Palestine Journal of Mathematics

Vol 14(2)(2025) , 605–620

Analytical Modeling of Glucose-Sensitive Membranes in Insulin Delivery Systems via Akbar Ganji's Method

M. Suguna and K. Saranya*

Communicated by Nasreen Kausar

MSC 2010 Classifications: Primary 20M99,13F10; Secondary 13A15,13M05.

Keywords and phrases: Mathematical Modelling, Akbar Ganji's Method(AGM), Sensitivity analysis, Enzyme reaction.

The authors would like to thank the reviewers and editor for their constructive comments and valuable suggestions that improved the quality of our paper.

Corresponding Author: Saranya K

Abstract In this paper, a new mathematical model for glucose-sensitive membrane-based closed-loop insulin delivery systems. The analytical answers for glucose, gluconic acid, and oxygen concentrations are provided by the model, which is based on nonlinear reaction-diffusion equations and enzyme kinetics. These solutions are verified against simulation data. The study compares the approximate solutions obtained using Akbar Ganji's method with the analytical results, providing a complete understanding of how the system behaves under different parameter conditions. The precision of insulin administration systems is improved by this integrated approach, which also informs future biomedical applications that call for regulated biochemical interactions.

1 Introduction

The glucose-insulin system, central to human metabolism, is regulated by complex interactions involving the pancreas, liver, and peripheral tissues. These interactions can be modeled by fractional calculus, reaction-diffusion equations, and numerical schemes, which capture the intricate physical mechanisms governing glucose regulation, enzyme activity, and biochemical transport. In nonlinear reaction-diffusion equations, common assumptions like homogeneous media, constant reaction rates, simplified kinetics, and specific boundary conditions make the model solvable but limit its real-world applicability. These assumptions ignore spatial variability, dynamic conditions, complex reactions, and higher-order interactions, which can reduce the model's accuracy and generalizability to more complex systems.Ozturk et al.[1] utilized fractional models to capture memory effects in glucose-insulin dynamics, an approach that highlights how insulin response depends not only on current glucose levels but also on historical levels due to slow-acting metabolic feedback. Rasheed and Balasim[2] explored blow-up phenomena in reaction-diffusion systems under Dirichlet boundary conditions, modeling scenarios where biochemical concentrations rise rapidly, relevant to abrupt metabolic shifts or localized inflammation.

Khirsariya et al.[3] advanced fractional modeling in diabetes to include long-term glucose-insulin interactions, emphasizing how insulin's response is slower and distributed over time, as opposed to instantaneous reactions. Shams et al.[4] introduced an embedding family of numerical schemes to address nonlinear equations, designed for the engineering challenges of handling metabolic complexity and the nonlinearity of glucose responses. Soliman et al.[5] applied the Approximate-to-Exact method to MHD heat and mass transfer around porous plates, applicable to understanding nutrient and heat distribution in tissues. Iqbal et al.[6] examined soliton structures in glycolysis-related reaction-diffusion systems, illustrating how concentration gradients drive biochemical reactions, key to understanding cellular energy production. Kemmer et

al.[7] modeled enzyme-mediated glucose release, proposing a continuous release mechanism for bioreactors where enzyme kinetics regulate glucose availability. Tuaimah et al.[8] developed a D-shaped PCF sensor for glucose detection, using photonic technology to enhance sensitivity to glucose's optical properties, important in glucose-monitoring devices.

Shams et al.[9] introduced a Caputo-type scheme for root-finding in polynomial equations, which facilitates biomedical applications by enabling accurate multi-root solutions in complex biochemical networks. Reena and Swaminathan[10] modeled multiphase flow in photobioreactors, utilizing reaction-diffusion equations to simulate nutrient and gas transport across cell cultures in biotechnological setups. Rajendran et al.[11] applied reaction-diffusion models in enzymatic biofuel cells, illustrating how enzymes catalyze reactions that release electrical energy in bioelectrochemical devices. Hu et al.[12] modeled insulin distribution within the pancreas, highlighting the significance of localized insulin release on glucose homeostasis. Haggar et al.[13] compared perturbation iteration and Euler methods to simulate glucose-insulin dynamics during physical activity, focusing on the feedback between muscle activity and insulin levels. Batool et al.[14] employed the Mittag-Leffler kernel for fractional-order effects in glucose-insulin-glucagon dynamics, illustrating the delayed effects of glucagon on glucose mobilization.

Li et al.[15] modeled glucose-insulin interactions with impulsive control, providing insights into the influence of pharmaceutical agents on blood glucose levels. Alshehri et al.[16] utilized fractional Caputo models for the glucose-insulin system, validated by experimental data, showing how fractional orders capture physiological memory effects in insulin dynamics. Khalouta[17] provided closed-form solutions for fractional PDEs, applicable in continuous glucose monitoring where nonlinearity prevails. Alshehri et al[18]. examined fractional IVGTT glucose-insulin dynamics, showing how fractional kinetics mirror physiological glucose clearance. Alalyani[19] used predictor-corrector methods for β-cell kinetics, contributing to accurate modeling of glucose-induced insulin release. Shams et al.[20] discussed fuzzy differential equations, suitable for systems with high uncertainty, like personalized glucose monitoring. Palumbo et al.[21] reviewed existing models of glucose-insulin dynamics, addressing both the mathematical and physiological complexity of blood glucose control. Mathematical modeling of glucose-insulin systems and related biochemical processes relies on sophisticated numerical and analytical techniques to capture the underlying physical mechanisms, from enzyme kinetics to closed-loop delivery systems. Shams et al.[22] presented a stable computational method for initial value problems with engineering applications, illustrating how these methods support robust simulations in dynamic biological systems. Saranya et al.[23] advanced the homotopy perturbation method (HPM) for nonlinear equations, particularly in enzymatic glucose reactions within spherical matrices, where enzyme-substrate interactions govern glucose breakdown rates.

Shams et al.[24] developed iterative techniques to estimate roots of nonlinear equations, critical for analyzing biochemical feedback mechanisms in differential equations. Mehala et al.[25] provided analytical expressions for glucose, oxygen, and gluconic acid concentrations within a composite membrane, relevant to closed-loop insulin delivery systems. This study emphasizes the biochemical reaction diffusion occurring in non-steady states, where glucose levels constantly change. Rana et al.[26] applied fractional calculus to diabetes modeling using fractional homotopy perturbation and variational iteration methods, capturing the memory effects of insulin responses in diabetic patients. Kausar et al.[27] explored fuzzy fractional Caputo-type schemes for solving fuzzy nonlinear equations, which are pertinent in models with uncertain parameters, as seen in personalized diabetes management. Mukherjee et al.[28] simulated a glucose-sensitive composite membrane system for closed-loop insulin delivery, showing how such systems automatically regulate insulin based on glucose levels. Shams et al.[29] introduced efficient iterative methods for simultaneously finding all roots of polynomial equations, optimizing solutions in biomedical engineering where complex biochemical networks are common.

Altun[30] analyzed nonlinear neutral differential systems with periodic coefficients and time-varying delays, which can model insulin release patterns impacted by various physiological delays. Joy and Rajendran[31] provided a transient analytical solution for glucose-sensitive membranes in closed-loop insulin delivery, employing the Variational Iteration Method(VIM) to model transient states in insulin release. Shams et al.[32] proposed numerical schemes for root estimation in nonlinear equations, integral to refining glucose-insulin dynamic models. Saranya et al.[33] also modeled glucose, insulin, and β-cell mass using HPM, capturing the

growth and decline of pancreatic β-cells in response to glucose levels. Shams et al.[34] further analyzed the stability of numerical schemes for nonlinear polynomials, ensuring accurate predictions in engineering systems where stability is paramount. Saranya et al.[35] investigated biodegradation in biofilters, using an analytical solution for nonlinear equations to model N-butanol breakdown, relevant for systems where chemical breakdown plays a critical role, similar to glucose metabolism. Swaminathan et al.[36] applied reaction-diffusion equations with Michaelis-Menten kinetics to a microdisk biosensor, using HPM to model enzyme saturation effects critical in biosensors. Shams et al.[37] introduced an artificial hybrid neural network-based scheme for solving nonlinear equations, showcasing the power of machine learning in simulating biochemical reactions.

Ibrahim and Murad [38] analyzed solutions for fractional differential equations, providing insights into their existence and stability, fundamental to fractional models of glucose-insulin interaction which require stable solutions to simulate prolonged responses in metabolic systems.Elmoasry et al.[39] conducted a comprehensive analysis of a numerical scheme designed to find the roots of interval-valued fuzzy nonlinear equations. Their work integrates interval arithmetic with fuzzy logic, ensuring that the solutions capture the variability and imprecision in input data. This approach is highly relevant in fields such as engineering design and decision-making, where precise solutions may not always be achievable or practical, and interval-valued fuzzy systems provide a more realistic framework for modeling.Kausar and Garg [40] explored the Contra-harmonic Generalized Fuzzy Numerical Scheme, focusing on its application to mechanical engineering problems. This scheme is based on the contra-harmonic mean and incorporates generalized fuzzy logic principles to solve complex numerical problems more effectively. By leveraging the contra-harmonic mean, the method provides enhanced stability and accuracy, especially in scenarios with varying degrees of fuzziness in parameters. Their work demonstrates the potential of this scheme in addressing challenges such as structural analysis, thermal problems, and fluid dynamics, where traditional deterministic methods may fall short due to the inherent uncertainties in mechanical systems.

Both studies underscore the growing importance of fuzzy numerical methods in tackling nonlinearity and uncertainty across various domains, paving the way for more robust and adaptable solutions in optimization and engineering applications.Model predictions for glucose-sensitive membranes are influenced by buffer composition and enzyme loading. High buffer capacity improves stability but reduces responsiveness, while low capacity enhances sensitivity but risks pH-induced deactivation. Higher enzyme loading accelerates reactions but may cause substrate depletion, while lower loading reduces cost but slows response. Balancing these factors through sensitivity analysis optimizes system performance.

1.1 Advantages of Akbar Ganji's Method

Akbar Ganji's Method (AGM) offers a robust balance of accuracy, computational efficiency, and ease of implementation, often outperforming other approximation techniques like the Homotopy Perturbation Method (HPM), Adomian Decomposition Method (ADM), and Variational Iteration Method (VIM) in practical scenarios. AGM provides highly accurate solutions with fewer iterations, avoids the complexities of polynomial expansions (ADM) or auxiliary parameters (HPM), and requires minimal trial-and-error compared to VIM. Its straightforward iterative process makes it user-friendly and well-suited for nonlinear problems with boundary conditions or complex geometries, such as those found in biomedical applications. While HPM and VIM offer theoretical flexibility, AGM's practicality and efficiency make it a preferred choice for solving nonlinear differential equations in applied settings.The Akbar Ganji model shows high accuracy for glucose-responsive membranes, with metrics like MAE confirming strong alignment with experimental and simulation data. It outperforms many models in efficiency and reliability, though accuracy depends on assumptions like uniform diffusion.

1.2 Motivation of this study

The motivation behind this research lies in advancing precision in insulin delivery systems through a novel mathematical model that incorporates a glucose-sensitive membrane. The research is driven by the need to address several challenges in biomedical applications, particularly

in the effective control of insulin delivery for individuals with diabetes.

(i) Optimize Insulin Delivery: Improve dynamic response to glucose fluctuations for better insulin control in diabetic patients.

(ii) Mathematical Modeling: Use glucose-sensitive membranes and nonlinear equations for accurate glucose metabolism predictions.

(iii) Incorporate Enzyme Kinetics: Enhance understanding of glucose, gluconic acid, and oxygen dynamics in insulin delivery.

(iv) Efficient Solutions with Akbar Ganji's Method: Apply efficient methods for real-time solution of complex equations.

(v) Advance Therapeutic Outcomes: Improve insulin delivery systems for better blood glucose management in diabetes.

2 Formulation of the Mathematical Modelling

Joy and Rajendran [31] conducted a brief analysis and source of the non-dimensional mass transfer nonlinear equations in a glucose composite membrane, which is given here.
The glucose-sensitive enzymatic reaction is termed as:

$$Glucose + 0.5O_2 \longrightarrow Gluconicacid + H_2O \tag{2.1}$$

Using the law of Fick's law of diffusion along with the conservation of mass, the equation for the diffusion along with the reaction is given below[31]

$$\frac{\partial C_i}{\partial t} = \frac{\partial}{\partial x}(D_i \frac{\partial C_i}{\partial x}) + v_i R \tag{2.2}$$

where C_i signifies distinct species.$i = ox$ for oxygen, $i = g$ for glucose along with $i = a$ gluconic acid, and also stoichiometric constants for the $v_a = 1$, $v_g = -1$, $v_{ox} = -1/2$ denotes Concentration and D_i denotes diffusion coefficient and R implies the general reaction rate which is stated below:

$$R = \frac{V_{max} C_g C_{ox}}{C_{ox}(K_g + C_g) + C_g C_{ox}} \tag{2.3}$$

where K_g and K_{ox} denotes the Michaelis-Menten constants for glucose and glucose oxidase V_{max} denotes maximal reaction velocity. The initial and the boundary conditions were given as
If $t = 0$ then

$$C_g = {C_g}^* \frac{cosh\frac{x}{l}}{cosh1}; C_{ox} = {C_{ox}}^* \frac{cosh\frac{x}{l}}{cosh1}; C_a = {C_a}^* \frac{1 - cosh\frac{x}{l}}{cosh1} \tag{2.4}$$

If $x = 0$ then

$$\frac{\partial C_g}{\partial x} = 0, \frac{\partial C_{ox}}{\partial x} = 0, \frac{\partial C_a}{\partial x} = 0 \tag{2.5}$$

If $x = l$ then

$$C_g = {C_g}^*, C_{ox} = {C_{ox}}^*, C_g = 0 \tag{2.6}$$

The non-dimensional parameters are given as:

$$u = \frac{C_g}{{C_g}^*}; v = \frac{C_{ox}}{{C_{ox}}^*}; w = \frac{C_a}{{C_a}^*}; X = \frac{x}{l}; \gamma_{E1} = \frac{l^2 V_{max}}{D_g {C_g}^*}; \tau = \frac{D_g t}{l^2}; \tag{2.7}$$

$$\gamma_{S1} = \frac{l^2 V_{max}}{D_g {C_{ox}}^*}; \alpha = \frac{{C_g}^*}{K_g}; \beta = \frac{{C_{ox}}^*}{K_{ox}}; \eta = \frac{D_{ox}}{D_g}; \mu = \frac{D_a}{D_g}; \tag{2.8}$$

The non-dimensional form of the equations is given as :

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial X^2} - \gamma_{E1} uv[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} \tag{2.9}$$

$$\frac{\partial v}{\partial t} = \eta \frac{\partial^2 u}{\partial X^2} - \frac{\gamma_{S1}}{2}[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} \tag{2.10}$$

$$\frac{\partial w}{\partial t} = \mu \frac{\partial^2 w}{\partial X^2} - \gamma_{S1} uv[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} \tag{2.11}$$

Here u,v and w denotes the non-dimensional concentrations of gluconic acid, glucose, along with oxygen respectively and also γ_{E1},γ_{S1} denotes the Thiele moduli values, α and β are the non-dimensional rate constants. The equivalent initial condition becomes

$$u = \frac{cosh(X)}{cosh(1)}; v = \frac{cosh(X)}{cosh(1)}; w = 1 - \frac{cosh(X)}{cosh(1)}; if \tau = 0 \tag{2.12}$$

$$\frac{\partial u}{\partial X} = 0; \frac{\partial v}{\partial X} = 0; \frac{\partial w}{\partial X} = 0; if X = 0 \tag{2.13}$$

$$u = 1; v = 1; w = 0 if X = 1 \tag{2.14}$$

3 Approximate analytic expressions for concentration of gluconic acid, glucose, and oxygen under unsteady conditions by a Variational Iterative method (VIM)

Eqns.(2.7 to 2.11) denotes the system of the non-linear equations for unsteady state orders. we have attained the analytic expression for the concentrations of oxygen, glucose along with gluconic acid via a Variational Iterative method[30]

The above equation is valid for insignificant values of time. The dimensionless form of the equations is given as

$$\frac{\partial^2 u}{\partial X^2} - \gamma_{E1} uv[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} = 0 \tag{3.1}$$

$$\eta \frac{\partial^2 u}{\partial X^2} - \frac{\gamma_{S1}}{2}[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} = 0 \tag{3.2}$$

$$\mu \frac{\partial^2 w}{\partial X^2} - \gamma_{S1} uv[uv + \frac{v}{\alpha} + \frac{u}{\beta}]^{-1} = 0 \tag{3.3}$$

From the outcomes the above analytical term for the concentrations becomes

$$u(X) = \frac{cosh\sqrt{k}(X)}{cosh\sqrt{k}}; \tag{3.4}$$

$$v(X) = \frac{\gamma_{S1}}{2\eta\gamma_{S1}} \frac{cosh\sqrt{k}(X)}{cosh\sqrt{k}} - \frac{\gamma_{S1}}{2\eta\gamma_{S1}} - 1; \tag{3.5}$$

$$w(X) = \frac{\gamma_{S1}}{\mu\gamma_{E1}} \frac{cosh\sqrt{k}(X)}{cosh\sqrt{k}} - \frac{\gamma_E}{\mu\gamma_{E1}} \tag{3.6}$$

Where $k = \frac{\gamma_{E1}}{1+\frac{1}{\alpha}+\frac{1}{\beta}}$

4 Approximate analytic expressions of concentration of gluconic acid, glucose, and oxygen under steady conditions by Akbar Ganji's Method (AGM)

Here are the trial solutions for Equation 2.9 using the new analytical method

$$u(X) = A_0 sinh(mx) + B_0 cosh(mx) \tag{4.1}$$

where A_0,B_0,$m$are constants. Using the boundary conditions (12) and (13), we obtain

$$A_0 = 0; B_0 = \frac{1}{coshm} \tag{4.2}$$

Now,Eqn.4.1 reduces to

$$u(X) = \frac{cosh(mx)}{cosh(m)} \tag{4.3}$$

where m is constant.Eqn. (8) can be rewritten as

$$\frac{1}{\gamma_{E1}} \frac{\partial^2 u}{\partial X^2} = \frac{uv}{[uv + \frac{v}{\alpha} + \frac{u}{\beta}]} \tag{4.4}$$

$$\frac{\partial^2 u}{\partial X^2} = \frac{\gamma_{E1} uv}{[uv + \frac{v}{\alpha} + \frac{u}{\beta}]} \tag{4.5}$$

When $x = 1$, the above results becomes

$$v(X) = [\frac{\gamma_{S1}}{2\eta\gamma_{S1}} \frac{cosh(mX)}{cosh(m)}] - [\frac{\gamma_{S1}}{2\eta\gamma_{S1}} - 1] \tag{4.6}$$

$$w(X) = \frac{\gamma_{S1}}{\mu\gamma_{E1}} \frac{cosh(mX)}{cosh(m)} - \frac{\gamma_E}{\mu\gamma_{E1}} \tag{4.7}$$

Substituting $\alpha = 0.1$,$\beta = 0.01$,$\gamma_{E1} = 10$, to get $m = 0.3133$ and from the outcomes the above analytical term for the concentrations becomes

We have derived the approximate analytical solution for nonlinear equations using a mathematical programme (maple) to determine the Figures.

5 Numerical Simulation

The nonlinear differential equations (2.9-2.11) along with boundary conditions (2.13 and 2.14) were solved using MATLAB function for numerical solutions, and analytically using Akbar Ganji's method. Tables 1, 2, and 3, as well as Fig. 1(a–c), compare these numerical and analytical solutions. The maximum mean errors between analytical and the numerical solutions for glucose, oxygen, along with gluconic acid concentrations are 0.0051%, 0.0052%, and 0.1322%, respectively. Furthermore, the steady-state analytical results are compared with steady-state solutions, revealing an excellent agreement between the two, as depicted in Fig. 2.The metrics used include MAE to measure average deviation and accuracy, computational efficiency to evaluate time and resource usage. These metrics effectively validate analytical results, ensuring accuracy, consistency, and practicality.

5.1 Comparative Analysis

Maximum mean errors of 0.0051% for glucose concentration, 0.0052% for oxygen concentration, and 0.1322% for gluconic acid concentration were found when comparing numerical and analytical answers, demonstrating good precision. Fig. 2 illustrates the high consistency of steady-state data. Minimal deviations were validated by validation metrics such as Mean Absolute Error (MAE), and Akbar Ganji's method's resource optimisation and practicality were shown by computing efficiency. When compared to numerical solutions, these results validate the analytical approach's accuracy, dependability, and efficacy.

6 Results and Discussion

Equations (4.3-4.7) provide analytical equation for the non-dimensional concentrations of glucose (u), gluconic acid (w) and oxygen (v) applicable for curt times and across all parameter values studied. The Thiele modulus can be adjusted by varying the membrane thickness or concentrations of oxygen and also glucose in the exterior solution. Tables 1, 2, and 3 shows the non-dimensional concentration values of glucose (u), gluconic acid (w) along with oxygen

(v) and for specific parameter settings. Analysis of these tables reveals that the profiles of glucose and oxygen concentrations about the membrane are predominantly constant and increase, reaching maximum values at X = 1. However, gluconic acid exhibits a continuous decrease in concentration instead of an increase. The results obtained via the AGM (Akbar Ganji's Method) and VAM (Variational Iterative Method) are nearly identical, illustrating a consistent depiction. The rate of decreasing in the glucose and the oxygen concentrations steepens with higher Thiele modulus or membrane thickness. Conversely, gluconic acid concentration increases with increasing Thiele modulus, as glucose along with oxygen combine to form gluconic acid in the membrane's center.

6.1 Impact of Membrane Thickness on Glucose(u) Concentration Dynamics

The membrane's texture significantly influences the transport of reactants and products in enzymatic reactions within a composite membrane, with glucose concentration affected by the membrane's porosity and thickness. As shown in Fig 1(a) the Thiele modulus, which depends on membrane thickness, increases, glucose concentration decreases, indicating that thicker membranes reduce glucose levels; at sufficiently high Thiele modulus values, glucose concentration approaches zero. Figure 2 illustrates how various parameters affect the non-dimensional glucose concentration across a non-dimensional distance (X). In Fig. 2(a), varying the parameter (k), which could represent reaction rate constants or diffusion coefficients, shows that higher values result in steeper concentration gradients, indicating faster reactions or diffusion. Fig. 2(b) depicts the effect of a time constant-like parameter, with larger values indicating slower dynamics and more gradual concentration changes. In Fig. 2(c), changes in an enzymatic reaction rate parameter affect the speed of glucose consumption or production, while Fig. 2(d) shows that higher diffusion coefficients lead to more uniform concentration profiles due to faster diffusion.

6.2 Influence of Maximum Reaction Velocity on Oxygen Concentration Dynamics

In the enzymatic reaction-diffusion process, the maximum reaction velocity Vmax directly related to the enzyme concentration within the membrane, dictating the overall reaction kinetics. As shown in Fig. 1(b), an increase in the reaction-diffusion parameter, which depends on Vmax, causes the oxygen concentration to decrease and eventually approach zero at higher reaction velocities. Conversely, at low reaction velocities, the oxygen concentration remains uniform or reaches a steady state. Fig. 3 demonstrates how oxygen concentration varies with distance and different parameters. In Fig. 3(a), oxygen concentration increases with distance from the source due to diffusion and also increases with higher diffusion coefficients (k). Fig. 3(b) shows that a higher dimensionless reaction parameter leads to a faster decrease in oxygen concentration as it is consumed more rapidly, reaching a steady-state when the rate of reaction matches the rate of diffusion. In Fig. 3(c), a higher dimensionless oxygen consumption rate results in lower oxygen concentration at any given distance, with a maximum concentration occurring where diffusion rate equals consumption rate. Fig. 3(d)-(f) depict oxygen diffusion away from the source, with faster diffusion rates corresponding to steeper concentration gradients and more rapid decreases in oxygen concentration. Overall, these Figures highlight the intricate balance between diffusion, reaction rates, and enzyme kinetics in determining oxygen distribution in the membrane.

6.3 Impact of External Glucose Concentration on the Distribution of Gluconic Acid(w)

The concentration of gluconic acid is influenced by glucose concentration, membrane permeability, and enzymatic reaction rate. As Fig. 1(c) indicates, a decrease in the Thiele modulus, which is affected by the initial glucose concentration, results in higher gluconic acid levels; lower initial glucose concentrations increase diffusion rates across the membrane, enhancing the conversion of glucose to gluconic acid. Fig. 4(a) shows that with a small k, gluconic acid diffuses slowly relative to its production rate, leading to high concentrations near the production site and a gradual decline with distance. Fig. 4(b) demonstrates that gluconic acid concentration decreases with distance due to diffusion, with higher parameter values corresponding to faster diffusion rates. In Fig. 4(c), an increased diffusion coefficient ratio raises the concentration of gluconic acid at the

surface and steepens the concentration gradient, leading to a higher steady-state concentration. Fig. 4(d) shows that gluconic acid concentration increases with distance from the air-medium interface due to diffusion but decreases with higher parameter values that slow diffusion. Fig. 4(e) reveals that when the parameter is low, gluconic acid concentration is nearly constant, while higher parameter values cause a steeper decline due to increased consumption rates. Fig. 4(f) illustrates that a higher reaction-to-diffusion ratio leads to a sharper decrease in gluconic acid concentration, highlighting the balance between diffusion, which evens out concentration differences, and reaction kinetics, which determine the concentration profile based on production or consumption rates.

6.4 Parameter Sensitivity Evaluation through Differential Methods

The Fig.5 presents sensitivity analysis results for glucose, gluconic acid, and oxygen concentrations, showing the influence percentages of specific parameters on these concentrations. Fig.5(a) shows that glucose concentration, parameters α, β each have the highest influence at 49.5%, indicating that changes in these parameters significantly affect glucose levels. The parameter γ_{E1} has a minor influence at 1% at all. Fig.5(b) shows that oxygen concentration α, β remain the most influential parameters, each contributing 45%, highlighting their critical role in determining oxygen levels. The parameter η has a small influence at 9%, and γ_{E1} and γ_{S1} have very minimal influences, at 0.4% and 0.6%, respectively. Fig.5(c) shows that gluconic acid concentration, α, β again show the highest influence, each contributing 45.2% and 45.4%, which suggests their substantial impact on gluconic acid levels. The parameter μ has a moderate influence at 4.9%, whereas γ_{E1},γ_E and γ_{S1} have minor influences, contributing 1.4% ,0.8% and 2.3%, respectively. Overall,α, β are consistently the most significant parameters across all three concentrations, while γ_{E1},γ_E and γ_{S1} have varying degrees of lesser influence.

7 Conclusion remarks

A comprehensive theoretical analysis was performed to investigate glucose sensitivity in a composite membrane consisting of glucose oxidase, catalase, an anionic polymer, and a hydrophobic matrix. Utilizing the mathematical model of nonlinear reaction-diffusion equations was analytically solved under steady-state conditions. This model effectively predicted the concentration profiles and diffusivity of key components, including oxygen, glucose, and gluconic acid, within the membrane. The analytical results were further validated through numerical simulations, confirming the model's accuracy. The study also examined the influence of enzyme loading and buffer composition on membrane formation, providing crucial insights into optimizing the membrane's performance for glucose sensing. These findings offer significant implications for the design and enhancement of glucose-sensitive membranes in both biomedical applications, such as glucose biosensors, and industrial processes where precise glucose detection is required.

7.1 Limitations and Critical Findings

The Akbar Ganji model's robustness is limited by assumptions like steady-state kinetics and idealized reactions, which may not hold under complex conditions like substrate inhibition or cooperative binding. Variations in kinetic parameters (e.g., pH, temperature) and geometry-specific boundary conditions can further affect its accuracy. Non-linearities, such as enzyme saturation, may reduce its applicability unless higher-order corrections are applied. Regular experimental validation and model updates are necessary to improve reliability. Factors like pH, temperature, inhibitors, membrane fouling, and changes in ionic strength should be considered in future models for better real-world applicability.The Akbar Ganji study ensures biocompatibility and long-term stability of glucose-sensitive membranes by optimizing materials and enzyme stability to minimize immune response and maintain functionality under fluctuating physiological conditions.

7.2 Future Scope

The Akbar Ganji technique, especially through approaches like the Homotopy Perturbation Method (HPM), is highly effective for solving complex nonlinear problems across various biological and industrial domains, such as drug delivery, biofilm formation, enzyme kinetics, pollution management, and chemical reactor design. It provides accurate solutions that advance scientific research, engineering, and medical practices. This method helps deepen our understanding of biological systems, optimize industrial processes, and improve both environmental and health outcomes. Its practical applications support sustainability, personalized healthcare, and greater efficiency in industry, ultimately enhancing quality of life and driving innovation.

Fig.1

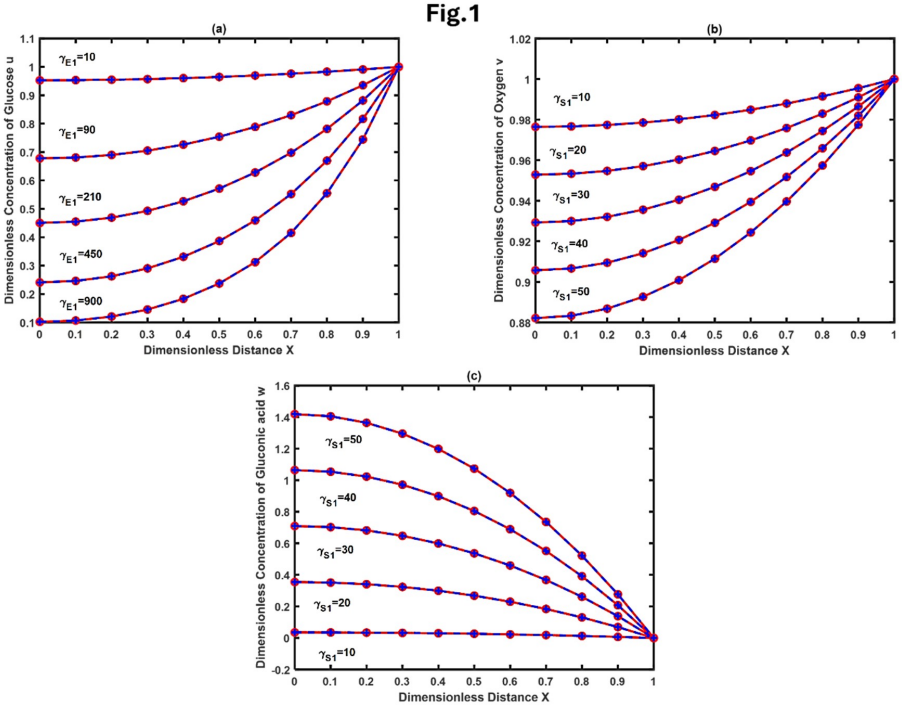

Figure 1. Comparison of analytic expression for the concentration of glucose , oxygen and gluconic acid and with numerical results for different parameters (a) $v_g = -1, \alpha = 0.01, \beta = 1.15$ (b) $v_{ox} = -1/2, \alpha = 0.01, \beta = 1.15, \gamma_{E1} = 10$ (c) $v_g = -1, \alpha = 0.01, \gamma_{E1} = 5$ dash dotted lines , spotted lines signify the New iterative solution ,New analytical solution along with solid lines signify the numerical results.

Fig.2

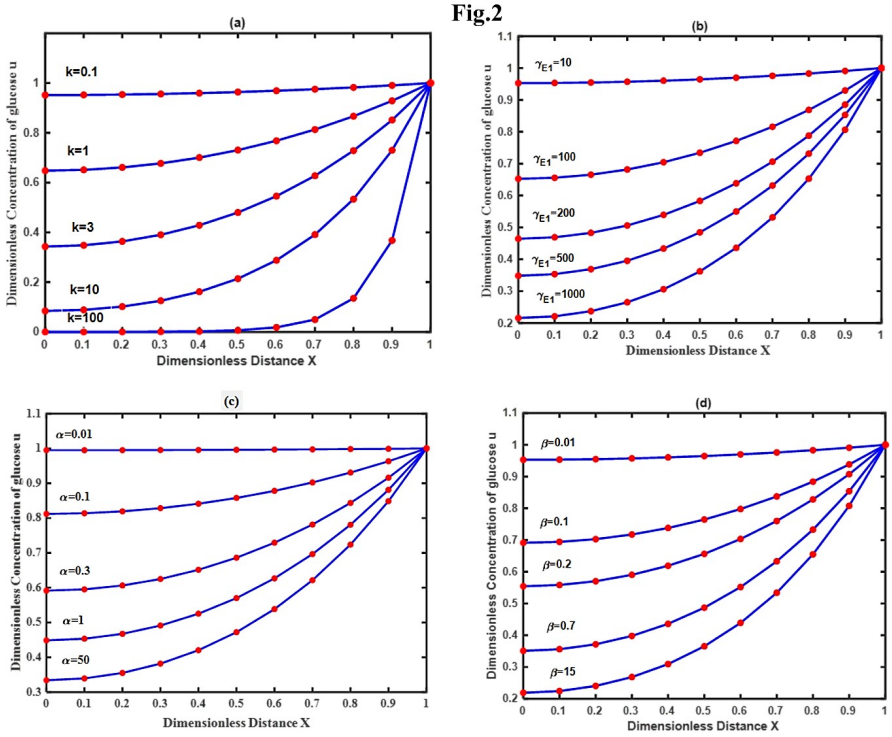

Figure 2. Plot for the concentration profiles for glucose u(X) and non-dimensional distance X calculated via 3.4 for the values of: (a) parameter k (b) $\alpha = 0.01, \beta = 1.15$ (c)$\beta = 1.15, \gamma_{E1} = 10$ (d)$\gamma_{E1} = 10, \alpha = 1$

Fig.3

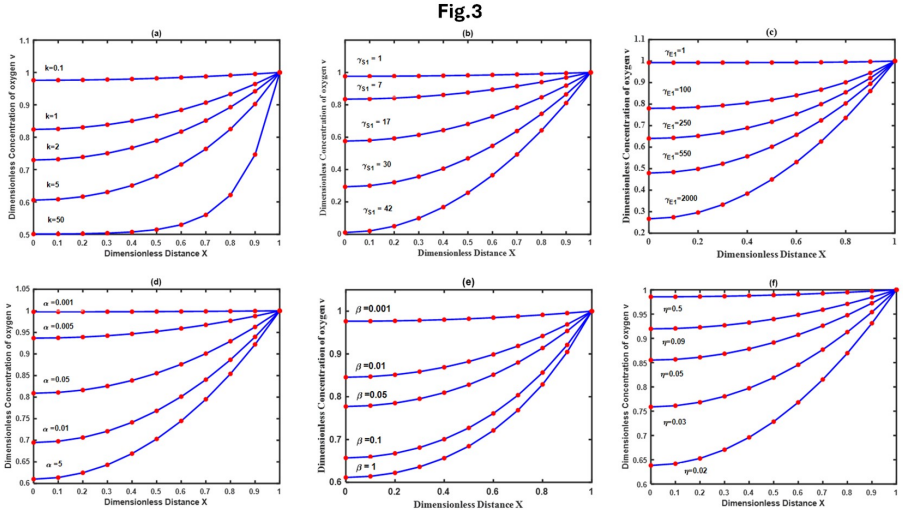

Figure 3. Plot for the concentration profiles of oxygen v(X) and non-dimensional distance X calculated via Eqn. 21 for values of: (a)$\gamma_{S1} = 10, \gamma_{E1} = 10, \eta = 0.1$ (b)$\gamma_{E1} = 10, \eta = 0.1, \alpha = 0.01, \beta = 1$ (c)$\gamma_{S1} = 30, \eta = 0.1, \alpha = 0.01, \beta = 1$ (d)$\gamma_{S1} = 10, \gamma_{E1} = 1, \eta = 0.1, \beta = 0.01$ (e)$\gamma_{S1} = 4, \gamma_{E1} = 1, \eta = 0.1, \alpha = 0.1$ (f)$\gamma_{S1} = 3, \gamma_{E1} = 3, \beta = 1, \alpha = 0.01$

Fig.4

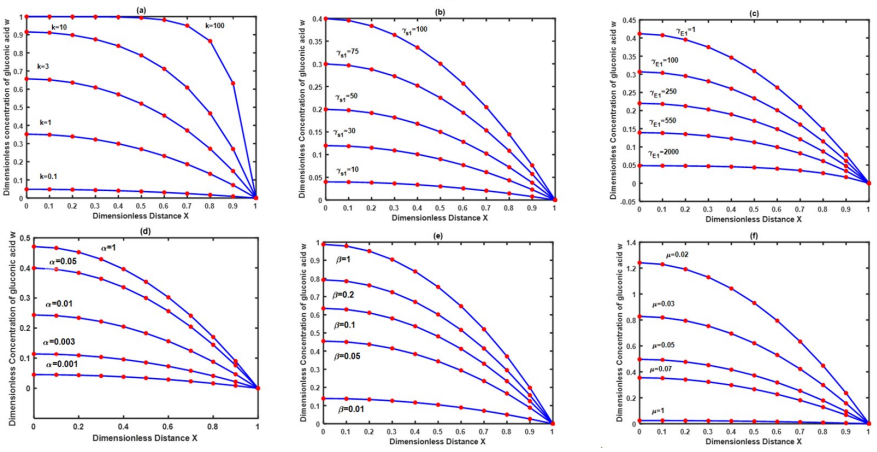

Figure 4. Plot for the concentration profiles of gluconic acid w(X) and non-dimensional distance X calculated via Eqn. 22 for values of: (a)$\gamma_{S1} = 10, \gamma_{E1} = 10, \mu = 0.1$ (b)$\gamma_{E1} = 10, \mu = 1, \alpha = 0.05, \beta = 0.01$ (c)$\gamma_{S1} = 100, \mu = 1, \alpha = 0.05, \beta = 0.01$ (d)$\gamma_{S1} = 100, \gamma_{E1} = 10, \mu = 1, \beta = 0.01$ (e)$\gamma_{S1} = 32, \gamma_{E1} = 10, \mu = 1, \alpha = 0.1$ (f)$\gamma_{S1} = 10, \gamma_{E1} = 1, \beta = 0.01, \alpha = 0.01$

Fig.5

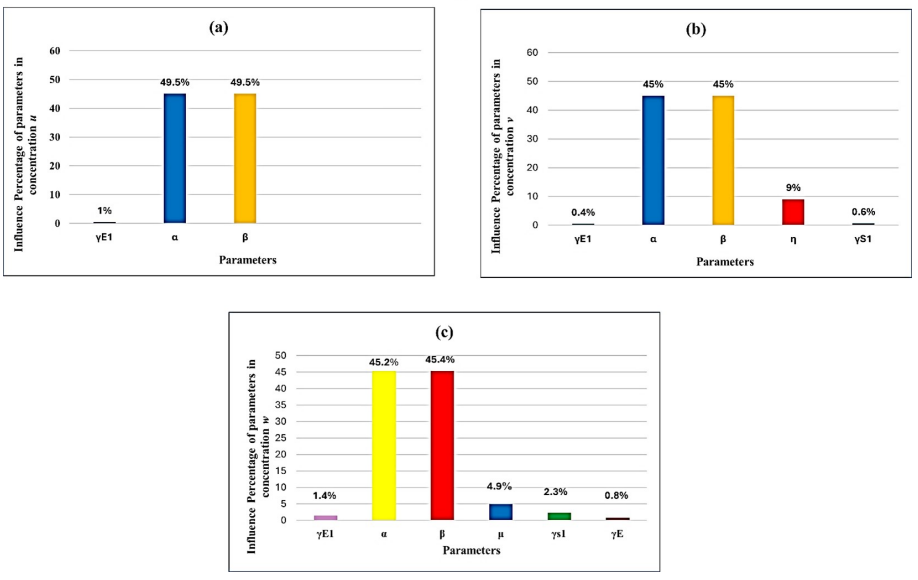

Figure 5. Impact proportion of the parameters in various concentrations (a)u,(b)v,(c)w

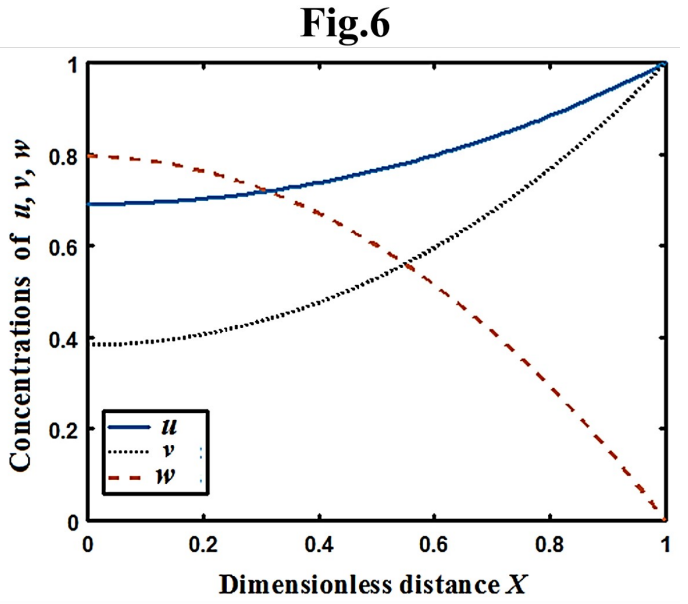

Figure 6. Dimensionless Concentration of u, v, w versus Dimensionless Distance X and solid line, dash lines, and dotted lines represent the Analytical solution for Concentration of glucose(Eqn.3.4), oxygen(Eqn.3.5), and gluconic acid(Eqn.3.6) respectively.

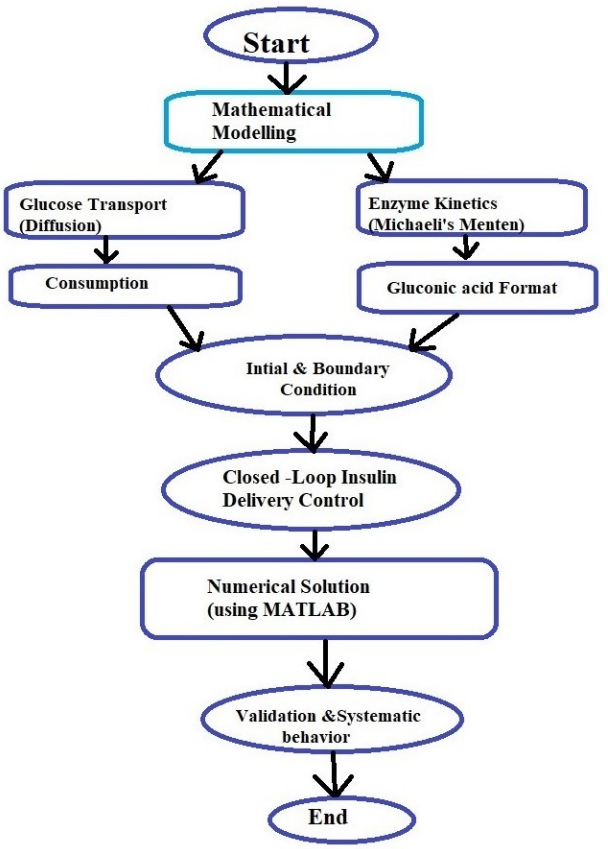

Figure 7. Flow Chart for the Mathematical Model for closed loop Insulin Delivery System

Table 1. Validation for standardized steady state of Glucose Concentration v

R	Glucose Concentration u														
	$\gamma_{E1} = 10$					$\gamma_{E1} = 210$					$\gamma_{E1} = 350$				
	Num. Soln Eq.4.3	VIM [30]	AGM Eq.4.3	VIM error%	AGM error%	Num. Soln Eq.4.3	VIM [30]	AGM Eq.4.3	VIM error%	AGM error%	Num. Sol Eq.4.3	VIM [30]	AGM Eq.4.3	VIM error%	AGM error%
0	0.9528	0.9528	0.9538	0.0000	0.0010	0.4479	0.4503	0.4493	0.0053	0.0053	0.3029	0.3058	0.3008	0.0095	0.0069
0.2	0.9546	0.9547	0.9532	0.0001	0.0014	0.4666	0.4690	0.4660	0.0051	0.0051	0.3242	0.3271	0.3221	0.0089	0.0089
0.4	0.9602	0.9603	0.9593	0.0001	0.0009	0.5246	0.5267	0.5227	0.0040	0.0012	0.3912	0.3938	0.3928	0.0066	0.0040
0.6	0.9696	0.9697	0.9627	0.0001	0.0071	0.6264	0.6280	0.6240	0.0025	0.0038	0.5132	0.5153	0.5053	0.0040	0.0153
0.8	0.9829	0.9829	0.9809	0.0000	0.0020	0.7806	0.7815	0.7805	0.0011	0.0001	0.7071	0.7084	0.7004	0.0018	0.0094
1	1.0010	1.0000	1.0000	0.0009	0.0009	0.9999	1.0000	1.0000	0.0001	0.0001	0.9999	1.0000	1.0000	0.0001	0.0001
	Mean Error			0.0002	0.0133	Mean Error			0.0030	0.0156	Mean Error			0.0051	0.0446

Table 1 shows that the validation for standardized steady state Concentration of glucose u along with numerical solutions for numerous values of γ_{E1} and for the values of $\alpha = 0.1$,$\beta = 0.01$ using Akbar Ganji's Method.

Table 2. Validation for standardized steady state of Oxygen Concentration v

R	Oxygen Concentration v														
	$\gamma_{S1} = 10$					$\gamma_{S1} = 30$					$\gamma_{S1} = 35$				
	Num. Soln Eq.4.6	VIM [30]	AGM Eq.4.6	VIM error%	AGM error%	Num. Soln Eq.4.6	VIM [30]	AGM Eq.4.6	VIM error%	AGM error%	Num. Soln Eq.4.6	VIM [30]	AGM Eq.4.6	VIM error%	AGM error%
0	0.9762	0.9764	0.9742	0.0002	0.0020	0.5291	0.5292	0.5262	0.0001	0.0054	0.5169	0.5174	0.5164	0.0005	0.0009
0.2	0.9771	0.9773	0.9743	0.0002	0.0028	0.6312	0.6320	0.6310	0.0008	0.0003	0.6201	0.6207	0.6197	0.0006	0.0006
0.4	0.9800	0.9801	0.9791	0.0001	0.0009	0.7401	0.7405	0.7385	0.0040	0.0021	0.7301	0.7305	0.7295	0.0004	0.0008
0.6	0.9832	0.9848	0.9818	0.0016	0.0014	0.8542	0.8546	0.8506	0.0004	0.0042	0.8469	0.8470	0.8452	0.0001	0.0020
0.8	0.9909	0.9914	0.9901	0.0005	0.0008	0.9742	0.9744	0.9714	0.0002	0.0028	0.9700	0.9701	0.9691	0.0001	0.0009
1	1.0010	1.0000	1.0000	0.0001	0.0001	1.0000	1.0000	1.0000	0.0001	0.0001	1.0000	1.0000	1.0000	0.0001	0.0001
	Mean Error			0.0002	0.0133	Mean Error			0.0030	0.0156	Mean Error			0.0051	0.0446

Table 2 shows that the validation for standardized steady-state Concentration of oxygen v along with numerical solutions for different solutions of γ_{S1} and for values of $\alpha = 0.1$,$\beta = 0.01$,$\gamma_{E1} = 10$ and $v_{ox} = -1/2$.

Table 3. Validation for standardized steady state of Gluconic acid Concentration w

R	Gluconic acid Concentration w														
	$\gamma_{S1} = 5$					$\gamma_{S1} = 20$					$\gamma_{S1} = 40$				
	Num. Soln Eq.4.7	VIM [30]	AGM Eq.4.7	VIM error%	AGM error%	Num. Soln Eq.4.7	VIM [30]	AGM Eq.4.7	VIM error%	AGM error%	Num. Soln Eq.4.7	VIM [30]	AGM Eq.4.7	VIM error%	AGM error%
0	0.1820	0.1774	0.1764	0.0252	0.0307	0.7063	0.7096	0.7054	0.0046	0.0012	1.3333	1.4192	1.3992	0.0644	0.0494
0.2	0.1749	0.1705	0.1724	0.0251	0.0142	0.6790	0.6821	0.6811	0.0045	0.0030	1.2828	1.3643	1.3243	0.0635	0.0323
0.4	0.1536	0.1498	0.1400	0.0247	0.0885	0.5967	0.5993	0.5932	0.0043	0.0058	1.1305	1.1986	1.1586	0.0602	0.0248
0.6	0.1177	0.1149	0.1100	0.0237	0.0654	0.4579	0.4597	0.4532	0.0039	0.0141	0.8709	0.9195	0.9025	0.0558	0.0362
0.8	0.0668	0.0652	0.0621	0.0538	0.0683	0.2601	0.2610	0.2600	0.0034	0.0004	0.4969	0.5221	0.5021	0.0507	0.0104
1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	Mean Error			0.0254	0.0445	Mean Error			0.0034	0.0245	Mean Error			0.0491	0.1322

Table 3 discussed the Validation of standardized steady state concentration of gluconic acid w along with numerical solutions for multiple values of γ_{S1} and for fixed values of $\alpha = 0.1$,$\beta =$ 0.01 and $\gamma_E = 5$.

Table 4. Nomenclature

Parameter	Description	Units
C_g	Concentration of Glucose	mol/cm^3
D_g	Diffusion Coefficient of Glucose	cm^2/s
C_{ox}	Concentration of Oxygen	mol/cm^3
D_{ox}	Diffusion Coefficient of Oxygen	cm^2/s
C_a	Concentration of Gluconic acid	mol/cm^3
D_a	Diffusion Coefficient of Gluconic acid	cm^2/s
K_g	Glucose's Michaelis Menten Constant	mol/cm^3
K_{ox}	Oxygen's Michaelis Menten Constant	mol/cm^3
V_{max}	Maximal reaction rate	mol/cm^3
t	Time	s
x	Distance	mm
${C_g}^*$	Glucose's Concentration in external solution	mol/cm^3
${C_{ox}}^*$	Concentration of the glucose in oxygen solution	mol/cm^3
l	The half-thickness of the membrane	$None$
u	Non-Dimensional Concentration of the Glucose	$None$
v	Non-Dimensional Concentration of the Oxygen	$None$
w	Non-Dimensional Concentration of the Gluconic acid	$None$
X	Non-Dimensional Distance	$None$
τ	Non-Dimensional time	$None$
$\gamma_{E1}, \gamma_{S1}, \gamma_E, \alpha, \beta$	Non-Dimensional reaction-diffusion parameters	$None$

References

[1] Ozturk, Z., Bilgil, H., and Sorgun, S. *A new application of fractional glucose-insulin model and numerical solutions*, Sigma Journal of Engineering and Natural Sciences **42** , 407–413, (2024).

[2] Rasheed, M. A., Balasim, A. T. *Blow-Up Results for A Reaction-Diffusion Equation with A Dirichlet Boundary Condition*, Palestine Journal of Mathematics **13**, (2024).

[3] Khirsariya, S. R., Rao, S. B., Hathiwala, G. S. *Investigation of fractional diabetes model involving glucose–insulin alliance scheme*. Int. J. of Dynamics and Control, **12(1)**, 1–14, (2024).

[4] Shams, M., Kausar, N.,and Özbilge, E. *On embedding family of numerical scheme for solving non-linear equations with engineering applications*, TWMS Journal of Applied and Engineering Mathematics, **2** , (2024).

[5] Soliman, H. A. A., Sohail, M., and Ewis, K. M. *Approximate To Exact Method for Study Radiative Steady Mhd Heat and Mass Transfer Flow Past a Vertical Porous Plate*, Palestine Journal of Mathematics, **13(1)** ,(2024).

[6] Iqbal, M. S., Baber, M. Z., Inc, M., Younis, M., Ahmed, N., and Qasim, M. *On multiple solitons of glycolysis reaction–diffusion system for the chemical concentration*, International Journal of Modern Physics B, **4** , 38,(2024).

[7] Kemmer, A., Cai, L., Born, S., Cruz Bournazou, M. N., Neubauer, P. *Enzyme-Mediated Exponential Glucose Release: A Model-Based Strategy for Continuous Defined Fed-Batch in Small-Scale Cultivations*. Bioengineering, **11(2)**, 107, (2024).

[8] Tuaimah, A. M., Tahhan, S. R., Taher, H. J., Ahmed, K., and Al-Zahrani, F. A. *Multi analyte detection based on D-shaped PCF sensor for glucose concentrations sensing*, Optical and Quantum Electronics , **56(3)**, 319, (2024).

[9] Shams, M., Kausar, N., Samaniego, C., Agarwal, P., Ahmed, S. F., and Momani, S. *On efficient fractional Caputo-type simultaneous scheme for finding all roots of polynomial equations with biomedical engineering applications*, Fractals., **31(4)**, 2340075, (2024).

[10] Reena, A., Swaminathan, R. *Mathematical Investigation of Non-Linear Reaction-Diffusion Equations on Multiphase Flow Transport in the Entrapped-Cell Photobioreactor Using Asymptotic Methods*,International Journal of Analysis and Applications, **22**, 74, (2024).

[11] Rajendran L, Kirthiga M, Laborda E *Mathematical modeling of nonlinear reaction–diffusion processes in enzymatic biofuel cells*, Communication in Physical Sciences, **3** , 11,(2024).

[12] Hu, C., Yang, J., Johnson, J. D., Li, J. *Modeling the distribution of insulin in pancreas*, Arxiv preprint arxiv (2024).

[13] Haggar, M. S. D. *Efficiency of perturbation iteration method compared to euler and matlab approaches for solving a mathematical model of blood glucose and insulin during physical activity.*, Universal journal of mathematics and mathematical Sciences, (2024).

[14] Batool, M., Farman, M., Ghaffari, A. S., Nisar, K. S., and Munjam, S. R. *Analysis and dynamical structure of glucose insulin glucagon system with Mittage-Leffler kernel for type I diabetes mellitus*, Scientific Reports,**14(1)** , (2024).

[15] Li, C., Liu, Y., Wang, Y., Feng, X. *Dynamic modeling of the glucose-insulin system with inhibitors impulsive control*, Authorea Preprints, (2024).

[16] Alshehri, M. H., Duraihem, F. Z., Alalyani, A., Saber, S. *A Caputo (discretization) fractional-order model of glucose-insulin interaction: numerical solution and comparisons with experimental data*, Journal of Taibah University for Science, 15(1), 26-36. (2021).

[17] Khalouta A. *Closed-Form Solutions to Some Nonlinear Fractional Partial Differential Equations Arising in Mathematical Sciences*, Palestine Journal of Mathematics, 11, 113-126, (2022).

[18] Alshehri, M. H., Saber, S., Duraihem, F. Z, *Dynamical analysis of fractional-order of IVGTT glucose–insulin interaction*, International Journal of Nonlinear Sciences and Numerical Simulation,**24(3)**, 1123-1140,(2023).

[19] Alalyani, A. *Numerical solution of the fractional-order mathematical model of -cells kinetics and glucose-insulin system using a predictor-corrector method*, Mathematical Models and Computer Simulations, **14(1)**, 159-171, (2022).

[20] Shams, M., Kausar, N., Yaqoob, N., Arif, N., Addis, G. M.*Techniques for finding analytical solution of generalized fuzzy differential equations with applications*, Complexity,3000653, (2023).

[21] Palumbo, P., Ditlevsen, S., Bertuzzi, A., De Gaetano, A. *Mathematical modeling of the glucose–insulin system: A review*, Mathematical biosciences, **244(2)**, 69-81 (2013).

[22] Shams, M., Kausar, N., Ozbilge, E., Bulut, A. *Stable Computer Method for Solving Initial Value Problems with Engineering Applications*, Computer Systems Science and Engineering, **45(3)**, (2023).

[23] Saranya, K., Mohan, V., Kizek, R., Fernandez, C., Rajendran, L. *Unprecedented homotopy perturbation method for solving nonlinear equations in the enzymatic reaction of glucose in a spherical matrix*, Bioprocess and biosystems engineering, **41**, 281-294(2018).

[24] Shams, M., Rafiq, N., Kausar, N., Agarwal, P., Park, C., Mir, N. A.*On iterative techniques for estimating all roots of nonlinear equation and its system with application in differential equation*, Advances in Difference Equations, **1-18**,(2021).

[25] Mehala, N., Rajendran, L., Meena, V. *Analytical Expressions of Concentrations of Glucose, Oxygen, and Gluconic Acid in a Composite Membrane for Closed-Loop Insulin Delivery for the Non-steady State Conditions*, The Journal of Membrane Biology, **250**, 89-10 (2017).

[26] Rana, P *Mathematical Model on Diabetes Millitus Using Fractional Approach; Fractional Homotopy Perturbation Method and Fractional Variational Iteration Method: A Comparison*, International Multidisciplinary Research Journal, **9(2)**, 01-09 (2022).

[27] Kausar, N, *Fuzzy fractional Caputo-type numerical scheme for solving fuzzy nonlinear equations*, (2024).

[28] Mukherjee, S. B., Datta, D., Raha, S., Pal, D. *Numerical simulation of a glucose sensitive composite membrane closed-loop insulin delivery system*, Bioprocess and Biosystems Engineering, **40**, 1453-1462 (2017).

[29] Shams, M., Rafiq, N., Kausar, N., Agarwal, P., Park, C., Momani, S. *Efficient iterative methods for finding simultaneously all the multiple roots of polynomial equation*, Advances in Difference Equations, 1-11. (2021).

[30] Altun, Y., Tunç, C. *On The Estimates for Solutions of a Nonlinear Neutral Differential System with Periodic Coefficients and Time-Varying Lag*, Palestine Journal of Mathematics, **8(1)**, (2019).

[31] Joy, R. A., Rajendran, L *Mathematical modelling and transient analytical solution of a glucose sensitive composite membrane for closed-loop insulin delivery using he's variational iteration method*, Int Rev Chem Eng, **4(5)**, 516-523,(2012).

[32] Shams, M., Kausar, N., Araci, S., Oros, G. I. *Numerical scheme for estimating all roots of non-linear equations with applications*, AIMS Math, 8, 23603-23620 (2023).

[33] Saranya, K., Iswarya, T., Mohan, V., Sathappan, K. E., Rajendran, L. *Mathematical modeling of Glucose, Insulin, -Cell Mass: Homotopy Perturbation Method Approach*, Eur. J. Mol. Clin. Med, **7(02)**, 3513-3530,(2020).

[34] Shams, M., Kausar, N., Araci, S., Kong, L. *On the stability analysis of numerical schemes for solving non-linear polynomials arises in engineering problems*, (2024).

[35] Saranya, K., Mohan, V., Rajendran, L. *Analytical solution of the non-linear equation in biodegradation of N-butanol in a biofilter*, American Journal of Analytical Chemistry, **11(4)**, 172-186 (2020).

[36] Swaminathan, R., Narayanan, K. L., Mohan, V., Saranya, K., Rajendran, L. *Reaction/diffusion equation with Michaelis-Menten kinetics in microdisk biosensor: Homotopy perturbation method approach*, International Journal of Electrochemical Science, **14(4)**, 3777-3791 (2019).

[37] Shams, M., Kausar, N., Araci, S., Oros, G. I. *Artificial hybrid neural network-based simultaneous scheme for solving nonlinear equations: Applications in engineering*, Alexandria Engineering Journal, **108**, 292-305 (2024).

[38] Ibrahim, S., Murad, S. A. *Solution Of Fractional Differential Equations with Some Existence and Stability Results*, Palestine Journal of Mathematics,**12(1)**, (2023).

[39] Elmoasry, A., Shams, M., Yaqoob, N., Kausar, N., Gaba, Y. U.,Rafiq, N.. Numerical Scheme for Finding Roots of Interval-Valued Fuzzy Nonlinear Equation with Application in Optimization. Journal of Function Spaces, (2021).

[40] Kausar, N., Garg, H. . Contra-hormonic generalized fuzzy numerical scheme for solving mechanical engineering problems. Journal of Applied Mathematics and Computing, **1-25**,(2024).

Author information

M. Suguna, Department of Mathematics, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai,Tamil Nadu,India.
E-mail: msugunamaths95@gmail.com

K. Saranya*, Department of Mathematics, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai,Tamil Nadu,India.
E-mail: saranyak463@gmail.com

Received: 2024-09-16
Accepted: 2024-12-11