EGT2
ENGINEERING TRIPOS PART IIA

Friday 2 May 2025 9.30 to 11.10

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 (a) Consider the enzyme catalysis reaction below:

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

Find an expression for the rate of product formation V as a function of the substrate concentration [S] and total enzyme concentration E_0, assuming that the equilibrium reactions are fast compared to the product formation rate. Sketch the curve $1/V = f(1/[\mathrm{S}])$ and indicate how the slope and intercepts of this curve relate to the reaction constants. [30%]

(b) Consider now the following set of reactions involving an allosteric interaction between the enzyme and I:

$$\begin{array}{ccccc}
\mathrm{E} + \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} & \mathrm{C}_1 & \xrightarrow{k_2} & \mathrm{E} + \mathrm{P} \\
+ & & + & & \\
\mathrm{I} & & \mathrm{I} & & \\
k_{-3} \Big\uparrow\Big\downarrow k_3 & & k_{-3} \Big\uparrow\Big\downarrow k_3 & & \\
\mathrm{C}_2 + \mathrm{S} & \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} & \mathrm{C}_3 & \xrightarrow{k_4} & \mathrm{E} + \mathrm{P} + \mathrm{I}
\end{array}$$

(i) Find an expression for the rate of product formation as a function V of [S], [I] and the total enzyme concentration E_0, assuming that all equilibrium reactions are fast. Sketch the curve $1/V = f(1/[\mathrm{S}])$ and indicate how the slope and intercepts of this curve are affected by the allosteric interaction. [50%]

(ii) Discuss the inhibitory nature of I in terms of k_2 and k_4. [20%]

2 (a) Based on the Hodgkin-Huxley model of action potential generation, explain with reasons what parameters of the model determine the following experimentally measurable quantities, and provide approximate values (with suitable physical units) for these quantities:

(i) The threshold value for depolarisation above which the neuron generates an action potential after a long period of quiescence. [10%]

(ii) The duration of the absolute refractory period. [10%]

(iii) The duration of the relative refractory period. [15%]

(b) A cylindrical axon of 0.125 mm radius and $\sqrt{2}$ cm length (without any branching) is stimulated at one of its endpoints with a brief electrical pulse. The stimulation is such that 1 ms after the end of the stimulation, the membrane is depolarised by 5 mV above the resting membrane potential at the location of the stimulation. The membrane capacitance is 1.0 $\frac{\mu\text{F}}{\text{cm}^2}$, the total membrane conductance at rest is 0.25 $\frac{\text{mS}}{\text{cm}^2}$, and the axial resistance is 1 kΩ mm. We measure the membrane potential at the midpoint of the axon.

(i) What is the time constant of the axon? [5%]

(ii) What is the length constant of the axon? [5%]

(iii) When will we measure the peak depolarisation? [10%]

(iv) What will be the peak depolarisation? [15%]

(v) What will be the peak depolarisation when the same stimulation, as described above, is applied to the two endpoints simultaneously? [10%]

(vi) We now apply a new kind of stimulation. It is also a brief electrical pulse delivered to one of the end points, but its strength is such that 1 ms after the end of the stimulation, the membrane would be depolarised by 20 mV above the resting membrane potential at the location of the stimulation if Na^+ channels were blocked. We apply this stimulation without blocking Na^+ channels. What will be the peak depolarisation in this case? [10%]

(vii) What will be the peak depolarisation when this new kind of stimulation is applied to the two endpoints simultaneously? [10%]

3 Figure 1 shows a microfluidic channel in which a fluid flow is forced along the x direction (i.e. from left to right on the figure). In such a system, the height h is typically of the order of 10 microns, the width W about a millimeter, and the length L a few centimeters, therefore $h \ll W \ll L$. A Newtonian fluid of viscosity μ enters at a pressure P_0, and exits on the opposite end at pressure P_1. The aim of this question is to find an expression for the flow rate through the channel as a function of the pressure drop. Due to the geometry of the vessel and incompressibility of the fluid, it is safe to assume that the velocity u of the fluid is in the x direction and does not depend on x and y.

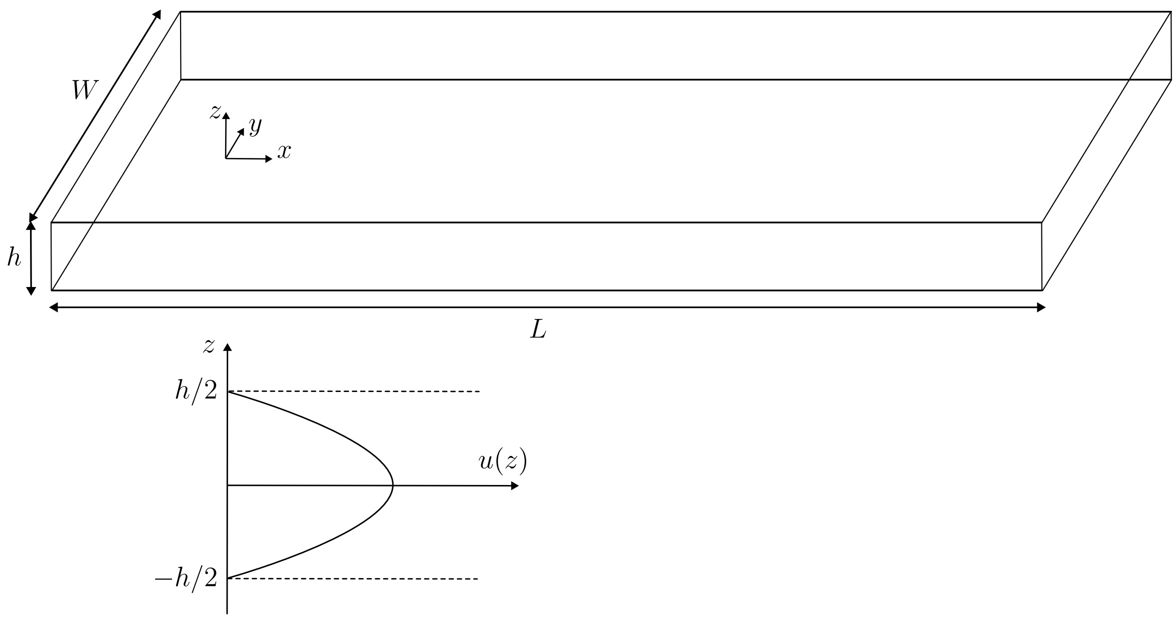

Fig. 1

(a) By balancing forces on a small volume element, show that:

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

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

where p is the pressure and τ is the shear stress in the fluid. [25%]

(b) Derive an expression for the flow profile $u(z)$ in the channel. [50%]

(c) Derive an expression for the flow rate Q through a cross section of the channel. [25%]

4 Figure 2 represents a single alveolus and a blood capillary in contact with it.

(a) Consider the following simplified model for oxygen binding to haemoglobin:

$$4O_2 + Hb \underset{k_-}{\overset{k_+}{\rightleftharpoons}} Hb(O_2)_4$$

List the key simplifications made to obtain this model. Derive an expression for the saturation curve of heamoglobin $Y([O_2])$, and sketch it. [25%]

(b) Find an expression for the flux per unit area of O_2 through the alveolar epithelium as a function of the concentration of O_2 in the blood (c_b), the partial pressure of oxygen in the alveolus (P_g), the thickness of the epithelium (d_e), the solubility of O_2 (σ), and the diffusion constant of O_2 in the epithelium (D_e). State your assumptions. [25%]

(c) Blood flows in the capillary at speed v. Let x denote the distance along the capillary, taking as the origin the location where the capillary comes in contact with the alveolar epithelium. The capillary cross-sectional area is uniform and can be approximated by d_a^2. The arc length of the capillary cross-section that is in contact with the epithelium is about d_a. Show that the concentration of O_2 along the capillary, $c_b(x)$, satisfies the following differential equation:

$$v\frac{d}{dx}\left(c_b + 4Hb_0\frac{c_b^4}{K + c_b^4}\right) = \frac{D_e}{d_a d_e}(\sigma P_g - c_b)$$

where K and Hb_0 are constants. [50%]

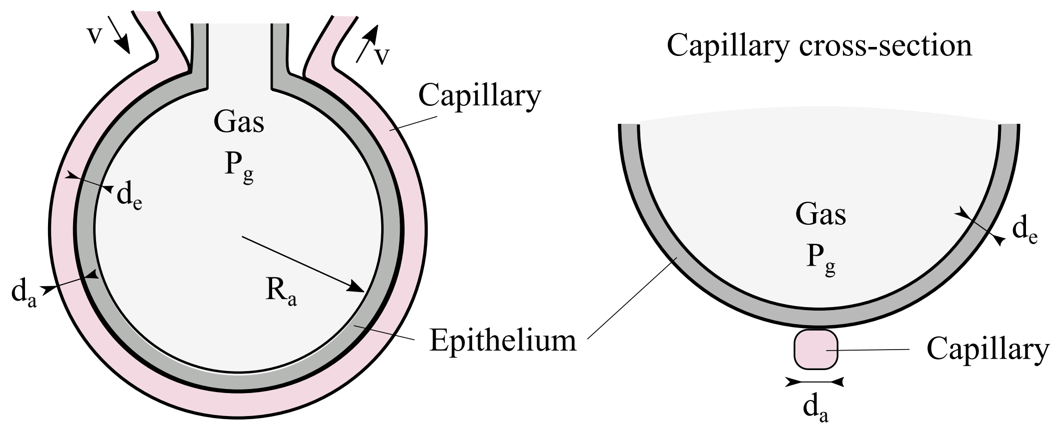

Fig. 2

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