Introduction to Biological Physics

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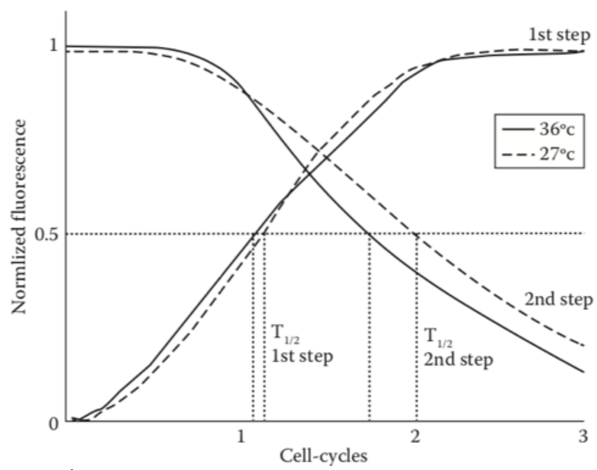
Exercise 1.

1. *A change in production rate.* A gene Y with simple regulation is produced at a constant rate β_1. The production rate suddenly shifts to a different rate β_2.
   a. Calculate and plot the gene product concentration Y(t).
   b. What is the response time (time to reach halfway between the steady states)?

2. *Cascades.* Consider a cascade of three activators, X → Y → Z. Protein X is initially present in the cell in its inactive from. The input signal of X, S_x, appears at time t = 0. As a result, X rapidly becomes active and binds the promoter of gene Y, so that protein Y starts to be produced at rate β. When Y levels exceed a threshold K_y, gene Z begins to be transcribed. All proteins have the same degradation/dilution rate α. What is the concentration of protein Z as a function of time? What is its response time with respect to the time of addition of S_x? What about a cascade of three repressors? Compare your solution to the experiments shown in the figure.



1 Rosenfeld and Alon, J. Mol. Biol. (2003) 329, 645–654

3. *Fan-out.* Transcription factor X regulates two genes, Y_1 and Y_2. Draw the resulting network, termed a fan-out with two target genes.The activation thresholds for these genes are K_1 and K_2. The activator X begins to be produced at time t = 0 at rate β. Its signal is degraded/diluted at rate α, and its signal S_x is present throughout. What are the times at which the gene products, the stable proteins Y_1 and Y_2, reach halfway to their maximal expression? Design a fan-out with three genes in which the genes are activated with equal temporal spacing, that is where they activated at times t_1, t_2, and t_3 such that $t_3 - t_2 = t_2 - t_1$.

4. *Positive feedback*. What is the effect of positive autoregulation on the response time? Use as a model the following linear equation:

   dX/dt= $\beta + \beta_1 X - \alpha X$

   Explain each term and solve for the response time. When might such a design be biologically useful? What happens when $\beta_1 > \alpha$?