UNIVERSITY COLLEGE LONDON

University of London

EXAMINATION FOR INTERNAL STUDENTS

For The Following Qualifications:-

B.Sc. *M.Sci.*

Mathematics 2503: Introductory Mathematical Biology

COURSE CODE	:	**MATH2503**
UNIT VALUE	:	**0.50**
DATE	:	**29-APR-05**
TIME	:	**14.30**
TIME ALLOWED	:	**2 Hours**

05-C0902-3-30

TURN OVER

All questions may be attempted but only marks obtained on the best **four** *solutions will count.*
The use of an electronic calculator is **not** *permitted in this examination.*

1. Suppose that a drug is administered to a patient through a feeding tube at rate γ (i.e. it accumulates in the stomach at rate γ). It is then transfered from the stomach to the bloodstream at rate α and there is eliminated by enzymes at rate $\beta \neq \alpha$.

   (a) Draw a network showing the transfer process involved in the model.

   (b) Write down suitable differential equations for the model using $S(t)$ for the stomach concentration at time time t, and $B(t)$ for the bloodstream concentration at time t.

   (c) Show that $S(t) = \frac{\gamma}{\alpha}(1 - e^{-\alpha t})$.

   (d) Hence solve the equation for $B(t)$ explicitly. What happens to the concentrations as $t \to \infty$?

   (e) When $\alpha = 2\beta$ find the time $T > 0$ taken for the concentration of the drug in the stomach to equal the concentration in the bloodstream.

2. (a) Explain in a couple of sentences what is meant by mass action reaction velocities.

   Consider the (hypothetical) reaction scheme

$$A + X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 3X$$

   The concentration a of the chemical A is maintained constant.

   (b) Write down the differential equation for the time evolution of $x(t)$, the concentration of X.

   (c) Solve explicitly the differential equation obtained in the previous part (b), assuming that $x(0) = x_0$.

   (d) By plotting dx/dt versus x show that the concentration always approaches a stable steady state x^* as $t \to \infty$ and find x^* in terms of k_1, k_{-1} and a.

   (e) Use part (d) to plot x as a function of time for the two initial conditions $x_0 \in \left(0, \sqrt{\frac{k_1 a}{3k_{-1}}}\right)$ and $x_0 \in \left(\sqrt{\frac{k_1 a}{3k_{-1}}}, \sqrt{\frac{k_1 a}{k_{-1}}}\right)$.

3. Consider in figure 1 the transfer of a tracer between the bloodstream (C1) and tissue (C2) and its removal from the bloodstream for excretion. Suppose that the concentration of the drug in the blood at time $t \geqslant 0$ is $x_1(t)$ and in the tissue is $x_2(t)$, and that $x_1(0) = x_{10}$, $x_2(0) = 0$. The transfer rates $f_{12} = 3x_1$, $f_{21} = 2x_2$ and the excretion rate is $f_{10} = 4x_1$. The tracer is not modified in the compartments or during the transfer between compartments.

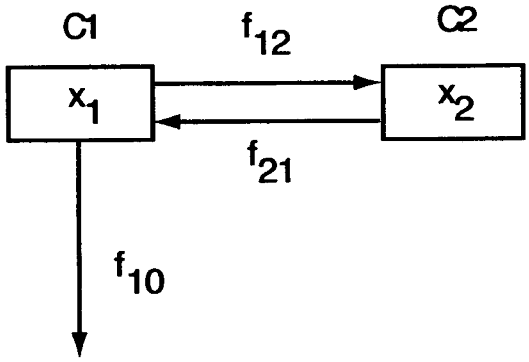

Figure 1: **Figure for Q1**

(a) Write down the differential equations for x_1, x_2 in matrix form $\dot{x} = Mx$ where $x = (x_1, x_2)^T$.

(b) Find the eigenvalues of M and two linearly independent eigenvectors y_1, y_2.

(c) By writing $(x_1(t), x_2(t))$ as a time-dependent sum of y_1, y_2 show that if $x_1(0) = 1$ and $x_2(0) = 0$ then

$$x_1(t) = \frac{1}{7}(e^{-t} + 6e^{-8t}),$$

and find a similar expression for $x_2(t)$.

(d) Sketch the phase plane (i.e. solution curves in $(x_1, x_2)-$space) to indicate what happens to solutions $(x_1(t), x_2(t))$ as $t \to \infty$ for different initial conditions.

4. Consider the 1-dimensional diffusion of a chemical C through a membrane of thickness h and diffusion constant D spanning the region $0 \leqslant x \leqslant h$. For $x \leqslant 0$ the concentration of C is maintained at 0, and for $x \geqslant h$ the concentration of C is also maintained at 0. Initially the chemical P is present at concentration $C_0(x)$ within the membrane.

   (a) Write down the diffusion equation for the concentration $C(x,t)$ of C for $x \in [0,h]$ and $t > 0$, together with the boundary conditions and initial conditions that $C(x,t)$ must satisfy.

   (b) Using separation of variables, or otherwise, show that the concentration $C(x,t)$ satisfies
   $$C(x,t) = \sum_{k=1}^{\infty} a_k \sin\left(\frac{k\pi x}{h}\right) \exp\left(-\frac{k^2\pi^2 D}{h^2}t\right),$$
   and find the a_k when $C_0(x) = \alpha(1 - x/h)$. (You may use that
   $$\int_0^h \sin\left(\frac{k\pi x}{h}\right) \sin\left(\frac{m\pi x}{h}\right) \mathrm{d}x = \frac{h}{2}\delta_{mk}$$
   where $\delta_{mk} = 1$ if $m = k$ and $\delta_{mk} = 0$ if $m \neq k$.)

   (c) Now suppose that in a new scenario, for $x \leqslant 0$ the concentration of C is maintained at a new value constant α, but that for $x \geqslant h$ the concentration of C is maintained at 0 as before. Initially there is no C present in the membrane. Find the new concentration as a function of x and t. (Hint: you may find it helpful to consider the new variable $U(x,t) = C_0(x) - C(x,t)$).

5. Consider the following set of reactions:

$$\begin{aligned}
\frac{1}{2}\text{glc} &\xrightarrow{J_1} \text{Pyr} + \text{NADH} + \text{ATP} \\
\text{Pyr} + \text{NADH} &\xrightarrow{J_2} \text{Lac} \\
\text{Pyr} &\xrightarrow{J_3} \text{AcCoA} + \text{NADH} + \text{CO}_2 \\
\text{Pyr} &\xrightarrow{J_4} \text{AcCoA} + \text{For} \\
\text{AcCoA} &\xrightarrow{J_5} \text{Ac} + \text{ATP} \\
\text{AcCoA} + 2\text{NADH} &\xrightarrow{J_6} \text{Et}
\end{aligned}$$

   (Here J_i is the steady state flux for the ith reaction in the list.)

   (a) Write down a stoichiometric matrix for the closed reaction system.

   (b) Write down a stoichiometric matrix for the open reaction system.

   (c) Suppose that the steady state fluxes J_1, J_2, J_4 are measured in an experiment. Find all possible values for J_3, J_5, J_6.

6. The stationary flux J of an ion A of valency z through a membrane thickness h is given by

$$J = -D\left(\frac{dC(x)}{dx} + \frac{z}{V_0}C(x)\frac{dV(x)}{dx}\right)$$

where D, V_0 are constants, $x \in [0, h]$ is position within the membrane, $C(x)$ is the concentration of the ion and $V(x)$ is the voltage at x.

Show that under the constant field assumption that the stationary flux is

$$J = \frac{-zP_A V_m}{V_0}\left(\frac{([A^2]\exp(zV_m/V_0) - [A^1])}{\exp(zV_m/V_0) - 1}\right)$$

where $P_A = D/h$ is the membrane permeability to ion A, $[A^1] = C(0,t)$ is the concentration of A at $x = 0$, $[A^2] = C(h,t)$ is the concentration of A at $x = h$ and $E = -V_m/h$ is the constant electric field.

Now suppose that on either side of the membrane there is an ionic solution of sodium chloride Na^+Cl^-; at concentration $[Na^+Cl^-]_1$ at $x = 0$ and $[Na^+Cl^-]_2$ at $x = h$. Let P_{Na} be the permeability of the membrane to sodium ions Na^+, and P_{Cl} the permeability of the membrane to chloride ions Cl^-.

(a) Find the final potential across the membrane in terms of the final concentrations $[Na^1_F]$, $[Na^2_F]$ and $[Cl^1_F]$, $[Cl^2_F]$ if the membrane is impermeable to sodium ions.

(b) What is the final state of the system if the membrane is made slightly permeable to sodium?