BE/APh161: Physical Biology of the Cell
Homework 1
Due Date: Wednesday, January 11, 2012

"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

Referee report: Read the vignettes from the new book that I am writing with Ron Milo entitled "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), Maja Bialecka (bialecka@caltech.edu) and my coauthor Ron (ron.milo@weizmann.ac.il) on the day the homework is due.

1. Who Are You?

It is said that you have more foreign cells in your body than those containing your own DNA. Make a simple estimate of the number of human cells you are made up of, the number of bacterial cells you harbor in your gut (assume there are 2 kg of bacteria in your gut), the number of human genes you carry and the number of genes associated with the more than 200 different species of bacteria you are carrying around.

2. To Build a Cell.

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 radiolabeled 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) Make an estimate of the composition of carbon, hydrogen, oxygen and nitrogen in the dry mass of a bacterium. That is, using what you know about the size and mass of a bacterium, the fraction of that mass that is "dry mass" (i.e. $\approx 30\%$) and the chemical constituents of a cell, figure out the approximate small integers (< 10) for the composition $C_mH_nO_pN_q$, that is, find m, n, p and q. Note that roughly half of the dry mass of a cell is protein and that the ratio of protein to (RNA+DNA) is 3:1. This is an exercise in estimating. I am not interested in super precise characterizations. Your arguments should be of the style: "I think the majority of cell is proteins, the typical amino acid has 5 carbons, there are roughly 300 amino acids per protein, blah, blah, blah...". Most importantly, explain your logic. We are most interested in careful descriptions of your approximations and logic.

(b) LB media is one of the famed growth media for studying bacterial growth and physiology. However, for more controlled experiments, a growth medium with only a single carbon source is used (so-called minimal media) which has 0.5 g of glucose for every 100 mL of media. Look up the minimal media recipe by visiting *http://www.thelabrat.com/protocols/m9minimal.shtml* - note that different people use different glucose concentrations and our 0.5 g of glucose per 100 mL is slightly different from the recipe you will find on the website. 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 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. What about nitrogen? What is the source of nitrogen in our minimal media and how many nitrogens does it take to make a cell and hence, how many cells can the media support if nitrogen is limiting?

(c) Estimate the number of sugars to make an *E. coli* cell and assume that your media is made up strictly of glucose as the carbon source. Note that in class, we flirted with these kinds of estimates when we examined the construction of a bacterium. 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.

(d) The estimate in the previous part of the problem was incomplete because we didn't consider the energetic cost of assembling all of the building blocks to make a cell. Begin by estimating how many ATPs it takes to make a cell. Given that it takes 4 ATPs for every polypeptide bond in a protein, what is a lower bound estimate on the number of ATPs to make a cell? How many sugars does it take to make those ATPs? How does this sugar consumption compare to that needed for the building materials themselves? How does your answer differ depending upon whether the growth is aerobic or not?

3. DNA replication rates.

Do problem 3.2 of PBoC.

4. RNA Polymerase and Rate of Transcription.

Do problem 3.3 of PBoC.