APh161: Physical Biology of the Cell
Homework 1
Due Date: Thursday, January 14, 2010

"The quality of a person's life is in direct proportion to their commitment to excellence, regardless of their chosen field of endeavor." - Vince Lombardi

Comments from RP to Class:

In my view, homeworks are one of the primary tools at a teacher's disposal to push an educational agenda. I am big on sports analogies, and the simple fact is this: if you want to shoot free throws like Kobe Bryant you have to practice your craft. It isn't always amusing, but it pays off later. As a result, I put lots of time into both thinking up problems and writing text that goes along with those homeworks that I think will give you the opportunity to practice things that will help you do science better later when it is "for real". The reading that goes along with my homeworks is a key part of the course material, so please read my commentaries (and argue with them if you have an alternative perspective).

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 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.

Referee report: Read the vignettes from the new book that I am writing with Ron Milo titled "Cell Biology By the Numbers" that are posted on the course website associated with this homework and write a referee report on each one. The report should focus on the following questions: Does the overall logic make sense? That is, is the point of the vignette clear and does the organization work in making this point? What suggestions do you have to make it more readable, clear and interesting? Did it teach you anything new? What would you suggest should be removed? Try to find extra biological numbers pertinent to the vignette. Bonus: join the community effort and contribute these numbers at www.BioNumbers.org

Please E-mail the report, as a Word or PDF file, to me (phillips@pboc.caltech.edu), Stephanie Johnson (stephj@caltech.edu) and my coauthor Ron (ron.milo@weizmann.ac.il) on the day the homework is due.

1. Manipulating Atomic Coordinates

This is basically prob. 2.4 of PBoC.

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 addition, having a sense of the sizes of the various molecular actors in the cell will permit us to make the kinds of estimates that will run through the course. For example, later, we will consider gene regulation and will be interested in how large a DNA sequence serves as the regulatory site for genes of interest. Part of our answer to that problem will depend upon the relative sizes of proteins and base pairs. 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 the atoms in ATP, phosphatidylcholine, B-DNA, and the green fluorescent protein (GFP) provided with this homework. More generally, you can do this by visiting sites such as:
"http://www.rcsb.org/pdb/home/home.do" (i.e. the Protein Data Bank). 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. In each drawing, use the tools provided within the software to provide relevant scale bars that characterize the size of these molecules.

(c) Later we will see that phosphatidylcholine is one of the molecules that can self assemble to form a lipid bilayer. 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. Now, revisit the cyanobacteria shown in class and do your own version of the estimate of the number of lipids in the membranes of these cells. Make sure to take into account the fraction of the surface taken up by membrane proteins (see the attached paper by Mitra *et al.* and the attached paper by Takamori *et al.*). Also, see the paper by van de Meene *et al.* that shows the multilayer structure of cyanobacterial membranes.

2. Sugar Budget.

The discovery of radioactivity revolutionized biology in a huge number of different ways. One way was that it showed that physicist's estimates on the age of the Earth were completely off base and hence that evolution had had far longer to act than originally thought. A second key outcome was that radioactive isotopes provided a means of following the paths of various molecules during their journey through the biochemical life of a cell. Indeed, the famous papers by Calvin on the biochemistry associated with photosynthesis were entitled "The Path of Carbon in Photosynthesis". In addition, radioactivity provided a means of quantifying the number of molecules of interest on the grounds that there is a linear relation between the number of radio labeled molecules and the intensity on a radiogram. Hence, over the years, much effort has gone into counting up the number of molecules of different types in living cells. Ultimately though, there has to be a carbon source and radioactivity has been a reliable tool in tracing the path of carbon (and other elements) in organisms.

(a) Estimate the number of sugars to make an *E. coli* cell. Note that in class, we flirted with these kinds of estimates when we examined the construction of a cyanobacterium. Now, it is your turn to exploit this kind of estimation to see what you come up with. Chap. 2 of PBoC should help you formulate your estimate. Remember to carefully state your assumptions. Also, for the moment, concentrate only on the building materials needed to make a cell and don't worry about the energy needed to assemble them.

(b) LB media is one of the famed growth media for studying bacterial cul-

tures. However, for more controlled experiments, a growth medium with only a single carbon source is used (so-called minimal media) which has 0.2 g of glucose for every 100 mL of media. A typical experiment involves 5 mL of minimal media which is inoculated with a small number of cells (let's assume one cell) which then grows and divides repeatedly until the culture saturates at roughly 5×10^9 cells per mL. Estimate the number of carbons in the 5 mL of growth media. Also, work out the fraction of these carbons that are used in the fully saturated culture. Extra Credit: use the recipe for LB posted with this homework to carry out a similar estimate for LB.

Molecular Volumes and Masses.

Do problem 2.2 of PBoC.

DNA replication rates.

Do problem 3.2 of PBoC.

RNA Polymerase and Rate of Transcription.

Do problem 3.3 of PBoC.