Version AJK/2

EGT2
ENGINEERING TRIPOS PART IIA

Monday 5 May 2014 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

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

1 Consider the following mechanism of enzyme activity, where the enzyme is E, the substrate S and the product P.

$$S + E \rightleftharpoons ES \qquad K_1 = \frac{[ES]}{[S][E]}$$

$$ES \xrightarrow{k_2} E + P$$

$$S + ES \rightleftharpoons SES \qquad K_3 = \frac{[SES]}{[S][ES]}$$

$$SES \xrightarrow{k_4} E + S + P$$

The equilibrium reactions are all supposed to be fast. The total concentration of enzyme is E_0 and the product creation rate is V.

(a) (i) In the limit where k_4=0, show that

$$\frac{V}{E_0} = \frac{k_2 s}{K_1^{-1} + s + K_3 s^2}, \text{ where } s = [S].$$

[20%]

(ii) Sketch the graphs of V as a function of s, and $1/V$ as a function of $1/s$. How do these graphs qualitatively differ from the standard Michaelis Menten case. [20%]

(iii) This type of enzyme kinetics is called substrate inhibition. Explain why. [10%]

(b) (i) Derive an expression for $\frac{V}{E_0}$ in the general case, where k_4 is non-zero. Sketch the curve of $V(s)$. [30%]

(ii) What condition on the kinetic and equilibrium constants must be satisfied for this inhibition mechanism to enhance the product creation rate at large substrate concentrations? [20%]

2 This question is about the Nernst potential.

(a) What is the formula for the Nernst potential? In your answer:

- explain the meaning of each symbol in the formula you provide,
- for each quantity, specify the units in which it is measured such that the formula is dimensionally consistent,
- for physical constants also provide their approximate value in the units you chose, for the other quantities state their typical values (or ranges) in living cells (such as neurons) in the units you chose. [20%]

(b) Under what condition are the following two statements equivalent: (1) the membrane potential in a neuron is at the Nernst potential of ion X, and, (2) the channel current for ion X is zero. [30%]

(c) In the Hodgkin-Huxley model, the Nernst potentials of ions are assumed to be constant in time, while the model is based on ionic currents. This seems an apparent contradiction. Explain with reasons what this contradiction is, and why in practice the assumption of fixed Nernst potentials may still be valid. [15%]

(d) In a very thin axon, 20 ms after a large number of action potentials have been fired at a very high rate, it is observed that no further action potentials can be elicited even with large current injections. Explain what mechanism can account for this observation. [35%]

(TURN OVER

3 A range of pressure-volume cycles in the left heart are presented in Fig. 1. The data has been collected on the same individual (dog) under various exercise conditions and under epinephrine treatment for some of them.

(a) (i) We consider first the greyed cycle on Fig. 1. For each of the segments 1-2, 2-3, 3-4 and 4-1, indicate the state of the mitral and aortic heart valves and estimate its typical duration. Provide values for the artery pressure P_a and pulmonary vein pressure P_v. [25%]

(ii) Explain the meaning of the dashed and solid straight lines on Fig. 1 for the epinephrine and control cases. What properties of the heart tissue can be measured from these lines? Estimate their value. [20%]

(iii) Establish a simplified quantitative model of the heart cycle and provide an expression for the cardiac output as a function of heart beat frequency. [25%]

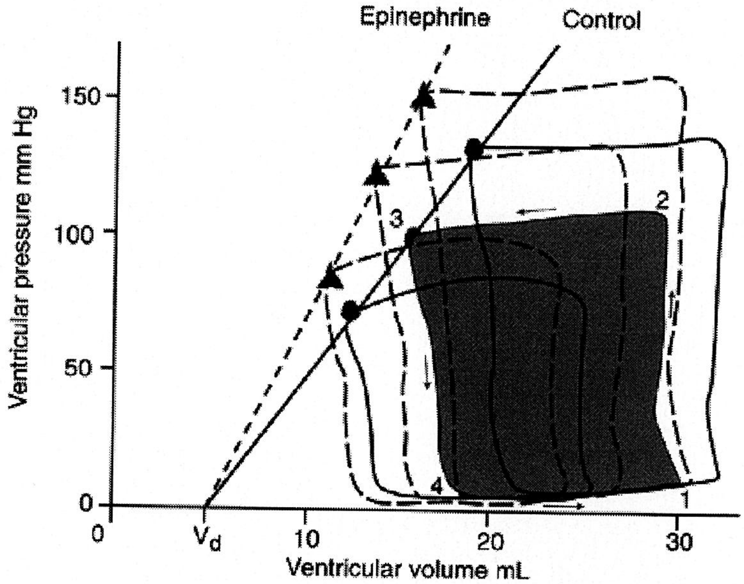

Fig. 1

(b) Velocity measurements in the circulatory system show that blood flow is pulsatile in the aorta but steady in capillaries. Explain how this is possible using a simple analytical model. [30%]

4 (a) In blood, dissolved carbon dioxide is largely transformed into bicarbonate ions through the following reaction:

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^- \qquad K = 4.30 \cdot 10^{-7}$$

Assuming that blood pH is approximately 7.4, determine the value of $\lambda = [HCO_3^-]/[CO_2]$ at the chemical equilibrium. [20%]

(b) We study in this question the balance between ventilation and perfusion of a gas in the lungs. The volume of air renewed in the lung per unit of time is $\dot{V}$ and the total blood flow rate is Q. Show that:

$$\frac{\dot{V}}{Q} = \frac{c_L - c_0}{c_i - c_a}$$

where c_i and c_a are the gas concentrations in the air entering and leaving the lungs respectively. c_0 and c_L are the gas concentrations in blood entering and exiting the lungs, respectively. [30%]

(c) In the case of carbon dioxide, show that the ventilation perfusion ratio takes the following form:

$$\frac{\dot{V}}{Q} = \sigma RT(1+\lambda)\frac{P_0 - P_a}{P_a}$$

where σ is the solubility of carbon dioxide in plasma, R the ideal gas constant and T the temperature. P_a and P_0 are the carbon dioxide partial pressures in the air exiting the lungs and in the blood entering alveoli capillaries, respectively. [50%]

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