BE/APh161: Physical Biology of the Cell
Homework 6
Due Date: Wednesday, February 23, 2022

"One of the principal objects of theoretical research in any department of knowledge is to find the point of view from which the subject appears in its greatest simplicity." - Josiah Willard Gibbs

1. The Failure of Equilibrium Fidelity.

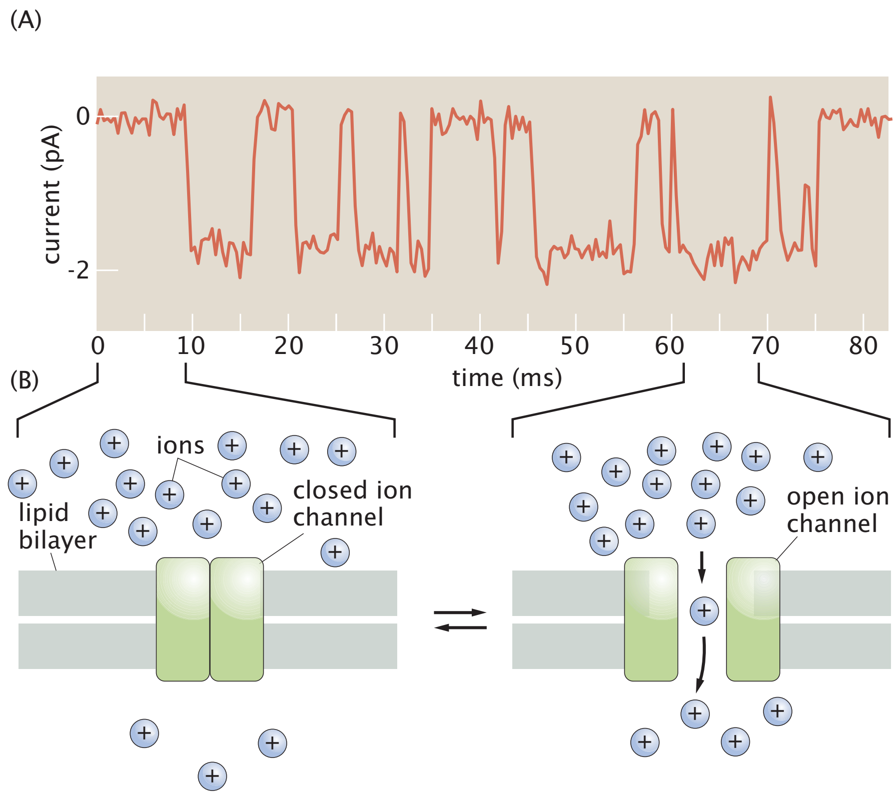
In the vignette on "Fidelity as Defiance," I worked out in words that for a simple two amino-acid view of protein translation, that the error rate is given by the ratio of the K_ds of the wrong and the right tRNAs. In this problem, flesh out the entire argument given in that vignette, and generalize beyond the case done in class to the case in which the concentration of the wrong and right tRNAs is different. That is, find an expression for the error rate in this case. Given the real biological situation, briefly explain why the number of wrong tRNAs is higher than the number of right tRNAs. Make sure you put in some approximate (but well justified) numbers. Explain why this model *fails* as a picture of translational fidelity.

2. Ion channel currents

Figure 1(A) shows a single-channel recording of the current passing through a voltage-gated sodium channel. The data reveal that the channel transitions between open and closed states as shown in Figure 1(B). When in the open state, Na^+ ions can flow from one side of the membrane to the other, resulting in a current across the membrane.

Given that ions have a typical diffusion constant of 1000 $\mu m^2/s$, given the difference between the sodium intracellular and extracellular concentrations shown in Figure 1(C), and using a rough guess for the radius of an ion channel, estimate the current that flows through the ion channel when in the open state strictly by thinking of it as a diffusion problem. That is, invoke Fick's law to find the flux through the channel and convert that flux into a current.

Recall that the charge of one monovalent ion is 1.6×10^{-19} C (Coulomb), and that 1 A = 1 C/s (Ampere = Coulomb/second). Compare your estimate to the current measured in Figure 1(A).



(C)

$D_{\text{small ions}} = 1000\ \mu m^2/s$

ion species	intracellular concentration (mM)	extracellular concentration (mM)
K^+	155	4
Na^+	12	145
Ca^{2+}	10^{-4}	1.5
Cl^-	4	120

Figure 1: Electrical current flowing through an ion channel. (A) Current flowing through a single voltage-gated sodium channel. (B) The channel recording reveals transitions through an open and a closed state. (C) The concentration gradient of Na^+ ions across the membrane can be used to estimate the current when the channel is open. (A, adapted from B. U. Keller et al., *J. Gen. Physiol.* 88:1, 1986; B, adapted from B. Hille, Ion Channels of Excitable Membranes. Sinauer Associates, 2001)

3. Secondary Transporters as Active Agents.

In class and in the vignettes, we talked in great detail about secondary transporters, membrane proteins that use an ion gradient to translocate molecules such as sugars up their concentration gradient. In this problem, you will repeat what I did in class (and vignettes), but instead of for the case of a symporter, rather for an antiporter. In this case, the ions move in an opposite direction to the sugar that is being transported up the gradient.

(A) Go through all the details of a derivation of the dynamics of the antiporter. That is, explain how the chemical potential of the sugar and ions allows us to compute the driving force for the flow of sugar and ions. Then, compute $\partial F/\partial N$ and make a plot of the driving force as a function of $N_{sugar}^{(in)}$. Use the same initial condition that I used in class and in the vignette.

(B) Plot the dynamics of the concentration of all four species - the number of sugars and ions both in and out as a function of time. Make sure you explain how you got to the dynamics.

(C) Now let's think about how the cell actually maintains a nonequilibrium steady state by pumping the ions back out again. For example, instead of letting the system run to equilibrium, imagine that an ion pump keeps pumping the H^+ ions back out so as to maintain the sugar pumping action. Let's imagine that as I did in the vignette we start out with all ions inside and then permit the ions to reach the point where 90% of them are on the interior and at that point, an ion pump pumps the ions back in so as to maintain this gradient. How much energy does it cost per ion to pump them back in? How does this compare to the energy available per sugar that is brought int? I have not worked through this part of the problem in a complete way so consider this as an exploratory problem.

4. The Art of Estimation Revisited

One of the main objectives of this course was to make sure you leave with a sense of how to do order of magnitude thinking and to obtain simple estimates for biological (and other) phenomena, yielding what Barbara McClintock referred to as a feeling for the organism.

Figure 2: Ground finch in the Galapagos.

In this problem, the goal is actually to make yourself do quick drills to get reinforce the habit of just making guesses about quantities. I like the Spanish proverb: "Habits are like cobwebs, then cables." We need to get into the estimation habit. Do not look up any facts - you can look at the included pictures and just make a quick statement based upon less than 60 seconds of staring. When appropriate, try to use the square root rule that we discussed in class. For each case, give a brief, but thorough description of how you came by your estimates. Don't just quote a single number. Give us some context about how you got your result. These problems are chosen from a wide variety of different biological contexts and give us the chance to practice our skills at many scales and in many contexts.

(a) What is the thickness of the beak of a ground finch? (in mm) Make an estimate of the beak-to-beak variation in beak size between adult ground finches. Use Figure 2 to help in making a rapid estimate. The biological significance of this estimate is that measurements have shown that a difference in beak thickness of less than 0.1 mm can mean the difference between life and death for finches faced with a drought where cracking harder and less desirable seeds becomes necessary.

Figure 3: Starling flock in Rome.

(b) How many starlings are in the flocks seen in Rome? How many kilograms of poop do these birds drop on Rome each day? Figures 3 and 4 can aid you in your thinking.

(c) When a bacterium is infected by a bacteriophage (a bacterial virus), what is the typical burst size of the viruses (i.e. how many viruses emerge from the cell after it lyses?) Begin by looking at Figure 5 and quickly telling us how big a bacterium is, how big a bacteriophage is. Then for figuring out the burst size, use Figure 5, but don't count. Do quick estimating by picking a lower and upper bound.

(d) How many atoms are in a "typical" amino acid? Figure 6 shows the *side chains* of the amino acids and should help you quickly make an estimate. Similarly, give an estimate of the typical mass of amino acids in Dalton units (remember, a Dalton is the mass of one hydrogen atom). How many atoms are in a typical base. Figure 7 shows various representations of bases and DNA. Similarly, give an estimate of the typical mass of nucleotides in Dalton

Figure 4: Consequences of starling flock in Rome.

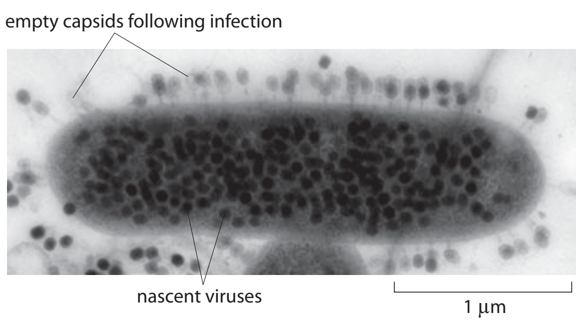


Figure 5: Burst size of an infected bacterium.

units.

(f) In this part of the problem, you are going to do an integral by eyeballing. Figure 8 shows the spectrum of radiation reaching the earth. By approximating the curve as a rectangle work out a simple statement for the flux of radiation on the earth from the sun in units of W/m^2. Then, using the blue region, figure out the flux 10 m below the surface of the ocean.

(g) Every time an electron microscope is used to take an image it corresponds to roughly a $1\mu m \times 1\mu m$ area. The electron microscope is used to explore the structure of the nanometer scale world of cells, for example. Biology is a subject characterized by great naturalist voyages in which figures such as Humboldt, Darwin, Wallace, Huxley and Hooker traveled around the

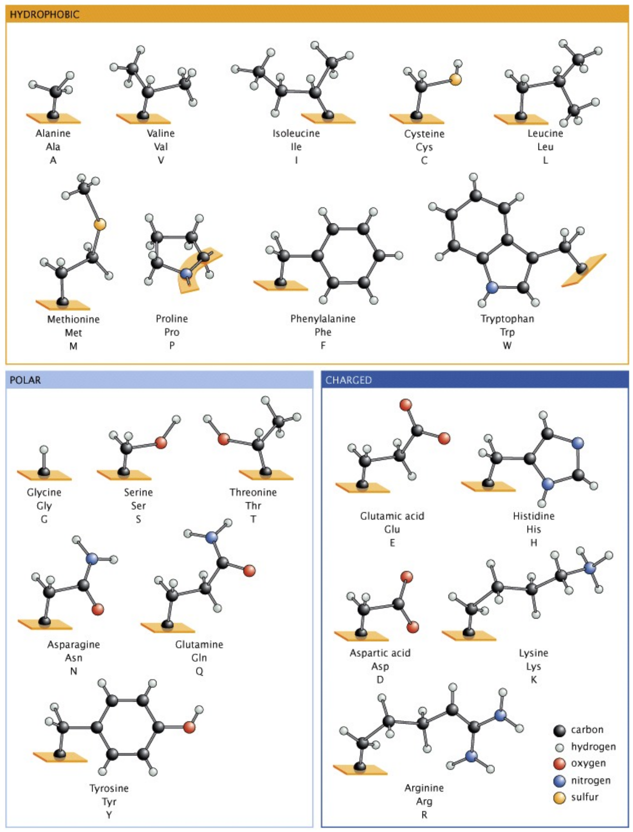


Figure 6: Amino acid side chains.

world to try and collect data on biological diversity. The point of this problem is to get a sense of the *microscopic* diversity explored. Make an estimate of the total area looked at in biological samples using electron microscopes in the history of science. How does this correspond to the area of the Earth? What do you conclude about the extent to which we have "explored" the microbial diversity on the planet?

N. Defiance

In a long series of vignettes, I argued that perhaps the real "secret of life" is defiance. Use a paragraph to explain what my argument about defiance

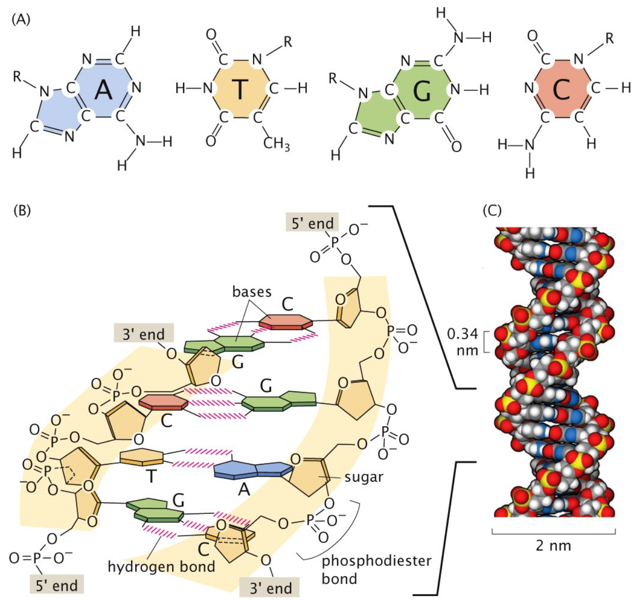


Figure 7: Structure of DNA.

is and give a succinct statement of how living organisms use the elements of the periodic table to make things that are clearly qualitatively different than, say, a rock.

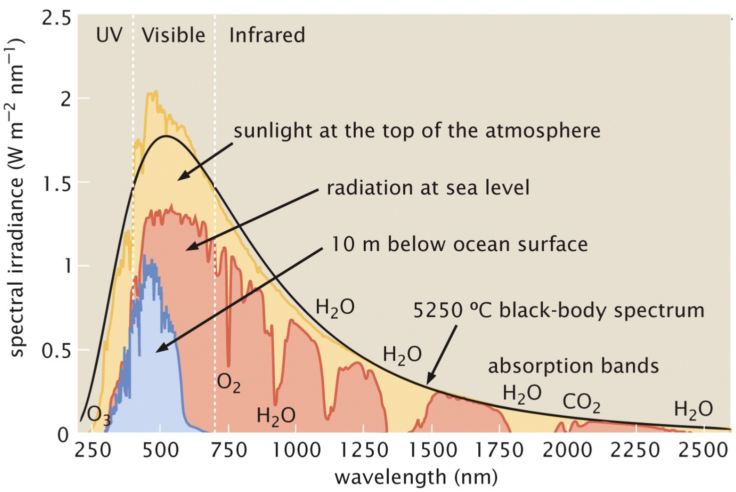


Figure 8: Spectrum of solar radiation reaching the Earth.