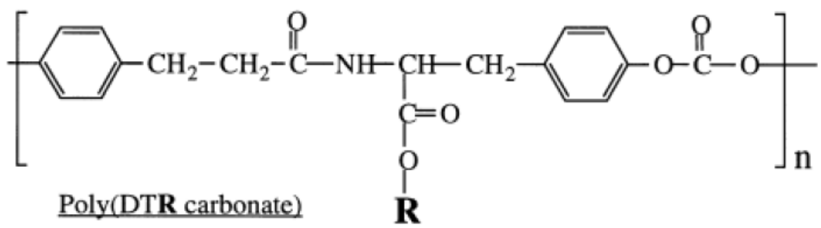
BE525; Problem Set#2, Due: March 7, 2023 11.59 pm via UBLearns

1. From the reading for lecture (Kumamoto et al., *Nat. Biotech*. **20**, 64-69 (2002)), we saw an example of how controlled release materials can be applied to create vaccines that attract immune cells to an immunization site. In this study, poly(ethylene-co-vinyl acetate) matrices were used. These are prepared by loading the polymer with a high amount of protein, such that the phase-separated protein forms a percolating network through the matrix, allowing for diffusion of the protein out of the sample once it is hydrated; as discussed in class, this leads to diffusion-based release much like a standard nondegradable matrix-based diffusion release.

    a. Based on your reading/analysis of the paper, cite what you think are the two most important limitations of the chosen matrix material for the given application, and explain your choices.

    b. Suggest an alternative material/release mechanism, and list two advantages and at least one potential issue with your alternative choice. Explain the advantages/issues you identify.

2. Given below are physical property data for poly(DPT-phenyl-carbonate) (PDPC), a degradable polycarbonate (note as shown below the 'R' group in the center of the structure is simply a hydrogen atom). This polymer has been shown to degrade with autocatalysis triggered by its acid breakdown products. You are going to encapsulate the small-molecule drug diltiazem within a slab matrix with dimensions as given below, and tests for the release rate of the drug will be performed with the matrix supported on an impermeable substrate as illustrated below in phosphate buffered saline at 37°C. Apply Charlier release theory for degradable polymers to answer the questions below.



*

(R = H) PDPC initial number average molecular weight: 125,000 g/mole

degradation rate constant: k = 0.075 day^{-1}*

approximate initial diffusion coefficient for diltiazem in the matrix: $D_o = 3.0\times10^{-11}\ cm^2/s$

(diffusion coefficient in water: ~$8\times10^{-6}\ cm^2/s$)

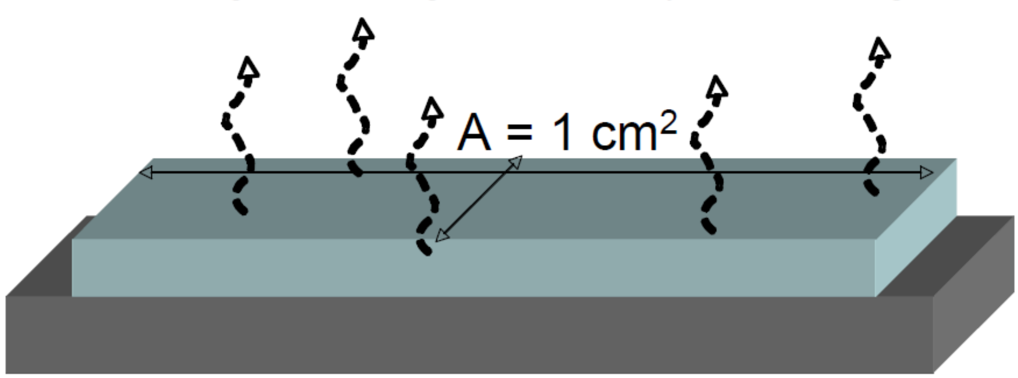
solubility of diltiazem in matrix: 0.001 g/cm^3

concentration of diltiazem encapsulated in matrix: 0.01 g/cm^3

surface area of matrix: 1 cm^2

matrix thickness: 500 μm

critical molecular weight of PDPC oligomers for solubility in saline: 2,500 g/mole



a. At what time after the start of release will release first deviate at least 10% from the predicted Higuchi release (pure diffusion from a nondegradable matrix)? By what percent have the diffusion coefficient of the drug and the molecular weight of the matrix changed at this time?

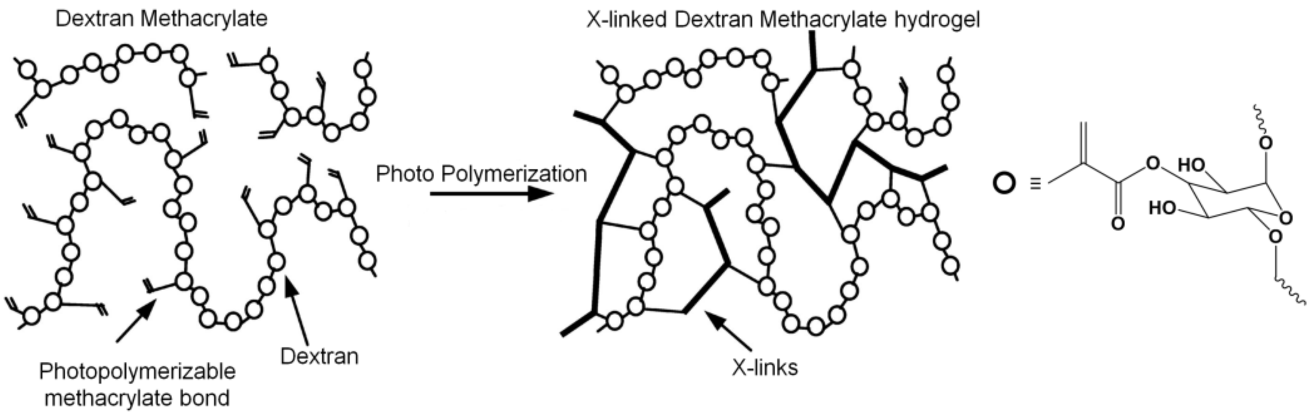
b. How long will this biodegradable matrix release drug?

c. How long would the matrix release drug if it had the same initial permeability to drug but were non-degradable?

d. Plot the drug release rate dQ/dt vs. time for the lifetime of the device.

*Tangpasuthadol, Kohn, et al. *Biomaterials* **21**, 2371-2378 (2000)

3. Non-ionic dextran methacrylate (dex-MA) hydrogel is prepared by photopolymerization through crosslinking of methacrylate bonds (see figure). The hydrogel is prepared with 10% (w/v) of dex-MA (i.e. 90% water) and is allowed to swell to equilibrium state. The equilibrium swelling shows water content 10 times of the initial water content (i.e. relaxed state after hydrogel formation). Based on the data provided below, calculate the molecular weight between the crosslinks (M_C) and crosslinking density ($\rho_x, \#/volume$) the hydrogel using Peppas-Merill Equation. Which molecular design of polymer can be changed to alter the swelling character of the hydrogel?



- $Molecular\ weight\ of\ dextran\ methacrylate\ (M) = 16\ \times 10^3 Da$
- $Dextran\ methacrylate/water\ Interaction\ parameter\ \ (\chi) = 0.47$
- $Molar\ volume\ of\ water\ (V_1) = 18\ cm^3/g$
- $Specific\ volume\ of\ polymer\ \left(v_{sp,2}\right) = 0.62\ cm^3/g$