MCB137/237: Physical Biology of the Cell
Spring 2019
Homework 1: Biological Numeracy And A Feeling for the Organism
( Due 1/31/19)
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“The greats weren’t great because at birth they could paint. The greats were great cause they paint a lot.” - Macklemore

Homeworks in MCB137/237

Whether it is in the context of professional sports, art, or science, it pays to practice. The idea of the homeworks during our course is to give you a venue to get your 10,000 hours of calculations and estimates in as a means to become proficient in the mathematical and physical modeling of living systems. Sometimes, the problems will ask you to redo a derivation we did in class in a new way, and sometimes they will propose a whole new biological phenomenon to attack. Regardless, if you spend more than five hours on a homework set, it means that you should come to office hours. Make sure to start working on your problems early on!

The objective of this homework is to get a feeling for the numbers in whatever problem you’re considering in biology. Just like you always need to check the units in your calculations, a more subtle sanity check of your theoretical results stems from having some expectation about the order of magnitude you will obtain.

When asked to do estimates, please do not provide multiple significant digits. You may use the Bionumbers website to look up information (examples are masses of amino acids (BNID 104877) and nucleotides (BNID 103828), the speed of the ribosome (BNID 100059), etc.), but please provide a citation to the Bionumber of interest as shown above. However, remember that the main point of many of the problems in this and future homeworks will be to do simple estimates and not to look quantities up.

Sometimes, the problems will be drawn directly from the 2nd edition of Physical Biology of the Cell (PBoC or PBoC2). In that case, I’ll make the effort to scan the problems and
include them as a figure. However, some of those problems might refer to information inside the book, which I will not scan. As a result, I highly recommend that you just get the book.

When you have to write Matlab code in order to make plots, you don’t need to include your actual code. However, all plots you generate need to have axes and lines that are clearly labeled.

Finally, please write each problem on a different piece of paper. This will make it easier for us to grade them.

A Feeling for the Numbers in Biology

In this section, we flex our quantitative muscles a little bit more to develop various estimates regarding biological systems.

1 Protein Sequences: The Frances Arnold Estimate Problem

In a 2001 Bioengineering seminar at Caltech, Professor Frances Arnold made a startling remark that it is the aim of the present problem to examine. The basic point is to try and generate some intuition for the HUGE, ASTRONOMICAL number of ways of choosing amino acid sequences. To drive home the point, she noted that if we consider a protein with 300 amino acids, there will be a huge number of different possible sequences.

(a) How many different sequences are there for a 300 amino acid protein?

But that wasn’t the provocative remark. The provocative remark was that if we took only one molecule of each of these different possible proteins, it would take a volume equal to five of our universes to contain all of these different distinct molecules.

(b) Estimate the size of a protein with 300 amino acids. Justify your result, but remember it is an estimate. Next, find an estimate of the size of the universe and figure out whether Frances was guilty of hyperbole or if her statement was on the money.

2 DNA Synthesis Over Your Lifetime

Estimate the total length of DNA your body will produce over your lifetime. Give the answer in meters and relate it to some astronomically appropriate quantity. Hint: Figure out a way to estimate what cell type is most numerous in your body by looking at Sender et al., Cell 164:337 (2016), which is provided on the course website. Then, figure out how often these cells need to be replaced by looking at, for example, BioNumbers.
Figure 1: Molecular contents of the bacterium *E. coli*. The illustration on the left shows the crowded cytoplasm of the bacterial cell. The cartoon on the right shows an order-of-magnitude molecular census of the *E. coli* bacterium with the approximate number of different molecules in *E. coli*. (Illustration of the cellular interior courtesy of D. Goodsell.)

**E. coli** by the Numbers

3 *E. coli* in culture

(a) A saturated *E. coli* culture contains approximately $10^9$ cells/ml. What’s the mass density of such culture? What’s the mean spacing between cells?

(b) DNA replication in *E. coli* introduces $10^{-9}$ mutations/bp on each DNA strand. Estimate the total number of mutations introduced in a saturated 5 ml culture. Hint: To estimate the total number of division in the culture, think of the number of cell divisions in the last round of replication before reaching saturation.

4 Building a bacterial cell

Do problems 2.5 and 3.7 from PBOC2 (shown in Figure 2). Together, these two problems are intended to get you thinking about the wondrous process whereby a clear liquid with simple chemical ingredients is converted into biomass. You can use Figure 1 or refer to BioNumbers to look up the composition of the cell.
2.5 Minimal media and *E. coli*

Minimal growth medium for bacteria such as *E. coli* includes various salts with characteristic concentrations in the mM range and a carbon source. The carbon source is typically glucose and it is used at 0.5% (a concentration of 0.5 g/100 mL). For nitrogen, minimal medium contains ammonium chloride (NH₄Cl) with a concentration of 0.1 g/100 mL.

(a) Make an estimate of the number of carbon atoms it takes to make up the macromolecular contents of a bacterium such as *E. coli*. Similarly, make an estimate of the number of nitrogens it takes to make up the macromolecular contents of a bacterium? What about phosphate?

(b) How many cells can be grown in a 5 mL culture using minimal medium before the medium exhausts the carbon? How many cells can be grown in a 5 mL culture using minimal medium before the medium exhausts the nitrogen? Note that this estimate will be flawed because it neglects the energy cost of synthesizing the macromolecules of the cell. These shortcomings will be addressed in Chapter 5.

3.7 The sugar budget in minimal medium

In rapidly dividing bacteria, the cell can divide in times as short as 1200 s. Make a careful estimate of the number of sugars (glucose) needed to provide the carbon for constructing the macromolecules of the cell during one cell cycle of a bacterium. Use this result to work out the number of carbon atoms that need to be taken into the cell each second to sustain this growth rate.

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Figure 2: Problems on building a bacterial cell from PBoC2.