

PREFACE

The goal of this book is to illustrate how classical genetics and molecular biology provide important insights for understanding genomics and bioinformatics. In an era when every day brings another sequenced genome, it is reasonable to ask how the wealth of genomic information can be captured in a book. My approach is to acknowledge that the information itself might rapidly become outdated. However, this is also an age when we carry hand-held devices that allow us to search the World Wide Web while waiting in the grocery line. Up-to-date information is readily available and we don't rely on a book to provide it. So if you are planning to use this book as a reference to look up the most recent information on a gene or a biological process, my advice is to search the Web instead. It will be easier to browse for information and the data could be more current.

On the other hand, if your interest is in thinking about what the genomic data tells us, this book might be able to help. The emphasis in this book is on the experimental strategies and intellectual foundations that allow us to interpret genetic information and to plan approaches for the next experimental questions. I view genomics and bioinformatics through the lenses of classical genetics and molecular biology. I have consciously tried to integrate what we are learning from studying genomics with what has also been learned from genetics and molecular biology while studying individual genes. Each of these approaches has a starting point that acts as the key experimental tool in probing new questions: classical genetics has mutant alleles, molecular biology depends on cloned genes, and genomics relies on genome sequence information. But these tools aren't mutually exclusive in terms of the questions they can answer: the same biological questions can be probed from different experimental starting points. In fact, when taken together, classical genetics, molecular biology, and genomics all help to provide a more *complete* answer than any of them would provide alone. It is not accurate to think of these as separate approaches using different tools but rather as different parts of the same approach, namely **genetic analysis**. Thus, this book is not so much about *what* we have learned—that will continue to change—but rather about *how* we have learned it. In other words, the book is about analysis, strategy, and experimental logic.

Course suitability

I have taught a course on advanced genetic analysis for more than a decade to undergraduate students (juniors and seniors) at Haverford College. These students have taken introductory genetics and have a general familiarity with biochemistry and with molecular and cellular biology; the book is written with that level of student preparation in mind. The topics included in this course change every year, but the approach of describing a few examples in depth has been consistent; this approach has been followed in writing this book. The book includes many more topics than could be included in my course, and yet I am keenly aware of how many

additional topics could be included. I have had to be selective in the topics, the organisms, and even the experimental approaches that I have presented.

I limited the book to genetic analysis in eukaryotes rather than attempting to include bacterial genetics, although many of the experimental strategies used in eukaryotic organisms are derived from similar approaches first developed in bacteria. I focus on five model eukaryotic organisms—the yeast *Saccharomyces cerevisiae*, the nematode worm *Caenorhabditis elegans*, the fruit fly *Drosophila melanogaster*, the flowering plant *Arabidopsis thaliana*, and the mouse *Mus musculus*. No one is likely to question the inclusion of these five organisms. However, some may ask why another model organism has been excluded. I apologize to those whose preferred model organism has been omitted.

For clarity, I have relied on relatively few examples from these organisms and discussed them repeatedly throughout the book. For instance, the *patched* gene in *Drosophila* (and other animals) and genes affecting dauer larva formation in *C. elegans* are discussed in four or more different chapters. Sex determination in flies and worms and hormone signaling in *Arabidopsis* are also discussed in more than one chapter. These particular examples illustrate well the powerful approaches arising from contemporary genetic analysis.

But this is not to suggest that these examples are the most important ones to know, or even necessarily the best ones to illustrate a particular aspect of genetic analysis. Dozens, even hundreds, of other genes and biological processes could have been used as effectively. I hope and expect that those who are teaching with this book will have their own examples. In fact, I welcome hearing about other genes and biological processes that could have been covered instead. Perhaps it would be helpful to describe how these examples are employed in my own class. Although I spend many class periods on *patched*, dauer larva formation, and some of the other examples included in the book, none of my examination questions and none of the student papers requires any specific information about *patched* itself or dauer larva formation. Instead, the students are asked to apply the experimental strategies from these examples to the analysis of other genes and biological questions. I would be pleased to learn that a reader has come away with an appreciation of these biological examples because they illustrate important principles of genetic analysis. But I would be even more pleased to learn that the examples described here served as a springboard for analyzing other genes and biological questions.

Organization of the book

The book is structured as four units. The first unit, *Genes and genomes*, reviews the fundamental findings of genetics and molecular biology from an historical perspective in Chapter 1 and introduces the five model organisms and their genome databases in Chapter 2. No biological question in these model organisms can be investigated or understood without relying on the genome databases, and all readers are encouraged to explore these remarkable resources. These two chapters lay out the principles of genetics and molecular biology that are the foundation for the remaining chapters.

The second unit, *Genes and mutants*, explains the crucial tools of mutant alleles, cloned genes, and genome sequences. Chapter 3 discusses the principles of genetic screens and selections to find mutants that affect a biological process, while Chapter 4 describes how these mutants are mapped, classified into genes, and characterized. Chapter 5 presents an overview of how genes are cloned, i.e. how the mutant phenotypes from Chapters 3 and 4 are connected to a DNA sequence. Chapter 6 reverses the process of Chapters 3, 4, and 5, and describes how a mutant phenotype is found for genes that have been previously cloned. Chapter 7 introduces the concept of genome-wide mutant screens, i.e. the chapter describes how deletion mutations have been created for every gene in yeast and how RNAi has been used to find mutant phenotypes for every gene in other organisms. The important comparison between genetic screens for mutations in Chapter 3 and genome-wide mutant screens in Chapter 7 is made.

The third unit, *Gene activity*, assumes that mutant alleles, cloned genes, and genome sequences are available for further genetic analysis. Chapter 8 discusses molecular approaches to the analysis of gene expression. This includes both the analysis of the expression pattern of individual genes and the analysis of entire genomes using microarrays and expression profiles. Lessons learned from expression studies with individual genes are applied to examining microarray data. Chapter 9 returns to the theme of using mutant alleles to examine gene activity and discusses approaches such as temperature-sensitive periods and mosaic analysis. These are compared with what is learned from molecular analysis of gene expression.

The fourth unit, *Gene interactions*, discusses the identification and analysis of the many genes typically involved in a single biological process. Chapter 10 describes how one gene is used to find other genes with related functions. Both genetic interactions involving suppressor and synthetic enhancer mutations and physical interactions between proteins are included. Chapter 11 provides a detailed description of the use of epistasis and other genetic interactions to create a logical pathway of interacting components. Chapter 12 moves from the linear genetic interaction pathways derived from comparing two genes to the more complex networks and systems of interactions that occur within an organism. This chapter provides an overview of the field known as systems biology or network biology and examines it in light of the more traditional genetic analysis discussed in the preceding chapters.

Pedagogical features

Genetic analysis can be considered from a number of different angles including the experimental techniques adopted, the information yielded from different model organisms, or the biological principles these studies illuminate. This multilayered quality is mirrored by the pedagogical structure of the book.

The first layer is the main **narrative text**, which leads the reader through the field in what I hope will be a progressive and engaging way.

The second layer is the inclusion of **case studies**. Almost every chapter includes a case study (and some include more than one). The case studies describe in more

detail how the genetic approaches discussed in the chapter were employed to study a particular gene or biological question. Many of the case studies are connected to one another or to another chapter. For example, the *patched* gene was found among the segment polarity mutants affecting *Drosophila* embryogenesis, as described in the case studies for Chapters 3 and 4; a description of how the *patched* gene was cloned from *Drosophila* and mammals is found in the case study for Chapter 5 and a gene disruption for *patched* in mice is described in the case study in Chapter 6. The case study in Chapter 8 describes how molecular analysis of gene expression was done in *Drosophila* embryogenesis (although not the *patched* gene itself), and a case study in Chapter 9 focuses on a mosaic analysis of *patched* in the *Drosophila* wing. Finally, genetic and physical interactions among *patched*, *hedgehog*, and *smoothed* are described in Chapter 11. Although the case studies are designed to be read in connection with the chapter itself, they can also be read as separate miniature histories of the genetic analysis of a gene or biological process.

The third and final layer of presentation comes in the form of **text boxes**. Almost all the chapters include text boxes that expand or speculate on a topic in the main text. Some of these text boxes arose directly from questions that students posed in class, and a few lay the groundwork for separate lectures in my advanced genetics or genomics courses. Although the text boxes are not crucial for understanding the main threads of the chapter, my opinion is that the topics in the text boxes are often as interesting as the topics in the main chapter.

Other learning features

The book includes a number of other learning features, to make it as reader-friendly as possible.

Frequent cross-references provide links to other sections and chapters.

Key literature articles are highlighted immediately after the section of text to which they relate.

Potentially unfamiliar terms are highlighted and defined in the margin of the page on which they appear.

A glossary is included at the end of the book, listing key terms used in the study of genetic analysis that may not be familiar from earlier courses.

One of the main goals of my teaching is to rouse students' imaginations to think creatively about new biological questions, including ones that I have not thought about. A similar goal lies behind this book. It is important to know the right answers, but it is even more important to be able to ask the right questions and know why an answer is right. I hope that this book will provide some stimulus to ask new questions. I believe that I sometimes learn as much from my students as they learn from me (which may be a commentary on my teaching ability). With that same philosophy of learning from each other, I encourage you to contact me with additional examples, ideas for new topics, corrections and updates, and other comments.

Philip Meneely
April 2008



Online resource centre

www.oxfordtextbooks.co.uk/orc/meneely

OXFORD UNIVERSITY PRESS ONLINE RESOURCE CENTRE

Home | About OUP | How to order | Help | You are not logged in | [LOG OUT](#)

Search this site [Go]

Home » Biosciences » Molecular Biology » Biosciences » Genetics » Meneely: Advanced Genetic Analysis

Meneely: Advanced Genetic Analysis

Select resources by type

Student resources

Topical updates Key updates on topics or tools presented in the book to keep you up-to-date with latest developments in the field

Guided tours of key websites With associated tutorials/activities

Lecturer resources

The following resources are password-protected and for adopting lecturers' use only.

Not yet registered for a password? Please complete the two steps below:

1. Inform your local sales representative that you are adopting this textbook. You may wish to do this via the [first point of contact](#) page.
2. Complete the [registration form](#). Please note your registration can only be processed if your sales representative is aware of your adoption.

Already registered for a password? Click on any resource below to log in.

Additional case studies Access additional cases studies for use in your teaching

Figures from the book Electronic versions of the figures from the book available to download

Journal club Suggested papers and discussion questions linked to topics covered in the book

About the book

[Learn more about the book](#)

[Buy the book](#)

[Lecturers order on](#)

[Penguin.com](#)

[Send us your feedback](#)

Sample Content

[Chapter 1: Genotyping methods](#)

Get Adobe PDF reader

(MS/IE)

Keep me updated about this site

Our email service will alert you

This book has been written with web usage in mind, so the reader is urged to consult the website associated with the book (www.oxfordtextbooks.co.uk/orc/meneely) for updates and additional resources as they are developed. Key resources on this site include the following

For registered adopters of the book:

- Figures from the book in electronic format, ready to download.
- Journal club: suggested papers and discussion questions linked to topics covered in the book.

Additional case studies for use in teaching.

For students:

- Guided tours of key websites, with associated tutorials/activities.
- Topical updates: key updates on topics or tools presented in the book to keep you up to date with the latest developments in the field.

Bookmark the site, or register for updates by visiting www.oxfordtextbooks.co.uk/orc/meneely and clicking on the 'Keep me updated about this site' link.