

Preface

The first two editions of *Molecular Biology*, written by David Freifelder, were published in 1983 and 1987. As stated in the preface to the second edition, Freifelder considered the book to be a multipurpose textbook “emphasizing basic molecular processes (such as the synthesis of DNA, RNA, and protein) and genetic phenomena in both prokaryotic and eukaryotic cells.” This third edition retains these goals, a fact emphasized by the revised title, *Molecular Biology: Genes to Proteins*. The book is intended for undergraduate and first year graduate students, who have completed full year courses in college biology, general chemistry and organic chemistry. Since the second edition of this book, the human genome sequence was determined. Structures for many enzymes and macromolecular machines that participate in DNA replication, RNA synthesis, and protein synthesis have been solved. New pathways such as the RNA interference pathway have been elucidated. These and many other important advances in the field of molecular biology necessitated a complete revision of the book. Significant changes in the way that we teach college science courses also contributed to the need for a complete revision. In 1987, instructors usually used standard slides to show how a nucleic acid, protein, or macromolecular complex looks and works. Today we view these structures in three-dimensions and manipulate them on our computer screens. Furthermore, the Internet now serves as an incredibly rich source of molecular biology information and data. Finally, molecular biology is now such an integral part of introductory biology, genetics, microbiology, cell biology, developmental biology, evolutionary biology and biochemistry courses that all students have encountered various aspects of molecular biology before they actually enroll in a molecular biology course.

Whenever possible the book uses a discovery approach so students learn about the experimental evidence relevant to the concepts discussed. This pedagogical approach provides historical and experimental background information, permitting students to see how molecular biologists examine clues and develop the hypotheses that ultimately lead to new advances in molecular biology. When teaching molecular biology, I find this approach helps students become part of the discovery process. In this way they begin to understand the pleasure and sense of satisfaction investigators derive from solving a molecular biology problem. Of course, space does not allow every concept to be presented in this way. Therefore, when faced with a choice of simply presenting a concept or omitting it, I opted to present the concept. This book differs from the previous two editions in introducing the scientists into the discovery process. I chose to do this, not because it is important for the students to memorize the scientist’s name, but rather because it is important for students to appreciate the human effort involved in the discovery process and to recognize that molecular biology is an evolving field. Thus, as additional experiments are performed we continue to obtain new information. Many of the students who enroll in a molecular biology course are interested in the medical sciences. In recognizing this interest, a major effort has been made to include interesting and important medical applications when they are relevant.

Chapter Organization

After an introduction to the field of molecular biology the book is divided into six sections: (1) protein structure and function, (2) nucleic acids and nucleoproteins, (3) genetics and virology, (4) DNA metabolism, (5) RNA synthesis and processing, and (6) protein synthesis. The material presented in the first two sections provides the basic information required to understand the chemical basis of molecular biology, while that provided in the third section provides information required to understand the biological basis of molecular biology. The order of the remaining chapters reflects the fact that genetic information in cells normally flows from DNA to RNA to protein. A major challenge in presenting new information in molecular biology, and indeed in most science courses, is that information presented in a later chapter is sometimes necessary to fully understand information in earlier chapters. This edition has tried to minimize this problem by introducing basic concepts and techniques that are required to understand molecular biology in the first three sections.

The book follows Freifelder's philosophy that "molecular biology must emphasize both molecules and biology, and that to be molecular, it must also be chemical and physical." With this philosophy in mind, the chapters' contents are as follows. **CHAPTER 1** provides a brief historical introduction to the field of molecular biology including the discovery of the double helix model, which provides a very clear example of structure-function relationships, a major theme in molecular biology and one that is emphasized throughout this book. **CHAPTER 2** introduces important information about the primary, secondary, tertiary, and quaternary structures of proteins and describes the structure of proteins and lipids in biological membranes. **CHAPTER 3** describes structure-function relationships in proteins. The chapter begins with an examination of specific proteins included specifically because they provide important insights into structure-function relationships encountered throughout the text. The second part of this chapter describes enzymes and enzyme kinetics, topics that are central to understanding the processes of DNA replication, repair, and recombination; RNA synthesis and processing; and protein synthesis. The third section of this chapter briefly describes the G-protein signal system. **CHAPTER 4** builds on the information provided in Chapter 1 about DNA structure, emphasizing conformational variations, helical stability, strand separation, helical reformation, circular DNA, and topoisomers. **CHAPTER 5** includes an examination of the physical techniques that are used to isolate and characterize nucleic acids and a discussion of techniques that use enzymes to manipulate DNA in the laboratory. **CHAPTER 6** describes the interactions between specific proteins and DNA to form nucleoprotein complexes. **CHAPTER 7** introduces concepts in genetic analysis that are essential for working in molecular biology, including a brief introduction to genetic recombination and descriptions of basic techniques used by molecular biologists to locate genes in bacteria, yeast, and higher organisms. **CHAPTER 8** provides some of the fundamental information that molecular biologists need to know about viruses. The information presented will help to place viral systems that are discussed in subsequent chapters in perspective. Some students and instructors may decide to skip this chapter but then refer back to appropriate sections when specific viruses are mentioned in subsequent chapters. **CHAPTER 9** presents both the general features of DNA replication and a detailed examination of the initiation, elongation, and termination stages of bacterial DNA replication. It also examines these stages in eukaryotes and the archaea. **CHAPTER 10** focuses on the different types of DNA damage that take place in cells and then explores the mechanisms that cells use to reverse DNA damage, excise and replace damaged elements, or tolerate the damage. **CHAPTER 11** explores homologous recombination models, based on

genetic and biochemical data. Individual steps of homologous recombination and the enzymes that carry out these reactions are described. **CHAPTER 12** examines transposons and other mobile elements with particular emphasis on the three types of reactions that can explain the movement of all mobile genetic elements. Some instructors may wish to assign the material covered in Chapter 11, Chapter 12, or both after completing Chapter 20. Chapters 11 and 12 are written in a way that makes this possible. **CHAPTER 13** examines bacterial RNA polymerase and its function in RNA synthesis. **CHAPTER 14** examines the mechanisms that bacteria use to regulate the synthesis of the different classes of RNA starting with the regulation of bacterial mRNA synthesis. **CHAPTER 15** examines the eukaryotic RNA polymerase II (the enzyme responsible for mRNA formation) and the general transcription factors that it requires for basal transcription. The chapter also describes how RNA polymerase II and the general transcription factors combine to form the basal transcription machinery. **CHAPTER 16** describes two types of transcriptional factors, transcription activators and Mediators, that interact with the basal transcription machinery to form the much more efficient transcription machine that is in fact responsible for eukaryotic mRNA synthesis. **CHAPTER 17** explores the various stages in cotranscriptional processing. It also describes RNA editing, messenger RNA export, and pathways for silencing messenger RNA. **CHAPTER 18** examines the role of RNA polymerase I and its accessory factors in synthesizing eukaryotic ribosomal RNA. It also describes the role of RNA polymerase III, and its accessory factors in synthesizing transfer RNA and other small RNA molecules, most notably the small nuclear RNA molecules (snRNAs) and the RNA polymerases present in mitochondria and chloroplasts. **CHAPTER 19** describes the structure and function of transfer RNA molecules and then examines how these molecules act along with mRNA and ribosomes to specify the amino acid sequences in proteins. **CHAPTER 20** examines ribosome structure and function so that students can learn how ribosomes are able to act as universal translators.

Supplements to the Text

Jones and Bartlett offers an array of ancillaries to assist instructors and students in teaching and mastering the concepts in this text. Additional information and review copies of any of the following items are available through your Jones and Bartlett sales representative, or by going to <http://www.jbpub.com/biology/>.

For the Student

Developed exclusively for the third edition of *Molecular Biology: Genes to Proteins*, the companion Web site offers a variety of resources to enhance understanding of molecular biology. The site contains a free on-line study guide with chapter outlines, quizzes to test comprehension and retention, and an interactive glossary. This Web site will also have links to relevant material such as animations, structural programs, and tutorials that are available on the Internet. This information will be organized in the same way as the chapters of this book. The URL for the Web site is <http://biology.jbpub.com/molecular>.

Laboratory Investigations in Molecular Biology presents well-tested protocols in molecular biology. The experiments are designed to guide students through realistic research projects and to provide students with instruction in methods and approaches that can be immediately translated into research projects conducted in modern research laboratories.

For the Instructor

Compatible with Windows and Macintosh platforms, the Instructor's ToolKit CD-ROM,

authored by Cheryl Ingram-Smith of Clemson University, provides instructors with the following traditional ancillaries:

- The **Instructor's Manual**, provided as a text file, includes chapter overviews, complete lecture outlines, and key terms from each chapter.
- The **PowerPoint® Image Bank** provides the illustrations, photographs, and tables (to which Jones and Bartlett holds the copyright or has permission to reproduce digitally) inserted into PowerPoint slides. You can quickly and easily copy individual images or tables into you existing lecture slides.
- The **PowerPoint Lecture Outline Slides** presentation package provides lecture notes and images for each chapter of *Molecular Biology: Genes to Proteins*. Instructors with the Microsoft PowerPoint software can customize the outlines, art, and order of presentation.

A Test Bank will be available to instructors through the Jones and Bartlett website. Visit www.jbpub.com/biology for more details.

A Note from the Author

I would like to tell a brief story that indicates just how far molecular biology has advanced in the past four decades. When I started out as a graduate student in the early 1960s we were all very excited about the rapid advances that were being made in molecular biology, especially the discovery of the genetic code. We viewed molecular biology as a discipline that soared above the other scientific disciplines that our classmates were studying. However, several of us were brought back down to earth one day when a young medical doctor, who was working as a postdoctoral fellow, challenged us to provide a single example of how molecular biology had actually benefited anybody in a clinical setting. After much consideration, we were only able to come up with one example. Molecular biology explained the cause of sickle cell anemia. However, the young doctor correctly pointed out that this knowledge did not really provide any benefit to individuals suffering from sickle cell anemia. As I wrote this book I thought about that challenge so many years ago. Molecular biology remains an exciting and rapidly developing discipline, but it also is a discipline that has a direct impact on our lives in so many different ways. There are so many examples of how molecular biology has contributed to our medical well being that it would take several books to describe them all. Therefore, a few examples will have to suffice. Techniques developed by molecular biologists help to detect bacterial and viral infections, produce new drugs and hormones, study the effectiveness of a chemotherapeutic agent used to treat a malignant disease, determine whether an individual has an inborn error of metabolism, and design drugs to treat diseases such as AIDS. Although initial attempts to cure inborn errors of metabolism by genetic engineering have been unsuccessful, and indeed some have proved dangerous to the subject, it seems likely that the next generation of molecular biologists will solve this problem as well as a host of other health-related problems.