University of St Andrews

MAY 2021 EXAMINATION DIET

SCHOOL OF MATHEMATICS & STATISTICS

MODULE CODE: **MT5854**

MODULE TITLE: Mathematical Oncology

EXAM DURATION: 2 hours

EXAM INSTRUCTIONS: Attempt ALL questions.

The number in square brackets shows the maximum marks obtainable for that question or part-question.

Your answers should contain the full working required to justify your solutions.

INSTRUCTIONS FOR ONLINE EXAMS:

Each page of your solution must have the page number, module code, and your student ID number at the top of the page. You must make sure all pages of your solutions are clearly legible.

1. Assume that the growth of a solid avascular tumour is governed by the ODE:

$$\frac{dV}{dt} = aV^{2/3} - bV, \quad V(0) = V_0, \tag{1}$$

where $V(t)$ represents the size of the tumour at time $t \geqslant 0$ and $a, b, V_0 \geqslant 0$.

(a) Solve the initial value problem (1) and find the formula of the time evolution of the tumour. **[2]**

(b) Show that the proposed model predicts the reduction of tumours with size larger than $\left(\frac{a}{b}\right)^3$, but not their full eradication. **[2]**

(c) If a tumour, at detection, is of size $8\left(\frac{a}{b}\right)^3$, how much time does in take to become $4\left(\frac{a}{b}\right)^3$. **[2]**

2. Some small 3-dimensional avascular tumours are better approximated by *circular cylinders* rather than spheroids. For such a tumour, let r_1, r_2 denote the radii of the (cylindrical) necrotic core and the whole (cylindrical) tumour respectively. A single nutrient diffuses freely in the tissue with constant diffusivity $D > 0$, and is consumed by the living cancer cells with a constant rate $k > 0$. If the concentration of the nutrient drops below a threshold value $c_1 \geqslant 0$ the cancer cells die; the concentration of the nutrient in the normal non-cancerous tissue is $c_2 > c_1$. Assume moreover the dynamics of the nutrient are much faster than the dynamics of the tumour growth.

(a) Show that the concentration of the nutrient c over the living part of the tumour is given by:

$$c(r) = \frac{1}{4}\frac{k}{D}r^2 + A\log r + B,$$

where r is the radial coordinate of the radial cylindrical coordinate system, and $A, B \in \mathbb{R}$ are constants. **[4]**

(b) Find the critical value of the radius r_2, which when exceeded by the tumour, a necrotic core begins to form.
(Hint: You will need to assign the proper boundary conditions on the living part of the tumour. Recall that the molecular-diffusion is driven by the flux $J = -D\frac{dc}{dr}$) **[3]**

(c) Find the relationship between the constants A, B and the necrotic radius r_1. **[3]**

(d) Show that if $r_2 \to \infty$ then $r_2 - r_1 \to C$, where C is a constant to be found. **[6]**

3. The growth of a tumour of density $N(t, x)$, where $(t, x) \in (0, \infty) \times \mathbb{R}$, is modelled by the following nonlinear reaction-diffusion equation

$$\frac{\partial N}{\partial t} = \frac{\partial}{\partial x}\left(D(N)\,\frac{\partial N}{\partial x}\right) + N\left(1 - \frac{N}{K}\right), \tag{2}$$

where the function $D : [0, \infty) \to (0, \infty)$ is continuously differentiable, and the carrying capacity $K > 0$ is constant.

(a) Derive a system of first order ODEs, along with suitable conditions at $\pm\infty$ for all involved functions, for a cancer growth wave solution of (2) that travels to the right with speed $c > 0$. **[5]**

(b) In the simpler case of linear diffusion with $D \equiv 1$, find the minimal cancer growth speed $c_{\min}$ for which a meaningful travelling-wave solution exists. **[5]**

4. (a) i. Show that the function

$$u(x, t) = \frac{1}{\sqrt{4D\pi t}} e^{-x^2/(4Dt)}$$

satisfies the one-dimensional diffusion equation

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} \qquad (3)$$ **[2]**

ii. Let $c(x,t) = w(t)u(x,t)$, where $u(x,t)$ satisfies (3). Show that if c is a solution to the equation

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + \rho c$$

with $D, \rho > 0$, then

$$c(x,t) = e^{\rho t}u(x,t).$$ **[3]**

iii. Considering the function

$$u(x_1, x_2, \ldots, x_n, t) = \Phi_1(x_1,t)\Phi_2(x_2,t)\ldots\Phi_n(x_n,t)$$

where every $\Phi_i(x_i,t)$, $i = 1\ldots n$ satisfies (3), show that

$$u(x_1, x_2, \ldots, x_n, t) = \frac{1}{\sqrt{(2D\pi t)^n}}e^{-(x_1^2+\cdots+x_n^2)/(2Dt)}$$ **[1]**

and that it satisfies the n-dimensional diffusion equation

$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x_1^2} + \cdots + \frac{\partial^2 u}{\partial x_n^2}\right).$$ **[3]**

(b) The growth of a glioma can be estimated from two-dimensional sections of a CT scan. Assuming radially symmetric growth, diffusion coefficient D and proliferation rate ρ, the equation governing the glioma growth, whose cells have density $c(\mathbf{r},t)$ is given by

$$\frac{\partial c}{\partial t} = D\nabla^2 c + \rho c$$

with $c(\mathbf{r},0) = \delta(\mathbf{r})$ and $\mathbf{n}\cdot\nabla c = 0$ on the boundary of the brain.

i. Write down the solution of the above equation. **[2]**

ii. If the detectable threshold density for the CT scan is c^* at radius r^* show that

$$r^* = 2\sqrt{D\rho t}\sqrt{1 - \frac{1}{\rho t}\log 4\pi Dtc^*}$$ **[3]**

iii. Using ii., estimate the average speed of glioma growth for large t. **[2]**

iv. If the glioma is detected when it has radius r_d and death occurs when it has radius r_l, provide and estimate the survival time of the patient. **[2]**

END OF PAPER
