MCB137L/237L: Physical Biology of the Cell
Spring 2025
Homework 11:
(Due 4/15/25 at 2:00pm)

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1 Uncovering phase separation in P-granule formation

In the paper by Brangwynne *et al.* (provided on the course website), the authors consider two mechanisms for the accumulation of P granules in the posterior end of the *C. elegans* embryo. First, they posit that P granules could migrate from the anterior end to the posterior end of the embryo. Second, they propose that anterior P granules could be preferentially disassembled or degraded.

(a) Read their paper and write a one-paragraph summary of it. Make sure to explain the various hypotheses they considered and how they tested them.

(b) In their Figure 4, they propose that, upon dissolution in the anterior end, the proteins that make up the P granules diffuse toward the posterior end to take part in granule formation at that location. Assume that these proteins have a reasonable diffusion constant, and estimate the time it takes for these molecules to diffuse throughout the embryo. How do these time scales compare to the overall rates of P granule formation?

2 Breaking the 2nd Law and Rectifying Thermal Noise

In a great *Physics Today* article (provided on the course website), Chris Jarzynski and colleagues state that "A liter of ordinary air weighs less than half a US penny, but it contains enough thermal energy to toss a 7-kg bowling ball more than 3 m off the ground. A gadget able to harvest that abundant energy by converting the erratic movement of colliding molecules into directed motion could be very useful indeed."

Check his assertion about the weight of the air in the room and the energy within it. Remember the meaning of k_BT as the energy scale of the particles in our system.

3 Ligand-Receptor Problem from the Perspective of Statistical Mechanics

In Homework 4, we calculated ligand-receptor binding from the perspective of rate equations and dissociation constants. In this problem we explore a third route to compute the probability of a receptor being bound by a ligand based on statistical mechanics. Note that you can complement this problems by reading the paper "A First Exposure to Statistical Mechanics for Life Scientists: Applications to Binding" (Garcia2007b) on the course website.

(a) Imitate the statistical mechanics protocol given in class by showing the states, energies, multiplicities and weights for a lattice consisting of Ω lattice sites and L ligands. Find an expression for p_{bound} in terms of the difference in energy of a ligand when in solution, ε_{sol} and the energy when the ligand is bound to the receptor, ε_b.

(b) Consider that the lattice sites in our lattice model (Figure 1 of Homework 4) have size v and hence that the concentration is $[L] = L/\Omega v$ and use that insight to arrive at an expression for the dissociation constant in terms of the microscopic parameters ε_{sol} and ε_b. Do this by comparing the results of this part of the problem with your result from Homework 4.

4 Ion Channels and Statistical Mechanics

In this problem, we will derive a mathematical description of the current passing through a voltage-gated ion channel. To model this channel, we assume that it can exist in an open or closed configuration as shown in Figure 1A. The thermal fluctuations in the cell result in the channel switching between these states over time as presented in Figure 1B. Figure 1C shows how these fluctuations in channel state can be directly read out from the current flowing through the channel.

(a) Use the statistical mechanics protocol (i.e. calculating the states and weights of the system) to calculate the probability of the channel being in the open state, p_{open}. Assume that the open state has an energy ε_{open}, and that the energy of the closed state is ε_{closed}.

(b) Plot p_{open} as a function of $\Delta\varepsilon = \varepsilon_{open} - \varepsilon_{closed}$. Explain what happens in the limits $\varepsilon_{open} \ll \varepsilon_{closed}$ and $\varepsilon_{open} \gg \varepsilon_{closed}$. What significance does $\Delta\varepsilon = 0$ have for p_{open}?

In a simple model of a voltage-gated ion channel, $\Delta\varepsilon = q(V^* - V)$. Here, V is the voltage applied to the membrane and q is the effective gating charge, which describes the movement of charges along the membrane as the channel configuration changes. You can learn more about this model in section 17.3.1 of PBoC2.

(c) What is the significance of V^*? Namely, what happens to the probability of being open when $V = V^*$.

(d) On the website, you will find measurements of p_{open} vs. V for a sodium-gated ion channel. Write your expression for p_{open} as a function of V instead of as a function of $\Delta\varepsilon$. Estimate V^* from the data using what you learned in (c). Now that you have V^*, to estimate q, make a plot where you overlay the data and the model prediction for three different values of q corresponding to 1, 3 or 5 electron charges (note that q is positive, so here we are talking about the *absolute value* of the electron charge).

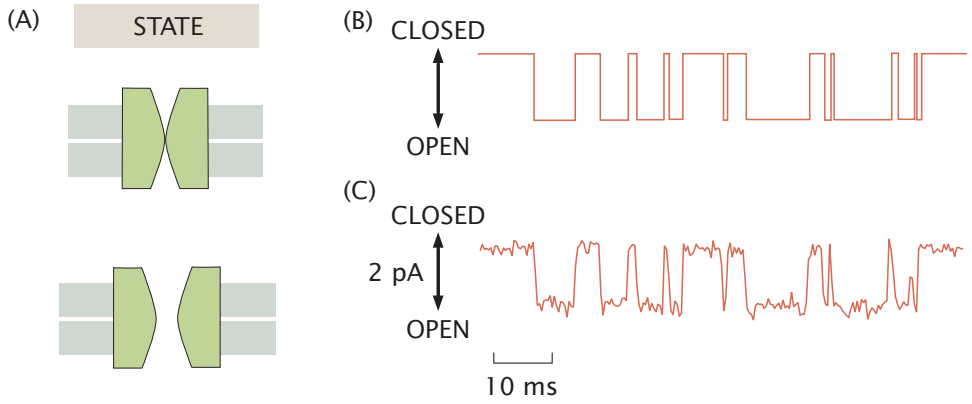

Figure 1: Current through an ion channels. (A) The ion channel can exist in a closed or open configuration, (B) fluctuating in time between these two states. (C) The current flowing through the channel is directly related to the state of the channel.