Continuum Diffusion Equations

- the motion of a particle is unpredictable, but the average motion of many particles follows a simple law
- imagine the release of trillions of random walking particles

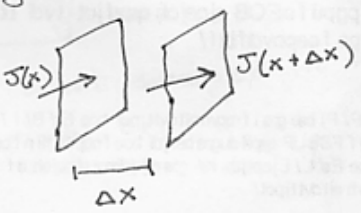
SHOW FIGURE

- particles are uniform in y, z ; not in x
- at each time point, imagine particles hopping to the left or right
- particles will move to the spacer bins
- the # of particles that move accross the boundary is the flux J
- the flux is opposite the concentration gradient

Fick's Law $\boxed{J = -D\frac{dc}{dx}}$

- How does the concentration change in time?
  - if flux is positive, concentration goes down in time
  - if $\Delta x \to 0$ (spacing between boundaries goes to 0)

$$\frac{dc}{dt} = -\frac{dJ}{dx}$$



The Diffusion Equation

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \quad \text{(one dimension)}$$

more generally,

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

microscopic theory,

$$\frac{\partial p(r,t)}{\partial t} = D\nabla^2 p(r,t)$$

SHOW COORDINATE SYSTEM FIGURE

Diffusion at steady-state

- time derrivative is zero $\frac{\partial c}{\partial t} = 0$

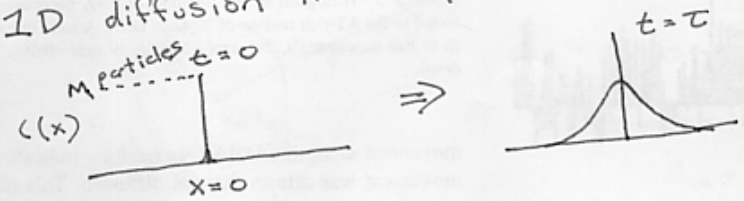
$$\nabla^2 c = 0$$

(note that the diffusion const is gone)

- many solutions for different geometries and boundary conditions are available (see book)

Time-dependent Solutions

- 1D diffusion from a point



$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}$$

look up or use Laplace or Fourier transforms, which is essentially the same as looking it up

$$c(x,t) = \frac{M}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$

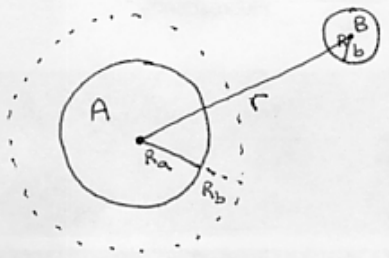
M is total number of particles

Gaussian ⇒ same as what emerged in the random walk derrivation

Diffusion-limited reactions

- speed only depends on the diffusion constant and is independent of the intrinsic chemical process itself
- reactions cannot be faster than the diffusion controlled rate

• Diffusion-limited binding in solution



- Diffusion of molecules towards a central reacting molecule A
- B disappears when it reacts with A
- A much larger than B

$R_a + R_b \rightarrow R_a$

$\mathcal{D}_B >> \mathcal{D}_A$

(imagine an antibiotic diffusing to a ribosome)

@ steady-state

$$\nabla^2 C_B = 0 = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial C_B}{\partial r}\right)$$

$$\frac{\partial}{\partial r}\left(r^2 \frac{\partial C_B}{\partial r}\right) = 0$$

$$r^2 \frac{\partial C_B}{\partial r} = A$$

$$\frac{\partial C_B}{\partial r} = \frac{A}{r^2}$$

$$C_B = -\frac{A}{r} + B$$

Boundary conditions

@ $r = R_a$ $\quad C_B = 0$ (B disappears when it hits A)

@ $r \rightarrow \infty$ $\quad C_B = C_0$ (bulk concentration of B)

$$0 = -\frac{A}{R_A} + B \Rightarrow 0 = \frac{-A}{R_A} + C_0 \Rightarrow A = R_A C_0$$

$C_0 = B$

$$\boxed{C_B = \frac{-R_A C_0}{r} + C_0}$$

- the rxn rate equals the flux at the surface multiplied by the surface area

$$J(r) = -D_B \frac{\partial c_B}{\partial r}$$

$$= -D_B \left(\frac{R_A C_0}{r^2} \right)$$

@ surface

$$J(R_B) = -\frac{D_B C_0}{R_A}$$

the surface area of a sphere $A = 4\pi R_A^2$

collision frequency $= |J| \cdot \text{Area}$

$$= \left(4\pi R_A^2\right)\left(-\frac{D_B C_0}{R_A}\right)$$

$$= \underbrace{4\pi R_A D_B}_{k_+} C_0$$

↑ Diffusion-limited rate

$$\boxed{k_+ = 4\pi R_B D_B}$$

when both molecules are about equal size

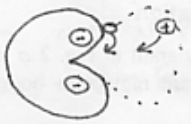
$$k_+ = 4\pi (R_A + R_B)(D_A + D_B)$$

putting in realistic numbers

$$k_+ \sim 4 \times 10^9 \frac{1}{M \cdot S}$$

Acetylcholinesterase $k_+ = 1.1 \times 10^{10} \frac{1}{M \cdot S}$

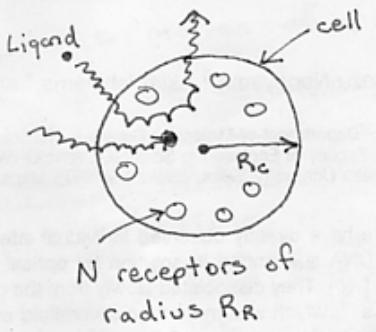
- hydrolyzes the neurotransmitter acetylcholine to terminate the synaptic response



- binding site is a cleft that is lined by negatively charged + aromatic groups that form electrostatic channels to the active site
- electristatic funnel that extends out from the active site via coolombic interactions

Binding to membrane receptors on the cell surface

(Berg + Purcell, 1977) to 'Effect on intake...'



N receptors of radius R_R

- if the ligand collides with any part of the cell surface, the cell restricts diffusion such that the ligand has a high probability of hitting the surface again

- number of receptors per cell:

  bacterium 10 to 10,000

  eukaryote 5,000 to 1,000,000

- Derivation in MCB Chap 8.8 (combines bulk diffusion to the cell w/ a random walk - and escape probability - on the surface)

- Diffusion-limited association rate:

$$k_+ = 4\pi R_c \mathcal{D}_L \left(\frac{N R_R}{4R_c + N R_R}\right)$$

- 2 limits:

  ① very few receptors on the cell surface

  $N R_R \ll R_c$, $k_+ \to \pi \mathcal{D}_L N R_R$

  cell is irrelevant, receptor is target

  ② many receptors cover the surface

  $N R_R \gg R_c$, $k_+ \to 4\pi R_c \mathcal{D}_L$

  reduced to diffusion-limited collisions w/ the cell

- What is the critical number of receptors, where both terms are important?

$$k_+ = 4\pi R_c \mathcal{D}_L \underbrace{\left(\frac{N R_R}{4R_c + N R_R}\right)}_{\text{when this term} = 0.5} \quad \Rightarrow \quad 4R_c = N_c R_R$$

$$N_c \sim \frac{4R_c}{R_R}$$

$R_R \sim 2\,nm = 0.002\,\mu m$

bacterium $R_c \sim 0.3\,\mu m$ $N_c \sim \frac{1.2}{0.002} = 600$

eukaryote $R_c \sim 10\,\mu m$ $N_c \sim \frac{40}{0.002} = 20{,}000$

5400 → 6% coverage

180,000 → 18% coverage

Range 0.1–0.9

N ← dominates 2,000 – 180,000 → 60 – 5400

cell-size dominant