Biochemical Thermodynamics: Applications of Mathematica

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Preface

This book is about calculations on the thermodynamics of biochemical reactions that is based on Legendre transforms of the Gibbs energy that bring in the pH, pMg, and concentrations of coenzymes and ligands as independent variables. Chemical reactions are studied under the constraints of constant temperature and constant pressure, but biochemical reactions are studied under the additional constraints of pH and, perhaps, pMg or free concentrations of other metal ions. In considering systems of biochemical reactions, it may be useful to constrain concentrations of various coenzymes. In considering macromolecule-ligand binding it may be useful to constrain the ligand concentration. For example, the binding of oxygen by hemoglobin can be treated at specified concentrations of molecular oxygen. As more intensive variables are specified, more thermodynamic properties of a system are defined, and the equations that represent thermodynamic properties as functions of independent variables become more complicated. Since more independent variables are involved in biochemical thermodynamics than in chemical thermodynamics, the equations for calculating properties become more complicated. Thanks to the development of mathematical applications for personal computers, these complicated calculations can be carried out much more easily. Thermodynamic calculations on such systems require the use of computers, and Mathematica is a very convenient application because of its symbolic capabilities, its calculation of partial derivatives, and its facilities for construction of databases, tables, and plots. The fact that Mathematica can be used to derive these very complicated functions and take partial derivatives to obtain other properties makes it possible to make calculations that would previously have been considered impractical. Therefore, this book has been written in Mathematica. Mathematica makes it possible to intermingle text with calculations, as illustrated by a number of recent books. In this book, the calculations of biochemical thermodynamics are described in words, equations are derived by use of Mathematica, and then evaluated for specified values of independent variables. All the Mathematica calculations are shown, and so the data, equations and programs can be used for the calculation of properties of reactants at other specified values of independent variables.

The main question that thermodynamics deals with is the direction of spontaneous change when a system is initially in a specified state. The state of a biochemical reaction system is described by specifying concentrations of reactants, temperature, pH, ionic strength, and concentrations of free metal ions that are bound by reactants. Concentrations of coenzymes and ligands like molecular oxygen can also be specified. Thermodynamics is important in biochemistry because it can tell us whether a given enzyme-catalyzed reaction or ligand binding will go to the right or to the left under specified conditions. It can also give us the equilibrium composition. Enzymes determine the reactions that are catalyzed in a given system and their rates, but enzymes do not determine the directions of reactions or the amount of energy that is stored, transferred, or is required to synthesize a needed reactant. In a cell, certain reactions are needed to store energy and other reactions are needed to use this energy for necessary purposes of life. If we want to understand how energy is stored and used, we need to know the apparent equilibrium constants $K'$ of the reactions involved under the ambient conditions and also heats of reaction. Other biochemical reactions, like the binding of oxygen by hemoglobin do not require enzyme catalysis, but the equilibrium extents of binding reactions and the influence of other ligands are determined by thermodynamics. With knowledge of pKs, a measurement of the apparent equilibrium constant $K'$ of a biochemical reaction at a single pH and ionic strength makes it
possible to calculate $K'$ as a function of pH and ionic strength. When enthalpies of reaction are available and enthalpies of acid dissociation are known, a measurement of $K'$ at a single temperature, pH, and ionic strength makes it possible to calculate $K'$ and other transformed thermodynamic properties as functions of temperature, pH, and ionic strength.

The apparent equilibrium constants of about 500 enzyme-catalyzed reactions have been determined under various sets of conditions, and enthalpy changes have been measured calorimetrically for some of these reactions or can be calculated from the effect of temperature on the apparent equilibrium constant. In principle these data can be used to calculate standard Gibbs energies of formation and standard enthalpies of formation for the species of about 1000 reactants. The current number of known species matrices is 199. For 94 of these reactants, the $\Delta_f H^0$ of all species are known. Further analysis of existing experimental data and new measurements will make it possible to extend the current database BasicBiochemData3.

The most efficient way to store thermodynamic information on enzyme-catalyzed reactions is to store data on species because then apparent equilibrium constants and other transformed thermodynamic properties of reactants and reactions can be calculated for specified conditions. Such a database makes it possible to calculate apparent equilibrium constants and transformed thermodynamic properties for many more reactions than it takes to make the data table. An even larger data set can be based on analogies because of similarities in the underlying chemistry of some reactions. Such a database can be used to calculate apparent equilibrium constants that are too large to measure directly. The number of apparent equilibrium constants that can be calculated from a database increases exponentially with the number of reactants in the database. The calculation of species properties from different enzyme-catalyzed reactions reveals inconsistencies between different equilibrium and calorimetric experiments.

Apparent equilibrium constants cannot be determined experimentally on reactions that go nearly completion. Calorimetric measurements of enthalpies of reaction do not have this problem. Proteins may be reactants in enzyme-catalyzed reactions. When apparent equilibrium constants can be measured on reactions involving proteins, the thermodynamic properties of the reaction site in the protein can be calculated.

It is assumed that the reader has had some introduction to thermodynamics at the level of an undergraduate course in physical chemistry. My previous book "Thermodynamics of Biochemical Reactions," Wiley, Hoboken, NJ (2003) provides a more complete introduction to the structure of thermodynamics and its relation to statistical mechanics. This successor book is needed because more recent research has clarified the structure of biochemical thermodynamics and opened up new possibilities for learning about the flow of energy in living things. Three aspects of these calculations are as follows:

1. Experimental data on enzyme-catalyzed reactions are in the form of apparent equilibrium constants $K'$, heats of reaction, and pKs (and corresponding heats of dissociation), but the most efficient way to store the thermodynamic properties of biochemical reactions is by means of small matrices that give standard Gibbs energies of formation, standard enthalpies of formation, charge numbers, and numbers of hydrogen atoms in each species of a reactant. The bridge between treating enzyme-catalyzed reactions in terms of species and in terms of reactants, like ATP, which is a sum of species, is provided by the Legendre transform $G^\prime = G - n_c(H)\mu(H^+)$, where $G^\prime$ is the transformed Gibbs energy of the system, $G$ is the Gibbs energy of the system, $n_c(H)$ is the amount of the hydrogen component in the system (total amount of hydrogen atoms), and $\mu(H^+)$ is the specified chemical potential of hydrogen ions, which is determined by the pH. The standard transformed Gibbs energy of a biochemical reaction is given by $\Delta_r G'^0 = -RT\ln K'$. The dependence of thermodynamic properties on ionic strength can be calculated using the extended Debye-Hückel equation, which involves a temperature-dependent parameter. When a reactant consists of pseudoisomers that are at equilibrium at a specified pH, isomer group thermodynamics has to be used to calculate the standard transformed Gibbs energy of formation $\Delta_r G'^0$ of the reactant. This process leads to functions of temperature, pH, and ionic strength that are too complicated to be written out by hand, but Mathematica can be used to derive these functions and to calculate the standard transformed enthalpy of formation, standard transformed entropy of formation, average number of hydrogen ions bound, and other thermodynamic properties by taking partial derivatives.

2. Going from the experimental thermodynamic properties $K'$ and transformed enthalpies of reaction to properties of species involves the concept of the inverse Legendre transform $(G = G' + n_c(H)\mu(H^+))$. Computer programs can be written to go from the experimental properties directly to the standard Gibbs energies of formation and standard enthalpies of formation of the species involved in a reactant. These programs are more complicated than the programs using properties of species to derive the standard transformed thermodynamic properties of reactants.
3. Equilibrium compositions of systems of chemical reactions or systems of enzyme-catalyzed reactions can only be calculated by iterative methods, like the Newton-Raphson method, and so computer programs are required. These computer programs involve matrix operations for going back and forth between conservation matrices and stoichiometric number matrices. A more global view of biochemical equilibria can be obtained by specifying steady-state concentrations of coenzymes. These are referred to as calculations at the third level to distinguish them from the first level (chemical thermodynamic calculations in terms of species) and the second level (biochemical thermodynamic calculations at specified pH in terms of reactants).

In Mathematica reactants need to named with words starting with lower case letters because words starting with capital letters refer to operations. Also the names of reactants need to be as short as convenient and cannot involve spaces, subscripts, superscripts, hyphens, dots or other symbols that are Mathematica operations. Therefore, ATP is referred to as atp both in the text and in computer programs. Most of these abbreviated names will be recognized immediately, but a glossary of names is provided in the Appendix.

The Appendix contains a copy of the Mathematica notebook BasicBiochemData3.nb, Tables of Transformed Thermodynamic Properties, the Glossary of Names of Reactants, the Glossary of Symbols for Thermodynamic Properties, a List of Mathematica programs, and Sources of Biochemical Thermodynamic Information on the Web. The Mathematica package BasicBiochemData3.m, which is also available at

http://library.wolfram.com/inforcenter/MathSource/5704

contains all of the species data at 298.15 K and zero ionic strength. It also contains functions of pH and ionic strength for the standard transformed Gibbs energies of formation of 199 reactants at 298.15 K; these functions are named atp, adp,... The functions are also given for the average number of hydrogen atoms in the reactant at 298.15 K as functions of the pH and ionic strength; these functions are named atpNH, adpNH,... Since $\Delta H^\circ$ values are known for all species of 94 reactants at 298.15 K and zero ionic strength, the functions of temperature, pH, and ionic strength are given for these 94 reactants for the following transformed thermodynamic properties: $\Delta G^\circ$ (named atpGT, adpGT,...), $\Delta H^\circ$ (named atpHT, adpHT,...), $\Delta S^\circ$ (named atpST, adpST,...), and $N_H$ (named atpNHT, adpNHT,...).

Since functions of pH and ionic strength for $\Delta G^\circ$ and $N_H$ are known for 199 reactants at 298.15 K, $\Delta G^\circ$ and $\Delta N_H$ are calculated in Chapter 12 for 229 enzyme-catalyzed reactions as functions of pH and ionic strength. Since $\Delta G^\circ$ and $\Delta H^\circ$ are known for all the species of 94 reactants, functions of temperature, pH, and ionic strength that yield $\Delta G^\circ$, $\Delta H^\circ$, $\Delta S^\circ$, and $N_H$ for 90 enzyme-catalyzed reactions are given in Chapter 13.

It is not necessary to be a programmer in order to use the programs and procedures illustrated in this book. Names of reactants, temperatures, pHs, and ionic strengths are readily changed in using the various programs.

The CD at the back of the book contains the whole book in Mathematica. It can be downloaded into a personal computer with Mathematica installed, but it can be read on a computer with MathReader, which is freely available from Wolfram Research, Inc. (100 Trade Center Drive, Champaign, IL 61820-7237, and www.wolfram.com). A chapter can be downloaded into a personal computer as a notebook. The following chapters do not require that BasicBiochemData3 be loaded: Chapters 2, 3, 5, 6, and 14. Chapters 1, 4, 7, 8, 9, 10, 11, 12, 13, and 15 need BasicBiochemData3 to be loaded by typing <<BiochemThermo'BasicBiochemData3' (see Use of Mathematica).

I am indebted to Irwin Oppenheim for my introduction to Legendre transforms. I am indebted to Robert N. Goldberg for many helpful discussions of biochemical thermodynamics. I am indebted to the National Institutes of Health for support of the research on which this book is based (5-RO1-0948358). At Wiley I am indebted to my Editor Darla Henderson and Editorial Assistant Christine Moore.

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Use of Mathematica

Even if you are not familiar with Mathematica (Wolfram Research, Inc. 100 Trade Center Drive, Champaign, IL 61820-7237 and www.wolfram.com), you should be able to read this book. The concepts and calculations in biochemical thermodynamics are explained in words in the textual parts of the book. And the results of calculations are discussed in words. When Mathematica is used to make tables and figures, explanatory titles are given. Names of biochemical reactants in Mathematica call up mathematical functions of temperature, pH, and ionic strength or mathematical functions of pH and ionic strength at $T = 298.15$ K (25 °C). Since names of mathematical functions in Mathematica have to start with lowercase letters and cannot contain dots, dashes, or spaces, short names like atp are used for reactants. There is a complete list of these short names and the corresponding scientific names in the Appendix 3.

BasicBiochemData3 contains functions of pH and ionic strength that give standard transformed thermodynamic properties of 199 reactants for which values of $\Delta_f G^\circ$ are known for all species that have significant concentrations in the pH 5 to pH 9 range. Using ATP as an example, these two functions are as follows:

- atp: This function of pH and ionic strength yields the standard transformed Gibbs energy of formation of ATP at 298.15 K.
- atpNH: This function of pH and ionic strength yields the average number of hydrogen atoms in ATP at 298.15 K.

For 94 of these reactants $\Delta_f G^\circ$ and $\Delta_f H^\circ$ are known for all species that have significant concentrations in the pH 5 to pH 9 range. Using ATP as an example, these four functions are as follows:

- atpGT: This function of $T$, pH, and ionic strength yields the standard transformed Gibbs energy of formation of ATP.
- atpHT: This function of $T$, pH, and ionic strength yields the standard transformed enthalpy of formation of ATP.
- atpST: This function of $T$, pH, and ionic strength yields the standard transformed entropy of formation of ATP.
- atpNHT: This function of $T$, pH, and ionic strength yields the average number of hydrogen atoms in ATP.

Since Mathematica is a high level language that uses words like Integrate and abbreviations like D for differentiate, you can see what mathematical operations are involved in a program. Everything that is involved in making these calculations is shown. When a calculation is made, a semicolon is often put at the end of the input so that the result is not shown immediately. When calculations are performed in your computer, the semicolon can be deleted to see what the result is, but semicolons are used in the book to save space.

The CD contains the whole book in Mathematica. When you put the CD in your computer, you will see a list of chapters and appendices. If Mathematica is installed in your computer, you can click on a chapter or appendix, and it will come up on the screen. If it is Chapter 2, 3, 5, 6, or 14, all the calculations can be run by using Kernel/Evaluation/Evaluate Notebook. This will take a few seconds or a couple of minutes depending on the chapter. When you load a new chapter, you can also run a cell at a time in the order they are in the chapter. The values of arguments in programs can be changed to make calculations at different temperatures, pHs, and ionic strengths. Each chapter should be opened in a fresh workspace.

If you want to run programs in Chapters 1, 4, 7, 8, 9, 10, 11, 12, 13, or 15, BasicBiochemData3 is needed (see Appendix 1). BasicBiochemData3.nb and BasicBiochemData3.m are also available at

http://library.wolfram.com/infocenter/MathSource/5704

Note that there is a BasicBiochemicalData3.m file in the CD that is not in the printed book. When the notebook BasicBiochemData3.nb was made, a package version BasicBiochemData3.m was made automatically. The package consists of the Mathematica input without the text. The package BasicBiochemData3.m needs to be installed in your personal computer as described in the following Instructions for the use of the package BasicBiochemData3.m. When it is installed, it possible to load it into a workspace by use of <<BiochemThermo'BasicBiochemData3'. The value of a mathematical function can be calculated using ReplaceAll (/_.x->). For example, the standard transformed Gibbs energy of formation of ATP in kJ mol$^{-1}$ at
298.15 K, pH 7, and ionic strength 0.25 M can be calculated by typing \texttt{atp/pH->7/is->.25}. This value can also be obtained by typing \texttt{atpGT/t->298.15/pH->7/is->.25}.

In calculations on enzyme-catalyzed reactions, one of the ways a reaction equation can be entered is in the form \texttt{atp+h2o+de==adp+pi}. Note that hydrogen ions are never shown in a reaction equation at specified pH. Other programs may require that the reaction equation be written in the form \texttt{ec3x61x3=adp+pi-(atp+h2o)}, where the name of the reaction is the EC (Enzyme Nomenclature) number with decimal points replaced by x's. It is especially simple to change the ranges of independent variables in tables and figures.

When a change is made in a chapter, the chapter can be saved in your computer, but the version in the CD cannot be changed. If you do not want to save the whole chapter, you can copy a calculation and paste it into a new notebook, where it can be saved where you want it in your computer. When you make a new notebook it needs to contain the programs that are used.

Mathematica provides for several styles of programming: functional programming, procedural programming, rule-based programming, and recursion. Almost all of the programs in this book are examples of functional programming. This is a style that is quite distinct from what is available in traditional computer languages. A functional program is a mathematical function and the inputs to the program are the arguments of the function. When the program is run, the function is applied to its arguments. The way of writing a functional program looks like a mathematical equation. For example, a function of \(x\) and \(y\) is written as \texttt{functionname[x_,y_]:=body}, where \(x\) and \(y\) are arguments. The body of the function can be a single expression or a series of expressions. The := is referred to as a delayed assignment. When the program is typed in, nothing is returned. But when the name of the function is typed in with values for the arguments, the program returns the result of the calculation. For example,

\begin{verbatim}
In[260]:=
square[x_] := x^2
In[261]:=
square[5]
Out[261]=
   25
\end{verbatim}

\textit{Instructions for the use of the package BasicBiochemData3.m}

When the 199 small matrices of species data or the 774 functions are needed, the command \texttt{<<BiochemThermo'BasicBiochemData3'}} is used to make this information available. It is necessary for the user of this book to put \texttt{BasicBiochemData3.m} in their computer so that \texttt{<<BiochemThermo'BasicBiochemData3'}} will work. To load this package properly, it is first necessary to create a folder named BiochemThermo and put \texttt{BasicBiochemData3.m} into this folder. Then it is necessary to find out where to put this folder as follows: Open a \texttt{Mathematica} session and evaluate \texttt{$UserBaseDirectory}. On my Mac computer, this yields /Users/robertalberty/Library/Mathematica. In this \texttt{Mathematica} file, you will find \texttt{Applications}. Put the folder BiochemThermo (with \texttt{BasicBiochemData3.m} in it) into this \texttt{Applications} directory. Now this package becomes available whenever you load it using \texttt{<<BiochemThermo'BasicBiochemData3'}}
When this package is loaded, all the species data on 199 reactants and the 774 functions under this package will be available for calculations. Each chapter should be opened in a fresh workspace. A whole chapter can be run by use of Kernel/Evaluation/Evaluate Notebook. The properties for adenosine triphosphate are named atpsp, atp, atpNH, atpGT, atpHT, atpST, and atpNHT. These functions are all protected; that is, none of them can be changed without unprotecting them. These thermodynamic values are based on the usual conventions of chemical thermodynamic tables that $\Delta_f G^o = \Delta_f H^o = 0$ for elements in defined reference states and for $H^+$ ($\alpha=1$).

Additional conventions are that $\Delta_f G^o = \Delta_f H^o = 0$ for glutathione$^{2-}$, NAD$^{\text{ox} -1}$, NADP$^{\text{ox} 3-}$, retinal$^0$, thioredoxin$^{\text{ox} 0}$, and ubiquinone$^{\text{ox} 0}$.

**Sources of Biochemical Thermodynamic Information on the Web**

In the lists of references in the chapters, some have URLs (Uniform Resource Locator). These URLs in the CD that contains this book are active in the sense that if you click on them in a computer connected with the Web, the data source will come up on your screen. These URLs are all given in one place in Appendix 6, which includes a short description of their content.

Biochemical Thermodynamics:
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Chapter 1  Thermodynamics of the Dissociation of Weak Acids

1.1 Basic Chemical Thermodynamics for Dilute Aqueous Solutions

1.2 Database BasicBiochemData3

1.3 Treatment of Activity Coefficients

1.4 Calculation of pH = -log[H+]

1.5 Calculation of Activity Coefficients for Ionic Species

1.6 pKs of Weak Acids at Various Ionic Strengths

1.7 pKs of Weak Acids at Various Ionic Strengths and Temperatures

1.8 Standard Thermodynamic Properties for Acid Dissociations

1.9 Discussion

References

1.1 Basic Chemical Thermodynamics for Dilute Aqueous Solutions

The first law of thermodynamics introduces a thermodynamic property $U$ of a system that is referred to as the internal energy. The change in the internal energy in a change in state of a system is given by $\Delta U = q + w$, where $q$ is the heat flow into the system and $w$ is the work done on the system. The second law of thermodynamics introduces the entropy $S$, and it has two parts. The change in entropy in a reversible change from one state of a system to another is given by $\Delta S = q/T$, where $T$ is the thermodynamic temperature. According to the second part of the second law, when a change takes place spontaneously in an isolated system, $\Delta S$ is greater than zero. This is very important because it provides a way to calculate whether a specified change in state can take place in a system on the basis of thermodynamic measurements. The entropy provides the criterion for spontaneous change and equilibrium at specified internal energy and volume: $(dS)_{U,V} \geq 0$. Thus the entropy of an isolated system increases to a maximum in a spontaneous change. These conclusions apply to systems consisting of phases that are uniform in composition and do not have gradients of temperature or concentration in them. According to the third law of thermodynamics, the entropy of a pure crystalline substance is equal to zero at absolute zero. The molar entropy of a crystalline substance at room temperature can be determined by making heat capacity measurements down to close to absolute zero.

The enthalpy $H$ of a system is defined by

$$ H = U + PV $$

(1.1-1)

The enthalpy provides the criterion for spontaneous change and equilibrium at specified internal energy and pressure:
Thus the enthalpy of a system decreases to a minimum in a spontaneous change at specified $U$ and $V$. Gibbs (1) introduced what we now refer to as the **Gibbs energy** $G$ that he defined with

$$G = U + PV - TS = H - TS$$

(1.1-2)

The Gibbs energy is especially useful in considering chemical reactions because it provides the criterion for spontaneous change and equilibrium at specified temperature and pressure: $(dG)_{T,P} \leq 0$. It decreases to a minimum in a system at specified temperature and pressure when a spontaneous change occurs. Equations 1.1-1 and 1.1-2 are called **Legendre transforms**. Note that Legendre transform 1.1-1 introduces $P$ as an independent variable, and Legendre transform 1.1-2 introduces $T$ as an independent variable. The transformed Gibbs energy $G'$ at specified pH will be introduced in Chapter 3. The transformed Gibbs energy provides the criterion for spontaneous change and equilibrium when temperature, pressure and pH are independent variables: $(dG')_{T,P,pH} \leq 0$. More information on Legendre transforms is given in Chapter 3. More information on introductory thermodynamics is given in textbooks on physical chemistry (2) and in "Thermodynamics of Biochemical Reactions" (3).

### 1.2 Database BasicBiochemData3

A long time ago chemists realized that the most efficient way to store thermodynamic data on chemical reactions is by making tables of standard thermodynamic properties of species. The NBS Tables of Chemical Thermodynamic Properties (4) gives $\Delta_f G^\circ$, $\Delta_f H^\circ$, and $S_m^\circ$ for species at 298.15 K at xero ionic strength. Since the standard molar entropy $S_m^\circ$ is not available for many species of biochemical interest, the standard entropies of formation $\Delta_f S^\circ$ are used. This property of a species is calculated by using

$$\Delta_f G^\circ = \Delta_f H^\circ - T\Delta_f S^\circ$$

(1.2-1)

Because of this relation $\Delta_f S^\circ$ is redundant, but it is of interest because the factors determining the entropy are quite different from those determining the enthalpy. The standard thermodynamic properties of some of the species of interest in biochemistry are available in the NBS Tables, but these tables are limited to inorganic species and $\mathrm{C}_1$ and $\mathrm{C}_2$. When the equilibrium constant $K$ has been determined for a chemical reaction of biochemical interest and the standard Gibbs energies of formation are available in the NBS Tables for all the species but one, the standard Gibbs energy of that one species can be calculated from the value for $K$ (see next section). When $\Delta_f H^\circ$ is available for all the species but one, the standard enthalpy of formation of that one species can also be calculated. When the properties are unknown for two species, it may be useful to assign $\Delta_f G^\circ = 0$ and $\Delta_f H^\circ = 0$ to one of the species. This was done in 1992 for adenosine so that $\Delta_f G^\circ$ and $\Delta_f H^\circ$ for all the species in the ATP series could be calculated (5). But when $\Delta_f G^\circ$ and $\Delta_f H^\circ$ became available for adenosine in dilute aqueous solution in 2001 (6), it became possible to calculate the properties of all species in the ATP series with respect to the elements.

A database on the thermodynamic properties of species of biochemical interest has been developed in Mathematica (7) as a package. In this package, BasicBiochemData3 (8), small matrices for 199 reactants (sums of species) contain the data at 298.15 K and zero ionic strength. There is a row in the matrix for each species that gives $\{\Delta_f G^\circ, \Delta_f H^\circ, z, N_H\}$ to $\Delta_f G^\circ$ and $\Delta_f H^\circ$ are given in kJ mol$^{-1}$. $N_H$ is the number of hydrogen atoms in the species. $N_H$ is not needed in this chapter, but it will play a key role in Chapter 3. The package BasicBiochemData3 exists in two forms: (1) as a Mathematica notebook BasicBiochemData3.nb, and as (2) a Mathematica package with the name BasicBiochemData3.m. The notebook form, which contains only the Mathematica input, is the first item in the Appendix of this book. The package form is loaded as follows:

```
In[2]:= Off[General::spell1];
Off[General::spell];
In[4]:= << BiochemThermo`BasicBiochemData3`
```
Chapter 1 Thermodynamics of the Dissociation of Weak Acids

Now the species matrices can be obtained by typing in the name of the reactant with the suffix sp. The species properties for the reactants in $\text{atp} + \text{h2o} = \text{adp} + \text{pi}$ are given by

$O_\text{t}[5]= \{(-2768.1, -3619.21, -4, 12), (-2811.48, -3612.91, -3, 13), (-2838.18, -3627.91, -2, 14)\}$

$O_\text{t}[6]= \{(-1906.13, -2626.54, -3, 12), (-1947.1, -2620.94, -2, 13), (-1971.98, -2638.54, -1, 14)\}$

$O_\text{t}[7]= \{(-1096.1, -1299., -2, 1), (-1137.3, -1302.6, -1, 2)\}$

$O_\text{t}[8]= \{(-237.19, -285.83, 0, 2)\}$

The names of these data matrices start with a lower case letter because capital letters are used for Mathematica operations. The names cannot contain - or a period because these are mathematical operations. $pKs$ less than 3 and more than 10 are generally ignored in the database because their effects are not significant in the range pH 5 to pH 9. The reason for using matrices in Mathematica is that the individual properties can be retrieved. $\Delta_f G^\circ (\text{ATP}^4\text{−})$ is given by

$\Delta_f G^\circ (\text{ATP}^4\text{−})$ is given by

$\Delta_f G^\circ (\text{HATP}^3\text{−})$ is given by

$\Delta_f G^\circ (\text{ATP}_4\text{−})$ is given by

1.3 Treatment of Activity Coefficients

The dissociations of weak acids play important roles in the thermodynamics of enzyme-catalyzed reactions, and so they are discussed first. Their dissociation constants determine the effects of pH on apparent equilibrium constants. The National Bureau of Standards Tables of Chemical Thermodynamic Properties (4) give the properties of species in water at 298.15 K and zero ionic strength, but biochemists are concerned with properties at ionic strengths in the physiological range. The ionic strength is defined by $I = (1/2)\sum z_j^2 c_j$, where $z_j$ is the charge number of the $j$th species and $c_j$ is its molar concentration. The Gibbs energy of formation $\Delta_f G_j$ of species $j$ in an aqueous solution is given by
Chapter 1 Thermodynamics of the Dissociation of Weak Acids

\[ \Delta_t G_j = \Delta_t G_j^0 + RT \ln \gamma_j = \Delta_t G_j^0 + RT \ln \gamma_j + RT n c_j \]  

(1.3-1)

where \( \Delta_t G_j^0 \) is the standard Gibbs energy of formation of ion \( j \) at zero ionic strength and \( \gamma_j \) is its activity coefficient. The standard Gibbs energy \( \Delta_t G_j^0 \) of formation of species \( j \) is relative to the elements it contains, each taken as \( \Delta_t G^0(\text{element}) = 0 \) for a reference form. Neutral species in water are not significantly affected by the ionic strength, but activity coefficients \( \gamma_j \) of ions in the physiological range of ionic strengths can be represented by the extended Debye-Hückel equation (9):

\[ \ln \gamma_j = -\alpha \frac{Z_j^2}{1 + (1 + B Z_j^2)} \]  

(1.3-2)

where the Debye-Hückel constant \( \alpha \) is a function of temperature, as shown in the next section, and \( B = 1.6 \text{ L}^{1/2} \text{ mol}^{-1/2} \) is an empirical constant that is taken to be independent of temperature.

At 298.15 K, the coefficient \( \alpha \) in the Debye-Hückel equation is 1.17582 kg \( ^{1/2} \text{ mol}^{1/2} \) (10). The original Debye-Hückel equation does not have the \( (1 + B Z_j^2) \) in the denominator. It is a limiting law, which means it is approached as the ionic strength approaches zero. The empirical term in the denominator leads to estimates at higher ionic strength, but should not be used above about 0.35 M. The exact thermodynamics of aqueous solutions containing ions is very complicated (11), but we will be concerned here with what might be called practical calculations. Substituting equation 1.3-2 into equation 1.3-1 yields

\[ \Delta_t G_j = \Delta_t G_j^0 - RT \frac{Z_j^2}{1 + (1 + B Z_j^2)} + RT n c_j \]  

(1.3-3)

We will actually use this equation in the form

\[ \Delta_t G_j(I) = \Delta_t G_j^0(I) + RT n c_j \]  

(1.3-4)

where the standard Gibbs energy of formation of species \( j \) at ionic strength \( I \) is given by

\[ \Delta_t G_j^0(I = 0) = \Delta_t G_j^0(I = 0) - RT \frac{Z_j^2}{1 + (1 + B Z_j^2)} \]  

(1.3-5)

Thus we will consider the standard Gibbs energy of formation of species \( j \), \( \Delta_t G_j^0(I) \), to be a function of ionic strength. A table of standard formation properties of species can be prepared for a specified ionic strength and can be used at that ionic strength without having to deal with activity coefficients.

The standard enthalpy of formation of species \( j \) at ionic strength \( I \) is obtained by applying the Gibbs-Helmholtz equation: \( H = -T^2 \{ \partial(G/T)/\partial T \} \) to equation 1.3-5.

\[ \Delta_t H_j^0(I) = \Delta_t H_j^0(I=0) - RT^2 \frac{Z_j^2}{1 + (1 + B Z_j^2)} \]  

(1.3-6)

Table 1.1 gives the coefficients in the Debye-Hückel equation, and in the equations for \( \Delta_t G_j^0(I) \) and \( \Delta_t H_j^0(I) \) that have been calculated by Clarke and Glew (10).
Table 1.1 Debye-Hückel constant $\alpha$ in kg$^{1/2}$ mol$^{-1/2}$ and the coefficients of the ionic strength terms for $\Delta_f G^\circ$ in kJ mol$^{-3/2}$ kg$^{1/2}$, $\Delta_f H^\circ$ in kJ mol$^{-3/2}$ kg$^{1/2}$ and $\Delta_f S^\circ$ in J mol$^{-3/2}$ kg$^{1/2}$ K$^{-1}$

<table>
<thead>
<tr>
<th>$t/^\circ C$</th>
<th>$\alpha$</th>
<th>$RT\alpha$</th>
<th>$RT^2 \partial \alpha / \partial T$</th>
<th>$R(\alpha + T \partial \alpha / \partial T)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.12938</td>
<td>2.56494</td>
<td>1.075</td>
<td>13.3258</td>
</tr>
<tr>
<td>10</td>
<td>1.14717</td>
<td>2.70073</td>
<td>1.213</td>
<td>13.8221</td>
</tr>
<tr>
<td>20</td>
<td>1.16589</td>
<td>2.84196</td>
<td>1.3845</td>
<td>14.4174</td>
</tr>
<tr>
<td>25</td>
<td>1.17582</td>
<td>2.91482</td>
<td>1.4775</td>
<td>14.7319</td>
</tr>
<tr>
<td>30</td>
<td>1.18599</td>
<td>2.98934</td>
<td>1.5775</td>
<td>15.0646</td>
</tr>
<tr>
<td>40</td>
<td>1.20732</td>
<td>3.14349</td>
<td>1.8</td>
<td>16.1057</td>
</tr>
</tbody>
</table>

Clarke and Glew did not give the entropy coefficient, but this is discussed in Chapter 15 and in papers on temperature effects (12,13).

The equilibrium constant $K_k$ for reaction $k$ between species at a specified ionic strength can be calculated using

$$
\Delta_f G^\circ_k = -RT \ln K_k = \sum_{j=1}^{N} v_{jk} \Delta_f G^\circ_j
$$

where $v_{jk}$ is the stoichiometric number for species $j$ in reaction $k$ and $N$ is the number of species involved in chemical reaction $k$. Whenever a thermodynamic property of a reaction is given, the chemical reaction must be specified because there are different ways to write chemical equations, and so it is important to know the way a chemical equation is written. The equilibrium constant $K_k$ is written in terms of concentrations in biochemical thermodynamics because equation 1.3-4 is written in terms of concentrations. Thus for the dissociation of a weak acid, $HA = H^+ + A^-$, the dissociation constant is given by

$$
K_k = [H^+][A^-]/[HA] = 10^{-pK_k} = 10^{-pK_k}
$$

where $pK_k = -\log K_k$ and $pH = -\log [H^+]$. This is not the $pH$ obtained with a pH meter, but the required adjustment is calculated in the next section.
1.4 Calculation of $\text{pH} = -\log [\text{H}^+]$

The symbol $\text{pH}_c$ can be used to distinguish $\text{pH}_c = -\log [\text{H}^+]$ from $\text{pH}_a = -\log \{ \gamma (\text{H}^+) [\text{H}^+] \}$ obtained with a glass electrode. Equation 1.3-2 can be used to show that (12)

$$\text{pH}_a - \text{pH}_c = a t^{1/2} / \ln(10) (1 + 1.6 t^{1/2}) \quad (1.4-1)$$

This is the adjustment to be subtracted from the pH measured with a pH meter to yield the pH used in equation 1.3-7. $\text{pH}_c$ is lower than $\text{pH}_a$ because the ion atmosphere of $\text{H}^+$ reduces its activity.

To calculate the adjustments shown in equation 1.4-1 as a function of temperature, we need the temperature dependence of the Debye-Hückel constant $a$. Clarke and Glew (10) have provided tables that show that

$$\text{In}[19]:= a = 1.10708 - 0.00154508 t + 5.95584 \times 10^{-6} t^2$$

$$\text{Out}[19]= 1.10708 - 0.00154508 t + 5.95584 \times 10^{-6} t^2$$

where $t$ is the temperature in Kelvins. The dark type is input in Mathematica (7), and the next line is output from Mathematica. A lower case $t$ is used here because capital letters in Mathematica are used for operations. In Mathematica an asterix is used as the multiply sign and $^*$ is used to indicate an exponent. The value of $a$ at a specified temperature can be calculated by use of the ReplaceAll operation (/.$t$>).

$$\text{In}[20]:= a /. t -> 298.15$$

$$\text{Out}[20]= 1.17585$$

The units of $a$ are $\text{kg}^{1/2} \text{mol}^{-1/2}$.

In Mathematica the right hand side of equation 1.4-1 is given by

$$\text{In}[21]:= a \times \text{is}^{2.5} / (\text{Log}[10] \times (1 + 1.6 \times \text{is}^{0.5}))$$

$$\text{Out}[21]= \frac{\text{is}^{2.5} \times (1.10708 - 0.00154508 t + 5.95584 \times 10^{-6} t^2)}{(1 + 1.6 \times \text{is}^{0.5}) \text{Log}[10]}$$

where $\text{is}$ is the symbol for ionic strength and $\text{Log}[10]$ is $\ln 10$. The pH adjustment at 298.15 K, pH 7.00, and ionic strength 0.25 M can be calculated by use of the ReplaceAll operation:

$$\text{In}[22]:= a \times \text{is}^{2.5} / (\text{Log}[10] \times (1 + 1.6 \times \text{is}^{0.5})) \times \text{t} -> 298.15 \times \text{pH} -> 7.0 \times \text{is} -> .25$$

$$\text{Out}[22]= 0.141851$$

Equation 1.4-1 yields the following table.
Table 1.2 Adjustments (as functions of ionic strength and Celsius temperature) to be subtracted from $pH_a$ measured with a pH meter to obtain $pH_c = - \log[H^+]$.

In[23]:=
PaddedForm[TableForm[a*is^-.5/(Log[10]*(l+1.6*is^.5))/.is->{0,.05,1.15,2.25}/.t->{283.15,298.15,313.15},TableHeadings->{{"O","O.05","0.10","0.15","0.20","0.25"},{"lo C","25 C","40 C"}}],[3,2]]

Out[23]//PaddedForm=

<table>
<thead>
<tr>
<th></th>
<th>10 C</th>
<th>25 C</th>
<th>40 C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>0.00</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>0.10</td>
<td>0.08</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>0.15</td>
<td>0.12</td>
<td>0.12</td>
<td>0.13</td>
</tr>
<tr>
<td>0.20</td>
<td>0.13</td>
<td>0.13</td>
<td>0.14</td>
</tr>
<tr>
<td>0.25</td>
<td>0.14</td>
<td>0.14</td>
<td>0.15</td>
</tr>
</tbody>
</table>

1.5 Calculation of Activity Coefficients for Ionic Species with Different Charge Numbers

The activity coefficients $\gamma$ of ions in water at 298.15 K are given as a function of ionic strength by equation 1.3-2:

In[24]:=
\[ \gamma = \exp[-1.17582 z^2 * is^-.5 / (1 + 1.6 * is^.5)] \]

Note that when a semicolon is put at the end of input, Mathematica does not print output. The effect of ionic strength on the activity coefficient of an ion is very sensitive to the charge number. At 298.15 K and 0.25 M ionic strength, the activity coefficients of ions with 1, 2, 3, and 4 charges are given by

In[25]:=
\[ \gamma / . is \to .25 / . z \to \{1, 2, 3, 4\} \]

Out[25]= \{0.72136, 0.270775, 0.0528895, 0.0053757\}

Figure 1.1 gives the activity coefficients at 298.15 K for ions with charge numbers of 1, 2, 3, and 4 as a function of ionic strength.

In[26]:=
Plot[Evaluate[\[ \gamma / . z \to \{1, 2, 3, 4\} \]], \{is, 0, .4\}, AxesLabel -> {"I/M", "\gamma"}];
Chapter 1 Thermodynamics of the Dissociation of Weak Acids

Figure 1.1 Activity coefficients as a function of ionic strength at 298.15 K in water for ions with charge numbers 1, 2, 3, and 4.

The standard Gibbs energy of formation $\Delta_f G_j^\circ(I)$ of ion $j$ in aqueous solution is given by equation 1.3-5, where $RTa = 2.91482 \text{ kJ mol}^{-1/2} \text{ kg}^{1/2}$ at 298.15 K. The Mathematica expression for the adjustment from $I = 0$ to $I$ is given by

$$In[27]:= \text{stdgibbse} = -2.91482 * z^2 * \text{is}^{0.5} / (1 + 1.6 * \text{is}^{0.5});$$

The effect of ionic strength on the standard Gibbs energy of formation of an ion is quite sensitive to the charge number. The effects on $\Delta_f G_j^\circ$ for $z = 1, 2, 3,$ and $4$ are given by

$$In[28]:= \text{stdgibbse} /. \text{is} -> .25 /. z \to \{1, 2, 3, 4\}$$

$$Out[28]= \{-0.809672, -3.23869, -7.28705, -12.9548\}$$

where the adjustments of the standard Gibbs energies are given in kJ mol$^{-1}$. Figure 1.2 gives the standard Gibbs energies of formation at 298.15 K as functions of ionic strength for ions with charge numbers of 1, 2, 3, and 4.

$$In[29]:= \text{Plot}[\text{Evaluate}[\text{stdgibbse} /. z \to \{1, 2, 3, 4\}],$$

$$\{\text{is}, 0, .4\}, \text{AxesLabel} \to \{"I/M", \"\Delta_f G_j^\circ\"\}, \text{AxesOrigin} \to \{0, -15\};$$
Chapter 1 Thermodynamics of the Dissociation of Weak Acids

1.6 pKs of Weak Acids at Various Ionic Strengths

Package BasicBiochemData3 can be used to calculate pKs for weak acids at 298.15 K and desired ionic strengths. This database contains 60 reactants that have a total of 82 pKs. In the program calcpK, it is necessary to give the number of the pK. pKs are numbered 1, 2, 3, ..., from the highest to the lowest. This program is used here to calculate the pKs for all the weak acids in the database at five ionic strengths. The logarithm of the acid dissociation $K(298.15 \text{ K}, I)$ is given as a function of ionic strength by the following equation:

$$\ln K(298.15 \text{ K}, I) = \ln K(298.15 \text{ K}, I=0) + \alpha I^{1/2} \sum_j z_j^2 / (1 + 1.6 I^{1/2})$$

Note that $\alpha = 1.17582 \text{ kgl}^{-1} \text{ mol}^{-1/2}$ at 298.15 K in Clarke and Glew (10). The following program (8) uses this equation to obtain pKs at 298.15 K at desired ionic strengths.

In[30]:=

calcpK[speciesmat_, no_, is_] := Module[{lnkzero, sigmanuzsq, lnK}, (*Calculates pKs for a weak acid at 298.15 K at specified ionic strengths (is) when the number no of the pK is specified. pKs are numbered 1, 2, 3, ..., from the highest pK to the lowest pK, but the highest pK for a weak acid may be omitted if it is outside of the range 5 to 9. For H3PO4, pK1=calcpK[psp,1,0] = 7.22.*)

lnkzero = (speciesmat[[no+1, 1]] - speciesmat[[no, 1]])/(8.31451*0.29815);

sigmanuzsq = speciesmat[[no, 3]]^2 - speciesmat[[no+1, 3]]^2 + 1;

lnk = lnkzero + (1.17582*is^0.5*sigmanuzsq) / (1 + 1.6*is^0.5);

N[-(lnk/Log[10])]]

This is the first Mathematica program in this book, and so it is important to observe its structure. In the Module the first list in {...} gives the names of expressions to be kept within the program. The purpose and operation of the program are described in (*...*). The first line of the program calculates $\ln K(I=0)$. The second line calculates $\sum z_j^2$. The third line calculates $\ln K$, and the last line calculates $pK = -\ln K/\log(10)$. The pKs of atp at 298.15 K and ionic strengths of 0, 0.05, 0.10, 0.15, and 0.25 M are calculated using

In[31]:=

calcpK[atsp, 1, {0, .05, .1, .15, .25}]
Chapter 1 Thermodynamics of the Dissociation of Weak Acids

When a program is to be used many times, it should have just one argument so that it can be applied to a list of species properties using Map in Mathematica. This can be done with the program calcpK298is (14). This program derives a list of functions of ionic strength that yield the successive pKs of a reactant at 298.15 K.

In[33]:=
calcpK298is[speciesmat_] :=
Module[{glist, hlist, zlist, nHlist, glistis, ghydionis}, (*This program derives the functions of ionic strength that yields the pKs at 298.15 K for weak acids. The first function of ionic strength is for the acid with the fewest hydrogen atoms. The program has a single argument so that it can be used with Map. The functions can be evaluated by use of calcpK298is[species]/.is→(0, .05, .1, .15, .25), for example.*)
{glist, hlist, zlist, nHlist} = Transpose[speciesmat];
glistis = Table[glist[[i]] - 2.91482*zlist[[i]]^2/is^.5/(1+1.6*is^.5), {i, 1, Length[zlist]}];
ghydionis = -2.91482/is^.5/(1+1.6*is^.5);
Table[((glistis[[i-1]] - glistis[[i]]) + ghydionis) / (8.31451*29815*Log[10])) , {i, 2, Length[zlist]}]]

In the second line of the program, Length[zlist] is used to calculate the number of pKs the reactant has. The Mathematica operation Table makes a list of values. The ionic strength dependencies of the two pKs of atp can be calculated as follows:

In[34]:=
TableForm[calcpK298is[species]/.is→(0, .05, .1, .15, .25),
TableHeadings→{"atp pK1", "atp pK2"}, {"I=0", "I=0.05", "I=0.1", "I=0.15", "I=0.25"}]}

Out[34]/TableForm=

<table>
<thead>
<tr>
<th></th>
<th>I=0</th>
<th>I=0.05</th>
<th>I=0.1</th>
<th>I=0.15</th>
<th>I=0.25</th>
</tr>
</thead>
<tbody>
<tr>
<td>atp pK2</td>
<td>4.67761</td>
<td>4.17303</td>
<td>4.03424</td>
<td>3.94497</td>
<td>3.82652</td>
</tr>
</tbody>
</table>

BasicBiochemData3 contains data on the following 60 weak acids at 298.15 K and zero ionic strength.

In[35]:=
lisreactantsdata = {acetatesp, acetylphossp, adeninesp, adenosinesp, adpasp, ammoniasp, amppsp, arabinose5phossp, atpasp, bgpasp, citratesp, citrateisosp, co2tosp, coAsp, cysteineLsp, deoxyribose1phossp, deoxyribose5phossp, deoxyadenosinesp, deoxympsp, deoxyadpasp, deoxyatpasp, dihydroxyacetonephossp, fructose6phossp, fructose16phossp, fumaratesp, galactose1phossp, galactose6phossp, gluconolactone6phossp, glucose6phossp, glucoselphossp, glutathioneredsp, glyceraldehydepophossp, glycerol1phossp, h2asasp, idasp, impasp, inosinesp, itasp, malatasp, malylcoAsp, mannitolphossp, mannose1phossp, mannose2phossp, methylimaleatesp, methylmalonylcoAsp, nicotinamideribonucleotidesp, oxalatasp, pepasp, phosphoglycerate2sp, phosphoglycerate3sp, phosphoserinesp, pispp, prppsp, pppasp, riboselphossp, ribose5phossp, ribulose5phossp, sorbitol6phossp, succinatesp, succinylocoAsp, thioredoxinredsp};

Map is used to apply calcpK298is to these species matrices. The functions of ionic strength for the 60 reactants are joined together by use of Join. Then the functions are evaluated at five ionic strengths.

In[36]:=
Join[TableForm[calcpK298is[lisreactantsdata]/.is→(0, .05, .1, .15, .25)];
Before making a table it is necessary to Flatten the matrix of pKs. This makes a table of pKs at I = 0, 0.05, 0.10, 0.15, and 0.25 M for 82 pKs.

In[37]:= Dimensions[Flatten[Join[Map[calcpK298is, listreactantsdata]] /. is -> {0, 0.05, .1, .15, .25}, 1]]
Out[37]= {82, 5}

The names of the rows are given by the following list.

Table 1.3 pKs of weak acids in water at 298.15 K at ionic strengths 0, 0.05, 0.10, 0.15, and 0.25 M.

\[
\text{In[39]}:=
\text{PaddedForm[}
\text{TableForm[Flatten[Join[Map[calcpK298isr, listreactantsdata]]/. is \to \{0, .05, .1, .15, .25\}, 1],}
\text{TableHeadings \to \{names, \{"I=0", "I=0.05", "I=0.1", "I=0.15", "I=0.25"\}\},}
\text{TableSpacing \to \{1, 1\}\}, \{3, 2\}\]}
\]

\text{Out[39]\text{//PaddedForm=}

<table>
<thead>
<tr>
<th></th>
<th>I=0</th>
<th>I=0.05</th>
<th>I=0.1</th>
<th>I=0.15</th>
<th>I=0.25</th>
</tr>
</thead>
<tbody>
<tr>
<td>acetate pK1</td>
<td>4.75</td>
<td>4.59</td>
<td>4.54</td>
<td>4.51</td>
<td>4.47</td>
</tr>
<tr>
<td>acetylphos pK1</td>
<td>8.69</td>
<td>8.35</td>
<td>8.26</td>
<td>8.20</td>
<td>8.12</td>
</tr>
<tr>
<td>acetylphos pK2</td>
<td>5.11</td>
<td>4.94</td>
<td>4.90</td>
<td>4.87</td>
<td>4.83</td>
</tr>
<tr>
<td>adenine pK1</td>
<td>4.20</td>
<td>4.20</td>
<td>4.20</td>
<td>4.20</td>
<td>4.20</td>
</tr>
<tr>
<td>adenosine pK1</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
</tr>
<tr>
<td>adp pK1</td>
<td>7.18</td>
<td>6.67</td>
<td>6.53</td>
<td>6.44</td>
<td>6.33</td>
</tr>
<tr>
<td>adp pK2</td>
<td>4.36</td>
<td>4.02</td>
<td>3.93</td>
<td>3.87</td>
<td>3.79</td>
</tr>
<tr>
<td>amp pK1</td>
<td>6.73</td>
<td>6.39</td>
<td>6.30</td>
<td>6.24</td>
<td>6.16</td>
</tr>
<tr>
<td>amp pK2</td>
<td>3.99</td>
<td>3.82</td>
<td>3.77</td>
<td>3.74</td>
<td>3.71</td>
</tr>
<tr>
<td>arabinose5phos pK1</td>
<td>6.69</td>
<td>6.35</td>
<td>6.26</td>
<td>6.20</td>
<td>6.12</td>
</tr>
<tr>
<td>atp pK1</td>
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<td>6.74</td>
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<td>6.47</td>
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<tr>
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<td>4.17</td>
<td>4.03</td>
<td>3.94</td>
<td>3.83</td>
</tr>
<tr>
<td>bpq pK1</td>
<td>7.96</td>
<td>7.29</td>
<td>7.10</td>
<td>6.98</td>
<td>6.83</td>
</tr>
<tr>
<td>citrate pK1</td>
<td>6.39</td>
<td>5.89</td>
<td>5.75</td>
<td>5.66</td>
<td>5.54</td>
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<tr>
<td>citrate pK2</td>
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<td>4.27</td>
<td>4.19</td>
</tr>
<tr>
<td>citrateiso pK1</td>
<td>6.40</td>
<td>5.90</td>
<td>5.76</td>
<td>5.67</td>
<td>5.55</td>
</tr>
<tr>
<td>citrateiso pK2</td>
<td>4.71</td>
<td>4.38</td>
<td>4.28</td>
<td>4.22</td>
<td>4.15</td>
</tr>
<tr>
<td>co2tot pK1</td>
<td>10.30</td>
<td>9.99</td>
<td>9.90</td>
<td>9.84</td>
<td>9.76</td>
</tr>
<tr>
<td>co2tot pK2</td>
<td>6.37</td>
<td>6.20</td>
<td>6.15</td>
<td>6.12</td>
<td>6.08</td>
</tr>
<tr>
<td>coa pK1</td>
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<td>8.21</td>
<td>8.16</td>
<td>8.14</td>
<td>8.10</td>
</tr>
<tr>
<td>cysteineL pK1</td>
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<td>8.21</td>
<td>8.16</td>
<td>8.13</td>
<td>8.09</td>
</tr>
<tr>
<td>deoxyribose1phos pK1</td>
<td>6.69</td>
<td>6.35</td>
<td>6.26</td>
<td>6.20</td>
<td>6.12</td>
</tr>
<tr>
<td>deoxyribose5phos pK1</td>
<td>6.69</td>
<td>6.35</td>
<td>6.26</td>
<td>6.20</td>
<td>6.12</td>
</tr>
<tr>
<td>deoxyadenosine pK1</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
</tr>
<tr>
<td>deoxyamp pK1</td>
<td>6.73</td>
<td>6.39</td>
<td>6.30</td>
<td>6.24</td>
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Chapter 1 Thermodynamics of the Dissociation of Weak Acids

This table can be helpful in estimating the pKs of other weak acids from their structures. In using this table it is important to remember that \(-\log [H^+]\) is used in the expression for the acid dissociation constant in terms of pH. To obtain pKs based on \(-\log (\gamma (H^+) [H^+] )\), add 0, 0.08, 0.11, 0.12, and 0.14 at ionic strengths of 0, 0.05, 0.10, 0.15, and 0.25 M, respectively, at 298.15 K as indicated by Table 1.3. PaddedForm rounds the output to two figures to the right of the decimal point. There is a list of full names of reactants in the Appendix of this book. The reactants bpg, nmn, pep, and prpp are bisphosphoglycerate, nicotinamidemononucleotide, phosphoenolpyruvate, and 5-phosphoribosyl-alpha-pyrophosphate, respectively.

Note that, except for ammonia, adenine, and adenosine, the pKs always decrease as the ionic strength increases; in other words, the acids become stronger as the ionic strength increases. For a weak acid dissociation represented by \(HA = H^+ + A^-\) increasing the ionic strength stabilizes \(H^+ + A^-\) more than \(HA\). The pK shift is greater when \(HA\) is an ion. There is no shift in pK with ionic strength for weak acids like the ammonium ion because there is a single charge on each side of the dissociation equation.

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1.7 pKs of Weak Acids at Various Ionic Strengths and Temperatures

When $\Delta f H^\circ$ values are known for all the species of a weak acid at 298.15 K in addition to $\Delta f G^\circ$, the pKs at temperatures other than 298.15 K can be calculated on the assumption that $\Delta f H^\circ$ is constant over the range of temperature. If $\Delta f H^\circ$ is independent of temperature, $\Delta f S^\circ$ is also independent of temperature. BasicBiochemData3 contains data on 27 weak acids for which $\Delta f H^\circ$ values are known. In order to calculate pKs at temperatures other than 298.15 K, we need to do two things: (1) Express the standard Gibbs energies of formation of species as functions of temperature. (2) Express the coefficient of the ionic strength term as a function of temperature. When the standard enthalpies of formation of species at $I = 0$ are independent of temperature, their standard Gibbs energies of formation are given by

$$
\Delta f G_j^\circ(T) = \frac{T}{298.15} \Delta f G_j^\circ(298.15 \text{ K}) + (1 - \frac{T}{298.15}) \Delta f H_j^\circ(298.15 \text{ K})
$$

(1.7-1)

The coefficient $RT\alpha$ in equation 1.2-5 is given as a function of temperature by

$$
RT\alpha = 9.20483 \times 10^{-3} T - 1.28467 \times 10^{-5} T^2 + 4.95199 \times 10^{-8} T^3
$$

(1.7-2)

The program `calcpKT(8)` can be used to calculate the pK of a weak acid at a series of temperatures.

```
In[40]:=

In[41]:=

In[42]:=

In[43]:=

In[44]:=

In[45]:=
```

The two pKs of ATP are each calculated at three ionic strengths and three temperatures as follows:

```
In[41]:= atp10 = calcpKT[atpS, 1, 0, {273.15, 298.15, 313.15}];
In[42]:= atp11 = calcpKT[atpS, 1, .10, {273.15, 298.15, 313.14}];
In[43]:= atp125 = calcpKT[atpS, 1, .25, {273.15, 298.15, 313.14}];
In[44]:= atp20 = calcpKT[atpS, 2, 0, {273.15, 298.15, 313.15}];
In[45]:= atp21 = calcpKT[atpS, 2, .10, {273.15, 298.15, 313.14}];
```