

# MCB137L/237L: Physical Biology of the Cell

## Spring 2020

### Homework 4: Diffusion as the null model of biological dynamics

(Due 2/20/20 at 3:30pm)

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#### 1 *E. coli* in culture

(a) A saturated *E. coli* culture contains approximately  $10^9$  cells/mL. What's the mean spacing between cells in such a culture?

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

#### 2 Diffusion times

Make a log-log plot of the diffusion time (in seconds) as a function of length (in  $\mu\text{m}$ ) using Python. Plot multiple lines considering the diffusion constants for ions and for a typical protein *inside a cell*. Finally, mark a few relevant biological sizes along the x-axis such as the size of an axon, a synaptic cleft, an *E. coli* cell, and a eukaryotic nucleus.

#### 3 Ion channel currents

Figure 1A 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 1B. 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.

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 1C, 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  $1.6 \times 10^{-19}$  C (Coulomb), and that  $1 \text{ A} = 1 \text{ C/s}$  (Ampere = Coulomb/second). Compare your estimate to the current measured in Figure 1A.

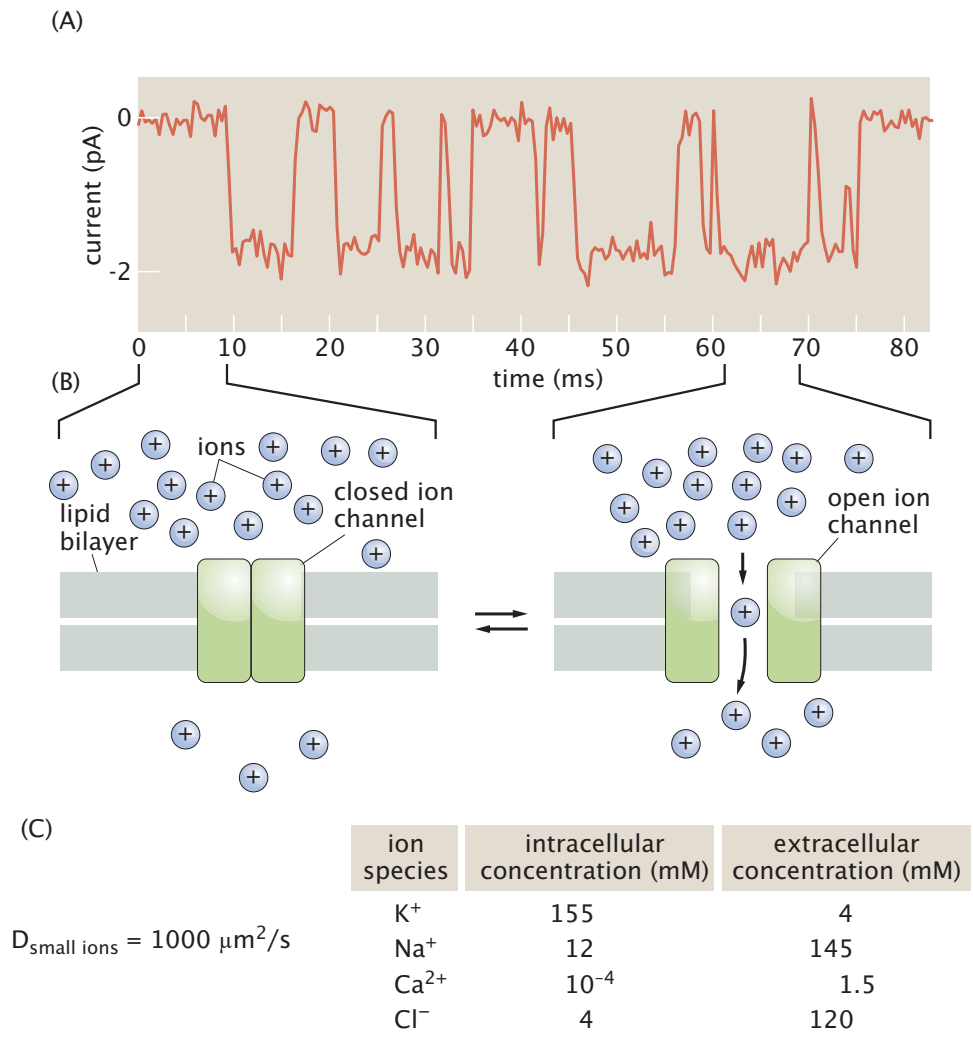


Figure 1: Electrical current flowing through an ion channel. (A) Current flowing through a single voltage-gated sodium channel. (B) The channel recording reveals transitions through an open and a closed state. (C) The concentration gradient of Na<sup>+</sup> ions across the membrane can be used to estimate 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)

## 4 Metabolic rates

Solve problem 3.8 from PBoC (Figure 2).

- **3.8 Metabolic rates**

Assume that 1 kg of bacteria burn oxygen at a rate of 0.006 mol/s. This oxygen enters the bacterium by diffusion through its surface at a rate given by  $\Phi = 4\pi DRc_0$ , where  $D = 2 \mu\text{m}^2/\text{ms}$  is the diffusion constant for oxygen in water,  $c_0 = 0.2 \text{ mol}/\text{m}^3$  is the oxygen concentration, and  $R$  is the radius of the typical bacterium, which we assume to be spherical.

**(a)** Show that the amount of oxygen that diffuses into the bacterium is greater than the amount used by the bacterium in metabolism. For simplicity, assume that the bacterium is a sphere.

**(b)** What conditions does (a) impose on the radius  $R$  for the bacterial cell? Compare it with the size of *E. coli*.

Figure 2: Metabolic rates. Problem 3.8 from PBoC

## 5 Diffusion on a microtubule

Read the great 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) 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). Fit the data in the figure (provided on the course website) "by eye" in order to determine the value of  $D$ . To make this possible, plot the expected relation between  $\langle x^2 \rangle$  and  $t$  for different values of  $D$  and decide which value of  $D$  better recapitulates the data. EXTRA CREDIT: Write a chi<sup>2</sup> minimization program to determine the diffusion constant. Make sure to plot the chi<sup>2</sup> as a function of  $D$ .

(b) In their Figure 3, they argue that a diffusive mechanism can be faster than one of directed motion on short length scales. Explain how this assertion is supported by the plot shown in their Figure 3b, and reproduce the plot in Python.