Further Mathematical Biology: Supplementary Questions

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Morphogen Gradients.

Question 1.

A one-dimensional field $0 \leq x \leq X_0$ contains corn of density $C(x,t)$. The corn undergoes logistic growth in the absence of external factors. A corn-loving plague of locusts $L(x,t)$ descends on the field, entering from $x = 0$. The locusts migrate through the field by random motion and chemotaxis, consuming corn in the process. We describe this situation as follows:

$$\frac{\partial C}{\partial t} = \lambda_0 C(C_0 - C) - \lambda_1 LC, \quad \frac{\partial L}{\partial t} = \mu \frac{\partial^2 L}{\partial x^2} - \chi \frac{\partial}{\partial x}\left(L \frac{\partial C}{\partial x}\right),$$

with

$$L(0,t) = L_0, \quad L(X_0,t) = 0 \quad \text{for } t \geq 0$$
$$C(x,0) = C_0 \text{ for } 0 \leq x \leq X_0,$$
$$L(x,0) = 0 \text{ for } 0 < x \leq X_0.$$

(a) By writing

$$C = C_0 c, \quad L = L_0 l, \quad x = X_0 x, \quad t = T\tau,$$

and choosing T appropriately, show that the model equations can be rewritten in terms of c, l, s and τ in the following form:

$$\frac{\partial c}{\partial \tau} = \lambda_0^* c(1-c) - \lambda_1^* lc, \quad \frac{\partial l}{\partial \tau} = \frac{\partial^2 l}{\partial x^2} - \chi^* \frac{\partial}{\partial x}\left(l \frac{\partial c}{\partial x}\right).$$

How are λ_0^*, λ_1^* and χ^* defined?

(b) Determine the steady state (time-independent) solutions of the transformed equations for the cases $\lambda_0^* > \lambda_1^*$ and $\lambda_0^* < \lambda_1^*$.

(c) Comment briefly on the results from part (b).

Question 2.

Bacteria have a tendency to move towards sources of food. The following model has been proposed to describe this process as it occurs in a one-dimensional region ($0 \leq x \leq 1$):

$$\frac{\partial a}{\partial t} = \frac{\partial^2 a}{\partial x^2} - k, \quad \frac{\partial b}{\partial t} = -\chi \frac{\partial}{\partial x}\left(ab \frac{\partial a}{\partial x}\right) + \alpha b,$$

$$a(0,t) = 0, \quad a(1,t) = 1, \quad b(x,0) = \left\{ \begin{array}{ll} (1 - x/x^*) & 0 \leq x \leq x^* \\ 0 & x^* < x < 1 \end{array} \right),$$

where $a(x,t)$ and $b(x,t)$ are the nutrient and bacteria densitites and χ, α, k and x^* are positive constants, with $0 < x^* < 1$.

(a) Determine the steady state nutrient concentration $a(x)$, and substitute this into the equation for $b(x,t)$.

(b) Use the method of characteristics to construct an analytical solution for $b(x,t)$ in the special case $k = 0$.

(c) Use your results to sketch the solution for

$$0 < t < \frac{1}{\chi} \ln\left(\frac{1}{x^*}\right) \quad \text{and} \quad \frac{1}{\chi} \ln\left(\frac{1}{x^*}\right) < t.$$

(d) Explain briefly how the long time behaviour of the bacteria differs for the cases $\alpha > \chi$ and $\alpha < \chi$.

Domain growth.

Question 1.

The following equations describe the growth of a two-dimensional, circular colony of cells:

$$0 = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right) - \lambda H(c - c_N), \tag{1}$$

$$R\frac{dR}{dt} = \int_0^R P(c)\, rdr \quad \text{where} \quad P(c) = \begin{cases} pc > 0 & \text{if } c > c_N, \\ -q < 0 & \text{if } c \leq c_N, \end{cases} \tag{2}$$

$$c = 1 \;\text{ when }\; r = R(t), \quad \frac{\partial c}{\partial r} = 0 \;\text{ when }\; r = 0, \tag{3}$$

$$c, \;\frac{\partial c}{\partial r} \;\text{ continuous across }\; r = R_N(t), \tag{4}$$

$$c = c_N \;\text{ when }\; r = R_N(t), \tag{5}$$

$$R = 1 \;\text{ when }\; t = 0. \tag{6}$$

In equation (1), $H(.)$ denotes the Heaviside step function ($H(x) = 1$ if $x \geq 0$ and $H(x) = 0$ if $x < 0$), λ, p, q and c_N are positive constants, with $0 < c_N < 1$.

(a) You are given that $c(r, t)$ represents the local oxygen concentration, $r = R(t)$ the position of the outer boundary of the colony and $R_N(t)$ the position of the interface separating proliferating and dead cells. Provide a brief description of equations (1)-(6).

(b) Given that there is initially no necrotic region, use equation (1) and the corresponding boundary conditions to derive an expression relating $c(r, t)$ to $R(t)$ prior to the appearance of dead cells.

(c) Determine the size of the colony $R = R^*$ at which dead cells first appear. By assuming that R^* and λ satisfy $R^* > 1$ and $0 < \lambda < 4(1 - c_N)$, show that the time t_N at which necrosis is initiated is given by

$$t_N = \frac{1}{p}\ln\left\{\frac{(1 - c_N)(8 - \lambda)}{(1 + c_N)\lambda}\right\}.$$

(d) A cytotoxic drug is applied to the cells at $t = 0$. The drug modifies equation (2) in the following way

$$R\frac{dR}{dt} = \int_0^R (P(c) - d) rdr, \tag{7}$$

where the positive constant d denotes the dose of drug applied to the cells. By assuming that $R_N = 0$ and studying the differential equation for $R(t)$ that arises from equation (7), show that the cell colony will be eliminated if $d > p$. What is the limiting behaviour of the colony when $(1 + c_N)/2 < d/p < 1$?

Question 2.

The following equations describe the effect of an externally-supplied poison β on the growth of a radially-symmetric cluster of mold.

$$0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial \beta}{\partial r}\right) - \beta_\infty H(\beta),$$

$$R^2\frac{dR}{dt} = \int_0^R (s - \beta) r^2 dr,$$

$$\text{with } \frac{\partial \beta}{\partial r} = h(\beta_\infty - \beta) \text{ on } r = R(t),$$

$$\frac{\partial \beta}{\partial r} = 0 \text{ at } r = 0,$$

$$\text{and } R = R_0 \text{ at } t = 0.$$

In the equations, β_∞, h, s and R_0 are positive constants and $H(.)$ denotes the Heaviside step function.

(a) Provide a brief description of the model equations.

(b) Given that initially $\beta(r,t) > 0$ for $0 < r < R(t)$, derive an expression relating $\beta(r,t)$ to $R(t)$ prior to the appearance of a central region in which $\beta = 0$.

(c) For the case $h = 2$, explain how the number and structure of the steady state solutions change with s/β_∞. What concentration of poison would you recommend to be confident of eradicating the mold?

Question 3.

Carefully justify the following model for growth of a cylindrical circular tumour:

$$
\begin{aligned}
\frac{\partial C}{\partial t} &= \frac{D}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right) - \lambda, \quad 0 \leq r \leq R(t),\\
C(r,t) &= C_*, \quad r = R(t),\\
\frac{\partial C}{\partial r}(0,t) &= 0,\\
R\frac{dR}{dt} &= \int_0^{R(t)} P(C) r dr,\\
R(t=0) &= R_0,
\end{aligned}
$$

where D, λ and C_* are positive constants.

(a) Describe briefly all terms in the equations [4 marks].

(b) Let the function $P(C)$ be given by

$$P(C) = P_0\left(\frac{C}{C_*}\right)^\alpha, \quad \alpha > 0.$$

Nondimensionalise the model with the scalings $r = R_0\rho$, $t = \tau/P_0$, $C = C_* c$, $P(C) = P_0 p(c)$, $R(t) = R_0 s(\tau)$. Assuming $R_0^2 P_0/D \ll 1$, obtain an approximate, quasi-steady equation for the dimensionless variable c, which you should solve to find c in terms of $s(\tau)$. Given a condition for the minimum value of c to be positive. Why is this necessary?

(c) Use the dimensionless version of the governing equations to show that, with P as defined in part (b), the tumour boundary position is governed by the ODE:

$$s\frac{ds}{d\tau} = \frac{2}{\mu(\alpha+1)}\left\{1 - \left(1 - \frac{\mu s^2}{4}\right)^{\alpha+1}\right\}. \tag{8}$$

(d) Show that $s = 0$ is the only possible steady state for the tumour boundary. By considering the behaviour of equation (8) for small s, determine the stability of this steady state.

Age-structured and discrete-to-continuum models.

Question 1.

The evolution of an age-structured population $n(t,a)$ may be modelled by von Foerster's equation:

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

$$\text{with}\quad n(0,a)=f(a),\quad n(t,0)=B(t)=\int_0^\infty \beta(\theta)n(t,\theta)d\theta,$$

where μ is a positive constant.

(a) Discuss briefly the assumptions underlying the model, providing a physical interpretation of the functions $f(a)$ and $\beta(a)$.

(b) Use the method of characteristics to show that

$$n(t,a)=\begin{cases} f(a-t)e^{-\mu t} & \text{for } 0<t<a, \\ B(t-a)e^{-\mu a} & \text{for } a<t. \end{cases}$$

where $B(t)$ is defined implicitly by

$$B(t)=\int_0^t \beta(\theta)B(t-\theta)e^{-\mu\theta}d\theta+e^{-\mu t}\int_t^\infty \beta(\theta)f(\theta-t)d\theta.$$

(c) Show that if the long time behaviour of the population has the separable form $n(t,a)=e^{\gamma t}F(a)$ then the growth rate γ satisfies

$$1=\int_0^\infty \beta(\theta)e^{-(\gamma+\mu)\theta}d\theta.$$

(d) Assuming further that

$$\beta(a)=\begin{cases} \beta^* & \text{if } a_m-1<a<a_m+1, \\ 0 & \text{otherwise,} \end{cases}$$

determine the unique value of $a_m=a_m(\beta^*,\mu)$ for which the population evolves to a time-independent distribution ($\gamma=0$). What value of a_m yields a steady state age-distribution in the limit as $\mu\to\infty$?

Question 2.

(a) The evolution of an age-structured population $v(a,t)$ satisfies

$$v_t+r(a)v_a=-\mu(V,a)v,\quad \text{for}\quad 0<a<L,\ 0<t,$$

$$\text{with}\quad v(0,t)=2v(L,t)\quad\text{and}\quad v(a,0)=v_{init}(a),$$

$$\text{and}\quad V(t)=\int_0^L \xi_v(a)v(a,t)da.$$

where $r(a),\xi_v(a),\mu(V,a)$ and $v_{init}(a)$ are known functions. Describe briefly the assumptions underlying the model equations and provide a physical interpretation of the functions $r(a),\xi_v(a),\mu(V,a)$ and $v_{init}(a)$.

(b) The evolution of a second population $u(a,t)$ satisfies

$$u_t+(r(a)u)_a=-\mu(U,a)u,\quad \text{for}\quad 0<a<L,\ 0<t,$$

$$\text{with}\quad u(0,t)=2u(L,t)\quad\text{and}\quad u(a,0)=u_{init}(a),$$

$$\text{and}\quad U(t)=\int_0^L \xi_u(a)u(a,t)da.$$

where $\xi_u(a)$ and $u_{init}(a)$ are known functions. Under what conditions (*i.e.* for what choices of $\xi_u(a)$ and $u_{init}(a)$) are the evolution of $u(a,t)$ and $v(a,t)$ equivalent?

(c) You are given that

$$\xi_v(a) = 1, \;\; r(a) = (1 + \alpha a), \;\; \mu(V, a) = \mu_0 + \mu_1 V \;\text{ for }\; 0 \leq a \leq L.$$

By seeking a separable solution of the form $v(a, t) = A(a)V(t)$ for $0 \leq a \leq L$ and t sufficiently large, identify conditions under which the population eventually dies out. [*Note: here "t sufficiently large" means that the evolution of* $v(a, t)$ *is independent of the initial conditions.*]

Question 3.

Two populations of left and right moving cells are distributed along the real line which is decomposed into a series of boxes of width Δx. We denote by $L_i(t)$ the number of cells in the i-th box that are moving to the left at time t and by $R_i(t)$ the number of cells in the i-th box that are moving to the right. The following system of discrete equations describe how the system changes from time t to time $t + \Delta t$:

$$L_i(t + \Delta t) = L_{i+1}(t) + k_L \Delta t R_i(t) - k_R \Delta t L_i(t),$$
$$R_i(t + \Delta t) = R_{i-1}(t) + k_R \Delta t L_i(t) - k_L \Delta t R_i(t),$$

where the parameters k_L and k_R are non-negative constants.

(a) Provide a brief physical interpretation of the above equations.

(b) Assume that the box size Δx is sufficiently small to identify continuous cell densities $\rho_L(i\Delta x, t) = \rho_L(x, t)$ and $\rho_R(i\Delta x, t) = \rho_R(x, t)$ with $L_i(t)$ and $R_i(t)$. Use the discrete equations from (a) to show that in the limit as $\Delta x, \Delta t \to 0$, $\rho_L(x, t)$ and $\rho_R(x, t)$ solve

$$\frac{\partial \rho_L}{\partial t} - v\frac{\partial \rho_L}{\partial x} = k_L \rho_R - k_R \rho_L, \tag{9}$$

$$\frac{\partial \rho_R}{\partial t} + v\frac{\partial \rho_R}{\partial x} = k_R \rho_L - k_L \rho_R. \tag{10}$$

How is the constant v defined? What assumptions are made about Δt and Δx when deriving equations (9) and (10)?

(c) Suppose now that $k_{LR}, \; k_{RL} \gg 1$. Obtain a relationship for ρ_R in terms of ρ_L and then use it to eliminate ρ_R from equation (9) and obtain a partial differential equation for ρ_L. Solve the resulting PDE for ρ_L.

(d) Use the solution for ρ_L from part (c) to describe the behaviour of the two cell populations for the cases (i) $k_L > k_R$ and (ii) $k_L = k_R$.

FitzHugh-Nagumo Equations.

Question 1.

Consider an experimental scenario where a nerve axon is bathed in sea water, which is a good conductor and thus of low resistivity. Additionally, a silver wire is placed down the centre of the axon, greatly decreasing the internal resistivity.

Assuming these resistivities are sufficiently low, one can non-dimensionalise the Fitzhugh Nagumo equations into the form

$$\begin{aligned}
&\frac{1}{\delta}\frac{\partial^2 u}{\partial x^2} = \frac{\partial u}{\partial \tau} + J_{ion}(u, v), \\
&\frac{\mathrm{d}v}{\mathrm{d}\tau} = -\gamma v + u,
\end{aligned}$$

where $J_{ion}(u, v)$ is a non-dimensionalised ionic current term, typically of unit magnitude, and the non-dimensional constant δ satisfies $0 < \delta \ll 1$.

Suppose one ensures no currents can pass through the ends of the axon so that one additionally has the boundary conditions

$$\left.\frac{\partial u}{\partial x}\right|_{x=0} = 0 = \left.\frac{\partial u}{\partial x}\right|_{x=L}.$$

(a) By considering the expansion $u = u_0(x, \tau) + \delta u_1(x, \tau) + \ldots$, and the assumption that

$$\frac{\partial^2 u}{\partial x^2}, \frac{\partial u}{\partial \tau}, J_{ion} \sim \mathcal{O}(1),$$

show that $u = u_0(\tau)$ at leading order.

(b) Show further that, for sufficiently large time, $u_0(\tau)$ is given by the solution of the ordinary differential equations

$$\begin{aligned}
\frac{\mathrm{d}u_0}{\mathrm{d}\tau} + J_{ion}(u_0, q_0) &= 0, \\
\frac{\mathrm{d}q_0}{\mathrm{d}\tau} &= -\gamma q_0 + u_0,
\end{aligned}$$

where $q_0 = q_0(\tau)$, at the first non-trivial order in δ even if $v(x, \tau = 0)$ is not spatially constant.