EGT2
ENGINEERING TRIPOS PART IIA

Monday 6 May 2024 14.00 to 15.40

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.*

*Write your candidate number **not** your name on the cover sheet.*

STATIONERY REQUIREMENTS
Single-sided script paper

SPECIAL REQUIREMENTS TO BE SUPPLIED FOR THIS EXAM
CUED approved calculator allowed
Engineering Data Book

10 minutes reading time is allowed for this paper at the start of the exam.

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

You may not remove any stationery from the Examination Room.

1 Researchers have collected data about the activity of an enzyme E with and without introducing an inhibitor, and would like to identify the mechanism of action of this inhibitor in the creation of a product P. They consider in particular these two mechanisms: competitive inhibition and uncompetitive inhibition.

(a) Competitive inhibition.

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

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

Find an expression for the rate of product formation as a function of the substrate concentration [S], the inhibitor concentration [I] and total enzyme concentration E_0. [35%]

(b) Uncompetitive inhibition.

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

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

Find an expression for the rate of product formation as a function of the substrate concentration [S], the inhibitor concentration [I] and total enzyme concentration E_0. [35%]

(c) Using the data below, identify a likely mechanism for the inhibition process. Justify your answer. [30%]

Substrate concentration (mmol/L)	Rate of product formation without inhibitor (mmol/L/min)	Rate of product formation with inhibitor (mmol/L/min)
0.710	0.200	0.180
0.400	0.180	0.150
0.310	0.160	0.110
0.098	0.120	0.070
0.066	0.100	0.050
0.040	0.070	0.040

2 This question is about ion flux at the Nernst potential.

(a) Give the formula for the Nernst–Planck equation, describing the flux of an ion along an ion channel, and explain the meaning of each symbol in it. [10%]

(b) Give the formula for the Nernst potential of an ion, and explain the meaning of each symbol in it. [5%]

(c) Prove that whenever the membrane potential is equal to the Nernst potential, the following equation holds: [25%]

$$\int_0^L \frac{J(x,t)}{c(x,t)}\,dx = 0$$

where x is the position along the channel, t is time, J is the flux of the ion, c is its concentration, and L is the length of the channel.

(d) Based on the equation in part (c), explain with reasons if the membrane potential being equal to the Nernst potential of the ion implies that the flux of the ion is zero everywhere inside the channel. [10%]

(e) Answer if each of the following statements is always true for the steady state of an ion channel. (You can assume that the channel is only permeable to a single ion.) [20%]

- (i) No individual ions move along the channel;
- (ii) There is no net movement of ions along the channel;
- (iii) The flux of the ion is constant as a function of space along the channel;
- (iv) The flux of the ion is zero everywhere along the channel.

(f) The equation in part (c) holds at any time (when the condition from which it was derived holds). What is its form when the channel is in steady state? Describe the meaning of any symbols that are different from those in the equation in part (c) and explain how they depend on time and space. [20%]

(g) Prove that whenever the membrane potential is equal to the Nernst potential, and the channel is in steady state, the flux of the ion is zero everywhere inside the channel. [10%]

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3 Consider a Bingham fluid flowing in a cylindrical rigid vessel of radius R and length L, in steady state. A Bingham fluid has a rheology defined by the following constitutive equation:

$$\tau = \tau_y + \eta\dot{\gamma}$$

where τ is the shear stress, $\dot{\gamma}$ is the shear rate, and τ_y and η are constants. The following equations characterise force balance at the steady state in a cylindrical vessel in polar coordinates, where x is the coordinate along the flow direction, and $p(x,r)$ is the pressure field in the fluid.

$$\frac{\partial p}{\partial x} = \frac{1}{r}\frac{\partial (r\tau)}{\partial r}$$

$$\frac{\partial p}{\partial r} = 0$$

(a) What is the minimum pressure drop ΔP_c across the vessel required to have a non-zero flow rate through the vessel? [25%]

(b) Find a mathematical expression of the flow profile in the case where the material is flowing, as a function of the pressure drop ΔP and other parameters defined above. [50%]

(c) Sketch the flow profiles for the following conditions: $\Delta P = \Delta P_c/2$, $\Delta P = 2\Delta P_c$, $\Delta P \gg \Delta P_c$. [25%]

4 (a) The Krogh cylinder model allows us to estimate the oxygen concentration c in tissues as a function of the distance to the closest capillary. Explain the interpretation of the Krogh cylinder radius R_0 in this model. [10%]

(b) Using appropriate assumptions, show that the concentration profile takes the following form:

$$\frac{c(r)}{c_c} = 1 + \Phi\left(\frac{r^2}{R_0^2} - R^{*2} - 2\ln\left(\frac{r}{R_0 R^*}\right)\right)$$

where r is the distance to the centre of the closest capillary, c_c is the oxygen concentration in the capillary, and Φ and R^* are constants. Find expressions for Φ and R^* as a function of the radius R_0 of the Krogh cylinder, the radius R_c of the capillary, the concentration c_c of oxygen in the capillary, the rate of oxygen consumption per unit time ρ and the coefficient of diffusion D of the oxygen in the tissue. [50%]

(c) Figure 1 shows the line defined by:

$$\Phi\left(R^{*2} - 2\ln\left(R^*\right) - 1\right) = 1$$

Explain the significance of this line and show how it is derived mathematically. [20%]

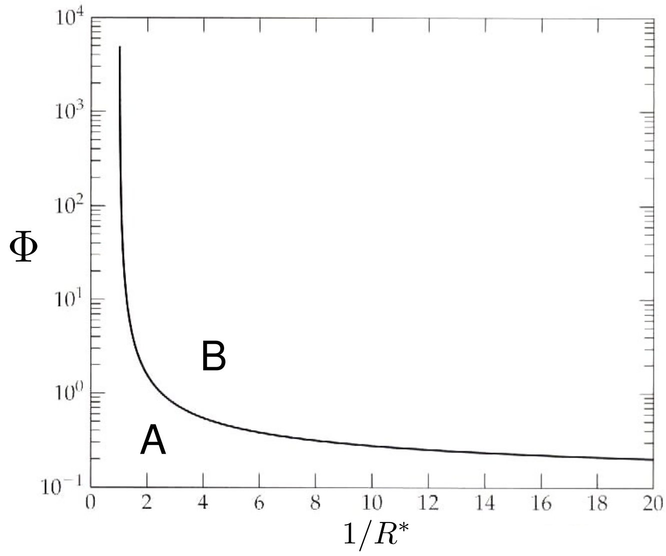

Fig. 1

(d) Sketch the oxygen concentration profiles for two tissues whose oxygenation states are in domain A and domain B respectively. [20%]

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