Further Mathematical Biology: Supplementary Questions

Michaelmas Term 2017

Morphogen Gradients.

Question 1.

A one-dimensional field $0 \le x \le X_0$ 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

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

(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 $\lambda_0^* < \lambda_1^*$. (i) $c=0,\ l=1-x$ (ii) $c=1-\frac{\lambda_1}{\lambda_0}l$, $0=\frac{\chi^*\lambda_1}{2\lambda_0}l^2+l-\left(1+\frac{\chi^*\lambda_1}{2\lambda_0}\right)(1-x)$

(c) Comment briefly on the results from part (b). $\boxed{\text{require } \lambda_1<\lambda_0 \text{ s.t. } c\geq 0.}$ (take +ve root).

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 ($0 \le x \le 1$):

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

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

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:

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

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

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

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

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

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

In equation (1), $H(.)$ denotes the Heaviside step function ($H(x) = 1$ if $x \ge 0$ 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

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

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 growth of a radially-symmetric tumour in response to an externally-supplied nutrient such as oxygen:

$$\frac{\partial n}{\partial t} + \frac{1}{r^2}\frac{\partial}{\partial r}(r^2 v n) = k(c)n, \tag{8}$$

$$\frac{dR}{dt} = v(R,t), \tag{9}$$

$$0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial c}{\partial r}\right) - \lambda n H(c - c_N),$$

$$\text{where } k(c) = \begin{cases} k_+ & \text{if } c > c_N \\ -k_- & \text{if } c \le c_N, \end{cases}$$

$$c(R,t) = c_\infty, \qquad \frac{\partial c}{\partial r}(0,t) = 0 = v(0,t),$$

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

$$R(0) = R_0,$$

and $0 \le R_N(t) < R(t)$ is defined so that

$$R_N(t) = 0 \text{ if } c(r,t) > c_N \text{ for } 0 < r < R(t),$$
$$c(R_N, t) = c_N \quad \text{otherwise.}$$

In these equations, $n(r,t)$ denotes the tumour cell density, $v(r,t)$ the cell velocity, $c(r,t)$ the local oxygen concentration, $R(t)$ the position of the outer tumour radius and $R_N(t)$ the interface between the proliferating and dead cells. The parameters λ, c_N, c_∞, R_0 and $k_\pm$ are positive constants.

(a) By assuming that the tumour is fully occupied by cells so that $n \equiv 1$ for $0 \le r \le R(t)$, use equation (8) to obtain an expression for $v(r,t)$ in terms of $k(c)$.

(b) Use the result from part (a) to show that

$$R^2 \frac{dR}{dt} = \int_0^{R(t)} k(c) r^2 dr.$$

(c) By solving for $c(r,t)$ and assuming that $R_0 < R^* = \sqrt{6(c_\infty - c_N)/\lambda}$, explain briefly how the tumour evolves. In particular, show that, since $k_- > 0$, the tumour eventually achieves a steady state, which you should determine. (**Note:** you do NOT need to solve the ODEs for $R(t)$.) * hard question

* need to include more steps.

Question 3.

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

not well worded (ie too vague/imprecise)

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

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

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

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

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

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 4.

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

$$\frac{\partial C}{\partial t} = \frac{D}{r}\frac{\partial}{\partial r}\left(r \frac{\partial C}{\partial r}\right) - \lambda, \quad 0 \le r \le R(t),$$

$$C(r,t) = C_*, \quad r = R(t),$$

$$\frac{\partial C}{\partial r}(0,t) = 0,$$

$$R\frac{dR}{dt} = \int_0^{R(t)} P(C) r dr,$$

$$R(t=0) = R_0,$$

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 $r = R_0\rho$, $t = \tau/P_0$, $C = C_*c$, $P(C) = P_0p(c)$, $R(t) = R_0s(\tau)$. Assuming $R_0^2P_0/D \ll 1$, 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:

$$s\frac{ds}{d\tau} = \frac{2}{\mu(\alpha+1)}\left\{1 - \left(1 - \frac{\mu s^2}{4}\right)^{\alpha+1}\right\}. \tag{10}$$

(d) Show that $s = 0$ is the only possible steady state for the tumour boundary. By considering the behaviour of equation (10) 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

$$v_t + r(a)v_a = -\mu(V,a)v, \quad \text{for } 0 < a < L,\ 0 < t,$$
$$\text{with } v(0,t) = 2v(L,t) \text{ and } v(a,0) = v_{init}(a),$$
$$\text{and } V(t) = \int_0^L \xi_v(a)v(a,t)da.$$

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

$$u_t + (r(a)u)_a = -\mu(U,a)u, \quad \text{for } 0 < a < L,\ 0 < t,$$
$$\text{with } u(0,t) = 2u(L,t) \text{ and } u(a,0) = u_{init}(a),$$
$$\text{and } U(t) = \int_0^L \xi_u(a)u(a,t)da.$$

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

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

By seeking a separable solution of the form $v(a,t) = A(a)V(t)$ for $0 \le a \le L$ 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

$$\frac{\partial \rho_L}{\partial t} - v\frac{\partial \rho_L}{\partial x} = k_L\rho_R - k_R\rho_L, \tag{11}$$
$$\frac{\partial \rho_R}{\partial t} + v\frac{\partial \rho_R}{\partial x} = k_R\rho_L - k_L\rho_R. \tag{12}$$

How is the constant v defined? What assumptions are made about Δt and Δx when deriving equations (11) and (12)?

(c) Suppose now that $k_L, k_R \gg 1$. Obtain a relationship for ρ_R in terms of ρ_L and then use it to eliminate ρ_R from equation (11) and obtain a partial differential equation for ρ_L. Solve the resulting PDE for ρ_L.

[need to prescribe compatible initial data]

(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

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

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

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

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

Morphogen Gradients

Q1, $c_\tau = l_\tau = 0 \Rightarrow c = 0$ or $0 = \lambda_0(1-c) - \lambda_1 l$

$\Rightarrow l = \frac{\lambda_0}{\lambda_1}(1-c) \; : c = 1 - \frac{\lambda_1}{\lambda_0} l.$

case (i) : $c \equiv 0 \Rightarrow l_{xx} = 0$ with $l(0)=1,\ l(1)=0$

$\Rightarrow l = 1 - x.$

case (ii) : $c = 1 - \frac{\lambda_1}{\lambda_0} l.$

NOTE: $c(0) = 1 - \frac{\lambda_1}{\lambda_0}$

$\Rightarrow$ require $\boxed{\lambda_1 < \lambda_0}$ for phys real sol's.

now $0 = l_{xx} - \chi^*(l c_x)_x$ where $c_x = -\frac{\lambda_1}{\lambda_0} l_x.$

$$\Rightarrow \quad l_x\left(1 + \frac{\chi^* \lambda_1}{\cancel{2}\lambda_0} . l\right) = C, \text{ const.}$$

$$\Rightarrow \quad l + \frac{\chi^*\lambda_1}{2\lambda_0} l^2 = \left(1 + \frac{\chi^*\lambda_1}{2\lambda_0}\right)(1-x) \quad \text{s.t. } l(0)=1,\ l(1)=0.$$

$$\Rightarrow \boxed{\left(\chi^*\frac{\lambda_1}{\lambda_0}\right) l = -1 + \sqrt{1 + 2\chi^*\frac{\lambda_1}{\lambda_0}\left(1 + \frac{\chi^*\lambda_1}{2\lambda_0}\right)(1-x)}} \quad (*)$$

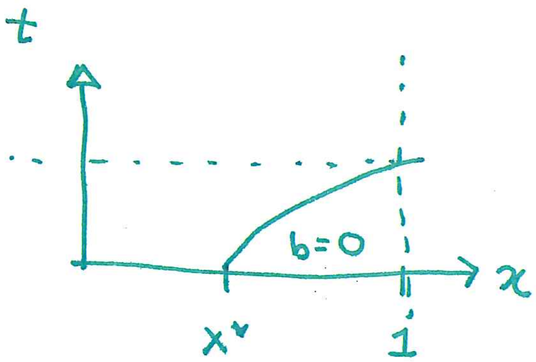
unique st. state if $\lambda_1 > \lambda_0$ with $c = 0,\ l = 1 - x.$

two steady states if $\lambda_1 < \lambda_0$ $\begin{cases} c = 0,\ l = 1 - x \\ c = 1 - \frac{\lambda_1}{\lambda_0} l, \ l \text{ defined by } (*) \end{cases}$

Morphogen Gradients

1/ $a_{xx} = 0 \qquad a = x. \qquad a_x = 1$

$$b_t = -\chi (a b a_x)_x + \alpha b \quad \text{with} \quad b(x,0) = \begin{cases} 1 - x/x^* \\ 0 \end{cases}$$



$$b_t + \chi (b x)_x = \alpha b$$

$$b_t + \chi x b_x = (\alpha - \chi) b.$$

$$\frac{dt}{d\tau} = 1 \qquad \frac{dx}{d\tau} = \chi x \qquad \frac{db}{d\tau} = (\alpha - \chi) b$$

with $t = 0, \ x = r, \ b = \begin{cases} 1 - r/r^* \\ 0 \end{cases}$ where $\tau = 0$

$$t = \tau \qquad x = r e^{\chi \tau} \qquad b = \begin{cases} (1 - r/x^*) e^{(\alpha - \chi)\tau} & 0 < r < x^* \\ 0. \end{cases}$$

$$\Rightarrow r = x e^{-\chi t}$$

$$b(x,t) = \begin{cases} \left(1 - \frac{x e^{-\chi t}}{x^*}\right) e^{(\alpha - \chi) t} & 0 < x < x^* e^{\chi t} \\ 0 & x^* e^{\chi t} < x < 1 \end{cases}$$

$$x = 1 = x^* e^{\chi t} \qquad t = \frac{1}{\chi} \ln\left(\frac{1}{x^*}\right).$$

for $\underline{0 < t < \frac{1}{\chi} \ln\left(\frac{1}{x^*}\right)}$: $b = \begin{cases} \left(1 - \frac{x e^{-\chi t}}{x^*}\right) e^{(\alpha - \chi) t} \\ 0 \end{cases}$

$\underline{\frac{1}{\chi} \ln\left(\frac{1}{x^*}\right) < t}$: $b = \left(1 - \frac{x e^{-\chi t}}{x^*}\right) e^{(\alpha - \chi) t}$

ie $b > 0 \ \forall \ x \in [0,1]$

$\alpha > \chi$: popⁿ explodes/unbdd near $x = 0$

$\alpha < \chi$: popⁿ becomes extinct

Domain Growth: Q1

(a) usual stuff – as per lectures.

(b) $0 = \frac{1}{r}\frac{\partial}{\partial r}\left(r\,\partial c/\partial r\right) - \lambda$

$C = 1$ on $r = R$

$C_r = 0$ @ $r = 0$

with $c > c_N \;\forall\; r \in (0, R]$

$$\Rightarrow \quad C = \frac{\lambda r^2}{4} + A\ln r + B \quad \equiv 1 - \frac{\lambda}{4}(R^2 - r^2).$$

(c) $$\frac{R\,dR}{dt} = \int_0^R pcr\,dr = p\int_0^R r\left(1 - \frac{\lambda}{4}(R^2 - r^2)\right)dr = \frac{pR^2}{2}\left(1 - \frac{\lambda R^2}{8}\right).$$

$$\Rightarrow \frac{dR}{dt} = \frac{pR}{2}\left(1 - \frac{\lambda R^2}{8}\right) \quad \text{or,} \quad \frac{d}{dt}(R^2) = pR^2\left(1 - \frac{\lambda R^2}{8}\right).$$

(logistic growth for $A = R^2$)

Dead cells first appear when $C_{min} = c(0,t) = C_N = 1 - \frac{\lambda R^2}{4}$

when $R = R^* = \sqrt{\frac{4}{\lambda}(1 - C_N)}$

The time t_N at which this happens s.t.

$$pt_N = \int_1^{R^{*2}} \frac{d(R^2)}{R^2\left(1 - \lambda R^2/8\right)} = \int_1^{R^{*2}} \frac{dV}{V(1 - \lambda V/8)}$$

$$= \int_1^{R^{*2}} \left(\frac{1}{V} + \frac{\lambda/8}{1 - \lambda V/8}\right)dV = \ln\left(\frac{R^{*2}}{1 - \lambda R^{*2}/8}\cdot\frac{(1 - \lambda/8)}{1}\right)$$

where $R^{*2} = \frac{4}{\lambda}(1 - C_N) \Rightarrow 1 - \lambda R^{*2}/8 = 1 - \frac{1}{2}(1 - C_N) = \frac{1}{2}(1 + C_N)$

$$\Rightarrow pt_N = \ln\left(\frac{(1 - \lambda/8)}{\lambda}\cdot\frac{(1 - C_N)}{(1 + C_N)}\,8\right) = \ln\left(\frac{(8 - \lambda)}{\lambda}\cdot\frac{(1 - C_N)}{(1 + C_N)}\right)$$

) Domain Growth Q1

$$\frac{R\,dR}{dt} = \int_0^R (pc - d)\, r\,dr \qquad \text{where } c = 1 - \frac{\lambda}{4}(R^2 - r^2)$$

as before

$$= \frac{pR^2}{2}\left(1 - \frac{\lambda R^2}{8}\right) - \frac{dR^2}{2}$$

$$\Rightarrow \frac{dV}{dt} = pV\left(1 - \frac{\lambda V}{8}\right) - dV = V\left((p-d) - \frac{p\lambda V}{8}\right)$$

$$= (p-d)V\left(1 - \frac{p\lambda}{8(p-d)}\cdot V\right) \qquad \left(V = R^2\right)$$

if $d > p$ then $V \to 0$ as $t \to \infty$. ie cells eliminated

if $\boxed{p > d}$ then $\exists$ nontriv st. st.

$$V = R^2 = \frac{8}{\lambda}\cdot\left(1 - d/p\right).$$

need to check sol^n is valid ie $C_{min} = C(0,t) > C_N$.

ie $$1 - \frac{\lambda}{4}.R^2 = 1 - 2(1 - d/p) > C_N$$

$$\Leftrightarrow \quad \frac{d}{p} > \frac{1}{2}(1 + C_N)$$

ie if $\frac{(1+C_N)}{2} < \frac{d}{p} < 1$ then $\exists$ nontriv st. st.

with $R^2 = \frac{8}{\lambda}\left(1 - d/p\right)$

Domain Growth : Q2

(a),(b) $n=1$ in (8) $\Rightarrow \frac{1}{r^2}\frac{\partial}{\partial r}(r^2 v) = k(c)$, with $v(0,t)=0$

$\Rightarrow v(r,t) = \frac{1}{r^2}\int_0^r \rho^2 k(c(\rho,t))\,d\rho.$

(c) Consider separately

case 1 : $R_N = 0$, no cell death

case 2 : $0 < R_N < R$; cell death occurs

$\Rightarrow \frac{dR}{dt} = v(R,t) = \frac{1}{R^2}\int_0^R k(c) r^2\,dr$

Case 1 : $R_N = 0$ ($c > c_N \ \forall\, r \in (0,R)$)

$$0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial c}{\partial r}\right) - \lambda \quad \text{with} \quad c = c_\infty \text{ on } r = R, \quad c_r = 0 \text{ @ } r=0$$

$$\Rightarrow \boxed{c = c_\infty - \frac{\lambda}{6}(R^2 - r^2)}.$$

[NB: general sol^n is $c(r,t) = A(t) + \frac{B(t)}{r} + \frac{\lambda r^2}{6}$; impose BCs to determine A, B]

where $R(t)$ satisfies

$$R^2\frac{dR}{dt} = \int_0^R k(c) r^2\,dr \equiv \int_0^R k_+ r^2\,dr = \frac{k_+ R^3}{3}$$

$$\Rightarrow \frac{dR}{dt} = \frac{k_+ R}{3} \quad \text{with} \quad R(0) = R_0 < R^* = \left[\frac{6}{\lambda}(c_\infty - c_N)\right]^{1/2}$$

(NB constraint guarantees $R_N = 0$ at $t=0$ ie $c > c_N \ \forall\, r \in (0,R)$ at $t=0$.)

$$\Rightarrow R(t) = R_0 e^{k_+ t/3}$$

Growth continues at exp. rate until necrosis is initiated at $t = t_N$ where $R = R^* = \left[\frac{6}{\lambda}(c_\infty - c_N)\right]^{1/2}$. Since $R(t) = R_0 e^{k_+ t/3}$, we deduce that $R^* = R_0 e^{k_+ t_N/3}$

$$\Rightarrow \boxed{t_N = \frac{3}{k_+}\ln\left(\frac{R^*}{R_0}\right)}$$

case 2 : $0 < R_N < R$

$$\left.\begin{array}{l} 0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial c}{\partial r}\right) - \lambda H(c - c_N) \\ c_r = 0 \text{ @ } r = 0 \\ c = c_\infty \text{ on } r = R, \\ c, c_r \text{ cts on } r = R_N \\ c = c_N \text{ on } r = R_N. \end{array}\right\} \Rightarrow c = \begin{cases} c_N & 0 < r < R_N \\ \hat{A} + \frac{\hat{B}}{r} + \frac{\lambda r^2}{6} & R_N < r < R \end{cases}$$

impose BCs to determine $\hat{A}(t)$, $\hat{B}(t)$ & $R_N(t)$:

Domain Growth
Q2 (ct'd)

$$c = \begin{cases} c_N & 0 < r < R_N \\ c_N + \frac{\lambda}{6}(r^2 - R_N^2) - \frac{\lambda R_N^3}{3}\left(\frac{1}{R_N} - \frac{1}{r}\right) & R_N < r < R \end{cases}$$

with

$$\boxed{c_\infty - c_N = \frac{\lambda}{6}(R-R_N)^2(R+2R_N)}$$

algebraic expression for R_N in terms of R.

where $R(t)$ solves

$$R^2\frac{dR}{dt} = -\int_0^{R_N} k_- r^2 dr + \int_{R_N}^{R} k_+ r^2 dr$$

$$= \frac{k_+}{3}(R^3 - R_N^3) - \frac{k_-}{3}R_N^3.$$

steady state when $\frac{dR}{dt} = 0 \Rightarrow 0 = \frac{k_+}{3}(R_S^3 - R_{NS}^3) - k_- R_{NS}^3$

$$\Rightarrow R_{NS}^3 = R_S^3 \Big/ \left(1 + \frac{k_-}{k_+}\right) \equiv \theta^3 R_S^3, \text{ say}$$

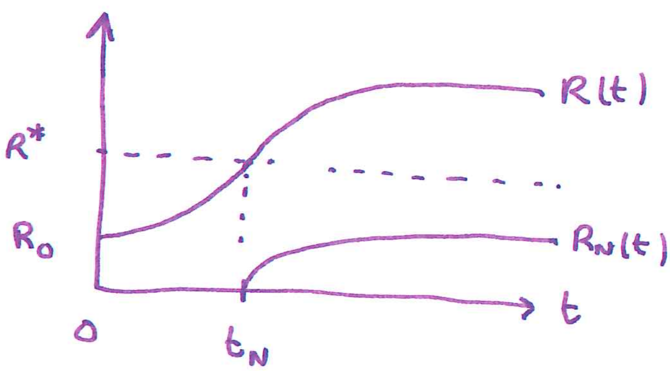
where $0 < \theta^3 = \left(1 + \frac{k_-}{k_+}\right)^{-1} < 1.$

with $R_{NS} = \theta R_S$ then R_S satisfies

$$c_\infty - c_N = \frac{\lambda}{6}.(1-\theta)^2(1+2\theta)R_S^3$$

$$\Rightarrow R_S^3 = \frac{6}{\lambda}(c_\infty - c_N).\frac{1}{(1-\theta)^2(1+2\theta)} \quad \text{with } R_{NS} = \theta R_S$$

summary



$0 < t < t_N$: tumour grows exponentially until necrotic core develops

$t_N < t$: growth slows when necrosis initiates until tumour attains st. st. with $R = R_S$, $R_N = R_{NS}$.

(feedback for student)

Re Q2,

$$c(r) = \begin{cases} c_N \\ c_N + \frac{\lambda}{6}(r^2 - R_N^2) - \frac{\lambda R_N^2}{3r}(r - R_N) \end{cases}$$

$\Rightarrow$ $$c_\infty - c_N = \frac{\lambda}{6}(R^2 - R_N^2) - \frac{\lambda R_N^2}{3R}(R - R_N)$$

$\Rightarrow$ (algebra) $$\boxed{\frac{6}{\lambda}(c_\infty - c_N) = R^2\left(1 - \frac{R_N}{R}\right)^2\left(1 + \frac{R_N}{R}\right)} \quad (*)$$

Also, $$R^2 \frac{dR}{dt} = \frac{k_+}{3}(R^3 - R_N^3) - \frac{k_-}{3} R_N^3$$

$\Rightarrow$ at steady state, $\frac{dR}{dt} = 0$ and $$\boxed{\frac{R_N}{R} = \left(1 + \frac{k_-}{k_+}\right)^{-1/3}}$$

Now sub with R_N/R in $(*)$ $\Rightarrow$ result

NB, your analysis looks fine,
give or take factor of 6!

Tumour Growth Q3

(a) standard bookwork.
care needed to interpret mixed BC.

b) $$\left.\begin{aligned} 0 &= \frac{1}{r^2}(r^2\beta_r)_r - \beta_\infty . \\ \beta_r &= 0 \quad \text{at} \quad r=0 \\ \beta_r &= h(\beta_\infty - \beta) \quad \text{on} \quad r=R . \end{aligned}\right\}$$

$$\beta = \frac{\beta_\infty r^2}{6} + A + \frac{B}{r} .$$ with $B=0$ s.t. $\beta_r = 0$ at $r=0$.

$$\beta_r = \frac{\beta_\infty r}{3}$$

$\Rightarrow$ BC at $r=R$ supplies: $$\frac{\beta_\infty R}{3} = h\left(\beta_\infty - \frac{\beta_\infty R^2}{6} - A\right)$$

$$\Rightarrow A = \beta_\infty\left(1 - \frac{R^2}{6} - \frac{1}{h}\cdot\frac{R}{3}\right).$$

$$\Rightarrow \beta(r,t) = \beta_\infty - \frac{\beta_\infty}{h}\cdot\frac{R}{3} - \frac{\beta_\infty}{6}(R^2 - r^2)$$

s'pose $h=2$ $$\beta(r,t) = \beta_\infty - \frac{\beta_\infty R}{6} - \frac{\beta_\infty}{6}(R^2 - r^2)$$

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

$$= \int_0^R \left\{ s - \beta_\infty + \frac{\beta_\infty R}{6} + \frac{\beta_\infty}{6}(R^2 - r^2)\right\} r^2\,dr$$

$$= \frac{R^3}{3}\left(s - \beta_\infty + \frac{\beta_\infty R}{6}\right) + \frac{\beta_\infty}{6}\cdot R^5 \underbrace{\left(\frac{1}{3} - \frac{1}{5}\right)}_{\frac{2}{15}}$$

$$R^2\frac{dR}{dt} = \frac{R^3}{3}\left\{ s - \beta_\infty + \frac{\beta_\infty R}{6} + \frac{\beta_\infty R^2}{15}\right\}$$

$$\frac{dR}{dt} = \frac{\beta_\infty R}{3}\left(\frac{s}{\beta_\infty} - 1 + \frac{R}{6} + \frac{R^2}{15}\right)$$

* $\beta_\infty > S \Rightarrow \begin{cases} R = 0 \text{ is stable st. state} \\ \exists \text{ unstable s.t. st. with } 2R/15 = -\frac{1}{6} + \sqrt{\frac{1}{36} + 15.(1 - S/\beta_\infty).4} \end{cases}$
* otherwise if $S > \beta_\infty$, $\frac{dR}{dt} > 0 \Rightarrow$ growm until $\beta_{min} = 0$

$$\beta_{min} = \beta(0,t) = \beta_\infty - \frac{\beta_\infty R^2}{6} - \frac{\beta_\infty R^2}{6}$$

$= 0$ when $6 - R - R^2 = 0$

when $R^2 + R - 6 = (R-2)(R+3) = 0$

when $\underline{R = 2.}$

for $R > 2$, $\beta = \begin{cases} 0 & 0 < r < R_N \\ \frac{\beta_\infty r^2}{6} + A + \frac{B}{r} & R_N < r < R. \end{cases}$

with A, B chosen s.t.

$$\frac{\beta R_N^2}{6} + A + \frac{B}{R_N} = 0.$$

$$\frac{\beta R_N}{3} - \frac{B}{R_N^2} = 0 \quad \Rightarrow B = \frac{\beta R_N^3}{3}$$

$$\Rightarrow A = -\frac{\beta R_N^2}{6} - \frac{\beta R_N^2}{3}$$

$$\Rightarrow \beta = \begin{cases} 0 \\ -\frac{\beta R_N^3}{3}\left(\frac{1}{R_N} - \frac{1}{r}\right) + \frac{\beta}{6}(r^2 - R_N^2) \end{cases}$$

where R_N chosen s.t. $\beta_r = h(\beta_\infty - \beta)$ on $r = R$.

and $0 = \int_{R_N}^{R} (S - \beta) r^2 dr.$

Tumour Growth : Q3

drug/poison satisfies :
$$\begin{cases} 0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial \beta}{\partial r}\right) - \beta_\infty \\ \beta_r = 0 \quad \text{at} \quad r=0 \\ \beta_r = h(\beta_\infty - \beta) \quad \text{on} \quad r = R(t) \end{cases}$$

$$\Rightarrow \quad \beta(r,t) = A(t) + \frac{B(t)}{r} + \frac{\beta_\infty r^2}{6}.$$

impose BCs at $r=0, R(t)$ to determine $A(t)$, $B(t)$.

Tumour Growth : Q4

[Earlier parts standard just algebra].

$$\left(1-\frac{\mu s^2}{4}\right)^{1+\alpha} \approx 1 - \frac{\mu s^2}{4}\cdot(1+\alpha) + O(s^4)$$

ie it's an exponent now perform Taylor series expansion of this term, with $s^2 \ll 1$

(d) $$s\frac{ds}{d\tau} = \frac{2}{\mu(1+\alpha)}\cdot\left\{1 - \overbrace{\left(1-\frac{\mu s^2}{4}\right)^{1+\alpha}}^{\left(1-\frac{\mu s^2}{4}\right)^{1+\alpha}}\right\} \quad (*)$$

If $s \ll 1$, then ODE reduces to give

$$s\frac{ds}{d\tau} \approx \frac{2}{\mu(1+\alpha)}\left\{1 - \left(1 - (1+\alpha)\frac{\mu s^2}{4}\right) + O(s^4)\right\}$$

$$\Rightarrow s\frac{ds}{d\tau} \approx \frac{2}{\mu(1+\alpha)}\cdot\frac{(1+\alpha)\mu s^2}{4} \approx \frac{s^2}{2}.$$

$$\Rightarrow \frac{ds}{d\tau} = \frac{s}{2}$$: exponential growth ie $s=0$ is unstable steady state.

B, you could instead define $\boxed{A(t) = \pi s^2}$. Then $(*)$ supplies

$$\frac{dA}{d\tau} = \frac{4\pi}{\mu(1+\alpha)}\cdot\left\{1 - \left(1 - \frac{\mu}{4\pi}A\right)^{1+\alpha}\right\}$$

(viii)

Age-Structured Models

Q1,

(a) * $n(0,a) = f(a)$: $f(a)$ defines initial age distribution of population (at $t=0$).

* $\underbrace{n_t + n_a}_{\text{ageing}} = \underbrace{-\mu n}_{\text{death}}$: PDE describes how age distribution evolves over time. Population ages at same rate as "real" time & individuals die at constant rate μ (which is indep of age).

* $n(t,0) = B(t) = \int_0^\infty \beta(\theta) n(t,\theta)\, d\theta$; $B(t)$ = birth rate ie rate at which new individuals of age $a=0$ enter pop^n. We assume that individuals of age a reproduce at rate $\beta(a)$ s.t. total birth rate at time t, $B(t) = \int_0^\infty \beta(\theta) n(t,\theta)\, d\theta$.

(b) as per Q1, with $\mu(\theta) = \mu$, constant.

(c) S'pose $n(t,a) \sim e^{\gamma t} F(a)$. Then

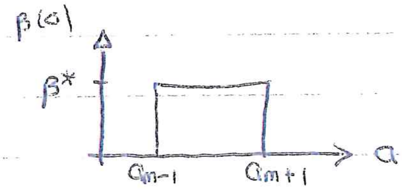
$$B(t) = \int_0^\infty \beta(\theta) n(t,\theta)\, d\theta \sim e^{\gamma t} \underbrace{\int_0^\infty \beta(\theta) F(\theta)\, d\theta}_{= I_F\text{, say}}$$

But
$$B(t) = e^{\gamma t} I_F = \int_0^t \beta(\theta) B(t-\theta) e^{-\mu\theta}\, d\theta + \underbrace{e^{-\mu t}\int_t^\infty \beta(\theta) f(\theta - t)\, d\theta}_{\to 0 \text{ as } t\to\infty}.$$

$$\sim \int_0^t \beta(\theta) e^{\gamma(t-\theta)} e^{-\mu\theta}\, d\theta \; I_F$$

In limit as $t \to \infty$ we have

$$1 \sim \int_0^\infty \beta(\theta) e^{-(\gamma+\mu)\theta}\, d\theta, \quad \text{as req}^d,$$



(d) S'pose $\beta(a) = \begin{cases} \beta^* & a_{m-1} < a < a_{m+1} \\ 0 & \text{o/w} \end{cases}$

For time-indep sol^n, $\gamma = 0 \Rightarrow 1 \approx \int_0^\infty \beta(\theta) e^{-\mu\theta}\, d\theta$
$= \beta^* \int_{a_{m-1}}^{a_{m+1}} e^{-\mu\theta}\, d\theta$.

1 (ct'd) $\quad 1 = \frac{\beta^*}{\mu}\left(e^{-\mu(a_m-1)} - e^{-\mu(a_m+1)}\right)$

$\Rightarrow e^{\mu a_m} = \frac{\beta^*}{\mu}(e^{\mu} - e^{-\mu})$ ie $\boxed{a_m = \frac{1}{\mu}\ln\left(\frac{\beta^*}{\mu}(e^{\mu} - e^{-\mu})\right)}$

$\Rightarrow a_m \to \ln\beta^*$ as $\mu \to \infty$.

3, $\left.\begin{aligned} &n_t + (1+\beta\phi)n_\phi = -\mu n \\ &n(\phi,0) = f(\phi) \\ &n(0,t) = 2n(1,t) \end{aligned}\right\}$

[comment: I think Q3 is on FMB Sheet 4].

Seek soln's: $n(\phi,t) \sim e^{\gamma t}N(\phi) \Rightarrow (1+\beta\phi)\frac{dN}{d\phi} = -(\mu+\gamma)N$

$\Rightarrow \ln\left|\frac{N(\phi)}{N(0)}\right| = -\frac{\mu+\gamma}{\beta}\ln(1+\beta\phi)$

$\Rightarrow N(\phi) = N(0)(1+\beta\phi)^{-(\mu+\gamma)/\beta}$

where $N(0) = 2N(1)$ if

$$\ln 2 = \frac{\mu+\gamma}{\beta}\ln(1+\beta).$$

For t-indep soln's, $\gamma = 0 \Rightarrow \boxed{\mu = \mu^*(\beta) = \frac{\beta\ln 2}{\ln(1+\beta)}}$

Age-Structure : Q2

$$\left.\begin{aligned} v_t + r(a) v_a &= -\mu(V, a) v \\ V(t) &= \int_0^L \xi_v\, v(a,t)\, da. \end{aligned}\right\} \quad (*_1)$$

$$\left.\begin{aligned} u_t + (r(a) u)_a &= -\mu(U, a) u. \\ U(t) &= \int_0^L \xi_u .\, u(a,t)\, da. \end{aligned}\right\} \quad (*_2)$$

Let ~~u(a,t)~~ $v = r(a) u(a,t)$ in $(*_2)$ & multiply by $r(a)$

$$\Rightarrow \quad v_t + r(a) v_a = -\mu(V, a) v$$

$$V(t) = \int \xi_u . u(a,t)\, da = \int \frac{\xi_u}{r(a)} . v(a,t)\, da.$$

ie let $\boxed{\xi_v = \xi_u(a)/r(a)}$.

s'pose $\xi_v = 1$, $r(a) = 1 + \alpha a$, $\mu(V, a) = \mu_0 + \mu_1 V$. Then $(*_1)$ supplies

$$v_t + (1 + \alpha a) v_a = -(\mu_0 + \mu_1 V).v \quad , \quad V(t) = \int_0^L v(a,t)\, da$$

Let $v(a,t) = V(t) A(a)$.

$$\frac{V_t}{V} + (1 + \alpha a) \frac{A'}{A} = -(\mu_0 + \mu_1 V)$$

$$\Rightarrow \underbrace{\frac{V_t}{V} + (\mu_0 + \mu_1 V)}_{t\text{-dep.}} = \underbrace{-(1 + \alpha a) \frac{A'}{A}}_{a\text{-dep.}} = \underbrace{\gamma}_{\text{sep}^n \text{ const.}}$$

$$V_t = V(\gamma - \mu_0 - \mu_1 V) \quad , \quad \frac{A'}{A} = \frac{-\gamma}{1 + \alpha a}. \quad \left\{ \text{with } 1 = \int_0^L A(a)\, da \right.$$

$$\ln A = -\frac{\gamma}{\alpha} \ln(1+\alpha a) + C.$$

$$A = C / (1+\alpha a)^{\gamma/\alpha}. \Rightarrow A(a) = \frac{A(0)}{(1+\alpha a)^{\gamma/\alpha}}.$$

$$A(0) = 2A(L) \Rightarrow (1+\alpha L)^{\gamma/\alpha} = 2.$$

$$\Rightarrow \gamma = \frac{\alpha . \ln 2}{\ln(1+\alpha L)}. \quad : A(a) = \frac{A(0)}{(1+\alpha a)^{\gamma/\alpha}}$$

$$A(0) = 1 \Big/ \left[\int_0^L \frac{da.}{(1+\alpha a)^{\gamma/\alpha}} \right]$$

recall that $V_t = (\gamma - \mu_0 - \mu_1 V) V$

$$\Rightarrow \begin{cases} V \to \dfrac{\gamma - \mu_0}{\mu_1} & \text{if } \gamma = \dfrac{\alpha \ln 2}{\ln(1+\alpha L)} > \mu_0. \\ V \to 0 & \text{if } \gamma < \mu_0. \end{cases}$$

Discrete-to-Continuum: Q3

$i-1$	i	$i+1$	$\dots$

(a)
$$L_i(t+\Delta t) = \underbrace{L_{i+1}(t)}_{\substack{\text{cell moves left}\\ \text{from box } (i+1) \text{ into}\\ \text{box } i}} + \underbrace{k_L \Delta t . R_i(t)}_{\substack{\text{cell moving}\\ \text{right in box } i\\ \text{switches dir}^n\\ \text{\& starts moving left}}} - \underbrace{k_R \Delta t \, L_i(t)}_{\substack{\text{cell in box } i \text{ switches from}\\ \text{moving left to moving right}}}.$$

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

[similar interpretation].

(b) Suppose
$$\begin{cases} \rho_L(x,t) = \rho_L(i\Delta x, t) \approx L_i(t) \\ \rho_R(x,t) = \rho_R(i\Delta x, t) \approx R_i(t). \end{cases}$$

ie replace discrete spatial variable (box # i) by cts indep vble or spatial coordinate x. Then

$$\rho_L(x, t+\Delta t) = \rho_L(x+\Delta x, t) + k_L \Delta t . \rho_R(x,t) - k_R \Delta t . \rho_L(x,t).$$

Perform Taylor series expansion:

$$\cancel{\rho_L(x,t)} + \Delta t . \frac{\partial \rho_L}{\partial t}(x,t) + O(\Delta t^2) = \cancel{\rho_L(x,t)} + \Delta x . \frac{\partial \rho_L}{\partial x}(x,t) + O(\Delta x^2)$$
$$+ k_L \Delta t . \rho_R(x,t) - k_R \Delta t . \rho_L(x,t)$$

Divide by Δt ~~& take limit as $\Delta x, \Delta t \to 0$~~

$$\frac{\partial \rho_L}{\partial t} = \left(\frac{\Delta x}{\Delta t}\right) \frac{\partial \rho_L}{\partial x} + k_L \rho_R - k_R \rho_L . + O(\Delta t, \Delta x).$$

Take limit as $\Delta x, \Delta t \to 0$:

$$\Rightarrow \boxed{\frac{\partial \rho_L}{\partial t} - v \frac{\partial \rho_L}{\partial x} = k_L \rho_R - k_R \rho_L} \quad \text{where} \quad \boxed{v = \lim_{\Delta x, \Delta t \to 0} \frac{\Delta x}{\Delta t}}$$

Equation for $\rho_R(x,t)$ follows similarly

Age-Structure : Q3 (ct'd).

(c) Given (from earlier)

$$(*) \quad \begin{cases} \rho_{Lt} - v\rho_{Lx} = k_L \rho_R - k_R \rho_L \\ \rho_{Rt} + v\rho_{Rx} = k_R \rho_L - k_L \rho_R . \end{cases}$$

where $k_L, k_R >> 1$

Let $k_L = \bar{k}_L/\varepsilon$, $k_R = \bar{k}_R/\varepsilon$. Then, at leading order (*) supplies :

$$\rho_R \approx \frac{k_R}{k_L} \cdot \rho_L .$$

Add PDEs for ρ_L, ρ_R :

$$(\rho_L + \rho_R)_t - v(\rho_L - \rho_R)_x = 0$$

Sub for $\rho_R = \frac{k_R}{k_L} \cdot \rho_L$

$$\Rightarrow \quad \left(1 + \frac{k_R}{k_L}\right)\rho_{Lt} - v\left(1 - \frac{k_R}{k_L}\right)\rho_{Lx} = 0.$$

1D wave equation for $\rho_L(x,t)$

$$\rho_{Lt} - \bar{V}\rho_{Lx} = 0 \qquad \bar{V} = \frac{v(1 - k_R/k_L)}{(1 + k_R/k_L)}$$

$$\Rightarrow \begin{cases} \rho_L(x,t) = R(x - \bar{V}t) \\ \rho_R(x,t) = \frac{k_R}{k_L} \cdot R(x - \bar{V}t) \end{cases} \quad \text{where } \rho(x,0) = R(x)$$

$k_L > k_R \Rightarrow \bar{V} > 0 \Rightarrow \rho_L, \rho_R$ move left to right

$k_R > k_L \Rightarrow \bar{V} < 0 \Rightarrow \rho_L, \rho_R$ move right to left.

FMB : Sheet 4

Q1, $N_t + N_a = -\mu(a) N$ with $\begin{cases} N(0,a) = F(a) \\ N(t,0) = B(t) = \int_0^\infty \beta(a) N(t,a)\, da. \end{cases}$

(a) Method of characteristics : $N(t,a) = \tilde{N}(s,r)$ where $\begin{cases} s & \text{param's char's} \\ r & \text{param's data.} \end{cases}$

$$\frac{dt}{ds} = 1 = \frac{da}{ds}, \quad \frac{d\tilde{N}}{ds} = -\mu(a)\tilde{N}$$

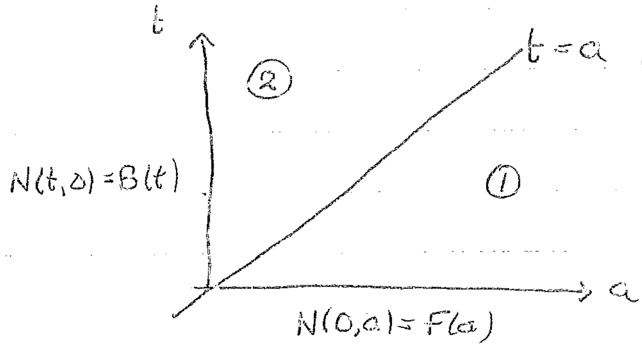
with either * $t=0,\ a=r,\ \tilde{N} = F(r)$ when $s=0$ (region (1))
or, * $t=r,\ a=0,\ \tilde{N} = B(r)$ " " (region (2))

In region (1) : $t=s,\ a=s+r \Rightarrow r = a-t.$

$$\frac{1}{\tilde{N}}\frac{d\tilde{N}}{ds} = -\mu(s+r) \Rightarrow \tilde{N}(s,r) = F(r)\exp\left(-\int_{\hat{s}=0}^{s} \mu(\hat{s}+r)\, d\hat{s}\right)$$

$$\Rightarrow N(t,a) = F(a-t)\exp\left(-\int_{\tau=a-t}^{a} \mu(\tau)\, d\tau\right)$$

solution valid for $0 < t < a$.



In region (2) : $t = s+r,\ a = s$

$$\frac{1}{\tilde{N}}\frac{d\tilde{N}}{ds} = -\mu(s)$$

$$\Rightarrow \tilde{N}(s,r) = B(r)\exp\left(-\int_{\hat{s}=0}^{s} \mu(\hat{s})\, d\hat{s}\right)$$

$$\Rightarrow N(t,a) = B(t-a)\exp\left(-\int_{\tau=0}^{a} \mu(\tau)\, d\tau\right) \quad \text{for } 0 < a < t.$$

where $$B(t) = \int_0^\infty \beta(a) N(t,a)\, da = \underbrace{\int_0^t \beta(a) N(t,a)\, da}_{\text{region (2)}} + \underbrace{\int_t^\infty \beta(a) N(t,a)\, da}_{\text{region (1)}}$$

$$\Rightarrow B(t) = \int_0^t \beta(a) B(t-a) e^{-\int_0^a \mu(\tau)d\tau}\, da + \int_t^\infty \beta(a) F(a-t) e^{-\int_{a-t}^{a} \mu(\theta)d\theta}\, da.$$

1 (ct'd)

(b) Suppose: $\beta(a) = \beta$, $\mu(a) = \mu$, $N(t,a) \sim e^{\gamma t} S(a)$ as $t \to \infty$.

Then

$$B(t) = \int_0^\infty \beta(a) N(t,a)\,da \sim \beta e^{\gamma t} \int_0^\infty S(a)\,da \quad \text{as } t \to \infty.$$

$$\Rightarrow B(t) \sim \beta I e^{\gamma t} \quad \text{where } I = \int_0^\infty S(a)\,da.$$

Now, from part (a),

$$B(t) = \beta \int_0^t B(t-\tau) e^{-\mu\tau}\,d\tau + \underbrace{\beta \int_t^\infty F(\tau - t) e^{-\mu t}\,d\tau}_{\to 0 \text{ as } t \to \infty}.$$

$$\Rightarrow B(t) \sim \beta I e^{\gamma t} \approx \beta \int_0^t \underbrace{\left(\beta I e^{\gamma(t-\tau)}\right)}_{=B(t-\tau)} e^{-\mu\tau}\,d\tau.$$

$$\Rightarrow 1 \sim \beta \int_0^t e^{-(\gamma+\mu)\tau}\,d\tau = \frac{\beta}{\gamma+\mu}\left(1 - e^{-(\gamma+\mu)t}\right)$$

$$\to \frac{\beta}{\gamma+\mu} \quad \text{as } t \to \infty.$$

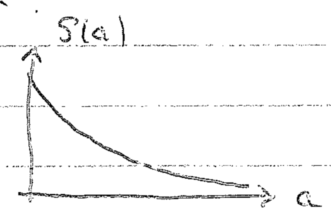
$$\Rightarrow \boxed{\gamma \sim \beta - \mu,} \quad \text{as req}^d,$$

From part (a), $N(t,a) \sim B(t-a) e^{-\mu a}$ for $a < t$.

where $B(t) \sim \beta I e^{\gamma t}$

$$\Rightarrow N(t,a) \sim e^{\gamma t} S(a) \sim \beta I e^{\gamma(t-a)} e^{-\mu a}$$

$$\Rightarrow S(a) = \beta I e^{-(\gamma+\mu)a} = \beta I e^{-\beta a}$$



here $I = \int_0^\infty S(a)\,da = 1$, wlog.

Note: $S(a)$ indep of whether $\gamma > 0$, $\gamma = 0$, $\gamma < 0$.

However,

$$N(t,a) \sim e^{\gamma t} S(a) \sim \beta e^{\gamma t} . e^{-\beta a} \quad \text{where } \gamma \sim \beta - \mu.$$

$$\Rightarrow \beta - \mu = \gamma \begin{cases} > 0 & : \text{population explodes as } t \to \infty. \\ = 0 & : \text{population attains eq}^m. \\ < 0 & : \text{pop}^n \text{ becomes extinct} \end{cases}$$

Q2, $\frac{1}{\delta} u_{xx} = u_\tau + J_{ion}(u,v)$, $v_\tau = -\gamma v + u$ $\quad 0 < \delta << 1, \quad u_x|_{x=0,L} = 0.$

(a) $u = u_0(x,\tau) + \delta u_1(x,\tau) + \dots$

$$\frac{1}{\delta}\left(u_{0xx} + \delta u_{1xx} + \dots \right) = u_{0\tau} + \delta u_{1\tau} + \dots + J_{ion}(u_0, v_0).$$

$O(1/\delta)$: $u_{0xx} = 0 \Rightarrow u_0 = u_0(\tau) \quad \because u_{0x}|_{x=0,L} = 0.$

comment: what about initial cond^{n}s: in practice, $\exists$ rapid transient, during which influence of ICs lost (scale eg $\tau = \delta t$)

(b) Equation for v: $v_{0\tau} = -\gamma v_0 + u_0(\tau).$

$$\Rightarrow v_0(x,\tau) = \underbrace{v_*(x) e^{-\gamma\tau}}_{v_0(x,0) = v_*(x)} + e^{-\gamma\tau}\int_0^\tau e^{\gamma s} u_0(s)\,ds.$$

For τ suff large $\left(\tau > \frac{1}{\gamma}\ln\left(\frac{1}{\delta^2}\sup v_*\right),\ x \in [0,L]\right)$

$$\left| v_0(x,\tau) - e^{-\gamma\tau}\int_0^\tau e^{\gamma s} u_0(s)\,ds \right| \le \delta^2$$

Define $q_0(\tau) = e^{-\gamma\tau}\int_0^\tau e^{\gamma s} u_0(s)\,ds.$

$\Rightarrow v_0(x,\tau) = q_0(\tau) + O(\delta^2)$ for τ suff large

where $\frac{dq_0}{d\tau} = -\gamma q_0 + u_0.$

At the next order in δ, $u_{1xx} = u_{0\tau} + J_{ion}(u_0, q_0).$

$v_0 = q_0$ at leading order.

$$\Rightarrow u_1(x,\tau) = \frac{x^2}{2}\left(u_{0\tau} + J_{ion}(u_0,q_0)\right) + \alpha x + \beta.$$

where $u_{1x} = 0$ @ $x = 0, L$ $\Rightarrow \alpha = 0$ & $\left[u_{0\tau} + J_{ion}(u_0,q_0)\right] L = 0$

$\Rightarrow u_{0\tau} + J_{ion}(u_0, q_0) = 0$, as req^d.