

Preface

The field of biochemistry is entering an exciting new era in which genomic information is being integrated into molecular-level descriptions of the physical processes that make life possible. Our understanding of how biological macromolecules work at the level of atoms and interactions is also enabling great strides to be made in molecular medicine—where the path between the identification of a target and the development of therapeutics that modulate its functions is becoming ever shorter. Key to making future advances in these areas is a new generation of molecular biologists and biochemists who are able to harness the tools and insights of physics and chemistry to exploit the emergence of genomic and systems-level information in biology. This book is the result of a decade-long series of discussions among the three of us, in which we considered how biology students should best prepare themselves to take advantage of the growing depth of information concerning molecular mechanisms in biology.

The central theme of this book is that the ways in which proteins, DNA, and RNA work together in a cell are connected intimately to the structures of these biological macromolecules. These structures, in turn, depend on interactions between the atoms in these molecules, and on the interplay between energy and entropy, which results in the remarkable ability of biological systems to self-assemble and control their own replication. This book is not intended to be a comprehensive reference, nor does it contain the most recent biological breakthroughs and discoveries. Our goal in this textbook is to integrate fundamental concepts in thermodynamics and kinetics with an introduction to biological mechanism at the level of molecular structure. We have done so by choosing biological examples to illustrate the basic physical and chemical principles that underlie how biological molecules function.

We have written this textbook with an undergraduate audience in mind, particularly those students who have chosen biology or the health sciences as their principal area of study. We assume that students have taken introductory courses in physics and chemistry, and have been introduced to differential calculus at a basic level. We anticipate that the book will also be useful for graduate students in biology who have not taken courses in physical chemistry, or who seek to learn more about structural biology. We also hope that the book will be useful for scientists wishing to refresh their knowledge of the elementary principles of biological structure, thermodynamics, and kinetics.

The development of this textbook has been anchored, over the last few years, by the creation of a one-semester undergraduate course at the University of California at Berkeley, offered jointly by faculty in the departments of Chemistry and of Molecular and Cell Biology. This course has merged the first part of a traditional course in biochemistry with a new way of teaching physical chemistry to biology undergraduates. There are two aspects of this course that are a departure from past practice. The first is the integration of structural biology with physical chemistry, as mentioned earlier. The second aspect, and perhaps the more radical one for a course aimed at biology undergraduates, is to develop the laws of thermodynamics and the concept of free energy through statistical analysis of molecular

interactions and behavior rather than on the more abstract concepts underlying heat engines. It is our experience that biology students take to the statistical treatment of energy and entropy more readily because this approach allows us to link thermodynamics and structure in an intuitively obvious way. Our initial hesitation concerning the implementation of this approach reflected a concern that the mathematical preparation of typical biology students might leave them ill-prepared to grapple with the statistical approach to thermodynamics. But, to our satisfaction, we have found that students understand these concepts readily, as witnessed by the growing enrollment in this class each year since its inception at Berkeley. The majority of these students are majors in Molecular and Cell Biology, with another large group of them majoring in Bioengineering.

The organization of our textbook follows how a course could be developed over one semester. We begin by introducing the nature of biological macromolecules and the structures that they form, placing these ideas in the broad context of how evolution proceeds while obeying physical laws. The first chapter provides an overview of DNA, RNA, and proteins and also reviews the processes of replication, transcription, and translation. A more detailed discussion of the structures of biological molecules is provided in Chapters 2 through 5, including a discussion of how evolutionary processes have shaped the architecture of proteins. Chapters 6, 7, and 8 provide a quantitative treatment of energy and the statistical basis for the concept of entropy, culminating in the development of the Boltzmann distribution and the idea that the energies of different molecular configurations determine the probabilities of observing them. The concept of free energy is introduced in Chapter 9 and, along with chemical potential, is developed further in Chapter 10, which applies these ideas to acid-base equilibria and to protein folding. Chapter 11 takes the concept of chemical potential one step further, by linking it to voltages through applications in redox chemistry and an analysis of how action potentials are transmitted in nerve cells.

Chapters 12 to 14 are concerned with the principles of molecular recognition, developing the ideas of affinity and specificity, with applications to drug interactions, protein-DNA, protein-RNA and protein-protein interactions, followed by a treatment of allosteric systems. Chapters 15 to 17 introduce kinetic concepts, including an analysis of enzyme mechanisms and transport properties (the material in these chapters could be presented in a course before Chapters 12 to 14 are covered). Finally, Chapters 18 and 19 bring together all of the ideas introduced in the earlier chapters by discussing two particularly interesting aspects of the self-assembly of biological systems: the folding of proteins and RNA, and the fidelity of replication and translation.

We have organized the book in a modular fashion, with each chapter broken into separate parts, some of which could be omitted according to instructor preference. While Chapters 6 to 19 assume that the student is familiar with the structural principles introduced in Chapters 1 to 5, an instructor could begin with Chapter 6, provided that the students have been introduced to proteins, DNA, and RNA in an earlier course (we believe that the earlier chapters could then serve as an excellent refresher). Each chapter has an associated set of problems—as anyone who has taken physical chemistry knows, working through problems is an important aspect of learning the material, and we hope that the problems at the end of each chapter can serve as a nucleus for generating assignments for the students to work through on their own.

There are two topics that might belong in an undergraduate biophysical chemistry course that we have purposely omitted. One is quantum mechanics, and the other concerns methods of instrumental analysis and structure determination in biochemistry. At Berkeley, students are introduced to these topics in a separate course that follows the one based on our book.

ONLINE RESOURCES

Accessible from www.garlandscience.com/TMOL, the Student and Instructor Resource Websites provide learning and teaching tools created for *The Molecules of Life*. The Student Resource Site is open to everyone, and users have the option to register in order to use book-marking and note-taking tools. The Instructor Resource Site requires registration and access is available to instructors who have assigned the book to their course. To access the Instructor Resource Site, please contact your local sales representative or email science@garland.com. Below is an overview of the resources available for this book. On the Website, the resources may be browsed by individual chapters and there is a search engine. You can also access the resources available for other Garland Science titles.

FOR STUDENTS

Animations and Videos

The animations and videos dynamically illustrate important concepts from the book, and make many of the more difficult topics accessible.

Flashcards

Each chapter contains a set of flashcards, built into the Website, that allow students to review key terms from the text.

Glossary

The complete glossary is available on the Website and can be searched and browsed as a whole or sorted by chapter.

FOR INSTRUCTORS

Figures

The images from the book are available in two convenient formats: PowerPoint® and JPEG. Figures are searchable by figure number, figure name, or by keywords used in the figure legend from the book. There is one PowerPoint presentation for each chapter.

Animations and Videos

The animations and videos that are available to students are also available on the Instructor's Website in two formats. The WMV formatted movies are created for instructors who wish to use the movies in PowerPoint presentations on Windows® computers; the QuickTime formatted movies are for use in PowerPoint for Apple® computers or Keynote® presentations. The movies can easily be downloaded to your computer by using the "download" button on the movie preview page.

Solutions Manual

A complete solutions manual is provided for all problems in the text.