Version ML/2

EGT2
ENGINEERING TRIPOS PART IIA

Monday 29 April 2019 9.30 to 11.10

Module 3G2 – CRIB

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%]

Answer: Both non-competitive and uncompetitive inhibitors bind to the enzyme allosteric sites, away from the active site of the substrate, but uncompetitive inhibitors can only bind to the substrate-enzyme complex, whereas non-competitive inhibitors can bind to the empty enzyme as well as the enzyme substrate complex.
Reaction diagrams:

Uncompetitive inhibition:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \overset{k_2}{\rightarrow} E + P$$
$$C_1 + I \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_2$$

Non-competitive inhibition:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \overset{k_2}{\rightarrow} E + P$$
$$C_1 + I \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_2$$
$$E + I \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_3$$
$$C_3 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_2$$

(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%]

Answer: The differential equations for the uncompetitive case are

$$\begin{aligned}
\frac{dS}{dt} &= k_{-1}C_1 - k_1 SE \\
\frac{dI}{dt} &= k_{-3}C_2 - k_3 IC_1 \\
\frac{dE}{dt} &= (k_{-1} + k_2)C_1 - k_1 SE \\
\frac{dC_1}{dt} &= k_1 SE - (k_2 + k_{-1})C_1 + k_{-3}C_2 - k_3 C_1 I \\
\frac{dC_2}{dt} &= k_3 IC_1 - k_{-3}C_2 \\
\frac{dP}{dt} &= k_2 C_1
\end{aligned}$$

The conservation of the number of enzyme molecules leads to

$$E + C_1 + C_2 = E0$$

The quasi-steady-state assumption implies that the rates of change of E, C_1 and C_2 are zero which, combined with the differential equations leads to

$$k_3 I C_1 = k_{-3} C_2$$

and

$$k_1 S E = (k_{-1} + k_2) C_1$$

These are now combined into new constants:

$$\frac{I C_1}{C_2} = \frac{k_{-3}}{k_3} = K_I$$

and

$$\frac{S E}{C_1} = \frac{k_{-1} + k_2}{k_1} = K_M$$

Using these new constants, the second quasi-steady-state equation is combined with the conservation equation to yield

$$S\left(E_0 - C_1 - \frac{I C_1}{K_I}\right) = K_M C_1$$

Which, after rearranging, gives the rate V as

$$V = k_2 C_1 = \frac{k_2 S E_0}{K_M + S(1 + I/K_I)}$$

The Lineweaver-Burk plot is $1/V$ against $1/S$, which is linear:

$$\frac{1}{V} = \frac{K_M}{k_2 E_0}\frac{1}{S} + \frac{1 + I/K_I}{k_2 E_0}$$

and its slope is independent of the inhibitor concentration I.

(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

Answer: Plotting $1/V$ against $1/S$ (Lineweaver-Burk plot) reveals that the slopes of the two lines (with and without inhibitor) are quite different, which implies that this is a noncompetitive inhibitor.

(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%]

Answer: Both types of allosteric inhibitors decrease the maximum rate of production, whereas competitive inhibition results in an increase of substrate concentration without a decrease in the production rate. So when an increase in substrate concentration is desired, competitive inhibitors are fine, but when a decrease of production rate is needed, noncompetitive or uncompetitive inhibitors are called for. It is much easier to design inhibitors that are competitive with known substrates, because they are structurally similar to the substrate.

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 $d = 2\,\mu$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%]

Answer:

$$r_{\text{inner}} = r_{\text{outer}} \sqrt{\frac{1}{e}}$$
$$d_{\text{outer}} = \sqrt{e}\, d \simeq 3.3\,\mu\text{m}$$

(b) The membrane capacitance (per unit area) of both the axon and the myelin sheath is $C_{\text{m}} = 1\,\mu\text{F/cm}^2$. 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) $g_{\text{m}} = 0.1\,\text{mS/cm}^2$. 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%]

Answer:

$$\tau_{\text{m}} = \tau_{\text{my}} = C_{\text{m}}\, R_{\text{m}} = C_{\text{m}}/g_{\text{m}} = 10\,\text{ms}$$

(c) The space constant of the axon at the nodes of Ranvier is $\lambda_{\text{m}} = 0.5\,\text{mm}$, 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%]

Answer:

$$\lambda_{\text{m}} = \sqrt{\frac{r_{\text{inner}}\, R_{\text{m}}}{2\, R_{\text{a}}}}$$
$$\lambda_{\text{my}} = r_{\text{outer}} \sqrt{\frac{R_{\text{m}}}{4\,\Delta r\, R_{\text{a}}\, e}}$$
$$= \sqrt{\frac{r_{\text{inner}}}{2\,\Delta r}}\,\lambda_{\text{m}} = \sqrt{\frac{d}{4\,\Delta r}}\,\lambda_{\text{m}}$$
$$\simeq 2.9\,\text{mm}$$

(d) We regard an action potential as a spatially and temporally point-like pulse, reaching a depolarisation of $\Delta V = 100\,\mathrm{mV}$ 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%]

Answer:

$$V(x,u) = \bar{V}\,\lambda_{\mathrm{my}}\,\frac{1}{\sqrt{4\,\pi\,\lambda_{\mathrm{my}}^2\,u}}\,e^{-\frac{x^2}{4\,\lambda_{\mathrm{my}}^2\,u}}\,e^{-u} \qquad \text{where } u = \frac{t}{\tau_{\mathrm{my}}}$$

$$u_{\mathrm{spike}} = \frac{t_{\mathrm{spike}}}{\tau_{\mathrm{my}}} = \frac{1}{10}$$

$$\Delta V = V\left(x=0, u_{\mathrm{spike}}\right) = \bar{V}\,\frac{1}{\sqrt{4\,\pi\,u_{\mathrm{spike}}}}\,e^{-u_{\mathrm{spike}}}$$

$$\bar{V} \simeq 124\,\mathrm{mV}$$

(e) The depolarisation needed to reach the firing threshold at a node of Ranvier is $V_{\mathrm{thresh}} = 10\,\mathrm{mV}$. 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 $x \gg \lambda_{\mathrm{my}}$ and you may find the following approximation useful: $\frac{1}{\sqrt{y}}\,e^{-y} \simeq e^{-y}$ for $y \geq 1$. [30%]

Answer:

The maximal voltage at distance $x \gg \lambda_{\mathrm{my}}$ from the point of action potential generation is reached at (unitless) time

$$u_{\mathrm{max}} = \frac{x}{2\,\lambda_{\mathrm{my}}}$$

Thus, the maximal voltage at distance x is

$$\begin{aligned} V_{\mathrm{max}} = V(x, u_{\mathrm{max}}) &= \bar{V}\,\lambda_{\mathrm{my}}\,\frac{1}{\sqrt{4\,\pi\,\lambda_{\mathrm{my}}^2\,u_{\mathrm{max}}}}\,e^{-\frac{x^2}{4\,\lambda_{\mathrm{my}}^2\,u_{\mathrm{max}}}}\,e^{-u_{\mathrm{max}}} \\ &= \frac{\bar{V}}{\sqrt{2\,\pi}}\,\frac{1}{\sqrt{\frac{x}{\lambda_{\mathrm{my}}}}}\,e^{-\frac{x}{\lambda_{\mathrm{my}}}} \\ &\simeq \frac{\bar{V}}{\sqrt{2\,\pi}}\,e^{-\frac{x}{\lambda_{\mathrm{my}}}} \end{aligned}$$

In order for active propagation of the action potential to be preserved, the maximal voltage needs to be higher than the threshold at the next node of Ranvier so that an action potential is generated there, too:

$$
\begin{aligned}
V_{\text{thresh}} &< V_{\text{max}} \\
V_{\text{thresh}} &< \frac{\bar{V}}{\sqrt{2\,\pi}}\, e^{-\frac{x}{\lambda_{\text{my}}}} \\
x &< \left[\ln \frac{\bar{V}}{V_{\text{thresh}}} - \frac{1}{2}\,\ln(2\,\pi)\right] \lambda_{\text{my}} \\
&\simeq 1.3\,\lambda_{\text{my}}
\end{aligned}
$$

(This shows that our initial assumption of $x \gg \lambda_{\text{my}}$ was not entirely unjustified.)

$$\simeq 3.8\,\text{mm}$$

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%]

Answer: For each vessel,

$$Q_0 = -\frac{A_0^2}{8\pi\mu}\frac{\partial p}{\partial x}$$

Total

$$Q = NQ_0 = -\frac{NA_0^2}{8\pi\mu}\frac{\partial p}{\partial x} = -\frac{A_0 A}{8\pi\mu}\frac{\partial p}{\partial x}$$

Therefore,

$$\frac{\partial p}{\partial x} \propto \frac{Q}{A_0 A}$$

Because the flow is incompressible, Q must be a constant at each level, therefore,

$$\frac{\partial p}{\partial x} \propto \frac{1}{A_0 A}$$

$$\frac{\partial p}{\partial x}L_v \propto \frac{L_v}{A_0 A}$$

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

Answer:

$$\Delta p \propto \frac{L_v}{A_0 A}$$

Using the data in the table:

Ascending Aorta	Femoral Artery	Arteriole	Capillary	Venule
$\frac{5}{2\times 2}$	$\frac{10}{0.2\times 3}$	$\frac{0.15}{2\times 10^{-5}\times 125}$	$\frac{0.06}{3\times 10^{-7}\times 600}$	$\frac{0.15}{2\times 10^{-5}\times 570}$
1.25	17	60	333	13

This shows that most of the viscous dissipation occurs in the capillaries.

 (cont.

(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%]

Answer:

$$8\pi\mu Q = -\frac{\partial p}{\partial x} A^2(p)$$

The left hand side is a constant. Therefore,

$$\int_0^L dx = -\frac{1}{8\pi\mu Q} \int_{p_0}^{p_1} A^2(p) dp$$

$$L = -\frac{1}{8\pi\mu Q} A_0^2 \int_{p_0}^{p_1} (1+\gamma p)^2 dp$$

where $\gamma = C/A_0$.

$$\begin{aligned} \frac{8\pi\mu Q}{A_0^2} L &= \frac{1}{3\gamma} (1+\gamma p)^3 \Big|_{p_1}^{p_0} \\ &= (p_0 - p_1) \left\{ 1 + \gamma(p_0 + p_1) + \frac{\gamma^2}{3}(p_0^2 + p_0 p_1 + p_1^2) \right\} \end{aligned}$$

Because Q increases with γ ($\propto C$, the compliance), for a given pressure difference, the flow rate increases with increasing compliance, thus making flow easier in a vessel with increasing compliance.

(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%]

Answer:

$$V = \int_0^L A(x) dx$$

$$V = \int_{p_0}^{p_1} A(p) \frac{dx}{dp} dp$$

$$\frac{dp}{dx} = -\frac{8\pi\mu Q}{A^2}$$

$$\frac{dx}{dp} = -\frac{A^2}{8\pi\mu Q}$$

Therefore,

$$\begin{aligned} V &= -\int_{p_0}^{p_1} \frac{A^3(p)}{8\pi\mu Q} dp = -\frac{1}{8\pi\mu Q} \int_{p_0}^{p_1} A^3(p) dp \\ &= -\frac{1}{8\pi\mu Q} \int_{p_0}^{p_1} (A_0 + Cp)^3 dp \\ &= -\frac{A_0^3}{8\pi\mu Q} \int_{p_0}^{p_1} (1 + \gamma p)^3 dp \\ &= \frac{A_0^3}{32\pi\mu Q} \frac{1}{\gamma} \, (1 + \gamma p)^4 \Big|_{p_1}^{p_0} \\ &= \frac{A_0^3}{32\pi\mu Q} (p_0 - p_1) \, \{4(p_0 - p_1) + O(\gamma)\} \end{aligned}$$

The total volume of the veins is large compared to the other vessels and they are highly compliant (much more than arteries) allowing for the blood to flow through a small pressure drop.

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

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:

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

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

Answer: In cylindrical coordinates, we consider a small volume element located in (r, θ, x), with dimensions along these directions $\mathrm{d}r$, $r\mathrm{d}\theta$ and $\mathrm{d}x$. Since u only depends on r, shear forces are only in the x direction. Considering first the force balance in the x direction, we get:

$$p(r,x) \times r\mathrm{d}\theta\ \mathrm{d}r - p(r, x+\mathrm{d}x) \times r\mathrm{d}\theta\ \mathrm{d}r - \tau(r) \times r\mathrm{d}\theta\ \mathrm{d}x + \tau(r+\mathrm{d}r) \times (r+\mathrm{d}r)\mathrm{d}\theta\ \mathrm{d}x = 0$$

This can be rewritten as:

$$-\frac{\partial p}{\partial x} \times r\mathrm{d}\theta\ \mathrm{d}r\ \mathrm{d}x + \frac{\partial (r\tau)}{\partial r} \times \mathrm{d}\theta\ \mathrm{d}r\ \mathrm{d}x = 0$$

leading to:

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

The force balance along the radial direction provides the next equation:

$$p(r,x) \times r\mathrm{d}\theta\ \mathrm{d}x - p(r+\mathrm{d}r, x) \times (r+\mathrm{d}r)\mathrm{d}\theta\ \mathrm{d}x + \underbrace{2p(r,x) \times \mathrm{d}r \sin(\mathrm{d}\theta/2)\ \mathrm{d}x}_{\text{from the lateral sides}} = 0$$

This can be rewritten as:

$$-\frac{\partial (rp)}{\partial r} \times \mathrm{d}\theta\ \mathrm{d}r\ \mathrm{d}x + p(r,x) \times \mathrm{d}\theta\ \mathrm{d}r\ \mathrm{d}x = 0$$

Using the product rule on the first term, we get after simplification:

$$-\frac{\partial p}{\partial r} = 0$$

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

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

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

Answer: The fluid is single phase, incompressible, and its constitutive model is $\tau = \mu\frac{\mathrm{d}u}{\mathrm{d}r}$. The fluid's

inertia is negligible, and the flow is steady in a rigid wall vessel. The boundary conditions are $u(r = R) = 0$ ("no-slip" boundary condition at the vessel wall) and $\frac{\mathrm{d}u}{\mathrm{d}r}\big|_{r=0} = 0$ (axial symmetry). For real blood flow, several of these assumptions are questionable (multiphase and non-uniform, rate-dependent viscosity, compliant vessel, pulsatile flow).

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

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

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

Answer: The tube hematocrit Hct_T is measured from a snapshot of the blood flowing in the tube. The discharge hematocrit Hct_D is measured from the composition of the blood that leaves the tube.

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

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

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 $\mathrm{Hct}_T/\mathrm{Hct}_D$. [30%]

Answer: By substituting the expression of $u(r)$ in the definitions of the tube and discharge hematocrits, we get:

$$\mathrm{Hct}_T = \mathrm{Hct}_0 \frac{\int_0^{R-\delta} 2\pi r \mathrm{d}r}{\int_0^R 2\pi r \mathrm{d}r} = \mathrm{Hct}_0 \frac{\pi(R-\delta)^2}{\pi R^2} = \mathrm{Hct}_0 \left(1 - \frac{\delta}{R}\right)^2$$

$$\text{and} \quad \mathrm{Hct}_D = \mathrm{Hct}_0 \frac{\frac{R^2}{4\mu}\frac{\Delta P}{L}\int_0^{R-\delta} 2\pi r\left(1 - \frac{r^2}{R^2}\right)\mathrm{d}r}{\frac{R^2}{4\mu}\frac{\Delta P}{L}\int_0^{R} 2\pi r\left(1 - \frac{r^2}{R^2}\right)\mathrm{d}r} \overset{\rho = r/R}{=} \mathrm{Hct}_0 \frac{\int_0^{1-\delta/R} \rho(1-\rho^2)\mathrm{d}\rho}{\int_0^1 \rho(1-\rho^2)\mathrm{d}\rho}$$

$$= \mathrm{Hct}_0 \frac{\left[\rho^2/2 - \rho^4/4\right]_0^{1-\delta/R}}{\left[\rho^2/2 - \rho^4/4\right]_0^1} = \mathrm{Hct}_0 \left(1 - \frac{\delta}{R}\right)^2 \left[2 - \left(1 - \frac{\delta}{R}\right)^2\right]$$

Hence:

$$\frac{\mathrm{Hct}_T}{\mathrm{Hct}_D} = \frac{1}{2 - (1 - \delta/R)^2}$$

(iii) Give an estimate of δ, with justification, and sketch $\mathrm{Hct}_T/\mathrm{Hct}_D$ 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%]

Answer: The length δ is the width of the red blood cells (RBCs) depletion zone due to their finite

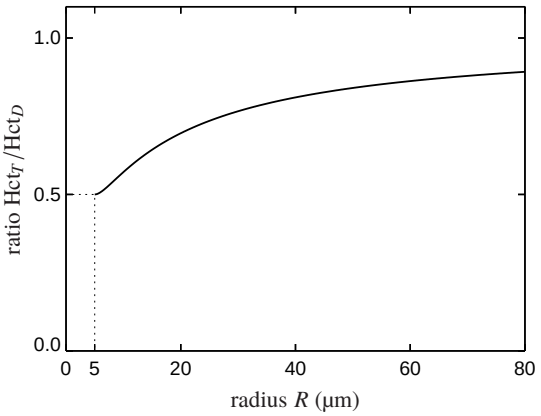

Fig. 1

size. It can be assumed to be similar to the radius of a RBC, of the order of a few μm. Figure 1 shows the hematocrit ratio as a function of R obtained using the simple model with $\delta = 5\,\mu\mathrm{m}$. The model is valid only when $R > \delta$. The RBCs are distributed in the axial core of the vessel, where the velocity is higher. Therefore, their mean velocity is higher than the mean velocity of blood and their discharge hematocrit will be greater than the tube hematocrit measured from a snapshot (that is, $\mathrm{Hct}_T/\mathrm{Hct}_D < 1$). As R increases, the width δ of the "cell-free" layer near the wall becomes negligible and both hematocrits tend to the same value. The resulting increase of $\mathrm{Hct}_T/\mathrm{Hct}_D$ with R is called the Fåhræus effect.

When the diameter of the vessel is near, or smaller than the size of the RBCs, these flow in file and both hematocrits again tend to the same value, so that the ratio increases when R decreases below δ.

NOT REQUIRED TO GET FULL MARK: Figure 2 below gives, with a dashed line, a fit to experimental observations which shows this increase at low R. The solid line is the simple model (same as in figure 1). Note that a log scale is used for the x-axis in Figure 2.

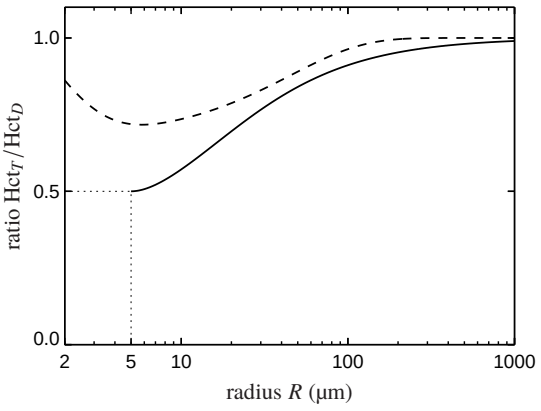

Fig. 2

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