PHYSICAL CHEMISTRY

Principles and Applications in Biological Sciences

Ignacio Tinoco, Jr.
University of California, Berkeley

Kenneth Sauer
University of California, Berkeley

James C. Wang
Harvard University

CHEMISTRY

Principles and Applications in Biological Sciences

PRENTICE-HALL, INC., ENGLEWOOD CLIFFS, NEW JERSEY 07632

Library of Congress Cataloging in Publication Data

Tinoco, Ignacio.
PHYSICAL CHEMISTRY.

Includes bibliographies and index.
1. Biological chemistry. 2. Chemistry, Physical and theoretical. I. Sauer, Kenneth, (date) joint author. II. Wang, James C., joint author. III. Title.
QH345.T56 541'.02'4574 77-25417
ISBN 0-13-665901-2

PHYSICAL CHEMISTRY
Principles and Applications in Biological Sciences
Ignacio Tinoco, Jr., Kenneth Sauer, and James C. Wang

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

PRENTICE-HALL INTERNATIONAL, INC., *London*
PRENTICE-HALL OF AUSTRALIA PTY. LIMITED, *Sydney*
PRENTICE-HALL OF CANADA, LTD., *Toronto*
PRENTICE-HALL OF INDIA PRIVATE LIMITED, *New Delhi*
PRENTICE-HALL OF JAPAN, INC., *Tokyo*
PRENTICE-HALL OF SOUTHEAST ASIA PTE. LTD., *Singapore*
WHITEHALL BOOKS LIMITED, *Wellington, New Zealand*

PHYSICAL CHEMISTRY

PHYSICAL

Ignacio Tinoco, Jr.

University of California, Berkeley

Kenneth Sauer

University of California, Berkeley

James C. Wang

Harvard University

Preface

We have been teaching a course in physical chemistry for the biological science majors at Berkeley for the past fifteen years. Most of the students are undergraduates from biochemistry, physiology, bacteriology, botany, and zoology departments. They include most of the premedical students. In addition a few graduate students in the biological sciences are always represented. We have found it difficult to find a suitable text for these students. Standard physical chemistry texts have too much material irrelevant to the biochemist, and they mainly ignore macromolecules and biological systems. Life science physical chemistry texts often omit too much fundamental physical chemistry, and although they discuss biological problems, they do so only at an elementary level. Modern physical methods used by molecular biologists and biochemists, such as density gradient sedimentation, fluorescence energy transfer, and electron microscopy, are usually not included.

We have written a book to provide a fundamental understanding of the physical chemistry important to biochemists and biologists. Each physical chemical principle is related and applied to biological problems. We thus try to teach basic physical chemistry, while motivating the student by stressing biochemical applications. We also discuss most of the physical methods and ideas that modern biological scientists use.

The book contains an introductory chapter describing the types of problems in biology or medicine to which physical chemistry can be applied. The next four chapters cover thermodynamics. The emphasis is on solution thermodynamics. One complete chapter deals with the equilibrium constant, activities, and free energy. A chapter on physical equilibria includes equilibrium dialysis, active transport, surfaces, and the use of colligative properties in measuring molecular weights.

Transport properties are treated in Chapter 6. A short discussion on kinetic theory of gases is followed by a thorough description of diffusion, viscosity, sedimentation, and electrophoresis. The application of each of these properties to the determination of size and shape of macromolecules is stressed. Molecular weights, axial ratios, hydration, and flexibility of nucleic acids and proteins are described.

There are two chapters on kinetics. The kinetics and mechanisms of reactions in solution are emphasized. The chapter on enzyme kinetics includes a discussion of temperature-jump kinetics.

The first eight chapters require only a minimum of mathematical knowledge beyond algebra. Although calculus is used in these chapters, only differentiation and integration of powers of x are required. Partial derivatives are introduced, but the text and problems mainly can be understood without them. The next four chapters assume more mathematical confidence on the part of the students. The mathematical steps are explained in detail (as before), but the student will feel more confident with a course in calculus for background.

Chapter 9 introduces quantum mechanics to provide a vocabulary for spectroscopy and chemical structure. A particle in a box is treated and applied to the free electron model for conjugated molecules. Qualitative discussions of molecular orbitals, and molecular structure and reactivity are given. The spectroscopy chapter deals mainly with electronic spectra of organic molecules. Ultraviolet and visible absorption, fluorescence, circular dichroism, and optical rotatory dispersion are discussed. Application of each of these methods to the study of proteins and nucleic acids is included. A short section on nuclear magnetic resonance is presented.

The application of statistical methods to macromolecules is emphasized in Chapter 11. Cooperative binding of small molecules to a macromolecule is described. The random walk is applied to diffusion and polymer dimensions. Helix-coil transitions in polypeptides and polynucleotides are discussed. The statistical thermodynamic definitions of energy, work, and entropy are described.

The last chapter gives the basic fundamentals of x-ray diffraction. Applications to structures of macromolecules are discussed. Qualitative descriptions of neutron scattering, electron microscopy, and their application to biological samples are given.

The Appendices contain tables of thermodynamic data, conversion factors, abbreviations, and structures of biological molecules mentioned in the text. The reader is encouraged to keep looking through the Appendix while using the book.

At Berkeley we have found it possible to cover most of the book in two quarters. This keeps the students and the instructor working hard. Two semesters or three quarters might be a more reasonable time to spend on the material covered in the book. The first five chapters form a complete treatment of the thermodynamics most useful for the biological scientists. The remaining chapters can essentially stand by themselves. The instructor can teach them in any order or omit any of them. For example, the applications in the spectroscopy chapter do not require knowledge of quantum mechanics.

We have tried to make this book useful to students and instructors with a wide range of backgrounds. There are many worked examples in the text; there are many problems at the end of each chapter. Each chapter has a summary and also a review of the mathematics needed for the chapter. The first half of the book uses less mathematics (and describes it more fully) than the last half. There are references to the current literature for most chapters. We hope that the readers of this book will tell us about aspects of the book which need improving.

We are happy to acknowledge the many people who contributed to this project. In the past several years, the students of Chemistry 109A,B at Berkeley and the teaching assistants made many helpful suggestions. Our faculty colleagues who also taught the course were often properly critical. Dr. Leonard Peller, University of California, San Francisco, read essentially the entire book and made detailed criticisms. Dr. Helen Berman carefully reviewed Chapter 12. Reviewers chosen by Prentice-Hall gave useful suggestions. Drs. Paul Hartig, Che-Hung Lee, and Esther Yang kindly contributed original data. Suzanne Pfeffer and Robert Sauer solved all the problems from several chapters and helped to clarify their presentation. We wish to thank all of these people.

We are grateful to Marshall Tuttle who typed and retyped the various editions of the manuscript. His cheery disposition encouraged us to continue.

Berkeley, California

Cambridge, Massachusetts

IGNACIO TINOCO, JR.
KENNETH SAUER
JAMES C. WANG

Contents

11 MOLECULAR DISTRIBUTIONS AND STATISTICAL THERMODYNAMICS 481

12 X-RAY DIFFRACTION AND RELATED TOPICS 548

1 Introduction

Physical chemistry is a group of principles and methods that are helpful in solving many different types of problems. Just as the methods of algebra can be applied to many problems, so can the methods of thermodynamics. In the following chapters we shall present the principles of thermodynamics, kinetics, quantum mechanics, and statistical thermodynamics. We shall also discuss various experimentally measurable properties, such as viscosity, light absorption, and x-ray diffraction. All these experimental and theoretical methods can give us useful information about the part of the universe we are interested in. We will stress biochemical and biological applications in this book, but it is up to the reader to see how the methods presented can be applied to other specific problems of interest. For applications of physical chemistry to other areas, the reader is directed to standard physical chemistry texts. Biochemistry and molecular biology texts can provide specific information about such areas as enzyme mechanisms, metabolic paths, and structure of membranes. Finally, a good physics textbook is useful for learning or reviewing the fundamentals of forces, charges, photons, and energy. A list of such books is given at the end of the chapter.

In this introductory chapter we shall give a few examples of the types of problems that physical chemistry can solve.

Energy Efficiency

The minimum amount of food that an average, adult human being at rest needs every day to survive corresponds to about 1500 kcal of energy. This is the basal metabolic rate of a 60-kg human; it is equal to 70 W of power. Light daily activity, such as walking, studying, and eating, increases the human energy requirement to about 2000 kcal day^{-1}, or roughly 100 W. The energy we eat is food energy converted from solar energy by photosynthesis. We convert this food energy directly to heat or to some form of work outside the body. There is obviously a long chain of energy-converting steps involved in this solar-energy to human-energy process. It is to our advantage to understand these steps and to be able to improve their efficiency. The efficient conversion of energy from one form to another is the subject of thermodynamics.

The amount of solar energy reaching the earth's atmosphere is 1.4 kW m^{-2} (2 cal min^{-1} cm^{-2}), but only about one half of this reaches the surface of the earth. This is the total energy input available to us for food productivity. Naturally occurring photosynthesis in plants is only about 1% efficient, so about 100 kcal of food can be grown per day per square meter of the earth's surface. This means that a minimum of 20 m^2 is needed to raise food for one person. However, in the United States we spend about 10 cal of energy to produce and prepare 1 cal of food (Steinhart and Steinhart, 1974). Figure 1.1 shows how this added energy has increased over the years. The energy input occurs about one fourth at the farm (fertilizer, machinery, irrigation), one third in refrigeration and cooking, and the rest in the processing industry. How can knowledge of physical chemistry and thermodynamics help? Just knowing the amounts of energy involved may make us more conscious of the real cost of eating highly processed foods. But more important is the fact that thermodynamics can tell us the maximum possible efficiency for performing a certain task. The first and second laws of thermodynamics tell us the maximum amount of heat or work that can be transferred in a particular process for a given energy input. Analysis of U.S. energy uses shows an average efficiency of only 10% of the maximum efficiency possible (*Physics Today*, 1975). For example, refrigeration efficiency is only 4% of theoretical thermodynamic efficiency, and truck transportation is 10% of theoretical efficiency. Improving refrigeration and transport efficiency would allow us to have food variety all year round yet not spend 10 times its food-energy value.

How about human efficiency? The energy cost of transportation can be defined as the amount of power used divided by the weight and velocity of the moving object. The energy cost is unitless; it is energy input per time (power) divided by the weight (a force) times distance moved per time. The minimum cost of walking occurs at a velocity of 3.8 mph for a 150-lb human. The metabolic rate for this fast walker is about 450 W and the cost of transport is 0.38. The minimum cost of transport for a bicyclist is 0.1 and is the most efficient transportation by an animal; only large fish or whales may be as efficient. Freight trains and freight steamers are the most efficient form of any kind of transportation; their minimum cost is about 0.01 (Tucker, 1975).