

Physical Chemistry:
Principles & Applications in
Biological Sciences 3rd ed

Third Edition

PHYSICAL CHEMISTRY

**Principles and Applications
in Biological Sciences**

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Preface to Third Edition

The third edition has been revised to make it obvious to students in the biological sciences why they need to learn physical chemistry. We start with a chapter which describes important problems in biology and medicine currently being studied by physical methods. Each succeeding chapter starts with sections on concepts and applications which show how the concepts the students learn in the chapter apply to biological and biochemical problems. Molecular interpretations of macroscopic properties—thermodynamics and transport properties—are emphasized in the next five chapters (Chapters 2–6). For example, in Chapter 3 we give an extensive discussion of entropy as a measure of disorder. The structures of proteins and nucleic acids are described in Chapter 3 so that they can be used in applications, examples, and problems freely afterwards.

Chapter 6 (MOLECULAR MOTION AND TRANSPORT PROPERTIES) has been changed extensively. Discussion of the Boltzmann energy distribution and the random walk has been introduced. The section on gel electrophoresis has been expanded to mirror the many new applications in separating proteins and very large DNAs, as well as in studying binding of proteins to nucleic acids.

Chapters 7 and 8 (KINETICS: RATES OF CHEMICAL REACTIONS, and ENZYME KINETICS) have been rearranged so that temperature-jump kinetics is now in the kinetics chapter where it belongs logically. The kinetics of competing substrates are discussed with application to the fidelity of DNA replication.

The chapter on MOLECULAR STRUCTURE AND INTERACTIONS: THEORY (Chapter 9, originally titled QUANTUM MECHANICS) now begins with intermolecular and intramolecular forces and the use of semi-empirical methods to calculate molecular conformations. This leads into the discussion of quantum mechanics.

The chapter on MOLECULAR STRUCTURE AND INTERACTIONS: SPECTROSCOPY (Chapter 10) has an increased emphasis on nuclear magnetic resonance. Two-dimensional NMR and magnetic resonance imaging are treated.

Chapter 11 (MOLECULAR DISTRIBUTIONS AND STATISTICAL THERMODYNAMICS) has been shortened because some of the material has been introduced in earlier chapters. Discussion of quantum mechanical distributions has been deleted.

Chapter 12 (MACROMOLECULAR STRUCTURES AND X-RAY DIFFRACTION) has a more detailed discussion of how a structure is obtained from a measured diffraction pattern. Scanning tunneling and atomic force microscopes are described.

There are now more problems at the end of each chapter; many old problems have been improved or deleted. Essentially all of the problems are biologically relevant. The references and suggested readings have been brought up to date and expanded.

Throughout the book we have tried to make the writing clearer and more explicit; the important equations are explained in words. The students, teaching assistants, and faculty in the biophysical chemistry courses at Berkeley pointed out sections that were unclear, and several reviewers of this new edition made very helpful comments. We are particularly grateful to our colleagues, Professor David Wemmer and Dr. Joseph Monforte, who made detailed comments and who contributed their homework and exam problems. Joan Tinoco prepared the Index. We would also like to acknowledge the following reviewers: James E. Davis, Harvard University; Eckard Münck, Carnegie Mellon University; Donald J. Nelson, Clark University; T. M. Schuster, University of Connecticut; Maurice Schwartz, University of Notre Dame; George Strauss, Rutgers University; and Jimmy W. Viers, Virginia Polytechnic Institute and State University.

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Introduction

Physical chemistry is a group of principles and methods helpful in solving many different types of problems. In the following chapters we will present the principles of thermodynamics, transport properties, kinetics, quantum mechanics and molecular interactions, spectroscopy, and scattering and diffraction. We will also discuss various experimentally measurable properties, such as enthalpy, electrophoretic mobility, light absorption, and x-ray diffraction. All these experimental and theoretical methods can give useful information about the part of the universe you are interested in. We will emphasize the molecular interpretation of these methods, and stress biochemical and biological applications, but it is up to you to see how the methods presented here can be applied to the problems that interest you. By learning the principles behind the methods, you will be able to judge the conclusions obtained from them. This is the first step in inventing new methods, or discovering new concepts.

Chapters 2 through 5 of this book cover the fundamentals of thermodynamics, and their applications to chemical reactions and physical processes. Much of this should be a review of material covered in beginning chemistry courses, so the applications to biological macromolecules can be emphasized. Chapter 6 describes the effect of sizes and shapes of molecules on their motions in gases, liquids, and gels. The driving forces are either random thermal forces which cause diffusion, or the directed forces in sedimentation, flow, and electrophoresis. Chapter 6 thus covers transport properties. Chapter 7 describes general kinetics, and Chapter 8 concentrates on the kinetics of enzyme-catalyzed reactions. Chapter 9 deals with molecular structures and intermolecular interactions. Quantum mechanical principles are introduced so that bonding and spectroscopy can be understood. Calculations of protein and nucleic acid conformations by the use of classical force fields (Coulomb's law, van der Waals potential) are described. Chapter 10 includes the main spectroscopic methods used for studying molecules in solution: ultraviolet, visible, and infrared absorption; circular dichroism and optical rotatory dispersion; and nuclear magnetic resonance. Chapter 11 introduces the principles of statistical thermodynamics and describes their biochemical applications. Topics such as helix-coil transitions in polypeptides (proteins) and polynucleotides (nucleic acids), and binding of small molecules to macromolecules are

emphasized. Chapter 12 starts with the scattering of electromagnetic radiation from one electron, and proceeds through the diffraction of x rays by crystals. New scanning microscope methods are introduced. The Appendices contain numerical data used throughout the book, unit conversion tables, and the structures of many of the biological molecules mentioned in the text.

Other books will be useful as background sources and to provide more depth of coverage. For applications of physical chemistry to other areas, there are standard physical chemistry texts. Biochemistry and molecular biology texts can provide specific information about such areas as enzyme mechanisms, metabolic paths, and structures of membranes. Finally, a good physics textbook is useful for learning or reviewing the fundamentals of forces, charges, electromagnetic fields, and energy. A list of books is given at the end of this chapter.

In the next sections we present a few examples of problems that physical chemistry can solve. They should be read for pleasure, not for memorization. The aim is simply to illustrate some current research from the scientific literature, and to point out the principles and methods which are used. We hope to motivate you to learn the material discussed in the following chapters. It will help if you pick an article with a title that interests you from a journal such as *Nature* or *Science*, or even *Scientific American*, to learn how this book will make it easier for you to understand the article.

THE HUMAN GENOME

A goal of the Human Genome Project is to learn the complete sequence of all three billion (3×10^9) base pairs which make up the genetic information of humans—the human genome. Genes are sequences of base pairs in double-stranded DNA. In human sperm the DNA is packaged in 23 chromosomes: 22 autosomes plus a male Y chromosome or a female X chromosome. In human eggs the DNA is packaged in 22 autosomes plus a female X chromosome. Thus, each of us acquires 23 pairs of chromosomes; the XX pair makes us female, the XY male. Nobody knows how many human genes there are; estimates range from 50,000 to 100,000. It is known that less than 10% of the human DNA consists of genes. The rest may be structural regions that fold the DNA into a required three-dimensional shape, or sequences that have lost their function during evolution. There are long regions of highly repetitive sequences which are useful for distinguishing human DNA from other species, but do not have known biological functions. Identifying genes and learning their arrangement on the chromosomes is of great importance in medicine, but learning about the rest of the DNA may be a more fundamental advance.

The DNA sequence with its alphabet of four letters (A, C, G, T) is transcribed into the RNA alphabet (A, C, G, U). The RNA is translated into a protein sequence of 20 amino acids in a three-letter code.* As there are 4^3 (64) three-letter words with an alphabet of four letters, the code must be redundant. In the genetic dictionary most amino acids are coded

* The structures and names of the nucleic acid bases and the protein amino acids are given in Appendix A.9.