The University Of Sheffield.

MAS377

SCHOOL OF MATHEMATICS AND STATISTICS **Autumn Semester 2020–21**

MAS377 Mathematical Biology

This is an open book exam.
Answer all questions.
You can work on the exam during the 24 hour period starting at 10am (GMT), and you must submit your work within 2 hours 30 mins of accessing the exam paper or by the end of the 24 hour period (whichever is earlier).
Late submission will not be considered without extenuating circumstances.
Unless it is explicitly stated otherwise, it is intended that calculations are performed by hand (possibly with the aid of a calculator). To gain full marks, you will need to show your working. By uploading your solutions you declare that your submission consists entirely of your own work, that any use of sources or tools other than material provided for this module is cited and acknowledged, and that no unfair means have been used.

1 A human population exposed to an infectious disease is separated into three compartments, S (susceptible), I (infected) and R (recovered). Over a short time period, the dynamics of the three compartments are governed by the following ordinary differential equations,

$$\frac{dS}{dt} = -\beta SI + \omega R \tag{1}$$

$$\frac{dI}{dt} = \beta SI - \gamma I \tag{2}$$

$$\frac{dR}{dt} = \gamma I - \omega R \tag{3}$$

where β, ω and γ are all positive constants.

(i) What process is represented by the parameter, ω? ***(2 marks)***

(ii) Show that the total population size, $N = S + I + R$ is constant. Hence re-write the system in the form,

$$\frac{dS}{dt} = f(S, I) \tag{4}$$

$$\frac{dI}{dt} = g(S, I) \tag{5}$$

where you should find explicit expressions for $f(S, I)$ and $g(S, I)$. ***(3 marks)***

(iii) Assume that $R_0 = \beta N/\gamma > 1$. Sketch a phase portrait of the system. This should clearly show the biologically-feasible region, the nullclines, equilibria and qualitative directions of flow. You should also add one trajectory with initial conditions $S(0) = N - 1, I(0) = 1$ (with $N \gg 1$). Describe the dynamics along this trajectory. ***(8 marks)***

(iv) This system yields two equilibria, one at $(S^*, I^*) = (N, 0)$ and a second at $(S^*, I^*) = (\hat{S}, \hat{I})$. Find $\hat{S}$ and $\hat{I}$, expressing $\hat{I}$ as a function of $R_0 = \beta N/\gamma$. ***(3 marks)***

(v) Find the Jacobian of the system and use it to determine how the stability of $(\hat{S}, \hat{I})$ depends on R_0. ***(6 marks)***

(vi) Suppose it is decided that an additional *exposed* compartment is needed for realism. After contracting the disease, susceptible individuals first move to this compartment for $1/\epsilon$ time units before moving to the infected/infectious compartment. Exposed individuals are not infectious. Re-write the system of equations (1)-(3) including an additional compartment, E, to represent this updated system. **You do not need to analyse this model.** ***(3 marks)***

2 The *hes1* gene codes for a protein that represses its own transcription. A model of *hes1* gene expression is given by

$$\frac{dM}{dt} = -\mu M + f(P) \tag{6}$$

$$\frac{dC}{dt} = kM - (\mu + \gamma)C \tag{7}$$

$$\frac{dP}{dt} = \gamma C - \mu P, \tag{8}$$

where M represents the amount of mRNA, and C and P represent intermediate and mature forms of the protein product of the gene. Only the mature form regulates transcription, and γ is the rate of maturation of the protein. Parameters μ, k and γ are positive constants, and

$$f(P) = \begin{cases} 1 - \phi P, & 0 \leq P \leq 1/\phi \\ 0, & P > 1/\phi \end{cases}$$

where $\phi > 0$

(i) Show graphically that the model has a unique steady state (M_*, C_*, P_*), and find an explicit expression for P_*. ***(5 marks)***

(ii) Determine the Jacobian matrix for the system (6)–(8) at the steady state. ***(1 mark)***

(iii) Show that the eigenvalues λ of the Jacobian matrix satisfy

$$(\lambda + \mu)^2(\lambda + \mu + \gamma) + k\gamma\phi = 0. \tag{9}$$

Show graphically, or otherwise, that Eq. (9) always has one negative real solution. ***(4 marks)***

(iv) Show that Eq. (9) has pure imaginary solutions $\lambda = \pm i\omega$ if and only if

$$\phi = \phi_H = \frac{2\mu(2\mu + \gamma)^2}{k\gamma}, \tag{10}$$

and that if this condition is met, then $\omega^2 = \mu(3\mu + 2\gamma)$. ***(9 marks)***

(v) The model undergoes a Hopf bifurcation as ϕ increases through the value $\phi = \phi_H$, and the two complex eigenvalues have positive real part when $\phi > \phi_H$. What kind of solution will Eqs. (6)–(8) have when $\phi > \phi_H$? ***(1 mark)***

(vi) For a fixed value of μ, show that the minimum value of ϕ_H occurs when $\gamma = 2\mu$. If $\mu = 0.03\text{min}^{-1}$, what is the period of oscillation at the Hopf bifurcation when $\gamma = 2\mu$? ***(5 marks)***

End of Question Paper