Modeling the Diffusion of Large Molecules (drugs) from an Aqueous Solution into a Hydrogel

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Introduction
Studies on alginates, as a base to store biological substances, have shown promising results to transport large molecules, including drugs, to parts of the body. These alginates have been used to store liver cells that mature and replicate liver functions, and to store pancreatic cells for producing insulin. It shows a human pancreatic islet encapsulated in an alginate-based capsule before implantation in a type-I diabetic patient. The capsule contains two islets after dithizone staining.

When these alginates or gels are placed into the body, the antibodies will attack the foreign substances. It is proposed to use a thin layer of instructive polymers improve bio compatibility. For this system to work, nutrients must diffuse inward to the cells, and proteins and waste must diffuse outward, while the body’s defenses are kept out. This lead us to questions, what controls the diffusion rate? The alginate or the proteins and waste must diffuse outward, while the body’s defenses are kept out.

To develop a model that can be used to explain the diffusion of large molecules into alginates.

Model
Figure 2 shows the proposed model based on the theoretical calculations for the diffusion of a large molecule into a sphere. The surface coating is a thin permeable membrane.

\[ \frac{M_{w}}{M_{e}} = 1 - \sum_{n=1}^{\infty} \frac{6\alpha (\alpha + 1)^n}{9 + 9\alpha + \alpha^2} \]

\[ \alpha = \frac{3\nu}{4\pi a^2 K_{eff}} \]

The model explains diffusion from a well-stirred solution of limited volume into a spherical system. The rate of the concentrations of the system at time, t, and at equilibrium.

\[ D_{eff}, \text{Diffusion Coefficient} = \text{The rate in which one substance is transported into another substance.} \]

\[ K_{eq}, \text{Partition Coefficient} = \text{The equilibrium ratio concentration of the outside one substance versus the concentration of the inside that has been diffused.} \]

\[ K_{eff} = K_{alg} + P_{alg} \cdot P_{mem} \]

\( K_{alg} \) is the partition coefficient for pure alginate.

\( P_{alg} \) is the volume fraction of pores where the diffusing species can accumulate in the alginate bead.

\( P_{mem} \) is the area density of pores in the membrane.

Results – Does It Work?

Figure 4 shows the results from our model (solid line). It also shows the results from experiment involving the diffusion of bovine serum albumin into containing bovine immunoglobin g. (data points). The line diamonds show the results for an alginate with no surface coating. (Data is from Dr. Kaitlin Bratlie)

To validate our model we compared to experimental results prepared by Prof. Beatlie. We fit the effective diffusion coefficient and partition coefficient using the root mean square minimization.

The diffusion coefficient controls the rate of accumulation, which was found to be 1.5 x 10^{-10} m^2/s.

The partition coefficient controls the saturation at large time scales. The partition coefficient is highly sensitive to the surface treatment. We found that the surface coating has no impact on the rate of diffusion. For this experiment the effective partition coefficient was found to range between 0.125 and 0.55.

Conclusions
The model that was developed predicts the diffusion coefficient and the partition coefficient. This model can fit to other situations that deal with alginates or similar compounds.

Future research will involve understanding the physical interpretation of \( P_{alg} \) and \( P_{mem} \). These will be studied using atomistic simulations.


