BE/APh161: Physical Biology of the Cell
Homework 7
Due Date: Wednesday, Feb. 22, 2017

"There is plenty of room at the top. It's the middle thats crowded. Be great!" -The guy at Idyllwild

1. Gravity in Cell Biology.

(a) In a very interesting recent paper, the laboratory of Cliff Brangwynne at Princeton University asked the question of whether or not objects within cells experience the force of gravity in any meaningful way. Please read the entirety of their paper and summarize those parts of the paper having to do with the gravitational sedimentation of the droplets within the nucleus. Give a one-paragraph description of their experiment and specifically comment on the experiments on sedimentation velocity and the sedimentation length.

(b) Work out the equation of motion for a droplet and use it to rationalize the variable plotted on the x-axis in Figure 4(k).

(c) Use a simple argument balancing gravitational potential energy (make sure to include the buoyant force) and thermal forces to work out the sedimentation length scale. Use your argument to explain their equation at the bottom of pg. 1256. (NOTE: Never, ever write science with equations without numbering each and every equation!) Use your results to explain how to think about Figure 5(d). Give an argument about when we should expect for gravity to matter and when it should not and why.

2. Multiplicities and entropy.

Do problem 5.5 of PBoC2. My reason for assigning this problem is that I want you to develop intuition for the way that entropy is computed in preparation for the following problem on hydrophobicity.

3. Hydrophobicity and statistical mechanics.

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.

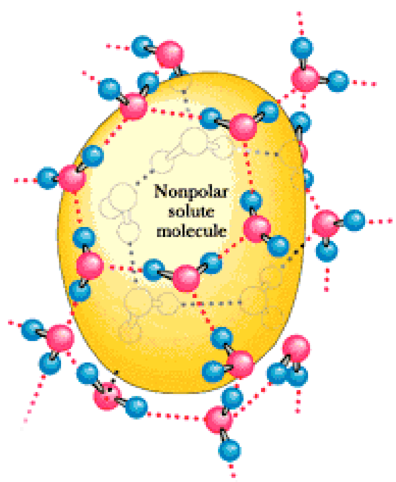

Figure 1: Schematic of the clathrate structure adopted by water molecules surrounding a hydrophobic molecule.

(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 of the water molecule (three of the edges) oriented towards that face 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.

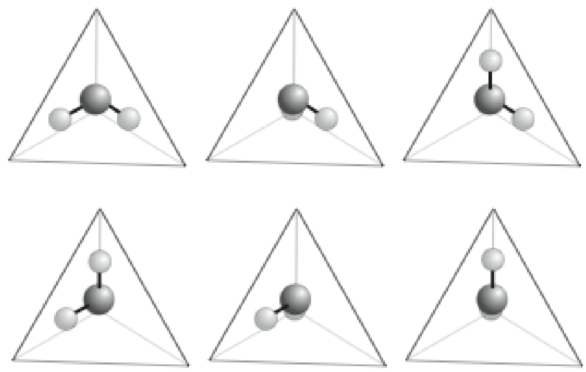

Figure 2: Schematic of the arrangements available to a water molecule when in a complete network of other water molecules.

(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 simple rule of thumb 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 several of these residues (you choose which ones) when they are not properly sequestered from water. Report your energies in units of k_BT. Similarly, make an estimate for the hydrophobic free energy γ that we used in class when discussing the critical micelle concentration.

NOTE: this problem provides a highly idealized toy model of hydrophobicity. The hydrophobic effect is much more subtle than I have made it sound.