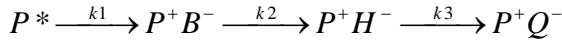Example problems integrating thermodynamics and kinetics.
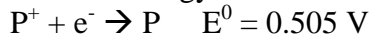
1) In one type of photosynthetic organism, the following series of reactions occur in the reaction center (an integral membrane protein complex):

$$P* \xrightarrow{k1} P^+B^- \xrightarrow{k2} P^+H^- \xrightarrow{k3} P^+Q^-$$

a) First let's consider these reactions to be irreversible (no back reactions). In this reaction, k1=1/(3.0 x 10^{-12}) seconds, k2=1/(0.9x10^{-12}) seconds and k2 = 1/(200 x 10^{-12}) seconds. After 100x10^{-12} seconds, what fraction of the initial excited state P* will have converted to P^+Q^-?
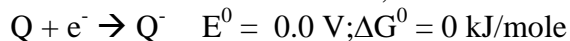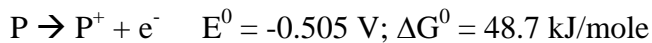
We can see that k3<<k1, k2. Therefore k3 is rate limiting. In other words, P* essentially instantly converts to P^+H^-. Therefore we can really look at this as P* → P^+Q^- with a rate constant of k3. These reactions are all first order. Therefore the integrated rate law for P* decay is P*(t) = P*(0) exp (-k3 t). For t = 100 x 10^{-12} we have P*(t) = P*(0) exp(-0.5). Thus P*(t)/P*(0) = 0.61. We can see that at 100 x 10^{-12} seconds, 39% of the initial excited state P* will have converted to P^+Q^-.

b) Consider the following half reactions and electronic transitions:

              P → P*   energy between the ground and excited state is 134 kJ/mole
              $P^+ + e^- \to P$ $E^0 = 0.505$ V
              $Q + e^- \to Q^-$ $E^0 = 0.0$ V

At equilibrium and 25 C, what fraction of the reaction centers are still in the excited state, P*?

We need to come up with an equilibrium constant for the reaction P* → P^+Q^-. So let's add up energies:

              P* → P   -134 kJ/mole
              $P \to P^+ + e^-$ $E^0 = -0.505$ V; $\Delta G^0 = 48.7$ kJ/mole
              $Q + e^- \to Q^-$ $E^0 = 0.0$ V; $\Delta G^0 = 0$ kJ/mole

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              P* → P^+Q^- $\Delta G = -85.3$ kJ/mole

So K_{eq} = exp(-ΔG^0/RT) = 8.9 x 10^{14}. Thus, only one reaction center in every 10^{15} or so is in the excited state. Interestingly, this small number of molecules can be detected by fluorescence from P* and this has been used to measure the equilibrium constant. It compares very well with the values calculated above.

2) Consider a transcription system in which gene A makes a protein that shuts down the production of gene B and gene B makes a protein that allows the production of gene A. Assume that we start with a little bit of A and B in the cell to begin with and that the protein made by A and the protein made by B are both degraded with a first order rate kd. Also assume that transcription from A only occurs when B is bound to it and then has a zero order rate constant kt. Transcription

from B only occurs when A is NOT bound to it and also has a zero order rate constant kt. The dissociation constants for both the B protein to the A gene and for the A protein to the B gene are both K_S. The question is, once the system has reached a steady state in the concentration of the A and B proteins, what will that concentration of each be?

So the rate at which A is made will depend on the fraction of the A gene that is on times the zero order rate constant that determines the rate of transcription. A zero order rate constant just means that the rate constant is independent of concentrations. In the case of a gene, if all the components are around to do the transcription, the polymerase just keeps making transcript at a constant rate. So, this is:

$$\frac{dA}{dt} = (fraction.active)k_t - [A]k_d$$

The fraction active we have calculated before. Since it is only active when B is bound, that is just

$$fraction.active = \frac{[OB]}{[O]+[OB]}$$

Here O stands for the operator (the part of the gene that B binds to). As we have seen in the past, when we substitute for [OB] by using the dissociation equilibrium equation with K_S as the dissociation constant, we get

$$fraction.active = \frac{[B]}{K_S +[B]}$$

So

$$\frac{dA}{dt} = \frac{[B]}{K_S +[B]}k_t - [A]k_d$$

Similarly

$$\frac{dB}{dt} = \frac{[O]}{[O]+[OA]}k_t - [B]k_d = \frac{K_S}{K_S +[A]}k_t - [B]k_d$$

Remember that the B gene is only working when A is NOT bound. That is why the equation lacks the term in the numerator.

Now, once the system hits steady state (A and B both), the rates of A and B change will be zero.

$$0 = \frac{[B]}{K_S + [B]}k_t - [A]k_d$$

$$\frac{[B]}{K_S + [B]}k_t = [A]k_d$$

and

$$0 = \frac{K_S}{K_S + [A]}k_t - [B]k_d$$

$$\frac{K_S}{K_S + [A]}k_t = [B]k_d$$

You now have two equations and two variables. You can solve for [A] and [B]. This just involves algebra and solving a quadratic, but it is not hard. Doing it for [A] I get (I am going to drop the brackets to make it easier to type):

$$B = \frac{K_S}{K_S + A}\frac{k_t}{k_d}$$

$$\therefore 0 = \frac{\dfrac{K_S}{K_S + A}\dfrac{k_t}{k_d}}{K_S + \dfrac{K_S}{K_S + A}\dfrac{k_t}{k_d}}k_t - Ak_d = \frac{\dfrac{1}{K_S + A}\dfrac{k_t}{k_d}}{1 + \dfrac{1}{K_S + A}\dfrac{k_t}{k_d}}k_t - Ak_d$$

$$0 = \frac{1}{K_S + A}\frac{k_t^2}{k_d} - Ak_d\left(1 + \frac{1}{K_S + A}\frac{k_t}{k_d}\right) = \frac{1}{K_S + A}\frac{k_t^2}{k_d} - Ak_d - \frac{A}{K_S + A}k_t$$

$$0 = \frac{k_t^2}{k_d} - Ak_d(K_S + A) - Ak_t$$

$$0 = -\frac{k_t^2}{k_d} + Ak_d(K_S + A) + Ak_t$$

$$0 = k_d A^2 + (k_d K_S + k_t)A - \frac{k_t^2}{k_d}$$

$$A = \frac{-(k_d K_S + k_t) \pm \sqrt{(k_d K_S + k_t)^2 + 4k_d \dfrac{k_t^2}{k_d}}}{2k_d}$$

$$A = \frac{-(k_d K_S + k_t) \pm \sqrt{(k_d K_S)^2 + 2k_d K_S k_t + k_t^2 + 4k_t^2}}{2k_d}$$

$$A = \frac{-(k_d K_S + k_t) \pm \sqrt{(k_d K_S)^2 + 2k_d K_S k_t + 5k_t^2}}{2k_d}$$

Now I just divide by k_d (which under the square root means dividing by k_d^2) and I get:

$$[A] = 0.5\left\{-K_S - \frac{k_t}{k_d} + \sqrt{K_S^2 + 2K_S \frac{k_t}{k_d} + 5\left(\frac{k_t}{k_d}\right)^2}\right\}$$

The point is that you can do this for large numbers of systems that control each other (control networks) and simply end up with a bunch of equations to solve in parallel and then get the computer to solve them (either analytically or numerically) for you. This is a very important concept in biology these days and is at the heart of systems biology and biological networks. You should be able to take a simple system like this and write down the equations for the rates and the set of equations that would have to be solved to give the concentrations when the system hits steady state (which is what living things exist in when they are stable).