Physics 347   **Assignment #3**   **Due Oct 23 (in class)**

Reading:
You should have read Ch. 6, sections 6.1.1, 1.2, 1.3, 6.4. Please begin reading all of
Chapter 8.

Problem 1: Force of an optical trap:

A transparent bead in solution trapped by the focus of a laser (as is the set up for an

optical trap) has an energy as a function of its position, *x*, given by $U(x)=\frac{1}{2}kx^2$.

Here *k* is the spring constant, or what the experimentalists call the trap stiffness of the
optical trap. A particle that is in a solution at temperature, *T*, will undergo motion while
in the trap that can be observed and recorded experimentally.

a) Use the Boltzmann distribution for the probability of observing the particle at a given
position, *P(x)*, and calculate the average squared displacement of the particle in the trap,
$\langle x^2 \rangle$. Note that *x* is a continuous variable, not discrete.

b) Based on your findings in (a), if you built an optical trap how would you go about
determining the trap stiffness, *k*?

Problem 2: Entropy Change upon Equilibration:

The zeroth law states that two systems brought into thermal contact will have their
temperatures become the same. Consider two boxes of ideal gas each containing N
molecules in a volume, V. Box 1 starts at temperature $T_{i,1}$ and box 2 starts at a
temperature $T_{i,2}$. Thus their initial energies are $E_{i,1} = 3/2\ N\ k_b\ T_{i,1}$ and $E_{i,2} = 3/2\ N\ k_b\ T_{i,2}$
respectively.

Now the two boxes are brought into thermal contact, and allowed to reach equilibrium
where their temperatures will be the same. Answer the following questions:

a) What is the final temperature in terms of the initial temperatures? (Use energy
conservation, and that the final energy is shared equally between both boxes).

b) Show that the change in entropy of the system is (you'll need to use the formula for the
entropy of an ideal gas derived in class)

$$\Delta S_{tot}=k_B\frac{3}{2}N\ln\frac{(T_{i,1}+T_{i,2})^2}{4T_{i,1}T_{i,2}}$$

c) Show that this change in entropy is always $\Delta S_{tot}\geq0$. (Hint: let X = $T_{i,1}/T_{i,2}$ and

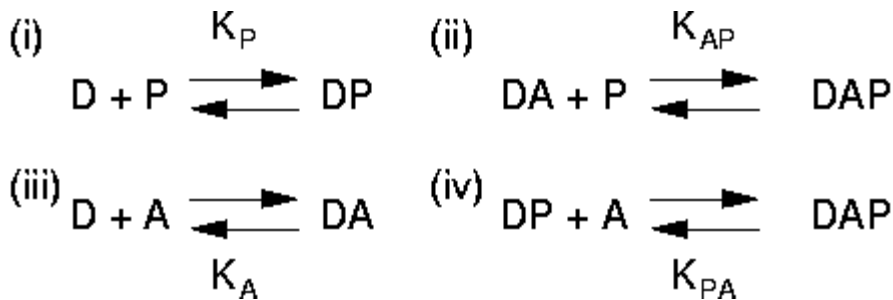express the change in entropy in terms of X. Is this function ever < 0?

d) Under what initial conditions will the change in entropy be zero?

Problem 3: RNA Folding

Consider the RNA sequence GCAAUGC. Use the simple RNA folding model presented in class to answer the following questions. Only draw those structures which can form stacks (or no stacks). Do not consider any structures that just have a single base-pairings. In the model, each stack contributes an energy $-E_s$ (with $E_s > 0$).

(a) Draw the four possible structures that this sequence can adopt in our simple model?

(b) What is the minimum energy structure? What is the minimum energy?

(c) Using the above structures, evaluate the partition function via
$$Z = \sum_i \exp(-E_i/kT)$$ where E_i is the energy of each structure.

(d) If $E_s = 4kT$, what is the probability of the minimum energy structure?

(e) The above calculation did not include the entropy of the unstacked free bases of the RNA. If every unpaired base contributes α states, what are the entropies of each of the above 6 structures.

(f) Go and join the crowd to solve RNA structure problems. Play eteRNA at http://eterna.cmu.edu Finish the Tutorial and become a puzzle master by solving 10 puzzles. One of these puzzles must be Difficulty Level 2. Submit a screen shot of your puzzle master status and the completion of the Level 2 problem.

Problem 4: RNA Polymerase Binding with TF

(i)
$$D + P \underset{}{\overset{K_P}{\rightleftharpoons}} DP$$

(ii)
$$DA + P \underset{}{\overset{K_{AP}}{\rightleftharpoons}} DAP$$

(iii)
$$D + A \underset{K_A}{\overset{}{\rightleftharpoons}} DA$$

(iv)
$$DP + A \underset{K_{PA}}{\overset{}{\rightleftharpoons}} DAP$$

The RNA Polymerase (RNAP) can be aided in binding to its binding site via the action of transcription factors which bind to other binding sites near the promoter. The promoter can thus exist in a variety of bound and unbound states for all the various binding configurations of RNAP and transcription factors. The probability of the promoter being bound by RNAP is simply the ratio of the concentrations of RNAP bound states to the total concentration of all promoter states.

(a) Consider case (i), where RNAP at concentration $[P]$ simply binds and unbinds to its binding site on a given promoter sequence. The amount of free unbound sequence is $[D]$ and the amount of RNAP bound promoter is $[DP]$. At equilibrium, the ratio $[D][P]/[DP]=K_P$ with K_P being the dissociation constant for this reaction in units of concentration. The probability of RNAP bound promoter is given by $p_{bound}=[DP]/D_{tot}$, where $D_{tot}=[D]+[DP]$. Show that $p_{bound}=P/(K_P+P)$ (I've dropped the concentration notation of "[ ]").

(b) Consider now the case where in addition to the binding site for RNAP, there is also a binding site for a transcription factor at concentration $[A]$. Now the three other reactions are also occurring. The dissociation constants are given by: $[DA][P]/[DAP]=K_{AP}$, $[D][A]/[DA]=K_A$, and $[DP][A]/[DAP]=K_{PA}$. The probability of RNAP binding is given by $p_{bound}=([DP]+[DAP])/([D]+[DA]+[DP]+[DAP])$.
Show that this is

$$p_{bound}=\frac{P/K_P+(K_P/K_{AP})A/K_A P/K_P}{1+P/K_P+A/K_A+(K_P/K_{AP})A/K_A P/K_P}$$

(c) The ratio of dissociation constants $f=(K_P/K_{AP})$ gives the effect of enhancement on the probability of RNAP binding due to the presence of the transcription factor. For $f>1$ the transcription factor enhances transcription. For the case $f=1$ show that the result in (b) reduces down to what you found in (a). This makes sense since the binding of "A" has no effect on the binding of RNAP in this case.

(d) The rate of production of mRNA is given by $r=v\,p_{bound}$ where v is the maximal rate of expression. In most treatments of biological networks, we never explicitly keep track of the RNAP concentration as it is assumed to be constant. If P is constant, using the results from (b), show that the mRNA production rate can be written solely in terms of the concentration of the transcription factor as $r=\dfrac{v_0+v_A A/K_A^{eff}}{1+A/K_A^{eff}}$ where v_0 is the rate when A=0, v_A is the rate when $A\to\infty$ and K_A^{eff} is an effective dissociation constant for the transcription factor. Give v_0, v_A and K_A^{eff} in terms of the

constants P, K_P, K_A, f, v .

(e) Sketch r as a function of A for the two cases $f > 1$ and $f < 1$. So what is the effect of the transcription factor for these two different cases?