

# Abstract

Targeted drug delivery to the desired site and controlled release rate increase treatment efficacy, reduce side effects and patient burden, protect the drug from degrading factors in the body, and reduce treatment costs. In this field, hydrogels are most commonly used as drug delivery systems. Fabrication and design of appropriate hydrogel properties to encapsulate and protect the drug, transport it to the desired location, and changing the structure of the hydrogel to cause drug release at a specific rate requires a series of complex studies and experiments. In this dissertation, mathematical modeling of hydrogel properties is presented to predict key parameters for designing the desired properties of hydrogels, such as shear modulus, crosslink density, mesh size, and drug release rate. The proposed approach could be useful in all hydrogel applications where the design of desired hydrogel properties is crucial. The developed mathematical model could reduce the number of experiments required for hydrogel development, thereby shortening research time, reducing research costs, and reducing the consumption of chemicals and energy, contributing to more environmentally friendly research.

Mathematical modeling of the drug release technology involves a detailed analysis of two key mechanisms, namely diffusion and the kinetics of adsorption and desorption of the drug in the case of electrostatic interactions with the hydrogel surface. The mass transfer by diffusion is directly related to the mesh sizes, as they allow complete encapsulation of the drug when the hydrodynamic radius of the drug is larger than the mesh size. On the other hand, increasing the mesh size allows diffusion of the drug. The release rate can be controlled by adjusting the mesh size, which acts as steric barrier. Therefore, the dissertation aims to develop a mathematical model to predict the mesh size in a hydrogel network as a function of the concentration of biopolymers and crosslinking agents. The theory of polymer-polymer interactions was introduced, which allows the analysis of the mechanical properties of hydrogels as a consequence of the interactions between the polymer chains that occur during the crosslinking process. Based on the observed predominant effect of hydrogen and ionic interactions, we developed a generalized mathematical model to predict the shear modulus, crosslink density, and mesh size in the hydrogel as a function of polymer and crosslinking agent concentration. The model was further modified to respond to hydrogels in an environment with different pH and temperature values. Using the developed model in already known correlations between mesh size and diffusion coefficient, the drug release rate was predicted in cases where diffusion is the predominant transport phenomenon and drugs do not form interactions with hydrogels.

Additionally, the research involves a detailed analysis of the kinetics of adsorption and desorption of proteins on or from the hydrogel surfaces. The kinetics of adsorption as a function of temperature and ionic strength of the release medium was studied by mathematical modeling of lysozyme release in addition to the already well-developed model for predicting the diffusivity of lysozyme. For the first time, we presented the mechanism for determining the initial (maximum) rate of protein adsorption on the hydrogel surface. At the same time, it was possible to similarly determine the initial (minimum) rate of protein desorption from the surface. The slowing of the adsorption rate and the acceleration of the desorption rate with increasing ionic strength were accurately evaluated mathematically with appropriate parameters. Implementation of the mathematical model for studying adsorption and desorption kinetics into the previously developed model for predicting drug release by the diffusion mechanism allows development of a generalized mathematical model for predicting targeted drug delivery with controlled release as a function of hydrogel design parameters (concentration and type of polymers and crosslinking agents, and understanding of the theory of polymer-polymer interactions during the crosslinking process).