Reading Assignment for Lectures 10-12: PKT Chapter 6

Problem Set 2 (due next Friday, Oct. 4) is now posted on the website. As I produce solutions, I may update it with further hints and comments.

Equilibrium, Macrostates, and thermodynamic variables:

Equilibrium means somewhat different things in cases A and B.

B. Equilibrium for a small system in contact with a (thermal) bath:

In case B, the small system—whatever state it starts in—exchanges energy (in the case of thermal contact, which I use below as my example) or particles, etc., with the reservoir. The reservoir is so large that (by definition) its overall properties do not change in any way as energy flows in/out to/from the small system; on the other hand, the energy of the small system CAN change appreciably. Over a period of time, the small system losses whatever memory it had of its starting state, and it comes "into equilibrium" with the reservoir. In this equilibrium state energy continues to flow between the reservoir and the small system. The microstate of the small system is not fixed because of this energy exchange with the bath. Each microstate n has some probability of occurring.

Key Result: The Boltzmann distribution: (I state this result here without proof. I will justify it later.)

The probability P_n of finding the system in the particular microstate n is proportional to the Boltzmann factor $e^{-\frac{E_n}{k_B T}} \equiv e^{-\beta E_n}$, where $\beta \equiv \dfrac{1}{k_B T}$, T is the temperature of the bath and $k_B = 1.38 \times 10^{-23}$ J/K is called Boltzmann's constant and, in effect, defines the Kelvin temperature scale.

To normalize this (discrete) probability, we need to multiply by an overall factor, defined as 1/Z, so $\boxed{P_n = \dfrac{e^{-\beta E_n}}{Z}}$. Normalisation requires $1 = \sum_n P_n$, from which it follows that $\boxed{Z = \sum_n e^{-\beta E_n}}$, which is called the "partition function." These weightings define the "canonical" or "thermal" ensemble.

Note: Z enters here simply as a normalization factor in the probability distribution; however, we will see it in another connection when we turn to thermodynamics.

Comment: A trick to calculate the average energy:

$\langle E \rangle = \sum_n P_n E_n = \dfrac{1}{Z} \sum_n E_n e^{-\beta E_n}$. But, $Z = \sum_n e^{-\beta E_n}$, so $\dfrac{dZ}{d\beta} = -\sum_n E_n e^{-\beta E_n}$ and

$$\boxed{\langle E \rangle = -\frac{1}{Z}\frac{dZ}{d\beta} = -\frac{d}{d\beta}\ln Z}$$

I am going to stop here and do an example which applies the Boltzmann result (PKT, Chapter 6):

Ligand Receptor Binding (a simple model):

Ligand molecules in solution (usually but not always dilute) can bind to one or more specialized receptor sites.

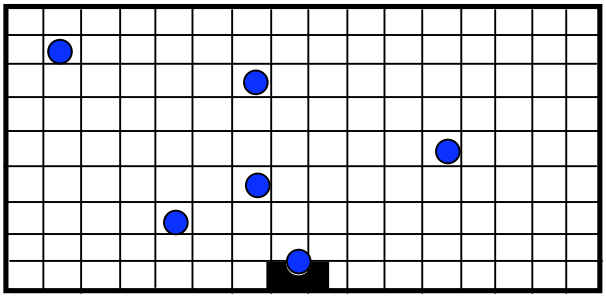
There is an attractive interaction between the ligand L and the receptor R, so that the energy of the ligand molecule is lower when bound and higher when floating in solution. On the other hand, there are more "states" available to the ligand molecule when it is in solution than when it is bound.

This is the classic energy-entropy trade-off.

$L + R \leftrightarrow LR$, where energy drives equilibrium to the right and entropy drives it to the left.

Examples:
Oxygen binding to myoglobin/hemoglobin
"Transcription factors" binding to DNA

Suppose there are N_L (identical) ligand molecules L and a single receptor R.
Following PKT, we will model the solution as a lattice of N_V cells, each of a size just large enough to contain one ligand. This will allow us to see the effect of what is called "excluded volume", i.e., the non-zero size of the ligand molecules (although, as far as I know, this effect is not usually important in biological applications.



R

To apply the Boltzmann rules, we need to enumerate all the distinct microstates n along with their Boltzmann weights $e^{-\beta E_n}$.

We assume that in the solution each ligand has an (aqueous) interaction energy ε_S ("solution"), while any single ligand molecule that binds to the receptor has a lower energy ε_B ("bound"). The (positive) energy difference $\Delta\varepsilon \equiv \varepsilon_S - \varepsilon_B$ is the energetic effect which drives the binding.
Note: This sign convention differs from PKT, who use the negative quantity $\Delta\varepsilon = \varepsilon_B - \varepsilon_S$ on p. 221.
The two classes of states are:

No bound ligands:

Energy: $E = N_L\varepsilon_S$

Number of distinct microstates of this type: $\dfrac{N_V!}{N_L!(N_V - N_L)!}$ (Binomial distribution, again!~)

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?

One bound ligand:

Energy: $E = (N_L - 1)\varepsilon_S + \varepsilon_B$

Number of distinct microstates of this type: $\dfrac{N_V!}{(N_L - 1)!(N_V - N_L + 1)!}$

how many ways are there to attach one of the (identical) ligands to the binding site and to distribute the remaining (N_L-1) ligands among the N_V cells?

It follows then that the probability of a bound microstate (any bound microstate) is:

$$P_B = \frac{1}{Z}\frac{N_V!}{(N_L - 1)!(N_V - N_L + 1)!}e^{-\beta\left[(N_L - 1)\varepsilon_S + \varepsilon_B\right]}$$

with $Z = \dfrac{N_V!}{N_L!(N_V - N_L)!}e^{-\beta[N_L\varepsilon_S]} + \dfrac{N_V!}{(N_L - 1)!(N_V - N_L + 1)!}e^{-\beta\left[(N_L - 1)\varepsilon_S + \varepsilon_B\right]}$.

Now divide through by $\dfrac{N_V!}{N_L!(N_V - N_L)!}e^{-\beta[N_L\varepsilon_S]}$,

noticing that $\dfrac{\dfrac{N_V!}{(N_L-1)!(N_V-N_L+1)!}}{\dfrac{N_V!}{N_L!(N_V-N_L)!}} = \dfrac{N_L!(N_V-N_L)!}{(N_L-1)!(N_V-N_L+1)!} = \dfrac{N_L}{N_V-N_L+1}$, giving

$$P_B = \frac{\dfrac{N_L}{N_V-N_L+1}e^{\beta\Delta\varepsilon}}{1+\dfrac{N_L}{N_V-N_L+1}e^{\beta\Delta\varepsilon}} = \frac{c_L}{(1-c_L)e^{-\beta\Delta\varepsilon}+c_L},$$ (single receptor) PKT have $e^{+\beta\Delta\varepsilon}$ here

where I have written the concentration of ligand molecules in solution (relative to the close-packing density) as $c_L \equiv \dfrac{N_L}{N_V}$ $(0 \le c_L \le 1)$ and I have neglected $\dfrac{1}{N_V}$, which is always negligible.

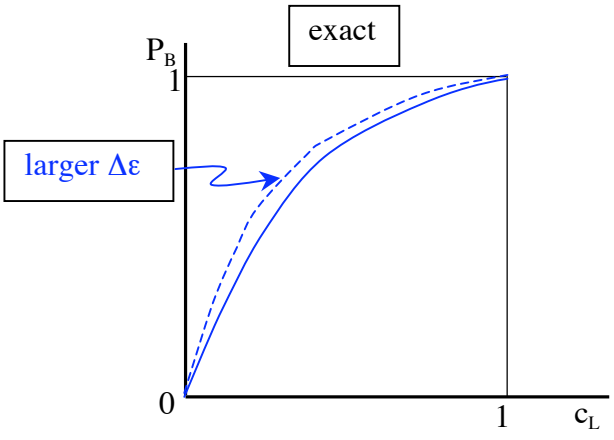
Normally c_L is small relative to one, so this is usually simplified: $P_B = \dfrac{c_L}{e^{-\beta\Delta\varepsilon}+c_L}$. (Hill Equation)

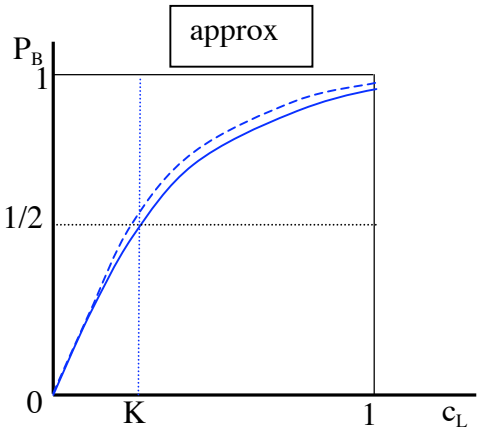
(this is the form derived in PKT; I think you learn more by keeping the full result, see below)

Comments:

1. $c_L \equiv \dfrac{N_L}{N_V}$ is dimensionless. To convert to usual (chemical) units (number/volume), multiply above and below by individual cell volume v_0: $c_L = \dfrac{v_0}{v_0}\cdot\dfrac{N_L}{N_V} = v_0\dfrac{N_L}{V} = v_0\cdot[L]$.

2. What does this look like?





Note:

(a) For the exact form P_B goes to 1 as c_L goes to 1 (last ligand forced onto biding site).

(b) Increasing $\Delta\varepsilon$ increases P_B. (lowers energy of the binding state)

(c) Increasing c_L increases P_B. (pushes equilibrium towards binding)

(d) Increasing N_V decreases c_L and, therefore, decreases P_B. (increasing the volume V increases entropy of free ligands)

(e) When $c_L = K = e^{-\beta\Delta\varepsilon}$, P_B = ½. PKT would have $e^{+\beta\Delta\varepsilon}$