Homework # 5

1. In a feedback control system governed by

$$\begin{aligned}\frac{\mathrm{d}u_1}{\mathrm{d}t} &= f(u_n) - k_1 u_1,\\ \frac{\mathrm{d}u_j}{\mathrm{d}t} &= u_{j-1} - k_j u_j, j = 2, 3, \cdots, n;\end{aligned}$$

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,

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} A, \qquad (1)$$

has been widely used in biochemistry to model the conformational changes of a single protein undergoing though 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,

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

is the same as the net flux from state $B \to$ state C, and also the net flux from $C \to A$. 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^*:

$$E \underset{k_{-1}}{\overset{k_1[S]}{\rightleftharpoons}} ES \xrightarrow{k_2} E^*.$$

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

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

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

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

and the probability density function

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

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