

I: Life and Energy

- 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)
- **Lecture 2:** Solutions and chemical potential; Osmotic pressure (B Lentz).
- Lecture 3: Mother Nature plays dice: the Boltzmann distribution, partition functions and entropy. (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:

$$PV=Nk_B T^*$$

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

$$1.99 \text{ cal/K/mol} = 8.33 \text{ J/K/mol} \text{ or } 1.38 \times 10^{-23} \text{ J/K in molecular units}$$

From this, you can show that:

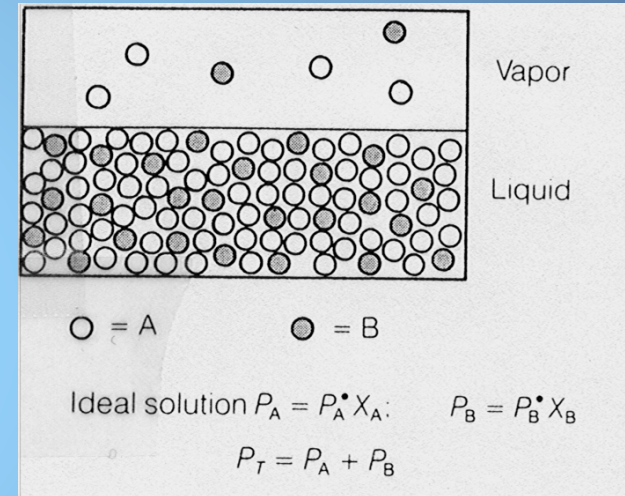
$$\mu = \mu_v^0(T, P=1) + k_B T \ln P = \mu_v^\dagger(T, \frac{N}{V}=1) + k_B T \ln \frac{N}{V}$$

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 total 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:

$$\mu_i = \left(\frac{\partial G}{\partial n_i} \right)_{T, P, n_{j \neq i}} = \mu_i^* + k_B T \ln X_i \quad \mu_i^* = \mu \text{ of pure component } i \text{ at } T, P.$$

We can prove this to ourselves using the statistical approaches in Lecture 3. 5

Real Dilute Solutions

Very low solute concentration:

Henry's Law applies to chemical potentials of solutes.

Raoult's Law applies to chemical potential of low vapor pressure solvent (e.g., water).

Henry's Law

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

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

Not identical!

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

$\mu_i^0 = \mu$ of solute in an imaginary state at unit concentration but surrounded by solvent.

$$X_i = \frac{n_i}{\sum_j n_j}$$

Raoult's Law

Low vapor Pressure Solvent:

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

$\mu_0^\circ = \mu$ of pure solvent (component 0) at T,P;

8/28/2015 standard state for solvent.

•• dilute solutions often 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

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

$\gamma_i =$ “*activity coefficient*” is a function of X_i !

$\gamma_i(0) = 1$; $\gamma_i \rightarrow 0$ 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 $\varepsilon \ll 1$

Conditions of Equilibria

Recall that the basic condition of equilibrium in 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 work function differential dG at fixed T and P \Rightarrow

$$G = \sum n_i \mu_i$$

Write the total differential of G for both n_i and μ_i as variables:

$$dG_{tot} = \sum n_i d\mu_i + \sum \mu_i dn_i$$

Work Function for the Combined 1st and 2nd Law:

$$dG_{WF} = -SdT + Vdp - dw - \sum n_i d\mu_i$$

At Equilibrium, $dG_{tot} = dG_{WF} = 0$

At fixed T, P, and no work done:

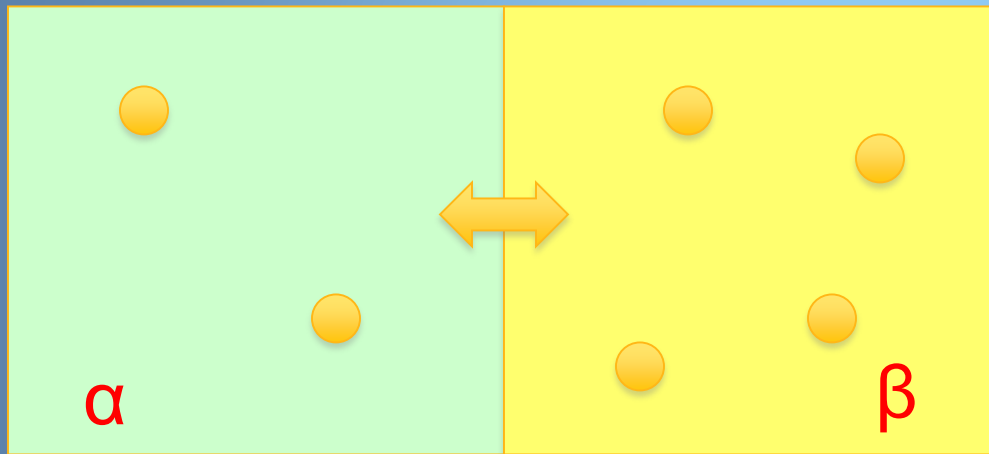
$$\sum n_i d\mu_i = 0$$

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.



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

Partition coefficient

Balance between unitary and cratic terms

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

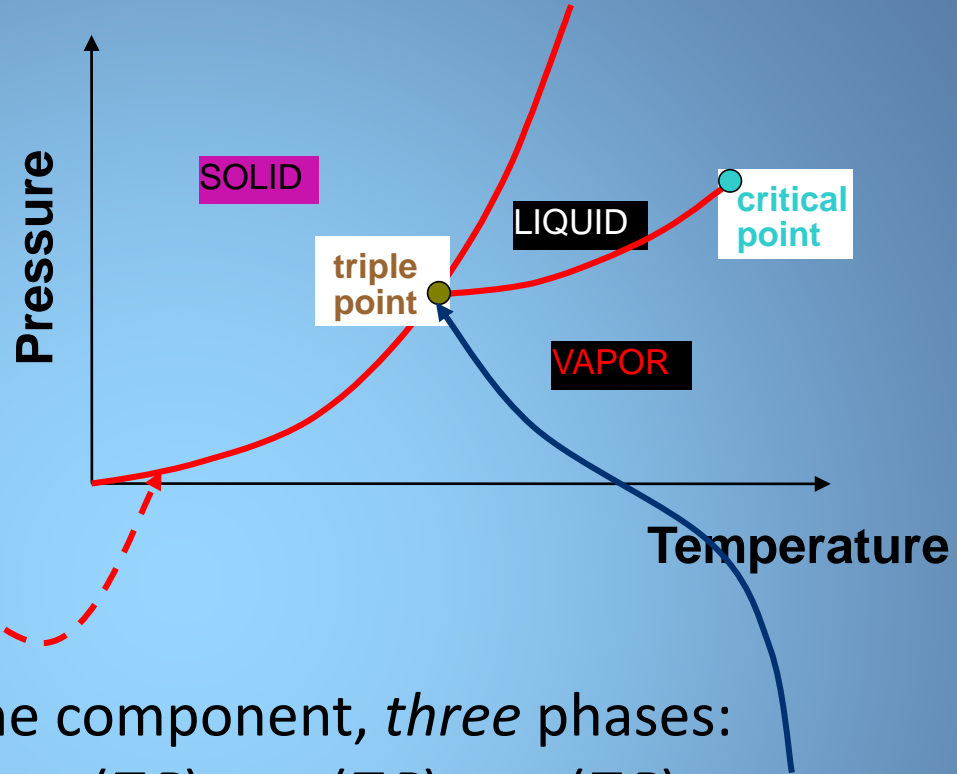
$$\mu_i^{\alpha} = \mu_i^{\beta} = \mu_i^{\gamma} = \dots; \text{ for each } i$$

Single Component Phase Diagram: T and P

One component, *two* phases:

$$\int_A(T,P) = \int_B(T,P)$$

Pick **any** T , then the requirement of phase equilibrium $\Rightarrow P$ is defined \Rightarrow a “phase line”



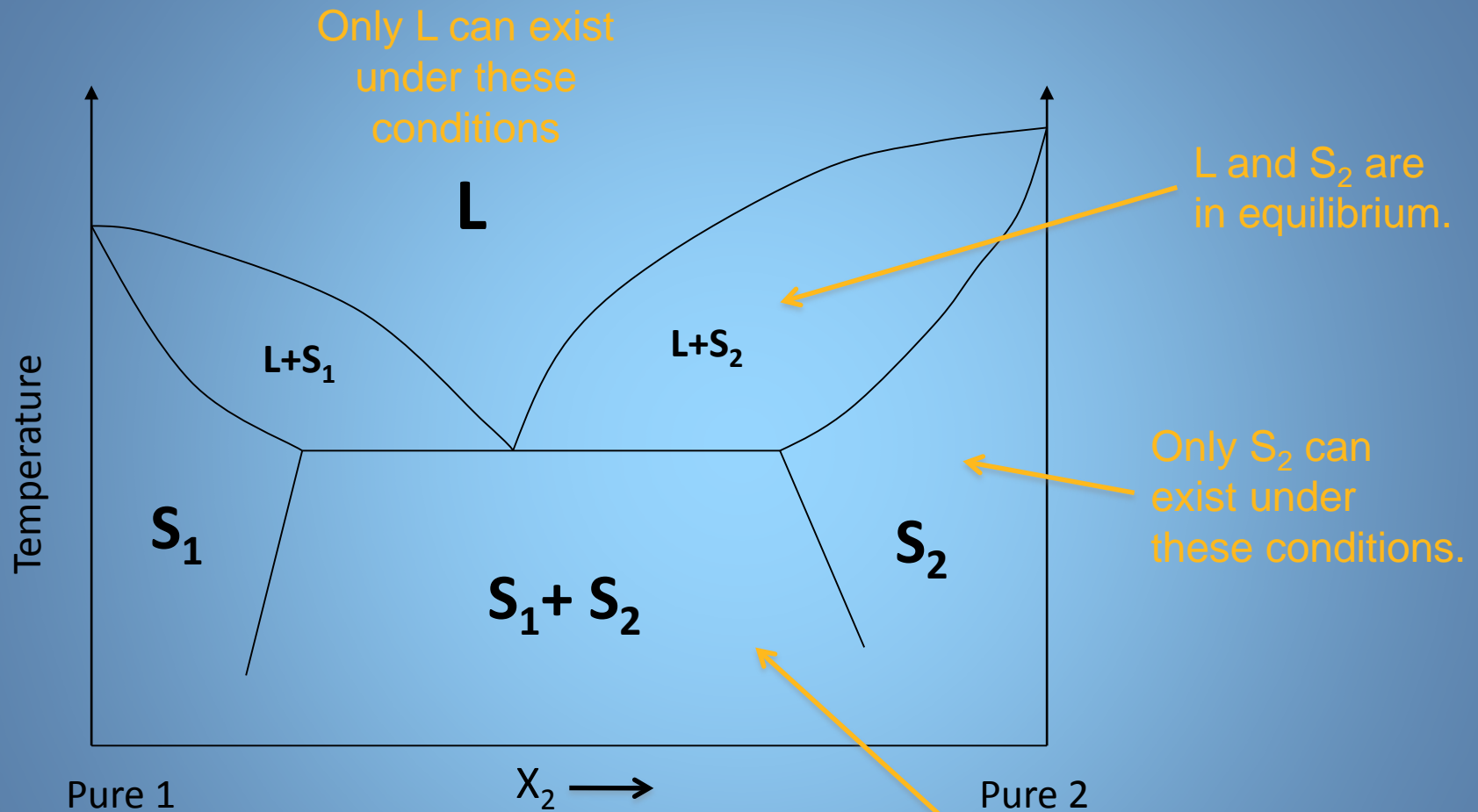
One component, *three* phases:

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

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

Gibbs Phase Rule: $\text{Deg Freedom} = 2 - \text{Phases} + \text{Components}$

Phase Diagrams for Two-Component Systems: T & X_i



Often describes equilibrium between lipids in different "domains" in a biomembrane.

S₁ and S₂ are in equilibrium under these conditions.

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:

where v_i is the stoichiometry of reactant M_i .

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

$$\sum_j v_j M_j$$

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

$$dG = \sum_j v_j \mu_j d\epsilon$$

This leads to the condition of **Chemical Equilibrium**:

$$\sum_j v_j \mu_j = 0$$

Eq Constant.

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

$$\sum_j v_j \mu_j^0 = -k_B T \sum_j v_j \ln \{ a_j \}$$

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

Cratic

Unitary₁₃

Chemical Equilibria -2-

Reactants (A) \longleftrightarrow Products (B)

$$-k_B T \ln K_{eq} = -\sum_{i \in A} \nu_i \mu_i^0 + \sum_{i \in B} \nu_i \mu_i^0 = \Delta G^0$$

ΔG^0 = *Standard* Free Energy Change for the reaction = 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.

ΔG^0 = negative \Rightarrow product wants to form.

Why not go completely to product???

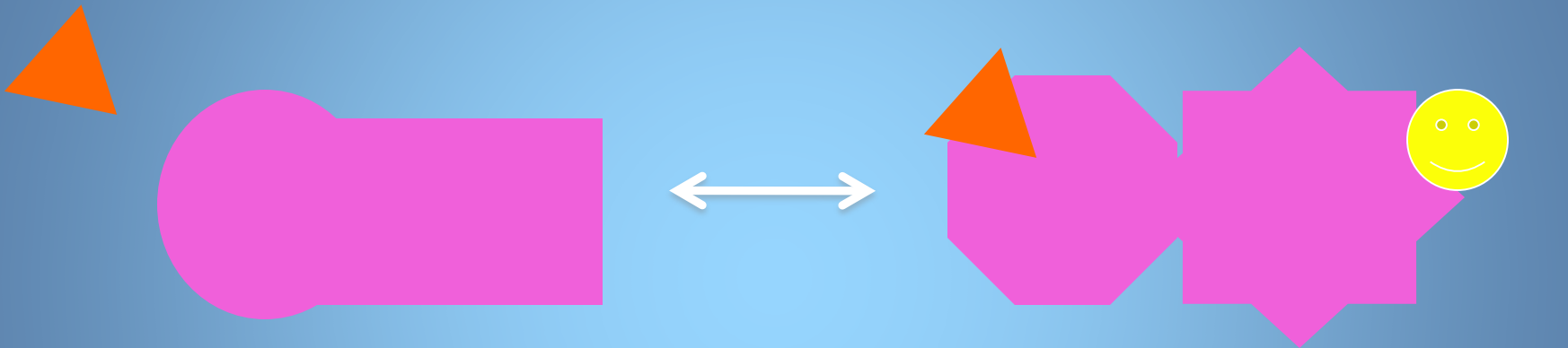
ENTROPY is max when we have a mix of products and reactants. Equilibrium is again the balance between these unitary and cratic effects.

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

$$\Delta H^0 = \frac{\partial[\Delta G^0 / T]}{\partial[1/T]} = -k_B \frac{\partial \ln K_P}{\partial[1/T]} = k_B T^2 \frac{\partial \ln K_P}{\partial T}$$

Binding Equilibria

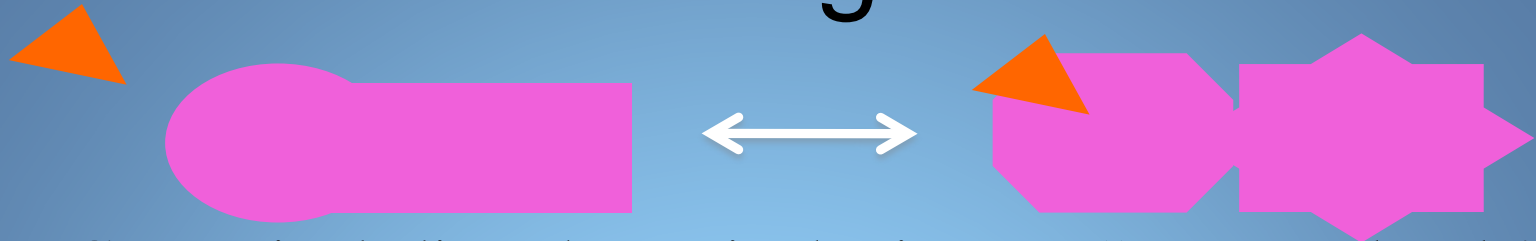
Binding is at the center of all biological mechanism!



Binding always reflects a **playoff** between the favorable free energy (mainly due to a reduction in internal energy) of occupying a binding site (**unitary effect**) and the **unfavorable entropy change** (**cratic effect**) 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 “macromolecule” (M)

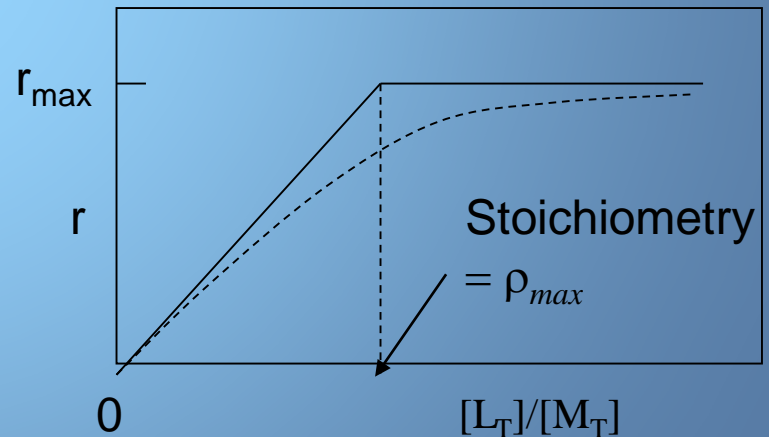


The "site association constant" (K_a) is simply the equilibrium constant for this reaction, where $[L]$ is free ligand concentration. From this, one easily obtains the fraction of sites occupied, v .

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

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

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



$$\kappa = \frac{[ML_n]}{[M][L]^n}; \quad r = \frac{nk_a[L]}{1 + k_a[L]}^{16}$$

Detecting Binding

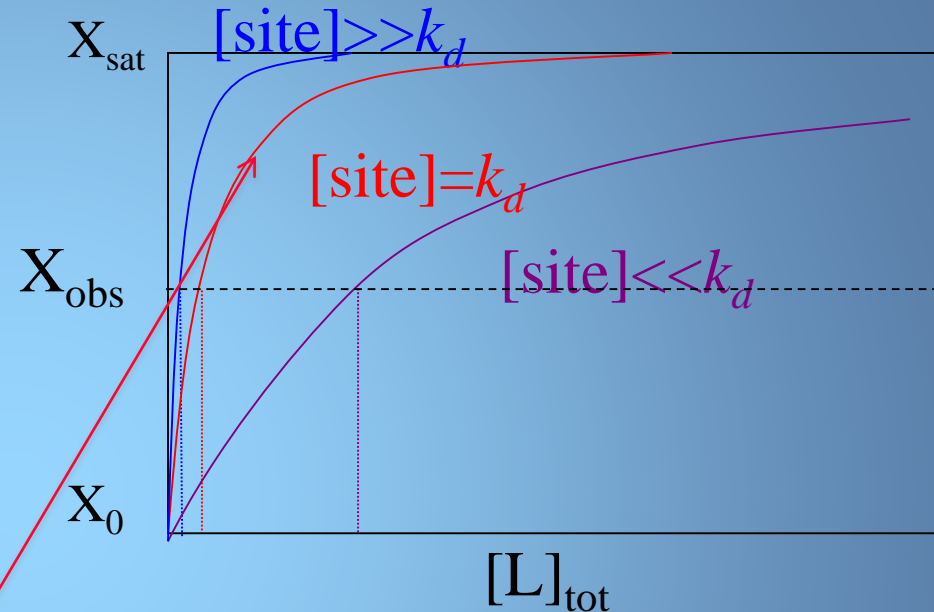
Direct Measurement: measure “ligand” [L] and “protein-ligand complex” [PL] by **equilibrium dialysis** or by **potentiometric measurement** of free ligand activity (a_L) *versus* total protein concentration ([P]).

Most often, measure a quantity X that is proportional to [PL] and use this quantity at increasing ligand concentration ($[L]_{tot}$) to determine the fraction of sites occupied.

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

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

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.

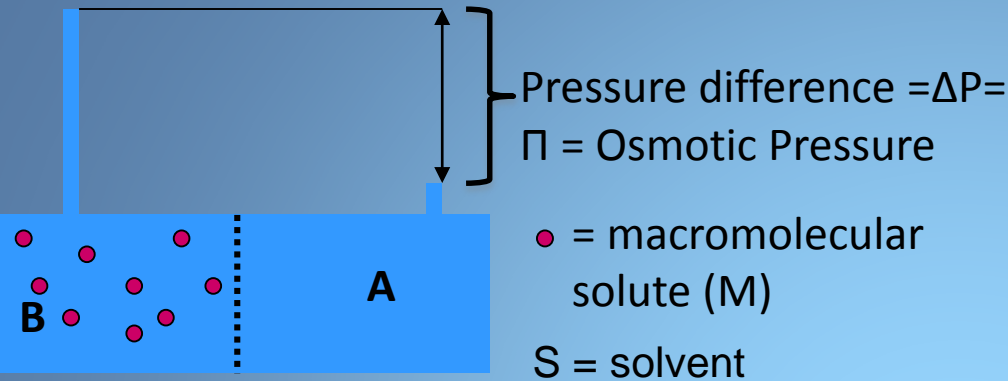


$$\frac{X - X_0}{X_{sat} - X_0} = \frac{1}{2[P]_{tot}} \left\{ a \pm \sqrt{a^2 - 4[P]_{tot} \frac{[L]_{tot}}{n}} \right\}$$

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

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 another experiment may be needed.

Osmotic Pressure



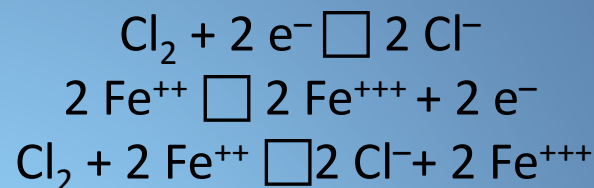
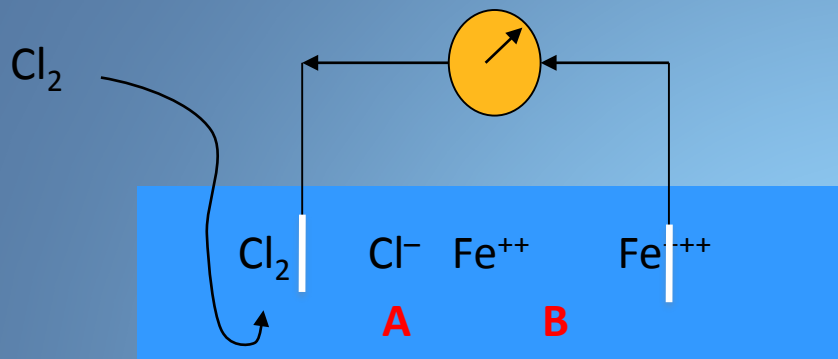
Semipermeable membrane: water pass between A and B but not M. At constant volume, the system will maximize S (minimize X_S in B) to achieve equilibrium. \Rightarrow move water from A to B, \Rightarrow increased pressure in B.

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

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



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

$$\sum_i \mu_i \nu_i - w = 0 \Rightarrow -\mu_{\text{Fe}^{2+}} + \mu_{\text{Fe}^{3+}} - \frac{1}{2} \mu_{\text{Cl}_2} + \mu_{\text{Cl}^-} - eV_{EMF} = 0$$

The work performed by an ionic gradient:

$$-eV_{EMF} = \mu^{\circ}_{\text{Fe}^{3+}} - \mu^{\circ}_{\text{Fe}^{2+}} - \left(\frac{1}{2} \mu^{\circ}_{\text{Cl}_2} - \mu^{\circ}_{\text{Cl}^-}\right) + k_B T \ln \frac{a_{\text{Fe}^{3+}} a_{\text{Cl}^-}}{a_{\text{Fe}^{2+}} \sqrt{a_{\text{Cl}_2}}}$$

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

$$V_{EMF}^0 = -\frac{\mu^{\circ}_{\text{Fe}^{3+}} - \mu^{\circ}_{\text{Fe}^{2+}} - \left(\frac{1}{2} \mu^{\circ}_{\text{Cl}_2} - \mu^{\circ}_{\text{Cl}^-}\right)}{e} = E^0_{\text{Fe}^{3+}/\text{Fe}^{2+}} - E^0_{\text{Cl}_2/\text{Cl}^-}$$

Electromotive force can report activities using Ion-Specific Electrodes.

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] 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?
- 5] 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?