Introduction to quantitative biology
Problem Set #3
Due by 2026/10/23

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?
    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/negative values indicate CW/CCW rotations. 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 the data consistent with typical properties of *E. coli* chemotaxis?
    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.
        ii. Next, choose N random times in the window T uniformly, and examine the same statistics as above. Check this simulation as well.
    d. Read this recent paper [https://www.nature.com/articles/s41567-025-03111-4] before class on 10/20. The paper quantifies and compares the information that *E. coli* extracts via its chemosensing circuit to the theoretical physical limit from particle encounters.
        i. Simulate the signal trajectory $s(t)$ and the history of particle encounters $r(t)$ in a static gradient without tumble response: as described in the text, both quantities can be written as stochastic differential equations with known parameters. Analyze and make sense of the results of your simulations. What are the correlations between $s(t)$ and $r(t-\tau)$ for different lag τ?
        ii. Bonus: Predict the current signal $s(t)$ given all past encounters $\{r(t')|t' < t\}$. Use any method you can think of to make this prediction, but whatever method, it should ideally be able to generalize across random instances.
    e. A "robot" *E. coli* is created to deliver a drug into 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?

2. Cooperativity: Simulate the MWC model for cooperativity. Pay attention to what it means to simulate. Explain your choice for parameters. In what parameter regimes do you observe cooperativity? What happens to intermediate states in and out of these regimes?

[1] From Bialek's *Biophysics*.