

Homework # 5

1. In a feedback control system governed by

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

the feedback function 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. 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. 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?

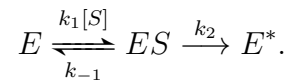
(b) Compute the steady state probabilities p_A^{ss} , p_B^{ss} , and p_C^{ss} , and show that, in the steady state, the net (probabilistic) flux from state A to B ,

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

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 $J^{ss} = 0$?

3. Consider single enzyme kinetics in which an E combines with an substrate molecule S to form ES , and then drops a product molecule P and returns E^* :



So the probability for the three states of the enzyme E , ES , and E^* are

$$\begin{aligned}\frac{dP_E(t)}{dt} &= -k_1[S]P_E + k_{-1}P_{ES}, \\ \frac{dP_{ES}(t)}{dt} &= k_1[S]P_E - (k_{-1} + k_2)P_{ES}, \\ \frac{dP_{E^*}(t)}{dt} &= k_2P_{ES}.\end{aligned}$$

(a) What is the probability distribution for the “random time” T from state E to state E^*

$$F_T(t) = \Pr \{T \leq t\} = P_{E^*}(t),$$

and the probability density function

$$f_T(t) = \frac{\Pr \{t < T \leq t + dt\}}{dt} = \frac{d}{dt}F_T(t)?$$

(b) What is the mean time according to the distribution?