1. Consider a reversible enzyme reaction

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} P + E$$

in which there is only one enzyme molecule, and the concentrations for substrate S and product P are kept at constant c_S and c_P. The enzyme can go either forward and complete a cycle, turning an S to a P:

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} P + E,$$

or backward and complete a cycle, turning a P to an S:

$$P + E \underset{k_2}{\overset{k_{-2}}{\rightleftharpoons}} ES \xrightarrow{k_{-1}} S + E.$$

(a) With constant c_S and c_P and treating E and ES as two states of the enzyme, write the transition probability matrix for the 2-state Markov system.

(b) Compute the steady state probabilities of states E and ES, as well as the net forward flux of the single enzyme in steady state.

2. The enzyme kinetics shown below is known as reversible Michaelis-Menten-Briggs-Haldane mechanism:

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} P + E.$$

Let us consider that there is one enzyme molecule, and constant concetrations for S and P, at c_S and c_P. Again, as discussed in Problem 1, the enzyme can either cycle forward or backward. To compute the times and probabilities of the two types of cycles, one considers the following "extended scheme"

$$E^- \xleftarrow{k_{-1}} ES' \underset{k_{-2}c_P}{\overset{k_2}{\rightleftharpoons}} E \underset{k_{-1}}{\overset{k_1 c_S}{\rightleftharpoons}} ES \xrightarrow{k_2} E^+,$$

in which we denote ES' as the enzyme-product complex formed by the enzyme binds a product.

Compute the probability distributions for the forward and backward cycle times, as well as the probability of cycling forward p^+ and backward $p^- = 1 - p^+$.

3. Consider the 3-state Markov system

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} A.$$

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

$$\frac{d}{dt}\mathbf{p} = \mathbf{p}\mathbf{Q},$$

where $\mathbf{Q}$ is a 3×3 matrix. Write the $\mathbf{Q}$ out in terms of the k's.

(b) Compute the steady state probabilities p_A^{ss}, p_B^{ss}, and p_C^{ss}, and the steady state flux J^{ss}.

(c) What is the condition for $J^{ss} = 0$?