ENGINEERING TRIPOS PART IIA

Thursday 22 April 2010 2.30 to 4

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.*

Attachment: Figure for question 1 (1 page), to be submitted with the solution.

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) The steady-state activation curves and time constant curves for the gating variables in the Hodgkin-Huxley model are shown on the left and right panel of Fig. 1, respectively, such that each pair of curves corresponding to the same variable uses a unique symbol (triangle, cross, or circle).

(i) On the copy provided, mark each curve with the name of the gating variable (m, n, or h) to which it belongs. [20%]

(ii) For each gating variable, name the ion that is passed through the corresponding channel. [10%]

(iii) For each ion listed in response to the previous question, select the voltage value from the following set that you think is closest to its equilibrium (Nernst-) potential: $0\,\mathrm{mV}$, $+15\,\mathrm{mV}$, $-15\,\mathrm{mV}$, $+115\,\mathrm{mV}$, $-115\,\mathrm{mV}$ (with the resting membrane potential of the cell defined to be $0\,\mathrm{mV}$). [15%]

(b) Anode break excitation (or postinhibitory rebound) is the paradoxical-looking phenomenon of a neuron generating an action potential after the sudden arrest of a prolonged period (hundreds of milliseconds) of hyperpolarisation, that was maintained by negative external current injection. Explain how the Hodgkin–Huxley model can account for this. (Hint: think of the steady-state activation values and time constants of the various gates in the Hodgkin–Huxley model – see also Fig. 1.) [40%]

(c) For each of the following changes in the membrane properties of a neuron, decide if it increases / decreases / does not affect the membrane time constant and the membrane space constant. Assume that all other properties are unchanged.

(i) Increasing membrane resistance, R_{m}.

(ii) Increasing axial resistance, R_{a}.

(iii) Decreasing membrane capacitance, C_{m}.

[15%]

A copy of Fig. 1 is provided on a separate sheet. This should be handed in with your answers.

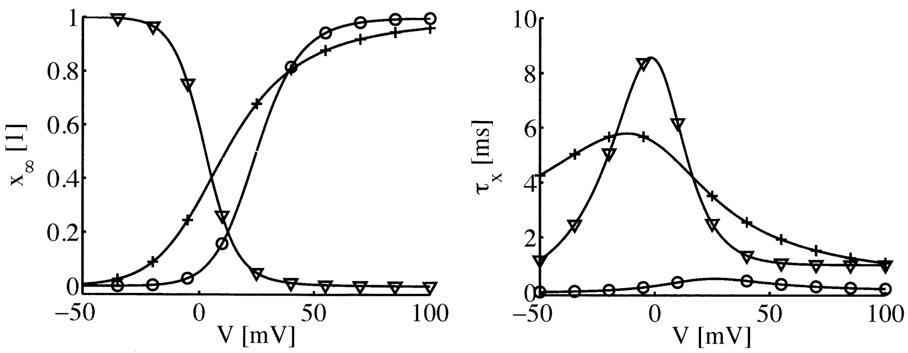


Fig. 1

Steady-state activation curves (left) and time constant curves (right) for the gating variables in the Hodgkin-Huxley model for Question 1.

2 The following data may be useful for any part of this question:

Atomic weight of hydrogen	1 g/mol
Atomic weight of carbon	12 g/mol
Atomic weight of oxygen	16 g/mol
Atomic weight of potassium	39 g/mol

The equilibrium constants above relate to ratios of concentrations measured in moles/litre.

(a) Consider the dissociation reaction of water,

$$H_2O \rightleftharpoons OH^- + H^+$$

(i) What is the equilibrium constant, K_{eq}, of the reaction? [15%]

(ii) What fraction of water molecules are dissociated at pH = 7? [10%]

(b) Lactic acid, also known as milk acid, is a chemical compound that plays a role in several biochemical processes. In animals, lactate is constantly produced during normal metabolism and especially during muscle exercise.

(i) The equilibrium constant of the dissociation reaction of lactic acid,

$$CH_3CH(OH)COOH \rightleftharpoons CH_3CH(OH)COO^- + H^+$$

is $K_A = 1.4 \times 10^{-4}$. Three solutions of lactic acid are made, with concentrations of 1 M, 0.1 M and 0.01 M. What is the pH and the fraction of dissociated molecules in each solution? [25%]

(ii) The pH of all the solutions in part (b).(i) are changed to 2 by adding an acid or a base as needed. What fraction of the lactic acid molecules are now dissociated in each case? [15%]

(c) 1 mole of potassium lactate ($KC_3H_5O_3$) is dissolved in a litre of water.

(i) Find the equilibrium constant K_B of the following reaction:

$$CH_3CH(OH)COO^- + H_2O \rightleftharpoons CH_3CH(OH)COOH + OH^-$$ [10%]

(ii) Assuming that the resulting solution is fairly basic, find its pH. [25%]

3 Consider a cylindrical blood vessel of radius R subjected to a constant pressure difference Δp between both ends. The position along the vessel is x, and the radial distance is r. The blood pressure is represented by the function $p(r,x)$, the blood velocity, which is aligned with the vessel axis, by the function $u(r)$ and the blood shear stress by the function $\tau(r)$. The x axis is oriented so that the velocity $u(r)$ is positive.

(a) (i) By considering force balance on a fluid element, show that:

$$-\frac{\partial p}{\partial x}+\frac{1}{r}\frac{\partial(r\tau)}{\partial r}=0$$

$$\text{and} \quad \frac{\partial p}{\partial r}=0$$

[30%]

(ii) Hence, derive the following expression for the shear stress:

$$\tau=\frac{r}{2}\frac{dp}{dx}$$

[10%]

(b) The rheological behaviour of blood is modelled using the Casson equation:

$$\sqrt{-\tau}=\sqrt{\tau_y}+\sqrt{-\mu\frac{du}{dr}}$$

where τ_y is the blood yield stress. Show that the velocity profile $u(r)$ satisfies the following differential equation in any region where $\frac{du}{dr}\neq 0$:

$$\mu\frac{du}{dr}=\frac{1}{2}\frac{dp}{dx}\left(r-2\sqrt{R_c r}+R_c\right)$$

Find the expression of R_c in the above equation and comment on what it represents. What happens if $R_c > R$? [15%]

(c) Assuming $R_c < R$, find the analytical expression of the solution. It will be useful to consider two different domains, for $R > r > R_c$ and for $R_c > r > 0$. [30%]

(d) A 35 cm long tube, internal diameter 1 mm, is filled with blood. At what pressure difference Δp_0 between the tube ends does the blood begin to flow? Use $\mu = 3.5\cdot 10^{-3}$ Pa·s and $\tau_y = 5\cdot 10^{-3}$ Pa. [15%]

4 A spherical tumor, of radius R_T, is surrounded by capillary vessels that maintain a stationary and uniform oxygen concentration c_0 at the surface of the tumor. The oxygen uptake in the tumor, ρ, is also constant and uniform over the volume of the tumor. The oxygen concentration in the tissue is represented by the function $c(r)$, where r is the distance from the tumor center. The flux $\Phi(r)$ of oxygen in the tumor is related to the oxygen concentration c by Fick's law: $\Phi = -D\nabla c$, where D is the coefficient of diffusion of oxygen in the tissue.

(a) By considering a small volume element in the tissue, establish the following differential equation for the oxygen concentration:

$$D\Delta c - \rho = 0$$ [25%]

(b) What are the boundary conditions of this differential equation? Find its solution. [25%]

(c) What is the critical size of the tumor, above which it gets partially necrosed? Use the following physiological values:
$D = 2 \cdot 10^{-5}$ cm^{2}s^{-1}, $\rho = 1.2 \cdot 10^{-7}$ mol cm^{-3}s^{-1}, and $c_0 = 0.1$ mM. [15%]

(d) Assuming all parts of the tumor are properly oxygenated, calculate the total amount of oxygen consumed by the tumor per unit of time. [10%]

(e) The blood irrigating the tumor comes from a single arteriol of cross-sectional area a. Blood flows in this vessel at a speed u_a and its oxygen concentration is c_0 when it reaches the tumor. Identify another physiological constraint on the tumor size. Use $a = (50\mu\text{m})^2$ and $u_a = 1$ cm s^{-1}. [15%]

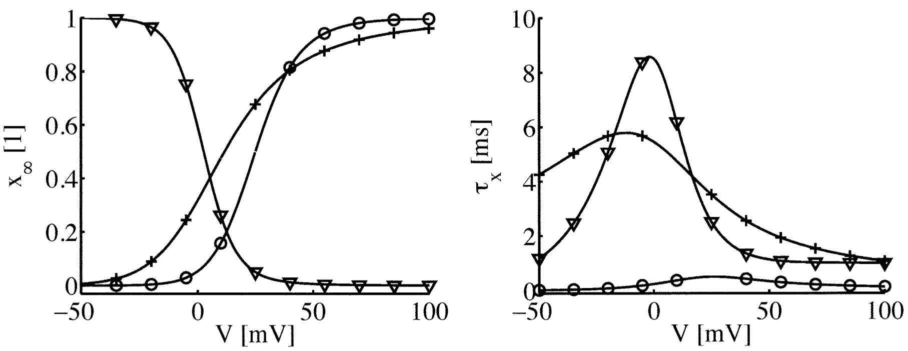
(f) Explain why drugs which block the formation of new blood vessels can slow down the growth of tumors. [10%]

END OF PAPER

Version: final

ENGINEERING TRIPOS PART IIA

Thursday 22 April 2010, Module 3G2, Question 1.



Extra copy of Fig. 1:

Steady-state activation curves (left) and time constant curves (right) for the gating variables in the Hodgkin-Huxley model for Question 1.

Version: final