9/15

Constitutive Expression for N for molecular diffusion

1. Emperical - Fick
2. Theory
   - analogy to current & heat
   - thermodynamics
   - statistical mechanics

Example - classical thermodynamics

- reduce free energy of a chemical system by reducing chemical potential;
- this can be accomplished by net movement of molecular species down a gradient of chemical potential $\underset{\sim}{\nabla} \mu_i$ ← chemical potential of molecular species, i

$\underset{\sim}{N}$ - flux $\dfrac{\text{molecular species}}{\text{area} \cdot \text{time}}$

c_i - conc. $\left(\dfrac{\text{molecules}}{\text{vol}}\right)$

$$\underset{\sim}{N} = \alpha_i \, c_i \boxed{\underset{\sim}{\nabla} \mu_i}$$

α_i ↑ mobility of species

$\boxed{\underset{\sim}{\nabla} \mu_i}$ — driving force

mobility is theoretically derived from movement of a particle in a solvent

 e.g. Stokes - Einstein theory.

Deen 1.5 (size, viscosity, structure)

$$\mu_i = RT \ln(\gamma_i y_i)$$

$y_i = \dfrac{c_i}{c_T}$ ← total solution

T — abs. temp.

γ_i — activity coeff. of species i

R — gas constant.

y_i — mole fraction of species in solution

γ_i parameterizes nonideal molecular interactions (% of high concentrations) under dilute conditions ($y_i \ll 1$)

$\gamma_i \to 1$ (ideal behavior)

issue: many biological systems are non-ideal

$\therefore \underline{\nabla} \mu_i = RT \underline{\nabla} (\gamma_i \ln y_i) \Rightarrow$ for $\gamma_i = 1$

$\underline{N} = -\underbrace{[\alpha_i RT]}_{\text{diffusion coefficient for species } i} \underline{\nabla} c_i$

$\therefore \underline{\nabla} \mu_i = RT \underline{\nabla} (\ln[\gamma_i y_i])$

$\Rightarrow$ for $\gamma_1 = 1$:

$\underline{N} = -\underbrace{[\alpha_i RT]}_{D_i} \underline{\nabla} c_i$

If $\gamma_i \neq 1$, then D_i is a function of γ_i, which maybe a function of c_i

$\Rightarrow \underline{N} = -\underline{\nabla}(D_i c_i)$

So, if $\gamma_i \neq 1$, D_i ~~D_i~~ is not constant, then $\underline{N} = \underbrace{\boxed{-D_i \nabla c_i}}_{\text{Fick's Law}} - \underbrace{c_i \nabla D_i}_{\text{potential}}$ esp. in cellular situations

potential extra contribution in non-ideal solutions

Back to mass cons. eq:

$$\frac{\partial c}{\partial t} = -\underline{\nabla}(-D \underline{\nabla} C) + R$$

Assume D is constant (no nonidealities)

$$\frac{\partial c}{\partial t} = D \nabla^2 c + R$$

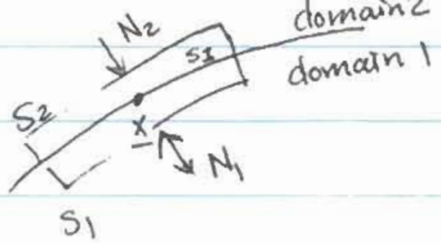
Can we solve this equ for $c(\underline{x}, t)$?

Need 1 Initial condition - specify $c(x, t_0) = C(x)$

2 Boundary conditions - @ 2 $\underline{x}$ locations specify

IC/BC con. laws &/or constitutive expressions

Conservation eqns – around points @ a boundary or interface



But here, as $V \to 0$

$$\frac{S}{V} \to \infty$$

so, $\int_V [\ \ ]\, dV$ can be neglected.

n_I is unit normal vector on S_I

Then cons. eqn for species is $0 = + \int_{S_1} - \underline{n}_I - N_1\, dS' - \int_{S_2} - \underline{n}_I \cdot \underline{N}_2\, dS$

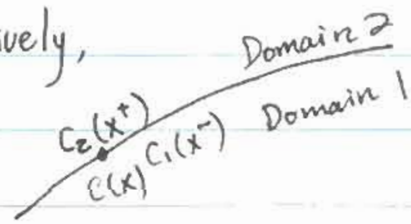
net generation @ interfacial surface

$$+ \int_{S_I} R_s\, ds$$

Take limit $S \to 0$ $\quad 0 = \underline{n}_I \cdot (\underline{N}_1 - \underline{N}_2) + R_s$

BC "flux matching"

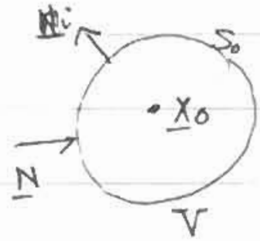
Alternatively,



Assume both domains are in equilibrium w/ one another.

$$\frac{C_2(\underline{x}^+)}{C_1(\underline{x}^-)} = K \text{ equilibrium partition coefficient}$$

Can have "BC" @ an interior point



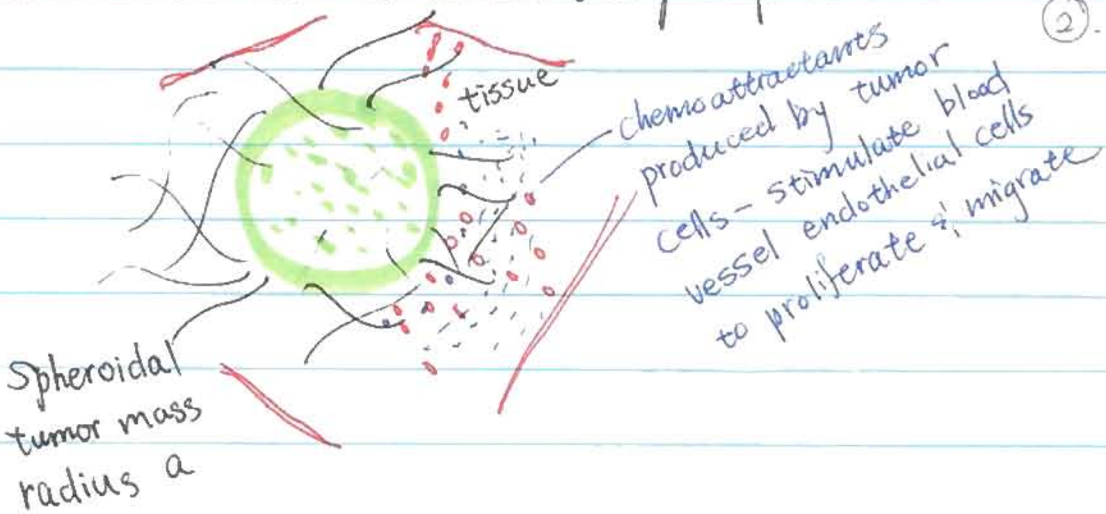
no generation and symmetric properties.

mass cons. eqn

$\lim V \to 0 \Rightarrow 0 = -\underline{n}_I \cdot \underline{N}\ ; \Rightarrow \boxed{0 = \underline{N}}$ "no flux" symmetry condition @ an interior point.

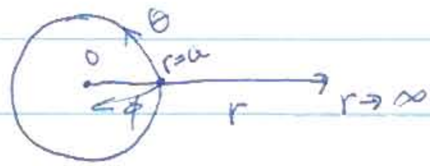
m - palmer @

Let's formulate a model for an example problem



Determine conc profile of chemoattractant in tissue

$$\frac{\partial c}{\partial t} = D\nabla^2 c + R \quad \text{in 3-D radial coordinates}$$



Assume angular symmetry (no gradient w/ respect to θ, ϕ)

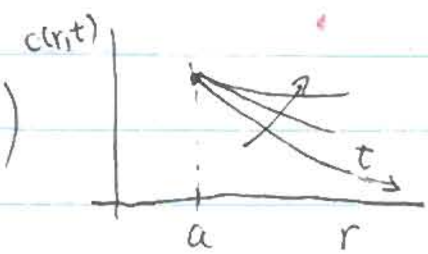
$$\nabla^2 c = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial c}{\partial r}\right)$$

Assume for $r > a$, $R = 0$

- i.e, negligible degredation by tissue enzymes, negligible update by tissue cells, negligible loss to blood cells.

Then

$$\frac{\partial c}{\partial t} = \frac{D}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial c}{\partial r}\right)$$



To stant simply, think about time scales

- attractant profile establishment is much (10x? 100x?).
  faster than time scale for tumor size change and endothelial cell response

$\Rightarrow$ assume attractant profile we are interested in is SS fory any given a.

i.e. $\frac{\partial c(r)}{\partial t} \to 0$

$$\frac{\partial c}{\partial t} = 0 = \frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{dc}{dr}\right)$$

Solution by simple double integration $c(r) = \frac{B_1}{r} + B_2$

(B_1, B_2 are ~~undet~~ undetermined coeff).

Determine $B1$, $B2$.

BC: $r=a$ flux matching

$$0 = \underset{\substack{\text{in tumor}\\ \text{molecules/time}}}{R_{gen}} + (2\pi a^2)\, D \left.\frac{dc}{dr}\right|_{r=a}$$

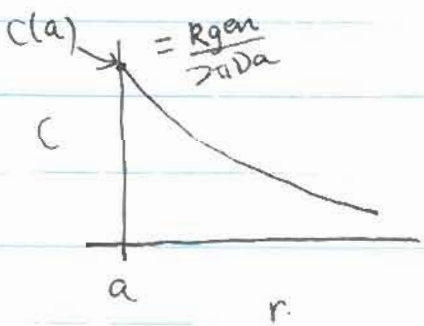
$\uparrow$ $\frac{\text{molecules}}{\text{~~vol~~. dist. time}}$

$r \to \infty$ $\boxed{c \to 0}$?

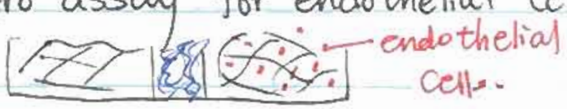
$\frac{dc}{dr} \to 0$?

can get B_1, B_2

$$c(r) = \frac{R_{gen}}{2\pi D r}$$



In vitro assay for endothelial cell response to tumor chemoattractant.



- steady state diffusion eqn, same assumptions

$$0 = \frac{D}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right)$$ solve by simple $\iint$

$c(r) = B_1 \ln r + B_2$ now, in 2D cylindrical coordinates

B_1, B_2 undertermined constants $\nabla^2 c = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial c}{\partial r}\right)$

BC $r=a$ flux matching $\quad 0 = R_{gen} + (2\pi a) D \left.\frac{dc}{dr}\right|_{r=a}$ $\quad$ {no. solution}

$r \to \infty$, $c \to 0$