

# BE/APh161: Physical Biology of the Cell

## Homework 6

### Due Date: Wednesday, Feb. 26, 2020

“A new concept appears in physics, the most important invention since Newton’s time: the field. It needed great scientific imagination to realize that it is not the charges nor the particles, but the field in the space between the charges and the particles which is essential for the description of physical phenomena.” - Albert Einstein and Leopold Infeld, **The Evolution of Physics**

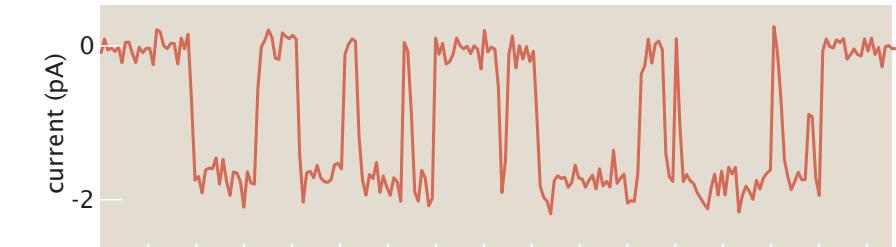
#### 1. Ion Channel Currents

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,  $\text{Na}^+$  ions can flow from one side of the membrane to the other, resulting in a current across the membrane.

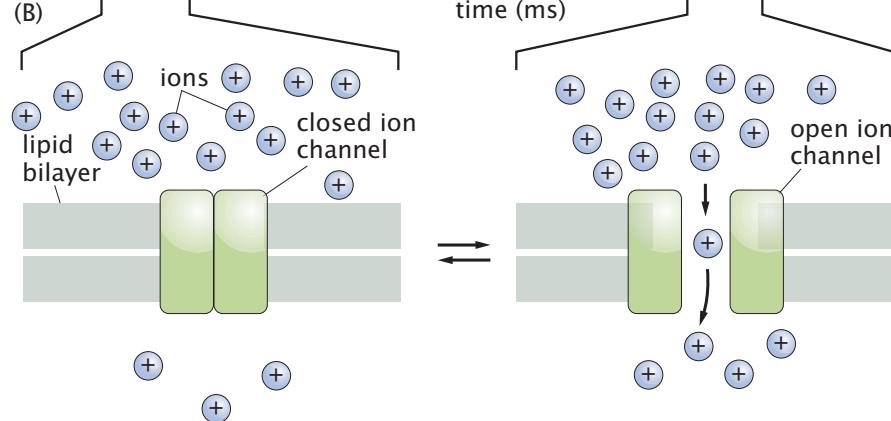
(A) Given that ions have a typical diffusion constant of  $1000 \mu\text{m}^2/\text{s}$ , given the difference between the sodium intracellular and extracellular concentrations shown in Figure 1(C), and using a rough guess for the radius of an ion channel, estimate the current that flows through the ion channel when in the open state. Recall that the charge of one monovalent ion is  $1.6 \times 10^{-19} \text{ C}$  (Coulomb), and that  $1 \text{ A} = 1 \text{ C/s}$  (Ampere = Coulomb/second). Compare your estimate to the current measured in Figure 1(A).

(B) In class, we discussed the driving force for spontaneous change in systems that are out of equilibrium in which a constraint has been removed. In the case of the ion channel described above, the constraint that is removed is that when the channel is open, the impermeable membrane separating the cellular interior from the external environment is no longer impermeable as shown in Figure 2. In this part of the problem reproduce the graphs shown in Figure 2 by first doing the relevant calculations for the entropy as a function of the number of particles on the left side and then by making the plot itself. Let’s use numbers relevant to *E. coli* by imagining that the boxes are each  $1 \mu\text{m}^3$  in size and that the size of the lattice sites are  $1 \text{ nm}^3$ . Imagine that the total number of ions in the system is  $L_{tot} = 10^6$ . Write the total entropy as  $S_{tot} = S_L(L) + S_R(L_{tot} - L)$ , where  $S_L$  is the entropy in the left part of

(A)



(B)



(C)

	ion species	intracellular concentration (mM)	extracellular concentration (mM)
$D_{\text{small ions}} = 1000 \mu\text{m}^2/\text{s}$	$\text{K}^+$	155	4
	$\text{Na}^+$	12	145
	$\text{Ca}^{2+}$	$10^{-4}$	1.5
	$\text{Cl}^-$	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  $\text{Na}^+$  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)

the container and  $S_R$  is the entropy of the right part of the container. Make sure to explain all of your steps.

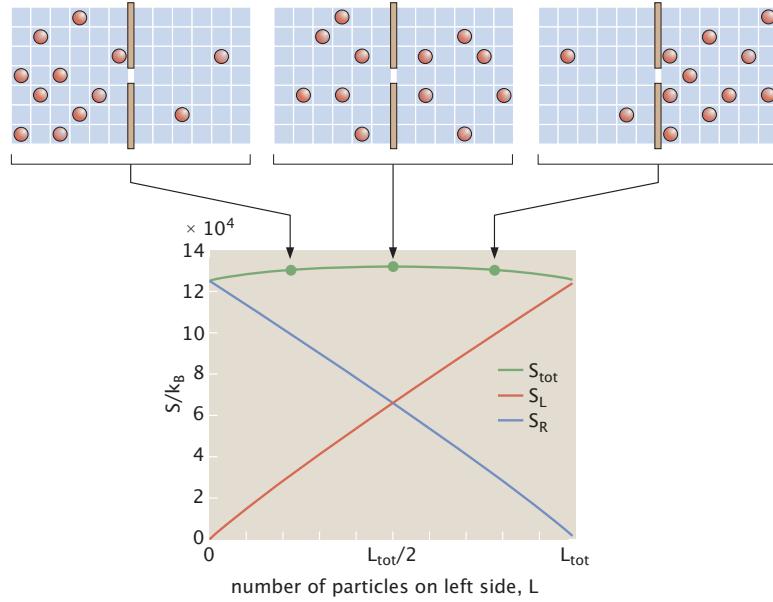


Figure 2: Maximization of entropy with respect to particle number.

## 2. Diffusion on a microtubule

Read the paper by Helenius *et al.* (provided on the course website) dissecting the mechanism of microtubule depolymerization by the kinesin MCAK. Here, they show how the MCAK molecular motor diffuses along the microtubule towards both ends, triggering the depolymerization of a few tubulin dimers before falling off the microtubule.

(A) Write a one paragraph summary of the paper. What questions were they considering, how did they answer those questions, what was learned?

(B) In their Figure 2b, they show the mean squared displacement of MCAK  $\langle x^2 \rangle$  as a function of time  $t$ . Remember that, using dimensional analysis, we concluded that  $\langle x^2 \rangle = Dt$ , where  $D$  is the diffusion constant (there's a difference of a factor of two between our expression and the one used by Helenius *et al.*, but we can ignore that for now). Using the data in the figure (provided on the course website), write a chi<sup>2</sup> minimization program to determine the

diffusion constant. Alternatively, you can fit “by eye” by plotting the expected relation between  $\langle x^2 \rangle$  and  $t$  for different values of  $D$ .

### **3. Antenna model of microtubule length control.**

(A) Do problem 15.7 of PBOC2.

(B) Go beyond the model described in the problem by now writing an equation for the entire probability distribution of finding a microtubule of length  $L$  at time  $t$  using the chemical master equation described in class. Using the parameters from the previous part of the problem, give a description of the expected steady-state distribution. Comment on what kind of distribution is obtained and what we might learn from this as well as how to test these ideas experimentally. Note that this is the problem that I argue we could attempt to convince the authors of the original paper to test.