Version AJK/2

EGT2
ENGINEERING TRIPOS PART IIA

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27 April 2018 9.30 to 11.10

Module 3G2

MATHEMATICAL PHYSIOLOGY - SOLUTIONS

*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
Supplementary page: one extra copy of Fig. 3 (Question 4)
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.

1 (a) Consider the following enzymatic reaction.

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

Using a quasi steady state assumption, find the expression of the rate V of product P formation as a function of the kinetic constants and concentrations of substrate S and enzyme E.

Explain how these parameters could be extracted from a graph of $1/V$ as a function of 1/[S]. [30%]

Answer: The transformation from C to P is usually very fast (this is the purpose of the enzyme). It is therefore reasonable to use the steady-state assumption on C, i.e. that $\frac{d[\mathrm{C}]}{dt} = 0$.

$$k_1[\mathrm{S}][\mathrm{E}] = (k_2 + k_{-1})[\mathrm{C}] \Rightarrow \quad \frac{[\mathrm{S}][\mathrm{E}]}{[\mathrm{C}]} = \frac{(k_2 + k_{-1})}{k_1} \equiv K_M$$

K_M is called the Michaelis constant.

Assuming again that the total amount of enzyme molecules is constant ($[\mathrm{E}] + [\mathrm{C}] = E_0$), we obtain an expression analogous to the case of the fast equilibrium, but with a different constant K_M.

$$\begin{aligned} \Rightarrow \quad [\mathrm{C}] &= E_0 \frac{[\mathrm{S}]}{[\mathrm{S}] + K_M} \\ \Rightarrow \quad V &= k_2 E_0 \frac{[\mathrm{S}]}{[\mathrm{S}] + K_M} \end{aligned} \tag{1}$$

$$\frac{1}{V} = \frac{1}{V_{\max}} + \frac{K_{\mathrm{M}}}{V_{\max}} \frac{1}{[\mathrm{S}]}$$

so a plot of $1/V$ vs. $1/[\mathrm{S}]$ is a straight line with y-intercept $1/V_{\max}$ and slope $K_{\mathrm{M}}/V_{\max}$.

(b) Explain what an enzyme inhibitor is. Describe qualitatively two different types of enzyme inhibition. [15%]

Answer: An enzyme inhibitor is a molecule that affects negatively the rate of product formation of an enzyme. The inhibitor may mind on the active site of the enzyme, therefore preventing the binding to the substrate and its conversion into the product; this is called competitive inhibition. The enzyme may also have several binding sites for the substrate and the inhibitor. In this case, the presence on the inhibitor on the enzyme prevents or slow down the rate of product formation.

(c) The liver produces an enzyme called alcohol dehydrogenase (ADH) responsible for the first step of the degradation and elimination of alcohol in the body. Unfortunately, the

enzyme reacts in the same way with ethylene glycol (EG), a common chemical used in anti-freeze fluids. This reaction initiates the formation of a toxic product, oxalic acid. The crucial reaction to limit is:

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

The Michaelis Menten constant characterising this reaction is $K_M = 10^{-4}$ M.

(i) Fomepizole (F) currently is the most effective treatment for EG poisoning. Its key biochemical property is to react with ADH in the following manner:

$$\mathrm{F} + \mathrm{ADH} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{D} \qquad\qquad K = \frac{k_3}{k_{-3}} = 10^6 \ \mathrm{M}^{-1}$$

What should be the concentration of Fomepizole in the body to reduce the rate of production of oxalic acid by 95% if the concentration of ethylene glycol is 5 x 10^{-5} M? [40%]

Answer: Fomepizole essentially acts as a competitive inhibitor. Therefore, we first have to find the expression of the rate of enzyme reaction in the presence of a competitive inhibitor I.

$$\begin{aligned} \mathrm{S} + \mathrm{E} &\underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{C}_1 \xrightarrow{k_2} \mathrm{P} + \mathrm{E}. \\ \mathrm{E} + \mathrm{I} &\underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{C}_2 \end{aligned}$$

we define new combinations of the rate constants:

$$\begin{aligned} \frac{[\mathrm{S}][\mathrm{E}]}{[\mathrm{C}_1]} &= \frac{(k_2 + k_{-1})}{k_1} \equiv K_M \\ \frac{[\mathrm{I}][\mathrm{E}]}{[\mathrm{C}_2]} &= \frac{k_{-3}}{k_3} \equiv K_I = K^{-1} = 10^{-6} \end{aligned}$$

Using the conservation equation, we get

$$\begin{aligned} [\mathrm{S}](E_0 - [\mathrm{C}_1] - [\mathrm{C}_2]) &= K_M[\mathrm{C}_1] \\ [\mathrm{I}](E_0 - [\mathrm{C}_1] - [\mathrm{C}_2]) &= K_I[\mathrm{C}_2] \end{aligned}$$

Rearranging gives the following equation for the C_1

$$[\mathrm{S}](E_0 - [\mathrm{C}_1] - \frac{[\mathrm{I}](E_0 - [\mathrm{C}_1])}{K_I + [\mathrm{I}]}) = K_M[\mathrm{C}_1]$$

yielding the expressions:

$$\begin{aligned}[\mathrm{C_1}] &= \frac{[\mathrm{S}]E_0K_I}{[\mathrm{S}]K_I+[\mathrm{I}]K_M+K_IK_M}\\ [\mathrm{C_2}] &= \frac{[\mathrm{I}]E_0K_M}{[\mathrm{S}]K_I+[\mathrm{I}]K_M+K_IK_M}\end{aligned}$$

Thus the overall rate of the reaction is:

$$\begin{aligned}V &= k_2[\mathrm{C_1}] = \frac{k_2[\mathrm{S}]E_0}{[\mathrm{S}]+K_M(1+[\mathrm{I}]/K_I)}\\ V &= \frac{V_{\max}[\mathrm{S}]}{[\mathrm{S}]+K'_M} \text{ with } K'_M = K_M(1+[\mathrm{I}]/K_I)\end{aligned}$$

If we want the rate of product formation to be reduced by 95%, we need the rate with inhibitor to match 5% of the rate with no inhibitor:

$$\frac{k_2[\mathrm{S}]E_0}{[\mathrm{S}]+K_M(1+[\mathrm{I}]/K_I)} = 0.05\frac{k_2[\mathrm{S}]E_0}{[\mathrm{S}]+K_M}$$

$$[\mathrm{S}]+K_M(1+[\mathrm{I}]/K_I) = 20([\mathrm{S}]+K_M)$$

Accounting for the numerical values involved in this problem, we have:

$$[5\cdot10^{-5}+10^{-4}(1+[\mathrm{I}]10^6) = 20(5\cdot10^{-5}+10^{-4})$$

$$1+[\mathrm{I}]10^6 = \frac{3\cdot10^{-3}-5\cdot10^{-5}}{10^{-4}} \approx 30$$

$$[\mathrm{I}] \approx 30\mu\mathrm{M}$$

This is the amount of fomepizole in the body in its free form, i.e. excluding D. It would also be acceptable to look for [F]+[D] in this question.

(ii) On 31 December 2002, the BBC reported the following news item (slightly reworded for the exam paper):

Mrs Middleton, from Forfar in Angus, drank antifreeze left on a table by a relative who she was helping decorate her house.
"There was a four to five hour waiting time at the accident and emergency department, but I got taken in after about 30 seconds. The doctors say about 100 millilitres of antifreeze is sufficient to kill you - I had between half a cupful and a cupful of the stuff. I think it's all the more dangerous because it doesn't taste bad - I thought it was particularly strongly-flavoured water. It didn't taste bitter."
She added: "The medical staff at Ninewells were concerned about me because they previously had a patient who died 22 hours after taking it. I was thinking that I was all right and that I had more important things to do but the doctor was saying to me 'you could die here, woman, you must stay'."

Doctors at Ninewells Hospital in Dundee gave her a choice of gin, vodka or whisky. She chose whisky - known as the "water of life" - and was given two cupfuls to drink immediately.

Explain why the doctors made such an unusual offer to a patient in a critical condition. [15%]

Answer: We know that the enzyme binds to both ethanol (its natural substrate) and ethylene glycol. Ethanol is therefore a competitive inhibitor of the enzyme reaction with ethylene glycol. The more ethanol is present, the less enzyme is available for the production of oxalic acid from EG.

2 Consider a simple 1D diffusion model where cells move at constant velocity v either in the (+) or (-) direction along the x axis, with a probability per unit time p_+ to switch from + to -, and p_- to switch from - to +. The 1D density of cells at a particular location x and time t is $n(x,t)$.

(a) Write conservation equations for the cell density functions $n_+(x,t)$ and $n_-(x,t)$ of the (+) and (-) cell populations respectively. [20%]

Answer: Consider a small element dx and apply mass conservation to it for each of the n^+ and n^- populations.

$$\frac{\partial n_+}{\partial t} = -\frac{\partial (v n_+)}{\partial x} + p_- n_- - p_+ n_+$$

$$\frac{\partial n_-}{\partial t} = \frac{\partial (v n_-)}{\partial x} + p_+ n_+ - p_- n_-$$

(b) Use the result above to derive the following differential equation for the cell flux J defined as $J = v\,(n_+ - n_-)$.

$$\frac{\partial J}{\partial t} = -2\,J p - v^2\,\frac{\partial (n)}{\partial x} - v\,\Delta p\,n$$

where $2p = p_+ + p_-$ and $\Delta p = p_+ - p_-$. You may use the following identity in your answer:

$$(n_+ - n_-)(p_+ + p_-) + (n_+ + n_-)(p_+ - p_-) = 2(p_+ n_+ - p_- n_-)$$

[30%]

Answer: We need to find an expression involving $J = v(n_+ - n_-)$ and its derivative, so let's start there:

$$\frac{\partial J}{\partial t} = v(\frac{\partial n_+}{\partial t} - \frac{\partial n_-}{\partial t})$$

This can now be combined with the result of the previous question.

$$\frac{\partial J}{\partial t} = v^2 \left(-\frac{\partial (n_+)}{\partial x} + p_- n_- - p_+ n_+ - \left(\frac{\partial (n_-)}{\partial x} + p_+ n_+ - p_- n_- \right) \right)$$

$$\frac{\partial J}{\partial t} = -v^2\,\frac{\partial n}{\partial x} - 2v\,(p_+ n_+ - p_- n_-)$$

$$\frac{\partial J}{\partial t} = -v^2\,\frac{\partial n}{\partial x} - v\,((n_+ - n_-)(p_+ + p_-) + (n_+ + n_-)(p_+ - p_-))$$

$$\frac{\partial J}{\partial t} = -v^2\,\frac{\partial n}{\partial x} - 2Jp - nv\,\Delta p$$

 (cont.

(c) Making a suitable assumption, show that the cell density n satisfies Fick's law, with an additional drift term. Find the expression of the effective coefficient of diffusion of the cells, as well as the mean speed of the cells due to the drift term. [30%]

Answer: We make a quasi steady state assumption, by saying that after a short transient (of duration of the order of $1/p$) the term $\frac{\partial J}{\partial t} = 0$. Rearranging the terms above, we get:

$$J = -\frac{v^2}{2p}\frac{\partial n}{\partial x} - \frac{vn\,\Delta p}{2p}$$

It may be useful for clarity to rewrite the equation as follows:

$$J = -D\frac{\partial n}{\partial x} + \bar{v}n$$

The first term corresponds to Fick's law, with a coefficient of diffusion $D = \frac{v^2}{2p}$. The second term generates a migratory flux whose amplitude $\bar{v}n$ is controlled by the difference between p_+ and p_-. The mean velocity if the cells is $\bar{v} = -\frac{v\,\Delta p}{2p}$.

(d) Explain how this analysis could be exploited to model chemotaxis. [20%]

Answer: The constants p_+ and p_- are handles in the model that can be connected to external stimuli from the cells environment. There would be typically two other ingredients to model chemotaxis: a model that relates the amount and gradient of an external chemical species to a biochemical signal in the cell (such as a proportion of activated membrane receptors) and a link between this signal and the probabilities p_+ and p_-. The relative values of p_+ and p_- determines if the external species is chemo-attractant or chemo-repellent.

3 Consider blood flowing in an artery. The mean blood velocity at a location x along the artery is $u(x,t)$. The vessel has a homogeneous compliance c. The density of blood is ρ. We define along the vessel the cross-sectional area $A(x,t) = A_0 + cP(x,t)$ where $P(x,t)$ is the blood pressure.

(a) Explain why blood velocity can be assumed to be independent of the radial distance r in the vessel. State the physical principles used in the course to derive the equations below.

$$c\left(\frac{\partial P}{\partial t} + u\frac{\partial P}{\partial x}\right) + A\frac{\partial u}{\partial x} = 0$$

$$\rho\left(\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right) = -\frac{\partial P}{\partial x}$$

[30%]

Answer: Blood flows in arteries are intermittent with high Womersley number. The flow is therefore inertial, and viscosity can be neglected.

Under such approximation, viscous forces from the vessel wall do not have enough time to produce the generic Poiseuille profile expected in steady state. The flow profile is fairly flat (independent of radial position) as a result.

The first equation accounts for mass/volume conservation in a vessel element, assuming incompressibility which is reasonable for blood in physiological conditions. The second equation is a momentum equation (F=ma).

(b) Derive a second order linear partial differential equation (the wave equation) from the equations above, making suitable assumptions in your derivation. [30%]

Answer:

For small amplitude deviations from the rest shape, we can linearise the previous equations by removing all second order terms in u or P. This implies that $u\frac{\partial P}{\partial x}$ and $u\frac{\partial u}{\partial x}$ are negligible, and that $A \approx A_0$.

$$\rho\frac{\partial u}{\partial t} + \frac{\partial P}{\partial x} = 0 \tag{2}$$

$$c\frac{\partial P}{\partial t} + A_0\frac{\partial u}{\partial x} = 0 \tag{3}$$

This can be simplified into a wave equation:

$$\frac{\partial^2 P}{\partial t^2} = \frac{A_0}{c\rho}\frac{\partial^2 P}{\partial x^2} \tag{4}$$

A number of students did not replace A with A_0. In this case, the equation is not fully linearised and the answer was incomplete as a result.

(c) Check that functions of the form $P(x,t) = f(x - vt)$ are solution of the wave equation derived above. Explain what v represents and find its analytical expression as a function of the physical parameters involved in this problem. [20%]

Answer: v represents the wave speed. Let's write $P(x,t) = f(z)$ with $z(x,t) = x - vt$. Using the chain rule, we get:

$$\frac{\partial P}{\partial x} = \frac{df}{dz}\frac{\partial z}{\partial x} = \frac{df}{dz}$$

$$\frac{\partial P}{\partial t} = \frac{df}{dz}\frac{\partial z}{\partial t} = -v\frac{df}{dz}$$

Differentiating one more time provides:

$$\frac{\partial^2 P}{\partial x^2} = \frac{d^2 f}{dz^2}$$

$$\frac{\partial^2 P}{\partial t^2} = v^2\frac{d^2 f}{dz^2}$$

Hence:

$$\frac{\partial^2 P}{\partial t^2} = v^2\frac{\partial^2 P}{\partial x^2}$$

which is the wave equation.

By analogy with the previous question, we get $v = \sqrt{A_0/c\rho}$.

(d) Use the data available on Fig. 1 and Fig. 2 to comment on the suitability of this model. [20%]

Answer: Graphs in fig 2 shows that the graphs of the pressure over time measured at different location along the artery are fairly similar to each other, but shifted in time. The shift in time seems to be proportional to the distance. We measure a lag of 60 ms for a distance of 30 cm. This corresponds to a speed of 5 m/s.

For arteries, the wave speed data in Fig 1 shows that the wave speed is roughly 4-6 m/s, which consistent with the measurement above. This validates the expression derived above.

To get full mark on this question, more was however expected to go from the physical parameters (geometry, Youngs modulus E) to the speed value. The main unknown in the expression of the wave speed is the compliance. How to get it?

The compliance relates area changes to pressure changes: $dA = cdP$. So we need to find a relationship between dA and dP.

For a cylindrical vessel, the internal pressure is related to the tension in the material: $P = \frac{h\sigma}{R}$. The stress comes from the material's deformation: $\sigma \approx E\frac{R-R_0}{R_0}$. This leads to:

$$dP = \frac{Eh}{RR_0}dR$$

as a function of

with $dR = R - R_0$. But we need an expression involving $dA = 2\pi RdR$

$$dP = \frac{Eh}{2\pi R_0^3} dA$$

Note that in this first order calculation, $R \approx R_0$. This leads to an expression for the compliance c:

$$c = \frac{2\pi R_0^3}{Eh}$$

Back to the wave speed! We have:

$$v^2 = \frac{A_0}{c\rho} = \frac{\pi R_0^2 Eh}{\rho 2\pi R_0^3} = \frac{Eh}{\rho 2R_0}$$

All these values are now available in the table or databooks:
$\rho = 10^3 \text{kg/m}^3$, $E \approx 5\ 10^5$ Pa, and $h/2R_0 = 7\ 10^{-2}$m.
This leads to $v \approx$6 m/s which is consistent with observations.

The fact that the curves evolve over time, and in particular get sharper, however suggests that non-linear effects are likely to be involved.

Site		Ascending aorta	Descending aorta	Abdominal aorta	Femoral artery	Carotid artery	Arteriole	Capillary	Venule	Inferior vena cava	Main pulmonary artery
Internal diameter d_i	cm	1·5	1·3	0·9	0·4	0·5	0·005	0·0006	0·004	1·0	1·7
		1·0–2·4	0·8–1·8	0·5–1·2	0·2–0·8	0·2–0·8	0·001–0·008	0·0004–0·0008	0·001–0·0075	0·6–1·5	1·0–2·0
Wall thickness h	cm	0·065		0·05	0·04	0·03	0·002	0·0001	0·0002	0·015	0·02
		0·05–0·08		0·04–0·06	0·02–0·06	0·02–0·04				0·01–0·02	0·01–0·03
h/d_i		0·07		0·06	0·07	0·08	0·4	0·17	0·05	0·015	0·01
		0·055–0·084		0·04–0·09	0·055–0·11	0·053–0·095					
Length	cm	5	20	15	10	15	0·15	0·06	0·15	30	3·5
						10–20	0·1–0·2	0·02–0·1	0·1–0·2	20–40	3–4
Approximate cross-sectional area	cm^2	2	1·3	0·6	0·2	0·2	2×10^{-5}	3×10^{-7}	2×10^{-5}	0·8	2·3
Total vascular cross-sectional area at each level	cm^2	2	2	2	3	3	125	600	570	3·0	2·3
Peak blood velocity	$cm\,s^{-1}$	120	105	55	100		0·75	0·07	0·35	25	70
		40–290	25–250	50–60	100–120		0·5–1·0	0·02–0·17	0·2–0·5	15–40	
Mean blood velocity	$cm\,s^{-1}$	20	20	15	10						15
		10–40	10–40	8–20	10–15						6–28
Reynolds number (peak)		4500	3400	1250	1000		0·09	0·001	0·035	700	3000
α (heart rate 2 Hz)		13·2	11·5	8	3·5	4·4	0·04	0·005	0·035	8·8	15
Calculated wave-speed c_0	$cm\,s^{-1}$	580		770	840	850				100	350
Measured wave-speed c	$cm\,s^{-1}$	500		700	900	800				400	250
		400–600		600–750	800–1030	600–1100				100–700	200–330
Young's modulus E	$Nm^{-2}\times10^5$	4·8		10	10	9				0·7	6
		3–6		9–11	9–12	7–11				0·4–1·0	2–10

Fig. 1

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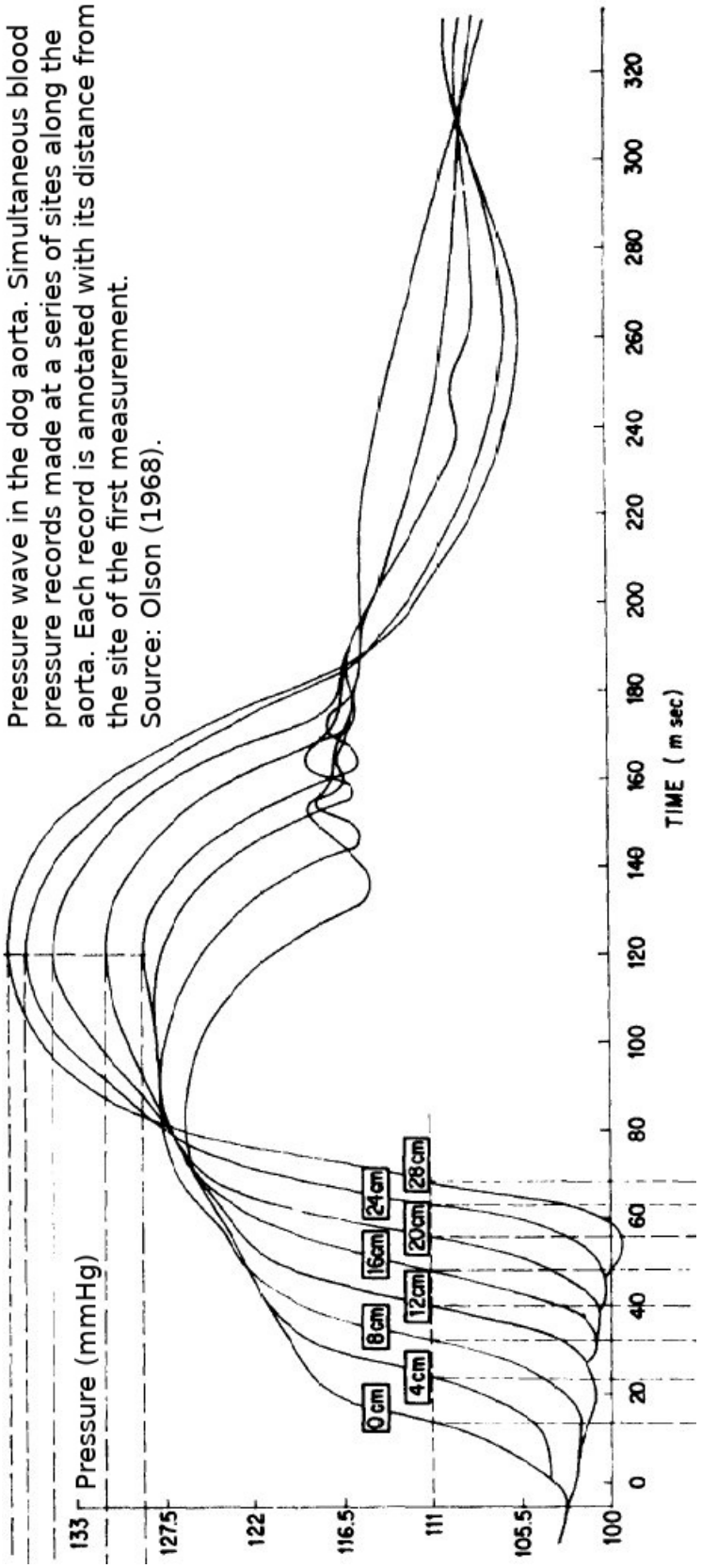
Pressure wave in the dog aorta. Simultaneous blood pressure records made at a series of sites along the aorta. Each record is annotated with its distance from the site of the first measurement.
Source: Olson (1968).
Pressure (mmHg)
133
127.5
122
116.5
111
105.5
100
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
TIME (m sec)
0 cm
4 cm
8 cm
12 cm
16 cm
20 cm
24 cm
28 cm

Fig. 2

4 (a) What ions carry the main currents that contribute to action potential generation in the Hodgkin-Huxley model? [10%]

Answer: The ions that carry the main currents in the Hodgkin-Huxley model are: sodium ion (Na^+), potassium ion (K^+), and to a lesser degree the chloride (Cl^-) ion.

(b) Imagine you want to design a drug that accelerates the upstroke of the action potential, but leaves other characteristics of the action potential unchanged as much as possible. Which rate constants would be its ideal targets and how should they be affected? [30%]

Answer: The upstroke of the action potential is mainly determined by the positive feedback between membrane voltage and the activating gate of the Na^+current (m). Thus, the ideal targets are the rate constants of m: α_m and β_m. They should both be increased.

(c) The time-evolution of the four variables in the Hodgkin-Huxley model during an action potential evoked by a brief current pulse (denoted by I) is given in Fig. 3. Sketch on the additional copy of Fig. 3 how the dynamics of the system will change qualitatively for the same stimulation if the inactivating gate is blocked ($h = 1$ at all times), and all other variables start from the same initial condition as in the normal case. Describe in words the changes you expect before, during, and after the upstroke of the action potential and explain why you expect them. [60%]

Answer: The inactivating variable is the h variable that belongs to the Na^+current.

The changes in the dynamics caused by setting $h = 1$ are shown in blue in Fig. 3, and can be described as follows.

- Before upstroke: Since $h = 1$, the Na^+conductance is increased at rest, which means that the resting membrane potential is higher than normal. However, the variables are started from values corresponding to a normal resting state. As a consequence, the membrane potential, V is slightly increasing towards the new resting membrane potential, and so are m and n which both have monotonically increasing steady-state curves. (If the new resting membrane potential is above the firing threshold, and the stiumulus comes late enough, the cell might even start firing before stimulus onset.)
- During upstroke: Since the Na^+conductance is increased, the positive feedback between the Na^+current and the membrane potential is accelerated, and therefore the upstroke of the action potential is much faster. Thus, V, m, and n are all rising faster than normal, but V and m are still faster than n.
- After upstroke: The Na^+channel never shuts off, it remains open. The K^+channel slowly opens up, too, which eventually brings down a little the membrane potential, V, and hence m, but is insufficient

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to cause proper depolarisation. The cell settles at a new equilibrium potential which is much higher than the normal resting membrane potential (depolarization block). As a results, V, m, and n all level off at abnormally high values.

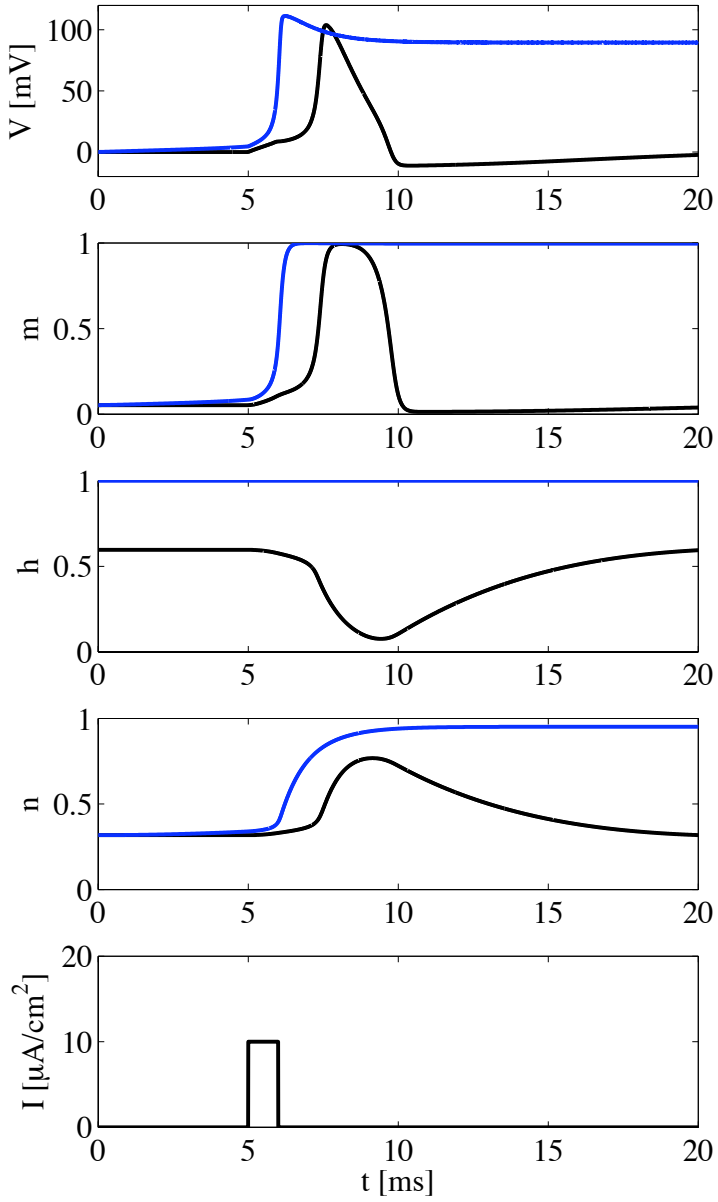

Fig. 3

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Comments on Questions

Q1 Enzyme kinetics

25 attempts (100% of the group), Average mark 16.3/20, Maximum 20/20, Minimum 10/20.

Enzyme kinetics was, as always, a popular topic. A good number of students achieved 20/20. Very few struggled with the first two parts, and most students demonstrated an excellent understanding of enzyme inhibition. Part c was less straight forward, but many students took the time to explain properly what the problem was about and delivered a correct answer.

Q2 Cell diffusion model

21 attempts, Average mark 13.4/20, Maximum 20, Minimum 2.

A very popular question. Students were overall very capable with conservation equations and turning these into a transport equation. Extracting a well defined coefficient of diffusion and mean velocity was more difficult. It was nice to see a number of students making sure that their expression of the mean velocity was dimensionally correct. The use of the model to account for chemotaxis was well understood.

Q3 Pressure waves in arteries

16 attempts, Average mark 12.2/20, Maximum 19, Minimum 3.

This question was overall well answered; the averaged is slightly pulled down by a few outlier marks from students who did not have time to finish it properly. Most of the students could explain well the qualitative questions and demonstrated a good understanding of the problem. In part (a), very few students actually stated that viscosity could be neglected in the force balance equation equation. In part (b), many students forgot that the area A was also a function of P, and did not linearise the equations correctly as a result. A should be replaced by A_0 to keep the set of equations linear. In (d), a range of answers were accepted. Few students calculated the wave speed from the physiological data. Marks were also given to students carefully reflecting on the assumptions made earlier and how they were justified based on the data in the table.

Q4 Electrophysiology

13 attempts, Average mark 10.8/20, Maximum 8, Minimum 15.

Most students answered part (a) correctly, many could answer part (b) mostly correctly, identifying the m gate as critical, but only few stated explicitly that both rate constants of m need to be modified (decreased), and very few students predicted all changes correctly in (c), especially that the opening of the n gate is also going to be faster due the upstroke of V being accelerated (which itself is due to the increased Na+ conductance), even missing some effects that would have been obvious by just looking at the part of the figure that was provided with the question (e.g. that h opening is almost double its normal resting state opening and hence there is also double as much Na+ influx right from the beginning).