Preface

The fast pace of modern molecular biology research is driven by intellectual curiosity and major challenges in medicine, agriculture, and industry. No discipline in biology has ever experienced the explosion in growth and popularity that molecular biology is now undergoing. There is intense public interest in the Human Genome Project and genetic engineering, due in part to fascination with how our own genes influence our lives. With this fast pace of discovery, it has been difficult to find a suitable, up-to-date textbook for a course in molecular biology. Other textbooks in the field fall into two categories: they are either too advanced, comprehensive, and overwhelmingly detailed, with enough material to fill an entire year or more of lectures, or they are too basic, superficial, and less experimental in their approach. It is possible to piece together literature for a molecular biology course by assigning readings from a variety of sources. However, some students are poorly prepared to learn material strictly from lectures and selected readings in texts and the primary literature that do not match exactly the content of the course. At the other end, instructors may find it difficult to decide what topics are the most important to include in a course and what to exclude when presented with an extensive array of choices. This textbook aims to fill this perceived gap in the market. The intent is to keep the text to a manageable size while covering the essentials of molecular biology. Selection of topics to include or omit reflects my view of molecular biology and it is possible that some particular favorite topic may not be covered to the desired extent. Students often complain when an instructor teaches "straight from the textbook," so adding favorite examples is encouraged to allow instructors to enrich their course by bringing to it their own enthusiasm and insight.

Approach

A central theme of the textbook is the continuum of biological understanding, starting with basic properties of genes and genomes, RNA and protein structure and function, and extending to the complex, hierarchical interactions fundamental to living organisms. A comprehensive picture of the many ways molecular biology is being applied to the analysis of complex systems is developed, including advances that reveal fundamental features of gene regulation during cell growth and differentiation, and in response to a changing nvironment, as well as developments that are more related to commercial and medical applications. Recent advances in technology, the process and thrill of discovery, and ethical considerations in molecular biology research are emphasized.

The text highlights the process of discovery – the observations, the questions, the experimental designs to test models, the results and conclusions – not just presenting the "facts." At the same time the language of molecular biology is emphasized, and a foundation is built that is based in fact. It is not feasible to examine every brick in the foundation and still have time to view the entire structure. However, as often as possible real examples of data are shown, e.g. actual results of an EMSA, Western blot, or RNA splicing assay. Experiments are selected either because they are classics in the field or because they illustrate a particular approach frequently used by molecular biologists to answer a diversity of questions.

Organization

The textbook is designed for a one-term course on molecular biology (or molecular genetics) for undergraduate students who are primarily majoring in biology or chemistry, with a large percentage of premedical students. First-year graduate students with a minimal background in molecular genetics/biology would also benefit from this course. Students would be expected to have completed, at a minimum, a two-term introductory biology course and to have completed at least 1 year of chemistry. Each chapter opens with a conceptual statement and historical perspective, followed by explanation and elaboration. Chapters end with a list of key references from the primary literature, and a series of analytical questions.

The book begins with a five chapter sequence that should be a review for most students, but with more detail than they would have encountered in an introductory biology or genetics course. Students of molecular biology need to have a solid grasp of these concepts so they may need to refresh their understanding of them. Depending on the curriculum at a particular institution, more or less time may need to be spent on these introductory chapters. Chapter 1 is a brief history of genetics and the beginnings of molecular biology. Chapter 2 discusses the structure and chemical properties of DNA. Chapter 3 discusses the organization of genomes and eukaryotic chromatin. Chapter 4 deals with the versatility of RNA structure and function, and Chapter 5 provides an overview of the flow of genetic information from DNA to RNA to protein and covers basic protein structure and function. The genetic code for amino acids is presented along with protein structure and function. This order reflects the view that to understand protein structure and function it is essential to first understand the flow of genetic information and where the primary sequence of amino acids derives from, and the consequences of alterations in the genetic code.

Chapters 6 and 7 cover DNA replication, telomere maintenance, and DNA repair and recombination. Although some instructors prefer to cover DNA replication later in a course, my view is that the information is essential early on, particularly to be able to understand many of the experimental strategies used in studying genes and their activities at the molecular level.

There is always debate on where to place methods and techniques – scattered throughout, in an appendix, or as specific chapters. I have mainly taken the latter approach, with the intent that this textbook will be a useful resource for students well beyond the course. Many undergraduate programs now include a research component and having a compilation of the standard techniques in molecular biology along with theoretical background and how they arose from basic research provides an essential aid. My approach in teaching is to cover some of the very basic methods in a series of "recombinant DNA technology" lectures, but to introduce others as needed to understand experiments discussed throughout the course. For example, Chapters 8 and 9, which cover recombinant DNA technology, molecular cloning, and tools for analyzing gene expression would certainly not be covered from start to finish. Covering method after method would become tedious. In addition, appreciation of the concepts behind techniques is much greater after students have acquired more experience in molecular biology.

Eukaryotic molecular biology is emphasized, although where details are better understood from bacteria, these are included. When fundamental processes such as DNA replication, repair, and recombination are discussed, the focus is on eukaryotes because the basic process is similar to that in prokaryotes, although the components of the machinery and the specific names of the players may differ. Prokaryotic transcription is given a separate chapter (Chapter 10), however, since some aspects of transcriptional regulation are fundamentally different than in eukaryotes, e.g. the concept of the operon, attenuation, and riboswitches. The basic transcription apparatus is introduced in Chapter 10 and how transcripts are initiated, elongated, and terminated is covered.

Chapter 11 covers the control of transcription in eukaryotes, introducing the regulatory elements, the general transcription factors, the interaction of DNA-binding proteins and DNA targets, the role of coactivators and corepressors, and regulated nuclear import of transcription factors. Chapter 12 covers the emerging field of epigenetics and monoallelic gene expression.

Chapter 13 introduces RNA processing and post-transcriptional gene regulation in eukaryotes, while Chapter 14 covers the mechanism of translation, with a focus on eukaryotic translation.

Chapters 15–17 cover some of the many applications of molecular biology. Chapter 15 introduces genetically modified organisms and their use in basic and applied research. Chapter 16 covers genome analysis, including DNA typing, genomics, and proteomics. Chapter 17 covers aspects of medical molecular biology including the molecular biology of cancer, gene therapy, and human behavior.

The course length is easily adjustable. The book is designed so that more or less time can be spent on particular topics according to an instructor's preference. The material in boxes can be treated as supplementary material if the course is too long for the needs of a particular class. On the other hand, there will be additional readings in these sections for students who want to go beyond the material in the main text to gain a deeper understanding of a particular topic.

Special features

Unique aspects of the book include a cohesive discussion of epigenetics and medical molecular biology, and the use of boxes to highlight molecular tools (Tool boxes), and to provide a more detailed treatment of material that will be of interest to the very keen student (Focus boxes). In addition, the textbook has a strong emphasis on biomedical research, which will appeal to the many premedical students who are likely to take the course prior to taking the MCATs. "Disease boxes" use diseases resulting from defects in a key gene to illustrate many principles of molecular biology. These examples place complex regulatory pathways, such as nucleotide excision repair, in a relevant context, making them more memorable for students.

- Book features:
  - Tool boxes explore key experimental methods and techniques in molecular biology
  - Focus boxes offer more detailed treatment of topics, delve into experimental strategies, and suggest areas for further exploration
  - Disease boxes illustrate key principles of molecular biology by examining diseases that result from key gene defects
  - Chapter-opening quotes, outlines, and introductions
  - End-of-chapter analytical questions
  - End-of-book glossary.
- Interactive website features:
  - Interactive animations (based on art from the book and identified in the book with a special icon)
  - Interactive student tutorials and pdb files
  - Interactive student exercises
  - Answers to end-of-chapter analytical questions
  - Additional student and instructor resources
  - Downloadable artwork from the text.
- CD-ROM features:
  - Downloadable artwork from the text
  - Sample interactive animation and tutorial
  - Sample syllabus
  - Link to website.

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