The University Of Sheffield.

SCHOOL OF MATHEMATICS AND STATISTICS **Autumn Semester 2017–18**

MAS377 Mathematical Biology **2 hours**

Marks will be awarded for your best ***three*** *answers.*

1 The dynamics of two interacting species, with densities M and N, are governed by the following ordinary differential equations,

$$\frac{dM}{dt} = M(a - bM + cN) \quad (1)$$

$$\frac{dN}{dt} = N(u - vN + wM), \quad (2)$$

where a, b, c, u, v, w are positive constants.

(i) Describe the type of interaction between these two species. ***(2 marks)***

(ii) Besides the unstable equilibrium at $(0, 0)$, this model yields three possible equilibria given by $(M_+, 0)$, $(0, N_+)$ and (M^*, N^*).

(a) Draw a phase portrait for the case where all these equilibria exist in the biologically-feasible region (i.e. $M, N \geq 0$). This should clearly show the nullclines, equilibria, qualitative directions of flow and two example trajectories. ***(5 marks)***

(b) Using the phase portrait, determine a condition on w for the equilibrium (M^*, N^*) to exist in the biologically-feasible region. ***(3 marks)***

(c) Using the phase portrait or otherwise, find the two equilibrium densities M_+ and N_+. ***(2 marks)***

(iii) (a) Calculate the Jacobian matrix, J, at a general equilibrium (M_e, N_e). Substitute in the equilibria for $(M_+, 0)$ and $(0, N_+)$ and determine whether it is ever possible for one species to be driven to extinction. ***(7 marks)***

(b) *Without calculating the equilibrium densities M^* and N^**, use the Jacobian to show that (M^*, N^*) is a stable node provided $w < vb/c$. How does this relate this to the condition found in part (ii)(b)? What can you conclude? ***(6 marks)***

2 Consider a human population that is exposed to an infectious disease. A proportion $v \in [0,1]$ of newborn offspring are vaccinated at birth and are thus born immune. Partitioning the population in to either susceptible (S), infected (I) or recovered/immune (R) compartments, the dynamics of this population are given by the ordinary differential equations,

$$\frac{dS}{dt} = \mu(1-v) - \beta SI - \mu S \quad (3)$$

$$\frac{dI}{dt} = \beta SI - (\gamma+\mu)I \quad (4)$$

$$\frac{dR}{dt} = \mu v + \gamma I - \mu R, \quad (5)$$

where μ, β, γ are positive constants, and the total population $S+I+R=1$.

(i) Give biological definitions of the parameters β and γ. ***(2 marks)***

(ii) Explain why this system may be fully described using only the equations for dS/dt and dI/dt. ***(2 marks)***

(iii) Find the densities (S_{df}, I_{df}) at the disease-free equilibrium, and show that the endemic equilibrium is given by,

$$S^* = \frac{\gamma+\mu}{\beta}, I^* = \frac{\mu}{\beta}\left[\frac{1-v}{S^*} - 1\right]. \quad (6)$$

(5 marks)

(iv) (a) Find the Jacobian matrix of the system at a general equilibrium (S_e, I_e). ***(2 marks)***

(b) Substitute both the disease-free, (S_{df}, I_{df}), and endemic, (S^*, I^*), equilibria in to the Jacobian, and thus conclude whether the disease persists or dies out when: (1) $v < (1-S^*)$, and (2) $v > (1-S^*)$. ***(9 marks)***

(v) Let $\mu = 0.1$, $\gamma = 0.9$ and $\beta = 2$. Sketch a bifurcation diagram for this system, plotting both S_{df} and S^* as the parameter v is varied between 0 and 1 on the x-axis. Use a solid line to denote a stable equilibrium and a dashed line for an unstable equilibrium. Name the type of bifurcation that occurs at $v = 0.5$. ***(5 marks)***

3 The regulated transcription of a gene is represented by the differential equation

$$\frac{dm}{dt} = -\mu m + f(t), \quad t \geq 0,$$

where $m(t)$ represents the concentration of the mRNA transcript associated with the gene, and μ is a positive constant.

(i) What are the meanings of the parameter μ and the function $f(t)$?
(2 marks)

(ii) Show that if $m(0) = 0$ and $f(t) = \frac{1}{2}(1 + \cos \omega t)$, then

$$m(t) = A + B(\mu \cos \omega t + \omega \sin \omega t) - Ce^{-\mu t},$$

where A, B and C are constants that you should determine. ***(7 marks)***

(iii) Show that, as $t \to \infty$, $m(t)$ approaches the periodic solution

$$m_P(t) = A + \tilde{B} \cos[\omega(t - \tau)],$$

where $\tilde{B}$ and τ are constants that you should determine. Show that

$$0 < \tau < \frac{\pi}{2\omega}.$$

You may find the identity $\cos(\alpha - \beta) = \cos\alpha \cos\beta + \sin\alpha \sin\beta$ helpful.
(8 marks)

(iv) Show that, as $t \to \infty$, the ratio ρ between the maximum and minimum concentrations of mRNA is given by

$$\rho = \frac{\sqrt{\mu^2 + \omega^2} + \mu}{\sqrt{\mu^2 + \omega^2} - \mu}.$$

(v) If the period of $f(t)$ is 120 min, and $\mu = 0.03$ min^{-1}, show that, as $t \to \infty$, peaks of mRNA concentration occur approximately 20 min after peaks of $f(t)$, and that the fold-difference between maxima and minima of mRNA concentration is approximately 3. ***(5 marks)***

4 A model for the expression of an autoregulatory gene is given by

$$\frac{dM}{dt} = f(P) - \mu M \quad (7)$$

$$\frac{dP}{dt} = kM - \nu P, \quad (8)$$

where M and P represent the concentration of mRNA and protein, and μ, ν and k are positive constants, and

$$f(P) = \frac{\theta^m}{\theta^m + P^m}, \quad \theta > 0, \ m \geq 1.$$

(i) Sketch $f(P)$ for $m = 1$ and for $m > 1$. State whether the model represents autoactivation or autorepression. ***(5 marks)***

(ii) Sketch the nullclines for the equations (7) and (8) and show that the model has a unique steady state (M_*, P_*). Show graphically that P_* is an increasing function of θ. Show that P_* is the positive solution of the equation

$$P^{m+1} + \theta^m P = \frac{k}{\mu\nu}\theta^m. \quad (9)$$

(6 marks)

(iii) By linearising the model around the steady state, show that the steady state is always stable, and that it is a stable spiral if

$$-4k\phi > (\mu - \nu)^2,$$

where $\phi = \frac{df}{dP}(P_*)$. ***(7 marks)***

(iv) Show that $\frac{df}{dP} = -m\theta^{-m}P^{m-1}f(P)^2$.

By evaluating this expression at the steady state P_* and using the steady state conditions and (9), show that

$$\phi = -m\left(\frac{\mu\nu}{k}\right)^2\left(\frac{k}{\mu\nu} - P_*\right).$$

Using your result from (ii), show that if $\mu \neq \nu$, then the steady state is a stable spiral only for sufficiently small values of θ. ***(7 marks)***

End of Question Paper