APh161: Physical Biology of the Cell
Homework 5
Due Date: Tuesday, February 22, 2005

"Problems worthy of attack prove their worth by hitting back." - Piet Hein

Reading: Chaps. 9 and 11 of Howard.

1. How Big is a Genome: Your Turn

In class I showed two classic pictures of a ruptured bacteriophage and a ruptured bacterium with their DNA extended around them in the microscope image. In this problem I want you to carry out a clean estimate of the radius of gyration of this DNA like we did in class, but more carefully. These figs. are reproduced on the course website.

(a) As a first step, you need to derive the relation between the end-to-end distance (which I already did in class) and the radius of gyration R_G. First, reproduce the derivation of the end-to-end distance itself. Next, using the definition of the radius of gyration as

$$\langle R_G^2 \rangle = \frac{1}{N} \sum_{i=1}^{N} \langle (\mathbf{R}_i - \mathbf{R}_{CM})^2 \rangle, \tag{1}$$

demonstrate the claim I made in class that

$$\langle R_G^2 \rangle = \frac{\langle R^2 \rangle}{6}. \tag{2}$$

Recall that

$$\mathbf{R}_{CM} = \frac{1}{N} \sum_{i=1}^{N} \mathbf{R}_i. \tag{3}$$

(b) The objective of this part of the problem is for you to first, derive a relation between the radius of gyration of DNA in solution and the number of base pairs. Remember that the number of steps in the random walk is *not*

equal to the number of base pairs. Rather, it is the number of Kuhn lengths where the Kuhn length is equal to twice the persistence length and hence ≈ 100 nm. Next, make a plot of the radius of gyration of DNA in solution as a function of the number of base pairs. Use that plot to comment on the size that human DNA would have in solution and don't forget that our DNA is divided up into chromosomes.

(c) Use all of the machinery you developed above in order to make explicit estimates of the size of the DNA exploding out of the bacteriophage and the bacterium which you can get on the course website. Make sure that you remember that the bacteriophage in that picture is bacteriophage T2 with a genome length of around 150,000bp.

(d) Write down a probability distribution $p(n_R; N)$ for the number of right pointing segments n_R for a polymer chain with a total number of segments N. In addition, use the expression

$$S = k_B \ln \Omega(n_R, N), \tag{4}$$

to compute the entropy of different configurations of the chain. Using this expression and the assumption that the entirety of the free energy of packing a polymer is associated with changing its entropy, estimate (in $k_B T$ units) the free energy of compaction to take the DNA with the size it has in solution and put it in a phage capsid.

2. 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? Comment on how you would do this same calculation for two large spherical particles in three-dimensions in a "gas" of smaller spherical particles of radius a.

3. 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.

(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.

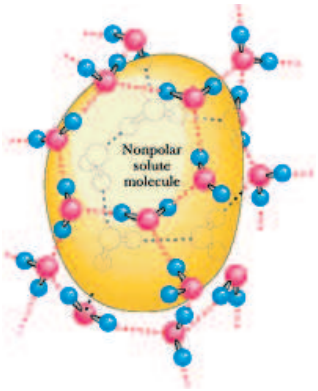

Figure 1: Schematic of the clathrate structure adopted by water molecules surrounding a hydrophobic molecule.

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

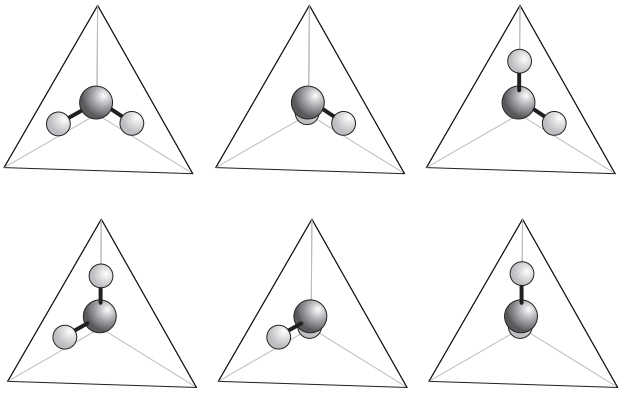

Figure 2: Schematic of the arrangements available to a water molecule when in a complete network of other water molecules.