# Biophysical Chemistry

## Molecules to Membranes

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# Preface

Today there is an unprecedented explosion of interest and experimental investigation in the fields of biochemistry, physiology, and biophysical sciences. The development of the techniques of molecular biology and immunology and the availability of computer analysis have led to a phenomenally rapid pace in the acquisition of new information, especially with respect to the biology of the cell. As information relating to the control and integration of cellular processes becomes available, more interest is turning toward understanding the interdependence of cellular processes on a larger scale. The inevitable consequence of this is the growing interdisciplinary nature of modern biochemical and biophysical studies. As the focus broadens, so does the base of researchers and graduate students who are being attracted into these fields to pursue their interests in what was traditionally more the province of biology. This increased diversity of backgrounds is good, but it carries with it a cost in the heterogeneity of the preparation of modern students. Not too many years ago, a candidate for graduate studies in biochemistry or biophysics was most likely to have been a chemistry or physics major in undergraduate school and consequently had been exposed to, if had not mastered, many of the intricacies of physical processes and their treatment in quantitative terms. We have found in our teaching over the last several years that entering students are less likely to have been exposed to rigorous courses in physical chemistry and engineering physics. However, the direction of modern biochemical and biophysical studies is moving quickly toward areas where scientists will need to understand and use the disciplines of surface chemistry, electrochemistry, quantum mechanics, and mathematical modeling to understand the molecular processes in cells and at subcellular levels.

This textbook had its origins in a course entitled "Water and Its Properties" taught in the Department of Biochemistry at Boston University School of Medicine. Originally, the course was intended to instill in graduate students of biochemistry, biophysics, and physiology some understanding of the ways in which knowledge of solutions and solution thermodynamics could be used to explain and to predict the behavior of cells. This is clearly necessary in modern biochemistry if cellular events such as metabolic processes, stimulus responses, cellular differentiation, or the functional controls of cells are to be understood and the effects of perturbations, of illnesses, of drugs, etc., are to be quantitatively predicted. As the backgrounds of our students became more heterogeneous, we found that an increasing amount of prerequisite material needed to be reviewed before the complexities of cellular processes could be systematically taught. It was from this need to level the ground and still provide a challenging and meaningful graduate course leading to an appreciation of the biophysical chemistry of cellular systems that this book was born. Therein lie the reasons for the choice of material, the style of presentation, and the limitations of the coverage of areas of interest in this volume. It is worth acknowledging that we have in our minds the addition of a second volume to this text, thereby extending both the breadth and the depth of coverage of the subject.

The text is designed to be used in a single-semester course in the first or second year of graduate school but certainly could also form the basis of an advanced course for undergraduates in biophysics or chemistry. The text assumes that all students using it will be familiar with basic physics (including electrostatics), general introductory inorganic and organic chemistry, and cell biology. A background in physical chemistry is not presumed but is certainly valuable. A knowledge of calculus and algebra is assumed, but students are not expected to be particularly familiar with advanced areas such as partial differential calculus.

Because the subsequent discussions in the second and third parts depend on a thermodynamic vocabulary, the first part is a rather lengthy discussion of the basic principles of equilibrium thermodynamics. Experience has taught many teachers that students are usually left baffled by a single rigorous exposure to thermodynamics, an exposure that we do assume all readers of this book have had. We therefore have chosen to cover, in a semirigorous but conversational tone, both old ground and some ground not traditionally taught extensively in undergraduate sections on thermodynamics. The ideal use of the chapters on thermodynamics would be as a study guide to a more traditional and rigorous presentation of the subject, probably available already in a textbook in the student's library. The student or professor who already feels adequately prepared in this area might opt to simply use these chapters as a quick refresher.

The second part of the book deals with the structure and behavior of solutions of ions and molecules. The first chapter of the part begins with a qualitative look at the structure and properties of bulk water, the substance most generally considered the solvent of biological systems. It is in the second part that our dual teaching objectives will become apparent. We aim to discuss the treatment of dilute and moderately concentrated homogeneous solutions of polar and nonpolar molecules with a focus on the important role played by water as the solvent. In addition, we attempt to demonstrate the principles used in model building through the use of both thermodynamic cycles and mechanistic information and then test the resulting models against empirical evidence. Because a theory is only as good as its assumptions and only as valid as the experimental evidence supporting it, great emphasis is placed on the analysis of assumptions and the examination of the effect of modifications in the model. Such an approach leads to an analysis of ion–solvent interactions starting with Born's hypothesis and of ion–ion interactions starting with Debye and Hückel. We then go on to discuss a solvent-structure view of homogeneous solutions of organic ions, small nonpolar organic molecules, and macromolecules.

Cells and cellular organisms are not dilute, homogeneous solution systems however. The third part of the book builds on the first two as it extends the physical principles necessary to understand the nonhomogeneous and nonequilibrium nature of biological processes. To understand the formation of the cell membrane, the properties of systems containing both lipids and water are examined. This is followed by a discussion of transport phenomena in terms of both nonequilibrium thermodynamics and mechanistic models, the focus being on diffusion and conduction. We believe that one of the most important frontier interdisciplinary fields for the biological scientist is bioelectrochemistry, and so we discuss in a qualitative fashion the structure and behavior of the electrified regions at the juncture of phases. Finally, having laid the foundation for interpreting the behavior of cellular systems on the basis of principles of multiphasic, nonideal, surface-dominated physical chemistry, we consider the role of biological membranes in terms of the forces acting at the membrane and the constraints they impose on the behavior of the cellular system.

We have included a limited number of questions for problem sets and review and as well have attempted to assemble glossaries of formulas and terms so that the reader needs only to go to other texts when interested in significantly greater depth or encounters some area that needs significant remedial review. Our hope is that this text will help both teachers and students in the field to be able to appreciate, and inspire the use of, the powerful tools available through the science of physical chemistry, and will serve to help prepare biological scientists for the inevitable and exciting application of principles of materials science, quantum mechanics, and electrochemistry to biological problems.

We would like to thank our colleagues and our students for their critiques of our effort. Of all the friends and colleagues who aided our efforts, Dr. Cindy McCrone stands as the individual to be most credited for guiding this book to its final completion. Without her eternal patience with the red pencil and unerring sense of teaching clarity and style, this volume would be at best an uncut, unpolished stone. It should be noted however that any errors remaining in this book are entirely our own responsibility and in no way reflect on the readers who were kind enough to evaluate the manuscript for us.

Boston, Massachusetts

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# Introduction

CHAPTER 1

# Molecules, Membranes, and Modeling

Imagine yourself standing outside a country home on an early spring morning just before dawn. Take a deep breath and shiver to the taste of the sweet morning air. Listen carefully to hear the chirping of morning birds. As the sun reaches the horizon, glinting shafts of light reach your eyes. Another deep breath and you feel a peace that comes from a resonance between you and the world at your doorstep. Your eyes close and for a fleeting moment you understand the universe in its simplest most basic terms. Savor that moment, for your eyes open again and now you are drawn back to the reality—you are reading the introduction to a book on physical chemistry. If you are mildly perturbed at being returned to this apparently less appealing reality, you have just demonstrated a facility with a key and exquisitely valuable tool in the study of science, the **Gedanken experiment** (thought experiment). The use of thought trips will be of fundamental importance in the approach that this book takes toward understanding biophysical processes. That virtually any student has access to one of the most profound and sophisticated theoretical techniques available to a scientist is an important lesson to learn. This is just one of the lessons that this short experiment or mind trip has pointed out to us already. Are there other lessons?

What are the consequences of scenes imagined? For one, the reader, who is a biological organism , has interacted with the physical universe, experiencing the electric field vectors of photons (light), detecting molecular vibrations (sound), and identifying alterations in local chemical potential (smell and taste). As part of the process, the reader has converted stored energy sources to sustain the life support processes of the heart, lungs, kidneys, immunological system, etc. This support machinery has allowed the specially adapted cells of the nervous system to recall previously collected, sorted, standardized, and analyzed physical events (light, sound, smell) that were interpreted as information and to sort this information into a creative memory trace that we call imagination. It seems only rational that if the biological organism can perceive and interact with the physical forces that surround it, then at some fundamental level those physical forces and processes are the same for the organism and the physical universe. This implies that a fundamental understanding of the physics and chemistry of the universe will lead to an understanding of biological processes and behavior. It is on this assumption that the fields of biophysics and biophysical chemistry are built. The imagined observer at the door could be content with the "feeling" of universal understanding or could use the tool of Gedanken experimentation along with experimental science to attempt to understand a wide variety of questions. These might include the origins of the photons and the laws governing their propagation; the mechanism of the production of sound by the birds or perhaps the laws governing its propagation through the air and the mechanics of its perception in the ear; and the identity and molecular behavior of the molecules giving rise to the smell of the fresh air or perhaps the nature of their interaction with the specialized olfactory cells of the observer. On the other hand, the reader might choose to focus on the nature and novelty of the beast that, being able to imagine an experience such as this sunrise while actually studying a book on physical chemistry, would consider the physics and chemistry of quantum electrodynamics, wave propagation theory, and ketone, aldehyde, or amine chemistry. What is it about the human biological being, its materials, and its organization that gives it such a charmed view of the universe? How can we understand this seemingly unique biological ability and can it be understood in the same terms as the rest of the physical universe?

Understanding a biological system in terms of physical forces and materials requires some sense of what the similarities and differences are between biological systems and physical systems. As a first approximation, animate and inanimate systems share much at the basic and fundamental levels and differ mostly in the types and magnitudes of complexity. For example, at the atomic level, biological systems are made up primarily of atoms of carbon, hydrogen, nitrogen, oxygen, and a small variety of other elements. The complex variety that occurs when these simple atoms are arranged into macromolecules and multifaceted, multicompartmentalized cells and organs seems to distinguish the biological system from other systems. This complex heterogeneity is something of a matter of scale however. A galaxy, a global weather system, or a coastline certainly has enormous complexity. The complexity of biological systems seems to be one of high density; in other words, biological systems seem to concentrate complex molecules together in complex envelopes called cells that are themselves concentrated into complex systems called organs that perform complex functions in organisms that frequently live in complexly constructed communities. An astronomical magnitude of complexity can therefore be found in an ant hill or under a microscope, not to mention in a city or nation-state. Yet at every level of the complexity that derives from an enormous number of degrees of freedom in the interactions of the parts, these biological systems are subject to the same forces and laws of nature as are other systems.

It is worth explicitly mentioning that there are a number of major theoretical physical constructs used to describe the behavior of everything in the universe. These are sometimes called the great theories of physics. They include:

1. **Classical or Newtonian mechanics**, which describes the motion of large material objects, such as planets and satellites, and the trajectory of balls and missiles.
2. **Quantum mechanics**, which describes the motion and behavior of submicroscopic objects. This theory explains behavior on a scale where classical mechanics is known to be incorrect, namely, the movement of subatomic particles such as electrons and protons.
3. **Relativity**, which describes high-speed motion and is based on the fundamental concept that all aspects of nature obey the same set of invariant laws. Like the quantum theory, relativistic theory describes motion in cases where classical mechanics is known to be incorrect.
4. **Electromagnetism**, which explains the behavior of electricity, magnetism, and electromagnetic radiation.
5. **Thermodynamics**, which describes the behavior of large numbers of particles and discusses these behaviors in terms of heat, temperature, and work.

The behavior of chemical and biological systems is consistent with these theories, and they are the source of the fundamental unity that binds different systems together. It will be necessary to invoke aspects of these physical theories as an understanding of biological systems is built. Although biological systems have great complexity, the threads of these theories will be found over and over again running through the analysis. In this book, it will seem that preference is being given to the theories of thermodynamics. This is not an unjustified conclusion, but it is important that the reader does not take such a dependence on thermodynamic formulation to suggest a lack of relevance of the other theoretical constructs. For the subjects chosen and the depth and slant of their presentation, thermodynamics is the most convenient and simplest approach. Taking a thermodynamic approach is also often the best strategy for describing extremely complex systems completely. Finally, thermodynamics is one of the most valuable tools of the chemist. After mastering this material with a thermodynamic scheme, the student will invariably be ready to extend an interest to the application of the other theories to biological problems.

If biological systems are so complex, how are they ever to be accurately described, much less understood? In fact, it is more likely that an understanding of biological processes will be attained long before a detailed description will be available. Evolution is a good case in point. The form,