Version AK/2

EGT2
ENGINEERING TRIPOS PART IIA

Thursday 21 April 2016 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.*

*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.

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

1 (a) Explain what competitive inhibition is in the context of enzyme kinetics. [20%]

(b) Write a set of reactions with their rate constants to model competitive inhibition, and derive an expression for the rate of product formation V. [30%]

(c) Use a graphical representation to illustrate the effect of the inhibitor concentration on the product formation rate. [10%]

(d) The following data show how the rate of product formation V depends on the concentrations of substrate S and inhibitor I for two particular enzyme reactions. In each case, indicate if it is consistent with a competitive inhibition model, and if it is, extract as much information as you can about the equilibrium constants.

(i)

	[S] (μmol L^{-1})	3	5	10	30	90	900
No inhibitor	V (μmol L^{-1} min^{-1})	10.4	14.5	22.5	33.8	40.5	44.5
[I]=0.01 μmol L^{-1}	V (μmol L^{-1} min^{-1})	4.1	6.4	11.3	22.6	33.8	44.4

[20%]

(ii)

	[S] (μmol L^{-1})	3	5	10	30	90	900
No inhibitor	V (μmol L^{-1} min^{-1})	10.4	14.5	22.5	33.8	40.5	44.5
[I]=0.01 μmol L^{-1}	V (μmol L^{-1} min^{-1})	2.1	2.9	4.5	6.8	8.1	8.8

[20%]

2 Certain organisms, such as the colonial algae Volvox, have all their cells arranged on the surface of a sphere, with only a single cell in the thickness of the layer. To survive, these cells need to collect oxygen and nutrients from their environment. In this question, we investigate if diffusion is sufficient as a transport mechanism to keep the organism healthy. We will focus on oxygen transport.

(a) Consider such a spherical organism with radius R. Assume the cells at the surface consume an amount ρ of oxygen per unit time and area. What is the total amount of oxygen consumed by the whole organism per unit time? [10%]

(b) What is the maximal amount of oxygen that the organism can collect per unit time in the steady state through diffusion alone, as a function of R, the coefficient of diffusion D of oxygen in the organisms environment (mostly water), and the concentration of oxygen c_0 away from the organism? [35%]

(c) Under what condition is diffusive transport sufficient to keep the organism properly oxygenated? [10%]

(d) Write the expression for the oxygen concentration at the surface of the organism when $R = \frac{1}{2}\frac{Dc_0}{\rho}$. [35%]

(e) The radius R of *Volvox carteri* ranges from about 100 µm to 500 µm. Is diffusive transport sufficient to supply the cells with oxygen? If it isn't, suggest other mechanisms that might help. The following figures might inform your answer:
$\rho = 10^{14}\text{cm}^{-2}\ \text{s}^{-1}$, $c_0 = 10^{17}\text{cm}^{-3}$ and $D = 2 \cdot 10^{-5}\ \text{cm}^2\ \text{s}^{-1}$. [10%]

3 (a) What are the units of measurement (if any) for the following physical quantities?

- (diffusion) flux
- diffusion coefficient
- electrovalency
- electric field
- Faraday constant
- universal gas constant
- Nernst potential
- ionic concentration
- dielectric constant
- channel permeability

[20%]

(b) This question is about the Nernst potential.

(i) Derive the value of the Nernst potential of an ion, defined as the membrane potential (electric potential difference between the two ends of a channel) when the flux of the ion is zero everywhere inside the channel. Start from the Nernst–Planck equation describing the flux of an ion:

$$J(x,t) = -D\left(\frac{\partial}{\partial x}c(x,t) + \frac{zF}{RT}\,c(x,t)\,\frac{\partial}{\partial x}\phi(x,t)\right)$$

where x is one-dimensional space, t is time, J is the flux, ϕ is the electric potential, F is the Faraday constant, R is the universal gas constant, T is absolute temperature, D is the diffusion coefficient, c is the concentration, and z is the valence of the ion. In your derivation, you can use the following definitions: let L denote the length of the channel, $V(t) = \phi(L,t) - \phi(0,t)$ denote the membrane potential, and $c_{\mathrm{i}}(t) = c(0,t)$ and $c_{\mathrm{e}}(t) = c(L,t)$ denote the concentration of the ion at the intra- and extra-cellular end of the channel, respectively. [20%]

(ii) Demonstrate with a derivation that the converse of the previous situation may not always hold, i.e. the flux of an ion may not be zero everywhere at the moment when the membrane potential reaches its Nernst potential. [20%]

(iii) In order to prove that the flux of an ion is zero at the Nernst potential, one must take the steady state limit. What defines this steady state limit, what are the

relevant boundary conditions, what are the assumptions underlying these boundary conditions, and why are these assumptions justified? [20%]

(c) Beside the usual currents of the Hodgkin–Huxley model responsible for action potential generation, some neurons also include a so-called A-type potassium current. The single gating variable, a, of this A-type current activates slowly with depolarisation, and deactivates even more slowly with hyperpolarisation, such that it could be modelled simply as having a steady-state value a_∞ that switches from 0 to 1 at a threshold voltage of 50 mV, and a time constant τ_a that is 200 ms and 20 ms below and above this threshold, respectively.

(i) Sketch and describe in words the behaviour of a in time when the cell is made to fire at around 60 Hz for several hundred milliseconds. For simplicity, assume that the maximal conductance of the A-type current is near zero, so that it has no visible effect on the membrane potential. [10%]

(ii) Sketch and describe in words the membrane potential trace of the cell in response to the stimulation described above when the maximal conductance of the A-type current is well above zero. [10%]

4 (a) Explain why capillaries have small holes called fenestrations. Give an approximate value for their diameter. [10%]

(b) Consider a capillary of length L oriented along the x axis. The hydrostatic pressure inside the capillary is denoted $P_c(x)$, while the hydrostatic pressure in the surrounding tissue is P_i. The osmotic pressures in blood and tissue are π_c and π_i respectively. Write down the expression for the total pressure difference $\Delta P(x)$ that drives the movement of water through the capillary wall as a function of $P_c(x)$, P_i, π_c and π_i. Write a simple relationship that relates $\Delta P(x)$, the flux of water $\phi(x)$ moving through the vessel wall per unit of capillary length, and the permeability per unit length K_f. [15%]

(c) The flow rate of blood along the capillary is denoted $q(x)$. The influx at the entry $x = 0$ and exit $x = L$ are assumed to be identical, $q(0) = q(L) = Q$. The capillary hydrodynamic resistance, ρ, is defined by $\frac{dP_c}{dx} = -\rho q(x)$ and is constant along the capillary. Assume at this stage that P_i, π_c and π_i are homogeneous along the capillary.

(i) Derive the differential equation satisfied by the blood hydrostatic pressure $P_c(x)$ in this model. [15%]

(ii) Show that the following expression is solution of the problem:

$$P_c(x) = P_i + \pi_c - \pi_i - \frac{P_c(0) - P_c(L)}{2} \frac{\sinh\left(\sqrt{\rho K_f}\,(x - L/2)\right)}{\sinh\left(\sqrt{\rho K_f} L/2\right)}$$

[20%]

(iii) Find the relationship between the entry flow rate Q and the pressure drop along the capillary $P_c(L) - P_c(0)$. [15%]

(iv) What is the amount of water filtrating through the tissue? [10%]

(d) Is the approximation that $q(0) = q(L)$ physiologically realistic? What would happen in the tissue if $q(0)$ and $q(L)$ were different. [15%]

END OF PAPER