# Thermodynamics V - Free Energy and Physical Equilibria

Tinoco Chapter 5

# One Component Systems

## Phase Equilibria

- an equilibrium between one component in two different phases, e.g. solid/liquid or liquid/gas
- the molar Gibbs free energy (chemical potential) for the two phases must be equal at constant T and P ($\Delta G=0$ for an equilibrium)
- if the same standard state is used for both phases, the activities for the two phases must also be equal
- if the external conditions (T and/or P) are changed, then the equilibrium shifts until the potentials are again equal

Example: Liquid water in equilibrium with water vapour. If the system is heated, the more water will evaporate, raising the vapour pressure until the chemical potential of the liquid and gas phases are once again equal

- the change in G with T at constant P is:

$$\left(\frac{\partial \overline{G}}{\partial T}\right)_P = -\overline{S}$$

- so a plot of $\overline{G}$ vs T is linear, with a slope of $-\overline{S}$
- the slope will be different for each phase

$$\overline{S}_{vapour} >> \overline{S}_{liquid} > \overline{S}_{solid}$$

and the lines will intersect at the freezing and boiling points for that pressure

- G always increases with increasing P with the greatest changes observed in the vapour phase
- the variation of $\overline{G}$ with P is

$$\left(\frac{\partial \overline{G}}{\partial P}\right)_T = \overline{V}$$

thus the greatest change is observed for the vapour phase as it has the largest molar volume

- the same plot of $\overline{G}$ vs T has the same three lines but the intersections are moved such that both the freezing and boiling points shift to higher temperature with an increase in pressure
- the shift in freezing point assumes that the molar volume of the liquid is greater than that of the solid. This is true for most substances, the most notable exception being water.

# Classius-Clapeyron Equation

- for a phase equilibrium between liquid and gas phases:

$$A \ (l) \rightleftharpoons A \ (g)$$
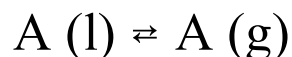
  the equilibrium constant is:

$$K = \frac{a_A(g)}{a_A(l)}$$

- the activity of the pure liquid is 1 and if the gas is ideal $a_A(g) = P_A(atm)$. Thus

$$K = P_A$$

  the equilibrium constant is equal to the equilibrium vapour pressure

- the dependence of equilibrium constants on T gives

$$\ln \frac{P_2}{P_1} = -\frac{\Delta \overline{H}_{vap}}{R} \left( \frac{1}{T_2} - \frac{1}{T_1} \right)$$

  the Clausius-Clapeyron equation which gives the variation of vapour pressure with T

- this can be used to calculate normal boiling points using vapour pressures measured at two different temperatures - first the data is used to determine the enthalpy of vaporization, then using one measured vapour pressure and T and the temperature at which the vapour pressure is 1 atm can be calculated

- a plot of lnP vs 1/T has a slope of $-\Delta \overline{H}_{vap} / R$ and can be used to determine vapour pressure at any T or boiling point at any P (see Tinoco Fig 5.2 b)
- this equation does assume that $\Delta \overline{H}_{vap}$ does not vary with T
- if the plot of lnP vs 1/T is curved, then the enthalpy of vaporization is changing with T

- the analogous equation for melting points is:

$$\frac{T_2 - T_1}{P_2 - P_1} = T \frac{\Delta \overline{V}_{fus}}{\Delta \overline{H}_{fus}}$$

where T is the average of $T_1$ and $T_2$ and

$\Delta \overline{V}_{fus} = \overline{V}(l) - \overline{V}(g) =$ molar volume change of fusion

- be careful with units, if P is in atm, $\Delta V$ in $m^3$ and $\Delta H$ in J, the conversion factor of 9.869 x $10^{-6}$ $m^3$ atm $J^{-1}$ must be applied

# Phase Diagrams

- plot P vs T for all three phases of a pure substance

$$\frac{dP}{dT} = \frac{\Delta\overline{H}}{T\Delta\overline{V}}$$

- slope of line depends on molar enthalpy and volume changes for phase transitions
- Tinoco Fig 5.2a - phase diagram for water
- there are two lines, one separating solid from liquid (fusion) the other separating solid and liquid from vapour (sublimation and evaporation respectively)
- two phases can only exist together at P and T conditions along these lines
- can determine vapour pressure at any T and bp, mp at any P
- normal bp is T where P = 1atm on L/V line
- normal mp is the T where P = 1 atm on the S/L line
- all three phases can exist together at the triple point where S/L and L/V lines meet - 273.16 K and 0.006 atm for water
- critical point is top end of L/V line - beyond this point liquid cannot exist
- note that for water, the slope for the S/L line is slightly negative - unlike most substances, $\Delta\overline{V}$ for water is negative, the molar volume for water is greater than that for ice

# Partial Molar Volumes

- a solution by definition contains two or more components
- the properties of a solution, like the properties of a pure substance, depend on the P and T of the system, but also depends on the composition of the solution
- the molar quantities (e.g. molar volume) which are used to describe pure substances cannot be used to describe solutions containing those same substances
- for solutions, partial molar quantities must be used

- water and ethanol have molar volumes of 0.018 L and 0.058 L at 298 K
- a mixture of 1 mole of water and 1 mole of ethanol has a volume of 0.072 L ≠ 0.018 + 0.058 L
- the attractive forces between water and ethanol molecules is greater than that between water molecules or between ethanol molecules, thus on mixing, the volume shrinks
- if the attractive forces between the two components is less than those within the individual components, on mixing, the volume increases

- for an ideal solution, the attractive forces between the two components are the same as those within the individual components and the final volume is equal to the sum of the initial volumes

- the volume after mixing (V) can be determined using:
$$V = n_1\overline{V}_1 + n_2\overline{V}_2$$
where $\overline{V}_i$ is the partial molar volume for the $i$th component

- partial molar volumes vary with the composition of the solution, but can be determined using the above equation
  - a series of solutions is made up at T and P all with $n_1$ moles of component 1 and with various moles of component 2
  - a plot of V vs $n_2$ will have a tangential slope at any given $n_2$ of $\overline{V}_2$ for that composition of solution
  - $\overline{V}_1$ at that composition can then be calculated using the equation above

# Two or More Component Systems - Solutions

For a one component system:

$$\mu^*(l) = \mu^*(g) = \mu^\circ(g) + RT \ln \frac{P^*}{1\,atm}$$

where * indicates the pure component.

For a two component system, the chemical potential in each phase for each component is still equal:

$$\mu_1(l) = \mu_1(g) = \mu_1^\circ(g) + RT \ln \frac{P_1}{1\,atm}$$

The standard state for the component is the same regardless of whether it is 1 or 2 component system:

$$\mu^\circ(g) = \mu_1^\circ(g)$$

From above:

$$\mu^\circ(g) = \mu^*(l) - RT \ln \frac{P^*}{1\,atm} = \mu_1^\circ(g)$$

$$\mu_1(l) = \mu_1^\circ(g) + RT \ln \frac{P_1}{1\,atm}$$

$$\mu_1(l) = \mu^*(l) + RT \ln \frac{P_1^*}{1\,atm} + RT \ln \frac{P_1}{1\,atm}$$

$$\mu_1(l) = \mu^*(l) - RT \ln \frac{P_1}{P_1^*}$$

$$\mu_1(l) = \mu^*(l) + RT \ln \frac{P_1}{P_1^*}$$

- this equation relates the potential of a component of a solution to the potential of the same species in the pure state at the same temperature
- they are related through the ratio of the vapour pressure of the component in the solution to the vapour pressure of the component in the pure state

- for some solutions the ratio of the two vapour pressures is equal to the mole fraction for the component:

$$\frac{P_1}{P_1^*} = X_1$$

- this is Raoult's law, and these are ideal solutions

**Ideal Solutions**
- an ideal solution is one where the intermolecular forces between the molecules are equal whether the molecules are alike or not
- $\Delta H_{mix} = 0$ and $\Delta V_{mix} = 0$
- the solvent and solute obey Raoult's law over the entire range of $X$
- e.g. a mixture of benzene and toluene - similar shape and electronic structure

# Raoult's Law

$$P_1 = X_1 P_1 *$$

- the vapour pressure of a component of a mixture is equal to its mole fraction multiplied by the vapour pressure of the pure substance
- non-ideal solutions can exhibit positive or negative deviations from Raoult's law

## Positive deviation

- the intermolecular forces between unlike molecules are less than those between like molecules
- the molecules have a greater tendency to evaporate than in an ideal solution and the vapour pressure is greater than that for an ideal solution
- e.g. $CS_2$ and acetone

## Negative deviation

- the intermolecular forces between unlike molecules are stronger than those between like molecules
- the vapour pressure is lower than that for an ideal solution
- e.g. $CHCl_3$ and acetone

# Henry's Law

- Raoult's law works when one component in a two component system is in excess - the solvent
- the vapour pressure of the small quantity component - the solute - does not follow Raoult's law, but is linear with concentration and follows Henry's law

$$P_2 = kX_2$$

    where k is the Henry's law constant for that solute and has the units of atm or torr
- Henry's law can also be written:

$$P_2 = k'm_2$$

    where m is the molality of the solution and k' has units of atm mol$^{-1}$ kg of solvent
- Tinoco Table 5.1 for Henry's law constants


- normally used for dissolution of gases, but also applicable to nongaseous solutes which are volatile
- holds only for dilute solutions
- does not hold where the solute reacts with the solvent
    e.g. $CO_2$, $H_2S$, $NH_3$, HCl in water
- does not hold where the solute complexes with something else in solution
    e.g. Complexation of $O_2$ with heme groups in blood versus normal dissolution of $O_2$ in aqueous solution
- both of these deviations from Henry's law result in an increase in solubility

# Real Solutions

- ideal solutions obey Raoult's law for both the solvent and solute over the entire range of $X$
- for dilute solutions where there is no interaction between the solute and the solvent, the solvent obey's Raoult's law and the solute obey's Henry's law - these are "ideal dilute solutions"
- in both of these situations, the activity coefficients are assumed to be 1
- for real solutions, the activity coefficients are not 1 and deviations from both Raoult's and Henry's laws are observed

# Colligative Properties

- properties of solutions with a common origin
- changes are due to changes in chemical potential of solvent in solution versus pure solvent
- in dilute solution, they depend only on the number of solute molecules and not on the kind of solute
- by preparing a solution with a known weight of solute, these properties can be used to determine the number of molecules in solution and therefore the molecular weight of the solute
- includes vapour pressure lowering, freezing point depression, boiling point elevation and osmotic pressure
- once one colligative property for a solution is measured, the others can be calculated
- applies to ideally dilute solutions (obey Raoult's law) with non-volatile, non-electrolyte solutes

# Vapour Pressure Lowering

Raoult's law applies
$$P_1 = X_1 P_1*$$
The molar fraction of the solute $X_2 = (1 - X_1)$
$$P_1* - P_1 = \Delta P = X_2 P_1*$$

- the vapour pressure of the solution $P_1$ is lower than that of the pure solvent $P_1*$ and the change is proportional to the mole fraction of the solute
- this is not an effect of changes in intermolecular forces - occurs even in ideal solutions where solute-solvent and solvent-solvent interactions are equal
- decrease in the vapour pressure is an entropy effect
  - the dissolution of a solute is spontaneous ($\Delta S$ is positive) - the solution has a higher entropy than the pure solvent
  - only the solvent evaporates from the solution - final state for evaporation from pure solvent or solution is the same
  - therefore the positive entropy change for evaporation from solution is smaller than that for the pure solvent, and the solvent in the solution has a lesser tendency to evaporate

- solute molecular weight ($M_2$) can be found using:

$$M_2 = \frac{wt_2}{n_1} \cdot \frac{P_1{}^*}{\Delta P}$$

- this method for determining molecular weight is limited
  - vapour pressures cannot be measured as accurately as other parameters
  - vapour pressures are quite sensitive to temperature
  - for high molecular weights, the change in vapour pressure is too small to measure
  - for high molecular weight solutes, there may be more change in the vapour pressure due to impurities than to the solute under study
    e.g. proteins cannot be studied in the presence of buffers

# Boiling Point Elevation

- the boiling point is the temperature at which the vapour pressure is equal to the external pressure
- dissolution of a non-volatile solute in a solvent causes a decrease in the vapour pressure and therefore an increase in the boiling point
- only the solvent evaporates - the vapour phase is pure solvent

- the chemical potential of the solvent in a solution differs from the potential of the pure solvent by a factor of $RT\ln X_1$

$$\mu_1(l) = \mu^*(l) + RT\ln\frac{P_1}{P_1^*} = \mu^*(l) + RT\ln X_1$$

- in a plot of potential vs T, this lowers the line relative to the pure solvent, leading to a higher T for the intersection between the liquid and vapour phases (the line for the vapour phase doesn't move as the solute is nonvolatile so the vapour consists solely of the solvent)

- the relation between the elevation of the boiling point and the concentration of the solution can be determined to be:

$$\Delta T_b = \frac{RT_b^2 M_1}{\Delta \overline{H}_{vap}} m_2 = K_b m_2$$

$T_b$ = boiling point of pure solvent
$M_1$ = molecular weight of solvent
$m_2$ = molality of solution
$\Delta H_{vap}$ = molar enthalpy of evaporation for solvent
$K_b$ = molal boiling-point elevation constant

- this equation can be rearranged to determine the molecular weight of the solute ($M_2$)

$$M_2 = \frac{wt_2}{kg\ solvent} \cdot \frac{K_b}{\Delta T_b}$$

wt$_2$/kg solvent = mass of solute er 1 kg solvent

# Freezing Point Depression

- freezing point depression works in the same manner as boiling point elevation
- in this case only the solvent freezes (not the solute) so solid phase is pure solvent
- in a plot of potential vs T, the line for the solid phase doesn't move but again, the line for the liquid phase is lower relative to the pure solvent, leading to a lower T for the intersection between the liquid and solid phases

- the change in the freezing point can be calculated using:

$$\Delta T_f = \frac{RT_f^2 M_1}{\Delta \overline{H}_{fus}} m_2 = K_f m_2$$

$T_f$ = freezing point of pure solvent
$M_1$ = molecular weight of solvent
$m_2$ = molality of solution
$\Delta H_{fus}$ = molar enthalpy of fusion for solvent
$K_f$ = molal freezing-point depression constant

- the equation to find the molecular weight of the solute by freezing-point depression is:

$$M_2 = \frac{wt_2}{kg\ solvent} \cdot \frac{K_f}{\Delta T_f}$$

wt$_2$/kg solvent = mass of solute er 1 kg solvent

- the net result on the phase diagram is lower of both the solid/liquid and liquid/vapour lines and no change in the solid/vapour line

# Solubility

- for freezing point depression, we considered a solid in equilibrium with a solution where the solid was pure solvent
- if instead the solid is pure solute, then the equilibrium represented is solubility rather than fusion
- in this case, the temperature dependence is:

$$\ln \frac{X_2(T_2)}{X_2(T_1)} = \frac{-\Delta \overline{H}_{sat}}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

$X_2(T_2)$, $X_2(T_1)$ = solute solubility at $T_2$ and $T_1$
$\Delta H_{sat}$ = $H_2$(solution)-$H_2$(solid) = molar enthalpy of dissolution in saturated solution

- works best for slightly soluble solutes - equation assumes ideal behaviour
- in dilute solution, mole fraction is proportional to molarity and molality - any convenient concentration units can be used

# Osmotic Pressure

- adding a solute to a solvent decreases the chemical potential of the solvent
$$\mu_1(l) = \mu^*(l) + RT \ln X_1$$
- when the solution is separated from the pure solvent by a semipermeable membrane, the solvent will move from the side with the higher potential (pure solvent) to the side with lower potential (solution)
- osmotic pressure is the pressure that must be applied to a solution to keep it in equilibrium with the pure solvent at the same temperature
(See Tinoco Fig 5.25)

- the osmotic pressure ($\Pi$) of a solution is proportional to the concentration of the solution
$$\Pi = cRT$$
$\Pi$ = osmotic pressure in atm
c = concentration in mol $L^{-1}$
R = gas constant = 0.08205 L atm $K^{-1}mol^{-1}$

- to determine the molecular weight of the solute, the equation is written

$$\Pi = \frac{w}{M}RT$$

w = concentration in g L$^{-1}$
M = molecular weight of solute in g mol$^{-1}$

- a series of measurements at different concentrations are made, and a plot of $\Pi$/w versus w is extrapolated to w=0 (ideal solution) - the intercept will be RT/M (Tinoco Fig 5.26)
  - for an ideal solution, $\Pi$/w does not vary with w and the slope is zero
  - a non-zero slope indicates variation from ideality
  - a positive slope is more common indicates non-ideal behaviour
  - a negative slope indicates increasing molecular weight with increasing concentration and is explained by aggregation of the solute

- osmotic pressure measurements are the most useful for determining molecular weights of molecules
    - the magnitude of the change in osmotic pressure is considerably larger than that for the other colligative properties and more accurate measurements can be made
    - the pressure measured is due to any solutes which cannot pass through the semi-permeable membrane used - a membrane can be selected to be permeable to everything but the solute of interest e.g. soluble to solvent and buffers but not high molecular weight proteins

# Ligand Binding

- this is the binding of a small molecule, the ligand, to a macromolecule (preotein, culceic acid etc)
- commonly studied using equilibrium dialysis

## Equilibrium Dialysis

- solution containing macromolecule is contained within a semipermeable membrane (dialysis bag)
- membrane often made from reformulated cellulose and can have various pore sizes and characteristics
- the dialysis bad is placed in a solution containing the ligand
- the macromolecule cannot pass through the pores of the membrane, but the ligand molecules and solvent can
- ligand passes from the solution outside the membrane to the solution inside the membrane where it then binds to the macromolecule
- the solution is stirred to speed up the approach to equilibrium at which point all concentrations remain constant
- if no macromolecule is present:
  - the concentration of all species are the same inside and outside the bag
  - if macromolecule is present the concentration of

free ligand is the same inside and outside the bag
*   the total concentration of ligand inside the bag is greater than that outside due to the macromolecule - ligand complex

$$M + L \rightleftharpoons M{\bullet}L$$

$$K = \frac{[M \cdot L]}{[M][L]}$$
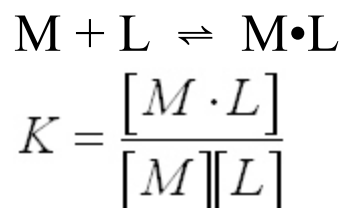
*   Generally, the concentrations of free (M) and bound (M•L) macromolecule cannot be measured directly
*   total ligand inside ($c_L$(inside)) and outside ($c_L$(outside)) and total macromolecule ($c_M$) concentrations are usually known, or can be measured

$c_M = [M] + [M{\bullet}L]$
$c_L$(inside) $= [L] + [M{\bullet}L]$
$c_L$(outside) $= [L]$
$c_L$(bound) $= [M{\bullet}L] = c_L$(inside) $- c_L$(outside)

*   [L] is the concentration of free ligand inside and outside the membrane - at equilibrium, the chemical potential and therefore the concentration of the free ligand must be equal on either side of the membrane, regardless of the presence or absence of bound ligand

- the equilibrium constant can then be expressed as

$$K = \frac{c_L(bound)}{\{c_M - c_L(bound)\}c_L(outside)}$$

## Scatchard Equation

- the average number of ligand molecules bound per macromolecule ($v$) is:

$$v = \frac{c_L(bound)}{c_M}$$

- the equilibrium constant now becomes:

$$K = \frac{v}{(1-v)c_L(outside)} = \frac{v}{(1-v)[L]}$$

$or$

$$\frac{v}{[L]} = K(1-v)$$

- $v$ ranges from 0 when no ligands are bound to the maximum number of ligands the macromolecule can bind (N)

- for N identical and independent binding sites per macromolecule - same K and binding at one site does not effect binding at the others - replace $v$ by $v/N$ and rearrange to obtain Scatchard equation

$$\frac{v}{[L]} = K(N - v)$$

    [L] is the concentration of ligand on the solvent side of membrane
    $v$ is determined from the concentration of ligand inside the membrane

- Scatchard plot ($v/[L]$ vs $v$) has a slope of -K, a y-intercept of NK and an x-intercept of N
  (Tinoco Fig 5.5)
- if Scatchard plot is not linear, binding sites are not identical or not independent


- macromolecules are polymers and it is often convenient to define binding on a per monomer basis
    $r$ = number of bound L per monomer unit
    $n$ = number of binding sites per monomer unit

$$\frac{r}{[L]} = K(n - r)$$

- See Tinoco p 202 and Fig 5.8 for example based on intercalation to DNA

# Cooperative and Anticooperative Binding

- there is often interaction between identical binding sites on one macromolecule
- cooperative binding
  - binding of one ligand makes it easier for next ligand to bind
  - may be caused by conformational changes
  - limit is all-or-none binding where once one ligand binds, the binding for the other sites increase such that all N ligands bind at once - macromolecule either has no ligands or all sites filled
- anticooperative binding
  - binding of one ligand makes it more difficult for next ligand to bind
  - e.g.  binding of $H^+$ to multiple acidic groups on protein - in fully deprotonated form, multiple negative charges attract protons, as each proton is bound, charge decreases and there is less attraction for next proton
  - limit is excluded-site binding where binding of ligand prevents binding at another site

- studied by plotting the fraction of sites bound (*f*) vs concentration of ligand

$$f = v/N$$

  - sigmoidal curve indicates cooperative binding
  - curve that fits Scatchard equation indicates identical, independent sites
  - Tinoco Fig 5.9

- from the Scatchard equation, for cooperative binding:

$$\frac{f}{(1-f)} = K[L]^n$$

$$\log \frac{f}{(1-f)} = n\log[L] + \log K$$

  *n* = Hill constant

  *K* = constant, not the binding constant for one L

- Hill constant varies from 1 for no cooperativity to N for all-or-one binding
- Hill plot, log f/(1-f) vs log[L] is used to determine *n*
- Tinoco Fig 5.10