ENGINEERING TRIPOS PART IIA

Monday 6 May 2013 9.30 to 11

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

1 (a) Explain the assumptions behind the Michaelis Menten model for enzyme kinetics. Write down the chemical reactions involved and introduce the relevant kinetic constants. [30%]

(b) Find the expression for the product creation rate V as a function of the substrate concentration S_0, the Michaelis Menten constant K_M and the maximal product creation rate V_{max}. [30%]

(c) The data presented in Table 1 were measured for a particular enzyme-catalysed reaction by monitoring the product formation rate at various substrate concentrations, keeping the enzyme concentration constant. Calculate the values of V_{max} and K_M. What would V be for substrate concentrations equal to 2.5×10^{-5}M and 5×10^{-5}M? What would V be if the enzyme concentration is doubled for a substrate concentration equal to 5×10^{-5}M? [40%]

Substrate concentration (Molar)	Product formation rate V (10^{-9} moles liter^{-1} min^{-1})
6.25×10^{-6}	15.0
7.50×10^{-5}	56.25
1.00×10^{-4}	60
1.00×10^{-3}	74.9
1.00×10^{-2}	75

Table 1

2 (a) Explain what the tube and discharge hematocrit represent. [20%]

(b) Considering a perfectly cylindrical vessel of radius R, write down the expressions of the tube and discharge hematocrits as a function of the local volume fraction of red blood cell $h_{ct}(r)$ and the velocity profile $u(r)$, where r is the radial position in cylindrical polar coordinates. [30%]

(c) In a simple model, the local hematocrit $h_{ct}(r)$ takes the following values:

$$\begin{cases} h_{ct}(r) = \mathrm{H}_{ct_0} & \text{for } 0 \leq r \leq R - \delta \\ h_{ct}(r) = 0 & \text{for } R - \delta < r \leq R \end{cases}$$

where H_{ct_0} is a positive constant.

(i) What does δ represent and what would be its approximate value? [10%]

(ii) Assuming that the velocity profile corresponds to a simple Poiseuille flow, derive an expression for the ratio of the tube and discharge hematocrits and sketch this as a function of the tube radius. [40%]

3 (a) In what physical units are the following quantities measured? (use combinations of the following standard SI units: m, s, mol, kg, C, V, A, Ω, S, F)

- Diffusion coefficient
- Concentration
- Electrovalency
- Permeability
- Membrane time constant
- Gating variables in the Hodgkin-Huxley model
- Membrane capacitance in the Hodgkin-Huxley model (assuming membrane currents are measured in $\mu\mathrm{A/cm^2}$, membrane potential in mV and time in s)
- Axial resistance in the cable equation
- Input resistance
- Propagation speed of the action potential

[20%]

(b) In an experiment, the sodium current through the membrane of a cell is measured while holding the membrane potential at a fixed value. The normal values of the intracellular and extracellular concentrations of sodium are $c_\mathrm{i} = 50$ mM and $c_\mathrm{e} = 437$ mM, respectively. Before the experiment, both quantities are lowered to $1/100^{\mathrm{th}}$ of these normal values. The experiment is conducted at room temperature, $T = 293$ K. Answer the following questions with regard to this experiment using the following physical constants: $R = 8.314\ \mathrm{J/(mol\,K)}$ and $F = 96485\ \mathrm{C/mol}$. Make sure you provide the appropriate physical units with your answers.

(i) What is the Nernst potential of sodium under these conditions? [10%]

(ii) What is the sodium current at the Nernst potential? [5%]

(iii) The sodium current is measured at 0 mV and is found to be $I = -5.47\ \mathrm{nA\,cm^{-2}}$. What is the sodium conductance of the membrane? [10%]

(iv) What is the permeability of the membrane for sodium? [15%]

(v) The sodium current is also measured at half the Nernst potential and is found to be $I = -2.26\ \mathrm{nA\,cm^{-2}}$. How can it be possible that the magnitude of this current is less than half of that measured at 0 mV, ie. that the sodium current does not appear to be a linear function of the membrane potential? [20%]

(vi) Normal sodium concentrations are restored both inside and outside the cell. What are the values of the sodium current at the following values of the membrane potential:

– Nernst potential;

– half the Nernst potential;

– 0 mV?

[20%]

4 At the end-stage of renal disease, over 90% of the blood filtration function is typically lost. Dialysis is one of the main treatments for such disease. Hemodialysis consists in connecting the bloodstream to a dialysis machine in order to remove toxic solutes accumulating in the blood. The key principle involved in hemodialysis is a transfer across a membrane of the solute from the blood to a second solution, called a dialysate. The main objective in the machine design is to maximise the removal of solute from the blood in each pass. In this question, the filtration rates obtained with two simple designs are quantified and compared.

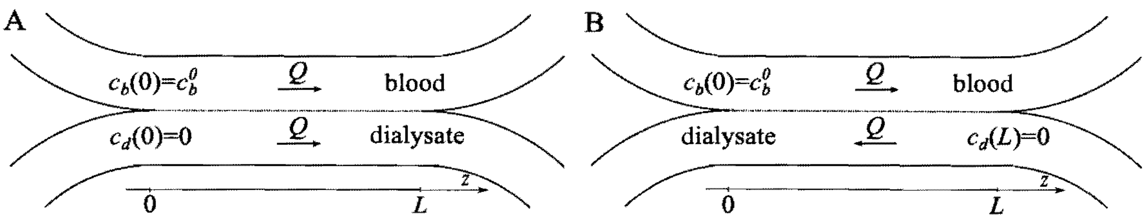

Fig. 1

As shown in figure 1, the flow rates in the blood and dialysate vessels are assumed to be identical and equal to Q. The concentrations of a particular solute along the vessels are $c_b(z)$ in the blood vessel and $c_d(z)$ in the dialysate vessel. The solute concentration in blood entering the dialyser is c_b^0 and the solute concentration in the dialysate entering the machine is negligible. The flux per unit length $\phi(z)$ of solute across the membrane is due to passive diffusion and controlled by the following relationship: $\phi(z) = K(c_b(z) - c_d(z))$, where K is the membrane permeability.

(a) Consider first the case of the co-current flow geometry depicted in figure 1A, in which the blood and dialysate flow alongside each other, in the same direction, over a length L.

(i) Show that $\frac{dc_b}{dz} = -\frac{dc_d}{dz} = -\frac{\phi}{Q}$ [15%]

(ii) Write down a first order differential equation for $\phi(z)$ and find its solution. Find the expression of $c_b(z)$ and $c_d(z)$ and sketch their graphs. [20%]

(iii) The total mass transfer rate $\dot{M}$ is defined by: $\dot{M} = \int_0^L \phi \, dz$. What is its maximum value, obtained when L tends to infinity? [10%]

(b) Consider next the case of the counter-current flow geometry depicted in figure 1B. Here, the blood and dialysate flow alongside each other, but in opposite directions, over a length L.

(i) Show that $\phi(z)$ is constant. [15%]

(ii) Show that: $\begin{cases} c_b^0 - c_b(L) = c_d(0) = \frac{\phi L}{Q} \\ c_b^0 - c_d(0) = c_b(L) = \frac{\phi}{K} \end{cases}$ [15%]

(iii) What is the maximum value of $\dot{M}$ in this geometry, obtained when L tends to infinity? [15%]

(c) What is the most efficient dialysis geometry? Briefly justify your answer. [10%]

END OF PAPER