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 space between bins.
- The # of particles that move across the boundary is the flux J.
- The flux is opposite the concentration gradient.

**Fick's Law**

\[ J = -D \frac{dc}{dx} \]

- 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**

\[ \frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \]  
(one dimension)

more generally,

\[ \frac{\partial c}{\partial t} = D \nabla^2 c \]

**SHOW COORDINATE SYSTEM FIGURE**
Diffusion at steady-state

- Time derivative 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

\[ c(x, t) = \frac{M}{\sqrt{4\pi D t}} \exp\left(-\frac{x^2}{4Dt}\right) \]

\( M \) is total number of particles

Gaussian \( \Rightarrow \) same as what emerged in the random walk derivation
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 $B$
  \[
  R_A + R_B \rightarrow R_A
  \]
  \[
  B \gg \Delta A
  \]
  (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 $C_B = 0$  \quad ($B$ disappears when it hits $A$)

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

\[
O = -\frac{A}{R_A} + B  \implies  O = -\frac{A}{R_A} + C_0  \implies  A = R_A C_0
\]

\[
C_0 = B
\]

\[
C_B = -\frac{R_A C_0}{r} + C_0
\]
- the rxn rate equals the flux at the surface multiplied by the surface area

\[ J(r) = -D_b \frac{\partial c}{\partial r} = -D_b \left( \frac{r A_c}{r^2} \right) \]

\( A \) surface

\[ J(r_0) = - \frac{D_b c_0}{R_A} \]

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

collision frequency = \( |J| \cdot \text{Area} \)

\[ = \left( 4\pi R_A^2 \right) \left( \frac{D_b c_0}{R_A} \right) \]

\[ = \frac{4\pi R_A D_b c_0}{k_+} \]

\( k_+ \) diffusion-limited rate

when both molecules are about equal size

\[ k_+ = \frac{4\pi R_A D_b c_0}{R_A + R_B} \]

putting in realistic numbers

\[ k_+ = 4 \times 10^{-1} \text{ M}^{-1}\text{S} \]

Acetylcholinesterase \( k_+ = 1.1 \times 10^{10} \text{ M}^{-1}\text{S} \)
- 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
- electrostatic funnel that extends out from the active site via coulombic interactions
Binding to membrane receptors on the cell surface

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

- 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:

\[ k_+ = 4\pi R_c D_L \left( \frac{N_R}{4R_c + N_R} \right) \]

- Z limits:
  1. Very few receptors on the cell surface
     - \( N_R R_c \ll R_c \), \( k_+ \to \frac{4\pi R_c D_L}{N_R} \)
     - Cell is irrelevant, receptor is target
  2. Many receptors cover the surface
     - \( N_R R_c \gg R_c \), \( k_+ \to 4\pi R_c D_L \)

- Reduced to diffusion-limited collisions w/ the cell

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

\[ k_+ = 4\pi R_c D_L \left( \frac{N_R R_c}{4R_c + N_R} \right) \]

\[ k_+ = N_c R_c \]

\[ N_c = \frac{4R_c}{N_R} \]

- S400 = 6% coverage
- 120,000 = 13% coverage

- Bacterium: \( R_c = 0.3 \mu m \), \( N_c = 12 \), \( N_R = 5,000 \), \( D_L = 600 \)
- Eukaryote: \( R_c = 10 \mu m \), \( N_c = 40 \), \( N_R = 20,000 \), \( D_L = 0.002 \mu m \)

Cell-size range: 0.002 - 120,000

\( R_c \approx \frac{2nm}{0.002 \mu m} \)