

PREFACE

Recent advances that allow scientists to quickly and accurately sequence a genome have revolutionized our view of the structure and function of genes as well as our understanding of evolution. A new era of genetics is under way—one that allows us to fully embrace Dobzhansky's famous statement that "Nothing in biology makes sense except in the light of evolution." *Genetics: Genes, Genomes, and Evolution* reflects the excitement of this new era, presenting the fundamental principles of genetics and molecular biology from an evolutionary perspective informed by genome analysis.

By using what has been learned from the analyses of bacterial and eukaryotic genomes as the basis of our book, we are able to unite evolution, genomics, and genetics in one narrative approach. Genome analysis is inherently both molecular and evolutionary, and we approach every chapter from this unified perspective. Thus, rather than relying on separate chapters on genome analysis or evolutionary principles and expecting the student to synthesize them with the principles of classical genetics, we include these as part of each topic. Similarly, the study of genomes has provided a deeper appreciation of the profound relationships between all organisms; we reflect this in our decision not to separate bacterial from eukaryotic evolution, genetics, and genomics. There are chapters in which bacterial genetics, molecular genetics, or evolutionary principles are more prominent, but all chapters include and integrate these concepts.

Audience and approach

This book is written to be an introductory genetics text that emphasizes the connections within and between topics. For several years, we have used drafts of this book in the first semester of our introductory genetics and molecular biology course—a second-year class—at Haverford College, a small US liberal arts institution; the book includes the topics that we are typically able to cover in one semester. The students in this class have usually taken college-level chemistry classes but are just beginning the biology curriculum.

The four of us have co-taught this course numerous times. The resulting synergy has energized our efforts and allowed us to combine our broad, but overlapping, areas of expertise to deliver a student-focused, coherent approach to teaching modern genetics. We have found that students who have completed our introductory genetics class have a highly integrated view of biology and a strong conceptual framework that allows them and us to fill in more detailed information in later upper-level courses. We feel that this integrated approach provides them with a uniquely flexible and contemporary view of genetics, genomics, and evolution.

Instructors and students can choose from numerous introductory genetics or molecular biology books, many of which attempt to cover all aspects of genetics and molecular biology. So what makes ours different? We have tried to maintain an accessible narrative voice and provide analogies and references that engage students; in addition, we have attempted to include the amount of detail appropriate for students at this level and that can be covered in a single term. We have integrated the topics across many fields of biology, including both eukaryotes and bacteria, drawing parallels and comparisons between them. Perhaps most importantly, however, our text uses genomes and the information

gained from genome analysis as its foundation, providing a truly contemporary approach to understanding genetics and evolution.

The book does not assume any particular scientific background in biology or other sciences, but most students will likely have a broad background either from a prior college biology or chemistry course or from advanced courses in high school.

Organization

The core of the book covers the topics found in most introductory genetics courses, with a strong molecular biology component needed to understand genome structure and function. These topics are introduced and developed after a discussion of evolutionary history as recorded in the genome, and evolutionary perspectives are emphasized throughout. Thus, you will find chapters that cover traditional topics in introductory genetics such as Mendelian genetics, single and two-factor crosses, X-linkage, pedigree analysis, mapping, meiosis, and linkage, but this coverage has been integrated with information about genomes from a wide range of organisms and viewed through the lens of evolution.

A chapter-by-chapter guide

We begin the Prologue of this book with the Five Great Ideas of Biology, as outlined by Sir Paul Nurse. We use these ideas throughout the text to interconnect concepts about the chemistry of biological molecules, the idea of a gene, cells as basic building blocks of life, the organization of living systems, and natural selection and evolution. As such, these ideas provide a framework for the information presented in the text. We have found that many students are adept at acquiring biological information on specific topics but are challenged when asked to make connections between concepts and topics. However, once these integration skills have been emphasized and developed, the depth of understanding increases dramatically. We therefore model this approach explicitly throughout the text.

In **Chapter 1**, we introduce a recent study of the genomes of Darwin's finches that identified genes that contribute to the differences in beak shape among these species. In this way, we link one of the most important and familiar examples of natural selection among Darwin's finches with the underlying genetic and genomic basis for the differences observed among these birds. Using this example in our opening chapter prepares students to think across scales, from DNA to molecules to phenotypes to species and then to evolution in a community of organisms. This perspective has only become possible because of our ability to sequence and compare genomes.

We then move on to describe in **Chapter 2** the structure of DNA and the Central Dogma, highlighting features of the DNA molecule that have an impact on its function. We point out modifications to the traditional view of the Central Dogma and introduce students to the basic structure of a gene. **Chapter 3** covers the structure of the genome and the variation in genome organization found in different species, which are both the outcome of, and the ingredients for, natural selection. This chapter discusses the structure of chromosomes, extrachromosomal DNA, and changes in the genome, and is one of the most important for integrating genomic findings with evolutionary and genetic principles.

In **Chapter 4**, we discuss DNA replication and repair, tying these topics to Darwin's concept of "descent with modification," a fundamental principle of natural selection and evolution. Several challenges to DNA replication that arise from its length and anti-parallel

structure are presented, along with the processes that have evolved to address these challenges. We introduce the many types of mutation that occur and how the occurrence of such mutations and the effects of selection can be revealed by comparing the genomes of different organisms. These comparisons provide us with the ability to reconstruct evolutionary history and develop phylogenetic trees based on DNA sequence changes.

The next section of the text, comprising **Chapters 5 to 9**, discusses Mendelian genetics, meiosis, the inheritance of two genes, sex-linked traits, and linkage and mapping. These chapters present all the material found in a traditional genetics course, framed in the context of genomics and evolution. For example, the relationship of the process of meiosis to Mendel's Laws of Segregation and independent assortment is explored in a progressive approach that encourages students to think between topics and across scales.

We then bring these fundamental concepts of genetics and genomes together in **Chapter 10** on complex traits and genome-wide association studies, which focuses primarily on human traits and diseases. We explore how these studies build upon the basic principles outlined in earlier chapters, to identify contributing genes and causative mutations. While chapters on complex traits are found in many books, an approach that shows how genome-wide associations integrate genomic variation, complex phenotypes, and evolutionary history is novel.

Chapter 11 introduces the process of horizontal gene transfer, originally found among bacteria, but now known to occur in other types of organisms too. **Chapters 12 and 13** focus on the essential processes of transcription and translation that link genotype to phenotype.

In **Chapter 14**, operons in bacteria are introduced as an example of gene regulatory networks and are followed by a discussion of transcriptional regulatory networks in eukaryotic organisms, using recent information from many genome annotation projects such as ENCODE. The tools of genetic analysis are covered in **Chapter 15**, beginning with Beadle and Tatum's experiments in *Neurospora* and Jacob and Monod's work with *lac* mutants, and moving into a discussion of more recent genetic screens for the identification of genes essential to embryonic development in *Drosophila*.

The final section of the text moves beyond individuals to populations and communities of organisms. Population genetics with a human focus is the subject of **Chapter 16** where we explore the assumptions of the Hardy-Weinberg equilibrium model. We review the many different types of evolutionary change that can operate, in addition to natural selection, to shape the genetic structure of a population and the imprints these leave at the level of the genome. Long-term studies of bacterial populations are featured as a method to explore evolution experimentally. **Chapter 17** concludes the text by introducing the relatively new field of metagenomics, in which genomic information is extracted directly from communities of organisms living in their natural environments, revealing evidence for their interdependence and co-evolution.

Pedagogical features

We have used many pedagogical features in the text to improve the accessibility for students and allow instructors to tailor each chapter for their own courses. Each chapter begins with an introductory paragraph—**IN A NUTSHELL**—which provides a brief preview of the upcoming chapter content, while **KEY POINTS** highlighting important concepts are found throughout the text. A summary paragraph concludes each chapter, followed by a **CHAPTER CAPSULE**, which presents a bulleted list of the important ideas we have discussed.

Boxes that expand on specific topics are found in every chapter and are grouped into several categories. **COMMUNICATING GENETICS** boxes present the terminology, notation, and diagrammatic conventions used to communicate genetics concepts. **TOOL BOXES** illustrate how the biological processes described in the chapter form the bases for essential experimental techniques. Other boxes feature *A Human Angle*, *An Historical Perspective*, or *Quantitative Toolkits* to a topic presented in the chapter, each giving a different flavor to the study of genetics. The *Going Deeper* boxes provide more advanced content about a process or system than is included in the main text of each chapter to allow instructors to include more details without losing the connections between the topics. We regard all of these boxes as an essential feature of the book, allowing each instructor to adjust the content for the particular audience and emphasis in different classes.

Every chapter also includes **study questions and problems**, for which all of the solutions are provided online. One goal of these questions is to have students work through examples that integrate more than one concept introduced in the chapter or from more than one chapter. We use realistic examples in the problems; since few experimental problems map neatly onto the concepts from only one chapter, we ask the students to do a similar integration of ideas with the result that they will gain a more unified view of the subject. For example, our chapter on meiosis has questions that draw on natural variation, Mendelian principles, and sex determination and sex linkage—concepts that were introduced in previous chapters or that will be covered in the next chapter. In addition, problems on the comparative genomics of Darwin's finches are contained in several chapters of the book to emphasize the connections to what has been covered before.

Supplements

Accompanying online resources include the solutions for all of the study problems, instructional videos for each chapter, and Journal Clubs that lead the class through a structured discussion of a publication from the scientific literature.

The **videos** have one of us walking students through the solution of a problem from the text, highlighting a research technique or providing additional analysis of an original research figure in a 5-minute summary.

The **Journal Clubs** offer the possibility of an active learning environment that reverses the typical pedagogical process in most large introductory courses. Class time could be spent discussing the Journal Club, reinforcing students' understanding of the chapter by exploring a more detailed example from the original literature, for instance.

We describe the learning features and supplements package in more detail in our guide to Teaching and Learning with *Genetics* on p. xviii.

Acknowledgements

We would like to sincerely acknowledge all the helpful feedback we have received from our students in the years since we first began purposefully reconfiguring our introductory genetics class to integrate genomics and evolution more fully. The assistance of the students in the class, the teaching assistants, and the peer tutors has been indispensable. They have encouraged us to improve and clarify our explanations, and have provided input on figures, study questions, and solutions. The students' responses have shaped every part of this book, and we regard them as contributors.

We would also like to thank our colleagues in the Biology Department at Haverford College for their suggestions and their patience as the four of us worked to make this idea a reality. Others at Haverford College have provided assistance as well, including those who provided technical support in creating videos and helped with the administrative tasks associated with this project.

We would like to thank our editor, Jonathan Crowe, for his insightful suggestions, his patience, and his unflagging support of this endeavor.

Finally, we want to acknowledge the steadfast support of our friends and families during the development of this text.

Haverford, PA

March 2017