Further Mathematical Biology: Problem Sheet 1

Michaelmas Term 2020

Question 1.

Use the Law of Mass Action to write ordinary differential equation models for the following reaction schemes:

(a)

$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} D + B; \tag{1}$$

(b)

$$A + 2B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} D + B; \tag{2}$$

(c)

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

Question 2.

Consider the reaction

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SE = C \xrightarrow{k_2} P + E, \tag{4}$$

where S, E, C and P are substrate, enzyme, complex and product, respectively, and k_1, k_{-1} and k_2 are positive rate constants.

(a) Use the Law of Mass Action, which you should state, to write down four equations for the concentrations s, e, c and p of S, E, C and P, respectively.

(b) Initially $s = s_0$, $e = e_0$, $c = 0$ and $p = 0$, where s_0 and e_0 are constant. Show that the total amount of enzyme is conserved.

(c) Hence show that the system may be reduced to the following pair of equations

$$\frac{\mathrm{d}s}{\mathrm{d}t} = -k_1 e_0 s + (k_1 s + k_{-1})c, \tag{5}$$

$$\frac{\mathrm{d}c}{\mathrm{d}t} = k_1 e_0 s - (k_1 s + k_{-1} + k_2)c. \tag{6}$$

(d) With the non-dimensionalisation

$$u = \frac{s}{s_0}, \qquad v = \frac{c}{e_0}, \qquad \lambda = \frac{k_2}{k_1 s_0}, \qquad K = \frac{k_{-1} + k_2}{k_1 s_0}, \qquad \epsilon = \frac{e_0}{s_0}, \tag{7}$$

use the rescaling in time $\sigma = k_1 e_0 t/\epsilon$ to show that if $\epsilon \ll 1$ then there is an initial fast transient solution given by

$$u(\sigma) \approx 1 \quad \text{and} \quad \frac{\mathrm{d}v(\sigma)}{\mathrm{d}\sigma} \approx 1 - (1 + K)v(\sigma). \tag{8}$$

(e) Now use the rescaling in time $\tau = k_1 e_0 t$ to show that the outer solution is given by

$$\frac{\mathrm{d}u(\tau)}{\mathrm{d}\tau} \approx -u + (u + K - \lambda)v \quad \text{and} \quad v \approx \frac{u}{u+K}. \tag{9}$$

(f) Show that the null clines for Equations (5) and (6) are given by, respectively,

$$c = \frac{Ds}{\alpha + s} \quad \text{and} \quad c = \frac{Ds}{\beta + s},$$

where α, β and D are to be found in terms of k_1, k_{-1}, k_2 and e_0.

(g) Sketch the null clines and draw the phase trajectory which begins at $s(0) = s_0$, $c(0) = 0$. Indicate the fast transient and pseudo-steady-state portions on the trajectory.

Question 3.

An allosteric enzyme E reacts with a substrate S to produce a product P according to the mechanism

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \overset{k_2}{\longrightarrow} P + E, \tag{10}$$

$$S + C_1 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_2 \overset{k_4}{\longrightarrow} C_1 + P, \tag{11}$$

where the k_i's are rate constants and C_1 and C_2 are enzyme-substrate complexes.

(a) With lowercase letters denoting concentrations, and initial conditions $s(0) = s_0$, $e(0) = e_0$, $c_1(0) = 0$, $c_2(0) = 0$ and $p(0) = 0$, write down the ordinary differential equation model for this system based on the Law of Mass Action.

(b) If

$$\epsilon = \frac{e_0}{s_0} \ll 1, \qquad \tau = k_1 e_0 t, \qquad u = \frac{s}{s_0}, \qquad v_i = \frac{c_i}{e_0}, \tag{12}$$

show that the non-dimensional reaction mechanism reduces to

$$\begin{aligned} \frac{\mathrm{d}u}{\mathrm{d}\tau} &= f(u, v_1, v_2), \\ \epsilon\frac{\mathrm{d}v_1}{\mathrm{d}\tau} &= g_1(u, v_1, v_2), \\ \epsilon\frac{\mathrm{d}v_2}{\mathrm{d}\tau} &= g_2(u, v_1, v_2), \end{aligned}$$

where f, g_1 and g_2 should be determined.

(c) Hence show that for $\tau \gg \epsilon$ the uptake of u is governed by

$$\frac{\mathrm{d}u}{\mathrm{d}\tau} = -r(u) = -u\frac{A + Bu}{C + u + Du^2},$$

where A, B, C and D are positive parameters.

(d) When $k_2 = 0$ sketch the uptake rate, $r(u)$, as a function of u and compare it with the Michaelis-Menten uptake rate.

Question 4.

Many physiological processes involve the conversion of fructose-G phosphate (FGP) to adenosine diphosphate (ADP). There are two parallel conversion mechanisms:

$$\text{FGP} \xrightarrow{k_1} \text{ADP} \qquad \text{and} \qquad \text{FGP} + 2(\text{ADP}) \xrightarrow{k_2} 3(\text{ADP}). \tag{13}$$

(a) Explain why the second of these reactions is described as autocatalytic.

(b) For the rest of this question, suppose further that ADP is converted into an end product with rate constant k_3, and that FGP is supplied at a constant rate (by other reactions). Write down an ordinary differential equation model describing the dynamics of the system.

(c) Using a suitable non-dimensionalisation, show that this model reduces to

$$\frac{\mathrm{d}u}{\mathrm{d}t} = \delta - ku - uv^2, \tag{14}$$

$$\frac{\mathrm{d}v}{\mathrm{d}t} = ku + uv^2 - v, \tag{15}$$

where you should define all new constants and variables.

(d) Show that this system has a unique steady state.

(e) Show that if k is sufficiently large, then the steady state is stable, but that when $0 < k < 1/8$ it is unstable.

(f) Show further that when $k < 1/8$, suitable levels of autocatalysis can induce oscillations in the concentrations of FGP and ADP.