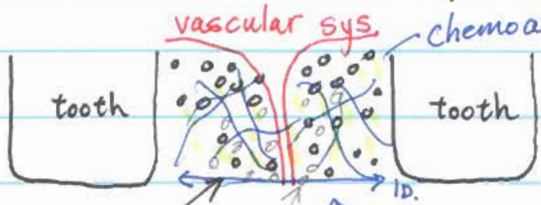
Motivating Example 9/28

- bacterial infection + periodental inflammation



bacteria.

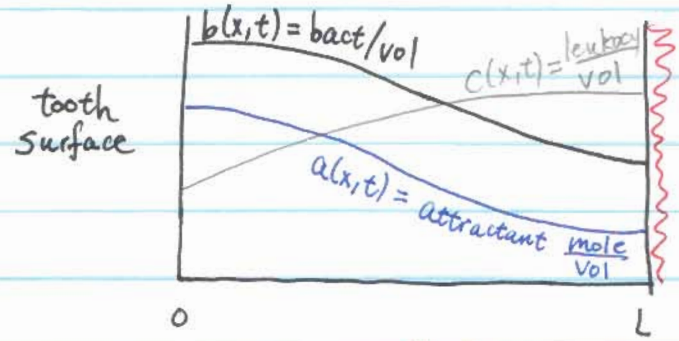
connective tissue - extracellular matrix + fibroblasts, microphages

neutrophil leukocytes from bloodstream

Dynamic competition between bacterial proliferation vs. killing by leukocytes

Phagocytic killing

Schematic illustration of situation



So, tooth-to-tooth distance is $2L$

$c(x,t)$ is bad if it's too big, cause damage via inflammation

severity of infection

severity of inflammation

Goal - determine how $\boxed{b(x,t)}$ and $\boxed{c(x,t)}$ depend on certain molecular and cellular proportions.

Let's write species conservation eqns.

batteria: $\frac{\partial b}{\partial t} = -\frac{\partial N_b}{\partial x} + R_b$

attractant: $\frac{\partial a}{\partial t} = -\frac{\partial N_a}{\partial x} + R_a$

leukocytes: $\frac{\partial c}{\partial t} = -\frac{N_c}{\partial x} + R_c$

bact. random motility coefficient

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

down density gradient

Specific batterial killing attractant by leukocytes.

$$R_b = k_g b - k_k bc$$

bacteria specific growth rate constant.

D_b, k_g, k_k are all emperically measurable.

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

attractant diffusion coefficient

$$R_a = k_p b - k_u ac$$

attractant uptake rate constant

attractant production rate constant.

$$-\frac{k_d a}{k_m + a}$$

Maximum proteolycetic degradation rate constant

Michaelis-Menten constant

Michaelis-Menten enzyme rxn expression

k_p, k_u, k_d, k_m, all measurable

leukocyte random motility coefficient

$$N_c = \underbrace{-D_c \frac{\partial c}{\partial x}}_{\text{random migration term.}} + \left[\chi \frac{\partial a}{\partial x} \right] c$$

Chemotactic Velocity

leukocyte Chemotatic migration coefficient.

D_c, χ are measurable

most critical for disease

leuk death rate constant, measurable

?

$R_c = -k_s(b)c$ tike C_{blood}.

neglect. alternative problem formulation

no proliferation

Model: Standard diffusion. Nonlinear rxn terms

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

$$\frac{\partial a}{\partial t} = D_a \frac{\partial^2 a}{\partial x^2} + k_p b - \boxed{k_u ac} - \boxed{\frac{k_d a}{K_m + a}}$$

Nonlinear trasport terms.

$$\frac{\partial c}{\partial t} = D_c \frac{\partial^2 c}{\partial x^2} - \boxed{\chi \frac{\partial^2 a}{\partial x^2} c - \chi \frac{\partial a}{\partial x}\frac{\partial c}{\partial x}} - k_s c$$

I.C. $t=0$ $b(x,0) = b_i(x) > 0$.

$a(x,0) = a_i(x) = 0$.

$c(x,0) = c_i(x)$

find S.S. solution for $b(x,0) = 0$

B.C. $x=0$; $N_b = 0$, $N_a = 0$, $N_c = 0$

$$D_b \frac{\partial b}{\partial x} = 0 \qquad D_a \boxed{\frac{\partial a}{\partial x}} = 0 \qquad D_c \frac{\partial c}{\partial x} - \chi \cancel{\frac{\partial a}{\partial x}} c = 0 \quad \to 0.$$

$$D_c \frac{\partial c}{\partial x} = 0$$

$X = L$: $0 = N_b + R_b$

blood density in bloodsteam

$$0 = -D_b \frac{\partial b}{\partial x} - h_b(b - \cancel{b_{blood}}) \quad \to 0$$

bacterial tissue to blood transfer coefficient

If $h_a, k_b \to \infty$, then could impose $a=0$, $b=0$

$$0 = N_a + R_a$$

$$0 = -D_a \frac{\partial a}{\partial x} - h_a(a - \underbrace{a_{blood}}_{\to 0})$$

attractant tissue to blood transfer-coefficient

measurable quantity

$$0 = N_c + R_c$$

$$0 = -D_c \frac{\partial c}{\partial x} + \chi \frac{\partial a}{\partial c} c + h_c\left[C_{blood} - c\right]$$

Analysis - start by scaling variables to ascertain relative contributions of terms

Define scaled variables: $\tau = \frac{t}{t^*}$, $\xi = \frac{x}{x^*}$, $u = \frac{b}{b^*}$, $v = \frac{a}{a^*}$, $w = \frac{c}{c^*}$

$t^* = \frac{1}{k_g}$, $x^* = L$, $b^* = \frac{b_i}{\cancel{b_i}}$, $\boxed{a^* = k_m ?}$ leave undefined until later. $C^* \equiv C_{blood}$

Obtain

bacteria: $\frac{\partial u}{\partial \tau} = \Delta_b \frac{\partial^2 u}{\partial \xi^2} + u - \theta_{uw}$ } dimensionless or unitless

$\Delta_b = \frac{D_b}{k_g L^2}$, $\theta = \frac{k_k C_{blood}}{k_g}$

governed by $\frac{\partial u}{\partial \tau} = u - \theta u w = \boxed{(1-\theta w)}u$

$\frac{\partial u}{\partial \tau} > 0$

Is $1 - \theta w < 0$ or > 0 $\frac{\partial u}{\partial \tau}$

$L \sim 10^{-1}$ cm

$D_b \sim 10^{-9}$

$k_g \sim 0.3\ hr^{-1}$

$\Rightarrow \Delta_b \sim 10^{-3}$

$C_{blood} \sim 10^{-6}$ leuk/cm^3 k_k $\Rightarrow \theta \to 1$

to a good approx, bacterial dynamics