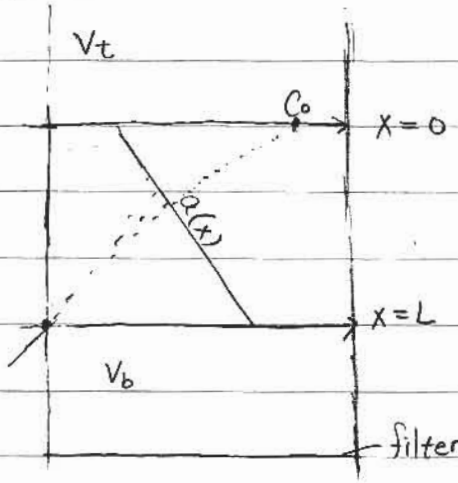
Problem 3.1 BE.430 Homework 3

a)



Assumptions:

- $\frac{\partial a}{\partial x} = \alpha$, chemoattractant gradient is constant.
- No leukocyte death: $-k_s C = 0$.
- Negligible attractant update
- $t=0$ is when $\frac{\partial a}{\partial x}$ is a constant

Note: α is chemoattractant gradient $a(r,t)$ is chemoattrant concentration.

- Conservation Equation for Leukocytes:

$$\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial x^2} - \chi a \frac{\partial c}{\partial x} - \chi \frac{\partial^2 a}{\partial x^2}^{\to 0} \quad \therefore \boxed{\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial x^2} - \chi \alpha \frac{\partial c}{\partial x}}$$

- Boundary Conditions:

$\boxed{@\ x=0,\ C=C_0}$
$\boxed{@\ x=L,\ C=0}$ because there's no accumulation of leukocytes @ $x=L$, all the cells fall through once they reach the bottom of the matrix.

- Initial Condition:

Assuming $t=0$ when the attractants concentration gradient becomes a constant. and the cells start to migrate.

$\boxed{\therefore\ C(x)=0}$

b) $\frac{\partial c}{\partial t}^{0} = D_c \frac{\partial^2 c}{\partial x^2} - \chi a \frac{\partial c}{\partial x} = 0.$

S.S.

$$\sim D_c r^2 - \chi a r = 0$$

$$r=0,\ r=\frac{\chi a}{D_c}$$

$$C(x) = A_1 + A_2 e^{\frac{\alpha \chi}{D_c} r}$$

$$C(x)\big|_{x=0} = C_0 \Rightarrow A_1 + A_2 = C_0$$

$$C(x)\big|_{x=L} = 0 \Rightarrow A_1 + A_2 e^{\frac{\alpha \chi}{D_c} L} = 0$$

$$A_2\left(1 - e^{\frac{\alpha \chi}{D_c} L}\right) = C_0$$

$$A_2 = \frac{C_0}{1 - e^{\frac{\alpha \chi}{D_c} L}}$$

$$A_1 = \frac{C_0 - C_0 e^{\frac{\alpha \chi}{D_c} L} - C_0}{1 - e^{\frac{\alpha \chi}{D_c} L}}$$

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b) $$C(x) = \frac{C_0 e^{\frac{\alpha\chi}{D_c}L}}{e^{\frac{\alpha\chi}{D_c}L}-1} - \frac{C_0 e^{\frac{\alpha\chi}{D_c}x}}{e^{\frac{\alpha\chi}{D_c}L}-1}$$ @ Steady state

$$N_c(x)\Big|_{x=L} = -D_c\frac{\partial c}{\partial x} = \frac{D_c C_0 e^{\frac{\alpha\chi}{D_c}x}}{e^{\frac{\alpha\chi}{D_c}L}-1}\cdot\frac{\alpha\chi}{D_c}\Big|_{x=L} = \frac{C_0 e^{\frac{\alpha\chi}{D_c}L}}{e^{\frac{\alpha\chi}{D_c}L}-1}\cdot\alpha\chi \quad \left(\text{unit: } \frac{\#\text{ cells}}{m^2\cdot s}\right)$$

$$\int_0^t \frac{C_0\alpha\chi e^{\frac{\alpha\chi}{D_c}L}}{e^{\frac{\alpha\chi}{D_c}L}-1}\,dt = T_c(t) = \frac{C_0\alpha\chi t e^{\frac{\alpha\chi}{D_c}L}}{e^{\frac{\alpha\chi}{D_c}L}-1} \quad \left(\text{unit: } \frac{\#\text{ cells}}{m^2}\right)$$

$T_c(t)$ is the amount of cells exiting the matrix / unit cross-sectional area.

Total # of cells on filter = $T_c(t)\cdot A_c$ (A_c: cross-sectional area)

↳ $$K(t,\alpha) = \frac{C_0 A_c \alpha\chi t e^{\frac{\alpha\chi}{D_c}L}}{e^{\frac{\alpha\chi}{D_c}L}-1} \text{ (\# cells)} \quad \text{(Eq. 1)}$$

Obtaining χ:

- After counting the cells on the filter after a certain time, we can obtain $K(t,\alpha)$ & t.
- We set C_0, L, & A_c and we assume that D_c is known.
- We can calculate α @ $t=0$ by determining the attractant conc. in V_b & V_t; take their difference and divide by L because it's in steady state.

$$\alpha = \frac{a(x=L)-a(x=0)}{L}$$

- Using all the parameters, we can calculate χ using Eq. 1.

Problem 3.1

b) $T_{diff} \sim \frac{L^2}{\pi^2 D}$; $T_\chi \sim \frac{L}{\chi\alpha}$ Because leukocytes migrate very slowly, in order for the gradient to became constant $\therefore L \ll D$ and $L \ll \chi\alpha$ shortly, we need to make L very small. Thus, we want to minimize the time constants because they show the respective windows of time @ which the system will reach steady state.

c) It is possible that $\chi = 0$, & $D_c = D_{co}(1 + p \times a)$ where p is a coefficient characterizing the Δ in cell random motility with attractant concentration.

Conservation equation for leukocytes:

$$\frac{\partial C}{\partial t} = -\frac{\partial}{\partial x}\left[-D_{co} p \frac{\partial a}{\partial x} C - D_{co}(1+pa)\frac{\partial C}{\partial x}\right]$$

$$= \cancel{D_{co} p \frac{\partial^2 a}{\partial x^2} C^0} + D_{co} p \frac{\partial a}{\partial x}\frac{\partial C}{\partial x} + D_{co} p \frac{\partial a}{\partial x}\frac{\partial C}{\partial x} + D_{co}(1+pa)\frac{\partial^2 C}{\partial x^2}$$

$$= D_{co}(1+pa)\frac{\partial^2 C}{\partial x^2} + 2 D_{co} p \frac{\partial a}{\partial x}\frac{\partial C}{\partial x}$$

↑ Constant.

If p is negative, it would cause a similar effect on the system as when $\chi \neq 0$.

Also, if a(x) is very small, $1 + pa \sim 1$, hence the diffusion term would also look like the decoupled diffusion term in the previous conservation of species equation w/ $\chi \neq 0$.

Problem 3.2 BE.430 Homework 3

3.2 Conservation of Species Equation:

$$\cancel{\frac{\partial c'}{\partial t}}^{\,0} = \frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{dc'}{dr}\right) - \frac{K_{max}[c'(r)+C_0]}{K_M+[c'(r)+C_0]}$$

Assumptions:
- Steady State

where

Homogeneous Boundary Conditions:

$r = r_0,\ c' = 0$

$r = 0,\ \frac{dc'}{dr} = 0$

Find Green's Function:

$$\frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{dc'}{dr}\right) = \frac{K_{max}[c'(r)+C_0]}{K_M+[c'(r)+C_0]}$$

$$\mathcal{L} = \frac{D}{r^2}\cdot 2r\cdot\frac{d}{dr} + \frac{D}{r^2}\cdot r^2\cdot\frac{d^2}{dr^2};\quad a_0 = D;\ a_1 = \frac{D}{r};\ a_2 = 0$$

- Solutions to $\mathcal{L}c' = 0$ are: $C_1'(r) = -\frac{A_1}{r} + A_2 \Rightarrow \boxed{C_1'(r) = 1}$

$$C_2'(r) = -\frac{B_1}{r} + B_2 \Rightarrow \boxed{C_2'(r) = -\frac{r_0}{r} + 1}$$

- Applying Boundary Conditions: $\frac{dC_1'(0)}{dt} = \frac{A_1}{r^2} = 0;\ A_1 = 0 \therefore$ let $A_2 = 1$

$$C_2'(r_0) = -\frac{B_1}{r_0} + B_2 = 0;\ \therefore \text{let } B_1 = r_0,\ B_2 = 1$$

- Find denominator of Green Function:

$$c(z) = a_0(z)\left[C_1'(z)\left.\frac{dC_2'}{dr}\right|_z - C_2'(z)\left.\frac{dC_1'}{dr}\right|_z\right] = D\left[1\cdot\frac{r_0}{z^2} - 0\right] = \frac{Dr_0}{z^2}$$

$$G = \begin{cases} \dfrac{C_2'(z)\,C_1'(r)}{c(z)}, & r \le z \\ \dfrac{C_1'(z)\,C_2'(r)}{c(z)}, & r \ge z \end{cases} = \boxed{\begin{cases} \dfrac{1\left(-\frac{r_0}{z}+1\right)}{\frac{Dr_0}{z^2}}, & r \le z \\ \dfrac{\left(-\frac{r_0}{r}+1\right)1}{\frac{Dr_0}{z^2}}, & r \ge z \end{cases}}$$

$C_0'(r) = C_0$; $C_1'(r) = 0$ (initial guess)

From these two starting conditions, Green's Function will be used in the iterative process to find $C_2'(r)$, $C_3'(r)$, etc...

$$C_2'(r) = \int_0^r \left[-\frac{z^2}{r_0 D} \cdot \frac{r_0}{r} + \frac{z^2}{r_0 D} \right] Q \, dz + \int_r^{r_0} \left[\frac{-z^2}{r_0 D} \frac{r_0}{z} + \frac{z^2}{r_0 D} \right] Q \, dz$$

where $Q = \dfrac{K_{max} C_0}{K_M + C_0}$

$$= \left[\frac{-z^3}{3rD} + \frac{z^3}{3r_0 D} \Big|_0^r + \frac{-z^2}{2D} + \frac{z^3}{3r_0 D} \Big|_r^{r_0} \right] Q$$

$$= \left[\frac{-r^2}{3D} + \frac{r^3}{3r_0 D} - \frac{r_0^2}{2D} + \frac{r_0^2}{3D} + \frac{r^2}{2D} - \frac{r^3}{3r_0 D} \right] Q$$

$$\boxed{C_2'(r) = \left(\frac{r^2}{6D} - \frac{r_0^2}{6D} \right) \left(\frac{K_{max} + C_0}{K_M + C_0} \right)}$$

$$C_3'(r) = \int_0^r \left[\frac{-z^2}{r_0 D} \cdot \frac{r_0}{r} + \frac{z^2}{r_0 D} \right] \left[\frac{K_{max} C_0 + K_{max} C_2'(z)}{K_M + C_0 + C_2'(z)} \right] dz +$$

$$\int_r^{r_0} \left[\frac{-z^2}{r_0 D} \cdot \frac{r_0}{z} + \frac{z^2}{r_0 D} \right] \left[\frac{K_{max} C_0 + K_{max} C_2'(z)}{K_M + C_0 + C_2'(z)} \right] dz$$

Analytical solutions to subsequent iterations would require a computer to obtain. However, by inspection, $C_3'(r)$ looks like it will have "arctan( )" in its analytical expression.

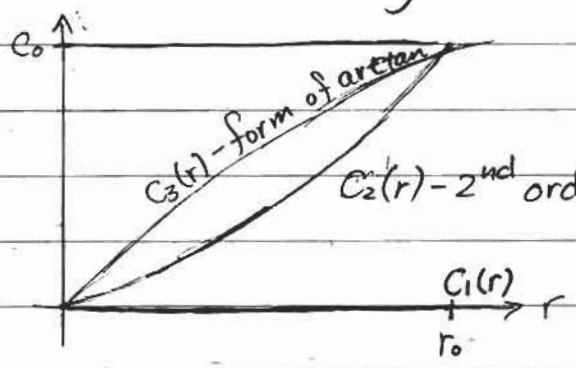
- Conditions under which this iterative process will give a useful answer
  - This series of iterations would provide a useful solution if C' is a complete metric space where all Cauchy sequences converge.
-

- In this case, we can find the point of convergence by invoking the Banach fixed point theorem which gaurantees the existence and uniqueness of fixed points of certain self mapping metric spaces.
- To find the fixed function point $C'^{*}(r)$, we first have to prove that $\mathcal{L}$ is a contraction mapping such that

$$d(\mathcal{L}C_n', \mathcal{L}C_{n-1}') \leq \alpha d(C_n', C_{n-1}')$$

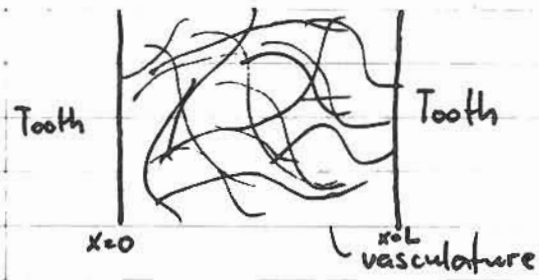
where d is the distance function of C' & $0 < \alpha < 1$

- An alternative way of determining whether $\mathcal{L}$ might be a contracting operator or not is looking at this graphically.



∴ From looking at the graphs after each iteration, it seems like $\mathcal{L}$ is a contracting operator.

Problem 3.3 - Periodontal infection model with uniformly distributed vasculature



Assume generally.
- no penetration of bacteria, attractant, cells into tooth
- homogeneously distributed vasculature
- 1-D system

Of course, there are many many answers to this problem. However, there is one major key point and we'll present it here.

3 species of interest: bacteria (b), attractant (a), leukocytes (c)

Species conservation:

bacteria: $\frac{\partial b}{\partial t} = -\frac{\partial}{\partial x}(N_b) + \mathcal{R}_b$

attractant: $\frac{\partial a}{\partial t} = -\frac{\partial}{\partial x}(N_a) + \mathcal{R}_a$

leukocytes: $\frac{\partial c}{\partial t} = -\frac{\partial}{\partial x}(N_c) + \mathcal{R}_c$

Constitutive expressions:

bacteria: $N_b = -D_b \frac{\partial b}{\partial x}$

$$\mathcal{R}_b = \underbrace{k_g b}_{\text{proliferation}} - \underbrace{k_k b \cdot c}_{\text{killing by leukocytes}}$$

attractant: $N_a = -D_a \frac{\partial a}{\partial x}$

$$R_a = \underbrace{k_p b}_{\text{production}} - \underbrace{\frac{K_d a}{K+a}}_{\text{enzymatic degradation}} - \underbrace{k_u a c}_{\text{uptake by cells}}$$

leukocytes: $N_c = -D_c \frac{\partial c}{\partial x} + \chi \frac{\partial a}{\partial x} c$

$$R_c = \underbrace{-k_s c}_{\text{leukocyte death}} + \underbrace{h_c (c_{blood} - c)}_{\text{leukocyte transfer at vasculature}}$$

Now, vasculature distributed homogeneously
Transfer term is in reaction term.

Combining:

$$\frac{\partial b}{\partial t} = D_b \frac{\partial^2 b}{\partial x^2} + k_g b - k_k b c$$

$$\frac{\partial a}{\partial t} = D_a \frac{\partial^2 a}{\partial x^2} + k_p b - \frac{k_d a}{K+a} - k_u a c$$

$$\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial x^2} - \chi \frac{\partial^2 a}{\partial x^2} c - \chi \frac{\partial a}{\partial x} \frac{\partial c}{\partial x} - k_s c + h_c (c_{blood} - c)$$

Boundary conditions:

$$\frac{\partial b}{\partial x}\Big|_{x=0} = \frac{\partial b}{\partial x}\Big|_{x=L} = 0$$

$$\frac{\partial a}{\partial x}\Big|_{x=0} = \frac{\partial a}{\partial x}\Big|_{x=L} = 0$$

$$\frac{\partial c}{\partial x}\Big|_{x=0} = \frac{\partial c}{\partial x}\Big|_{x=L} = 0$$

no flux conditions for all species.

It is important to realize that at steady-state, due to prior diffusion processes, the concentration / density profiles will become constant if we are dealing with no flux boundary conditions on both sides.

We will also obtain constant profiles if we have initially constant profiles.

$$\Rightarrow \frac{\partial}{\partial x} = 0$$

Let's say, we are only interested in steady-state profiles for medical reasons.

$$\cancel{\frac{\partial b}{\partial t}}^{\,0} = k_g b - k_K bc \qquad (1)$$

$$\cancel{\frac{\partial a}{\partial t}}^{\,0} = k_p b - \frac{k_d a}{K+a} - k_u ac \qquad (2)$$

$$\cancel{\frac{\partial c}{\partial t}}^{\,0} = -k_s c + h_c (c_{blood} - c) \qquad (3)$$

(3) $\Rightarrow$ $c = \dfrac{h_c c_{blood}}{k_s + h_c}$

(1) $\Rightarrow$ $c = \dfrac{k_g}{k_K}$

Here, we might have a solution if (3) = (1), no solution if (3) ≠ (1). This is also an opportunity to solve for c_{blood} if it was unknown.

We can also readjust our model by setting our killing term to $-k_K c$ assuming no dependence on b. We can then solve for b.

$$b = \frac{k_K}{k_g} c = \frac{k_K h_c c_{blood}}{k_g (k_s + h_c)}$$

We can also solve for a with (2). (not shown)

This is one of the simplest analyses. You can solve for the transient solution, do a scaling analysis, etc, eliminate terms.
As long as $\frac{\partial}{\partial x} = 0$ is recognized and a plausible analysis is given, you should receive full credit.