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Theoretical Analysis of Immobilized Oxidase Enzyme Electrode in the Presence of Two Oxidants

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Abstract

In this paper, mathematical model of Martens and Hall (Analytical chemistry 66, 2763-2770 (1994 [1])) for an immobilized oxidase enzyme electrode is discussed. The model involves the system of non-linear reaction diffusion equations under the steady state conditions. A simple and closed-form of approximate analytical expressions for the concentrations of the immobilization of three enzyme substrates has been derived by solving the system of non-linear reaction diffusion equations using new approach of homotopy perturbation method. Approximate polynomial expression of concentration of substrate, oxygen and oxidized mediator and current was obtained in terms of the Thiele moduli and the small values of parameters B_s, B_o and B_m (normalized surface concentration of substrate, oxygen and oxidized mediator). Furthermore, in this work the numerical simulation of the problem is also reported using Matlab program. An agreement between analytical expressions and numerical results is noted.

Keywords

Mathematical Modelling, Enzyme Electrodes, Non-linear Reaction, Diffusion Equation, New Homotopy Perturbation Method

1. Introduction

There have been many publications on models for enzyme electrodes. Schulmeister *et al.* [2] have described models for multilayer and multi enzyme electrodes under diffusion control such that enzyme kinetic are linear. Here the reaction and diffusion system is described by a parabolic differential equation with linear in homogeneities Schulmeister *et al.* [3]. A model for two substrate enzyme electrode has been developed by Leypoldt and Gough where the non-linear enzyme reaction was taken into account.

This model was employed to describe the behavior of a glucose oxidase (Go_x) electrode Leypoldt *et al.* [4]. The transient response of a mediated amperometric enzyme electrode was studied by Bergel and Comtat, employing an implicit finite difference method Bergel *et al.* [5]. Recently Indira and Rajendran *et al.* [6] have derived analytical expressions for the concentrations of substrate, oxygen and mediator in an amperometric enzyme electrode. Logambal *et al.* [7] and Anitha *et al.* [8] have developed the approximate analytical expressions for steady state concentrations of oxidized mediator, substrate and reduce mediator of an enzyme-membrane electrode by the Adomian decomposition method and Homotopy perturbation method. To our knowledge no simple analytical expressions that describe the concentration of substrate, oxygen and oxidized mediator for various values of the Thiele moduli and the normalized parameters have been derived. In this paper we have derived that analytical expressions corresponding to the concentrations of substrate, oxygen, and oxidized mediator in an oxidase enzyme electrode using new Homotopy perturbation method.

2. Mathematical Formulation of the Boundary Value Problem

The details of the model adopted have been fully described in Mertens and Hall [1] and so we only present a brief summary here. **Figure 1** represents the general kinetic reaction scheme of an enzyme membrane electrode geometry Gooding *et al.* [9]

$$E_{OX} + S \to ES \to_{red} + P \tag{1}$$

$$E_{red} + O_2 \to E_{OX} + H_2O_2 \tag{2}$$

$$E_{red} + Med_{OX} \to E_{OX} + Med_{red} \tag{3}$$

We assume that the concentrations of all reactants and enzyme intermediates remain constant for all time. Also the concentration of total active enzyme $[E_t]$ and the reactants in the bulk electrode remain constant. We can consider that the diffusion of the reactants can be described by Fick's second law and the enzymes are assumed to be uniformly dispersed throughout the matrix. The enzyme activity is not a function of position. The coupled three non linear reaction/diffusion equations in normalized form are

$$\frac{d^2F_s}{dx^2} = \Phi_s^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1} \tag{4}$$

$$\frac{d^2F_o}{dx^2} = \Phi_o^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1}\frac{F_oB_o}{F_oB_o+F_mB_m} \tag{5}$$

$$\frac{d^2F_m}{dx^2} = \Phi_m^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1}\frac{F_mB_m}{F_oB_o+F_mB_m} \tag{6}$$

The boundary conditions becomes

$$F_s = F_o = F_m = 1 \ \ at \quad x = 1 \tag{7}$$

$$\frac{dF_o}{dx} = \frac{dF_s}{dx} = 0,\ F_m = 1 \ \text{at}\ x = 0 \tag{8}$$

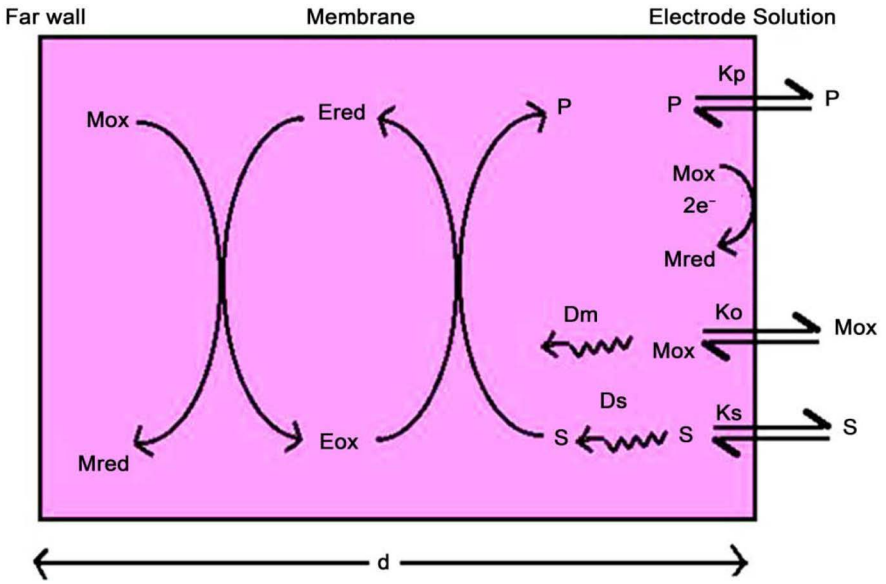

Figure 1. Schematic diagram of reaction scheme of an enzyme membrane electrode geometry [8].

The normalized parameters are

$$\begin{aligned} F_s &= \frac{[S]}{[S]_b}; F_o = \frac{[O_2]}{[O_2]_b}; F_m = \frac{[Med_{OX}]}{[Med_{OX}]_b}; \; x = \frac{y}{d}; \\ B_s &= \frac{[S]_b}{\beta_s}; B_o = \frac{[O_2]_b}{\beta_o}; B_m = \frac{[Med_{OX}]_b}{\beta_m}; \\ \Phi_s^2 &= \frac{d^2 k_3 [E_t]}{D_s [S]_b}; \Phi_o^2 = \frac{d^2 k_3 [E_t]}{D_m [O_2]_b}; \Phi_m^2 = \frac{d^2 k_3 [E_t]}{D_m [Med_{OX}]_b} \end{aligned} \tag{9}$$

where F_s, F_o, and F_m represent the normalized concentrations of substrate, oxygen and oxidized mediator and B_s, B_o, and B_m are the corresponding normalized surface concentrations. The surface concentration is the ratio of the bulk concentration and the reaction constants. Φ_s, Φ_o, and Φ_m denote the Thiele moduli of substrate, oxygen and oxidized mediator, respectively. Thiele modulus Φ^2 represents the ratio of the characteristic time of the enzymatic reaction to that of substrate diffusion. d is the thickness of the enzyme layer. The normalized current J_{OX} is given by,

$$J_{OX} = \left(\frac{dF_m}{dx} \right)_{x=0} \tag{10}$$

3. Analytical Expressions of Concentrations of Substrate, Oxygen and Oxidized Mediator under Steady-State Condition

Recently, many authors have applied the Homotopy perturbation method to solve the various non linear problems in physical and chemical engineering sciences [10]-[12]. This method is a combination of Homotopy in topology and classic perturbation techniques. Ji-Huan He used the HPM to solve the Lighthill equation [13], the duffing Equ-

ation [14] and Blasius Equation [15]. The idea has been used to solve non-linear boundary value problems, integral equations and many other problems [16]-[18]. The HPM is unique in its applicability, accuracy and efficiency. The HPM uses the imbedding parameter p as a small parameter and only a few iterations are needed to find the asymptotic solution with good accuracy. Using the new approach to Homotopy perturbation method, the analytical expressions of steady state concentrations of substrate, oxygen and oxidized mediator (Appendix A) can be obtained as follows:

$$F_s(x) = \frac{Cosh\sqrt{A}x}{Cosh\sqrt{A}} \tag{11}$$

$$F_o(x) = \frac{Cosh\sqrt{B}x}{Cosh\sqrt{B}} \tag{12}$$

$$F_m(x) = e^{\sqrt{E}x} - \frac{\left(e^{\sqrt{E}} - 1\right)Sinh\sqrt{E}x}{Sinh\sqrt{E}} \tag{13}$$

$$where \quad A = \frac{\Phi_s^2\left(B_o + B_m\right)B_s}{\left(B_o + B_m\right)B_s + B_s + B_o + B_m}$$

$$B = \frac{\Phi_o^2 B_o B_s}{\left(B_o + B_m\right)B_s + B_s + B_o + B_m}; \quad E = \frac{\Phi_m^2 B_m B_s}{\left(B_o + B_m\right)B_s + B_s + B_o + B_m}$$

Recently Anitha and Rajendran [8] have derived that analytical expressions corresponding to the concentrations of substrate, oxygen and oxidized mediator in an oxidase enzyme electrode using Homotopy perturbation method. From Equation (10), we can obtain the current as follows:

$$J_{OX} = \left|\sqrt{E} - \frac{\left(e^{\sqrt{E}} - 1\right)\sqrt{E}}{Sinh\sqrt{E}}\right| \tag{14}$$

Equation (11) to Equation (13) represents the new simple and closed-form of approximate analytical expression of concentrations of substrate, oxygen and oxidized mediator.

4. Discussion

Equation (11) to Equation (13) represent the new closed approximate analytical expression of the non-steady state concentration of substrate, oxygen and oxidized mediator for all values of *kinetic and diffusion parameters.* The concentration depends on parameters such as B_s, B_o and B_m and Φ_s, Φ_o and Φ_m (Thiele *moduli*).

Figure 2 shows the dimensionless non-steady state concentration of substrate, oxygen and oxidized mediatorversus dimensionless distance for various values of the dimensionless parameters B_s. From this figure, it is inferred that the concentration of substrate and oxygen decreases when B_s (surface concentration of substrate) increases. Also concentration mediator decreases due to consumption by the enzyme reaction and reaching the minimum at the centre of the membrane ($x = 0.5$). Then the concentration of the mediator increases from $x = 0.5$ to $x = 1$ due reoxidation of the electrode.

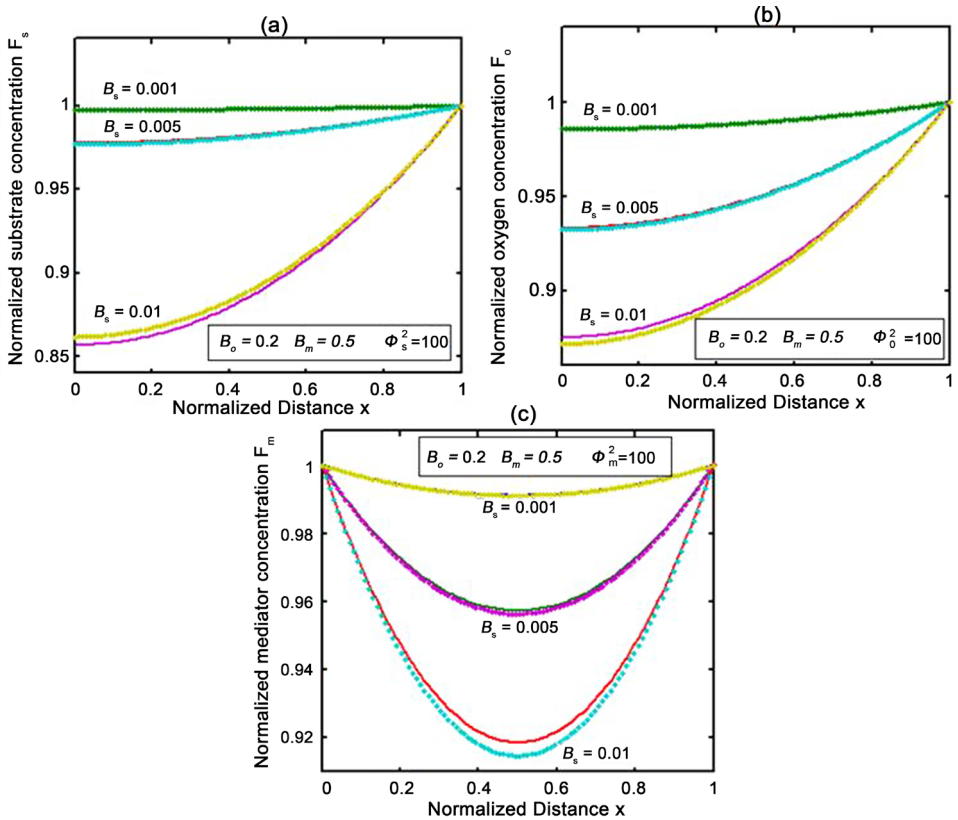

Figure 2. (a)-(c): Plot of analytical expression of concentration of substrate oxygen and mediator for various values of parameter B_s using Equations (11)-(13). Dotted line represents numerical solution and solid line represents the analytical solution.

Figure 3 represents the dimensionless non-steady state concentration profiles of substrate, oxygen and mediator for various values of Thiele modulus. Thiele Modulus depends upon thickness of the enzyme layer or amount of enzyme immobilized in the matrix (refer Equation 9). This parameter express the relative importance of diffusion and reaction in the enzyme layer when it is small, kinetics are the dominant and when Thiele modlus is large internal diffusion usually limits the overall rate of reaction. From this figure, we can observed that, the concentration of substrate, oxygen and mediator increases when Thiele modulus decreases. For small values of Thiele modulus, the reaction rate is small compared to the diffusion rate and the concentration becomes nearly uniform. Also the minimum values of the mediator is zero for the large value of Thiele modulus. Concentration is uniform for very small values of Thiele modules (Φ_i less than 0.1).

Figure 4 represents the concentration of substrate, oxygen and mediator verse the normalized distance for various values B_o. From this figure, it is inferred that the concentrate of substrate and oxygen increases when B_s decreases and become uniform for very small values of B_o. Here also concentration mediator decreases slowly from x = 0 to $x = 0.5$. Then from $x = 0.5$ to $x = 1$ the concentration increases due to reoxidation at the electrode.

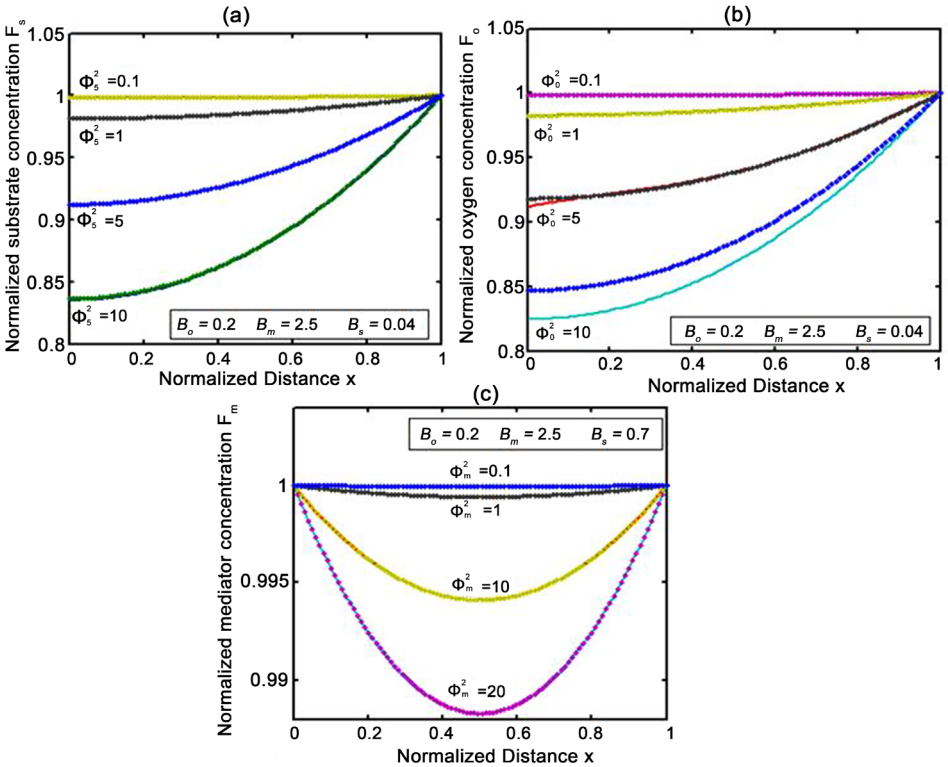

Figure 3. (a)-(c): Plot of concentration of substrate oxygen and mediator for various values of parameter Φ_o^2, Φ_s^2 and Φ_m^2 using Equations (11)-(13). Dotted line represents numerical simulation and solid line represents the analytical expression.

Figure 5 represents normalized current density J_{ox} verses Thiele modules/B_o for various values of dimensionless parameter B_s, B_o, B_m and Φ_m. From this figure it is observed that, the current density increases when B_s, B_o, B_m (surface concentration of substrate, oxygen, mediator) decreases. The most accessible parameters in the design of a sensor are the thickness of the membrane and the actual loading of active enzyme in the matrix. Also the maximum current decreases with decreases of membrane thickness or actual loading of active enzymes due to decrease in the total amount of enzyme presence in the system.

Tables 1-3 represent the comparison of analytical expression of concentration of the substrate, oxygen and mediator (F_s, F_o, F_m) for various of Thiele modules. The maximum average relative error between the analytical results and numerical results is 1.62%. This error is less than pervious published analytical result [8].

5. Conclusion

In this paper, steady state nonlinear differential equations in biofiltration model have been solved analytically. Approximate analytical expressions pertaining to the concentrations of substrate, oxygen and oxidized mediator are derived using homotopy perturbation method. These analytical solutions are compared with the numerical simulation results. These analytical results provide a good understanding of the system and

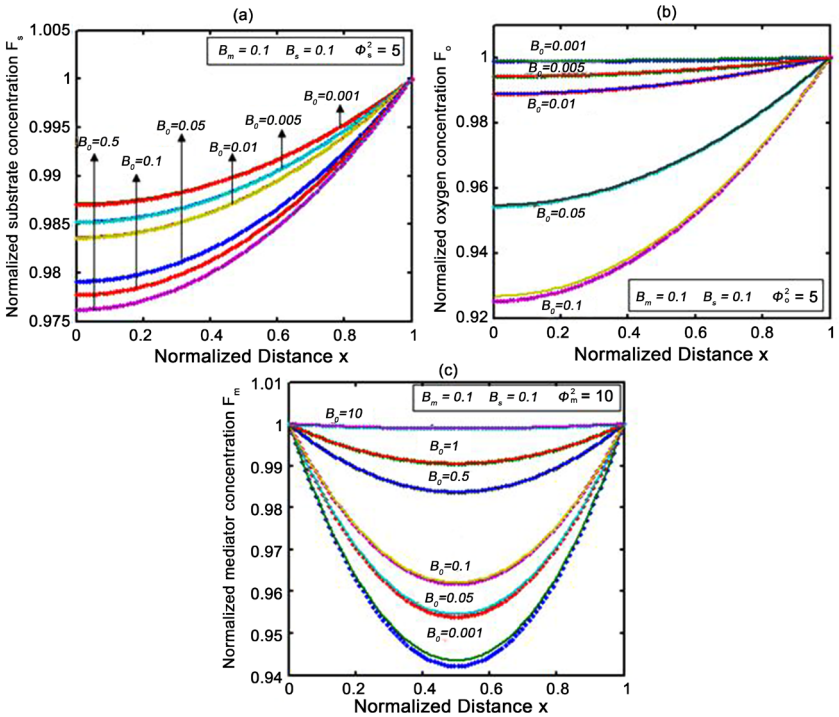

Figure 4. (a)-(c): Plot of concentration of substrate oxygen and mediator for various values of parameter, B_0 using Equations (11)-(13). Dotted line represents numerical simulation and solid line represents the analytical expression.

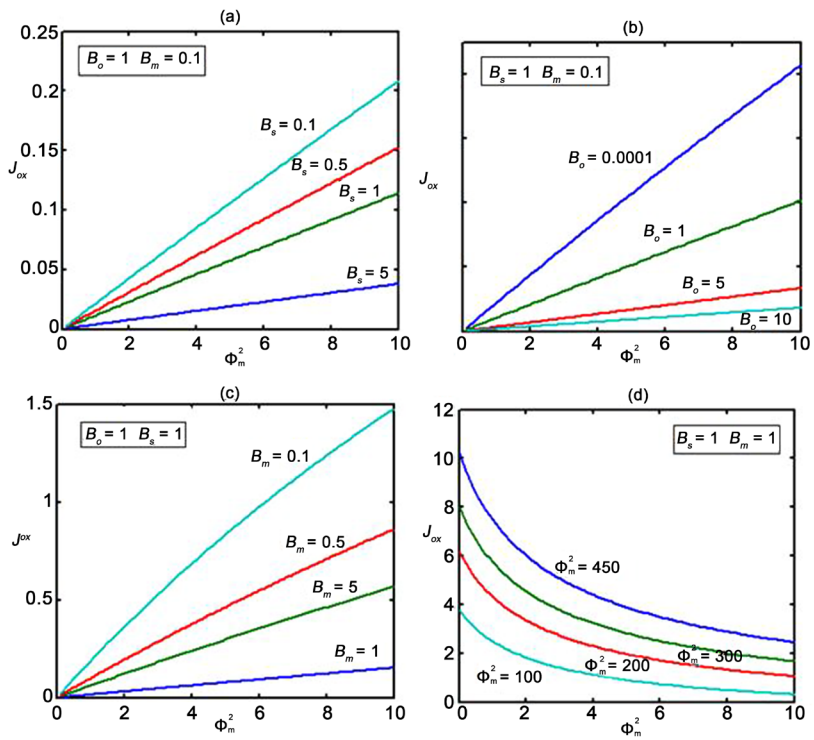

Figure 5. (a)-(d): Normalized current density J_{ox} verses the lie Modules/B_o for various values of the parameters using Equation (14).

Table 1. Comparison of normalized substrate concentration F_s with the numerical result for various values of Φ_s^2 and some fixed values of normalized parameters $b_s = 0.04$, $b_o = 2.5$ and $b_m = 0.2$.

F_s	$\Phi_s^2 = 0.1$					$\Phi_s^2 = 1$					$\Phi_s^2 = 5$					$\Phi_s^2 = 10$				
x	Numerical	Anitha *et al.* [8]	This Work Equation (11)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (11)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (11)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (11)	Error of Anitha (%)	Error of this work (%)
0	0.9981	0.9981	0.9981	0.00	0.00	0.9813	0.9810	0.9813	0.03	0.00	0.9118	0.9052	0.9122	0.72	0.04	0.8352	0.8104	0.8363	2.97	0.13
0.2	0.9982	0.9982	0.9982	0.00	0.00	0.9821	0.9818	0.9821	0.03	0.00	0.9153	0.9090	0.9156	0.69	0.03	0.8416	0.8180	0.8427	2.80	0.13
0.4	0.9984	0.9984	0.9984	0.00	0.00	0.9843	0.9841	0.9843	0.02	0.00	0.9257	0.9204	0.9260	0.57	0.03	0.8609	0.8407	0.8618	2.35	0.10
0.6	0.9988	0.9988	0.9988	0.00	0.00	0.9880	0.9879	0.9880	0.01	0.00	0.9433	0.9393	0.9435	0.42	0.02	0.8934	0.8787	0.8941	1.65	0.08
0.8	0.9993	0.9993	0.9993	0.00	0.00	0.9933	0.9932	0.9933	0.01	0.00	0.9679	0.9659	0.9681	0.21	0.02	0.9395	0.9317	0.9399	0.83	0.04
1	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000`	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00
		Average error		0.00	0.00		Average error		0.02	0.00		Average error		0.44	0.02		Average error		1.77	0.08

Table 2. Comparison of normalized oxygen concentration F_o with the numerical results for various values of Φ_o^2 and some fixed values of normalized parameters $b_s = 0.04$, $b_o = 2.5$ and $b_m = 0.2$.

F_o	$\Phi_o^2 = 0.1$					$\Phi_o^2 = 1$					$\Phi_o^2 = 5$					$\Phi_o^2 = 10$				
x	Numerical	Anitha *et al.* [8]	This Work Equation (12)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (12)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (12)	Error of Anitha (%)	Error of this work (%)	Numerical	Anitha *et al.* [8]	This Work Equation (12)	Error of Anitha (%)	Error of this work (%)
0	0.9982	0.9982	0.9982	0.00	0.00	0.9827	0.9122	09827	0.03	0.00	0.9118	0.9122	0.9182	0.04	0.70	0.8244	0.8490	0.8469	2.98	2.73
0.2	0.9983	0.9983	0.9983	0.00	0.00	0.9834	0.9157	0.9834	0.03	0.00	0.9220	0.9157	0.9214	0.68	0.07	0.8315	0.8548	0.8529	2.80	2.57
0.4	0.9985	0.9985	0.9985	0.00	0.00	0.9855	0.9263	0.9855	0.02	0.00	0.9316	0.9263	0.9311	0.57	0.05	0.8525	0.8725	0.8708	2.35	2.15
0.6	0.9989	0.9989	0.9989	0.00	0.00	0.9889	0.9438	0.9889	0.01	0.00	0.9477	0.9438	0.9474	0.41	0.03	0.8876	0.9022	0.9010	1.65	1.51
0.8	0.9994	0.9994	0.9994	0.00	0.00	0.9938	0.9684	0.9938	0.01	0.00	0.9705	09684	0.9703	0.22	0.02	0.9368	0.9445	0.9439	0.82	0.76
1	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.0	1.0000	1.0000	1.0000	0.00	0.00
	Average error			0.00	0.00	Average error			0.02	0.00	Average error			0.32	0.15	Average error			1.77	1.62

Table 3. Comparison of normalized mediator concentration F_m with the numerical result for various values of Φ_m^2 and some fixed values of normalized parameters b_s = 0.07, b_o = 2.5 and b_m = 0.2.

F_m		Φ_m^2 = 0.1				Φ_m^2 = 1				Φ_m^2 = 10				Φ_m^2 = 20				
x	Numerical	Anitha *et al.* [8]	This Work Equation (13)	Error of Anitha	Error of this work	Numerical	Anitha *et al.* [8]	This Work Equation (13)	Error of Anitha	Error of this work	Numerical	Anitha *et al.* [8]	This Work Equation (13)	Error of Anitha	Error of this work	Numerical	Anitha *et al.* [8]	This Work Equation (13)	Error of Anitha	Error of this work
0	1	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00
0.2	1	1.0000	1.0000	0.00	0.00	0.9996	0.9996	0.9996	0.00	0.00	0.9962	0.9962	0.9962	0.00	0.00	0.9924	0.9924	0.9924	0.00	0.00
0.4	1	0.9999	0.9999	0.00	0.01	0.9994	0.9994	0.9994	0.00	0.00	0.9944	0.9943	0.9944	0.01	0.00	0.9987	0.9986	0.9987	0.01	0.00
0.6	1	0.9999	0.9999	0.00	0.01	0.9994	0.9994	0.9994	0.00	0.00	0.9944	0.9943	0.9944	0.01	0.00	0.9987	0.9986	0.9987	0.0\1	0.00
0.8	1	1.0000	1.0000	0.00	0.00	0.9996	0.9996	0.9996	0.00	0.00	0.9962	0.9962	0.9962	0.00	0.00	0.9924	0.9924	0.9924	0.00	0.00
1	1	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00	1.0000	1.0000	1.0000	0.00	0.00
	Average error			0.00	0.00	Average error			0.00	0.00	Average error			0.00	0.00	Average error			0.00	0.00

the optimization of the parameters in enzyme model. The extension of the prodecure to other immobilized oxidase enzyme electrode systems at steady and non-steady state condition seems possible.

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Nomenclature

Symbols:

Parameters	Description	Units
$[E_t]$	Total active enzyme concentration in the matrix	mmol/L
$[E_{ox}]$	Enzyme concentration of the oxidized mediator	mmol/L
[ES]	Enzyme concentration of the substrate	mmol/L
$[E_{red}]$	Reduced enzyme concentration	mmol/L
$[O_2]$	Concentration of oxygen at any position in the enzyme layer	mmol/L
$[O_2]_b$	Oxygen concentration in the bulk electrolyte	mmol/L
[S]	Concentration of substrate at any position in the enzyme layer	mmol/L
$[S]_b$	Substrate concentration in the bulk electrolyte	mmol/L
[Medox]	Concentration of oxidised mediator at any position in the enzyme layer	mmol/L
$[Medox]_b$	Oxidised mediator concentration in the bulk electrolyte	mmol/L
D_o	Diffusion coefficient of oxygen	$cm^2 \cdot s^{-1}$
D_s	Diffusion coefficient of substrate	$cm^2 \cdot s^{-1}$
D_m	Diffusion coefficient of mediator	$cm^2 \cdot s^{-1}$
d	Enzyme layer thickness	cm
y	Distance from the electrode	cm
$k1$, $k4$, $k5$	Rate constants	$L \cdot mol^{-1} \cdot s^{-1}$
$k2$, $k3$	Rate constants	s^{-1}
K_o	Partitioning coefficient for oxygen	None
K_s	Partitioning coefficient for substrate	None
K_m	Partitioning coefficient for mediator	None
B_o	Normalized surface concentration of oxygen	None
B_s	Normalized surface concentration of the substrate	None
B_m	Normalized surface concentration of mediator	None
F_o	Normalized oxygen concentration	None
F_s	Normalized substrate concentration	None
F_m	Normalized mediator concentration	None
x	Normalized distance from the electrode	None
J_{ox}	Normalized current	None

Greek symbols:

Φ_o^2	Thiele modulus for the oxygen	Normalized
Φ_s^2	Thiele modulus for the substrate	Normalized
Φ_m^2	Thiele modulus for the mediator	Normalized
o	Oxygen	Subscripts
s	Substrate	Subscripts
m	Mediator	Subscripts
ox	Oxidized species	Subscripts
red	Reduced species	Subscripts
t	Total	Subscripts
∞	Bulk solution	Subscripts

Appendix: A

Approximate Analytical Solution of Equations (4)-(6) Using New Approach of Homotopy Perturbation Method.

Here, we have indicated how to obtain the solution of Equations (4)-(6) using the initial and boundary conditions Equation (7) & Equation (8). We consider the following non-linear differential equation.

$$L(u)+N(u)-f(r)=0, r\in\Omega \tag{A1}$$

where L is a linear operator, N is a non-linear operator, u is an unknown function, and $f(r)$ is a given continuous function. We construct a homotopy which satisfies.

$$(1-p)\left[L(u)\right]+p\left[L(u)+N(u)-f(r)\right]=0 \tag{A2}$$

Here p [0, 1] is an embedded parameter. Using the above Equation (A2), we can construct the homotopy [8] for the Equations (4)-(6), as follows:

$$\begin{aligned}&(1-p)\left[\left(\frac{d^2F_s}{dx^2}\right)-\Phi_s^2\left(1+\frac{1}{F_o(x=0)B_o+F_m(x=0)B_m}+\frac{1}{F_s(x=0)B_s}\right)^{-1}\right]\\&+P\left[\left(\frac{d^2F_s}{dx^2}\right)-\Phi_s^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1}\right]=0\end{aligned} \tag{A3}$$

$$\begin{aligned}&(1-p)\left[\left(\frac{d^2F_o}{dx^2}\right)-\Phi_s^2\left(1+\frac{1}{F_o(x=0)B_o+F_m(x=o)B_m}+\frac{1}{F_s(x=0)B_s}\right)^{-1}\right]\\&\frac{F_oB_o}{F_o(x=0)B_o+F_m(x=0)B_m}+P\left[\left(\frac{d^2F_o}{dx^2}\right)-\Phi_s^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1}\right]\\&\frac{F_oB_o}{F_oB_o+F_mB_m}=0\end{aligned} \tag{A4}$$

$$\begin{aligned}&(1-p)\left[\left(\frac{d^2F_m}{dx^2}\right)-\Phi_m^2\left(1+\frac{1}{F_o(x=0)B_o+F_m(x=0)B_m}+\frac{1}{F_s(x=0)B_s}\right)^{-1}\right]\\&\frac{F_mB_m}{F_o(x=0)B_o+F_m(x=0)B_m}+P\left[\left(\frac{d^2F_o}{dx^2}\right)-\Phi_s^2\left(1+\frac{1}{F_oB_o+F_mB_m}+\frac{1}{F_sB_s}\right)^{-1}\right]\\&\frac{F_mB_m}{F_oB_o+F_mB_m}=0\end{aligned} \tag{A5}$$

Supposing the approximate solutions of Equations (4)-(6) have the form

$$\left.\begin{aligned}F_s&=F_{s,0}+pF_{s,1}+p^2F_{s,2}+\cdots\cdots\cdots\\F_o&=F_{o,0}+pF_{o1}+p^2F_{o,2}+\cdots\cdots\cdots\\F_m&=F_{m,0}+pF_{m,1}+p^2F_{m,2}+\cdots\cdots\end{aligned}\right\} \tag{A6}$$

Substituting Equation (A6) into Equations (A3)-(A5) (respectively), and equate the terms with the identical powers of p, we obtain.

$$P^0 : \frac{d^2F_{s,0}}{dx^2} - \Phi_s^2\left(1+\frac{1}{F_o(x=0)B_o + F_m(x=0)B_m} + \frac{1}{F_s(x=0)B_s}\right)^{-1} = 0 \tag{A7}$$

$$P^0 : \frac{d^2F_{o,0}}{dx^2} - \Phi_o^2\left(1+\frac{1}{F_o(x=0)B_o + F_m(x=0)B_m} + \frac{1}{F_s(x=0)B_s}\right)^{-1} \frac{F_oB_o}{F_o(x=0)B_o + F_m(x=0)B_m} = 0 \tag{A8}$$

$$P^0 : \frac{d^2F_{m,0}}{dx^2} - \Phi_m^2\left(1+\frac{1}{F_o(x=0)B_o + F_m(x=0)B_m} + \frac{1}{F_s(x=0)B_s}\right)^{-1} \frac{F_mB_m}{F_o(x=0)B_o + F_m(x=0)B_m} = 0 \tag{A9}$$

The above equations can be written as

$$P^0 : \frac{d^2F_{s,0}}{dx^2} - \left(\frac{\Phi_s^2(B_o+B_m)B_s}{(B_o+B_m)B_s + B_o + B_m + B_s}\right)F_s = 0 \tag{A10}$$

$$P^0 : \frac{d^2F_{o,0}}{dx^2} - \left(\frac{\Phi_o^2 B_oB_s}{(B_o+B_m)B_s + B_o + B_m + B_s}\right)F_o = 0 \tag{A11}$$

$$P^0 : \frac{d^2F_{m,0}}{dx^2} - \left(\frac{\Phi_m^2 B_mB_s}{(B_o+B_m)B_s + B_o + B_m + B_s}\right)F_m = 0 \tag{A12}$$

The initial approximations boundary conditions Equation (7) and Equation (8) are as follows.

$$F_{s,0}(x=1) = 1; F_{o,0}(x=1) = 1; F_{m,0}(x=1) = 1 \tag{A13}$$

$$F_{m,0}(x=0) = 1; \ \frac{dF_{o,0}(x=0)}{dx} = \frac{dF_{s,0}(x=0)}{dx} = 0 \tag{A14}$$

And

$$F_{s,i}(x=1) = 0; F_{o,i}(x=1) = 0; F_{m,i}(x=1) = 0 \ i = 1,2,3,\cdots \tag{A15}$$

$$F_{m,i}(x=0) = 0; \frac{dF_{o,i}(x=0)}{dx} = \frac{dF_{s,i}(x=0)}{dx} = 0 \ \ i = 1,2,3,\cdots \tag{A16}$$

Solving the Equations (A7)-(A9) and using the boundary conditions Equation (A13) and Equation (A14) we get

$$F_{s,0}(x) = \frac{Cosh\sqrt{A}x}{Cosh\sqrt{A}} \tag{A17}$$

$$F_{o,0}(x) = \frac{Cosh\sqrt{B}x}{Cosh\sqrt{B}} \tag{A18}$$

$$F_{m,0}(x) = e^{\sqrt{E}x} - \frac{\left(e^{\sqrt{E}} - 1\right)Sinh\sqrt{E}x}{Sinh\sqrt{E}} \tag{A19}$$

where

$$A = \frac{\Phi_s^2 \left(B_o + B_m\right) B_s}{\left(B_o + B_m\right) B_s + B_s + B_o + B_m}$$

$$B = \frac{\Phi_o^2 B_o B_s}{\left(B_o + B_m\right) B_s + B_s + B_o + B_m}$$

$$E = \frac{\Phi_m^2 B_m B_s}{\left(B_o + B_m\right) B_s + B_s + B_o + B_m}$$

Using the basic assumptions underlying the homotopy method, we obtain since the

$$F_s(x) = {}_p\underrightarrow{\lim}_1 F_{s,i} \approx F_{s,0} \tag{A20}$$

$$F_o(x) = {}_p\underrightarrow{\lim}_1 F_{o,i} \approx F_{o,0} \tag{A21}$$

$$F_m(x) = {}_p\underrightarrow{\lim}_1 F_{m,i} \approx F_{m,0} \tag{A22}$$

value of the first order iteration $F_{s,1}$, $F_{o,1}$, $F_{m,1}$ is negligible. Substituting Equations (A 17)-(A19) in Equations (A 20)-(A22), Equations (4)-(6) of the text.

Appendix: B

Matlab Program to Find the Numerical Solution of Equations (4)-(6)

```
function pdex4
m = 0;
x = linspace (0,0.5);
t = linspace (0,100);
sol = pdepe (m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
xlabel('Distance x')
ylabel('u1(x,2)')
figure
plot(x,u2(end,:))
xlabel('Distance x')
ylabel('u2(x,2)')
figure
plot(x,u3(end,:))
xlabel('Distance x')
ylabel('u3(x,2)')
% --------------------------------------------------------------
function [c,f,s] = pdex4pde(x,t,u,DuDx)
Bs=0.5;
Bo=0.05;
Bm=0.1;
A=0.1;
J=0.1;
E=0.1;
```

```
c = [1;1;1];
f = [1;1;1].* DuDx;
F1 =-A/(1+1/(u(2)*Bo+u(3)*Bm)+1/(u(1)*Bs));
F2 =-J/(1+1/(u(2)*Bo+u(3)*Bm)+1/(u(1)*Bs))*(u(2)*Bo/(u(2)*Bo+u(3)*Bm));
F3 =-E/(1+1/(u(2)*Bo+u(3)*Bm)+1/(u(1)*Bs))*(u(3)*Bm/(u(2)*Bo+u(3)*Bm));
s = [F1; F2; F3];
% --------------------------------------------------------------
functionu0 = pdex4ic(x)
u0 = [0; 0; 1];
% --------------------------------------------------------------
function [pl,ql,pr,qr] = pdex4bc(xl,ul,xr,ur,t)
pl = [0; 0 ; ul(3)-1];
ql = [1; 1 ; 0];
pr = [ur(1)-1; ur(2)-1 ; ur(3)-1];
qr = [0; 0; 0];
```