SECOND PUBLIC EXAMINATION

Honour School of Mathematics Part C: Paper C5.12

MATHEMATICAL PHYSIOLOGY

2025

You may submit answers to as many questions as you wish but only the best two will count for the total mark.

You must start a new booklet for each question which you attempt. Indicate on the front sheet the numbers of the questions attempted. A booklet with the front sheet completed must be handed in even if no question has been attempted.

Do not turn this page until you are told that you may do so

1. Note: Equation numbers labelled in red refer to those in the exam paper.

(a) [4 marks] [Bookwork]
The v-nullcline given by setting $\mathrm{d}v/\mathrm{d}t = 0$, which gives $w = f(v) = -v(v-\alpha)(v-1)$. The w-nullcline given by setting $\mathrm{d}w/\mathrm{d}t = 0$, which gives $v = 0$. [1 mark]

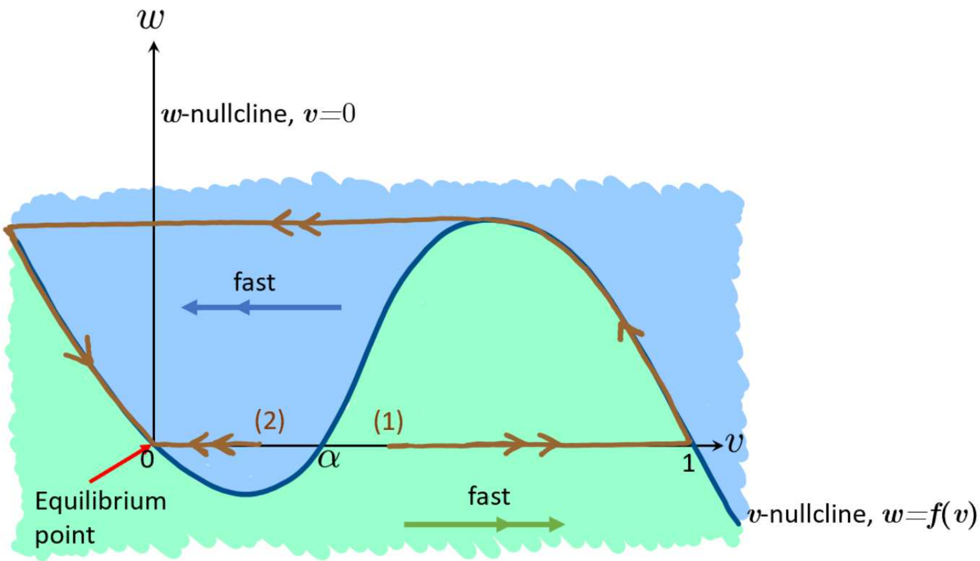


Figure 1: Phase plane for system (1). [2 marks]

If we start at point (1) then we move quickly to the right until we arrive at the v-nullcline. We then move up the v-nullcline until we reach its local maximum. Following this, we move quickly to the right until we reach the v-nullcline once more. The excursion completes by moving down the v-nullcline until we reach $(0,0)$. Note that if we start at point (2) we move back to $(0,0)$ and no excursion takes place. [1 mark]

(b) We are given

$$\epsilon\frac{\mathrm{d}v}{\mathrm{d}t} = \frac{\gamma w(v+\beta)}{(v+\delta)} - \frac{v}{v+\beta}, \tag{1a}$$

$$\frac{\mathrm{d}w}{\mathrm{d}t} = \frac{1}{1+v^2} - w, \tag{1b}$$

with $v(0) = 0$, $w(0) = 1/\gamma$, where $0 < \epsilon \ll 1$, $\gamma = 3$, $\beta = 1/4$ and $\delta = 2$.

(i) [6 marks] [Standard techniques]
The v-nullcline is given by setting $v' = 0$, which gives

$$w = \frac{v(v+\delta)}{\gamma(v+\beta)^2}. \quad \text{[1 mark]} \tag{2}$$

When $v = 0$, $w = 0$ and when $v \to \infty$, $w \to 1/\gamma$. [1 mark]
Calculating $\mathrm{d}w/\mathrm{d}v$ for (2) and setting this equal to zero shows that there is one turning point at (v^*, w^*) where

$$v^* = \frac{\beta\delta}{\delta - 2\beta} = \frac{1}{3}, \tag{3}$$

$$w^* = \frac{\delta^2}{4\beta\gamma(\delta-\beta)} = \frac{16}{21}. \tag{4}$$

[1 mark]
The w-nullcline given by setting $w' = 0$, which gives

$$w = \frac{1}{1+v^2}. \qquad \text{[1 mark]} \tag{5}$$

When $v = 0$, $w = 0$ and when $v \to \infty$, $w \to 0$. The w-nullcline decays monotonically to zero. [1 mark]

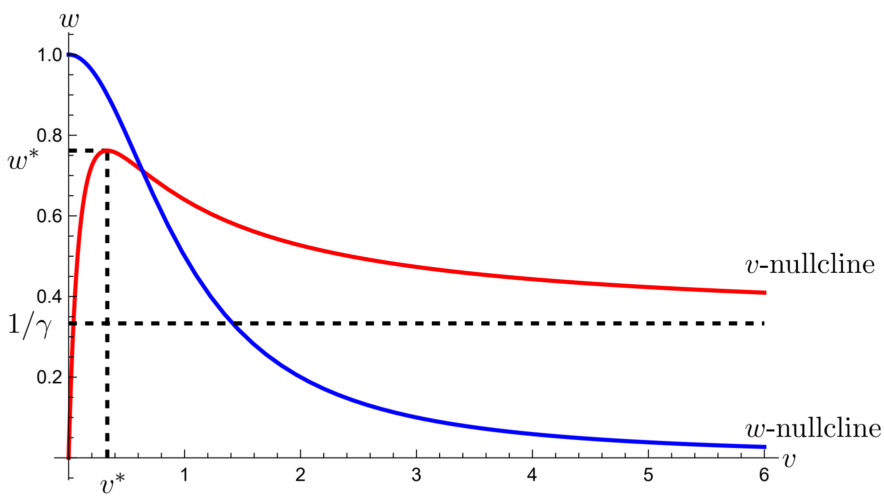


Figure 2: Nullclines of v (red) and w (blue). [1 mark]

(ii) [3 marks] [Standard techniques]
Rescaling $t = \epsilon\tau$ in the fast phase and substituting into (1) gives, to leading order in ϵ:

$$\frac{\mathrm{d}v}{\mathrm{d}\tau} = \frac{\gamma w(v+\beta)}{v+\delta} - \frac{v}{v+\beta}, \tag{6}$$

$$\frac{\mathrm{d}w}{\mathrm{d}\tau} = 0. \tag{7}$$

[1 mark] Integrating (7) and applying the initial condition gives $w = /\gamma$ on the fast timescale. [1 mark]
Since $\mathrm{d}v/\mathrm{d}\tau > 0$ when we lie above the v-nullcline this means that the trajectory moves to the right until it reaches the v-nullcline. The value of v is given by solving for v in (3), which gives $v = \beta^2/(\delta - 2\beta) = 1/24$. [1 mark]

(iii) [2 marks] [Standard techniques]
In the subsequent slow phase, we lie on the v-nullcline. Since $\mathrm{d}w/\mathrm{d}t > 0$ below the w nullcline this means we move up the v-nullcline until we reach the turning point at $w = w^*$. [2 marks]

(iv) [3 marks] [New idea. Candidates have not seen an example where the trajectory turns around without moving towards another nullcline]
Once we reach (v^*, w^*) we move quickly to the right. However, unlike in the classical Fitzhugh–Nagumo equation in part (a), there is no v-nullcline to reach. Thus, v continues to grow until it gets large. This overall motion takes place on an $\mathrm{O}(1)$ timescale. [1 mark]
We thus rescale $v = V/\epsilon$ but leave t unscaled. Substituting into (1) gives, to leading

order in ϵ,

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \gamma w - 1, \tag{8a}$$

$$\frac{\mathrm{d}w}{\mathrm{d}t} = -w. \tag{8b}$$

[1 mark] We must match to the end point of the previous motion up the v-nullcline, which originates at $v = v^*$ and $w = w^*$ as appropriate initial conditions for this part of the motion, which corresponds to $V = 0$ and $w = w^*$ at $t = 0$, where we have reset the origin of time for this part of the motion. [1 mark]

(v) [5 marks] [Standard techniques to solve equation. New idea to interpret the results]

We may solve (8) subject to the matching conditions to give

$$V = \gamma w^*(1 - \mathrm{e}^{-t}) - t, \tag{9}$$

$$w = w^* \mathrm{e}^{-t}. \tag{10}$$

[1 mark]

$V' = 0$ when $t = \log \gamma w^*$ and so

$$V = \gamma w^* \left(1 - \frac{1}{\gamma w^*}\right) - \log(\gamma w^*), \tag{11}$$

$$w = \frac{1}{\gamma} \tag{12}$$

at this point [1 mark] Thus we can plot the full trajectory:

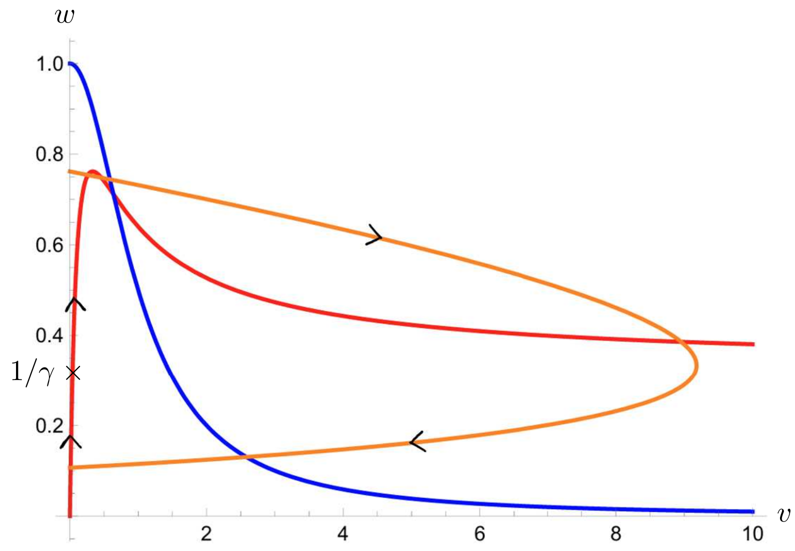


Figure 3: Trajectory of oscillation cycle. For illustrative purposes we have chosen $\epsilon = 0.05$. As $\epsilon \to 0$ the orange trajectory will coincide with the peak of the v-nullcline and the location of the maximum value of v on the orange curve will tend to infinity and coincide with the red curve. [2 marks]

As mentioned in part (iv), this differs from the motion of the excursion in part (a) because in this case there is no v-nullcline to reach and instead, v becomes large and the trajectory turns around. [1 mark]

(vi) [2 marks] [Unifying physical understanding and interpretation]

As we reduce λ the w-nullcline will fall until eventually the equilibrium point will occur to the left of the maximum of the v-nullcline. The critical value of λ when the equilibrium point coincides with the maximum of the v-nullcline is when $\lambda = w^*(1 + v^{*2}) = \lambda^* = 160/189$. When $\lambda > \lambda^*$ we have a limit cycle and when $\lambda \leqslant \lambda^*$ the motion will comprise a fast transition from $v = 0$ to $v = \beta^2/(\delta - 2\beta) = 1/24$ and then a slow motion up the v-nullcline until the equilibrium point is reached. [2 marks]

2. Note: Equation numbers labelled in red refer to those in the exam paper.

(a) [4 marks] [Bookwork]
Equation (1a) is an electrodiffusion equation in steady state. [1 mark] The first term represents molecular diffusion and the second term represents electrodiffusion. [1 mark] Equations (1b) and (1c) represent imposed concentrations and electric potentials at $x = 0$ and $x = 1$. [1 mark] J represents the flux of ions in the $-x$ direction, and is a constant at all locations in x, so represents the flux out of the membrane at $x = 0$. [1 mark]

(b) [4 marks] [Straightforward calculation]
Integrating (1) gives

$$c' + c\phi' = J$$
$$\Rightarrow \left(c\mathrm{e}^{\phi}\right)' = J\mathrm{e}^{\phi}.$$

[1 mark]
Integrating once more and applying (2) gives

$$c = J\mathrm{e}^{-\phi} \int_0^x \mathrm{e}^{\phi(s)}\, \mathrm{d}s + c_L \mathrm{e}^{\phi_L - \phi}. \tag{1}$$

[1 mark]
Finally, applying (3) gives

$$c = \left(c_R \mathrm{e}^{\phi_R} - c_L \mathrm{e}^{\phi_L}\right) \mathrm{e}^{-\phi} \frac{\int_0^x \mathrm{e}^{\phi(s)}\, \mathrm{d}s}{\int_0^1 \mathrm{e}^{\phi(s)}\, \mathrm{d}s} + c_L \mathrm{e}^{\phi_L - \phi}. \tag{2}$$

[1 mark]
and

$$J = \frac{c_R \mathrm{e}^{\phi_R} - c_L \mathrm{e}^{\phi_L}}{\int_0^1 \mathrm{e}^{\phi(s)}\, \mathrm{d}s}. \tag{3}$$

[1 mark]

(c) [2 marks] [Bookwork but requires candidates to recall definition of Nernst potential]

The Nernst potential corresponds to the potential difference $\phi_R - \phi_L \equiv V$ when the flux $J = 0$. [1 mark] Setting $J = 0$ and rearranging (3) immediately gives the expression for the Nernst potential,

$$V = \phi_R - \phi_L = \log\left(\frac{c_L}{c_R}\right).$$

[1 mark]

(d) [8 marks] [New material]
Substituting (2) into (2) and multiplying both sides by e^{ϕ} gives

$$\phi''\mathrm{e}^{\phi} = -J \int_0^x \mathrm{e}^{\phi(s)}\, \mathrm{d}s - c_L \mathrm{e}^{\phi_L}.$$

[1 mark] Differentiating with respect to x and dividing both sides by e^{ϕ} gives

$$\phi''' + \phi''\phi' = -J$$

$$\Rightarrow \quad \phi''' + \left(\frac{1}{2}\left(\phi'\right)^2\right)' = -J \tag{4}$$

as required. [1 mark]
Defining $v = \phi'$ then (4) becomes, upon integration,

$$v' + \frac{1}{2}v^2 = A, \tag{5}$$

where A is a constant of integration. Now, since $v' = \phi'' = -c = -c_L\mathrm{e}^{-\phi_L+\phi}$, this means that

$$A = -c_L + \frac{1}{2}\left(\phi'(0)\right)^2 = 0$$

since we are given this extra condition in the question. [2 marks]
Equation (5) may then be solved using separation of variables:

$$\int \frac{\mathrm{d}v}{v^2} = \frac{1}{2}\left(x + a\right), \tag{6}$$

$$\Rightarrow \quad \phi' = -\frac{2}{(x+a)}, \tag{7}$$

$$\phi = -2\log\left(x + a\right) + b, \tag{8}$$

where a and b are constants of integration. [2 marks] Applying (1b,c) gives

$$a = \frac{1}{\mathrm{e}^{(\phi_L-\phi_R)/2} - 1},$$

$$b = \phi_L - 2\log\left(\mathrm{e}^{(\phi_L-\phi_R)/2} - 1\right),$$

[1 mark] and so

$$\phi = \phi_L - 2\log\left[\left(\mathrm{e}^{(\phi_L-\phi_R)/2} - 1\right)x + 1\right]. \tag{9}$$

[1 mark]

(e) [New material]

(i) [3 marks] When $c = O(\epsilon)$, equation (2) to leading order in ϵ is simply

$$\phi'' = 0$$

$$\Rightarrow \quad \phi = (\phi_R - \phi_L)x + \phi_L.$$

[1 mark] Equation (1a) at leading order in ϵ is

$$\hat{c}' + \hat{c}\phi' = \hat{J},$$

$$\Rightarrow \quad \hat{c}' + (\phi_R - \phi_L)\hat{c} = \hat{J},$$

$$\Rightarrow \quad \hat{c} = \frac{\hat{J}}{\phi_R - \phi_L} + B\mathrm{e}^{-(\phi_R-\phi_L)x},$$

where B is a constant to be determined. Applying (1b) gives

$$\hat{c} = \frac{\hat{J}}{\phi_R - \phi_L} + \left(\hat{c}_L - \frac{\hat{J}}{\phi_R - \phi_L}\right) \mathrm{e}^{-(\phi_R - \phi_L)x}.$$

Applying (1c) gives

$$\hat{J} = \frac{\hat{c}_R \mathrm{e}^{\phi_R} - \hat{c}_L \mathrm{e}^{\phi_L}}{\mathrm{e}^{\phi_R} - \mathrm{e}^{\phi_L}} \left(\phi_R - \phi_L\right).$$

[2 marks]

(ii) [4 marks] Replacing $c = c_0 + \epsilon c_1$, $\phi = \phi_0 + \epsilon \phi_1$ and $J = \epsilon \hat{J}$ in (1) gives

$$c_0 + \epsilon c_1 = \epsilon \hat{J} \mathrm{e}^{-\phi_0 - \epsilon\phi_1} \int_0^x \mathrm{e}^{\phi_0(s) + \epsilon\phi_1(s)} \, \mathrm{d}s + c_R \mathrm{e}^{\phi_R - \phi_0 - \epsilon\phi_1}. \tag{10}$$

[1 mark]

Expanding the exponentials and considering the result at $O(1)$ we obtain an equation that is identically satisfied [1 mark] while at $O(\epsilon)$ we get

$$c_1 = \hat{J} \mathrm{e}^{-\phi_0} \int_0^x \mathrm{e}^{\phi_0(s)} \, \mathrm{d}s - c_L \mathrm{e}^{\phi_L - \phi_0} \phi_1. \tag{11}$$

[1 mark]

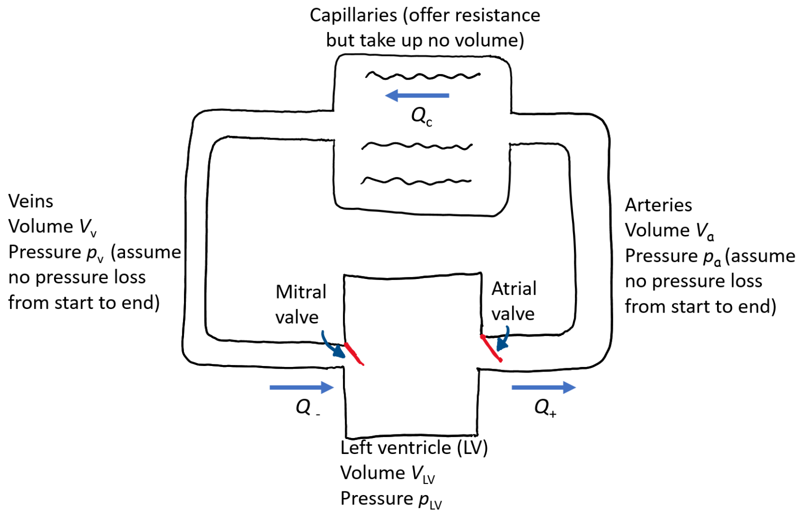
Considering this at $x = 1$ and using the fact that $c_1(1) = 0$ (since the concentration is not perturbed at $x = 1$), we have

$$\hat{J} = \frac{c_L \phi_{1R} \mathrm{e}^{\phi_L}}{\displaystyle\int_0^1 \mathrm{e}^{\phi_0(x)} \, \mathrm{d}x}. \tag{12}$$

[1 mark]

3. Note: Equation numbers labelled in red refer to those in the exam paper.

(a) [7 marks] [Bookwork]



[2 marks]
The blood is incompressible but blood vessels are compliant; C_a, C_v and C_{LV} are the compliances of the arteries, veins and left ventricle, respectively. [1 mark]
R_a, R_v and R_c are the resistances of the arteries, veins and capillaries, respectively. [1 mark]
The system (1) is obtained from equations expressing mass conservation:

$$\frac{\mathrm{d}V_a}{\mathrm{d}t} = Q_+ - Q_c,$$
$$\frac{\mathrm{d}V_v}{\mathrm{d}t} = Q_c - Q_-,$$
$$\frac{\mathrm{d}V_{LV}}{\mathrm{d}t} = Q_- - Q_+.$$

Here, V_a, V_v and V_{LV} are the volumes of blood in the arteries, veins and capillaries; Q_+ is the flux of blood leaving the left ventricle, Q_- is the flux of blood entering the left ventricle, and Q_c is the flux of blood entering the capillaries, as shown in the sketch above. We relate the volumes to the pressure and compliance via

$$V_a = V_a^* + C_a p_a, \qquad V_v = V_v^* + C_v p_v, \qquad V_{LV} = V_{LV}^* + C_{LV} p_{LV},$$

where V_a^*, V_v^* and V_{LV}^* are baseline constant values. The fluxes are given by

$$Q_c = \frac{p_a - p_v}{R_c}, \qquad Q_+ = \frac{[p_{LV} - p_a]_+}{R_a}, \qquad Q_- = \frac{[p_v - p_{LV}]_+}{R_v},$$

where $[]_+$ represents the positive part, and enforces no backflow. [3 marks]

(b) [3 marks] [New material requiring physical interpretation]

If the arterial pressure falls from the steady state, then, due to the delay τ, the right-hand side of (2b) will be positive, so the heart rate will rise. [1 mark] A rise in heart rate will make the right-hand side of (2a) positive, which will cause a rise in arterial pressure. This will allow the arterial pressure to regulate itself. [1 mark] The parameter τ is a delay that corresponds to the time taken for the heart rate to respond to a change in blood pressure. [1 mark] An example of this is if you stand up quickly (blood pressure falls as blood pools in the feet); the heart rate rises to increase the pressure to prevent you from going light-headed.

(c) [2 marks] [Straightforward calculation]
The steady state of the system is determined by setting $p(t) = p^*$, $f = f^*$ where p^* and f^* are constants. This gives

$$p^* = f^* = \frac{\gamma}{\beta}.$$

(d) [5 marks] [New idea]
Linearizing via $p = p^* + A\mathrm{e}^{\lambda t}$, $f = f^* + B\mathrm{e}^{\lambda t}$ gives

$$\begin{pmatrix} 1+\lambda & -1 \\ \delta \mathrm{e}^{-\lambda\tau} + \beta\delta & \lambda \end{pmatrix} \begin{pmatrix} A \\ B \end{pmatrix} \begin{pmatrix} 0 \\ 0 \end{pmatrix},$$

where

$$\delta = -g'(p^*) = \frac{\beta^2}{\gamma(1+\beta)^2} > 0. \tag{1}$$

[2 marks]
Thus, for non-trivial solutions we require

$$\lambda^2 + \lambda + \delta(\beta + \mathrm{e}^{-\lambda\tau}) = 0. \tag{2}$$

[1 mark]
If $\lambda \in \mathbb{R}$ then $\delta(\beta + \mathrm{e}^{-\lambda\tau}) > 0$ and so

$$\lambda = \frac{-1 \pm \sqrt{1 - 4\delta(\beta + \mathrm{e}^{-\lambda\tau})}}{2} < 0.$$

This means that if $\lambda \in \mathbb{R}$ then the system is always stable. [2 marks]

(e) [8 marks] [New idea]
The result from part (d) means that you can only get an instability if $\lambda \in \mathbb{C}$ and $Re(\lambda) > 0$. [1 mark] We can identify when this first happens by setting $\lambda = \mathrm{i}z$ where $z \in \mathbb{R}$. [1 mark] Substituting into (2) gives

$$-z^2 + \mathrm{i}z + \delta(\beta + \cos(\tau) - \mathrm{i}\sin(\tau)) = 0.$$

Equating real parts gives

$$z^2 = \delta(\beta + \cos(z\tau)). \tag{3}$$

Equating imaginary parts gives

$$z = \delta \sin(z\tau). \tag{4}$$

Equations (3) and (4) may be rearranged to give

$$\cos^2(z\tau) = \left(\frac{z^2}{\delta} - \beta\right)^2,$$
$$\sin^2(z\tau) = \frac{z^2}{\delta^2},$$

and so adding these equations gives

$$z^4 + (1 - 2\delta\beta)z^2 + (\beta^2 - 1)\delta = 0. \tag{5}$$

[2 marks] We are asked to look at the case when $\beta = 1/2$ and $\gamma = 1/9$. In this case, $\delta = 1$ from (1) [1 mark] and so (5) reduces to

$$z^4 = \frac{3}{4},$$
$$\Rightarrow \quad z = \left(\frac{3}{4}\right)^{1/4} = z^\dagger, \text{ say.}$$

[1 mark]

The period of the oscillation is $2\pi/z^\dagger$ [1 mark] and the time at which stability is lost is

$$\tau = \tau^* = \frac{1}{z^\dagger} \arcsin\left(\frac{z^\dagger}{\delta}\right).$$

[1 mark]