

EGT2
ENGINEERING TRIPOS PART IIA

Monday 29 April 2019 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

Engineering Data Book

CUED approved calculator allowed

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) Explain the difference between noncompetitive and uncompetitive enzyme inhibition, and write reaction equations for each, indicating the rate constants. [20%]

(b) For *uncompetitive* inhibition *only*, derive the rate of product formation as a function of the substrate and inhibitor concentrations, and draw the corresponding Lineweaver-Burk plots, indicating how the plot changes when the inhibitor is introduced. [40%]

(c) The data in Table 1 show the rate of product formation V for a particular enzyme as a function of substrate concentration S in the absence and presence of inhibitor I . Is the data consistent with I being a noncompetitive or uncompetitive inhibitor? Justify your answer, optionally including plots in your answer. [20%]

	S	3	10	30
No inhibitor	V	10.5	22.0	34.1
With inhibitor I	V	2.2	4.6	6.9

Table 1

(d) Explain what would make a noncompetitive or uncompetitive (as opposed to a competitive) inhibitor desirable as a drug for the inhibition of a particular enzyme? [20%]

2 This question is about the propagation of action potentials in a myelinated (and cylindrical) axon.

(a) The inner diameter of the cylindrical axon (without the myelin sheath) is $d = 2 \mu\text{m}$. We know that d is optimal for propagation speed given the outer diameter of the axon including the myelin sheath, d_{outer} . Compute the value of d_{outer} . [15%]

(b) The membrane capacitance (per unit area) of both the axon and the myelin sheath is $C_m = 1 \mu\text{F}/\text{cm}^2$. Voltage gated channels in the axon are confined to nodes of Ranvier, otherwise the axon membrane is passive with a total membrane conductance (per unit area) $g_m = 0.1 \text{mS}/\text{cm}^2$. The myelin sheath has the same membrane conductance (per unit area) as the axon membrane. What is the time constant at the nodes of Ranvier, τ_m , and between the nodes of Ranvier, τ_{my} ? [15%]

(c) The space constant of the axon at the nodes of Ranvier is $\lambda_m = 0.5 \text{mm}$, and each layer of the myelin sheath between the nodes of Ranvier is $\Delta r = 15 \text{nm}$ thick. What is the space constant between the nodes of Ranvier, λ_{my} ? [20%]

(d) We regard an action potential as a spatially and temporally point-like pulse, reaching a depolarisation of $\Delta V = 100 \text{mV}$ at the location where it is initiated 1 ms after it has been initiated. Using the formula for the voltage response function for a pulse point current injection into an infinite cable, compute the constant \bar{V} that scales the voltage response function. [20%]

(e) The depolarisation needed to reach the firing threshold at a node of Ranvier is $V_{\text{thresh}} = 10 \text{mV}$. Using the same formula for the spread of membrane potential in the axon as above, compute the maximal distance, x , between two consecutive nodes of Ranvier at which active propagation of the action potential is preserved. In order to simplify your derivation, you can assume that $x \gg \lambda_{\text{my}}$ and you may find the following approximation useful: $\frac{1}{\sqrt{y}} e^{-y} \simeq e^{-y}$ for $y \geq 1$. [30%]

3 Assuming Poiseuille flow through systemic vessels, it can be shown that the flux 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) 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

$$\frac{\partial P}{\partial x} L_v \propto \frac{L_v}{AA_0}$$

where $A = NA_0$. [20%]

(ii) Using the data in Table 2, explain why most of the viscous dissipation occurs in the capillaries. [20%]

(b) For a compliant vessel with 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 :

$$A = A_0 + CP$$

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

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

(ii) Derive an expression for the volume of blood contained in the vessel and explain why veins contain a large portion of the blood. [30%]

Site	Ascending aorta	Descending aorta	Abdominal aorta	Femoral artery	Carotid artery	Arteriole	Capillary	Venule	Inferior vena cava	Main pulmonary artery
Internal diameter d_i	1.5 1.0-2.4	1.3 0.8-1.8	0.9 0.5-1.2	0.4 0.2-0.8	0.5 0.2-0.8	0.005 0.001-0.008	0.0006 0.0004-0.0008	0.004 0.001-0.0075	1.0 0.6-1.5	1.7 1.0-2.0
Wall thickness h	0.065 0.05-0.08 0.07	0.065 0.05-0.08 0.07	0.05 0.04-0.06 0.06	0.04 0.02-0.06 0.07	0.03 0.02-0.04 0.08	0.002 0.001-0.002 0.002	0.0001 0.0001-0.0001 0.0001	0.0002 0.0002-0.0002 0.0002	0.015 0.01-0.02 0.015	0.02 0.01-0.03 0.01
h/d_i	0.055-0.084	0.055-0.084	0.04-0.09	0.055-0.11	0.053-0.095	0.4	0.17	0.05	0.015	0.01
Length	5	20	15	10	15	0.15	0.06	0.15	30	3.5
Approximate cross-sectional area	cm^2	cm^2	cm^2	cm^2	cm^2	cm^2	cm^2	cm^2	cm^2	cm^2
Total vascular cross-sectional area at each level	2	2	2	3	3	$0.1-0.2$ 2×10^{-5}	$0.02-0.1$ 3×10^{-7}	$0.1-0.2$ 2×10^{-5}	20-40	3-4
Peak blood velocity	120 40-290	105 25-250	55 50-60	100 100-120	10-20	0.75 0.5-1.0	0.07 0.02-0.17	0.35 0.2-0.5	25	70
Mean blood velocity	20 10-40	20 10-40	15 8-20	10 10-15	0.2				15-40	15
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}	cm s^{-1}	cm s^{-1}	cm s^{-1}	cm s^{-1}				100	350
Measured wave-speed c	500	500	700	900	800				400	250
Young's modulus E	$\text{Nm}^{-2} \times 10^5$	$\text{Nm}^{-2} \times 10^5$	$\text{Nm}^{-2} \times 10^5$	$\text{Nm}^{-2} \times 10^5$	$\text{Nm}^{-2} \times 10^5$				100-700	200-330
	4-8	4-8	10	10	9				0.7	6
	3-6	3-6	9-11	9-12	7-11				0.4-1.0	2-10

Table 2

4 Consider a cylindrical blood vessel of radius R and length L subjected to a constant pressure difference $\Delta P > 0$ between the two ends. Let r and x denote the radial and longitudinal positions in the vessel, respectively. Blood pressure is represented by the function $p(r, x)$, blood velocity (aligned with the vessel axis) by the function $u(r)$, blood shear stress by the function $\tau(r)$, and local hematocrit by the function $h_{ct}(r)$. The x -axis is oriented so that $u(r)$ is positive.

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

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

and that
$$\frac{\partial p}{\partial r} = 0$$
 [30%]

(ii) Assuming blood is Newtonian with viscosity μ , the resulting velocity profile is given by:

$$u(r) = \frac{R^2 \Delta P}{4\mu L} \left(1 - \frac{r^2}{R^2}\right)$$

Discuss the validity of all the assumptions made to obtain this result. [15%]

(b) The tube hematocrit Hct_T and the discharge hematocrit Hct_D are defined as:

$$\text{Hct}_T = \frac{\int_0^R 2\pi r h_{ct}(r) dr}{\int_0^R 2\pi r dr} \quad \text{and} \quad \text{Hct}_D = \frac{\int_0^R 2\pi r h_{ct}(r) u(r) dr}{\int_0^R 2\pi r u(r) dr}$$

(i) Explain qualitatively what these two values of hematocrit represent. [10%]

(ii) In a simple model, $h_{ct}(r)$ takes the following values:

$$h_{ct}(r) = \begin{cases} \text{Hct}_0 & \text{for } 0 \leq r \leq R - \delta \\ 0 & \text{for } R - \delta \leq r \leq R \end{cases}$$

where Hct_0 is a positive constant, and δ is the thickness of the cell-free plasma layer. Assuming that $u(r)$ follows the equation in (a)(ii), derive an expression for the hematocrit ratio $\text{Hct}_T/\text{Hct}_D$. [30%]

(iii) Give an estimate of δ , with justification, and sketch $\text{Hct}_T/\text{Hct}_D$ as a function of R (for $R > \delta$), also explaining the physical interpretation of the curve. How does the hematocrit ratio vary with R when $R < \delta$? [15%]

END OF PAPER