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Analytical Expressions for the Steady-State Concentrations of Glucose, Oxygen and Gluconic Acid in a Composite Membrane for Closed-Loop Insulin Delivery

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Abstract The mathematical model of Abdekhodaie and Wu (J Membr Sci 335:21–31, 2009) of glucose-responsive composite membranes for closed-loop insulin delivery is discussed. The glucose composite membrane contains nanoparticles of an anionic polymer, glucose oxidase and catalase embedded in a hydrophobic polymer. The model involves the system of nonlinear steady-state reaction–diffusion equations. Analytical expressions for the concentration of glucose, oxygen and gluconic acid are derived from these equations using the Adomian decomposition method. A comparison of the analytical approximation and numerical simulation is also presented. An agreement between analytical expressions and numerical results is observed.

Keywords Glucose-sensitive membrane · Insulin delivery · Enzymatic reaction · Reaction–diffusion equation · Adomian decomposition method

Introduction

Many people in the world suffer from diabetes. Diabetes is a chronic disorder of glucose metabolism and one of the major causes of heart and renal illnesses. Insulin-dependent diabetes requires treatment with insulin delivered by injection several times a day or by a pump to control glucose levels. Therefore, various kinds of insulin-delivering systems containing a glucose membrane have been studied (Abdekhodaie and Wu 2009). Some of these systems consist of immobilized glucose oxidase and catalase in pH-responsive polymeric hydrogels (Abdekhodaie and Wu 2005; Albin et al. 1990; Traitel et al. 2000; Podual et al. 2000; Hassan et al. 1997; Zhang and Wu 2002; Zhang et al. 2004; Wu et al. 2003a, b). The pH-sensitive hydrogels can be divided into cationic and anionic types. Cationic hydrogels, consisting of amino groups, swell in response to pH decreases at high glucose levels. Anionic hydrogels shrink due to the protonization of acidic groups. In this way the permeability of the hydrogel to the insulin can be varied, enabling dosage control. However, the weak mechanical properties of homogeneous hydrogels constitute a drawback (Wu et al. 2003a, b; Bae and Kim 1993). To overcome this problem, composites of hydrophilic and hydrophobic polymers have been developed (Abdekhodaie and Wu 2009; Wu et al. 2003a, b; Bae and Kim 1993; Cifková et al. 1990; Schwendeman et al. 1992; Zhang and Wu 2004; Yam et al. 2000).

There have been only a few theoretical modeling studies of cationic glucose-sensitive membranes (Abdekhodaie and Wu 2005, 2009). Abdekhodaie and Wu (2009) have developed a mathematical model to describe a dynamic process of diffusion of reactants, coupled with an enzymatic reaction inside a glucose composite membrane containing anionic nanoparticles, glucose oxidase and catalase embedded in a hydrophobic polymer. To our knowledge, no analytical solutions of this model have been reported. However, in general, analytical solutions of nonlinear differential equations are more interesting and

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useful than purely numerical solutions as they are amenable to various kinds of manipulation and data analysis. For this reason, the purpose of the present study is to derive simple approximate analytical expression for the steady-state concentrations of reactants in a membrane for closed-loop insulin delivery using the Adomian decomposition method (Adomian 1984, 1995; Siddiqui et al. 2010; Wazwaz and Gorguis 2004; Sweilam and Khader 2010; Adomian and Witten 1994; Lesnic 2007; Magyari 2008; Rida 2010; Wazwaz 2000). This method has already been used to solve effectively, easily and accurately a large class of linear and nonlinear ordinary (deterministic or stochastic) differential equations, with approximations that converge rapidly. Hariharan and Kannan (2010) solved the one-dimensional reaction–diffusion problem using the Adomian decomposition method. As far as we are aware, the present study is the first application of the Adomian decomposition method to solve the system of nonlinear second-order reaction–diffusion equations pertinent to membrane science.

The Mathematical Model

Building upon earlier study, Abdekhodaie and Wu (2009) presented a concise discussion and derivation of the dimensionless mass transport nonlinear equations in the glucose composite membrane, which is summarized briefly below. For the glucose membrane consisting of a pH-sensitive hydrogel and immobilized enzymes (glucose oxidase and catalase), the reaction of the glucose oxidation catalyzed by the glucose oxidase is

$$\text{Glucose} + \text{O}_2 \xrightarrow{\textit{Glucose oxidase}} \text{Gluconic acid} + \text{H}_2\text{O}_2 \tag{1}$$

The catalase catalyzes the conversion of hydrogen peroxide to oxygen and water:

$$\text{H}_2\text{O}_2 \xrightarrow{\textit{Catalase}} \text{H}_2\text{O} + \frac{1}{2}\text{O}_2 \tag{2}$$

When the catalase is in excess, all hydrogen peroxide is reduced. Thus, the overall reaction becomes

$$\text{Glucose} + \frac{1}{2}\text{O}_2 \xrightarrow{\textit{Glucose oxidase, catalase}} \text{Gluconic acid} + \text{H}_2\text{O} \tag{3}$$

The corresponding governing equations for non-steady-state conditions in Cartesian coordinates for the planar diffusion and reaction in a membrane for closed-loop insulin delivery are (Abdekhodaie and Wu 2009)

$$\frac{\partial C_i}{\partial t} = \frac{\partial}{\partial x}\left(D_i \frac{\partial C_i}{\partial x}\right) + \upsilon_i R = 0 \tag{4}$$

where, $i = g$ for glucose, $i = OX$ for oxygen and $i = a$ for gluconic acid. The stoichiometric coefficients υ_i are $\upsilon_g = -1$, $\upsilon_{OX} = -0.5$ and $\upsilon_a = 1$. The reaction rate R is

$$R = \frac{v_{\text{Max}}\, C_g\, C_{OX}}{C_{OX}(K_g + C_g) + C_g K_{OX}} \tag{5}$$

For the steady-state condition, Eq. 4 becomes

$$D_g \frac{d^2 C_g}{dx^2} - \frac{v_{\text{Max}}\, C_g\, C_{OX}}{C_{OX}(K_g + C_g) + C_g K_{OX}} = 0 \tag{6}$$

$$D_{OX} \frac{d^2 C_{OX}}{dx^2} - \frac{v_{\text{Max}}\, C_g\, C_{OX}}{2[C_{OX}(K_g + C_g) + C_g K_{OX}]} = 0 \tag{7}$$

$$D_a \frac{d^2 C_a}{dx^2} + \frac{v_{\text{Max}}\, C_g\, C_{OX}}{C_{OX}(K_g + C_g) + C_g K_{OX}} = 0 \tag{8}$$

where D_g, D_{OX} and D_a are the diffusion coefficients of glucose, oxygen and gluconic acid, respectively; C_g, C_{OX} and C_a are the concentrations of glucose, oxygen and gluconic acid, respectively; x is the spatial coordinate; and v_{max} is the maximum reaction rate that is proportional to the concentration of enzyme ($C_{\text{enz}}$is glucose oxidase) in the membrane. K_g and K_{OX} are the Michaelis-Menten constants for glucose and glucose oxidase, respectively. The boundary conditions are

$$\frac{dC_{OX}}{dx} = 0;\ \frac{dC_g}{dx} = 0;\ \frac{dC_a}{dx} = 0 \text{ at } x = 0 \tag{9}$$

$$C_{OX} = C_{OX}^*;\ C_g = C_g^*;\ C_a = 0 \text{ at } x = l \tag{10}$$

where C_{OX}* and C_g* are the concentrations of oxygen and glucose in the external solution, $x = 0$ corresponds to the membrane center and l is the half-thickness of the membrane. We introduce the following set of dimensionless variables:

$$u = \frac{C_g}{C_g^*};\ v = \frac{C_{OX}}{C_{OX}^*};\ w = \frac{C_a}{C_{OX}^*};\ X = \frac{x}{l};\ \gamma_{E1} = \frac{l^2 v_{\text{Max}}}{D_g C_g^*};$$
$$\gamma_{S1} = \frac{l^2 v_{\text{Max}}}{D_{OX} C_{OX}^*};\ \gamma_E = \frac{l^2 v_{\text{Max}}}{D_a C_{OX}^*};\ \alpha = \frac{C_g^*}{K_g};\ \beta = \frac{C_{OX}^*}{K_{OX}} \tag{11}$$

Using these variables, Eqs. 6–8 can be cast into the following dimensionless form:

$$\frac{d^2 u}{dX^2} - \gamma_{E1} uv \left[uv + \frac{v}{\alpha} + \frac{u}{\beta}\right]^{-1} = 0 \tag{12}$$

$$\frac{d^2 v}{dX^2} - \frac{\gamma_{S1} uv}{2} \left[uv + \frac{v}{\alpha} + \frac{u}{\beta}\right]^{-1} = 0 \tag{13}$$

$$\frac{d^2 w}{dX^2} + \gamma_E uv \left[uv + \frac{v}{\alpha} + \frac{u}{\beta}\right]^{-1} = 0 \tag{14}$$

Here, u, v and w are the dimensionless concentrations of glucose, oxygen and gluconic acid, respectively, and

Table 1 Numerical values of the parameters used in this study

Parameter	Unit	Numerical value of parameter used in Abdekhodaie and Wu (2009)	Numerical value of parameter used in this study					
			Fig. 1	Fig. 2	Fig. 3	Fig. 4	Fig. 5	Fig. 6
$\alpha = C_g^*/K_g$	–	8.9 and 35	0.1	0.5	0.5	0.1	0.5	0.5
$\beta = C_{OX}^*/K_{OX}$	–	0.39	0.01	0.01	0.1	1–0.001	0.1–5	0.01–5
X (dimensionless distance)	–	0–1	0–1	0–1	0–1	0–1	0–1	0–1
l (membrane thickness)	cm	0–0.025	0.3×10^{-2}–0.3	0.3×10^{-2}–0.3	0.3×10^{-2}–0.3	0.3×10^{-2}–0.3	0.3×10^{-2}–0.3	0.3×10^{-2}–0.3
$\gamma_{E1} = \frac{l^2 v_{\mathrm{Max}}}{D_g C_g^*}$	–	0 to 0.42×10^2	1–100	–	0.01	10	0.001	0.01
$\gamma_{s1} = \frac{l^2 v_{\mathrm{Max}}}{D_{OX} C_{OX}^*}$;	–	0 to 21.8×10^2	0.01	1–100	0.005	0.05	10	0.05
$\gamma_E = \frac{l^2 v_{\mathrm{Max}}}{D_u C_{OX}^*}$;	–	0 to 8.12×10^2	–	0.001	0.1–20	–	–	–

The fixed values of the dimensional parameters are $C_{OX}^* = 0.274 \times 10^{-6}$, $C_g^* = 5.5 \times 10^{-6}$and 22 $\times 10^{-6}$, $D_g = 6.75 \times 10^{-6}$, $D_{OX} = 2.29 \times 10^{-5}$, $K_{OX} = 6.992 \times 10^{-5}$, $K_g = 6.187 \times 10^{-7}$, $\upsilon_{\mathrm{Max}} = 2.5 \times 10^{-6}$, and 25.8×10^{-6}. These are dimensional parameters used in Abdekhodaie and Wu (2009)

Table 2 Comparison of normalized analytical steady-state concentration of glucose u with numerical results for various values of X and for some fixed values of parameters $\alpha = 0.1$, $\beta = 0.01$ and $\gamma_{S1} = 0.01$

X	Concentration of glucose u											
	u (when $\gamma_{E1} = 1$)			u (when $\gamma_{E1} = 10$)			u (when $\gamma_{E1} = 50$)			u (when $\gamma_{E1} = 100$)		
	This study Eq. 17	Numerical	% of deviation	This study Eq. 17	Numerical	% of deviation	This study Eq. 17	Numerical	% of deviation	This study Eq. 17	Numerical	% of deviation
0	0.9954	0.9955	0.01	0.9551	0.9551	0.00	0.7785	0.7793	0.10	0.5647	0.5718	1.26
0.2	0.9956	0.9957	0.01	0.9569	0.9569	0.00	0.7874	0.7883	0.11	0.5850	0.589	0.68
0.4	0.9962	0.9962	0.00	0.9622	0.9624	0.02	0.8139	0.8152	0.16	0.6359	0.6409	0.78
0.6	0.9971	0.9972	0.01	0.9712	0.9716	0.04	0.8581	0.8601	0.23	0.7207	0.7061	2.03
0.8	0.9983	0.9972	0.11	0.9838	0.9844	0.06	0.9201	0.9232	0.34	0.8426	0.8502	0.90
1	1.0000	0.9984	0.16	1.0000	1.0000	0.00	1.0000	1.0000	0.00	1.0000	1.0000	0.00

Table 3 Comparison of normalized analytical steady-state concentration of oxygen v with numerical results for various values of X and for some fixed values of $\alpha = 0.5$, $\beta = 0.01$ and $\gamma_{E1} = 0.001$

X	Concentration of oxygen v											
	v (when $\gamma_{S1} = 1$)			v (when $\gamma_{S1} = 10$)			v (when $\gamma_{S1} = 50$)			v (when $\gamma_{S1} = 100$)		
	This sudy Eq. 18	Numerical	% of deviation	This study Eq. 18	Numerical	% of deviation	This study Eq. 18	Numerical	% of deviation	This study Eq. 18	Numerical	% of deviation
0	0.9976	0.9978	0.02	0.9762	0.9779	0.17	0.8906	0.8963	0.64	0.8049	0.8079	0.37
0.2	0.9977	0.9978	0.01	0.9772	0.9788	0.16	0.8949	0.9004	0.61	0.8125	0.8155	0.37
0.4	0.9980	0.9981	0.01	0.9801	0.9815	0.14	0.9081	0.913	0.54	0.8355	0.8384	0.34
0.6	0.9985	0.9986	0.01	0.9849	0.9860	0.11	0.9302	0.934	0.40	0.8744	0.877	0.30
0.8	0.9992	0.9992	0.00	0.9917	0.9923	0.06	0.9615	0.9636	0.22	0.9302	0.9319	0.18
1	1.0000	0.9899	1.01	1.0000	1.0000	0.00	1.0000	1.0000	0.00	1.0000	1.0000	0.00

Table 4 Comparison of normalized analytical steady-state concentration of gluconic acid w with numerical results for various values X and some fixed values of $\alpha = 0.5$, $\beta = 0.1$, $\gamma_{E1} = 0.01$ and $\gamma_{S1} = 0.005$

X	Concentration of gluconic acid w											
	w (when $\gamma_E = 1$)			w (when $\gamma_E = 5$)			w (when $\gamma_E = 10$)			w (when $\gamma_E = 20$)		
	This study Eq. 19	Numerical	% of deviation	This study Eq. 19	Numerical	% of deviation	This study Eq. 19	Numerical	% of deviation	This study Eq. 19	Numerical	% of deviation
0	0.0384	0.03846	0.16	0.1922	0.1923	0.05	0.3845	0.3846	0.02	0.7691	0.7691	0.00
0.2	0.0369	0.03689	0.03	0.1845	0.1844	0.05	0.3691	0.3689	0.05	0.7383	0.7378	0.07
0.4	0.0323	0.03218	0.37	0.1615	0.1609	0.37	0.3230	0.3218	0.37	0.6460	0.6436	0.37
0.6	0.0246	0.02433	1.10	0.1230	0.1217	1.05	0.2461	0.2433	1.14	0.4922	0.4866	1.14
0.8	0.0138	0.01335	2.90	0.0692	0.0667	3.57	0.1384	0.1335	3.54	0.2768	0.2669	3.58
1	0.0000	0.0000	0.00	0.0000	0.0000	0.00	0.0000	0.0000	0.00	0.0000	0.0000	0.00

γ_{E1}, γ_{S1} and γ_E are the corresponding Thiele modulus values. α and β are the dimensionless rate constants. The corresponding boundary conditions (9 and 10) become

$$\frac{du}{dX} = 0;\ \frac{dv}{dX} = 0;\ \frac{dw}{dX} = 0 \text{ when } X = 0 \tag{15}$$

$$u = 1;\ v = 1;\ w = 0 \text{ when } X = 1 \tag{16}$$

Analytical Determination of the Concentrations of Glucose, Oxygen and Gluconic Acid under Steady-State Condition

In order to solve the boundary value problem, Eq. 12–16, we used the Adomian decomposition method (Adomian 1984, 1995; Siddiqui et al. 2010; Wazwaz and Gorguis 2004; Sweilam and Khader 2010; Adomian and Witten 1994; Lesnic 2007; Magyari 2008; Rida 2010; Wazwaz 2000; Danish et al. 2011). The basic principle of this method is described in Appendix A. Detailed derivations of the dimensionless concentrations u, v and w of glucose, oxygen and gluconic acid are described in Appendix B. As a result, we have obtained

$$u(X) = 1 - \frac{\gamma_{E1}\alpha\beta\omega}{2} + \frac{5\alpha^2\beta^2\gamma_{E1}\omega^3[2\gamma_{E1}\beta + 5\gamma_{S1}\alpha]}{48} + \left[\frac{\gamma_{E1}\alpha\beta\,\omega}{2} - \frac{\alpha^2\beta^2\gamma_{E1}\omega^3[2\gamma_{E1}\beta + \gamma_{S1}\alpha]}{8}\right]X^2 + \left[\frac{\alpha^2\beta^2\gamma_{E1}\omega^3}{48}[2\gamma_{E1}\beta + \gamma_{S1}\alpha]\right]X^4 \tag{17}$$

$$v(X) = \left[1 - \frac{\gamma_{S1}\alpha\beta\omega}{4} + \frac{5\alpha^2\beta^2\gamma_{S1}\omega^3}{96}[2\gamma_{E1}\beta + 5\gamma_{S1}\alpha]\right] + \left[\frac{\gamma_{S1}\alpha\beta\,\omega}{4} - \frac{\alpha^2\beta^2\gamma_{S1}\omega^3}{16}[2\gamma_{E1}\beta + \gamma_{S1}\alpha]\right]X^2 + \left[\frac{\alpha^2\beta^2\gamma_{S1}\omega^3}{96}[2\gamma_{E1}\beta + \gamma_{S1}\alpha]\right]X^4 \tag{18}$$

$$w(X) = \left[\frac{\gamma_E\alpha\beta\omega}{2} - \frac{5\alpha^2\beta^2\gamma_{E1}\omega^3}{48}[2\gamma_{E1}\beta + 5\gamma_{S1}\alpha]\right] - \left[\frac{\gamma_E\alpha\beta\,\omega}{2} - \frac{\alpha^2\beta^2\gamma_E\omega^3}{8}[2\gamma_{E1}\beta + \gamma_{S1}\alpha]\right]X^2 - \left[\frac{\alpha^2\beta^2\gamma_E\omega^3}{48}[2\gamma_{E1}\beta + \gamma_{S1}\alpha]\right]X^4 \tag{19}$$

where

$$\omega = [\alpha + \beta + \alpha\beta]^{-1} \tag{20}$$

This is the approximation involving three terms of the expansion (Eq. A5) only. The accuracy of expressions 17–19 can be improved by taking into account higher-order terms.

Numerical Simulation

The differential Eqs. 12–14 with boundary conditions 15 and 16 have also been solved numerically using SCILAB/MATLAB software (www.scilab-enterprises.com). A respective script pdex4 is provided in Appendix D. The default parameters employed in Abdekhodaie and Wu (2009) and in this study are given in Table 1. The numerical solution is compared with our analytical results in Tables 2, 3, 4 and Figs. 1, 2, 3. The comparison reveals that the relative difference between the analytical dimensionless concentrations u, v and w of glucose, oxygen and gluconic acid and numerical reference results does not exceed 3 % for all values of the parameters considered in the simulations.

Results and Discussion

Equations 17–19 represent the analytical expressions for the dimensionless concentrations of glucose $u(X)$, oxygen

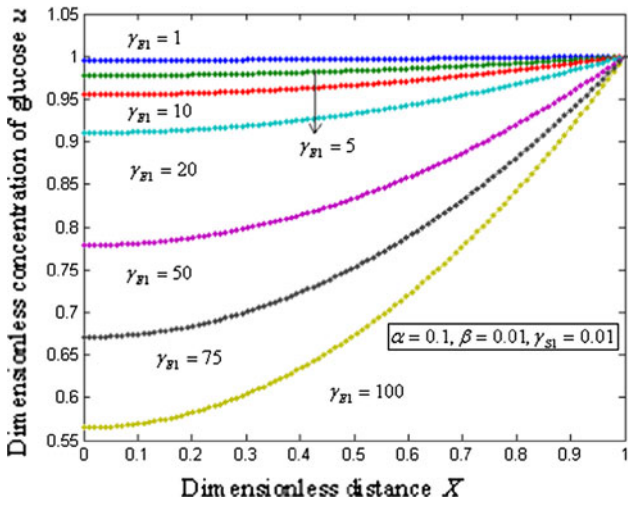

Fig. 1 Dimensionless concentration of glucose versus dimensionless distance X, calculated for $\alpha = 0.1$, $\beta = 0.01$ and $\gamma_{S1} = 0.01$. *Solid lines* represent the analytical solution presented in this study (Eq. 17) and *dotted lines*, the numerical solution

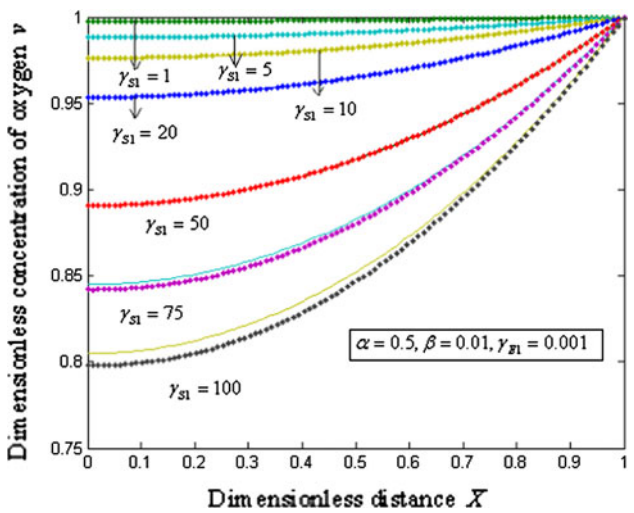

Fig. 2 Dimensionless concentration of oxygen versus dimensionless distance X calculated for $\alpha = 0.5$, $\beta = 0.01$ and $\gamma_{e1} = 0.001$. *Solid lines* represent the analytical solution presented in this study (Eq. 18) and *dotted lines*, the numerical solution

$v(X)$ and gluconic acid $w(X)$ valid for all values of parameters γ_{E1}, γ_{S1}, γ_E, α and β considered in this study (see Table 1). The Thiele modulus γ_{E1}, γ_{S1} or γ_E can be varied by changing either the thickness of the membrane or the concentration of oxygen and glucose in the external solution. This parameter describes the relative importance of diffusion and reaction in the enzyme layer. When it is small, the kinetics are the dominant resistance; the overall uptake of glucose, oxygen and gluconic acid in the enzyme matrix is kinetically controlled. Under these conditions, the glucose concentration profile across the membrane is essentially uniform. The overall kinetics are determined by

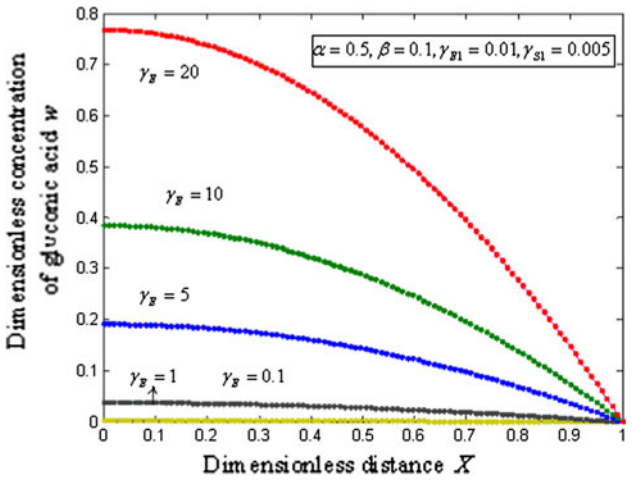

Fig. 3 Dimensionless concentration of gluconic acid versus dimensionless distance X calculated for $\alpha = 0.5$, $\beta = 0.1$, $\gamma_{E1} = 0.01$ and $\gamma_{S1} = 0.005$. *Solid lines* represent the analytical solution presented in this study (Eq. 19) and *dotted lines*, the numerical solution

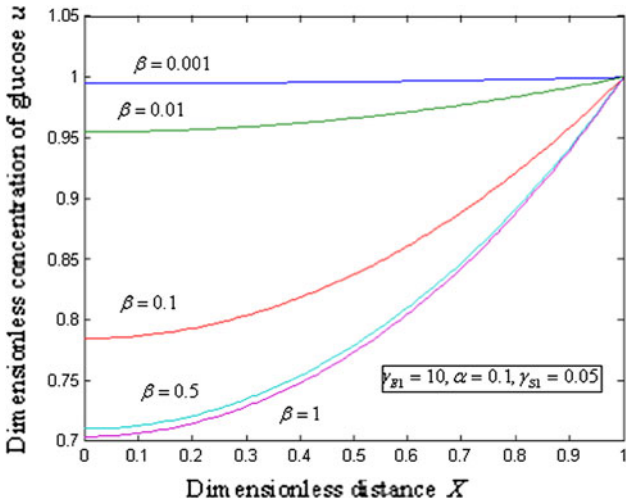

Fig. 4 Typical normalized steady-state concentration of glucose u calculated from Eq. 17 for different values of the parameter β

the maximal reaction rate. In contrast, when the Thiele modulus is large, diffusion limitations are the principal determining factor. Adding Eqs. 12–14 and integrating twice, we also obtain the following simple relation between concentrations of glucose, oxygen and gluconic acid.

$$\frac{u}{\gamma_{E1}} + \frac{2v}{\gamma_{s1}} + \frac{2w}{\gamma_E} = \frac{1}{\gamma_{E1}} + \frac{2}{\gamma_{S1}} \tag{21}$$

Figure 1 presents the dimensionless concentration of glucose $u(X)$ for $\alpha = 0.1$, $\beta = 0.01$ and $\gamma_{S1} = 0.01$ and various values of γ_{E1}. From this figure, it is evident that the concentration of glucose increases when γ_{E1} or the thickness of the membrane decreases. Also, the value of $u(X)$ is largest at $X = 1$. The value of the dimensionless

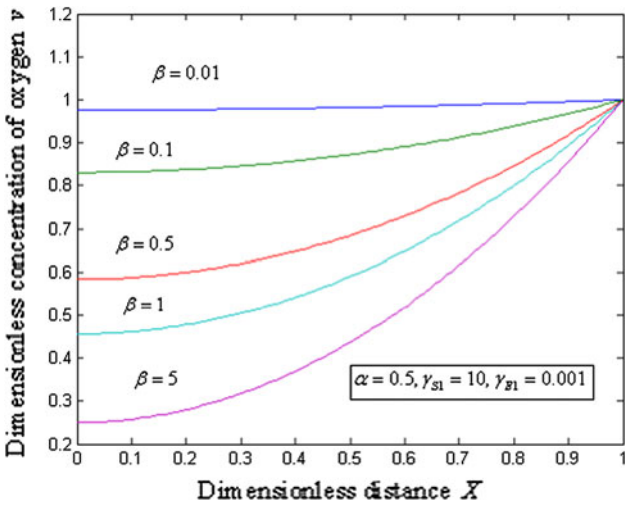

Fig. 5 Typical normalized steady-state concentration of oxygen v calculated from Eq. 18 for different values of the parameter β

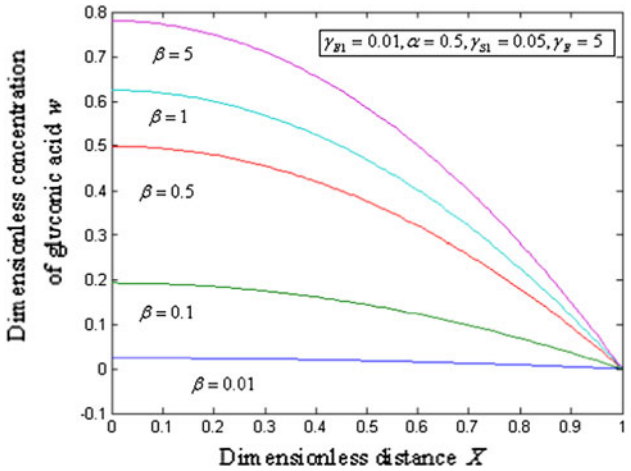

Fig. 6 Typical normalized steady-state concentration of gluconic acid w calculated from Eq. 19 for different values of the parameter β

concentration of oxygen $v(X)$versus the dimensionless distance is plotted in Fig. 2. From this figure, it is inferred that the concentration of oxygen increases when γ_{S1} decreases. Furthermore, the concentration of oxygen reaches the steady-state value when $\gamma_{S1} \leq 10$. Figure 3 presents the concentration of gluconic acid $w(X)$ as a function of X for various values of parameters. From this figure, it is obvious that the concentration of gluconic acid $w(X)$ increases when γ_E increases. It also decreases with increasing X, approaching zero at $X = 1$.

The normalized steady-state concentration of glucose against dimensionless distance is plotted in Fig. 4. From this figure, we conclude that the value of $u(X)$ increases when the reaction–diffusion parameter β or the Michaelis-Menten constant for glucose decreases. Figure 5 illustrates the concentration of oxygen as a function of dimensionless distance X for various values of β. In this figure, the value of $v(X)$ is equal to 1 when $X = 1$ for all values of the reaction–diffusion parameter β. In Fig. 6, the concentration of gluconic acid increases when β increases.

Conclusions

We analyzed the theoretical model describing the process of reaction and diffusion in glucose-responsive composite membranes, previously described by Abdekhodaie and Wu (2009). The system of nonlinear, steady-state reaction–diffusion equations of the model has been solved analytically. The accuracy of the approximate analytical solutions has been verified by comparison with numerical solutions. The analytical results can be employed to analyze the effects of membrane formulation such as enzyme loading, the type of buffer in the external solution and optimization of the design of glucose-sensitive membranes.

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Appendix A: Basic Concepts of the Adomian Decomposition Method

The Adomian decomposition method (Adomian 1984, 1995; Siddiqui et al. 2010; Wazwaz and Gorguis 2004; Sweilam and Khader 2010; Adomian and Witten 1994; Lesnic 2007; Magyari 2008; Rida 2010; Wazwaz 2000; Danish et al. 2011) consists of decomposing the nonlinear differential equation

$$F[x, y(x)] = 0 \tag{A1}$$

into two components

$$L[y(x)] + N[y(x)] = 0 \tag{A2}$$

where L and N are the linear and the nonlinear parts of F, respectively. The operator L is assumed to be an invertible operator. Solving for $L(y)$ leads to

$$L(y) = -N(y) \tag{A3}$$

Applying the inverse operator L to both sides of Eq. A3 yields

$$y = -L^{-1}(N(y)) + \phi(x), \tag{A4}$$

where $\phi(x)$ is the function that satisfies the condition $L(\phi) = 0$. Now suppose that the solution y can be represented as an infinite series of the form

$$y = \sum_{n=0}^{\infty} y_n \tag{A5}$$

The Adomian decomposition method assumes that the nonlinear term $N(y)$ can be written as an infinite series in terms of the Adomian polynomials A_n:

$$N(y) = \sum_{n=0}^{\infty} A_n \tag{A6}$$

where the Adomian polynomials A_n of $N(y)$ are evaluated using the formula

$$A_n(x) = \frac{1}{n!}\frac{d^n}{d\lambda^n} N\left(\sum_{n=0}^{\infty}(\lambda^n y_n)\right)\Big|_{\lambda=0} \tag{A7}$$

where $\lambda \in [0,1]$is a hypothetical parameter (28).

Substituting Eqs. A5 and A6 in A4 gives

$$\sum_{n=0}^{\infty} y_n = \phi(x) - L^{-1}\left(\sum_{n=0}^{\infty} A_n\right) \tag{A8}$$

By equating the terms in the linear system of Eq. A8 one obtains the recurrence formula:

$$y_0 = \phi(x),\ y_{n+1} = -L^{-1}(A_n) \quad n \geq 0 \tag{A9}$$

However, in practice all terms of the series (A6) cannot be determined, and the solution is approximated by the truncated series $\sum_{n=0}^{N} y_n$.

Appendix B: Analytical Solutions for the Concentrations of Glucose, Oxygen and Gluconic Acid

The solution of Eqs. 12–14 allows us to predict the concentration profiles of glucose, oxygen and gluconic acid. We write Eqs. 12–14 in the operator form and derive its general solution using the Adomian decomposition method (16–25). The operator form is

$$L\begin{bmatrix} u(X) \\ v(X) \\ w(X) \end{bmatrix} = N\begin{bmatrix} u(X) \\ v(X) \\ w(X) \end{bmatrix} = \begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{u(X)v(X)}{u(X)v(X) + v(X)/\alpha + u(X)/\beta} \tag{B1}$$

where $L = \frac{d^2}{dX^2}$. Applying the inverse operator L^{-1} to both sides of Eq. B1 yields, in agreement with Eqs. A4, A6 and A8

$$\begin{bmatrix} u(X) \\ v(X) \\ w(X) \end{bmatrix} = \sum_{n=0}^{n=\infty} \begin{bmatrix} u_n(X) \\ v_n(X) \\ w_n(X) \end{bmatrix} = \begin{bmatrix} P_u \\ P_v \\ P_w \end{bmatrix} X + \begin{bmatrix} Q_u \\ Q_v \\ Q_w \end{bmatrix} + L^{-1}\begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{u(X)v(X)}{u(X)v(X) + v(X)/\alpha + u(X)/\beta}$$
$$= \begin{bmatrix} P_u \\ P_v \\ P_w \end{bmatrix} X + \begin{bmatrix} Q_u \\ Q_v \\ Q_w \end{bmatrix} + L^{-1}\sum_{n=0}^{n=\infty} \begin{bmatrix} A_{n,u} \\ A_{n,v} \\ A_{n,w} \end{bmatrix} \tag{B2}$$

where P_u, P_v, P_w, Q_u, Q_v and Q_w are the integration constant and the Adomain polynomial coefficients $A_{n,i}(X)$ $(i = u, v, w)$ can be obtained using Eq. A7. By equating the terms of Eq. B2 and using the boundary conditions 15 and 16, we get

$$\begin{bmatrix} u_0(X) \\ v_0(X) \\ w_0(X) \end{bmatrix} == \begin{bmatrix} P_u \\ P_v \\ P_w \end{bmatrix} X + \begin{bmatrix} Q_u \\ Q_v \\ Q_w \end{bmatrix} = \begin{bmatrix} 1 \\ 1 \\ 0 \end{bmatrix} \tag{B3}$$

The first two Adomain polynomial coefficients $A_{n,i}(X)$ $(i = u, v, w)$ are

$$\begin{bmatrix} A_{0,u} \\ A_{0,v} \\ A_{0,w} \end{bmatrix} = \begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{\alpha\beta}{\alpha\beta + \alpha + \beta} \tag{B4}$$

$$\begin{bmatrix} A_{1,u} \\ A_{1,v} \\ A_{1,w} \end{bmatrix} = \begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{\alpha\beta[\beta u_1(X) + \alpha v_1(X)]}{(\alpha\beta + \alpha + \beta)^2} \tag{B5}$$

From the above equations we obtain $u_1(X)$, $v_1(X)$, $w_1(X)$ and $u_2(X)$, $v_2(X)$, $w_3(X)$ as follows:

$$\begin{bmatrix} u_1(X) \\ v_1(X) \\ w_1(X) \end{bmatrix} = L^{-1}\begin{bmatrix} A_{0,u} \\ A_{0,v} \\ A_{0,w} \end{bmatrix} = \begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{\alpha\beta(-1 + X^2)}{2(\alpha + \beta + \alpha\beta)} \tag{B6}$$

and

$$\begin{bmatrix} u_2(X) \\ v_2(X) \\ w_2(X) \end{bmatrix} = L^{-1} \begin{bmatrix} A_{1,u} \\ A_{1,v} \\ A_{1,w} \end{bmatrix} = \begin{bmatrix} \gamma_{E1} \\ \gamma_{S1}/2 \\ -\gamma_E \end{bmatrix} \frac{(\alpha\beta)^2[2\gamma_1\beta + \gamma_{s1}\alpha][5 - 6X^2 + X^4]}{48(\alpha + \beta + \alpha\beta)^3} \tag{B7}$$

Adding Eqs. B3, B6 and B7 we obtain Eqs. 14–16 in the text.

Appendix C

Nomenclature

C_g	Concentration of glucose (mol/cm^3)
C_{OX}	Concentration of oxygen (mol/cm^3)
C_a	Concentration of gluconic acid (mol/cm^3)
D_g	Diffusion coefficient of glucose (cm^2/s)
D_{OX}	Diffusion coefficient of oxygen (cm^2/s)
D_a	Diffusion coefficient of gluconic acid (cm^2/s)
K_g	Michaelis-Menten constant for glucose (mol/cm^3)
K_{OX}	Michaelis-Menten constant for glucose oxidase (mol/cm^3)
$v_{\max}$	Maximal reaction rate (mol/s cm^3)
x	distance (mm)
C_g*	Concentration of glucose in the external solution (mol/cm^3)
C_{OX}*	Concentration of glucose in the oxygen solution (mol/cm^3)
l	Half thickness of the membrane (mm)
u	Dimensionless concentration of glucose
v	Dimensionless concentration of oxygen
w	Dimensionless concentration of gluconic acid
X	Dimensionless distance
γ_{E1}, γ_{S1}, γ_E, α, β	Dimensionless reaction diffusion parameters

Appendix D

The SCILAB/MATLAB program for the numerical solution of the system of nonlinear second-order differential Eqs. 6–8 for the glucose composite membrane is given in the supplementary material for this article.

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