves 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 integrated throughout. Present throughout the book are frequent references to human genetics, including discussions of metabolic diseases, the fragile-X syndrome, imprinting, the genetic basis of cancer, expansion of unstable repeats in diseases such as Huntington disease, the relationship of DNA repair enzymes to hereditary colon cancer, the controversial mitochondrial "Eve," genetic diseases associated with defective mitochondria, DNA typing in individual identification, the Human Genome Project, and many other special topics. Although applications to human genetics are often stressed, the book is also liberally supplied with applications to other animals as well as plants.

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. Chapter 1 also includes a discussion of the experimental evidence that DNA is the genetic material, and introduces the concepts of genome and proteome.
- **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 discuss how and why these methods are used to study DNA markers such as SNPs, RFLPs, and other key approaches that form the basis of modern genetic analysis.

- **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 in the discussion of human genetic analysis.

An important principle of genetics, too often ignored or given inadequate treatment, is that of the complementation test and how complementation differs from segregation or other genetic principles. Chapter 3 includes a clear and concise description of complementation, with examples, showing how complementation is used in mutation screens to group mutations into categories corresponding to genes.

- **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, Chapter 8 includes a discussion of repetitive DNA sequences in eukaryotic genomes and the molecular structures of centromeres and telomeres.
- **Chapter 8** covers the principles of cytogenetics, including the human genome 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. We emphasize the importance of polyploidy in plant evolution, including recent new evidence bearing on the origin of polyploids, and examine genome evolution in the cereal grains.

- **Chapter 9** deals with the principles of genetics in prokaryotes, beginning with the genetics of mobile DNA, plasmids, and integrons, and their relationships to the evolution of multiple antibiotic resistance. There is a thorough discussion of mechanisms of genetic recombination in microbes, including transformation, conjugation, and transduction, as well as discussion of temperate and virulent bacteriophages.
- **Chapters 10 and 11** deal with molecular genetics in the strict sense. These chapters include the classical principles of gene expression and gene regulation. For the first time we include broader aspects of gene regulation that are topics of much current research: chromatin remodeling complexes, imprinting and other epigenetic modifications of gene expression, transcriptional and post-transcriptional cosuppression, riboswitches, “kissing complexes,” and RNA interference (RNAi).
- **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. Also discussed are methods used in large-scale genomic sequencing and a summary of what new principles have emerged from genomic sequencing. Functional genomics is introduced by examining how DNA microarrays (“DNA chips”) 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*.
- **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.
- **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.
- **Chapter 16** covers organelle genetics, including genetic defects in human mitochondrial DNA.
- **Chapters 17 and 18** deal with population and evolutionary genetics and include an overview of the principles of molecular evolution. The discussion also includes the population genetics of the *CCR5* receptor mutation that confers resistance to AIDS caused by HIV virus, as well as DNA typing in criminal investigations, paternity testing, the effects of inbreeding, and the evolutionary mechanisms that drive changes in allele frequency. 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. There is also a section on the genetic determinants of human behavior with examples of the approach

using “candidate” genes that led to the identification of the “natural Prozac” polymorphism in the human serotonin transporter gene.

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 all of the “classic” papers are old papers. Many of them are very recent, including the report of the human genome sequence.

The pieces are called Connections because each connects the material in the text to something that broadens or enriches its implications. Some of the Connections raise issues of ethics in the application of genetic knowledge, social issues that need to be addressed, or issues related to the proper care of laboratory animals. 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

To make the genetic information explosion on the Internet available to the student, we developed the feature called GeNETics on the Web, which make use of Internet resources. Genetics is a dynamic science, and through this venue we can introduce the newest discoveries as soon as they appear and keep the textbook up to date.

The addresses of the relevant genetic sites are not printed in the book. Instead, the sites are accessed through the use of key words that are highlighted in each exercise. The key words are maintained as hot links at the publisher’s web site

<http://www.jbpub.com/genetics>

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

Problems

Each chapter provides about 60 problems for solution, graded in difficulty, for the students to test their understanding. The problems are of several different types:

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.

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.

Fill-ins are a set of problems in which students are asked to recognize a key term in the context in which it is used. Few things are more intimidating to a student than a long list of unfamiliar words whose meanings they are supposed to know. But understanding the meaning of a word when one sees it in context and being able to draft a concise dictionary definition of it are two very different things. In learning genetics, it is the understanding of key terms in context that is the more important, and these fill-ins are designed to emphasize this level of understanding.

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. So, forever in hope but against all experience, we 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 Terms* or look up any technical terms they may have forgotten. The *Dictionary* includes not only the *Key Terms*, but also genetic terms that students are likely to encounter in exploring the Internet or in their further reading.

Further Reading

Each chapter also 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 as a learning aid. 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

An unprecedented offering of traditional and interactive multimedia supplements is available 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:

- The Computerized TestBank contains over a thousand questions and complete answers. It uses Diploma software, a format which allows the instructor to easily generate tests and quizzes from a single chapter or collection of chapters. Diploma allows you to create paper, Internet, or network tests. The questions, authored by Elena Lozovsky of Harvard University, are a mix of factual, descriptive, and quantitative types. A typical chapter contains multiple-choice, fill-in-the-blank, and short answer questions. In addition to being available in the convenient Diploma format, each chapter's TestBank is also provided as Rich Text files.

- The Kaleidoscope Media Viewer is an easy-to-use multimedia tool which provides many of the illustrations from the text specially enhanced for classroom presentation. You can select images you need by chapter, topic, and figure number and easily generate your own slide shows, print the files for transparency creation, or insert the images into the PowerPoint presentations already prepared for you.
- Microsoft Word files of the *Student Solutions Manual and Supplemental Problems* are provided. This manual is 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.
- A PowerPoint presentation containing the detailed outline for each chapter of *Genetics: Analysis of Genes and Genomes*, Sixth Edition is also 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 the images from the Kaleidoscope Media Viewer.

GenETics on the Web

<http://www.jbpub.com/genetics>

Updated and expanded for this edition, the student web site GenETics on the Web now offers more ways for students to support course content and to explore the genetics field. Students also will find Animated Flashcards that reinforce important terms and Crossword Puzzles that provide an exciting way to review course material. Additional 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 supplemental text, available to all students, is comprised of two parts. Firstly, it contains a complete set of solutions for all of the end-of-chapter problems in the text. Secondly, it contains hundreds of supplemental problems with complete solutions. These problems, also written by Elena Lozovsky of Harvard University, are a great resource for students seeking an extra advantage. The problems are designed to test their knowledge of each chapter's content, but particularly to provide practice thinking and working through some of the more difficult concepts in genetics.

Cogito: Electronic Companion to Genetics™, Version 2.0

This Mac/IBM CD-ROM, prepared by Philip Anderson and Barry Ganetzky of the University of Wisconsin, Madison, reviews important genetics concepts covered in class using state-of-the-art interactive multimedia. It consists of hundreds of animations, diagrams, and videos that dynamically explain difficult concepts to students. In addition, it contains over 400 interactive multiple-choice, "drag and drop," true/false, and fill-in problems. Brand new to this version are review screens and self-test questions on genomics, a new HTML format, readable through any current Web browser on any platform, and improved navigation and quicker loading and playing of animations. These resources will prove invaluable to students in a self-study environment and to instructors as a lecture-enhancement tool.

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.

Visual Genetics Plus: Tutorial and Laboratory Simulations

This Mac/IBM CD-ROM, created by Alan W. Day and Robert L. Dean of the University of Western Ontario, is already in use at over 200 institutions worldwide. Visual Genetics 3.0 continues to provide a unique, dynamic presentation tool for viewing key genetic and molecular processes in the classroom. With this expanded version of the Virtual Genetics Lab 2.0, instructors can assign 17 comprehensive lab simulations. You can also bring the lab into the classroom, as the program allows you to perform on-screen tasks such as the selection of mutant colonies, using a pipette to make a dilution series, inoculating mutants to petri dishes to test for response to growth factors, and then to analyze and interpret the data. Through the testing feature and presentation capabilities, you can offer a complete lab environment. Site Licenses and Instructor Copies are available.