I: Life and Energy

- May 21: Monday
- Lecture 1: What is life? An attempt at definition.
- Energy, heat, and work: Temperature and thermal equilibrium. The First Law. Thermodynamic states and state functions. Reversible and real processes. The Second Law and free energy. Why do living systems need energy? (B Lentz)
- **May 23: Tuesday**
- Lecture 2: Solutions and chemical potential; Osmotic pressure (B Lentz).
- May 25: Wednesday
- Lecture 3: Mother Nature plays dice: the Boltzmann distribution, partition functions and en
  tropy. (B Lentz)

Chemical Thermodynamics

While Thermodynamics is familiar to engineers and physicists, the thermodynamics most useful in Biophysics is that familiar to chemists: solution, reaction, and phase equilibria.

We have already defined the thermodynamic quantity essential to describing these phenomena, the chemical potential or molar Gibbs free energy:

$$\mu_i = \left(\frac{\partial G}{\partial n_i}\right)_{T,P,n_{j\neq i}} = \mu_i^0 + \text{concentration dependent term}$$

We will use this quantity to describe:

1] solutions
2] chemical equilibria
3] phase equilibria
4] binding equilibria
5] osmotic effects

Solutions

We will review four types of solutions:

Ideal Gas: precursor to the ideal solution

Ideal Solutions

Dilute Solutions that behave according to Raoult's and Henry's Laws.

Non-Ideal or Real Solutions.

Ideal Gas

An Ideal Gas is a hypothetical state in which the particles in the gas have a mass but do not interact, and occupy no significant volume.

Boyle observed experimentally that a very dilute gas behaved according to the following equation of state:

$PV=Nk_BT$*

*Note that k_B (Boltzmann constant) has units of energy/temperature/molecule or per mol, depending on the context in which it is used:

1.99 cal/K/mol=8.33J/K/mol or 1.38×10^{-23} J/K in molecular units

From this, you can show that:

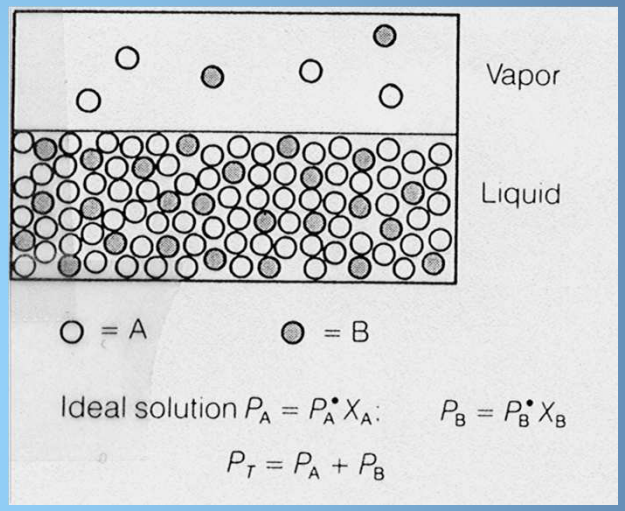
$$\mu = \mu_v^0(T, P=1) + k_B T \ln P = \mu_v^\dagger(T, \frac{N}{V}=1) + k_B T \ln \frac{N}{V}$$

We shall see that this is easily derived from the canonical partition function for a non-interacting particle mixture, but you can derive it from Boyle's Law using the t differential of G.

Ideal Solution

An Ideal Solution might better be called an Ideal Mixture, since, as in an Ideal Gas, no distinction is made between solute and solvent.

In an Ideal Mixture, all components have the same size and they interact with each other uniformly.



All components of an ideal solution have chemical potentials of the form:

$$\mu_i = \left(\frac{\partial G}{\partial n_i}\right)_{T,P,n_{j\neq i}} = \mu_i^{\bullet} + k_B T \ell n X_i$$

$\mu_i^{\bullet}$ = μ of pure component *i* at T,P.

We will prove this to ourselves using a statistical approach in Lecture 3.

Real Dilute Solutions

At very low solute concentration, chemical potentials of solutes vary linearly as the logs of their mole fractions (Henry's Law), and the chemical potential of low vapor pressure solvent (*e.g.*, water) also varies with the log of its mole fraction (Raoult's Law).

Henry's Law

Solutes: $$\mu_i = \mu_{i,x}^{\circ}(T,P) + k_B T \ln X_i = \mu_{i,c}^{\circ} + k_B T \ln c_i$$

Not identical!

NOTE: X_i = mole fraction is the "natural" unit of concentration!

μ_i° is the "unitary" chemical potential
$k_B \ln X_i$ is the "cratic" chemical potential

Raoult's Law

μ_i^0 = μ of solute in an imaginary state at unit concentration but surrounded by solvent.

Low vapor Pressure Solvent: $$\mu_0 \approx \mu_{0,L}^{\circ}(T,P) - k_B T \sum_{i>0} X_i$$

μ_0° = μ of pure solvent (component 0) at T,P; standard state for solvent.

∴ dilute solutions c
called ideal, but are not!

Real Solutions

$$\mu_i = \mu_{i,x}^{\circ} + k_B T \ln a_i$$

a_i is the activity of component i

$a_i = \gamma_i (X_i) \times X_i$

γ_i = *"activity coefficient"* is a function of X_i!

$\gamma_i (0) = 1$; $\gamma_i \backslash 0$ as X_i increases.

In itself, this expresses nothing and is not very useful! Only if we know γ is it useful. *Useful* when $\gamma = 1 - \varepsilon$, with $\varepsilon << 1$

Conditions of Equilibria

Recall that the basic condition of equilibrium is a system is that the entropy be maximized or, equivalently, that the free energy be minimized.

There are many types of equilibria, but often we are interested in determining the number of molecules present in an open system.

- ✚ molecules distributing between two phases
- ✚ molecules A & B reacting to form molecule C
- ✚ a ligand molecule moving from solution to a binding site on a protein

These are all examples of MASS EQUILIBRIUM in an OPEN SYSTEM.

Equilibrium: Gibbs-Duhem Equation

For Open Systems, the condition that dG = 0 leads to a well known expression for mass equilibrium at fixed T and P.

Recall that Integrating the total differential dG at fixed T and P ⇨

$$G = \sum n_i \mu_i$$

$$dG = \sum n_i d\mu_i + \sum \mu_i dn_i = 0 = -dw - \sum n_i d\mu_i ; \text{fixed } T \ \& \ P$$

At dw=0, $\Rightarrow$

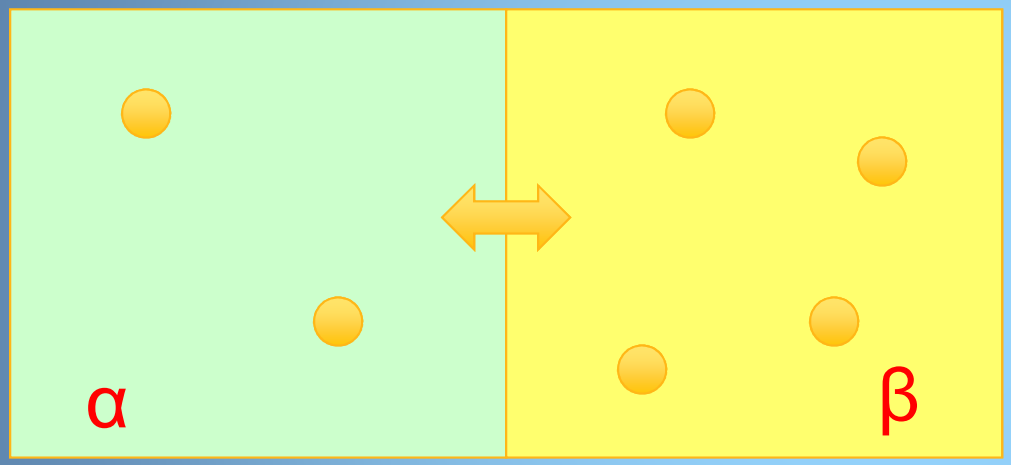
$$\sum n_i d\mu_i = 0$$

This is the famous Gibbs-Duhem Equation.

It established the condition of mass equilibrium in an open system

Gibbs-Duhem 2: Phase Equilibrium

The Gibbs-Duhem Equation establishes the principle that the chemical potentials of the components of a mixture cannot change independently. This provides us with the conditions of phase and chemical equilibrium.



$$\ell n\left(\frac{a_\alpha}{a_\beta}\right) = \frac{\mu_\beta^0}{\mu_\alpha^0} = \ell n K_p$$

Partition coefficient

Balance between unitary and cratic terms

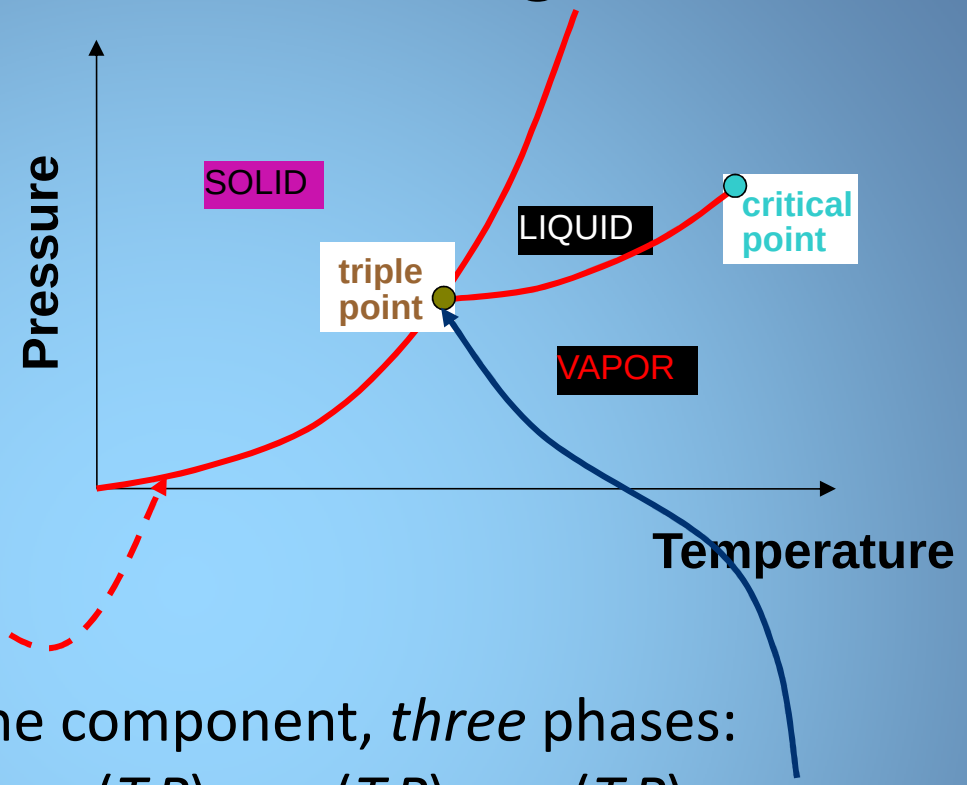
For Phase Equilibrium, the Gibbs-Duhem Equation implies the condition of equilibrium:

$$\mu_i^\alpha = \mu_i^\beta = \mu_i^\gamma = \cdots; \text{ for each } i$$

Single Component Phase Diagram: *T* and *P*

One component, *two* phases:

$\mu_A(T,P) = \mu_B(T,P)$



Pick any *T*, then the requirement of phase equilibrium => *P* is defined => a "phase line"

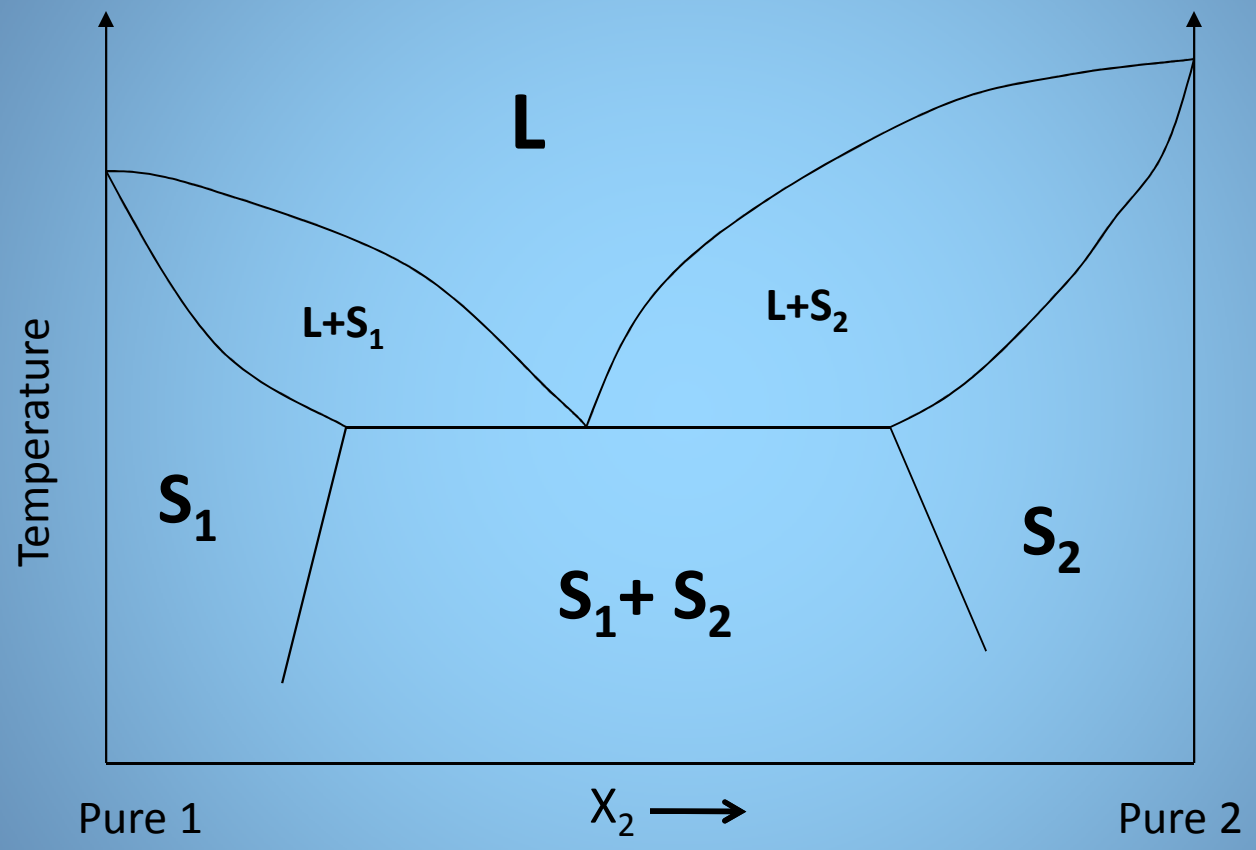
One component, *three* phases:

$\mu_A(T,P) = \mu_B(T,P) = \mu_C(T,P)$

Only one pair of values of *T* and *P* can satisfy these two equalities

Gibbs Phase Rule: Deg Freedom = 2 – Phases + Components

Phase Diagrams for Two-Component Systems: T & X_i



Gibbs-Duhem 3: Chemical Equilibrium

In a chemical reaction, several types of molecules are converted to other types by a rearrangement of electronic motions. Equilibrium is also achieved when there is a balance between the unitary and cratic contributions to the chemical potential of each species.

Any Chemical Reaction can be written as:

$$\sum_j \nu_j M_j$$

where ν_i is the stoichiometry of reactant M_i.

e.g.: 3A+B $\longleftrightarrow$ 2C; ν = -3,-1,2; reactants, products

The change in Gibbs Free Energy (dG) for a small change in extent of reaction (dε) is

$$dG = \sum_j \nu_j \mu_j d\varepsilon$$

$$\sum_j \nu_j \mu_j^0 = -k_B T \sum_j \nu_j \ell n\{a_j\}$$

$$K_{eq} = \prod_j a_j^{\nu_j} = e^{-\sum_j \nu_j \mu_j^0 / k_B T}$$

Cratic Unita

This leads to the condition of Chemical Equilibrium:

$$\sum_j \nu_j \mu_j = 0$$

e.g.

$$K_{AB \leftrightarrow C} = \frac{a_C^2}{a_A^3 a_B}$$

Chemical Equilibria -2-

Reactants (A) $\longleftrightarrow$ Products (B)

$$-k_B T \ln K_{eq} = -\sum_{i \in \mathbf{A}} \nu_i \mu_i^{\circ} + \sum_{i \in \mathbf{B}} \nu_i \mu_i^{\circ} = \Delta G^{\circ}$$

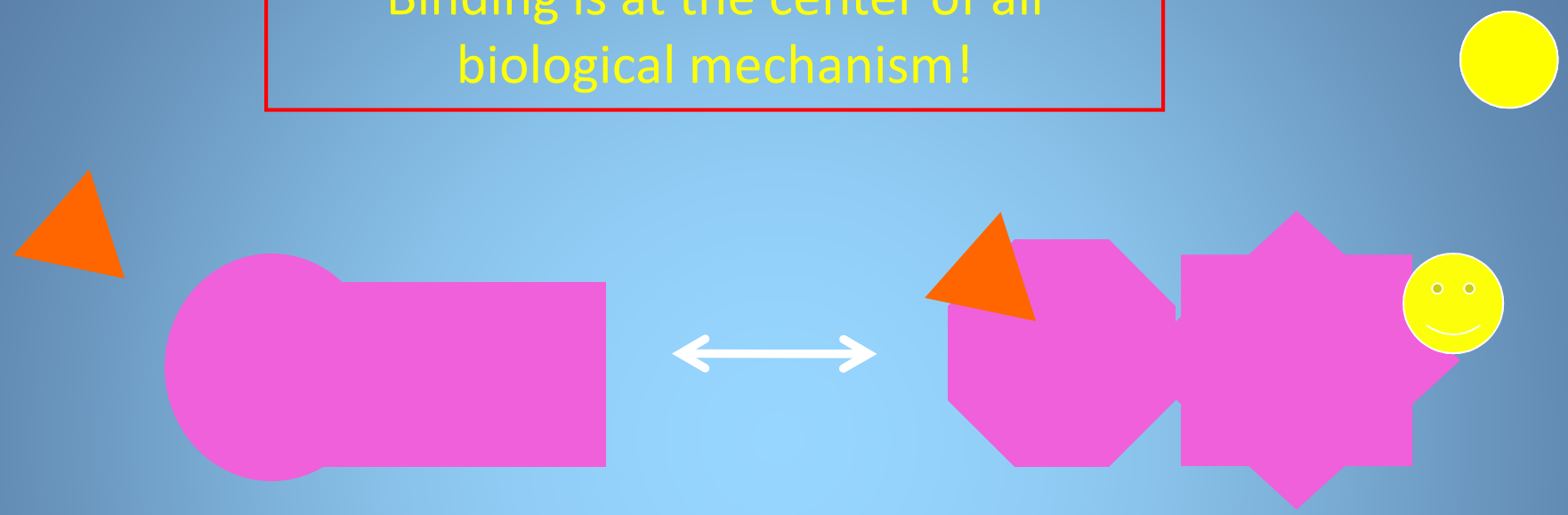
ΔG^0 is the *Standard* Free Energy Change for the reaction. This is the free energy difference between the products and reactants in their standard chemical potential states. This is a measure of how much the reactants *intrinsically* want to convert to product. If ΔG^0 is negative, entropic considerations (embodied in the ratio of activities of products over reactants) are all that keeps the reaction from proceeding all the way to products. Equilibrium is again the balance between these unitary and cratic effects.

The van 't Hoff equation gives the reaction's standard enthalpy change:

$$\Delta H^{\circ} = \frac{\partial[\Delta G^{\circ}/T]}{\partial[1/T]} = -k_B \frac{\partial \ln K_P}{\partial[1/T]} = k_B T^2 \frac{\partial \ln K_P}{\partial T}$$

Binding Equilibria

Binding is at the center of all biological mechanism!



Binding always reflects a playoff between the favorable free energy (mainly due to a reduction in internal energy) of occupying a binding site and the unfavorable entropy change associated with bringing ligands out of solution to binding sites.

The balance between these two effects determines the fraction of sites occupied at any free ligand concentration.

Binding 2

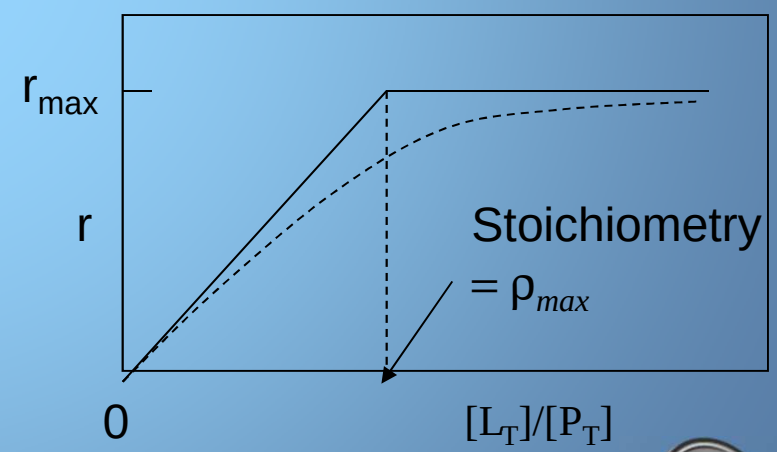
Simplest Case: single ligand to a single site on a protein :

$$M + L \leftrightarrow ML$$

The "site association constant" (K_a) is simply the equilibrium constant for this reaction, where [L] is free ligand concentration. From this, one easily obtains the fraction of sites occupied, *v*.

$$K_a = \exp\left\{\frac{\mu_{ML}^0 - \mu_L^0 - \mu_M^0}{k_B T}\right\} = \frac{a_{ML}}{a_L a_M}; \quad \nu = \frac{K_a a_L}{1 + K_a a_L}$$

$$\Delta G^0 = \mu_{ML}^0 - \mu_L^0 - \mu_M^0 = \text{unitary site binding free energy}$$



If P contains *n* equivalent sites, the number bound, *r*, is easily obtained. Here the equilibrium constant, κ, is a "stoichiometric" binding constant for the association of *n* ligands with P.

$$\kappa = \frac{[PL_n]}{[P][L]^n}; \qquad r = \frac{n\kappa[L]}{1 + \kappa[L]}$$

Detecting Binding

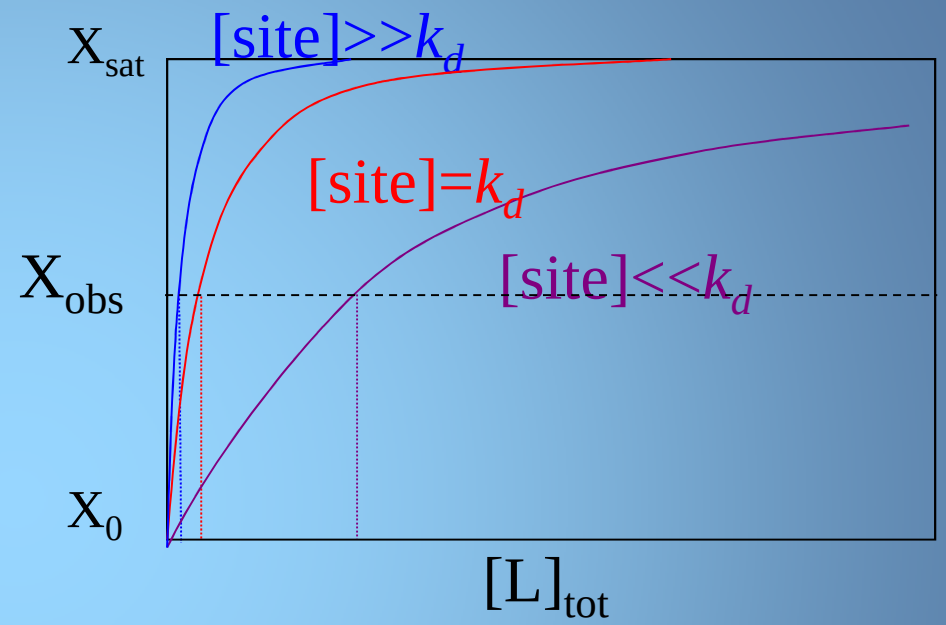
Direct Measurement: We can often measure [L] and [PL] by equilibrium dialysis or by parallel potentiometric measurement of free ligand activity (a_L) in buffer versus total macromolecule concentration ([M]).

Most often, we do not know the free and bound ligand concentrations but measure a quantity X that is proportional to [PL]. We use the values of this quantity at increasing ligand concentration ($[L]_{tot}$) to determine the fraction of sites occupied.

$$\nu = \frac{X - X_0}{X_{sat} - X_0} = \frac{\Delta X}{\Delta X_T} = \frac{K[L]}{1 + K[L]}$$

$$X = \Delta X_T \frac{K[L]}{1 + K[L]} + X_0$$

The binding isotherm is approximately hyperbolic, and it takes a minimum of three parameters to define an hyperbola. A carefully planned experiment will define both K and X_{sat}. Get X_0 by inspection.

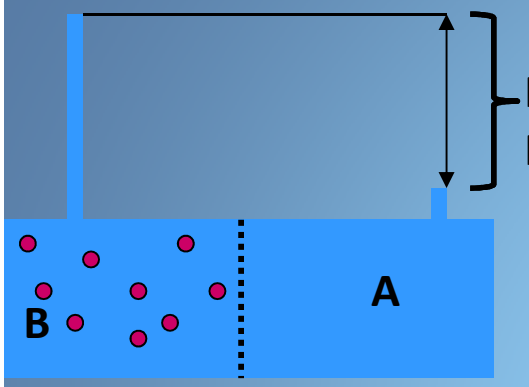


$$\frac{X - X_0}{X_{sat} - X_0} = \frac{1}{2[P]_{tot}} \left\{ a \pm \sqrt{a^2 - 4[P]_{tot} \frac{[L]_{tot}}{n}} \right\}$$

$$a = \frac{1}{nK} + \frac{[L]_{tot}}{n} + [P]_{tot}$$

When multiple ligands bind, we must also estimate n, the stoichiometry. In general, the information in a single binding isotherm is insufficient to obtain n, and a second experiment may be needed.

Osmotic Pressure



Pressure difference =ΔP=
Π = Osmotic Pressure

● = macromolecular solute (M)

S = solvent

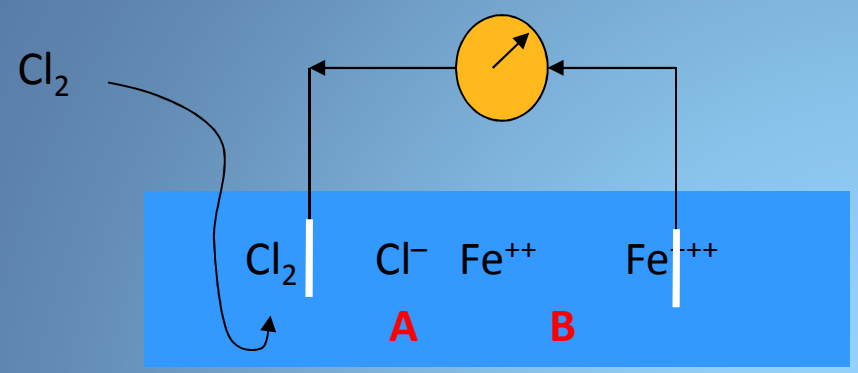
If we allow water to pass between A and B at constant volume, and no movement of macromolecules, the system will maximize S (minimize X_S) to achieve equilibrium. This will involve moving water from A to B, leading to an increase in pressure on B.

$$\mu_S^B = \mu_S^*(T, P+\delta P) + k_B T \cdot \ell n X_S^B \approx \mu_S^*(T, P+\delta P) - k_B T \cdot X_M^B = \mu_S^A = \mu_S^*(T, P)$$

from definition of G: $\left(\frac{\partial \mu_S^*}{\partial P}\right)_{T,N_S} = v_S = \left(\frac{\partial V}{\partial N_S}\right)_{T,P}$

$$\mu_S^*(T, P+\Delta P) = \mu_S^*(T,P) + \int_P^{P+\Delta P} v_S dP = \mu_S^*(T,P) + v_S \Delta P; \quad \rightarrow \quad v_S \Pi = k_B T \cdot X_M^B$$

Ionic Equilibria: Electromotive Force



$Cl_2 + 2\,e^- \rightarrow 2\,Cl^-$

$2\,Fe^{++} \rightarrow 2\,Fe^{+++} + 2\,e^-$

$Cl_2 + 2\,Fe^{++} \rightarrow 2\,Cl^- + 2\,Fe^{+++}$

The Rxn is favorable but can occur only if electron can get from B to A.

Chemical Rxns that produce an electrical potential (V^{EMF}) have the ability to do work.

Gibbs-Duhem when $dw \neq 0$: $-dw - \sum n_i d\mu_i = 0$

$$\sum_i \mu_i \nu_i - w = 0 \Rightarrow -\mu_{Fe2+} + \mu_{Fe3+} - \tfrac{1}{2}\mu_{Cl_2} + \mu_{Cl-} - eV_{EMF} = 0$$

The work performed by an ionic gradient:

$$-eV_{EMF} = \mu^o{}_{Fe3+} - \mu^o{}_{Fe2+} - (\tfrac{1}{2}\mu^o{}_{Cl_2} - \mu^o{}_{Cl^-}) + k_B T \ln \frac{a_{Fe^{3+}} a_{Cl^-}}{a_{Fe^{2+}} \sqrt{a_{Cl_2}}}$$

The ability of an electrode couple to do work: Standard EMF

$$V^0_{EMF} = -\frac{\mu^o{}_{Fe3+} - \mu^o{}_{Fe2+} - (\tfrac{1}{2}\mu^o{}_{Cl_2} - \mu^o{}_{Cl^-})}{e} = E^0_{Fe^{3+}/Fe^{2+}} - E^0_{Cl_2/Cl^-}$$

Electromotive force can report activities using Ion-Specific Electrodes.

Electromotive force can do work: Electric Cars

Study Questions

1] What is an Ideal Solution? How does the chemical potential of a solute in an ideal solution differ from that in a dilute solution?

2] Derive the chemical potential of a component of an ideal from Boyle's Law.

3] Can you suggest two physical reasons for the activity coefficient being less than one? That is, for the effective concentration to be less than the real concentration.

4] Explain how one derives the Gibbs Phase Rule.

5] In all types of equilibria, we see that there is a unifying principle: the unitary free energy is balanced by the cratic free energy at equilibrium. What does this mean in simple terms?

6] We saw that binding of one ligand to a site on a macromolecule can affect the way another ligand binds to a different site. What is this called? If a ligand were to bind to the second site, would this alter binding to the first site?