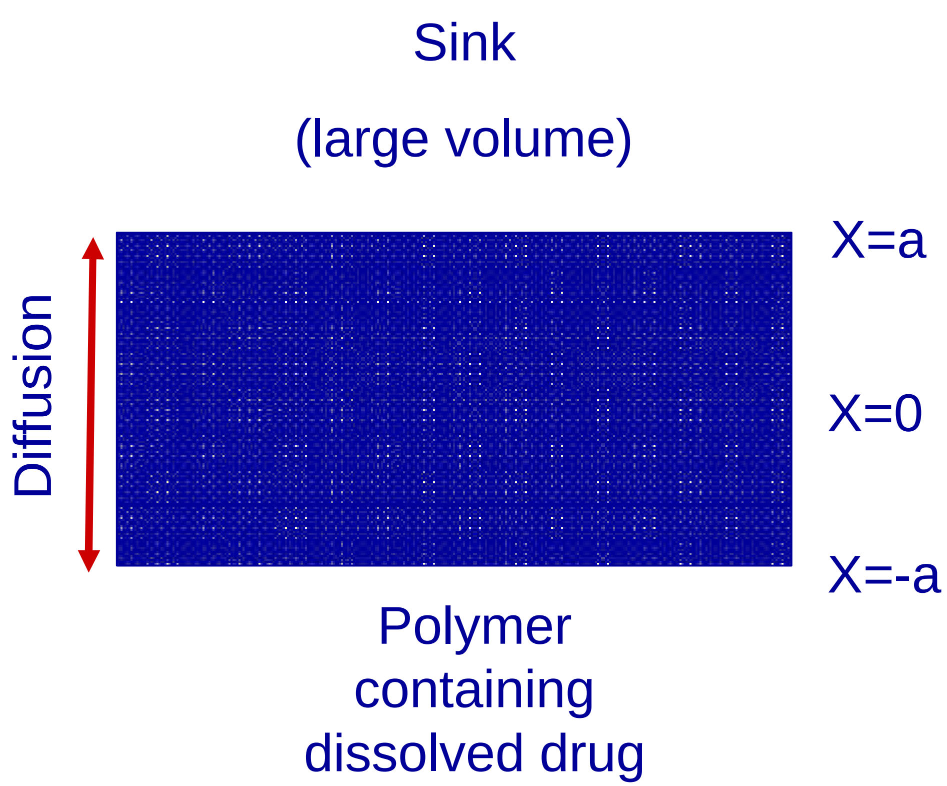
Controlled Release

Drug Dissolved in Matrix

Unsteady-state Diffusion



- Fick's Second Law

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

- Initial Condition
  - $C=C_0$ $\quad -a<x<a,\ t=0$
- Boundary Condition
  - $C=0$ $\quad x=-a$
- Boundary Condition
  - $C=0$ $\quad x=a$

Analytical Solution

- Using separation of variables, Laplace transforms or other suitable technique

$$\frac{M_t}{M_\infty} = 1 - \frac{8}{p^2}\sum_{n=0}^{\infty}\left(\frac{1}{(2n+2)^2}\exp\frac{\left(-D_m(2n+1)^2 p^2\right.}{4a^2}t\right)$$

M_∞ is the fraction released

M_t is the amount released at time t

D_m is the diffusivity of the drug in the polymer

a is the half - thickness of the polymer

Analytical solution

- Previous solution

$$\frac{M_t}{M_\infty} = 1 - \frac{8}{p^2}\sum_{n=0}^{\infty}\left(\frac{1}{(2n+1)^2}\exp\left(\frac{-D_m(2n+1)^2 p^2}{4a^2}t\right)\right)$$

- Equivalent solution, more useful for short times

$$\frac{M_t}{M_\infty} = 2\left(\frac{D_m t}{a^2}\right)^{1/2}\left(p^{-1/2} + 2\sum_{n=1}^{\infty}(-1)^n \operatorname{ierfc}\left(\frac{na}{(D_m t)^{1/2}}\right)\right)$$

ierfc is the complementary error function

ierfc values can be looked up in a table just like erf(x)

Short time approximation

$$\frac{M_t}{M_\infty} = 2\left(\frac{D_m t}{a^2}\right)^{1/2}\left(p^{-1/2} + 2\sum_{n=1}^{\infty}(-1)^n \operatorname{ierfc}\left(\frac{na}{(D_m t)^{1/2}}\right)\right)$$

- What happens to the argument of ierfc as t? 0?

$$\text{As t} \to 0, \left(\frac{na}{(D_m t)^{1/2}}\right) \to \quad ?$$

- Given that $erfc(x) \to 0 \quad \text{as x} \to \infty$

  Then what happens to $\frac{M_t}{M_\infty}$ as $t \to \infty$

- Short time approximation

$$\frac{M_t}{M_\infty} \cong 2\left(\frac{D_m t}{pa^2}\right)^{1/2} \qquad 0 \le \frac{M_t}{M_\infty} \le 0.6$$

Late time approximation

$$\frac{M_t}{M_\infty} = 1 - \frac{8}{p^2}\sum_{n=0}^{\infty}\left(\frac{1}{(2n+1)^2}\exp\left(\frac{-D_m(2n+1)^2 p^2}{4a^2}t\right)\right)$$

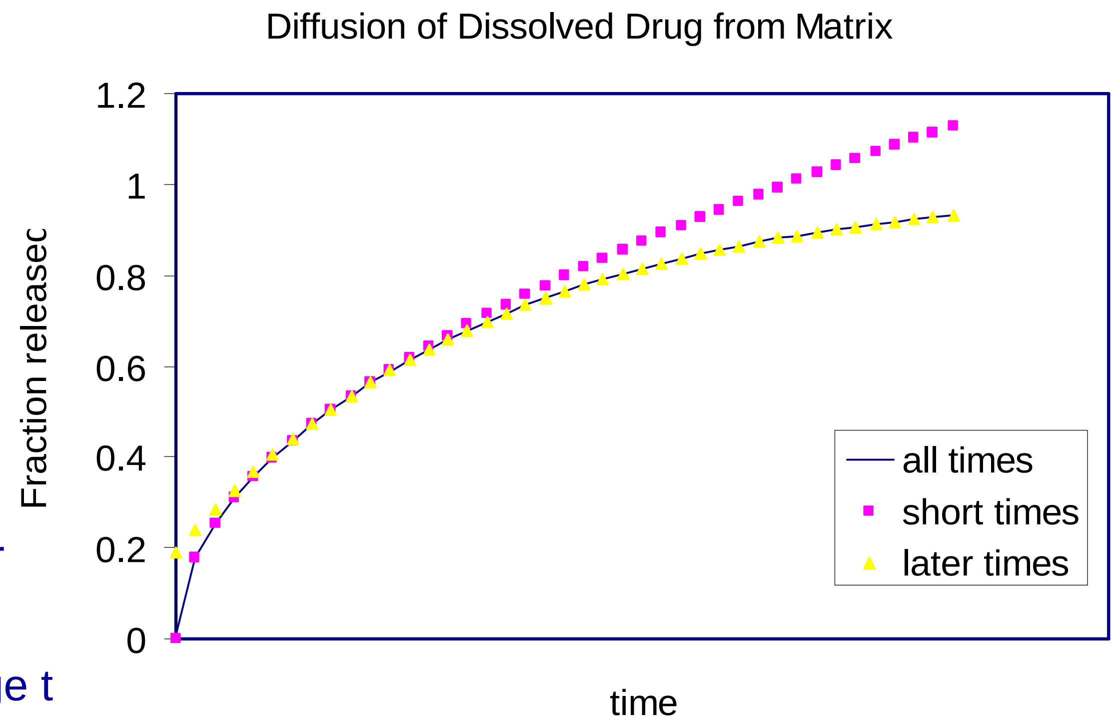
- What happens to the exponential term as t grows very large?

$$\text{As t} \rightarrow \infty \qquad \exp\left(\frac{\left(-D_m(2n+1)\right)^2 p^2}{4a^2}t\right) \rightarrow \quad 1$$

- What happens to the fraction released?
  - Use only the first term (n=0) of the series

$$\frac{M_t}{M_\infty} \cong 1 - \frac{8}{p^2}\exp\left(\frac{-D_m p^2}{4a^2}t\right)^{1/2} \qquad 0.4 \le \frac{M_t}{M_\infty} \le 1$$

Release Profiles



- Does it make sense?
  - What is the fraction released for
    - Short time approximation, t=0
    - Long time approximation, large t
  - Range of validity
    - For what F does the short time approximation overlap the full solution?
    - For what F does the long time approximation overlap the full solution?
    - For what F do the two approximate solutions overlap?
  - Note the value of fraction released for
    - Short time approximation, large t
    - Long time approximation, small t
    - Approximations do not hold outside their range

Rate of drug release

- Differentiate M/M_{inf} w.r.t. time
- Early times

$$Q_t \cong M_\infty \left(\frac{D_m}{pa^2 t} \right)^{1/2}$$

- Late times

$$Q_t \cong \frac{2D_m M_\infty}{a^2} \exp\left(\frac{-p^2 D_m}{4a^2} t \right)$$

- Rate is never zero order

Release profiles