



The
University
Of
Sheffield.

MAS377

SCHOOL OF MATHEMATICS AND STATISTICS

**Spring Semester
2011–2012**

MAS377 Mathematical Biology

2 hours

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

- 1 A model for fishing in a lake is given in nondimensional form by

$$\begin{aligned}\frac{df}{dt} &= sf(1-f) - fn \\ \frac{dn}{dt} &= \alpha f - n,\end{aligned}$$

where $f(t)$ and $n(t)$ represent the number of fish in the lake, and the number of fishermen, respectively, and s and α are positive constants.

- (i) Suggest a mechanistic interpretation for each of the terms in the model.
(4 marks)
- (ii) Find the steady state solutions of the model and determine their stability. Describe briefly what your results mean in terms of the long term outcome of fishing in the lake.
(11 marks)
- (iii) Sketch the phase portrait of the model, showing examples of model trajectories. Explain how the qualitative nature of the phase portrait depends on the model parameters.
(10 marks)

2 A model for the expression of a single gene is given by

$$\begin{aligned}\frac{dM}{dt} &= -\mu M + \alpha \\ \frac{dP}{dt} &= \beta M - \mu P,\end{aligned}$$

where $M(t)$ and $P(t)$ represent mRNA and protein, respectively, and α , β and μ are positive constants.

- (i) Assuming initial conditions $M(0) = 0, P(0) = 0$, show that the time T_1 taken for the protein level to reach half its steady state value is given by the solution of

$$e^{\mu T_1} = 2(1 + \mu T_1).$$

(10 marks)

- (ii) A common simplification in cellular network models is to set mRNA dynamics to steady state, modelling explicitly only the protein dynamics. Show that this assumption leads to the reduced model

$$\frac{dP}{dt} = \frac{\alpha\beta}{\mu} - \mu P,$$

and that the time T_2 taken for the protein level to rise from 0 to half its steady state level is given by T_2 , where

$$e^{\mu T_2} = 2.$$

By comparing your expressions for T_1 (from part (i)) and T_2 graphically, show that $T_2 < T_1$. *(8 marks)*

- (iii) Using the approximation $e^x \approx 1 + x + x^2/2$, show that

$$T_1 - T_2 \approx \frac{\sqrt{2 \ln 2}}{\mu}.$$

Does this approximation provide an under- or overestimate of the true value of $T_1 - T_2$? Calculate T_2 and estimate T_1 if $\mu = 0.03\text{min}^{-1}$. *(7 marks)*

- 3** The *hes1* gene encodes a transcription factor that represses its own transcription. A simple model of *hes1* regulation is given by

$$\begin{aligned}\frac{dm}{dt} &= -d_m m + k_m g(p) \\ \frac{dp}{dt} &= k_p m - d_p p,\end{aligned}$$

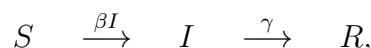
where $m = m(t)$ and $p = p(t)$ represent mRNA and protein, respectively. d_m , d_p , k_m and k_p are positive constants, and $\frac{dg}{dp} < 0$ for $p > 0$.

- (i) Show **graphically** that the model has a unique steady state. **(2 marks)**
- (ii) By linearising the model equations about the steady state, determine whether or not the steady state is stable to small perturbations. Show that if $d_m = d_p$, the steady state is always a spiral. **(8 marks)**
- (iii) Write down a revised differential equation model of the *hes1* system that includes transcription and translation time delays. Does the inclusion of time delays affect the steady state value of the system? **(3 marks)**
- (iv) Linearise the delay equations about their steady state, deriving a 2nd order delay differential equation for perturbations about the protein steady state. Show that this equation depends only on the total delay (i.e. on the sum of the transcription and translation delays). Assuming that $d_m = d_p = d$, show that the linearised system has a pure imaginary eigenvalue for a critical value of the total time delay if $\gamma k_m k_p > d^2$. **(10 marks)**
- (v) Show that the corresponding oscillatory period of the solution of the linearised system is

$$T = \frac{2\pi}{\sqrt{\gamma k_m k_p - d^2}},$$

where γ is the gradient of the function $g(p)$ evaluated at the steady state. **(2 marks)**

- 4 The following flow diagram represents the dynamics of an SIR epidemic model without births or deaths:



where β and γ are positive constants.

- (i) Write down a set of equations to describe these dynamics and explain why the system can be fully described using only two of the equations. **(6 marks)**
- (ii) Define the basic reproductive ratio of the disease, R_0 , in words. Give an expression for R_0 in terms of your model parameters. **(4 marks)**
- (iii) Find the nullclines and draw phase portraits of the system for the two general cases, $R_0 < 1$ and $R_0 > 1$, showing clearly which parts of the phase plane can be accessed by system trajectories. Use your phase portraits to explain what disease dynamics the two cases correspond to. **(12 marks)**
- (iv) An outbreak of chicken pox is predicted in a town of population 2000. The transmission coefficient is estimated to be $\beta = 0.00075$ and the daily recovery rate is $\gamma = 0.15$. Find how many individuals in the town must be vaccinated for herd immunity to prevent the outbreak. **(3 marks)**

- 5 A reaction diffusion model is given by

$$\begin{aligned} \frac{\partial U}{\partial t} &= a - bU + \frac{U^2}{V} + \frac{\partial^2 U}{\partial x^2} \\ \frac{\partial V}{\partial t} &= U^2 - V + D \frac{\partial^2 V}{\partial x^2}, \end{aligned}$$

where $U(x, t)$ and $V(x, t) > 0$ are the concentrations of two chemicals at position x and time t , and a , b and D are positive constants.

- (i) Show that the model has a unique spatially uniform steady state (U_*, V_*) and find expressions for U_* and V_* . **(4 marks)**
- (ii) Show that (U_*, V_*) is stable to *spatially uniform* perturbations if and only if $b > 0$ and $b(1 - a) < 1 + a$. **(8 marks)**
- (iii) By considering the growth rate of spatially periodic perturbations to (U_*, V_*) , find **three** additional inequalities that the parameters must satisfy in order for diffusion-driven instability to occur. **(13 marks)**

End of Question Paper