Mathematical Biology Assignment 2

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September 24, 2019

Normally I would paraphrase the the questions, but instead I have appended the question sheet to the end

1. (a) Given the reaction occurs stepwise

   We have $i = 0, 1$ and $j = 0$ so we can write the system as:

$$S_{0,j} \underset{\beta}{\overset{2\alpha}{\rightleftharpoons}} S_{1,j} \underset{2\beta}{\overset{\alpha}{\rightleftharpoons}} S_{2,j}$$
$$S_{i,0} \underset{\gamma}{\overset{\delta}{\rightleftharpoons}} S_{i,1}$$

   So the DE system is:

$$\frac{\partial S_{00}}{\partial t} = -2\alpha S_{00} - \delta S_{00} + \beta S_{10} + \gamma S_{01}$$
$$\frac{\partial S_{01}}{\partial t} = -2\alpha S_{01} - \gamma S_{01} + \beta S_{11} + \delta S_{00}$$
$$\frac{\partial S_{10}}{\partial t} = -\alpha S_{10} - \beta S_{10} - \delta S_{10} + 2\beta S_{20} + 2\alpha S_{00} + \gamma S_{11}$$
$$\frac{\partial S_{11}}{\partial t} = -\alpha S_{11} - \beta S_{11} - \gamma S_{11} + 2\beta S_{21} + 2\alpha S_{01} + \delta S_{10}$$
$$\frac{\partial S_{20}}{\partial t} = -2\beta S_{20} - \delta S_{20} + \alpha S_{10} + \gamma S_{21}$$
$$\frac{\partial S_{21}}{\partial t} = -2\beta S_{21} - \gamma S_{21} + \alpha S_{11} + \delta S_{20}$$

   With the condition that

$$\sum_i \sum_j S_{ij} = 1$$

   Or in full

$$S_{00} + S_{01} + S_{10} + S_{11} + S_{20} + S_{21} = 1$$

   (b) Noting that S_{ij} is the proportion of channels with i open m gates and j open h gates,

$$m = \frac{1}{2}S_{10} + \frac{1}{2}S_{11} + S_{20} + S_{21}$$
$$h = S_{01} + S_{11} + S_{21}$$

And taking the derivative with respect to t gives

$$\begin{aligned}
\frac{dm}{dt} &= \frac{1}{2}\frac{dS_{10}}{dt} + \frac{1}{2}\frac{dS_{11}}{dt} + \frac{dS_{20}}{dt} + \frac{dS_{21}}{dt} \\
&= \frac{1}{2}(-2\alpha S_{10} - \beta S_{10} - \delta S_{10} + 2\beta S_{20} + 2\alpha S_{00} + \gamma S_{11}) \\
&+ \frac{1}{2}(-2\alpha S_{11} - \beta S_{11} - \gamma S_{11} + 2\beta S_{21} + 2\alpha S_{01} + \delta S_{10}) \\
&+ (-2\beta S_{20} - \delta S_{20} + \alpha S_{10} + \gamma S_{21}) + (-2\beta S_{21} - \gamma S_{21} + \alpha S_{11} + \delta S_{20}) \\
\\
&= S_{00}\left(\alpha\right) + S_{01}\left(\alpha\right) + S_{10}\left(-\alpha - \frac{1}{2}\beta - \frac{1}{2}\delta + \frac{1}{2}\delta + \alpha\right) + S_{11}\left(\frac{1}{2}\gamma - \alpha - \frac{1}{2}\beta - \frac{1}{2}\gamma + \alpha\right) \\
&+ S_{20}\left(\beta - 2\beta - \delta + \delta\right) + S_{21}\left(\beta + \gamma - 2\beta - \gamma\right) \\
\\
&= \alpha S_{00} + \alpha S_{01} - \frac{1}{2}\beta S_{10} - \beta S_{11} - \beta S_{20} - \beta S_{21} \\
&= \alpha(S_{00} + S_{01}) - \beta(\frac{1}{2}S_{10} + \frac{1}{2}S_{11} + S_{20} + S_{21}) \\
\frac{dm}{dt} &= \alpha(1-m) - \beta m
\end{aligned}$$

By using

$$m = \frac{1}{2}S_{10} + \frac{1}{2}S_{11} + S_{20} + S_{21} 1 - m = S_{00} + S_{01}$$

As for h:

$$\begin{aligned}
\frac{dh}{dt} &= \frac{dS_{01}}{dt} + \frac{dS_{11}}{dt} + \frac{dS_{21}}{dt} \\
&= -2\alpha S_{01} - \gamma S_{01} + \beta S_{11} + \delta S_{00} \\
&- \alpha S_{11} - \beta S_{11} - \gamma S_{11} + 2\beta S_{21} + 2\alpha S_{01} + \delta S_{10} \\
&- 2\beta S_{21} - \gamma S_{21} + \alpha S_{11} + \delta S_{20} \\
\\
&= S_{00}\left(\delta\right) + S_{01}\left(-2\alpha - \gamma + 2\alpha\right) + S_{10}(\delta) \\
&+ S_{11}\left(\beta - \alpha - \beta - \gamma + \alpha\right) + S_{20}\left(\delta\right) + S_{21}\left(2\beta - 2\beta - \gamma\right) \\
\\
&= \delta S_{00} - \gamma S_{01} - \gamma S_{11} + \delta S_{20} - \gamma S_{21} \\
\frac{dh}{dt} &= \delta(1-h) - \gamma h
\end{aligned}$$

Using $S_{00} + S_{10} + S_{20} = 1 - h$

(c) We were given

$$S_{00} = (1-m)^2(1-h), \quad S_{10} = 2m(1-m)(1-h), \quad S_{20} = m^2(1-h)$$
$$S_{01} = (1-m)^2 h, \quad S_{11} = 2m(1-m)h, \quad S_{21} = m^2 h$$

Subbing into the S_{21} DE

LHS:

$$\begin{aligned}\frac{\partial S_{21}}{\partial t} &= \frac{\partial (m^2 h)}{\partial t} \\ &= 2mh\frac{\partial m}{\partial t} + m^2\frac{\partial h}{\partial t} \\ &= 2mh(\alpha(1-m) - \beta m) + m^2(\delta(1-h) - \gamma h) \\ &= 2\alpha mh(1-m) - 2\beta m^2 h + \delta m^2(1-h) - \gamma m^2 h\end{aligned}$$

RHS

$$\begin{aligned}\frac{\partial S_{21}}{\partial t} &= -2\beta S_{21} - \gamma S_{21} + \alpha S_{11} + \delta S_{20} \\ &= -2\beta m^2 h - \gamma m^2 h + 2\alpha m(1-m)h + \delta m^2(1-h) \\ &= 2\alpha mh(1-m) - 2\beta m^2 h + \delta m^2(1-h) - \gamma m^2 h\end{aligned}$$

And clearly $LHS = RHS$.

2. Steady states

$$\begin{aligned}0 = I^* + Av(a-v)(v-1) - w \\ 0 = bv - w\end{aligned}$$

So the nullclines are

$$\begin{aligned}w &= I^* + Av(a-v)(v-1) \\ w &= bv\end{aligned}$$

With $0 < a < 1$.

For $I^* = 0$, the fixed point is $w = v = 0$.

The oscillatory behaviour occurs when the fixed point v^* exists between the two extrema of the v nullcline

$$\begin{aligned}\frac{\partial w}{\partial v} = A\frac{\partial}{\partial v}\left(av^2 - v^3 - av + v^2\right) &= 0 \\ A\left(2av - 3v^2 - a + 2v\right) &= 0 \\ 2v(1+a) - 3v^2 - a &= 0 \\ 3v^2 - 2v(1+a) + a &= 0 \\ v &= \frac{1 + a \pm \sqrt{a^2 - a + 1}}{3}\end{aligned}$$

So for oscillatory behaviour, $v^* \in \left(\frac{1+a-\sqrt{a^2-a+1}}{3}, \frac{1+a+\sqrt{a^2-a+1}}{3}\right)$. If this is satisfied, due to the small parameter ϵ, the system will quickly jump to the v nullcline. If the fixed point exists between a local maximum and a local minimum of the v nullcline, the system will oscillate between these two extrema.

So for any v^* within this range, the requirement for I^* is:

$$\begin{aligned}bv^* &= I^* + Av^*(a-v^*)(v^*-1) \\ I^* &= bv^* - Av^*(a-v^*)(v^*-1)\end{aligned}$$

3. (a) As stated in the question: this is an age system, so $n(t,a)\delta a$ is the number of people in ages $a, a+\delta a$ at time t.
   - $\beta(a)$ is effectively a birth probability/number for individuals at age a, i.e. the number of individuals that an individual at age a will reproduce (with age 0).
   - $B(t)$ is the convolution integral of $\beta * n$. It takes the integral of the birth probability with the number of individuals at all ages. It is the number of individuals born (i.e. age 0) at time t.

   (b) First note:
$$\frac{dN}{dz} = \frac{\partial N}{\partial a}\frac{\partial a}{\partial z} + \frac{\partial N}{\partial t}\frac{\partial N}{\partial t} = \frac{\partial N}{\partial a} + \frac{\partial N}{\partial t}$$
   The equation along the curves $n(t,a) = n(t(z), a(z)) = N(z)$
$$\begin{aligned}\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} &= -\mu(a)n\\ \frac{\partial N}{\partial t} + \frac{\partial N}{\partial a} &= -\mu(a)N\\ \frac{dN}{dz} &= -\mu(a)N\end{aligned}$$

   (c) i. Integrating (3) gives
$$\begin{aligned}\frac{\partial t}{\partial z} &= 1, & \frac{\partial a}{\partial z} &= 1\\ t &= z + t_0, & a &= z + a_0\\ t &= z, & a &= z + \theta\end{aligned}$$

   $z = 0$ gives $t = 0$ and $a = \theta$.

   ii.
$$\begin{aligned}\frac{dN}{dz} &= -\mu(a)N\\ \frac{1}{N}\frac{dN}{dz} &= -\mu(z+\theta)\\ \log N &= \int_0^z -\mu(\tau+\theta)d\tau\\ N &= e^C \exp\left\{-\int_0^z \mu(\tau+\theta)d\tau\right\} N \qquad = e^C \exp\left\{-\int_\theta^{z+\theta}\mu(\tau)d\tau\right\}\end{aligned}$$
   So the $z = 0$ condition is the $N(0) = n(0,\theta) = F(\theta)$ Hence
$$\begin{aligned}N(0) &= e^C \exp\left\{-\int_\theta^\theta \mu(\tau)d\tau\right\}\\ F(\theta) &= e^C \exp\{0\}\\ \implies e^C &= F(\theta)\end{aligned}$$
$$N(z) = F(\theta)\exp\left\{-\int_\theta^{z+\theta}\mu(\tau)d\tau\right\}$$
   We can write $\theta = a - t$, and using $z + \theta = a$, we arrive at
$$n(t,a) = F(a-t)\exp\left\{-\int_{a-t}^{a}\mu(\tau)d\tau\right\}$$

(d) i. Again, integrating (3)

$$\begin{aligned}\frac{\partial t}{\partial z} &= 1, & \frac{\partial a}{\partial z} &= 1\\ t &= z + t_0, & a &= z + a_0\\ t &= z + \theta, & a &= z\end{aligned}$$

ii.

$$\begin{aligned}\frac{dN}{dz} &= -\mu(a)N\\ \frac{1}{N}\frac{dN}{dz} &= -\mu(z)\\ \log N &= \int_0^z -\mu(\tau)d\tau\\ N &= e^{C_2}\exp\left\{-\int_0^z \mu(\tau)d\tau\right\}\end{aligned}$$

The $z = 0$ condition instead gives $N(0) = n(\theta, 0) = B(\theta)$,

$$\begin{aligned}N(0) &= e^{C_2}\exp\left\{-\int_0^0 \mu(\tau)d\tau\right\}\\ B(\theta) &= e^{C_2}e^0\\ \implies e^{C_2} &= B(\theta)\end{aligned}$$

And hence

$$N = B(\theta)\exp\left\{-\int_0^z \mu(\tau)d\tau\right\}$$

Then, using

$$t - a = z + \theta - z = \theta, \quad \text{and,} \quad a = z$$

We get

$$N(z) = B(t-a)\exp\left\{-\int_0^a \mu(\tau)d\tau\right\}$$

And hence

$$n(t,a) = B(t-a)\exp\left\{-\int_0^a \mu(\tau)d\tau\right\}$$

(e) Using the definition of B: And the fact that

$$n(t,a) = \begin{cases} F(a-t)\exp\left\{-\int_{a-t}^a \mu(\tau)d\tau\right\} & 0 < t < a\\ B(t-a)\exp\left\{-\int_0^a \mu(\tau)d\tau\right\}, & t > a\end{cases}$$

$$\begin{aligned}B(t) &= \int_0^\infty \beta(a)n(t,a)da\\ &= \int_0^\infty \beta(\tau)n(t,\tau)d\tau\\ &= \int_0^t \beta(\tau)n(t,\tau)d\tau + \int_t^\infty \beta(\tau)n(t,\tau)d\tau\\ B(t) &= \int_0^t \beta(\tau)B(t-\tau)\exp\left\{-\int_0^\tau \mu(q)dq\right\}d\tau + \int_t^\infty \beta(\tau)F(\tau-t)\exp\left\{-\int_{\tau-t}^\tau \mu(\tau)d\tau\right\}d\tau\end{aligned}$$

4. (a) The steady state distribution obeys $\frac{\partial c}{\partial t} = 0$

$$D\frac{\partial^2 c}{\partial x^2} - kc = 0$$
$$\frac{\partial^2 c}{\partial x^2} = \frac{k}{D}c$$

Given that $kD > 0$,

$$c(x) = Ae^{\sqrt{kD}x} + Be^{-\sqrt{kD}x}$$

To satisfy the two BCs:

$$c(0) = c_0 = A + B$$
$$\frac{\partial c}{\partial x}\Big|_L = 0 = \sqrt{\frac{k}{D}}\left(Ae^{\sqrt{k/D}L} + Be^{-\sqrt{k/D}L}\right)$$
$$0 = Ae^{\sqrt{k/D}L} + Be^{-\sqrt{k/D}L}$$
$$B = -Ae^{2\sqrt{k/D}L}$$
$$\implies A - Ae^{2\sqrt{k/D}L} = c_0$$
$$A = \frac{c_0}{1 - e^{2\sqrt{k/D}L}}$$

$$c(x) = \frac{c_0}{1 - e^{2\sqrt{k/D}L}}\left(e^{\sqrt{k/D}x} - e^{2\sqrt{k/D}L}e^{-\sqrt{k/D}x}\right)$$

(b)

$$c = \theta$$
$$\frac{c_0}{1 - e^{2\sqrt{k/D}L}}\left(e^{\sqrt{k/D}x_\theta} - e^{2\sqrt{k/D}L}e^{-\sqrt{k/D}x_\theta}\right) = \theta$$
$$e^{\sqrt{k/D}x_\theta} - e^{2\sqrt{k/D}L}e^{-\sqrt{k/D}x_\theta} = \frac{\theta(1 - e^{2\sqrt{k/D}L})}{c_0}$$
$$e^{\sqrt{k/D}x_\theta} - e^{\sqrt{k/D}(2L - x_\theta)} = \frac{\theta(1 - e^{2\sqrt{k/D}L})}{c_0}$$

x_θ is the solution to this expression.

(c) If we write the equation as:

$$e^{-2\sqrt{k/D}L}e^{\sqrt{k/D}x_\theta} - e^{-\sqrt{k/D}x_\theta} = e^{-2\sqrt{k/D}L}\frac{\theta(1 - e^{2\sqrt{k/D}L})}{c_0}$$
$$e^{-2\sqrt{k/D}L}e^{\sqrt{k/D}x_\theta} - e^{-\sqrt{k/D}x_\theta} = \frac{\theta(e^{-2\sqrt{k/D}L} - 1)}{c_0}$$

Sending $L \to \infty$, we get $e^{-L} \to 0$. So the equation becomes

$$\begin{aligned}
-e^{-\sqrt{k/D}x_\theta} &= -\theta/c_0 \\
e^{-\sqrt{k/D}x_\theta} &= \theta/c_0 \\
-\sqrt{k/D}x_\theta &= \log(\theta/c_0) \\
x_\theta &\to \frac{\log(c_0/\theta)}{\sqrt{k/D}} \\
x_\theta &\to \sqrt{\frac{D}{k}} \log(c_0/\theta)
\end{aligned}$$

So when the column is infinitely long, we find that the distance x_θ, where the cells become able to divide relates to the chemical concentration at the bottom of the column, the threshold θ, the rates of diffusion and chemical consumption. The ratio of diffusion to consumption, and bottom concentration to

x_θ will be the point where cells can no longer divide. Hence it makes sense that it increases with diffusion and base nutrient c_0, and similarly how it decreases with consumption rate and threshold θ.

5. (a) And note

$$\begin{aligned}
\frac{\partial}{\partial x} &= \frac{\partial z}{\partial x}\frac{\partial}{\partial z} \\
\frac{\partial N}{\partial t} &= \frac{dN}{dz}\frac{\partial z}{\partial t} = -c\frac{dN}{dz} = -cN' \\
\frac{\partial N}{\partial x} &= \frac{dN}{dz}\frac{\partial z}{\partial x} = \frac{dN}{dz} = N'
\end{aligned}$$

And apply this to the equation:

$$\begin{aligned}
\frac{\partial n}{\partial t} &= \frac{\partial}{\partial x}\left(n\frac{\partial n}{\partial x}\right) + n(1-n) \\
-cN' &= \frac{d}{dz}\left(NN'\right) + N(1-N) \\
-cN' &= (N')^2 + NN'' + N(1-N) \\
NN'' &= -cN' - N'^2 - N(1-N) \\
N'' &= -\frac{N'}{N}\left(c + N'\right) + N - 1
\end{aligned}$$

Letting $P(z) = N'(z) = \frac{dN}{dz}$, gives the system

$$\begin{aligned}
N'(z) &= P(z) \\
P'(z) &= -\frac{P(z)}{N(z)}\left(c + P(z)\right) + N(z) - 1
\end{aligned}$$

(b) Make the change of variables on z:

$$\zeta = \int_0^z \frac{1}{N(\eta)} d\eta$$

$$\begin{aligned}\frac{\partial}{\partial z}N(z) &= \frac{\partial N}{\partial \zeta}\frac{1}{N(z)}\\ N(z)\frac{\partial N(z)}{\partial z} &= \frac{\partial N(\zeta)}{\partial \zeta}\\ N(z)P(z) &= P(\zeta)\end{aligned}$$

so that

$$\begin{aligned}N' &= NP\\ P' &= -P\left(c+P\right)+N(N-1)\end{aligned}$$

Clearly the N nullclines are for $P=0$ and $N=0$
P nullclines with $P=0$:

$$\begin{aligned}-P\left(c+P\right)+N(N-1) &= 0\\ 0\left(c+0\right)+N(N-1) &= 0\\ N-1=0, \quad N &= 0\\ N &= 1\end{aligned}$$

Nullclines of the second equation with $N=0$:

$$\begin{aligned}-P\left(c+P\right) &= 0\\ P=0, \quad P &= -c\end{aligned}$$

Hence the fixed points are

$$(N,P)=\begin{cases}(1,0)\\(0,0)\\(0,-c)\end{cases}$$

(c) Typo in this question - should be $N(z)$ against z.

(d)

$$\begin{aligned}P(z)=N'(z) &= c(N(z)-1)\\ N(z) &= ke^{cz}+1\\ N'(z) &= kce^{cz}\\ N''(z) &= kc^2e^{cz}=cN'(z)=c^2(N(z)-1)\end{aligned}$$

With BC $N=0$ at $z=z_c$, giving

$$\begin{aligned}N(z_c)=0 &= ke^{cz_c}+1\\ k &= -e^{-cz_c}\end{aligned}$$

$$\begin{aligned}-cN' &= \left(N'\right)^2+NN''+N(1-N)\\ -c^2ke^{cx} &= k^2c^2e^{2cx}+kc^2e^{cx}(ke^{cx}+1)+(ke^{cx}+1)(-ke^{cx})\\ -c^2 &= kc^2e^{cx}+c^2(ke^{cx}+1)-ke^{cx}+1\end{aligned}$$

$$
\begin{aligned}
-cN' &= (N')^2 + NN'' + N(1-N) \\
-c^2(N(z)-1) &= (c(N(z)-1))^2 + N(z)(c^2(N(z)-1)) + N(z)(1-N(z)) \\
-c^2N(z) + c^2 &= c^2N^2(z) - 2c^2N^2(z) + c^2 + c^2N^2(z) - N(z) + N(z) - N^2(z) \\
-c^2N(z) &= c^2N^2(z) - 2c^2N^2(z) + c^2N^2(z) - N^2(z)
\end{aligned}
$$

$z > z_c$ refers to $x - ct > z_c$, i.e. for early time, and position sufficiently towards infinity

School of Mathematical Sciences

Mathematical Biology (Honours)

Assignment 2 question sheet

Due: Friday, 20 September, by 11am
(bring to lecture, or leave in box on office door)

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1. An ion channel has gates / subunits of two different types, M and H, say, which can be either open or closed. Suppose the channel has two M gates and one H gate. Let S_{ij} denote the proportion of channels with i open M gates and j open H gates, and let m and h denote the proportion of open M and H gates, respectively.

   (a) Assume that changes in the state of a channel occur stepwise, so, for example, a channel with no open gates must first become one with one open gate (it cannot jump straight to the state of having two or three open gates). If the rates of opening and closing are α and β, respectively, for M gates, and δ and γ for H gates, write down the ODEs governing the S_{ij} where $i = 0, 1, 2$, $j = 0, 1$. (*Hint:* It may help to draw out the reaction scheme, as in §3.3.2 of the notes.)

   (b) Write down expressions for m and h in terms of the S_{ij}. Hence show they satisfy
   $$\frac{dm}{dt} = \alpha(1-m) - \beta m, \qquad \frac{dh}{dt} = \delta(1-h) - \gamma h.$$

   (c) By substituting into one of the equations you derived in part (a), verify that the solutions for the S_{ij} in terms of m and h given in lectures are indeed solutions of the relevant equations, provided m and h satisfy the equations above.
   [10 marks]

2. The Fitzhugh-Nagumo model for an action potential is:
   $$\varepsilon \frac{dv}{dt} = I^* + Av(a-v)(v-1) - w$$
   $$\frac{dw}{dt} = bv - w,$$
   where $0 < a < 1$, $\varepsilon \ll 1$, and I^* represents the externally applied current . Show that the system can spontaneously oscillate if $I^* > 0$. Give an explicit criterion for such oscillations to occur, in terms of A, a, b and v^* (where v^* denotes the value of v at a homogeneous steady state of the equations with $I^* > 0$). [6 marks]

3. **(An age-structured model for a population)**. Consider a generalised version of the age-structured model for chemotherapy from lectures, which we now interpret as an age-structured model for a population which reproduces asexually. Individuals in the population can take any age, $a \in [0, \infty)$, and we assume their death rate is dependent only on their age, so $\mu = \mu(a)$. The governing equation is thus

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

where $n(t, a)\, \delta a$ is the number of individuals with ages between a and $a + \delta a$ at time t. We impose the more general initial and boundary conditions

$$n(0, a) = F(a), \qquad n(t, 0) = B(t) = \int_0^\infty \beta(a) n(t, a)\, da,$$

where $\mu(a)$, $F(a)$ and $\beta(a)$ are positive-valued functions. We solve this model using the **method of characteristics**.

(a) Give a biological interpretation of the functions $\beta(a)$ and $B(t)$.

(b) Consider the curves in the (a, t) plane given by $a = a(z)$, $t = t(z)$, for some parameter z. Hence, along these curves, $n(t, a) = n(t(z), a(z)) = N(z)$. By making a change of variable, show that along such curves, equation (1) can be reduced to

$$\frac{dN}{dz} = -\mu(a)N, \tag{2}$$

provided

$$\frac{\partial t}{\partial z} = 1, \qquad \frac{\partial a}{\partial z} = 1. \tag{3}$$

(c) Now consider the case $0 < t < a$.

i. Integrate (3) to obtain a and t as functions of z, imposing the conditions

$$t = 0, \quad a = \theta, \quad \text{at } z = 0, \quad (\text{where } 0 < \theta < \infty).$$

Sketch some examples of these curves in the (a, t) plane. What condition is obeyed by $N(z)$ when $z = 0$?

ii. By integrating (2) with respect to z and imposing the condition at $z = 0$, show that

$$N(z) = F(\theta) \exp\left\{ -\int_\theta^{z+\theta} \mu(\tau)\, d\tau \right\},$$

and hence that

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

(d) Now consider the case $t > a$.

i. Integrate (3) to obtain a and t as functions of z, imposing the conditions

$$t = \theta, \quad a = 0, \quad \text{at } z = 0.$$

Again, sketch some examples of these curves in the (a, t) plane. What condition is now obeyed by $N(z)$ when $z = 0$?

ii. By integrating (2) with respect to z and imposing the condition at $z = 0$, show that

$$N(z) = B(\theta) \exp \left\{ -\int_0^z \mu(\tau)\, d\tau \right\},$$

and hence that

$$n(t, a) = B(t - a) \exp \left\{ -\int_0^a \mu(\tau)\, d\tau \right\} \quad \text{for } t > a,$$

(e) Using your answers to the previous two parts, show that $B(t)$ satisfies the integral equation:

$$B(t) = \int_0^t \beta(\tau) B(t-\tau) \exp \left\{ -\int_0^\tau \mu(q)\, dq \right\} d\tau + \int_t^\infty \beta(\tau) F(\tau-t) \exp \left\{ -\int_{\tau-t}^\tau \mu(q)\, dq \right\} d\tau.$$

[18 marks]

4. **(Nutrient consumption)** Yeast cells can be grown in such a way that the cells form a cylindrical column, which becomes taller as the cells proliferate. Consider a column of length, L, and let x denote the distance up the column. The bottom of the column ($x = 0$) sits in a dish containing a constant concentration, c_0, of nutrient (*e.g.* glucose). There is no flux of nutrient out of the top of the column, and nutrient transport is assumed to be by diffusion only. Cells are assumed to consume nutrient at a constant rate. Hence the nutrient concentration, c, satisfies

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} - kc$$

subject to $c(x, 0) = 0$, $c = c_0$ at $x = 0$ and $\dfrac{\partial^2 c}{\partial c^2} = 0$ at $x = L$.

(a) Find the steady-state distribution of nutrient, c.

(b) The yeast cells are *proliferative* (able to divide) if $c > \theta$ (where $0 < \theta < c_0$) and *quiescent* if $c < \theta$. Find an expression for the distance x_θ at which the cell type switches from proliferative to quiescent.

(c) What happens to x_θ as $L \to \infty$? [6 marks]

5. **(A modified Fisher's equation)** Let $n(x, t)$ be the density of a population of cells in a scratch assay (as described in §5.2 of the lecture notes). We consider the possibility that the cells' random motion increases with their density, so we model the situation with a modified version of Fisher's equation in which the diffusion coefficient is proportional to n. In dimensionless variables, the equation is

$$\frac{\partial n}{\partial t} = \frac{\partial}{\partial x} \left(n \frac{\partial n}{\partial x} \right) + n(1 - n).$$

(a) Look for travelling wave solutions of the form $n(x, t) = N(z)$ where $z = x - ct$, $c > 0$, and find the pair of equations satisfied by $N(z)$ and $P(z) = N'(z)$.

(b) Make the change of variables $\zeta = \displaystyle\int_0^z \frac{1}{N(\eta)}\, d\eta$ to remove the singularity at $N = 0$ (this can be thought of as a nonlinear 'stretch' of z). Show that $(N, P) = (1, 0)$ is a fixed point of the transformed system, and that there are two others, both with $N = 0$.

(c) We are interested in solutions such that $N(-\infty) = 1$ and $N(\infty) = 0$. For each of the two fixed points with $N = 0$, suppose there is a trajectory connecting (1,0) to this point; sketch the shape of the solution $N(\zeta)$ against ζ for this trajectory.

(d) By looking for a solution of the original travelling wave problem in the form $P(z) = c(N(z) - 1)$, show that an exact solution exists for a particular value of c (which you should state). Find the particular solution that satisfies $N = 0$ at $z = z_c$. Referring to one of the solutions sketched in the previous part, explain why this solution will satisfy $N(z) = 0$ for $z > z_c$. [10 marks]

Total: 50 marks