9/13

Chemical Subsystem

Grodzinsky Chapter 2

Deen 1.2, 1.4, 1.6, 2.2, 2.4, 2.6, 2.7, 2.8, 3.2, 3.3, 3.4. Appendix } next 3 weeks

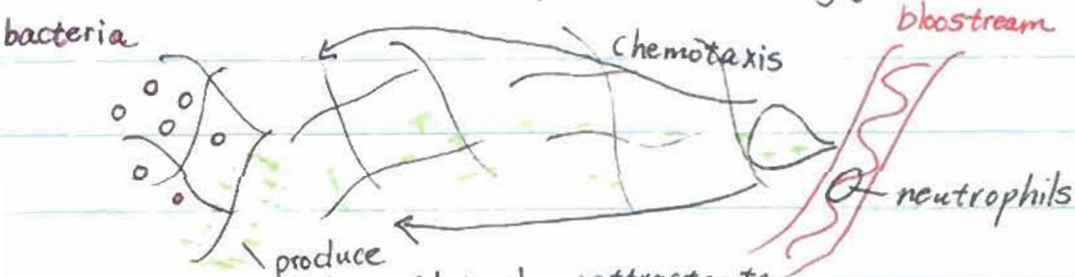
Molecular Species transport influenced by Chemical driving forces
(also some analogies to cell motility)

Start w/ dilute solution, low concentration

Begin w/ formulation formalism - setting up problems
situations → models → math

start with example situation - concentration profiles of chemoattractant species in tissue

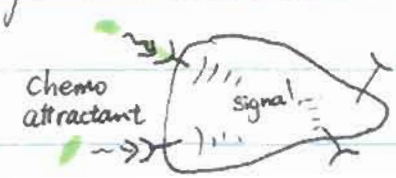
Tissue matrix - ECM (proteins, proteoglycans, ...)



If bacteria proliferate faster than when neutrophils gets to them, ∴.

Chemoattractants attract the neutrophils to exit the bloodstream

Neutrophils must be able to perceive gradient in concentration of chemoattra



sensitivity: relative gradient $\equiv \frac{\Delta c}{c} < 0.01$ (1%)

concentrations $\sim 10^{-9}$ M (moles/ℓ)

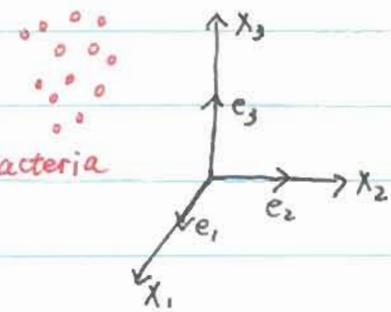
We decide peptide concentration as function of spatial position and time

3-D rectangular coordinates

Vector $\underline{x} = (x_1, x_2, x_3)$

$= x_1 \underline{e_1} + x_2 \underline{e_2} + \underline{e_3} x_3$

$e_i \equiv$ unit vector in each coordinate direction



vector norm (magnitude) $\|\underline{x}\| = |(x_1^2 + x_2^2 + x_3^2)^{1/2}|$

so, $\|\vec{e}_1\| = \|\vec{e}_2\| = \|\vec{e}_3\| = 1$

so, @ any point t, in time we want to calculate

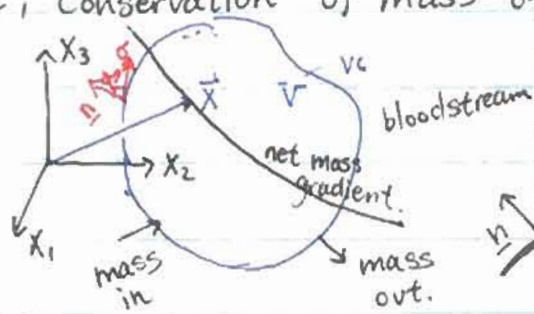
$c(\underline{x}, t)$ and $\underline{\nabla} c = \frac{\partial c}{\partial x_1}\vec{e}_1 + \frac{\partial c}{\partial x_2}\vec{e}_2 + \frac{\partial c}{\partial x_3}\vec{e}_3$

[moles / vol] or [#/vol]

We need an eqn. governing $\vec{c}(x,t)$

Eqns governing our variables of interest will arise from ~~concentration~~ conservation laws.

- Here, Conservation of mass of chemoattractant species



$\bar{V}$ - volume of control volume

S' - surface area of control volume.

start w/ control volume surrounding $\bar{x}$

$\underline{n}$ unit normal vector @ any point on surface of control volume
$\|\underline{n}\| = 1$ w/ angle between n & σ
$\underline{n} \cdot \underline{\sigma} = \|\underline{n}\| \|\underline{\sigma}\| \cos\phi = 0$ (normal)

Eqns governing our variables of interest will arise from conservation laws.
- Here, conservation of mass of chemoattractant species

Let $\int_V [\ ]\, dV$ = volume integral of quantity $[\ ](\underline{x}, t)$

$\int_S [\ ]\, dS$ = surface integral of quantity $[\ ](\underline{x}, t)$

Mass conservation eqn. for chemoattractant molecular species is

$$\underbrace{\frac{d}{dt}\int_V c(x,t)\,dV}_{\text{rate of accumulation in volume}} = \underbrace{-\int_S n \cdot N(x,t)\,dS}_{\text{net flux into volume}} + \underbrace{\int_V R(x,t)\,dV}_{\text{net generation}}$$

molar flux

$\underline{N}(x,t)$ $\frac{\text{moles}}{\text{area-time}}$

$R(\underline{x},t)$, $\frac{\text{moles}}{\text{vol-time}}$

net generation

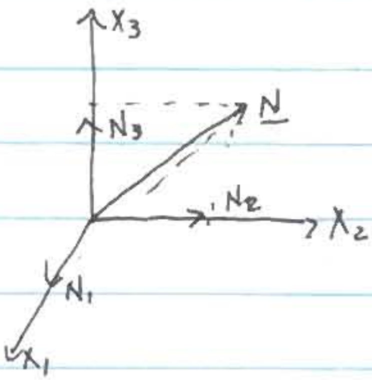
Apply Divergence Theorem to convert surface integral to volume integral

$$\int_S \underline{n} \cdot \underline{N}\, dS = \int_V \nabla \cdot \underline{N}\, dV$$

Divergence operator

In 3-D rectangular

$$\nabla \cdot \underline{N} = \frac{\partial N_1}{\partial x_1} + \frac{\partial N_2}{\partial x_2} + \frac{\partial N_3}{\partial x_3}$$



Obtain $\int_V \left(\frac{\partial c}{\partial t} + \nabla \cdot \underline{N} - R \right) dV = 0$

Recognize volume integral was created for arbitrary central volume ~~where~~ surrounding $\underline{x}$; take limit as $V \to 0$

Shrink volume down to lim of 0.

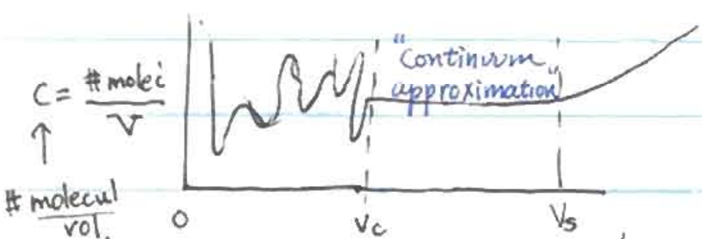
$\therefore \frac{\partial c}{\partial t} = -\nabla \cdot \underline{N} + R$

species was conserved @ an interior point of our space of interest

Wait! What does $V \to 0$ mean?

It does not mean $V = 0$

It means V is "small" relative to ... ?



Loose sense of volume w/ respect to x. as V↑

need $V_s \ll$ system
$V_c \ll V_s$
↘ ~0

only then will $c(x,t)$ have meaning

For volume V, if statistical distribution of molecule is random + independent (Gaussian), then expected standard deviation is # of molecules found is $\#^{1/2}$ if expected number is #

Then relative expected fluctuation magnitude is $\frac{\#^{1/2}}{\#} = \#^{-1/2} \equiv \frac{1}{(\underset{\text{Vol}}{V}\,\underset{\#/\text{vol}}{C})^{1/2}}$

For this problem, a typical concentration magnitude is $C \sim 10^{-9}$ moles/l

error tolerance ~1%

So, need $[V_c (10^{-9} \text{ moles}/\ell)(6 \times 10^{23} \#/\text{mol})]^{-1/2} < 10^{-2}$

$\Rightarrow \boxed{V_c \gtrsim 10^{-2}\, n\ell}$

$V_c = L^3$; $V_c = 10^{-2} n\ell \Rightarrow \sim 10\,\mu m$.

Neutraphil: 5-10 μm, intercapillary space ~100-300 μm

Back to (continuum approximation) species mass conservation equ:

$\frac{\partial c}{\partial t} = -\nabla \cdot \underline{N} + R$; want to calculate $c(\underline{x}, t)$

need $\underline{N}$, R in terms of C

$\boxed{\text{Conservation laws}}$ + $\boxed{\text{constitutive relations}}$

$\underline{N}$ - need constitutive relation

- experimental observation: emperical data

<u>or</u> - theory

In absence of nonchemical driving forces, typically for pure molecular diffusion

$\underline{N} = -[\overset{\swarrow \text{diff}}{D}][\nabla C]$ Fick's Law

coefficient \ divergence.

Where does it come from?

- theory: random walk model of particles
- " : analogy to Ohm's Law
- emperical data: Fick (studied oxygen dissolving in H_2O)