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Steady-State Substrate and Product Concentrations for Non-Michaelis-Menten Kinetics in an Amperometric Biosensor – Hyperbolic Function and PadéApproximants Method

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A theoretical model is presented for an amperometric biosensor with inhibition of the substrate. This model is based on the non-stationary diffusion equations which contains a non-linear term connected to the enzymatic reaction of non-Michaelis-Menten kinetics. This paper describes the analytical representation of concentrations for steady-state conditions and for all parameter values. Hyperbolic function and Padé approximants method are used to evaluate the analytical expressions of concentration of substrate, product, substrate flux and current. A comparison of our estimated analytical results with the numerical simulation and previous analytical results available is provided. This observed a good agreement.

Keywords: Mathematical modeling; Non-linear equation; Hyperbolic function method; Padé approximants method; Amperometric biosensor; Non-Michaelis-Menten kinetics; Substrate Inhibition; Steady-state.

1. INTRODUCTION

Biosensors are analytical instruments that closely combine elements of biorecognition and a physical transducer to detect target compounds. An amperometric biosensor is a tool used in a solution to measure the concentration of a specific particular chemical or biochemical substances [1-7]. In biosensor, many enzymes are inhibited by their substrates. In the literature, the theoretical model has been widely applied as an essential tool to study and optimize the analytical characteristics of biosensors. Practical biosensors contain a multilayer enzyme membrane; Exploratory monolayer membrane-containing biosensors are widely used to study the biochemical behavior of biosensors. The inhibition of substrates is often considered a biochemical oddity and experimental annoyance.

To reduce the biosensor properties, the biosensor model was constructed with a substrate and product inhibition. Visuvasam et al. [8] discussed the non-steady state model of a biosensor based on microdisk enzymes where the enzyme reacts directly to the electrode itself and is based on a diffusion equation containing a non-linear term related to the enzymatic reaction kinetics of Michaelis-Menten. Dong et al. [9] and Lyons et al. [10] reported analytical expression for the steady-state current at a chemical sensor with a microdisk. The current at a microdisk biosensor where an enzyme is present in bulk solution has been described by Galceran and coworkers [11]. But there was no reported model for immobilized enzymes on the microdisk. Kirthiga et al. [12] discussed non-linear reaction-diffusion equations in a mono-enzymatic biosensor that includes a Michaelis – Menten kinetics equation.Rasi et al.[13] presented the estimated analytical expressions for the steady-state substrate and co-substrate concentration of different enzyme kinetics over amperometric biosensors. Manimozhi et al.[14] used the homotopy perturbation method (HPM) and the variational iteration method (VIM) to find a steady-state substrate concentrations.Already the analytical expression for steady-state concentrations of substrate and product with substrate inhibition using the Adomian decomposition method was discussed by Anitha et al. [15]. Senthamarai et al. [16] evaluated the non-steady state substrate concentration in the action of biosensor at mixed enzyme kinetics. In this paper, for all values of reaction/diffusion parameters, we have derived an analytical expression corresponding to the steady-state concentrations of substrate, product, and current using the Hyperbolic function method, and Padé approximants method. Also, our analytical results are compared with numerical simulation.

2. MATHEMATICAL FORMULATION OF THE PROBLEMS

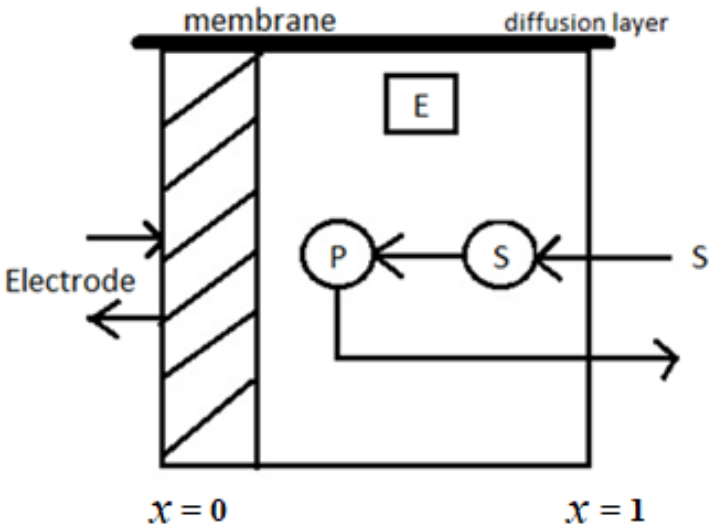

Figure 1. Schematic representation of biosensor.

In the enzyme reaction,

$$E + S \leftrightarrow ES \rightarrow E + P \quad (1)$$

the substrate (S) binds to the enzyme (E) in order to form an enzyme-substrate complex ES. The substrate is converted to product (P) while it is part of this complex. The rate of the product's appearance depends on its substrate concentration. Figure.1 [15] illustrates the basic model used in this work and a definition of the coordinate system.

For example, the simplest scheme of non-Michaelis-Menten kinetics may have been obtained by adding to the Michaelis-Menten scheme (Equation (1)), a stage of enzyme-substrate complex (ES) interaction with another substrate molecule (S) (Equation (2)) after the non-active complex (ESS) is generated as follows [6]:

$$ES + S \leftrightarrow ESS \tag{2}$$

The steady-state non-linear differential equations for the substrate inhibition are

$$D_s \frac{d^2 s(x)}{dx^2} = \frac{V_{\max} s(x)}{k_m + s(x) + \frac{(s(x))^2}{k_s}} \tag{3}$$

$$D_p \frac{d^2 p(x)}{dx^2} = \frac{-V_{\max} s(x)}{k_m + s(x) + \frac{(s(x))^2}{k_s}} \tag{4}$$

where D_s, D_p are the diffusion coefficients of the substrate and product in the enzyme layer. $s(x)$ and $p(x)$ are the concentration of substrate and product in the enzyme layer. V_{max} is the maximal enzymatic rate, k_M denotes the Michaelis-Menten constant and d is the thickness of the enzyme layer. The equations are resolved for the following boundary conditions [6].

$$\frac{ds}{dx}(x=0) = 0, s(x=d) = s^* \tag{5}$$

$$p(x=0) = 0, p(x=d) = 0 \tag{6}$$

The current density I of the biosensor is expressed as follows:

$$I = n_e F D_p \left.\frac{dp(x)}{dx}\right|_{x=0} \tag{7}$$

The steady-state enzyme surface activity rate (V_s), following the scheme (1,2) is defined by

$$V_s^* = \frac{V_{\max} d s^*}{k_m + s^* + \frac{(s^*)^2}{k_s}} \tag{8}$$

At steady-state conditions, the substrate flux (J_s) through the Nernst diffusion layer is equal to the enzymatic rate (V_s) on the surface:

$$J_s = \frac{D_s (s_0 - s^*)}{\delta} = \frac{V_{\max} d s^*}{k_m + s^* + \frac{(s^*)^2}{k_s}} \tag{9}$$

where s_0 is the concentration of substrate in the bulk solution, s^* is the concentration of substrate at $x = d$ and δ is thickness of the diffusion layer. We introduce the set of dimensionless variables as follows:

$$S(\chi) = \frac{s(x)}{s^*}, P(\chi) = \frac{p(x)}{s^*}, \chi = \frac{x}{d}, \varphi_s^2 = \frac{V_{\max} d^2}{D_s k_m}, \varphi_p^2 = \frac{V_{\max} d^2}{D_p k_m}, \alpha = \frac{s^*}{k_m}, \beta = \frac{(s^*)^2}{k_m k_s}$$

(10)

where S(χ) and P(χ) indicate the dimensionless concentration of substrate and product respectively. $\varphi_s^{\,2}$ and $\varphi_p^{\,2}$ denote the corresponding reaction diffusion parameters. χ represents the dimensionless distance. α and β represents the saturation parameters. The governing non-linear reaction/diffusion equations (3) and (4) are expressed in the following non-dimensionless form:

$$\frac{d^2S(\chi)}{d\chi^2} = \frac{\varphi_s^{\,2}S(\chi)}{1+\alpha S(\chi)+\beta(S(\chi))^2} \quad (11)$$

$$\frac{d^2P(\chi)}{d\chi^2} = \frac{-\varphi_p^{\,2}S(\chi)}{1+\alpha S(\chi)+\beta(S(\chi))^2} \quad (12)$$

The boundary conditions are given by:

$$\frac{dS}{d\chi}(\chi=0)=0, S(\chi=1)=1 \quad (13)$$

$$P(\chi=0)=0, P(\chi=1)=0 \quad (14)$$

The dimensionless current is reduced to

$$\psi = \frac{Id}{n_e F D_p s^*} = \left.\frac{dP(\chi)}{d\chi}\right|_{\chi=0} \quad (15)$$

3. ANALYTICAL EXPRESSION OF CONCENTRATION OF SUBSTRATE AND PRODUCT USING HYPERBOLIC FUNCTION METHOD

The hyperbolic function method is used to obtain an approximate analytical expression for the steady-state concentrations of the substrate in an amperometric biosensor with substrate inhibition using the specified boundary conditions (equation (13)). He also proposed the exponential function method for solving the non-linear equations [17]. Our method is a special case of exponential function method. The analytical expression of the dimensionless concentration of the substrate is obtained using the hyperbolic function method (Appendix-A) as follows:

$$S(\chi) = \frac{\cosh(m\chi)}{\cosh(m)} \quad (16)$$

Then, the concentration of product can be obtained by using the relation (B4) (Appendix-B) as follows:

$$P(\chi) = \frac{\varphi_p^{\,2}}{\varphi_s^{\,2}}\left(\chi + \frac{1}{\cosh(m)}(1-\chi-\cosh(m\chi))\right) \quad (17)$$

where,

$$m = \frac{\varphi_s}{\sqrt{1+\alpha+\beta}} \quad (18)$$

The dimension current, ψ

$$\psi = \left.\frac{dP(\chi)}{d\chi}\right|_{\chi=0} = \frac{{\varphi_p}^2}{{\varphi_s}^2}\left(1-\frac{1}{\cosh(m)}\right) = \frac{D_s}{D_p}\left(1-\sec h\left(d\sqrt{\frac{V_{\max}}{D_s k_m\left(1+\frac{s^*}{k_m}\left(1+\frac{s^*}{k_m}\frac{k_m}{k_s}\right)\right)}}\right)\right) \tag{19}$$

4. ANALYTICAL EXPRESSION OF CONCENTRATION OF SUBSTRATE AND PRODUCT USING PADÉ APPROXIMANTS METHOD

In mathematics, the "best" approximation of a function by a rational function of the given order is a Padé approximants. Under this methodology, the approximation's power series correlates with the power series of the function it approximates. Henri Padé invented the method, but it goes back to Georg Frobenius, who introduced the idea and studied the features of rational power series approximations. More recently, Ji-Huan He solved the one-dimensional convection-diffusion equation and its fractional modification for E reaction arising in rotating disk electrodes [18] using this method. Also, He developed the Taylor series and Padé approximants solution for fractal Bratu-type equations arising in the electrospinning process [19] and lane-emden equation [20]. He also proposed the exponential function method for solving the non-linear equations [21]. Saravana Kumar et al. [22] discussed an E-reaction convection-diffusion equation in rotating disk electrodes and solved the equations using the Taylor series method and the Pade approximants method. The Padé approximants also gives the function a better approximants than truncating the Taylor series, and it may still perform where the Taylor series does not converge. Padé approximants are widely used in computer calculations for these purposes. The analytical expression of concentration of substrate and product are obtained using Padé approximants method (Appendix -C) for α = 0.1, β = 0.02, ${\varphi_s}^2 = 0.1, {\varphi_p}^2 = 5$ and $a = 0.9567737660$ are as follows:

$$S(\chi) = \frac{9.5677 + 0.4217\,\chi^2 + 0.2664\times10^{-2}\,\chi^4}{10 - 0.8059\times10^{-2}\,\chi^2 + 0.1871\times10^{-3}\,\chi^4} \tag{20}$$

$$P(\chi) = \frac{2.16131\,\chi - 2.14719\,\chi^2 - 1.74179\times10^{-3}\,\chi^3 - 1.24244\times10^{-2}\,\chi^4 + 4.04331\times10^{-5}\,\chi^5}{1 - 8.05895\times10^{-4}\,\chi^2 + 1.87077\times10^{-5}\,\chi^4} \tag{21}$$

5. ESTIMATION OF PARAMETERS

From the equation (3) we can get the steady-state surface rate (V_s^*) of enzyme activity as follows:

$$V_s^* = \frac{V_{\max} d s^*}{k_m + s^* + \frac{(s^*)^2}{k_s}} \tag{22}$$

This equation can be rewritten as

$$\frac{s^*}{V_s^*} = \left(\frac{k_m}{d\,V_{\max}}\right) + \left(\frac{1}{d\,V_{\max}}\right)s^* + \left(\frac{1}{d\,k_s V_{\max}}\right)\left(s^*\right)^2 \qquad (23)$$

This is of the form $y = a + bx + cx^2$. Fitting a second degree parabola curve using least square, we can find Michaelis-Menten constant (k_m), maximal enzymatic rate $(V_{\max})$ and thickness of the enzyme layer (d).

6. NUMERICAL SIMULATION

The non-linear differential equations (11) and (12) with the boundary conditions (13) and (14) are solved numerically by using the function pdex4 in Scilab/Matlab, numerical software. The analytical solutions (equations (16) and (17)) are compared with the numerical solutions in Figures.2-3. The concentration of substrate by Padé approximants (equation (20)) and by Hyperbolic function method (equation (16)) are compared with a numerical solution in Figure.5.

Table.1 and Table.2 represent the comparison between numerical and analytical results by Padé approximants and Hyperbolic function method. Also, the average relative errors are given in the respective tables. From Table.1and Table.2 it is confirmed that the Padé approximants method is the effective method for obtaining the analytical expressions for steady-state concentrations of substrate and product in an amperometric biosensor compared to the hyperbolic function method. Padé technique can be used in solving large scale of nonlinear differential equations in chemical sciences.

Table 1. Comparison of numerical solution of concentration of substrate with the analytical solutionsby hyperbolic function method and Padé approximants method for $\alpha = 0.1, \beta = 0.02$ and for different values of $\varphi_s{}^2$.

	$\varphi_s{}^2 = 0.1$					$\varphi_s{}^2 = 1$					$\varphi_s{}^2 = 5$					$\varphi_s{}^2 = 15$				
χ	Num	Hyp (Eq.16)	Padé (Eq.20)	Error % for Hyp	Error % for Padé	Num	Hyp (Eq.16)	Padé (Eq.20)	Error % for Hyp	Error % for Padé	Num	Hyp (Eq.16)	Padé (Eq.20)	Error % for Hyp	Error % for Padé	Num	Hyp (Eq.16)	Padé (Eq.20)	Errorr % for Hyp	Error % for Padé
0	0.957	0.912	0.957	0.02	0	0.667	0.675	0.668	1.12	0.03	0.22	0.238	0.220	8.27	0.14	0.043	0.051	0.0447	14.46	3.62
0.25	0.959	0.917	0.959	0.02	0	0.687	0.694	0.687	1.02	0.01	0.255	0.272	0.255	6.74	0.16	0.065	0.075	0.0677	10.94	3.61
0.5	0.968	0.933	0.968	0.02	0	0.748	0.752	0.748	0.56	0.01	0.371	0.384	0.372	3.39	0.13	0.155	0.167	0.1601	5.141	3.56
0.75	0.981	0.960	0.981	0	0	0.848	0.852	0.848	0.53	0.01	0.592	0.606	0.593	2.28	0.10	0.385	0.398	0.398	3.374	3.24
1	1	1	1	0	0	1	1	1	0	0	1	1	1	0	0	1	1	1	0	0
Average Error %				0.01	0	**Average Error %**			0.66	0.01	**Average Error %**			4.14	0.11	**Average Error %**			6.78	2.81

Table 2. Comparison of numerical solution of concentration of product with the analytical solution by hyperbolic function method and Padé approximants method for $\alpha = 0.1,\ \beta = 0.02, \varphi_s{}^2 = 5$ and for different values of $\varphi_p{}^2$.

χ	$\varphi_p{}^2 = 0.1$					$\varphi_p{}^2 = 1$					$\varphi_p{}^2 = 5$					$\varphi_p{}^2 = 15$				
	Num	**Hyp (Eq.17)**	**Padé (Eq.21)**	**Error % for Hyp**	**Error % for Padé**	**Num**	**Hyp (Eq.17)**	**Padé (Eq.21)**	**Error % for Hyp**	**Error % for Padé**	**Num**	**Hyp (Eq.17)**	**Padé (Eq.21)**	**Error % for Hyp**	**Error % for Padé**	**Num**	**Hyp (Eq.17)**	**Padé (Eq.21)**	**Errorr % for Hyp**	**Error % for Padé**
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.25	0.003	0.003	0.003	3.12	0	0.032	0.031	0.032	3.09	0	0.162	0.156	0.162	3.34	0.06	0.485	0.469	0.4851	3.36	0.08
0.5	0.005	0.005	0.005	2.08	0	0.048	0.047	0.048	3.09	0.21	0.242	0.235	0.242	3.05	0.12	0.727	0.705	0.7263	3.05	0.14
0.75	0.004	0.004	0.004	2.38	0	0.042	0.041	0.042	3.27	0.19	0.211	0.204	0.210	3.32	0.24	0.633	0.612	0.6312	3.26	0.22
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Average Error %				1.52	0	**Average Error %**			1.89	0.08	**Average Error %**			1.94	0.08	**Average Error %**			1.93	0.09

Table 3. Comparison of numerical solution of concentration of substrate with our analytical results and the previous analytical results for $\alpha = 5,\ \beta = 2.5$ and for different values of $\varphi_s{}^2$.

χ	$\varphi_s{}^2 = 0.1$									$\varphi_s{}^2 = 5$								
	Num	**Hyp (Eq.17)**	**Padé (Eq.21)**	**HPM [14]**	**ADM [15]**	**Error % for Hyp**	**Error % for Padé**	**Error % for HPM**	**Error % for ADM**	**Num**	**Hyp (Eq.17)**	**Padé (Eq.21)**	**HPM [14]**	**ADM [15]**	**Error % for Hyp**	**Error % for Padé**	**Error % for HPM**	**Error % for ADM**
0	0.941	0.944	0.941	0.941	0.941	0.34	0	0.02	0	0.695	0.764	0.695	0.695	0.693	9.83	0	0.115	0.345
0.25	0.944	0.947	0.944	0.940	0.944	0.31	0.01	0.44	0.01	0.715	0.778	0.715	0.699	0.712	8.81	0.05	2.18	0.3634
0.5	0.956	0.958	0.955	0.959	0.955	0.21	0.03	0.34	0.02	0.773	0.821	0.772	0.749	0.770	6.13	0.194	3.14	0.414
0.75	0.974	0.9753	0.974	0.970	0.974	0.15	0.03	0.40	0.04	0.866	0.894	0.867	0.847	0.866	3.20	0.127	2.16	0.035
1	1	1	1	1	1	0	0	0	0	1	1	1	1	0.999	0	0	0	0.01
Average Error %						0.20	0.01	0.24	0.01	**Average Error %**					5.59	0.075	1.519	0.233

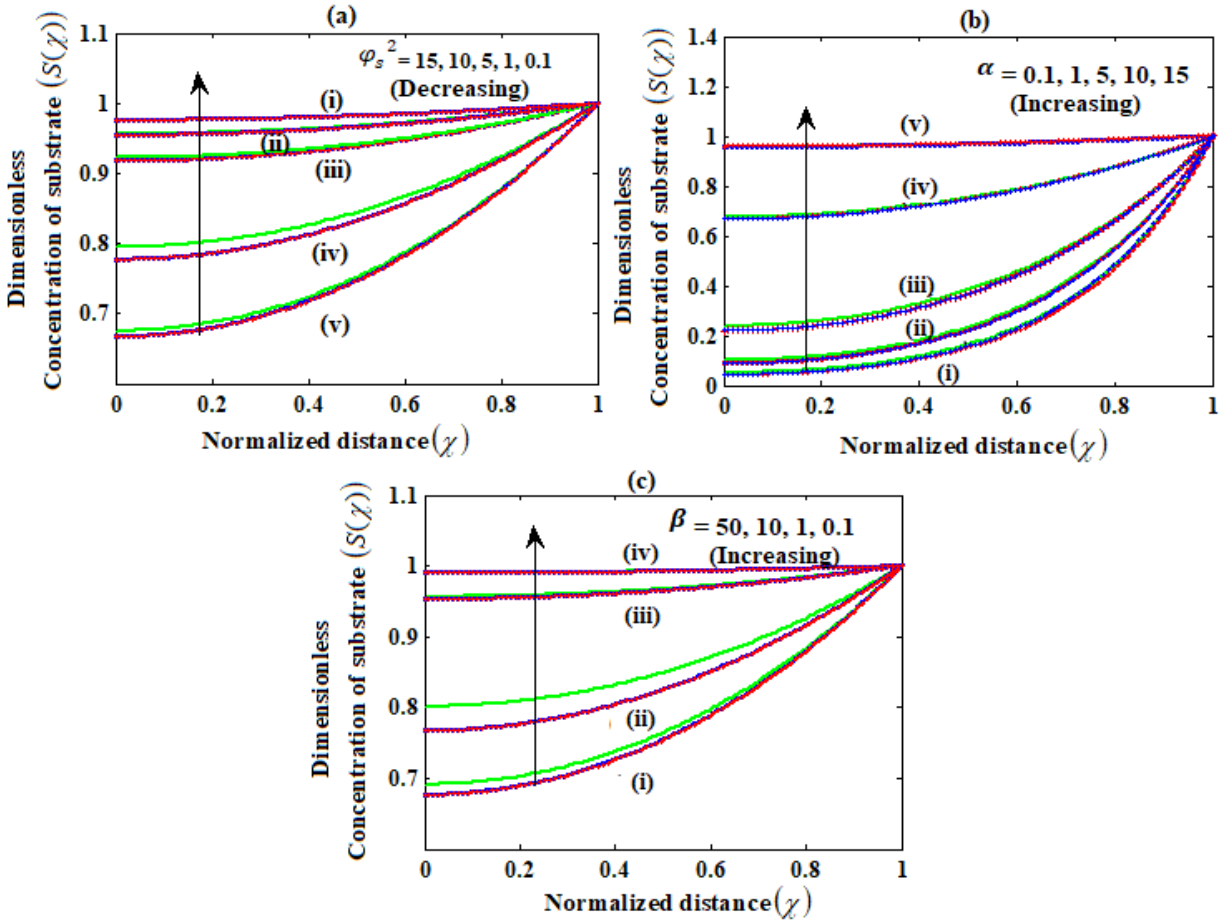

Figure 2. Dimensionless concentration of substrate, $S(\chi)$versus normalized distance,χ**(a) (a)**for $\alpha = 0.1, \beta = 0.02$ and for different values of $\varphi_s{}^2$.**(b)** for $\varphi_s{}^2 = 1, \beta = 0.02$ and for different values of α. **(c)**for $\varphi_s{}^2 = 1, \alpha = 0.1$and for different values of β. where green line represents the analytical result (equation 16) by hyperbolic function method, blue line represents the analytical result (equation 20) by Padé approximants method and red line represent the numerical method.

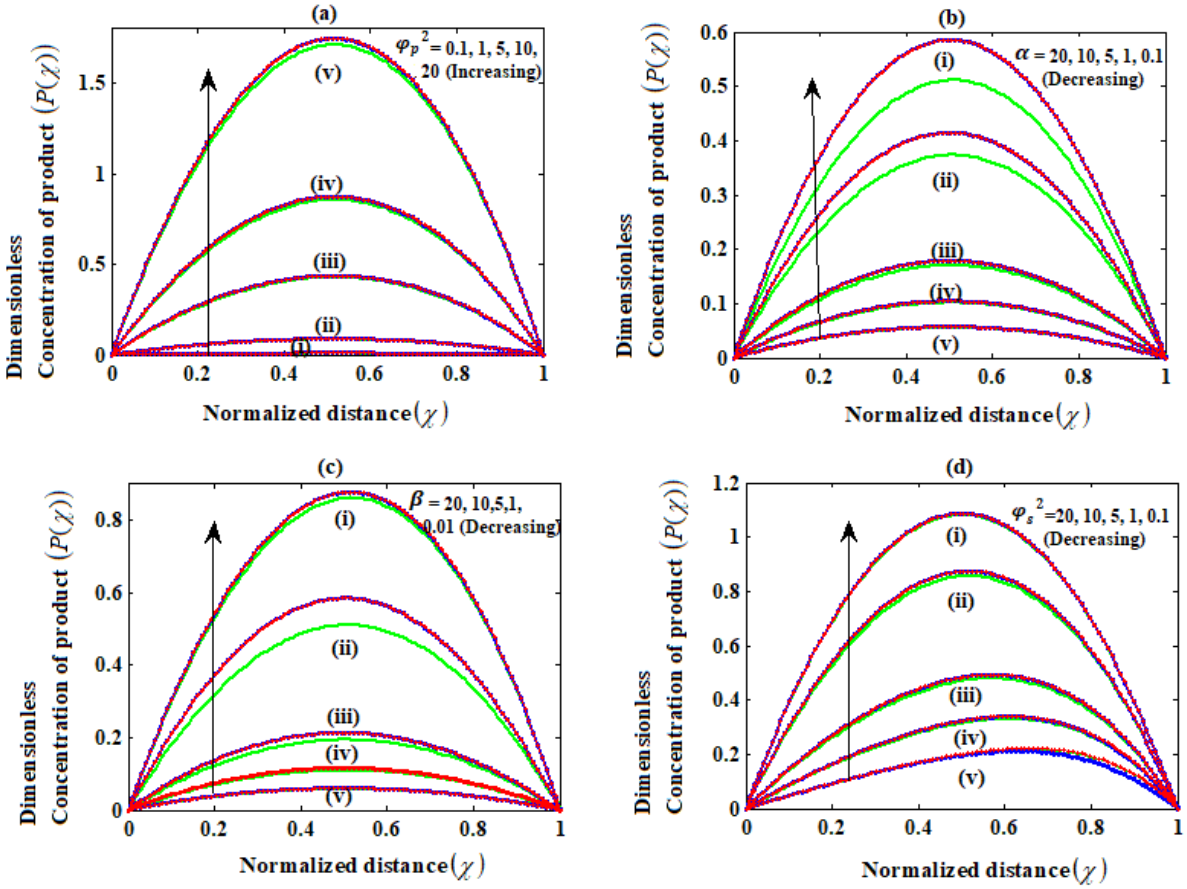

Figure 3. Dimensionless concentration of product, $P(\chi)$versus normalized distance,χ **(a)** for $\alpha = 0.1, \beta = 0.02, {\varphi_s}^2 = 1$ and for various value of ${\varphi_p}^2$. **(b)**for ${\varphi_s}^2 = 0.1, {\varphi_p}^2 = 10, \beta = 1$ and for various value of α. **(c)**for ${\varphi_s}^2 = 0.1, {\varphi_p}^2 = 1, \alpha = 0.1$ and for various value of β. **(d)**for $\alpha = 0.1, \beta = 0.02, {\varphi_p}^2 = 10$ and for various value of ${\varphi_s}^2$. where green line represents the analytical result (equation 17) by hyperbolic function method, blue line represents the analytical result (equation 21) by Padé approximants method and red line represent the numerical solution.

7. RESULT AND DISCUSSION

The nonlinear equations (11) and (12) are solved analytically using the Hyperbolic function method. Equations (16), (17) and (20), (21) are the simple and closed-form of analytical expressions for the concentration of substrate and product for different values of parameters such as substrate reaction-diffusion parameter $({\varphi_s}^2)$, product reaction-diffusion parameter $({\varphi_p}^2)$, and saturation parameters (α and β) respectively. The concentration of substrate and product depends upon the Thiele module and saturation parameters. The Thiele module, ${\varphi_i}^2 = V_{max} d^2 / D_i k_m$ basically compares the enzyme reaction rate and the enzyme layer diffusion rate. If the Thiele module is small (${\varphi_i}^2 < 1$),then the biosensor response predominates in enzyme kinetics. The total amount of active enzyme governs the overall kinetics. The response is under diffusion control, if the Thiele module is

large($\varphi_i{}^2 > 1$), which is observed at high catalytic activity and active membrane thickness or low reaction rate constant or diffusion coefficient values.

Figure.2a shows the concentration of substrate versus normalized distance for different values of a parameter. It is observed from this figure that the concentration of the substrate decreases when $\varphi_s{}^2$ increases. Figure.2band Figure.2c shows the concentration of substrate versus normalized distance for various values of parameters. It follows from these figures that the concentration of substrate increases when α and β increases. Figure.3a represents the concentration of product versus normalized distance for different values of parameters. It is observed from this figure that the concentration of product increases when $\varphi_p{}^2$ increases. Figure.3b, Figure.3c,andFigure.3d shows that the concentration of product versus normalized distance for various values of parameters. It is observed from those figures that the concentration of the product decreases whenα, β and $\varphi_s{}^2$increases. It follows from the figures that the concentration of the substrate attains its maximum at $\chi = 1$ and minimum at$\chi = 0$. Also, the concentration of the product attains its maximum at $\chi = 0.5$and minimum at $\chi = 0$and$\chi = 1$.

In Table.3, our analytical result for the concentration substrate is compared with the previous analytical results [14,15]. From this Table, it is observed that the Padé approximants method is an effective method when compared to other methods (Hyperbolic function method, Homotopy perturbation method, Adomian decomposition method).Figure.4a represents the dimensionless current, Ψ for all values of parameters. Figure.4b represents the substrate flux (J_s) versus for all values of parameters. From Figure.4a, it is observed that the value of the current increases when increases and reaches the maximum value and then decreases. The maximum value of the current depends on high enzyme activity and high substrate concentration.

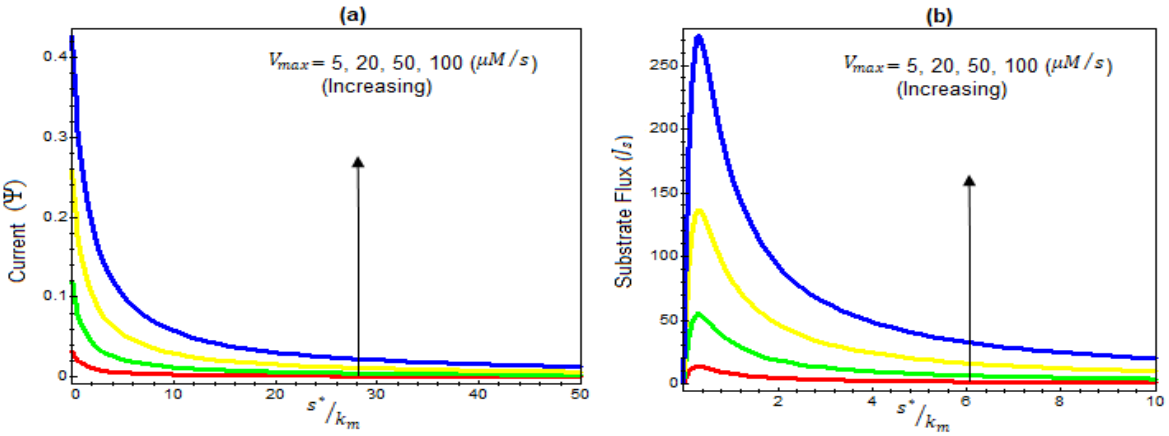

Figure.4a Dimensionless current (Ψ) (equation (19)) versus $\frac{S^*}{K_m}$ for $D_s = D_p = 300\,\mu m^2/s$, $K_m = 100\mu\text{M}, K_s = 10\mu\text{M}, d = 20\mu\text{m}$ and for different values of V_{max}.Figure.4b Substrate flux (J_s) (equation (9)) versus $\frac{S^*}{K_m}$ for , $K_m = 100\mu\text{M}, K_s = 10\mu\text{M}, d = 20\mu m$ and for different values of V_{max}.

7. CONCLUSION

This paper discusses the modeling of the amperometric biosensor with substrate inhibition. The approximate analytical expression for the concentration of the substrate, product, and current is obtained. We have successfully used the hyperbolic function approach to construct solutions for nonlinear differential equations. Also, the approximate analytical expression for the concentration of the substrate, product is obtained using Padé approximants. The primary result of this work is to calculate the concentration of substrate, product, substrate flux, and current for all values of parameters. Our simple and closed-form of analytical results are validated by the numerical result.But this method is also readily computable.Consequently, considering the solution of nonlinear differential equations, the proposed approach is worthy of further research. Also, it may find new and interesting solutions for a given nonlinear system in physical and chemical sciences.

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Nomenclature:

Parameter	Meaning	Unit
s	Concentration of Substrate	μM
p	Concentration of Product	μM
S	Dimensionless Concentration of Substrate	None
P	Dimensionless Concentration of Product	None
x	Distance	cm
χ	Dimensionless Distance	None
s^*	Concentration of substrate at $x = d$	μM
${\varphi_s}^2$	Substrate reaction diffusion parameter	None
${\varphi_p}^2$	Product reaction diffusion parameter	None
α	Saturation Parameter	None
β	Saturation Parameter	None
F	Faraday constant (96485 C/mol)	C/mol
D_s	Diffusion Coefficient of the substrate	$\mu m^2/s$
D_p	Diffusion Coefficient of the product	$\mu m^2/s$
K_m	Michaelis-Menten Constant	μM
K_s	Inhibition Constant	μM
V_{max}	Maximal enzymatic rate	$\mu M/s$
d	Thickness of the enzyme layer	μm
δ	Thickness of the diffusion layer	μm
I	Current density of the biosensor	$\mu A/cm^2$
Ψ	Dimensionless Current	None
J_s	Substrate Flux	μM

n_e	Number of electrons involved in charge transfer at the electrode surface	None

APPENDIX A:

Analytical solution of nonlinear equations (Eq.11 and Eq.12) using hyperbolic function method.

By using hyperbolic function method, we can assume that the trail function of concentration of substrate (equation (11)) is the hyperbolic function of the form,

$$S(\chi) = A_1 \cosh(m\chi) + B_1 \sinh(m\chi) \quad \text{(A1)}$$

Using the boundary conditions (equation (13) and (14)), we can obtain the constant

$$A_1 = \frac{1}{\cosh(m)},\ B_1 = 0$$

The function $S(\chi)$ becomes

$$S(\chi) = \frac{\cosh(m\chi)}{\cosh(m)} \quad \text{(A2)}$$

where, m is a constant. Also

$$\frac{dS}{d\chi} = \frac{m\sinh(m\chi)}{\cosh(m)} \quad \text{(A3)}$$

$$\frac{d^2S}{d\chi^2} = \frac{m^2\cosh(m\chi)}{\cosh(m)} \quad \text{(A4)}$$

Next, we have to find the constant m by substituting the equations (A2) to (A4) in the equation (11), we get

$$1 + \alpha\left(\frac{\cosh(m\chi)}{\cosh(m)}\right) + \beta\left(\frac{\cosh(m\chi)}{\cosh(m)}\right)^2 = \frac{\varphi_s^{\,2}}{m^2} \quad \text{(A5)}$$

When $\chi = 1$, the above equation becomes

$$1 + \alpha + \beta = \frac{\varphi_s^{\,2}}{m^2} \quad \text{(A6)}$$

Hence,

$$m = \frac{\varphi_s}{\sqrt{1+\alpha+\beta}} \quad \text{(A7)}$$

Using the relation between $S(\chi)$ and $P(\chi)$(equation ($B4$)), we can obtain $P(\chi)$

$$P(\chi) = \frac{\varphi_p^{\,2}}{\varphi_s^{\,2}}\left[\chi + \frac{1}{\cosh(m)}\left(1 - \chi - \cosh(m\chi)\right)\right] \quad \text{(A8)}$$

APPENDIX B:

Relation between the concentration of substrate and product.

Adding equations (11) and (12) we get,

$$\frac{d^2}{d\chi^2}\left(\frac{S(\chi)}{\varphi_s^{\,2}}+\frac{P(\chi)}{\varphi_p^{\,2}}\right)=0 \tag{B1}$$

Integrating twice the above equation we get the following equation.

$$\frac{S(\chi)}{\varphi_s^{\,2}}+\frac{P(\chi)}{\varphi_p^{\,2}}=C_1\chi+C_2 \tag{B2}$$

From the above equation, we can obtain the dimensionless concentration of product in terms of concentration of substrate as follows:

$$P(\chi)=\varphi_p^{\,2}\left[C_1\chi+C_2-\frac{S(\chi)}{\varphi_s^{\,2}}\right] \tag{B3}$$

The constants C_1 and C_2 can be obtained using the boundary conditions given by the equations (13) and (14). Using the boundary condition (equation (13)), we get $C_2=S(0)/\varphi_s^{\,2}$ and the boundary condition (equation (14)), we get $C_1=(1-S(0))/\varphi_s^{\,2}$.

Hence, $P(\chi)=\dfrac{\varphi_s^{\,2}}{\varphi_p^{\,2}}\left(\left(\dfrac{1-S(0)}{\varphi_s^{\,2}}\right)\chi+\dfrac{S(0)}{\varphi_s^{\,2}}-\dfrac{S(\chi)}{\varphi_s^{\,2}}\right)$ (B4)

APPENDIX C:

Analytical solution of nonlinear equation (Eq.11 and Eq.12) using Taylor series and Pade approximants method.

Consider the Maclaurin series (Taylor's series at $\chi = 0$) for dimensionless concentration of substrate, $S(\chi)$.

$$S(\chi)=S(0)+S'(0)\frac{\chi}{1!}+S''(0)\frac{\chi^2}{2!}+S'''(0)\frac{\chi^3}{3!}+S''''(0)\frac{\chi^4}{4!}+..... \tag{C1}$$

Let us consider, $S(0)=a$ where a is constant. From the boundary conditions (equation(12)),we get $S'(0)=0$. From equation (11),

$$S''(0)=\frac{\varphi_s^{\,2}a}{1+\alpha a+\beta a^2} \tag{C2}$$

$$S'''(0)=0 \tag{C3}$$

$$S''''(0)=\frac{{\varphi_s}^2 a\left(1-\beta a^2\right)}{\left(1+\alpha a+\beta a^2\right)^3} \tag{C4}$$

$$S^{(5)}(0)=0 \tag{C5}$$

$$S^{(6)}(0)=\frac{{\varphi_s}^5 a\left(1-5\alpha a-\alpha\beta a^3+7\beta^2 a^4-20\beta a^2-a^2+a^4\beta\right)}{\left(1+\alpha a+\beta a^2\right)^5} \tag{C6}$$

$$S^{(7)}(0)=0 \tag{C7}$$

$$S^{(8)}(0)=\frac{{\varphi_s}^6 a\left(1-a^2-35\alpha a-201\beta a^2+90\alpha^2 a^2+394\alpha\beta a^3+687\beta^2 a^4+2a^4\beta+a^5\beta^2\alpha-a^6\beta^2-127a^6\beta^3\right)}{\left(1+\alpha a+\beta a^2\right)^7} \tag{C8}$$

Consider,

$$S(\chi)\approx c_0+c_1\chi+c_2\chi^2+c_3\chi^3+c_4\chi^4+c_5\chi^5+c_6\chi^6+c_7\chi^7+c_8\chi^8 \tag{C9}$$

where,

$$c_0=a \tag{C10}$$

$$c_1=0 \tag{C11}$$

$$c_2=\frac{{\varphi_s}^2 a}{2\left(1+\alpha a+\beta a^2\right)} \tag{C12}$$

$$c_3=0 \tag{C13}$$

$$c_4=\frac{{\varphi_s}^2 a\left(1-\beta a^2\right)}{48\left(1+\alpha a+\beta a^2\right)^3} \tag{C14}$$

$$c_5=0 \tag{C15}$$

$$c_6=\frac{{\varphi_s}^5 a\left(1-5\alpha a-\alpha\beta a^3+7\beta^2 a^4-20\beta a^2-a^2+a^4\beta\right)}{34560\left(1+\alpha a+\beta a^2\right)^5} \tag{C16}$$

$$c_7=0 \tag{C17}$$

$$c_8=\frac{{\varphi_s}^6 a\left(1-a^2-35\alpha a-201\beta a^2+90\alpha^2 a^2+394\alpha\beta a^3+687\beta^2 a^4+2a^4\beta+a^5\beta^2\alpha-a^6\beta^2-127a^6\beta^3\right)}{1393459200\left(1+\alpha a+\beta a^2\right)^7} \tag{C18}$$

The Padé approximants is a rational fraction and is equal to Maclaurin series as follows:

$$S(\chi)=\frac{a_0+a_1\chi+a_2\chi^2+a_3\chi^3+a_4\chi^4}{1+b_1\chi+b_2\chi^2+b_3\chi^3+b_4\chi^4} \tag{C19}$$

Substitute equation (C9) instead of $S(\chi)$, we get

$$c_0+c_1\chi+c_2\chi^2+c_3\chi^3+c_4\chi^4+c_5\chi^5+c_6\chi^6+c_7\chi^7+c_8\chi^8=\frac{a_0+a_1\chi+a_2\chi^2+a_3\chi^3+a_4\chi^4}{1+b_1\chi+b_2\chi^2+b_3\chi^3+b_4\chi^4} \quad \text{(C20)}$$

$$\Rightarrow c_0+(c_1+c_0b_1)\chi+(c_2+c_1b_1+c_0b_2)\chi^2+(c_3+c_2b_1+c_1b_2+c_0b_3)\chi^3+(c_4+c_3b_1+c_2b_2+c_1b_3+c_0b_4)\chi^4+(c_5+c_4b_1+c_3b_2+c_2b_3+c_1b_4)\chi^5+(c_6+c_5b_1+c_4b_2+c_3b_3+c_2b_4)\chi^6+(c_7+c_6b_1+c_5b_2+c_4b_3+c_3b_4)\chi^7+(c_8+c_7b_1+c_6b_2+c_5b_3+c_4b_4)\chi^8=a_0+a_1\chi+a_2\chi^2+a_3\chi^3+a_4\chi^4 \quad \text{(C21)}$$

Equating the coefficients of $\chi^0,\chi,\chi^2,\chi^3,\chi^4,\chi^5,\chi^6,\chi^7,\chi^8$, we get

$$c_0=a_0 \quad \text{(C22)}$$

$$c_1+c_0b=a_1 \quad \text{(C23)}$$

$$c_2+c_1b_1+c_0b_2=a_2 \quad \text{(C24)}$$

$$c_3+c_2b_1+c_1b_2+c_0b_3=a_3 \quad \text{(C25)}$$

$$c_5+c_4b_1+c_3b_2+c_2b_3+c_1b_4=0 \quad \text{(C26)}$$

$$c_6+c_5b_1+c_4b_2+c_3b_3+c_2b_4=0 \quad \text{(C27)}$$

$$c_7+c_6b_1+c_5b_2+c_4b_3+c_3b_4=0 \quad \text{(C28)}$$

$$c_8+c_7b_1+c_6b_2+c_5b_3+c_4b_4=0 \quad \text{(C29)}$$

Since $c_1=0,c_3=0,c_5=0,c_7=0$

Solving equation (C26)and(C28),we get $b_1=0$ and $b_3=0$. Solving equation (C27) and (C29), we get

$b_2=\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}$ and $b_4=\frac{({c_6}^2-c_4c_8)}{{c_2}^2-c_2c_6}$.

Hence, $a_0=a,a_1=0,a_2=c_2+a\left(\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}\right),a_3=0,a_4=c_4+c_2\left(\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}\right)+a\left(\frac{{c_6}^2-c_4c_8}{{c_2}^2-c_2c_6}\right)$

Substituting the values of $a_i,\forall i=0$ to 4 and $b_j,\forall j=1$ to 4 in equation (C19), we get

$$S(\chi)=\frac{a+\left(c_2+a\left(\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}\right)\right)\chi^2+\left(c_4+c_2\left(\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}\right)+a\left(\frac{{c_6}^2-c_4c_8}{{c_2}^2-c_2c_6}\right)\right)\chi^4}{1+\left(\frac{c_8c_2-c_6c_4}{{c_4}^2-c_6c_2}\right)\chi^2+\left(\frac{{c_6}^2-c_4c_8}{{c_2}^2-c_2c_6}\right)\chi^4} \quad \text{(C30)}$$

In order to find the unknown constant "*a*" we have to substitute the equations (C10)- (C18) in equation (C30) ,and using the boundary condition $S(1)=1$ and substitute $\alpha=0.1,\beta=0.02,{\varphi_s}^2=0.1$,we get the unknown constant $a=0.9568$ .Hence,

$$S(\chi)=\frac{9.5677+0.4217\,\chi^2+0.2664\times10^{-2}\,\chi^4}{10-0.8059\times10^{-2}\,\chi^2+0.1871\times10^{-3}\,\chi^4} \quad \text{(C31)}$$

Using the relation between $S(\chi)$ and $P(\chi)$ in equation (B4) and using the above equation (C31) for $\alpha = 0.1, \beta = 0.02, \varphi_s^{\,2} = 0.1$ and $\varphi_p^{\,2} = 5$ we get,

$$P(\chi) = \frac{2.16131\ \chi - 2.14719\ \chi^2 - 1.74179 \times 10^{-3}\ \chi^3 - 1.24244 \times 10^{-2}\ \chi^4 + 4.04331 \times 10^{-5}\ \chi^5}{1 - 8.05895 \times 10^{-4}\ \chi^2 + 1.87077 \times 10^{-5}\ \chi^4} \tag{C32}$$

Note:

By equation (C30), for $\alpha = 0.1, \beta = 0.02$,

(i) $\varphi_s^{\,2} = 1$, the value of $a = 0.6675$.

(ii) $\varphi_s^{\,2} = 5$, the value of $a = 0.2203$.

(iii) $\varphi_s^{\,2} = 15$, the value of $a = 0.0447$.

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