BE/APh161: Physical Biology of the Cell
Homework 7
Due Date: Friday, March 12, 2021

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

(A) In class (see the vignettes about Newtonian fluids), 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

$$\rho(\frac{\partial v_i}{\partial t} + v_j \frac{\partial v_i}{\partial x_j}) = \frac{\partial \sigma_{ij}}{\partial x_j}. \tag{1}$$

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

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

Explain all the steps in the derivation including any comments about mass conservation and the continuity equation. Make sure you show off your new skills in indicial notation, taking care to show us each time you are summing over repeated indices.

(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

$$x^* = \frac{x}{L}, \tag{3}$$

a dimensionless velocity of the form

$$v^* = \frac{v}{U}, \tag{4}$$

a "characteristic pressure" p^*

$$p^* = \frac{L}{\eta U} p \tag{5}$$

and the "characteristic time"

$$t^* = \frac{t}{(L/U)}. \tag{6}$$

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

$$\rho \frac{\partial v_i}{\partial t} = \rho \frac{\partial (v_i^* U)}{\partial t^*} \frac{dt^*}{dt} = \frac{\rho U^2}{L} \frac{\partial v_i^*}{\partial t^*} \tag{7}$$

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

$$\frac{\partial v_i^*}{\partial t^*} + v_j^* \frac{\partial v_i^*}{\partial x_j^*} = -\frac{1}{Re} \frac{\partial p^*}{\partial x_i^*} + \frac{1}{Re} \nabla_*^2 v_i^*, \tag{8}$$

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

$$Re = \frac{\rho L U}{\eta}. \tag{9}$$

(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 roughly 5 pN of a typical motor?

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

$$\frac{\partial v_i}{\partial x_i} = \nabla \cdot \mathbf{v} = 0. \tag{10}$$

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

$$\Delta p = B\frac{\Delta V}{V}, \tag{11}$$

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 1, 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.

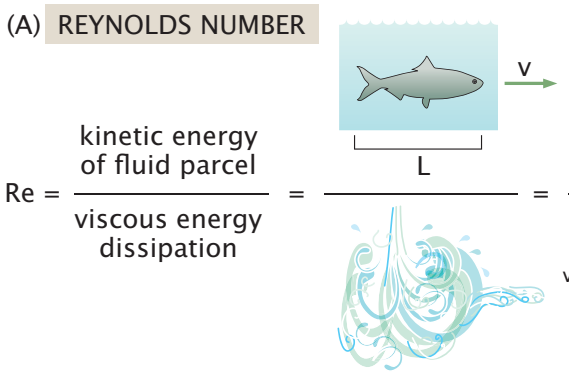

Figure 1: Getting a feeling for the Reynolds number.

2. Phenotypic Properties of MWC Molecules

(A) In the vignette on the Monod-Wyman-Changeux model (see the week of February 1), we discussed the statistical mechanics of a broad array of different proteins that switch back and forth between inactive and active states. Define the concept of allostery and give examples from biology that demonstrate why the allostery concept that is represented in the MWC model is so important.

(B) We are going to explore the key properties of leakiness, dynamic range, the effective Hill coefficient and the EC_{50}. To begin, derive the probability that an MWC molecule with two binding sites for ligand will be active. Then, make a plot of the activity of an MWC molecule as a function of the concentration of the ligand that regulates it. On that plot give graphical interpretations of all of the key phenotypic properties of the molecule listed above. Let's choose the parameters such that the energy difference between active and inactive states is a few k_BT and the $K_A = 10$ nM and $K_I = 100$ nM. Explain how the sign of $\Delta\varepsilon$ controls whether active or inactive state is favored without ligand. For the choice of K_A and K_I we have chosen here, which state is favored by the binding of the ligand?

(C) Write expressions for each of the four properties listed above by using their definitions. You will *not* be able to find analytic expressions for all of these properties, but you can define them in terms of $p_{active}(c)$. Then, simplify

your expressions for these various properties in the limit where $K_I/K_A >> 1$.

N-3. Your Philosophy of Biology.

Choose to answer one of the following questions in a several paragraph discussion.

a) The history of engineering has been characterized repeatedly by a transition from enlightened empiricism to rational design. For example, the flying buttresses of European cathedrals originally did not come from a deep understanding of the quantitative principles of structural mechanics. Now, companies like Boeing design their airplanes knowing very well what the stresses and strains are like within the materials from doing finite element calculations of elasticity. Give your position on the future of bioengineering and whether you think the field is currently in the enlightened empiricism stage or the rational design stage? Will medicine become a rational design topic and do you think it should?

b) The mantra of this course is that quantitative data demands quantitative models. Explain in what sense modern biology has become quantitative and defend the mantra as a tool for understanding biological phenomena.

N-2. Defiance

In a long series of vignettes, I argued that perhaps the real "secret of life" is defiance, in keeping with the Schrödinger quote that headlines this homework. Use a paragraph to explain what my argument about defiance is and give a succinct statement of how living organisms use the elements of the periodic table to make things that are clearly qualitatively different than, say, a rock.

N-1 Your Turn. A Feeling for the Organism.

Pose an order of magnitude problem about real world biology and then make the corresponding estimate. Please take this seriously and try to build on everything we have done the entire term. Formulate a particular "I wonder" question that you find exciting and that you imagine others will find interesting as well. Then, make clear statements about what assumptions you

need to make in order to construct the relevant estimate. Once you obtain your estimate, make a rational discussion of why the values take the values they do and how you think this corresponds to what we know from data.

N. Your Turn.

In this final problem, I want you to construct a thoughtful syllabus for how you would teach a course on Physical Biology. You have ten weeks, two classes of 90 minutes each per week. Make sure to give a sense of whether your homeworks will involve computation, whether you will give an exam, etc. But more importantly, what is the content? What do you want students to leave the course with? What are the top five skills you want them to leave with? What are the top five insights you want them to leave with? You have 20 lectures, so I want to hear what each and every lecture will be about. How much powerpoint? How many calculations on the blackboard. For this problem, send a pdf (nothing but pdf accepted and zero credit for stuff like powerpoint or word files) to the TAs and Rob.