Lecture 12: Introduction to Thermo and Stat. Mech. (continued)

Reading Assignment for Lectures 10-12: PKT Chapter 6
Tutorial Tuesday: I will respond to questions about homework.

3. Relation to "chemical equilibrium." Consider the dissociation reaction $AB \leftrightarrow A+B$.

Chemists characterize ratio of equilibrium concentrations by an equilibrium constant: $\frac{[A][B]}{[AB]} = K(T)$.

("Law of Mass Action") K(T) is the "dissociation constant"

In this situation, $RL \leftrightarrow R+L$, so we would expect $\frac{[R][L]}{[RL]} = K(T)$, i.e. $[RL] = \frac{[R][L]}{K}$.

But, $P_B = \frac{[RL]}{[R]+[RL]} = \frac{[R][L]/K}{[R]+[R][L]/K} = \frac{[L]}{K+[L]}$.

Identifying [L] with the ligand concentration c_L, we can see that this is the same as our result with $K = e^{-\beta\Delta\varepsilon}(1-c_L)$.

Note:

(a) In this representation, we can identify K with the concentration at which the binding site is equally likely to be occupied or unoccupied.

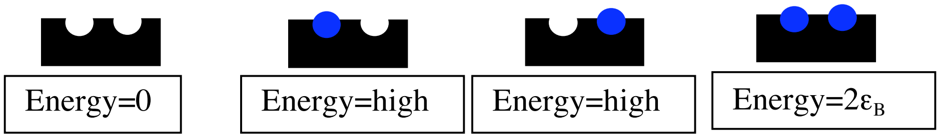
(b) We have, thus, derived the "law of mass action" from statistical mechanics.

(c) At low ligand concentration, $K = K(T) = e^{-\beta\Delta\varepsilon}$.

(d) At high ligand concentrations, the effective equilibrium constant decreases. This concentration dependence of the "equilibrium constant" is a real effect, going beyond the simple chemical approach (which is, in fact, a low-concentration approximation).

4. Cooperative binding and higher-order effects.

In biological systems, it is often required to bind two (or more) ligands to make the reaction proceed. We can model this process by postulating a receptor R which likes to bind two ligands but penalizes with high energy the binding of single ligands:



Assume "high" energy to infinity (easy enough to do the more-general case).

What is P_B for this case?

No bound ligands:

Energy: $E = N_L \varepsilon_S$

Number of distinct microstates of this type: $\frac{N_V!}{N_L!(N_V-N_L)!}$

the argument is the same as for the coin-toss problem: how many ways are there to distribute N_L identical ligands among the N_V cells?

Two bound ligands:

Energy: $E = (N_L-2)\varepsilon_S + 2\varepsilon_B$

Number of distinct microstates of this type: $\frac{N_V!}{(N_L-2)!(N_V-N_L+2)!}$. Now , calculate

$$\frac{2-\text{bound}\quad\text{multiplicity}}{0-\text{bound}\quad\text{multiplicity}} = \frac{N_L!(N_V-N_L)!}{(N_L-2)!(N_V-N_L+2)!} = \frac{N_L(N_L-1)}{(N_V-N_L+2)(N_V-N_L+1)} = \frac{c^2}{(1-c)^2}$$

Now, calculate the probability of finding the double receptor bound to two ligands:

$$\boxed{P_B = \frac{c_L^2}{e^{-2\beta\Delta\varepsilon}(1-c_L)^2 + c_L^2}}$$

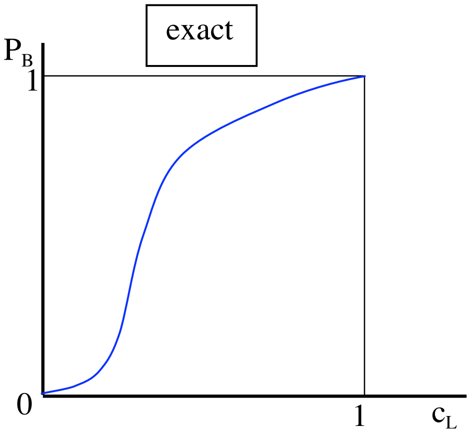
(exact, double receptor)

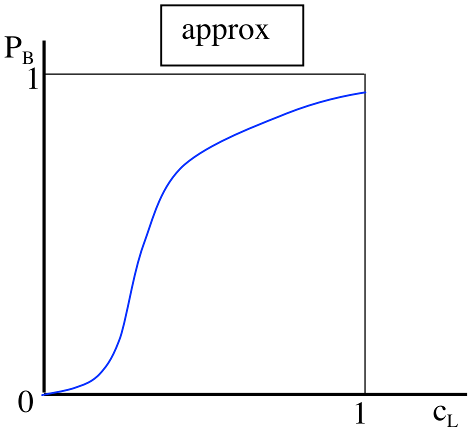
PKT would have $e^{+2\beta\Delta\varepsilon}$

or, neglecting the (1-c_L),

$$\boxed{P_B = \frac{c_L^2}{e^{-2\beta\Delta\varepsilon} + c_L^2} = \frac{c_L^2}{K_1^2 + c_L^2}}$$

(Hill equation)



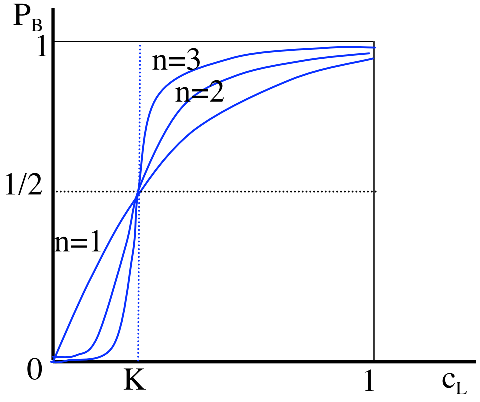


Note:

A. This "cooperative" binding leads to a slower onset of binding at low ligand density but, then, a more rapid rise. This is getting closer to a "switch" which turns on (the transcription or the enzyme) at a specific level of c_L. You can see the potential advantage for "control" processes.

B. This can be extended to higher order:

$$P_B = \frac{c_L^n}{K_1^n + c_L n}$$ is called the "Hill function," with n the "Hill coefficient."



C. Myoglobin is n=1; hemoglobin is n~3.

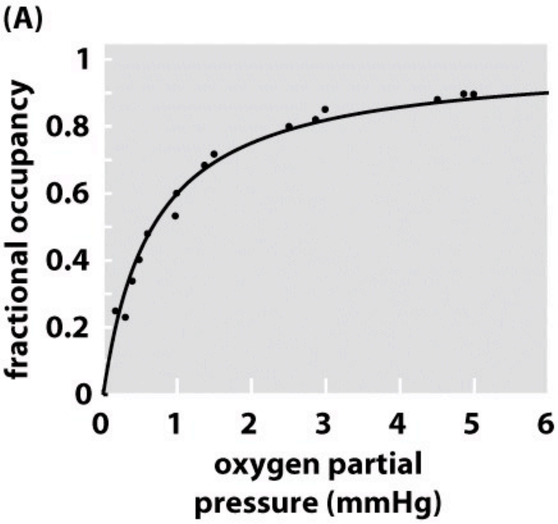


Figure 6.26 Physical Biology of the Cell (© Garland Science 2009)

Myoglobin:
Oxygen binding
Hill coefficient n=1
(for hemoglobin n~3)

Return now to general discussion of Thermo and Stat Mech:

A. Equilibrium for a large system: Thermodynamics and thermodynamic variables.

May be isolated or in contact with a thermal reservoir.

Equilibrium is what happens when you put a bunch of material (e.g., a set of atoms or molecules) into a big box (volume=V), you isolate it (or you let it sit in contact with a heat bath at fixed temperature T), and you wait a long time until nothing further seems to be happening. Initially, there may be inhomogeneities of density, pressure, temperature, etc., and the corresponding flows of matter, energy, etc. Eventually, for most (but not all!) systems. You reach a situation in which—macroscopically speaking!—all flows have stopped and the material is in an apparently time-independent and spatially uniform (homogeneous) state. It is this situation that is called "equilibrium."

Example: gas in room, fluid in container.

This equilibrium situation is sometimes referred to as a "macrostate." Many properties of such an equilibrium macrostate are determined by a very small number of variables.
E, T; V, P; N, μ; etc. Thus, for a gas, just knowing N,V,T tells you a lot, e.g., P(N,V,T).

Ex: Ideal gas (good approx to this room) $P(N,V,T) = \dfrac{Nk_BT}{V}$.

You don't have to know the microstate of the gas to predict the pressure; a small number of "thermodynamic variables" suffices.

Q: How can this be?

A: Many distinct microstates sharing only certain global properties (e.g., N,V, E or N, V, T, etc.) will exhibit the same behavior when appropriate averaged quantities (like P) are measured.

Many microstates correspond to the same macrostates.

Just as many microstates (++-+---+-+…) correspond to the same average <M>~0 in the coin-toss.

The properties of these equilibrium macrostates are what thermodynamics describes.

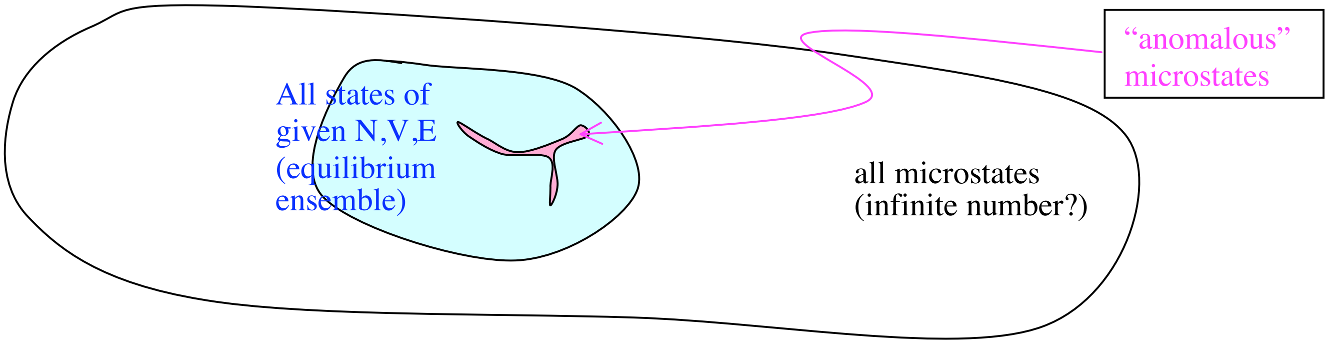
The variables which serve to characterize such states are called "thermodynamic variables."

The "average" quantities, which can be predicted with certainty I will call "thermodynamic quantities."

These predictable quantities are sums/averages over single particles or small clusters of particles, e.g.,

the energy of non-ideal gas: $E = \sum_{n=1}^{N} \frac{\vec{p}_n^{\,2}}{2m} + \sum_{\text{pairs } m,n} V(\vec{r}_m - \vec{r}_n) + \ldots$

Upshot for a LARGE system at equilibrium (with "sufficient" specification of thermodynamic variables):
The collection of microstates that make up the equilibrium macrostate is called an equilibrium "ensemble."
When you make a measurement, you are choosing a particular microstate from this ensemble.
(Almost) all microstates in this ensemble have (almost) the same values of thermodynamic quantities.
Thus, with high probability, the value of such a quantity for a particular microstate is the same as the average value over the entire ensemble.



Comments:
1. Think of the coin-toss outcomes as an ensemble. N is a thermodynamic variable, M is an extenisve thermodynamic quantity, m=M/N is an intensive thermodynamic quantity.
2. "Anomalous" microstates do occur in the ensemble; however, they occur with very low probability. Thus, the probability of finding (+++++…) with M=N is $2^{-N} = e^{-N\ln 2}$, which is negligible for $N=10^{23}$.
3. "Small" fluctuations in measured values of thermodynamic quantities over the ensemble are to be expected. For extensive quantities, these fluctuations are typically of order $\sqrt{N}$; for intensive quantities, they are typically of order $1/\sqrt{N}$.
4. Lots of quantities you might want to measure are NOT thermodynamic, e.g., the position of a particular particle of gas.
5. Much is going on "at equilibrium": local fluctuations of density, temperature, etc.
6. Equilibrium is not completely homogeneous, e.g., inhomogeneous regions near walls.
7. Q: Is equlilibrium a consequence of (e.g.) Newtonian mechanics? Will every system necessarily approach equilibrium?
A: This is a hard question. Answer is "No, not necessarily, but, yes, almost always." Examples.

Thermodynamic variables/quantities:
Thermodynamic variables are all interrelated.
Once you know "enough" information to specify the marcostate, then other variables/quantities are all determined.
What these minimal sets of variables are depends on what kind of a system you are looking at.
Furthermore, for a particular system, you still have a lot of choice.
E.g., for a gas (not necessarily ideal::
E, V, N
T, P, μ, n=N/V, ε=E/N
Thus, (T,V,N) is a common choice; but, (T,P,N) or (E,V,N) or (T,V,μ) are all OK (depends on experimental set-up).

Thermodynamic quantities X are either extensive (doubling the "size" doubles X) or intensive (doubling the size leaves X unchanged).

Examples:

For gas in room, E is extensive but P is intensive.

Note:

You can't specify the system completely without at least one extensive variable; otherwise, you don't know how "big" it is.

The intensive variables are all related to one another; thus, P(T,n) or P(T,μ).

How mathematically to characterize extensivity/intensivity?

Suppose Q (q) is a thermodynamic quantity which is extensive (intensive) and X, Y, Z (x, y, z) are thermodynamic variables that are extensive (intensive).

Consider Q(X): The condition of extensivity requires that $Q(\lambda X)=\lambda Q(X)$.

It is sometimes convenient to express this in the form of a differential equation, by differentiating both sides with respect to λ and then setting λ to 1,

$Q(X)=X\dfrac{dQ}{dX}$, which implies $\dfrac{dX}{X}=\dfrac{dQ}{Q}$, i.e., $\ln Q=\ln X+\text{const}$, or $Q=CX$, so the only possible dependence is linear.

Now, suppose Q is an extensive variable of X, and Y, which are both extensive:

Then, $Q(\lambda X,\lambda Y)=\lambda Q(X,Y)$ for any positive λ.

This constitutes a functional equation that Q has to satisfy, so it puts some limits on the possible form of Q(X,Y). Mathematically, we say "Q is a homogeneous function of (X,Y) of degree 1."

$$Q(X,Y)=X\frac{\partial Q}{\partial X}+Y\frac{\partial Q}{\partial Y}.$$

I claim that solution of this condition is $Q(X,Y)=Xf\left(\dfrac{X}{Y}\right)$.

Equivalently, $Q(X,Y)=Yg\left(\dfrac{X}{Y}\right)=Xh\left(\dfrac{Y}{X}\right)=\ldots$

Check: $\dfrac{\partial Q}{\partial X}=f+\dfrac{X}{Y}f'$, $\dfrac{\partial Q}{\partial Y}=-\dfrac{X^2}{Y^2}f'$, so $X\dfrac{\partial Q}{\partial X}+Y\dfrac{\partial Q}{\partial Y}=\left(Xf+\dfrac{X^2}{Y}f'\right)-\dfrac{X^2}{Y}f'=Q$

Generally, $Q(X,Y,Z,\ldots)=Xf\left(\dfrac{Y}{X},\dfrac{Z}{X},\ldots\right)$, i.e., Q can be written as a product of (any) one of the (extensive) variables times an arbitrary function of (extensive-variable) ratios.