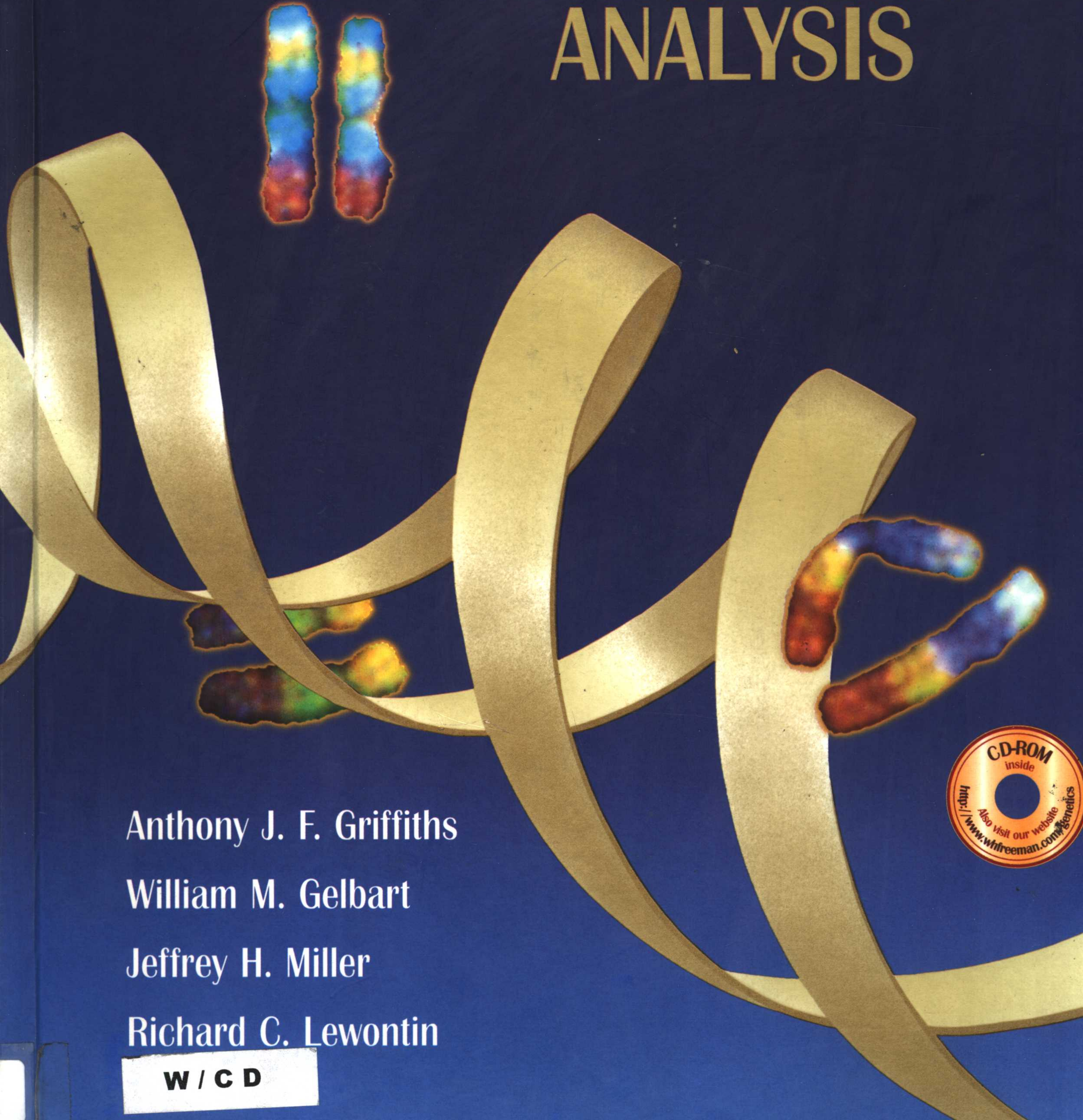
MODERN GENETIC ANALYSIS



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Preface

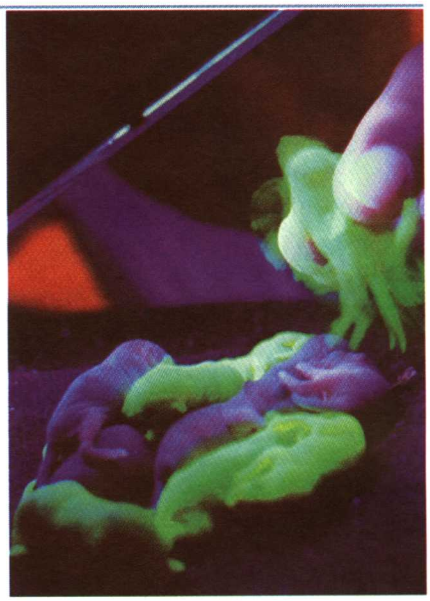


Figure 1-10

AS TEACHERS OF GENETICS and the authors of *An Introduction to Genetic Analysis,* we are aware of the quiet revolution in the way that genetics is taught to beginning students. Many instructors are finding that a strictly chronological, or historical, approach no longer fits their method of teaching genetics, nor does it meet their students' needs. More and more, molecular genetics is being introduced earlier in the course and integrated with phenotypic and genotypic analysis.

Modern Genetic Analysis was written for instructors and students who need a textbook that supports the "DNA first" approach. This departure from the traditional historical unfolding of genetics has had some significant side effects—chief among them, a more streamlined presentation in which genetic principles stand in bolder relief.

Regardless of whether the presentation is traditional or modern, it is essential that students learn to think like geneticists. Thus, as in *An Introduction to Genetic Analysis,* the focus is on teaching students to analyze data and draw conclusions.

Modern Approach

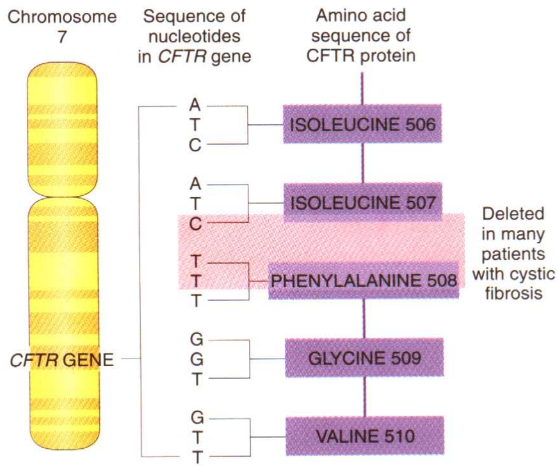


Figure 3-28

After an introductory chapter on the relations between genes and phenotypes, there is a chapter on the structure of genes and genomes. This immediately establishes a framework of the molecular nature of the hereditary material on which its various properties can be hung. Chapters 3 through 5 deal with gene function and gene inheritance, which are related back to the structural nature of the genome. Chapter 4, "The Inheritance of Genes," presents the inheritance patterns of single genes. Increasing complexity stepwise, Chapter 5, "Recombination of Genes," covers the principles at work when two genes or more are analyzed. We add further to the complexity of genetics in Chapter 6, "Gene Interaction," in which inheritance patterns are related to functional gene interactions at the molecular level.

Thus, in the first six chapters, the core of our modern view of gene structure and function is presented. However, instead of segregating Mendel's work in its own chapter, we have extracted the principles deduced by Mendel and integrated them where they belong pedagogically, alongside the cellular and molecular structures that drive them. Our belief is that this new organization of material will help those students who have trouble retrospectively fitting molecular biology onto a framework of Mendelian genetics. Moreover, because molecular biology is introduced first, we provide an opportunity for a vertical integration of concepts at the organismal, cellular, chromosomal, protein, and DNA levels. Finally, we hope that this new approach will enable students to understand how genetics is done in the "real world," where classical and molecular approaches are not segregated but complement each other.

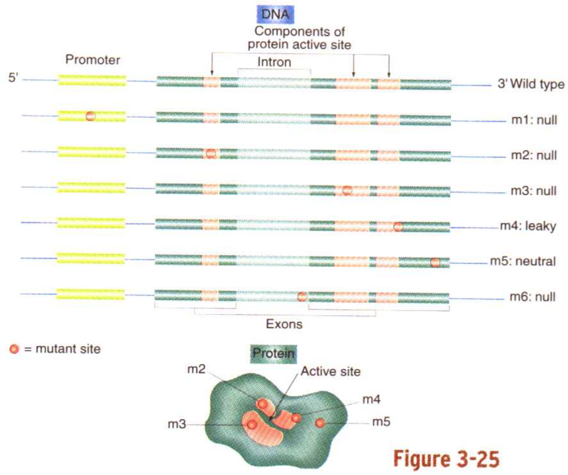


Figure 3-25

In keeping with the book's title, we have strived for currency throughout the text. We have included the latest approaches in genomics, including a section on functional genomics embracing DNA chip technology and the yeast two-hybrid system. As another example, programmed cell death is considered in the contexts of both normal biology and the genetics of cancer.

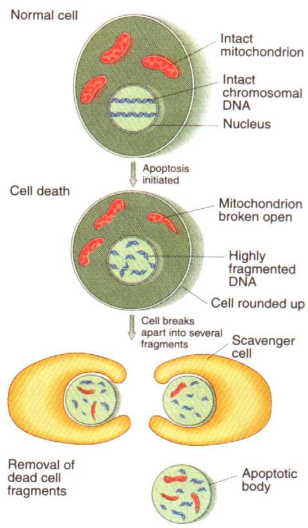


Figure 15-4

Focus on Principles

A primary goal in writing *Modern Genetic Analysis* was that the understanding and application of core genetic principles take priority over historical details. We hope that students will more readily recognize and grasp fundamental principles and themes if their presentation is not encumbered by excessive detail. Thus the focus is on overarching principles of genetics rather than the historical experiments that generated them. The principles are used to explain to students how genetics is done today. For instance, in Chapter 3, we introduce the common themes of complementarity of nucleic acid sequences and specificity of protein–nucleic acid interactions. Students then see these themes again in subsequent chapters, applied in the analyses of DNA replication, protein synthesis, and regulation of gene expression.

In all chapters, we stress the vertical relation between DNA, protein products, and phenotype. The chapters on recombinant DNA technology focus on how recombinant DNA technology is used to isolate and characterize genes, rather than on the techniques themselves. Here the students will see how recombinant DNA techniques were used to clone the human genes for albinism and alkaptonuria. In Chapter 11, "Applications of Recombinant DNA Technology," a section deals with transgenic crops currently in use in agriculture. The chap-

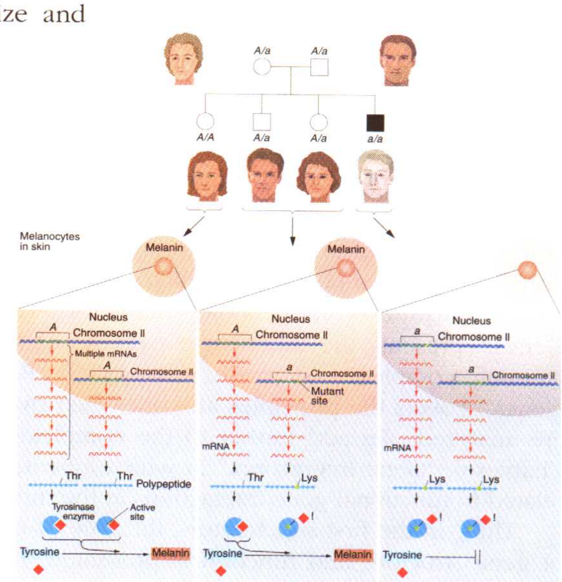
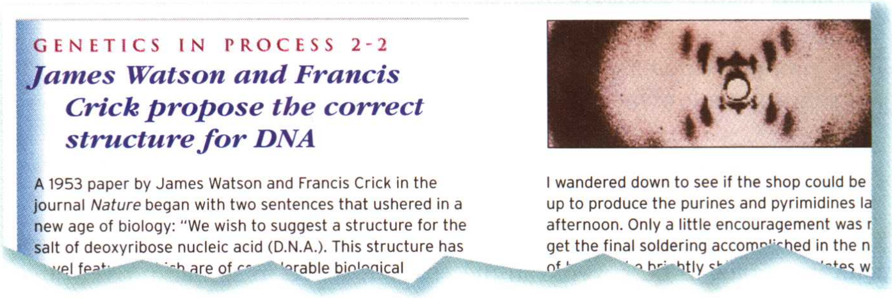


Figure 4-20

ters on developmental genetics emphasize the importance of signal transduction cascades in all aspects of a cell's or an organism's development and the important and varied switch mechanisms that underlie all developmental decisions.

Although we do not want the details of historical experiments to distract from the core principles, it is enriching in a well-rounded study of genetics for the students to be exposed to some of the landmark experiments in genetics. Students benefit from learning how these key experiments were conceived and carried out. These important investigations are set apart from the text in sections called "Genetics in Process." Here, students will read about the way that Archibald Garrod inferred the nature of inborn errors of metabolism, about the research that led Charles Yanofsky to deduce that gene and protein structure are colinear, about Watson and Crick's model for the structure of DNA, including Watson's own description of the first assembly of the metal model, and about Luria and Delbruck's method of deducing the random nature of mutations.


GENETICS IN PROCESS 2-2

James Watson and Francis Crick propose the correct structure for DNA

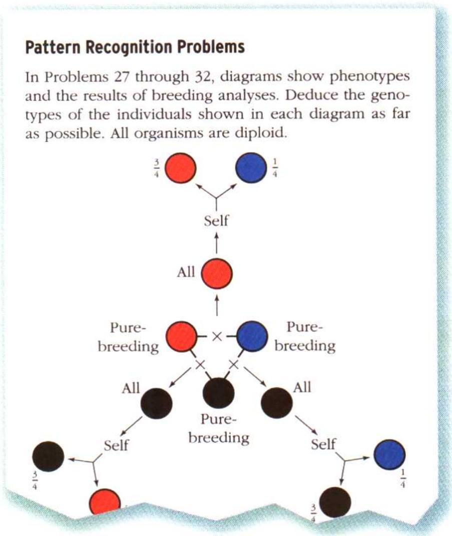
A 1953 paper by James Watson and Francis Crick in the journal *Nature* began with two sentences that ushered in a new age of biology: "We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has

I wandered down to see if the shop could be up to produce the purines and pyrimidines la afternoon. Only a little encouragement was r get the final soldering accomplished in the n

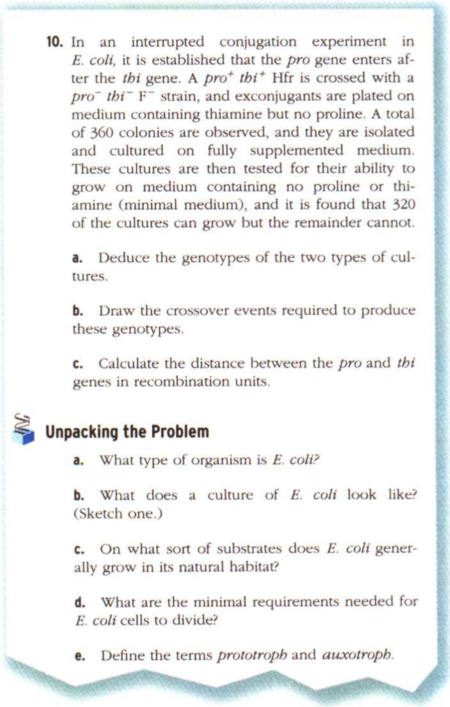
Focus on Genetic Analysis

We focus on the questions that underlie much of modern genetics, such as, "How many genes affect this phenotypic difference? Are the genes linked? Are the mutations allelic? What is the cellular function of the gene?" In short, the focus is on the modes of inference used in genetics today.

PROBLEMS at the end of each chapter have been created for students to apply and exercise their analytical skills. Problems are arranged to start from the simple and proceed to the more complex. All problems have been classroom tested. Of particular interest is a new type of problem called *Pattern Recognition*. These problems are symbolic representations of the results of simple cross systems, shown graphically with a minimum number of words. They have been designed to aid students in recognizing hereditary patterns in data, a key skill in genetic analysis. Most chapters also include a problem containing an exercise titled *Unpacking the Problem*. Such exercises reveal the underlying levels of knowledge that must be applied for a problem to be solved constructively. The unpacking exercise


Pattern Recognition Problems

In Problems 27 through 32, diagrams show phenotypes and the results of breeding analyses. Deduce the genotypes of the individuals shown in each diagram as far as possible. All organisms are diploid.


10. In an interrupted conjugation experiment in *E. coli*, it is established that the *pro* gene enters after the *thi* gene. A pro^+ thi^+ Hfr is crossed with a pro^- thi^- F^- strain, and exconjugants are plated on medium containing thiamine but no proline. A total of 360 colonies are observed, and they are isolated and cultured on fully supplemented medium. These cultures are then tested for their ability to grow on medium containing no proline or thiamine (minimal medium), and it is found that 320 of the cultures can grow but the remainder cannot.

a. Deduce the genotypes of the two types of cultures.

b. Draw the crossover events required to produce these genotypes.

c. Calculate the distance between the *pro* and *thi* genes in recombination units.

Unpacking the Problem

a. What type of organism is *E. coli?*

b. What does a culture of *E. coli* look like? (Sketch one.)

c. On what sort of substrates does *E. coli* generally grow in its natural habitat?

d. What are the minimal requirements needed for *E. coli* cells to divide?

e. Define the terms *prototroph* and *auxotroph*.

accesses this underlying knowledge and even addresses fundamental misunderstandings that sometimes prevent students from solving problems successfully.

Each chapter also includes several SOLVED PROBLEMS that walk students through the way in which geneticists apply principles to experimental data. The Solved Problems prepare students for solving problems on their own.

SOLVED PROBLEM

2. The leaves of pineapples can be classified into three types: spiny (S), spine tip (ST), and piping (nonspiny) (P). In crosses between pure strains followed by intercrosses of the F_1, the following results were obtained:

		Phenotypes	
Cross	**Parental**	**F_1**	**F_2**
1	ST × S	ST	99 ST:34 S
2	P × ST	P	120 P:39 ST
3	P × S	P	95 P:25 ST:8 S

a. Assign gene symbols. Explain these results in terms of the genotypes produced and their ratios.

b. Using the model from part a, give the phenotypic ratios you would expect if you crossed (1) the F_1 progeny from piping × spiny with the spiny parental stock, and (2) the F_1 progeny of piping × spiny with the F_1 progeny of spiny × spiny tip.

SOLUTION

a. First, let's look at the F_2 ratios. We have clear 3:1 ratios in crosses 1 and 2, indicating single-gene segregations. Cross 3, however, shows a ratio that approximates a 12:3:1 ratio. This ...

Students' Study Aids

KEY CONCEPTS at the beginning of each chapter give an overview of the main principles to be covered in the chapter, stated in simple prose without genetic terminology. They provide a strong pedagogic direction for the reader.

KEY CONCEPTS

- **Normal cell proliferation is modulated by cell cycle regulation.**
- **Apoptosis is a normal self-destruction mechanism that eliminates damaged and potentially harmful cells.**
- **Signaling systems permit proliferation and apoptosis to be coordinated within a population of cells.**
- **In cancer, cells proliferate out of control and avoid fail-safe destruction mechanisms through the accumulation of a series of special mutations in the same somatic cell.**
- **Many of the classes of genes that are mutated to cause cancers are important components of the ce... that directly or indirectly contribute to growth control and differentiation.**

Highlighted MESSAGES appear throughout each chapter to serve as convenient milestones at which the reader can pause and contemplate the material just presented.

MESSAGE

Protein architecture is the key to gene function. The specific amino acid sequence determines the general shape, binding properties, and reactivity of the protein.

Each chapter SUMMARY provides a short distillation of the chapter material and an immediate reinforcement of the concepts. Summaries are useful in text review, especially in preparing for exams.

SUMMARY

The basis of the transmission of genes through cell and organismal generations is DNA replication. DNA replication precedes both asexual and sexual cell division. During DNA replication the two halves of the double helix separate, and the single strands serve as templates for new polymerization of nucleotides. Hence each daughter DNA molecule is half old and half new; this mechanism of replication is called ...

At the end of each chapter, the student is asked to create a CONCEPT MAP. Concept maps grew out of the constructivist movement in education, which asserts that student learning is most effective when new information confronts previous understanding. The concept map provides a powerful method for resolving such confrontation and for visualizing concept integration.

CONCEPT MAP

Draw a concept map interrelating as many of the following terms as possible. Note that the terms are in no particular order.

DNA double helix / genome / nucleus / homologs / ploidy / *n* / haploid / diploid / chromosome

Supplements

The following supplementary materials are available to accompany *Modern Genetic Analysis.*

Solutions Manual

William Fixsen, Harvard University, 0-7167-3282-3

The *Solutions Manual* contains worked-out answers to all the problems in the textbook.

Modern Genetic Analysis Web Site

W. H. Freeman with Sumanas, Inc. with contributions from William Sofer, The State University of New Jersey at Rutgers

This multimedia learning tool complements and enriches the textbook. All the features of the CD-ROM function within the context of the book's coverage. Practice tools such as interactive quizzes in every chapter help students review for exams. The Modern Genetic Analysis Web site, at www.whfreeman.com/genetics, will be updated regularly.

Modern Genetic Analysis 1.0 CD-ROM

(hybrid format for Windows and Macintosh)

Packaged with every copy of the textbook, the Modern Genetic Analysis 1.0 CD-ROM is the same as the Web site with these two additions: (1) original animations on topics such as transcription, DNA replication, and complementation bring the textbook figures to life; and (2) for instructors, the text's entire illustration program and the original animations are available in a Presentation Manager, which allows the preparation of a series of illustrations, animations, and videos for lecture. Source files for the illustrations are provided so that images can be exported into presentation software programs.

Instructor's Resource Manual and Test Bank

Sally Allen, University of Michigan, and Ewen Harrison

Printed: 0-7167-3422-2, Windows: 0-7167-3421-4, Macintosh: 0-7167-3420-6

The *Instructor's Resource Manual* contains over 700 test questions in multiple-choice, true-false, and matching formats. It also contains complete sample exams and teaching hints. Electronic versions of the test questions let professors edit and rearrange questions and add their own.

Transparency Set

0-7167-3423-0

A full-color *overhead transparency set* of 130 key illustrations from the textbook is available free of charge to qualified adopters. The *overhead transparency set* also includes 100 transparency masters of text illustrations and tables.

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Contents in Brief

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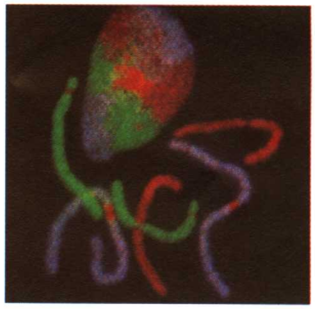

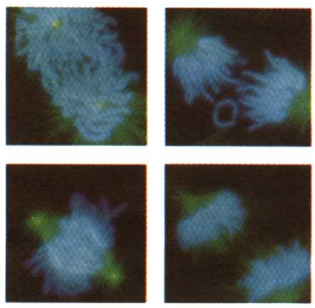

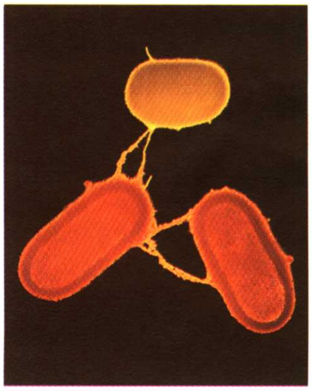

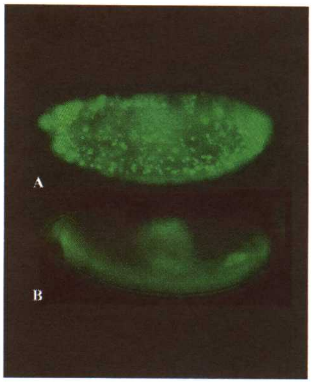
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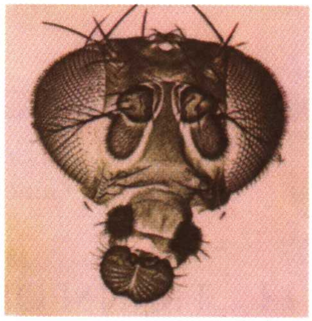

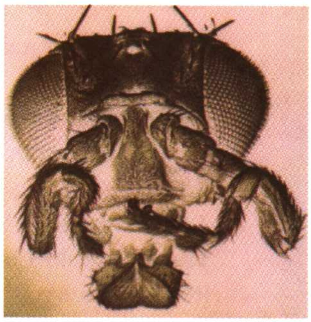

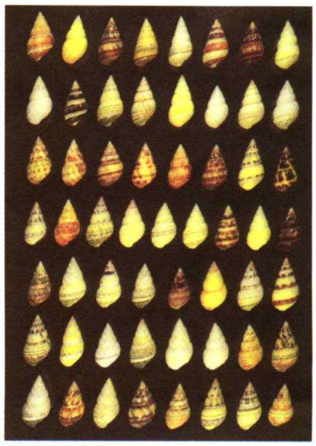

1 GENETICS AND THE ORGANISM

Genetic variation in the color of corn kernels. Each kernel represents a separate individual with a distinct genetic makeup. The photograph symbolizes the history of humanity's interest in heredity. Humans were breeding corn thousands of years before the rise of the modern discipline of genetics. Extending this heritage, corn today is an important research organism in classical and molecular genetics.

(William Sheridan, University of North Dakota; photo by Travis Amos.)

KEY CONCEPTS

- **Genetics has unified the biological sciences by revealing uniform hereditary systems.**
- **Genetics is of direct relevance to human affairs.**
- **Genetics may be defined as the study of genes.**
- **Genetic variation contributes to variation in nature.**
- **Variation is the basis for much of genetic analysis.**
- **The genetic approach can be used to dissect any biological process.**

Why study genetics? There are two basic reasons. First, genetics has come to occupy a pivotal position in the entire subject of biology. For any serious student of plant, animal, or microbial life, an understanding of genetics is thus essential. Second, genetics, like no other scientific discipline, has become central to numerous aspects of human affairs. It touches our humanity in many different ways. Indeed, genetic issues seem to surface daily in our lives, and no thinking person can afford to be ignorant of its discoveries. In this chapter we take an overview of the science of genetics, showing how it has come to occupy its crucial position. In addition we provide a perspective from which to view the subsequent chapters.

First we need to define what genetics is. Some define it as the study of heredity, but hereditary phenomena have been interesting to humans since before the dawn of civilization. Long before biology or genetics existed as the scientific disciplines we know today, ancient peoples were improving plant crops and domesticated animals by selecting desirable individuals for breeding. They also must have puzzled about the inheritance of individuality in humans, and asked such questions as "Why do children resemble their parents?" and "How can various diseases run in families?" However, genetics as a set of principles and analytical procedures did not begin until the 1860s when an Augustinian monk named Gregor Mendel (Figure 1-1) performed a set of experiments that pointed to the existence of biological elements called **genes.** The word *genetics* comes from "genes," and genes provide the focus for the subject. Whether geneticists study at the molecular, cellular, organismal, family, population, or evolutionary level, genes are always central in their studies. Simply stated, genetics is the study of genes.

Figure 1-1 Gregor Mendel. (Moravian Museum, Brno.)

What are genes? Genes are composed of a thread-like double-helical macromolecule called **deoxyribonucleic acid,** abbreviated **DNA.** DNA, the hereditary material that passes from one generation to the next, dictates the inherent properties of a species. The information encoded in DNA is in the form of a sequence of chemical subunits called **nucleotides.** Each cell in an organism typically contains one or two sets of the basic complement of DNA, called a **genome.** The genome itself is made up of one or more extremely long molecules of DNA that are assembled into structures called **chromosomes.** Genes are simply the functional units of chromosomal DNA. Each gene not only encodes the structure of some cellular product, but also bears control buttons that determine when, where, and how much of that product is synthesized (Figure 1-2). Most genes encode protein products. Proteins are the most important determinants of the properties of cells and organisms: when you

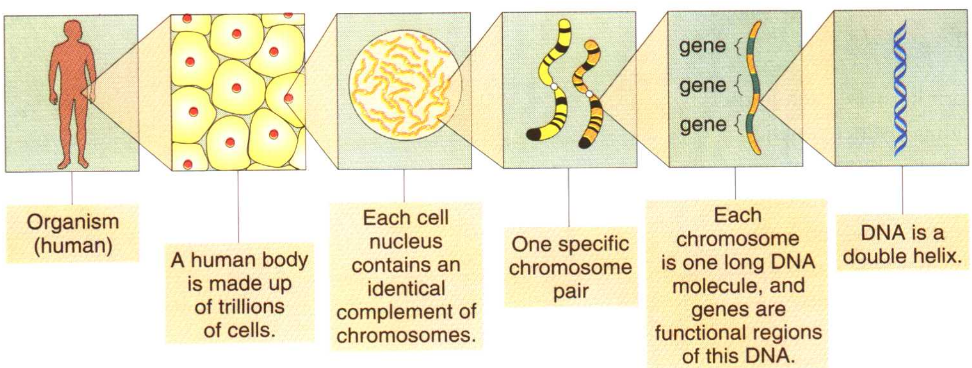

Figure 1-2 Successive enlargements of an organism to focus on the genetic material.