Chapter 20: Chemical Equilibrium

> Consider the shift in the position of equilibrium of the reaction PCl_5 (g) $\rightleftarrows$ PCl_3 (g) + Cl_2(g) when the total pressure is increased. LeChâtelier's Principle predicts that the position of equilibrium shifts in the direction with the smaller numbers of moles of gas. However, the equilibrium constant, K_p, is not a function of pressure. How can the position of equilibrium shift while the K_p is unaffected by a change in pressure?

Chemical equilibrium is the thermodynamic theory that most directly relates structure to function. For example, the goal of the development of a new pharmaceutical is to design a compound that has a large equilibrium constant for binding to a target enzyme while showing negligible equilibrium constants for binding to other enzymes. The position of equilibrium determines "how far" a reaction progresses. All chemical systems eventually reach equilibrium, unless a continual source of energy or materials is supplied. The position of equilibrium is determined by the Second Law of thermodynamics. To apply the Second Law, the system and surroundings are taken as a composite system. The composite is isolated. The change in total entropy for the composite system is zero at equilibrium and the entropy is maximized. At equilibrium at constant temperature and pressure, the maximization of the total entropy corresponds to the minimization of the Gibbs energy for the reaction. At equilibrium at constant temperature and pressure, the Gibbs energy of the products is equal to the reactants, $\Sigma \, \nu_i \, \bar{\mu}_i = 0$, Eq. 15.3.13. Chemical equilibrium is dynamic. Even though concentrations are constant over time, the reactions still take place with the overall forward reaction rate equal to the overall reverse reaction rate.

The position of equilibrium is determined by the **Law of Mass Action**. Consider the general gas phase reaction: a A(P_A) + b B(P_B) $\rightleftarrows$ c C(P_C) d D(P_D), where A is at partial pressure P_A, B is at partial pressure P_B, etc. The Law of Mass Action gives the equilibrium constant as:

$$K_p = \frac{(P_C/P^\circ)^c (P_D/P^\circ)^d}{(P_A/P^\circ)^a (P_B/P^\circ)^b} \qquad \text{(equilibrium)}$$

where P° is the standard state pressure, making K_p unitless. This equilibrium constant is designated as K_p because the quotient is expressed as the ratio of the partial pressures of the products to the reactants. The equilibrium constant K_p is a function <u>only</u> of temperature. For example, the reaction:

$$CO \text{ (g)} + H_2O \text{ (g)} \rightleftarrows CO_2 \text{ (g)} + H_2 \text{ (g)}$$
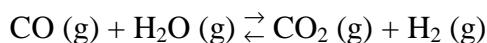
can be used to illustrate the independence of K_p on initial conditions. The partial pressures of the reactants and products at equilibrium for several initial mixtures of CO and H_2O at 1259 K are:

Initial conditions	P_{CO} (bar)	P_{H2O} (bar)	P_{CO2} (bar)	P_{H2} (bar)	K_p
equal CO & H_2O	0.279	0.279	0.221	0.221	0.627
more H_2O	0.121	0.421	0.179	0.179	0.629
more CO	0.396	0.136	0.184	0.184	0.629

The last column is the ratio calculated from the experimental pressures: $K_p = (P_{CO_2}P_{H_2})/(P_{CO}P_{H_2O})$, which is constant to within experimental and round-off error. K_p is constant even though the initial partial pressures of the reactants are very different for each experiment. K_p is only a function of temperature. The Law of Mass Action was established empirically in 1864 using similar observations on 300 different reactions.[1]

The response of a reaction at equilibrium to changes in conditions is summarized by **LeChâtelier's Principle**:

A system perturbed from equilibrium shifts its equilibrium position to relieve the applied stress.

For example, for an increase in temperature, the reaction shifts in the endothermic direction to relieve the stress. As we develop the theory of chemical equilibrium, we will need to verify that the theory agrees with the Law of Mass Action and LeChâtelier's Principle.

The position of equilibrium, from a fundamental thermodynamic perspective, is established by minimizing the Gibbs energy of the reaction. What is the relationship between the Gibbs energy and the equilibrium constant? Chemical reactions are characterized by the reaction Gibbs energy under standard state conditions using Eq. 15.4.17:

$$\Delta_r G^\circ = \sum_{i=1}^{n_s} \nu_i \, \Delta_f G_i^\circ \qquad \text{(cst. T\&P)} \qquad (15.4.17)$$

However, a reaction at equilibrium is not very likely to have partial pressures for each reactant and product equal to 1 bar. The key to unifying the Law of Mass Action with thermodynamic principles is through the calculation of the reaction Gibbs energy under non-standard state conditions.

20.1 Gibbs Energy and Chemical Equilibrium

The Equilibrium Extent Depends on the Standard State Reaction Gibbs Energy: What is $\Delta_r G$ under non-standard conditions? Consider the general gas phase reaction:

$$a \, A(P_A) + b \, B(P_B) \rightleftarrows c \, C(P_C) \ d \, D(P_D) \qquad\qquad 20.1.1$$

The chemical potential of each reactant and product is given by Eq.16.6.20° assuming the constituents can be treated as ideal gases. For example for A:

$$\mu_A = \mu_A^\circ + RT \ln(P_A/P^\circ) \qquad\qquad \text{(ideal gas) } (16.6.20°)$$

At constant T and P, the change in Gibbs energy during the course of the reaction is given by:

$$dG = \mu_A \, dn_A + \mu_B \, dn_B + \mu_C \, dn_C + \mu_D \, dn_D \qquad \text{(cst. T\&P)} \qquad 20.1.2$$

The progress of the reaction is expressed using the extent, Eq. 3.1.4, $dn_i = \nu_i d\xi$. Substituting for the changes in moles of reactants and products in terms of the extent gives:

$$dG = (c \, \mu_C + d \, \mu_D - a \, \mu_A - b \, \mu_B) \, d\xi \qquad \text{(cst. T\&P)} \qquad 20.1.3$$

The chemical potentials are constant, since the partial pressures of each reactant and product are held constant, Sec. 8.4. Integrating the last equation to the completion of the reaction gives the reaction Gibbs energy:

$$\int_{G_{reactants}}^{G_{products}} dG = \int_0^1 (c \, \mu_C + d \, \mu_D - a \, \mu_A - b \, \mu_B) \, d\xi \qquad \text{(cst. T\&P)} \qquad 20.1.4$$

$$\Delta_r G = c\,\mu_C + d\,\mu_D - a\,\mu_A - b\,\mu_B \qquad \text{(cst. T\&P)} \qquad 20.1.5$$

Substituting for each chemical potential under the given reaction conditions using Eq. 16.6.20° gives:

$$\Delta_r G = c\left[\mu_C^\circ + RT\ln\frac{P_C}{P^\circ}\right] + d\left[\mu_D^\circ + RT\ln\frac{P_D}{P^\circ}\right] - a\left[\mu_A^\circ + RT\ln\frac{P_A}{P^\circ}\right] - b\left[\mu_B^\circ + RT\ln\frac{P_B}{P^\circ}\right]$$

$$\text{(cst. T\&P, ideal gas)} \quad 20.1.6°$$

Rearranging terms to collect all the standard state chemical potentials gives:

$$\Delta_r G = c\,\mu_C^\circ + d\,\mu_D^\circ - a\,\mu_A^\circ - b\,\mu_B^\circ + RT\left[c\ln\frac{P_C}{P^\circ} + d\ln\frac{P_D}{P^\circ} - a\ln\frac{P_A}{P^\circ} - b\ln\frac{P_B}{P^\circ}\right] \qquad 20.1.7°$$

The first term is the standard state reaction Gibbs energy:

$$\Delta_r G^\circ \equiv c\,\mu_C^\circ + d\,\mu_D^\circ - a\,\mu_A^\circ - b\,\mu_B^\circ \qquad \text{(cst. T\&P)} \qquad 20.1.8$$

Substituting this definition into Eq. 20.1.7° gives the reaction Gibbs energy under non-standard conditions in the final form:

$$\Delta_r G = \Delta_r G^\circ + RT\ln\left[\frac{(P_C/P^\circ)^c(P_D/P^\circ)^d}{(P_A/P^\circ)^a(P_B/P^\circ)^b}\right] \qquad \text{(cst. T\&P, ideal gas)} \quad 20.1.9°$$

Using this equation, we can calculate the reaction Gibbs energy for any given set of conditions and not just standard states. The term in brackets is the reaction quotient, Q:

$$\Delta_r G = \Delta_r G^\circ + RT\ln Q \quad \text{with } Q = \left[\frac{(P_C/P^\circ)^c(P_D/P^\circ)^d}{(P_A/P^\circ)^a(P_B/P^\circ)^b}\right] \qquad \text{(cst. T\&P, ideal gas) 20.1.10°}$$

Example 20.1.1:
The water-gas shift reaction is a historically important process in the gasification of solid fuels. In gasification, the solid fuel is burned with limiting oxygen to produce a mixture of CO and H_2, which is called Syngas. Syngas is then treated with high pressure steam to enhance the production of H_2. The result is an equilibrium mixture: $CO + H_2O \rightleftarrows CO_2 + H_2$. Gasification fueled the "gas-light" era and may again be important for the gasification of coal and biomass for the production of H_2 for transportation fuels and chemical feedstocks. Biomass gasification increases our energy self-sufficiency and decreases CO_2 emissions compared to fossil fuel utilization, assuming sustainable harvesting practices. Calculate the reaction Gibbs energy under the given conditions at 298.2 K:

$$CO \text{ (g, 10.0 bar)} + H_2O \text{ (g, 10.0 bar)} \rightleftarrows CO_2 \text{ (g, 5.00 bar)} + H_2 \text{ (g, 2.00 bar)}$$
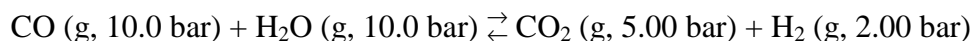
Answer: The first step is to calculate the standard state reaction Gibbs energy and then secondly to adjust to the given non-standard conditions. At standard state:

	CO (g, 1 bar) +	H$_2$O (g, 1 bar) $\rightleftarrows$	CO$_2$ (g, 1 bar) +	H$_2$ (g, 1 bar)	units
$\Delta_f G^\circ$	-137.17	-228.57	-394.36	0	kJ mol^{-1}

$\Delta_rG° = [\Sigma products] – [\Sigma reactants] = [-394.36 + 0] – [-137.17 + (-228.57)]$ kJ mol^{-1}
$= -28.62$ kJ mol^{-1}

Then correcting to non-standard state conditions, using Eq. 20.1.10°:

$$Q = \frac{(5.00)(2.00)}{(10.0)(10.0)} = 0.100$$

$\Delta_rG = \Delta_rG° + RT \ln Q = -28.62$ kJ mol^{-1} + 8.314 J K^{-1} mol^{-1}(1 kJ/1000 J)(298.2 K) ln 0.100
$= -28.62$ kJ mol^{-1} + (-5.71 kJ mol^{-1}) = -34.33 kJ mol^{-1}

The kinetics of the water-gas shift reaction are slow at room temperature, so the process is run at high temperatures and pressures in the presence of a catalyst. However, the equilibrium is not as favorable at high temperatures. New membrane technologies to separate and remove the H_2 product improve the efficiency of the overall process.[2]

Compare 20.1.5 and Eq. 15.1.12 under equilibrium conditions: the reaction Gibbs energy at equilibrium is zero:

$$\Delta_rG = \Delta_rG° + RT \ln Q_{eq} = 0 \qquad K_p = Q_{eq} = \left[\frac{(P_C/P°)^c(P_D/P°)^d}{(P_A/P°)^a(P_B/P°)^b} \right]_{eq}$$

(equilibrium, cst. T&P)   20.1.11°

The reaction quotient at equilibrium is the equilibrium constant, $K_p = Q_{eq}$. Solving Eq. 20.1.11° for the standard state reaction Gibbs energy gives the central and important expression:

$$\Delta_rG° = – RT \ln K_p \qquad\qquad \text{(cst. T)} \qquad 20.1.12°$$

The equilibrium constant is a function of temperature only because $\Delta_rG°$ is defined at standard state pressures of 1 bar for each reactant and product. Eq. 20.1.12° can also be used to solve for the equilibrium constant in terms of the standard state reaction Gibbs energy:

$$\ln K_p = \frac{-\Delta_rG°}{RT} \qquad\qquad 20.1.13°$$

Solving for K_p shows the exponential dependence of the equilibrium constant on the standard state reaction Gibbs energy (which is of the form discussed in *General Pattern ℘4*):

$$K_p = e^{\frac{-\Delta_rG°}{RT}} \qquad\qquad 20.1.14°$$

Does the dependence on reaction conditions agree with our expectations based on experimental observations? Substituting Eq. 20.1.12° into Eq. 20.1.11° provides a useful relationship for verifying LeChâtelier's Principle:

$$\Delta_rG = RT \ln \frac{Q}{K_p} \qquad\qquad 20.1.15°$$

If the partial pressures of the reactants are too high, then $Q \sim$ [products]/[reactants] gives $Q < K_p$. The ratio, Q/K_p, is less than one and the corresponding reaction Gibbs energy is negative. The

forward direction is the spontaneous direction for the reaction. If the partial pressures of the products are too high, then $Q > K_p$. The ratio Q/K_p is greater than one and the corresponding reaction Gibbs energy is positive. The backwards direction is the spontaneous direction for the reaction. Now consider starting with the system at equilibrium. If a small amount of a reactant is added to the equilibrium reaction mixture, Q decreases and $\Delta_r G < 0$. The reaction runs in the forward direction, which decreases the partial pressures of the reactants, resisting the change. On the other hand, if a small amount of a product is added, Q increases and $\Delta_r G > 0$. The reaction runs in the backwards direction, which decreases the partial pressures of the products, again resisting the change. The response of the system to perturbations from equilibrium based on Eq. 20.1.15° agrees with LeChâtelier's Principle. The position of equilibrium is such a central issue in chemistry that we should take special care to understand the underlying factors.

The Entropy and Gibbs Energy of Mixing Play a Central Role in Determining the Position of Equilibrium: Using the schematic gas-phase reaction $A + B \rightleftarrows C + D$, let's see if we can tease out the contributing factors governing the position of equilibrium. The relationship of Q to the extent of the reaction is through the partial pressures of each reactant and product. The initial values of the mole amounts of reactants are n_{Ao} and n_{Bo}. Assume that we start with only reactants so that $n_{Co} = 0$ and $n_{Do} = 0$. From the stoichiometry for this example, the mole amounts are:

$$n_A = n_{Ao} - \xi, \quad n_B = n_{Bo} - \xi, \quad n_C = \xi, \quad n_D = \xi \qquad \qquad 20.1.16$$

The Gibbs energy at any point during the reaction is just the sum of the Gibbs energies for each product and reactant:

$$G = n_A \mu_A + n_B \mu_B + n_C \mu_C + n_D \mu_D \qquad \qquad \text{(cst. T\&P)} \qquad 20.1.17$$

$$G = n_A \left[\mu_A^\circ + RT \ln\left(\frac{P_A}{P^\circ}\right)\right] + n_B \left[\mu_B^\circ + RT \ln\left(\frac{P_B}{P^\circ}\right)\right] + n_C \left[\mu_C^\circ + RT \ln\left(\frac{P_C}{P^\circ}\right)\right] + n_D \left[\mu_D^\circ + RT \ln\left(\frac{P_D}{P^\circ}\right)\right]$$

$$\text{(cst. T\&P, ideal gas)} \qquad 20.1.18°$$

The partial pressures are expressed in terms of the mole fractions using Dalton's Law of partial pressures, $P_i = y_i P$, with P the total pressure, $y_i = n_i/n$, and $n = \Sigma n_i$. Collecting terms, as we did for Eqs. 20.1.7-20.1.9, gives:

$$G = (n_A \mu_A^\circ + n_B \mu_B^\circ + n_C \mu_C^\circ + n_D \mu_D^\circ)$$
$$+ n_A RT \ln y_A + n_B RT \ln y_B + n_C RT \ln y_C + n_D RT \ln y_D$$
$$+ n_A RT \ln\left(\frac{P}{P^\circ}\right) + n_B RT \ln\left(\frac{P}{P^\circ}\right) + n_C RT \ln\left(\frac{P}{P^\circ}\right) + n_D RT \ln\left(\frac{P}{P^\circ}\right)$$

$$\text{(cst. T\&P, ideal gas)} \qquad 20.1.19°$$

The total moles of gas is $n = n_A + n_B + n_C + n_D$, and we can use:

$$n_A RT = nRT \left(\frac{n_A}{n}\right) = nRT \, y_A \qquad \qquad 20.1.20$$

and parallel expressions for each reactant and product to simplify Eq. 20.1.19°:

$$G = (n_A \mu_A^\circ + n_B \mu_B^\circ + n_C \mu_C^\circ + n_D \mu_D^\circ) + nRT (y_A \ln y_A + y_B \ln y_B + y_C \ln y_C + y_D \ln y_D)$$
$$+ nRT \ln\left(\frac{P}{P^\circ}\right) \qquad \qquad \text{(cst. T\&P, ideal gas)} \qquad 20.1.21°$$

The first term, which is expressed in the standard state values, is just the Gibbs energy of the reactants and products at each stage of the reaction, but as <u>pure</u>, <u>unmixed</u> constituents at standard state pressure. The term in the mole fractions is the Gibbs energy of mixing of the constituents to give the reaction mixture.[3] Remember from Eq. 16.8.16° that for ideal gases, the Gibbs energy of mixing is given by $\Delta_{mix}G = -T\Delta_{mix}S$. The Gibbs energy of the reaction is stabilized by the favorable entropy of mixing of the reactants and products. The last term adjusts for the overall pressure of the reaction mixture. For a constant pressure reaction, P is constant. These terms are diagramed in Figure 20.1.1 for a reaction at a constant total pressure of 1 bar. The top-most line is the term $G°(pure) = (n_A\mu_A^\circ + n_B\mu_B^\circ + n_C\mu_C^\circ + n_D\mu_D^\circ)$, which varies <u>linearly</u> with the extent of the reaction between the pure reactants and the pure products.
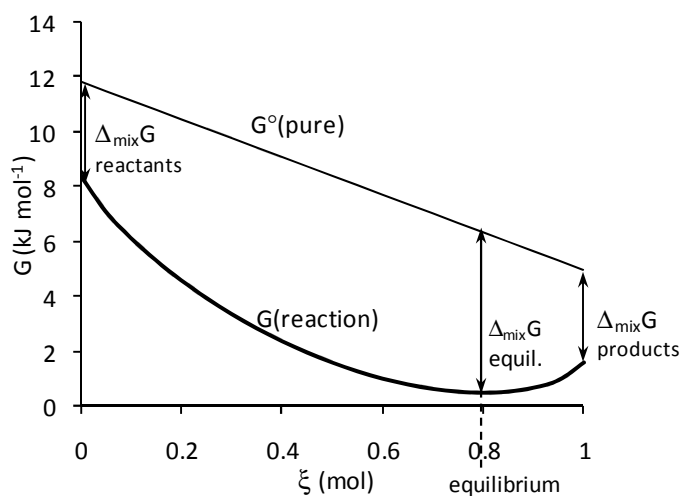

Figure 20.1.1: The Gibbs energy of the reaction includes the Gibbs energy of each pure reactant and product and the Gibbs energy of mixing to form the reaction mixture.

The lower curve is the Gibbs energy during the course of the reaction. At the beginning of the reaction, the Gibbs energy is less than the pure reactants because of the Gibbs energy of mixing of the reactants. The Gibbs energy of mixing is also important at completion for the products. At equilibrium, the Gibbs energy of mixing is even more stabilizing, because there are four constituents in the mixture, A, B, C, and D. Were it not for this additional Gibbs energy of mixing, $A + B \rightarrow C + D$ would always go to completion giving $\xi = 1$ if spontaneous or remain at $\xi = 0$ if non-spontaneous. The entropy of mixing and the corresponding Gibbs energy of mixing play a central role in determining the position of equilibrium.

   Another useful viewpoint is to consider the relationship of the Gibbs energy during the reaction, Figure 20.1.1, to the reaction Gibbs energy, Δ_rG. In direct analogy with the reaction enthalpy, Eq. 8.4.19, the reaction Gibbs energy is the slope of the Gibbs energy at a given extent. The corresponding derivative for the Gibbs energy is:

$$\left(\frac{\partial G}{\partial \xi}\right)_{T,P} = \sum_{i=1}^{n_s} \nu_i\, G_i = \Delta_rG \qquad\qquad \text{(cst. T\&P)} \qquad 20.1.22$$

This relationship is shown diagrammatically in Figure 20.1.2. If the extent of the reaction is less than equilibrium, the slope of the Gibbs energy curve is negative giving $\Delta_r G < 0$ and the reaction is spontaneous in the forward direction. If the extent of the reaction is greater than equilibrium, the slope of the Gibbs energy curve is positive giving $\Delta_r G > 0$ and the reaction is spontaneous in the backward direction. The Gibbs energy is at minimum at equilibrium, where $\Delta_r G = 0$.
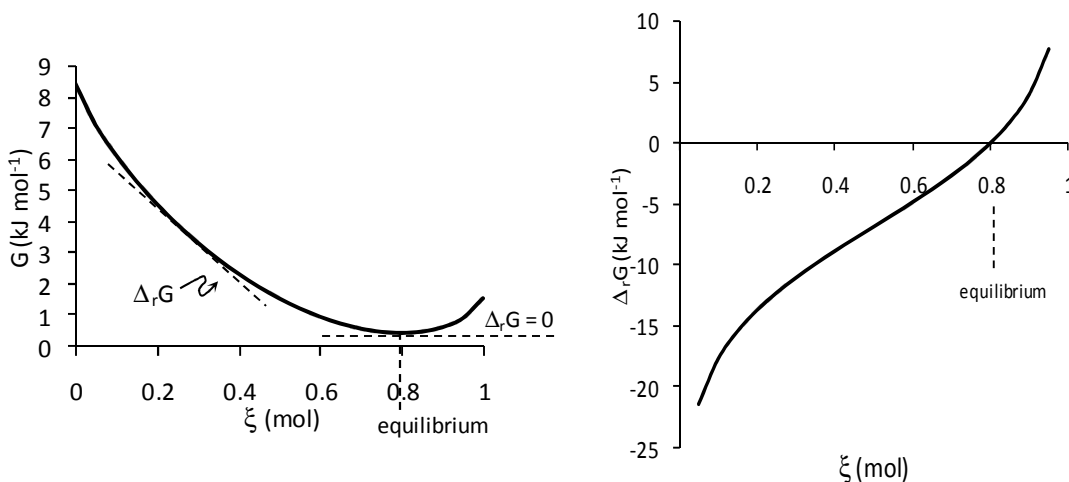

Figure 20.1.2: The Gibbs energy during the reaction is at minimum at equilibrium, where $\Delta_r G = 0$. The reaction Gibbs energy is the slope of the G vs. ξ curve at a given extent.

Eq. 20.1.10° is specific for two reactants and two products. Eq. 20.1.22 gives the reaction Gibbs energy for the general case for which:

$$K_p = \prod_{i=1}^{n_s} \left(P_i/P^\circ\right)^{\nu_i} \qquad \text{(ideal gas)} \qquad 20.1.23°$$

The Π symbol indicates a continued product, $\Pi\, x_i = x_1 x_2 x_3 x_4 \ldots$.

The position of equilibrium is determined by $\Delta_r G^\circ$ and the reaction stoichiometry. So far, other than changing initial amounts of the reactants and products, we have no control of the position of equilibrium. How can we gain additional control, if the reaction conditions aren't favorable? The reaction Gibbs energy is a function of temperature.

The Equilibrium Constant Depends on Temperature: The dependence of the standard state reaction Gibbs energy on temperature is given by the Gibbs-Helmholtz relationship, Eq. 16.3.12:

$$\left(\frac{\partial\left(\frac{\Delta_r G^\circ}{T}\right)}{\partial T}\right)_p = -\frac{\Delta_r H^\circ}{T^2} \qquad\qquad 20.1.24$$

We can convert this last expression into a relationship for $\ln K_p$ by dividing both sides of the equation by $-R$:

$$\left(\frac{\partial\left(\frac{-\Delta_r G^\circ}{RT}\right)}{\partial T}\right)_p = \frac{\Delta_r H^\circ}{RT^2} \qquad\qquad 20.1.25$$

Using Eq. 20.1.13°, $\ln K_p = -\Delta_r G°/RT$, the Gibbs-Helmholtz relationship reduces to:

$$\left(\frac{\partial \ln K_p}{\partial T}\right)_p = \frac{\Delta_r H°}{RT^2} \qquad \text{20.1.26}$$

This relationship is called the **van 't Hoff equation**. This result is in accord with LeChâtelier's principle. For endothermic reactions, $\Delta_r H°/RT^2 > 0$ and K_p increases with increasing temperature. For an increase in temperature the reaction shifts in the endothermic direction, resisting the change. For exothermic reactions, the derivative is negative and K_p decreases with increasing temperature. The general form for the temperature dependence in Eq. 20.1.26 is outlined in *General Pattern ℘9*, Sec. 17.1. As discussed in the general pattern, we can integrate:

$$\int d \ln K_p = \int_{T_1}^{T_2} \frac{\Delta_r H°}{RT^2} \, dT \qquad \text{20.1.27}$$

Assuming $\Delta_r H°$ is constant over the temperature range, the integrated result is:

$$\ln \frac{K_{p,T_2}}{K_{p,T_1}} = -\frac{\Delta_r H°}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) \qquad \text{(cst. } \Delta_r H°) \qquad \text{20.1.28}$$

$$K_{p,T2} = K_{p,T1} \, e^{\frac{-\Delta_r H°}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)} \qquad \text{(cst. } \Delta_r H°) \qquad \text{20.1.29}$$

In addition, using *General Patterns ℘4* and *℘9*, Eqs. 17.1.22° and 20.1.26 can be recast as:

$$d \ln K_p = -\frac{\Delta_r H°}{R} \, d\left(\frac{1}{T}\right) \qquad \text{20.1.30}$$

$$\ln K_p = -\frac{\Delta_r H°}{RT} + \ln C \qquad \text{(cst. } \Delta_r H°) \qquad \text{20.1.31}$$

The plot of $\ln K_p$ as a function of $1/T$ gives a straight line, assuming constant $\Delta_r H°$, with a slope of $-\Delta_r H°/R$, Figure 20.1.3. This plot is called a **van 't Hoff plot**. The temperature variation is exponential at low temperatures and at high temperatures reaches a constant value.
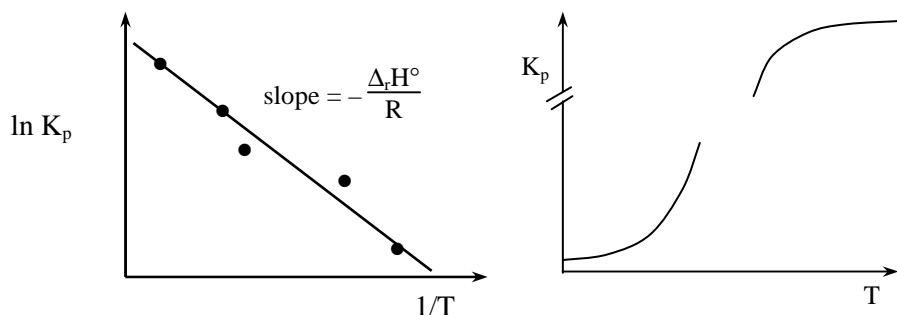

Figure 20.1.3: Variation of the equilibrium constant for an endothermic process, $\Delta_r H° > 0$.

If the reaction enthalpy is not constant over the temperature range, the plot of $\ln K_p$ versus $1/T$ shows systematic curvature. Geochemists, chemical engineers, and environmental chemists often

work under extreme conditions of heat or cold. For moderate changes in temperature, the temperature variation of the enthalpy is given by Eq. 8.5.5 assuming $\Delta_r C_p$ is constant over the temperature range: $\Delta_r H_T^\circ = \Delta_r H_o^\circ + \Delta_r C_p\, T$, where $\Delta_r H_o^\circ$ is the reaction enthalpy extrapolated to $T = 0$ K. The integral in Eq. 20.1.27 is then:

$$\ln \frac{K_{P,T_2}}{K_{P,T_1}} = \int_{T_1}^{T_2} \frac{\Delta_r H_o^\circ}{RT^2} + \frac{\Delta_r C_p T}{RT^2}\ dT = \int_{T_1}^{T_2} \frac{\Delta_r H_o^\circ}{RT^2}\, dT + \int_{T_1}^{T_2} \frac{\Delta_r C_p}{RT}\, dT \qquad \text{(cst. } \Delta_r C_p) \qquad 20.1.32$$

$$\ln \frac{K_{P,T_2}}{K_{P,T_1}} = -\frac{\Delta_r H_o^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) + \frac{\Delta_r C_p}{R}\ln \frac{T_2}{T_1} \qquad \text{(cst. } \Delta_r C_p) \qquad 20.1.33$$

   Over large temperature ranges, the reaction heat capacity and reaction enthalpy are expressed as power series in the temperature, Eqs. 8.5.14 and 8.5.21:

$$\Delta_r C_p = \Delta_r a + \Delta_r b T + \Delta_r c T^2 \qquad\qquad (8.5.14)$$

$$\Delta_r H^\circ = \Delta_r H_o^\circ + \Delta_r a T + \frac{\Delta_r b}{2} T^2 + \frac{\Delta_r c}{3} T^3 \qquad\qquad (8.5.21)$$

The integral in Eq. 20.1.27 is then:

$$\ln \frac{K_{P,T_2}}{K_{P,T_1}} = \int_{T_1}^{T_2} \frac{\Delta_r H_o^\circ}{RT^2} + \frac{\Delta_r a}{RT} + \frac{\Delta_r b}{2R} + \frac{\Delta_r c}{3R} T\ dT \qquad\qquad 20.1.34$$

which integrates to:

$$\ln \frac{K_{P,T_2}}{K_{P,T_1}} = -\frac{\Delta_r H_o^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) + \frac{\Delta_r a}{R}\ln \frac{T_2}{T_1} + \frac{\Delta_r b}{2R}(T_2 - T_1) + \frac{\Delta_r c}{6R}(T_2^2 - T_1^2) \qquad 20.1.35$$

Eqs. 20.1.33 and 20.1.35 add "correction terms" to the basic form in 20.1.28 for successively wider variations in temperature. Alternatively, the integrals in Eq. 20.1.27 can be done as indefinite integrals:

$$\ln K_p = -\frac{\Delta_r H_o^\circ}{RT} + \frac{\Delta_r a}{R}\ln T + \frac{\Delta_r b}{2R} T + \frac{\Delta_r c}{6R} T^2 + I \qquad\qquad 20.1.36$$

where I is the combined integration constant. The integration constant is determined from one known K_p at the corresponding temperature.

Entropy and the Variation of K_p with Temperature: In general, $\Delta_r G^\circ$, $\Delta_r H^\circ$, and $\Delta_r S^\circ$ are functions of temperature. The reaction Gibbs energy is determined from the equilibrium constant as a function of temperature using Eq. 20.1.12, $\Delta_r G^\circ = -RT \ln K_p$. The van 't Hoff equation allows the reaction enthalpy, $\Delta_r H^\circ$, to be determined from the temperature variation of the equilibrium constant. The reaction entropy is then calculated using the definition of the reaction Gibbs energy, $\Delta_r G^\circ = \Delta_r H^\circ - T\, \Delta_r S^\circ$:

$$\Delta_r S^\circ = \frac{\Delta_r H^\circ - \Delta_r G^\circ}{T} \qquad\qquad 20.1.37$$

Alternately, the dependence of the equilibrium constant on the reaction enthalpy and entropy can be separated by substituting the definition of the reaction Gibbs energy into Eq. 20.1.13°:

$$\ln K_p = \frac{-(\Delta_r H° - T\Delta_r S°)}{RT} = \frac{-\Delta_r H°}{RT} + \frac{\Delta_r S°}{R} \qquad\qquad 20.1.38$$

If we assume that $\Delta_r H°$ and $\Delta_r S°$ are temperature independent, this last equation is in the form of a straight line with a slope of $-\Delta_r H°/R$ and an intercept of $\Delta_r S°/R$, as in Figure 20.1.3. This interpretation is useful in explaining the influence of the reaction entropy on the equilibrium constant. The value of the reaction entropy shifts the line up and down in the vertical direction on the $\ln K_p$ axis. However, it is important to remember that $\Delta_r S°$ is temperature dependent. The intercept of the graph gives $\Delta_r S°$ at roughly the average temperature of the plotted data points. In general it is better to use Eq. 20.1.37 to calculate the reaction entropy at a given specific temperature, than to use the intercept of the van 't Hoff plot.

For Real Gases the Equilibrium Constant is written in Terms of Fugacities: The thermodynamic equilibrium constant should be independent of total pressure. However, studies of reactions at high pressures show that K_p is a function of pressure. The K_p for the synthesis of ammonia, at a range of total pressures, is given in Table 20.1.1.

Table 20.1.1: K_p for ½ N_2 + $^3/_2$ H_2 $\rightleftarrows$ NH_3 as a function of total pressure at 723 K.[4]

Total pressure (atm)	K_p	$K\gamma$	K_f
10	0.00659	0.995	0.00655
50	0.00690	0.945	0.00650
100	0.00725	0.880	0.00636
600	0.01294	0.497	0.00642

Our treatment of gas phase equilibria to this point has assumed ideal gas behavior. At high pressures, gases are no longer ideal. The change in equilibrium constant with large changes in total pressure results from the non-ideal behavior of the reactants and products. Under extreme changes in pressure, we need to recast the equilibrium expression in terms of the fugacity. The chemical potential of a real gas is given by Eq. 16.7.1, $\mu_i = \mu_i° + RT \ln(f_i/P°)$. Using the fugacities in the derivation of Eqs. 20.1.6°-20.1.10°, we find that:

$$\Delta_r G° = -RT \ln K_f \qquad \text{with} \quad K_f = \frac{(f_C/P°)^c (f_D/P°)^d}{(f_A/P°)^a (f_B/P°)^b} \qquad \text{(equilibrium, cst. T)} \quad 20.1.39$$

The fugacity based equilibrium constant can be factored into a pressure dependent term and the corresponding ratio of fugacity coefficients using Eq. 16.7.10, $f_i = \gamma_i P_i$:

$$K_f = \left[\frac{\gamma_C{}^c \gamma_D{}^d}{\gamma_A{}^a \gamma_B{}^b}\right]\left[\frac{(P_C/P°)^c (P_D/P°)^d}{(P_A/P°)^a (P_B/P°)^b}\right] = K_\gamma K_p \qquad \text{(equilibrium)} \qquad 20.1.40$$

For the ammonia synthesis, K_γ was approximated, using the Law of Corresponding States and Figure 16.7.1. The results are listed in Table 20.1.1. The resulting equilibrium constant in terms of fugacities is constant to within experimental error and the error inherent in using the Law of

Corresponding States to estimate the fugacity coefficients. For real gases we simply exchange the fugacity for the measured partial pressure. The result is the pressure independent thermodynamic equilibrium constant based on fugacities, K_f.

The pressure independence of the equilibrium constant leaves an important issue to be resolved. LeChâtelier's Principle predicts a shift in the position of equilibrium with total pressure. How can the position of equilibrium shift if K_p, or K_f for real gases, is constant?

20.2 Gas Phase Chemical Equilibria and LeChâtelier's Principle

K_p, K_c, and K_x Differ if $\Delta_r n_g \neq 0$: At times working with partial pressures is inconvenient. The equilibrium expression can be evaluated using mole fractions or gas phase concentrations when necessary. Substituting Dalton's Law of partial pressures for each constituent into the Law of Mass Action, with $P_i = y_i P$ and total pressure P, gives:

$$K_p = \frac{(P_C/P^\circ)^c (P_D/P^\circ)^d}{(P_A/P^\circ)^a (P_B/P^\circ)^b} = \frac{(y_C P/P^\circ)^c (y_D P/P^\circ)^d}{(y_A P/P^\circ)^a (y_B P/P^\circ)^b} = \left(\frac{y_C^c y_D^d}{y_A^a y_B^b}\right)\left(\frac{P}{P^\circ}\right)^{\Delta_r n_g}$$
20.2.1

where $\Delta_r n_g$ is the change in number of moles of gas for the reaction, $\Delta_r n_g = c + d - a - b$, as given in Eq. 8.3.1°. The first term on the right is the equilibrium constant expressed in terms of mole fractions, K_x.

$$K_p = K_x \left(\frac{P}{P^\circ}\right)^{\Delta_r n_g} \qquad \text{with } K_x = \frac{y_C^c y_D^d}{y_A^a y_B^b}$$
20.2.2

Alternatively, Dalton's Law can be expressed in terms of the gas phase concentrations, $P_i = n_i RT/V = c_i RT$:

$$K_p = \frac{(P_C/P^\circ)^c (P_D/P^\circ)^d}{(P_A/P^\circ)^a (P_B/P^\circ)^b} = \frac{(c_C RT/P^\circ)^c (c_D RT/P^\circ)^d}{(c_A RT/P^\circ)^a (c_B RT/P^\circ)^b} = \left(\frac{c_C^c c_D^d}{c_A^a c_B^b}\right)\left(\frac{RT}{P^\circ}\right)^{\Delta_r n_g}$$
20.2.3

The ratio of concentrations has units in general. To insure the concentration based equilibrium constant is unitless, divide and multiply each concentration term by the standard state concentration, c°:

$$K_p = \frac{((c_C/c^\circ) c^\circ RT/P^\circ)^c ((c_D/c^\circ) c^\circ RT/P^\circ)^d}{((c_A/c^\circ) c^\circ RT/P^\circ)^a ((c_B/c^\circ) c^\circ RT/P^\circ)^b} = \frac{(c_C/c^\circ)^c (c_D/c^\circ)^d}{(c_A/c^\circ)^a (c_B/c^\circ)^b}\left(\frac{c^\circ RT}{P^\circ}\right)^{\Delta_r n_g}$$
20.2.4

$$K_p = K_c \left(\frac{c^\circ RT}{P^\circ}\right)^{\Delta_r n_g} \qquad \text{with } K_c = \frac{(c_C/c^\circ)^c (c_D/c^\circ)^d}{(c_A/c^\circ)^a (c_B/c^\circ)^b}$$
20.2.5

K_p is the true thermodynamic equilibrium constant, assuming ideal gas behavior. In other words, K_p is independent of the total pressure and the partial pressures of the reactants and products. K_c and K_x are not true thermodynamic equilibrium constants because they depend on the total pressure. On the other hand, if $\Delta_r n_g = 0$, as in the water-gas shift reaction, $K_p = K_x = K_c$, or you can even use moles directly in the equilibrium expression.

Example 20.2.1: *Dissociation*

Calculate the degree of dissociation of PCl_5 at 1.00 bar and 10.0 bar total pressure, starting with 2.00 moles of PCl_5. $K_p = 0.460$ at 229 K. The reaction is PCl_5 (g) $\overset{\rightarrow}{\leftarrow}$ PCl_3 (g) + Cl_2 (g).

Answer: The reaction is in the general form of a dissociation. The change in number of moles of gas for the reaction is $\Delta_r n_g = 1$. Using Eq. 20.2.2 the equilibrium position is given by:

$$K_p = K_x \left(\frac{P}{P^\circ} \right) \qquad \text{at P = 1.00 bar, } K_x = 0.460 \qquad \text{and at P = 10.0 bar, } K_x = 0.0460$$

The moles fractions can be calculated using the following table using "a" as the initial moles of the reactant:

$$PCl_5 \quad \overset{\rightarrow}{\leftarrow} \quad PCl_3 \text{ (g)} + Cl_2 \text{ (g)}$$

moles: $\quad a - \xi \qquad \xi \qquad \xi \qquad\qquad$ giving $\quad n_{tot} = a - \xi + \xi + \xi = a + \xi$

mole fraction: $\dfrac{a - \xi}{a + \xi} \qquad \dfrac{\xi}{a + \xi} \qquad \dfrac{\xi}{a + \xi}$ $\qquad\qquad$ 20.2.6

where n_{tot} is the total moles of gases. Substitution of the mole fractions into K_x gives:

$$K_x = \frac{y_{PCl_3}\, y_{Cl_2}}{y_{PCl_5}} = \frac{\left(\dfrac{\xi}{a + \xi} \right)\left(\dfrac{\xi}{a + \xi} \right)}{\left(\dfrac{a - \xi}{a + \xi} \right)} = \frac{\xi^2}{a^2 - \xi^2} \qquad\qquad 20.2.7$$

Solving for the extent: $\quad \xi = \left(\dfrac{K_x}{1 + K_x} \right)^{1/2} a$ $\qquad\qquad$ 20.2.8

Eqs. 20.2.6-20.2.8 are applicable for any reaction with stoichiometry $A \overset{\rightarrow}{\leftarrow} B + C$. With P = 1.00 bar, a = 2.00 mol, and $K_x = 0.460$, then $\xi = 1.12_3$ mol. The degree of dissociation is:

$$\alpha = \frac{\xi}{a} 100\% = 56.1\%$$

At 10.0 bar, giving $K_x = 0.0460$, then $\xi = 0.419_4$ and $\alpha = 21.0\%$ dissociated. The shift in the equilibrium position is as predicted by LeChâtelier's Principle; for an increase in total pressure the reaction shifts in the direction with the smaller number of moles of gas. The change in pressure for this problem might be accomplished by placing the reaction in a cylinder that is fitted with a piston, and then compressing the reaction mixture to 10.0 bar.

Example 20.2.2: *Addition of an Inert Gas at Constant Volume*

Calculate the position of the equilibrium if 1.00 mole of an inert gas is added to the reaction mixture in the last problem. The effect of an inert gas is different if the gas is added at constant pressure or at constant volume. For this problem assume the system is at constant volume.

Answer: The partial pressure of a substance is the pressure the substance would exert if alone in the vessel. For a constant volume system, addition of an inert gas does not change the partial pressures of the reactants and products, so the position of equilibrium does not change. The inert gas can be any substance that does not participate in the reaction, including helium, argon, nitrogen, or even oxygen if oxygen is unreactive.
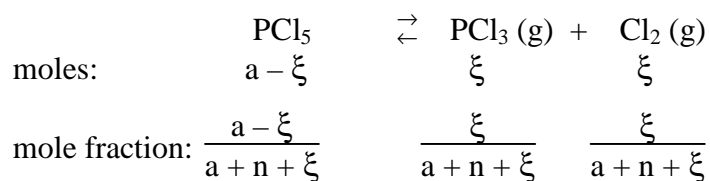

Example 20.2.3: *Addition of an Inert Gas at Constant Pressure*
Calculate the position of the equilibrium if 3.00 moles of an inert gas is added to the reaction in Example 20.2.1. Assume the system is at a constant pressure of 1.00 bar.

Answer: Let the initial moles of reactant be a and the moles of added inert gas be n. After the addition of the inert gas, the mole fractions are based on:

$$n_{total} = a - \xi + \xi + \xi + n = a + n + \xi$$

and the mole fractions are now:

$$\begin{array}{cccc} & PCl_5 & \overset{\rightarrow}{\underset{\leftarrow}{}} \; PCl_3\,(g) \; + & Cl_2\,(g) \\ \text{moles:} & a - \xi & \xi & \xi \\ \text{mole fraction:} & \dfrac{a-\xi}{a+n+\xi} & \dfrac{\xi}{a+n+\xi} & \dfrac{\xi}{a+n+\xi} \end{array}$$

Substitution of the mole fractions into K_x gives:

$$K_x = \frac{\left(\dfrac{\xi}{a+n+\xi}\right)\left(\dfrac{\xi}{a+n+\xi}\right)}{\left(\dfrac{a-\xi}{a+n+\xi}\right)} = \frac{\xi^2}{(a+n+\xi)(a-\xi)} = \frac{\xi^2}{a(a+n) - n\xi - \xi^2}$$

Rearranging: $(1 + K_x)\xi^2 + K_x\, n\xi - K_x\, a(a+n) = 0$

Solving for the extent using the quadratic formula with a = 2 and n = 3 gives ξ = 1.304 mol and the degree of dissociation, α = 65.2%. Why does the degree of dissociation increase? Consider the equilibrium expression in terms of partial pressures. At constant pressure, the addition of an inert gas increases the volume of the system. The partial pressures of the reacting gases then decrease, since $P_i = n_i RT/V$. The effect of the perturbation on the product side is greater than the reactant side because of the two partial pressures in the numerator of the equilibrium expression. The equilibrium position shifts to the right, compared to Example 20.2.1.
  We can check our results for errors by using the equilibrium extent to calculate the corresponding equilibrium constant. For ξ = 1.304 mol:

$$y_{PCl_5} = \frac{a-\xi}{a+n+\xi} = \frac{2-1.304}{2+3+1.304} = 0.13133$$

$$y_{PCl_3} = y_{Cl_2} = \frac{\xi}{a+n+\xi} = \frac{1.304}{2+3+1.304} = 0.24578$$

giving $K_x = y_{PCl_3}\, y_{Cl_2}/y_{PCl_5} = 0.460$, which verifies our calculation.

We have developed the connection between thermodynamics and the equilibrium expression for homogeneous gas phase reactions. However, most chemists work in solution.

20.3 Equilibria in Solution and Heterogeneous Equilibria

The central connection between thermodynamics and equilibrium is through the chemical potential. For a component in solution, from Eqs. 19.1.3 and 19.1.11:

$$\mu_A = \mu_A^*(l) + RT \ln a_A \qquad \text{(solvent, Raoult's Law SS)} \qquad (19.1.3)$$

$$\mu_i = {}^x\mu_i^\dagger(l) + RT \ln a_i \qquad \text{(solute, Henry's Law SS)} \qquad (19.1.11)$$

The corresponding equilibrium expression is easily determined by substitution of the chemical potentials in terms of the solution activities into Eq. 20.1.5. Repeating the steps in Eqs. 20.1.6°-20.1.10°, we find that:

$$\Delta_r G = \Delta_r G^\circ + RT \ln Q \qquad \text{with} \quad Q = \left[\frac{a_C{}^c a_D{}^d}{a_A{}^a a_B{}^b} \right] \qquad \text{(cst. T\&P)} \qquad 20.3.1$$
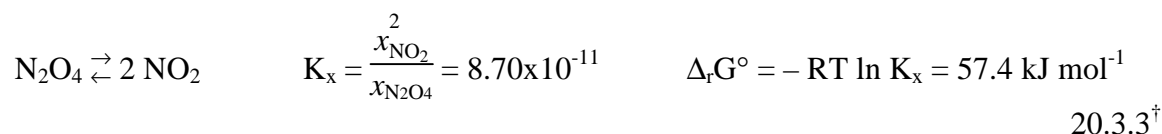
$$\Delta_r G^\circ = - RT \ln K_a \qquad \text{with} \quad K_a = \left[\frac{a_C{}^c a_D{}^d}{a_A{}^a a_B{}^b} \right]_{eq} \qquad \text{(equilibrium, cst. T)} \quad 20.3.2$$

No assumptions of ideality are necessary. G. N. Lewis's cleaver definition of the activity for a real solution allows us to easily convert our relationships for gas phase reactions to the condensed phase; we just exchange activities for partial pressures. Little more needs to be said about the fundamental thermodynamics of reactions in solution.

You can use any concentration measure that is convenient, Eqs. 19.1.17. You just need to remember that the standard state chemical potentials depend on the choice of concentration measure, and then $\Delta_r G^\circ = - RT \ln K_a$ is expressed in the appropriate concentration units. We have used "x", "c", and "m" superscripts to differentiate the standard states. However, most publications drop these superscripts and instead you need to determine the concentration measure from context. The Raoult's Law and Henry's Law standard states are summarized in Figure 18.3.3.

For an ideal-dilute solution, the activity coefficients are one. The equilibrium expression then reduces to a relationship in mole fractions, molarities, or molalities instead of activities: K_x, K_c, K_m. What are the ramifications of the choices of different concentration measures?

The Choices for Standard States Change the Value of the Equilibrium Constant: The numerical value for the concentration based equilibrium constant and reaction Gibbs energy depend on the choice of concentration measure. Consider for example the dissociation of N_2O_4 in chloroform assuming an ideal dilute solution:

$$N_2O_4 \overset{\rightarrow}{\underset{\leftarrow}{}} 2 \, NO_2 \qquad K_x = \frac{x_{NO_2}^2}{x_{N2O4}} = 8.70 \times 10^{-11} \qquad \Delta_r G^\circ = - RT \ln K_x = 57.4 \text{ kJ mol}^{-1}$$

$$20.3.3^\dagger$$

Using Eqs. 2.2.7 and 2.2.11, the mole fractions can also be converted into molarity and molality units for the same experiment, Table 20.3.1.

Table 20.3.1: Equilibrium concentrations in different units for $N_2O_4 \overset{\rightarrow}{\underset{\leftarrow}{}} 2\,NO_2$ at 298.2 K.

	x_i	c_i (mol L^{-1})	m_i (mol kg^{-1})
NO_2	1.47×10^{-6}	1.85×10^{-3}	1.85×10^{-3}
N_2O_4	2.48×10^{-2}	0.324	0.335

The equilibrium constants calculated in terms of molarity and molality, K_c and K_m, respectively, are significantly different from K_x in magnitude, but equally valid. Assuming ideal behavior with $\gamma_{NO2} \cong 1$ and $\gamma_{N2O4} \cong 1$:

$$K_c = \frac{(c_{NO2}/c^\circ)^2}{c_{N2O4}/c^\circ} = 1.09 \times 10^{-5} \qquad\qquad K_m = \frac{(m_{NO2}/m^\circ)^2}{m_{N2O4}/m^\circ} = 1.06 \times 10^{-5}$$

$$\Delta_r G^\circ = -\,RT\,\ln K_c = 28.4 \text{ kJ mol}^{-1} \qquad\qquad \Delta_r G^\circ = -\,RT\,\ln K_m = 28.5 \text{ kJ mol}^{-1}$$

$$20.3.4^\dagger$$

The corresponding reaction Gibbs energies also differ and the values correspond to unit concentration standard states in each corresponding concentration unit.

The equilibrium constants listed in standard references are often based on unit molality standard states. However, work in the laboratory is often done on a molarity basis. How are equilibrium constants converted between concentration measures? Equilibrium constant conversions for molality and molarity standard states in dilute solution are based on Eqs. 2.2.8 and 2.2.12. To help with the unit conversions, note that $(1 \text{ L kg}^{-1}) = m^\circ/c^\circ$. Eq. 2.2.8 can be written:

$$m \cong \frac{c}{d_{soln}}\,(1 \text{ g L kg}^{-1} \text{ mL}^{-1}) = \frac{c}{d_{soln}}\,(m^\circ/c^\circ)(1 \text{ g mL}^{-1}) \qquad \text{(very dilute)} \quad 20.3.5$$

Equilibrium expressions involve terms of the form m/m° or c/c°. Solving this last equation for these ratios gives:

$$m/m^\circ = c/c^\circ\,(1 \text{ g mL}^{-1}/d_{soln}) \quad \text{and} \quad c/c^\circ = m/m^\circ\,(d_{soln}/1 \text{ g ml}^{-1}) \quad \text{(very dilute)} \quad 20.3.6$$

Consider the reaction, $a\,A + b\,B \overset{\rightarrow}{\underset{\leftarrow}{}} c\,C + d\,D$, with $\Delta_r\nu = c + d - a - b$. Substitution for m/m° into K_m using Eqs. 20.3.6 gives:

$$K_m = \frac{(m_C/m^\circ)^c\,(m_D/m^\circ)^d}{(m_A/m^\circ)^a\,(m_B/m^\circ)^b} \cong \frac{[c_C/c^\circ\,(1 \text{ g mL}^{-1}/d_{soln})]^c\,[c_D/c^\circ\,(1 \text{ g mL}^{-1}/d_{soln})]^d}{[c_A/c^\circ\,(1 \text{ g mL}^{-1}/d_{soln})]^a\,[c_B/c^\circ\,(1 \text{ g mL}^{-1}/d_{soln})]^b}$$

$$\cong \frac{(c_C/c^\circ)^c(c_D/c^\circ)^d}{(c_A/c^\circ)^a\,(c_B/c^\circ)^b}\left(\frac{1 \text{ g mL}^{-1}}{d_{soln}}\right)^{\Delta_r\nu}$$

$$K_m \cong K_c\left(\frac{1 \text{ g mL}^{-1}}{d_{soln}}\right)^{\Delta_r\nu} \qquad\qquad\qquad \text{(very dilute)} \quad 20.3.7$$

Substitution for c/c° into K_c using Eqs. 20.3.6 gives similarly:

$$K_c = K_m\,(d_{soln}/1 \text{ g ml}^{-1})^{\Delta_r\nu} \qquad\qquad\qquad \text{(very dilute)} \quad 20.3.8$$

The density of very dilute aqueous solutions is often close to that of pure water; at physiological temperature $d_{H_2O}^{37°C} = 0.9935$ g mL^{-1}. For a reaction with stoichiometry $A \rightleftarrows B + C + D$, $K_c \cong K_m(0.9935)^2$, which corresponds to a 1.3% difference. Reactions with large $\Delta_r\nu$ and solution densities different than ~1.0 have significant differences between K_m and K_c.

   The theory of chemical equilibrium that we have developed is easy to implement for homogenous solution, but what happens in heterogeneous reactions?
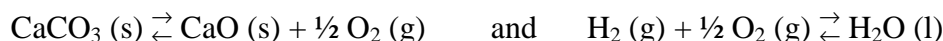
The Activity of Pure Constituents is 1: For a pure substance in a condensed phase at modest pressures, the chemical potential is equal to the standard state chemical potential, $\mu_A = \mu_A^*$:

$$\mu_A = \mu_A^* + RT \ln a_A = \mu_A^* \qquad \text{so that } a_A = 1 \qquad\qquad 20.3.9$$

The activity of a pure condensed phase is equal to one. Another equivalent viewpoint is that the concentration of a pure phase is $x_A = 1$, which corresponds to the standard state on a mole fraction basis. If a pure substance is in its standard state, the activity coefficient is equal to one so that $a_A = \gamma_A x_A = 1$.

Example 20.3.1: *Equilibria with pure condensed phases*
Give the equilibrium expression for the reactions:

$$CaCO_3 \text{ (s)} \rightleftarrows CaO \text{ (s)} + \tfrac{1}{2} O_2 \text{ (g)} \qquad \text{and} \qquad H_2 \text{ (g)} + \tfrac{1}{2} O_2 \text{ (g)} \rightleftarrows H_2O \text{ (l)}$$

Answer: For the dissociation of $CaCO_3$: $K_p = \dfrac{a_{CaO} \, P_{O_2}^{1/2}}{a_{CaCO_3}} = P_{O_2}^{1/2}$.

For the formation of pure liquid water: $K_p = \dfrac{a_{H_2O}}{P_{H_2} \, P_{O_2}^{1/2}} = \dfrac{1}{P_{H_2} \, P_{O_2}^{1/2}}$

In Dilute Solution the Solvent Activity is Approximated by the Mole Fraction: How does the solvent in dilute solution affect the position of equilibrium? Consider as a simple example the autoprotolysis of water and the corresponding equilibrium expression:

$$H_2O \text{ (l)} \rightleftarrows H^+ \text{ (aq)} + OH^- \text{ (aq)} \qquad\qquad K_w = \frac{(a_{H^+})(a_{OH^-})}{a_{H_2O}} \qquad\qquad 20.3.10$$

In dilute solution, we use a Henry's law standard state for the solutes and a Raoult's law standard state for the solvent. The activity coefficient of the solvent in dilute solution is near one, especially in comparison with any ionic solutes. In dilute solution, the equilibrium expression can be adequately approximated as:

$$K_w = \frac{(a_{H^+})(a_{OH^-})}{x_{H_2O}} \qquad\qquad \text{(dilute solution)} \qquad\qquad 20.3.11$$

The concentration of the solvent <u>does</u> have an effect on the position of equilibrium if the solvent is a reactant or product. In an ideal dilute solution, the mole fraction of the solvent approaches one, $x_{H_2O} \rightarrow 1$, and to the accuracy available from most experimental determinations, we can

often approximate the equilibrium expression as $K_w = (a_{H^+})(a_{OH^-})$. General Chemistry texts sometimes give the impression that the concentrations of pure liquids and solids and the solvent in dilute solution are "left out" of the equilibrium expression. Rather, the concentrations of pure condensed phases are always included; they are, however, always rigorously equal to 1. In dilute solution, except for studies with high accuracy, we also approximate the mole fraction of water as 1. The ability to approximate the activity of the solvent as ≈ 1 results from the choice of a Raoult's law standard state for the solvent.

The Gibbs Phase Rule Determines the Number of Independent Variables: When solving for the equilibrium position of a chemical reaction, we first need to know the number of independent variables. We then need to specify the values for the independent variables before the problem can be solved. This first step of laying out the variables for the calculation is necessary to ensure the problem is completely determined and solvable. Consider several chemical reactions at equilibrium occurring in one or more phases. The number of independent variables is given by the Gibbs Phase Rule, $D = f + p$, Eqs. 18.5.6 and 18.5.9. The variance, f, is the number of intensive variables that can be changed independently without disturbing the number of phases in equilibrium. The degrees of freedom, D, is the number of independent variables that appear in the expression for the total differential of the Gibbs energy.
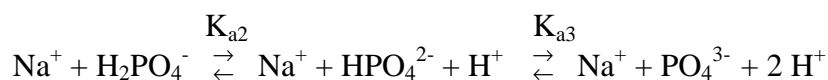

Example 20.3.2:
Phosphate equilibria play an important role in biochemical systems. Determine the variance of a solution made from NaH_2PO_4 and water at constant temperature and pressure. Use the variance to determine dG for an open system and for a closed system at equilibrium.

Answer: The constituents are the same as Example 14.2.1: Na^+, H^+, $H_2PO_4^-$, HPO_4^{2-}, PO_4^{3-}, and H_2O. There are 2 components: NaH_2PO_4 and H_2O. The solution is a single phase system giving the variance at constant temperature and pressure: $f'' = c - p = 2 - 1 = 1$. With one phase there is one extensive variable, giving $D'' = f'' + p = 2$ total independent variables. For an open system at constant temperature and pressure, dG then has two terms:

$$dG = \mu_{NaH_2PO_4}\, dn_{NaH_2PO_4} + \mu_{H_2O}\, dn_{H_2O}$$

The mole amounts of the two constituents are conventionally calculated using the solution concentration and total solution mass. The concentration is the intensive variable, with $x_{NaH_2PO_4} + x_{H_2O} = 1$, and the solution mass is the extensive variable to specify the phase size. For a closed system, $dn_{NaH_2PO_4} = dn_{H_2O} = 0$ giving $dG = 0$. The closed system is at equilibrium. At equilibrium the chemical potentials are constrained as:

$$Na^+ + H_2PO_4^- \underset{\rightleftarrows}{\overset{K_{a2}}{}} Na^+ + HPO_4^{2-} + H^+ \underset{\rightleftarrows}{\overset{K_{a3}}{}} Na^+ + PO_4^{3-} + 2\,H^+$$

$$\mu_{NaH_2PO_4} = \mu_{Na^+} + \mu_{H_2PO_4^-} = \mu_{Na^+} + \mu_{HPO_4^{2-}} + \mu_{H^+} = \mu_{Na^+} + \mu_{PO_4^{3-}} + 2\,\mu_{H^+}$$

The hydrogen ion activity is uniquely determined by specifying just the NaH_2PO_4 concentration, no other information beyond the equilibrium constants is necessary. For studying chemical reactions involving phosphate in a closed system, the moles of Na^+ ions will be constant and have no effect on the chemical equilibrium. In addition, if the moles of water is unchanged in the

reaction, then $dn_{H_2O} = 0$. For such a reaction the change in Gibbs energy is just
$dG = \mu_{H_2PO_4^-} \, dn_{H_2PO_4^-}$.

The Biochemist's Standard State is at pH = 7: Biochemical systems are commonly buffered at a pH near 7. As a consequence, equilibrium expressions are often specified at pH 7 and biochemistry references quote transformed standard state reaction Gibbs energies, $\Delta_r G^{o'}$, at pH 7. The hydrolysis of ATP is an interesting example. The free energy for most processes in living cells is derived from the hydrolysis of ATP. Surprisingly, the standard state reaction Gibbs energy for the hydrolysis of ATP is <u>unfavorable</u>, $\Delta_r G^o = 3.06$ kJ mol^{-1} at 298.2 K, Example 15.4.4. However, under standard state conditions the hydrogen ion activity is 1. The standard state reaction Gibbs energy is then not a useful measure of the free energy available from the hydrolysis of ATP at physiological pH. The standard state needs to be transformed to a pH of 7. The reaction, written using the primary ions in solution at pH 7, is:

$$ATP^{4-} + H_2O \rightleftharpoons ADP^{3-} + HPO_4^{2-} + H^+ \qquad \Delta_r G^o = 3.06 \text{ kJ mol}^{-1} \text{ (298.2 K)} \qquad 20.3.12$$

Near pH 7 ATP, ADP, and inorganic phosphate each have two predominant forms:

$$HATP^{3-} \rightleftharpoons ATP^{4-} + H^+ \qquad\qquad K_{ATP} = [ATP^{4-}][H^+]/[HATP^{3-}] \qquad 20.3.13$$
$$HADP^{2-} \rightleftharpoons ADP^{3-} + H^+ \qquad\qquad K_{ADP} = [ADP^{3-}][H^+]/[HADP^{2-}] \qquad 20.3.14$$
$$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+ \qquad\qquad K_{Pi} = [HPO_4^{2-}][H^+]/[H_2PO_4^-] \qquad 20.3.15$$

with the division by the standard state concentration m^o implied for each term to keep the equilibrium constants unitless. The ratio of these species changes with pH. As the reaction Gibbs energy is adjusted to pH 7, the shift in protonation states also needs to be addressed.

   For a reaction in a closed system, the mole amount of each reactant and product is a dependent variable that is fixed by the requirement of equilibrium (Sec. 15.2). To run the reaction at constant pH, a reservoir with H$^+$ ions at constant activity is used to supply or absorb H$^+$ ions in sufficient quantity to keep the H$^+$ activity constant for the reaction. The reaction system is therefore open with respect to H$^+$ and the moles of H$^+$ ions is an independent variable. Consider, first, just the equilibrium for the dissociation of $H_2PO_4^-$, Eq. 20.3.15. Consider five constituents, $H_2PO_4^-$, HPO_4^{2-}, H$^+$, Na$^+$, and H_2O. The chemical constraint is charge balance. The number of components is c = N_s – no. of reactions – no. chemical constraints = 3. The components are chosen as the moles of H_2O, n_{H_2O}, the total moles of phosphate, n_{Pi}, and the total moles of H, n_H, as given by the mass balance expressions:

$$n_{Pi} = n_{H_2PO_4^-} + n_{HPO_4^{2-}} \qquad \text{or equivalently} \qquad [P_i] = [H_2PO_4^-] + [HPO_4^{2-}]$$
$$n_H = 2 \, n_{H_2PO_4^-} + n_{HPO_4^{2-}} + n_{H^+} \qquad\qquad\qquad 20.3.16$$

(see Examples 14.2.1 and 20.3.2). Water is not involved in the acid dissociation reaction, $\nu_{H_2O} = 0$, giving $dn_{H_2O} = 0$ and also $dn_{Na^+} = 0$.

   The Gibbs energy at constant temperature and pressure can be written, neglecting water:

$$G = \mu_{H_2PO_4^-} \, n_{H_2PO_4^-} + \mu_{HPO_4^{2-}} \, n_{HPO_4^{2-}} + \mu_{H^+} \, n_{H^+} \qquad (\text{cst. T\&P, } \nu_{H_2O} = 0) \quad 20.3.17$$

However, the mole amounts are not independent, because there are only two chemical components in addition to water. The constraint of constant pH corresponds to fixing the H$^+$

activity, $pH = -\log(a_{H^+})$, which in turn constrains the chemical potential, $\mu_{H^+} = \mu_{H^+}^\circ + RT \ln a_{H^+}$. We can transform the Gibbs energy to make the H^+ chemical potential an independent variable by defining the Legendre transform (Sec. 16.2):[5,6]

$$G' \equiv G - \mu_{H^+} n_H \qquad\qquad 20.3.18$$

where G' is a new state function with $n_{H_2PO_4^-}$, $n_{HPO_4^{2-}}$, and μ_{H^+} as independent variables This transformation allows us to focus on the H^+ chemical potential instead of the total moles of H. Applying the Legendre transform defined by Eq. 20.3.18 using Eqs. 20.3.16 for the total moles of H gives:

$$G' = (\mu_{H_2PO_4^-} n_{H_2PO_4^-} + \mu_{HPO_4^{2-}} n_{HPO_4^{2-}} + \mu_{H^+} n_{H^+}) - \mu_{H^+}(2\, n_{H_2PO_4^-} + n_{HPO_4^{2-}} + n_{H^+})$$

$$= (\mu_{H_2PO_4^-} - 2\,\mu_{H^+})\, n_{H_2PO_4^-} + (\mu_{HPO_4^{2-}} - \mu_{H^+})\, n_{HPO_4^{2-}} \qquad \text{(cst. T\&P,}v_{H_2O}=0) \quad 20.3.19$$

The transformed chemical potentials are defined by the terms in parentheses:[5,6]

$$\mu'_{H_2PO_4^-} \equiv \mu_{H_2PO_4^-} - 2\,\mu_{H^+} \qquad \text{and} \qquad \mu'_{HPO_4^{2-}} \equiv \mu_{HPO_4^{2-}} - \mu_{H^+} \qquad \text{(cst. pH)} \quad 20.3.20$$

With these definitions, Eq. 20.3.19 becomes:

$$G' = \mu'_{H_2PO_4^-} n_{H_2PO_4^-} + \mu'_{HPO_4^{2-}} n_{HPO_4^{2-}} \qquad \text{(cst. T,P,\& pH;}v_{H_2O}=0) \quad 20.3.21$$

There is no term for the chemical potential of the H^+ ion. Recall that the definition of the Legendre transform to define the Gibbs energy as $G \equiv H - TS$ accomplished a similar simplification: $dG = -SdT + VdP = V\,dP$ at constant T. Further, for the acid dissociation in a closed system, $dn_{H_2PO_4^-} = -\,d\xi$ and $dn_{HPO_4^{2-}} = d\xi$:

$$dG' = -\,\mu'_{H_2PO_4^-}\, d\xi + \mu'_{HPO_4^{2-}}\, d\xi \qquad \text{(cst. T,P,\& pH, closed)} \quad 20.3.22$$

At equilibrium, $dG' = 0$, and the transformed chemical potentials of the phosphate containing species are equal, $\mu'_{H_2PO_4^-} = \mu'_{HPO_4^{2-}}$ (compare Eq. 15.2.25). At equilibrium, all the phosphate species are, in this sense, equivalent. The chemical potential of the phosphate component is simply called μ'_{Pi} with $\mu'_{Pi} \equiv \mu'_{H_2PO_4^-} = \mu'_{HPO_4^{2-}}$. Consider, again, Eq. 20.3.21. The equivalence of the transformed chemical potentials allows the terms for both protonation states to be combined into a single term using the mass balance from Eqs. 20.3.16:

$$dG' = \mu'_{H_2PO_4^-}\, dn_{H_2PO_4^-} + \mu'_{HPO_4^{2-}}\, dn_{HPO_4^{2-}} = \mu'_{Pi}\, dn_{Pi} \qquad \text{(cst. T,P,\& pH)} \quad 20.3.23$$

This last result shows that at constant pH, the phosphate contribution to the chemical potential reduces to a single term that combines all phosphate species into a single component, as required by the Gibbs phase rule (Example 20.3.2). The parallel treatment for ATP and ADP using Eqs. 20.3.13 and 20.3.14 shows that $HATP^{3-}$ and ATP^{4-} can be combined together as a single component, $[ATP] \equiv [HATP^{3-}] + [ATP^{4-}]$ and also $HADP^{2-}$ and ADP^{3-} can be combined together as a single component $[ADP] \equiv [HADP^{2-}] + [ADP^{3-}]$. At constant pH the hydrolysis of ATP is written:

$$ATP + H_2O \rightleftarrows ADP + P_i + H^+ \qquad\qquad K' = \frac{[ADP][P_i]}{[ATP]} \qquad \text{(cst. pH)} \quad 20.3.24$$
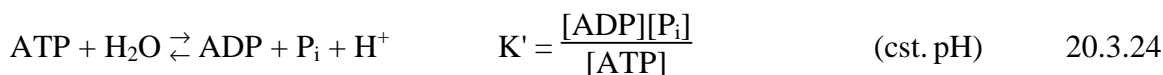
and we no longer need to consider the shift in protonation states of ATP, ADP, and phosphate, and the H^+ activity no longer appears in the equilibrium expression. The disadvantage of this approach is that the transformed standard state reaction Gibbs energy and the corresponding

equilibrium constant are now dependent on pH. The transformed standard state reaction Gibbs energy is given by the differences in transformed chemical potentials as usual: $\Delta_r G^{o\prime} = \Sigma\, \nu_i\, \mu^{o\prime}$. Using the corresponding definitions to Eqs. 20.3.20 for each reactant and product component relates the transformed, constant pH $\Delta_r G^{o\prime}$ to the conventional standard state $\Delta_r G^o$ as:[5,6]

$$\Delta_r G^{o\prime} = \Delta_r G^o + \nu_{H^+}\, \mu_{H^+} = \Delta_r G^o + \nu_{H^+}\, RT\, \ln a_{H^+} \qquad \text{(cst. pH)} \qquad 20.3.25$$

where ν_{H^+} is the stoichiometric coefficient for the free H^+ ion. The transformed standard state can be specified at any pH. The effective free energy at the given pH is $\Delta_r G^{o\prime}$.

Example 20.3.3: *The Biochemist's Standard State*

Calculate the transformed standard state reaction Gibbs energy and equilibrium constant for the hydrolysis of ATP at pH 7 at 298.15 K.

Answer: The stoichiometric coefficient for H^+ ion in Eq. 20.3.24 is +1. The hydrogen ion activity at pH 7 is 1.005×10^{-7}. Using Eq. 20.3.25 and $\Delta_r G^o = 3.06$ kJ mol^{-1} from Example 15.4.4:

$$\Delta_r G^{o\prime} = \Delta_r G^o + \nu_{H^+}\, RT\, \ln a_{H^+}$$
$$= 3.06 \text{ kJ mol}^{-1} + 8.3145 \text{ J K}^{-1} \text{ mol}^{-1}(298.15 \text{ K})(1 \text{ kJ}/1000 \text{ J}) \ln 1.005 \times 10^{-7}$$
$$= 3.06 \text{ kJ mol}^{-1} - 39.94 \text{ kJ mol}^{-1} = -36.88 \text{ kJ mol}^{-1}$$

$$K' = e^{-\Delta_r G^o/RT} = e^{-(-3.688 \times 10^4)/(8.3145 \text{ J K}^{-1} \text{ mol}^{-1}\, 298.15 \text{ K})} = e^{14.88} = 2.89 \times 10^6$$

At pH 7, the hydrolysis of ATP is a significant source of free energy. The shift in effective free energy can be understood using LeChâtelier's principle. The decrease in $[H^+]$ from the unit activity standard state to pH 7 shifts the position of equilibrium to the right, favoring hydrolysis.

Example 20.3.4: *Free Energy Under Physiological Conditions*

The transformed standard state reaction free energy for the hydrolysis of ATP corresponds to ATP, ADP, and P_i at unit activity, which is very different than the conditions in a living cell. Estimates of these concentrations for a resting state cell are: $[ATP] = 3.0 \times 10^{-4}$ m, $[ADP] = 1.0 \times 10^{-4}$ m, and $[P_i] = 1.0 \times 10^{-3}$ m. Neglecting activity coefficients, estimate the reaction Gibbs energy for the hydrolysis of ATP in a resting state cell.

Answer: Find the reaction Gibbs energy under non-standard state conditions using Eq. 20.1.10°:

$$\Delta_r G' = \Delta_r G^{o\prime} + RT \ln \frac{[ADP]/m^o\ [P_i]/m^o}{[ATP]/m^o} = \Delta_r G^{o\prime} + RT \ln \frac{[ADP][P_i]}{[ATP]}$$

with the division by the standard state concentration m^o implied for each term.

$$\Delta_r G' = -36.88 \text{ kJ mol}^{-1} + 8.314 \text{ J K}^{-1} \text{ mol}^{-1} (1 \text{ kJ}/1000 \text{ J}) \ln \frac{(1.0 \times 10^{-4})(1.0 \times 10^{-3})}{3.0 \times 10^{-4}}$$
$$\Delta_r G' = -36.88 \text{ kJ mol}^{-1} - 19.8 \text{ kJ mol}^{-1} = -56 \text{ kJ mol}^{-1}$$

Biochemical processes typically occur in many small steps so that the free energy demand for each individual process is well matched to the energy available from the hydrolysis of ATP.

20.4 Probabilities of Energy States Determine the Equilibrium Constant

   Statistical mechanics provides an interpretation of equilibrium that shows the interrelationship of molecular structure and thermodynamic function. The equilibrium constant, at the most fundamental level, is completely determined by the available energy levels of the reactants and products. Consider an isomerization or conformational change, $A \rightleftarrows B$, as a simple example. The available energy levels for the reactants and products are schematically represented in Figure 20.6.1a, with the reactant and product energies are placed on the same numerical scale with a common zero. The equilibrium constant for the reaction can be determined by considering both sets of states together, without noting which belong to the reactant or product, Figure 20.6.1b. The probability of occurrence of each state is given by the Boltzmann distribution, Eq. 8.9.5, $p_i = e^{-\varepsilon_i/RT}/q$, and the occupation is given by $n_i = n_{tot}\, e^{-\varepsilon_i/RT}/q$, where n_{tot} is the total number of molecules. The equilibrium constant is the sum of molecules in product states divided by the sum of molecules in reactant states, Figure 20.4.1c.
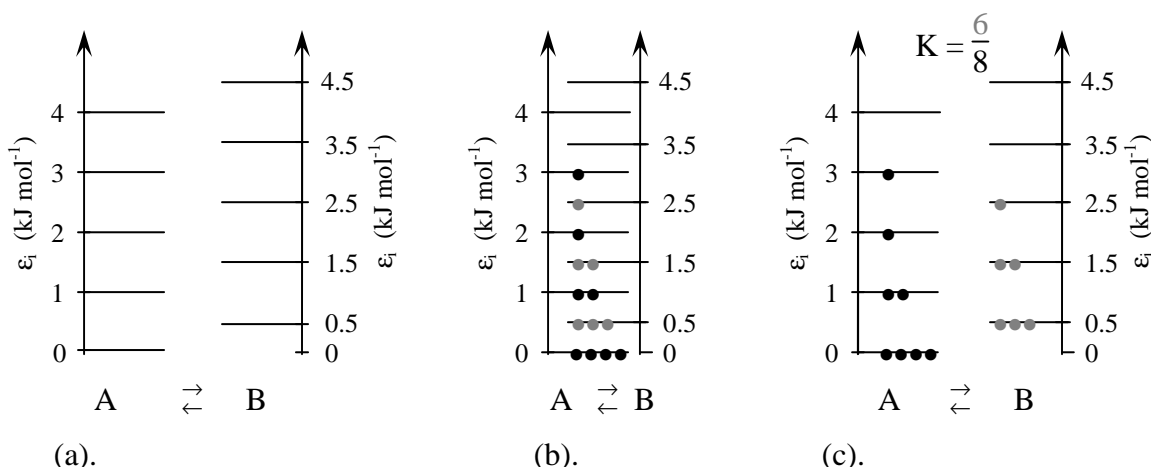

Figure 20.4.1: (a). The energy states for the reactant and product are placed on the same scale. (b). To calculate the equilibrium constant, the energy levels are filled without considering the constituent. The population of a state is determined by the energy of the state alone. (c). The equilibrium constant is given by the sum of the Boltzmann populations for the product energy states divided by the reactant energy states.

Equivalently, the equilibrium constant is also the ratio of the sum of Boltzmann probabilities or weighting factors of the product states divided by the sum of the reactant states:

$$K = \frac{\displaystyle\sum_{\substack{product \\ states}} n_i}{\displaystyle\sum_{\substack{reactant \\ states}} n_i} = \frac{\displaystyle\sum_{\substack{product \\ states}} n_{tot}\, e^{-\varepsilon_i/RT}/q}{\displaystyle\sum_{\substack{reactant \\ states}} n_{tot}\, e^{-\varepsilon_i/RT}/q} = \frac{\displaystyle\sum_{\substack{product \\ states}} e^{-\varepsilon_i/RT}/q}{\displaystyle\sum_{\substack{reactant \\ states}} e^{-\varepsilon_i/RT}/q} = \frac{\displaystyle\sum_{\substack{product \\ states}} e^{-\varepsilon_i/RT}}{\displaystyle\sum_{\substack{reactant \\ states}} e^{-\varepsilon_i/RT}} \qquad (A \rightleftarrows B,\ \text{same } \varepsilon=0)$$

$$\Sigma \; molecules \qquad \Sigma \; molecules \qquad \Sigma \; probabilities \qquad \Sigma \; weighting\ factors \qquad\qquad 20.4.1°$$

For the example in Figure 20.6.1, assume A and B have equally spaced states at 1 kJ mol^{-1} intervals and the lowest state for B is 0.5 kJ mol^{-1} higher than A. The occupations at 298 K are shown in Figure 20.6.1b. The resulting equilibrium constant is K = 6/8. The statistical interpretation of equilibrium is amazingly simple, yet extremely powerful.

Example 20.4.1: *Conformational Equilibria*

   The molecular mechanics based steric energy difference between the *anti-* and *gauche*-forms of butane is $\Delta\varepsilon$ = -3.26 kJ mol^{-1}, Figure 12.4.2:

   butane (*gauche*) $\overset{\rightarrow}{\leftarrow}$ butane (*anti*)
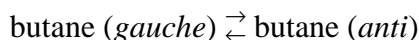
Assume there are no significant changes in vibrations between the two conformers. Also remember $\Delta_r H° = \Delta_r U° + \Delta_r n_g RT$, where $\Delta_r n_g$ is the change in the number of moles of gas. Since we are calculating the difference in energy between two conformers, $\Delta_r n_g = 0$, giving $\Delta_r H° = \Delta_r U° = \Delta\varepsilon$. Calculate the equilibrium constant for the ratio of *anti-* to *gauche*-forms using (a) $\Delta_r G° = \Delta_r H° - T \Delta_r S°$ and (b) using Eq. 20.4.1°.

Answer: (a). There are two equivalent *gauche*-conformers and one *anti*-conformer. The reaction entropy, assuming no significant change in vibrations (or rotational constants), is:

   $\Delta_r S° = S_{anti} - S_{gauche} = R \ln (1/2) = -5.76$ J K^{-1} mol^{-1}
   $\Delta_r G° = G_{anti} - G_{gauche} = \Delta_r H° - T\Delta_r S°$:
   $\Delta_r G° = -3.26$ kJ mol^{-1} $-$ (298.2 K)(-5.76 J K^{-1} mol^{-1})(1 kJ/1000 J) = -1.54$_3$ kJ mol^{-1}

and the equilibrium constant is: $K = e^{-\Delta_r G°/RT} = \dfrac{[anti]}{[gauche]} = 1.86_3$

(b). The *anti*-conformer has the lowest energy, which we assign as $\varepsilon_{anti} = 0$. Then the *gauche*-conformer has an energy $\varepsilon_{gauche} = 3.26$ kJ mol^{-1}. Table 20.4.1 lists the Boltzmann weighting factors and probabilities at 298.15 K.

Table 20.4.1. Calculation of the Boltzmann factors for *gauche-* and *anti*-conformations of butane at 298.2 K. There are two *gauche*-conformations and one *anti*-conformation.

Conformation	ε_i (kJ mol^{-1})	ε_i/RT	$e^{-\varepsilon_i/RT}$	$e^{-\varepsilon_i/RT}/q$
gauche	3.26	1.31$_5$	0.2685	0.174$_7$
gauche	3.26	1.31$_5$	0.2685	0.174$_7$
anti	0	0	1	0.650$_7$
			q=1.536$_9$	

To calculate q we sum the weighting factors in column 4. Then we use q to calculate the probabilities in the last column. The ratio of the *anti-* to *gauche*-probabilities is:

   $K_p = \dfrac{\Sigma \text{ probability for } anti}{\Sigma \text{ probability for } gauche} = \dfrac{0.650_7}{0.174_7 + 0.174_7} = 1.86_3$

The Gibbs energy and statistical approaches are equivalent, but take different points of view.

The statistical interpretation of equilibrium is indispensible for relating microscopic structure to macroscopic function, so we should derive Eq. 20.4.1°. If you haven't covered Chapt. 12 on the statistical definition of entropy, you can skip to the next section.

The Reaction Gibbs Energy and Equilibrium Constant are Expressed as Probabilities: We can relate molecular probabilities to the equilibrium constant in an elegant and illuminating way using the statistical definition of entropy. Consider an internal degree of freedom, such as vibration or a conformational change. The molar internal energy and entropy for an internal degree of freedom are given by Eqs. 12.2.6 and 12.4. 24° as sums over individual molecule energy states:

$$U - U(0) = \sum_i p_i \, \varepsilon_i \qquad S = -R \sum_i p_i \ln p_i \qquad \text{(internal,molar) (12.2.6, 12.4.24°)}$$

where $U(0)$ is the internal energy of the substance at absolute zero as the reference state. Allowing for differences in reference states, the Gibbs energy is given as:

$$G - G(0) = U - U(0) + PV - TS \qquad\qquad 20.4.2$$

Substituting Eqs. 12.2.6, 12.4.24° and $PV = nRT$ into this last equation gives an expression for the molar Gibbs energy of a substance:

$$G - G(0) = \sum_i p_i \, \varepsilon_i + RT + RT \sum_i p_i \ln p_i \qquad \text{(internal, molar)} \qquad 20.4.3°$$

Collecting terms in the sums gives:

$$G - G(0) = RT \sum_i p_i \, (\varepsilon_i/RT + \ln p_i) + RT \qquad \text{(internal, molar)} \qquad 20.4.4°$$

For the system at equilibrium, the Boltzmann distribution, Eq. 8.9.5, gives $\ln p_i = -\varepsilon_i/RT - \ln q$:

$$G - G(0) = RT \sum_i p_i \, (\varepsilon_i/RT - \varepsilon_i/RT - \ln q) + RT \qquad \text{(internal, molar)} \qquad 20.4.5°$$

Canceling terms and simplifying the last equation using $\sum p_i = 1$ results in:

$$G - G(0) = -RT \ln q + RT \qquad \text{(internal, molar)} \qquad 20.4.6°$$

For each constituent, k, in the chemical reaction:

$$G_k = G_k(0) - RT \ln q_k + RT \qquad \text{(internal, molar)} \qquad 20.4.7°$$

For the reaction $A \rightleftarrows B$, and referencing the energies to the same scale, $G_A(0) = G_B(0)$, the reaction Gibbs energy is, using Eq. 20.4.7° for A and B:

$$\Delta_r G = G_B - G_A = -RT \ln\left(\frac{q_B}{q_A}\right) \qquad (A \rightleftarrows B, \text{ internal, same } \varepsilon=0) \quad 20.4.8°$$

Specifying standard state pressure to convert $\Delta_r G$ to $\Delta_r G°$ has no effect on the internal degrees of freedom. Finally we use $K_p = e^{-\Delta_r G°/RT}$ to solve for the equilibrium constant. Solving for K_p gives Eq. 20.4.1°:

$$K_p = \left(\frac{q_B}{q_A}\right) = \frac{\displaystyle\sum_{\substack{product \\ states}} e^{-\varepsilon_i/RT}}{\displaystyle\sum_{\substack{reactant \\ states}} e^{-\varepsilon_i/RT}} \qquad (A \rightleftarrows B, \text{ internal, same } \varepsilon=0) \quad 20.4.9°$$

This result is restricted to the stoichiometry $A \rightleftarrows B$, considering internal degrees of freedom, and using a common energy zero for the reactant and product. We will derive a more general result in Chapter 32. However, the simple interpretation of this last equation is maintained in the more general result; the equilibrium constant is the sum of Boltzmann weighting factors for the products divided by the reactants. The equilibrium constant is completely determined by the available energy levels of the reactants and products and the random distribution of molecules over those energy states.

20.5 Binding Isotherms Characterize Molecular Association

Molecular recognition is the study of the intermolecular forces that allow the specific binding of one molecule to another. Molecular recognition is a central issue in protein-protein binding, protein-oligonucleotide binding, supramolecular chemistry, self-assembly, binding to surfaces in chromatographic separations, binding to surfaces in sensor applications, and guest-host chemistry. **Guest-host chemistry** is the study of tight-binding interactions between small molecules. However, whatever the specific identity of the partners in a binding interaction, the principles are the same. Molecular recognition depends on hydrogen-bonding, electrostatic, and Van der Waals forces, which act between binding partners and between the binding partners and the solvent. Guest-host chemistry is a typical example of a binding interaction study.

   β-Cyclodextrin is a typical host, Figure 20.5.1. β-Cyclodextrin, CD, is a cylindrical molecule with a hydrophobic cavity. Hydroxyl groups extend from the top and bottom of the cylinder, providing sites for strong hydrogen bond formation. Cyclodextrins are natural products produced by bacteria from starch. Naphthalenes with polar substituents are examples of good guests for cyclodextrins.
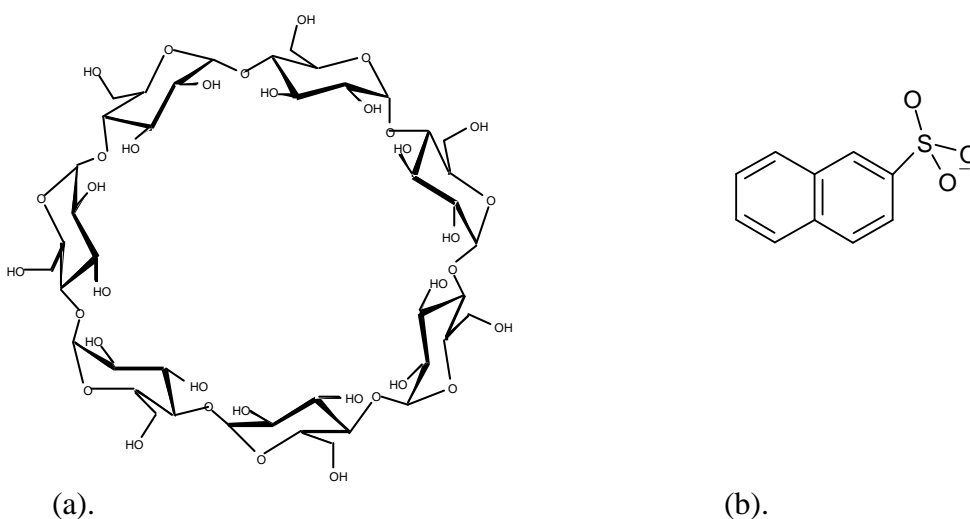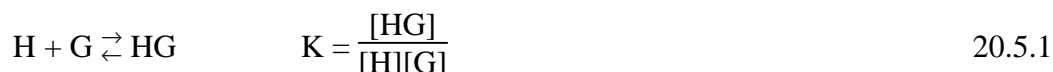

(a).   (b).

Figure 20.5.1: (a). β-Cyclodextrin (cycloheptaamylose) has an internal hydrophobic cavity. (b). A typical cyclodextrin guest, 2-naphthalene sulfonate ion.

Consider the binding of a host and guest and the corresponding equilibrium expression:

$$H + G \rightleftarrows HG \qquad\qquad K = \frac{[HG]}{[H][G]} \qquad\qquad\qquad 20.5.1$$

The equilibrium constant is called an association constant. This type of association is traditionally studied by determining the degree of association, α_{HG}:

$$\alpha_{HG} = \frac{[HG]}{[H]_o} \qquad\qquad\qquad 20.5.2$$

The total host concentration, $[H]_o$, determines the mass balance with free and bound forms of the host:

$$[H]_o = [H] + [HG] \qquad\qquad\qquad 20.5.3$$

Substituting the mass balance into Eq. 20.5.2 gives the degree of association as:

$$\alpha_{HG} = \frac{[HG]}{[H] + [HG]} \qquad\qquad\qquad 20.5.4$$

The degree of association can be determined using NMR, absorption, and fluorescence spectroscopy, among other techniques. Solving the equilibrium expression for the complex concentration, $[HG] = K\,[H][G]$, and substitution into Eq. 20.5.4 gives:
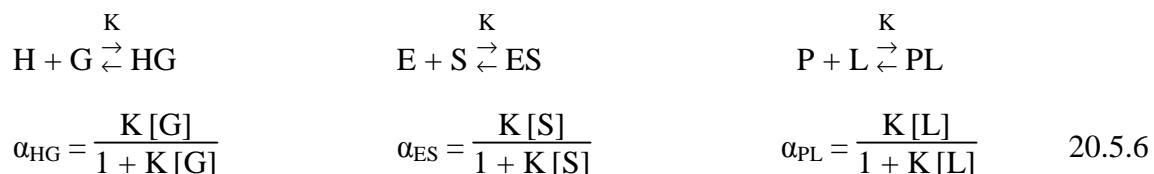
$$\alpha_{HG} = \frac{K\,[H][G]}{[H] + K\,[H][G]} = \frac{K\,[G]}{1 + K\,[G]} \qquad\qquad\qquad 20.5.5$$

This result is often called the **binding isotherm**. Strong binding corresponds to large K. Note the limiting behavior of this expression. For low guest concentration or for weak binding, the $K\,[G]$ term in the denominator can be neglected and the binding isotherm reduces to: $\alpha_{HG} \approx K\,[G]$. In the limit that the guest concentration is large or for strong binding, the degree of association approaches one. When $\alpha_{HG} = 1$ the complex formation is said to be saturated. The general form of this last equation occurs in many different circumstances and is the basis for a general pattern.

℘10

General Pattern ℘10: Saturation Binding (Scatchard and Langmuir):

   Enzyme-substrate or ligand-protein binding are entirely equivalent to guest-host binding. The only difference is that the host is a large protein instead of a small molecule:[7]

$$H + G \overset{K}{\rightleftarrows} HG \qquad\qquad E + S \overset{K}{\rightleftarrows} ES \qquad\qquad P + L \overset{K}{\rightleftarrows} PL$$

$$\alpha_{HG} = \frac{K\,[G]}{1 + K\,[G]} \qquad\qquad \alpha_{ES} = \frac{K\,[S]}{1 + K\,[S]} \qquad\qquad \alpha_{PL} = \frac{K\,[L]}{1 + K\,[L]} \qquad 20.5.6$$

where E is the enzyme and S is the substrate or P is the protein with L the ligand. These binding isotherms assume one binding site. Any reaction with the same stoichimetry as Eqs. 20.5.6 can be handled in an analogous fashion.

The binding of molecules from the gas phase onto a surface also leads to saturation binding. Consider an adsorbate, A, that combines with a free site on a surface (see Sec. 5.3 for a parallel kinetic derivation):

$$A\ (g) + B_\sigma \overset{K_\sigma}{\underset{\leftarrow}{\rightarrow}} A_\sigma \qquad\qquad 20.5.7\ (5.3.4)$$

where B_σ is a free binding site on the surface, A_σ is the adsorbed species, K_σ is the equilibrium constant for adsorption. We assume all sites are equivalent and that the probability a site is occupied is independent of the occupancy of adjacent sites. With these assumptions, the equilibrium constant for the process in terms of the surface concentrations is given by:

$$K_\sigma = \frac{[A]_\sigma}{[B]_\sigma\, P_A} \qquad\qquad \text{(equilibrium)} \qquad 20.5.8$$

where P_A is the partial pressure of A in the gas phase. The **fractional coverage** of A on the surface, θ_A, is given by the ratio:

$$\theta_A = \frac{[A]_\sigma}{[B]_{o\sigma}} \qquad\qquad 20.5.9\ (5.3.2)$$

where $[B]_{o\sigma}$ is the total concentration of binding sites on the surface. The fractional coverage is equivalent to the degree of association of the adsorbate with binding sites on the surface, $\theta_A = \alpha_{A\sigma}$. The surface concentration of A can readily be obtained from θ_A by rearranging this last equation:

$$[A]_\sigma = [B]_{o\sigma}\, \theta_A \qquad\qquad 20.5.10\ (5.3.3)$$

The concentration of remaining free sites on the surface is $[B]_{o\sigma}\,(1 - \theta_A)$, Figure 5.3.1. Using Eq. 20.5.10 for the surface concentration of A and the corresponding equation for the free sites gives:

$$K_\sigma = \frac{[B]_{o\sigma}\theta_A}{[B]_{o\sigma}(1 - \theta_A)\, P_A} = \frac{\theta_A}{(1 - \theta_A)\, P_A} \qquad\qquad 20.5.11$$

Solving this last equation for the fractional coverage at equilibrium gives:

$$\theta_A = \frac{K_\sigma\, P_A}{1 + K_\sigma\, P_A} = \frac{b\, P_A}{1 + b\, P_A} \qquad\qquad \text{(equilibrium)} \quad 20.5.12\ (5.3.11)$$

where the equilibrium constant is often called b, $K_\sigma = b$. This equation is called the **Langmuir adsorption isotherm**. Notice the limiting behavior of Eq. 20.5.12. For low partial pressures or for weak binding, the bP_A term in the denominator can be neglected and the Langmuir isotherm reduces to: $\theta_A \approx b\, P_A$. For large partial pressures or for strong binding, the fractional coverage approaches one; the surface is saturated. The Langmuir adsorption isotherm and the binding isotherms in Eqs. 20.5.5 and 20.5.6 are directly comparable. For brevity we will continue to discuss the example of guest-host binding, realizing that our comments are equally valid for surface adsorption and protein-ligand binding.

The plot of the degree of association versus free guest concentration from Eq. 20.5.5 is given in Figure 20.5.2a.
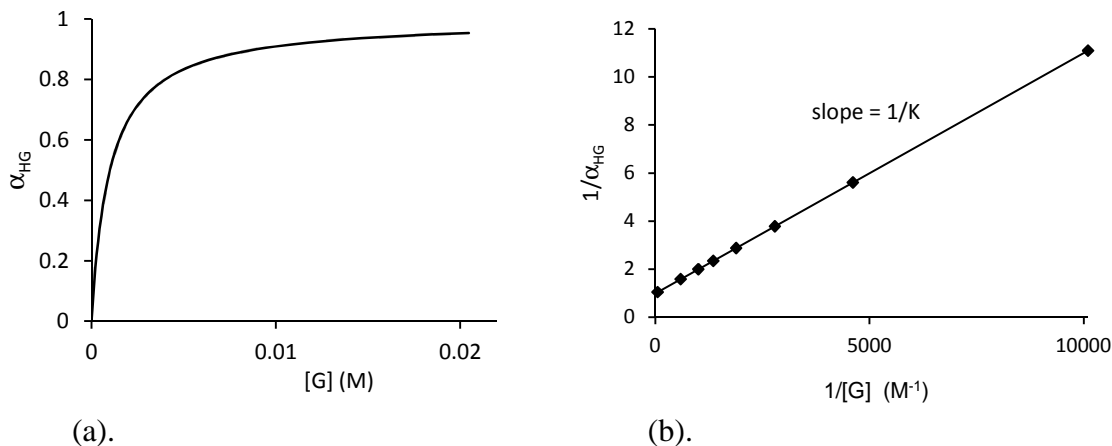
(a).   (b).

Figure 20.5.2: (a). Binding isotherm for a reaction of the type: $H + G \rightleftarrows HG$ versus free guest concentration using Eq. 20.5.5. (b) The binding isotherm in the double reciprocal form. For these example plots $[H]_o = 0.010$ M and $K = 1000$.

The approach to the limit of $\alpha_{HG} = 1$ with increasing free guest concentration shows the saturation behavior of the binding. Eq. 20.5.5 is in a form that is easily treated by non-linear curve fitting. Linearized forms of the binding isotherm are sometimes used to verify the functional form and determine the binding constant. Inverting Eq. 20.5.5 gives a double reciprocal plot that gives a slope of 1/K and an intercept of 1, Figure 20.5.2b and Example 5.3.1:

$$\frac{1}{\alpha_{HG}} = \frac{1}{K}\frac{1}{[G]} + 1 \qquad\qquad 20.5.13$$

Alternatively, Eq. 20.5.5 can be rearranged to give, Figure 20.5.3a:

$$\frac{\alpha_{HG}}{[G]} = K - K\,\alpha_{HG} \qquad\qquad 20.5.14$$

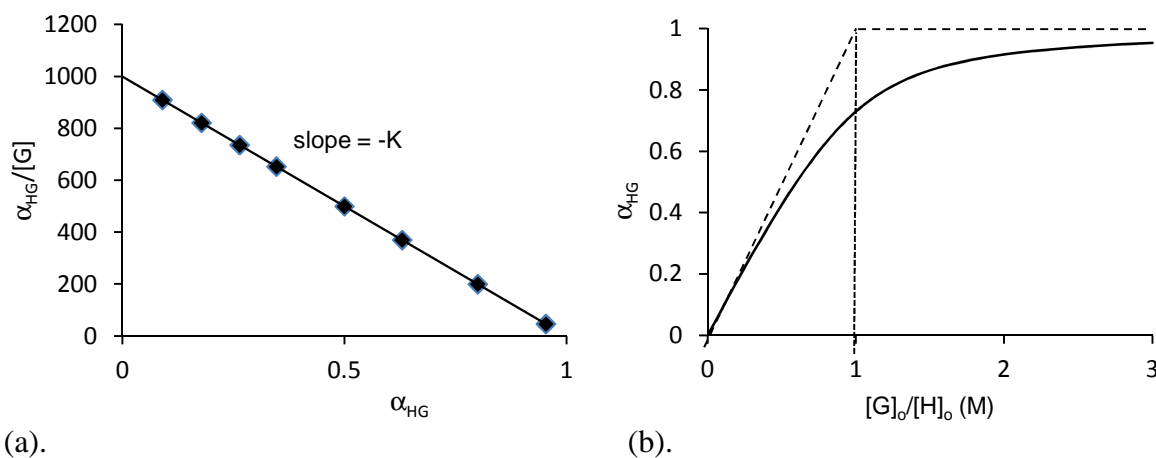(a).   (b).

Figure 20.5.3: (a). Scatchard plot for a host-guest binding isotherm. (b). Direct plot of the degree of association versus the analytical guest-host ratio: $r = [G]_o/[H]_o$. The intersection of the initial slope and $\alpha = 1$ gives the stoichiometry of the complex.

This rearranged form of the binding isotherm is called the Scatchard equation. The Scatchard form is commonly used in ligand binding studies in biochemistry. A plot of $\alpha_{HG}/[G]$ versus α_{HG} gives a straight line with slope $= -K$. These results can be extended to multiple binding sites.[7]

For some types of experiments, it difficult to find the free guest concentration, $[G]$. In addition, double-reciprocal and Scatchard plots sometimes give highly correlated fit parameters (see Sec. 3.2 for a discussion of between fit parameter correlation coefficients). An alternative course is to solve the equilibrium expression to find the degree of association in terms of the analytical concentrations, $[H]_o$ and $[G]_o$. The mass balance equation for the host is given by Eq. 20.5.3 and for the guest:

$$[G]_o = [G] + [HG] \qquad\qquad 20.5.15$$

Solving Eqs. 20.5.3 and 20.5.15 for the free guest and host concentrations gives:

$$[G] = [G]_o - [HG] \qquad\qquad 20.5.16$$
$$[H] = [H]_o - [HG] \qquad\qquad 20.5.17$$

Substitution of the mass balances into the equilibrium expression, Eq. 20.5.1, results in:

$$K = \frac{[HG]}{([H]_o - [HG])([G]_o - [HG])} \qquad\qquad 20.5.18$$

Cross-multiplying and rearranging gives a quadratic expression:

$$K[HG]^2 - (1 + K([H]_o + [G]_o)\,[HG] + K[H]_o\,[G]_o = 0 \qquad\qquad 20.5.19$$

Substitution of the coefficients into the quadratic formula gives:[8]

$$[HG] = \frac{(1+K([H]_o+[G]_o)) \pm \sqrt{(1+K\,([H]_o+[G]_o))^2 - 4K^2[H]_o[G]_o}}{2K} \qquad\qquad 20.5.20$$

Only the negative root gives meaningful concentrations. Expressing $[HG]$ as a function of the mole ratio of the guest and host is useful. Multiplying and dividing the equilibrium constant by $[H]_o$ gives:

$$[HG] = \frac{(1+K[H]_o\,(1+[G]_o/[H]_o)) - \sqrt{(1+K[H]_o\,(1+[G]_o/[H]_o))^2 - 4K^2[H]_o{}^2\,[G]_o/[H]_o}}{2K[H]_o/[H]_o} \qquad\qquad 20.5.21$$

The mole ratio of the guest to host is $r \equiv [G]_o/[H]_o$ giving:

$$[HG] = [H]_o\left(\frac{(1+K[H]_o\,(1+r)) - \sqrt{(1+K[H]_o\,(1+r))^2 - 4K^2[H]_o{}^2\,r}}{2K[H]_o}\right) \qquad\qquad 20.5.22$$

This last equation is applicable to any chemical equilibrium with the same stoichiometry. Similarly, the free concentrations of guest and host can also be calculated:[8]

$$[G] = [H]_o\left(\frac{-(1+K[H]_o\,(1-r)) + \sqrt{(1+K[H]_o\,(1-r))^2 + 4K[H]_o\,r}}{2K[H]_o}\right) \qquad\qquad 20.5.23$$

$$[H] = [H]_o\left(\frac{-(1+K[H]_o\,(r-1)) + \sqrt{(1+K[H]_o\,(r-1))^2 + 4K[H]_o}}{2K[H]_o}\right) \qquad\qquad 20.5.24$$

Alternatively, the mass balance equations, Eqs. 20.5.16 and 20.5.17, can be used with Eq. 20.5.22 to calculate the free guest and host concentrations. The degree of association for the complex is given by dividing Eq. 20.5.22 by $[H]_o$.

[www] Though algebraically cumbersome, the forms of Eqs. 20.5.22-20.5.24 are easily used in non-linear curve fitting, and are included in the "Nonlinear Least Squares Curve Fit" applet on the textbook Web site and on the companion CD.

Although it is important not to mix kinetic and equilibrium arguments, it is useful to point out that the Michaelis-Menten enzyme kinetics mechanism gives a rate law, Eq. 4.2.32, that is in essentially the same form. The use of double reciprocal and Scatchard type plots are common in analyzing the results of enzyme kinetics experiments. The similarity of the Michaelis-Menten mechanism with saturation binding should not be surprising, since the Michaelis-Menten mechanism is a reversible first-step mechanism treated using the steady state approximation.

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20.6 Isothermal Titration Calorimetry Does a Complete Thermodynamic Characterization

Isothermal titration calorimetry, ITC, is the most reliable way to characterize binding interactions. In ITC, guest-host reactions are run as titrations in an adiabatic solution calorimeter.[9] Heat flow to or from the sample cell is monitored as a function of added titrant. Titration calorimetry is an important tool in biochemistry, molecular biology, medicinal chemistry, and other areas that study molecular recognition.
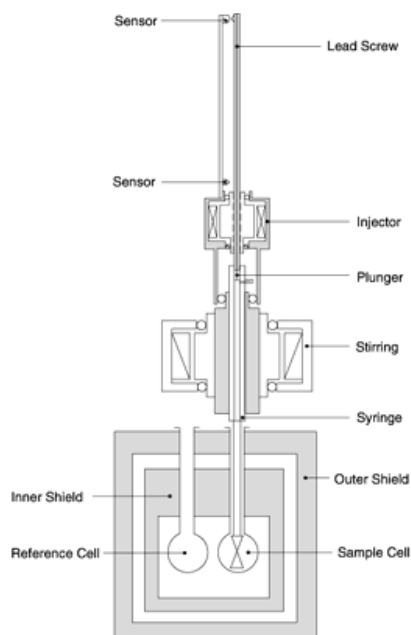

Figure 20.6.1: An isothermal titration calorimeter has a sample and reference cell and operates as an adiabatic, differential calorimeter to keep the sample and reference temperatures equal. Titrant is added using a stepper-motor driven syringe.

Thermometric titrations have become especially important in studies of protein and nucleic acid binding. For example, the reaction enthalpy and association constant of binding of an inhibitor to an enzyme is a common determination. Once the equilibrium constant and reaction enthalpy are known, it is straightforward to calculate $\Delta_r G°$ and $\Delta_r S°$ from $\Delta_r G° = -RT \ln K$ and $\Delta_r G° = \Delta_r H° - T\Delta_r S°$. A thermometric titration then provides a complete thermodynamic characterization of the chemical reaction, giving $\Delta_r G°$, $\Delta_r H°$, and $\Delta_r S°$.

An isothermal titration calorimeter directly measures heat evolved or absorbed during the titration using the same principle as a differential scanning calorimeter. However, the instrument is run in an isothermal mode with the heat flow instead caused by the chemical reaction. A computer controlled, stepper-motor driven syringe is utilized for injecting the titrant, Figure 20.6.1. Heat is released or absorbed from the sample cell in direct proportion to the amount of binding that occurs upon each injection of titrant.

The titration curve is then analyzed using non-linear fitting models based on Eq. 20.5.20 to calculate the reaction stoichiometry, K, $\Delta_r H$, and $\Delta_r S$. Since the calorimeter is at constant pressure, the reaction enthalpy is:

$$\Delta_r H = \frac{q_{rx}}{n_{rx}} \qquad\qquad 20.6.1$$

where q_{rx} is the heat transfer for the reaction at completion and n_{rx} is the number of moles of the limiting reactant in solution.

The Steepness of the Titration Curve Determines the Equilibrium Constant: The ITC titration curve for the guest-host reaction:[10]

$$CD + naphthaleneSO_3^- \rightarrow [CD \cdots naphthaleneSO_3^-] \qquad\qquad 20.6.2$$
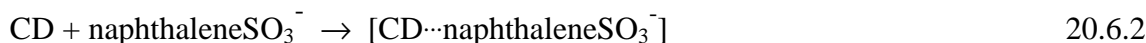
is shown in Figure 20.6.2. The guest, 2-naphthalene sulfonate ion, is added as the titrant. The titration is done in discrete steps of volume V_{inj} (typically 10 µL). A small volume of titrant is added and then heat is transferred to or from the sample cell until the temperatures of the sample and reference cells are equalized. Then the process is repeated with a second addition of titrant, and so on until the titration is complete. As the titration proceeds, the titrant that is added increases the total volume of the solution, which pushes some of the solution up into the stem of the sample cell. Once the solution is pushed into the stem any unreacted host will no longer be available for reaction with the guest. This dilution effect is often small and we neglect these effects in this section. The corrections are discussed in the Addendum. The total concentration of the host is $[H]_o$. For the ith step of the titration the volume of added titrant is: $V_{guest} = i\, V_{inj}$. Neglecting dilution corrections, the concentration of the guest titrant in the sample cell is given by:

$$[G]_o = M_{guest}\, i\, V_{inj}\, /V_{cell} \qquad\qquad \text{(neglecting dilution)} \quad 20.6.3$$

V_{cell} is the volume of the sample cell. The horizontal axis of the titration plot is given as the molar ratio, r, as used in Eq. 20.5.22:

$$r = \frac{[G]_o}{[H]_o} = \frac{\text{total moles guest added}}{\text{initial moles host}} = \frac{M_{guest}\, i\, V_{inj}}{M_{host}\, V_{cell}} \qquad\qquad 20.6.4$$

where M_{guest} is molar concentration of the titrant, M_{host} is the initial concentration of the host in the sample cell.
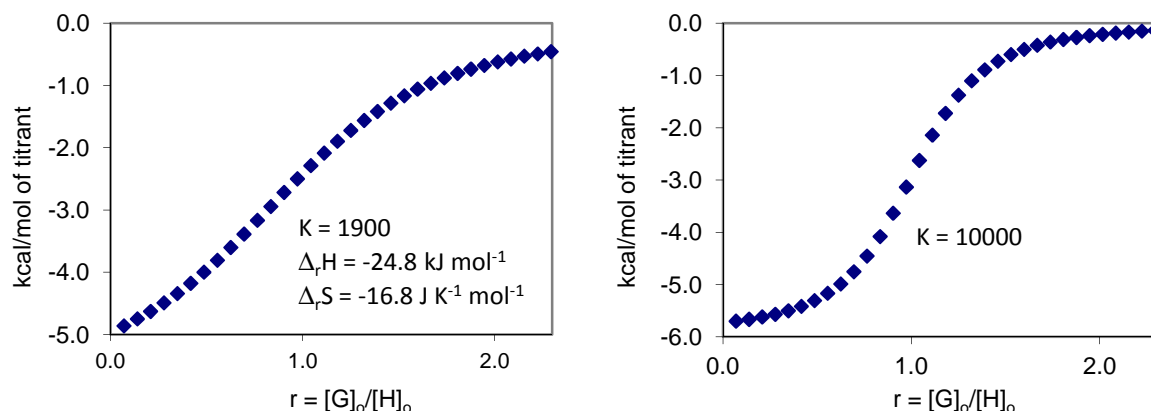

Figure 20.6.2. (a). Thermogram for the titration of β-cyclodextrin with naphthalenesulfonate. (b). Schematic titration curve showing the effect of increasing the equilibrium constant with the same reaction enthalpy as in (a).

The concentration of guest-host complex is given by Eq. 20.5.23. The change in number of moles of guest-host complex from step i-1 to step i is:

$$\Delta n_{HG,i} = [HG]_i\, V_{cell} - [HG]_{i-1}\, V_{cell} \qquad\qquad 20.6.5$$

The heat transferred after an addition of titrant is then given by the change in number of moles as:[11]

$$q_i = \Delta n_{HG,i}\, \Delta_r H° \qquad\qquad \text{(neglecting dilution)}\quad 20.6.6$$

where $\Delta_r H°$ is the reaction enthalpy. The vertical axis of the thermogram is plotted as:

$$q_{i,m} = \frac{q_i}{n_{inj}} \qquad\qquad \text{(neglecting dilution)}\quad 20.6.7$$

where n_{inj} is the number of moles of added titrant at each step, $n_{inj} = V_{inj}\, M_{guest}$. Eqs. 20.6.3-20.6.7 and 20.5.23 are then used in non-linear curve fitting to calculate K and $\Delta_r H°$.

Qualitatively, increasing $\Delta_r H°$ for the reaction increases the range along the vertical axis. Increasing the equilibrium constant causes a sharper transition, just as in acid-base titrations, Figure 20.6.2b.

20.7 Summary – Looking Ahead

The position of equilibrium determines "how far" a reaction runs. $\Delta_r G° = -RT \ln K_p$ is an important equation because it relates thermochemistry to chemical equilibrium. Thermochemistry is based on the determination of heat transfer and chemical equilibrium is based on the determination of concentrations. Thermochemistry is studied using calorimeters and equilibrium is generally studied using spectrophotometers. The underlying principle is the maximization of the entropy of the universe, which at constant temperature and pressures corresponds to the minimization of the Gibbs energy. At equilibrium the Gibbs energies of the

reactants and products are equal, subject to the reaction stoichiometry, $\Sigma \, v_i \, \bar{\mu}_i = 0$. To find the equilibrium expression for a gas phase reaction with real gases, we replace the partial pressures in the equilibrium expression with fugacities. To find the equilibrium expression for a non-ideal condensed phase reaction, we replace the concentrations in the equilibrium expression with activities. Thermodynamic equilibrium constants are functions only of temperature. For practical applications, we often use equilibrium constants, such as K_c and K_x for gas phase processes, that are functions of total pressure. Even though K_p is constant, the position of equilibrium does shift with total pressure if $\Delta v_i \neq 0$. With an increase in temperature, the position of equilibrium shifts in the endothermic direction, because the equilibrium constant increases for an endothermic process and decreases for an exothermic process. Isothermal titration calorimetry bridges the world of thermochemistry and chemical equilibrium and does a complete thermodynamic characterization of chemical reactions.

We have not yet discussed chemical equilibrium in the presence of electric fields. Electric fields are important in electrochemical cells and membrane systems. Electrochemistry is a convenient experimental approach to the study of many different types of chemical reactions, including, but not restricted to, redox reactions. Many biogeoenvironmental and biochemical reactions are redox reactions.

20. 8 Addendum: Dilution Corrections for Titration Calorimetry

The most commonly used ITC calorimeters in use in biochemistry laboratories have a fixed volume sample cell. During each titration step, some titrant and some analyte are excluded from the sample cell, which must be accounted for when calculating the heat effect for a given titration step. The adjustments for the excluded portions are given using the correction factors:[12]

$$\phi_{guest,i} = \frac{1}{\left(1 + \dfrac{iV_{inj}}{2V_{cell}}\right)} \qquad \text{and} \qquad \phi_{host,i} = \frac{\left(1 - \dfrac{iV_{inj}}{2V_{cell}}\right)}{\left(1 + \dfrac{iV_{inj}}{2V_{cell}}\right)} \qquad \text{20.8.1}$$

Then the corrected amounts for the guest and host at step i is:

$$n_{guest,i} = i \, V_{inj} \, M_{guest} \, \phi_{guest,i} \qquad\qquad n_{host,i} = V_{cell} \, M_{host} \, \phi_{host,i} \qquad\qquad \text{20.8.2}$$

Then $[G]_o = n_{guest,i}/V_{cell}$ and $[H]_o = n_{host,i}/V_{cell}$ for use in Eq. 20.5.22. The corrected heat effect for the ith step is calculated as:[12]

$$q_{i,corr} = Q(i) + \frac{iV_{inj}}{V_{cell}}\left(\frac{Q(i) + Q(i\text{-}1)}{2}\right) - Q(i\text{-}1) \qquad\qquad \text{20.8.3}$$

where Q(i) is the total enthalpy for the ith step, and Q(i-1) is for the preceding step. Each Q(i) is the total enthalpy for preparing the solution at equilibrium in the titration volume at step i starting from the beginning of the titration. These corrections are easily implemented in dedicated curve fitting software.

Chapter Summary

1. The reaction Gibbs energy under non-standard conditions is:

$$\Delta_r G = \Delta_r G^\circ + RT \ln Q \quad \text{with} \quad Q = \left[\frac{(P_C/P^\circ)^c (P_D/P^\circ)^d}{(P_A/P^\circ)^a (P_B/P^\circ)^b}\right]$$

2. At equilibrium $K_p = Q_{eq}$ and $\Delta_r G^\circ = -RT \ln K_p$.

3. Alternate important forms relating the equilibrium constant and reaction Gibbs energy are:

$$\ln K_p = \frac{-\Delta_r G^\circ}{RT} \qquad \text{and} \qquad K_p = e^{\frac{-\Delta_r G^\circ}{RT}}$$

4. The effect of changing reactant and product partial pressures on the position of equilibrium are conveniently predicted using LeChâtelier's Principle in the quantitative form:

$$\Delta_r G = RT \ln \frac{Q}{K_p}$$

5. The entropy and Gibbs energy of mixing plays a central role in determining the position of equilibrium. Assuming constant T and P and ideal gas behavior, the Gibbs energy during the course of a reaction is:

$$G = (n_A \mu_A^\circ + n_B \mu_B^\circ + n_C \mu_C^\circ + n_D \mu_D^\circ) + nRT \sum_{i=1}^{n_s} y_i \ln y_i + nRT \ln\left(\frac{P}{P^\circ}\right)$$

The second term is the Gibbs energy of mixing, which for ideal mixtures is entirely entropic, $\Delta_{mix}G = -T\Delta_{mix}S$. G is minimized at equilibrium.

6. For a general reaction: $K_p = \prod_{i=1}^{n_s} \left(P_i/P^\circ\right)^{\nu_i}$

7. The equilibrium constant depends on temperature as given by the van 't Hoff equation:

$$\left(\frac{\partial \ln K_p}{\partial T}\right)_P = \frac{\Delta_r H^\circ}{RT^2}$$

Assuming a constant reaction enthalpy over the temperature interval:

$$\ln \frac{K_{p,T_2}}{K_{p,T_1}} = -\frac{\Delta_r H^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

8. For moderate changes in temperature assuming a constant reaction heat capacity change:

$$\ln \frac{K_{p,T_2}}{K_{p,T_1}} = -\frac{\Delta_r H_o^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) + \frac{\Delta_r C_p}{R} \ln \frac{T_2}{T_1}$$

Over large temperature ranges:

$$\ln \frac{K_{p,T_2}}{K_{p,T_1}} = -\frac{\Delta_r H_o^\circ}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) + \frac{\Delta_r a}{R} \ln \frac{T_2}{T_1} + \frac{\Delta_r b}{2R}(T_2 - T_1) + \frac{\Delta_r c}{6R}(T_2^2 - T_1^2)$$

$$\ln K_p = -\frac{\Delta_r H_o^\circ}{RT} + \frac{\Delta_r a}{R} \ln T + \frac{\Delta_r b}{2R} T + \frac{\Delta_r c}{6R} T^2 + I$$

9. For equilibria with non-ideal gases we substitute the fugacity for the partial pressure:

$$\Delta_r G^\circ = -\,RT \ln K_f \qquad \text{with} \quad K_f = \frac{(f_C/P^\circ)^c (f_D/P^\circ)^d}{(f_A/P^\circ)^a (f_B/P^\circ)^b}$$

$$K_f = \left[\frac{\gamma_C^{\,c}\,\gamma_D^{\,d}}{\gamma_A^{\,a}\,\gamma_B^{\,b}}\right]\left[\frac{(P_C/P^\circ)^c (P_D/P^\circ)^d}{(P_A/P^\circ)^a (P_B/P^\circ)^b}\right] = K_\gamma\,K_p$$

10. In concentration units the equilibrium expressions for gas phase reactions are:

$$K_p = K_x \left(\frac{P}{P^\circ}\right)^{\Delta_r n_g} \text{ with } K_x = \frac{y_C^{\,c}\,y_D^{\,d}}{y_A^{\,a}\,y_B^{\,b}} \quad \text{and} \quad K_p = K_c \left(\frac{RT}{P^\circ}\right)^{\Delta_r n_g} \text{ with } K_c = \left(\frac{c_C^{\,c}\,c_D^{\,d}}{c_A^{\,a}\,c_B^{\,b}}\right)$$

11. If $\Delta_r n_g \neq 0$, K_x and K_c are not true thermodynamic equilibrium constants.

12. For gas phase dissociations with stoichiometry $A \rightleftarrows B + C$, starting only with A in initial amount a in moles:

$$K_x = \frac{y_{PCl_3}\,y_{Cl_2}}{y_{PCl_5}} = \frac{\xi^2}{a^2 - \xi^2}$$

13. The position of equilibrium for a constant volume reaction is insensitive to added inert gas. At constant pressure, the shift in equilibrium position with added inert gas is consistent with LeChâtelier's Principle as quantitatively expressed through $K_p = K_x(P/P^\circ)^{\Delta_r n_g}$.

14. For reactions in solution, replace the partial pressure by the solution activity of each species:

$$\Delta_r G = \Delta_r G^\circ + RT \ln Q \qquad \text{with} \quad Q = \left[\frac{a_C^{\,c}\,a_D^{\,d}}{a_A^{\,a}\,a_B^{\,b}}\right]$$

$$\Delta_r G^\circ = -\,RT \ln K_a \qquad \text{with} \quad K_a = \left[\frac{a_C^{\,c}\,a_D^{\,d}}{a_A^{\,a}\,a_B^{\,b}}\right]_{eq}$$

15. The standard state chemical potential and reaction Gibbs energies depend on the concentration measure chosen. Unit molality is not the same concentration as unit molarity.

16. The activity of a pure phase is equal to one, referred to a Raoult's Law standard state.

17. In dilute solution the solvent activity is given by the mole fraction, referred to a Raoult's Law standard state.

18. The variance, determined by the Gibbs phase rule, is the number of independent intensive variables that appear in the expression for the total differential of the Gibbs energy.

19. The biochemist's standard state, $\Delta_r G_B^{\circ\prime}$, is a Henry's Law standard state on a molality basis defined using a Legendre transformation at constant pH, $a_{H^+}^\circ = 1.005 \times 10^{-7}$:
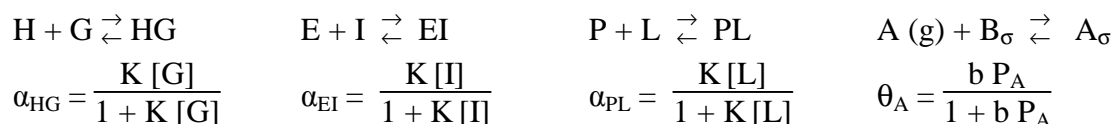
$$\Delta_r G^{\circ\prime} = \Delta_r G^\circ + \nu_{H^+} RT \ln a_{H^+}$$

20. The equilibrium constant is the ratio of molecules, the ratio of the sum of Boltzmann probabilities, or the ratio of the Boltzmann weighting factors of the product states divided by the reactant states. For a reaction $A \rightleftarrows B$ with the energies of the reactants and products on the same scale with a common energy zero:

$$K = \frac{\displaystyle\sum_{\substack{product \\ states}} n_i}{\displaystyle\sum_{\substack{reactant \\ states}} n_i} = \frac{\displaystyle\sum_{\substack{product \\ states}} n_{tot}\,e^{-\varepsilon_i/RT}/q}{\displaystyle\sum_{\substack{reactant \\ states}} n_{tot}\,e^{-\varepsilon_i/RT}/q} = \frac{\displaystyle\sum_{\substack{product \\ states}} e^{-\varepsilon_i/RT}/q}{\displaystyle\sum_{\substack{reactant \\ states}} e^{-\varepsilon_i/RT}/q} = \frac{\displaystyle\sum_{\substack{product \\ states}} e^{-\varepsilon_i/RT}}{\displaystyle\sum_{\substack{reactant \\ states}} e^{-\varepsilon_i/RT}}$$

21. Molecular recognition is the study of the intermolecular forces that allow the specific binding of one molecule to another.

22. Guest-host chemistry is the study of tight-binding interactions between small molecules.

23. For guest-host binding, $H + G \rightleftarrows HG$, the degree of association is defined as: $\alpha_{HG} = [HG]/[H]_o$, where $[H]_o$ is the total, analytical concentration of the host.

24. The binding isotherm for guest-host complexation is: $\alpha_{HG} = \dfrac{K\,[G]}{1 + K\,[G]}$

25. For the ith step of the titration the volume of added titrant is: $V_{guest} = i\,V_{inj}$. Neglecting dilution corrections, the concentration of the guest in the sample cell is given by: $[G]_o = M_{guest}\, i\, V_{inj}/V_{cell}$, where V_{cell} is the volume of the sample cell.

26. The change in number of moles of guest-host complex from step i-1 to step i is: $\Delta n_{HG,i} = [HG]_i\,V_{cell} - [HG]_{i-1}\,V_{cell}$. The heat transferred after an addition of titrant is then: $q_i = \Delta n_{HG,i}\,\Delta_r H°$, where $\Delta_r H°$ is the reaction enthalpy. The vertical axis of the thermogram is normalized to the amount of titrant added in a single step: $q_{i,m} = q_i/n_{inj}$.

℘10 *General Pattern 10: Saturation Binding*: The algebraic form for binding isotherms is:

$$H + G \rightleftarrows HG \qquad E + I \rightleftarrows EI \qquad P + L \rightleftarrows PL \qquad A\,(g) + B_\sigma \rightleftarrows A_\sigma$$

$$\alpha_{HG} = \frac{K\,[G]}{1 + K\,[G]} \qquad \alpha_{EI} = \frac{K\,[I]}{1 + K\,[I]} \qquad \alpha_{PL} = \frac{K\,[L]}{1 + K\,[L]} \qquad \theta_A = \frac{b\,P_A}{1 + b\,P_A}$$

Alternate linearized forms of the binding isotherms include the double-reciprocal and Scatchard equations, respectively:

$$\frac{1}{\alpha_{HG}} = \frac{1}{K}\frac{1}{[G]} + 1 \qquad\qquad \frac{\alpha_{HG}}{[G]} = K - K\,\alpha_{HG}$$

Double-reciprocal and Scatchard plots are often visually diagnostic, but are often not the most accurate form for curve fitting to extract the association constant. Non-linear curve fitting of plots of α_{HG} versus $r = [G]_o/[H]_o$ are often preferable. Solution of the equilibrium expression, subject to the mass balance constraints, gives the guest-host complex concentration, the free guest, and free host concentrations as:

$$[HG] = [H]_o\left(\frac{(1+K[H]_o\,(1+r)) - \sqrt{(1+K[H]_o\,(1+r))^2 - 4K^2[H]_o{}^2\,r}}{2K[H]_o}\right)$$

$$[G] = [H]_o\left(\frac{-(1+K[H]_o\,(1-r)) + \sqrt{(1+K[H]_o\,(1-r))^2 + 4K[H]_o\,r}}{2K[H]_o}\right)$$

$$[H] = [H]_o\left(\frac{-(1+K[H]_o\,(r-1)) + \sqrt{(1+K[H]_o\,(r-1))^2 + 4K[H]_o}}{2K[H]_o}\right)$$

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*Molecular Recognition and Supramolecular Chemistry*

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Problems: Chemical Equilibrium

1. Determine $\Delta_r G°$ at 298.2 K for the reaction: $AgCl\ (s) \rightleftarrows Ag^+\ (aq) + Cl^-\ (aq)$. The K_{sp} for AgCl is 1.8×10^{-10}.

2. Nitrogen dioxide forms a dimer in the equilibrium: $2\ NO_2\ (g) \rightleftarrows N_2O_4\ (g)$. The standard state reaction Gibbs energy for the dimerization of NO_2 is -4.77 kJ mol^{-1} at 298.2 K. In a reaction mixture, the partial pressure of NO_2 is 0.332 bar and of N_2O_4 is 0.986 bar. Is the reaction at equilibrium, and if not what is the spontaneous direction for the reaction?

3. Under standard conditions, one of the steps in the photosynthetic production of glucose does not occur spontaneously:

fructose-6-P + glyceraldehyde-3-P $\rightleftarrows$ erythrose-4-P + xyulose-5-P
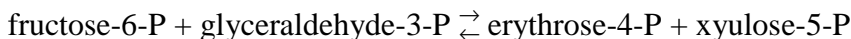
where $\Delta_r G°' = +6.28$ kJ mol^{-1} at 298.2 K. The "P" indicates the phosphorylated form of the sugar; fructose-6-P is fructose-6-phosphate. Can this reaction take place spontaneously in a chloroplast where the concentrations are: [fructose-6-P] = 53.0×10^{-5} M, [glyceraldehyde-3-P] = 3.20×10^{-5} M, [erythrose-4-P] = 2.00×10^{-5} M, and [xyulose-5-P] = 2.10×10^{-5} M ?

4. At 298.15 K the $\Delta_r G°$ for the dissociation of water to H^+ and OH^- is 79.89 kJ mol^{-1}. Calculate $\Delta_r G$ for the reaction conditions specified below.

H_2O (l) $\rightleftarrows H^+$ (aq, $a_{H^+} = 1.005 \times 10^{-7}$) + OH^- (aq, $a_{OH^-} = 1.005 \times 10^{-7}$)
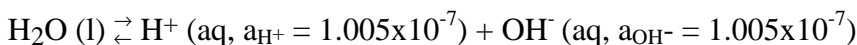
5. In rivers and lakes, bacteria catalyze the oxidation of Fe(II) to Fe(III):

$4\ Fe^{2+} + O_2(g) + 4\ H^+ \rightleftarrows 4\ Fe^{3+} + 2\ H_2O$

with $\Delta_f G°(Fe^{2+}) = -78.90$ kJ mol^{-1}, $\Delta_f G°(Fe^{3+}) = -4.70$ kJ mol^{-1}, and $\Delta_f G°(H_2O) = -237.13$ kJ mol^{-1}. Calculate the reaction Gibbs energy for $m_{Fe2+} = 1.00 \times 10^{-6}$ m, $m_{Fe3+} = 1.00 \times 10^{-5}$m, $P_{O_2} = 0.200$ bar, $m_{H^+} = 1.00 \times 10^{-6}$ m at 298.15 K (neglect activity coefficients).

6. The equilibrium constant for the dissociation N_2O_4 (g) $\rightleftarrows 2\ NO_2$ (g) is $K_p = 0.146$ at 298.2 K. Assume that the initial amount of N_2O_4 is 0.300 mol with no initial NO_2. Find the equilibrium partial pressures for the dissociation assuming that the reaction is run under constant pressure conditions at (a) 0.500 bar and at (b) 5.00 bar. (c). Does the shift in equilibrium position with applied pressure agree with LeChâtelier's Principle?

7. Calculate the equilibrium partial pressures at 298.2 K for the dimerization of NO_2: $2\ NO_2$ (g) $\rightleftarrows N_2O_4$ (g). The standard state reaction Gibbs energy for the dimerization of NO_2 is -4.77 kJ mol^{-1} at 298.2 K. Assume the initial amount of NO_2 is 0.300 moles at a constant total pressure of 1.00 bar. [Hint: you may use successive approximations to solve for the equilibrium position.]

8. Calculate the equilibrium partial pressures and the degree of dissociation for the reaction:

SO_2Cl_2 (g) $\rightleftarrows SO_2$ (g) + Cl_2 (g)

The equilibrium constant is $K_p = 2.78$ at 110°C. Assume a constant total pressure of 0.500 bar with 2.00 moles of SO_2Cl_2, only, initially placed in the reaction vessel.

9. Consider a gas phase dissociation with the stoichiometry A (g) $\rightleftarrows$ B (g) + C (g). (a). Show that the equilibrium expression can be directly expressed in terms of the degree of dissociation as:

$$K_p = \frac{\alpha^2}{1 - \alpha^2} (P/P°) \qquad\qquad\qquad P20.9.1$$

(b). Solve for the degree of dissociation.

<u>10</u>. For the reaction H_2S (g) $\rightleftarrows H_2$ (g) + ½ S_2 (g) the degree of dissociation of H_2S is 0.305 at 1125°C and 1.00 bar total pressure. Calculate K_p at 1125°C.

<u>11</u>. The K_p and K_x based equilibrium expressions are convenient to use for reactions at constant pressure. K_c based expressions are convenient for reactions at constant volume. Consider dissociation with the stoichiometry: A (g) $\rightleftarrows$ B (g) + C (g). Set up the K_p expression in terms of the extent of the reaction, ξ, as in Example 20.2.1. Show that the K_p expression reduces to:

$$K_c = \frac{(x/c°)^2}{c_{Ao}/c° - x/c°}$$

where c_{Ao} is the initial concentration of A and x is the final concentration of B and C. Assume the reaction is run at constant volume.

<u>12</u>. Calculate the equilibrium partial pressures and the degree of dissociation for the reaction:

$$SO_2Cl_2 \text{ (g)} \rightleftarrows SO_2 \text{ (g)} + Cl_2 \text{ (g)}$$

The equilibrium constant is $K_p = 2.78$ at 110.°C. Assume the reaction starts with 2.00 moles of SO_2Cl_2, only, initially placed in the reaction vessel with an initial pressure of 0.500 bar. Assume the reaction runs at constant volume (see Problem 8 for the constant pressure version of this problem).

<u>13</u>. For the reaction $BeSO_4(s) \rightleftarrows BeO$ (s) + SO_3 (g), $K_p = 1.71 \times 10^{-19}$ at 400.0 K and 9.70×10^{-11} at 600.0 K. (a). Predict, without doing the numerical calculation, if the reaction is endothermic or exothermic. (b). Calculate $\Delta_r H°$ for this temperature range and $\Delta_r G°$ and $\Delta_r S°$ at 400.0 K.

<u>14</u>. The autoprotolysis constant for water, K_w, is the equilibrium constant for the reaction:

$$H_2O \text{ (l)} \overset{K_w}{\rightleftarrows} H^+ \text{ (aq)} + OH^- \text{ (aq)}$$
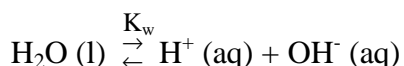
The temperature dependence for K_w is given in the table, below.[1] (a). Assume $\Delta_r H°$ is constant. Calculate $\Delta_r H°$ for this temperature range and $\Delta_r G°$ and $\Delta_r S°$ at 298.2 K. (b). Neutral pH is the pH that gives $a_{H+} = a_{OH-}$. Calculate the pH of a neutral solution at each temperature.

| T (°C)	0.0	10.0	25.0	35.0	40.0
K_w	1.15×10^{-15}	2.97×10^{-15}	1.01×10^{-14}	2.07×10^{-14}	2.88×10^{-14}

<u>15</u>. In the last problem for the autoprotolysis of water, we assumed that the reaction enthalpy was temperature independent. Assume the temperature dependence of the reaction enthalpy is given by $\Delta_r H_T° = \Delta_r H_o° + \Delta_r C_p T$, with $\Delta_r C_p = -186.6 \pm 2.7$ J K^{-1} mol. The temperature dependence of ln K is then just the first two terms of Eq. 20.1.36:

$$\ln K = -\frac{\Delta_r H_o°}{RT} + \frac{\Delta_r C_p}{R} \ln T + c$$

where c is a constant. Calculate $\Delta_r H^\circ$, $\Delta_r G^\circ$, and $\Delta_r S^\circ$ at 298.2 K. A more complete table for the autoprotolysis constant for water, K_w, is given in the table, below.[1] [Hint: subtract $\Delta_r C_p \ln T$ from both sides of the above equation and plot ($\ln K - \Delta_r C_p \ln T$) along the vertical axis.]

T (°C)	0.0	5.0	10.0	15.0	20.0	25.0	30.0
K_w	1.15×10^{-15}	1.88×10^{-15}	2.97×10^{-15}	4.57×10^{-15}	6.88×10^{-15}	1.01×10^{-14}	1.46×10^{-14}

T (°C)	35.0	40.0	45.0	50.0	100.0	150.0
K_w	2.07×10^{-14}	2.88×10^{-14}	3.94×10^{-14}	5.31×10^{-14}	5.43×10^{-13}	2.3×10^{-12}

16. In the atmosphere NO and NO_2 approach equilibrium (see Ch. 5 Problems 10-12):

$$NO\ (g) + \tfrac{1}{2}\ O_2\ (g) \rightleftarrows NO_2(g)$$
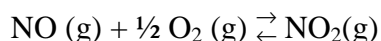
Because NO and NO_2 are rapidly interconverted, the concentration of NO and NO_2 in the atmosphere are usually combined and quoted as [NO_x]. The equilibrium constant is $K_p = 1.168 \times 10^5$ at 335.15 K and 4075. at 400.15 K. (a). Calculate the standard state reaction enthalpy at the average temperature, assuming the reaction enthalpy is constant over the temperature range. (b). Calculate the standard state reaction Gibbs energy and entropy at 335.15 K. (c). The molar constant pressure heat capacities are 29.844 J K^{-1} mol^{-1} for NO, 29.355 J K^{-1} mol^{-1} for O_2, and 37.20 J K^{-1} mol^{-1} for NO_2. Calculate $\Delta_r H^\circ$, $\Delta_r S^\circ$, and $\Delta_r G^\circ$ at 298.15 K.

17. The density at equilibrium for gas phase reaction mixtures can be used to calculate the equilibrium constant for the chemical reaction. Consider a gas phase dissociation with the stoichiometry A (g) $\rightleftarrows$ B (g) + C (g), giving at equilibrium (see Problem 9):

$$K_p = \frac{\xi^2}{a^2 - \xi^2}\ (P/P^\circ) = \frac{(\xi/a)^2}{1 - (\xi/a)^2}\ (P/P^\circ) = \frac{\alpha^2}{1 - \alpha^2}\ (P/P^\circ) \tag{P20.9.1}$$

Assume only A is initially placed in the reaction vessel. The total moles of gas is then determined by $n_{tot} = a + \xi = a(1 + \alpha)$. Now consider the density of the gas mixture. The total mass of the reaction mixture is constant, $w = a\mathfrak{M}_A$, where $\mathfrak{M}_A$ is the molar mass of reactant A. However, the total moles of gas changes as the reaction progresses, if $\Delta_r n_g \neq 0$. For a reaction at constant temperature and pressure, the change in moles of gas will cause a change in volume as the reaction progresses from the initial state. The density of the reaction gas mixture at equilibrium, assuming each constituent is ideal, is given by the ideal gas law:

$$d = w/V_{eq} = \frac{a\mathfrak{M}_A}{n_{tot}\ RT/P} = \frac{a\ \mathfrak{M}_A}{a(1 + \alpha)\ RT/P} = \frac{1}{1 + \alpha}\left(\frac{\mathfrak{M}_A\ P}{RT}\right) \tag{P20.17.1°}$$

$COCl_2$ dissociates according to the reaction: $COCl_2$ (g) $\rightleftarrows$ CO (g) + Cl_2 (g). The density of the reaction mixture at equilibrium at 724. K and 1.00 bar total pressure is 1.16 g L^{-1}. Calculate the degree of dissociation, K_p, and $\Delta_r G^\circ$ at 724. K.

18. The density of an equilibrium mixture of N_2O_4 (g) and NO_2 (g), at 1.00 bar pressure, is 3.62 g L^{-1} at 15.°C. Only N_2O_4 was initially placed in the reaction vessel. Calculate K_p and $\Delta_r G^\circ$ at 15.°C. [Hint: write the equilibrium expression in terms of the degree of dissociation.]

19. Create an Excel spreadsheet based on Eq. 20.1.21° to reproduce Figure 20.1.1. Assume the total pressure is constant at 1.00 bar and the standard state chemical potentials of A, B, C, and D

are 6.24, 5.64, 2.78, and 2.22 kJ mol^{-1}, respectively. Assume 1.00 mol for A and B initially, with no C and D.

20. Dissociations with the stoichiometries A $\rightleftarrows$ B + C and A $\rightleftarrows$ 2 B have significantly different equilibrium positions, given the same equilibrium constant and initial conditions. (a). First, assume the equilibrium constant for both reactions is $K_p = 1.33$ and the initial moles of reactant is 1.00 mol, with no initial products at 1.00 bar total pressure. Calculate the degree of dissociation for each reaction. (b). Qualitatively sketch diagrams of the form in Figure 20.1.1 and discuss the effect of the entropy of mixing in determining the difference in equilibrium position for the two reaction stoichiometries. (See also Problems 6, 8, and 9.)

21. Derive an expression for the Gibbs energy for the dissociation A $\rightleftarrows$ B + C as a function of the extent of the reaction. Your derivation will parallel Eqs. 20.1.16-20.1.21°, but for the new stoichiometry. Create an Excel spreadsheet based on your expression to produce a plot similar to Figure 20.1.1. Assume the total pressure is constant at 1.00 bar and the standard state chemical potentials of A, B, and C are 6.00, 2.95, and 2.34 kJ mol^{-1}, respectively. Assume 1.00 mol for A initially, with no B and C.

22. Calculate the pH and degree of dissociation of 0.100 m acetic acid in water at 25°C using the Debye-Hückel approximation and $K_a = 1.75 \times 10^{-5}$. (The acid dissociation constant is determined on a molal basis. Neglect the autoprotolysis of water.) Compare to the degree of dissociation calculated neglecting activity coefficients.

23. Calculate the pH and degree of hydrolysis of 0.100 m ammonia in water at 25°C using the Debye-Hückel approximation and $K_b = 1.78 \times 10^{-5}$. (The hydrolysis constant is determined on a molal basis. Neglect the autoprotolysis of water.) Compare to the degree of hydrolysis calculated neglecting activity coefficients.

24. The K_{sp} for PbCl$_2$ in water is 1.70×10^{-5}. (a). Calculate the solubility of PbCl$_2$ in pure water. (b). Show that the solubility of a 1:2 electrolyte with charges $z_+ = 2$ and $z_- = -1$ in a m-molal solution of NaNO$_3$ (or other uni-positive : uni-negative non-participating electrolyte) is given by:

$$m_s = 10^{0.509|z_+ \, z_-| \, (m/m°)^{1/2}} \left(\frac{K_{sp}}{4} \right)^{1/3}$$

Use the Debye-Hückel approximation at 25°C for the activity coefficients. Calculate the solubility of PbCl$_2$ in 0.100 m KNO$_3$.

25. The K_{sp} for PbCl$_2$ in aqueous solution is 1.70×10^{-5} on a molal basis at 298.15 K. (a). Calculate the K_{sp} of PbCl$_2$ in pure water on a molarity concentration basis. (b). Calculate the K_{sp} of PbCl$_2$ on a molarity basis in a 0.200-M solution of KNO$_3$, assuming a very dilute solution. The density of 0.200 M KNO$_3$ is 0.9905 g mL^{-1}.

26. The hydrolysis of ammonia is given by: NH$_3$ (aq) + H$_2$O $\rightleftarrows$ NH$_4^+$ + OH$^-$ with $K_b = 1.78 \times 10^{-5}$ at 25°C on a molal basis. Calculate K_b on a molarity concentration basis. The density of 0.100 M ammonia is 0.994 g mL^{-1} at 25°C

27. Nimodipine is a dihydropyridine calcium channel blocker that was developed for the treatment of high blood pressure:
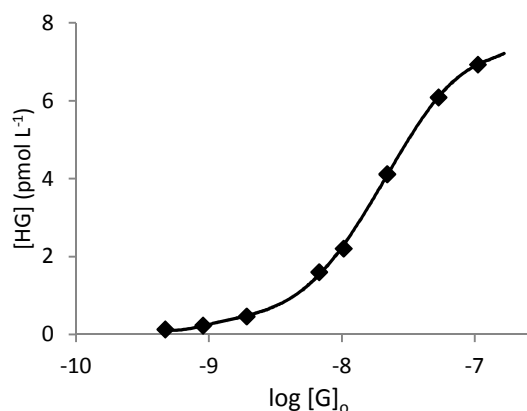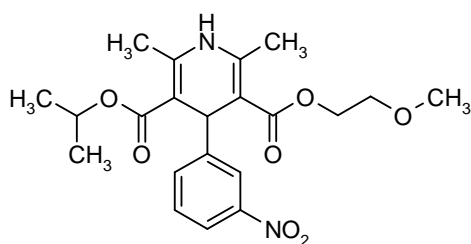
This class of calcium channel blockers are antagonists that block the flow of Ca^{2+} ions out of cardiac muscle cells. A receptor site for nimodipine is found in the plasma membrane of striated muscle tissue, or sarcolemma. Isolated sarcolemma membranes were used in a binding study with tritium-labeled nimodipine. Tritiated-nimodipine was incubated with the purified membranes in the absence of Ca^{2+} ion and then filtered. The concentration of bound nimodipine was determined by liquid scintillation counting of the membranes trapped on the filters. Consider the membrane bound protein receptor as the host and nimodipine as the guest. The concentration of bound guest as a function of the total concentration of guest is given in the table below.[2] The effective concentration of the host membrane receptors is $[H]_o = 9.3 \pm 0.4$ pmol L^{-1}.

$[G]_o$ (pmol L^{-1})	0.468	0.9	1.92	6.75	10.3	21.9	53.4	105.4
$[HG]$ (pmol L^{-1})	0.134	0.234	0.468	1.606	2.21	4.12	6.09	6.93

28. Leukotriene-B_4 is important in activating the inflammatory response:[3]
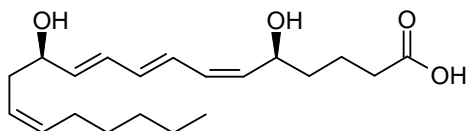
Developing leukotriene-B_4 antagonists may be helpful in managing chronic obstructive pulmonary disease, severe asthma, rheumatoid arthritis, inflammatory bowel disease, and cystic fibrosis. A receptor site for leukotriene-B_4 is a membrane bound protein in polymorphonuclear leukocytes, PMNLs. Isolated PMNL membranes were used in a binding study with radio-iodine labeled leukotriene-B_4. The leukotriene was incubated with the purified membranes and then filtered. The concentration of bound leukotriene was determined by liquid scintillation counting of the membranes trapped on the filters. Consider the membrane bound protein receptor as the host and leukotriene-B_4 as the guest. The concentration of bound guest as a function of the total concentration of guest is given in the table below.[3] The effective concentration of the host membrane receptors is $[H]_o = 33 \pm 12$ pmol L^{-1}.

$[G]_o$ (pmol L^{-1})	8.33	16.7	38.7	86.4	183	322	401	464	1000	2080
$[HG]$ (pmol L^{-1})	0.56	1.26	2.66	5.19	9.67	14.3	14.3	16.8	21.7	27.8

29. The organic dye eosin binds to the protein lysozyme. Binding to lysozyme quenches the fluorescence of the protein at 340 nm.[4] If I_H is the fluorescence intensity of the free form of

lysozyme and I_{HG} is the fluorescence intensity of the bound form of the protein, then the observed intensity is the mole fraction weighted average:

$$I_{obs} = \alpha_H I_H + \alpha_{HG} I_{HG} = (1 - \alpha_{HG}) I_H + \alpha_{HG} I_{HG} = (I_{HG} - I_H) \alpha_{HG} + I_H \qquad \text{P20.29.1}$$

where α_H is the mole fraction of the free host protein, $\alpha_H = n_H/(n_H + n_{HG}) = [H]/[H]_o$, and α_{HG} is the mole fraction of the guest-host complex, $\alpha_{HG} = n_{HG}/(n_H + n_{HG}) = [HG]/[H]_o$. Solving Eq. P20.29.1 for the degree of association gives:

$$\alpha_{HG} = \frac{[HG]}{[H]_o} = \frac{I_H - I_{obs}}{I_H - I_{HG}} \qquad \text{P20.29.2}$$

The fluorescence intensity of free lysozyme in buffer alone is $I_H = 1.541$. The fluorescence intensity, I_{obs}, as a function of the concentration of eosin with $[H]_o = 3.00 \times 10^{-6}$ M lysozyme in each solution is:[4]

$[G]_o$ (M)	5.00×10^{-6}	10.0×10^{-6}	20.0×10^{-6}	50.0×10^{-6}
I_{obs}	1.198	1.064	0.855	0.494

The fluorescence intensities are relative and in arbitrary units, which makes fluorescence intensity effectively unitless. Calculate the association constant of eosin with lysozyme. Assume that the fluorescence of lysozyme is negligible in the bound form, $I_{HG} \approx 0$. [Hints: a Scatchard plot is not appropriate for this experiment, because the free eosin concentration is not known. There is only one unknown, so use of a curve fitting program is not necessary. Using "goal seek" in a spreadsheet format is useful for finding the optimum value for an adjustable parameter in a non-linear equation.]

30. Finding the optimum value for a single adjustable parameter in a non-linear equation is easily handled using the "goal seek" option in a spreadsheet, rather than using non-linear least squares curve fitting programs. However, the spreadsheet approach makes the determination of the uncertainty of the final fit value more involved than using non-linear least squares curve fitting algorithms. However, least squares curve fitting programs are often set up to fit two or more adjustable parameters, not just one parameter. The uncertainty for fitting procedures for a single parameter are easily handled using the following approach.

The general formula for propagation of errors for the two-parameter function f(x,y) is (Appendix 1):

$$\delta^2 f = \left(\frac{\partial f}{\partial x}\right)_y^2 \delta^2 x + \left(\frac{\partial f}{\partial y}\right)_x^2 \delta^2 y$$

Consider a non-linear function f(b,x), with the adjustable parameter b and independent variable x. The adjustable parameter is often an equilibrium constant and the x variable is a concentration or a mole ratio (see the previous problem). Let the value of the measured observables at a series of x values be $y_1 = f(b,x_1)$, $y_2 = f(b,x_2)$, $y_3 = f(b,x_3)$, ... for n values of x. The y values are often absorbances, fluorescence intensities, or chemical shifts. The uncertain variables are the y_i values. The uncertainty in the fit parameter, b, is then given by:

$$\delta^2 b = \left(\frac{\partial b}{\partial y_1}\right)^2 \delta^2 y_1 + \left(\frac{\partial b}{\partial y_2}\right)^2 \delta^2 y_2 + ...$$

with the sum over all n data points. If we assume that the derivatives are all approximately equal, then the last equation reduces to:

$$\delta^2 b \approx \left(\frac{\partial b}{\partial y}\right)^2 \sum_{i=1}^{n} \delta^2 y_i \qquad \text{or} \qquad \left(\frac{\delta^2 b}{n-1}\right) \approx \left(\frac{\partial b}{\partial y}\right)^2 \left(\frac{\sum_{i=1}^{n} \delta^2 y_i}{n-1}\right)$$

Dividing both sides of the equation by n–1 converts the uncertainties to variances, s_b and s_y. Taking the square root and inverting the derivative gives:

$$s_b \approx \frac{1}{\left(\frac{\partial y}{\partial b}\right)} s_y$$

where $(\partial y/\partial b)$ is approximately evaluated numerically as the change in a typical y value for a small change in the fit parameter:

$$\left(\frac{\partial y}{\partial b}\right) = \frac{f(b+\delta b,x) - f(b,x)}{\delta b}$$

where x is a typical x-value and δb is a small change in the fit parameter. The derivative is easily calculated by finding the y-value for the optimal b-value , f(b,x), and then changing b by a small amount and finding the new y-value, f(b+δb,x).

Using these last two equations, find the uncertainty in the association constant for the previous fluorescence quenching problem.

31. NMR is an important technique for measuring formation constants in guest-host chemistry. For example, if a given proton in the host shows a chemical shift difference between the free and bound forms, then the chemical shift of the proton is strongly concentration dependent. The dependence is due to changes in the mole fractions of the free and bound forms. Assume the reactions are rapid on the NMR time scale: rate $> 1/\nu_o$ with ν_o the resonance frequency. If δ_H is the chemical shift of the free form of the host and δ_{HG} is the chemical shift of the bound form of the host, then the observed chemical shift is the mole fraction weighted average, assuming the reactions are rapid:

$$\delta_{obs} = \alpha_H\, \delta_H + \alpha_{HG}\, \delta_{HG}$$

where α_H is the mole fraction of the free host, $\alpha_H = n_H/(n_H + n_{HG}) = [H]/[H]_o$, and α_{HG} is the mole fraction of the guest-host complex, $\alpha_{HG} = n_{HG}/(n_H + n_{HG}) = [HG]/[H]_o$. Given that $\alpha_H + \alpha_{HG} = 1$, the observed chemical shift reduces to:

$$\delta_{obs} = (1 - \alpha_{HG})\, \delta_H + \alpha_{HG}\, \delta_{HG} = (\delta_{HG} - \delta_H)\, \alpha_{HG} + \delta_H$$

The mole fraction of the bound guest-host complex is calculated by Eq 20.5.22:

$$\delta_{obs} = (\delta_{HG} - \delta_H) \left(\frac{(1+K[H]_o\,(1+r)) - \sqrt{(1+K[H]_o\,(1+r))^2 - 4K^2[H]_o^2\, r}}{2K[H]_o}\right) + \delta_H$$

Although somewhat daunting looking, this equation is easily used in non-linear curve fitting with the "Nonlinear Least Squares Curve Fitting" applet on the text Web site and the companion CD.

In particular, the guest and host can be a hydrogen-bonded pair. NMR is an important technique in studies of hydrogen bonding.

The formation of the hydrogen bond between the sterically crowded alcohol, below, and pyridine has been studied:[5]
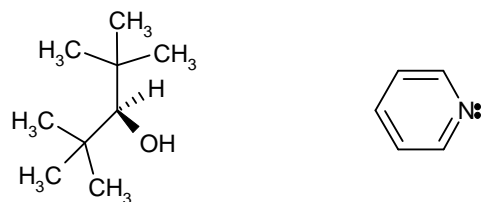
2,2,4,4-tetramethyl-pentan-3-ol   pyridine

Consider the alcohol as the host and pyridine as the guest. The chemical shift of the alcohol hydrogen is given in the table, below, as a function of the concentration of pyridine in benzene solution. The alcohol concentration is fixed in each solution at 0.100 M. The chemical shift of the free alcohol is $\delta_H = 1.105$ ppm. The chemical shift difference, $(\delta_{HG} - \delta_H)$, and $K[H]_o$ are treated as the two variable parameters in the curve fitting. The binding constant is expected to be ≈ 1, since the formation of a single hydrogen bond is a weak interaction.

$[G]_o$ (M)	0	0.136	0.271	0.543	0.814	1.628	3.799
δ_{obs} (ppm)	1.105	1.594	2.000	2.630	3.111	3.970	4.901

32. Derive Eq. 20.5.23.

33. Derive Eq. 20.5.24.

34. An alternative form for the concentration of the guest-host complex often encountered in biochemical studies is based on the dissociation equilibria:

$$HG \rightleftarrows H + G \qquad\qquad K_D = \frac{[H]\,[G]}{[HG]}$$

where K_D is the dissociation constant. The relationship to the association constant and Eq. 20.5.1 is $K_D = 1/K$. (a). Show that the guest-host concentration is given by:

$$[HG] = \frac{([H]_o + [G]_o + K_D) - \sqrt{([H]_o + [G]_o + K_D)^2 - 4\,[H]_o\,[G]_o}}{2}$$

(b). Find the relationship in terms of the guest-host ratio, $r = [G]_o/[H]_o$.

35. Determine if the following statements are true or false. If the statement is false, describe the changes that are necessary to make the statement true, if possible. If the statement is true, but too restrictive, give the more general statement.

(a). The relationship $\Delta_r G° = -RT \ln K_p$ shows that $\Delta_r G°$ is the reaction Gibbs energy at equilibrium.
(b). The position of equilibrium for a constant volume process is determined by the extent of the reaction, ξ.
(c). The position of equilibrium is unaffected by addition of an inert gas, such as helium, since the inert gas will not participate in the reaction.

(d). The position of equilibrium for the reaction types $2A \rightleftarrows B + C$ and $A + B \rightleftarrows C + D$ will be the same if the equilibrium constants are the same.

(e). The rate of the reaction $2A \rightarrow B + C$ increases with temperature so the equilibrium position of the reaction shifts to the right with an increase in temperature.

(f). The rate of the reaction $2A \rightarrow B + C$ is fast so the equilibrium constant for the reaction is large.

<u>36</u>. The ITC titration of the enzyme ribonuclease A with the ligand 2'CMP is given in the table below. Consider ribonuclease A as the host and 2'CMP as the guest. The host concentration in the titration cell was 6.272×10^{-5} M, the guest concentration in the automated buret was 2.19×10^{-3} M, the titration cell volume was 1.4389 mL, and the titrant was added in 9.00 μL increments. The association constant was determined to be 6.99×10^5 and the reaction enthalpy was -70.6 kJ mol^{-1} using non-linear curve fitting. (a). Calculate $\Delta_r G^\circ$ and $\Delta_r S^\circ$. (b). Use the fit values to reproduce the titration curve. Neglect any corrections for exclusion of material from the constant volume titration cell (as discussed in the addendum). [Hint: construct a spreadsheet using Eq. 20.5.22. Show the titration curve with the calculated and experimental values, for comparision.]

i V_{inj} (μL)	9	18	27	36	45	54	63	72	81	90	99
q/n_{inj} (kJ mol^{-1})	-68.3	-67.3	-64.2	-56.3	-35.6	-14.6	-6.41	-3.61	-2.33	-1.64	-1.3

<u>37</u>. Eq. 20.5.22 can be used directly in non-linear curve fitting for finding association constants from ITC titration curves. The results for each step in an ITC experiment are given by Eqs. 20.6.5-20.6.7. Consider the first two steps in the titration. The sum of the $q_{i,m}$ values for the first two steps gives, using Eqs. 20.6.6 and 20.6.7:

$$q_{tot} = q_{1,m} + q_{2,m} = q_2/n_{inj} + q_1/n_{inj} = (\Delta n_{HG,2} + \Delta n_{HG,2}) \, \Delta_r H^\circ / n_{inj}$$

Then using Eq. 20.6.5 the total calorimetric enthalpy is given in terms of [HG] as:

$$q_{tot} = q_{1,m} + q_{2,m} = q_2/n_{inj} + q_1/n_{inj} = ([HG]_2 - [HG]_1 + [HG]_1 - [HG]_o) \, \Delta_r H^\circ \, V_{cell}/n_{inj}$$

$$q_{tot} = q_{1,m} + q_{2,m} = q_2/n_{inj} + q_1/n_{inj} = [HG]_2 \, \Delta_r H^\circ \, V_{cell}/n_{inj}$$

since $[HG]_o = 0$. Solving for $[HG]_2 \, \Delta_r H^\circ$ gives:

$$q_{tot} \, n_{inj}/V_{cell} = \Delta_r H^\circ \, [HG]_2$$

In a similar fashion, if we add the calorimetric enthalpies for the first n steps:

$$q_{tot} \, n_{inj}/V_{cell} = (q_{1,m} + q_{2,m} + \ldots + q_{2,n}) \, n_{inj}/V_{cell} = \Delta_r H^\circ \, [HG]_n$$

Eq. 20.5.22 can then be used to calculate the concentration of the host-guest complex:

$$q_{tot}\left(\frac{n_{inj}}{V_{cell} \, [H]_o}\right) = \Delta_r H^\circ \left(\frac{(1+K[H]_o \, (1+r)) - \sqrt{(1+K[H]_o \, (1+r))^2 - 4K^2[H]_o^2 \, r}}{2K[H]_o}\right)$$

where r is the guest-host ratio at the nth step of the titration. The two adjustable parameters for curve fitting are $a = \Delta_r H^\circ$ and $b = K[H]_o$.

Use the data in the last problem to find the association constant and reaction enthalpy for the binding of ribonuclease A with 2'CMP.

38. Comparison of Eqs. 20.1.17 and 20.1.5 might at first seem conflicting:

$$G = n_A \mu_A + n_B \mu_B + n_C \mu_C + n_D \mu_D \qquad (20.1.17)$$
$$\Delta_r G = c \mu_C + d \mu_D - a \mu_A - b \mu_B \qquad (20.1.5)$$

Derive Eq. 20.1.5 from Eq. 20.1.17, thus showing that the two equations are consistent. [Hint: remember that the reaction Gibbs energy is the Gibbs energy for the products minus the Gibbs energy for the reactants.]

39. Calculate the equilibrium constant for the *anti-* to *gauche*-conformers for dichloroethane from $\Delta_r G°$ and also the statistical approach. Use molecular mechanics to estimate of the difference in steric energy. Assume no significant change in vibrations between the two conformers.

40. The dimer of methylvinylketone is shown below, at left. The bond with free rotation is marked. Consider only the axial conformer for the $-CO-CH_3$ side chain. Calculate the equilibrium constant for the two low energy conformers. (b). Which face of the carbonyl is more susceptible to nucleophilic attack? Nucleophilic attack will be perpendicular to the trigonal plane of the sp^2 hybridized carbon, as shown by the arrows for one possible conformation at right. According to Cram's rule, the less hindered side is most susceptible to attack by nucleophiles. You may use molecular mechanics, semi-empirical AM1, *ab initio* HF/6-31G*, or B3LYP/6-31G* density functional methods to determine the energies.
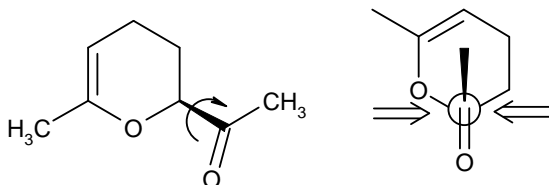
41. The next two problems develop a model for the equilibrium profile of NO in the lower troposphere. In the atmosphere, NO and NO_2 approach equilibrium (see Problem 16 and Ch. 5 Problems 10-12):

$$NO\,(g) + \tfrac{1}{2} O_2\,(g) \underset{\leftarrow}{\overset{\rightarrow}{}} NO_2(g) \qquad \text{P20.41.1}$$

In a given initial volume, let the number of moles of NO be "a", the moles of O_2 be "b", and the moles of other gases in the atmosphere be "n". These last contributions include primarily N_2 with small amounts of H_2O vapor, CO_2, and Ar. Assume that the initial amount of NO_2 is zero and the reaction runs at constant total pressure, P. To help simplify the relationships for the mole fractions, define $\alpha \equiv \xi/a$ as the fraction of NO oxidized, $r \equiv b/a$, and $q \equiv n/a$. Show that the equilibrium expression is:

$$K_p = \frac{\alpha}{1 - \alpha}\left(\frac{1 + r + q - \alpha/2}{r - \alpha/2}\right)^{1/2} (P/P°)^{-1/2} \qquad \text{P20.41.2°}$$

The concentration of NO_x in the atmosphere is typically in the ppm range. Correspondingly, r and q are much larger than α. Let $P_{NO,o}$ be the initial partial pressure of NO, before any oxidation occurs. Show that an excellent approximation is then:

$$K_{eff} \cong \frac{\alpha}{1-\alpha} \qquad \text{with} \quad K_{eff} = K_p \left(\frac{r}{r+q}\right)^{\frac{1}{2}} (P/P^\circ)^{\frac{1}{2}} \qquad (P_{NO,o} \ll P_{O_2}, P_{N_2}) \quad \text{P20.41.3}^\circ$$

$\underline{42}$. Use Eq. P20.41.2° to determine the equilibrium partial pressure of NO up to an altitude of 2000 m in the troposphere. Use the barometric formula, Eqs. 1.3.16° and 1.3.17, to estimate the total pressure as a function of altitude. Assume that r and q are constant with altitude (that is, the atmosphere is well-mixed before any oxidation occurs). Assume also that the temperature in the troposphere decreases 6.0 K per 1000 m; in other words, the environmental lapse rate is $\gamma = -0.006$ K m^{-1}. For the oxidation, Eq. P20.41.1, $\Delta_r G^\circ = -35.24$ kJ mol^{-1} and $\Delta_r H^\circ = -57.07$ kJ mol^{-1}. Assume $\Delta_r H^\circ$ is constant over the temperature range. Assume the temperature is 298.15 K and the total pressure is 1.00 bar at sea level. The initial partial pressure at sea level for O_2 is 0.200 bar and for NO is 1.00×10^{-5} bar (10 ppm) before any oxidation.

The barometric formula is derived assuming the temperature is constant at each altitude. However, for a realistic model, we also need to take into account the decrease in temperature with altitude. An easy way to take both pressure and temperature effects into account is to use an average temperature of 282.7 K with the barometric formula to calculate the pressure profile in the atmosphere. Separately, the variation of temperature is then determined using $\gamma = -0.006$ K m^{-1} starting at 298.2 K at sea level, h = 0.

$\underline{43}$. Consider the reaction $A + B \rightleftarrows C + D$ in solution from a thermodynamic perspective and from a kinetic perspective. The equilibrium constant is a function of the solution activities, but the rate law is conventionally written in terms of the concentrations:

$$K_a = \frac{a_C\, a_D}{a_A\, a_B} \qquad\qquad \upsilon = \frac{1}{V}\frac{d\xi}{dt} = k_f\,[A][B] - k_r[C][D]$$

(a). Use detailed balance to prove that the rate law is also expressible in terms of the solution activities:

$$\upsilon = \frac{1}{V}\frac{d\xi}{dt} = k_f'\, a_A\, a_B - k_r'\, a_C\, a_B$$

(b). Relate the two sets of rate constants, k_f and k_r with k_f' and k_r', given the activity coefficients for each species.

$\underline{44}$. *Challenge Problem*: In the previous problem, we showed that the rate law for a reaction is best expressed in terms of activities, rather than concentrations, for consistency with detailed balance. However, by convention in concentration based kinetic expressions, the activity coefficients of the reactants and products are incorporated into the rate constants. The activity of a species deviates from the analytical concentration because of solute-solvent interactions. Rationalize the fact that solute-solvent interactions of the reactants and products have an effect on chemical reactions rates. However, be careful to separate thermodynamic and kinetic concerns. Assume that the kinetics follow Arrhenius behavior, and reason through the reaction profile, Figure 4.5.2.

$\underline{45}$. The temperature dependence of isomerization is conveniently followed by experimental techniques that have additive response of the two forms in equilibrium. The equilibrium constant of the two forms is given by:

$$A \rightleftarrows B \qquad \text{with} \quad K = [B]/[A] \qquad\qquad\qquad \text{P20.45.1}$$

One example of an experimental technique with additive response is infrared spectroscopy. The wave number of an IR band is the mole fraction weighted average of the two forms:

$$\tilde{\nu}_{obs} = \tilde{\nu}_A \, x_A + \tilde{\nu}_B \, x_B \qquad \text{(additive response)} \qquad P20.45.2$$

where x_A and x_B are the mole fractions of A and B, respectively. The absorption wave numbers of the pure components are $\tilde{\nu}_A$ and $\tilde{\nu}_B$, respectively.

(a). Let the total analytical moles be a, with $n_A + n_B = a$, where n_A and n_B are the number of moles of A and B. The total volume of the solution is V. Show that the corresponding concentrations are related by $[A] + [B] = [a]$, with concentrations in moles per liter.

(b). Show that the observed wave number is given in terms of the concentrations as:

$$\tilde{\nu}_{obs} = \tilde{\nu}_A \frac{[A]}{[a]} + \tilde{\nu}_B \frac{[B]}{[a]} \qquad \text{(additive response)} \qquad P20.45.3$$

(c). Using P20.43.1 show that the equilibrium concentrations are given by:

$$[A] = \frac{1}{1+K}[a] \qquad [B] = \frac{K}{1+K}[a] \qquad\qquad P20.45.4$$

(d). Using Eqs. P20.43.2-P20.43-4, show that the equilibrium constant is determined by:

$$K = \frac{\tilde{\nu}_{obs} - \tilde{\nu}_A}{\tilde{\nu}_B - \tilde{\nu}_{obs}} \qquad \text{(additive response)} \qquad P20.45.5$$

<u>46</u>. The infrared absorption of an intramolecular hydrogen-bonded amine (see Problem Ch. 10.13: N-[2-(dimethylamino)ethyl]-N-methylguanidium ion) as a function of temperature is at:

T (°C)	25.0	30.0	35.0	40.0	45.0
$\tilde{\nu}_{obs}$ (cm^{-1})	1520	1540	1548	1570	1573

Equilibrium is established between the closed and open forms; the closed form is hydrogen-bonded and the open form is not hydrogen-bonded: $C \rightleftarrows O$. The wave number of the closed form is: $\tilde{\nu}_C = 1505$ cm^{-1} and the open form is $\tilde{\nu}_O = 1580$ cm^{-1}. Using Eq. P20.45.5, determine the equilibrium constant and reaction Gibbs energy as a function of temperature.

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