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Research article

Analysis of amperometric biosensor utilizing synergistic substrates conversion: Akbari-Ganji's method

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Abstract: The biological recognition of enzymes was the basis of enzyme-based chemical biosensors. It is essential for a biosensor to function under normal operating conditions so that enzymes can catalyze biochemical reactions. The mechanism of a modified enzymemembrane electrode in a catalytic cycle was described using a mathematical model. The nonlinear terms associated with enzyme kinetics were presented in this model. The Akbari-Ganji's method (AGM) was used to calculate the semi-analytical expressions for species concentration and normalized current. For all possible values of the Thiele modulus, normalized surface concentration of the oxidized mediator, and normalized surface concentration of the substrate, a simple and approximate hyperbolic expression of concentrations of an oxidized mediator, substrate, and reduced mediator were derived. The numerical simulation was then verified using semi-analytical results. The numerical simulation and semi-analytical predictions agreed well with each other.

Keywords: mathematical modeling; nonlinear differential equations; Akbari-Ganji's method; numerical simulation; amperometric biosensor; immobilized enzyme

Abbreviations:

	$[Med_{OX}]_b$: Oxidized mediator concentration at the enzyme					
	layer electrode boundary, units: <i>mM</i> ;					
$[E_T]$: Total enzyme concentration, units: mM ;	$[Med_{OX}]_{\infty}$: Oxidized mediator concentration in bulk					
$[E_{OX}]$: Enzyme concentration of the oxygen, units: mM ;	solution units: mM :					
[<i>ES</i>]: Enzyme concentration of the substrate, units: <i>mM</i> ;						
$[E_{red}]$: Reduced enzyme concentration, units: mM ;	[5]: Concentration of substrate at any position in the enzyme					
[Medox]: Concentration of oxidized mediator at any	layer, units: <i>mM</i> ;					
position in the engume lower units: mM :	$[S]_b$: Concentration of substrate at any position in the					
position in the enzyme rayer, units. <i>mm</i> ,	enzyme layer electrode boundary, units: mM ; [S] _{∞} : Substrate concentration in bulk solution, units: mM ;					
$[Med_{red}]$: Concentration of reduced mediator at any position						
in the enzyme layer, units: <i>Molcm</i> ⁻³ ;	k_1 k_2 k_4 : Rate constants units: $M^{-1}s^{-1}$:					
D_M : Diffusion coefficient of oxidized mediator, units:	$k + k_{2}$: Pate constants units: e^{-1} :					
$cm^2s^{-1};$	κ_{-1}, κ_2 . Kate constants, units. S ,					
	ϕ_{2}^{2} : Thiele modulus for the oxidized mediator, units: None					

 D_S : Diffusion coefficient of substrate, units: cm^2s^{-1} ;

 ψ_O

d: Thickness of the planar matrix, units: cm;

1. Introduction

The development of biosensing in recent decades has affected several fields, including environmental and biomedical monitoring. In modern biosensors, miniaturization, mass production, and simple transport processes are possible. Biological fluids constantly change, making biosensors an excellent real-time tool for monitoring these changes. Polymer membranes have been widely used as carriers for immobilizing enzymes in recent years [1]. Biocatalysts immobilized on membranes perform optimally. Catalytic reactions can be more selective toward desired products when substrate partitioning occurs at the membrane/fluid interphase (see [2]). A new approach to enzyme immobilization [3] based on molecular recognition has recently been used successfully for building chemically active membranes [4] as well as for building enzymatic biosensors. A great deal of effort has gone into developing biosensors with biologically sensitive components and transformers in the past decades, devices that have many possible applications [5]. Robeson demonstrated certain changes in membrane chemistry [6]. By enhancing the membrane area per unit volume, separation can be expedited by altering the membrane geometry. Recent research has identified increased surface area as a research priority for membranes [7].

Experiments were performed using a two-substrate model for enzyme electrodes incorporating nonlinear enzyme reactions [8]. Models of glucose oxidation electrodes have been developed using this approach [9]. When the mediators and natural co-substrates are both present in the assay solution, it has been found that the mediators cannot solely replace the co-substrate, so a three-substrate model is required. The calibration curve of the enzyme electrode is complex in these cases [10]. Although biosensors have been extensively tested experimentally, very few studies have focused on modeling or theoretical design. Efficient and productive biosensor design can be enhanced using a digital model [11-13]. The semi-analytical properties of biosensors have been optimized using mathematical models (see [14–17]). Biosensor models have been studied under steady-state [18, 19] and transient conditions [20, 21] using synergistic substrate conversion schemes.

А theoretical model for an enzyme-membrane amperometric oxidase electrode was recently presented by Loghambal et al. [22]. Novel enzyme electrodes were numerically analyzed in [23, 24]. Semi-analytical expressions of the substrate concentration for planar, cylindrical, and spherical particles under steady-state conditions were derived [25]. Lyons et al. [26] examined the problem of describing the transport and kinetics of catalytic reactions in a bounded region such as a conductive polymer-modified electrode.

Biological sensors have been assessed using electrochemical impedance spectroscopy, which is both nondestructive and sensitive to electrochemical properties [27-29]. An analysis of the influence of complex homogeneous and heterogeneous reactions on the sensor response was performed using mathematical models. A one-dimensional model for amperometric sensors was developed by Bartlett et al. and coworkers [30-32] based on the Michaelis-Menten approximation. Michaelis-Menten kinetics assumes a very large substrate concentration and that complex-forming reactions are equilibrated. A porous rotating disk electrode was recently analyzed by Visuvasam et al. [33]. The mathematical solution is semi-analytical, and more often, it is numerical. This method can be applied to various systems, and has been described in several publications [34-37]. This model can be understood better by reading [38–42] and its references.

This paper presents a semi-analytical solution for the model. By solving the system of nonlinear reactiondiffusion equations using Akbari-Ganji's (AGM) method (see [43, 44]), we can derive semi-analytical expressions for the substrate and oxidized and reduced mediator concentrations. These models provide information about the enzyme electrode mechanisms and their kinetics. These modeling results can be helpful for sensor design and optimization, and for determining how the electrode will react.

2. Mathematical formulation of the problem

The dimensionless nonlinear mass transport equation for this model was derived by Gooding and Hall [23]. A solid substrate encases the biological layer, and an outer permeable electrode is in contact with the sample in the enzyme-membrane geometry. This model employs a permeable electrode to facilitate the penetration of the substrate and co-substrate into the enzyme layer, where it reduces to the form of a co-substrate that diffuses oxygen back to the electrode. In the presence of two oxidants, immobilized oxidase can be described by the following general reaction scheme [23]:

$$E_{ox} + S \xrightarrow[k_{-1}]{k_1} ES \xrightarrow{k_2} E_{red} + P, \qquad (2.1)$$

$$E_{\text{red}} + O_2 \xrightarrow{k_3} E_{\text{ox}} + H_2O_2, \qquad (2.2)$$

$$E_{red} + Med_{ox} \xrightarrow{\kappa_4} E_{ox} + Med_{red}$$
 (2.3)

with respect to the m^{th} reaction, k_m and k_{-m} represent the forward and backward rate constants, where m = 1, 2, 3, ..., respectively. If $[E_T]$ is the total enzyme concentration in the matrix, then at all times

$$[E_T] = [E_{\text{OX}}] + [\text{ES}] + [E_{\text{red}}], \qquad (2.4)$$

where $[E_{OX}]$, [ES], and $[E_{red}]$ are the oxidized mediator, enzyme-substrate complex, and reduced mediator enzyme concentrations, respectively. When a substrate diffuses into an enzyme layer at steady-state, its diffusion rate is equal to its reaction rate within the matrix. We consider a planar matrix of thickness y = d, where diffusion is only considered in the y-direction (see Figure 1).



Figure 1. The geometry representation of enzyme-membrane electrode. The thicknesses of the layers are shown next to their boundaries [23].

On the enzyme electrode, the governing equations for the planar diffusion and reaction are as follows [23]:

$$D_M \frac{d^2 [\text{Med}_{\text{OX}}]}{dy^2} = k_4 [E_{\text{red}}] [\text{Med}_{\text{OX}}]$$

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$$= [E_{OX}][S] \frac{k_2 k_1}{k_{-1} + k_2}$$

$$= k_2 [E_T] \left(\frac{\beta_S}{[S]} + \frac{\beta_O}{[Med_{OX}]} + 1 \right)^{-1}, \quad (2.5)$$

$$D_S \frac{d^2[S]}{dy^2} = k_1 [E_{OX}][S] - k_{-1}[ES]$$

$$= [E_{OX}][S] \left(k_1 - \frac{k_{-1} k_1}{k_{-1} + k_2} \right)$$

$$= k_2 [E_T] \left(\frac{\beta_S}{[S]} + \frac{\beta_O}{[Med_{OX}]} + 1 \right)^{-1}, \quad (2.6)$$

$$D_M \frac{d^2 [Med_{red}]}{dy^2} = -k_4 [E_{red}] [Med_{OX}]$$

$$= -k_2 [E_T] \left(\frac{\beta_S}{[S]} + \frac{\beta_O}{[Med_{OX}]} + 1 \right)^{-1}, \quad (2.7)$$

and from the above equations, we have

$$D_M \frac{d^2[\text{MedOX}]}{dy^2} = D_S \frac{d^2[S]}{dy^2}$$
$$= -D_M \frac{d^2[\text{Med}_{\text{red}}]}{dy^2}$$
$$= \frac{k_2 [E_T]}{\frac{\beta S}{[S]} + \frac{\beta O}{[\text{Med}^O \text{OX}]} + 1}, \qquad (2.8)$$

where D_M and D_S are the diffusion coefficient of the mediator and substrate within the enzyme layer. [Med_{OX}], [Med_{red}], and [S] are the concentration of oxidized, reduced mediators and the substrate within the enzyme layer.

and

$$\beta_O = (k_2/k_4)$$

 $\beta_{S} (= (k_{-1} + k_2) / k_1)$

are the rate constants in dimensionless form.

The corresponding boundary conditions are the following: at the far wall, y = 0,

$$\frac{d \left[\operatorname{Med}_{OX}\right]}{dy} = \frac{d[S]}{dy} = \frac{d \left[\operatorname{Med}_{\mathrm{red}}\right]}{dy} = 0.$$
(2.9)

At the electrode, y = d,

$$[\operatorname{Med}_{OX}] = [\operatorname{Med}_{OX}]_b = K_O [\operatorname{Med}_{OX}]_{\infty},$$

$$[S] = [S]_b = K_S [S]_{\infty}, \ [\operatorname{Med}_{\operatorname{red}}] = 0, \qquad (2.10)$$

where $[Med_{OX}]_b$ and $[S]_b$ are the bulk concentration of the oxidized mediator and substrate at the enzyme layer electrode boundary. They are the bulk solution and concentrations and are the equilibrium partition coefficients for the oxidized mediator and the substrate, respectively.

By defining the following dimensionless variables, we can reduce the nonlinear differential Eqs (2.5)–(2.7) to dimensionless form

$$F_{O} = \frac{[\text{Med}_{OX}]}{[\text{Med}_{OX}]_{b}}, \quad F_{S} = \frac{[\text{S}]}{[\text{S}]_{b}}, \quad F_{R} = \frac{[\text{Med}_{red}]}{[\text{Med}_{red}]_{b}}, \quad \chi = \frac{y}{d},$$
$$B_{O} = \frac{[\text{Med}_{OX}]_{b}}{\beta_{O}}, \quad B_{S} = \frac{[\text{S}]_{b}}{\beta_{S}}, \quad \phi_{O}^{2} = \frac{d^{2}k_{2} [E_{T}]}{D_{M} [\text{Med}_{OX}]_{b}},$$
$$\mu_{S} = \frac{D_{M} [\text{Med}_{OX}]_{b}}{D_{S} [S]_{b}}, \quad (2.11)$$

where F_O , F_S , and F_R are the normalized concentration of the oxidized mediator, substrate, and reduced mediator, respectively, and χ is the normalized distance. B_O and B_S are the normalized surface concentration of the oxidized mediator and substrate. ϕ_O is the Thiele modulus for the oxidized mediator. Non-dimensionalized expressions for the oxidized mediator, substrate, and reduced mediator are as follows:

$$\frac{d^2 F_O}{d\chi^2} = \phi_O^2 \left[\frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right], \qquad (2.12)$$

$$\frac{d^2 F_S}{d\chi^2} = \mu_S \phi_O^2 \left[\frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right], \quad (2.13)$$

$$\frac{d^2 F_R}{d\chi^2} = -\phi_O^2 \left[\frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right].$$
 (2.14)

From the above equations, we obtain the following relations:

$$\frac{d^2 F_O}{d\chi^2} = \frac{1}{\mu_s} \frac{d^2 F_S}{d\chi^2}$$
$$= -\frac{d^2 F_R}{d\chi^2}$$
$$= \phi_O^2 \left[\frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right]. \quad (2.15)$$

Corresponding boundary conditions are given by:

$$F'_{O} = 0, \ F'_{S} = 0, \ F'_{R} = 0 \ \text{at} \ \chi = 0,$$
 (2.16)

$$F_O = 1, F_S = 1, F_R = 0 \text{ at } \chi = 1.$$
 (2.17)

From Eq (2.14), we get

$$\frac{d^2 F_O}{d\chi^2} = \frac{1}{\mu_S} \frac{d^2 F_S}{d\chi^2}$$
(2.18)

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$$\frac{d^2 F_R}{d\chi^2} = -\frac{1}{\mu_S} \frac{d^2 F_S}{d\chi^2}.$$
 (2.19)

Solving Eqs (2.18) and (2.19) we get

$$F_O(\chi) = \frac{1}{\mu_S} \left(F_S(\chi) - 1 \right) + 1, \tag{2.20}$$

$$F_R(\chi) = \frac{1}{\mu_S} \left(1 - F_S(\chi) \right).$$
 (2.21)

The following expression gives the normalized current response:

$$I = -\left(\frac{dF_R}{d\chi}\right)_{\chi=1}.$$
 (2.22)

3. Approximate analytical expressions for the oxidized mediator, substrate, and reduced mediator using AGM

AGM [45–49] was used to solve the boundary value problem and its associated boundary conditions represented by Eqs (2.12)–(2.17), which has a minimum number of unknowns. This is an appropriate and simple method for nonlinear differential equations [50]. This is a particular case of the exponential function method proposed by He et al. [51]. Using this method, a general semi-analytical expression for the normalized concentrations can be obtained as follows:

$$F_S(\chi) \approx \frac{\cosh(b\chi)}{\cosh(b)},$$
 (3.1)

$$F_O(\chi) \approx 1 - \frac{1}{\mu_S} \left(1 - \frac{\cosh(b\chi)}{\cosh(b)} \right),$$
 (3.2)

$$F_R(\chi) \approx \frac{1}{\mu_S} \left(1 - \frac{\cosh(b\chi)}{\cosh(b)} \right),$$
 (3.3)

where

$$b = \phi_0 \sqrt{\frac{\mu_S B_O B_S}{B_O + B_S + B_O B_S}}.$$
 (3.4)

From these relations, the following current response formula is derived:

$$I = -\left(\frac{dF_R}{d\chi}\right)_{\chi=1} = \frac{b}{\mu_S} \tanh(b).$$
(3.5)

4. Previous analytical results for concentration for the oxidized mediator, substrate, and reduced mediator [52]

Loghambal et al. [52] derived the approximate semianalytical expressions for the concentration for the oxidized

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mediator, substrate, and reduced mediator using the adomian decomposition method

$$F_O(\chi) \approx 1 + \frac{\phi_0^2 B_O B_S}{2(B_O + B_S + B_O B_S)} (5w_1 - 1 + (1 - 6w_1)\chi^2 + w_1\chi^4), \tag{4.1}$$

$$F_S(\chi) \approx \mu_S(F_O(\chi) - 1) + 1,$$
 (4.2)

$$F_R(\chi) \approx 1 - F_O(\chi). \tag{4.3}$$

The normalized current becomes

$$I = \frac{\phi_O^2 B_O B_S (1 - 4w_1)}{B_O + B_S + B_O B_S},$$
(4.4)

where

$$w_1 = \phi_O^2 B_O B_S (B_S + B_O \mu_S) / 12 (B_O + B_S + B_O B_S)^2$$

5. Numerical simulation

Numerical methods are used to solve the nonlinear differential Eqs (2.12)–(2.14). A numerical solution of the nonlinear differential Eqs (2.12)–(2.14) has been performed via MATLAB. Comparing our numerical solutions with our analytical results is shown in Figures 2–4 regarding species concentrations. The numerical solution, which is shown in Figures 2–4, yields a satisfactory result when compared to the AGM.

6. Discussion

Equations (3.1)–(3.3) provide semi-analytical expressions of the concentrations of the substrate, oxygen, and reduced mediators that are obtained by using AGM with the normalized current given in Eq (3.5). Figure 2a–c depicts the normalized steady-state concentrations of species obtained using Eq (2.12)–(2.14) for various values of ϕ_0 and for some fixed values of μ_S , B_O , and B_S . The concentration is uniform when $\phi_0 \leq 1$ for all species. Figure 2a,b shows that for some fixed values of other parameters μ_S , B_O , and B_S , the normalized concentrations of the oxidized mediator and substrate decrease with the increasing Thiele modulus. In contrast, this modulus has an opposite effect on the normalized concentrations of the reduced mediator for some fixed values of the μ_S , B_O and B_S as shown in Figure 2c.



Figure 2. Comparison of the concentration profile with simulation results for various values of normalized parmeter ϕ_0 : (a) substrate (Eq (3.1)); (b) oxidized mediator (Eq (3.2)); (c) reduced mediator (Eq (3.3)). Solid line represents the semi-analytical result and (...) represents the numerical result.

Figure 3a–c illustrates the normalized concentrations of substrates, the oxidized mediator and reduced mediator, versus the dimensionless distance, respectively. Figure 3a,b shows that, for some fixed values of the parameters $\mu_{\rm S}$, ϕ_0 , and $B_{\rm S}$ concentrations of substrates and the oxidized mediator decrease as $B_{\rm O}$ increases. Figure 3c illustrates that for some constant measurements of the parameters $\mu_{\rm S}$, ϕ_0 , and $B_{\rm S}$, the normalized surface concentrations of the reduced mediator increase as $B_{\rm O}$ increases.

According to Eqs (2.12)–(2.14), the normalized steadystate concentrations of substrate and various mediator species can be determined for various values of B_S as shown in Figure 4a–c. We conclude that when the dimensionless parameter B_S increases, the concentrations of substrate and oxidized mediator decrease for some fixed values of the parameters μ_S , ϕ_0 , and B_O in Figure 4a,b. In Figure 4c, it can be seen that the influence of the increasing dimensionless parameter B_S can result in normalized concentrations of the mediator increasing, even when the other parameter is at fixed values.



Figure 3. Comparison of the concentration profile with simulation results for various values of normalized parmeter B_0 : (a) substrate (Eq (3.1)); (b) oxidized mediator (Eq (3.2)); (c) reduced mediator (Eq (3.3)). Solid line represents the semi-analytical result and (...) represents the numerical result.



Figure 4. Comparison of the concentration profile with simulation results for various values of normalized parmeter B_S : (a) substrate (Eq (3.1)); (b) oxidized mediator (Eq (3.2)); (c) reduced mediator (Eq (3.3)). Solid line represents the semi-analytical result and (...) represents the numerical result.

Figure 5a–c illustrates the normalized concentrations of substrates, oxidized mediator, and reduced mediator versus the dimensionless distance χ , respectively. Figure 5a,b shows that, for some fixed values of the parameters ϕ_0 , B_S , and B_O , concentrations of substrates and reduced mediator decrease as μ_S increases. Figure 5c illustrates that for some constant measurements of the parameters ϕ_0 , B_S , and B_O , the normalized surface concentrations of the oxidized mediator increase as μ_S increases.



Figure 5. Comparison of the concentration profile with simulation results for various values of normalized parmeter $\mu_{\rm S}$: (a) substrate (Eq (3.1)); (b) oxidized mediator (Eq (3.2)); (c) reduced mediator (Eq (3.3)). Solid line represents the semi-analytical result and (...) represents the numerical result.

The effect of the various parameters on the current in the three-dimensional is displayed in Figure 6a– c. The dependencies of the steady-state current *I* on the concentration of the substrate, oxygen, and reduced mediators versus the Thiele modulus are displayed in Figure 6. It is noticed from these figures that the steadystate current increases as the values of the parameters μ_S , ϕ_0 , B_O , and B_S increase. The proposed empirical concentration models are compared with the corresponding numerical data in Tables 1 and 2.



Figure 6. Three-dimensional plot for normalized current *I* versus Thiele modulus and (a) $B_{\rm O}$ (b) $\mu_{\rm S}$ (c) $B_{\rm S}$ using (3.5).

Table 1. Comparison of normalized current *I* in Eq (3.5) and previous results in Eq (4.4) with simulation results when $B_O = 0.1, B_S = 0.01$, and $\mu_S = 0.05$ and for various values of parameter (ϕ_O^2) Thiele module.

ϕ_{0}^{2}	Previous results in Eq (4.4)	Our results in Eq (3.5)	Numerical
1	0.009	0.009	0.0090
25	0.223	0.224	0.2230
50	0.441	0.447	0.4410
75	0.655	0.668	0.6520
100	0.864	0.887	0.8380

7. Conclusions

An amperometric enzyme-based biosensor combines chemistry, biology, electrochemistry, materials science, polymer synthesis, enzymology, and electrochemistry to provide a powerful analytical tool.

Our main goal was to develop a biosensor that responds to oxidase linked tests independently of biorecognition matrix thickness for oxidase linked tests. The mathematical models (2.12)–(2.14) of the biosensor utilizing the synergistic scheme of substrates conversion can be successfully used to investigate the peculiarities of the biosensor response and sensitivity at steady as well as at

transition state. In the amperometric biosensor system, a nonlinear differential equation was used to determine the semi-analytical solution of the species concentration. Using the AGM, an approximate general semi-analytical expression for the concentration of substrate, mediator and current of amperometric biosensor at the enzyme-membrane electrode geometry is derived for all values of parameters ϕ_{O}^{2} , B_{O} , and B_{S} . The effects of these parameters on the concentration and effectiveness were also explored. The results were satisfactory compared to those of the numerical simulation. It is possible to determine the qualitative behavior of biosensors by using this hypothetical model. Furthermore, the results of this study provide an option for extending this method to measure substrate concentrations and diffusion currents. As the reciprocal of the squares of the Thiele modulus decreases, the current density increases. The results of this study can be used to optimize and design biosensors.

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Conflict of interest

All authors declare no conflicts of interest in this paper.

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$\phi_{O}^{2} =$	0.01					$\phi_{O}^{2} =$	1				
X	Previous	Our	Numerical	Error	Error	X	Previous	Our	Numerical	Error	Error
	results	results		in	for		results	results		in	for
	in	in		Eq (4.1)	Eq (3.1)		in	in		Eq (4.1)	Eq (3.1)
	Eq (4.1)	Eq (3.1)					Eq (4.1)	Eq (3.1)			
0	0.9999	0.9999	1	0.01	0.01	0	0.9955	0.9955	0.9955	0.00	0.00
0.2	0.9999	0.9999	1	0.01	0.01	0.2	0.9957	0.9957	0.9957	0.00	0.00
0.4	0.9999	0.9999	1	0.01	0.01	0.4	0.9962	0.9962	0.9962	0.00	0.00
0.6	0.9999	0.9999	1	0.01	0.01	0.6	0.9971	0.9971	0.9971	0.00	0.00
0.8	0.9999	0.9999	1	0.01	0.01	0.8	0.9984	0.9984	0.9984	0.00	0.00
1	1	1	1	0	0	1	1	1	1	0.00	0.00
Average deviation			0.05	0.05	Avera	age deviation			0.00	0.00	
$\phi_{O}^{2} = 25$				$\phi_{O}^{2} = 100$							
X	Previous	Our	Numerical	Error	Error	χ	Previous	Our	Numerical	Error	Error
	results	results		in	for		results	results		in	for
	in	in		Eq (4.1)	Eq (3.1)		in	in		Eq (4.1)	Eq (3.1)
	Eq (4.1)	Eq (3.1)					Eq (4.1)	Eq (3.1)			
0	0.8889	0.8889	0.8889	0.00	0.00	0	0.5801	0.5795	0.5773	0.46	0.45
0.2	0.8933	0.8923	0.8923	0.00	0.00	0.2	0.5965	0.5966	0.5939	0.43	0.42
0.4	0.9066	0.9058	0.9060	0.00	0.02	0.4	0.6462	0.6463	0.6440	0.34	0.34
0.6	0.9288	0.9282	0.9282	0.00	0.00	0.6	0.7295	0.7296	0.7279	0.22	0.22
0.8	0.9599	0.9596	0.9599	0.00	0.03	0.8	0.9484	0.9485	0.8479	0.85	0.83
1	1	1	1	0.00	0.00	1	1	1	1	0.00	0.00
Average deviation		0.00	0.05	Avera	Average deviation			0.38	0.37		

Table 2. Comparison of concentration of oxidized mediator in Eq (3.1) and previous in Eq (4.1) with simulation results when $B_O = 0.1$, $B_S = 0.01$, and $\mu_S = 0.05$, and for various values of parameter (ϕ_O^2) Thiele module.

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