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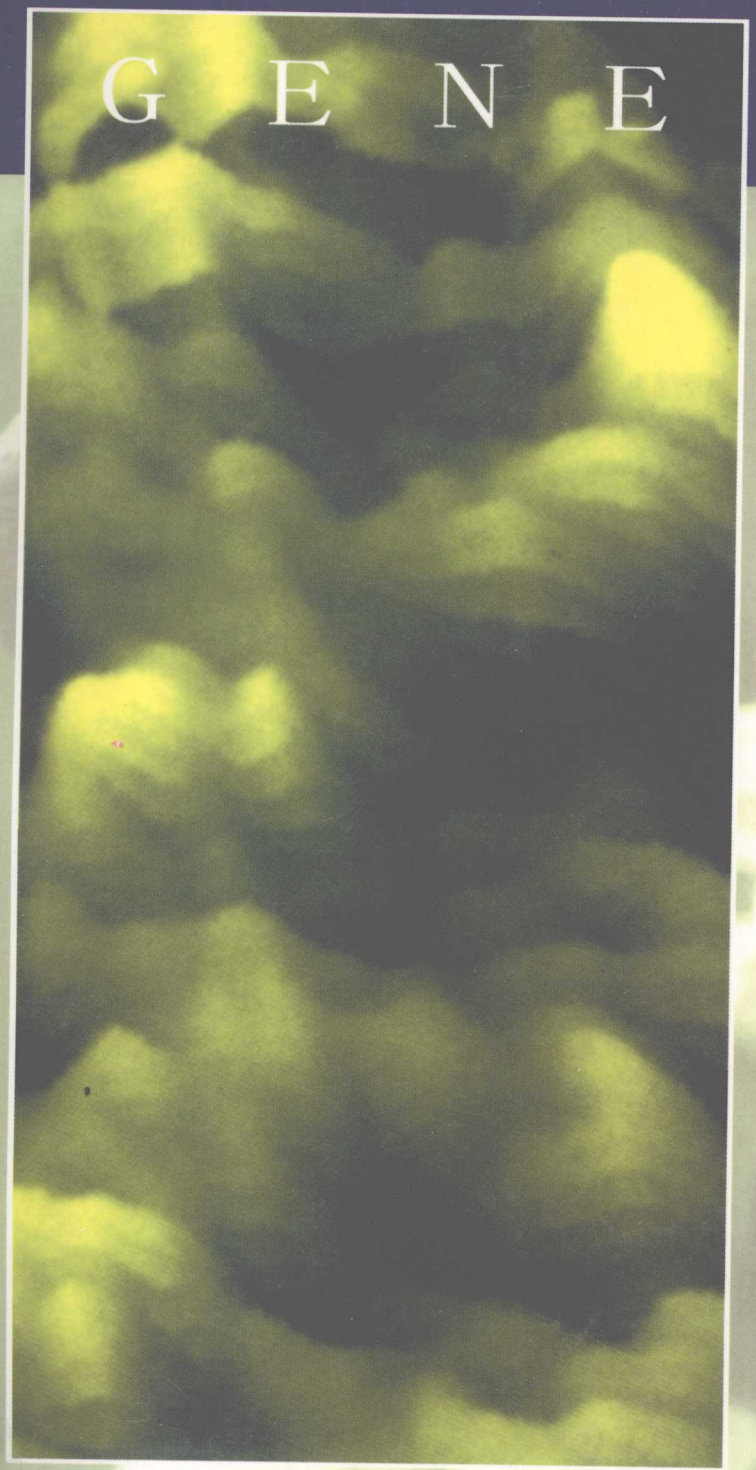

THE CONTINUITY OF LIFE

生命的延续

（英文影印版）

Daniel J. Fairbanks
W. Ralph Anderson

随赠光盘

中国协和医科大学出版社
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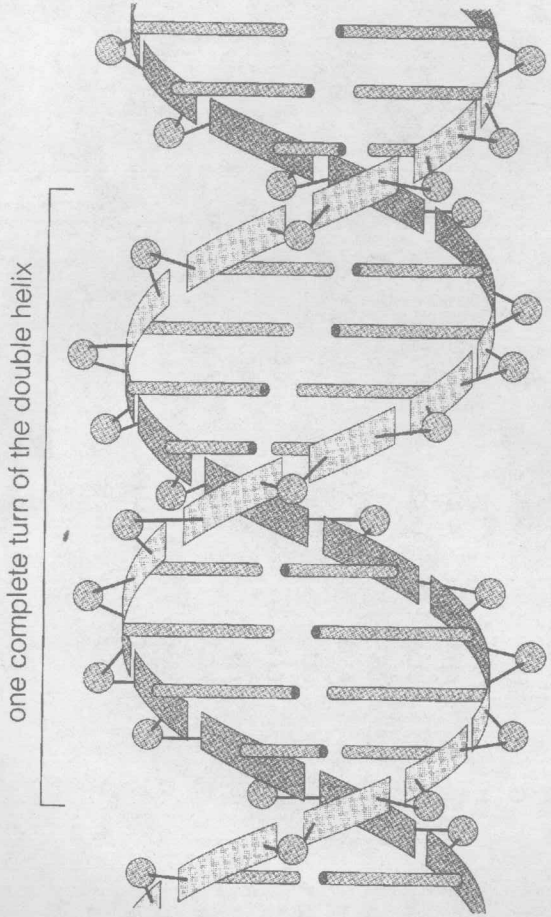
THE WATSON-CRICK MODEL OF DNA

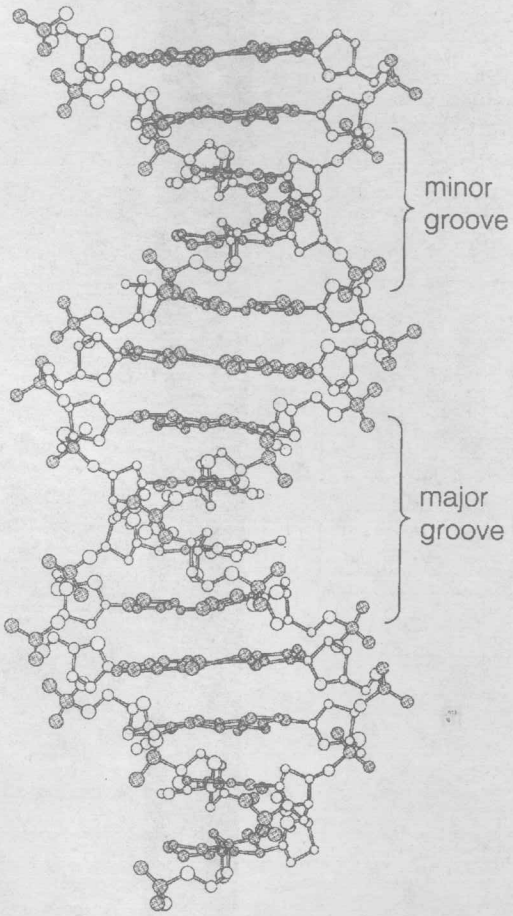


= deoxyribose sugar

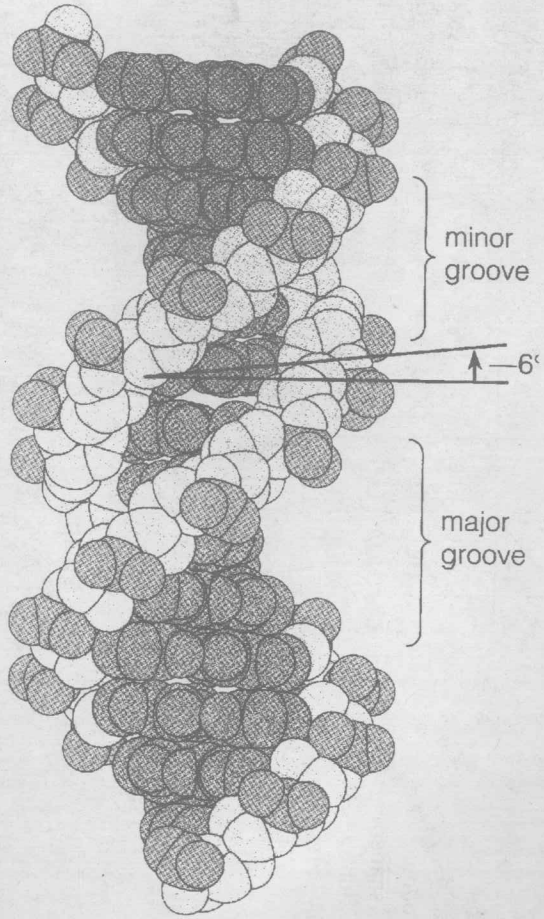
= phosphate linkage

= base pair

a The sugar-phosphate backbone and the nitrogenous base pairs in the DNA molecule.



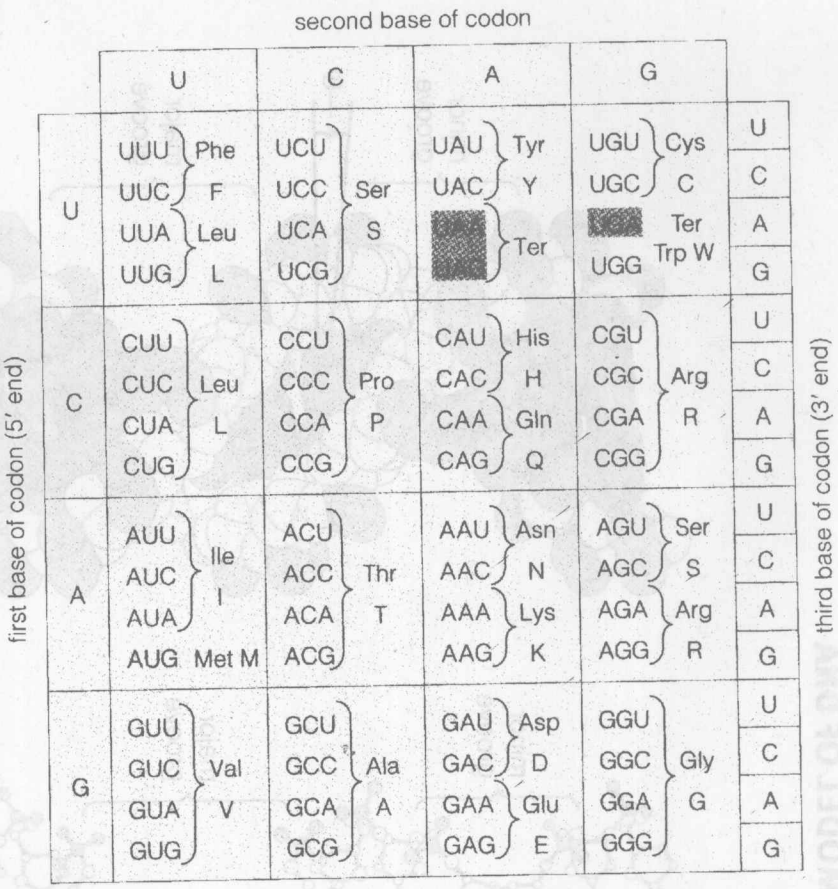
b The positioning of the nucleotides in the DNA molecule.



c A space-filling diagram of B-DNA.

THE GENETIC CODE

The three-letter and one-letter abbreviations of the amino acids. "Ter" denotes termination codon. The initiation codon, AUG, is shaded green, and the three termination codons—UAA, UAG, and UGA—are shaded red.



Amino Acids and Their Symbols			Codons					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Asparagine	Asn	N	AAC	AAU				
Aspartic acid	Asp	D	GAC	GAU				
Cysteine	Cys	C	UGC	UGU				
Glutamic acid	Glu	E	GAA	GAG				
Glutamine	Gln	Q	CAA	CAG				
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AUU			
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Lysine	Lys	K	AAA	AAG				
Methionine	Met	M	AUG					
Phenylalanine	Phe	F	UUC	UUU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				
Valine	Val	V	GUA	GUC	GUG	GUU		

Some Type II Restriction Endonucleases with Their Restriction Sites, Shown After Cleavage

Restriction Endonuclease	Source	Restriction Site	Type of Cut
AluI	*Arthobacter luteus*	5′ AG CT 3′ 3′ TC GA 5′	Blunt
BalI	*Brevibacterium albidum*	5′ TGG CCA 3′ 3′ ACC GGT 5′	Blunt
BamHI	*Bacillus amyloliquifaciens*	5′ G GATCC 3′ 3′ CCTAG G 5′	Staggered
BglII	*Bacillus globigii*	5′ A GATCT 3′ 3′ TCTAG A 5′	Staggered
ClaI	*Clostridium formoaceticum*	5′ GCG C 3′ 3′ C GCG 5′	Staggered
DraI	*Deinococcus radiophilus*	5′ TTT AAA 3′ 3′ AAA TTT 5′	Blunt
EcoRI	*Escherichia coli*	5′ G AATTC 3′ 3′ CTTAA G 5′	Staggered
EcoRV	*Escherichia coli*	5′ GAT ATC 3′ 3′ CTA TAG 5′	Blunt
HaeIII	*Haemophilus aegyptius*	5′ GG CC 3′ 3′ CC GG 5′	Blunt
HindIII	*Haemophilus influenzae*	5′ A AGCTT 3′ 3′ TTCGA A 5′	Staggered
PstI	*Providencia stuarti*	5′ CTGCA G 3′ 3′ G ACGTC 5′	Staggered
SacI	*Streptomyces achromogenes*	5′ GAGCT C 3′ 3′ C TCGAG 5′	Staggered
SalI	*Streptomyces alba*	5′ G TCGAC 3′ 3′ CAGCT G 5′	Staggered
TaqI	*Thermus aquaticus*	5′ T CGA 3′ 3′ AGC T 5′	Staggered
XhoI	*Xanthomonas holica*	5′ C TCGAG 3′ 3′ GAGCT C 5′	Staggered

χ^2 Critical Values for Different Levels of Probability

Degrees of Freedom	Probability Level									
	0.95	0.90	0.70	0.50	0.30	0.20	0.10	0.05	0.01	0.001
1	0.004	0.016	0.15	0.46	1.07	1.64	2.71	3.84	6.64	10.83
2	0.10	0.21	0.71	1.39	2.41	3.22	4.61	5.99	9.21	13.82
3	0.35	0.58	1.42	2.37	3.67	4.64	6.25	7.82	11.35	16.27
4	0.71	1.06	2.20	3.36	4.88	5.99	7.78	9.49	13.28	18.47
5	1.15	1.61	3.00	4.35	6.06	7.29	9.24	11.07	15.09	20.52
6	1.64	2.20	3.83	5.35	7.23	8.56	10.65	12.59	16.81	22.46
7	2.17	2.83	4.67	6.35	8.38	9.80	12.02	14.07	18.48	24.32
8	2.73	3.49	5.53	7.34	9.52	11.03	13.36	15.51	[illegible]	26.13
9	3.33	4.17	6.39	8.34	10.66	12.24	14.68	16.92	21.67	27.88
10	3.94	4.87	7.27	9.34	11.78	13.44	15.99	18.31	23.21	29.59
11	4.58	5.58	8.15	10.34	12.90	14.63	17.28	19.68	24.73	31.26
12	5.23	6.30	9.03	11.34	14.01	15.81	18.55	21.03	26.22	32.91
13	5.89	7.04	9.93	12.34	15.12	16.99	19.81	22.36	27.69	34.53
14	6.57	7.79	10.82	13.34	16.22	18.15	21.06	23.69	29.14	36.12
15	7.26	8.55	11.72	14.34	17.32	19.31	22.31	25.00	30.58	37.70
20	10.85	12.44	16.27	19.34	22.78	25.04	28.41	31.41	37.57	45.32
25	14.61	16.47	20.87	24.34	28.17	30.68	34.38	37.65	44.31	52.62
30	18.49	20.60	25.51	29.34	33.53	36.25	40.26	43.77	50.89	59.70
50	34.76	37.69	44.31	49.34	54.72	58.16	63.17	67.51	76.15	86.66

PREFACE

Which should a genetics professor teach first, Mendelian genetics or molecular genetics? Most textbook authors have chosen to begin with transmission genetics, an organization that parallels the historical development of the discipline. With this approach students are often left with the impression that the field of transmission genetics is finished, and that molecular genetics is the frontier. However, the application of molecular tools to genetic analysis has brought transmission genetics firmly into the molecular arena. To understand transmission genetics in today's world, students need a strong molecular background.

Our book begins with genetics at its most fundamental level: the molecular information encoded in DNA. It takes readers through the transfer of genetic information from DNA to RNA to protein and finally to the outward characteristics that we observe in organisms. It proceeds in a logical fashion from molecules to cells to organisms to populations.

This organization offers several advantages for students and professors. Because students enter the genetics course with basic knowledge of DNA and genes from earlier biology courses, they can begin to forge connections between molecular and Mendelian concepts from the first week of class. They are exhilarated to encounter modern molecular concepts and techniques from the start rather than feeling that the course is replaying ideas they already know. As the term goes on, this organization gives professors the power to explain in a multidimensional way how genetics actually works. And with this approach, they can teach their students the way most geneticists think when tackling real genetic research.

OBJECTIVES

In writing *Genetics: The Continuity of Life*, we address four major objectives:

1. *Integrate modern molecular biology with all other areas of genetics.* Because of its unique organization, our book teaches the entire realm of genetics in a modern context, like no other book does. For example, as students confront Mendelian genetics, they do so with a molecular foundation and can relate Mendelian principles to the underlying molecular causes. The linkage between genotype at the DNA level and phenotype at the level of observation is a key theme of every chapter—a theme that can work only if we begin with molecular genetics.

2. *Teach students how to conduct genetic analysis.* After each major concept, we provide students with *real genetic data* that have been published in scientific journals, and show them how to analyze and interpret the data step by step, applying the concepts they just learned. We highlight key publications in the history of genetics as well as recent research. The advantage of such an approach is twofold: First, students learn how scientists acquire, organize, analyze, and interpret real genetic data. They learn about specific problems that scientists have faced and see how the scientists confronted those problems. Second, by

analyzing key experiments that helped to build the science of genetics, students become acquainted with the history and development of genetics. Rather than simply reading about the history, they analyze the work of scientists who made genetics what it now is. No other book delves as deeply into analysis of real experiments as ours does.

3. *Present genetics using a clear, friendly style that conveys the excitement of scientific discovery, stimulates imagination, and invites students to learn more.* The writing style of our book is conversational. We want students to feel that they are discussing genetics, not just reading about it. The book is illustrated with excellent drawings and photographs that visually portray the concepts discussed in the text. The artwork is integrated with the text so that students have the chance to work step by step through a diagram until they understand the concept. We have also interwoven the worked examples with the conceptual part of the text so that they fit together coherently.

Throughout, we have tried to convey the passion for scientific discovery that motivates most geneticists. Genetics is a dynamic science with important advances and applications appearing in the news almost weekly. As students sense how exciting genetics can be, they begin to imagine how they can contribute to the science of genetics as researchers. We hope that they will go beyond the book and seek information from both current and historical sources. To help them, we provide carefully chosen suggested readings and free online access to articles through *InfoTrac College Edition*.

4. *Provide students with a resource for study that assists them in their careers long after they have completed the course.* We view a genetics textbook as a resource not only for a genetics course, but also for a scientific career. Most students will not learn all of the information in our book in a single-semester genetics course. We hope, however, that during their course, they will become so familiar with their genetics textbook that they can turn to it for easily accessible additional information years after completing the course. Although the rapid progress of genetic discovery ensures that many of the details in any genetics textbook will become outdated shortly after its publication, the core principles and experimental examples that constitute the central messages of our book will remain informative and valuable for years to come.

ORGANIZATION

Genetics: The Continuity of Life includes 28 chapters: an introductory chapter followed by six major parts. The first chapter introduces students to the importance of genetics and genetic analysis, the purpose of model organisms, and the concept of the gene. The first four parts provide core principles, beginning with the molecular foundations of genetics and moving sequentially through the genetics of cells, organisms, and populations. The fifth part focuses on four special topics in genetics: transposable elements, development, cancer, and immunity. The final part discusses applications of genetics in medicine, forensics, agriculture, and industry and concludes by examining of the legal and ethical issues that such applications raise.

Part I: Molecular Foundations of Genetics

Part I provides students with the molecular background to understand the material in the rest of the book. Chapter 2 introduces students to DNA structure and replication. After providing fundamental information about gene expression, Chapter 3 focuses on transcription and RNA processing in both prokaryotes and eukaryotes. Chapter 4 covers translation and the processing and functions of proteins. Chapter 5 discusses mutation at the molecular level. Chapter 6 ties the concepts from the previous four chapters together to show how genetic variation at the DNA level is expressed as outward phenotypic variation, setting the stage for the chapters that follow.

Part II: Genetics of Cells

Part II covers genetics at the cellular level in prokaryotes and eukaryotes. Chapter 7, on the genetics and genome organization of bacteria, includes recent studies on whole genome sequencing as well as classical genetic mapping. In this chapter students also learn about bacterial culture techniques and bacterial viruses, information that is important for understanding recombinant DNA methodology. Chapter 8 reviews gene regulation in both prokaryotes and eukaryotes with a focus on how it influences the phenotype. Chapter 9 introduces the fundamental techniques of molecular biology, such as DNA cloning, genetic engineering of eukaryotic genes for expression in bacteria, the polymerase chain reaction, gel electrophoresis of nucleic acids and proteins, DNA sequencing, and computerized use of DNA sequence databases. This chapter provides the foundation for understanding the applications of molecular biology in eukaryotic genetics. Chapter 10 introduces students to the organization of the eukaryotic genome, culminating with an analysis of the complete DNA sequence of the *Saccharomyces cerevisiae* genome as an example of whole genome organization in eukaryotes. The review of mitosis, meiosis, and life cycles in Chapter 11 sets the stage for the next part.

Part III: Genetics of Organisms

In Part III the advantages of a molecular foundation become apparent. Chapter 12 discusses Mendelian genetics. Most students will have studied Mendelian genetics be-

fore, both in high school and in an introductory biology course in college. Rather than review the same material they have already encountered (but may not fully understand), this chapter presents Mendelian genetics in an entirely new light. It begins with a discussion of Mendel's experiments as he perceived them, and shows how he derived the fundamental principles of inheritance from the results of his experiments. Then the chapter brings Mendel's work into a modern context, showing how an understanding of gene expression and mutation at the molecular level can explain Mendelian principles at the phenotypic level. The chapter also introduces students to probability analysis and teaches them to use the binomial distribution and chi-square analysis. The chapter concludes with the story of the origin of genetics and applies statistical analysis to questions raised about Mendel's research. Chapter 13 teaches such important genetic concepts as incomplete dominance, codominance, multiple alleles, pleiotropy, penetrance, variable expressivity, and epistasis, all in a molecular context. With a strong background in the molecular basis of inheritance, students can grasp these concepts with ease. This chapter also introduces students to DNA markers and their use in genetics research. Chapter 14 describes the molecular basis of sex determination in humans and *Drosophila*, and the inheritance of X-linked alleles. Chapter 15 discusses chromosome mapping, starting with the classical approaches in model organisms, then moving to DNA marker-based chromosome mapping in humans and other species. The chapter ends with an explanation of how mapped DNA markers are used to clone important genes through chromosome walking and jumping. Chapter 16 discusses the fine structure of the gene. It shows how classical studies in fungal genetics led researchers to develop models of recombination and gene conversion at the molecular level. Then it discusses intragenic recombination and fine-structure mapping of mutations. Chapter 17 introduces students to the fundamentals of cytogenetics, including alterations in chromosome number and structure, and ends by showing how molecular analysis has played a role in human cytogenetics. Chapter 18 discusses extranuclear inheritance, focusing on mitochondrial and plastidial genomes and their inheritance.

Part IV: Genetics of Populations

In Part IV Chapter 19 introduces population genetics and provides detailed discussions of selection, inbreeding, and random genetic drift. Chapter 20 outlines quantitative genetics with a focus on the genetic basis for continuous variation and the relationship between heritability and the effectiveness of selection. Chapter 21 introduces students to the genetic basis of evolution, highlighting the contribution of molecular biology to an understanding of human origins.

Part V: Gene Expression and the Organism

Part V treats four important topics in current research on gene expression. Transposable elements were introduced in Chapter 10, but Chapter 22 discusses them in more detail, especially the transposable elements of maize and *Drosophila*. Chapter 23 covers developmental genetics, highlighting studies of *Caenorhabditis elegans*, *Drosophila melanogaster*, and mammals. The chapter concludes with a discussion of the emerging field of plant developmental genetics. Chapter 24 introduces students to the genetic basis of cancer. They learn how genes regulate the cell cycle and how mutations in those genes can cause cancer to develop. The chapter also provides practical information on cancer prevention and treatment. Chapter 25 discusses the genetic basis of immunity with a focus on human immunity. It also introduces students to immune system dysfunction including autoimmune disorders and HIV infection.

Part VI: Applications of Genetics

Throughout the book we discuss many applications of genetics, but Part VI shows students how genetics is used in applied research. Chapter 26 presents applications to medicine and forensics. Topics include the Human Genome Project and its implications, genetic testing and screening, DNA fingerprinting, genetic pharmacology, gene therapy, and clinical genetics. We introduce new examples and refer students to examples from previous chapters. Chapter 27 reviews the applications of genetics in agriculture and industry from prehistory to modern times. It tells the genetic origin of domesticated plants and animals and shows how genetic erosion threatens our food supply. This discussion leads into modern breeding and biotechnology of agricultural species. Chapter 28 addresses the legal and ethical issues that arise from applications of genetics. After a historical discussion of the eugenics movement, we discuss current legal and ethical issues, such as protection of intellectual property, confidentiality and informed consent, admissibility of DNA evidence in court, and safety issues associated with recombinant DNA research. The chapter concludes with a discussion of the importance of science education as a means of encouraging people in all walks of life to properly inform themselves about scientific issues.

PEDAGOGICAL FEATURES

A single goal guided the development of pedagogical features in this book: Provide students with a straightforward, accessible presentation that integrates genetic concepts and analysis. Genetics is a rigorous and challenging discipline; accordingly, our book is designed to help students focus on learning genetic concepts and analysis with as little distraction as possible. We have

integrated the artwork and photographs with the text to enliven and clarify the discussion, and we have avoided using sidebars and other features that can distract students from an intensive study of core principles.

Focus on Analysis: Examples and Problems

Nine out of ten instructors state that analyzing and solving problems is the greatest challenge for students in a genetics course. Students *learn* genetics by *doing* genetic analysis, and for this reason every genetics textbook provides students with questions and problems to help them practice genetic analysis. Most also provide worked examples at the end of each chapter to show students step by step how to interpret and analyze data. In many of these texts, the worked examples and end-of-chapter problems use fabricated data that are easy to analyze mathematically.

Our approach to teaching genetic analysis departs from this standard method. We require students to work as much as possible with real data from published research, which are not as mathematically simple as fabricated data. With such an approach, students, like professional researchers, must wrestle with ambiguities, sampling error, alternative interpretations of data, and tentative conclusions. Although this approach may challenge students, it also prepares them to understand genetics in the real world.

In addition, our worked examples are woven into the text so that genetic concepts and analysis are presented in a unified way. We have carefully chosen the worked examples from published data that clearly illustrate each major concept.

The end-of-chapter problems range from easy conceptual exercises to analyses that require students to synthesize information from various parts of the chapter. Like the worked examples, many of the end-of-chapter problems are based on published data.

Our website (http://www.brookscole.com/biology) and *InfoTrac* provide online resources that supplement the book's focus on analysis. Our website contains additional questions and problems that we regularly update to include recent research. Many of the questions and problems at the website ask students to consult published research that is available in *InfoTrac College Edition*, an online resource with recent original articles from leading journals such as *Science*, *Annual Review of Genetics*, *Annual Review of Microbiology*, and *Evolution*.

Study Aids

Each chapter begins with a set of key concepts that give students an overview of what they are about to study. Following each major topic in the chapter is a boldfaced concept review, which reinforces the key ideas of that topic. We highlight key terms in boldface and define the most important key terms in a glossary at the end of the book. Each chapter concludes with a summary of the major principles discussed in the chapter.

Design and Layout

The design and layout of our book are also intended to capture interest and facilitate learning. The illustrations and text are placed to complement one another visually and to help students avoid turning pages as they compare the illustrations with the text. The judicious use of colors in the text and illustrations help students focus on concepts and organize their thoughts as they study.

Suggested Readings

Each chapter ends with an annotated list of suggested readings. Rather than simply list a long set of references, we have chosen readings that will guide students to excellent sources of further information. Some of the readings are review articles that provide more detailed information than that found in our book. Others are important original research that helped scientists develop the concepts discussed in the chapter. In some cases, we refer students to books or collections of articles. Besides the suggested readings at the end of the chapter, we provide references for all data in the worked examples and end-of-chapter problems so that students can consult the original sources to enhance their study. We also give full references for reprinted illustrations and photographs in the figure captions, rather than at the end of the book, so that students can easily consult these sources as well.

Technology-Based Resources and Supplements

A host of valuable resources accompany this book. The website for this book is available free to students and provides online study aids, reviews of current articles, specific information about each chapter in the text, supplemental questions and problems, career tips, and links to genetics-related sites. **InfoTrac College Edition** delivers online access to full-length articles from more than 700 periodicals. Students can log on to this online library with their personal ID and perform searches, read assigned articles, use articles as a resource to analyze assigned problems from the website, and print articles for their personal use. The Brooks/Cole **BioLink** is a lecture presentation tool and image bank that allows instructors to assemble images and related text (captions and titles) for electronic presentation in lectures and to post lecture notes and URLs to a course website. BioLink includes over 2000 images, animations, and Quicktime® movies, including more than 100 images from this book. **Genetics Updates**, an online genetics newsletter, features concise essays on current topics and issues in the field of genetics with links to related sites. The **Instructor's Resource**

Manual contains sample syllabi, chapter outlines, lists of main concepts, solutions to all questions and problems from the book, teaching hints, hints on how to use media and web materials, and a conversion guide to illustrate how to move from a Mendel-first approach to a molecular-first approach using *Genetics: The Continuity of Life*. The **Student Companion to Genetics: The Continuity of Life** contains detailed solutions to all end-of-chapter questions and problems. ***Current Perspectives in Genetics***, by Shelly Cummings, features some 50 selected articles in molecular, transmission, population, and human genetics as a complement to genetics courses. **Transparencies** with over 100 color reproductions of art from the book are available to instructors. ***Genetics on the Web***, by Daniel J. Kurland, gives students exercises to become proficient with the Internet as they study genetics; this book includes a list of URL sites and online materials for each topic in genetics.

ACKNOWLEDGMENTS

The writing, assembly, publication, and distribution of this textbook has been a major cooperative effort on the part of many dedicated professionals who have worked together for the past 6 years. The idea for this book began in 1992 when Cecie Starr and Daniel Fairbanks had a delightful telephone conversation about biology. Cecie suggested that her publisher, Jack Carey, approach Daniel about the possibility of writing a genetics textbook. Daniel and Jack agreed that the time had come to develop an excellent genetics textbook with a molecular-first approach. Ralph Andersen soon joined on as coauthor. Daniel wrote most of the text while Ralph did most of the background library research and prepared many of the worked examples and end-of-chapter problems. Ralph also managed the day-to-day activities of our joint laboratory, allowing us to continue to conduct and publish our research during the time we were working on the textbook.

Numerous reviewers from universities and colleges throughout the country generously provided comments and criticisms at each stage of manuscript development. Their comments have proved invaluable in helping us decide how to organize the book and what to emphasize, and in ensuring accuracy. We are grateful to the reviewers for pointing out errors in the manuscript, but accept full responsibility ourselves for any errors that remain. The names of the reviewers are listed on the following page. We also thank our student assistants at BYU—Michelle Aliff, Carol Gregory, Gordon Harkness, Amy Allgaier, Adam Scrumm, Matthew Tonioli, Paula Randall, Angela Hawkes, Michelle Blauer, and Jeremy Beard—for their contributions in assisting us with the research and clerical work for this book.

The experienced team of professionals at Brooks/Cole and Wadsworth Publishing companies have generously shared their diverse skills to make this book possible. Publishers Jack Carey and Gary Carlson have worked tirelessly to coordinate all aspects of the text and ancillary development. Kristin Milotich, Kerri Abdinoor, Marie Carigma-Sambilay, and Larisa Lieberman have managed the many details associated with the development of the book and its ancillaries. Elmarie Hutchinson, with her skilled developmental editing, taught us how to write clearly and how to reach students with the interweaving of text, examples, and illustrations. Mary Arbogast oversaw the editing and assembly of the final manuscript. She spent many hours on the telephone helping us through the unfamiliar process of the final stages of text development. John Walker supervised a group of professionals who developed the captivating design of the book and its cover. The marketing team of Halee Dinsey, Marlene Veach, and Rita Frumkin enthusiastically developed the most detailed and informative marketing brochure ever produced for a genetics textbook.

Jonathan Peck of Dovetail Publishing Services brilliantly orchestrated the efforts of artists, copyeditor, compositor, proofreader, and photo researcher. He put countless hours into the production of this book and, in the process, became a true friend. Brian Jones is a remarkable copyeditor who meticulously scrutinized every sentence and every mathematical exercise. His queries demonstrated to us that his fascination with genetics, and his devotion to improving the quality of our book, went well beyond his duties as a copyeditor. Our special thanks go to the artists of Precision Graphics, and to Marcus Alan Vincent whose artwork makes this book so understandable and visually appealing. We also thank the many authors, artists, photographers, and publishers who so generously gave permission to adapt their drawings and reprint their photographs. We especially thank Cecie Starr and Stephen Wolfe for allowing us to adapt many drawings from their books. Our photo researcher, Stuart Kenter, acquired many photographs to highlight the chapter opening pages and to illustrate concepts throughout the book. We are grateful to Stephanie Gintowt, Cindy Marschat, and their collegues at New England Typographic Services for their skillful typesetting and layout.

We ultimately owe our ability to write this book to those who taught us genetics, and we express our heartfelt gratitude to them for shaping our careers. Their devotion to teaching is reflected in the content of this book. We also thank the thousands of students who completed our genetics courses and collectively taught us how to teach genetics. Finally, we cannot find appropriate words to express our love and appreciation to our families, who supported us so completely in the long and demanding process of writing a textbook.

September 1998

Daniel J. Fairbanks
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