



Development of a multiphysics model to characterize the responsive behavior of urea-sensitive hydrogel as biosensor



K.B. Goh, Hua Li*, K.Y. Lam

School of Mechanical and Aerospace Engineering, Nanyang Technological University, Nanyang Avenue, Singapore 639798, Republic of Singapore

ARTICLE INFO

Keywords:

Multiphysics model
Urea-sensitive hydrogel
Urease
Bioelectrochemistry

ABSTRACT

A remarkable feature of biomaterials is their ability to deform in response to certain external bio-stimuli. Here, a novel biochemo-electro-mechanical model is developed for the numerical characterization of the urea-sensitive hydrogel in response to the external stimulus of urea. The urea sensitivity of the hydrogel is usually characterized by the states of ionization and denaturation of the immobilized urease, as such the model includes the effect of the fixed charge groups and temperature coupled with pH on the activity of the urease. Therefore, a novel rate of reaction equation is proposed to characterize the hydrolysis of urea that accounts for both the ionization and denaturation states of the urease subject to the environmental conditions. After examination with the published experimental data, it is thus confirmed that the model can characterize well the responsive behavior of the urea-sensitive hydrogel subject to the urea stimulus, including the distribution patterns of the electrical potential and pH of the hydrogel. The results point to an innovative means for generating electrical power via the enzyme-induced pH and electrical potential gradients, when the hydrogel comes in contact with the urea-rich solution, such as human urine.

1. Introduction

According to Mayo clinic the chronic kidney disease (CKD) is characterized by the gradual loss of kidney functions over time (Ficalora, 2013). As the CKD progresses to the advanced-stage, a dangerous level of urea and electrolytes build-up in the human system, which increases the risk of cardiovascular, hyperlipidemia, anemia and metabolic bone diseases (Thomas et al., 2008). Therefore, the urea and electrolytes levels in the human blood and urine are measured for CKD patients during medical evaluation, since it provides access to the state of health of the kidney. As such, there were great attempt to develop the urea biosensors to estimate the blood urea nitrogen (BUN) levels for CKD patients by means of integrating urease into the hydrogel (Dezhong et al., 1996; Kovács et al., 2003; Liu et al., 1996). However, it is evident from the open literature that the performance of the hydrogel in response to the external stimulus of urea is still poorly understood. Therefore, in this paper, a multiphysics model is developed to investigate the responsive behavior of the hydrogel subject to the external stimulus of urea at different environmental conditions.

It is found in the open literature that the urea-sensitive hydrogel-based biosensors were synthesized using the pH- or temperature-sensitive hydrogels, i.e. poly(vinyl alcohol) (Jha et al., 2008;

Marchenko et al., 2015), polyaniline (Buron et al., 2014), poly(*o*-phenylenediamine) (Chirizzi and Malitesta, 2011), poly(carbamoylsulfonate) (Eggenstein et al., 1999), and poly(3-cyclohexyl thiophene) (Pandey et al., 2000). Moreover, most researchers opted for gamma radiation (Hamdy et al., 2008), covalent binding (Chen and Chiu, 1999, 2000; Chen et al., 1994; Miyata et al., 1997), or physical entrapment (Hamilton and Breslin, 2014) for the amalgamation of the urease with the polymer network chains for the synthesis of the urea-sensitive hydrogel. As such, it is reported that the integration of the urease with the polymer network chains improved the mechanical properties of the hydrogel and stability of the urease, which may then prolong the life shelf of the biosensors (Novick and Dordick, 1998; Teixeira et al., 2012).

As mentioned above, despite the extensive experimental investigations carried out on the urea-sensitive hydrogel, very few efforts were made via theoretical modeling and numerical simulation for the examination of the hydrogels. From the open literature, it is found that most of the published mathematical models were unable to capture the coupled biochemo-electro-mechanical behavior of the hydrogel. For example, the published mathematical models were inadequate in predicting the volumetric behavior of the hydrogels in response to the urea, where the simulated diffusion and reaction of the reactive solutes were associated with the urea hydrolysis and not the

* Corresponding author.

E-mail address: lihua@ntu.edu.sg (H. Li).

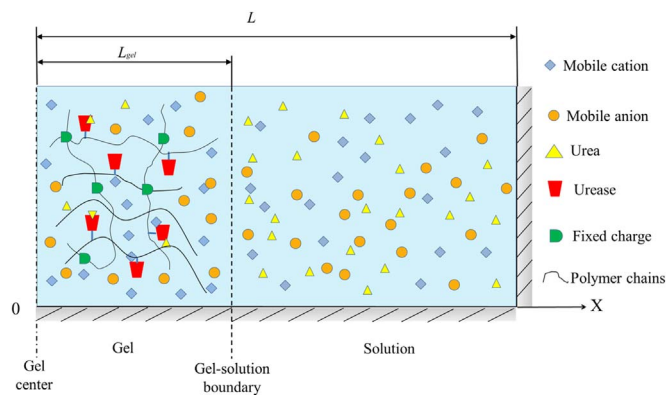


Fig. 1. Schematic diagram of the urea-sensitive hydrogel system.

concomitant mechanical behavior of the hydrogels (Blaedel and Kissel, 1975; Chen and Chiu, 2000), including Moynihan et al. (1989) and Chowdhury and Bhattacharya (1997), where they modelled the kinetic parameters of the urea-sensitive hydrogel via the mass balance and Michaelis-Menten equations.

It is known that the mathematical correlation presented by Ogawa and Kokufuta may be the first work to attempt to predict the mechanical deformation of the hydrogels in response to urea (Ogawa and Kokufuta, 2002). The mathematical correlation was obtained from the experimental pH-responsive equilibrium swelling of the hydrogel, where the correlation was limited to the swelling at pH 4–7 immersed in 5 mM maleate-buffer solution of 35 °C. Therefore, the correlation was unable to estimate the equilibrium swelling ratio of the hydrogel at different environmental conditions other than the prescribed conditions. It is also noted that the influence of environmental pH on the activity of the urease was accounted for in their reaction-diffusion model, while the effect of pH coupled with temperature on the performance of the urease was excluded. Moreover, the effect of the fixed charge groups in the hydrogels was also neglected by all the published models mentioned above on the distribution pattern of the concentration of the reactive mobile ions. In order to overcome these limitations of the published mathematical models, a multi-effect-coupling urea-stimulus (MECurea) model is proposed in this paper to investigate the performance of the hydrogels in response to urea.

2. Formulation of the MECurea model

In order to formulate the model, a few components are prescribed delicately, given as follows: (a) the movement of mobile solutes between the hydrogel and surrounding solution; (b) the enzymatic hydrolysis reaction of urea within the hydrogel; (c) the interaction between the mobile ions and fixed charge in the hydrogel; (d) the swelling forces arising from the biochemical reactions and (f) the swelling behavior of the hydrogels, as illustrated in Fig. 1.

The present MECurea model is formulated based on the following assumptions:

- (i) The hydrogel is maintained at the isothermal condition, such that the rate of reaction r_k is constant.
- (ii) The urease is immobilized and distributed uniformly within the hydrogel, where the activity of the urease is also constant.
- (iii) The optimum temperature T_{OP} of urease is equal to the temperature at the midpoint of transition between active and inactive forms T_{eq} , such that $\Delta H_{eq} \approx 2\Delta G_{cat}$, where ΔH_{eq} is the enthalpy change associated with the conversion of an active to an inactive enzyme, and ΔG_{cat} is the activation energy of the catalytic reaction (Peterson et al., 2004).
- (iv) The hydrogel has a macroporous nature such that the diffusivity coefficients D_k of the mobile solutes are the same in both the

hydrogels and surrounding solution.

- (v) The solution flow is very slow and thus the convection term is neglectable, where the urea hydrolysis in the diluted buffer solution is also neglected.

2.1. Conservation of mass

In the MECurea model, at least six mobile ions and one molecule are considered in the present system, namely the hydrogen ion (H^+), hydroxide ion (OH^-), ammonium ion (NH_4^+), bicarbonate ion (HCO_3^-), cation and anion species, and urea. The Nernst-Planck equation is used to characterize the fluxes of the mobile solutes, given as follows (Li et al., 2009)

$$\nabla \cdot \left(\mathbf{C}^{-1} D_k \left[\nabla C_k + \frac{z_k F}{RT} C_k \nabla \Phi \right] \right) = v_k r_k \quad (k = H^+, OH^-, \dots, N) \quad (1)$$

where \mathbf{C}^{-1} the inverse of the right Cauchy-Green tensor and $\mathbf{C}^{-1} = \mathbf{F}^{-1} \mathbf{F}^{-T}$. D_k , C_k , z_k , v_k and r_k indicate the diffusivity tensor (m^2/s), concentration (mM), valence number, stoichiometric coefficient in the chemical reaction, and rate of chemical reaction for the k th mobile species. R , T , F , and Φ denote the universal gas constant (8.314 J/mol K), absolute temperature (K), Faraday constant (96487 C/mol), and electrostatic potential of the hydrogel. For the non-ionic solute where the charge $z_k = 0$, the Nernst-Planck Eq. (1) is reduced to Fick's first law of diffusion.

2.2. Conservation of momentum

The bioelectrochemistry reaction within the hydrogel gives rise to the swelling pressure, resulting in the configurational changes or swelling deformation of the urea-sensitive hydrogel. It is known that the swelling of the hydrogel progresses, until the swelling forces are balanced by the restrictive forces exerted by the elastic structure of the polymer network chains to achieve the equilibrium hydration state. In order to formulate this phenomenon, the law of conservation of linear momentum is employed, given as follows

$$\nabla \cdot \mathbf{P} = \mathbf{0} \quad (2)$$

where \mathbf{P} is the Piola stress.

2.3. Free energy imbalance inequality for constitutive equation

In order to develop the equations of state for the hydrogel subject to the isothermal condition, the local free energy imbalance inequality is written as follows (Drozdov and deClaville Christiansen, 2015c)

$$\dot{W} - (u_1 + u_2 + u_3) \leq 0 \quad (3)$$

where \dot{W} is temporal increase of the Helmholtz free energy density of the hydrogel, while u_1 , u_2 and u_3 denote the rate of work per volume expanded into the system by the mechanical, electric and chemical fields.

The free energy density of an idealized ionic hydrogel is defined as a sum of four components (Drozdov and deClaville Christiansen, 2015b): (i) the free energy density of stretching of the polymer network chains W_1 , (ii) the free energy density of mixing the polymer and solvent W_2 , (iii) the free energy density due to entropy mixing of mobile ions and solvent W_3 , and (iv) the free energy density of the electric field formed by mobile ions and bound charges W_4

$$W = W_1 + W_2 + W_3 + W_4 \quad (4)$$

The free energy density of elastic stretching of the polymer network chains is given as (Hong et al., 2008)

$$W_1 = \frac{1}{2} N k_B T [\text{tr}(\mathbf{F}^T \mathbf{F}) - 2 \ln(\det \mathbf{F}) - 3] \quad (5)$$

where $N k_B T$ is the ground-state shear modulus G , N is the number of

Download English Version:

<https://daneshyari.com/en/article/5031205>

Download Persian Version:

<https://daneshyari.com/article/5031205>

[Daneshyari.com](https://daneshyari.com)