1 Testing the French Flag model

NOTE: You need to download the Bicoid data set again. The one you used in class is outdated. Get the new data set from this link, or from “Bicoid dosage full data set” corresponding to class on 2/28 on the course website.

In class we discussed the French Flag model of positional information in the context of the development of the cephalic furrow in *Drosophila* embryos. Specifically, we posited that Bicoid concentration dictates the position of the cephalic furrow. To test this model, we invoked the experiment by Liu *et al.*, where they measured cephalic furrow position as a function of different dosages of the *bicoid* gene in embryos. An exponential gradient of Bicoid is described by

\[ Bcd(x, \lambda, \alpha, Bcd_0) = Bcd_0 \alpha e^{-x/\lambda}, \]

(1)

where \(x\) is the position along the embryo, \(Bcd_0\) is the Bicoid concentration at \(x = 0\), \(\lambda\) is the decay constant of the gradient and \(\alpha\) is the Bicoid dosage, with \(\alpha = 1\) corresponding to the wild-type. We predicted that, given a position of the cephalic furrow in the wild-type \(x_{CF}\), if the dosage of Bicoid is changed the new cephalic furrow will be located at

\[ x_{new} = \lambda \ln \alpha + x_{CF}, \]

(2)

where \(x_{new}\) is the position of the cephalic furrow under this new Bicoid dosage. We then went on to test our theoretical prediction by analyzing the position of the cephalic furrow (in fraction of embryo length) in a sample image of an embryo with 0.52x Bicoid Dosage \((\alpha = 0.52)\) using our Matlab code (available on the course website).

(a) Modify the code we wrote in class to analyze three images for the Bicoid wild-type data set \((1.0x)\) in order to determine the average \(x_{CF}\). Given the measurement of \(\lambda = 0.191\) by Liu *et al.*, plot the prediction for the new cephalic furrow position as a function of the Bicoid...
dosage on a linear-log plot (linear y-axis vs. log x-axis). Your prediction should appear as a line on these axes. Make sure to indicate which embryos of the data set you analyzed.

(b) Now use the same code to analyze three embryos for each mutant dosage (0.52x, 1.57x, and 2.34x). Plot this data on top of the prediction (your prediction should appear as a line and your analysis results should be points). You can plot each data point independently or plot the average cephalic furrow position for each dosage. Make sure to indicate which embryos of the data set you analyzed.

(c) Comment on how well your prediction matches the data. What could be going on? You might want to read the article by Jeremy Gunawardena on our “pathetic thinking” provided on the course website.

Regulatory biology

2 Protein-mRNA ratio

In this problem we go beyond the calculation on mRNA production we did in class, and think about how transcription and translation shape the protein-to-mRNA ratio inside cells.

(a) In class, we described the temporal evolution of the number of mRNA molecules using the equation

\[ m(t + \Delta t) = m(t) + r_m \Delta t - \gamma_m m(t)\Delta t. \]  

(3)

Here, \( m(t) \) is the number of mRNA at time \( t \), \( r_m \) is the rate of mRNA production, and \( \gamma_m \) is the mRNA decay rate. Write the corresponding equation for the number of protein molecules given a rate of protein production per mRNA of \( r_p \) and a protein decay rate \( \gamma_p \). Make sure to incorporate the fact that the number of mRNA molecules present will determine how many proteins are produced in a time interval \( \Delta t \).

(b) Calculate the ratio of protein to mRNA in steady state, \( p_{SS}/m_{SS} \) and show that it is given by \( r_p/\gamma_p \). Find typical values for the various model parameters in \( E. coli \) and estimate the ratio of proteins to mRNA molecules. How do your numbers compare to those measured in Figure 3C of Taniguchi et al., which is provided on the course website?

3 Measuring Bicoid translation

Using flies with different dosages of Bicoid-GFP, Petkova et al. measured the relation between the number of \textit{bicoid} mRNA molecules deposited by the mother, and the resulting number of Bicoid proteins. Read their paper (available on the course website) and make sure you understand how their Figure 3 is generated.

In the previous problem, you calculated the protein-mRNA ratio in steady state. Assuming that Bicoid-GFP is in steady state, use Figure 3 from Petkova et al. to estimate the ratio \( r_p/\gamma_p \). Use the value for the degradation rate obtained by Drocco et al. discussed in Homework 6 in order to calculate \( r_p \).
4 Phase diagram for the logistic equation

In Homework 3, we solved the logistic equation numerically. This equation can describe the saturation of a bacterial culture by accounting for a limited food supply

\[ \frac{dN}{dt} = rN \left( 1 - \frac{N}{K} \right), \]  \hspace{1cm} (4)

where \( N \) is the number of cells, \( r \) is the growth rate, and \( K \) is the carrying capacity or maximum population size. Note that this equation can also be written as

\[ \frac{dN}{dt} = rN - \frac{rN^2}{K}. \]  \hspace{1cm} (5)

Here, we can identify a “cell production” term and “cell destruction” term.

Like we did for the case of the constitutive promoter, plot a phase diagram where both production and destruction terms are plotted. Use this plot to graphically show that there are two stable points at which the production and destruction are balanced out.