1 A Feeling for the Numbers in Biology: Your Turn

Over the semester, we will do many estimates about each biological phenomenon we address. To cement these skills, you will prepare two short estimates. Your first estimate will consist of a written vignette in the style of *Cell Biology by the Numbers*. You will present your second estimate in a 5-minute presentation at the end of the semester. Some examples of interesting estimates are

- How many proteins are in a viral capsid?
- What is the energy cost to a host cell in order to create a new virus after it has been infected?
- What is the cell-to-cell variability in the number of copies of the *lacZ* gene?
- What is the largest osmotic shock a cell can suffer without bursting?

Your first task is to write a short paragraph describing the estimate you’re interested in writing a vignette about. Note that the objective at this point is not for you to have a finished estimate, but to have an outline of the calculation you plan to do so that we can give you feedback. Send this paragraph as an email to Hernan, Gabriella and Liz by 2/14.

**Bacterial growth revisited**

2 Growth Curves and the Logistic Equation

In class, we discussed the exponential growth equation. This equation has been the basis for the study of microbiology for years (read, for example, F. Neidhardt, *Bacterial Growth: Constant Obsession with dN/dt*, *J of Bacteriology* 181:7405 (1999) provided on the course
If the number of cells is given by \( N \) and the growth rate is \( r \), then this equation takes the form
\[
\frac{dN}{dt} = rN.
\]  
(1)

We solved this equation in a variety of ways, both numerically and analytically, and found a solution given by
\[
N(t) = N_0 e^{rt},
\]  
(2)
where \( N_0 \) is the number of cells at \( t = 0 \).

(a) Of course, the solution shown above cannot be correct forever. For fast-growing \( E. \ coli \) estimate how long it would take for a single cell to produce enough progeny to cover the whole surface of the Earth.

A more realistic scenario is to account for the fact that, sooner or later, bacteria will run out of resources and halt their growth. For example, a liquid bacterial culture will saturate at a density of about \( 10^9 \) cells/ml. To account for these limited resources, we introduce a growth rate that depends on the number of cells, \( r_{\text{new}} \)
\[
r_{\text{new}} = r \left( 1 - \frac{N}{K} \right),
\]  
(3)
where \( K \) represents the maximum population size. Note that when \( N \) is very small compared to \( K \), \( r_{\text{new}} = r \) and growth is exponential. However, as \( N \) approaches \( K \) the growth rate will decrease. Thus, we get the so-called logistic equation
\[
\frac{dN}{dt} = r_{\text{new}} N = r N \left( 1 - \frac{N}{K} \right),
\]  
(4)

(b) What is the number of cells at which there is no growth and the population reaches steady state? Justify how you impose steady state on the logistic equation in order to figure out this number.

(c) In class, we wrote Matlab code to solve Equation 1 numerically. Modify your code to now solve the logistic equation. For reasonable choices of \( r \) and \( K \), plot number of cells as a function of time for both exponential and logistic growth.

(d) Feel free to look at section “Computational Exploration: Growth Curves and the Logistic Equation” on page 103 of PBoC2.

### Diffusion

#### 3 Diffusion times

Make a log-log plot of the diffusion time (in seconds) as a function of length (in \( \mu m \)) using Matlab. 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, \( E. \ coli \), and an eukaryotic nucleus.

#### 4 Random walks and biological polymers
Physicists know how to solve just a handful of problems. Fortunately, many dissimilar phenomena in physics and biology alike can be mapped onto such problems for which we know a solution. Here, we explore the mathematical connection between diffusion and the spatial arrangement of polymers such as DNA, actin, and microtubules.

(a) Read the introduction to Section 8.2 of PBoC (“Random Walk Models of Macromolecules View Them as Rigid Segments Connected by Hinges”) to learn more about how polymers can be thought of as chains of connected rigid segments. Pay close attention to Figures 8.1 and 8.2. Here, the Kuhn length $a$ is defined as the length of the segments. Look up the Kuhn length for DNA, actin, and microtubules in order to get a feeling for these polymers. Note that you might find reference to the persistence length $\xi_p = a/2$ instead of the Kuhn length.

(b) Now, think of a polymer chain of $N$ segments in 1D. As shown in Figure 8.3 of PBoC each segment can either be pointing to the right or to the left. Given $n_R$ and $n_L$ segments pointing to the right and left, respectively, the position of the end of the chain is given by $L = (n_R - n_L) a$. Map this problem onto the diffusion problem we solved in class by noting that each segment can be randomly pointing to the left or right. In particular, calculate $\langle n_R - n_L \rangle$ and $\langle (n_R - n_L)^2 \rangle$ and show that the size of the polymer is given by

$$\text{size} \approx \sqrt{\langle L^2 \rangle} = a\sqrt{N} \quad (5)$$

by repeating the derivation we did in class.

(c) Use the derived formula to estimate the genome length (in \(\mu\text{m}\) and bp) of the bacteriophage T2 shown in Figure 1.16 of PBoC and of the E. coli in Figure 8.5 of PBoC. All relevant figures from PBoC can also be found in Figure and below.
Figure 8.1: Random walk model of a polymer. Schematic representation of (A) a one-dimensional random walk and (B) a three-dimensional random walk as an arrangement of linked segments of length $a$.

Figure 8.2: DNA as a random walk. (A) Structure of DNA on a surface as seen experimentally using atomic-force microscopy. (B) Representation of the DNA on a surface as a random walk. (Adapted from P. A. Wiggins et al., Nat. Nanotech. 1:37, 2006.)

Figure 8.5: Illustration of the spatial extent of a bacterial genome that has escaped the bacterial cell. The expanded region in the figure shows a small segment of the DNA and has a series of arrows on the DNA, each of which has a length equal to the persistence length in order to give a sense of the scale over which the DNA is stiff. (Adapted from an original by Ruth Kavenoff.)

Figure 1.16: Electron microscopy image of a bacteriophage genome that has escaped its capsid. Simple arguments from polymer physics can be used to estimate the genomic size of the DNA by examining the physical size of the randomly spread DNA. We will perform these kinds of calculations in Chapter 8. (Adapted from G. Stent, Molecular Biology of Bacterial Viruses. W. H. Freeman, 1963.)

Figure 1: Figures 8.1, 8.2, 8.5 and 1.16 from PBoC.
Figure 2: Figure 8.3 from PBoC.

Figure 8.3: Random walk configurations. The schematic shows all of the allowed conformations of a polymer made up of three segments ($2^3 = 8$ conformations) and their corresponding degeneracies.