Part II

Mathematical Biology

Paper 1, Section I

6C Mathematical Biology

Consider a birth-death process in which births always give rise to 3 offspring, with rate λ, while the death rate per individual is β. Draw a transition diagram and write down the master equation for this system.

Show that the population mean is given by

$$\langle n \rangle = \frac{3\lambda}{\beta}\left(1 - e^{-\beta t}\right) + n_0 e^{-\beta t},$$

where n_0 is the initial population mean, and that the population variance satisfies

$$\sigma^2 \to \frac{6\lambda}{\beta} \quad \text{as} \quad t \to \infty.$$

Paper 2, Section I

6C Mathematical Biology

In an SIR model for an infectious disease the population N is divided into susceptible $S(t)$, infected $I(t)$ and recovered (non-infectious) $R(t)$. The disease is assumed to be non-lethal, so the total population does not change in time.

Consider the following SIR model,

$$\frac{dS}{dt} = fR - \beta IS, \quad \frac{dI}{dt} = \beta IS - \nu I, \quad \frac{dR}{dt} = \nu I - fR,$$

and explain the meaning of each of the terms in the equations. Assume that at $t = 0$, $S \simeq N$, while $I, R \ll N$.

(a) Setting $f = 0$, show that if $\beta N < \nu$ no epidemic occurs.

(b) Now take $f > 0$ and suppose that there is an epidemic. Show that the system has a nontrivial fixed point and that it is stable for small disturbances. Show that the eigenvalues of the Jacobian matrix are complex for sufficiently small f but real for sufficiently large f. Give a qualitative sketch of $I(t)$ in the two cases.

Paper 3, Section I

6C Mathematical Biology

A gene product with concentration g is produced by a chemical S of concentration s, is autocatalysed and degrades linearly according to the kinetic equation

$$\frac{dg}{dt} = f(g,s) = s + k\frac{g^2}{1+g^2} - g,$$

where $k > 2$ is a constant.

First consider the case $s = 0$. Show that there are two positive steady states, and determine their stability. Sketch the reaction rate $f(g,0)$.

The system starts in the steady state $g = 0$ with $s = 0$. The value of s is then increased to the value s_1, held at this value for a long time, and then reduced to zero. Show that, if s_1 is greater than a value $s_c(k)$, a biochemical switch can be achieved to a state $g = g_* > 0$ whose value you should determine. Give a clear mathematical specification of the value $s_c(k)$. [An explicit formula is not needed.]

For the case $k \gg 1$, use a suitable approximate form of $f(g,s)$ to show that $s_c(k) \simeq Ck^{-1}$ where C is a constant that you should derive.

Paper 4, Section I

6C Mathematical Biology

The concentration $C(x,t)$ of a morphogen obeys the differential equation

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2} + f(C),$$

in the domain $0 \leqslant x \leqslant L$, with boundary conditions $C(0,t) = 0$ and $\partial C(L,t)/\partial x = 0$, with D a positive constant and $f(C)$ a nonlinear function of C with $f(0) = 0$ and $f'(0) > 0$. Linearising the dynamics around $C = 0$, and representing $C(x,t)$ as a suitable Fourier expansion, find the condition on L such that the system is linearly stable. Express your answer in terms of D and $f'(0)$.

Paper 3, Section II

13C Mathematical Biology

Consider the reaction-diffusion system in one spatial dimension $-\infty < x < \infty$,

$$\begin{aligned} \frac{\partial u}{\partial t} &= D\frac{\partial^2 u}{\partial x^2} + f(u) + \rho(u-v), &(1)\\ \epsilon\frac{\partial v}{\partial t} &= \frac{\partial^2 v}{\partial x^2} + u - v, &(2) \end{aligned}$$

where $D > 0$ is the activator diffusion constant, $\rho > 0$ is a constant, and $0 < \epsilon \ll 1$ so that the inhibitor v is a fast variable relative to the activator u. The nonlinear function $f(u)$ is taken to have the properties $f(0) = 0$ and $f'(0) = -r$ with $0 \leqslant r \leqslant 1$.

(a) Setting $\epsilon = 0$, show that the inhibitor dynamics can be solved to express the Fourier amplitude $\hat{v}(k,t)$ of the inhibitor in terms of the Fourier amplitude $\hat{u}(k,t)$ of the activator.

(b) Using the relation found in part (a), and linearising around the state $u = 0$, find the dynamics of perturbations around $u = 0$ and thus the growth rate $\sigma(k)$ as a function of the wavenumber k.

(c) From the result in (b), show that the threshold of a pattern-forming instability lies along a curve in the $r - \rho$ plane given by

$$\rho_c(r) = \left(\sqrt{r} + \sqrt{D}\right)^2, \qquad (3)$$

along which the critical wavenumber is

$$k_c = \left(\frac{r}{D}\right)^{1/4}. \qquad (4)$$

Paper 4, Section II

14C Mathematical Biology

Consider a population subject to the following birth-death process. When the number of individuals in the population is n, the probability of an increase from n to $n+1$ per unit time is $\gamma+\beta n$ and the probability of a decrease from n to $n-1$ is $\alpha n(n-1)$, where α, β, and γ are constants.

Draw a transition diagram and show that the master equation for $P(n,t)$, the probability that at time t the population has n members, is

$$\frac{\partial P}{\partial t} = \alpha n(n+1)P(n+1,t) - [\alpha n(n-1)+\gamma+\beta n]\, P(n,t) + [\gamma+\beta(n-1)]\, P(n-1,t). \quad (1)$$

Show that $\langle n\rangle$, the mean number of individuals in the population, satisfies

$$\frac{d\langle n\rangle}{dt} = -\alpha\langle n^2\rangle + (\alpha+\beta)\langle n\rangle + \gamma.$$

Deduce that, in a steady state,

$$\langle n\rangle = \frac{\alpha+\beta}{2\alpha} \pm \sqrt{\frac{(\alpha+\beta)^2}{4\alpha^2} + \frac{\gamma}{\alpha} - (\Delta n)^2},$$

where Δn is the standard deviation of n. Given the form of the expression above, when is the choice of the minus sign not admissible?

Show that, under conditions to be specified, the master equation (1) may be approximated by a Fokker-Planck equation of the form

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial n}\left[g(n)P(n,t)\right] + \frac{1}{2}\frac{\partial^2}{\partial n^2}\left[h(n)P(n,t)\right].$$

Find the functions $g(n)$ and $h(n)$.

In the case $\alpha \ll \gamma$ and $\alpha \ll \beta$, find the leading-order approximation to n_* such that $g(n_*) = 0$. Defining the new variable $x = n - n_*$, explain how an approximate form of $P(x)$ may be obtained in the neighbourhood of $x=0$ in the steady-state limit, showing clearly the dependence of $P(x)$ on the properties of the functions $g(n)$ and $h(n)$ at $n = n_*$. Deduce leading order estimates for $\langle n\rangle$ and $(\Delta n)^2$ in terms of α, β and γ.

Compare your results to those obtained from the master equation above and give justification of why the conditions for applicability of the Fokker-Planck equation hold in this case.

Paper 1, Section I
6C Mathematical Biology

Consider the discrete delay equation

$$x_{n+1} = x_n \exp\left[r\left(1 - x_{n-1}\right)\right],$$

with $r > 0$ a constant.

(a) Find the positive fixed point x^* of the model. Setting $x_n = x^* + u_n$, with $|u_n| \ll 1$, determine the linearised stability equation for u_n.

(b) Find the range of r for which the fixed point x^* is stable and for which perturbations decay monotonically in time.

(c) Find the range of r for which the decay of perturbations to x^* is oscillatory.

(d) Find the critical value r^* for x^* to become unstable, and show that at that value of r the system exhibits oscillations of period $p > 1$. Find p.

Paper 2, Section I
6C Mathematical Biology

Two species with populations N_1 and N_2 compete according to the equations

$$\begin{aligned}
\frac{dN_1}{dt} &= r_1 N_1 \left(1 - \frac{N_1}{K_1} - b_{12}\frac{N_2}{K_1}\right) \\
\frac{dN_2}{dt} &= r_2 N_2 \left(1 - b_{21}\frac{N_1}{K_2}\right),
\end{aligned}$$

so that only species 1 has limited carrying capacity. Assume that the parameters $r_1, r_2, K_1, K_2, b_{12}$, and b_{21} are all strictly positive.

(a) Rescale the variables N_1, N_2 and t to leave three parameters, $\rho = r_1/r_2$, $\alpha = b_{12}K_2/K_1$ and $\beta = b_{21}K_1/K_2$ and determine the steady states.

(b) Assuming $\beta > 1$, investigate the stability of the biologically relevant steady states and sketch the phase plane trajectories.

(c) Assuming $\beta > 1$, show that irrespective of the size of the parameters the principle of competitive exclusion holds. Briefly describe under what ecological circumstances species 2 becomes extinct.

Paper 3, Section I

6C Mathematical Biology

A biological population contains n individuals. The population increases or decreases according to the transition rates

$$n \xrightarrow{\lambda} n+1 \qquad\qquad n \xrightarrow{\beta n^2} n-2\,.$$

(a) Derive the master equation for $P(n,t)$, the probability that the population contains n individuals at time t, and a corresponding equation for $\langle n \rangle$. What condition does the latter imply on the steady state?

(b) The Fokker-Planck equation has the form:

$$\frac{\partial}{\partial t}P(n,t) = -\frac{\partial}{\partial n}\big[A(n)P(n,t)\big] + \tfrac{1}{2}\frac{\partial^2}{\partial n^2}\big[B(n)P(n,t)\big]\,. \qquad (1)$$

Derive the Fokker-Planck equation from your master equation. Deduce the forms of $A(n)$ and $B(n)$ for this system.

(c) Give brief arguments why in the steady state (1) has the approximate solution $(2\pi\sigma^2)^{-1/2}\exp(-(n-\mu)^2/2\sigma^2)$ and derive the corresponding values of σ and μ.

(d) Comment on the relation to the steady-state condition you have derived in (a). Under what conditions on β and λ is the Fokker-Planck equation likely to give an accurate description of the steady state?

Paper 4, Section I
6C Mathematical Biology

An allosteric enzyme E reacts with substrate S to produce a product P according to the mechanism

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1$$
$$C_1 + S \xrightarrow{k_2} C_2 \xrightarrow{k_3} C_1 + P \ ,$$

where the k_is are rate constants, and C_1 and C_2 are enzyme-substrate complexes.

(a) With lowercase letters denoting concentrations, write down the differential equation model based on the Law of Mass Action for the dynamics of e, s, c_1, c_2 and p.

(b) Show that the quantity $c_1 + c_2 + e$ is conserved and comment on its physical meaning.

(c) Using the result in (b), assuming initial conditions $s(0) = s_0$, $e(0) = e_0$, $c_1(0) = c_2(0) = p(0) = 0$, and rescaling with $\epsilon = e_0/s_0$, $\tau = k_1 e_0 t$, $u = s/s_0$, and $v_i = c_i/e_0$, show that the reaction mechanism can be reduced to

$$\frac{du}{d\tau} = f(u, v_1, v_2)\,,$$
$$\epsilon\frac{dv_1}{d\tau} = g_1(u, v_1, v_2)\,,$$
$$\epsilon\frac{dv_2}{d\tau} = g_2(u, v_1, v_2)\,.$$

Determine f, g_1 and g_2 and express them in terms of the three dimensionless quantities $\alpha = k_{-1}/k_1 s_0$, $\beta = k_2/k_1$ and $\gamma = k_3/k_1 s_0$.

(d) On time scales $\tau \gg \epsilon$, show that the rate of production of P can be expressed in terms of the rescaled substrate concentration u in the form

$$\frac{dp}{dt} = A\frac{u^2}{\alpha + u + (\beta/\gamma)u^2}\ ,$$

where A is a constant. Compare this relation to the Michaelis-Menten form by means of a sketch.

Paper 3, Section II
13C Mathematical Biology

A chemical species of concentration $C(\mathbf{x},t)$ diffuses in a two-dimensional stationary medium with diffusivity $D(C)$. Write down an expression for the diffusive flux $\mathbf{J}$ that enters Fick's law and then show that C obeys the partial differential equation

$$\frac{\partial C}{\partial t} = \boldsymbol{\nabla}\cdot\left(D(C)\boldsymbol{\nabla} C\right). \tag{1}$$

Suppose that at time $t=0$ an amount $2\pi M$ of the chemical is deposited at the origin and diffuses outward in a circularly symmetric manner, so that $C = C(r,t)$ for $r>0, t>0$, where r is the radial coordinate. Assume the diffusivity is $D = kC$ for some constant k. Show, by dimensional analysis or otherwise, that an appropriate similarity solution has the form

$$C = \frac{M^\alpha}{(kt)^\beta} F(\xi)\,, \qquad \xi = \frac{r}{(Mkt)^\gamma} \qquad \text{and} \qquad \int_0^\infty \xi F(\xi)\, d\xi = 1\,,$$

where the exponents α, β, γ are to be determined, and derive the ordinary differential equation satisfied by F.

Solve this ordinary differential equation, subject to appropriate boundary conditions, and deduce that the chemical occupies a finite circular region of radius

$$r_0(t) = (NMkt)^{1/4}\,,$$

with N a constant which you should find.

Still assuming that $D = kC$, show that if a term αC is added to the right-hand side of (1), a solution of the form $C(r,t) = G(r,\tau)e^{\alpha t}$ can be found, where $\tau(t)$ is a time-like variable satisfying $\tau(0)=0$. Show that a suitable choice of τ reduces the dynamics to

$$\frac{\partial G}{\partial \tau} = k\boldsymbol{\nabla}\cdot(G\boldsymbol{\nabla} G)\,,$$

and that the previous analysis can be applied to find the concentration. Describe the evolution in the cases $\alpha = 0, \alpha > 0$, and $\alpha < 0$.

[*Hint: In plane polar coordinates*

$$\boldsymbol{\nabla} C(r,t) \equiv \left(\frac{\partial C}{\partial r}, 0, 0\right) \qquad \text{and} \qquad \boldsymbol{\nabla}\cdot(V(r,t),0,0) \equiv \frac{1}{r}\frac{\partial}{\partial r}(rV)\,.\Big]$$

Paper 4, Section II
14C Mathematical Biology

Consider the standard system of reaction-diffusion equations

$$\begin{aligned} u_t &= D_u \nabla^2 u + f(u,v) \\ v_t &= D_v \nabla^2 v + g(u,v)\,, \end{aligned}$$

where D_u and D_v are diffusion constants and $f(u,v)$ and $g(u,v)$ are such that the system has a stable homogeneous fixed point at $(u,v) = (u_*, v_*)$.

(a) Show that the condition for a Turing instability can be expressed as

$$f_u + d g_v > 2\sqrt{dJ}\,,$$

where $d = D_u/D_v$ is the diffusivity ratio and $J = f_u g_v - f_v g_u > 0$ is the determinant of the stability matrix of the homogeneous system evaluated at (u_*, v_*).

(b) Show that this result implies that a Turing instability at equal diffusivities ($d = 1$) is not possible.

(c) Show that the result in (b) also follows directly from the structure of the reaction-diffusion equations linearised about the homogeneous fixed point in the case $D_u = D_v$.

(d) Using the example

$$\begin{pmatrix} -1 & -1 \\ 1+\delta & 1-\delta \end{pmatrix},$$

for the stability matrix of the homogeneous system, show that the diffusivity ratio at which Turing instability occurs can be made as close to unity as desired by taking δ sufficiently small.

Paper 1, Section I

6E Mathematical Biology

(a) Consider a population of size $N(t)$ whose per capita rates of birth and death are be^{-aN} and d, respectively, where $b > d$ and all parameters are positive constants.

(i) Write down the equation for the rate of change of the population.

(ii) Show that a population of size $N^* = \dfrac{1}{a} \log \dfrac{b}{d}$ is stationary and that it is asymptotically stable.

(b) Consider now a disease introduced into this population, where the number of susceptibles and infectives, S and I, respectively, satisfy the equations

$$\frac{dS}{dt} = be^{-aS} S - \beta SI - dS \,,$$
$$\frac{dI}{dt} = \beta SI - (d+\delta) I \,.$$

(i) Interpret the biological meaning of each term in the above equations and comment on the reproductive capacity of the susceptible and infected individuals.

(ii) Show that the disease-free equilibrium, $S = N^*$ and $I = 0$, is linearly unstable if

$$N^* > \frac{d+\delta}{\beta} \,.$$

(iii) Show that when the disease-free equilibrium is unstable there exists an endemic equilibrium satisfying

$$\beta I + d = be^{-aS}$$

and that this equilibrium is linearly stable.

Paper 2, Section I

6E Mathematical Biology

Consider a stochastic birth–death process in a population of size $n(t)$, where deaths occur in pairs for $n \geqslant 2$. The probability per unit time of a birth, $n \to n+1$ for $n \geqslant 0$, is b, that of a pair of deaths, $n \to n-2$ for $n \geqslant 2$, is dn, and that of the death of a lonely singleton, $1 \to 0$, is D.

(a) Write down the master equation for $p_n(t)$, the probability of a population of size n at time t, distinguishing between the cases $n \geqslant 2$, $n = 0$ and $n = 1$.

(b) For a function $f(n)$, $n \geqslant 0$, show carefully that

$$\frac{d}{dt}\langle f(n)\rangle = b\sum_{n=0}^{\infty}(f_{n+1} - f_n)p_n - d\sum_{n=2}^{\infty}(f_n - f_{n-2})np_n - D(f_1 - f_0)p_1 \ ,$$

where $f_n = f(n)$.

(c) Deduce the evolution equation for the mean $\mu(t) = \langle n\rangle$, and simplify it for the case $D = 2d$.

(d) For the same value of D, show that

$$\frac{d}{dt}\langle n^2\rangle = b(2\mu + 1) - 4d\big(\langle n^2\rangle - \mu\big) - 2dp_1$$

Deduce that the variance σ^2 in the stationary state for $b, d > 0$ satisfies

$$\frac{3b}{4d} - \frac{1}{2} < \sigma^2 < \frac{3b}{4d} \, .$$

Paper 3, Section I

6E Mathematical Biology

The population density $n(a,t)$ of individuals of age a at time t satisfies the partial differential equation

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -d(a)n(a,t) \tag{1}$$

with the boundary condition

$$n(0,t) = \int_0^\infty b(a)n(a,t)\,da\,, \tag{2}$$

where $b(a)$ and $d(a)$ are, respectively, the per capita age-dependent birth and death rates.

(a) What is the biological interpretation of the boundary condition?

(b) Solve equation (1) assuming a separable form of solution, $n(a,t) = A(a)T(t)$.

(c) Use equation (2) to obtain a necessary condition for the existence of a separable solution to the full problem.

(d) For a birth rate $b(a) = \beta e^{-\lambda a}$ with $\lambda > 0$ and an age-independent death rate d, show that a separable solution to the full problem exists and find the critical value of β above which the population density grows with time.

Paper 4, Section I

6E Mathematical Biology

A marine population grows logistically and disperses by diffusion. It is moderately predated on up to a distance L from a straight coast. Beyond that distance, predation is sufficiently excessive to eliminate the population. The density $n(x,t)$ of the population at a distance $x < L$ from the coast satisfies

$$\frac{\partial n}{\partial t} = rn\Big(1 - \frac{n}{K}\Big) - \delta n + D\frac{\partial^2 n}{\partial x^2}\,, \tag{$*$}$$

subject to the boundary conditions

$$\frac{\partial n}{\partial x} = 0 \text{ at } x = 0\,, \quad n = 0 \text{ at } x = L\,.$$

(a) Interpret the terms on the right-hand side of ($*$), commenting on their dependence on n. Interpret the boundary conditions.

(b) Show that a non-zero population is viable if $r > \delta$ and

$$L > \frac{\pi}{2}\sqrt{\frac{D}{r-\delta}}\,.$$

Interpret these conditions.

Paper 3, Section II

13E Mathematical Biology

Consider an epidemic spreading in a population that has been aggregated by age into groups numbered $i = 1, \ldots, M$. The ith age group has size N_i and the numbers of susceptible, infective and recovered individuals in this group are, respectively, S_i, I_i and R_i. The spread of the infection is governed by the equations

$$\begin{aligned} \frac{dS_i}{dt} &= -\lambda_i(t) S_i\,, \\ \frac{dI_i}{dt} &= \lambda_i(t) S_i - \gamma I_i\,, \\ \frac{dR_i}{dt} &= \gamma I_i\,, \end{aligned} \tag{1}$$

where

$$\lambda_i(t) = \beta \sum_{j=1}^{M} C_{ij} \frac{I_j}{N_j}\,, \tag{2}$$

and C_{ij} is a matrix satisfying $N_i C_{ij} = N_j C_{ji}$, for $i, j = 1, \ldots, M$.

(a) Describe the biological meaning of the terms in equations (1) and (2), of the matrix C_{ij} and the condition it satisfies, and of the lack of dependence of β and γ on i.

State the condition on the matrix C_{ij} that would ensure the absence of any transmission of infection between age groups.

(b) In the early stages of an epidemic, $S_i \approx N_i$ and $I_i \ll N_i$. Use this information to linearise the dynamics appropriately, and show that the linearised system predicts

$$\mathbf{I}(t) = \exp\left[\gamma(\mathbf{L} - \mathbf{1})t\right] \mathbf{I}(0)\,,$$

where $\mathbf{I}(t) = [I_1(t), \ldots, I_M(t)]$ is the vector of infectives at time t, $\mathbf{1}$ is the $M \times M$ identity matrix and $\mathbf{L}$ is a matrix that should be determined.

(c) Deduce a condition on the eigenvalues of the matrix $\mathbf{C}$ that allows the epidemic to grow.

Paper 4, Section II

14E Mathematical Biology

The spatial density $n(x,t)$ of a population at location x and time t satisfies

$$\frac{\partial n}{\partial t} = f(n) + D\frac{\partial^2 n}{\partial x^2}\,, \qquad (*)$$

where $f(n) = -n(n-r)(n-1)$, $0 < r < 1$ and $D > 0$.

(a) Give a biological example of the sort of phenomenon that this equation describes.

(b) Show that there are three spatially homogeneous and stationary solutions to $(*)$, of which two are linearly stable to homogeneous perturbations and one is linearly unstable.

(c) For $r = \frac{1}{2}$, find the stationary solution to $(*)$ subject to the conditions

$$\lim_{x\to-\infty} n(x) = 1, \quad \lim_{x\to\infty} n(x) = 0 \quad \text{and} \quad n(0) = \frac{1}{2}\,.$$

(d) Write down the differential equation that is satisfied by a travelling-wave solution to $(*)$ of the form $n(x,t) = u(x-ct)$. Let $n_0(x)$ be the solution from part (c). Verify that $n_0(x-ct)$ satisfies this differential equation for $r \neq \frac{1}{2}$, provided the speed c is chosen appropriately. [*Hint: Consider the change to the equation from part (c).*]

(e) State how the sign of c depends on r, and give a brief qualitative explanation for why this should be the case.

Paper 1, Section I

6B Mathematical Biology

Consider a bivariate diffusion process with drift vector $A_i(\mathbf{x}) = a_{ij}x_j$ and diffusion matrix b_{ij} where

$$a_{ij} = \begin{pmatrix} -1 & 1 \\ -2 & -1 \end{pmatrix}, \quad b_{ij} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix},$$

$\mathbf{x} = (x_1, x_2)$ and $i, j = 1, 2$.

(i) Write down the Fokker–Planck equation for the probability $P(x_1, x_2, t)$.

(ii) Plot the drift vector as a vector field around the origin in the region $|x_1| < 1$, $|x_2| < 1$.

(iii) Obtain the stationary covariances $C_{ij} = \langle x_i x_j \rangle$ in terms of the matrices a_{ij} and b_{ij} and hence compute their explicit values.

Paper 2, Section I

6B Mathematical Biology

Consider the system of predator-prey equations

$$\frac{dN_1}{dt} = -\epsilon_1 N_1 + \alpha N_1 N_2 \ ,$$
$$\frac{dN_2}{dt} = \epsilon_2 N_2 - \alpha N_1 N_2 \ ,$$

where ϵ_1, ϵ_2 and α are positive constants.

(i) Determine the non-zero fixed point (N_1^*, N_2^*) of this system.

(ii) Show that the system can be written in the form

$$\frac{dx_i}{dt} = \sum_{j=1}^{2} K_{ij} \frac{\partial H}{\partial x_j}, \qquad i = 1, 2 \ ,$$

where $x_i = \log(N_i/N_i^*)$ and a suitable 2×2 antisymmetric matrix K_{ij} and scalar function $H(x_1, x_2)$ are to be identified.

(iii) Hence, or otherwise, show that H is constant on solutions of the predator-prey equations.

Paper 3, Section I

6B Mathematical Biology

Consider a model for the common cold in which the population is partitioned into susceptible (S), infective (I), and recovered (R) categories, which satisfy

$$\frac{dS}{dt} = \alpha R - \beta S I\,,$$
$$\frac{dI}{dt} = \beta S I - \gamma I\,,$$
$$\frac{dR}{dt} = \gamma I - \alpha R\,,$$

where α, β and γ are positive constants.

(i) Show that the sum $N \equiv S + I + R$ does not change in time.

(ii) Determine the condition, in terms of β, γ and N, for an endemic steady state to exist, that is, a time-independent state with a non-zero number of infectives.

(iii) By considering a reduced set of equations for S and I only, show that the endemic steady state identified in (ii) above, if it exists, is stable.

Paper 4, Section I

6B Mathematical Biology

Consider a population process in which the probability of transition from a state with n individuals to a state with $n+1$ individuals in the interval $(t, t+\Delta t)$ is $\lambda n \Delta t$ for small Δt.

(i) Write down the master equation for the probability, $P_n(t)$, of the state n at time t for $n \geqslant 1$.

(ii) Assuming an initial distribution

$$P_n(0) = \begin{cases} 1\,, & \text{if } n = 1\,, \\ 0\,, & \text{if } n > 1\,, \end{cases}$$

show that

$$P_n(t) = \exp(-\lambda t)(1 - \exp(-\lambda t))^{n-1}\,.$$

(iii) Hence, determine the mean of n for $t > 0$.

Paper 3, Section II

13B Mathematical Biology

The larva of a parasitic worm disperses in one dimension while laying eggs at rate $\lambda > 0$. The larvae die at rate μ and have diffusivity D, so that their density, $n(x,t)$, obeys

$$\frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2} - \mu n\,, \qquad (D > 0,\ \mu > 0).$$

The eggs do not diffuse, so that their density, $e(x,t)$, obeys

$$\frac{\partial e}{\partial t} = \lambda n\ .$$

At $t = 0$ there are no eggs and N larvae concentrated at $x = 0$, so that $n(x,0) = N\delta(x)$.

(i) Determine $n(x,t)$ for $t > 0$. Show that $n(x,t) \to 0$ as $t \to \infty$.

(ii) Determine the limit of $e(x,t)$ as $t \to \infty$.

(iii) Provide a physical explanation for the remnant density of the eggs identified in part (ii).

[You may quote without proof the results

$$\begin{aligned}\int_{-\infty}^{\infty} \exp(-x^2)dx &= \sqrt{\pi} \\ \int_{-\infty}^{\infty} \frac{\exp(ikx)}{k^2+\alpha^2}dk &= \pi\exp(-\alpha|x|)/\alpha\ , \quad \alpha > 0\ .\ ]\end{aligned}$$

Paper 4, Section II

14B Mathematical Biology

Consider the stochastic catalytic reaction

$$E \leftrightharpoons ES, \qquad ES \rightarrow E + P$$

in which a single enzyme E complexes reversibly to ES (at forward rate k_1 and reverse rate k_1') and decomposes into product P (at forward rate k_2), regenerating enzyme E. Assume there is sufficient substrate S so that this catalytic cycle can continue indefinitely. Let $P(E,n)$ be the probability of the state with enzyme E and n products and $P(ES,n)$ the probability of the state with complex ES and n products, these states being mutually exclusive.

(i) Write down the master equation for the probabilities $P(E,n)$ and $P(ES,n)$ for $n \geqslant 0$.

(ii) Assuming an initial state with zero products, solve the master equation for $P(E,0)$ and $P(ES,0)$.

(iii) Hence find the probability distribution $f(\tau)$ of the time τ taken to form the first product.

(iv) Obtain the mean of τ.

Paper 4, Section I

6C Mathematical Biology

(a) A variant of the classic logistic population model is given by:

$$\frac{dx(t)}{dt} = \alpha \left[x(t) - x(t-T)^2\right]$$

where $\alpha, T > 0$.

Show that for small T, the constant solution $x(t) = 1$ is stable.

Allow T to increase. Express in terms of α the value of T at which the constant solution $x(t) = 1$ loses stability.

(b) Another variant of the logistic model is given by this equation:

$$\frac{dx(t)}{dt} = \alpha\, x(t-T)\,[1 - x(t)]$$

where $\alpha, T > 0$. When is the constant solution $x(t) = 1$ stable for this model?

Paper 3, Section I

6C Mathematical Biology

A model of wound healing in one spatial dimension is given by

$$\frac{\partial S}{\partial t} = rS(1-S) + D\,\frac{\partial^2 S}{\partial x^2}\,,$$

where $S(x,t)$ gives the density of healthy tissue at spatial position x at time t and r and D are positive constants.

By setting $S(x,t) = f(\xi)$ where $\xi = x - ct$, seek a steady travelling wave solution where $f(\xi)$ tends to one for large negative ξ and tends to zero for large positive ξ. By linearising around the leading edge, where $f \approx 1$, find the possible wave speeds c of the system. Assuming that the full nonlinear system will settle to the slowest possible speed, express the wave speed as a function of D and r.

Consider now a situation where the tissue is destroyed in some window of length W, i.e. $S(x,0) = 0$ for $0 < x < W$ for some constant $W > 0$ and $S(x,0)$ is equal to one elsewhere. Explain what will happen for subsequent times, illustrating your answer with sketches of $S(x,t)$. Determine approximately how long it will take for this wound to heal (in the sense that S is close to one everywhere).

Paper 2, Section I

6C Mathematical Biology

An activator–inhibitor system for $u(x,t)$ and $v(x,t)$ is described by the equations

$$\begin{aligned}\frac{\partial u}{\partial t} &= uv^2 - a + D\,\frac{\partial^2 u}{\partial x^2}\,, \\ \frac{\partial v}{\partial t} &= v - uv^2 + \frac{\partial^2 v}{\partial x^2}\,,\end{aligned}$$

where $a, D > 0$.

Find the range of a for which the spatially homogeneous system has a stable equilibrium solution with $u > 0$ and $v > 0$.

For the case when the homogeneous system is stable, consider spatial perturbations proportional to $\cos(kx)$ to the equilibrium solution found above. Give a condition on D in terms of a for the system to have a Turing instability (a spatial instability).

Paper 1, Section I

6C Mathematical Biology

An animal population has annual dynamics, breeding in the summer and hibernating through the winter. At year t, the number of individuals alive who were born a years ago is given by $n_{a,t}$. Each individual of age a gives birth to b_a offspring, and after the summer has a probability μ_a of dying during the winter. [You may assume that individuals do not give birth during the year in which they are born.]

Explain carefully why the following equations, together with initial conditions, are appropriate to describe the system:

$$\begin{aligned}n_{0,t} &= \sum_{a=1}^{\infty} n_{a,t} b_a \\ n_{a+1,t+1} &= (1-\mu_a) n_{a,t}\,,\end{aligned}$$

Seek a solution of the form $n_{a,t} = r_a \gamma^t$ where γ and r_a, for $a = 1,2,3\ldots$, are constants. Show γ must satisfy $\phi(\gamma) = 1$ where

$$\phi(\gamma) = \sum_{a=1}^{\infty} \left(\prod_{i=0}^{a-1} (1-\mu_i) \right) \gamma^{-a} b_a\,.$$

Explain why, for any reasonable set of parameters μ_i and b_i, the equation $\phi(\gamma) = 1$ has a unique solution. Explain also how $\phi(1)$ can be used to determine if the population will grow or shrink.

Paper 3, Section II

13C Mathematical Biology

(a) A stochastic birth-death process has a master equation given by

$$\frac{dp_n}{dt} = \lambda(p_{n-1} - p_n) + \beta\left[(n+1)p_{n+1} - np_n\right] ,$$

where $p_n(t)$ is the probability that there are n individuals in the population at time t for $n = 0, 1, 2, \ldots$ and $p_n = 0$ for $n < 0$.

(i) Give a brief interpretation of λ and β.

(ii) Derive an equation for $\frac{\partial \phi}{\partial t}$, where ϕ is the generating function

$$\phi(s,t) = \sum_{n=0}^{\infty} s^n p_n(t).$$

(iii) Assuming that the generating function ϕ takes the form

$$\phi(s,t) = e^{(s-1)\,f(t)} ,$$

find $f(t)$ and hence show that, as $t \to \infty$, both the mean $\langle n \rangle$ and variance σ^2 of the population size tend to constant values, which you should determine.

(b) Now suppose an extra process is included: k individuals are added to the population at rate $\epsilon(n)$.

(i) Write down the new master equation, and explain why, for $k > 1$, the approach used in part (a) will fail.

(ii) By working with the master equation directly, find a differential equation for the rate of change of the mean population size $\langle n \rangle$.

(iii) Now take $\epsilon(n) = an + b$ for positive constants a and b. Show that for $\beta > ak$ the mean population size tends to a constant, which you should determine. Briefly describe what happens for $\beta < ak$.

Paper 4, Section II

14C Mathematical Biology

A model of an infectious disease in a plant population is given by

$$\begin{aligned}\dot{S} &= (S+I) - (S+I)S - \beta IS\,, &(1)\\ \dot{I} &= -(S+I)I + \beta IS &(2)\end{aligned}$$

where $S(t)$ is the density of healthy plants and $I(t)$ is the density of diseased plants at time t and β is a positive constant.

(a) Give an interpretation of what each of the terms in equations (1) and (2) represents in terms of the dynamics of the plants. What does the coefficient β represent? What can you deduce from the equations about the effect of the disease on the plants?

(b) By finding all fixed points for $S \geqslant 0$ and $I \geqslant 0$ and analysing their stability, explain what will happen to a healthy plant population if the disease is introduced. Sketch the phase diagram, treating the cases $\beta < 1$ and $\beta > 1$ separately.

(c) Define new variables $N(t)$ for the total plant population density and $\theta(t)$ for the proportion of the population that is diseased. Starting from equations (1) and (2) above, derive equations for $\dot{N}$ and $\dot{\theta}$ purely in terms of N, θ and β. Without carrying out a full fixed point analysis, explain how this system can be used directly to show the same results you had in part (b). [*Hint: start by considering the dynamics of $N(t)$ alone.*]

(d) Suppose now that in an attempt to control disease, plants are culled at a rate k per capita, independently of whether the plants are healthy or diseased. Write down the modified versions of equations (1) and (2). Use these to build updated equations for $\dot{N}$ and $\dot{\theta}$. Without carrying out a detailed fixed point analysis, what can you deduce about the effect of culling? Give the range of k for which culling can effectively control the disease.

Paper 1, Section I
6C Mathematical Biology

Consider a birth-death process in which the birth and death rates in a population of size n are, respectively, Bn and Dn, where B and D are per capita birth and death rates.

(a) Write down the master equation for the probability, $p_n(t)$, of the population having size n at time t.

(b) Obtain the differential equations for the rates of change of the mean $\mu(t) = \langle n \rangle$ and the variance $\sigma^2(t) = \langle n^2 \rangle - \langle n \rangle^2$ in terms of μ, σ, B and D.

(c) Compare the equations obtained above with the deterministic description of the evolution of the population size, $dn/dt = (B - D)n$. Comment on why B and D cannot be uniquely deduced from the deterministic model but can be deduced from the stochastic description.

Paper 2, Section I
6C Mathematical Biology

Consider a model of an epidemic consisting of populations of susceptible, $S(t)$, infected, $I(t)$, and recovered, $R(t)$, individuals that obey the following differential equations

$$
\begin{aligned}
\frac{dS}{dt} &= aR - bSI, \\
\frac{dI}{dt} &= bSI - cI, \\
\frac{dR}{dt} &= cI - aR,
\end{aligned}
$$

where a, b and c are constant. Show that the sum of susceptible, infected and recovered individuals is a constant N. Find the fixed points of the dynamics and deduce the condition for an endemic state with a positive number of infected individuals. Expressing R in terms of S, I and N, reduce the system of equations to two coupled differential equations and, hence, deduce the conditions for the fixed point to be a node or a focus. How do small perturbations of the populations relax to the steady state in each case?

Paper 3, Section I

6C Mathematical Biology

Consider a nonlinear model for the axisymmetric dispersal of a population in two spatial dimensions whose density, $n(r,t)$, obeys

$$\frac{\partial n}{\partial t} = D\boldsymbol{\nabla}\cdot(n\boldsymbol{\nabla}n)\,,$$

where D is a positive constant, r is a radial polar coordinate, and t is time.

Show that

$$2\pi\int_0^\infty n(r,t)r\,dr = N$$

is constant. Interpret this condition.

Show that a similarity solution of the form

$$n(r,t) = \left(\frac{N}{Dt}\right)^{1/2} f\left(\frac{r}{(NDt)^{1/4}}\right)$$

is valid for $t>0$ provided that the scaling function $f(x)$ satisfies

$$\frac{d}{dx}\left(xf\frac{df}{dx}+\frac{1}{4}x^2 f\right) = 0\,.$$

Show that there exists a value x_0 (which need not be evaluated) such that $f(x)>0$ for $x<x_0$ but $f(x)=0$ for $x>x_0$. Determine the area within which $n(r,t)>0$ at time t in terms of x_0.

[*Hint: The gradient and divergence operators in cylindrical polar coordinates act on radial functions f and g as*

$$\boldsymbol{\nabla}f(r) = \frac{\partial f}{\partial r}\hat{\boldsymbol{r}} \quad , \quad \boldsymbol{\nabla}\cdot[g(r)\hat{\boldsymbol{r}}] = \frac{1}{r}\frac{\partial}{\partial r}(rg(r)). \qquad]$$

Paper 4, Section I

6C Mathematical Biology

Consider a model of a population N_τ in discrete time

$$N_{\tau+1} = \frac{rN_\tau}{(1+bN_\tau)^2},$$

where $r, b > 0$ are constants and $\tau = 1, 2, 3, \ldots$. Interpret the constants and show that for $r > 1$ there is a stable fixed point.

Suppose the initial condition is $N_1 = 1/b$ and that $r > 4$. Show, using a cobweb diagram, that the population N_τ is bounded as

$$\frac{4r^2}{(4+r)^2 b} \leqslant N_\tau \leqslant \frac{r}{4b}$$

and attains the bounds.

Paper 3, Section II

13C Mathematical Biology

Consider fluctuations of a population described by the vector $\mathbf{x} = (x_1, x_2, \ldots, x_N)$. The probability of the state $\mathbf{x}$ at time t, $P(\mathbf{x}, t)$, obeys the multivariate Fokker–Planck equation

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x_i}\big(A_i(\mathbf{x})P\big) + \frac{1}{2}\frac{\partial^2}{\partial x_i \partial x_j}\big(B_{ij}(\mathbf{x})P\big),$$

where $P = P(\mathbf{x}, t)$, A_i is a *drift* vector and B_{ij} is a symmetric positive-definite *diffusion* matrix, and the summation convention is used throughout.

(a) Show that the Fokker–Planck equation can be expressed as a continuity equation

$$\frac{\partial P}{\partial t} + \boldsymbol{\nabla} \cdot \mathbf{J} = 0,$$

for some choice of probability flux $\mathbf{J}$ which you should determine explicitly. Here, $\boldsymbol{\nabla} = (\frac{\partial}{\partial x_1}, \frac{\partial}{\partial x_2}, \ldots, \frac{\partial}{\partial x_N})$ denotes the gradient operator.

(b) Show that the above implies that an initially normalised probability distribution remains normalised,

$$\int P(\mathbf{x}, t)\, dV = 1,$$

at all times, where the volume element $dV = dx_1 dx_2 \ldots dx_N$.

(c) Show that the first two moments of the probability distribution obey

$$\begin{aligned} \frac{d}{dt}\langle x_k \rangle &= \langle A_k \rangle \\ \frac{d}{dt}\langle x_k x_l \rangle &= \langle x_l A_k + x_k A_l + B_{kl} \rangle. \end{aligned}$$

(d) Now consider small fluctuations with zero mean, and assume that it is possible to linearise the drift vector and the diffusion matrix as $A_i(\mathbf{x}) = a_{ij} x_j$ and $B_{ij}(\mathbf{x}) = b_{ij}$ where a_{ij} has real negative eigenvalues and b_{ij} is a symmetric positive-definite matrix. Express the probability flux in terms of the matrices a_{ij} and b_{ij} and assume that it vanishes in the stationary state.

(e) Hence show that the multivariate normal distribution,

$$P(\mathbf{x}) = \frac{1}{Z}\exp(-\frac{1}{2}D_{ij} x_i x_j),$$

where Z is a normalisation and D_{ij} is symmetric, is a solution of the linearised Fokker–Planck equation in the stationary state, and obtain an equation that relates D_{ij} to the matrices a_{ij} and b_{ij}.

(f) Show that the inverse of the matrix D_{ij} is the matrix of covariances $C_{ij} = \langle x_i x_j \rangle$ and obtain an equation relating C_{ij} to the matrices a_{ij} and b_{ij}.

Paper 4, Section II

14C Mathematical Biology

An activator-inhibitor reaction diffusion system is given, in dimensionless form, by

$$\frac{\partial u}{\partial t} = d\,\frac{\partial^2 u}{\partial x^2} + \frac{u^2}{v} - 2bu, \qquad \frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} + u^2 - v,$$

where d and b are positive constants. Which symbol represents the *concentration of activator* and which the *inhibitor*? Determine the positive steady states and show, by an examination of the eigenvalues in a linear stability analysis of the spatially uniform situation, that the reaction kinetics are stable if $b < \frac{1}{2}$.

Determine the conditions for the steady state to be driven unstable by diffusion, and sketch the (b, d) parameter space in which the diffusion-driven instability occurs. Find the critical wavenumber k_c at the bifurcation to such a diffusion-driven instability.

Paper 1, Section I

6B Mathematical Biology

A model of insect dispersal and growth in one spatial dimension is given by

$$\frac{\partial N}{\partial t} = D\frac{\partial}{\partial x}\left(N^2\frac{\partial N}{\partial x}\right) + \alpha N\,, \quad N(x,0) = N_0\delta(x),$$

where α, D and N_0 are constants, $D > 0$, and α may be positive or negative.

By setting $N(x,t) = R(x,\tau)\,e^{\alpha t}$, where $\tau(t)$ is some time-like variable satisfying $\tau(0) = 0$, show that a suitable choice of τ yields

$$R_\tau = (R^2 R_x)_x\,, \quad R(x,0) = N_0\,\delta(x)\,,$$

where subscript denotes differentiation with respect to x or τ.

Consider a similarity solution of the form $R(x,\tau) = F(\xi)/\tau^{\frac{1}{4}}$ where $\xi = x/\tau^{\frac{1}{4}}$. Show that F must satisfy

$$-\frac{1}{4}(F\xi)' = (F^2F')' \quad \text{and} \quad \int_{-\infty}^{+\infty} F(\xi)d\xi = N_0\,.$$

[You may use the fact that these are solved by

$$F(\xi) = \begin{cases} \frac{1}{2}\sqrt{\xi_0^2 - \xi^2} & \text{for } |\xi| < \xi_0 \\ 0 & \text{otherwise} \end{cases}$$

where $\xi_0 = \sqrt{4N_0/\pi}$.]

For $\alpha < 0$, what is the maximum distance from the origin that insects ever reach? Give your answer in terms of D, α and N_0.

Paper 2, Section I

6B Mathematical Biology

A bacterial nutrient uptake model is represented by the reaction system

$$\begin{aligned} 2S + E &\xrightarrow{k_1} C \\ C &\xrightarrow{k_2} 2S + E \\ C &\xrightarrow{k_3} E + 2P \end{aligned}$$

where the k_i are rate constants. Let s, e, c and p represent the concentrations of S, E, C and P respectively. Initially $s = s_0$, $e = e_0$, $c = 0$ and $p = 0$. Write down the governing differential equation system for the concentrations.

Either by using the differential equations or directly from the reaction system above, find two invariant quantities. Use these to simplify the system to

$$\begin{aligned} \dot{s} &= -2k_1 s^2(e_0 - c) + 2k_2 c\,, \\ \dot{c} &= k_1 s^2(e_0 - c) - (k_2 + k_3)c\,. \end{aligned}$$

By setting $u = s/s_0$ and $v = c/e_0$ and rescaling time, show that the system can be written as

$$\begin{aligned} u' &= -2u^2(1 - v) + 2(\mu - \lambda)v\,, \\ \epsilon v' &= u^2(1 - v) - \mu v\,, \end{aligned}$$

where $\epsilon = e_0/s_0$ and μ and λ should be given. Give the initial conditions for u and v.

[*Hint: Note that 2X is equivalent to X+X in reaction systems.*]

Paper 3, Section I

6B Mathematical Biology

A stochastic birth-death process has a master equation given by

$$\frac{dp(n,t)}{dt} = \lambda\,[p(n-1,t) - p(n,t)] + \beta\,[(n+1)\,p(n+1,t) - n\,p(n,t)]\ ,$$

where $p(n,t)$ is the probability that there are n individuals in the population at time t for $n = 0, 1, 2, \ldots$ and $p(n,t) = 0$ for $n < 0$.

Give the corresponding Fokker–Planck equation for this system.

Use this Fokker–Planck equation to find expressions for $\frac{d}{dt}\langle x\rangle$ and $\frac{d}{dt}\langle x^2\rangle$.

[*Hint: The general form for a Fokker–Planck equation in $P(x,t)$ is*

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x}(AP) + \frac{1}{2}\frac{\partial^2}{\partial x^2}(BP)\,.$$

You may use this general form, stating how $A(x)$ and $B(x)$ are constructed. Alternatively, you may derive a Fokker–Plank equation directly by working from the master equation.]

Paper 4, Section I

6B Mathematical Biology

Consider an epidemic model with host demographics (natural births and deaths). The system is given by

$$\begin{aligned}\frac{dS}{dt} &= -\beta IS - \mu S + \mu N\,,\\ \frac{dI}{dt} &= +\beta IS - \nu I - \mu I\,,\end{aligned}$$

where $S(t)$ are the susceptibles, $I(t)$ are the infecteds, N is the total population size and the parameters β, μ and ν are positive. The basic reproduction ratio is defined as $R_0 = \beta N/(\mu + \nu)$.

Show that the system has an endemic equilibrium (where the disease is present) for $R_0 > 1$. Show that the endemic equilibrium is stable.

Interpret the meaning of the case $\nu \gg \mu$ and show that in this case the approximate period of (decaying) oscillation around the endemic equilibrium is given by

$$T = \frac{2\pi}{\sqrt{\mu\nu(R_0 - 1)}}\,.$$

Suppose now a vaccine is introduced which is given to some proportion of the population at birth, but not enough to eradicate the disease. What will be the effect on the period of (decaying) oscillations?

Paper 3, Section II

12B Mathematical Biology

In a discrete-time model, adults and larvae of a population at time n are represented by a_n and b_n respectively. The model is represented by the equations

$$\begin{aligned} a_{n+1} &= (1-k)a_n + \frac{b_n}{1+a_n}, \\ b_{n+1} &= \mu\, a_n . \end{aligned}$$

You may assume that $k \in (0,1)$ and $\mu > 0$. Give an explanation of what each of the terms represents, and hence give a description of the population model.

By combining the equations to describe the dynamics purely in terms of the adults, find all equilibria of the system. Show that the equilibrium with the population absent $(a = 0)$ is unstable exactly when there exists an equilibrium with the population present $(a > 0)$.

Give the condition on μ and k for the equilibrium with $a > 0$ to be stable, and sketch the corresponding region in the (k, μ) plane.

What happens to the population close to the boundaries of this region?

If this model was modified to include stochastic effects, briefly describe qualitatively the likely dynamics near the boundaries of the region found above.

Paper 4, Section II

13B Mathematical Biology

An activator-inhibitor system is described by the equations

$$\begin{aligned}\frac{\partial u}{\partial t} &= u(c+u-v)+\frac{\partial^2 u}{\partial x^2}\,,\\ \frac{\partial v}{\partial t} &= v(au-bv)+d\,\frac{\partial^2 v}{\partial x^2}\,,\end{aligned}$$

where $a, b, c, d > 0$.

Find and sketch the range of a, b for which the spatially homogeneous system has a stable stationary solution with $u > 0$ and $v > 0$.

Considering spatial perturbations of the form $\cos(kx)$ about the solution found above, find conditions for the system to be unstable. Sketch this region in the (a, b)-plane for fixed d (for a value of d such that the region is non-empty).

Show that k_c, the critical wavenumber at the onset of the instability, is given by

$$k_c = \sqrt{\frac{2ac}{d-a}}\,.$$

Paper 4, Section I

6B Mathematical Biology

A stochastic birth–death process is given by the master equation

$$\frac{dp_n}{dt} = \lambda(p_{n-1} - p_n) + \mu\,[\,(n-1)p_{n-1} - np_n\,] + \beta\,[\,(n+1)p_{n+1} - np_n\,]\ ,$$

where $p_n(t)$ is the probability that there are n individuals in the population at time t for $n = 0, 1, 2, \ldots$ and $p_n = 0$ for $n < 0$. Give a brief interpretation of λ, μ and β.

Derive an equation for $\frac{\partial \phi}{\partial t}$, where ϕ is the generating function

$$\phi(s,t) = \sum_{n=0}^{\infty} s^n p_n(t)\,.$$

Now assume that $\beta > \mu$. Show that at steady state

$$\phi = \left(\frac{\beta-\mu}{\beta-\mu s}\right)^{\lambda/\mu}$$

and find the corresponding mean and variance.

Paper 3, Section I

6B Mathematical Biology

A delay model for a population of size N_t at discrete time t is given by

$$N_{t+1} = \max\left\{\,(r - N_{t-1}^2)N_t\,,\,0\,\right\}\ .$$

Show that for $r > 1$ there is a non-trivial equilibrium, and analyse its stability. Show that, as r is increased from 1, the equilibrium loses stability at $r = 3/2$ and find the approximate periodicity close to equilibrium at this point.

Paper 2, Section I

6B Mathematical Biology

(a) The populations of two competing species satisfy

$$\begin{aligned} \frac{dN_1}{dt} &= N_1[\,b_1 - \lambda(N_1 + N_2)\,]\,, \\ \frac{dN_2}{dt} &= N_2[\,b_2 - \lambda(N_1 + N_2)\,]\,, \end{aligned}$$

where $b_1 > b_2 > 0$ and $\lambda > 0$. Sketch the phase diagram (limiting attention to $N_1, N_2 \geqslant 0$).

The relative abundance of species 1 is defined by $U = N_1/(N_1 + N_2)$. Show that

$$\frac{dU}{dt} = AU(1-U)\,,$$

where A is a constant that should be determined.

(b) Consider the spatial system

$$\frac{\partial u}{\partial t} = u(1-u) \,+\, D\frac{\partial^2 u}{\partial x^2}\,,$$

and consider a travelling-wave solution of the form $u(x,t) = f(x - ct)$ representing one species ($u = 1$) invading territory previously occupied by another species ($u = 0$). By linearising near the front of the invasion, show that the wave speed is given by $c = 2\sqrt{D}$.

[You may assume that the solution to the full nonlinear system will settle to the slowest possible linear wave speed.]

Paper 1, Section I

6B Mathematical Biology

Consider an epidemic model where susceptibles are vaccinated at per capita rate v, but immunity (from infection or vaccination) is lost at per capita rate b. The system is given by

$$\begin{aligned} \frac{dS}{dt} &= -rIS + b(N - I - S) - vS \,, \\ \frac{dI}{dt} &= \ \ rIS - aI \,, \end{aligned}$$

where $S(t)$ are the susceptibles, $I(t)$ are the infecteds, N is the total population size and all parameters are positive. The basic reproduction ratio $R_0 = rN/a$ satisfies $R_0 > 1$.

Find the critical vaccination rate v_c, in terms of b and R_0, such that the system has an equilibrium with the disease present if $v < v_c$. Show that this equilibrium is stable when it exists.

Find the long-term outcome for S and I if $v > v_c$.

Paper 3, Section II

12B Mathematical Biology

The Fitzhugh–Nagumo model is given by

$$\begin{aligned} \dot{u} &= c\left(v + u - \tfrac{1}{3}u^3 + z(t)\right) \\ \dot{v} &= -\frac{1}{c}\left(u - a + b\,v\right), \end{aligned}$$

where $(1 - \frac{2}{3}b) < a < 1$, $0 < b \leqslant 1$ and $c \gg 1$.

For $z(t) = 0$, by considering the nullclines in the (u, v)-plane, show that there is a unique equilibrium. Sketch the phase diagram.

At $t = 0$ the system is at the equilibrium, and $z(t)$ is then 'switched on' to be $z(t) = -V_0$ for $t > 0$, where V_0 is a constant. Describe carefully how suitable choices of $V_0 > 0$ can represent a system analogous to (i) a neuron firing once, and (ii) a neuron firing repeatedly. Illustrate your answer with phase diagrams and also plots of v against t for each case. Find the threshold for V_0 that separates these cases. Comment briefly from a biological perspective on the behaviour of the system when $a = 1 - \frac{2}{3}b + \epsilon b$ and $0 < \epsilon \ll 1$.

Paper 4, Section II

13B Mathematical Biology

The population densities of two types of cell are given by $U(x,t)$ and $V(x,t)$. The system is described by the equations

$$\begin{aligned}\frac{\partial U}{\partial t} &= \alpha\, U(1-U) + \chi\,\frac{\partial}{\partial x}\left(U\,\frac{\partial V}{\partial x}\right) + D\frac{\partial^2 U}{\partial x^2}\,,\\ \frac{\partial V}{\partial t} &= V(1-V) - \beta\, UV + \frac{\partial^2 V}{\partial x^2}\,,\end{aligned}$$

where α, β, χ and D are positive constants.

(a) Identify the terms which involve interaction between the cell types, and briefly describe what each of these terms might represent.

(b) Consider the system without spatial dynamics. Find the condition on β for there to be a non-trivial spatially homogeneous solution that is stable to spatially invariant disturbances.

(c) Consider now the full spatial system, and consider small spatial perturbations proportional to $\cos(kx)$ of the solution found in part (b). Show that for sufficiently large χ (the precise threshold should be found) the spatially homogeneous solution is stable to perturbations with either small or large wavenumber, but is unstable to perturbations at some intermediate wavenumber.

Paper 4, Section I

5E Mathematical Biology

(i) A variant of the classic logistic population model is given by the Hutchinson–Wright equation

$$\frac{dx(t)}{dt} = \alpha\, x(t)\,[\,1 - x(t-T)\,]$$

where $\alpha, T > 0$. Determine the condition on α (in terms of T) for the constant solution $x(t) = 1$ to be stable.

(ii) Another variant of the logistic model is given by the equation

$$\frac{dx(t)}{dt} = \alpha\left[\,x(t-T) - x(t)^2\,\right],$$

where $\alpha, T > 0$. Give a brief interpretation of what this model represents.

Determine the condition on α (in terms of T) for the constant solution $x(t) = 1$ to be stable in this model.

Paper 3, Section I

5E Mathematical Biology

The number of a certain type of annual plant in year n is given by x_n. Each plant produces k seeds that year and then dies before the next year. The proportion of seeds that germinate to produce a new plant the next year is given by $e^{-\gamma x_n}$ where $\gamma > 0$. Explain briefly why the system can be described by

$$x_{n+1} = k\, x_n e^{-\gamma x_n}\,.$$

Give conditions on k for a stable positive equilibrium of the plant population size to be possible.

Winters become milder and now a proportion s of all plants survive each year ($s \in (0,1)$). Assume that plants produce seeds as before while they are alive. Show that a wider range of k now gives a stable positive equilibrium population.

Paper 2, Section I

5E Mathematical Biology

An activator-inhibitor system is described by the equations

$$\begin{aligned}\frac{\partial u}{\partial t} &= 2u + u^2 - uv + \frac{\partial^2 u}{\partial x^2}, \\ \frac{\partial v}{\partial t} &= a\left(u^2 - v\right) + d\,\frac{\partial^2 v}{\partial x^2},\end{aligned}$$

where $a, d > 0$.

Find the range of a for which the spatially homogeneous system has a stable equilibrium solution with $u > 0$ and $v > 0$.

For the case when the homogeneous system is stable, consider spatial perturbations proportional to $\cos(kx)$ to the equilibrium solution found above. Show that the system has a Turing instability when

$$d > \left(\tfrac{7}{2} + 2\sqrt{3}\right) a\,.$$

Paper 1, Section I

5E Mathematical Biology

The population density $n(a,t)$ of individuals of age a at time t satisfies

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu(a)\, n(a,t), \qquad n(0,t) = \int_0^\infty b(a)\, n(a,t)\, da$$

where $\mu(a)$ is the age-dependent death rate and $b(a)$ is the birth rate per individual of age a. Show that this may be solved with a similarity solution of the form $n(a,t) = e^{\gamma t} r(a)$ if the growth rate γ satisfies $\phi(\gamma) = 1$ where

$$\phi(\gamma) = \int_0^\infty b(a)\, e^{-\gamma a - \int_0^a \mu(s)\, ds}\, da.$$

Suppose now that the birth rate is given by $b(a) = Ba^p e^{-\lambda a}$ with $B, \lambda > 0$ and p is a positive integer, and the death rate is constant in age (i.e. $\mu(a) = \mu$). Find the average number of offspring per individual.

Find the similarity solution, and find the threshold B^* for the birth parameter B so that $B > B^*$ corresponds to a growing population.

Paper 4, Section II

11E Mathematical Biology

In a stochastic model of multiple populations, $P = P(\mathbf{x}, t)$ is the probability that the population sizes are given by the vector $\mathbf{x}$ at time t. The jump rate $W(\mathbf{x}, \mathbf{r})$ is the probability per unit time that the population sizes jump from $\mathbf{x}$ to $\mathbf{x} + \mathbf{r}$. Under suitable assumptions, the system may be approximated by the multivariate Fokker–Planck equation (with summation convention)

$$\frac{\partial}{\partial t} P = -\frac{\partial}{\partial x_i} A_i P + \frac{1}{2} \frac{\partial^2}{\partial x_i \partial x_j} B_{ij} P \,,$$

where $A_i(\mathbf{x}) = \sum_{\mathbf{r}} r_i W(\mathbf{x}, \mathbf{r})$ and matrix elements $B_{ij}(\mathbf{x}) = \sum_{\mathbf{r}} r_i r_j W(\mathbf{x}, \mathbf{r})$.

(a) Use the multivariate Fokker–Planck equation to show that

$$\begin{aligned} \frac{d}{dt} \langle x_k \rangle &= \langle A_k \rangle \\ \frac{d}{dt} \langle x_k x_l \rangle &= \langle x_l A_k + x_k A_l + B_{kl} \rangle . \end{aligned}$$

[You may assume that $P(\mathbf{x}, t) \to 0$ as $|\mathbf{x}| \to \infty$.]

(b) For small fluctuations, you may assume that the vector $\mathbf{A}$ may be approximated by a linear function in $\mathbf{x}$ and the matrix $\mathbf{B}$ may be treated as constant, i.e. $A_k(\mathbf{x}) \approx a_{kl}(x_l - \langle x_l \rangle)$ and $B_{kl}(\mathbf{x}) \approx B_{kl}(\langle \mathbf{x} \rangle) = b_{kl}$ (where a_{kl} and b_{kl} are constants). Show that at steady state the covariances $C_{ij} = \operatorname{cov}(x_i, x_j)$ satisfy

$$a_{ik} C_{jk} + a_{jk} C_{ik} + b_{ij} = 0 \,.$$

(c) A lab-controlled insect population consists of x_1 larvae and x_2 adults. Larvae are added to the system at rate λ. Larvae each mature at rate γ per capita. Adults die at rate β per capita. Give the vector $\mathbf{A}$ and matrix $\mathbf{B}$ for this model. Show that at steady state

$$\langle x_1 \rangle = \frac{\lambda}{\gamma}, \quad \langle x_2 \rangle = \frac{\lambda}{\beta} \,.$$

(d) Find the variance of each population size near steady state, and show that the covariance between the populations is zero.

Paper 3, Section II
11E Mathematical Biology

A fungal disease is introduced into an isolated population of frogs. Without disease, the normalised population size x would obey the logistic equation $\dot{x} = x(1-x)$, where the dot denotes differentiation with respect to time. The disease causes death at rate d and there is no recovery. The disease transmission rate is β and, in addition, offspring of infected frogs are infected from birth.

(a) Briefly explain why the population sizes x and y of uninfected and infected frogs respectively now satisfy

$$\begin{aligned} \dot{x} &= x\,[\,1 - x - (1+\beta)y\,] \\ \dot{y} &= y\,[\,(1-d) - (1-\beta)x - y\,]\,. \end{aligned}$$

(b) The population starts at the disease-free population size ($x = 1$) and a small number of infected frogs are introduced. Show that the disease will successfully invade if and only if $\beta > d$.

(c) By finding all the equilibria in $x \geqslant 0$, $y \geqslant 0$ and considering their stability, find the long-term outcome for the frog population. State the relationships between d and β that distinguish different final populations.

(d) Plot the long-term steady *total* population size as a function of d for fixed β, and note that an intermediate mortality rate is actually the most harmful. Explain why this is the case.

Paper 4, Section I
6B Mathematical Biology

The concentration $c(x,t)$ of a chemical in one dimension obeys the equations

$$\frac{\partial c}{\partial t} = \frac{\partial}{\partial x}\left(c^2 \frac{\partial c}{\partial x}\right), \qquad \int_{-\infty}^{\infty} c(x,t)\, dx = 1\,.$$

State the physical interpretation of each equation.

Seek a similarity solution of the form $c = t^{\alpha} f(\xi)$, where $\xi = t^{\beta} x$. Find equations involving α and β from the differential equation and the integral. Show that these are satisfied by $\alpha = \beta = -1/4$.

Find the solution for $f(\xi)$. Find and sketch the solution for $c(x,t)$.

Paper 3, Section I
6B Mathematical Biology

An epidemic model is given by

$$\begin{aligned} \frac{dS}{dt} &= -rIS\,, \\ \frac{dI}{dt} &= +rIS - aI\,, \end{aligned}$$

where $S(t)$ are the susceptibles, $I(t)$ are the infecteds, and a and r are positive parameters. The basic reproduction ratio is defined as $R_0 = rN/a$, where N is the total population size. Find a condition on R_0 for an epidemic to be possible if, initially, $S \approx N$ and I is small but non-zero.

Now suppose a proportion p of the population was vaccinated (with a completely effective vaccine) so that initially $S \approx (1-p)N$. On a sketch of the (R_0, p) plane, mark the regions where an epidemic is still possible, where the vaccination will prevent an epidemic, and where no vaccination was necessary.

For the case when an epidemic is possible, show that σ, the proportion of the initially susceptible population that has not been infected by the end of an epidemic, satisfies

$$\sigma - \frac{1}{(1-p)R_0}\log\sigma \approx 1.$$

Paper 2, Section I

6B Mathematical Biology

Consider an experiment where two or three individuals are added to a population with probability λ_2 and λ_3 respectively per unit time. The death rate in the population is a constant β per individual per unit time.

Write down the master equation for the probability $p_n(t)$ that there are n individuals in the population at time t. From this, derive an equation for $\frac{\partial \phi}{\partial t}$, where ϕ is the generating function

$$\phi(s,t) = \sum_{n=0}^{\infty} s^n p_n(t).$$

Find the solution for ϕ in steady state, and show that the mean and variance of the population size are given by

$$\langle n \rangle = 3\frac{\lambda_3}{\beta} + 2\frac{\lambda_2}{\beta}, \qquad \mathrm{var}(n) = 6\frac{\lambda_3}{\beta} + 3\frac{\lambda_2}{\beta}.$$

Hence show that, for a free choice of λ_2 and λ_3 subject to a given target mean, the experimenter can minimise the variance by only adding two individuals at a time.

Paper 1, Section I

6B Mathematical Biology

A population model for two species is given by

$$\begin{aligned} \frac{dN}{dt} &= aN - bNP - kN^2\,, \\ \frac{dP}{dt} &= -dP + cNP\,, \end{aligned}$$

where a, b, c, d and k are positive parameters. Show that this may be rescaled to

$$\begin{aligned} \frac{du}{d\tau} &= u(1 - v - \beta u)\,, \\ \frac{dv}{d\tau} &= -\alpha v(1 - u)\,, \end{aligned}$$

and give α and β in terms of the original parameters.

For $\beta < 1$ find all fixed points in $u \geqslant 0$, $v \geqslant 0$, and analyse their stability. Assuming that both populations are present initially, what does this suggest will be the long-term outcome?

Paper 3, Section II

13B Mathematical Biology

A discrete-time model for breathing is given by

$$V_{n+1} = \alpha C_{n-k}\,, \qquad (1)$$
$$C_{n+1} - C_n = \gamma - \beta V_{n+1}\,, \qquad (2)$$

where V_n is the volume of each breath in time step n and C_n is the concentration of carbon dioxide in the blood at the end of time step n. The parameters α, β and γ are all positive. Briefly explain the biological meaning of each of the above equations.

Find the steady state. For $k = 0$ and $k = 1$ determine the stability of the steady state.

For general (integer) $k > 1$, by seeking parameter values when the modulus of a perturbation to the steady state is constant, find the range of parameters where the solution is stable. What is the periodicity of the constant-modulus solution at the edge of this range? Comment on how the size of the range depends on k.

This can be developed into a more realistic model by changing the term $-\beta V_{n+1}$ to $-\beta C_n V_{n+1}$ in (2). Briefly explain the biological meaning of this change. Show that for both $k = 0$ and $k = 1$ the new steady state is stable if $0 < a < 1$, where $a = \sqrt{\alpha\beta\gamma}$.

Paper 2, Section II

13B Mathematical Biology

An activator–inhibitor system is described by the equations

$$\frac{\partial u}{\partial t} = \frac{au}{v} - u^2 + d_1 \frac{\partial^2 u}{\partial x^2}\,,$$
$$\frac{\partial v}{\partial t} = v^2 - \frac{v}{u^2} + d_2 \frac{\partial^2 v}{\partial x^2}\,,$$

where $a, d_1, d_2 > 0$.

Find the range of a for which the spatially homogeneous system has a stable equilibrium solution with $u > 0$ and $v > 0$. Determine when the equilibrium is a stable focus, and sketch the phase diagram for this case (restricting attention to $u > 0$ and $v > 0$).

For the case when the homogeneous system is stable, consider spatial perturbations proportional to $\cos(kx)$ of the solution found above. Briefly explain why the system will be stable to spatial perturbations with very small or very large k. Find conditions for the system to be unstable to a spatial perturbation (for some range of k which need not be given). Sketch the region satisfying these conditions in the $(a, d_1/d_2)$ plane.

Find k_c, the critical wavenumber at the onset of instability, in terms of a and d_1.

Paper 4, Section I

6A Mathematical Biology

A model of two populations competing for resources takes the form

$$\begin{aligned} \frac{dn_1}{dt} &= r_1 n_1 (1 - n_1 - a_{12} n_2)\,, \\ \frac{dn_2}{dt} &= r_2 n_2 (1 - n_2 - a_{21} n_1)\,, \end{aligned}$$

where all parameters are positive. Give a brief biological interpretation of a_{12}, a_{21}, r_1 and r_2. Briefly describe the dynamics of each population in the absence of the other.

Give conditions for there to exist a steady-state solution with both populations present (that is, $n_1 > 0$ and $n_2 > 0$), and give conditions for this solution to be stable.

In the case where there exists a solution with both populations present but the solution is not stable, what is the likely long-term outcome for the biological system? Explain your answer with the aid of a phase diagram in the (n_1, n_2) plane.

Paper 3, Section I

6A Mathematical Biology

An immune system creates a burst of N new white blood cells with probability b per unit time. White blood cells die with probability d each per unit time. Write down the master equation for $P_n(t)$, the probability that there are n white blood cells at time t.

Given that $n = n_0$ initially, find an expression for the mean of n.

Show that the variance of n has the form $Ae^{-2dt} + Be^{-dt} + C$ and find A, B and C.

If the immune system were modified to produce k times as many cells per burst but with probability per unit time divided by a factor k, how would the mean and variance of the number of cells change?

Paper 2, Section I

6A Mathematical Biology

The population density $n(a,t)$ of individuals of age a at time t satisfies

$$\frac{\partial n(a,t)}{\partial t} + \frac{\partial n(a,t)}{\partial a} = -\mu(a)n(a,t),$$

with

$$n(0,t) = \int_0^\infty b(a)n(a,t)da,$$

where $\mu(a)$ is the age-dependent death rate and $b(a)$ is the birth rate per individual of age a.

Seek a similarity solution of the form $n(a,t) = e^{\gamma t}r(a)$ and show that

$$r(a) = r(0)e^{-\gamma a - \int_0^a \mu(s)ds}, \quad r(0) = \int_0^\infty b(s)r(s)ds.$$

Show also that if

$$\phi(\gamma) = \int_0^\infty b(a)e^{-\gamma a - \int_0^a \mu(s)ds}da = 1,$$

then there is such a similarity solution. Give a biological interpretation of $\phi(0)$.

Suppose now that all births happen at age a^*, at which time an individual produces B offspring, and that the death rate is constant with age (i.e. $\mu(a) = \mu$). Find the similarity solution and give the condition for this to represent a growing population.

Paper 1, Section I

6A Mathematical Biology

In a discrete-time model, a proportion μ of mature bacteria divides at each time step. When a mature bacterium divides it is destroyed and two new immature bacteria are produced. A proportion λ of the immature bacteria matures at each time step, and a proportion k of mature bacteria dies at each time step. Show that this model may be represented by the equations

$$\begin{aligned} a_{t+1} &= a_t + 2\mu b_t - \lambda a_t\,, \\ b_{t+1} &= b_t - \mu b_t + \lambda a_t - k b_t\,. \end{aligned}$$

Give an expression for the general solution to these equations and show that the population may grow if $\mu > k$.

At time T, the population is treated with an antibiotic that completely stops bacteria from maturing, but otherwise has no direct effects. Explain what will happen to the population of bacteria afterwards, and give expressions for a_t and b_t for $t > T$ in terms of a_T, b_T, μ and k.

Paper 3, Section II

13A Mathematical Biology

An activator-inhibitor system is described by the equations

$$\begin{aligned} \frac{\partial u}{\partial t} &= \frac{\partial^2 u}{\partial x^2} + u - uv + au^2 \,, \\ \frac{\partial v}{\partial t} &= d\,\frac{\partial^2 v}{\partial x^2} + u^2 - buv \,, \end{aligned}$$

where $a, b, d > 0$.

Find and sketch the range of a, b for which the spatially homogeneous system has a stable stationary solution with $u > 0$ and $v > 0$.

Considering spatial perturbations of the form $\cos(kx)$ about the solution found above, find conditions for the system to be unstable. Sketch this region in the (d, b) plane for fixed $a \in (0, 1)$.

Find k_c, the critical wavenumber at the onset of the instability, in terms of a and b.

Paper 2, Section II

13A Mathematical Biology

The concentration $c(x,t)$ of insects at position x at time t satisfies the nonlinear diffusion equation

$$\frac{\partial c}{\partial t} = \frac{\partial}{\partial x}\left(c^m \frac{\partial c}{\partial x}\right) ,$$

with $m > 0$. Find the value of α which allows a similarity solution of the form $c(x,t) = t^\alpha f(\xi)$, with $\xi = t^\alpha x$.

Show that

$$f(\xi) = \begin{cases} \left[\frac{\alpha m}{2}(\xi^2 - {\xi_0}^2)\right]^{1/m} & \text{for } -\xi_0 < \xi < \xi_0 \,, \\ 0 & \text{otherwise,} \end{cases}$$

where ξ_0 is a constant. From the original partial differential equation, show that the total number of insects c_0 does not change in time. From this result, find a general expression relating ξ_0 and c_0. Find a closed-form solution for ξ_0 in the case $m = 2$.

Paper 4, Section I

6C Mathematical Biology

The master equation describing the evolution of the probability $P(n,t)$ that a population has n members at time t takes the form

$$\frac{\partial P(n,t)}{\partial t} = b(n-1)P(n-1,t) - [b(n)+d(n)]P(n,t) + d(n+1)P(n+1,t)\,, \qquad (1)$$

where the functions $b(n)$ and $d(n)$ are both positive for all n.

From (1) derive the corresponding Fokker–Planck equation in the form

$$\frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x}\{a_1(x)P(x,t)\} + \tfrac{1}{2}\frac{\partial^2}{\partial x^2}\{a_2(x)P(x,t)\}\,, \qquad (2)$$

making clear any assumptions that you make and giving explicit forms for $a_1(x)$ and $a_2(x)$.

Assume that (2) has a steady state solution $P_s(x)$ and that $a_1(x)$ is a decreasing function of x with a single zero at x_0. Under what circumstances may $P_s(x)$ be approximated by a Gaussian centred at x_0 and what is the corresponding estimate of the variance?

Paper 3, Section I

6C Mathematical Biology

Consider a model of insect dispersal in two dimensions given by

$$\frac{\partial C}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(rDC\frac{\partial C}{\partial r}\right),$$

where r is a radial coordinate, t is time, $C(r,t)$ is the density of insects and D is a constant coefficient such that DC is a diffusivity.

Show that under suitable assumptions

$$2\pi\int_0^\infty rC\,dr = N\,,$$

where N is constant, and interpret this condition.

Suppose that after a long time the form of C depends only on r, t, D and N (and is thus independent of any detailed form of the initial condition). Show that there is a solution of the form

$$C(r,t) = \left(\frac{N}{Dt}\right)^{1/2} g\left(\frac{r}{(NDt)^{1/4}}\right),$$

and deduce that the function $g(\xi)$ satisfies

$$\frac{d}{d\xi}\left(\xi g\frac{dg}{d\xi} + \frac{1}{4}\xi^2 g\right) = 0\,.$$

Show that this equation has a continuous solution with $g > 0$ for $\xi < \xi_0$ and $g = 0$ for $\xi \geqslant \xi_0$, and determine ξ_0. Hence determine the area within which $C(r,t) > 0$ as a function of t.

Paper 2, Section I

6C Mathematical Biology

Consider a birth-death process in which the birth rate per individual is λ and the death rate per individual in a population of size n is βn.

Let $P(n,t)$ be the probability that the population has size n at time t. Write down the master equation for the system, giving an expression for $\partial P(n,t)/\partial t$.

Show that

$$\frac{d}{dt}\langle n\rangle = \lambda\langle n\rangle - \beta\langle n^2\rangle\,,$$

where $\langle . \rangle$ denotes the mean.

Deduce that in a steady state $\langle n\rangle \leqslant \lambda/\beta$.

Paper 1, Section I

6C Mathematical Biology

Krill is the main food source for baleen whales. The following model has been proposed for the coupled evolution of populations of krill and whales, with $x(t)$ being the number of krill and $y(t)$ being the number of whales:

$$\frac{dx}{dt} = rx\left(1 - \frac{x}{K}\right) - axy\,,$$
$$\frac{dy}{dt} = sy\left(1 - \frac{y}{bx}\right)\,,$$

where r, s, a, b and K are positive constants.

Give a biological interpretation for the form of the two differential equations.

Show that a steady state is possible with $x > 0$ and $y > 0$ and write down expressions for the steady-state values of x and y.

Determine whether this steady state is stable.

Paper 3, Section II

13C Mathematical Biology

Consider the two-variable reaction-diffusion system

$$\frac{\partial u}{\partial t} = a - u + u^2 v + \nabla^2 u\,,$$
$$\frac{\partial v}{\partial t} = b - u^2 v + d\nabla^2 v\,,$$

where a, b and d are positive constants.

Show that there is one possible spatially homogeneous steady state with $u > 0$ and $v > 0$ and show that it is stable to small-amplitude spatially homogeneous disturbances provided that $\gamma < \beta$, where

$$\gamma = \frac{b-a}{b+a} \qquad \text{and} \qquad \beta = (a+b)^2.$$

Now assuming that the condition $\gamma < \beta$ is satisfied, investigate the stability of the homogeneous steady state to spatially varying perturbations by considering the time-dependence of disturbances whose spatial form is such that $\nabla^2 u = -k^2 u$ and $\nabla^2 v = -k^2 v$, with k constant. Show that such disturbances vary as e^{pt}, where p is one of the roots of

$$p^2 + (\beta - \gamma + dk^2 + k^2)p + dk^4 + (\beta - d\gamma)k^2 + \beta.$$

By comparison with the stability condition for the homogeneous case above, give a simple argument as to why the system must be stable if $d = 1$.

Show that the boundary between stability and instability (as some combination of β, γ and d is varied) must correspond to $p = 0$.

Deduce that $d\gamma > \beta$ is a necessary condition for instability and, furthermore, that instability will occur for some k if

$$d > \frac{\beta}{\gamma}\left\{1 + \frac{2}{\gamma} + 2\sqrt{\frac{1}{\gamma} + \frac{1}{\gamma^2}}\right\}.$$

Deduce that the value of k^2 at which instability occurs as the stability boundary is crossed is given by

$$k^2 = \sqrt{\frac{\beta}{d}}\,.$$

Paper 2, Section II

13C Mathematical Biology

A population of blowflies is modelled by the equation

$$\frac{dx}{dt} = R(x(t-T)) - kx(t)\,, \qquad (1)$$

where k is a constant death rate and R is a function of one variable such that $R(z) > 0$ for $z > 0$, with $R(z) \sim \beta z$ as $z \to 0$ and $R(z) \to 0$ as $z \to \infty$. The constants T, k and β are all positive, with $\beta > k$. Give a brief biological motivation for the term $R(x(t-T))$, in which you explain both the form of the function R and the appearance of a delay time T.

A suitable model for $R(z)$ is $\beta z \exp(-z/d)$, where d is a positive constant. Show that in this case there is a single steady state of the system with non-zero population, i.e. with $x(t) = x_s > 0$, with x_s constant.

Now consider the stability of this steady state. Show that if $x(t) = x_s + y(t)$, with $y(t)$ small, then $y(t)$ satisfies a delay differential equation of the form

$$\frac{dy}{dt} = -ky(t) + By(t-T)\,, \qquad (2)$$

where B is a constant to be determined. Show that $y(t) = e^{st}$ is a solution of (2) if $s = -k + Be^{-sT}$. If $s = \sigma + i\omega$, where σ and ω are both real, write down two equations relating σ and ω.

Deduce that the steady state is stable if $|B| < k$. Show that, for this particular model for R, $|B| > k$ is possible only if $B < 0$.

By considering B decreasing from small negative values, show that an instability will appear when $|B| > \left[k^2 + \frac{g(kT)^2}{T^2}\right]^{1/2}$, where $\pi/2 < g(kT) < \pi$.

Deduce that the steady state x_s of (1) is unstable if

$$\beta > k \exp\left[\left(1 + \frac{\pi^2}{k^2T^2}\right)^{1/2} + 1\right].$$

Paper 1, Section I

6B Mathematical Biology

A proposed model of insect dispersal is given by the equation

$$\frac{\partial n}{\partial t} = D\frac{\partial}{\partial x}\left[\left(\frac{n_0}{n}\right)\frac{\partial n}{\partial x}\right], \tag{1}$$

where $n(x,t)$ is the density of insects and D and n_0 are constants.

Interpret the term on the right-hand side.

Explain why a solution of the form

$$n(x,t) = n_0(Dt)^{-\beta}g(x/(Dt)^{\beta}), \tag{2}$$

where β is a positive constant, can potentially represent the dispersal of a fixed number n_0 of insects initially localised at the origin.

Show that the equation (1) can be satisfied by a solution of the form (2) if $\beta = 1$ and find the corresponding function g.

Paper 2, Section I

6B Mathematical Biology

A population with variable growth and harvesting is modelled by the equation

$$u_{t+1} = \max\left(\frac{ru_t^2}{1+u_t^2} - Eu_t, 0\right),$$

where r and E are positive constants.

Given that $r > 1$, show that a non-zero steady state exists if $0 < E < E_m(r)$, where $E_m(r)$ is to be determined.

Show using a cobweb diagram that, if $E < E_m(r)$, a non-zero steady state may be attained only if the initial population u_0 satisfies $\alpha < u_0 < \beta$, where α should be determined explicitly and β should be specified as a root of an algebraic equation.

With reference to the cobweb diagram, give an additional criterion that implies that $\alpha < u_0 < \beta$ is a sufficient condition, as well as a necessary condition, for convergence to a non-zero steady state.

Paper 3, Section I

6B Mathematical Biology

The dynamics of a directly transmitted microparasite can be modelled by the system

$$\begin{aligned}\frac{dX}{dt} &= bN - \beta XY - bX\,,\\ \frac{dY}{dt} &= \beta XY - (b+r)Y\,,\\ \frac{dZ}{dt} &= rY - bZ\,,\end{aligned}$$

where b, β and r are positive constants and X, Y and Z are respectively the numbers of susceptible, infected and immune (i.e. infected by the parasite, but showing no further symptoms of infection) individuals in a population of size N, independent of t, where $N = X + Y + Z$.

Consider the possible steady states of these equations. Show that there is a threshold population size N_c such that if $N < N_c$ there is no steady state with the parasite maintained in the population. Show that in this case the number of infected and immune individuals decreases to zero for all possible initial conditions.

Show that for $N > N_c$ there is a possible steady state with $X = X_s < N$ and $Y = Y_s > 0$, and find expressions for X_s and Y_s.

By linearising the equations for dX/dt and dY/dt about the steady state $X = X_s$ and $Y = Y_s$, derive a quadratic equation for the possible growth or decay rate in terms of X_s and Y_s and hence show that the steady state is stable.

Paper 4, Section I

6B Mathematical Biology

A neglected flower garden contains M_n marigolds in the summer of year n. On average each marigold produces γ seeds through the summer. Seeds may germinate after one or two winters. After three winters or more they will not germinate. Each winter a fraction $1-\alpha$ of all seeds in the garden are eaten by birds (with no preference to the age of the seed). In spring a fraction μ of seeds that have survived one winter and a fraction ν of seeds that have survived two winters germinate. Finite resources of water mean that the number of marigolds growing to maturity from S germinating seeds is $\mathcal{N}(S)$, where $\mathcal{N}(S)$ is an increasing function such that $\mathcal{N}(0) = 0$, $\mathcal{N}'(0) = 1$, $\mathcal{N}'(S)$ is a decreasing function of S and $\mathcal{N}(S) \to N_{max}$ as $S \to \infty$.

Show that M_n satisfies the equation

$$M_{n+1} = \mathcal{N}(\alpha\mu\gamma M_n + \nu\gamma\alpha^2(1-\mu)M_{n-1})\,.$$

Write down an equation for the number M_* of marigolds in a steady state. Show graphically that there are two solutions, one with $M_* = 0$ and the other with $M_* > 0$ if

$$\alpha\mu\gamma + \nu\gamma\alpha^2(1-\mu) > 1\,.$$

Show that the $M_* = 0$ steady-state solution is unstable to small perturbations in this case.

Paper 2, Section II

13B Mathematical Biology

Consider a population subject to the following birth–death process. When the number of individuals in the population is n, the probability of an increase from n to $n+1$ in unit time is $\beta n+\gamma$ and the probability of a decrease from n to $n-1$ is $\alpha n(n-1)$, where α, β and γ are constants.

Show that the master equation for $P(n,t)$, the probability that at time t the population has n members, is

$$\frac{\partial P}{\partial t}=\alpha n(n+1)P(n+1,t)-\alpha n(n-1)P(n,t)+(\beta n-\beta+\gamma)P(n-1,t)-(\beta n+\gamma)P(n,t)\,.$$

Show that $\langle n\rangle$, the mean number of individuals in the population, satisfies

$$\frac{d\langle n\rangle}{dt}=-\alpha\langle n^2\rangle+(\alpha+\beta)\langle n\rangle+\gamma\,.$$

Deduce that, in a steady state,

$$\langle n\rangle=\frac{\alpha+\beta}{2\alpha}\pm\sqrt{\frac{(\alpha+\beta)^2}{4\alpha^2}+\frac{\gamma}{\alpha}-(\Delta n)^2}\,,$$

where Δn is the standard deviation of n. When is the minus sign admissable?

Show how a Fokker–Planck equation of the form

$$\frac{\partial P}{\partial t}=\frac{\partial}{\partial n}[g(n)P(n,t)]+\frac{1}{2}\frac{\partial^2}{\partial n^2}[h(n)P(n,t)] \qquad (*)$$

may be derived under conditions to be explained, where the functions $g(n)$ and $h(n)$ should be evaluated.

In the case $\alpha\ll\gamma$ and $\beta=0$, find the leading-order approximation to n_* such that $g(n_*)=0$. Defining the new variable $x=n-n_*$, where $g(n_*)=0$, approximate $g(n)$ by $g'(n_*)x$ and $h(n)$ by $h(n_*)$. Solve $(*)$ for $P(x)$ in the steady-state limit and deduce leading-order estimates for $\langle n\rangle$ and $(\Delta n)^2$.

Paper 3, Section II

13B Mathematical Biology

The number density of a population of amoebae is $n(\mathbf{x},t)$. The amoebae exhibit chemotaxis and are attracted to high concentrations of a chemical which has concentration $a(\mathbf{x},t)$. The equations governing n and a are

$$\frac{\partial n}{\partial t} = \alpha n(n_0^2 - n^2) + \nabla^2 n - \boldsymbol{\nabla}\cdot(\chi(n) n \boldsymbol{\nabla} a)\,,$$
$$\frac{\partial a}{\partial t} = \beta n - \gamma a + D\nabla^2 a\,,$$

where the constants n_0, α, β, γ and D are all positive.

(i) Give a biological interpretation of each term in these equations and discuss the sign of $\chi(n)$.

(ii) Show that there is a non-trivial (i.e. $a \neq 0$, $n \neq 0$) steady-state solution for n and a, independent of $\mathbf{x}$, and show further that it is stable to small disturbances that are also independent of $\mathbf{x}$.

(iii) Consider small spatially varying disturbances to the steady state, with spatial structure such that $\nabla^2\psi = -k^2\psi$, where ψ is any disturbance quantity. Show that if such disturbances also satisfy $\partial\psi/\partial t = p\psi$, where p is a constant, then p satisfies a quadratic equation, to be derived. By considering the conditions required for $p = 0$ to be a possible solution of this quadratic equation, or otherwise, deduce that instability is possible if

$$\beta\chi_0 n_0 > 2\alpha n_0^2 D + \gamma + 2(2D\alpha n_0^2\gamma)^{1/2}\,,$$

where $\chi_0 = \chi(n_0)$.

(iv) Explain briefly how your conclusions might change if an additional geometric constraint implied that $k^2 > k_0^2$, where k_0 is a given constant.

Paper 1, Section I

6A Mathematical Biology

A delay model for a population N_t consists of

$$N_{t+1} = \frac{rN_t}{1 + b\,N_{t-1}^2}\ ,$$

where t is discrete time, $r > 1$ and $b > 0$. Investigate the linear stability about the positive steady state N^*. Show that $r = 2$ is a bifurcation value at which the steady state bifurcates to a periodic solution of period 6.

Paper 2, Section I

6A Mathematical Biology

The population of a certain species subjected to a specific kind of predation is modelled by the difference equation

$$u_{t+1} = a\,\frac{u_t^2}{b^2 + u_t^2}\ , \qquad a > 0\ .$$

Determine the equilibria and show that if $a^2 > 4\,b^2$ it is possible for the population to be driven to extinction if it becomes less than a critical size which you should find. Explain your reasoning by means of a cobweb diagram.

Paper 3, Section I

6A Mathematical Biology

A population of aerobic bacteria swims in a laterally-infinite layer of fluid occupying $-\infty < x < \infty$, $-\infty < y < \infty$, and $-d/2 < z < d/2$, with the top and bottom surfaces in contact with air. Assuming that there is no fluid motion and that all physical quantities depend only on z, the oxygen concentration c and bacterial concentration n obey the coupled equations

$$\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial z^2} - kn \,,$$
$$\frac{\partial n}{\partial t} = D_n \frac{\partial^2 n}{\partial z^2} - \frac{\partial}{\partial z}\left(\mu n \frac{\partial c}{\partial z}\right) \,.$$

Consider first the case in which there is no chemotaxis, so n has the spatially-uniform value $\bar{n}$. Find the steady-state oxygen concentration consistent with the boundary conditions $c(\pm d/2) = c_0$. Calculate the Fick's law flux of oxygen into the layer and justify your answer on physical grounds.

Now allowing chemotaxis and cellular diffusion, show that the equilibrium oxygen concentration satisfies

$$\frac{d^2 c}{dz^2} - \frac{kn_0}{D_c} \exp\left(\mu c / D_n\right) = 0 \,,$$

where n_0 is a suitable normalisation constant that need not be found.

Paper 4, Section I

6A Mathematical Biology

A concentration $u(x,t)$ obeys the differential equation

$$\frac{\partial u}{\partial t} = D u_{xx} + f(u) \,,$$

in the domain $0 \leqslant x \leqslant L$, with boundary conditions $u(0,t) = u(L,t) = 0$ and initial condition $u(x,0) = u_0(x)$, and where D is a positive constant. Assume $f(0) = 0$ and $f'(0) > 0$. Linearising the dynamics around $u = 0$, and representing $u(x,t)$ as a suitable Fourier expansion, show that the condition for the linear stability of $u = 0$ can be expressed as the following condition on the domain length

$$L < \pi \left[\frac{D}{f'(0)}\right]^{1/2} \,.$$

Paper 2, Section II

13A Mathematical Biology

The radially symmetric spread of an insect population density $n(r,t)$ in the plane is described by the equation

$$\frac{\partial n}{\partial t} = \frac{D_0}{r}\frac{\partial}{\partial r}\left[r\left(\frac{n}{n_0}\right)^2\frac{\partial n}{\partial r}\right] . \qquad (*)$$

Suppose Q insects are released at $r=0$ at $t=0$. We wish to find a similarity solution to $(*)$ in the form

$$n(r,t) = \frac{n_0}{\lambda^2(t)}\, F\left(\frac{r}{r_0\lambda(t)}\right) .$$

Show first that the PDE $(*)$ reduces to an ODE for F if $\lambda(t)$ obeys the equation

$$\lambda^5\,\frac{d\lambda}{dt} = C\,\frac{D_0}{r_0^2} ,$$

where C is an arbitrary constant (that may be set to unity), and then obtain $\lambda(t)$ and F such that $F(0)=1$ and $F(\xi)=0$ for $\xi \geqslant 1$. Determine r_0 in terms of n_0 and Q. Sketch the function $n(r,t)$ at various times to indicate its qualitative behaviour.

Paper 3, Section II

13A Mathematical Biology

Consider an epidemic model in which $S(x,t)$ is the local population density of susceptibles and $I(x,t)$ is the density of infectives

$$\frac{\partial S}{\partial t} = -\,rIS\ ,$$
$$\frac{\partial I}{\partial t} = D\,\frac{\partial^2 I}{\partial x^2} + rIS - aI\ ,$$

where r, a, and D are positive. If S_0 is a characteristic population value, show that the rescalings $I/S_0 \to I$, $S/S_0 \to S$, $(rS_0/D)^{1/2}\,x \to x$, $rS_0 t \to t$ reduce this system to

$$\frac{\partial S}{\partial t} = -\,IS\ ,$$
$$\frac{\partial I}{\partial t} = \frac{\partial^2 I}{\partial x^2} + IS - \lambda I\ ,$$

where λ should be found.

Travelling wavefront solutions are of the form $S(x,t) = S(z)$, $I(x,t) = I(z)$, where $z = x - ct$ and c is the wave speed, and we seek solutions with boundary conditions $S(\infty) = 1$, $S'(\infty) = 0$, $I(\infty) = I(-\infty) = 0$. Under the travelling-wave assumption reduce the rescaled PDEs to ODEs, and show by linearisation around the leading edge of the advancing front that the requirement that I be non-negative leads to the condition $\lambda < 1$ and hence the wave speed relation

$$c \geqslant 2(1-\lambda)^{1/2}\ , \qquad \lambda < 1\ .$$

Using the two ODEs you have obtained, show that the surviving susceptible population fraction $\sigma = S(-\infty)$ after the passage of the front satisfies

$$\sigma - \lambda \ln \sigma = 1\ ,$$

and sketch σ as a function of λ.

Paper 1, Section I

6A Mathematical Biology

A discrete model for a population N_t consists of

$$N_{t+1} = \frac{rN_t}{(1+bN_t)^2},$$

where t is discrete time and $r, b > 0$. What do r and b represent in this model? Show that for $r > 1$ there is a stable fixed point.

Suppose the initial condition is $N_1 = 1/b$, and that $r > 4$. Show, with the help of a cobweb, that the population N_t is bounded by

$$\frac{4r^2}{(4+r)^2\, b} \leqslant N_t \leqslant \frac{r}{4b},$$

and attains those bounds.

Paper 2, Section I

6A Mathematical Biology

Consider the reaction system

$$A \xrightarrow{k_1} X, \qquad B + X \xrightarrow{k_2} Y, \qquad 2X + Y \xrightarrow{k_3} 3X, \qquad X \xrightarrow{k_4} E,$$

where the ks are the rate constants, and the reactant concentrations of A and B are kept constant. Write down the governing differential equation system for the concentrations of X and Y and nondimensionalise the equations by setting $u = \alpha X$ and $v = \alpha Y$, $\tau = k_4 t$ so that they become

$$\frac{du}{d\tau} = 1 - (b+1)u + au^2 v, \qquad \frac{dv}{d\tau} = bu - au^2 v,$$

by suitable choice of α. Thus find a and b. Determine the positive steady state and show that there is a bifurcation value $b = b_c = 1 + a$ at which the steady state becomes unstable to a Hopf bifurcation. Find the period of the oscillations in the neighbourhood of b_c.

Paper 3, Section I

6A Mathematical Biology

Consider an organism moving on a one-dimensional lattice of spacing a, taking steps either to the right or the left at regular time intervals τ. In this random walk there is a slight bias to the right, that is the probabilities of moving to the right and left, α and β, are such that $\alpha - \beta = \epsilon$, where $0 < \epsilon \ll 1$. Write down the appropriate master equation for this process. Show by taking the continuum limit in space and time that $p(x,t)$, the probability that an organism initially at $x = 0$ is at x after time t, obeys

$$\frac{\partial p}{\partial t} + V\frac{\partial p}{\partial x} = D\frac{\partial^2 p}{\partial x^2}.$$

Express the constants V and D in terms of a, τ, α and β.

Paper 4, Section I

6A Mathematical Biology

The diffusion equation for a chemical concentration $C(r,t)$ in three dimensions which depends only on the radial coordinate r is

$$C_t = D\frac{1}{r^2}\left(r^2 C_r\right)_r. \qquad (*)$$

The general similarity solution of this equation takes the form

$$C(r,t) = t^\alpha F(\xi), \qquad \xi = \frac{r}{t^\beta},$$

where α and β are to be determined. By direct substitution into $(*)$ and the requirement of a valid similarity solution, find one relation involving the exponents. Use the conservation of the total number of molecules to determine a second relation. Comment on the relationship between these exponents and the ones appropriate to the similarity solution of the one-dimensional diffusion equation. Show that F obeys

$$D\left(F'' + \frac{2}{\xi}F'\right) + \frac{1}{2}\xi F' + \frac{3}{2}F = 0,$$

and that the relevant solution describing the spreading of a delta-function initial condition is $F(\xi) = A\exp(-\xi^2/4D)$, where A is a suitable normalisation that need not be found.

Paper 2, Section II

13A Mathematical Biology

Travelling bands of microorganisms, chemotactically directed, move into a food source, consuming it as they go. A model for this is given by

$$b_t = \frac{\partial}{\partial x}\left[Db_x - \frac{b\chi}{a}a_x\right], \qquad a_t = -kb,$$

where $b(x,t)$ and $a(x,t)$ are the bacteria and nutrient respectively and D, χ, and k are positive constants. Look for travelling wave solutions, as functions of $z = x - ct$ where c is the wave speed, with the boundary conditions $b \to 0$ as $|z| \to \infty$, $a \to 0$ as $z \to -\infty$, $a \to 1$ as $z \to \infty$. Hence show that $b(z)$ and $a(z)$ satisfy

$$b' = \frac{b}{cD}\left[\frac{kb\chi}{a} - c^2\right], \qquad a' = \frac{kb}{c},$$

where the prime denotes differentiation with respect to z. Integrating db/da, find an algebraic relationship between $b(z)$ and $a(z)$.

In the special case where $\chi = 2D$ show that

$$a(z) = \left[1 + Ke^{-cz/D}\right]^{-1}, \qquad b(z) = \frac{c^2}{kD}e^{-cz/D}\left[1 + Ke^{-cz/D}\right]^{-2},$$

where K is an arbitrary positive constant which is equivalent to a linear translation; it may be set to 1. Sketch the wave solutions and explain the biological interpretation.

Paper 3, Section II

13A Mathematical Biology

An activator–inhibitor reaction diffusion system in dimensionless form is given by

$$u_t = u_{xx} + \frac{u^2}{v} - bu, \qquad v_t = dv_{xx} + u^2 - v,$$

where b and d are positive constants. Which is the activitor and which the inhibitor? Determine the positive steady states and show, by an examination of the eigenvalues in a linear stability analysis of the spatially uniform situation, that the reaction kinetics is stable if $b < 1$.

Determine the conditions for the steady state to be driven unstable by diffusion. Show that the parameter domain for diffusion–driven instability is given by $0 < b < 1$, $bd > 3 + 2\sqrt{2}$, and sketch the (b, d) parameter space in which diffusion–driven instability occurs. Further show that at the bifurcation to such an instability the critical wave number k_c is given by $k_c^2 = (1 + \sqrt{2})/d$.

1/I/6B **Mathematical Biology**

A gene product with concentration g is produced by a chemical S of concentration s, is autocatalysed and degrades linearly according to the kinetic equation

$$\frac{dg}{dt} = f(g,s) = s + k\,\frac{g^2}{1+g^2} - g,$$

where $k > 0$ is a constant.

First consider the case $s = 0$. Show that if $k > 2$ there are two positive steady states, and determine their stability. Sketch the reaction rate $f(g,0)$.

Now consider $s > 0$. Show that there is a single steady state if s exceeds a critical value. If the system starts in the steady state $g = 0$ with $s = 0$ and then s is increased sufficiently before decreasing back to zero, show that a biochemical switch can be achieved to a state $g = g_2$, whose value you should determine.

2/I/6B **Mathematical Biology**

The population dynamics of a species is governed by the discrete model

$$N_{t+1} = f(N_t) = N_t \exp\left[r\left(1 - \frac{N_t}{K}\right)\right],$$

where r and K are positive constants.

Determine the steady states and their eigenvalues. Show that a period-doubling bifurcation occurs at $r = 2$.

Show graphically that the maximum possible population after $t = 0$ is

$$N_{max} = f(K/r).$$

2/II/13B **Mathematical Biology**

Consider the nonlinear equation describing the invasion of a population $u(x,t)$

$$u_t = m\,u_{xx} + f(u), \tag{1}$$

with $m > 0$, $f(u) = -u\,(u-r)(u-1)$ and $0 < r < 1$ a constant.

(a) Considering time-dependent spatially homogeneous solutions, show that there are two stable and one unstable uniform steady states.

(b) In the case $r = \frac{1}{2}$, find the stationary 'front' which has

$$u \to 1 \text{ as } x \to -\infty \quad \text{and} \quad u \to 0 \text{ as } x \to \infty. \tag{2}$$

[*Hint:* $f(u) = F'(u)$ *where* $F(u) = -\frac{1}{4}u^2(1-u)^2 + \frac{1}{6}(r - \frac{1}{2})u^2(2u-3)$.]

(c) Now consider travelling-wave solutions to (1) of the form $u(x,t) = U(z)$ where $z = x - vt$. Show that U satisfies an equation of the form

$$m\,\ddot{U} + v\,\dot{U} = -V'(U),$$

where $(\dot{\ \ }) \equiv \dfrac{d}{dz}(\ \ )$ and $(\ \ )' \equiv \dfrac{d}{dU}(\ \ )$.

Sketch the form of $V(U)$ for $r = \frac{1}{2}$, $r > \frac{1}{2}$ and $r < \frac{1}{2}$. Using conditions (2), show that

$$v\int_{-\infty}^{\infty} \dot{U}^2\,dz = F(1) - F(0).$$

Deduce how the sign of the travelling-wave velocity v depends on r.

3/I/6B **Mathematical Biology**

An allosteric enzyme E reacts with a substrate S to produce a product P according to the mechanism

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_1 \overset{k_2}{\rightharpoonup} E + P$$

$$S + C_1 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} C_2 \overset{k_4}{\rightharpoonup} C_1 + P,$$

where C_1 and C_2 are enzyme-substrate complexes. With lowercase letters denoting concentrations, write down a system of differential equations based on the Law of Mass Action which model this reaction mechanism.

The initial conditions are $s = s_0$, $e = e_0$, $c_1 = c_2 = p = 0$. Using $u = s/s_0$, $v_i = c_i/e_0$, $\tau = k_1 e_0 t$ and $\epsilon = e_0/s_0$, show that the nondimensional reaction mechanism reduces to

$$\frac{du}{d\tau} = f(u, v_1, v_2) \quad \text{and} \quad \epsilon \frac{dv_i}{d\tau} = g_i(u, v_1, v_2) \quad \text{for} \quad i = 1, 2,$$

finding expressions for f, g_1 and g_2.

3/II/13B **Mathematical Biology**

Consider the activator-inhibitor system in the fast-inhibitor limit

$$u_t = D\, u_{xx} - u\,(u - r)(u - 1) - \rho\,(v - u),$$

$$0 = v_{xx} - (v - u),$$

where D is small, $0 < r < 1$ and $0 < \rho < 1$.

Examine the linear stability of the state $u = v = 0$ using perturbations of the form $\exp(ikx + \sigma t)$. Sketch the growth-rate σ as a function of the wavenumber k. Find the growth-rate of the most unstable wave, and so determine the boundary in the r-ρ parameter plane which separates stable and unstable modes.

Show that the system is unchanged under the transformation $u \to 1 - u$, $v \to 1 - v$ and $r \to 1 - r$. Hence write down the equation for the boundary between stable and unstable modes of the state $u = v = 1$.

4/I/6B **Mathematical Biology**

A semi-infinite elastic filament lies along the positive x-axis in a viscous fluid. When it is perturbed slightly to the shape $y = h(x,t)$, it evolves according to

$$\zeta\, h_t = -A\, h_{xxxx}\,,$$

where ζ characterises the viscous drag and A the bending stiffness. Motion is forced by boundary conditions

$$h = h_0 \cos(\omega t) \quad \text{and} \quad h_{xx} = 0 \quad \text{at} \quad x = 0, \quad \text{while} \quad h \to 0 \quad \text{as} \quad x \to \infty.$$

Use dimensional analysis to find the characteristic length $\ell(\omega)$ of the disturbance. Show that the steady oscillating solution takes the form

$$h(x,t) = h_0 \operatorname{Re}\left[e^{\,i\omega t} F(\eta)\right] \quad \text{with} \quad \eta = x/\ell,$$

finding the ordinary differential equation for F.

Find two solutions for F which decay as $x \to \infty$. Without solving explicitly for the amplitudes, show that $h(x,t)$ is the superposition of two travelling waves which decay with increasing x, one with crests moving to the left and one to the right. Which dominates?

1/I/6B **Mathematical Biology**

A chemostat is a well-mixed tank of given volume V_0 that contains water in which lives a population $N(t)$ of bacteria that consume nutrient whose concentration is $C(t)$ per unit volume. An inflow pipe supplies a solution of nutrient at concentration C_0 and at a constant flow rate of Q units of volume per unit time. The mixture flows out at the same rate through an outflow pipe. The bacteria consume the nutrient at a rate $NK(C)$, where

$$K(C) = \frac{K_{\max} C}{K_0 + C},$$

and the bacterial population grows at a rate $\gamma N K(C)$, where $0 < \gamma < 1$.

Write down the differential equations for $N(t), C(t)$ and show that they can be rescaled into the following form:

$$\begin{aligned} \frac{dn}{d\tau} &= \alpha \frac{cn}{1+c} - n, \\ \frac{dc}{d\tau} &= -\frac{cn}{1+c} - c + \beta, \end{aligned}$$

where α, β are positive constants, to be found.

Show that this system of equations has a non-trivial steady state if $\alpha > 1$ and $\beta > \dfrac{1}{\alpha - 1}$, and that it is stable.

2/I/6B **Mathematical Biology**

A field contains X_n seed-producing poppies in August of year n. On average each poppy produces γ seeds, a number that is assumed not to vary from year to year. A fraction σ of seeds survive the winter and a fraction α of those germinate in May of year $n+1$. A fraction β of those that survive the next winter germinate in year $n+2$. Show that X_n satisfies the following difference equation:

$$X_{n+1} = \alpha\sigma\gamma X_n + \beta\sigma^2(1-\alpha)\gamma X_{n-1}.$$

Write down the general solution of this equation, and show that the poppies in the field will eventually die out if

$$\sigma\gamma[(1-\alpha)\beta\sigma + \alpha] < 1.$$

2/II/13B **Mathematical Biology**

Show that the concentration $C(\mathbf{x},t)$ of a diffusible chemical substance in a stationary medium satisfies the partial differential equation

$$\frac{\partial C}{\partial t} = \nabla \cdot (D \nabla C) + F\,,$$

where D is the diffusivity and $F(\mathbf{x},t)$ is the rate of supply of the chemical.

A finite amount of the chemical, $4\pi M$, is supplied at the origin at time $t = 0$, and spreads out in a spherically symmetric manner, so that $C = C(r,t)$ for $r > 0, t > 0$, where r is the radial coordinate. The diffusivity is given by $D = kC$, for constant k . Show, by dimensional analysis or otherwise, that it is appropriate to seek a similarity solution in which

$$C = \frac{M^{\alpha}}{(k\,t)^{\beta}}\, f(\xi)\,, \quad \xi = \frac{r}{(Mkt)^{\gamma}} \quad \text{and} \quad \int_0^{\infty} \xi^2 f(\xi)\, d\xi = 1\,,$$

where α, β, γ are constants to be determined, and derive the ordinary differential equation satisfied by $f(\xi)$.

Solve this ordinary differential equation, subject to appropriate boundary conditions, and deduce that the chemical occupies a finite spherical region of radius

$$r_0(t) = (75Mkt)^{1/5}\,.$$

[*Note: in spherical polar coordinates*

$$\nabla C \equiv \left(\frac{\partial C}{\partial r}\,, 0, 0\right) \quad \textit{and} \quad \nabla \cdot (V(r,t), 0, 0) \equiv \frac{1}{r^2}\frac{\partial}{\partial r}\,(r^2 V)\,.$$]

3/I/6B **Mathematical Biology**

Consider a birth and death process in which births always give rise to two offspring, with rate λ, while the death rate per individual is β.

Write down the master equation (or probability balance equation) for this system.

Show that the population mean is given by

$$\langle n \rangle = \frac{2\lambda}{\beta}(1 - e^{-\beta t}) + n_0 e^{-\beta t}$$

where n_0 is the initial population mean, and that the population variance satisfies

$$\sigma^2 \to 3\lambda/\beta \quad \text{as} \quad t \to \infty\,.$$

3/II/13B **Mathematical Biology**

The number density of a population of cells is $n(\mathbf{x},t)$. The cells produce a chemical whose concentration is $C(\mathbf{x},t)$ and respond to it chemotactically. The equations governing n and C are

$$\frac{\partial n}{\partial t} = \gamma n(n_0 - n) + D_n \nabla^2 n - \chi \nabla \cdot (n \nabla C)$$
$$\frac{\partial C}{\partial t} = \alpha n - \beta C + D_c \nabla^2 C.$$

(i) Give a biological interpretation of each term in these equations, where you may assume that α, β, γ, n_0, D_n, D_c and χ are all positive.

(ii) Show that there is a steady-state solution that is stable to spatially invariant disturbances.

(iii) Analyse small, spatially-varying perturbations to the steady state that satisfy $\nabla^2 \phi = -k^2 \phi$ for any variable ϕ, and show that a chemotactic instability is possible if

$$\chi \alpha n_0 > \beta D_n + \gamma n_0 D_c + (4\beta\gamma n_0 D_n D_c)^{1/2} \ .$$

(iv) Find the critical value of k at which the instability first appears as χ is increased.

4/I/6B **Mathematical Biology**

The non-dimensional equations for two competing populations are

$$\frac{du}{dt} = u(1 - v) - \epsilon_1 u^2,$$
$$\frac{dv}{dt} = \alpha \left[v(1 - u) - \epsilon_2 v^2 \right] \ .$$

Explain the meaning of each term in these equations.

Find all the fixed points of this system when $\alpha > 0$, $0 < \epsilon_1 < 1$ and $0 < \epsilon_2 < 1$, and investigate their stability.

1/I/6B Mathematical Biology

A large population of some species has probability $P(n,t)$ of taking the value n at time t. Explain the use of the generating function $\phi(s,t)=\sum_{n=0}^{\infty}s^nP(n,t)$, and give expressions for $P(n,t)$ and $\langle n\rangle$ in terms of ϕ.

A particular population is subject to a birth-death process, so that the probability of an increase from n to $n+1$ in unit time is $\alpha+\beta n$, while the probability of a decrease from n to $n-1$ is γn, with $\gamma>\beta$. Show that the master equation for $P(n,t)$ is

$$\frac{\partial P(n,t)}{\partial t}=(\alpha+\beta(n-1))P(n-1,t)+\gamma(n+1)P(n+1,t)-(\alpha+(\beta+\gamma)n)P(n,t)\ .$$

Derive the equation satisfied by ϕ, and show that in the statistically steady state, when ϕ and P are independent of time, ϕ takes the form

$$\phi(s)=\left(\frac{\gamma-\beta}{\gamma-\beta s}\right)^{\alpha/\beta}\ .$$

Using the equation for ϕ, or otherwise, find $\langle n\rangle$.

2/I/6B Mathematical Biology

Two interacting populations of prey and predators, with populations $u(t)$, $v(t)$ respectively, obey the evolution equations (with all parameters positive)

$$\begin{aligned}\frac{du}{dt}&=u(\mu_1-\alpha_1v-\delta u)\ ,\\ \frac{dv}{dt}&=v(-\mu_2+\alpha_2u)-\epsilon\ .\end{aligned}$$

Give an explanation in terms of population dynamics of each of the terms in these equations.

Show that if $\alpha_2\mu_1>\delta\mu_2$ there are two non-trivial fixed points with $u,v\neq0$, provided ϵ is sufficiently small. Find the trace and determinant of the Jacobian in terms of u,v and show that, when δ and ϵ are very small, the fixed point with $u\approx\mu_1/\delta$, $v\approx\epsilon\delta/\mu_1\alpha_2$ is always unstable.

2/II/13B **Mathematical Biology**

Consider the discrete predator-prey model for two populations N_t, P_t of prey and predators, respectively:

$$\left.\begin{aligned} N_{t+T} &= rN_t \exp(-aP_t) \\ P_{t+T} &= sN_t(1-b\exp(-aP_t)) \end{aligned}\right\}, \qquad (*)$$

where r, s, a, b are constants, all assumed to be positive.

(a) Give plausible explanations of the meanings of T, r, s, a, b.

(b) Nondimensionalize equations $(*)$ to show that with appropriate rescaling they may be reduced to the form

$$\left.\begin{aligned} n_{t+1} &= rn_t \exp(-p_t) \\ p_{t+1} &= n_t(1-b\exp(-p_t)) \end{aligned}\right\}.$$

(c) Now assume that $b < 1$, $r > 1$. Show that the origin is unstable, and that there is a nontrivial fixed point $(n, p) = (n_c(b, r), p_c(b, r))$. Investigate the stability of this point by writing $(n_t, p_t) = (n_c + n_t', p_c + p_t')$ and linearizing. Express the linearized equations as a second order recurrence relation for n_t', and hence show that n_t' satisfies an equation of the form

$$n_t' = A\lambda_1^t + B\lambda_2^t$$

where the quantities $\lambda_{1,2}$ satisfy $\lambda_1 + \lambda_2 = 1 + bn_c/r$, $\lambda_1\lambda_2 = n_c$ and A, B are constants. Give a similar expression for p_t' for the same values of A, B.

Show that when r is just greater than unity the λ_i $(i = 1, 2)$ are real and both less than unity, while if n_c is just greater than unity then the λ_i are complex with modulus greater than one. Show also that n_c increases monotonically with r and that if the roots are real neither of them can be unity.

Deduce that the fixed point is stable for sufficiently small r but loses stability for a value of r that depends on b but is certainly less than $e = \exp(1)$. Give an equation that determines the value of r where stability is lost, and an equation that gives the argument of the eigenvalue at this point. Sketch the behaviour of the moduli of the eigenvalues as functions of r.

3/I/6B **Mathematical Biology**

The SIR epidemic model for an infectious disease divides the population N into three categories of *susceptible* $S(t)$, *infected* $I(t)$ and *recovered* (non-infectious) $R(t)$. It is supposed that the disease is non-lethal, so that the population does not change in time.

Explain the reasons for the terms in the following model equations:

$$\frac{dS}{dt} = pR - rIS, \qquad \frac{dI}{dt} = rIS - aI, \qquad \frac{dR}{dt} = aI - pR.$$

At time $t = 0$, $S \approx N$ while $I, R \ll 1$.

(a) Show that if $rN < a$ no epidemic occurs.

(b) Now suppose that $p > 0$ and there is an epidemic. Show that the system has a non-trivial fixed point, and that it is stable to small disturbances. Show also that for both small and large p both the trace and the determinant of the Jacobian matrix are $O(p)$, and deduce that the matrix has complex eigenvalues for sufficiently small p, and real eigenvalues for sufficiently large p.

3/II/13B **Mathematical Biology**

A chemical system with concentrations $u(x,t), v(x,t)$ obeys the coupled reaction-diffusion equations

$$\frac{du}{dt} = ru + u^2 - uv + \kappa_1 \frac{d^2u}{dx^2} \; ,$$
$$\frac{dv}{dt} = s(u^2 - v) + \kappa_2 \frac{d^2v}{dx^2} \; ,$$

where r, s, κ_1, κ_2 are constants with s, κ_1, κ_2 positive.

(a) Find conditions on r, s such that there is a steady homogeneous solution $u = u_0$, $v = u_0^2$ which is stable to spatially homogeneous perturbations.

(b) Investigate the stability of this homogeneous solution to disturbances proportional to $\exp(ikx)$. Assuming that a solution satisfying the conditions of part (a) exists, find the region of parameter space in which the solution is stable to space-dependent disturbances, and show in particular that one boundary of this region for fixed s is given by

$$d \equiv \sqrt{\frac{\kappa_2}{\kappa_1}} = \sqrt{2s} + \frac{1}{u_0}\sqrt{s(2u_0^2 - u_0)} \; .$$

Sketch the various regions of existence and stability of steady, spatially homogeneous solutions in the (d, u_0) plane for the case $s = 2$.

(c) Show that the critical wavenumber $k = k_c$ for the onset of the instability satisfies the relation

$$k_c^2 = \frac{1}{\sqrt{\kappa_1 \kappa_2}} \left[\frac{s(d - \sqrt{2s})}{d(2\sqrt{2s} - d)} \right] .$$

Explain carefully what happens when $d < \sqrt{2s}$ and when $d > 2\sqrt{2s}$.

4/I/6B **Mathematical Biology**

A nonlinear model of insect dispersal with exponential death rate takes the form (for insect population $n(x,t)$)

$$\frac{\partial n}{\partial t} = -\mu n + \frac{\partial}{\partial x}\left(n\frac{\partial n}{\partial x}\right) . \qquad (*)$$

At time $t = 0$ the total insect population is Q, and all the insects are at the origin. A solution is sought in the form

$$n = \frac{e^{-\mu t}}{\lambda(t)} f(\eta); \quad \eta = \frac{x}{\lambda(t)}, \quad \lambda(0) = 0 . \qquad (\dagger)$$

(a) Verify that $\int_{-\infty}^{\infty} f \, d\eta = Q$, provided f decays sufficiently rapidly as $|x| \to \infty$.

(b) Show, by substituting the form of n given in equation ($\dagger$) into equation ($*$), that ($*$) is satisfied, for nonzero f, when

$$\frac{d\lambda}{dt} = \lambda^{-2} e^{-\mu t} \quad \text{and} \quad \frac{df}{d\eta} = -\eta .$$

Hence find the complete solution and show that the insect population is always confined to a finite region that never exceeds the range

$$|x| \leqslant \left(\frac{9Q}{2\mu}\right)^{1/3} .$$

1/I/6E **Mathematical Biology**

Consider a biological system in which concentrations $x(t)$ and $y(t)$ satisfy

$$\frac{dx}{dt} = f(y) - x \quad \text{and} \quad \frac{dy}{dt} = g(x) - y \ ,$$

where f and g are positive and monotonically decreasing functions of their arguments, so that x represses the synthesis of y and vice versa.

(a) Suppose the functions f and g are bounded. Sketch the phase plane and explain why there is always at least one steady state. Show that if there is a steady state with

$$\frac{\partial \ln f}{\partial \ln y} \frac{\partial \ln g}{\partial \ln x} > 1$$

then the system is multistable.

(b) If $f = \lambda/(1+y^m)$ and $g = \lambda/(1+x^n)$, where λ, m and n are positive constants, what values of m and n allow the system to display multistability for some value of λ?

Can $f = \lambda/y^m$ and $g = \lambda/x^n$ generate multistability? Explain your answer carefully.

2/I/6E **Mathematical Biology**

Consider a system with stochastic reaction events

$$x \xrightarrow{\lambda} x+1 \quad \text{and} \quad x \xrightarrow{\beta x^2} x-2 \ ,$$

where λ and β are rate constants.

(a) State or derive the exact differential equation satisfied by the average number of molecules $<x>$. Assuming that fluctuations are negligible, approximate the differential equation to obtain the steady-state value of $<x>$.

(b) Using this approximation, calculate the elasticity H, the average lifetime τ, and the average chemical event size $<r>$ (averaged over fluxes).

(c) State the stationary Fluctuation Dissipation Theorem for the normalised variance η. Hence show that

$$\eta = \frac{3}{4<x>} \ .$$

2/II/13E **Mathematical Biology**

Consider the reaction-diffusion system

$$\frac{\partial u}{\partial \tau} = \beta_u \left(\frac{u^2}{v} - u \right) + D_u \frac{\partial^2 u}{\partial x^2}$$
$$\frac{\partial v}{\partial \tau} = \beta_v \left(u^2 - v \right) + D_v \frac{\partial^2 v}{\partial x^2}$$

for an activator u and inhibitor v, where β_u and β_v are degradation rate constants and D_u and D_v are diffusion rate constants.

(a) Find a suitably scaled time t and length s such that

$$\begin{aligned} \frac{\partial u}{\partial t} &= \frac{u^2}{v} - u + \frac{\partial^2 u}{\partial s^2} \\ \frac{1}{Q}\frac{\partial v}{\partial t} &= u^2 - v + P\,\frac{\partial^2 v}{\partial s^2}\ , \end{aligned} \qquad (*)$$

and find expressions for P and Q.

(b) Show that the Jacobian matrix for small spatially homogenous deviations from a nonzero steady state of $(*)$ is

$$J = \begin{pmatrix} 1 & -1 \\ 2Q & -Q \end{pmatrix}$$

and find the values of Q for which the steady state is stable.
[*Hint: The eigenvalues of a* 2×2 *real matrix both have positive real parts iff the matrix has a positive trace and determinant.*]

(c) Derive linearised ordinary differential equations for the amplitudes $\hat{u}(t)$ and $\hat{v}(t)$ of small spatially inhomogeneous deviations from a steady state of $(*)$ that are proportional to $\cos(s/L)$, where L is a constant.

(d) Assuming that the system is stable to homogeneous perturbations, derive the condition for inhomogeneous *instability*. Interpret this condition in terms of how far activator and inhibitor molecules diffuse on average before they are degraded.

(e) Calculate the lengthscale L_{crit} of disturbances that are expected to be observed when the condition for inhomogeneous instability is just satisfied. What are the dominant mechanisms for stabilising disturbances on lengthscales (i) much less than and (ii) much greater than L_{crit}?

3/I/6E **Mathematical Biology**

Let x be the concentration of a binary master sequence of length L and let y be the total concentration of all mutant sequences. Master sequences try to self-replicate at a total rate ax, but each independent digit is only copied correctly with probability q. Mutant sequences self-replicate at a total rate by, where $a > b$, and the probability of mutation back to the master sequence is negligible.

(a) The evolution of x is given by

$$\frac{dx}{dt} = aq^L x \ .$$

Write down the corresponding equation for y and derive a differential equation for the master-to-mutant ratio $z = x/y$.

(b) What is the maximum length $L_{\max}$ for which there is a positive steady-state value of z? Is the positive steady state stable when it exists?

(c) Obtain a first-order approximation to $L_{\max}$ assuming that both $1 - q \ll 1$ and $s \ll 1$, where the selection coefficient s is defined by $b = a(1 - s)$.

3/II/13E **Mathematical Biology**

Protein synthesis by RNA can be represented by the stochastic system

$$\begin{aligned} x_1 &\xrightarrow{\lambda_1} x_1+1 \quad \text{and} \quad x_1 \xrightarrow{\beta_1 x_1} x_1-1 \\ x_2 &\xrightarrow{\lambda_2 x_1} x_2+1 \quad \text{and} \quad x_2 \xrightarrow{\beta_2 x_2} x_2-1 \end{aligned} \tag{1}$$

in which x_1 is an environmental variable corresponding to the number of RNA molecules per cell and x_2 is a system variable, with birth rate proportional to x_1, corresponding to the number of protein molecules.

(a) Use the normalized stationary Fluctuation–Dissipation Theorem (FDT) to calculate the (exact) normalized stationary variances $\eta_{11} = \sigma_1^2/{<}x_1{>}^2$ and $\eta_{22} = \sigma_2^2/{<}x_2{>}^2$ in terms of the averages ${<}x_1{>}$ and ${<}x_2{>}$.

(b) Separate η_{22} into an intrinsic and an extrinsic term by considering the limits when x_1 does not fluctuate (intrinsic), and when x_2 responds deterministically to changes in x_1 (extrinsic). Explain how the extrinsic term represents the magnitude of environmental fluctuations and time-averaging.

(c) Assume now that the birth rate of x_2 is changed from the "constitutive" mechanism $\lambda_2 x_1$ in (1) to a "negative feedback" mechanism $\lambda_2 x_1 f(x_2)$, where f is a monotonically decreasing function of x_2. Use the stationary FDT to approximate η_{22} in terms of $h = |\partial \ln f/\partial \ln x_2|$. Apply your answer to the case $f(x_2) = k/x_2$.

[*Hint: To reduce the algebra introduce the elasticity* $H_{22} = \partial \ln(R_2^-/R_2^+)/\partial \ln x_2$*, where* R_2^- *and* R_2^+ *are the death and birth rates of* x_2 *respectively.*]

(d) Explain the extrinsic term for the negative feedback system in terms of environmental fluctuations, time-averaging, and static susceptibility.

(e) Explain why the FDT is exact for the constitutive system but approximate for the feedback system. When, generally speaking, does the FDT approximation work well?

(f) Consider the following three experimental observations: (i) Large changes in λ_2 have no effect on η_{22}; (ii) When x_2 is perturbed by 1% from its stationary average, perturbations are corrected more rapidly in the feedback system than in the constitutive system; (iii) The feedback system displays lower values η_{22} than the constitutive system.

What does (i) imply about the relative importance of the noise terms? Can (ii) be directly explained by (iii), i.e., does rapid adjustment reduce noise? Justify your answers.

4/I/6E **Mathematical Biology**

The output of a linear perceptron is given by $y = \mathbf{w} \cdot \mathbf{x}$, where $\mathbf{w}$ is a vector of weights connecting a fluctuating input vector $\mathbf{x}$ to an output unit. The weights are given random initial values and are then updated according to a learning rule that has a time-constant τ much greater than the fluctuation timescale of the inputs.

(a) Find the behaviour of $|\mathbf{w}|$ for each of the following two rules

(i) $\tau \dfrac{d\mathbf{w}}{dt} = y\mathbf{x}$

(ii) $\tau \dfrac{d\mathbf{w}}{dt} = y\mathbf{x} - \alpha y^2 \mathbf{w}|\mathbf{w}|^2$, where α is a positive constant.

(b) Consider a third learning rule

(iii) $\tau \dfrac{d\mathbf{w}}{dt} = y\mathbf{x} - \mathbf{w}|\mathbf{w}|^2 \,.$

Show that in a steady state the vector of weights satisfies the eigenvalue equation

$$\mathbf{C}\mathbf{w} = \lambda \mathbf{w} \,,$$

where the matrix $\mathbf{C}$ and eigenvalue λ should be identified.

(c) Comment briefly on the biological implications of the three rules.