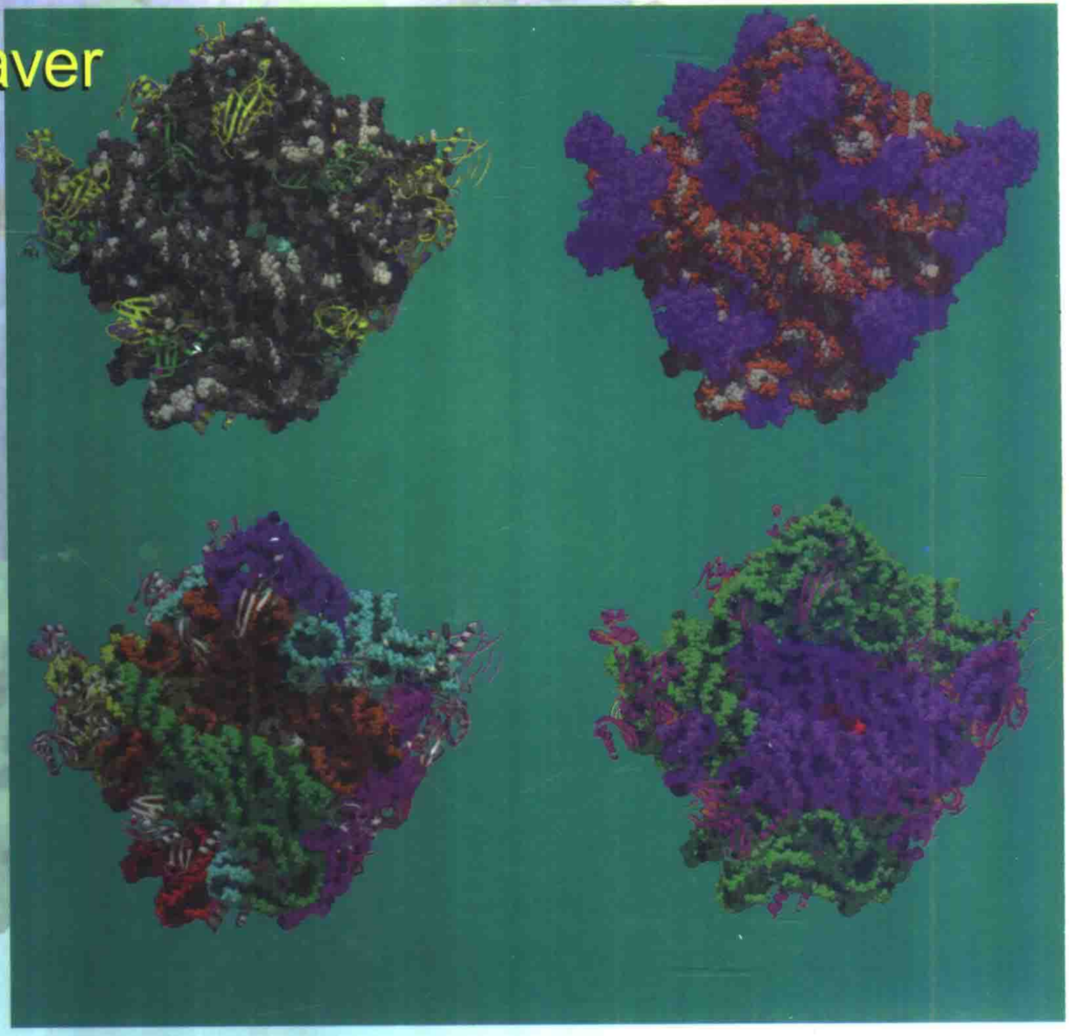
中国科学院研究生教学丛书

分子生物学（第二版）

MOLECULAR BIOLOGY

Robert F. Weaver



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MOLECULAR BIOLOGY

（第二版）

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内容简介

本书属于中国科学院推荐的研究生用原版教材。作者为美国著名分子生物学家 Robert F. Weaver。全书详尽地从分子水平上阐述了基因及其活动，包括了转录、翻译、DNA 复制、重组和转座等。在这次的新版中又新增了基因组学等重要内容。本书的特色在于理论与实验技术相结合，并有大量的背景资料，使读者能够扩大进一步阅读的范围。该书文字清晰、简练、准确，非常有利于读者直接掌握最新的专业知识和提高外语能力。

本书可供生命科学相关专业的研究生、科研和教学人员参考。

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《中国科学院研究生教学丛书》序

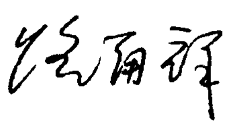
在21世纪曙光初露，中国科技、教育面临重大改革和蓬勃发展之际，《中国科学院研究生教学丛书》——这套琵聚了中国科学院新老科学家、研究生导师们多年心血的研究生教材面世了。相信这套丛书的出版，会在一定程度上缓解研究生教材不足的困难，对提高研究生教育质量起着积极的推动作用。

21世纪将是科学技术日新月异，迅猛发展的新世纪，科学技术将成为经济发展的最重要的资源和不竭的动力，成为经济和社会发展的首要推动力量。世界各国之间综合国力的竞争，实质上是科技实力的竞争。而一个国家科技实力的决定因素是它所拥有的科技人才的数量和质量。我国要想在21世纪顺利地实施“科教兴国”和“可持续发展”战略，实现邓小平同志规划的第三步战略目标——把我国建设成中等发达国家，关键在于培养造就一支数量宏大、素质优良、结构合理、有能力参与国际竞争与合作的科技大军。这是摆在我国高等教育面前的一项十分繁重而光荣的战略任务。

中国科学院作为我国自然科学与高新技术的综合研究与发展中心，在建院之初就明确了出成果出人才并举的办院宗旨，长期坚持走科研与教育相结合的道路，发挥了高级科技专家多、科研条件好、科研水平高的优势，结合科研工作，积极培养研究生；在出成果的同时，为国家培养了数以万计的研究生。当前，中国科学院正在按照江泽民同志关于中国科学院要努力建设好“三个基地”的指示，在建设具有国际先进水平的科学研究基地和促进高新技术产业发展基地的同时，加强研究生教育，努力建设好高级人才培养基地，在肩负起发展我国科学技术及促进高新技术产业发展重任的同时，为国家源源不断地培养输送大批高级科技人才。

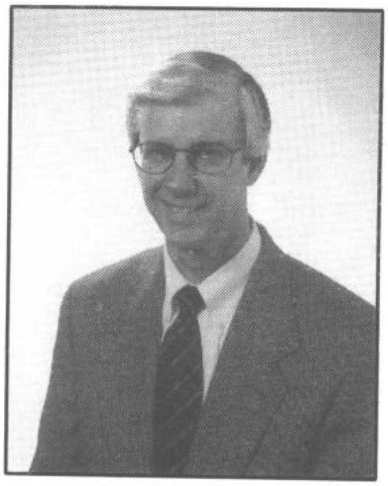
质量是研究生教育的生命，全面提高研究生培养质量是当前我国研究生教育的首要任务。研究生教材建设是提高研究生培养质量的一项重要的基础性工作。由于各种原因，目前我国研究生教材的建设滞后于研究生教育的发展。为了改变这种情况，中国科学院组织了一批在科学前沿工作，同时又具有相当教学经验的科学家撰写研究生教材，并以专项资金资助优秀的研究生教材的出版。希望通过数年努力，出版一套面向21世纪科技发展、体现中国科学院特色的高水平的研究生教学丛书。本丛书内容力求具有科学性、系统性和基础性，同时也兼顾前沿性，使阅读者不仅能获得相关学科的比较系统的科学基础知识，也能被引导进入当代科学研究的前沿。这套研究生教学丛书，不仅适合于在校研究生学习使用，也可以作为高校教师和专业研究人员工作和学习的参考书。

“桃李不言，下自成蹊。”我相信，通过中国科学院一批科学家的辛勤耕耘，《中国科学院研究生教学丛书》将成为我国研究生教育园地的一丛鲜花，也将似润物春雨，滋养莘莘学子的心田，把他们引向科学的殿堂，不仅为科学院，也为全国研究生教育的发展作出重要贡献。



To my parents

ABOUT THE AUTHOR



Rob Weaver was born in Topeka, Kansas, and grew up in Arlington, Virginia. He received his bachelor's degree in chemistry from The College of Wooster in Wooster, Ohio, in 1964. He earned his Ph.D. in boichemistry at Duke University in 1969, then spent two years doing postdoctoral research at the University of California, San Francisco, where he studied the structure of eukayotic RNA polymerases with William J. Rutter.

He joined the faculty of the University of Kansas as an assistant professor of biochemistry in 1971, was promoted to associate professor, and then to full professor in 1981. In 1984, he became chair of the Department of Biochemistry, and served in that capacity until he was named Associate Dean of the College of Liberal Arts and Sciences in 1995.

Prof. Weaver is the divisional dean for the science and mathematic departments within the college, which includes supervising 14 different departments and programs. As a professor of molecular biosciences, he teaches courses in introductory molecular biology and the molecular biology of cancer. He directs a research laboratory in which undergraduates and graduate students participate in research on the molecular biology of a baculovirus that infects caterpillars.

Prof. Weaver is the author of many scientific papers resulting from research funded by the National Institutes of Health, the National Science Foundation, and the American Cancer Society. He has also coauthored two genetics textbooks and has written two articles on molecular biology in the *National Geographic Magazine*. He has spent two years performing research in European Laboratories as an American Cancer Society Research Scholar, one year in Zurich, Switzerland, and one year in Oxford, England.

PREFACE

This textbook is designed for an introductory course in molecular biology. But what is molecular biology? The definition of this elusive term depends on who is doing the defining. In this book, I consider molecular biology to be the study of genes and their activities at the molecular level.

When I was a student in college and graduate school I found that I became most excited about science, and learned best, when the instructor emphasized the experimental strategy and the data that led to the conclusions, rather than just the conclusions themselves. Thus, when I began teaching an introductory molecular biology course in 1972, I adopted that teaching strategy and have used it ever since. I have found that my students react as positively as I did.

One problem with this approach, however, was that no textbook placed as great an emphasis on experimental data as I would have liked. So I tried assigning reading from the literature in lieu of a textbook. Although this method was entirely appropriate for an advanced course, it was a relatively inefficient process and not practical for a first course in molecular biology. To streamline the process, I augmented the literature readings with hand-drawn cartoons of the data I wanted to present. Later, when technology became available, I made transparencies of figures from the journal articles. But I really wanted a textbook that presented the concepts of molecular biology, along with experiments that led to those concepts. I finally decided that the best way to get such a book would be to write it myself. I had already coauthored a successful introductory genetics text in which I took an experimental approach—as much as possible with a book at that level. That gave me the courage to try writing an entire book by myself and to treat the subject as an adventure in discovery.

Organization

The book begins with a four-chapter sequence that should be a review for most students. Chapter 1 is a brief history of genetics. Chapter 2 discusses the structure and chemical properties of DNA. Chapter 3 is an overview of gene expression, and Chapter 4 deals with the nuts and bolts of gene cloning. All these are topics that the great majority of molecular biology students have already learned in an introductory genetics course. Still, students of molecular biology need to have a grasp of these concepts and may need to refresh their understanding of them. I do not deal specifically with these chapters in class; instead, I suggest students consult them if they need more work on these topics. These chapters are written at a more basic level than the rest of the book.

Chapter 5 describes a number of common techniques used by molecular biologists. It would not have been possible to include all the techniques described in this book in one chapter, so I tried to include the most common or, in a few cases, valuable techniques that are not mentioned elsewhere in the book. When I teach this course, I do not lecture on Chapter 5 as such. Instead, I refer students to it when we first encounter a technique in a later chapter. I do it that way to avoid boring my students with technique after technique. I also realize that the concepts behind some of these techniques are rather sophisticated, and the students' appreciation of them is much deeper after they've acquired more experience in molecular biology.

Chapters 6–9 describe transcription in prokaryotes. Chapter 6 introduces the basic transcription apparatus, including promoters, terminators, and RNA polymerase, and shows how transcripts are initiated, elongated, and terminated. Chapter 7 describes the control of transcription in four different operons, then Chapter 8 shows how bacteria and their phages control transcription of many genes at a time, often by providing alternative sigma factors. Chapter 9 discusses the interaction between prokaryotic DNA-binding proteins, mostly helix-turn-helix proteins, and their DNA targets.

Chapters 10–13 present control of transcription in eukaryotes. Chapter 10 deals with the three eukaryotic RNA polymerases and the promoters they recognize. Chapter 11 introduces the general transcription factors that collaborate with the three RNA polymerases and points out the unifying theme of the TATA-box-binding protein, which participates in transcription by all three polymerases. Chapter 12 explains the functions of gene-specific transcription factors, or activators. This chapter also illustrates the structures of several representative activators and shows how they interact with their DNA targets. Chapter 13 describes the structure of eukaryotic chromatin and shows how activators can interact with histones to activate or repress transcription.

Chapters 14–16 introduce some of the posttranscriptional events that occur in eukaryotes. Chapter 14 deals with RNA splicing. Chapter 15 describes capping and polyadenylation, and Chapter 16 introduces a collection of fascinating "other posttranscriptional events," including rRNA and tRNA processing, *trans*-splicing, and RNA editing. This chapter also discusses two kinds of posttranscriptional control of gene expression: (1) RNA interference; and (2) modulating mRNA stability (using the transferrin receptor gene as the prime example).

Chapters 17–19 describe the translation process in both prokaryotes and eukaryotes. Chapter 17 deals with initiation of translation, including the control of translation at the initiation step. Chapter 18 shows how polypeptides are elongated, with the emphasis on elongation in prokaryotes. Chapter 19 provides details on the structure and function of two of the key players in translation: ribosomes and tRNA.

Chapters 20–23 describe the mechanisms of DNA replication, recombination, and translocation. Chapter 20 introduces the basic mechanism of DNA replication, and some of the proteins (including the DNA polymerases) involved in replication. Chapter 21 provides details of the initiation, elongation, and termination steps in DNA replication in prokaryotes and eukaryotes. Chapters 22 and 23 describe DNA rearrangements that occur naturally in cells. Chapter 22 discusses homologous recombination and Chapter 23 deals with site-specific recombination and translocation.

New to the Second Edition

After the Introduction, all the chapters of this second edition have been extensively updated and include new information. Three major expansions of the first edition are evident:

- First, Chapter 24 on genomics is new. Since the first edition appeared, the total sequences of many complex genomes have been obtained, including the genomes of a worm, a fly, and a mustard plant. We even have a rough draft of the human genome, and a polished human genome sequence is on the horizon. These historic developments have already begun to revolutionize molecular biology. Now we can examine the activities of all the genes in an organism at once and see how they respond to various perturbations, including development and disease. The sequence of any genetic loci, including those involved in disease states, is instantly available from the sequence database. Genomes of related organisms can be compared to detect the effects of evolution and to pinpoint conserved DNA sequences that are likely to be keys to the function of gene products.
- Second, Chapter 22 of the first edition has been split in two (Chapters 22 and 23). Trying to force all of recombination and translocation into one chapter did not allow for enough treatment of either topic. Now Chapter 22 is devoted exclusively to homologous recombination, so the mechanism of that vital process can be analyzed in detail. A new discussion of meiotic recombination in yeast has also been added. Chapter 23 covers site-specific recombination—with λ integration and excision as the major example—and translocation. The translocation section has been considerably expanded and now includes new discussions of retroviruses, non-LTR retrotransposons such as LINES, nonautonomous retrotransposons such as Alu elements, and transposable group II introns.
- Third, Chapter 20 includes a new section on DNA damage and repair. These are important elements of molecular biology, and they also play a major role in human disease, especially cancer.

Supplements

- Visual Resource Library
  The presentation CD-ROM contains digital files for all of the line art, tables, and most of the photographs in the text in an easy-to-use format. This format is compatible with either PC or Macintosh.
- Text-Specific Website
  The following website, specific to this text, provides access to digital image files, updates, and web links for both students and instructors. Separate message boards for both instructor and student discussion are also available:

  www.mhhe.com/weaver2

ACKNOWLEDGMENTS

In writing this book, I have been aided immeasurably by the advice of many editors and reviewers. They have contributed greatly to the accuracy and readability of the book, but they cannot be held accountable for any remaining errors or ambiguities. For those, I take full responsibility. I would like to thank the following people for their help.

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