Quantitative principles in biological systems
Problem Set #1
Due by noon on 2025/03/06

1. Chemotaxis:
    a. A "post-00" *E. coli* decides to lie flat – rather than swim for food, it goes with the flow and waits for nutrient molecules to diffuse over.
        i. The bacterium is looking for a molecule of iron. Suppose iron is present at a concentration of 0.5 nM. How long would it take to swim to the nearest molecule? How long would it take for a molecule to diffuse over?
        ii. The bacterium needs ~10^{10} atoms of nitrogen to replicate itself. Suppose nitrogen is present at a concentration of 10 nM. How much nitrogen will the bacterium get in a day of lying flat?
        iii. *Prochlorococcus* cells are only 0.5 nm in length and do not swim. Can they get enough nitrogen to replicate within a day?
    b. A fun experiment is to tether a cell by one of its flagellum motors, which causes the whole cell rather than the flagellum to rotate. The file `omega.txt`[1] contains a time series of the angular velocity from such an experiment. Positive and negative values indicate clockwise and counterclockwise rotations, respectively. Measurements are taken sixty times per second.
        i. Is the data consistent with a Poisson process?
        ii. Is there anything about the data that is different from typical properties of *E. coli* chemotaxis? How might this difference change chemotactic behavior?

2. Cell cycle regulation:
    a. In a constant environment, an *E. coli* cell can grow and divide for more than one hundred generations, implying that there must be some regulation to maintain homeostasis against biological noise. This process can be observed using microfluidic channels to trap and track a single cell over time. The file `sizes.txt`[2] contains a time series of cell length from such an experiment.
        i. Plot cell size across time. You will be able to clearly identify cell divisions.
        ii. Plot cell size at birth $v_b(T)$ for generation T across generations. Would you describe $v_b(T)$ as a random walk?
        iii. How does $v_b(T+1)$ depend on $v_b(T)$? Are they correlated?
    b. Consider the stochastic map $v_b(T+1) = s v_b(T) + v_0 + \xi_T$, where s and v_0 are some constants. ξ_T is a random variable – its value is independently drawn at each T from a normal distribution with mean zero and standard deviation σ_v.
        i. Simulate the stochastic map with $s = 1$ and $v_0 = 0$. How well does this set of parameters capture the data?
        ii. Use the result from (a) to determine the values of s, v_0, and σ_v. How well does your stochastic map describe $v_b(t)$?
        iii. What do your results tell us about how cells maintain a homeostatic size?
    c. How might cells implement the regulation strategies that we explored in (b)? For example, do cells measure time or size?
        i. Assume that cell size grows exponentially at a constant rate λ and divides precisely in half. If cells measure time to grow for a constant time from birth to division, then what is the resulting map between $v_b(T+1)$ and $v_b(T)$?

3. Adaptation / Cooperativity:
    a. Simulate either the simple model for adaptation or the MWC model for cooperativity introduced in class. Set reasonable parameter values and explain your choice. In what parameter regimes do you observe adaptation or cooperativity?
    b. What questions do you still have about adaptation / cooperativity in chemotaxis? Pose a quantitative question, as precisely as you can. Design an experiment and analysis to test your hypotheses.

[1] From Bialek's *Biophysics*.
[2] Tanouchi et al. *Sci Data* (2017).