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Research Article

Mathematical Modelling and Analytical Expressions for Steady-state Concentrations of Non-linear Glucose-responsive Composite Membranes for Closed-loop Insulin Delivery: Akbari-Ganji and Differential Transform Methods

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Abstract

The dynamic mechanism comprising an enzymatic reaction and the diffusion of reactants and products inside a glucose-sensitive composite membrane is described using a mathematical model created by Abdekhodaie and Wu. A set of non-linear steady-state reaction-diffusion equations is presented in this theoretical model. These equations have been meticulously and accurately solved analytically, considering the concentrations of glucose, oxygen, and gluconic acid, using a novel approach of Akbari Ganji and differential transform methods. The high level of agreement between these analytical results and the numerical results for steady-state conditions is a testament to the model's precision. A numerical simulation was produced via the precise and widely used MATLAB software. A comprehensive graphic representation of the model's various kinetic parameters' effects has also been provided. Additionally, a theoretical analysis of the kinetic parameters, such as the maximal reaction velocity (V_{max}) and the Michaelis-Menten constants (Kg and Kox) for oxygen and glucose, pH profiles with membranes is presented. This expressed model is incredibly helpful when creating glucose-responsive composite membranes for closed-loop insulin delivery.

Keywords

Membrane Responsive to Glucose, Delivery of Insulin, Enzymatic Process, Equation of Reaction-diffusion, Akbari-Ganji Method, Differential Transform Method

1. Introduction

Worldwide, a large number of people have diabetes. Diabetes is a long-term glucose metabolic problem and a leading cause of kidney and heart disease. Insulin must be administered intravenously or via a pump multiple times a day to treat insulin-dependent diabetes and regulate blood sugar levels. As a result, numerous types of glucose membrane-containing insulin-delivering devices have been researched (Abdekhodaie & Wu). Immobilized glucose oxidase and catalase are found in specific systems (Abdekhodaie & Wu; Albin et al.,; Traitel et al.,; Podual et al.,; Hassan et al., ; Zhang & Wu, ;

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Zhang et al.,; Wu et al.). These systems are comprised of pH-responsive polymeric hydrogels [1-5].

There are two categories of pH-sensitive hydrogels: cationic and anionic. High glucose levels cause cationic hydrogels, made of amino groups, to swell in reaction to pH reductions. The protonation of acidic groups causes anionic hydrogels to contract. More theoretical modelling investigations of cationic glucose-sensitive membranes have been conducted (Abdekhodaie and Wu) [5]. Abdekhodaie and Wu created a mathematical model explaining the dynamic process of reactant diffusion and an enzymatic reaction within a glucose composite membrane made of hydrophobic polymer-embedded anionic nanoparticles, glucose oxidase, and catalase. No analytical solutions for this particular model have been documented. However, because they may be subjected to multiple manipulations and data analysis types, analytical solutions to nonlinear differential equations are generally more exciting and valuable than solely numerical solutions.

Hariharan and Kannan used the Adomian decomposition method to address the one-dimensional reaction-diffusion problem [6]. According to Rajendran et al., the nonlinear second-order reaction-diffusion equations relevant to membrane science can be solved using the Adomian decomposition approach [7]. Megala et al. generated analytical results for the homotopy perturbation method, allowing the construction of glucose-sensitive membranes for closed-loop insulin delivery [8]. The glucose-sensitive membranes for closed-loop insulin delivery can be developed in this paper study that produced analytical results by discussing the influence of several kinetic factors included in this model by Akbari-Ganji and differential transform methods.

2. Mathematical Formulation of the Problem

Abdekhodaie and Wu state that the reaction scheme for a glucose-sensitive membrane made up of immobilized enzymes like glucose oxidase and catalase and a pH-sensitive anionic hydrogel may be expressed as follows [5]:

$$Glucose \ + 0.5 \ O_2 \xrightarrow{Glucose \ \ oxidase,catalase} Gluconic \ \ acid + \ \ H_2O \tag{1}$$

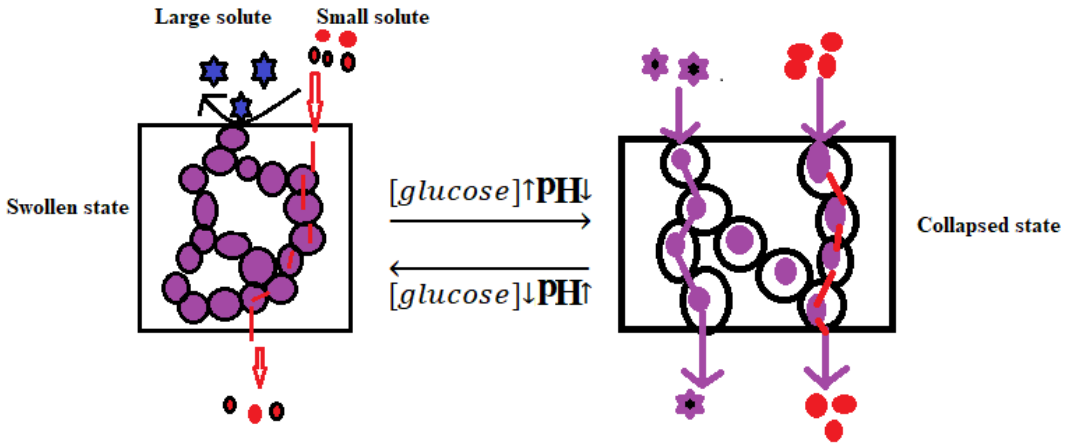

Figure 1. *Diagrammatic representation of the pore space within the composite membrane, the glucose-responsive volume change of the anionic hydrogel, and the solute permeation paths across the membrane as a function of molecule size.*

Figure 1 shows the suggested mechanism of the composite membrane's pH and glucose-responsive permeability to tiny and large solutes. Diffusion of glucose and oxygen from the medium into the membrane converts glucose to gluconic acid, lowering the pH and altering the membrane's permeability to solutes. This process indicates that when catalase is in excess, just half of an oxygen molecule is utilized for every glucose molecule. For non-steady state conditions, the appropriate governing non-linear differential equation inside the cationic glucose-sensitive membrane can be expressed as

$$D_i \frac{d^2 a_i(x)}{dx^2} - \frac{v_i \ V_{max} \ a_g a_{ox}}{a_{ox}(K_g + a_g) + K_{ox} \ a_g} = 0, a_i = a_g \ , a_{ox}, a_{ga} \tag{2}$$

Where $a_g, a_{ox} \ and \ a_{ga}$ are concentration of glucose, oxidase, and gluconic acid. D_i is the diffusion coefficient, K_g, K_{ox} are Michaelis–Menton constants for glucose, oxidase V_{max} is the maximal reaction velocity and v_i are $v_g = -1, v_{ox} \ = \frac{1}{2}, v_{ga} = 1$.

The boundary conditions are,

$$x = 0 \ \ \frac{\partial a_g}{\partial x} = 0, \frac{\partial a_{ox}}{\partial x} = 0, \frac{\partial a_{ga}}{\partial x} = 0. \tag{3}$$

$$x = l, \ \ a_g = a_g{}^*, a_{ox} \ = a_{ox}{}^*, a_{ga} = a_{ga}{}^*. 0 \ \ < x < l, \tag{4}$$

The following non-dimension parameters are introduce as,

$$U = \frac{a_g}{a_g^*}, V = \frac{a_{ox}}{a_{ox}^*}, W = \frac{a_{ga}}{a_{ox}^*} \quad \chi = \frac{x}{l}, \quad \gamma_{E1} = \frac{V_{max}\ l^2}{D_g\ a_g^*}, \gamma_{S1} = \frac{V_{max}\ l^2}{D_{ox}\ a_{ox}^*}, \gamma_E = \frac{V_{max}\ l^2}{D_{ga}\ a_{ox}^*}, \alpha = \frac{a_g}{K_g}, \beta = \frac{a_{ox}}{K_{ox}} \tag{5}$$

Where $U, V\ and\ W$ are the dimensionless concentration of the glucose, oxidase, and gluconic acid respectively, χ is the dimensionless distance, l is the relative thickness and $\gamma_{E1}, \gamma_{S1}\ and\ \gamma_E$ are corresponding Thiele modulus, α, β be the rate of constant.

The steady-state dimensionless form of equations (2) to (4) using the dimensionless parameters equation (5) are given as follows,

$$\frac{\partial^2 U(\chi)}{\partial \chi^2} - \gamma_{E1}\ U\ V[U\ V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \tag{6}$$

$$\frac{\partial^2 V(\chi)}{\partial \chi^2} - \frac{\gamma_{S1}}{2}\ U\ V[U\ V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \tag{7}$$

$$\frac{\partial^2 W(\chi)}{\partial \chi^2} + \gamma_E\ U\ V[U\ V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \tag{8}$$

Corresponding boundary conditions are,

$$\chi = 0 \quad \frac{\partial U(\chi)}{\partial \chi} = 0, \quad \frac{\partial V(\chi)}{\partial \chi} = 0, \frac{\partial W(\chi)}{\partial \chi} = 0$$

$$\chi = 1 \quad U = 1, V = 1, W = 0. \tag{9}$$

3. Expression of the Concentrations Analytically

3.1. Analytical Expression for the Concentration of Glucose, Oxidase, and Gluconic Acid Under the Steady State Condition Using Akbari-Ganji Method

The semi-analytical algebraic method known as the Akbari-Ganji Method (AGM) is used to solve nonlinear differential equations. It is regarded as a potent technique for resolving these equations, which can be more challenging than linear differential equations. To solve non-linear boundary value problems, Akbari and Ganji initially presented the Akbari-Ganji Method (AGM), which combines the conventional algebraic approach. Recently, Akbari and Ganji used the Akbari-Ganji approach with two expanding parameters to solve a few non-linear problems. The ability of the Akbari-Ganji to offer precise analytical suggestions for various non-linear chemical issues is a significant advantage. Akbari-Ganji's ability to tackle a wide range of non-linear problems with fewer iterations is fantastic. This approach's most important benefit is its adaptability to various chemical physics challenges. Various analytical methods for dealing with nonlinear boundary value problems [10-24].

Using this method (details in Appendix I), we get the approximate expressions (6) to (9) as follows.

$$U(\chi) = \frac{\cos\ h l\chi}{\cos h\ l} \tag{10}$$

$$V(\chi) = \frac{\cos h\ m\chi}{\cos h\ m} \tag{11}$$

$$W(\chi) = 1 - \frac{\cos h\ n\chi}{\cos h\ n} \tag{12}$$

Where $l = \sqrt{\frac{\gamma_{E1}\ \alpha\ \beta}{\alpha\ \beta+\alpha+\beta}}, \ m = \sqrt{\frac{\gamma_{S1}\ \alpha\ \beta}{2(\alpha\ \beta+\alpha+\beta)}}, \ n = \sqrt{\frac{\gamma_E\ \alpha\ \beta}{\alpha\ \beta+\alpha+\beta}}$ (13)

3.2. Use the Differential Transform Method (DTM) to Approximate the Analytical Expression for the Concentration Species

The differential transform method (DTM) is a semi-analytical approach to solving differential equations. Zhou was the first to propose the differential transform notion in electric circuit analysis, which addresses linear and nonlinear boundary value issues. DTM can be used to accurately calculate the nth derivative of an analytical function at a given place, even if the boundary conditions are unknown. The differential transform method (DTM) is an alternative iterative approach for determining analytical solutions to differential equations [25-33].

Using this method (details in Appendix II), we get the approximate expressions (6) to (9) as follows.

$$U(\chi) = l_1 - \frac{\gamma_{E1}\ \alpha\ \beta\ l_1 m_1}{2(l_1 m_1 \alpha\ \beta + l_1\alpha + m_1\beta)}\chi^2 \tag{14}$$

$$V(\chi) = m_1 - \frac{\gamma_{S1}\ \alpha\ \beta}{4(l_1 m_1 \alpha\ \beta + l_1\alpha + m_1\beta)}\chi^2 \tag{15}$$

$$W(\chi) = n_1 - \frac{\gamma_E\ \alpha\ \beta\ l_1 m_1}{2(l_1 m_1 \alpha\ \beta + l_1\alpha + m_1\beta)}\chi^2 \tag{16}$$

Where

$$l_1 = \frac{\beta m_1(2\alpha - \gamma_{E1}\alpha - 2)}{4\alpha(m_1\ \beta+1)} \pm$$
$$\sqrt{\alpha^2\beta^2 m_1{}^2(\gamma_{E1}{}^2 - 4\gamma_{E1} + 4) + \alpha\beta^2 m_1{}^2(4\gamma_{E1} + 8) + \beta\alpha^2 m_1(-4\gamma_{E1} + 8) + 4\beta^2 m_1{}^2 + 8\beta\alpha m_1 + 4\alpha^2 - 2\alpha}$$

$$m_1 = \frac{\pm(-\alpha\ \ l_1+\sqrt{-\gamma_{S1}\alpha^2\beta^2 l_1-\gamma_{S1}\alpha\beta^2+{l_1}^2\alpha^2)}}{2\beta(l_1\alpha+1)}$$

$$n_1 = \frac{\gamma_E\ \ \alpha\ \ \beta\ \ l_1 m_1}{2(l_1 m_1\alpha\ \ \beta+l_1\alpha+m_1\beta)} \quad (17)$$

4. Findings and Discussions

The analytical techniques for the glucose $U(\chi)$, oxygen $V(\chi)$, and gluconic acid $W(\chi)$, dimensionless concentrations are valid for all values of parameters $\gamma_{E1}, \gamma_{S1}, \gamma_E$ a, and b taken into account in this investigation. The Thiele modulus $\gamma_{E1}, \gamma_{S1}, \gamma_E$ can be changed by altering the membrane's thickness or the amount of glucose and oxygen in the external environment. This parameter describes the relative relevance of reaction and diffusion inside the layer of enzymes. When the enzyme matrix is small, its overall absorption of glucose, oxygen, and gluconic acid is kinetically controlled, making kinetics the major resistance. Under these circumstances, the profile of glucose concentration throughout the membrane is nearly constant. The maximal reaction rate dictates the total kinetics. On the other hand, diffusion restrictions are the main deciding factor when the Thiele modulus is high. Numerical simulations are used to compare the analytical results, which are presented in the following Figures. The Numerical simulations are presented in (Refer Appendix III) using pdex4 function in MATLAB.

Table 1. *The parameter values utilized in this study and Abdekhodaie and Wu).*

Parameter	Unit	Value
D_g	$cm^2 s^{-1}$	6.75×10^{-6}
D_{ox}	$cm^2 s^{-1}$	6.75×10^{-6}
K_{ox}	mol cm^{-3}	6.992×10^{-5}
K_g	mol cm^{-3}	6.187×10^{-7}
V_{max}	mol s^{-1} cm^{-3}	860×3
${a_{ox}}^*$	mol cm^{-3}	0.274
${a_g}^*$	mol cm^{-3}	5.5 *and* 22

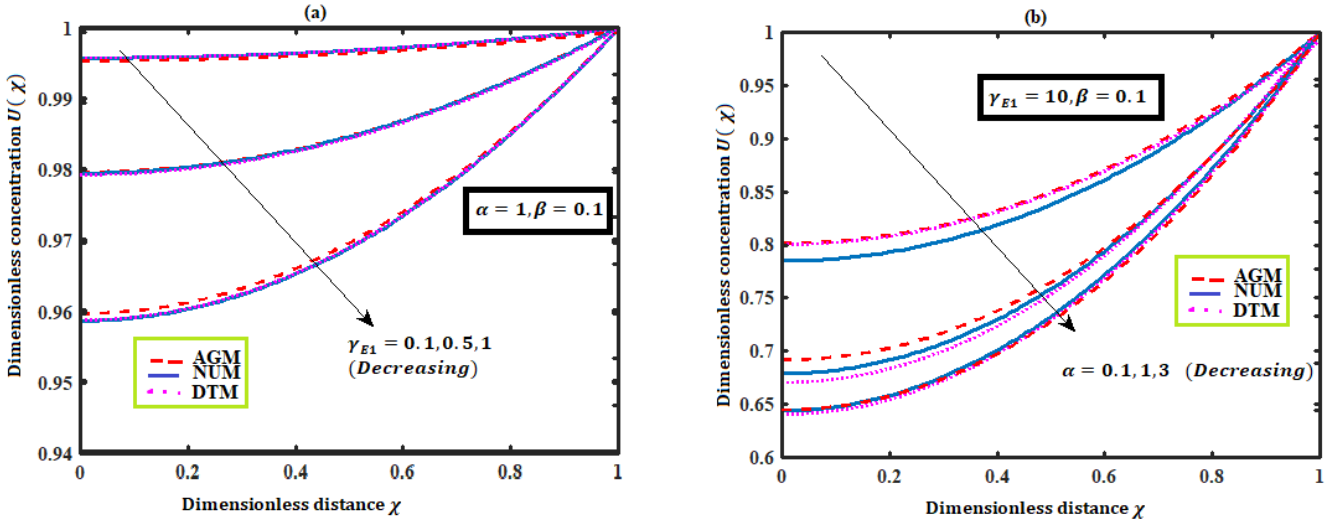

Figure 2. *The concentration $U(\chi)$ is compare to Dimensionless distance χ using in eqn. (10) & (14) for a) several values of non dimensional parameter γ_{E1} and fixed values of the parameter α and β b) several values of non dimensional parameter α and fixed values of the parameter γ_{E1} and β.*

From this Figure 2, it is evident that the concentration of glucose increases when γ_{E1} or the thickness of the membrane decreases. Also, the value of $U(\chi)$ is largest at $\chi = 1$. Diffusion reaction parameter α increases, the concentration of glucose decreases. From this figure 3, it is inferred that the concentration of oxygen increases when γ_{S1} decreases. Furthermore, the concentration of oxygen reaches the steady-state value when $\gamma_{S1} \geq 1$. Diffusion reaction parameter α increases, the concentration of oxygen decreases simultaneously.

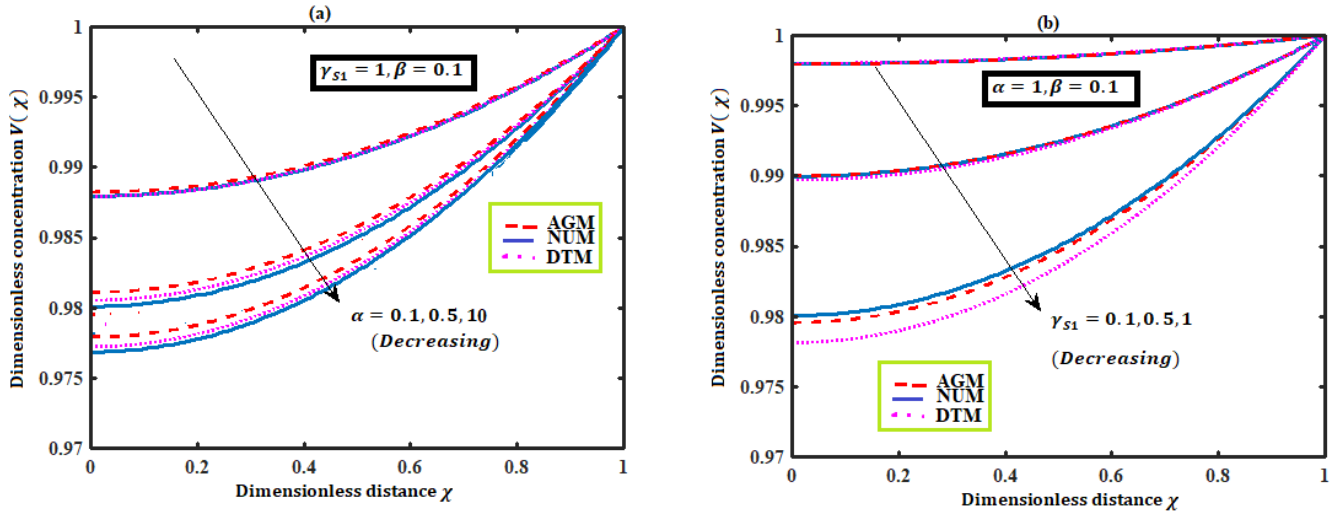

Figure 3. *The concentration $V(\chi)$ is compare to Dimensionless distance χ using in eqn. (11) & (15) for a) several values of non dimensional parameter α and fixed values of the parameter β, γ_{S1} b) several values of non dimensional parameter γ_{S1} and fixed values of the parameter α and β.*

From Figure 4, it is stated that the concentration of gluconic acid increases when γ_E increases. Furthermore, the concentration of gluconic acid reaches the steady-state value when $\gamma_E \leq 0.1$. Diffusion reaction parameter α increases, the concentration of gluconic acid increases simultaneously.

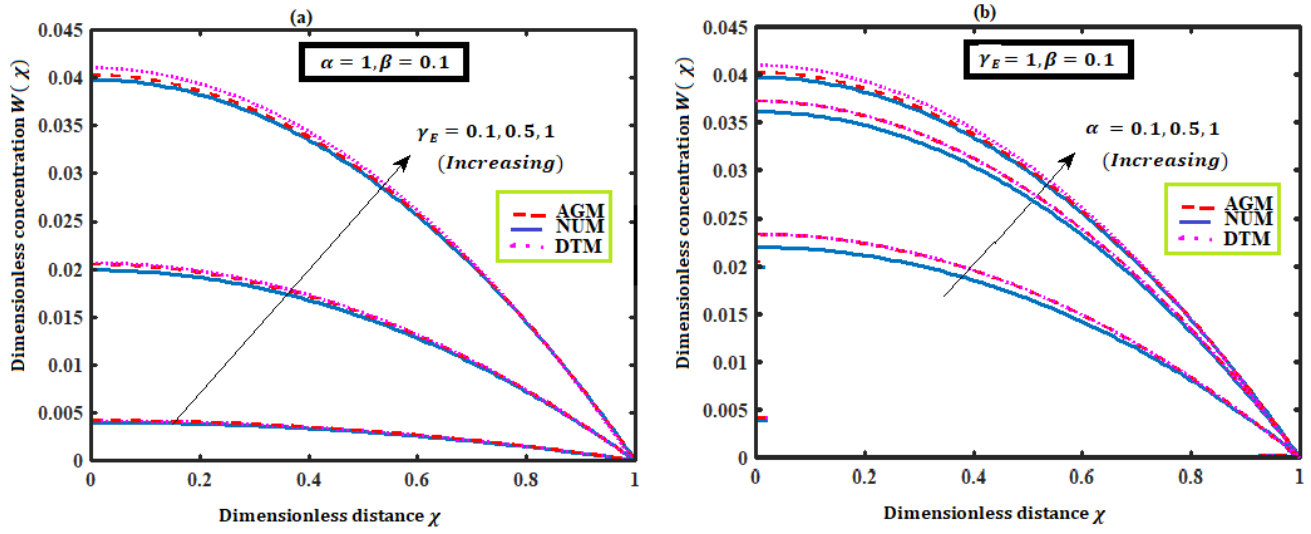

Figure 4. *The concentration $W(\chi)$ is compare to Dimensionless distance χ using in eqn. (12) & (16) for a) several values of non dimensional parameter γ_E and fixed values of the parameter α and β b) several values of non dimensional parameter α and fixed values of the parameter γ_E and β.*

5. Calculating the pH Profile Within the Membrane

The pH profile inside the membrane must be ascertained as Diffusion coefficient in Eq. (2.2), depending on the extent of polymer swelling, which is a function of pH. The Henderson–Hassel equation can determine a buffer's pH when gluconic acid is absent [9].

$$pH_1 = pK + \log \frac{[base]_1}{[acid]_1} \tag{18}$$

The quantities of buffer ions and gluconic acid within the membrane dictate pH in the presence of gluconic acid (pH_2).

$$pH_2 = pK + \log\left\{\frac{10^{pH_1-pK} - \frac{w(\chi)}{[buffer]}(1+10^{pH_1-pK})}{1+\frac{w(\chi)}{[buffer]}(1+10^{pH_1-pK})}\right\} \tag{19}$$

Applying equation (12) yields the pH in a gluconic acid concentration as follows:

$$\exp(\mathrm{p}H_2\text{-pK}) = \frac{10^{\mathrm{p}H_1-\mathrm{pK}}-\left(1-\frac{\cosh\left(\sqrt{\frac{\gamma_E\ \alpha\ \beta}{\alpha\beta+\alpha+\beta}}\right)\chi}{\cosh\left(\sqrt{\frac{\gamma_E\ \alpha\ \beta}{\alpha\beta+\alpha+\beta}}\right)}\frac{w(\chi)}{[buffer]}\right)\left(1+10^{\mathrm{p}H_1-\mathrm{pK}}\right)}{1+\frac{w(\chi)}{[buffer]}\left(1+10^{\mathrm{p}H_1-\mathrm{pK}}\right)}\} \tag{20}$$

Figure 5 plots exp(pH_2-pK) versus $\mathrm{p}H_1 - \mathrm{pK}$ for various parameter values. It observed that exp(pH_2-pK) increases when the values of the parameter $\frac{w(\chi)}{[buffer]}$, γ_E and α values change and decreases simultaneously.

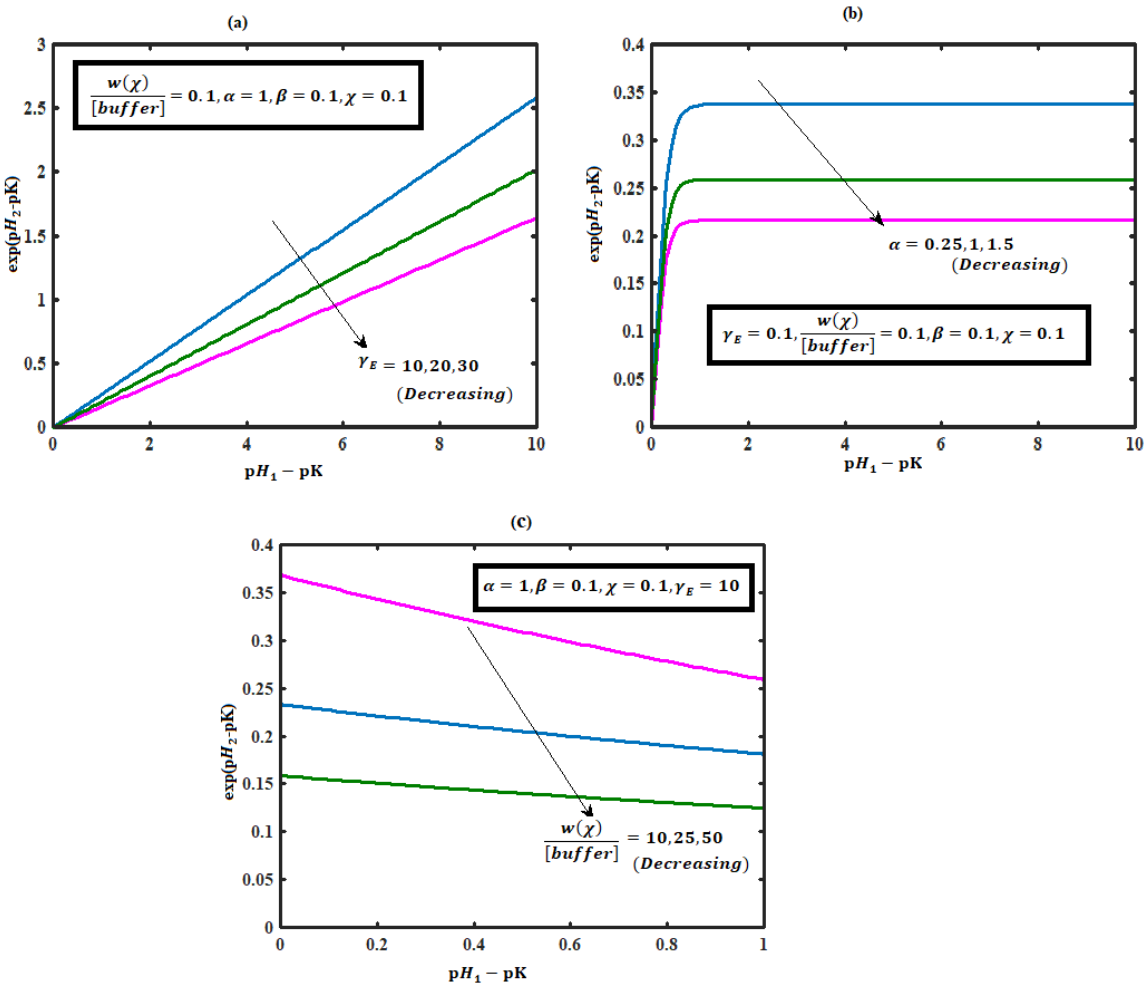

Figure 5. *The exp(pH_2-pK) versus $pH_1 - pK$ for various values of the parameter a) γ_E, b) α, c) $\frac{w(\chi)}{[buffer]}$ by using eqn. (20).*

6. Conclusions

A mathematical model has described the glucose sensitivity of a composite membrane with nanoparticles of an anionic polymer, glucose oxidase, and catalase embedded in a hydrophobic polymer. The model can forecast pH in the membrane at different glucose levels in the medium, time- and position-dependent concentrations and diffusivity of the associated solutes, water and polymer volume percentage, and more. The model may be used to examine how the type of buffer in the external solution and enzyme loading, among other aspects of membrane formulation, affect the membrane's sensitivity to glucose. According to the numerical simulation, improving the enzyme loading can increase the membrane's reaction to the step change in glucose concentration. Other design parameters in the model, such as particle content and charge density, can be examined using numerical

simulation in addition to the formulation parameter and external condition discussed in this research. Thus, the model helps design composite membranes sensitive to glucose for closed-loop insulin delivery. This theoretical model is also helpful for maximising the functionality of glucose-sensitive membranes and determining the parameters needed to enhance membrane design. This model has been analytically resolved using the Akbari-Ganji method and the differential transform method. The acquired analytical data were helpful in accurately predicting the diffusion and concentration values of glucose, oxidase and gluconic acid. The given methodology's comparison of the analytical results with those generated by the MATLAB program convincingly demonstrated correctness. In contrast, the analytical results from AGM are superior to those from DTM. Furthermore, pH profile with membrane is derived. Future studies can use this approach to solve non-steady state circumstances. Additionally, this theoretical model can be used to determine the parameters required to improve the design of gluconic acid delivery systems and to optimize their performance.

Nomenclature

a_g	concentration of Glucose (mol cm^{-3})
a_{ox}	concentration of Glucose Oxidase (mol cm^{-3})
a_{ga}	concentration of Gluconic Acid (mol cm^{-3})
U	Dimensionless Concentration of Glucose (none)
V	Dimensionless Concentration of Glucose Oxidase (none)
W	Dimensionless Concentration of Gluconic Acid (none)
${a_g}^* {a_{ox}}^* {a_{ga}}^*$	Initial Concentration of Species (mol cm^{-3})
l	Thickness of the Membrane (μm)
K_g	Michaelis–Menten Constant for Glucose (mol cm^{-3})
K_{ox}	Kox Michaelis–Menten Constant for Oxygen (mol cm^{-3})
V_{max}	Maximal Reaction Rate (mol s^{-1} cm^{-3})
$\gamma_{E1}, \gamma_{S1}, \gamma_E$	Thiele Modulus (none)
D_i	Diffusion Coefficient of Substrate ($cm^2 s^{-1}$)
α	Dimensionless Diffusion Reaction Parameter (none)
β	Dimensionless Diffusion Reaction Parameter (none)
χ	Normalized Electrode Distance (none)
x	Distance from Electrode (cm)

Abbreviations

AGM	Akbari Ganji Method
DTM	Differential Transform Method

Author Contributions

Ranjani Kesavan: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing

Swaminathan Rajagopal: Conceptualization, Formal Analysis, Project administration, Validation, Visualization

Karpagavalli Ramasamy: Conceptualization, Formal Analysis, Investigation, Project administration, Resources, Supervision, Validation, Visualization

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix

Appendix I: Akbari-Ganji Method

In section 3, From Equations (6) to (8)

$$\frac{\partial^2 U(\chi)}{\partial \chi^2} - \gamma_{E1}\ U\ V[U\ V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \tag{A-1}$$

$$\frac{\partial^2 V(\chi)}{\partial \chi^2} - \frac{\gamma_{S1}}{2} U V[U V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \quad \text{(A-2)}$$

$$\frac{\partial^2 W(\chi)}{\partial \chi^2} + \gamma_E U V[U V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \quad \text{(A-3)}$$

Corresponding boundary conditions are,

$$\chi = 0 \quad \frac{\partial U(\chi)}{\partial \chi} = 0, \frac{\partial V(\chi)}{\partial \chi} = 0, \frac{\partial W(\chi)}{\partial \chi} = 0$$

$$\chi = 1 \quad U = 1, V = 1, W = 0.0 \quad < x < 1 \quad \text{(A-4)}$$

Assume that solution of the equations (A-1) to (A-3)

$$U(\chi) = A \cos h \; l\chi + B \sinh l \; \chi \quad \text{(A-5)}$$

$$V(\chi) = A_1 \cos h \; m\chi + B_1 \sinh m \; \chi \quad \text{(A-6)}$$

$$W(\chi) = 1 + A_2 \cos h \; n\chi + B_2 \sinh n \; \chi \quad \text{(A-7)}$$

Here $A, B \; A_1, B_1, A_2, B_2, l, m$ and n are constants has to be obtained.
To solve equation (A-5), (A-6) using equation (A-4) to get
$A = \frac{1}{\cos hl}$, $B = 0$ and $A_1 = \frac{1}{\cos hm}$, $B_1 = 0$, are substitute in (A-5) and (A-6)

$$U(\chi) = \frac{cos \; hl\chi}{\cos h \; l} \quad \text{(A-8)}$$

$$V(\chi) = \frac{\cos h \; m\chi}{\cos h \; m} \quad \text{(A-9)}$$

To solve equation (A-7) using equation (A-4) to get $A_2 = -\frac{1}{\cos hn}$, $B_2 = 0$, substitute in equation (A-7)

$$W(\chi) = 1 - \frac{\cos h \; n\chi}{\cos h \; n} \quad \text{(A-10)}$$

Substitute equation (A-8) to (A-10) in to (A-1) to (A-3) and $\chi = 0$ we get,

$$l = \sqrt{\frac{\gamma_{E1} \; \alpha \; \beta}{\alpha \; \beta + \alpha + \beta}}, \; m = \sqrt{\frac{\gamma_{S1} \; \alpha \; \beta}{2(\alpha \; \beta + \alpha + \beta)}}, \; n = \sqrt{\frac{\gamma_E \; \alpha \; \beta}{\alpha \; \beta + \alpha + \beta}} \quad \text{(A-11)}$$

Appendix II: Differential Transform Method

From Equations in section 3 from (A-6) to (A-8)

$$\frac{\partial^2 U(\chi)}{\partial \chi^2} - \gamma_{E1} U V[U V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \quad \text{(A-12)}$$

$$\frac{\partial^2 V(\chi)}{\partial \chi^2} - \frac{\gamma_{S1}}{2} U V[U V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \quad \text{(A-13)}$$

$$\frac{\partial^2 W(\chi)}{\partial \chi^2} + \gamma_E U V[U V + \frac{V}{\alpha} + \frac{U}{\beta}]^{-1} = 0 \quad \text{(A-14)}$$

Corresponding boundary conditions are,

$$\chi = 0 \quad \frac{\partial U(\chi)}{\partial \chi} = 0, \frac{\partial V(\chi)}{\partial \chi} = 0, \frac{\partial W(\chi)}{\partial \chi} = 0$$

$$\chi = 1 \quad U = 1, V = 1, W = 0.0 \quad < x < 1 \quad \text{(A-15)}$$

The transformed equations (A-12) and (A-15) are follows

$$(n+2)(n+1)U(n+2) - \alpha \sum_{r=0}^{n} U(n)V(n-r) + \beta \sum_{r=0}^{n} W(r) = 0 \quad \text{(A-16)}$$

$$U(1) = 0, V(1) = 0, W(1) = 0 \quad \text{(A-17)}$$

$$\text{Assume that } U(0) = l_1 \quad \text{(A-18)}$$

Let $n = 0$ and substituting equation (A-17), (A-18) in equation (A-16),

$$2U(2) + \beta = 0 \quad \text{(A-19)}$$

$$\text{Therefore } U(2) = -\frac{\beta}{2} \quad \text{(A-20)}$$

The differential inverse transform $U(n)$ is defined as,

$$U(x) = \sum_{n=0}^{2} U(n)(\chi - \chi_0)^n \quad \text{(A-21)}$$

Let $\chi_0 = 0$, we get the following equation

$$U(\chi) = \sum_{n=0}^{2} U(n)(\chi)^n = l_1 - \frac{\gamma_{E1}\ \alpha\ \beta\ l_1 m_1}{2(l_1 m_1 \alpha\ \beta + l_1 \alpha + m_1 \beta)}\chi^2 \quad \text{(A-22)}$$

By using boundary condition $U(\chi) = 1$ when $\chi = 1$ as follows

$$l_1 = \frac{\beta m_1(2\alpha - \gamma_{E1}\alpha - 2)}{4\alpha(m_1\ \beta + 1)} \pm \sqrt{\alpha^2\beta^2 m_1{}^2(\gamma_{E1}{}^2 - 4\gamma_{E1} + 4) + \alpha\beta^2 m_1{}^2(4\gamma_{E1} + 8) + \beta\alpha^2 m_1(-4\gamma_{E1} + 8) + 4\beta^2 m_1{}^2 + 8\beta\alpha m_1 + 4\alpha^2 - 2\alpha} \quad \text{(A-23)}$$

Similarly, the same procedure of (A-13) to (A-17) we get the solution of $V(\chi)$ and $W(\chi)$.

Appendix III: MATLAB (pdex4) Numerical solution

```
function pdex4
  m = 0;
  x = linspace(0,1);
  t = linspace(0,1000);
  sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
  u1 = sol(:,:,1);
  u2 = sol(:,:,2);
  u3 = sol(:,:,3);
  %------------------------------------------------------------------
  %figure
  %plot(x,u1(end,:))
  %title('u1(x)')
  %xlabel('Dimensionless Distance x')
  %ylabel('Dimensionless concentration u')
  %------------------------------------------------------------------
  %figure
  %plot(x,u2(end,:))
  %title('u2(x)')
  %xlabel('Dimensionless Distance x')
  %ylabel('Dimensionless concentration v')
  % ------------------------------------------------------------------
  figure
```

```
plot(x,u3(end,:))
title('u3(x)')
xlabel('Dimensionless Distance x')
ylabel('Dimensionless concentration w')
%--------------------------------------------------------------------
function [c,f,s] = pdex4pde(x,t,u,DuDx)
c = [1; 1; 1];
f = [1; 1; 1].*DuDx;
alpha=0.5;
beta=0.1;
y = (u(1)* u(2))/(u(1) * u(2)+(u(2)/alpha)+(u(1)/beta));
gamma=8;
gamma1=1.1;
gamma2=1;
F =(-gamma*y);
F1 =(-(1/2)*gamma1*y);
F2 =(gamma2*y);
s=[F;F1;F2];
function u0 = pdex4ic(x) %create a initial conditions
u0 = [1; 0; 1];
% --------------------------------------------------------------------
function [pl,ql,pr,qr]= pdex4bc(xl,ul,xr,ur,t) %create a boundary conditions
pl = [0; 0; 0];
ql = [1; 1; 1];
pr = [ur(1)-1; ur(2)-1; ur(3)];
qr = [0; 0; 0];
```

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