ENGINEERING TRIPOS PART IIA

Monday 30 April 2012 2.30 to 4

Module 3G2

MATHEMATICAL PHYSIOLOGY

*Answer not more than **three** questions.*

All questions carry the same number of marks.

*The **approximate** percentage of marks allocated to each part of a question is indicated in the right margin.*

There are no attachments.

STATIONERY REQUIREMENTS
Single-sided script paper.

SPECIAL REQUIREMENTS
Engineering Data Book
CUED approved calculator allowed

You may not start to read the questions printed on the subsequent pages of this question paper until instructed that you may do so by the Invigilator

Version: Final version

1 (a) Consider the following set of reactions:

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

where $k_2 \gg k_1$. We are interested in calculating the evolution of all species concentrations over time.

(i) Write down differential equations describing the evolution of each concentration. [10%]

(ii) What assumption can you make in order to simplify the problem? [10%]

(iii) The initial conditions are [A](0)=$[A]_0$ and [B](0) = [C](0) = 0. Deduce simplified analytical expressions for [A](t), [B](t) and [C](t). [10%]

(b) Consider now the following reactions:

$$\mathrm{S+E} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C_1} \xrightarrow{k_2} \mathrm{P+E}$$

$$\mathrm{C_1+I} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{C_2}$$

(i) What type of inhibition mechanism do they account for? [10%]

(ii) Write down differential equations describing the evolution of the concentration of each species. [20%]

(iii) Using the steady-state assumption for C_1 and C_2, express the rate of product creation V as a function of the substrate concentration [S], total enzyme concentration E_0 and inhibitor concentration [I]. Use the following notations: $K_M \equiv \frac{(k_2+k_{-1})}{k_1}$ and $K_I \equiv \frac{k_{-3}}{k_3}$. [30%]

(iv) Sketch $1/V$ as a function of 1/[S]. How does the graph change if the inhibitor concentration is increased? Justify your answer. [10%]

2 (a) We measure the electrophysiological properties of two axons that have different radii but are otherwise identical. The radius of the thinner axon is $r_{\text{thin}} = 2\ \mu\text{m}$, the radius of the thicker one is $r_{\text{thick}} = 5\ \mu\text{m}$. Provide formulæ for the following quantities:

(i) the ratio of the time constants in the two axons, $\frac{\tau_{\text{thick}}}{\tau_{\text{thin}}}$, when both axons are unmyelinated;

(ii) the ratio of the space constants in the two axons, $\frac{\lambda_{\text{thick}}}{\lambda_{\text{thin}}}$, when both axons are unmyelinated;

(iii) the ratio of the time constants in the two axons, $\frac{\tau_{\text{thick}}}{\tau_{\text{thin}}}$, when both axons are myelinated, and the thickness of the myelin layer in both axons is optimal for high propagation speed;

(iv) the ratio of the space constants in the two axons, $\frac{\lambda_{\text{thick}}}{\lambda_{\text{thin}}}$, when both axons are myelinated, and the thickness of the myelin layer in both axons is optimal for high propagation speed.

[40%]

(b) With regard to the absolute and relative refractory periods in the Hodgkin-Huxley model:

(i) describe the experimental protocol by which the duration of these refractory periods can be measured; [30%]

(ii) explain how the behaviour of the different dynamical variables of the model accounts for these phenomena. [30%]

3 (a) Explain the physiological function of globular proteins in the context of micro-circulation. [25%]

(b) The function of the kidneys is to filtrate blood in order to regulate water content and ensure waste removal. The first stage takes place in the glomurelus where a large volume of water and small solutes (Na+, glucose, etc.) leaves the plasma and filtrates in to the so called Bowman's capsule. Figure 1 shows a simplified sketch of this region. Blood arrives in the afferent arteriole at a flow rate Q_i and flows along the capsule, modelled as a parallel vessel, over a distance L. During this process, water is free to filtrate through a porous epithelium into the capsule while large globular proteins remain in the blood plasma. As a result, the flow rates in the arteriole q_1 and in the capsule q_2 are both functions of the position x. The pressures in the arteriole P_1 and capsule P_2 are however assumed to be constant.

(i) The concentration of globular proteins in the blood is $c(x)$, with $c(0) = c_0$. Find a relationship between c, q_1, c_0 and Q_i. Deduce an expression for the osmotic pressure π in the blood as a function of q_1. [25%]

(ii) The filtration rate K_f is defined as the ratio between the water flux per unit length along the arteriole and the pressure difference between the arteriole and the Bowman's capsule (accounting for hydrostatic and osmotic effects). Express $\frac{dq_1}{dx}$ as a function of K_f, P_1, P_2 and π. [25%]

(iii) Use the results above to establish a first order ODE for $q_1(x)$. Without solving this equation, sketch the evolution of q_1, q_2 and π along the arteriole, paying attention to the limiting behaviour of these functions. [25%]

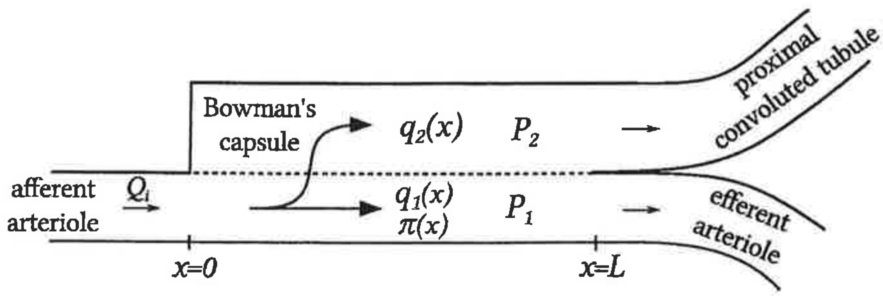

Fig. 1

4 We consider an unsteady flow in a compliant artery. Viscosity is neglected and the blood speed is assumed to be uniform across any section of the vessel. The blood velocity at time t and location x along the vessel is $u(x,t)$. The cross-section area is $A(x,t)$ and the blood pressure $P(x,t)$. The vessel has a compliance c so that $A(x,t) = A_0 + cP(x,t)$. The mass density ρ of the blood is constant.

(a) Justify why neglecting viscosity and assuming u is uniform across any vessel cross-section are reasonable assumptions in arteries. [15%]

(b) Using a mass or volume conservation argument, show that:

$$\frac{\partial A}{\partial t} + \frac{\partial (Au)}{\partial x} = 0$$

[15%]

(c) By considering forces and momentum, show that:

$$\rho \left(\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} \right) = -\frac{\partial P}{\partial x}$$

[35%]

(d) In the limit of small variations in pressure and velocity (i.e. to the first order in u and P), show that $P(x,t)$ satisfies the wave equation,

$$\frac{\partial^2 P}{\partial t^2} = v_w^2 \frac{\partial^2 P}{\partial x^2}$$

Find the expression of the wave velocity v_w as a function of the constants introduced above. [35%]

END OF PAPER