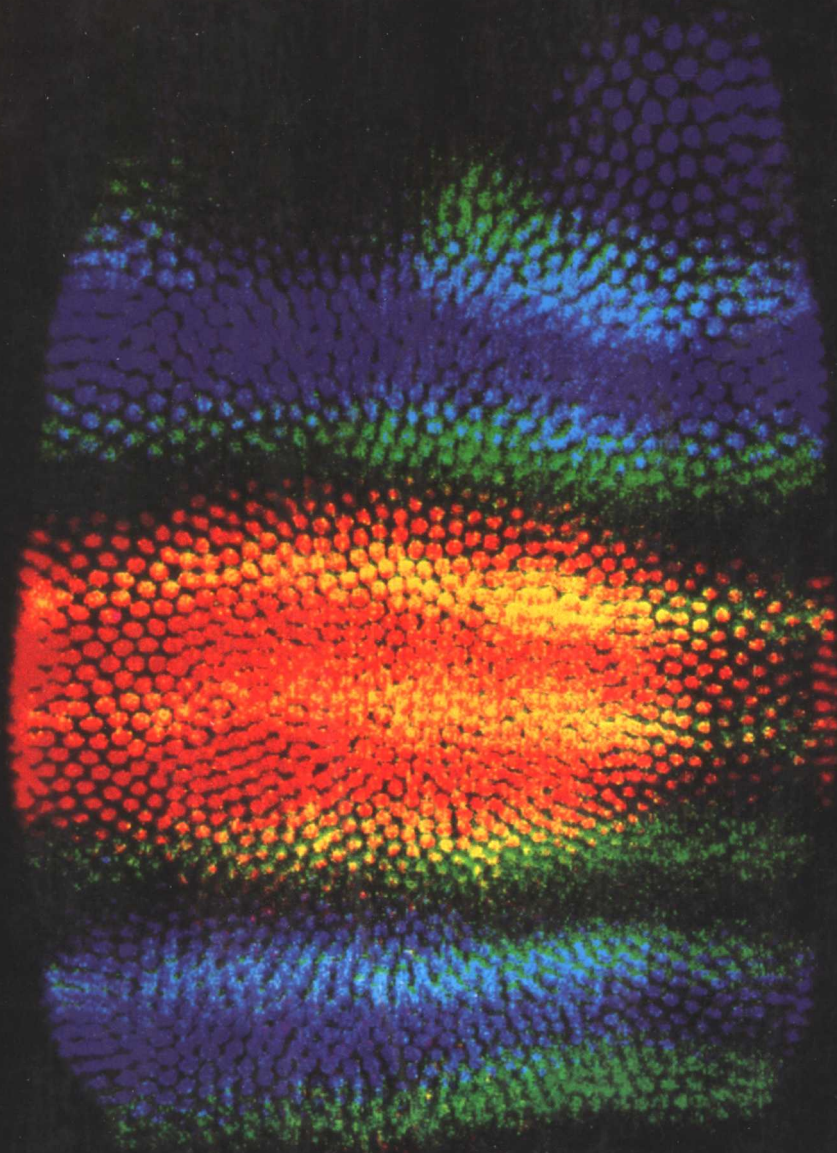


THIRD EDITION

# GENETICS

DANIEL L. HARTL



ATGTTTAC A TAATG TTTGGCAATAA G CTAGCTAG TCACCTTCAAGGAAAACGGC ACTCTG TTTTCCGTGCC CACCGATAG AACGGACGATGAATTTCTGGCAG

130

140

150

160

170

180

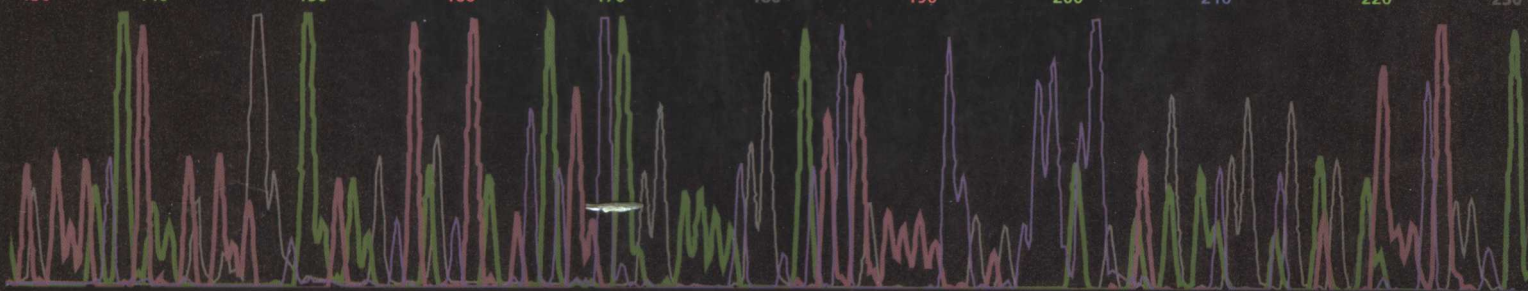
190

200

210

220

230



# GENETICS

THIRD EDITION

Daniel L. Hartl

HARVARD UNIVERSITY



Jones and Bartlett Publishers  
BOSTON LONDON



This book is printed on acid-free, recycled paper.

*Editorial, Sales, and Customer Service Offices*

Jones and Bartlett Publishers

One Exeter Plaza

Boston, MA 02116

617-859-3900

800-832-0034

Jones and Bartlett Publishers International

7 Melrose Terrace

London W6 7RL

England

Copyright © 1994, 1991, 1988 by Jones and Bartlett Publishers, Inc.

All rights reserved. No part of the material protected by this copyright notice may be reproduced or utilized in any form, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without written permission from the copyright owner.

Previous editions were published under the title *Basic Genetics*.

**Library of Congress Cataloging-in-Publication Data**

Hartl, Daniel L.

Genetics / Daniel L. Hartl. — 3rd ed.

p. cm.

Includes bibliographical references and index.

ISBN 0-86720-870-8

1. Genetics. I. Title.

QH430.H3733 1994

93-46845

CIP

*Acquisitions Editor:* Arthur C. Bartlett

*Developmental Editor:* Patricia Zimmerman

*Production Editor:* Judy Songdahl

*Manufacturing Buyer:* Dana L. Cerrito

*Design:* Deborah Schneck

*Illustrations:* Schneck-DePippo Graphics

*Typesetting:* Omegatype Typography

*Cover Design:* Marshall Henrichs

*Color Separation:* Flying Color Graphics

*Printing and Binding:* Rand McNally

*Cover Printing:* John P. Pow Company

*Cover:* An embryo of a *Drosophila* approximately 3 hours after fertilization showing the combined patterns of expression of the genes *Hairy*, *Krüppel*, and *giant*. Cells in which *hairy* is expressed fluoresce green, those in which *Krüppel* is expressed fluoresce red, and those in which *giant* is expressed fluoresce blue. The combined expression of *hairy* (green) and *Krüppel* (red) shows up as yellow. Even at this early stage in development, there is already considerable linear differentiation in the patterns of gene expression. Below the embryo is the trace of a fluorescence pattern obtained from an automated DNA-sequencing machine and the DNA sequence. (*Drosophila* embryo courtesy of James Langeland, Stephen Paddock, and Sean Carroll.)

Printed in the United States of America

98 97 96 95

10 9 8 7 6 5 4 3 2

# Introduction: For the Student

You are possibly wondering what you are going to learn by taking a course in genetics. Will the material be interesting? Is there any reason to study genetics other than to satisfy an academic requirement? At the end of the course, will you feel glad that you took it? Will there be any practical value to what you will learn? The purpose of this introduction is to reassure you that the answer to each question is yes. Furthermore, the study of genetics is relevant not only to biologists, but also to all members of our modern, complex, technological society. Understanding the principles of genetics will help you to make informed decisions about numerous matters of political, scientific, and personal concern.

At least 4000 years ago in Sumeria, Egypt, and other parts of the world, farmers recognized that they could improve their crops and their animals by selective breeding. Their knowledge was based on experience and very incomplete, but they did recognize that many features of plants and animals were passed from generation to generation. Furthermore, they discovered that desirable traits—such as size, speed, and weight of animals—could sometimes be combined by controlled mating and that, in plants, crop yield and resistance to arid conditions could be combined by cross-pollination. The ancient breeding programs were not based on much solid information because nothing was known about genes or any of the principles of heredity.

The scientific study of heredity is called **genetics**. The modern approach to genetics can be traced to the middle of the nineteenth century, when Gregor Mendel undertook his careful analyses of inheritance in peas. Mendel's experiments were simple and direct and brought forth significant principles that determine how traits are passed from one generation to the next. In Chapter 1, you will learn the rules followed by genes and chromosomes as they pass from generation to generation, and you will be able to calculate in many instances the probabilities that organisms with particular traits will be produced. The calculations require only simple arithmetic, and so there is no reason to be intimidated—even if higher mathematics is not a comfortable part of your repertory.

Mendel's kind of experiments, which occupied most of genetic research until the middle of the twentieth century, is called **transmission genetics**. Some people have called it formal genetics because the subject can be understood and the rules clearly seen without reference to the biochemical nature of genes or gene products. Geneticists of that period concerned themselves with a variety of organisms. One was the fruit fly, *Drosophila melanogaster*; others were corn (maize), chickens, mice, and, later, various fungi. The main reasons for the study of these model organisms were the following:

1. Genetic analysis needs traits that are easily detected and a large collection of variants (called mutants). *Drosophila* is extraordinary in this respect because natural populations include variants with different eye color, wing shape, bristle type, and so forth, and new mutations are readily detected in the laboratory. Corn is a good choice, too, because variants of kernel type and color are easily seen.
2. Genetic analysis requires sizable numbers of individuals. In genetic experiments, a sufficient number of organisms must be examined to determine the frequencies with which traits appear in each generation and to compare theoretical probabilities with observations. Again, *Drosophila* is excellent because hundreds of culture bottles can be maintained in a laboratory. Corn is good because a large number of plants can be grown in a fairly small plot of land. Although colonies of mice are maintained in smaller number, mice compensate for this limitation by possessing traits present in higher organisms and of direct relevance to human disease—for example, different mouse strains with hereditary diabetes, hypertension, cancer, and various immunological disorders have been developed.
3. Ideally, generation times should be short so that the transmission of traits from one generation to the next can be followed in a reasonable period of time. From this point of view, Mendel's original choice of peas was good, but not the best, because he could grow



only one or two crops per year. In *Drosophila*, the time interval between fertilization of an egg and production of a fertile adult is less than two weeks. Corn has its disadvantages in this respect (only one or two generations per year), but one compensation is its importance as an agricultural crop.

4. The organisms should be easy to maintain in the laboratory or field. Clearly, a population of fruit flies is more manageable than a pride of lions, and mice are more convenient than elephants.

Beginning about 1900, geneticists began to wonder about the biochemical nature of the gene. How could information be maintained in molecules, and how could this information be transmitted from one generation to the next? In what way is the information different in a mutant? At that time, there was no logical starting point for such an investigation, no experimental "handle." However, beginning in the 1920s and later in the 1940s, a few critical observations were made (they are documented in Chapter 4), that implicated a molecule discovered in 1869—deoxyribonucleic acid (DNA). With the discovery of the structure of DNA in 1953 by James Watson and Francis Crick, genetics entered the DNA age. Within a decade, there came an understanding of the chemical nature of genes and how genetic information is stored, released to a cell, and transmitted from one generation to the next. During the first three decades after the discovery of DNA structure, the body of genetic knowledge grew with a two-year doubling time. These were exciting times, indeed, and you will be presented with a distillation of these findings in the chapters of this book that deal with **molecular genetics**. Just to give a sample, we know with clarity how a gene is copied, how a mutation arises, how genes are turned on and off when their activity is needed or not needed, how patterns of embryonic development are initially established; we also know, by direct isolation of macromolecules, the chemical products of thousands of genes and, by elegant chemical procedures, the precise sequence of the DNA bases for many genes.

Since the early 1970s, genetics has undergone yet another revolution: the development of recombinant DNA technology. This technology is a collection of methods that enable genes to be transferred, at the will of the molecular geneticist, from one organism to another. This branch of genetics is known as **genetic engineering**. Genetic engineering has had an enormous effect on genetic research, particularly in our ability to understand gene expression and its regulation in plants and animals. Topics formerly unapproachable suddenly became amenable to experimental investigation. Currently, genetic engineering is giving us new tools of economic importance and of value in medical practice: projects of great interest include the genetic modification of plants and domesticated ani-

mals and the production of clinically active substances. New recombinant DNA strategies have made it possible to study whole **genomes** (the totality of genetic information in an organism) rather than single genes. The complete set of DNA instructions has been determined by direct DNA sequencing in a number of viruses (and in cellular organelles such as mitochondria), and programs are well underway to determine the complete DNA sequence of bacteria, yeast, nematodes, *Drosophila*, and even the complete DNA sequence in the human genome.

For the past fifty years or so, by far the greatest practical influence of genetics has been in the fields of agriculture and medicine. Studies of the genetic composition of economically important plants have enabled plant breeders to institute rational programs for developing new varieties. Among the more-important plants that have been developed are high-yield strains of corn and dwarf wheat, disease-resistant rice, corn with an altered and more-nutritious amino acid composition (high-lysine corn), and wheat that grows faster, allowing crops to be grown in short-season regions such as Canada and Sweden. The techniques for developing some of these strains are presented in this book. Often, new plant varieties have shortcomings, such as a requirement for increased amounts of fertilizer or decreased resistance to certain pests. How to overcome these shortcomings is a problem for the modern geneticist, who has the job of manipulating the inherited traits. Genetic engineering is also providing new procedures for such manipulations, and quite recently there have been dramatic successes.

Genetics has also made important contributions to medicine and modern clinical practice, and, once again, progress is accelerating because of the increased emphasis on genomic analysis. Genetic studies of the immune system have yielded information about immunological diseases and are enabling physicians to develop programs for organ transplantation. Recent genetic experiments have revealed thousands of new genetic markers in the human genome and have given us new methods for the detection of mutant genes—not only in affected persons, but also in their relatives and in members of the population at large. These methods have given genetic counseling new meaning. Human beings are heir to several thousand different inherited diseases. Married couples can be informed of the possibility of their producing an affected offspring and can now make choices between childbearing and adoption. Consider the relief afforded a woman and a man who learn that neither carries a particular defective gene and that they can produce a child without worry. Furthermore, even with the knowledge that an offspring might be affected with a genetic disorder, techniques are available to determine *in utero* if a fetus is, in fact, affected.

As a pedagogical aid, important terms are printed in **boldface** in the text. These terms are collected at the end

of each chapter in a section titled "Key Terms." You should know their meanings because they form the basic vocabulary of genetics. Each chapter also includes a summary at the end of the text. Sample problems are worked in the section titled "Examples of Worked Problems." Each chapter ends with a fairly large collection of problems. The first few problems test your knowledge of the vocabulary in the text and the more-elementary facts. The problems then increase in difficulty. It is essential that you work as many of the problems as you can because experience

has shown that practice with problems is a good way to learn genetics and to identify particular points or concepts that have been misunderstood. Sometimes, it is not even necessary to solve a problem completely but only to read the problem and decide whether you could solve it if asked to do so. The answers to all of the problems, and full explanations, are given at the back of the book. A problem will be more useful to you if you take a fair shot at it before turning to the answer.

# Contents

Introduction: For the Student xvii

## CHAPTER 1

### Principles of Heredity and Variation xx



- 1-1 Mendel and His Experiments 2
  - Particulate Hereditary Determinants 4
  - The Principle of Segregation 5
  - Some Genetic Terminology 6
  - The Principle of Independent Assortment 6
  - Testcrosses 9
  - Multiple Alleles 10
- 1-2 Mendelian Inheritance and Probability 10
- 1-3 Segregation in Pedigrees 13
- 1-4 Genes and Cellular Products 14
- 1-5 Deviations from Simple Dominance 15
  - The Absence of Dominance of Some Alleles 15
  - Codominance 17
- 1-6 The Effects of Genes on the Expression of Other Genes 18
  - Penetrance, Expressivity, and Pleiotropy 21
- Chapter Summary 22
- Key Terms 23
- Examples of Worked Problems 23
- Problems 25

## CHAPTER 2

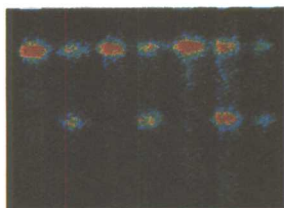
### Genes and Chromosomes 28



- 2-1 The Stability of Chromosome Complements 29
- 2-2 Mitosis 31
- 2-3 Meiosis 33
  - The First Meiotic Division 36
  - The Second Meiotic Division 39
- 2-4 Chromosomes and Heredity 40
  - Chromosomal Determination of Sex 40
  - X-linked Inheritance 40
  - Nondisjunction as Proof of the Chromosome Theory of Heredity 44
  - Sex Determination in *Drosophila* 45
- 2-5 Probability in Prediction and Analysis of Genetic Data 45
  - Using the Binomial Distribution in Genetics 45
  - Evaluating the Fit of Observed Results to Theoretical Expectations: The Chi-squared Method 47
- Chapter Summary 50
- Key Terms 51
- Examples of Worked Problems 52
- Problems 53

## CHAPTER 3

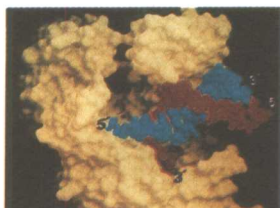
### Gene Linkage and Chromosome Mapping 56



- 3-1 Linkage and Recombination of Genes in a Chromosome 57
- 3-2 Crossing-over and Genetic Mapping 61
  - Crossing-over 62
  - Multiple Crossing-over 66
- 3-3 Gene Mapping from Three-Point Testcrosses 68
  - Interference in the Occurrence of Double Crossing-over 71
- 3-4 Mapping by Tetrad Analysis 71
  - The Analysis of Unordered Tetrads 72
  - The Analysis of Ordered Tetrads 75
  - Mitotic Recombination 77
- 3-5 Recombination within Genes 77
- 3-6 Complementation 78
- Chapter Summary* 81
- Key Terms* 82
- Examples of Worked Problems* 82
- Problems* 84

## CHAPTER 4

### The Chemical Nature and Replication of the Genetic Material 88



- 4-1 The Importance of Bacteria and Viruses in Genetics 90
- 4-2 Evidence That the Genetic Material Is DNA 92

- 4-3 The Chemical Composition of DNA 95
- 4-4 The Physical Structure of DNA: The Double Helix 98
- 4-5 What a Genetic Material Needs That DNA Supplies 100
- 4-6 The Replication of DNA 102
  - The Basic Rule for the Replication of Nucleic Acids 102
  - The Geometry of DNA Replication 103
- 4-7 DNA Synthesis 109
- 4-8 Discontinuous Replication 111
  - Fragments in the Replication Fork 112
  - Initiation by an RNA Primer 113
  - The Joining of Precursor Fragments 113
- 4-9 Determination of the Sequence of Bases in DNA 115
  - Gel Electrophoresis 116
  - The Sequencing Procedure 117
- 4-10 The Isolation and Characterization of Particular DNA Fragments 118
- Chapter Summary* 121
- Key Terms* 122
- Examples of Worked Problems* 123
- Problems* 124

## CHAPTER 5

### The Molecular Organization of Chromosomes 126



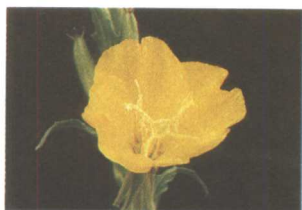
- 5-1 Genome Size and Evolutionary Complexity 128
- 5-2 The Supercoiling of DNA 129
- 5-3 The Structure of the Bacterial Chromosome 130
- 5-4 The Structure of Eukaryotic Chromosomes 132
  - The Nucleosome Is the Basic Structural Unit of Chromatin 132
  - The Arrangement of Chromatin Fibers in a Chromosome 134
- 5-5 Polytene Chromosomes 136
- 5-6 The Organization of Nucleotide Sequences in Eukaryotic Genomes 137



- 5-7 Nucleotide Sequence Composition 138
  - Unique Sequences 138
  - Highly Repetitive Sequences 138
  - Middle-Repetitive Sequences 140
- 5-8 Transposable Elements 140
- 5-9 Centromere and Telomere Structure 142
- Chapter Summary 145
- Key Terms 146
- Examples of Worked Problems 146
- Problems 147

## CHAPTER 6

### Variation in Chromosome Number and Structure 150



- 6-1 The Forms of Chromosomes 152
- 6-2 Polyploidy 153
- 6-3 Monoploidy 155
- 6-4 Extra or Missing Chromosomes 157
- 6-5 Human Chromosomes 158
  - Trisomy in Human Beings 159
  - Sex-Chromosome Abnormalities and Dosage Compensation 159
  - The Fragile-X Syndrome 161
  - Chromosome Abnormalities in Spontaneous Abortion 162
- 6-6 Abnormalities in Chromosome Structure 163
  - Deletions 163
  - Duplications 165
  - Inversions 166
  - Translocations 167
- 6-7 Chromosome Abnormalities and Cancer 168
- Chapter Summary 171
- Key Terms 172
- Examples of Worked Problems 173
- Problems 174

## CHAPTER 7

### Extranuclear Inheritance 176



- 7-1 Recognition of Extranuclear Inheritance 178
- 7-2 Organelle Heredity 179
  - Leaf Variegation in Four-o'clock Plants 180
  - Drug Resistance in *Chlamydomonas* 182
  - Respiration-defective Mitochondrial Mutants 183
  - Cytoplasmic Male Sterility in Plants 184
- 7-3 The Evolutionary Origin of Organelles 185
- 7-4 The Cytoplasmic Transmission of Symbionts 185
- 7-5 Maternal Effect in Snail-Shell Coiling 188
- 7-6 In Search of Mitochondrial "Eve" 189
- Chapter Summary 192
- Key Terms 194
- Examples of Worked Problems 194
- Problems 195

## CHAPTER 8

### Population Genetics and Evolution 196



- 8-1 Allele Frequencies and Genotype Frequencies 198
  - Calculating Allele Frequency 198
  - Enzyme Polymorphisms 199
  - Restriction Fragment Length Polymorphisms 201

8-2	Random Mating and the Hardy-Weinberg Principle	202
	Implications of the Hardy-Weinberg Principle	203
	Multiple Alleles	205
	X-linked Genes	206
8-3	DNA Typing and Population Substructure	207
8-4	Inbreeding	211
	The Effects of Inbreeding	212
8-5	Genetics and Evolution	212
8-6	Mutation and Migration	213
8-7	Natural Selection	214
	Selection in <i>Escherichia coli</i> : An Example	214
	Selection in Diploids	215
	Selection-Mutation Balance	216
	Heterozygote Superiority	217
8-8	Random Genetic Drift	217
	Chapter Summary	219
	Key Terms	221
	Examples of Worked Problems	221
	Problems	222

## CHAPTER 9

### Quantitative Genetics 224

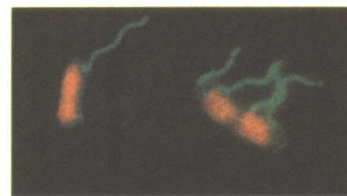


9-1	Quantitative Inheritance	226
	Continuous, Meristic, and Threshold Traits	227
	Distributions	227
9-2	Causes of Variation	230
	Genotypic Variance	231
	Environmental Variance	233
	Genotype-Environment Interaction and Genotype-Environment Association	235
9-3	Analysis of Quantitative Traits	236
	The Number of Genes Affecting a Quantitative Trait	237
	Broad-Sense Heritability	238
	Twin Studies	238

9-4	Artificial Selection	239
	Narrow-Sense Heritability	240
	Long-Term Artificial Selection	242
	Inbreeding Depression and Heterosis	242
9-5	Correlation Between Relatives	243
	Covariance and Correlation	243
	Estimation of Narrow-Sense Heritability	244
9-6	Linkage Analysis of Quantitative-Trait Loci	245
	Chapter Summary	247
	Key Terms	248
	Examples of Worked Problems	249
	Problems	250

## CHAPTER 10

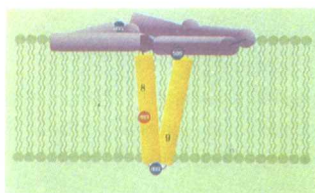
### Genes and Behavior 252



10-1	Chemotaxis in Bacteria	254
	Nonchemotactic Mutants	255
	The Cellular Components of Chemotaxis	259
	Molecular Mechanisms in Chemotaxis	260
	Sensory Adaptation	262
10-2	Animal Behavior	263
	Circadian Rhythms	263
	Love-Song Rhythms in <i>Drosophila</i>	266
	The Molecular Biology of <i>period</i> , a Clock Mutant	269
10-3	Learning Ability in Laboratory Rats	270
	Genotype-Environment Interaction	272
10-4	The Genetics of Human Behavior	273
	Severe Mental Disorders	275
	Sensory Perceptions	276
	Genetic and Cultural Effects on IQ Scores	277
	Race and IQ	278
	Chapter Summary	279
	Key Terms	280
	Examples of Worked Problems	281
	Problems	281

## CHAPTER 11

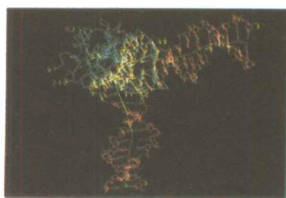
### The Genetics of Bacteria and Viruses 284



- 11-1 Bacterial Mutants 287
- 11-2 Bacterial Transformation 288
- 11-3 Conjugation 289
  - Plasmids 290
  - Hfr Cells 291
  - Time-of-Entry Mapping 293
  - F<sup>+</sup> Plasmids 296
- 11-4 Transduction 297
- 11-5 Bacteriophage Genetics 299
  - Plaque Formation and Phage Mutants 299
  - Genetic Recombination in the Lytic Cycle 300
  - The Arrangement of Genes in Phage Chromosomes 301
  - Fine Structure of the *rII* Gene in Bacteriophage T4 301
- 11-6 Lysogeny and *E. coli* Phage 302
  - Specialized Transducing Phage 305
- 11-7 Transposable Elements 306
  - Transposons in Genetic Analysis 308
- Chapter Summary* 310
- Key Terms* 311
- Examples of Worked Problems* 311
- Problems* 312

## CHAPTER 12

### Gene Expression 314



- 12-1 Proteins and Amino Acids 316
- 12-2 Relations Between Genes and Polypeptides 319

- 12-3 Transcription 320
  - General Features of RNA Synthesis 320
  - Messenger RNA 324
- 12-4 RNA Processing 325
- 12-5 Translation 330
- 12-6 The Genetic Code 335
  - Genetic Evidence for a Triplet Code 335
  - Elucidation of the Base Sequences of the Codons 337
  - A Summary of the Code 338
  - Transfer RNA and Aminoacyl Synthetase Enzymes 339
  - Redundancy and Wobble 341
  - The Sequence Organization of a Typical Prokaryotic mRNA Molecule 341
- 12-7 Overlapping Genes 342
- 12-8 Complex Translation Units 343
- 12-9 The Overall Process of Gene Expression 344
- Chapter Summary* 345
- Key Terms* 346
- Examples of Worked Problems* 347
- Problems* 348

## CHAPTER 13

### Genetic Engineering and Genome Analysis 350



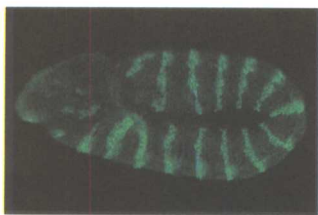
- 13-1 Cloning Strategies 352
  - The Production of Defined DNA Fragments 352
  - Recombinant DNA Molecules 354
  - Vectors 354
  - Joining DNA Fragments 356
  - The Insertion of a Particular DNA Molecule into a Vector 357
  - The Use of cDNA 358
  - The Detection of Recombinant Molecules 359
  - Screening for Particular Recombinants 360
- 13-2 Polymerase Chain Reaction 361



- 13-3 Reverse Genetics 363
  - Germ-Line Transformation in Animals 364
  - Genetic Engineering in Plants 367
  - Engineered Male Sterility with Suicide Genes 368
- 13-4 Applications of Genetic Engineering 369
  - Commercial Possibilities 370
  - Uses in Research 371
  - The Production of Useful Proteins 371
  - Genetic Engineering with Animal Viruses 372
  - The Diagnosis of Hereditary Diseases 373
- 13-5 The Analysis of Complex Genomes 373
  - Sizes of Complex Genomes 373
  - Manipulating Large DNA Fragments 374
  - Cloning Large DNA Fragments 375
  - Physical Mapping With Sequence-tagged Sites 377
- 13-6 Automated DNA Sequencing 380
  - Chapter Summary* 382
  - Key Terms* 383
  - Examples of Worked Problems* 384
  - Problems* 384
- 14-5 Alteration of DNA 402
  - Gene Dosage and Gene Amplification 402
  - Programmed DNA Rearrangements 403
  - DNA Methylation 405
- 14-6 Regulation of Transcription 406
  - Yeast Mating Type 406
  - Transcriptional Activator Proteins 407
  - Hormonal Regulation 409
  - Transcriptional Enhancers 410
  - The Logic of Combinatorial Control 412
  - Enhancer-Trap Mutagenesis 413
  - Alternative Promoters 414
- 14-7 Alternative Splicing 415
- 14-8 Translational Control 416
  - Multiple Proteins from a Single Segment of DNA 417
- 14-9 Is There a General Principle of Regulation? 417
  - Chapter Summary* 418
  - Key Terms* 420
  - Examples of Worked Problems* 420
  - Problems* 421

## CHAPTER 14

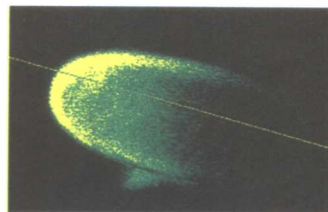
### Regulation of Gene Activity 386



- 14-1 Transcriptional Regulation in Prokaryotes 388
- 14-2 Lactose Metabolism and the Operon 390
  - Lac<sup>-</sup> Mutants 390
  - Inducible and Constitutive Synthesis and Repression 391
  - The Operator Region 392
  - The Operon Model 393
  - Positive Regulation of the Lactose Operon 394
- 14-3 Regulation of the Tryptophan Operon 396
  - Attenuation 398
- 14-4 Regulation in Eukaryotes 400
  - Important Differences in the Genetic Organization of Prokaryotes and Eukaryotes 401

## CHAPTER 15

### Genetic Control of Development 424



- 15-1 Genetic Determinants of Development 426
- 15-2 Early Embryonic Development in Animals 428
  - Early Development and Activation of the Zygote Genome 432
  - Composition and Organization of Oocytes 431
- 15-3 Genetic Control of Cell Lineages 432
  - Genetic Analysis of Development in the Nematode 432
  - Mutations Affecting Cell Lineages 434
  - Types of Lineage Mutations 434
  - The *lin-12* Developmental-Control Gene 437



- 15-4 Development in *Drosophila* 440  
 Maternal-Effect Genes and Zygotic Genes 442  
 The Genetic Basis of Pattern Formation in Early Development 443  
 Coordinate Genes 444  
 Gap Genes 446  
 Pair-Rule Genes 447  
 Segment-Polarity Genes 447  
 Homeotic Genes 448
- 15-5 Development in Higher Plants 451  
*Chapter Summary* 453  
*Key Terms* 455  
*Examples of Worked Problems* 455  
*Problems* 456

## CHAPTER 16

### Mutation, Recombination, and DNA Repair 458

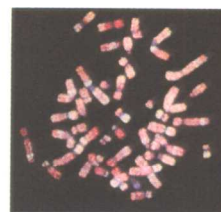


- 16-1 General Properties of Mutations 460
- 16-2 The Molecular Basis of Mutation 461  
 Base Substitutions 461  
 Additions and Deletions 462  
 Transposable-Element Mutagenesis 463
- 16-3 Spontaneous Mutations 464  
 The Nonadaptive Nature of Mutation 465  
 Measuring Mutation Rates 466  
 Hot Spots of Mutation 468  
 Mismatch Repair 469
- 16-4 Induced Mutations 469  
 Base-Analog Mutagens 470  
 Chemical Agents That Modify DNA 471  
 Misalignment Mutagenesis 472  
 Ultraviolet Irradiation 473  
 Ionizing Radiation 474
- 16-5 Mechanisms of DNA Repair 475
- 16-6 Reverse Mutations and Suppressor Mutations 478  
 Intragenic Suppression 478  
 Intergenic Suppression 479  
 Reversion as a Means of Detecting Mutagens and Carcinogens 481

- 16-7 Oligonucleotide Site-directed Mutagenesis 482
- 16-8 Recombination 484  
*Chapter Summary* 487  
*Key Terms* 489  
*Examples of Worked Problems* 489  
*Problems* 490

## CHAPTER 17

### Somatic-Cell Genetics and Immunogenetics 492



- 17-1 Somatic-Cell Genetics 494  
 Somatic-Cell Hybrids and Gene Mapping 494  
 The Production of Hybrid Cells 497
- 17-2 The Immune Response 498
- 17-3 Blood-Group Systems 501  
 The ABO Blood Groups 501  
 Rh Blood Groups 502  
 Applications of Blood Groups 504
- 17-4 Antibodies and Antibody Variability 504  
 Gene Splicing in the Origin of T-cell Receptors 507
- 17-5 Histocompatibility Antigens 508  
 Blood Groups, HLA, and Disease 510  
*Chapter Summary* 510  
*Key Terms* 512  
*Examples of Worked Problems* 512  
*Problems* 513

Glossary 517

Bibliography 539

Answers 545

Index 569

## CHAPTER OUTLINE

### MENDEL AND HIS EXPERIMENTS

Particulate Hereditary Determinants • The Principle of Segregation  
Some Genetic Terminology • The Principle of Independent Assortment  
Testercrosses • Multiple Alleles

### MENDELIAN INHERITANCE AND PROBABILITY

#### SEGREGATION IN PEDIGREES

#### GENES AND CELLULAR PRODUCTS

#### DEVIATIONS FROM SIMPLE DOMINANCE

The Absence of Dominance of Some Alleles • Codominance

#### THE EFFECTS OF GENES ON THE EXPRESSION OF OTHER GENES

Penetrance, Expressivity, and Pleiotropy

*Chapter Summary* • *Key Terms*

*Examples of Worked Problems* • *Problems*



**G**enetics is the study of inheritance. The fundamental concept of the science is that:

Inherited traits are determined by chemical entities that are transmitted from parents to offspring in reproduction.

The unit of inheritance is called a **gene**. The elements of heredity and the rules governing their transmission from generation to generation were discovered by Gregor Mendel in 1866 in experiments with garden peas. Although the molecular biology of genes and gene action was not understood until after the 1950s, Mendel's principles of inheritance formed the foundation for the development of genetics and much of modern biology. Mendel's breakthrough experiments and concepts are the subject of this chapter.

---

*Left:* Gregor Mendel carried out his genetic experiments in this small garden in the monastery of St. Thomas in Brno, Czech Republic. The flowers are maintained as a memorial. There is also a Mendel Museum, which is located in the wing of the building at the right. (Photographed by the author in 1990.)

## 1-1

### Mendel and His Experiments

During the period in which Mendel developed his theory of heredity, he was a monk and a teacher of science in a public high school in what is now Brno, Czechoslovakia. He lived in a monastery, and it was there that he carried out his experiments on heredity. The principal difference between Mendel's approach and that of other scientists who were interested in similar problems is that Mendel thought in quantitative terms about traits that could be classified into a small number of categories. He proceeded by posing simple questions to be answered by experiments and then looking for statistical regularities that might identify general rules.

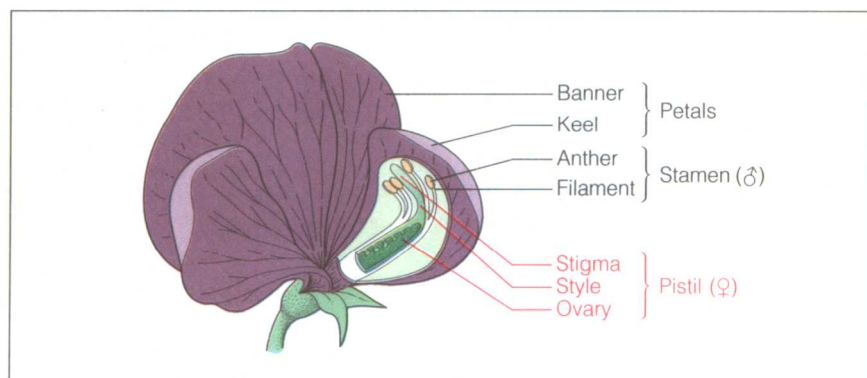
Mendel selected peas for his experiments for two reasons: (1) he had access to varieties that differed in observable alternative characteristics, and (2) his earlier studies of flower structure (Figure 1-1) indicated that peas usually reproduce by self-pollination, in which pollen produced in a flower is transferred to the stigma of the same flower. To produce hybrids by cross-pollination, he needed only to open the keel petal (enclosing the reproductive structures), remove the immature anthers before they had shed pollen, and dust the stigma with pollen taken from a flower on another plant.

Mendel recognized the need to study inherited characteristics that were uniform within any given line of peas but different between lines. Therefore, at the beginning of his experiments, he established **true-breeding** lines in which the plants produced only progeny like themselves when allowed to self-pollinate normally. These different lines (which bred true for flower color, pod shape, or any of the other well-defined characters that Mendel had selected for investigation—Figure 1-2) provided the parents for subsequent hybridization. A **hybrid** is the offspring of a cross between inherently unlike parents.

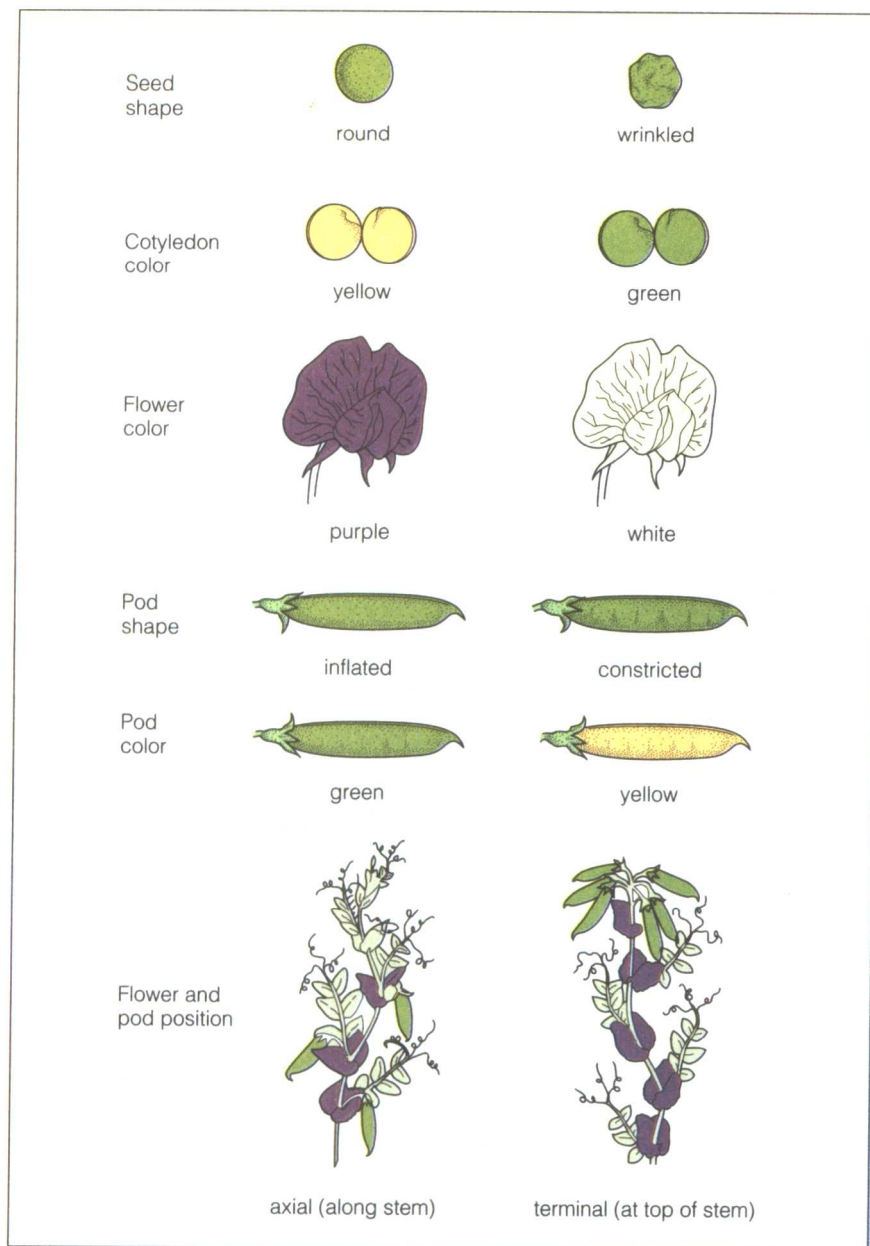
From an examination of a few of Mendel's original experiments, we will learn what his methods were and how he interpreted his results. One pair of characters that he studied was round versus wrinkled seeds. When pollen from a line of plants with wrinkled seeds was used to cross-pollinate plants from a line with round seeds, all of the hybrid seeds produced were round. He also performed the **reciprocal cross**, in which plants from the line with round seeds were used as the pollen parents and those from the line with wrinkled seeds as female parents. As before, all of the hybrid seeds were round.

**Figure 1-1**

A pea flower with section removed to show the reproductive structures. Each flower has a single ovary that develops into the seed pod, and each ovary contains as many as ten ovules, which give the seeds. The pistil is shown in green.







**Figure 1-2**

Six of the seven character differences in peas studied by Mendel (the seventh difference was long versus short stems). In each case, the characteristic shown at the left is seen in the hybrid.

When the hybrid seeds from the round  $\times$  wrinkled cross were allowed to undergo self-fertilization, the progeny were of two types—round and wrinkled—in definite numerical proportions. Mendel counted 5474 seeds that were round and 1850 that were wrinkled and noted that this ratio was approximately 3 : 1.

The hybrid progeny produced by crossing the lines with round and wrinkled seeds constitute the **F<sub>1</sub> generation**, and all of the F<sub>1</sub> seeds were round. The progeny produced by self-fertilization of the F<sub>1</sub> generation constitute the **F<sub>2</sub> generation**, and the F<sub>2</sub> progeny appeared in the proportions 3 round : 1 wrinkled. (The letter *F* in the F<sub>1</sub>, F<sub>2</sub> terminology stands for *filial*, referring to sons or daughters.) These results can be summarized in the following way:



Parental lines: round seeds  $\times$  wrinkled seeds

F<sub>1</sub>:

all round

F<sub>2</sub>:

3 round : 1 wrinkled

Similar results were obtained when Mendel made crosses between plants differing in six other pairs of alternative characteristics. The results of some of these experiments are summarized in Table 1-1. The principal observations were:

1. The F<sub>1</sub> hybrids possessed only one of the parental traits.
2. In the F<sub>2</sub> generation, both parental traits were present.
3. The trait that appeared in the F<sub>1</sub> generation was always present in the F<sub>2</sub> about three times as frequently as the alternative trait.

In the remainder of this section, we will see how Mendel followed up these basic observations and performed experiments that led to his concept of discrete genetic units and to the principles governing their inheritance.

### Particulate Hereditary Determinants

The prevailing concept of heredity in Mendel's time was that the traits of the parents became blended in the hybrid, as though the hereditary material consisted of fluids that became permanently mixed when combined. However, Mendel's observation that one of the parental characteristics was absent in F<sub>1</sub> hybrids and reappeared in unchanged form in the F<sub>2</sub> generation was inconsistent with the idea of blending. From this result, Mendel concluded that the traits from the parental lines were transmitted as two different elements of a *particulate nature* that retained their purity in the hybrids. The element associated with the trait seen in the F<sub>1</sub> hybrids (round seeds, in the example just used) he called **dominant**, and the other element, associated with the trait not seen in the hybrids but reappearing in their progeny (wrinkled seeds), he called **recessive**.

Table 1-1 Results of several of Mendel's experiments

Parental characteristics	F <sub>1</sub>	Number of F <sub>2</sub> progeny	F <sub>2</sub> ratio
round $\times$ wrinkled (seeds)	round	5474 round, 1850 wrinkled	2.96 : 1
yellow $\times$ green (cotyledons)	yellow	6022 yellow, 2001 green	3.01 : 1
purple $\times$ white (flowers)	purple	705 purple, 224 white	3.15 : 1
inflated $\times$ constricted (pods)	inflated	882 inflated, 299 constricted	2.95 : 1
long $\times$ short (stems)	long	787 long, 277 short	2.84 : 1