$$\boxed{\begin{array}{c}\text{More on Diffusion} \\ \text{and} \\ \text{Applications}\end{array}}$$

Diffusion

Is a result of random particle motion. which tends to disperse particles throughout the medium. Continuum limits of random walk processes can be used to derive flux formulae. Most common is

$$\vec{J} = -D \vec{\nabla} u \qquad D = \text{diffusivity}$$

Since $\vec{\nabla} u$ is the direction in which concentration u increases most rapidly, particles move <u>down</u> gradient.

$$\vec{J} = -D(x) \vec{\nabla} u$$

nonhomogeneous isotropic diffusion

$$\vec{J} = -\underline{D} \vec{\nabla} u$$

$\underline{D} \in \mathbb{R}^{3\times 3}$ yields anisotropic diffusion.

For particles of radius a, viscosity μ

$$D = \frac{kT}{6\pi\mu a} \qquad \text{Einstein formula}$$

Here T = temperature, k = Boltzman constant

EXAMPLE Reaction Diffusion Equation

$$U + V \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} W \qquad \text{buffering}$$

Law of mass action for source terms. If buffering sites are immobile then $D_v = D_w = 0$.

Since U allowed to diffuse in cell we arrive at the Rx-Diff system

$$\begin{aligned} u_t &= D_u \nabla^2 u - k_1 uv + k_{-1} w, \quad x \in \Omega \\ v_t &= \quad - k_1 uv + k_{-1} w \\ w_t &= \quad k_1 uv - k_{-1} w \end{aligned}$$

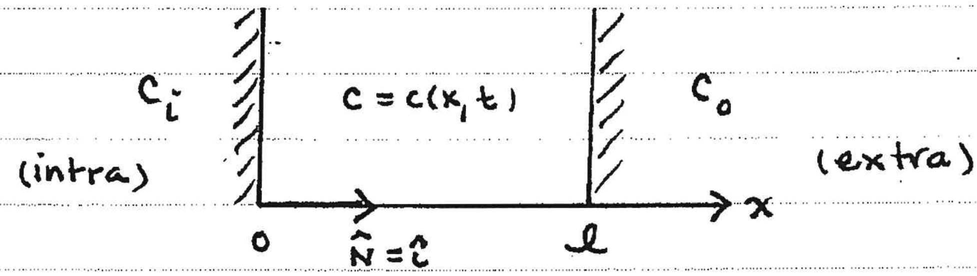
Boundary conditions needed to complete model

$$\vec{u}_t = D \nabla^2 \vec{u} + f(\vec{u}) \qquad D = \mathrm{diag}(D_u, 0, 0)$$

A common B.C. for diffusion is "no flux" as in $\vec{J} \cdot \hat{N}|_{\partial\Omega} = 0$ on $\partial\Omega$. For diffusion:

$$\vec{\nabla} u \cdot \hat{N} = \left.\frac{\partial u}{\partial n}\right|_{\partial\Omega} = 0$$

Diffusion thru a membrane (passive)



Diffusion equation for membrane

$$(1) \qquad \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \qquad c(0,t) = c_i \,, \quad c(\ell,t) = c_o$$

At equilibrium, $c_t = 0$ implies

$$c(x) = c_i + (c_o - c_i)\left(\frac{x}{\ell}\right)$$

Using $\vec{J} = -D \vec{\nabla} c$, one can compute the steady state flux thru membrane.

$$\boxed{J = \frac{D}{\ell}(c_i - c_o)} \qquad \vec{J} = J\hat{i}$$

If $c_i > c_o$ there is a steady flow out.

For cell membranes sometimes called "leaky" channels. Also, no energy is utilized hence <u>passive transport</u>

Facilitated Transport (of Oxygen in Muscle)

$$O_2 + Mb \underset{k_-}{\overset{k_+}{\rightleftarrows}} Mb\,O_2$$

where

			(gmm)
S	$= [O_2]$	oxygen	32
E	$= [Mb]$	myoglobin	17K
C	$= [Mb\,O_2]$	oxymyoglomin	17K

Here E and C are large (intracellular) molecules

Dimensional Reaction Diffusion Equations

(1) $S_t = D_s S_{xx} + F \qquad x \in (0, \ell)$

(2) $E_t = D_e E_{xx} + F$

(3) $C_t = D_c C_{xx} - F$

where ℓ is the membrane thickness.

$$F = k_{-1} C - k_+ S E$$

and the boundary conditions are

$$S(0,t) = S_0' \qquad S(\ell, t) = \beta S_0$$

$$E_x(0,t) = 0 \qquad E_x(\ell, t) = 0$$

$$C_x(0,t) = 0 \qquad C_x(\ell, t) = 0$$

The latter for E, C are "no flux" or Neumann B.C.

Dimensional Analysis

$$S = s S_0 \qquad E = E_0 e \qquad C = E_0 c$$

$$x = y\ell \qquad t = t_0 \tau$$

where $t_0 = (k_+ E_0)^{-1}$. Define dimensionless param:

$$\varepsilon = \frac{E_0}{S_0} \qquad \alpha = \frac{k_-}{k_+ S_0} \qquad \varepsilon_1 = \frac{D_s}{E_0 k_+ \ell^2} \qquad \varepsilon_2 = \frac{D_e}{E_0 k_+ \ell^2}$$

Since $D_e \approx D_c$ (large similar weight molecules)

(4) $\quad s_\tau = \varepsilon_1 s_{yy} + f \qquad s(0,\tau) = 1, \; s(1,\tau) = \beta$

(5) $\quad e_\tau = \varepsilon_2 e_{yy} + \frac{1}{\varepsilon} f \qquad$ Neumann

(6) $\quad c_\tau = \varepsilon_2 c_{yy} - \frac{1}{\varepsilon} f \qquad$ Neumann

and

(7) $\quad f = -se + \alpha c$

Parameter assumptions

(A1) $\quad 0 < \varepsilon \ll 1 \qquad$ E_0 low relative to S_0

(A2) $\quad \varepsilon_2 \ll \varepsilon_1 \qquad$ since large E molecules (move) diffuse more slowly than O_2.

Initial Condition Assumptions

$$s(y,0) = \text{any fn satisfying B.C. on } s$$

$$e(y,0) = 1 \qquad \text{throughout membrane}$$

$$c(y,0) = 0 \qquad \text{"} \qquad \text{"}$$

The latter mimics Michaelis Menten I. Cond.

Conservation of Myoglobin

Total amount of Mb (bound or not) is

$$v = e + c$$

Given (5)-(6), boundary and initial conditions

$$(8) \qquad v_\tau = \varepsilon_2 v_{yy} \qquad y \in (0,1),\ t > 0$$

$$(9) \qquad v_y(0,t) = v_y(1,t) = 0 \qquad \forall t > 0$$

$$(10) \qquad v(y,0) = 1 \qquad y \in (0,1)$$

The unique solution of (8)-(10) is $v(y,\tau) \equiv 1$

$$e + c = 1 \qquad \forall (y,\tau)$$

Quasi-Steady State

On account $\varepsilon \ll 1$, $\varepsilon_2 \ll 1$ eqn (5) $\Rightarrow$ $f = 0$ at QSS

$$c = \frac{s}{s + \alpha}$$

is dimensionless form of QSS

Dimensional Flux at Equilibrium

$$S_t + C_t = 0$$

Adding (1)-(2) yields

$$D_s S_{xx} + D_e C_{xx} = 0 \qquad x \in (0, \ell)$$

Integrate

$$(11) \qquad -J = D_s S_x + D_e C_x$$

where J is the (constant) equilibrium flux.
Integrate (11) over $(0, \ell)$ using B.C.

$$(12) \qquad -J\ell = D_s(\beta - 1)S_0 + D_e(C_\ell - C_0)$$

Don't know C_ℓ, C_0 so use QSS approximation in dimensional form

$$(13) \qquad C' = \left(\frac{E_0}{k_+}\right) \frac{S'}{\underline{K} + S} \qquad \underline{K} \equiv \frac{k_-}{k_+}$$

Since $S_\ell = S(\ell)$, $S_0 = S(0)$ in (13) to get C_ℓ, C_0.

After much algebra (12)-(13) yield flux

$$\boxed{J = \frac{D_s}{\ell}\left(\overbrace{1 + \mu\rho}^{>1}\right)(S_0 - S_\ell) \qquad \text{Facilated Diffusion}}$$

where facilitation factor $\mu\rho$ is

$$\mu\rho = \frac{D_e}{D_s}\frac{\underline{K}}{k_+}\frac{E_0}{(\underline{K} + S_\ell)(\underline{K} + S_0)}$$

Diffusion and Random walks

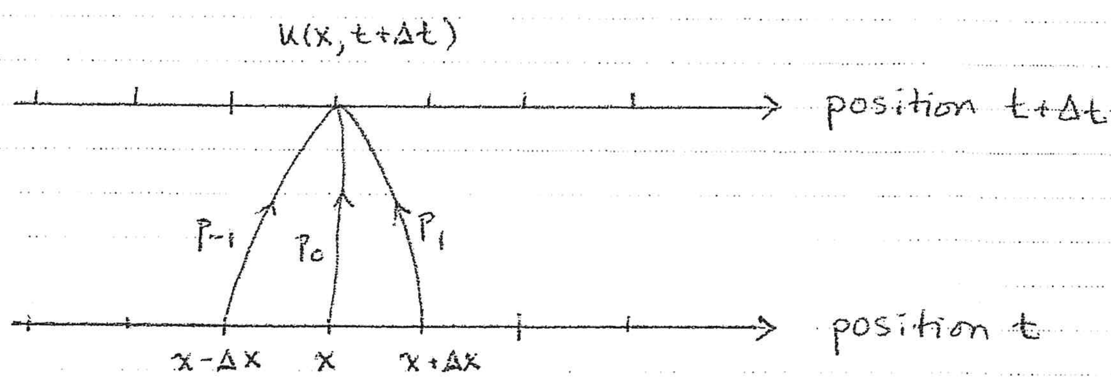
Diffusion can be viewed as the continuum limit of a discrete random walk process.

Let $X(t)$ be the random variable for the position of an organism and let $u(x,t)$ be probability density function.

$u(x,t)\Delta x$ = probability organism is located in the interval $(x, x+\Delta x)$ at time t

$$u(x,t)\Delta x = P(x < X(t) < x+\Delta x)$$

In a random walk one attributes probabilities to the organisms movement from time t to $t+\Delta t$.



Schematic illustrates a random walk where organism position at x, $t+\Delta t$ could have arisen from organism moving left or right Δx units with probabilties p_1, p_{-1} or remaining stationary with prob p_0.

For such a random walk (assuming independence)

$$u(x, t+\Delta t) = p_{-1}\, u(x-\Delta x, t) + p_0\, u(x, t) + p_1\, u(x+\Delta x, t)$$

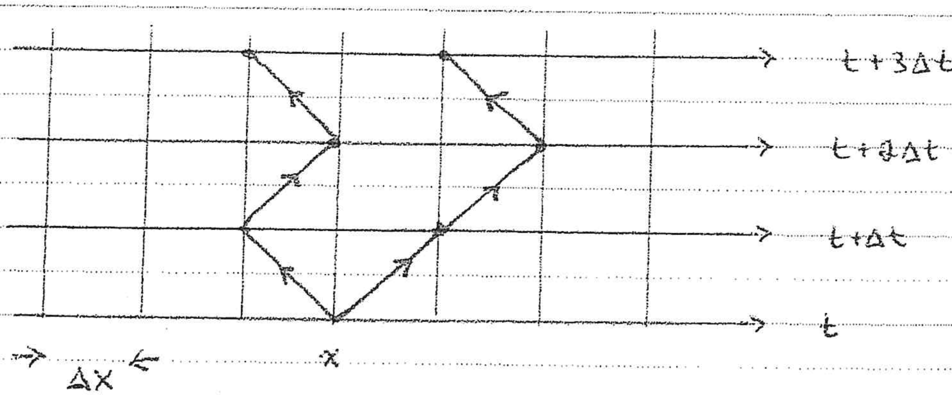
where

$$p_{-1} + p_0 + p_1 = 1$$

As a special case we consider $p = p = \frac{1}{2}$, $p_0 = 0$

$$(1) \qquad u(x, t+\Delta t) = \frac{1}{2} u(x-\Delta x, t) + \frac{1}{2} u(x+\Delta x, t)$$

Here the organism moves left/right Δx units with equal probability and with certainty moves (doesn't stay a posit. x)



Shows two potential realizations for the random walk.

Continuum Limit ($\Delta x, \Delta t \to 0$)

$$(1) \qquad u(x, t+\Delta t) = \tfrac{1}{2} u(x-\Delta x, t) + \tfrac{1}{2} u(x+\Delta x, t)$$

Seek a PDE that $u(x,t)$ satisfies. Expand each term in a Taylor series about (x,t):

$$u(x, t+\Delta t) = u + u_t \Delta t + \tfrac{1}{2} u_{tt} \Delta t^2 + O(\Delta t^3)$$

$$u(x+\Delta x, t) = u + \Delta x + \tfrac{1}{2} u_{xx} \Delta x^2 + O(\Delta x^3)$$

$$u(x-\Delta x, t) = u - u_x \Delta x + \tfrac{1}{2} u_{xx} \Delta x^2 + O(\Delta x^3)$$

After substituting these into the assumed rule (1) the u terms cancel:

$$(2) \qquad u_t \Delta t + \tfrac{1}{2} u_{tt} \Delta t^2 = \tfrac{1}{2} \Delta x^2 u_{xx} + \text{h.o.t.}$$

where h.o.t. denotes higher order terms. Dividing both sides by Δt and rearranging

$$(3) \qquad u_t = \left(\frac{\Delta x^2}{2\Delta t}\right) u_{xx} - \tfrac{1}{2} u_{tt} \Delta t + \text{h.o.t.}$$

fix constant $\qquad\qquad$ as $\Delta t \to 0$

and we arrive at the <u>diffusion eqn</u> for $u(x,t)$

$$(4) \qquad u_t = D\, u_{xx}$$

where

$$D = \frac{\Delta x^2}{2\Delta t}$$

Earlier we showed that

$$(5) \qquad u(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-x^2/4Dt} \qquad x \in \mathbb{R},\ t > 0$$

was a solution to the diffusion eqn (4).
It is readily verified that

$$\int_{\mathbb{R}} u(x,t)\,dx = 1$$

so the fundamental solution in (5) is the probability density function for the random walk. Moreover,

$$P(a < X(t) < b) = \int_a^b u(x,t)\,dx$$

is the probability the organism is in (a,b) at time t.

Connection to concentration

If the "organism" in the preceding discussion is a molecule and Ω contains N such molecules which randomly move (independently) then

$$c(x,t) = N\,u(x,t) = \text{molecular (\#) concentrat.}$$

and $c(x,t)$ also satisfies a diffusion equation

$$c_t = D c_{xx}$$

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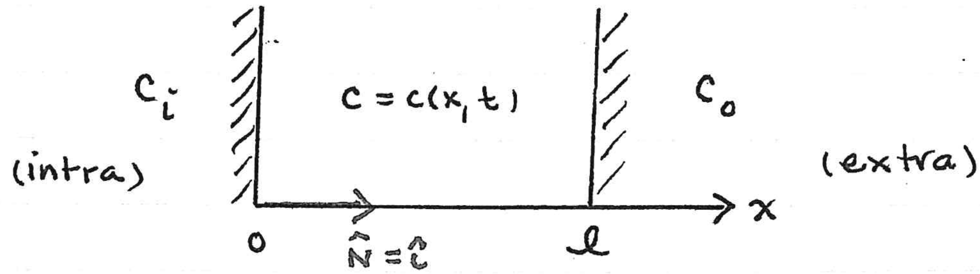

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