11.2 Glucose and membrane permeability

(a) Compute the time scale for molecules to empty out of a "spherical bacterium" of radius 1 μm due to the permeability of the membrane to various molecular species. In particular, use the relation $j = -P\Delta c$ between the flux of molecules j across the membrane and its permeability P. Make a plot of the time scale as a function of the parameter P using the data in Figure 11.11, and then estimate the time scale for glucose. The permeability for phosphorylated glucose is thought to be much lower due to its charge, which makes traversing the membrane much less favorable. How much longer will the glucose take to leak out if the permeability is 100-fold smaller in the phosphorylated than unphosphorylated state, for example?

(b) To go beyond the simple estimate of (a), write a differential equation for the rate of change of concentration of molecules assuming that the initial concentration within the cell is c_{in} and the concentration outside of the cell is $c_{\text{out}} = 0$. Solve the differential equation and find the time scale for the molecules to exit the cell. How does this compare with the simple estimate you made in (a)?

11.3 Mathematics of curvature

Consider the function $h(x_1, x_2) = x_1^2 + x_1 x_2 - 2x_2^2$, which we assume describes the shape of a deformed lipid bilayer membrane. As shown in Figure 11.14, x_1 and x_2 are the coordinates of the reference plane below the membrane.

(a) Make a plot of the height as a function of x_1 and x_2.

(b) Compute the principal radii of curvature as functions of x_1 and x_2.

(c) Compute the bending free energy for the piece of membrane corresponding to the square $0 \le x_1 \le 1$ and $0 \le x_2 \le 1$ in the reference plane.

11.6 Membrane deformation and adhesion in pipettes

The patch clamp technique is widely used in electrophysiology to study the gating properties of ion channels. A glass micropipette with an open tip is brought into contact with a cell or a vesicle containing the ion channel of interest. As a result of the strong adhesion between the glass and the lipid membrane, the membrane gets pulled into the pipette as shown in Figure 11.49.

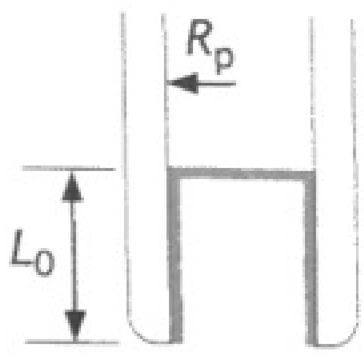

Figure 11.49: Membrane patch and pipette. Schematic showing the membrane patch shape (grey) at zero applied pressure. The pipette has a radius of R_p and as a result of adhesion, the membrane is pulled up the pipette by a distance L_0.

Although the glass-membrane adhesion is crucial to avoiding spurious leakage currents not resulting from the channels themselves, this adhesion can also have negative side effects. For example, as the membrane adheres to the pipette, it induces a tension that is different from the resting tension in the membrane patch, and this could lead to errors in the estimates of gating tension of mechanosensitive channels, for example. In this problem, we use our understanding of elasticity of membranes to estimate the size of this adhesion-induced tension.

(a) Consider the geometry shown in Figure 11.49, where the membrane patch has a cylindrical adhered domain and a circular free domain. The elastic energy associated with the patch comes from two contributions, namely, the stretch energy and the glass–bilayer adhesion energy. The stretch energy results from the fact that the membrane is stretched when it is pulled into the pipette. This contribution to the free energy has a quadratic dependence on the areal strain $\phi = (A - A_0)/A_0$, and is given by

$$G_{\text{stretch}} = \frac{1}{2} K_A \phi^2 A_0 \,, \tag{11.68}$$

where A_0 is the unstretched area of the membrane patch and $K_A \approx 50\, k_B T/\text{nm}^2$ is the stretch modulus.

The adhesion energy is proportional to the area of the contact domain A_{adh} and is given by $G_{\text{adh}} = -\gamma A_{\text{adh}}$, where γ is the adhesion energy (that is, the energy per unit area). Using these facts and the geometry shown in Figure 11.49, obtain the expression for the total elastic energy of the membrane patch in terms of the areal strain ϕ.

(b) Minimize the elastic energy with respect to ϕ to obtain the expression for the equilibrium areal strain. Compute the tension τ in the membrane patch in equilibrium using the relation $\tau = K_A \phi$. For $\gamma \sim 0.5\, k_B T/\text{nm}^2$, a typical value for glass–bilayer interaction, estimate the equilibrium areal strain and the tension in the patch.

(c) Assuming that the unstretched area of the patch is $A_0 = 2 \times \pi R_p^2$, what is the length of membrane tube L that lines the sides of the pipette? How does this length compare with the length computed from simple geometrical considerations, namely, by assuming that the membrane patch does not get stretched when it is drawn into the pipette.

(d) Show that membrane bending does not contribute significantly to the energy budget of the membrane patch. Do this by computing the bending energy of cylindrical membrane material within the pipette and compare the resulting energy with the stretch energy and adhesion energy you already obtained.

11.7 Bending modulus and the pipette aspiration experiment

The pipette aspiration experiment described in the chapter can be used to measure the bending modulus K_b as well as the area stretch modulus. Lipid bilayer membranes are constantly jostled about by thermal fluctuations. Even though a flat membrane is the lowest-energy state, fluctuations will cause the membrane to spontaneously bend. The goal of this problem is to use equilibrium statistical mechanics to predict the nature of bending fluctuations and to use this understanding as the basis of experimental measurement of the bending modulus. (Note: This problem is challenging and the reader is asked to consult the hints on the book's website to learn more of our Fourier transform conventions, how to handle the relevant delta functions, the subtleties associated with the limits of integration, etc.).

(a) Write the total free energy of the membrane as an integral over the area of the membrane. Your result should have a contribution from membrane bending and a contribution from membrane tension. Write your result using the function $h(\mathbf{r})$ to characterize the height of the membrane at position $\mathbf{r}$.

(b) The free energy can be rewritten using a decomposition of the membrane profile into Fourier modes. Our Fourier transform convention is

$$h(\mathbf{r}) = \frac{A}{(2\pi)^2} \int \tilde{h}(\mathbf{q}) e^{-i\mathbf{q}\cdot\mathbf{r}}\, d^2\mathbf{q}, \tag{11.69}$$

where $A = L^2$ is the area of the patch of membrane of interest. Plug this version of $h(\mathbf{r})$ into the total energy you

Use this result to plot the total free energy as a function of radius for several different tensions including the critical tension (that is, produce a figure analogous to Figure 11.47). How does the critical tension compare with the value obtained using the full solution of the partial differential equation?

11.9 Dynamin on tubules

In the chapter, we considered an experiment in which a tubule was pulled from a giant unilamellar vesicle and then dynamin was added into the solution. The dependence of nucleation on the radius was inferred by appealing to the force measured in the trap as shown in Figure 11.36. Here we rederive this force.

(a) Write a free energy for the tubule in terms of the bending energy and the tension.

(b) Find the force due to the bending energy and the surface tension by evaluating $f = -\partial G_{\text{tubule}}/\partial L$.

(c) Now consider the effect of the optical trap with stiffness k_{trap} on the free energy of the tubule/bead system. Assume that the equilibrium position of the bead corresponds to a tubule of length L_0 and write down the expression for the total free energy that includes the free energy of the tubule and the energy of the bead in the trap. Find the equilibrium value of the tubule length L^*, and show that it is a result of balancing the tubule force and the force applied by the optical trap.

11.10 Two-dimensional treatment of MscL

Consider a two-dimensional generalization of Equation 11.36.