Mathematical Modeling of Glucose Responsive Hydrogels

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Abstract

Diabetes mellitus affects 387 million people across the world according to the latest estimates of International Diabetes Foundation. Insulin is one of the major drugs required to keep the glucose level within desired limits in a diabetic patient. Insulin is generally administered to a patient as a subcutaneous injection and consists of two forms namely, basal and bolus. The basal dosage is required to maintain glucose during fasting conditions encountered overnight whereas a bolus dosage is given along with the meal. Usually, a type 1 diabetic patient requires three to four insulin injections throughout a day, leading to adherence issues. Furthermore, there are problems related to estimation of individualized insulin dosages that may lead to undesired outcomes [1]. Therefore, to overcome the above mentioned issues smart drug delivery systems are being developed that can meet the individual requirements of insulin and minimize its dosage. Hydrogels, network of hydrophilic polymers that can swell and hold a large amount of water while maintaining the structure, are one of the promising drug delivery systems. These hydrogels can swell in the presence of external stimuli such as pH, temperature, sound and electric field [2]. Novel hydrogel based drug delivery carriers comprising glucose oxidase and catalase have been developed that can deliver insulin in response to varying glucose levels [3]. The enzymes catalyze the conversion of glucose to gluconic acid that leads to change in the local pH inside the hydrogel and thus leads to its swelling.

We have modelled the observed swelling behavior of the hydrogel in presence of glucose using COMSOL Multiphysics®. An accurate description of the underlying phenomena requires estimation of: (i) Diffusive fluxes of ionic species and drug encapsulated, (ii) Enzymatic reaction kinetics of oxidation of glucose to gluconic acid, (iii) Electric potential generated inside hydrogel, and (iii) Deformation of hydrogel under osmotic pressure. We have used the transport of diluted species, structural mechanics, and electrostatics physics interfaces available in COMSOL Multiphysics to describe the above phenomena. The coupled set of equations is solved under a moving mesh frame to account for the large deformation of the hydrogel. The model has been validated for swelling behavior of sulfonamide group based hydrogels in presence of glucose [4], for the steady state response of hydrogel in response to glucose concentration (Figure 1). The model is also able to capture the observed swelling/de-swelling kinetics as the glucose concentration in the bulk solution undergoes step changes (Figure 2). The model is a mechanistic in nature. It also takes into account process parameters such as the composition of hydrogel: ionic polymer and its concentration, composition of the bulk solution and mechanical properties of the gel used. The model thus can be used for in silico design of

glucose sensitive hydrogels that can give desired swelling and/or drug release profiles.

Reference

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3.S. Marek, and N. A. Peppas. "Insulin release dynamics from poly (diethylaminoethyl methacrylate) hydrogel systems." AIChE Journal, 59.10 3578-3585, 2013.
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Figures used in the abstract

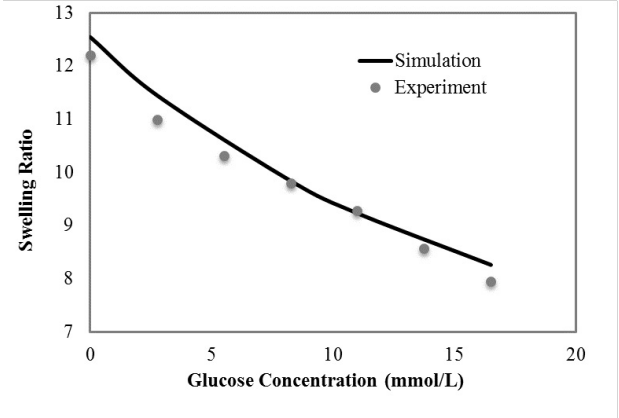

Figure 1: Steady state swelling of hydrogel at different glucose concentrations.

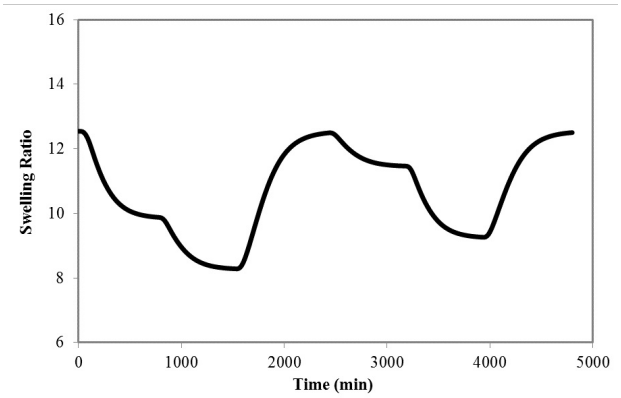

Figure 2: Transient response of hydrogel with step changes in glucose concentration.