Version ML/5

EGT2
ENGINEERING TRIPOS PART IIA

Friday 1 May 2026 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 An enzyme E catalyses the conversion of a substrate S into a product P according to the following mechanism:

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

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

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

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

All equilibrium reactions are assumed to be fast. The total enzyme concentration is E_0, and the rate of product formation is denoted by V.

(a) Consider first the case $k_2 = 0$ and $k_4 \neq 0$, so that the product is formed only from the complex SES.

(i) Derive the following expression for the rate law:

$$\frac{V}{V_{\max}} = \frac{K_1\,K_3\,s^2}{1 + K_1\,s + K_1\,K_3\,s^2}$$

where $V_{\max} = k_4\,E_0$ and $s = [\mathrm{S}]$. [15%]

(ii) Derive an expression for the value s_{h} of s at which $V = \dfrac{V_{\max}}{2}$. [10%]

(iii) In the limit $K_1 \gg K_3$, determine s_{h} and show that the rate law reduces to a standard Michaelis–Menten equation. [15%]

(iv) In the limit $K_3 \gg K_1$, determine s_{h} and show that

$$\frac{V}{V_{\max}} = \frac{s^2}{s_{\mathrm{h}}^2 + s^2}$$

Sketch V as a function of s, and explain how this behaviour differs from Michaelis–Menten kinetics. [20%]

(b) Next consider the case $k_4 = 0$ and $k_2 \neq 0$, so that the product is formed only from the complex ES.

(i) Derive an expression for $\dfrac{V}{k_2\,E_0}$. [20%]

(ii) On the same set of axes, sketch V as a function of s for $K_3 = 0$ (when the complex SES does not form), and for $K_3 \neq 0$. Explain why this type of enzyme kinetics is called *substrate inhibition*. [20%]

2 Blood is often modelled as a non-Newtonian fluid with a yield stress. Two commonly used constitutive laws are the Bingham and the Casson models. The Bingham model is

$$\tau = \tau_{\mathrm{y}} + \mu_{\mathrm{b}}\,\dot{\gamma}$$

where τ is the shear stress, $\dot{\gamma}$ the shear rate, τ_{y} the yield stress, and μ_{b} the viscosity. The Casson model is

$$\sqrt{\tau} = \sqrt{\tau_{\mathrm{y}}} + \sqrt{\mu_{\mathrm{c}}\,\dot{\gamma}}$$

where μ_{c} is the viscosity. For both models, $\dot{\gamma} = 0$ when $\tau \le \tau_{\mathrm{y}}$.

(a) Consider steady, fully developed flow in a cylindrical vessel of radius R, driven by a constant pressure gradient $G > 0$. Let r denote the radial coordinate. Then

$$\frac{1}{r}\frac{\partial(r\tau)}{\partial r} = G$$

(i) Show that both models predict a central plug region, and determine the plug radius R_{p} in terms of G and τ_{y}. [15%]

(ii) Assuming $R_{\mathrm{p}} < R$, derive expressions for $\dot{\gamma}(r)$ for each model in terms of G, R_{p}, and the relevant viscosity. [15%]

(iii) For each model, show that

$$\dot{\gamma}(r) \propto (r - R_{\mathrm{p}})^{n} \quad \text{as } r \to R_{\mathrm{p}} \text{ (with } r > R_{\mathrm{p}})$$

and determine the exponent n in each case. Comment briefly on which model is more suitable for describing blood. [20%]

(b) A yield stress τ_{y} and viscosity μ have been measured for blood. It is proposed to discriminate between the Bingham and Casson models by measuring the volumetric flow rate Q in the vessel of part (a). All models will now employ the measured τ_{y} and μ.

(i) Using integration by parts, show that Q can be written as an integral involving only $\dot{\gamma}(r)$. Verify your result by recovering Poiseuille's law,

$$Q_{\mathrm{n}} = \frac{\pi\, G\, R^{4}}{8\,\mu}$$

for the flow rate Q_{n} of a Newtonian fluid. [20%]

(ii) Let $\Delta Q = |Q_{\mathrm{b}} - Q_{\mathrm{c}}|$ denote the absolute difference between the flow rates predicted by the Bingham and Casson models, respectively. Using parts (a)(ii) and (b)(i), show that

$$\frac{\Delta Q}{Q_{\mathrm{n}}} = \frac{8}{21}\left(x^{4} - 7\,x + 6\,x^{1/2}\right), \quad \text{where } x = \frac{R_{\mathrm{p}}}{R}$$ [20%]

(iii) Comment briefly on whether such measurements could reliably discriminate between the two models. [10%]

3 Assuming Poiseuille flow through systemic vessels, it can be shown that the flux Q of blood in the x direction, through a cylindrical vessel with a cross-section area A_0, is given by

$$Q = -\frac{A_0^2}{8\,\pi\,\mu}\,\frac{\partial P}{\partial x}$$

where μ is the viscosity and P denotes the pressure.

(a) State the assumptions required for a Poiseuille flow. [10%]

(b) Assume that at each level (arteries, veins, capillaries, etc) there are N parallel vessels, each of the same radius and cross-sectional area A_0 and length L_v.

(i) Show that the pressure drop at each level is given by

$$\frac{\partial P}{\partial x}\,L_\mathrm{v} \propto \frac{L_\mathrm{v}}{A\,A_0}$$

where $A = N\,A_0$. [20%]

(ii) Using the data in Table 1, explain why most of the viscous dissipation occurs in the capillaries. [20%]

(c) A compliant vessel has length L, input pressure P_0, output pressure P_1 and zero external pressure. Assume a linear relationship between the cross-sectional area A and the internal pressure P:

$$A = A_0 + C\,P$$

where A_0 is the cross-sectional area for zero internal pressure and C is the compliance.

(i) Sketch the pressure, cross-sectional area, and the centerline velocity along the vessel. [20%]

(ii) Derive an expression for the flux in the x-direction through the vessel. Use this expression to explain why compliance makes flow easier in a vessel. [30%]

Site		Ascending aorta		Descending aorta	Abdominal aorta	Femoral artery	Carotid artery
Internal diameter d_i	cm	1·5		1·3	0·9	0·4	0·5
		1·0–2·4		0·8–1·8	0·5–1·2	0·2–0·8	0·2–0·8
Wall thickness h	cm		0·065		0·05	0·04	0·03
			0·05–0·08		0·04–0·06	0·02–0·06	0·02–0·04
h/d_i			0·07		0·06	0·07	0·08
			0·055–0·084		0·04–0·09	0·055–0·11	0·053–0·095
Length	cm	5		20	15	10	15
							10–20
Approximate cross-sectional area	cm^2	2		1·3	0·6	0·2	0·2
Total vascular cross-sectional area at each level	cm^2	2		2	2	3	3
Peak blood velocity	$cm\ s^{-1}$	120		105	55	100	
		40–290		25–250	50–60	100–120	
Mean blood velocity	$cm\ s^{-1}$	20		20	15	10	
		10–40		10–40	8–20	10–15	
Reynolds number (peak)		4500		3400	1250	1000	
α (heart rate 2 Hz)		13·2		11·5	8	3·5	4·4
Calculated wave-speed c_0	$cm\ s^{-1}$		580		770	840	850
Measured wave-speed c	$cm\ s^{-1}$		500		700	900	800
			400–600		600–750	800–1030	600–1100
Young's modulus E	$Nm^{-2} \times 10^5$		4·8		10	10	9
			3–6		9–11	9–12	7–11

Site		Arteriole	Capillary	Venule	Inferior vena cava	Main pulmonary artery
Internal diameter d_i	cm	0·005	0·0006	0·004	1·0	1·7
		0·001–0·008	0·0004–0·0008	0·001–0·0075	0·6–1·5	1·0–2·0
Wall thickness h	cm	0·002	0·0001	0·0002	0·015	0·02
					0·01–0·02	0·01–0·03
h/d_i		0·4	0·17	0·05	0·015	0·01
Length	cm	0·15	0·06	0·15	30	3·5
		0·1–0·2	0·02–0·1	0·1–0·2	20–40	3–4
Approximate cross-sectional area	cm^2	2×10^{-5}	3×10^{-7}	2×10^{-5}	0·8	2·3
Total vascular cross-sectional area at each level	cm^2	125	600	570	3·0	2·3
Peak blood velocity	$cm\ s^{-1}$	0·75	0·07	0·35	25	70
		0·5–1·0	0·02–0·17	0·2–0·5	15–40	
Mean blood velocity	$cm\ s^{-1}$					15
						6–28
Reynolds number (peak)		0·09	0·001	0·035	700	3000
α (heart rate 2 Hz)		0·04	0·005	0·035	8·8	15
Calculated wave-speed c_0	$cm\ s^{-1}$				100	350
Measured wave-speed c	$cm\ s^{-1}$				400	250
					100–700	200–330
Young's modulus E	$Nm^{-2} \times 10^5$				0·7	6
					0·4–1·0	2–10

Table 1

4 This question is about the spatial average of the Cl^- flux inside a Cl^- channel.

You can assume that the intra- and extra-cellular concentrations of Cl^- do not change over time. Unless otherwise noted, the spatial average of the flux inside the channel at time t is defined as $\bar{J}(t) = \frac{1}{L}\int_0^L J(x,t)\ \mathrm{d}x$, where $J(x,t)$ is the flux at position $x \in [0, L]$ and time t, and L is the length of the channel.

Explain with reasons what is the spatial average of the Cl^- flux under each of the following conditions, or explain with reasons why it cannot be determined. Support your explanations with mathematical derivations.

(a) The membrane potential momentarily equals the Cl^- Nernst potential. [15%]

(b) The membrane potential momentarily equals the Cl^- Nernst potential, and the spatial average of the flux inside the channel is defined as a weighted average, where the weighting factor for the flux at a given location is inversely proportional to the Cl^- concentration at that location. [10%]

(c) The membrane potential momentarily equals the Cl^- Nernst potential, and Cl^- flux inside the channel is unidirectional (its sign is the same everywhere inside the channel). [25%]

(d) The membrane potential has been held at the Cl^- Nernst potential for a millisecond. [15%]

(e) The membrane potential has been held at 10 mV above the Cl^- Nernst potential for a millisecond. [5%]

(f) The membrane potential has been held at 10 mV above the Cl^- Nernst potential for a millisecond, the conditions for the "long channel limit" are satisfied, the conductance of the channel for Cl^- is 20 pS, and the cross-sectional area of its pore is 0.4 nm^2. [30%]

END OF PAPER