Review of Mass Transfer

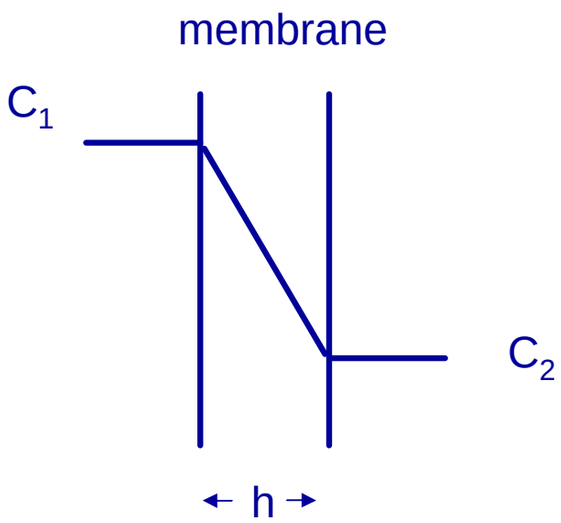
- Fick's First Law (one dimensional diffusion)
  - J flux (moles/area/time)
  - At steady-state or any instant in time

$$J = -D\frac{dC}{dx}$$

- Fick's Second Law
  - When concentration changes with time

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

Example – Fick's First Law



- SS valid if a high C_1 is maintained and
- C_2 remains << C_1 by removal of drug or large volume

- Determine amount of drug to pass through membrane in one hour

- D = 1×10^{-10} cm^2/s
- h = 2×10^{-3} cm
- A = 10 cm^2
- C_1 = 0.5 mol/L
- C_2 = 0

Example Fick's First Law

Soln

$$J = -D\frac{dC}{dx} = -D\frac{C_2 - C_1}{h}$$

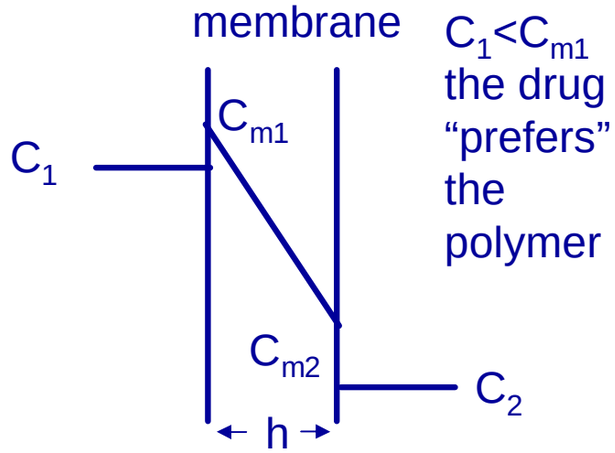
$$= -1\times10^{-10}\ cm^2/s \quad \frac{\left[0.5\ \frac{mol}{l} - 0\ \frac{mol}{l}\right]}{10\ cm^2}$$

$$J = 2.5\times10^{-11}\ \frac{mol}{s\ cm^2}$$

$$Amt = J \cdot A \cdot t$$

$$= 2.5\times10^{-11}\ \frac{mol}{s\ cm^2} \cdot 3600\ s \cdot 10\ cm^2 = 9\times10^{-7}\ mol \text{ in } 1\ hr$$

Partitioning



- So far we have assumed the drug has equal affinity for solution and membrane. This is unlikely.
- Preference is indicated by partitioning

- Flux across membrane

$$J = -D\frac{dCm}{dx} = -D\left[\frac{C_{m2} - C_{m1}}{h}\right]$$

- Cannot measure C_m
- Partition Coefficient relates C_m to C

$$K_{m1} = \frac{C_{m1}}{C_1} \qquad K_{m2} = \frac{C_{m2}}{C_2}$$

Partition Coefficient

- A measure of relative concentrations in membrane vs. solution at equilibrium
- If both solvents (1 and 2) are the same, then

$$K_{m1} = K_{m2} = K_m$$

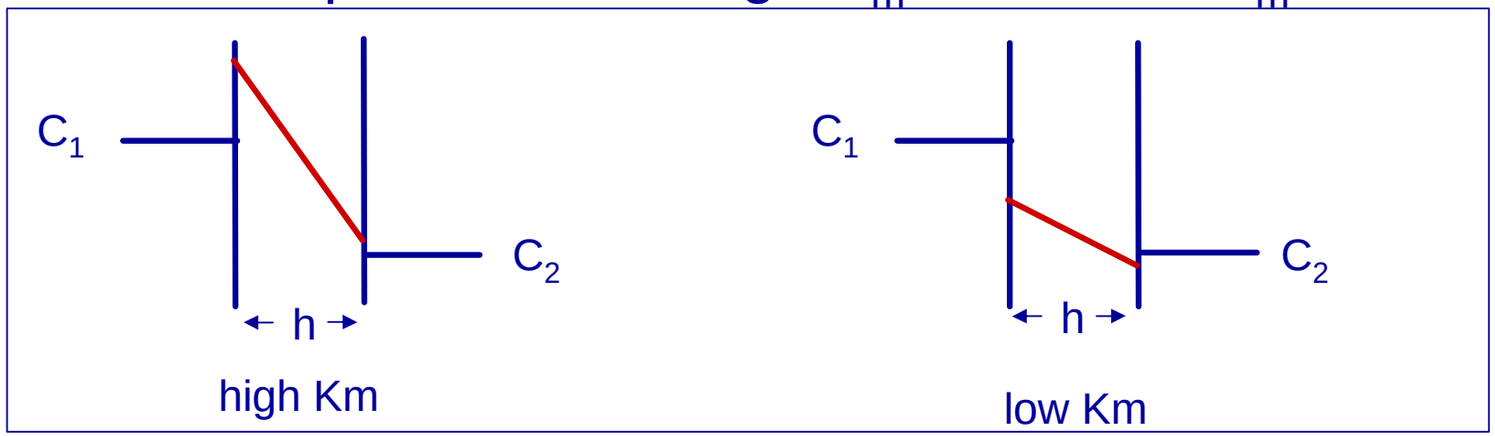
- Flux becomes

$$J = -D\frac{dCm}{dx} = -DK_m\left[\frac{C_2 - C_1}{h}\right]$$

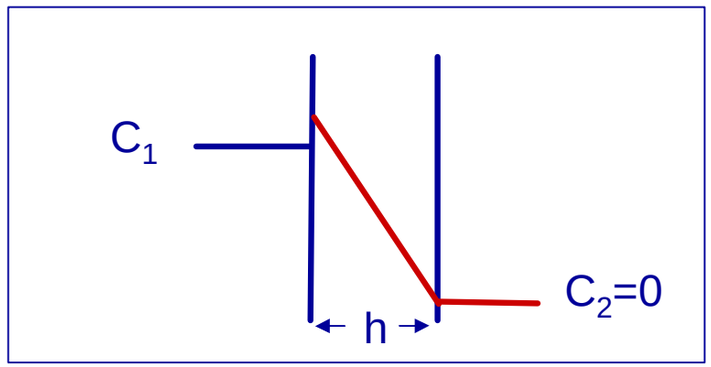
- The term [DK_m/h] is the *Permeability*

Partition Coefficient

- Sketch the profiles for a high K_m and a low K_m



- Sketch the profile for C2=0
  - Common situation: body acts as a sink to remove the drug



Example – Transdermal Delivery

- Digitoxin (used for heart failure; ointment)
- How much digitoxin can be delivered transdermally in one day
- Membrane control – skin acts as barrier membrane (stratum corneum, outermost layer)

- $K_{m1} = 0.014$
  - Between ointment and *s.c.*
- $D = 5.2 \times 10^{-10}$ cm^2/s
  - Through the *s.c.*
- $h = 2 \times 10^{-3}$ cm
  - Typical thickness of s.c.
- $A = 10$cm^2
  - Covered by ointment
- $C_1 = 0.01$ mg/cm^3
  - Saturation C of drug in ointment

Solution

Soln

$$J = -\frac{D K_{m1}}{h}\left(C_2^{\circ} - C_1\right)$$

$$J = 5.2 \times 10^{-10} \frac{cm^2}{s} \frac{(0.014)}{2.0 \times 10^{-3}\ cm} \left(0.01 \frac{mg}{cm^3}\right)$$

$$= 3.64 \times 10^{-11} \frac{mg}{s\ cm^2}$$

For 1 day $= 8.64 \times 10^4$ s and 10 cm^2 area

$$Amt = J \cdot A \cdot t = \boxed{3.15 \times 10^{-5}\ mg}$$

small. Formulability is a challenge w/ transdermal systems

Some K values

Steroid	K
Cortisol	5.5e-3
Estradiol	2e-1
Melengstiol acetate	18.87
Norethindrone	1.22
Norgestrel	3.19
19-Norprogesterone	33.3
Megesterol acetate	35.7
Mestranol	100
Progesterone	22.7
Testosterone	4.31

Reported by Sundaram and Kincl [93] in Kydonieus, Treatise in CDD

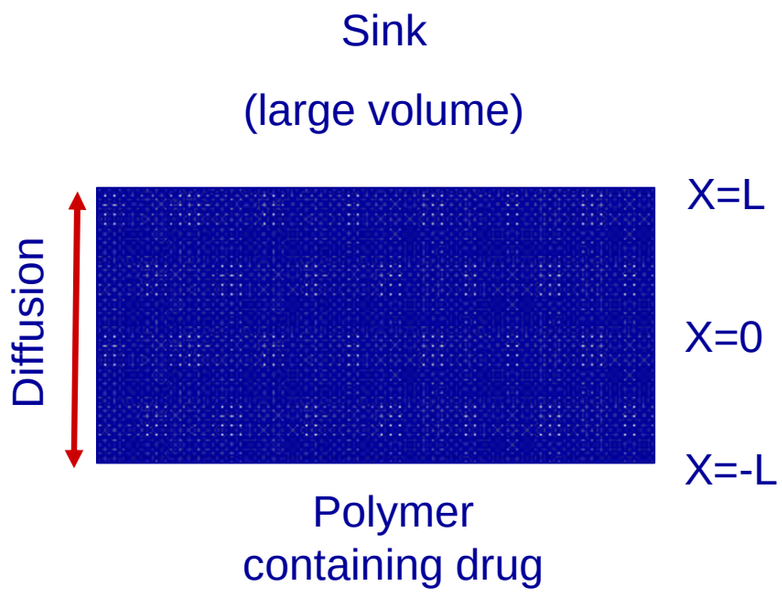
Fick's Second Law

- For one-dimensional unsteady-state diffusion

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2}$$

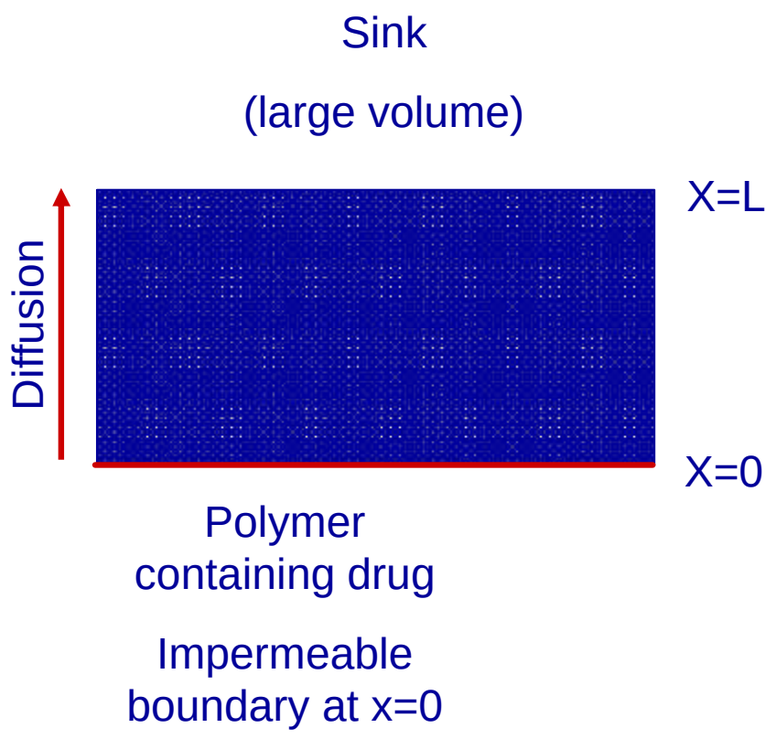
- How many IC's and BC's are needed?

Finite source



- IC
  - At t=0, $C=C_0$
- BC1
  - x=L, C=0
- BC2
  - X=0, dC/dx = 0 (symmetric)

Finite source, reflective boundary



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Solution method

- For cartesian (planar) systems
  - Separation of variables or Laplace Transforms
  - Error function solution
- We will investigate this later!