

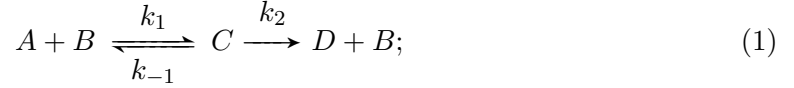
# FURTHER MATHEMATICAL BIOLOGY: PROBLEM SHEET 1

## MICHAELMAS TERM 2020

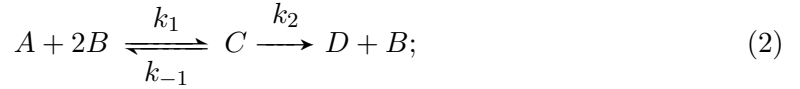
### Question 1.

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

(a)



(b)

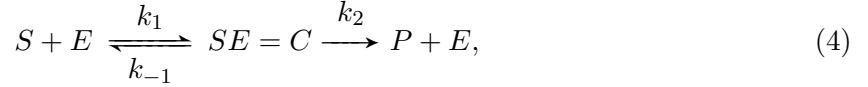


(c)



### Question 2.

Consider the reaction



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

$$\frac{ds}{dt} = -k_1 e_0 s + (k_1 s + k_{-1})c, \quad (5)$$

$$\frac{dc}{dt} = k_1 e_0 s - (k_1 s + k_{-1} + k_2)c. \quad (6)$$

- (d) With the non-dimensionalisation

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

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

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

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

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

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

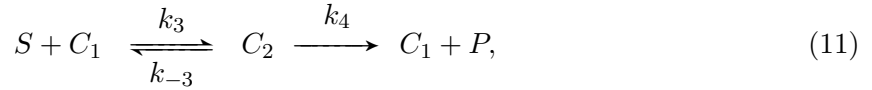
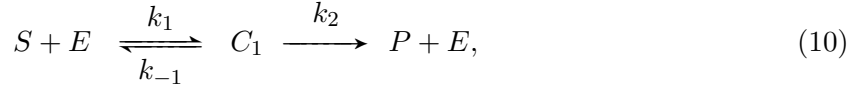
$$c = \frac{Ds}{\alpha + s} \quad \text{and} \quad c = \frac{Ds}{\beta + s},$$

where  $\alpha$ ,  $\beta$  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



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

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

show that the non-dimensional reaction mechanism reduces to

$$\begin{aligned} \frac{du}{d\tau} &= f(u, v_1, v_2), \\ \epsilon \frac{dv_1}{d\tau} &= g_1(u, v_1, v_2), \\ \epsilon \frac{dv_2}{d\tau} &= g_2(u, v_1, v_2), \end{aligned}$$

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

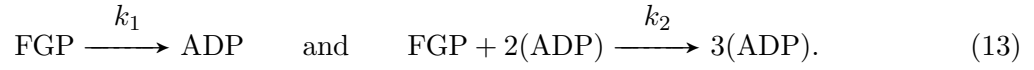
$$\frac{du}{d\tau} = -r(u) = -u \frac{A + Bu}{C + u + Du^2},$$

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:



- (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

$$\frac{du}{dt} = \delta - ku - uv^2, \quad (14)$$

$$\frac{dv}{dt} = ku + uv^2 - v, \quad (15)$$

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.