

国外优秀教材

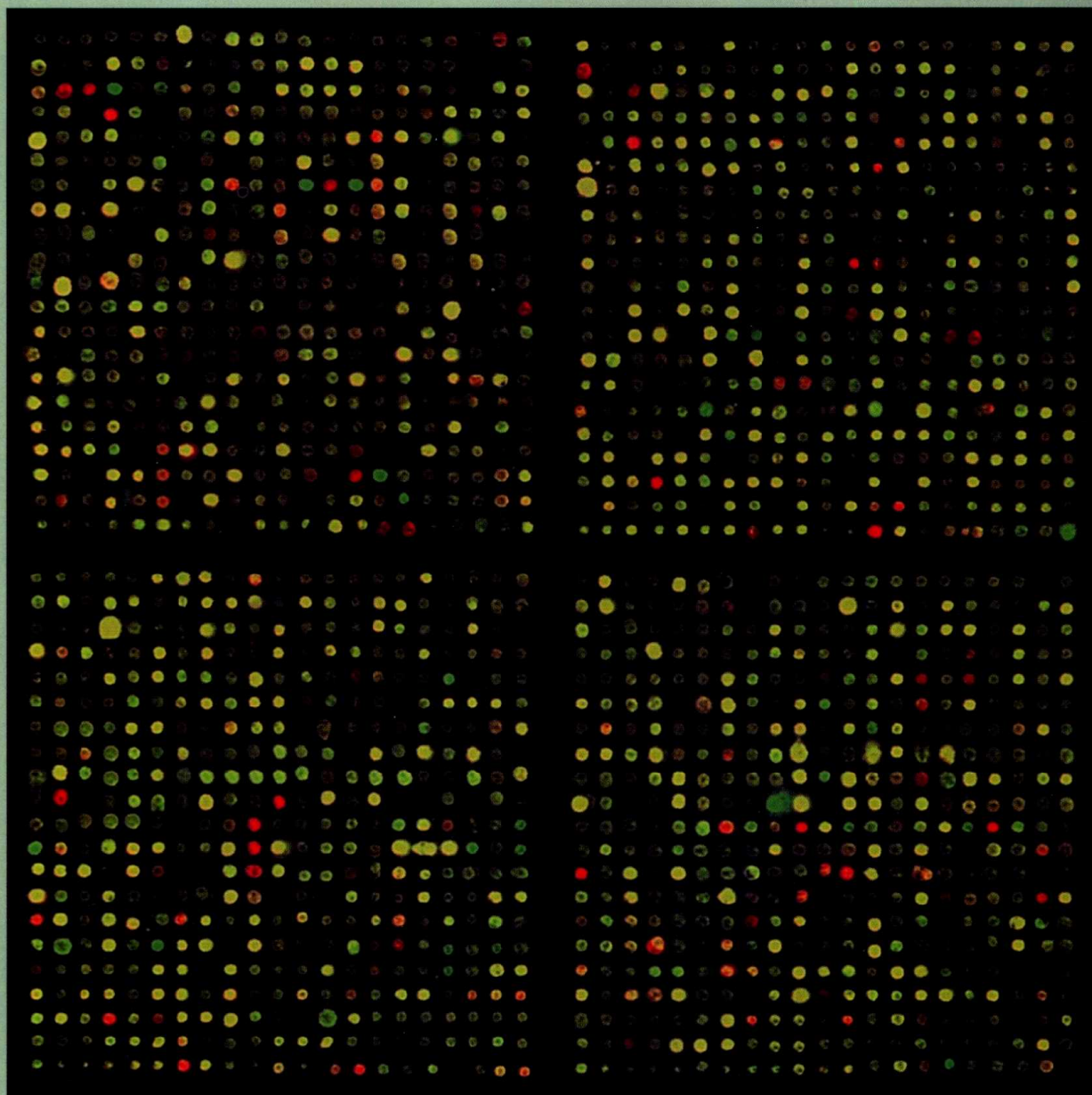
Genetics: Analysis of Genes and Genomes

遗传学——基因与基因组分析

第五版

Daniel L. Hartl
Elizabeth W. Jones

(影印版)



科学出版社



JONES AND BARTLETT PUBLISHERS

遗传学——基因与基因组分析

(第五版 影印版)

Genetics: Analysis of Genes and Genomes

(Fifth Edition)

Daniel L. Hartl
Elizabeth W. Jones

科学出版社

2002

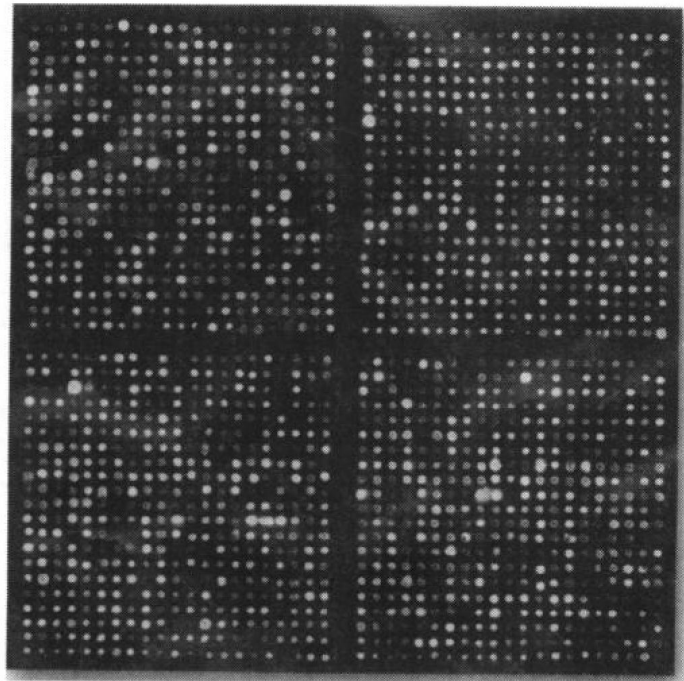
GENETICS

ANALYSIS OF GENES AND GENOMES

Fifth Edition

Daniel L. Hartl
Harvard University

Elizabeth W. Jones
Carnegie Mellon University



内 容 简 介

本书尝试在后基因组时代整合经典、分子和群体遗传学。

书中揭示了基因传递、突变、表达和调控的基本过程,介绍了传统和现代遗传学实验方法,运用遗传学和基因组学知识洞察历史和社会变迁。书中还精选遗传学经典论文,附章前提示和章末小结、各类习题和解答、名词概念解释、参考文献及主题索引。在<http://www.jbpub.com/genetics> 网址上,有更丰富的网络资源。适用于高等院校生物专业师生。

图字: 01-2002-0541

Original English Language Edition Published by

Jones and Bartlett Publishers, Inc.

One Exert Plaza

Boston, MA 02116

Copyright 2001

All Rights Reserved

图书在版编目(CIP)数据

遗传学: 基因与基因组分析 = Genetics: Analysis of Genes and Genomes / (美) 哈特尔 (Hartl, D. L.), (美) 琼斯 (Jones, E. W.) 著. —影印版. —北京: 科学出版社, 2002 (国外优秀教材)

ISBN 7-03-010311-4

I. 遗… II. ①哈…②琼… III. 遗传学-英文 IV. Q3

中国版本图书馆 CIP 数据核字 (2002) 第 018564 号

科学出版社 出版

北京东黄城根北街16号

邮政编码: 100717

<http://www.sciencep.com>

新蕾印刷厂 印刷

科学出版社发行 各地新华书店经销

*

2002 年 4 月第 一 版 开本: 850×1168 1/16

2002 年 4 月第一次印刷 印张: 55 1/4

印数: 1—3 000 字数: 1 272 000

定价: 88.00 元

(如有印装质量问题, 我社负责调换(环伟))

TO THE BEST TEACHERS WE EVER HAD—OUR PARENTS AND OUR STUDENTS

ABOUT THE AUTHORS

Daniel L. Hartl is Higgins Professor of Biology at Harvard University. He received his B.S. degree and Ph.D. from the University of Wisconsin. His research interests include molecular genetics, molecular evolution, and population genetics. Elizabeth W. Jones is a Professor of Biological Sciences at Carnegie Mellon University. She received her B.S. degree and Ph.D. from the University of Washington in Seattle. Her research interests include gene regulation and the genetic control of cellular form. Currently she is studying the function and assembly of organelles in the yeast *Saccharomyces*.

ABOUT THE COVER

DNA chip showing four 21×21 arrays of microspots of yeast DNA, each from a different gene, placed with precision by a robotic microarrayer. The chip has been hybridized with samples of fluorescently labeled DNA copied from messenger RNA extracted from a control culture and an experimental culture. The colors indicate the relative levels of gene expression: red, greater expression in the experimental culture; green, less expression in the experimental culture; and yellow, approximately equal expression. Each spot is 150–200 micrometers in diameter. The actual size of the entire array is approximately one square centimeter. [Courtesy of Jeffrey P. Townsend, Duccio Cavalieri, and the Harvard Center for Genomics Research]

P R E F A C E

GENETICS: ANALYSIS OF GENES AND GENOMES, Fifth Edition, embodies our belief that the time is ripe to teach transmission genetics, the molecular biology of gene expression and regulation, and evolutionary genetics as integrated subjects. For our own convenience in teaching genetics, and to fit the manner in which the overwhelming majority of college courses in genetics have been organized (including our own), there is a group of chapters that most geneticists would label “classical” genetics, another group that would qualify as “molecular” genetics, and still another group that would undoubtedly be called “population” genetics. We distinguish between these subfields because we agree with most geneticists and teachers of genetics that the distinction is still useful. In our opinion this organizational framework is optimal, not only for convenience in teaching, but also for transmitting to students some sense of the history of advances in genetics. Nevertheless, most modern geneticists recognize that the distinctions between these subfields have become increasingly artificial in the post-genomics era.

Classical or Molecular Genetics: Where to Start?

The distinction between classical genetics and molecular genetics began to appear about a half-century ago when the three-dimensional structure of DNA burst upon the scene. Methods for the direct study of DNA (and proteins) were then quite new and still in the earliest stages of development. The subfield of “classical” genetics became defined as the study of the patterns in which alternative organismic traits (phenotypes) are transmitted in family histories (pedigrees). The critical generalization was the fruit of Mendel’s experiments: the physical entities that are transmitted are not the traits themselves but “genes.” Classical genetics took upon itself the role of recognizing different forms of genes through their effects on visible traits and on mapping the genes along the chromosomes. Those working in the subfield of “molecular” genetics could not have cared less about ge-

netic transmission. In this arena the questions were: “At the molecular level, precisely how do alternative forms of a gene differ, how do they result in different expressed traits, and how does one alternative of a gene mutate into another alternative?” At this time the subfield of “population” genetics was almost divorced from the other two. Population genetics set for itself the task of understanding the patterns of transmission of complex traits whose expression depends on multiple genes as well as upon environmental factors, and not knowing either the genetics or the molecular biology, an adherence to statistical means, variances, and covariances was the only way to stay afloat.

But we are now (quite by coincidence, and happily) in a different millenium from that in which genetics as a science developed, and the previously

separate subdisciplines have been integrated. For example, many modern geneticists do population studies of DNA markers in individuals in pedigrees in which an inherited risk factor for a disease may be present. The goal is to find a genetic linkage between the occurrence of the disease and a genetic marker in the chromosomes. Then an examination of the complete genomic sequence of the chromosome yields a set of candidate genes in the region, which the geneticist uses to propose hypotheses for the molecular basis of the increased risk; these are then tested by further pedigree, population, and molecular studies. Is this approach “classical,” “molecular,” or “population” genetics? It is, in fact, all of the above, integrated.

Integration. That has been our goal in this edition. We discovered that an integration of the subfields can be achieved almost effortlessly and without sacrificing any of the traditional emphasis on such classical subjects as Mendel’s experiments. One practical advantage of this approach is that instructors no longer need to decide “Should I teach classical genetics first? Or should I teach molecular genetics first?” With an integrated approach, there is no longer a need to make this choice. Closely related aspects of both classical and molecular genetics are taught together, and they illuminate and reinforce each other. The appeal to students is tremendous. In previous years both of us have watched our undergraduates’ eyes glaze over when we first mentioned Mendel (as if, judging from the drooping eyelids, they were thinking, “Oh, we know this round and wrinkled stuff; wake us up when you come to something relevant to those of us in the modern world.”) This book is it: an integrated view of the modern world of genetics, with classical genetics, molecular genetics, and population genetics each taught with regard to its separate goals, aspirations, and history, but taught as one unified field that, even in our post-genomics era, still goes by the name “genetics.”

Instructional Goals

The overall aim of *Genetics: Analysis of Genes and Genomes*, Fifth Edition, is to provide a clear, comprehensive, rigorous, and balanced introduction to genetics and genomics at the college level. It is a guide to learning critically important and sometimes difficult subjects. 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 claim-

ing 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 solve problems of several types, including problems that ask the student to verbalize genetic principles in his or her own words, 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

This edition incorporates 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 that 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, GeNETtics 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. There is a Concise Dictionary of Genetics at the end of the book 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.

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 hy-

bridization, 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 through 8** deal with the molecular structure and replication of DNA and the molecular organization of chromosomes, as well as the molecular basis of mutation and the effects of mutagens, including the genetic effects of the Chernobyl nuclear accident. Chapter 6 also covers the molecular mechanisms of recombination and Chapter 7 the rapidly growing field of DNA repair. Chapter 8 includes a discussion of repetitive DNA sequences in eukaryotic genomes and the molecular structures of centromeres and telomeres.
- **Chapter 9** 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 poly-

ploidy in plant evolution, and examine genome evolution in the cereal grains as an example.

- **Chapter 10** 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 11 and 12** 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 in gene expression, transcriptional and post-transcriptional cosuppression, and RNA interference (RNAi).
- **Chapter 13** 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.
- **Chapters 14 and 15** deal with the genetic control of development. In Chapter 14 we focus on genetic analysis of development in nematodes (*Caenorhabditis elegans*) and *Drosophila*, and also include is a thorough examination of the genetic basis of floral development in *Arabidopsis thaliana*. 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. The discussion includes the population genetics of the CCR5 receptor muta-

tion that confers resistance to infection 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 special 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 first human chromosome sequenced, chromosome 22.

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. They illustrate other things as well. Because each Connection names the place where the research was carried out, the student will learn that great science is done in many universities and research institutions throughout the world. 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

More than in most fields of biology, genetic resources and genetic information are abundant on the Internet. The most useful sites are not always easy to find. A recent search of Internet sites using the AltaVista search engine and the keyword genetics yielded about 800,000 hits. Most of these are of limited usefulness, but quite a few are invaluable to the student and to

the practicing geneticist. The problem is how to find the really useful ones among the 800,000 sites.

To make the genetic information explosion on the Internet available to the student, we developed for the Fourth Edition and have updated for the Fifth Edition 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. The use of key words also allows an innovation: one exercise in each chapter makes use of a mutable site that changes frequently.

Problems

Each chapter provides about 50 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.

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 sec-

tion 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.

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, thanks to the creative efforts of J/B Woolsey Associates, with special thanks to John Woolsey and Patrick Lane. 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 "process labels" 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 13. 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 Tool Kit 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 Lecture Success Image Bank 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*, 5/e is also included. The presentation, designed to mirror the text, is flexibly constructed 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 Lecture Success Image Bank.

GenNETics on the Web

Corresponding to the end-of-chapter GeNETics on the Web exercises, this World Wide Web site offers genetics-related links, articles and monthly updates to other genetics sites on the Web. Material for this site is carefully selected and updated by the authors. Jones and Bartlett Publishers ensures that links for the site are regularly maintained. Visit the GeNETics on the Web site at

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

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

Cogito Learning Media Inc.

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. This CD-ROM is available for packaging exclusively with Jones and Bartlett Publishers texts.

Video Resource Library

A full complement of quality videos is available to qualified adopters. Genetics-related topics include: Origin and Evolution of Life, Human Gene Therapy, Biotechnology, the Human Genome Project, Oncogenes, and Science and Ethics.

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 new, greatly expanded version of the Virtual Genetics Lab 2.0, instructors can now assign 17 comprehensive lab simulations. You can also bring the lab into the class-

room, 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.

Acknowledgments

We are indebted to many colleagues whose advice and thoughtful reviews, comments, and advice have helped in the preparation of this and previous editions. Their expert recommendations are reflected in the content, organization, and presentation of the material.

Laura Adamkewicz, George Mason University,
Fairfax VA

Jeremy C. Ahouse, Brandeis University, Waltham MA

Mary Alleman, Duquesne University, Pittsburgh PA

Peter D. Ayling, University of Hull, Hull UK

John C. Bauer, Stratagene, Inc., La Jolla CA

Anna W. Berkovitz, Purdue University,
West Lafayette IN

Mary K. B. Berlyn, Yale University, New Haven CT

Pierre Carol, Université Joseph Fourier, Grenoble,
France

John Celenza, Boston University, Boston MA

Alan C. Christensen, University of Nebraska–Lincoln,
Lincoln NE

Leslie Dendy, University of New Mexico,
Los Alamos NM

Stephen J. DiSurney, University of Mississippi,
University MS

John W. Drake, National Institute of Environmental
Health Sciences, Research Triangle Park, NC

Kathleen Dunn, Boston College, Boston MA

Chris Easton, State University of New York,
Binghamton NY

Wolfgang Epstein, University of Chicago, Chicago IL

Robert G. Fowler, San Jose State University,
San Jose CA

David W. Francis, University of Delaware, Newark DE

Dan Garza, Florida State University, Tallahassee FL

Gail Gasparich, Towson University, Towson MD

Elliott S. Goldstein, Arizona State University, Tempe AZ

Jeffrey C. Hall, Brandeis University, Waltham MA

Mark L. Hammond, Campbell University,
Buies Creek NC

Steven Henikoff, Fred Hutchinson Cancer Research
Center, Seattle WA

Charles Hoffman, Boston College, Boston MA

Ivan Huber, Fairleigh Dickenson University, Madison NJ

Kerry Hull, Bishop's University, QC Canada

Lynn A. Hunter, University of Pittsburgh, Pittsburgh PA

Richard Imberski, University of Maryland,
College Park MD

Joyce Katich, Monsanto, Inc., St. Louis MO

Jeane M. Kennedy, Monsanto, Inc., St. Louis MO

Jeffrey King, University of Berne, Switzerland

Yan B. Linhart, University of Colorado, Boulder CO

K. Brooks Low, Yale University, New Haven CT

Sally A. MacKenzie, Purdue University,
West Lafayette IN

Gustavo Maroni, University of North Carolina,
Chapel Hill NC

Jeffrey Mitton, University of Colorado, Boulder CO

Robert K. Mortimer, University of California,
Berkeley CA

Gisela Mosig, Vanderbilt University, Nashville TN

Steve O'Brien, National Cancer Institute, Frederick MD

Kevin O'Hare, Imperial College, London UK

Ronald L. Phillips, University of Minnesota, St. Paul MN

Robert Pruitt, Purdue University, West Lafayette IN

Peggy Redshaw, Austin College, Sherman TX

Pamela Reinagel, California Institute of Technology,
Pasadena CA

Kenneth E. Rudd, National Library of Medicine,
Bethesda MD

Thomas F. Savage, Oregon State University, Corvallis OR

David Shepard, University of Delaware, Newark DE

Leslie Smith, National Institute of Environmental Health
Sciences, Research Triangle Park NC

Charles Staben, University of Kentucky, Lexington KY

Johan H. Stuy, Florida State University, Tallahassee FL

David T. Sullivan, Syracuse University, Syracuse NY

Jeanne Sullivan, West Virginia Wesleyan College,
Buckhannon WV

Irwin Tessman, Purdue University, West Lafayette IN

James H. Thomas, University of Washington, Seattle WA

David Ussery, The Technical University of Denmark,
Lyngby, Denmark

Denise Wallack, Muhlenberg College, Allentown PA

Kenneth E. Weber, University of Southern Maine,
Gorham ME

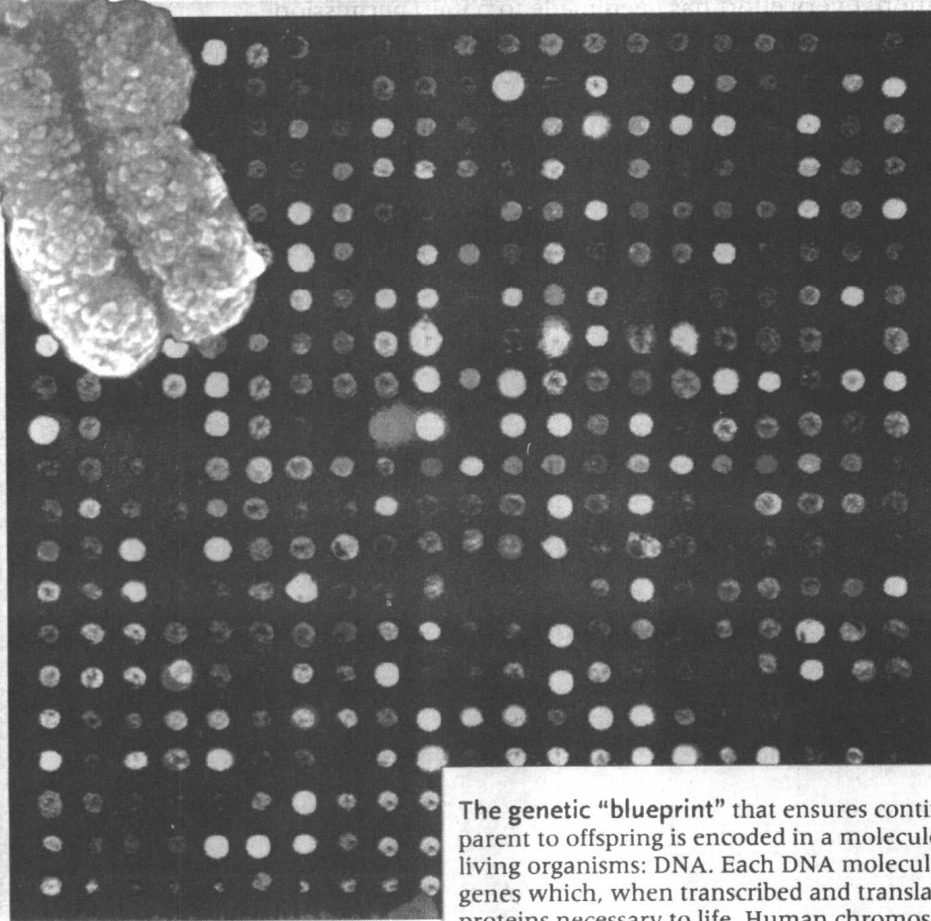
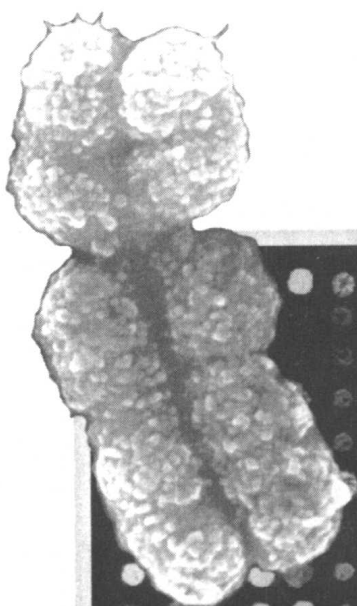
We especially want to acknowledge Elena Lozovsky of Harvard University for her work on the *Testbank*, *Student Solutions Manual*, and *Supplemental Problems*.

We also wish to acknowledge the superb art, production, and editorial staff who helped make this book possible: Tom Manning, Brian McKean, Judy Hauck, Anne Spencer, Therese Bräuer, Mary Hill, Tim Gleeson, and Elizabeth Pearson of Jones and Bartlett; Andrea Fincke, Bonnie Van Slyke, and Sally Steele of Thompson Steele; John Woolsey and Patrick Lane of J/B Woolsey Associates. Much of the credit for the attractiveness and readability of the book should go to them. Thanks also to Jones and Bartlett, the publishers, for their ongoing commitment to high quality in book production. We are also grateful to the many people, acknowledged in the legends of the illustrations, who contributed photographs, drawings, and micrographs from their own research and publications, especially those who provided color photographs for this edition. Every effort has been made to obtain permission to use copyrighted material and to make full disclosure of its source. We are grateful to the authors, journal editors, and publishers for their cooperation. Any errors or omissions are wholly inadvertant and will be corrected at the first opportunity.

CHAPTER

1

Introduction to Molecular Genetics and Genomics



The genetic “blueprint” that ensures continuity of life from parent to offspring is encoded in a molecule common to all living organisms: DNA. Each DNA molecule is subdivided into genes which, when transcribed and translated, produce the proteins necessary to life. Human chromosome four, shown here, contains approximately 2000 genes. New technologies, like that of the DNA microarray—or “chip”—offer researchers the means to read genetic blueprints. [DNA chip courtesy of Jeffrey P. Townsend, Duccio Cavalieri, and the Harvard Center for Genomics Research.]

B R I E F C O N T E N T S

Chapter	1	Introduction to Molecular Genetics and Genomics	1
Chapter	2	DNA Structure and DNA Manipulation	36
Chapter	3	Transmission Genetics: The Principle of Segregation	86
Chapter	4	Genes and Chromosomes	132
Chapter	5	Genetic Linkage and Chromosome Mapping	174
Chapter	6	Molecular Biology of DNA Replication and Recombination	222
Chapter	7	Molecular Mechanisms of Mutation and DNA Repair	264
Chapter	8	Molecular Organization of Chromosomes	310
Chapter	9	Human Karyotypes and Chromosome Behavior	344
Chapter	10	Genetics of Bacteria and Their Viruses	392
Chapter	11	Molecular Biology of Gene Expression	444
Chapter	12	Molecular Mechanisms of Gene Regulation	488
Chapter	13	Genetic Engineering and Genomics	540
Chapter	14	Genetic Control of Development	590
Chapter	15	Molecular Genetics of the Cell Cycle and Cancer	634
Chapter	16	Extranuclear Inheritance	676
Chapter	17	Population Genetics and Evolution	706
Chapter	18	The Genetic Basis of Complex Inheritance	748

CONTENTS

Preface xiii

Chapter 1 Introduction to Molecular Genetics and Genomics	1
1.1 DNA: The Genetic Material 2	
Experimental Proof of the Genetic Function of DNA 3	
Genetic Role of DNA in Bacteriophage 6	
Connection: Shear Madness 8	
1.2 DNA Structure: The Double Helix 9	
1.3 An Overview of DNA Replication 10	
1.4 Genes and Proteins 11	
Inborn Errors of Metabolism as a Cause of Hereditary Disease 12	
Connection: The Black Urine Disease 12	
Mutant Genes and Defective Proteins 15	
1.5 Gene Expression: The Central Dogma 16	
Transcription 18	
Translation 18	
The Genetic Code 19	
1.6 Mutation 21	
Protein Folding and Stability 23	
1.7 Genes and Environment 25	
1.8 Evolution: From Genes to Genomes, From Proteins to Proteomes 27	
The Molecular Unity of Life 27	
Natural Selection and Diversity 28	
Chapter End Material 29	
Chapter Summary • Key Terms	
• Review the Basics • Guide to Problem Solving • Analysis and Applications • Challenge Problems • Further Reading • GeNETics on the Web	

Chapter 2 DNA Structure and DNA Manipulation	36
2.1 Genomes and Genetic Differences Among Individuals 39	
DNA Markers as Landmarks in Chromosomes 39	
2.2 The Molecular Structure of DNA 41	
Polynucleotide Chains 41	
Base Pairing and Base Stacking 44	
Antiparallel Strands 47	
Connection: The Double Helix 48	
DNA Structure as Related to Function 48	
2.3 The Separation and Identification of Genomic DNA Fragments 49	
Restriction Enzymes and Site-Specific DNA Cleavage 50	
Gel Electrophoresis 52	
Nucleic Acid Hybridization 54	
The Southern Blot 57	
2.4 Selective Replication of Particular DNA Fragments 58	
Constraints on DNA Replication: Primers and 5'-to-3' Strand Elongation 59	
The Polymerase Chain Reaction 60	
2.5 The Terminology of Genetic Analysis 64	
2.6 Types of DNA Markers Present in Genomic DNA 65	
Single Nucleotide Polymorphisms (SNPs) 66	
Restriction Fragment Length Polymorphisms (RFLPs) 66	
Connection: Origin of the Human Genetic Linkage Map 68	
Random Amplified Polymorphic DNA (RAPD) 68	
Amplified Fragment Length Polymorphisms (AFLPs) 71	
Simple Tandem Repeat Polymorphisms (STRPs) 72	
2.7 Applications of DNA Markers 73	
Genetic Markers, Genetic Mapping, and "Disease Genes" 73	
Other Uses for DNA Markers 74	
Chapter End Material 76	
Chapter Summary • Key Terms	
• Review the Basics • Guide to Problem Solving • Analysis and Applications • Challenge Problems • Further Reading • GeNETics on the Web	

