Version ML/2 – CRIB

EGT2
ENGINEERING TRIPOS PART IIA

Friday 1 May 2015 9.30 to 11.00

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
CUED approved calculator allowed
Engineering Data Book

10 minutes reading time is allowed for this paper.

You may not start to read the questions printed on the subsequent pages of this question paper until instructed to do so.

1 (a) Determine if each statement below is universally true at steady-state inside an ion channel.

- The flux of the permeable ion is zero everywhere.
- The concentration of the permeable ion is constant in space.
- The electric potential is constant in space.
- The electric potential difference between the two ends of the channel is the Nernst potential of the permeable ion.
- The second spatial derivative of the electric field is proportional to the concentration of the permeable ion.

[25%]

Answer: For all statements: not true.

- The flux of a permeable ion is constant but not necessarily zero everywhere.
- The concentration of a permeable ion is not constant in space (for example, it may be a linear, or exponential function of space – as in the long and short channel limits, respectively).
- The electric potential is constant is not constant in space (for example, it may be a linear, or logarithmic function of space – as in the short and long channel limits, respectively).
- The electric potential difference between the two ends may be different from the Nernst potential of the permeable ion.
- It is the second derivative of the electric potential that is proportional to the concentration of an ion. As the electric field itself is the first spatial derivative of the electric potential, it is its first derivative that is proportional to the concentration of the ion – but for an ion channel even that is only true only if the permeable ion is the only charged particle that influences the electric potential (or field), which is rarely the case.

(b) The membrane resistance of a neuron is $4\,\mathrm{k\Omega\,cm^2}$, its membrane capacitance is $1\,\mu\mathrm{F/cm^2}$, and its resting membrane potential is at $-68.84\,\mathrm{mV}$. The Nernst potential of the ions for which there are permeable channels in the membrane are as follows:

$$V_{\mathrm{Na}^+} = +55\,\mathrm{mV}$$
$$V_{\mathrm{K}^+} = -75\,\mathrm{mV}$$
$$V_{\mathrm{Cl}^-} = -69\,\mathrm{mV}$$

and the Cl^- conductance is

$$g_{\mathrm{Cl}^-} = 0.04\,\mathrm{mS/cm^2}$$

 (cont.

(i) What are the membrane conductances for Na^+ and K^+ at the resting membrane potential? [15%]

Answer:

What we know:

$$\begin{aligned} R_\mathrm{m} = 4\,\mathrm{k\Omega\,cm^2} &= \frac{1}{g_{\mathrm{Na^+}} + g_{\mathrm{K^+}} + g_{\mathrm{Cl^-}}} \\ V_\mathrm{rest} = -68.84\,\mathrm{mV} &= \frac{g_{\mathrm{Na^+}}\,55\,\mathrm{mV} - g_{\mathrm{K^+}}\,75\,\mathrm{mV} - g_{\mathrm{Cl^-}}\,69\,\mathrm{mV}}{g_{\mathrm{Na^+}} + g_{\mathrm{K^+}} + g_{\mathrm{Cl^-}}} \\ g_{\mathrm{Cl^-}} &= 0.04\,\mathrm{mS/cm^2} \end{aligned}$$

From these we can derive:

$$\begin{aligned} \frac{1}{R_\mathrm{m}} = 0.25\,\mathrm{mS/cm^2} &= g_{\mathrm{Na^+}} + g_{\mathrm{K^+}} + g_{\mathrm{Cl^-}} \\ &= g_{\mathrm{Na^+}} + g_{\mathrm{K^+}} + 0.04\,\mathrm{mS/cm^2} \\ 0.21\,\mathrm{mS/cm^2} &= g_{\mathrm{Na^+}} + g_{\mathrm{K^+}} \\ V_\mathrm{rest} = -68.84\,\mathrm{mV} &= \frac{g_{\mathrm{Na^+}}\,55\,\mathrm{mV} - g_{\mathrm{K^+}}\,75\,\mathrm{mV} - 0.04\,\mathrm{mS/cm^2}\,69\,\mathrm{mV}}{0.25\,\mathrm{mS/cm^2}} \\ -14.45\,\mathrm{mV\,mS/cm^2} &= g_{\mathrm{Na^+}}\,55\,\mathrm{mV} - g_{\mathrm{K^+}}\,75\,\mathrm{mV} \\ g_{\mathrm{K^+}} &= 0.20\,\mathrm{mS/cm^2} \\ g_{\mathrm{Na^+}} &= 0.01\,\mathrm{mS/cm^2} \end{aligned}$$

(ii) The membrane is depolarised to $-60\,\mathrm{mV}$. Assuming the steady-state conductances of the ion channels are essentially constant between -69 and $-60\,\mathrm{mV}$, what is the time taken for the membrane potential to return to within $0.1\,\mathrm{mV}$ of the resting membrane potential? [25%]

Answer: The time constant of the membrane is $\tau_\mathrm{m} = R_\mathrm{m} C_\mathrm{m} = 4\,\mathrm{k\Omega\,cm^2}\,1\,\mu\mathrm{F/cm^2} = 4\,\mathrm{ms}$. When all conductances are constant, the membrane potential obeys simple exponentially decaying dynamics: $V(t) = V_\mathrm{rest} + (V_0 - V_\mathrm{rest})\,e^{-t/\tau_\mathrm{m}}$. Thus, we need to solve the following equation:

$$\begin{aligned} -68.74\,\mathrm{mV} &= -68.84\,\mathrm{mV} + 8.84\,\mathrm{mV}\,e^{-t/4\,\mathrm{ms}} \\ 0.1\,\mathrm{mV} &= 8.84\,\mathrm{mV}\,e^{-t/4\,\mathrm{ms}} \\ \frac{0.1}{8.84} &= e^{-t/4\,\mathrm{ms}} \\ \ln\frac{0.1}{8.84} &= -t/4\,\mathrm{ms} \\ t &= -4\ln\frac{0.1}{8.84}\,\mathrm{ms} \simeq 18\,\mathrm{ms} \end{aligned}$$

(iii) How does your answer to part (b)(ii) change if the conductance of the K^+ channel is instead approximated as a linear function of the membrane potential, v, between $v = -69\,\text{mV}$ and $-60\,\text{mV}$, where $g_{K^+}(v) = \left[\frac{v}{25\,\text{mV}} + 2.9536\right]\,\text{mS/cm}^2$?

[35%]

You may need the solution to the differential equation:

$$\frac{dy}{dt} = Ay^2 + By + C$$

which is:

$$y(t) = \alpha \tan(\beta t + \gamma) + \delta$$

with

$$\alpha = \frac{\sqrt{4AC - B^2}}{2A}$$
$$\beta = \frac{\sqrt{4AC - B^2}}{2}$$
$$\gamma = \arctan\left(\frac{2Ay(0) + B}{\sqrt{4AC - B^2}}\right)$$
$$\delta = -\frac{B}{2A}$$

In your calculations, you may also need the following identities:

$$\arctan(0 + bi) = k\pi/2 + \left[\frac{1}{2}\ln\left((1+b)^2\right) - \frac{1}{4}\ln\left(\left(1-b^2\right)^2\right)\right] i, \qquad \text{with}$$
$$k = \begin{cases} 0 & \text{for } |b| < 1 \\ 1 & \text{for } |b| > 1 \end{cases}$$
where $i = \sqrt{-1}$ is the imaginary number,

and

$$\tan(x \pm y) = \frac{\tan x \pm \tan y}{1 \mp \tan x \cdot \tan y}$$

Answer: In this case, the current balance equation of the cell is the following (ignoring units, which

are as above) :

$$\begin{aligned}
C_{\mathrm{m}}\frac{\mathrm{d}V}{\mathrm{d}t} &= g_{\mathrm{Na}^+}\,(V_{\mathrm{Na}^+}-V)+g_{\mathrm{K}^+}\,(V_{\mathrm{K}^+}-V)+g_{\mathrm{Cl}^-}\,(V_{\mathrm{Cl}^-}-V)\\
\frac{\mathrm{d}V}{\mathrm{d}t} &= 0.01\,(55-V)+[0.04V+2.9536]\,(-75-V)+0.04\,(-69-V)\\
&= 0.55-0.01V-3V-0.04V^2-221.52-2.9536V-2.76-0.04V\\
&= -0.04V^2+(-0.01-3-2.9536-0.04)\,V+0.55-221.52-2.76\\
&= -0.04V^2-6.0036V-223.73\\
V(t) &= \alpha\tan(\beta t+\gamma)+\delta\\
\frac{V(t)-\delta}{\alpha} &= \tan(\beta t+\gamma)\\
t &= \frac{\arctan\frac{V(t)-\delta}{\alpha}-\gamma}{\beta}
\end{aligned}$$

with

$$\begin{aligned}
V(0) &= -60\\
V(t) &= -68.74\\
\alpha &= -\frac{\sqrt{4\cdot 0.04\cdot 223.73-6.0036^2}}{2\cdot 0.04} = -\frac{0.4964\,i}{2\cdot 0.04} = -6.2050\,i\\
\beta &= \frac{\sqrt{4\cdot 0.04\cdot 223.73-6.0036^2}}{2} = 0.2482\,i\\
\gamma &= \arctan\left(\frac{2\cdot 0.04\cdot 60-6.0036}{\sqrt{4\cdot 0.04\cdot 223.73-6.0036^2}}\right) = \arctan\left(\frac{-1.2036}{0.4964\,i}\right) = \arctan(-2.4247\,i)\\
\delta &= -\frac{6.0036}{2\cdot 0.04} = -75.0450
\end{aligned}$$

Method 1 – requires computing 2 arctans: we directly substitute everything into the expression for t

$$\begin{aligned}
t &= \frac{\arctan\frac{-68.74+75.0450}{-6.2050\,i}-\arctan(-2.4247\,i)}{0.2482\,i}\\
&= \frac{\arctan\frac{6.305}{-6.2050\,i}-\arctan(-2.4247\,i)}{0.2482\,i}\\
&= \frac{\arctan 1.0161\,i-\arctan(-2.4247\,i)}{0.2482\,i}\\
&= \frac{\pi/2+2.4146\,i-\pi/2-0.4385\,i}{0.2482\,i}\\
&= \frac{2.4146\,i-0.4385\,i}{0.2482\,i}\\
&= \frac{1.9761\,i}{0.2482\,i}\\
&\simeq 8\,\mathrm{ms}
\end{aligned}$$

Method 2 – requires computing 1 arctan: we realise that γ can be rewritten as

$$\gamma = \arctan\frac{V(0)-\delta}{\alpha}$$

which allows us to rewrite t as

$$
\begin{aligned}
t &= \frac{\arctan\frac{V(t)-\delta}{\alpha} - \arctan\frac{V(0)-\delta}{\alpha}}{\beta} \\
&= \frac{\arctan\left(\tan\left(\arctan\frac{V(t)-\delta}{\alpha} - \arctan\frac{V(0)-\delta}{\alpha}\right)\right)}{\beta} \\
&= \frac{\arctan\left(\frac{\tan\left(\arctan\frac{V(t)-\delta}{\alpha}\right)-\tan\left(\arctan\frac{V(0)-\delta}{\alpha}\right)}{1+\tan\left(\arctan\frac{V(t)-\delta}{\alpha}\right)\cdot\tan\left(\arctan\frac{V(0)-\delta}{\alpha}\right)}\right)}{\beta} \\
&= \frac{\arctan\left(\frac{\frac{V(t)-\delta}{\alpha}-\frac{V(0)-\delta}{\alpha}}{1+\frac{V(t)-\delta}{\alpha}\cdot\frac{V(0)-\delta}{\alpha}}\right)}{\beta} \\
&= \frac{\arctan\left(\frac{\alpha\,[V(t)-V(0)]}{\alpha^2+[V(t)-\delta]\,[V(0)-\delta]}\right)}{\beta} \\
&= \frac{\arctan\left(\frac{-6.2050\,i\,[-68.74+60]}{(-6.2050\,i)^2+[-68.74+75.0450]\,[-60+75.0450]}\right)}{0.2482\,i} \\
&= \frac{\arctan\left(\frac{6.2050\,i\cdot 8.74}{-38.5020+6.305\cdot 15.045}\right)}{0.2482\,i} \\
&= \frac{\arctan(0.9623\,i)}{0.2482\,i} \\
&= \frac{1.9761\,i}{0.2482\,i} \\
&\simeq 8\,\text{ms}
\end{aligned}
$$

2 (a) Consider the following enzyme reaction:

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

(i) Assuming the equilibrium is fast, show that the speed of product creation V takes the form $V = V_{max}\frac{[\mathrm{S}]}{[\mathrm{S}]+K}$. Express V_{max} and K as a function of the other constants involved in the problem. [15%]

Answer: The speed of product creation is $V = k_2[C]$, so we must find [C].
From the fast equilibrium, we know that $K_1 = k_1/k_{-1} = \frac{[C]}{[S][E]}$.
The total amount of enzyme is also constant here, hence $E_0 = [E]+[C]$.
Combining these equations, we get $[C] = \frac{K_1E_0[S]}{1+K_1[S]} = \frac{E_0[S]}{K_1^{-1}+[S]}$.
We therefore get $V = k_2E_0\frac{[S]}{K_1^{-1}+[S]}$.
Hence $V_{max} = k_2E_0$ and $K = K_1^{-1} = k_{-1}/k_1$.

(ii) Sketch $1/V$ as a function of 1/[S] and explain how the values of V_{max} and K can be obtained from this graph. [15%]

Answer: Rearranging the equation above, we get:

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

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

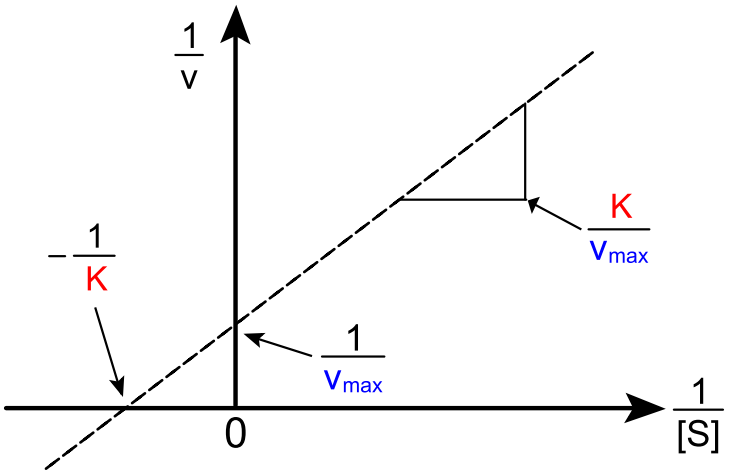

Fig. 1

(b) Consider the following mechanism of enzyme activity, where the enzyme is E, A and B are two different substrates, and P and Q are two products. The equilibrium reactions are all supposed to be fast.

$$\mathrm{A} + \mathrm{E} \rightleftharpoons \mathrm{EA} \qquad \mathrm{K}_1 = \frac{[\mathrm{EA}]}{[\mathrm{A}][\mathrm{E}]} \tag{1}$$

$$\mathrm{B} + \mathrm{EA} \rightleftharpoons \mathrm{EAB} \qquad \mathrm{K}_2 = \frac{[\mathrm{EAB}]}{[\mathrm{B}][\mathrm{EA}]} \tag{2}$$

$$\mathrm{EAB} \rightleftharpoons \mathrm{EPQ} \qquad \mathrm{K}_3 = \frac{[\mathrm{EPQ}]}{[\mathrm{EAB}]} \tag{3}$$

$$\mathrm{EPQ} \xrightarrow{k_4} \mathrm{E} + \mathrm{P} + \mathrm{Q} \tag{4}$$

(i) Express the product creation speed, V, as a function of the kinetic and thermodynamic constants, the total enzyme concentration E_0 and the concentrations of A and B. [25%]

Answer: Let's define $a = [\mathrm{A}]$, $b = [\mathrm{B}]$, $e = [\mathrm{E}]$, $e_{ab} = [\mathrm{EAB}]$, $e_{pq} = [\mathrm{EPQ}]$. The rate of product creation is $V = k_4 e_{pq}$. So we need to find e_{pq} as a function of a, b and other constants.
From the equilibrium constants, we get:

$$e_a = K_1 a e$$

$$e_{ab} = K_2 b e_a = K_2 K_1 b a e$$

$$e_{pq} = K_3 e_{ab} = K_3 K_2 K_1 b a e$$

The total enzyme concentration is $E_0 = e + e_a + e_{ab} + e_{pq}$. Hence:

$$e = E_0 - K_1 a e - K_2 K_1 b a e - K_3 K_2 K_1 b a e$$

$$e = \frac{E_0}{1 + K_1 a + K_2 K_1 b a + K_3 K_2 K_1 b a}$$

$$e = \frac{E_0}{1 + K_1 a (1 + K_2 b (1 + K_3))}$$

The product creation rate is therefore:

$$V = k_4 e_{pq} = k_4 K_3 K_2 K_1 b a e = \frac{E_0 k_4 K_3 K_2 K_1 b a}{1 + K_1 a (1 + K_2 b (1 + K_3))}$$

(ii) Assume that [B] is constant. Show that the speed of product creation from part (b)(i) takes the form obtained in part (a)(i), with A being the substrate. How would an increase of [B] change the graph of $1/V$ as a function of $1/[\mathrm{A}]$? Explain with reasons whether B can be considered an inhibitor or activator. [15%]

Answer: If [B] is constant, the product creation rate takes the form $V = V_{max} \frac{a}{a+K}$ with:

$$V_{max} = \frac{E_0 k_4 K_3 K_2 K_1 b}{K_1 (1 + K_2 b (1 + K_3))} \text{ and } K^{-1} = K_1 (1 + K_2 b (1 + K_3))$$

It is clear from these expressions that V_{max} increases with b, and K decreases with b. Hence B acts as an activator.

(iii) Assume instead that [A] is constant. Show that the speed of product creation from part (b)(i) takes the form obtained in part (a)(i), with B being the substrate. How would an increase of [A] change the graph of $1/V$ as a function of 1/[B]? Explain with reasons whether A can be considered an inhibitor or activator. [15%]

Answer: If [A] is constant, the product creation rate takes the form $V = V_{max}\frac{b}{b+K}$ with:

$$V_{max} = \frac{E_0 k_4 K_3 K_2 K_1 a}{K_1 K_2 (1+K_3) a} = \frac{E_0 k_4 K_3}{1+K_3} \text{ and } K = \frac{1+K_1 a}{K_1 K_2 (1+K_3) a}$$

V_{max} is therefore independent of a, and K decreases with a. Hence A acts as an activator.

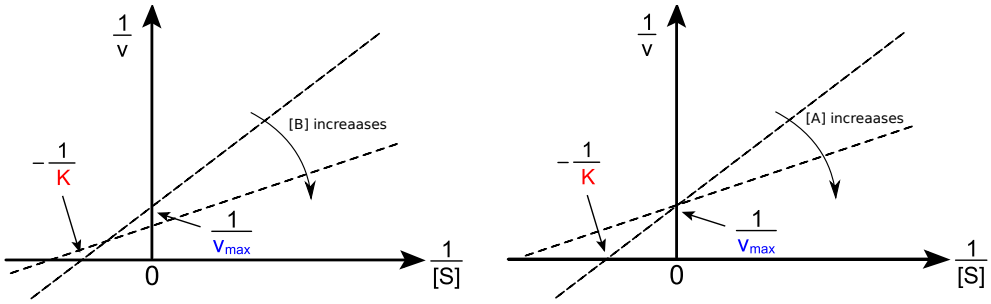

Fig. 2

(iv) Two substrates X and Y are known to react according to this mechanism, but the order in which they bind to the enzyme is unknown. Experimentally, it is found that doubling [X] while halving [Y] decreases the rate of product creation. Deduce from this whether X binds first or second. [15%]

Answer: The concentrations of A and B are changed so that their product $p = ab$ is constant. The expression of the rate of product creation is:

$$V = \frac{E_0 k_4 K_3 K_2 K_1 ba}{1+K_1 a(1+K_2 b(1+K_3))} = \frac{E_0 k_4 K_3 K_2 K_1 p}{1+K_1 a+K_2 K_1 p(1+K_3)}$$

Hence V is going to decrease with an increase of [A] at constant p. This implies that X is playing the role of A, i.e. binds first to the enzyme.

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

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

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

and

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

[30%]

Answer: We consider a small volume element located in (r,θ,x), with dimensions along these directions dr, $rd\theta$ and dx. Since u only depends on r, shear forces are only in the x direction. Considering first force balance in the x direction, we get:

$$p(r,x)(dr\cdot r\,d\theta)-p(r,x+dx)(dr\cdot r\,d\theta)-\tau(r)(dx\cdot r\,d\theta)+\tau(r+dr)(dx\cdot(r+dr)\,d\theta)=0$$

This can be rewritten as:

$$-\frac{\partial p}{\partial x}(dx\cdot dr\cdot r\,d\theta)+\frac{\partial(r\tau)}{\partial r}(dx\cdot dr\cdot d\theta)=0$$

leading to:

$$-\frac{\partial p}{\partial x}+\frac{1}{r}\frac{\partial(r\tau)}{\partial r}=0 \tag{5}$$

Force balance along the radial direction provides the next equation:

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

This can be rewritten as:

$$-\frac{\partial(pr)}{\partial r}(dx\cdot dr\cdot d\theta)+p(r,t)(dx\cdot dr\cdot d\theta)=0$$

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

$$-\frac{\partial p}{\partial r}=0 \tag{6}$$

(b) Assuming blood is Newtonian, derive the analytical expression of the flow profile $u(r)$. Discuss the validity of all the assumptions made to obtain this result. [30%]

Answer: The equation 6 shows that p is only a function x. Since τ is only a function of r, the equation 5 implies additionally that $\frac{dp}{dx}$ is constant.

We can now integrate Equ 5 with respect to r, and get:

$$\frac{\partial(r\tau)}{\partial r}=r\frac{dp}{dx}\Rightarrow\tau=\frac{r}{2}\frac{dp}{dx}+K/r$$

In the absence of a pressure gradient, the shear stress must be null everywhere, and therefore the integration constant K is zero. Hence the result.

$$\tau = \frac{r}{2}\frac{dp}{dx} \tag{7}$$

Combined with the rheological model for the fluid, $\tau = \mu\frac{dv}{dr}$, where μ is the fluid viscosity, we get:

$$\frac{dv}{dr} = \frac{r}{2\mu}\frac{dp}{dx} = \frac{r}{2\mu} \tag{8}$$

Integration with the condition that the velocity is zero along the vessel wall gives:

$$u(r) = \frac{r^2 - R^2}{4\mu}\frac{dp}{dx}$$

(c) Derive the relationship between fluid flux Q and pressure drop Δp. [20%]

Answer:

$$Q = \int_0^R 2\pi r u(r) dr = \frac{\pi R^4}{8\mu}\frac{\Delta p}{L}$$

(d) Use the expression obtained in part (c) to calculate the flow rate passing through the circulatory network pictured in Fig. 3 as a function of the vessels' geometry (see parameters in the figure), pressure drop, and blood viscosity. [20%]

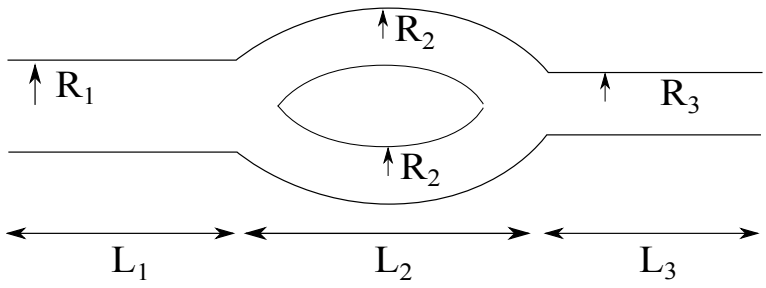

Fig. 3

Answer: There is a simple analogy with electric resistors. Δp is equivalent to a voltage, Q to a current, and the effective resistor is $\rho = \frac{8\mu L}{\pi R^4}$.
The resistance of the middle section with the two vessels in parallel is therefore $\frac{1}{2}\frac{8\mu L_2}{\pi R_2^4}$, and total resistance in the network is:

$$\rho_{tot} = \frac{8\mu L_1}{\pi R_1^4} + \frac{1}{2}\frac{8\mu L_2}{\pi R_2^4} + \frac{8\mu L_3}{\pi R_3^4}$$

$$\rho_{tot} = \frac{8\mu}{\pi}\left(\frac{L_1}{R_1^4} + \frac{L_2}{2R_2^4} + \frac{L_3}{R_3^4}\right)$$

The flow rate through the network writes:

$$Q = \frac{\pi \, \Delta p}{8\mu} \left(\frac{L_1}{R_1^4} + \frac{L_2}{2R_2^4} + \frac{L_3}{R_3^4} \right)^{-1}$$

4 (a) Explain the aim of the Krogh cylinder model and list the assumptions underlying the model. [30%]

Answer: The Krogh cylinder model is used to find a quantitative criteria for the proper oxygenation of tissues surrounding capillaries. It simplifies the complex network of capillaries by assuming that each capillary provides oxygen to cylindrical domains whose diameter represents the typical distance between capillaries. This strongly simplifies the use of a reaction-diffusion equation used in steady state (constant oxygen concentration in blood, and constant and uniform consumption of oxygen in tissues).

(b) Prove that the oxygen concentration profile within a Krogh cylinder of radius R_0 has the following form:

$$\frac{c(r)}{c_\mathrm{c}} = 1 + \frac{\rho R_0^2}{4 c_\mathrm{c} D}\left(\frac{r^2}{R_0^2} - \frac{R_\mathrm{c}^2}{R_0^2} - 2\ln\left(r/R_\mathrm{c}\right)\right)$$

where $c(r)$ is the concentration of oxygen at radial position r, R_c is the capillary radius, c_c is the oxygen concentration in blood, D is the coefficient of diffusion of oxygen in the tissue, and ρ is the rate at which oxygen is consumed per unit volume in healthy tissue. [35%]

Answer: In the steady state and cylindrical geometry:

$$\frac{D}{r}\frac{d}{dr}\left(r\frac{dc}{dr}\right) = \rho$$

The general solution is:

$$c(r) = \frac{\rho}{4D}r^2 + A\ln(r) + B$$

Using the following boundary conditions:

$$c(R_c) = c_c \text{ and } \frac{dc}{dr}(R_0) = 0$$

leads to the proposed relationship.

(c) Use this model to explain the role of capillary sphincters in capillary beds. [35%]

Answer: From part (b), we can establish a criteria for the proper oxygenation of the whole Krogh cylinder: $c(R_0) > 0$.

We denote $\Phi = \frac{\rho R_0^2}{4 c_c D}$ (dimensionless reaction rate) and define two dimensionless geometrical parameters: $r^* = r/R_0$ and $R^* = R_c/R_0$:

$$\frac{c(r)}{c_c} = 1 + \Phi\left(r^{*2} - R^{*2} - 2\ln\left(r^*/R^*\right)\right)$$

In this form, tissues are properly oxygenated when the concentration at $r = R_0$ ($r^* = 1$) is strictly positive. This provides the following condition:

$$\Phi\left(R^{*2} - 2\ln(R^*) - 1\right) < 1$$

If a tissue needs to increase its oxygen consumption ρ (for instance in muscles during physical exercise), other parameters need to change to keep Φ in the same range of values. Since the capillary radius and coefficient of diffusion of oxygen are not free to change dynamically, capillary sphincters offer a practical way to open or close additional capillaries, effectively reducing the distance between capillaries and the Krogh cylinder radius as a result. Since $\Phi = \frac{\rho R_0^2}{4c_c D}$, an increase in ρ would be associated with the opening of capillary sphincters.

END OF PAPER

Version ML/2 – CRIB

Comments on Questions

Q1 Electrophysiology

An unpopular question, where many candidates attempting did not even consider the the early easy parts, eg. which would have only required solving a simple linear equation of the form included in the examples paper. Unfortunately, there was a sign error in one of the constants provided in part (b) (the correct value of chloride Nernst potential is $V_{Cl^-} = -69\,\text{mV}$ instead of $69\,\text{mV}$), which changed the final solution to parts (i) and (iii) but not to part (ii). Thus, all candidates attempting part (i) and getting the wrong solution due to this error were awarded the maximum mark (3). No candidates got sufficiently far in solving part (iii) so that this error would have affected their result, therefore no corrections were made there. The version of the paper and crib submitted for archival has the corrected sign.

Q2 Enzyme reaction

All students selected this question. It was overall well answered, with a few students reaching 20/20. This part of the course is generally well understood. A few students got confused with the quasi-steady state and fast equilibrium assumptions on the first question.

Q3 Circulation

Very popular question. Most students answered correctly part a, although a few used a simplified 2D relationship and therefore missed some important contributions to the equations. Flow profiles and flow rates were well derived in most cases. In the last part, many students made the question more complicated that it was by missing the analogy with a simple network of resistors.

Q4 Krogh cylinder

This question is very closely related to the lecture material, and easy to answer if one remembers the derivations from the lecture notes. Almost all students could explain what the Krogh model is about, and list the key assumptions. Deriving the equation was more difficult, but nevertheless well answered by many. Establishing a quantitative criterion for proper oxygenation and linking this with capillary sphincters was more problematic.

Many students wrote a long paragraph of text instead of analysing the structure of the dimensionless numbers and spelling out the condition for necrosis.

M.L.