

PREFACE

Overburdening necessarily leads to superficiality. Teaching should be such that what is offered is perceived as a valuable gift, and not as a hard duty.

Albert Einstein

This is a textbook on concepts in biochemistry: concepts from physics, from chemistry, from biology. I have chosen proteins as the subject of the book because they provide the richest illustrations of those concepts. However, the book is not a description of the physical properties of proteins and their biological functions. Rather, my goal is to communicate a way of thinking about problems in biochemistry—in science, really. In this sense, I use proteins as a vehicle. But proteins are much more than a vehicle for this process: They are the most fascinating molecules that exist.

This book was born from teaching. Having taught biochemistry for about 20 years, I came to appreciate that students struggle with the sheer volume of material in introductory courses. They are asked to know an ever-growing amount of information (yet what a human being can reasonably learn and comprehend has not increased) at the expense of conceptual understanding. Over the past decade, more than 30 undergraduate students have worked in my research laboratory. I have noticed that the amount of material learned in the classroom that is actually retained in usable form is quite small. This is true even of students who completed the courses with excellent results. Why?

Biochemistry textbooks have become increasingly concentrated on biological aspects and on large amounts of information. Conversely, understanding chemical, physical, and mathematical aspects of biochemical topics have received less attention. Yet, already about 10 years ago the National Research Council (NRC) of the National Academies reached the conclusion that *"life science majors must acquire a much stronger foundation in the physical sciences... than they now get,"*¹ and recommended increasing connections between biological and physical sciences as a means to bridge the communication gap that exists between researchers in different disciplines. The NRC also emphasized the importance of raising the interest for research in undergraduate students as early as possible. I wanted to attempt something to help change this state of affairs.

¹National Research Council (2003). Bio 2010: Transforming Undergraduate Education for Future Research Biologists. National Academic Press.

I believe this book will be helpful for all those who seek a foundation in more physical aspects of biochemistry. The book contains a manageable amount of material for a one-semester course on proteins for advanced undergraduates and beginning graduate students in chemistry, biochemistry, biophysics, and biology. At the PhD level, courses on proteins often have a heterogeneous population of students, with varied backgrounds. Those courses are often taught on the basis of journal articles from the scientific literature. In these cases, I think this textbook will provide the necessary foundation for many students. Furthermore, chemistry departments whose concentration in biochemistry is limited may find this text appropriate for a course that fulfills their biochemistry requirement. The prerequisites for the course are one semester of calculus and a knowledge of introductory physical chemistry. A basic undergraduate general biochemistry course is helpful but not essential, because the book covers the basics of protein and DNA composition and structure. I have taught this course, with some variations, to beginning graduate and advanced undergraduate students in chemistry and biology. My hope is to endow students with a frame of thought that will help them tackle problems they will encounter in the course of their careers.

I designed this book to present essential concepts in biochemistry without overburdening students with too many facts or too much formalism. The book covers protein structure, evolution, stability, folding, ligand binding, and enzyme kinetics. I wanted to approach these topics from a perspective of probabilistic (statistical) and quantitative thinking. Therefore, the book begins with an introduction to statistical thermodynamics, applied to biological macromolecules. The concept of the partition function is introduced early and used throughout. With the exception of Chapter 3 (evolution), all chapters use the partition function method to solve various problems. Mathematics is essential in science, and many topics in biochemistry require mathematics. However, I have tried to keep the mathematical formalism to a minimum. When mathematics is used, I have tried to explain the meaning of formulas and procedures in plain English. Mathematics tends to scare biochemistry students. The barrier, however, is mainly one of language not of concepts; I have found that most students can follow a mathematical argument if it is explained in words. I have also sacrificed formalism to intuition. In so doing, I have taken approaches that purists may frown upon. I think this is a risk worth taking.

The book starts simple and becomes progressively more complex. Later chapters build on the previous ones: the book is meant to be read in sequence; it is not a reference text to look things up. Because of that, some sections may be assigned as homework reading, rather than covered in class. Each chapter ends with a set of problems of variable degrees of difficulty, not necessarily in order. The overall complexity of the problems tends to increase as the book progresses. Finally, each chapter includes a list of references, organized by topics. The references are listed under the topic for which they are most relevant, but some references are relevant for more than one topic. The references are not cited in line, to facilitate reading, but it should be fairly evident which references were used for a particular topic.

Some additional resources are highly recommended. One is the Protein Data Bank (PDB), which is the source of the protein structures that illustrate this book. The second is a means of visualization and rendering of those structures, such as the PyMol software. All protein structures in this book were produced with Open Source PyMol, which is free for everyone, and which I am pleased to acknowledge.

The third tool is the Kinemage web site, organized by Jane and David Richardson at Duke University. This site contains various tools that make the study of protein structure a wonderful experience. Students are strongly encouraged to visit those sites, download the programs, and begin exploring proteins.

I would like to acknowledge all the people who have helped me in this endeavor. I thank my editor at Garland, Summers Scholl, for her constant support and understanding during the writing of this book, and editorial assistant Michael Roberts for his help in the last stretch. I thank the reviewers of the manuscript, or of several of its chapters—namely, (in alphabetical order), Charles E. Bell (Ohio State University), David Case (Rutgers University), Athel Cornish-Bowden (CNRS, Marseille, France), Paul Raymond Gooley (University of Melbourne, Australia), Andrew Herr (University of Cincinnati College of Medicine), Anne Hinderliter (University of Minnesota, Duluth), Matt Junker (Kutztown University of Pennsylvania), Jim Morton (Lincoln University), Bill Pearson (University of Virginia), Gordon Rule (Carnegie Mellon University), Brian Shilton (University of Western Ontario), Nicolas Silvaggi (University of Wisconsin, Milwaukee), Jennifer Surtees (University at Buffalo School of Medicine and Biomedical Sciences), Christopher Taylorson (University College London, UK), Darren Thompson (University of Sussex, UK), Peter Tipton (University of Missouri, Columbia), and Honggao Yan (Michigan State University). All of their criticisms, major and minor, were extremely helpful.

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The views presented here, however, and any mistakes or errors remaining, are of my exclusive responsibility. I welcome any corrections from readers, which can be sent to science@garland.com.

I would also like to thank the colleagues in my department who have read and commented on various chapters: Antje Pokorny Almeida, on ligand binding; Chris Halkides, on enzyme kinetics; Mike Messina, on statistical thermodynamics; Pam Seaton, on NMR; and especially Hee-Seung Lee, who read and provided feedback on almost the entire manuscript. Their comments, suggestions, and corrections are deeply appreciated.

One of my motivations to write this book was to pass to students what I have learned. Therefore, I want to take this chance to thank the people from whom I myself have learned the most: my first mentor in science, Winchil Vaz (University of Coimbra, Portugal), for the many hours and years of great discussions; my PhD advisor, Tom Thompson (University of Virginia), from whom I learned so many things, among which is not to be afraid of starting to work on something I knew nothing about; and my post-doctoral advisor, Rod Biltonen (University of Virginia), from whom I learned to use the partition function in biochemical problems, and to whom, in this and many other senses, this book is a tribute.

Finally, I thank Antje for her support and patience during all the spoiled weekends and vacations for the past three years, while the most intense writing took place.

Paulo Almeida
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Art of Proteins: Concepts in Biochemistry The images from the book are available in two convenient formats: PowerPoint® and JPEG. They have been optimized for display on a computer. Figures are searchable by figure number, by figure name, or by keywords used in the figure legend from the book.

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