Modelling Drug Release from a Polymer

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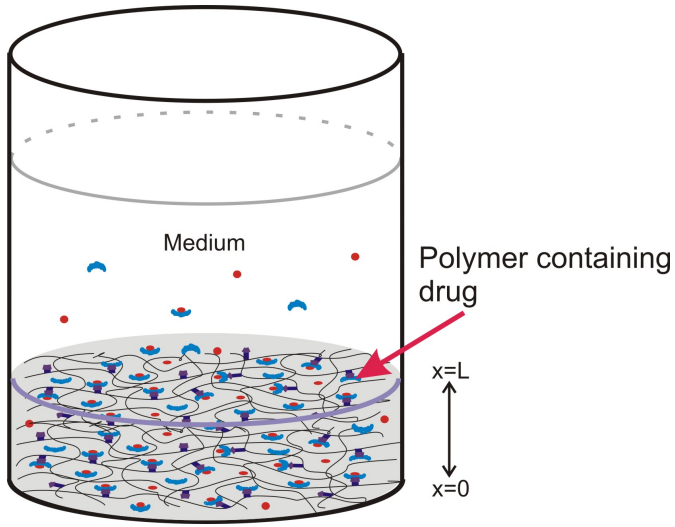
Problem Description

Task:
To model the diffusion of a drug from a polymeric wafer to a release medium, considering the effect of geometry on the rate of diffusion.



Approach:

Assumptions

- Planar System
- Diffusion through one surface only
- Initial uniform concentration of the drug in the polymer
- The release medium is a perfect sink
- Constant diffusion coefficient

Dimensional Analysis

Through Dimensional analysis and the Buckingham Pi theorem, the reduced formula for the time it takes half the drug to be released was found to be

$$\tau_{\frac{1}{2}} = \frac{H^2}{D} G\left(c_0 H^3\right)$$

where $G\left(c_0 H^3\right)$ is a function of the initial concentration and position of the drug.

Diffusion Equation

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

Where:

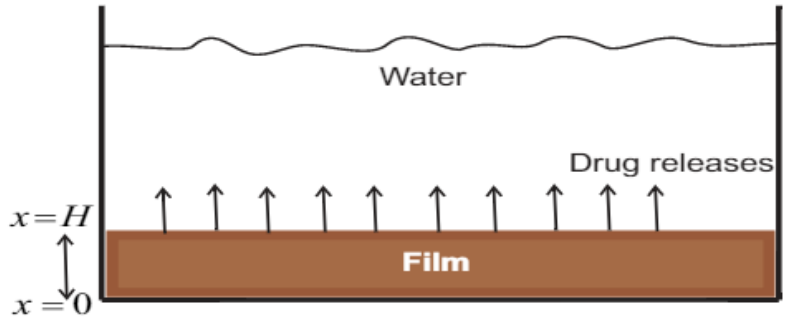
c = c(x,t) = concentration of drug in polymer

t = time

x = position

D = Diffusion Coefficient (constant)

Boundary and Initial Conditions



The polymer occupies $0 < x < H$

Boundary Conditions

$$c = 0 \text{ on } x = H, t > 0 \text{ (perfect sink condition)}$$

$$\frac{\partial c}{\partial x} = 0, \text{ on } x = 0, t > 0 \text{ (no flow condition)}$$

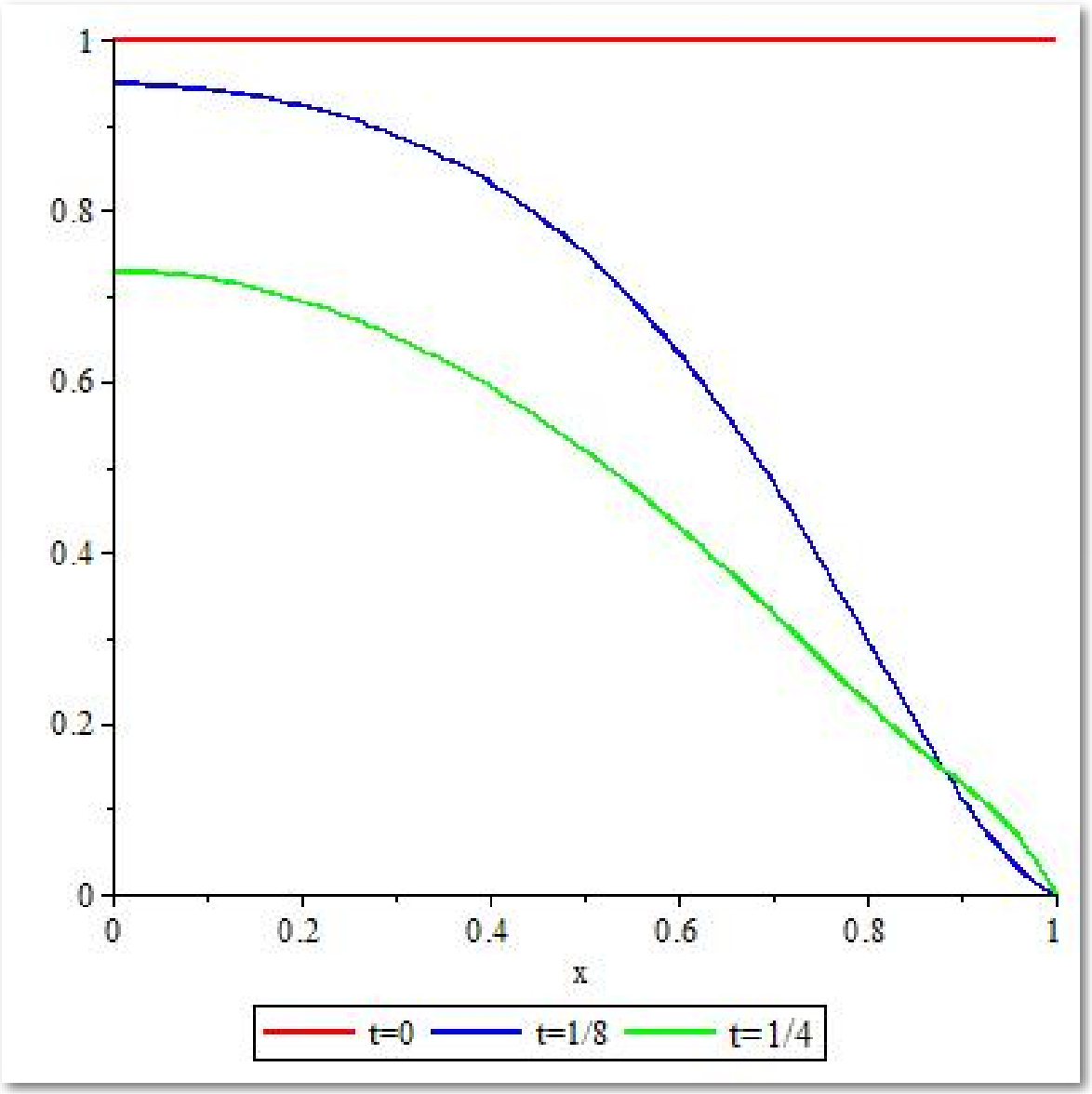
Initial Conditions

$$c = c_0, 0 < x < H, t = 0$$

PDE Solution

The initial boundary value problem was solved through separation of variables. The concentration was found to be:

$$c(x,t) = \sum_{n=0}^{\infty} \left[\left(\frac{c_0 (-1)^n}{\left(n + \frac{1}{2}\right)\pi} \right) cos \left(\frac{\left(n + \frac{1}{2}\right)\pi x}{H} \right) e^{\frac{-\left(n+\frac{1}{2}\right)\pi^2 Dt}{H^2}} \right]$$



c(x,t)

M(t) is defined as the amount of drug diffused from the polymer into the release medium, that is:
(the total amount of drug) - (the amount of drug left in the polymer at time t)

$$M(t) = AHc_0 - \int_0^H Ac(x,t)dx$$

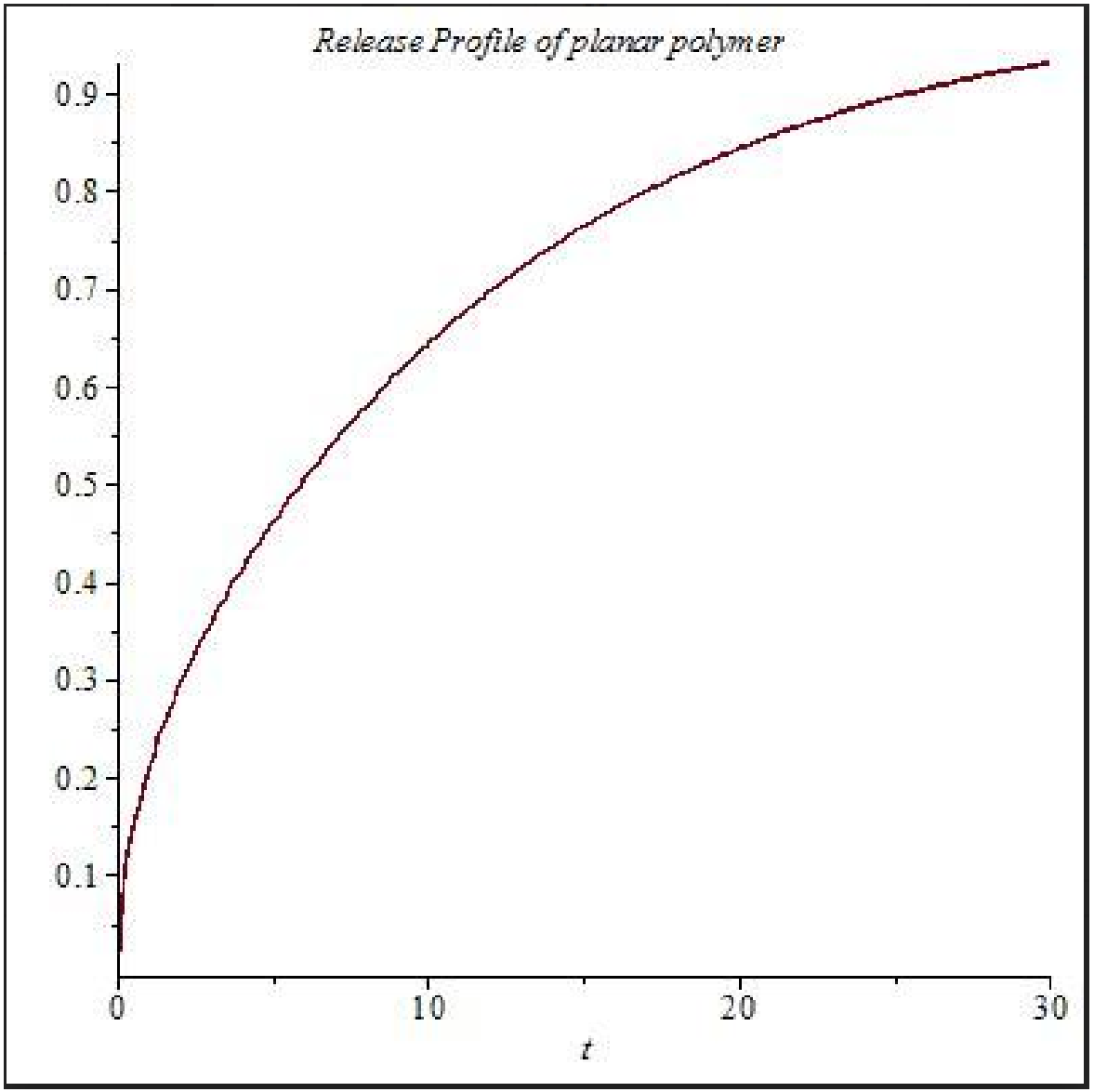
which is calculated to be:

$$M(t) = AHc_0 \left[1 - \frac{2}{\pi^2} \sum_{n=0}^{\infty} \left(\frac{1}{\left(n+\frac{1}{2}\right)^2} \right) e^{\frac{-\left(n+\frac{1}{2}\right)\pi^2 Dt}{H^2}} \right]$$

Release Profile

The release profile is a plot of $\frac{M(t)}{M(\infty)}$ against time. For the planar release profile:

$$\frac{M(t)}{M(\infty)} = \left[1 - \frac{2}{\pi^2}\sum_{n=0}^{\infty}\left(\frac{1}{\left(n+\frac{1}{2}\right)^2}\right)e^{\frac{-\left(n+\frac{1}{2}\right)\pi^2 Dt}{H^2}}\right]$$


Release Profile of planar polymer
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
10
20
30
t

Using the expression for $\frac{M(t)}{M(\infty)}$, then

$$\frac{M\left(\tau_{\frac{1}{2}}\right)}{M(\infty)} = 1 - \frac{2}{\pi^2}\sum_{n=0}^{\infty}\left(\frac{1}{\left(n+\frac{1}{2}\right)^2}\right) e^{\frac{-\left(n+\frac{1}{2}\right)^2\pi^2\tau_{1/2}}{H^2}} = \frac{1}{2}$$

Solving numerically for $\tau_{\frac{1}{2}}$:

$$\tau_{\frac{1}{2}} = 0.197\frac{H^2}{D}$$

$\therefore\ G\left(H^3 c_0\right)$ is a constant.

$\Longrightarrow$ The timescale over which the drug releases has no dependance on initial concentration c_0.
A parameter regime can be designed for the release of the drug over specific time intervals. For a H of 2mm:

- **1 day**: $D = 4.00x10^{-6} m^2/day$
- **1 week**: $D = 5.71x10^{-7} m^2/day$
- **1 month**: $D = 1.33x10^{-7} m^2/day$

Geometries

A similar analysis can be made to find the release profiles for polymers of different geometries.

Spherical

$$\frac{M(t)}{M(\infty)} = 1 - \frac{6}{\pi^2} \sum_{n=1}^{\infty} \left(\frac{(-1)^{n+1}}{n^2} \right) e^{-\frac{Dn^2\pi^2 t}{R^2}}$$

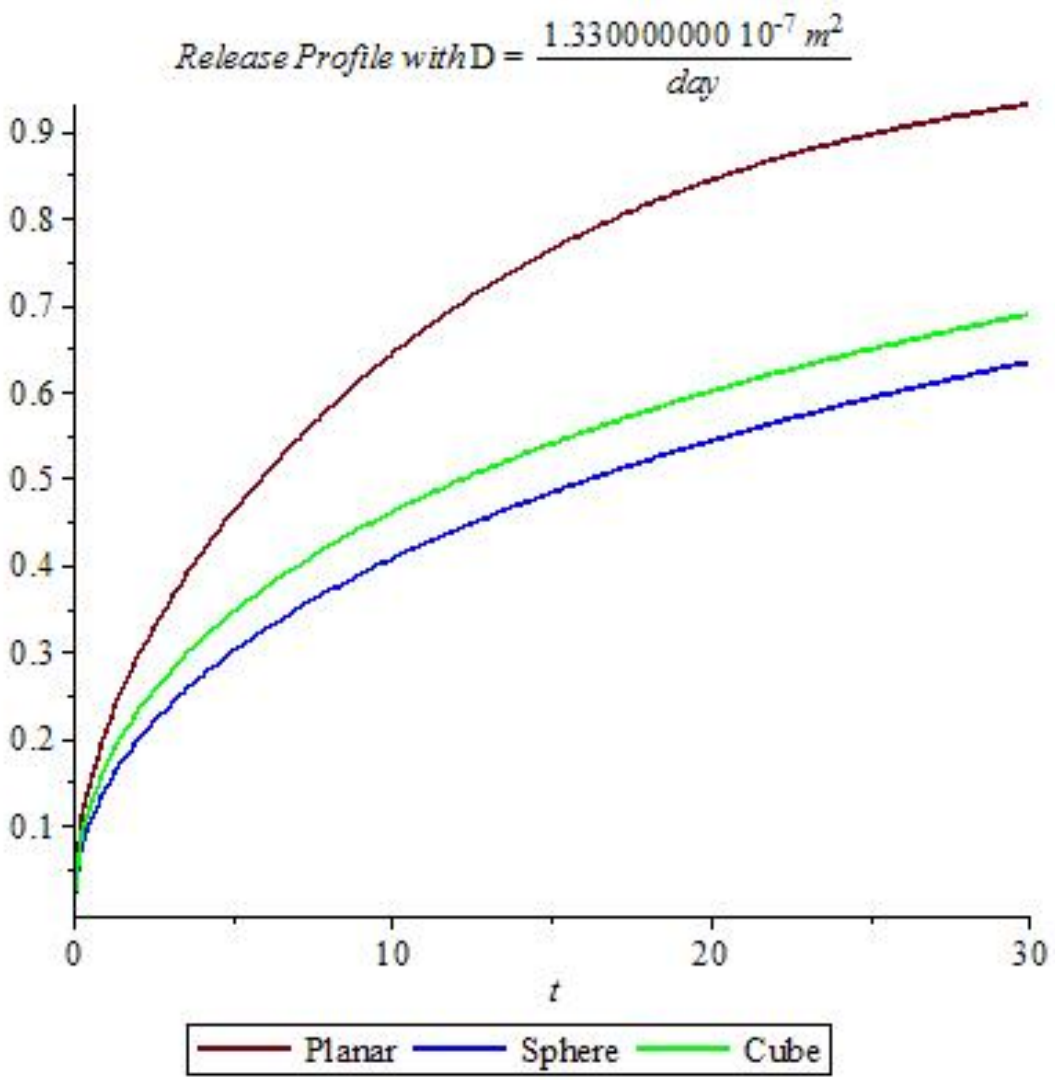
Cube

$$\frac{M(t)}{M(\infty)} = 1 - \frac{8}{\pi^6} \sum_{n,m,p=1}^{\infty} \left[\frac{\left(1-(-1)^n\right)^2 \left(1-(-1)^m\right)^2 \left(1-(-1)^p\right)^2}{(nmp)^2} \right] x \left(e^{-\frac{D\pi^2\left(n^2+m^2+p^2\right)t}{R^2}} \right)$$

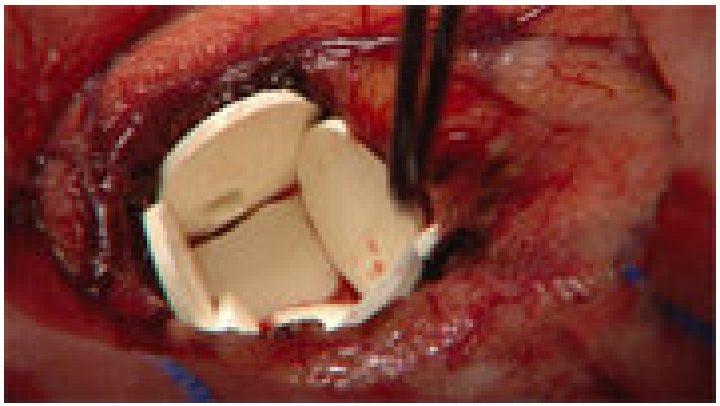
Cylindrical

$$\frac{M(t)}{M(\infty)} = 1 - \frac{32}{\pi^2}\left(\sum_{n=1}^{\infty}\frac{1}{q_n^2}e^{\frac{-q_n^2}{R^2}Dt} x \sum_{p=0}^{\infty}\frac{1}{(2p+1)^2}e^{\frac{-(2p+1)^2}{H^2}\pi^2 Dt}\right)$$

Where q_n are the roots of the Bessel function of the first kind of zero order.

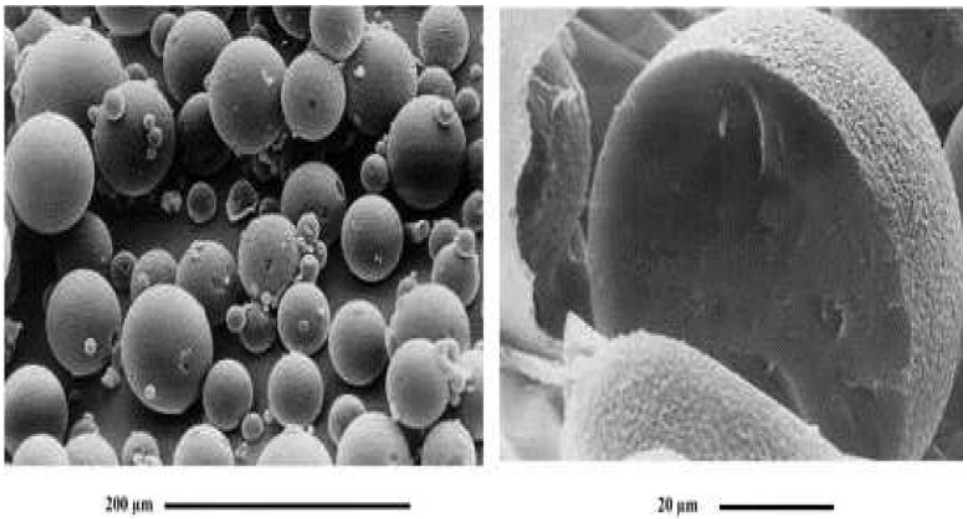

Release Profile with D = 1.330000000 10^-7 m^2 / day
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
10
20
30
t
Planar
Sphere
Cube

Applications



Planar - Gliadel Wafer

- Localised delivery
- Especailly potent drugs
- Eg. tumour removal



Spherical - Microsphere

- Long-term sustained release
- Injectable/inhalable
- Ease of mobility through narrow capillaries
- Eg. macular degeneration

Conclusions

- The amount of drug released M(t) depends exponentially on thickness H and diffusivity D, and is directly proportional to initial concentration c_0
- The timescale for drug release is dependant on D and strongly dependant on H. These parameters can be altered during drug manufacture.
- The timescale does not depend on c_0
- Polymer geometry affects the rate of diffusion of the drug.