APh161: Physical Biology of the Cell
Homework 1
Due Date: Tuesday, January 16, 2007

"Chance only favours the mind which is prepared." " – Louis Pasteur

Reading:

Read chap. 1 of Physical Biology of the Cell (PBOC) and write a referee report. Your referee report should be submitted by email to me and both TAs. The referee report should be divided into two sections: i) general comments - this should provide an overview of your impressions on the chapter, ii) specific comments - call attention to particular issues that need to be fixed.

This first homework has as its main objective the development of a feel for the numbers associated with various biological problems and the beginning of an ability to use important software for visualizing biological structures and examining biological sequence information. This particular homework will probably involve more searching around on the web than others. Please make sure to report your sources.

1. A Feeling for the Numbers: The Parts List of a White Blood Cell

In the figures attached to this homework, there is an electron micrograph of a white blood cell. Your goal in this problem is to imitate the molecular census I did in class for *E. coli*, but this time for this mammalian cell. In particular, use the picture to estimate the size of the nucleus (including its volume). Estimate the number of nucleosomes that wrap up the human genome in these cells. Estimate the number of proteins in the cytoplasm of one of these cells. Also, estimate the area of the plasma membrane and then the number of lipid molecules making up this membrane (Note: assume that half the mass of the plasma membrane is lipids, the other half is proteins).

2. A Feeling for the Numbers: Microbes as the Unseen Majority

One of the key arguments that I will make throughout the course is that

sometimes just having a feel for magnitudes is a useful guide to intuition. Indeed, our model building will usually follow the sequence: simple estimates and feeling for the numbers, simple toy models, more realistic models. For this problem, read the article entitled "Prokaryotes: The Unseen Majority" as the basis for your estimates.

(a) I argued that we will think of *E. coli* as our biological standard ruler. This cell has hall of fame status in biology and it is important that you have a sense of what these cells are like. Justify the assumption that a typical (i.e. *E. coli*) bacterial cell has a volume of 1 μm^3. Also, express this volume in femtoLiters. The claim is made (see the paper on prokaryotes as the unseen majority on the course website) that in the top 200 m of the world's oceans, there are roughly 10^{28} prokaryotes. Work out the total volume taken up by these cells in m^3 and km^3.

(b) In his famed book *The Story of Mankind*, Hendrik Willem van Loon makes an amazing estimate of the size of a box that all of the humans from all of history would have fit into. I read this when I was about 15 years old and found it really odd, but cool! Your task is to work out the size of a box that would hold (close packing) all of the current human inhabitants of the Earth. Compare this number to the volume of the box that will hold all of the bacteria in the top 200 m of the oceans.

(c) Also, recall that roughly 2-3 kg of bacteria are to be found in the waste factory of your large intestine. Make an estimate of the total number of bacteria inhabiting your intestine and then all of the intestines of all of the humans currently on the Earth.

(d) On the course website, there is a fascinating paper by Zimmerman and Trach in which they attempt to measure the crowding in the cellular interior. In table 3 they tell us their estimated macromolecular concentrations in the cellular interior. Use these numbers to make an estimate of the mean protein spacing. Also, estimate the number of lipid molecules in the cell membrane of *E. coli* by computing the approximate area of the cell membrane and dividing by the area taken up by each lipid (note: be careful because there are two lipid bilayer membranes in these cells), the total number of protein molecules and the number of water molecules. What is the number of base pairs of the

E. coli genome and what is the circumference of its circular chromosome? Comment on the relative size of the DNA molecule and the bacterium.

(e) If a particular protein in an *E. coli* cell is found there at nM concentrations, how many molecules are there per cell? Are you happy with the notion of a "concentration" in this case? Explain your reasoning. Make a plot of the number of copies of a molecule in an *E. coli* cell as a function of the concentration - make the plot for concentrations from nM to mM.

(f) Bacteriophage are the viruses that infect bacteria. Given that the concentration of phage is tenfold or more higher than that of bacteria, report the concentration of phage in the ocean in mg/mL. Then, use this to make an estimate of the total number of phage on the Earth. This number will come in handy in our initial estimates about evolution.

3. Manipulating Atomic Coordinates

Visualization of the various structures populating the cell is a key part of fulfilling the objective of structural biology to connect structure and function. In this problem, you will learn how to manipulate pdb files from the Protein Databank and to view them using one of the various plotting programs.

(a) Obtain coordinates for ATP, phosphatidylcholine, B-DNA, G-actin, the lambda repressor/DNA complex or lac repressor/DNA complex, hemoglobin, HIV gp120 complexed to an antibody, green fluorescent protein (GFP) and RNA polymerase. We will provide most of these coordinates for you with this homework - a few will be left for you so that you can at least see how this is done. You can do this by visiting sites such as "http://chemistry.gsu.edu/glactone/PDB/pdb.html" and the Protein Databank itself. You may have to search around a bit. Give a brief description of each one of these molecules and its role in cellular life.

(b) Download a structural viewing code such as VMD (University of Illinois), Rasmol (University of Massachusetts) or DeepView (http://www.expasy.ch/spdbv/) and create a plot of each of the molecules you downloaded above. You can download one of these programs under the "General Interest" part of the APh161 webpage. Experiment with the orientation of the molecule and make sure you print out pictures of each and every molecule.

(c) Later we will see that phosphatidylcholine is one of the molecules that can self assemble to form a lipid bilayer (see chap. 11 of Alberts et al.). Part of our analysis of such structures will be to consider their geometry. As a first step down that path, estimate the cross sectional area of the polar head of phosphatidylcholine. Make sure you get the coordinates for this molecule and plot it as well. Note that you will find this result useful for the estimate of the number of lipids in an *E. coli* cell in problem 1.

(d) ATP is the energy currency for many processes in biochemistry. The action of ATP is mediated by ATP binding onto other molecules which then exploit the energy associated with hydrolysis of ATP. Use your coordinates for ATP to estimate the size of the regions in which ATP might bind when it encounters other molecules.