

Problem Set 6

- You may use your course materials and/or any literature resources to formulate your solutions.
- Homework should be submitted electronically to the teaching assistant. Each collaborating team member name should be listed on the first page of the submitted homework.
- Problem Set 6 is due on **Thursday, April 13th, 2021** by **11:59 PM**.

Problem 1: Stability analysis of Collins toggle switch. (Gardner, T. S., C. R. Cantor, and J. J. Collins, 2000, Nature **403**, 520.)

The behavior of the toggle switch and the conditions of bistability can be understood using the following dimensionless model for the network:

$$\frac{du}{dt} = \frac{\alpha}{1+v^n} - u = f(u,v) \qquad (1)$$

$$\frac{dv}{dt} = \frac{\alpha}{1+u^n} - v = g(u,v) \qquad (2)$$

a) Identify each variable or parameter in the model as one of the following:

i. Concentration of a repressor of gene expression (there are two repressors)
ii. Max rate of synthesis of repressor
iii. Cooperativity of repression
iv. Degradation rate constant for repressor

b) Plot the nullclines (lines for which f(u,v) = 0 or g(u,v) = 0) for the system for $\alpha = 10$ and $n = 1$ **AND** 2. How many steady-state solutions exist for each case? Comment on the influence of the degree of cooperativity.

c) To gain intuition for this system, generate a phase portrait for the system and include the nullclines (separately or on the same graph). On your graph of the nullclines, identify the steady states and assess the character of each steady state (stable or unstable?).

d) Build the Jacobian for the system (for arbitrary α and n) at its steady states and write down the stability criterion. (You can leave your expression in terms of u_s and v_s, the concentrations of u and v at steady-state.) Use the stability criterion to explain the influence of the degree of cooperativity and the rate of synthesis on the stability of the center steady state (i.e., the one with $u = v$).

e) Find the numerical eigenvalues for the center steady state for $\alpha = 10$ and $n = 1$ and 2. How does the change in cooperativity affect the system?

Problem 2: Electrophoretic separation of mutant and wild-type protein.

Complete the calculations for the problem that we discussed in class on 5/04. You wish to separate a mutant protein with net charge of +1e from a native protein with a net charge of +2e. With a field of, E = 100 V/cm, how long will it take to separate native from mutant protein by 1 mm in water (viscosity = 10^{-3} kg/m-s)? Assume that the proteins are each spherical (radius = 2 nm) and diffusion is negligible.

Problem 3: Thermodynamics of cell-cell adhesion. (Bell, G.I., Dembo, M., and Bongrand, P., 1984, Biophys J. 45: 1051-64)

a) For two interacting cells with parameters listed in Table 1 (Best estimate), calculate the critical glycocalyx compressibility coefficient, γ^*, above which cells cross from Region III to Region II on the phase diagram presented in Figure 5. Refer to the section, "Minimization of Free Energy," on pages 1054-1055 for a description of the phase boundaries.

b) Compute and plot the number of bonds and cell-cell separation distance, S, at equilibrium for $\gamma = 0$ to $\gamma = \gamma^*$.

c) How do your results change for cells with a glycocalyx thickness coefficient of 2.0×10^{-6} cm?

d) In Region II of the phase diagram, how does S depend on γ at equilibrium?