

Homework # 4

1. In a biological system with feedback control, u_1, u_2, \dots, u_n are the n population sizes which are governed by

$$\begin{aligned}\frac{du_1}{dt} &= f(u_n) - k_1 u_1, \\ \frac{du_j}{dt} &= u_{j-1} - k_j u_j, j = 2, 3, \dots, n;\end{aligned}$$

in which the functional form for the feedback regulation of the n^{th} species on the 1^{st} species is given as

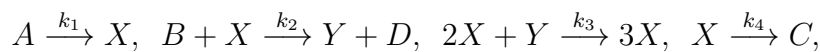
$$(i) f(u) = \frac{a + u^m}{1 + u^m}, \quad (ii) f(u) = \frac{1}{1 + u^m},$$

where constants $a, m > 0$.

(a) Determine which of these represents a positive feedback control and which a negative feedback control.

(b) Determine the steady states and show that with positive feedback multi-stability is possible while if $f(u)$ represents negative feedback there is only a unique steady state.

2. Consider the system of nonlinear chemical reaction



where k s are the rate constants, and the reactant concentrations of chemical species A and B are kept at constant values of a and b , respectively, for all time.

(a) Write the governing differential equation system, according to the *law of mass action*, for the concentrations of X and Y ; nondimensionalize the equation so that they becomes

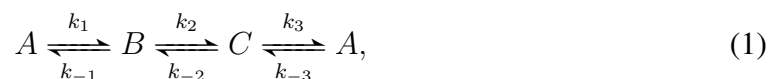
$$\frac{du}{d\tau} = 1 - (\beta + 1)u + \alpha u^2 v, \quad \frac{dv}{d\tau} = \beta u - \alpha u^2 v,$$

in which u and v are the corresponding variables for the concentrations of X and Y , $\tau = k_4 t$, $\alpha = (k_1 a)^2 k_3 / k_4^3$, and $\beta = k_2 b / k_4$.

(b) Determine the positive steady state and show that there is a bifurcation value $\beta_c = 1 + \alpha$ at which the steady state becomes unstable in a Hopf bifurcation way.

(c) Show that in the vicinity of $\beta = \beta_c$, the limit cycle has a period of $2\pi/\sqrt{\alpha}$.

3. The 3-state Markov system,



has been widely used in biochemistry to model the conformational changes of a single protein undergoing through its three different states A , B , and C . For example, A is non-active, B is partially active, and C is fully active.

(a) The probabilities for the states, $\vec{p} = (p_A, p_B, p_C)$, satisfies a differential equation

$$\frac{d}{dt}\vec{p}(t) = \vec{p}(t)\mathbf{Q},$$

where \mathbf{Q} is a 3×3 matrix. (See Sec. 6.2.5.1 of Qian's book chapter *Mathematicothermodynamics*.) Write the \mathbf{Q} out in terms of the k 's. Show that the sum of each and every row is zero. Discuss in probabilistic terms, what is the meaning of this result?

(b) Compute the steady state probabilities p_A^{ss} , p_B^{ss} , and p_C^{ss} , and show that, in the steady state, the net (probabilistic) flux from state A to B ,

$$J_{A \rightarrow B}^{ss} = k_1 p_A^{ss} - k_{-1} p_B^{ss},$$

is the same as the net flux from state $B \rightarrow$ state C , and also the net flux from $C \rightarrow A$. Since they are all the same, it is called the steady state flux J^{ss} of the biochemical reaction cycle in (1).

(c) What is the condition, in terms of all the k 's, for $J^{ss} = 0$?

Additional Problems for AMATH 523

4. Consider the reaction system with two biochemical species X and Y which degrade linearly, with rate constants b and d respectively, and X activates the synthesis of Y and Y activates the synthesis of X according to

$$\begin{aligned}\frac{dx(t)}{dt} &= \frac{ay^2}{k^2 + y^2} - bx, \\ \frac{dy(t)}{dt} &= \frac{cx^2}{h^2 + x^2} - dy,\end{aligned}$$

where $x(t)$, $y(t)$ are the concentrations of X , Y at time t , and a , b , c , d , k and h are positive constants. Nondimensionalize the system to reduce the relevant number of parameters. Show that there can be two or zero positive steady states. [Hint: You might need to use Descartes' rule of signs, which can be found from online wikipedia.]

Studying simple mathematical models like this was an active area of biological research. For examples see

<https://doi.org/10.1103/PhysRevLett.84.5447>

<https://doi.org/10.1073/pnas.110057697>