APh161: Physical Biology of the Cell
Homework 5
Due Date: Tuesday, February 14, 2006

"The heights by great men reached and kept were not attained by sudden flight, but they while their companions slept were toiling upward in the night." -Henry Wadsworth Longfellow

1. The Question of Depletion Forces.

In class I described a fascinating feature of soft condensed matter systems in general and biological structures in particular, namely, that many of the forces that drive structure formation in these systems are of an entropic character. One of the key examples of this idea is that of depletion forces in which two large objects are forced together by virtue of permitting the system more space for the remaining particles to wander around in. In this problem, we will consider a simple model of these forces. In particular, consider a two dimensional system of total area A in which two square particles of edge length b are in a gas of discs of radius a. Begin with the two large square particles pushed up against each other and then examine the free energy as a function of their separation. In particular, compute the partition function for an ideal gas of these discs and note how as the two square particles are separated this deprives the discs of available volume to wander around in. Compute the entropic attraction between our two square particles by differentiating the free energy with respect to the spacing x between the square particles. This entropic force is a so-called depletion force. What is the range of the interaction between the two square particles? Set up the equations to do this same calculation for 2 large spherical particles in three-dimensions.

2. Hydrophobic Effect: A Feeling for the Numbers

We continue with the theme of some of the interesting forces that arise in the crowded environs of the cellular interior. We have already examined depletion forces. A second hugely important class of forces are those associated with hydrophobicity. In class I gave a quick impression of the hydrophobic effect as an idea that is invoked often with great explanatory power. In this problem, you will estimate the magnitude of the interfacial energy that is assigned to having certain chemical groups in contact with water. This will

give us an idea of how much free energy is gained when different molecules come into contact and sequester these hydrophobic structural elements. The essential argument is that the water molecules that surround the hydrophobic region of a molecule are deprived of some of their entropy because they can adopt fewer hydrogen bonding configurations. In particular, the water molecules are thought to form cages known as clathrate structures such as are shown in the accompanying figure.

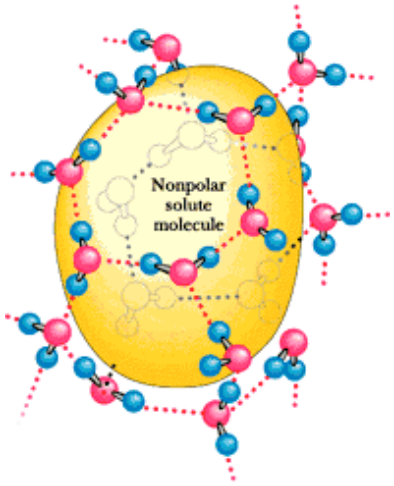

Figure 1: Schematic of the clathrate structure adopted by water molecules surrounding a hydrophobic molecule.

(a) Estimate the entropy lost for each water molecule by appealing to the schematic of the tetrahedron shown in the figure. The basic idea is that if we think of the O of the water molecule as being situated at the center of the tetrahedron then the two H atoms can be associated with any two adjacent vertices (or, there are a total of six configurations). However, when in the presence of the hydrophobic molecule, one of the faces of the tetrahedron can be thought of as facing that hydrophobic molecule and hence all configurations (three of the edges) facing that molecule are unavailable for hydrogen bonding. How many configurations are available now? Compute the entropy change of a single water molecule as a result of this configurational inhibition.

(b) Next, we need to estimate how many water molecules neighbor a given

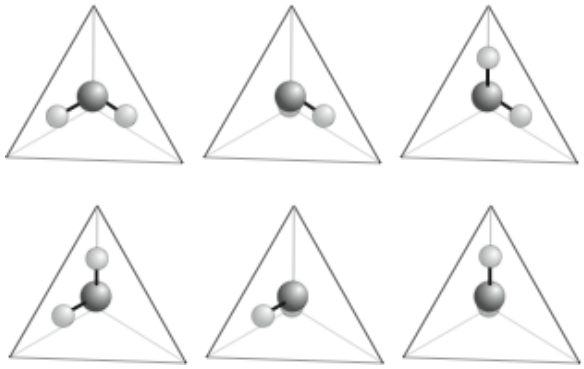

Figure 2: Schematic of the arrangements available to a water molecule when in a complete network of other water molecules.

hydrophobic molecule. Consider the case of methane and ethane and estimate the radius of sphere that represents the hydrophobic surface area they present. Next, estimate how many water molecules neighbor these molecules and hence the total free energy difference because of the lost entropy. Convert your result into an interfacial energy and use units both of J/m^2 and cal/mol $\mathring{A}^2$. Compare the result to the rule of thumb I quoted in class which is 25 cal/mol $\mathring{A}^2$.

(c) Since we have said that hydrocarbons are hydrophobic, go back and examine the 20 amino acids and decide which residues are hydrophobic. Further, estimate the free energy cost for each such residue when it is not properly sequestered from water. Report your energies in units of kT.

3. Diffusion to Capture: The Hard Way

In class I gave an intuitive derivation of the problem of diffusion to capture without ever solving the diffusion equation. In this problem, I want you to work out the features of diffusion to capture with a perfect absorber using the full machinery of the diffusion equation.

(a) Recall that we wish to solve for the steady-state condition in which we prescribe a far-field concentration c_0 and assume that the absorber (a sphere of radius a) is a perfect absorber ($c(a) = 0$). Write the diffusion equation in

spherical coordinates at steady-state (i.e. $\partial c/\partial t = 0$).

(b) Show that the resulting concentration profile is of the form

$$c(r) = A + \frac{B}{r}, \tag{1}$$

and use the conditions $c(a) = 0$ and $c(\infty) = c_0$ to determine the constants A and B.

(c) Compute the flux at the surface of the sphere and then use this to evaluate dn/dt and confirm the expression for the diffusive speed limit that I discussed in class.

(d) Recall Prof. Bob Austin's (Princeton Physics) quip that "physics isn't worth a damn unless you put in some numbers". Let's put in some numbers and actually evaluate the diffusive speed limit for several cases of interest. In particular, let's work out the rate for actin monomers to be incorporated onto a growing actin filament and for oxygen arriving at hemoglobin. That is, make an estimate of the size and diffusion constant for G-actin and O_2 and compare the rates that you find with the k_{on} for the actin polymerization reaction and for the uptake of oxygen by hemoglobin. Of course, you will have to make some assumptions about c_0 - try the critical concentration for actin and for oxygen, maybe you can find some reasonable numbers on the web. The discussion on pgs. 308 and 309 of Howard give an interesting discussion of the diffusion-limited speed limit. Note that we are making a simplifying assumption by treating the growing filament and the hemoglobin as stationary.