BE/APh161: Physical Biology of the Cell
Homework 7
Due Date: Wednesday, March 4, 2020

"How can the events in *space and time* which take place within the spatial boundary of a living organism be accounted for by physics and chemistry?" - Erwin Schrödinger **What is Life?**

1. Three Routes to Ligand-Receptor Binding

(A) Several weeks ago in class and then in homework, we derived the diffusion-limited on rate as the speed limit for chemical reactions. In this problem, we are going to use that analysis as a jumping off point for thinking about ligand-receptor binding problems. Imagine a situation in which we have a receptor fixed at some point in space as shown in the top right panel of Figure 1. Write a rate equation for the concentration of ligand-receptor pairs in terms of the concentration of ligands and receptors. Given that equation, derive an expression for the dissociation constant

$$K_d = \frac{[L][R]}{[LR]} \tag{1}$$

in terms of the on and off rates. Make sure you explain the dimensions of your on and off rates and hence, the dimensions of K_d.

(B) A second route to considering ligand-receptor interactions is to think of binding probabilistically with the probability that the receptor is occupied given by

$$p_{bound} = \frac{[LR]}{[R] + [LR]}. \tag{2}$$

Given the definition of the dissociation constant introduced in the previous part of the problem, find a simple expression for $p_{bound}([L])$ that is only a function of the concentration of ligand. (NOTE: for now, we are ignoring the subtlety that the amount of total ligand and free ligand are not actually the same, though in the case considered here with a single receptor we have somewhat finessed that point.) Make a plot of $p_{bound}([L])$ as a function of $[L]$ and comment on where K_d belongs on the axes.

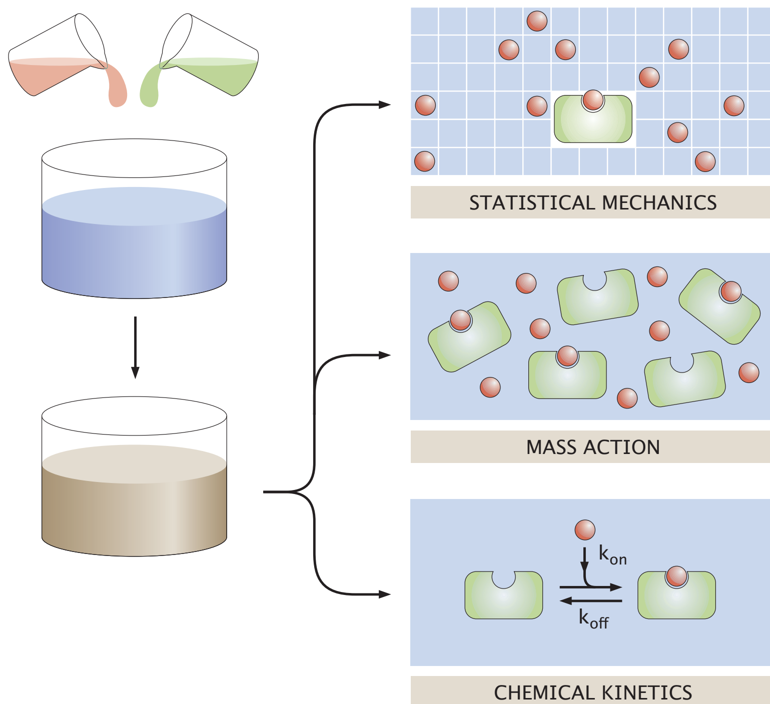

Figure 1: Three treatments of ligand-receptor binding.

(C) Our third route to ligand-receptor binding is to use statistical mechanics. 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. Consider that the lattice sites in our lattice model 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. Do this by comparing the results of this part of the problem with your result from part (B).

2. Digging deeper into the continuum field theory of a Newtonian fluid.

(A) In class, we exploited the continuum theory protocol to derive the Navier-Stokes equations. In this part of the problem, repeat that derivation by explaining how we obtain the equation of force balance

$$\rho(\frac{\partial v_i}{\partial t} + v_j \frac{\partial v_i}{\partial x_j}) = \frac{\partial \sigma_{ij}}{\partial x_j}. \tag{3}$$

Then, using the constitutive equation for the Newtonian fluid, $\sigma_{ij} = -p\delta_{ij} + 2\eta D_{ij}$, derive the Navier-Stokes equations themselves,

$$\rho(\frac{\partial v_i}{\partial t} + v_j \frac{\partial v_i}{\partial x_j}) = -\frac{\partial p}{\partial x_i} + \eta \nabla^2 v_i. \tag{4}$$

Explain all the steps in the derivation including any comments about mass conservation and the continuity equation.

(B) One of the most important superpowers of applied mathematics and physics is the act of rewriting the equations we use to describe the world around us in dimensionless form. This is not some trick or afterthought. Rather, it is about finding the natural variables of some problem of interest. For fluids, that natural variable is the Reynolds number and in this part of the problem we will see how the Reynolds number emerges from the act of writing the equations in dimensionless form. We introduce the “characteristic length” L and the “characteristic velocity” U, allowing us to then define four dimensionless variables, namely, a dimensionless spatial coordinate

$$x^* = \frac{x}{L}, \tag{5}$$

a dimensionless velocity of the form

$$v^* = \frac{v}{U}, \tag{6}$$

a "characteristic pressure" p^*

$$p^* = \frac{L}{\eta U} p \tag{7}$$

and the "characteristic time"

$$t^* = \frac{t}{(L/U)}. \tag{8}$$

Explain why each one of these is dimensionless. We use these definitions to rewrite the Navier-Stokes equations in dimensionless form. The way to do this is to take each term in the Navier-Stokes equation and to write them in dimensionless terms. For example, the first term on the left side is of the form

$$\rho \frac{\partial v_i}{\partial t} = \rho \frac{\partial (v_i^* U)}{\partial t^*} \frac{dt^*}{dt} = \frac{\rho U^2}{L} \frac{\partial v_i^*}{\partial t^*} \tag{9}$$

Using this strategy, show that you can rewrite the Navier-Stokes equations as

$$\frac{\partial v_i^*}{\partial t^*} + v_j^* \frac{\partial v_i^*}{\partial x_j^*} = -\frac{1}{Re} \frac{\partial p^*}{\partial x_i^*} + \frac{1}{Re} \nabla_*^2 v_i^*, \tag{10}$$

where my notation with ∇_*^2 means spatial derivatives are with respect to the dimensionless variable x^*. We have defined the Reynolds number as

$$Re = \frac{\rho L U}{\eta}. \tag{11}$$

(C) Given the definition of the Reynolds number, estimate the Reynolds numbers associated with a blue whale, a human swimmer, a flying bar-tailed godwit, a swimming Stentor cell, an *E. coli* cell and a 1 micron bead in an optical trap being dragged by a molecular motor such as myosin or kinesin.

(D) Estimate the drag force on a 1 micron bead being pulled along by a molecular motor using the Stokes drag, $F_{drag} = 6\pi\eta a v$, where a is the size of the bead and η is the viscosity. How does the force due to the drag compare to the stall force of the motor?

(E) One of the conditions we invoked in our discussion of the Newtonian fluid was that of incompressibility, captured mathematically as

$$\frac{\partial v_i}{\partial x_i} = \nabla \cdot \mathbf{v} = 0. \tag{12}$$

In this part of the problem, we are going to use simple physical reasoning to explore the legitimacy of this condition. Our starting point is the idea that we can write the change in the pressure of the fluid due to a change in volume as

$$\Delta p = B\frac{\Delta V}{V}, \tag{13}$$

where B is the so-called bulk modulus with a value of $B = 2.2$ GPa for water. If we subject our water to a change in pressure of 1 atm, what is the corresponding change in volume and what does your estimate tell you about the incompressibility condition?

(F) There is an alternative way for us to explore the meaning of the Reynolds number as the ratio of the kinetic energy to the viscous energy dissipation. As shown in Figure 2, we can make a simple analysis by considering the swimming of a fish. Consider a fish of size L swimming at speed v. Make a *scaling* estimate of the kinetic energy of the fluid parcel that is moved by the fish - this is not about factors of 2 or 1/5 or anything like that. Just construct a formula that depends upon the density of water ρ, the speed v and the size scale L that captures the kinetic energy of the fluid parcel. Our next task is to construct the denominator by making a scaling estimate of the energy dissipation due to viscous stresses. First, using the viscosity η, the speed v and the size scale L, find an order of magnitude expression for the viscous stress. This is a force per unit area. Turn that into a force scale by multiplying by the relevant area over which these stresses act. Finally, given that work = force $\times$ distance, work out the scaling of the viscous work. By now constructing the ratio of these two terms, show that you recover precisely the Reynolds number we had above.

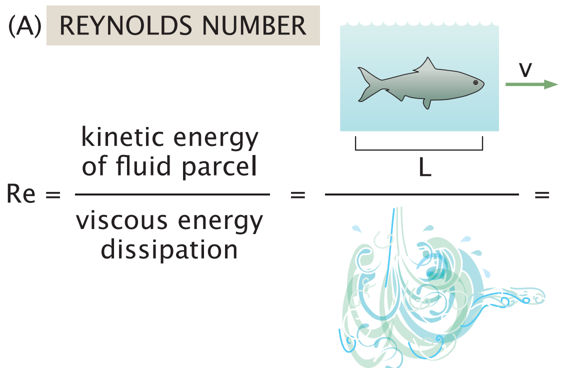

Figure 2: Getting a feeling for the Reynolds number.

3. A feeling for the numbers: stress in biology.

(A) One of the fundamental facts of life is changes in osmotic stress. To put it bluntly, sometimes the bacteria in our guts are all of a sudden exposed to pure water in a toilet bowl, resulting in a substantial hypoosmotic stress coming from a concentration change as much as $\Delta c = 1$ M. One simple equation of state for the osmotic pressure that results is the so-called van't Hoff equation which says that the osmotic pressure is given by the ideal solution form

$$\Pi = \Delta c k_B T, \tag{14}$$

where Δc is the concentration jump across the relevant cell membrane. Work out the stress in Pa units for an osmotic stress experiment.

(B) In class we discussed the phenomenon of cyclosis observed in cells such as the algae *Chara*. In this part of the problem, your aim is to make an estimate of the shear stresses that arise in the fluid medium within the cell. As a reminder, look at Figure 3 to get a sense of the dimensions. Given these structural details, and given that the flow speed at the outer radii is around 100 μm/s, make an estimate of the shear stresses within the cell. In addition, evaluate the Reynolds number within one of these cells and use those insights to simplify the Navier-Stokes equations to the form of the Stokes equations. Here I am asking you to explain the simplification that emerges in the low Reynolds number limit.

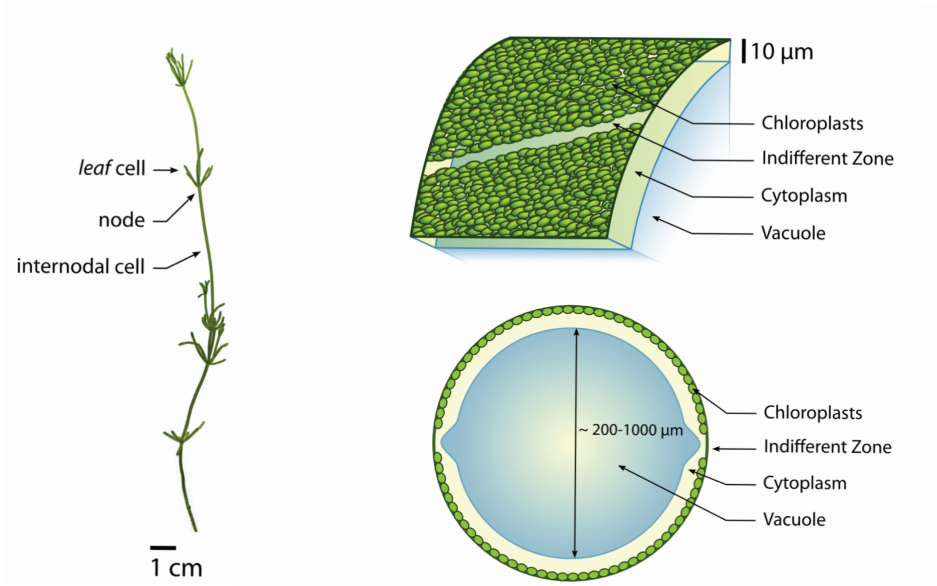

Figure 3: The anatomy of the internodal cell of *Chara*. (Courtesy of Jan Willem van de Meent)

4. Bacterial Foraging.

Work out problem 12.1 in PBoC2. This problem explores the very interesting question of the relative importance of directed motion and diffusion.