Preface

The objective of this book is to provide a unifying approach to the study of biophysical chemistry for the advanced undergraduate who has had a year of physics, organic chemistry, calculus, and biology. This book began as a revised edition of *Biophysical Chemistry: Molecules to Membranes,* which Elizabeth Simons and I coauthored. That short volume was written in an attempt to provide a concise text for a one-semester course in biophysical chemistry at the graduate level. The experience of teaching biophysical chemistry to biologically oriented students over the last decade has made it clear that the subject requires a more fundamental text that unifies the many threads of modern science: physics, chemistry, biology, mathematics, and statistics. This book represents that effort. This volume is not a treatment of modern biophysical chemistry with its rich history and many controversies, although a book on that topic is also needed. *The Physical Basis of Biochemistry* is an introduction to the philosophy and practice of an interdisciplinary field in which biological systems are explored using the quantitative perspective of the physical scientist. I have three primary objectives in this volume: one, to provide a *unifying* picture of the interdisciplinary threads from which the tapestry of biophysical studies is woven; two, to provide an insight into the power of the *modeling* approach to scientific investigation; and three, to communicate a sense of *excitement* for the activity and wholesome argument that characterize this field of study.

The students in this course are likely to be a cross section of quantitatively oriented biologists as well as aspiring chemists, physicists, and engineers with an interest in biological systems. This leads to a mixing of interests and disciplines brought to both the classroom and the laboratory. A fundamental assumption of a physical approach to biology and especially biophysical chemistry is that we can gain understanding of a biological phenomenon by describing and understanding its physical nature. Thus the tools of the physical scientist become available to the biologist in the exploration of the complexities of biological systems. In recent years, the skills of the biophysical chemist have emerged as prized commodities in both academic and industrial circles. The need for these skills will intensify as the practice in biotechnology and bioindustry moves from gene identification to the manufacture of gene products that will need both proper structure and function to be useful.

This edition is a response to these educational and real-world challenges. It reflects a recognition of the need to provide students (and professional practitioners) with an integrated presentation of the fundamental philosophy, logic, and physical foundations shared by the biology, chemistry, and physics on which biophysical chemistry is built. At the risk of repeating familiar information, certain topics are reviewed with the intention of presenting an integrated picture in a single volume. In addition, the modern student may be unprepared because curricular decisions about prerequisite courses have often eliminated material that is essential for the study of biophysical chemistry. For example, a colleague teaching a graduate course in protein structure and function recently complained that none of the students were familiar with the ideas of an electric dipole or the electromagnetic wave nature of an X-ray beam. Hence she complained, "Teaching hydration of proteins and X-ray crystallography was going very slowly." I have had students report that "we skipped electrostatics in (college?!) physics because we ran out of time." Whatever the reasons for these all-too-common stories, I hope the inclusion of "prerequisite" material in this volume will go some distance to ameliorate the problem.

Textbook writers can follow one of two paths when they undertake the task of assembling information in a book. The author can attempt to provide state-of-the-art description of the entire field—in a sense, attempting a cross between a library of monographs and an encyclopedia. Alternatively, one can present a focused, consistent perspective to give the student a clear point of view. Both approaches have their place in the educational process of the well-rounded student. This book adopts the latter approach. Rather than attempting a comprehensive account of the entire field of biophysical chemistry, I have presented the material as an interdisciplinary study that pursues one of the most interesting but complex subjects known. Two biophysical problems run through the text. One highlights Newtonian mechanics and the other, quantum mechanics. The first is the issue of macromolecular structure, especially with regard to protein folding. Its discussion culminates in an analysis of the protein misfolding problem that causes the amyloid diseases and with a discussion of molecular modeling. The second is bioenergetics and the transfer of photonic energy into electrochemical energy. This discussion concludes with an exploration of (quantum) mechanics of biological electron transfer.

There are five sections to this volume.

Part 1 explores the central philosophy of scientific study. The ideas of model making and system science investigations as basic tools to describe and explore a state space are explored in relation to biological systems.

Part 2 reviews the underlying physical principles leading to the central abstraction of the book: the potential energy surface. The physical review chapters are a natural venue for exploring the principles underlying certain of the biophysical chemist's laboratory arts. I have chosen to present some of this practical material as an example of the application of the physical theories under discussion. Centrifugation, X-ray crystallography, and electron microscopy are discussed. Many biologically oriented students will find these chapters a unifying exposure to the principles of Newtonian and quantum mechanics, and this will lead us to a study of thermodynamics.

Part 3 outlines the use of thermodynamics, spectroscopy, and microscopy as tools for the exploration of biochemical problems. We consider the basis of thermodynamic-energy accounting as a window into the properties, form, and structure of molecules and systems. Although classical thermodynamics is covered, a somewhat heavier emphasis on a statistical viewpoint is present. I try to balance the theoretical richness of thermodynamics with a practical feel for the uses of enthalpy, free energy, and phase-equilibria studies in characterizing biomolecular systems.

Part 4 shows how the principles developed in the first two sections can be used to build up a biophysical model. The system we use—aqueous biochemistry—starts with a consideration of the properties of water and then sequentially explores the interactions of water with the chemical components that make up biological systems. In the development of ion-solvent and ion-ion models, we learn how the great physical scientists brought us to where we are today. There is a certain "classical" coverage of material, but it is important for the modern student to see where the simplifications and abstractions originated in many of the ideas that have become our modern dogma. The section explores the interactions that lead to macromolecular structure, the properties of the cell membrane, and the structure of the electrified regions near cells and colloidal surfaces.

Part 5 takes the three-dimensional potential energy surface, which reflects the equilibrium state, and puts it into motion. This section explores the time-dependent actions of real-world processes. The major driving forces in biological systems are chemical and electrical gradients, and diffusion and conduction are the focus of this section, which concludes with an examination of the electromechanical phenomena of electrokinetics and the kinetics of chemical and electrochemical systems of biological importance: enzymes and electron transfer in proteins.

The *appendices* contain material that would have distracted from the flow of ideas in the main text. Just about all students of science—whether learning, teaching, or researching—have a joy and thrill at the art and craft of scientific endeavors outside their area of direct interest. I have used the appendices in some cases to provide a glimpse into these associated areas of interest that one may not feel justified in covering during classroom time.

A *further reading* section has been assigned to each chapter that will help the reader explore the subject matter touched on in that section more fully. I have attempted to include a wide range of levels of readings so that the interested reader can consult other literature with a minimum of difficulty. Some books listed are out of print but are usually available in libraries. In the primary literature I have made special effort to include references to applications of the physical methods to biological problems so that the student may see the practice of the art.

Most chapters are accompanied by *questions and problems* that amplify and extend the teaching points outlined in the preceding chapter. I have provided answers to certain questions, and in some cases the answers augment the material in the chapters.

I have made some nontraditional choices about the order of presentation. Because in general I have wished to build up to the study of biological systems from the foundations of physics and mathematical modeling, I have left the important treatment of thermodynamics until after the forces and observables making up the biochemical system have been presented. Thus thermodynamics follows quantum mechanics and a chapter on chemical structure. I believe there is value in shifting toward a fundamental statistical/quantum teaching of chemical systems, and this makes the systemic behavior reflected in thermodynamics derived from, rather than fundamental to, the teaching process. Of course this is also true for kinetic ideas, and I have located those topics toward the end of the presentations, so I may not have the true courage of my convictions! For the truly radical among us who wish to follow this approach, one might teach Chapters 1 through 12 and then add topics from chemical kinetics (Chapter 31). Then thermodynamics provides tools for the study of systems and can be used with a focus on building the structure of model systems. The last section on kinetic processes then explores the structural model as a time-dependent function.

On the other hand, the section on thermodynamics can be taught in a more traditional order, probably after the chapter on mechanics, which ends with a discussion of the equipartition of energy. The professor is then free to choose from the subsequent topics ranging from modeling, microscopy, molecular modeling, and even the later chapters on kinetic processes. The quantum mechanical core material will be best served taught from electrostatics through electromagnetics and then quantum mechanics and spectroscopy. The sections on electron kinetics and spectroscopy can be taught without an emphasis on quantum mechanics, but many of the unifying ideas will inevitably be lost.

I would like to thank and acknowledge the help and support provided by colleagues and my family over the last two years. I had the special delight and privilege of working closely with one of the great grammarians (and red-pencil users), my father, Dr. K. R.