Quantitative principles in biological systems
Problem Set #1
Due by noon on 2026/03/26

1. Chemotaxis:
   Based on Weitz and Bialek.
   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 um in length and do not swim. Can they get enough nitrogen to replicate within a day? [Hint: There might be more factors at play than at first glance.]
   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? Is the process memoryless? Do you need to calculate the correlations to check that the events are independent?
      ii. Is there anything about the data that is different from typical properties of *E. coli* chemotaxis? How might this difference change chemotactic behavior?
   c. Simulate a Poisson process.
      i. Consider a time window of length T and divide this window into many small bins of size dt. In each bin, generate a random number to determine if an event occurs, such that the average number of events per second is 10. Check that you have implemented a Poisson process by comparing your numerical simulations to analytical expressions.
      ii. Next, choose N random times in the window T uniformly, and examine the same statistics as above. Is this process still Poisson? Why or why not?
   d. A "robot" *E. coli* is created to deliver a drug inside a tumor in a host. Suppose the tumor secretes a known compound that forms an interstitial concentration gradient that is somewhat rugged. Can the mechanism of chemotaxis, as implemented in wildtype *E. coli*, successfully guide the robot bacterium to the tumor? Make a rough guess using order of magnitude analyses and scaling arguments.

2. Cell cycle regulation:
   a. In a constant environment, an *E. coli* cell can grow and divide for more than one hundred generations, suggesting 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?
      iv. Does the distribution of cell sizes follow Benford's law? Why or why not?
   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 $v_b(t)$?

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

    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, at a phenomenological level, 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. Cooperativity:
    a. Simulate the MWC model for cooperativity. Set reasonable parameter values and explain your choice. In what parameter regimes do you observe cooperativity? Check that intermediate states are depleted.
    b. What have you learned from our discussion of bacterial chemotaxis? Try to apply some of these learnings to your own research, e.g. by asking a question inspired by our discussion but about the biological system you are working on.