A12214H1

SECOND PUBLIC EXAMINATION

Honour School of Mathematics Part C: Paper C5.12
Honour School of Mathematics and Statistics Part C: Paper C5.12
Master of Science in Mathematical Sciences: Paper C5.12

Mathematical Physiology

TRINITY TERM 2025

Friday 13 June, 2:30pm to 4:15pm

You may submit answers to as many questions as you wish but only the best two will count for the total mark. All questions are worth 25 marks.

You should ensure that you observe the following points:

- start a new answer booklet for each question which you attempt.
- indicate on the front page of the answer booklet which question you have attempted in that booklet.
- cross out all rough working and any working you do not want to be marked. If you have used separate answer booklets for rough work please cross through the front of each such booklet and attach these answer booklets at the back of your work.
- hand in your answers in numerical order.

If you do not attempt any questions, you should still hand in an answer booklet with the front sheet completed. Approved calculators permitted.

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

1. (a) [4 marks] Consider the Fitzhugh–Nagumo equations:

$$\epsilon \frac{\mathrm{d}v}{\mathrm{d}t} = f(v) - w, \qquad \frac{\mathrm{d}w}{\mathrm{d}t} = v, \tag{1}$$

where $f(v) = -v(v-\alpha)(v-1)$, where ϵ and α are constants, with $0 < \epsilon \ll 1$ and $0 < \alpha < 1$. Sketch the nullclines on a (v, w) phase diagram and briefly explain how this system admits an excursion comprising fast and slow parts, illustrating this on the phase diagram.

(b) Now consider the following differential equation system:

$$\epsilon \frac{\mathrm{d}v}{\mathrm{d}t} = \frac{\gamma w(v+\beta)}{(v+\delta)} - \frac{v}{v+\beta}, \tag{2a}$$

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

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

(i) [6 marks] Draw the v- and w-nullclines on a phase-plane plot in (v, w) space taking care to show the location and values of any turning points, and the values that these curves asymptote to as $v \to \infty$.

(ii) [3 marks] By rescaling $t = \epsilon\tau$ show that the system starts with a fast phase in which w remains constant and state the value of v that is reached when this fast phase ends.

(iii) [2 marks] Explain why the next part of the motion takes place on the v-nullcline, and state the value of v at which this phase ends.

(iv) [3 marks] Explain why, following the motion in part (iii), v becomes large. By rescaling $v = V/\epsilon$, explain why the behaviour in this phase, to leading order in ϵ, is given by:

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \gamma w - 1, \qquad \frac{\mathrm{d}w}{\mathrm{d}t} = -w, \tag{3}$$

and state appropriate initial conditions for V and w for this system.

(v) [5 marks] Solve the system (3) and use the result to show that the system (2) exhibits periodic motion, and draw the trajectory for this motion on the phase plane. Comment on the difference between this motion and the motion of the excursion in part (a).

(vi) [2 marks] If (2b) is modified to

$$\frac{\mathrm{d}w}{\mathrm{d}t} = \frac{\lambda}{1+v^2} - w, \tag{4}$$

show that there exists a critical value of λ, the value of which you should find, above which the system displays periodic behaviour and below which the system relaxes to an equilibrium value.

2. Consider a membrane containing ions that lies in $0 < x < 1$. The ion concentration and electric potential at $x = 0$ and $x = 1$ are all held fixed.

   (a) [4 marks] Explain why the system may be described by

$$\left(c' + c\phi'\right)' = 0, \qquad 0 < x < 1 \qquad (1a)$$
$$c = c_L, \qquad \phi = \phi_L, \qquad x = 0, \qquad (1b)$$
$$c = c_R, \qquad \phi = \phi_R, \qquad x = 1, \qquad (1c)$$

   where primes denote differentiation with respect to x, and explain what the quantity $J = c' + c\phi'$ represents physically.

   (b) [4 marks] Find a relationship for $c(x)$ and J in terms of $\phi(x)$, c_L, c_R, ϕ_L and ϕ_R.

   (c) [2 marks] Explain what the Nernst potential is for such a system and use the relationship found in part (b) to find an expression for the Nernst potential in terms of c_L and c_R.

The electric potential is determined by Poisson's equation,

$$\phi'' = -c. \qquad (2)$$

   (d) (i) [2 marks] Show that the electric potential satisfies

$$\phi''' + \frac{1}{2}\left(\left(\phi'\right)^2\right)' = -J.$$

   (ii) [6 marks] In the specific case when $J = 0$ and $c_L = \phi'(0)^2/2$, find the solution for $\phi(x)$.

   (e) (i) [3 marks] Suppose that the ion concentration is low, so that $c = \epsilon\hat{c}$, $c_L = \epsilon\hat{c}_L$ and $c_R = \epsilon\hat{c}_R$ where $0 < \epsilon \ll 1$ and $\hat{c}$, $\hat{c}_L$ and $\hat{c}_R$ are all $O(1)$ quantities. Show that the flux $J = \epsilon\hat{J}$ to leading order in ϵ, where $\hat{J} = O(1)$, and find an expression for $\hat{J}$.

   (ii) [4 marks] Now suppose that ϕ_L, ϕ_R and c_R take the same values as in part (d)(ii), but $c_L = \phi'(0)^2/2 + \epsilon$, where, once again, $0 < \epsilon \ll 1$. Show that $J = \epsilon\overline{J}$ where

$$\overline{J} = -\frac{3}{\mathrm{e}^{\phi_R^* - \phi_L^*} + \mathrm{e}^{(\phi_R^* - \phi_L^*)/2} + 1}.$$

3. Consider the following mechanical model to describe blood circulation in the body:

$$\frac{\mathrm{d}p_a}{\mathrm{d}t} = \frac{[p_{LV} - p_a]_+}{R_a C_a} - \frac{p_a - p_v}{R_c C_a}, \tag{1a}$$

$$\frac{\mathrm{d}p_v}{\mathrm{d}t} = \frac{p_a - p_v}{R_c C_v} - \frac{[p_v - p_{LV}]_+}{R_v C_v}, \tag{1b}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}(C_{LV} p_{LV}) = \frac{[p_v - p_{LV}]_+}{R_v} - \frac{[p_{LV} - p_a]_+}{R_a}. \tag{1c}$$

Here, p_a, p_v and p_{LV} represent the pressure in the arteries, the veins, and the left ventricle, respectively, and t denotes time.

(a) [7 marks] Sketch a diagram of the blood circulation system containing the left ventrical, the arteries, the veins and the capillaries and use this to explain the physical origin of this model and the rationale for each of the terms. You should also explain what C_a, C_v, C_{LV}, R_a, R_v and R_c represent in your model.

Now consider the following coupled system

$$\frac{\mathrm{d}p}{\mathrm{d}t} = -p + f, \tag{2a}$$

$$\frac{\mathrm{d}f}{\mathrm{d}t} = g(p(t-\tau)) - [1 - g(p(t))]\,\beta. \tag{2b}$$

Here, p represents arterial pressure and f represents heart rate; $g(p) = \gamma/(\gamma + p)$, and β, τ and γ are all positive constants.

(b) [3 marks] By considering what happens to the heart rate in this model if the arterial pressure changes, and the subsequent response to the arterial pressure, explain how the heart rate can be used to regulate arterial pressure. You should also explain the relevance of the term τ in the model.

(c) [2 marks] Find the steady state of the system (2), say $p = p^*$, $f = f^*$.

(d) [4 marks] By linearizing about the steady state via $p = p^* + A\mathrm{e}^{\lambda t}$, $f = f^* + B\mathrm{e}^{\lambda t}$, show that if $\lambda \in \mathbb{R}$ then $\lambda < 0$.

(e) [9 marks] Hence explain why the system can only be unstable if $\lambda \in \mathbb{C}$. If $\beta = 1/2$ and $\gamma = 1/9$, determine the critical value of the delay time τ for which the system first becomes unstable together with the time period of oscillation when the stability is lost.