1. Retinal conformational change.

Retinal is a light-sensitive molecule embedded in the membrane of our eye's photoreceptors. Retinal conformational change converts light into metabolic energy, and is the chemical bases for animal vision. In class this week, we discussed a simple mathematical model for the dynamics of the two forms of retinal pictured below. In this model, we assume that molecules transition from state A to state B at an average rate of k. The average number of molecules in species A is governed by the equation

$$\frac{\mathrm{d}c_A}{\mathrm{d}t} = -kc_A.$$

With the initial condition $c_A(t = 0) = c_0$, we obtained the solution

$$c_A(t) = c_0 e^{-kt},$$

illustrating that the number of molecules in state A will decay exponentially with time.

a. Obtain a corresponding expression for the population of molecules in state B as a function of time, $c_B(t)$.

   We begin with an equation describing the average number of molecules in state B:

$$\frac{\mathrm{d}c_B}{\mathrm{d}t} = kc_B$$

   where k is the average rate of molecules transitioning from state A to state B as defined above. We also define the initial condition $c_B(t = 0) = (1 - c_0)$. We can re-arrange this differential equation in the typical mathematician-angering fashion to

$$c_B^{-1}\mathrm{d}c_B = k\mathrm{d}t,$$

   which integrates to

$$\ln(c_B) - \ln(1 - c_0) = kt,$$

   and can be expressed as

$$c_B = (1 - c_0)e^{kt}.$$

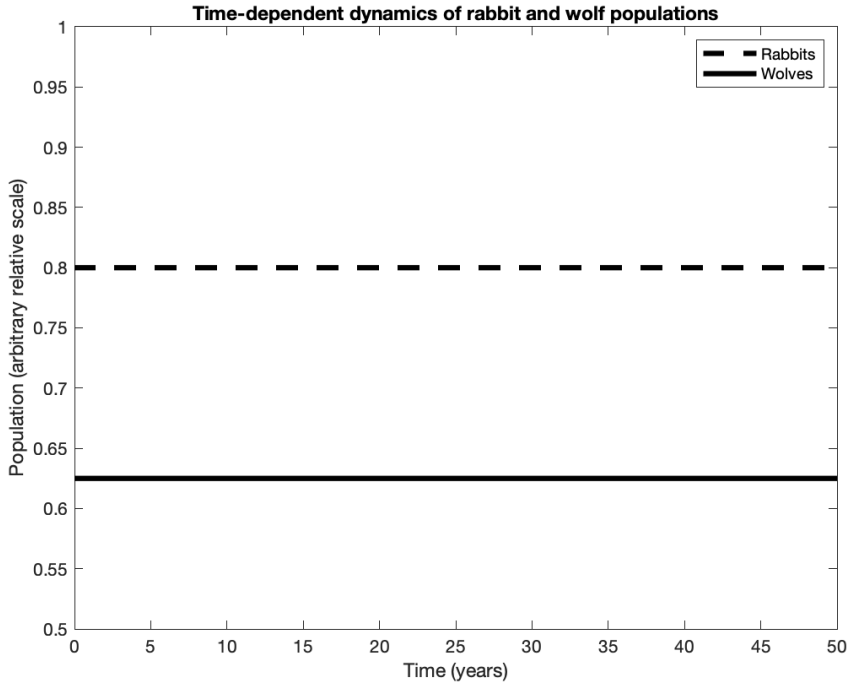
2. Lotka-Volterra model for population dynamics.

The Lotka-Volterra model discussed in class is comprised of a set of coupled differential equations that govern the time dynamics of a 'rabbit' population, $R(t)$, and a 'wolf' population $W(t)$. As we saw with our simulations of this model during class, most combinations of parameters yield coupled oscillations in the rabbit and wolf populations. In this problem, we will explore the conditions for steady state, in which the populations do not oscillate. One condition for steady state that we discussed in class was if both the rabbit and wolf populations are zero, $(R = 0, W = 0)$: If there are no wolves and rabbits, nothing happens!

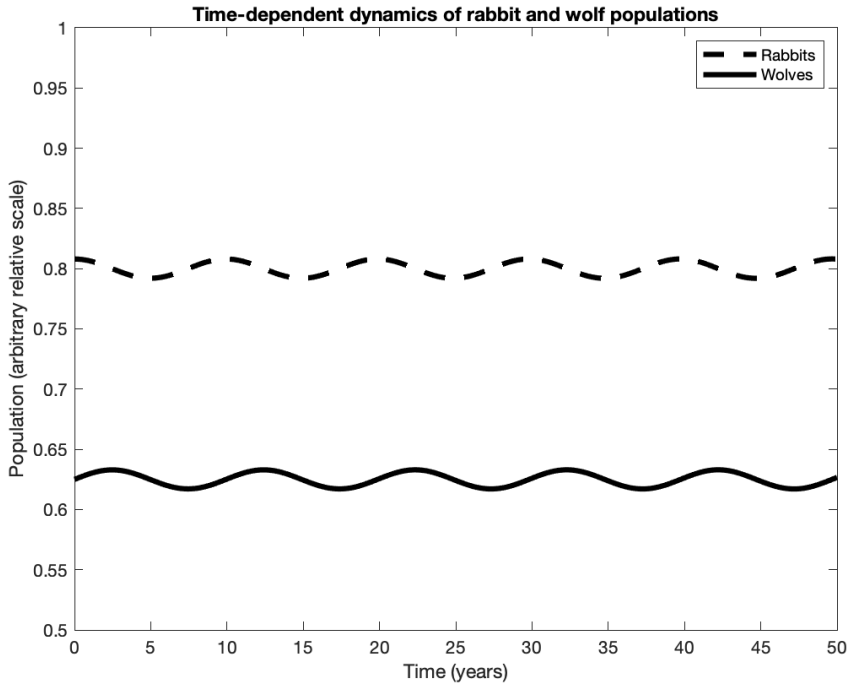
a. Determine one other combination of R and W values that produces a steady-state condition, by setting $\frac{\mathrm{d}R}{\mathrm{d}t}$ and $\frac{\mathrm{d}W}{\mathrm{d}t}$ equal to zero in the Lotka-Volterra model, and algebraically obtaining the non-zero solutions for R and W in terms of the system rate parameters (a, b, c, d).

   An infinite number of steady state solutions exist for $\left(R = \frac{a}{b}, W = \frac{d}{c}\right)$.

b. Using the simulation code from class, set the initial values of R and W to match the steady-state condition you obtained in (a.). Run The simulation to test whether the populations remain constant. Attach a sample plot.



c. Starting with the steady-state conditions, slightly increase the initial rabbit population, and run the simulation again. Does the system return to the steady state, or does it begin to oscillate? Why do you think this is the case? Attach a sample plot.



The system oscillates about the steady state situation.

3. SIR model for viral propagation.

The SIR model discussed in class is comprised of a set of coupled differential equations that govern the time-dynamics of a 'susceptible' population $S(t)$, an 'infectious' population $I(t)$, and a 'recovered' population $R(t)$. One useful application of viral models is to predict conditions under which a virus will become epidemic, that is, with a large local outbreak of infection. To investigate conditions most likely to produce prolonged outbreak, let's examine the differential equation describing the time dynamics of the infectious population:

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - \gamma I.$$

a. Mathematically solve for the condition on $S(t = 0)$ that corresponds to initial growth in infectious population:

$$\left.\frac{\mathrm{d}I}{\mathrm{d}t}\right|_{t=0} > 0,$$

and the condition on $S(t = 0)$ that corresponds to initial decay in infectious population:

$$\left.\frac{\mathrm{d}I}{\mathrm{d}t}\right|_{t=0} < 0.$$

These conditions, initial growth and initial decay of infected population, are given respectively by

$$S > \frac{\gamma}{\beta}, \qquad S < \frac{\gamma}{\beta}$$

b. Describe what your answer to (a.) tells you about the factors that determine whether a virus will produce a prolonged outbreak. Based on this prediction, what practical strategies could be used to avoid an epidemic?

The β term governs the infectivity of interactions between susceptible and infections people and the γ term governs the recovery of the infected population. Recovery rate is difficult to control but the infectivity of interactions can be managed quite effectively (as demonstrated by covid).

4. Answer these questions after reading Marshall et. al.

a. Describe what is meant by the term "flagellar length control" in this paper, and why this is an important topic of investigation in cell biology/biophysics.

Flagellar length control is the biological process that regulates the length of flagella. Flagellar length control is important to understand because it represents many complex biological processes being executed together to achieve some physically important goal; that is, because of the rate of interaction between motors and disassembly processes the flagella reaches a particular steady state length preferred by the cell.

b. What are two key assumptions of the "balance point" model?

Two key assumptions of the balance-point model are that the number of transport complexes are fixed, and the particles move at fixed velocity.

c. According to the model, how do the key assumptions described above contribute to flagellar length control?

As a consequence the rate of growth is inversely proportional to length and disassembly is constant.

d. Describe briefly at least one alternative to the balance point model mentioned in the paper.

One alternative proposed mechanism for flagella length control is a signal pathway that carries length information back to the cell and modulates the assembly rate. These competing models predict different time-scales on which the flagella would reach a steady length. As of this paper no measurement has shown clear preference for one model over another.

e. The authors used several experiments to test the balance-point model. Describe one example of an experimental result from this paper that supports the balance point model. Explain what was being measured, what was found, and how this result supports the model.

The authors observe length independence in their data, an important aspect of the balance-point model. They did so by modifying an allele of kinesin to halt transport and essentially disable assembly. They found that, as expected, the disassembly rate was independent of length.

f. The authors emphasize that their experimental strategies were specifically designed for their potential to invalidate the balance-point model. Describe one possible alternate result that could have invalidated the model.

The authors describe that finding a length dependence of disassembly rate which intersects the assembly length dependence in more than one place on some hypothetical rate vs length plot would invalidate the balance-point model. They note that length dependence which intersects at just one point could be allowed so long as assembly length dependence is stronger than disassembly length dependence.

5. Experimental testing of the balance-point model.

In this problem, you will compare theoretical predictions with data from *Marshall et. al* to test the assumptions of the balance-point model. Complete the following problems using the Matlab code you completed during class for the balance-point model, in combination with data from *Marshall et. al.* Use appropriate axes labels for all plots, and use a legend if plotting more than one data set in a figure. Include a brief caption stating parameters that were used for the plot.

a. Use the data from *Marshall et. al* to determine reasonable values for the constants A and D in the balance point model. Show how you obtained the values A and D by including any graphs you made to fit the model to the experimental data with explanation.

The balance-point model relates the elongation rate to the assembly rate A and disassembly rate D by

$$\frac{\mathrm{d}L}{\mathrm{d}t} = \frac{A}{L} - D.$$

We linearize this model by plotting the elongation rate from Figure 2E of *Marshall et. al.* on the vertical axis and $1/L$ on the horizontal axis. Then the slope of a fitted line will be the assembly rate and the intercept will the be disassembly rate. Uncertainties can be estimated by taking the standard deviation of the residuals and calculating the standard deviations of the slope and intercept[1]. Given the standard deviation of the residuals, σ_r, the standard deviation of the slope is found as

$$\sigma_A = \frac{\sigma_r}{\sqrt{\sum \left(\frac{1}{L} - \mu_{\frac{1}{L}}\right)^2}},$$

and the standard deviation of the intercept is found as

$$\sigma_D = \frac{\sigma_r}{\sqrt{\frac{1}{n} + \frac{\mu_{\frac{1}{L}}^2}{\sum \left(\frac{1}{L} - \mu_{\frac{1}{L}}\right)^2}}}.$$

[1]This should not be taken for a proper analysis, merely a fun thing to try. I have no idea if this is how uncertainties would actually be estimated from a linear fit.

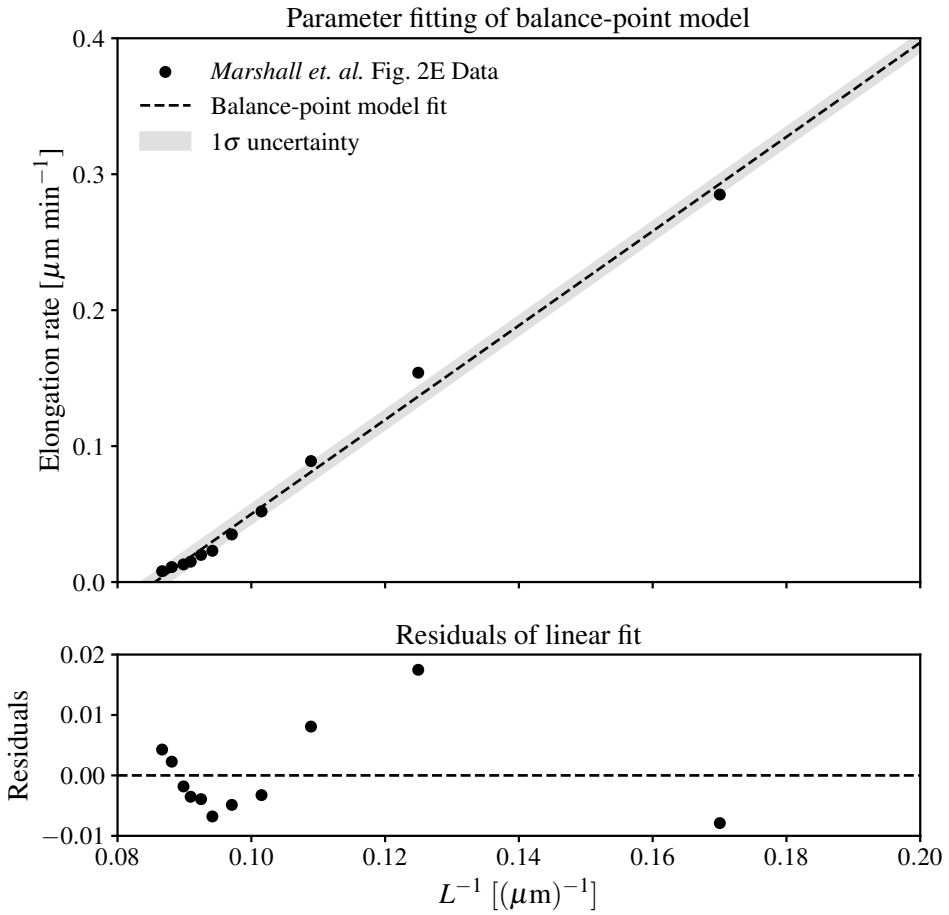


Figure 1: Linear fit of the balance-point model to data from *Marshall et. al.* Figure 2E with 1σ uncertainties estimated from residuals.

The best fit parameters for Figure 1 are found to be

$$A = 3.47 \pm 0.09 \text{ µm}^2 \text{ min}^{-1},$$
$$D = 0.30 \pm 0.01 \text{ µm min}^{-1}.$$

b. Set A and D in your Matlab code to the values you determined in part (a.). Set the initial length in your simulation to match the initial length for the green data points in Fig. 5B in *Marshall et. al.* Make a plot that shows your simulation of length vs. time for these parameters, along with the experimental data of length vs. time from Fig. 5B.

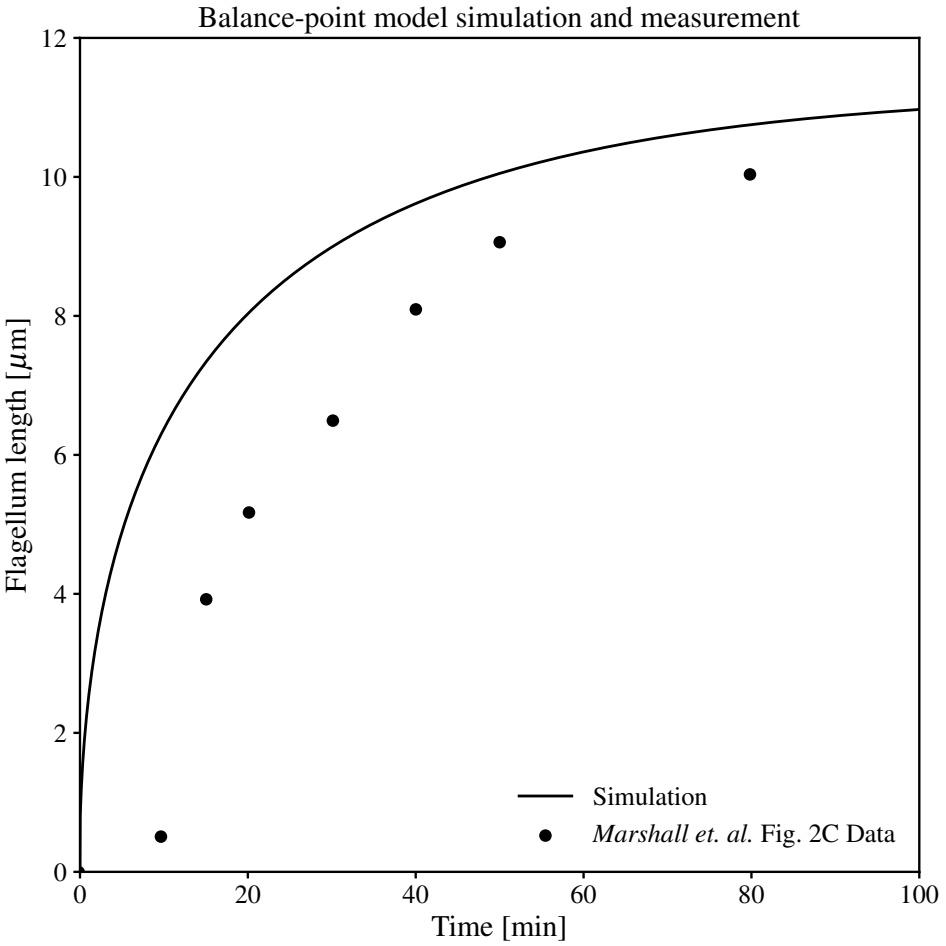


Figure 2: The simulation, with parameters found by linear fit shown in Figure 1, compared to measured data from *Marshall et. al.*

c. To what extent do your simulations agree with the experimental data in (b.)? Discuss any possible sources of disagreement between the theory and the experimental results.

The simulations show significant disagreement with experimental data as shown in Figure 2. However, the shape of the two lines shows strong agreement. The first two points show significant deviation from the exponential model which likely contributes to the overall disagreement. If the first measurement is neglected and the second point treated as the measurement made at $t = 0$ we get the relationship shown in Figure 3.

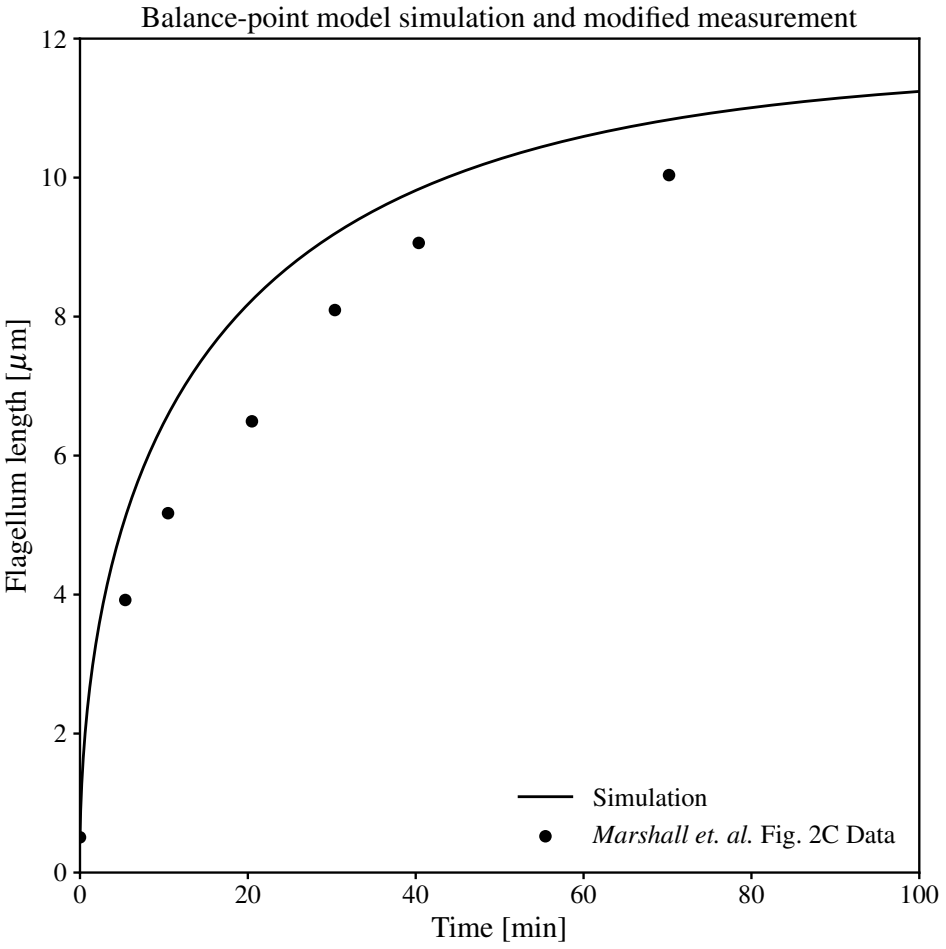


Figure 3: The simulation, with parameters found by linear fit shown in Figure 1, compared to measured data from *Marshall et. al.* The first measurement has been neglected and the time series re-indexed.

d. While keeping all other parameters constant, systematically vary the initial length of your simulated flagella. Make a plot that shows length vs. time for several values of the initial length and attach your plot here. Try some values that are below your predicted steady-state length, and some that are above it. Do your observations agree with qualitative trends in the experimental data in *Marshall et. al*?

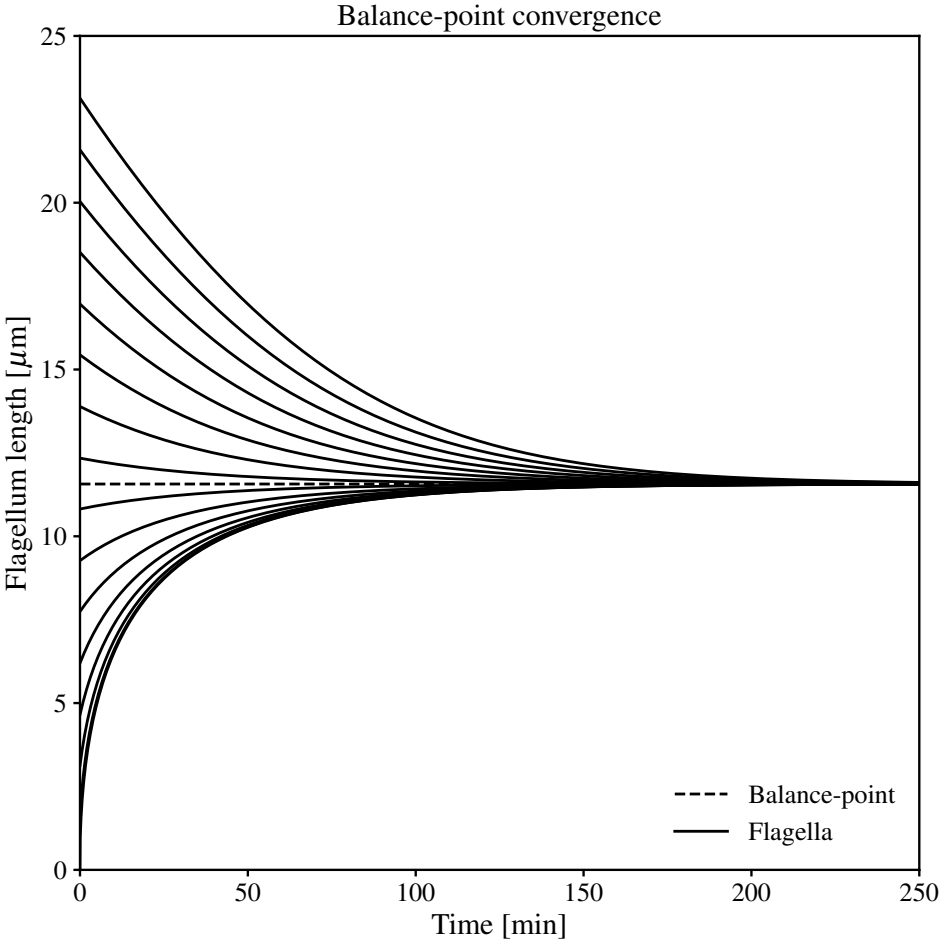


Figure 4: Many initial lengths shown to converge to the predicted steady state length given by A/D.

Shown in Figure 4 is the convergence of many different starting flagella lengths, with all other properties constant, to the steady state length predicted.