Homework Assignment 4
Due at 5 p.m. on Wednesday 2/5/14. Show calculations as well as answers.

1) For a polypeptide composed of N monomers that undergo C to H transitions non-cooperatively, the structural state of each monomer can be treated as a two level system. The energy of the C structure will be $\varepsilon_C = 0$ and the energy of the H structure will be $\varepsilon_H = \varepsilon$. Then the partition function for a single monomer is $Q = 1 + e^{-\varepsilon/k_BT} = 1 + s$. The partition function for a polypeptide composed of N monomers is

$$Q_N = \left(1 + e^{-\varepsilon/k_BT}\right)^N = (1 + s)^N \text{ where } s = e^{-\varepsilon/k_BT}.$$

a) Calculate the Internal Energy divided by T i.e. $\frac{U}{T}$ for this peptide if N=100 and s=1.5.

Note the internal energy U is negative. That is because we set the energy of the coil as zero...but because $s=1.5=[H]/[C]$, the helix is more stable. So its energy is lower than the energy of C... and that makes it negative.

b) Using your result from part a, calculate the entropy S for this peptide if N=100 and s=1.5.

c) Suppose s changes (i.e. the temperature changes) from 1.5 to 5. Calculate the change in helical fraction $\Delta f_H$, and the change in entropy $\Delta S$. Explain these changes.

2) As shown in the text (see section 23.11, equations 23.121 and 23.122) and in the lecture notes, the Zipper model has a simple equation for the partition function that can be used to determine helicity $f_H$: $q = q_0 \left(1 + \sigma \sum_{k=1}^{N} (N-k+1)s^k\right)$ where the term $N-k+1$ is the number of way you can arrange $k$ contiguous H monomers in a peptide chain N monomers long.

a) From the partition function equation given above for the zipper model, it is easily shown that the probability of observing a helical sequence of length k in a peptide N monomers long is:

$$p_k = \frac{q_0\sigma}{q} (N-k+1)s^k$$
For $N=30$, $s=1.0$, and $\sigma=0.0001$, determine the relative probability of observing a helical sequence of length $k=10$ versus $k=25$. Repeat the calculation for $s=5.0$.

b) For $N=30$ and $s=1.5$, and $\sigma=0.001$, what is the most probable helical length $k$. What is the most probable helical length $k$ if $s$ changes to 5?

c) In the text (see equations 23.121-23.123) it was stated that starting with the expression $q = q_0 \left( 1 + \sigma \sum_{k=1}^{N} (N-k+1)s^k \right)$, it can be shown that the partition function for the zipper model can be written as:

$$q = q_0 \left( 1 + \frac{\sigma s^2 (s^N + Ns^{-1} - (N + 1))}{(s-1)^2} \right)$$

Using this form for $q$ obtain an expression for the helical fraction $f_H = \frac{1}{N} \frac{s}{q} \frac{\partial q}{\partial s}$. Recall the rule for differentiating the quotient of two functions:

$$\frac{d}{dx} \left( \frac{f(x)}{g(x)} \right) = -\frac{1}{g^2(x)} \left( f(x) \frac{dg(x)}{dx} - g(x) \frac{df(x)}{dx} \right)$$

d) Using your expression for $f_H$ obtained in part c, determine $f_H$ for $N=30$, $s=1.5$, $\sigma=0.001$.

Note: You may get some pretty serious looking expressions if you just plow ahead with differentiating $q$ and then take the ratio of $dq/ds$ and $q$ to get $f_H$. That will be a lot of really hard and UNNECESSARY work. Because note...for $s=1.5$ and $N=30$, $q$ and $dq/ds$ simplify because terms like $s^{N+2}$ and $s^{N+1}$ are a lot bigger than everything else in the expressions for $q$ and $dq/ds$. So before you start substituting in numbers...SIMPLIFY $q$ and $dq/ds$ ...and then take their ration and simplify the expression for $f_H$.

3) In the lecture notes we did not obtain a general expression for the partition function for the Bragg-Zimm model. We constructed $q$ for this model by the laborious process of determining all the conformations and their corresponding statistical weights. In fact the Bragg-Zimm model has an expression for the partition function, but it involves matrix algebra. The Bragg-Zimm partition function equation uses a 2x2 matrix $\hat{M}$ called the statistical weight matrix to generate $q$. $\hat{M}$ has the following four elements:

i) the upper left hand element of the matrix (i.e. the CC matrix element) is the statistical weight assigned in the partition function to a C monomer that follows another C monomer. This weight is 1.
ii) Similarly in the lower left hand corner (i.e. the HC element) is the statistical weight assigned in the partition function to a C that follows a H. This is again a statistical weight of 1.

iii) In the upper right hand corner (i.e. the CH element) of the matrix is the statistical weight assigned in the partition function to a H that follows a C. This weight is $\sigma$.

iv) In the lower right hand corner (i.e. the HH element) is the statistical assigned to a H that follows another H. This weight is $s$.

With these rules the statistical weight matrix $\tilde{M}$ has the form:

$$\tilde{M} = \begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix}.$$ 

To obtain the partition function for a peptide $N$ monomers long we use the expression:

$$\frac{q}{q_0} = (1, 0) \tilde{M}^N (1, 1)$$

where $(1, 0)$ is a row vector with elements 1 and 0 and $(1, 1)$ is a column vector.

For example: Obtain the partition function for a Bragg-Zimm dimer ($N=2$):

Solution:

$$\frac{q}{q_0} = (1, 0) \tilde{M}^2 (1, 1) = (1, 0) \begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix} \begin{pmatrix} 1 & \sigma s \\ 1 & s \end{pmatrix} (1, 1)$$

$$= (1, \sigma s) (1, \sigma s) (1, 1) = (1 + \sigma s, \sigma s + \sigma s^2) (1, 1) = 1 + \sigma s + \sigma s + \sigma s^2 = 1 + 2\sigma s + \sigma s^2$$

Therefore the partition function is:

$$q = q_0 (1 + 2\sigma s + \sigma s^2)$$

a) Using statistical matrix approach as illustrated above for a Bragg-Zimm dimer, obtain the partition function for a Bragg-Zimm tetramer ($N=4$).

b) Using your expression for a Bragg-Zimm tetramer from part a, calculate the fractional helicity $f_H$ for $s=1.0$ and $\sigma=0.0001$.

c) As mentioned in lecture, for very large values of $N$, there is a simple form for the Bragg-Zimm partition function: $q \approx \frac{\lambda_1^{N+1} (1 - \lambda_2)}{\lambda_1 - \lambda_2}$, where

$$\lambda_{1,2} = \frac{1 + s \pm \sqrt{(1-s)^2 + 4\alpha s}}{2}.$$ Assumming $N=10000$, $s=1$, $\sigma=0.0001$, justify the approximation $\ln q \approx N \ln \lambda_1$.

d) Calculate the average number of helical monomers $\langle n \rangle$ and the fractional helicity $f_H$ assuming, $N=10000$, $s=1.0$, $\sigma=0.0001$.

4) For a protein with four ligand binding sites the general expression for the binding polynomial $Q$ is:

$$Q = [P](1 + 4k_1[L] + 6k_1k_2[L]^2 + 4k_1k_2k_3[L]^3 + k_1k_2k_3k_4[L]^4)$$

where the
microscopic equilibrium constants $k_1, k_2, k_3,$ and $k_4$ correspond to equilibria between the
ligand $L$ and the four partially filled or completely filled polymers.

a) In lecture we showed that if $k_1=k_2=k_3=k_4=k$ we obtain the expression for non-
cooperative binding $Q = \left[P\right](1 + k[L])^4$. Calculate the average number of sites bound
\(\langle \nu \rangle\) for $k=100$ and $[L]=0.01\text{M}$. Repeat for $k=100$, $[L]=0.001\text{M}$ and $[L]=0.0001\text{M}$

b) A model used to simulate cooperative binding in hemoglobin is to assume
$$
k_1 = \alpha^3 k; \quad k_2 = \alpha^2 k; \quad k_3 = \alpha k; \quad k_4 = k$$
The parameter $\alpha<1$ and so as more sites are filled with oxygen, the binding
affinity for the remaining sites increases. Using these forms for the microscopic
equilibrium constants, obtain an expression for $Q$ and the average number of sites
bound $\langle \nu \rangle$.

c) Using your results from part b and assuming $k=100$ and $\alpha=0.1$, calculate $\langle \nu \rangle$
for $[L]=0.01\text{M}$, $0.001\text{M}$, and $0.0001\text{M}$. Compare to the results for part a.

5) The cooperative binding of oxygen to tetrameric hemoglobin (Hb) is sometimes
represented by the empirical equation
$$f_B = \frac{KP_{O_2}^{\alpha_H}}{1+KP_{O_2}^{\alpha_H}}$$
where $P_{O_2}$ is the pressure of oxygen over a solution of Hb, $K$ is an equilibrium constant
associated with oxygen binding to Hb, and $\alpha_H$ is the Hill constant. For Hb $\alpha_H \approx 2.9$.

a) $P_{50}$ is defined as the pressure of oxygen at which the binding sites on Hb are half
filled i.e. $f_B = 0.5$. For Hb $P_{50}=0.0343\text{ atm}=26\text{ Torr}$. Calculate the equilibrium
constant $K$.

b) The partial pressure of oxygen in the lungs is 0.13 atm. Calculate the fraction of
sites bound $f_B$ for Hb in the lungs using the equation above.

c) Perform the same calculation as in part b only assume oxygen binds to Hb non-
cooperatively. Explain why we may have evolved a cooperative binding mode for
Hb.

6) Evaluate the translational partition function for Ar confined to a volume $1000\text{cm}^3$ at
$T=298\text{K}$. At what temperature will the translational partition function of Ne be the same
as Ar in the same volume?