

Second Edition

PHYSICAL CHEMISTRY

for the

BIOLOGICAL SCIENCES

Gordon G. Hammes • Sharon Hammes-Schiffer

WILEY

**PHYSICAL CHEMISTRY
FOR THE BIOLOGICAL
SCIENCES**

METHODS OF
BIOCHEMICAL ANALYSIS

Volume 55

A complete list of the titles in this series appears at the end of this volume.

PHYSICAL CHEMISTRY FOR THE BIOLOGICAL SCIENCES

SECOND EDITION

Gordon G. Hammes
Sharon Hammes-Schiffer

Part of Wiley Series in Methods of Biochemical Analysis

WILEY

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Preface to First Edition

Biology is the study of living species. The historic origin of biology is descriptive in nature, a classification and description of the various biological species. Modern biology is far different and seeks to understand living phenomena on a molecular basis. The incredible amount of information available and the databases of this information are staggering, the most obvious example being the nucleotide sequence of the human genome. In essence, biology has moved from a qualitative to a quantitative science. Inevitably, this requires a theoretical framework and associated mathematics. Physical chemistry provides this framework for molecular structure and chemical reactions, the components of all biological systems that ultimately must be understood.

Traditionally, physical chemistry has been a major training component for chemists, but not for biologists. This has been attributed to the relatively sophisticated mathematical underpinnings of rigorous physical chemistry. However, the concepts of physical chemistry can be understood and applied to biology with a minimum of mathematics.

This volume attempts to present physical chemistry in conceptual terms using mathematics only at an upper level of elementary calculus, a level required for all science students. Nevertheless, the approach is quantitative in nature, with explicit calculations and numerical problems. Examples from biology are used to illustrate the principles, and problems are appended at the end of each chapter. This book is intended to serve as a one-semester introduction to physical chemistry for undergraduate biology majors and as a refresher course for first-year graduate students. This book combines two volumes published earlier, *Thermodynamics and Kinetics for the Biological Sciences* and *Spectroscopy for the Biological Sciences*. These two books have been integrated with some additions and modification. The most notable addition is a chapter on the hydrodynamics of macromolecules. Hydrodynamics is the basis of several important laboratory techniques used in molecular biology, and understanding the underlying concepts will permit better use of the methods and development of new methods.

We begin with a discussion of thermodynamics, a subject that provides a convenient framework for all equilibrium phenomena. This is followed by chemical kinetics, the quantitative description of the time dependence of chemical reactions. For both subjects, multiple applications to biology are presented. The concepts associated with spectroscopy and structure determination are then considered. These topics deal with the molecular nature of matter and the techniques used to characterize molecules and their interactions. The concluding section of the book includes the important subjects of ligand binding to macromolecules, hydrodynamics, and mass

spectrometry. The coverage of this book represents the minimal knowledge that every biologist should have to understand biological phenomenon in molecular terms (in my opinion!).

I am indebted to my colleagues at Duke for their encouragement and assistance. In particular, Professors Jane and David Richardson, Lorena Beese, Leonard Spicer, Terrance Oas, Michael Fitzgerald, and Harvey Sage who have provided vital expertise. A special thanks also goes to Darla Henderson who as a Wiley editor has provided both encouragement and professional assistance in the preparation of this volume. As always, my wife Judy has provided her much appreciated (and needed) support.

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Preface to Second Edition

The impetus for preparing the second edition was twofold. First, the material in the first edition was brought up to date. Although the argument can be made that the principles of physical chemistry are timeless, new applications continually appear. We have tried to ensure that interested students will have access to the most recent developments in the areas covered in this book. Second, with the addition of a co-author, we have significantly expanded and upgraded some of the theoretical aspects of this book. The flavor of the first edition has been retained: students in the biological sciences can still obtain a working knowledge of physical chemistry without utilizing advanced calculus. However, the landscape has changed. Calculus, and even advanced calculus, is now routinely taught in high school so that many more college students have an understanding of advanced calculus. Also research in the biological sciences now includes many more applications of theory relative to ten years ago.

More specifically, five new chapters have been added. The first deals with some of the advanced aspects of thermodynamics and makes use of multivariable calculus. Two of the chapters discuss quantum mechanics in much more detail and at a higher level than the first edition. The additions include a discussion of hydrogen tunneling, as well as a chapter on atomic and molecular electronic structure, with brief treatments of Hartree-Fock and density functional theory. The last two new chapters discuss statistical mechanics. One chapter deals with the fundamentals of the subject, and the other discusses computer simulations, with an extensive treatment of molecular dynamics. Finally, an appendix has been added to introduce the fundamentals of electrochemistry.

As a result of these changes, the second edition contains more material than can be covered in a one semester course. However, the instructor can pick and choose the material to be included for such a course. In fact, this text is suitable for a traditional two semester physical chemistry course. Although a few traditional subjects are not covered, there is more than enough material for two semesters. We have intentionally not designed this text to be encyclopedic in nature to make it more accessible to students for self-study.

We are grateful to a number of people for their assistance in reviewing specific aspects of the book. These people include Professor Nicholas Winograd (Pennsylvania State University), Professor Terrance Oas (Duke University), and Professor Leonard Spicer (Duke University). We again want to thank Professors Jane and David Richardson for the marvelous color plates which have been retained from the first edition. Special thanks are due to Dr. Joshua Layfield, who prepared most of the figures for the new material in the second edition and provided valuable

insights. We also want to acknowledge the support of our spouses, Judy and Peter, who have provided much needed patience and encouragement in this father-daughter endeavor.

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THERMODYNAMICS

Heat, Work, and Energy

1.1 INTRODUCTION

Thermodynamics is deceptively simple or exceedingly complex, depending on how you approach it. In this book, we will be concerned with the principles of thermodynamics that are especially useful in thinking about biological phenomena. The emphasis will be on concepts, with a minimum of mathematics. Perhaps an accurate description might be rigor without *rigor mortis*. This may cause some squirming in the graves of thermodynamic purists, but the objective is to provide a foundation for researchers in experimental biology to use thermodynamics. This includes cell biology, microbiology, molecular biology, and pharmacology, among others. A more advanced treatment of some aspects of thermodynamics is presented in Chapter 4. Excellent texts are available that present a more complete exposition of thermodynamics (cf. Refs. 1–3).

In point of fact, thermodynamics can provide a useful way of thinking about biological processes and is indispensable when considering molecular and cellular mechanisms. For example, what reactions and coupled physiological processes are possible? What are the allowed mechanisms involved in cell division or in protein synthesis? What are the thermodynamic considerations that cause proteins, nucleic acids, and membranes to assume their active structures? It is easy to postulate biological mechanisms that are inconsistent with thermodynamic principles—but just as easy to postulate those that are consistent. Consequently, no active researcher in biology should be without a rudimentary knowledge of the principles of thermodynamics. The ultimate goal of this exposition is to understand what determines equilibrium in biological systems and how these equilibrium processes can be coupled together to produce living systems, even though we recognize that living organisms are not at equilibrium. Thermodynamics provides a unifying framework for diverse systems in biology. Both a qualitative and a quantitative understanding are important and will be developed.

The beauty of thermodynamics is that a relatively small number of postulates can be used to develop the entire subject. Perhaps the most important part of this development is to be very precise with regard to concepts and definitions, without

getting bogged down with mathematics. Thermodynamics is a macroscopic theory, not molecular. As far as thermodynamics is concerned, molecules need not exist. However, we will not be purists in this regard: If molecular descriptions are useful for understanding or introducing concepts, they will be used. We will not hesitate to give molecular descriptions of thermodynamic results, but we should recognize that these interpretations are not inherent in thermodynamics itself. It is important to note, nevertheless, that large collections of molecules are assumed so that their behavior is governed by Boltzmann statistics; that is, the normal thermal energy distribution is assumed. This is almost always the case in practice. Furthermore, thermodynamics is concerned with time-independent systems, that is, systems at equilibrium. Thermodynamics has been extended to nonequilibrium systems, but we will not be concerned with the formal development of this subject here.

The first step is to define the *system*. A thermodynamic system is simply that part of the universe in which we are interested. The only caveat is that the system must be large relative to molecular dimensions. The system could be a room, it could be a beaker, it could be a cell, etc. An *open system* can exchange energy and matter across its boundaries, for example, a cell or a room with open doors and windows. A *closed system* can exchange energy but not matter, for example, a closed room or box. An *isolated system* can exchange neither energy nor matter, for example, the universe or, approximately, a closed Dewar flask. We are free to select the system as we choose, but it is very important that we specify what it is. This will be illustrated as we proceed. The *properties* of a system are any measurable quantities characterizing the system. Properties are either *extensive*, proportional to the amount of material in the system, or *intensive*, independent of the amount of material. Examples of extensive properties are mass and volume. Examples of intensive properties are temperature, pressure, and color.

1.2 TEMPERATURE

We are now ready to introduce three important concepts: temperature, heat, and work. None of these are unfamiliar, but we must define them carefully so that they can be used as we develop thermodynamics.

Temperature is an obvious concept, as it simply measures how hot or cold a system is. We will not belabor its definition and will simply assert that thermodynamics requires a unique temperature scale, namely, the Kelvin temperature scale. The Kelvin temperature scale is related to the more conventional Celsius temperature scale by the definition

$$T_{\text{Kelvin}} = T_{\text{Celsius}} + 273.16 \quad (1-1)$$

Although the temperature on the Celsius scale is referred to as “degrees Celsius,” by convention degrees are not stated on the Kelvin scale. For example, a temperature of 100 °C is 373 K. (Thermodynamics is entirely logical—some of the conventions used are not.) The definition of *thermal equilibrium* is very simple: When two systems are at the same temperature, they are at thermal equilibrium.

1.3 HEAT

Heat flows across the system boundary during a change in the state of the system because a temperature difference exists between the system and its surroundings. We know of many examples of heat: Some chemical reactions produce heat, such as the combustion of gas and coal. Reactions in cells can produce heat. By convention, heat flows from higher temperature to lower temperature. This fixes the sign of the heat change. It is important to note that this is a convention and is not required by any principle. For example, if the temperature of the surroundings decreases, heat flows to the system, and the sign of the heat change is positive (+). A simple example will illustrate this sign convention as well as the importance of defining the system under consideration.

Consider two beakers of the same size filled with the same amount of water. In one beaker, A, the temperature is 25 °C, and in the other beaker, B, the temperature is 75 °C. Let us now place the two beakers in thermal contact and allow them to reach thermal equilibrium (50 °C). This situation is illustrated in Figure 1-1. If the system is defined as A, the temperature of the system increases, so the heat change is positive. If the system is defined as B, the temperature of the system decreases, so the heat change is negative. If the system is defined as A and B, no heat flow occurs across the boundary of the system, so the heat change is zero! This illustrates how important it is to define the system before asking questions about what is occurring.

The heat change that occurs is proportional to the temperature difference between the initial and final states of the system. This can be expressed mathematically as

$$q = C(T_f - T_i) \quad (1-2)$$

where q is the heat change, the constant C is the *heat capacity*, T_f is the final temperature, and T_i is the initial temperature. This relationship assumes that the heat capacity is constant, independent of the temperature. In point of fact, the heat capacity often changes as the temperature changes, so that a more precise definition puts this relationship in differential form:

$$dq = C dT \quad (1-3)$$

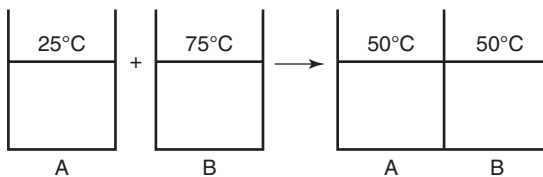


FIGURE 1-1. Illustration of the establishment of thermal equilibrium and importance of defining the *system* carefully. Two identical vessels filled with the same amount of liquid, but at different temperatures, are placed in contact and allowed to reach thermal equilibrium. A discussion of this figure is given in the text.

Note that the heat change and the heat capacity are extensive properties—the larger the system, the larger the heat capacity and the heat change. Temperature, of course, is an intensive property.

1.4 WORK

The definition of *work* is not as simple as that for heat. Many different forms of work exist, for example, mechanical work, such as muscle action, and electrical work, such as ions crossing charged membranes. We will use a rather artificial, but very general, definition of work that is easily understood. Work is a quantity that can be transferred across the system boundary and can always be converted to lifting and lowering a weight in the surroundings. By convention, work done on a system is positive: this corresponds to lowering the weight in the surroundings.

You may recall that mechanical work, w , is defined as the product of the force in the direction of movement, F_x , times the distance moved, x , or in differential form

$$dw = F_x dx \quad (1-4)$$

Therefore, the work to lower a weight is $-mgh$, where m is the mass, g is the gravitational constant, and h is the distance the weight is lowered. This formula is generally useful: for example, mgh is the work required for a person of mass m to walk up a hill of height h . The work required to stretch a muscle could be calculated with Eq. (1-4) if we knew the force required and the distance the muscle was stretched. Electrical work, for example, is equal to $-EIt$, where E is the electromotive force, I is the current, and t is the time. In living systems, membranes often have potentials (voltages) across them. In this case, the work required for an ion to cross the membrane is $-zF\Psi$, where z is the charge of the ion, F is the Faraday (96,489 coulombs/mole), and Ψ is the potential. A specific example is the cotransport of Na^+ and K^+ , Na^+ moving out of the cell and K^+ moving into the cell. A potential of -70 mV is established on the inside so that the electrical work required to move a mole of K^+ ions to the inside is $-(1)(96,489)(0.07) = -6750$ Joules. ($\Psi = \Psi_{\text{outside}} - \Psi_{\text{inside}} = +70$ mV.) The negative sign means that work is done by the system.

Although not very biologically relevant, we will now consider in some detail pressure–volume work, or $P - V$ work. This type of work is conceptually easy to understand, and calculations are relatively easy. The principles discussed are generally applicable to more complex systems, such as those encountered in biology. As a simple example of $P - V$ work, consider a piston filled with a gas, as pictured in Figure 1-2. In this case, the force is equal to the external pressure, P_{ex} , times the area, A , of the piston face, so the infinitesimal work can be written as

$$dw = -P_{\text{ex}} A dx = -P_{\text{ex}} dV \quad (1-5)$$

If the piston is lowered, work is done on the system and is positive, whereas if the piston is raised, work is done by the system and is negative. Note that the work done

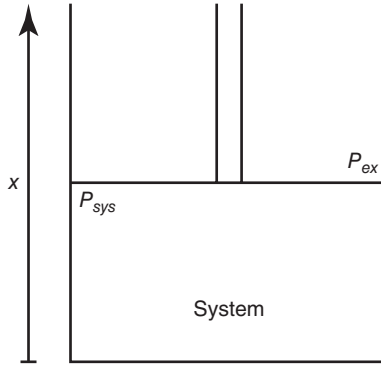


FIGURE 1-2. Schematic representation of a piston pushing on the system. P_{ex} is the external pressure and P_{sys} is the pressure of the system.

on or by the system by lowering or raising the piston depends on what the external pressure is. Therefore, the work can have any value from 0 to ∞ , depending on how the process is done. This is a very important point: the work associated with a given change in state depends on *how* the change in state is carried out.

The idea that work depends on how the process is carried out can be illustrated further by considering the expansion and compression of a gas. The $P - V$ isotherm for an ideal gas is shown in Figure 1-3. An ideal gas is a gas that obeys the ideal gas law, $PV = nRT$ (n is the number of moles of gas and R is the gas constant). The behavior of most gases at moderate pressures is well described by this relationship. Let us consider the expansion of the gas from P_1, V_1 to P_2, V_2 . If this expansion is done with the external pressure equal to zero, that is, into a vacuum, the work is zero. Clearly, this is the minimum amount of work that can be done for this change in state. Let us now carry out the same expansion with the external pressure equal to P_2 . In this case, the work is

$$w = - \int_{V_1}^{V_2} P_{ex} dV = -P_2(V_2 - V_1) \quad (1-6)$$

which is the striped area under the $P - V$ curve. The expansion can be broken into stages; for example, first expand the gas with $P_{ex} = P_3$ followed by $P_{ex} = P_2$, as shown in Figure 1-3. The work done by the system is then the sum of the two rectangular areas under the curve. It is clear that as the number of stages is increased, the magnitude of the work done increases. The maximum work that can be done by the system is when the external pressure is set equal to the pressure of the system minus a small differential pressure, dP , throughout the expansion. This can be expressed as

$$w_{max} = - \int_{V_1}^{V_2} PdV \quad (1-7)$$

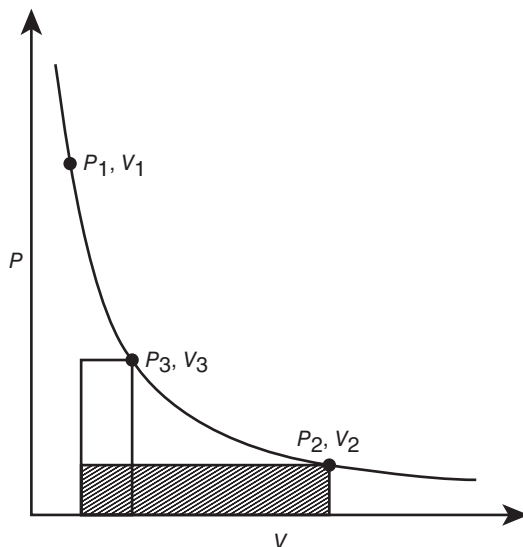


FIGURE 1-3. A P - V isotherm for an ideal gas. The narrow rectangle with both hatched and open areas is the work done in going from P_1, V_1 to P_3, V_3 with an external pressure of P_3 . The hatched area is the work done by the system in going from P_1, V_1 to P_2, V_2 with an external pressure of P_2 . The maximum amount of work done by the system for this change in state is the area under the curve between P_1, V_1 and P_2, V_2 .

By a similar reasoning process, it can be shown that for a compression the minimum work done on the system is

$$w_{\min} = - \int_{V_2}^{V_1} P dV \quad (1-8)$$

This exercise illustrates two important points. First, it clearly shows that the work associated with a change in state depends on how the change in state is carried out. Second, it demonstrates the concept of a *reversible path*. When a change in state is carried out such that the surroundings and the system are not at equilibrium only by an infinitesimal amount, in this case dP , during the change in state, the process is called reversible. The concept of reversibility is only an ideal—it cannot be achieved in practice. Obviously, we cannot really carry out a change in state with only an infinitesimal difference between the pressures of the system and surroundings. We will find this concept very useful, nevertheless.

Now let us think about a cycle whereby an expansion is carried out followed by a compression that returns the system back to its original state. If this is done as a one-stage process in each case, the total work can be written as

$$w_{\text{total}} = w_{\text{exp}} + w_{\text{comp}} \quad (1-9)$$

or

$$w_{\text{total}} = -P_2(V_2 - V_1) - P_1(V_1 - V_2) \quad (1-10)$$

or

$$w_{\text{total}} = (P_1 - P_2)(V_2 - V_1) > 0 \quad (1-11)$$

In this case, net work has been done on the system. For a reversible process, however, the work associated with compression and expansion is

$$w_{\text{exp}} = - \int_{V_1}^{V_2} PdV \quad (1-12)$$

and

$$w_{\text{comp}} = - \int_{V_2}^{V_1} PdV \quad (1-13)$$

so that the total work for the cycle is equal to zero. Indeed, for reversible cycles the net work is always zero.

To summarize this discussion of the concept of work, the work done on or by the system depends on how the change in state of the system occurs. In the real world, changes in state always occur irreversibly, but we will find the concept of a reversible change in state to be very useful.

Heat changes also depend on how the process is carried out. Generally, a subscript is appended to q , for example, q_P and q_V for heat changes at constant pressure and volume, respectively. As a case in point, the heat change at constant pressure is greater than that at constant volume if the temperature of a gas is raised. This is because not only must the temperature be raised, but the gas must also be expanded.

Although this discussion of gases seems far removed from biology, the concepts and conclusions reached are quite general and can be applied to biological systems. The only difference is that exact calculations are usually more difficult. It is useful to consider why this is true. In the case of ideal gases, a simple equation of state is known, $PV = nRT$, that is obeyed quite well by real gases under normal conditions. This equation is valid because gas molecules, on average, are quite far apart and their energetic interactions can be neglected. Collisions between gas molecules can be approximated as billiard balls colliding. This situation obviously does not prevail in liquids and solids where molecules are close together and the energetics of their interactions cannot be neglected. Consequently, simple equations of state do not exist for liquids and solids.

1.5 DEFINITION OF ENERGY

The first law of thermodynamics is basically a definition of the energy change associated with a change in state. It is based on the experimental observation that heat and work can be interconverted. Probably the most elegant demonstration of this is the experimental work of James Prescott Joule in the late 1800s. He carried out experiments in which he measured the work necessary to turn a paddle wheel in water and the concomitant rise in temperature of the water. With this rather primitive experiment, he was able to calculate the conversion factor between work and heat with