International Journal of Mathematical Archive-8(9), 2017, 39-51
Available online through www.ijma.info ISSN 2229 – 5046

NEW APPROACH OF HOMOTOPY PERTURBATION METHOD TO SOLVE THE NON-LINEAR EQUATION IN BIOSENSOR

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(Received On: 01-08-17; Revised & Accepted On: 30-08-17)

ABSTRACT

T*heoretical models of diagnostic biosensors system at two basic types of enzyme kinetics is discussed in the presence of diffusion. The models are based on non stationary diffusion equation containing a non linear term related to Michaelis-Menten and ping-pong kinetics. In this paper, approximate analytical solutions are obtained for the non-linear equations under steady-state conditions by using the new Homotopy perturbation method. Simple and closed forms of analytical expressions for concentrations of substrate, product and co-substrate and corresponding current response have been derived for all values of kinetics parameters. The numerical solution of the problem is also reported here by using Scilab program. Good agreement between analytical and simulation results is noted.*

Keywords: *Biosensor, Enzyme kinetic, Non-linear equations, Reaction/diffusion equation, New Homotopy perturbation method.*

1. INTRODUCTION

A biosensors are analytical devices made up of a biological entity, usually an enzyme that recognizes a specific analyte and a transducer that translates the changes in the bio-molecules into an electrical signal [1]. The biosensors yield a signal, which is proportional to the concentration of the measured analyte. The amperometric biosensors measure the faradic current that arises on the electrode by direct electrochemical oxidation or reduction processes. These devices have been widely used in environmental, medical and industrial applications because of their high selectivity, simplicity and low cost [2]. Mathematical models are found to be an effective tool in the modeling of analytical characteristics of biosensors [3]. We consider a system where a membrane biosensor is used for the analysis of a continuously owing analyte over the membrane surface. Although practical biosensors contain a multi-layer enzyme membrane [4], the model biosensors containing the exploratory monolayer membrane are widely used to study the biochemical behavior of biosensors [3, 5]. The action of biosensor can be modeled with differential equations of substrate and products diffusion and conversion in bio catalyzed membrane [6, 7].

The developed model is based on the reaction diffusion equations, containing a nonlinear term related to non Michaelis-Menten kinetics of the enzymatic reaction [8, 9]. Manimozhi *et al.* applied the variational iteration method (VIM) and homotopy perturbation method (HPM) for the solution of steady-state substrate concentration in the action of biosensor response at mixed enzyme kinetics [10]. Anitha *et al.* [11] gave the analytical expressions for steady-state concentrations of substrate and product in an amperometric biosensor with the substrate inhibition by using the Adomian decomposition method.

The purpose of this work is to solve a model for a steady-state substrate concentration at the diagnostic biosensor at mixed enzyme kinetics using HPM. To the researcher's knowledge no exact analytical expressions of substrate concentration $S(x)$, product with concentration profiles $P(x)$, co-substrate concentration $C(x)$ and corresponding current I response has been derived for all possible values of parameters under steady-state conditions [12]. The purpose of this communication is to derive approximate analytical expressions for the steady-state concentrations and current over the diagnostic of biosensor transducers for Michaelis-Menten and Ping-Pong kinetics using homotopy perturbation method.

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2. MATHEMATICAL FORMULATION OF THE BOUNDARY VALUE PROBLEM

We assume that the electrode has symmetrical geometry and diffusion is one-dimensional in space and is described with second Fick's law. Now we can write the system of nonlinear differential equations equation for the concentrations of substrate $S(x)$, product $P(x)$ and co-substrate $C(x)$ for the diagnostic biosensor system as follows [12]:

$$\frac{d^2S}{dx^2} - \vartheta(S,C) = 0,\ \frac{1}{\lambda}\frac{d^2P}{dx^2} - \vartheta(S,C) = 0,\ \frac{1}{\mu\,\rho}\frac{d^2C}{dx^2} - \vartheta(S,C) = 0 \tag{1}$$

The non- dimensional coordinates, variables and parameters are as follows:

$$x = \frac{\delta}{l},\ S = \frac{[S]}{K_S}, C = \frac{[C]}{K_C},\ P = \frac{[P]}{K_P},\ S_o = \frac{[S]}{K_S},\ \lambda = \frac{D_S}{D_P},\ \mu = \frac{D_S}{D_C},\ \rho = \frac{K_S}{K_C}\ and\ \varphi = \frac{\left(V_m / K_S\right)}{\left(I^2 / D_S\right)} \tag{2}$$

where D_S, D_C & D_P are diffusion coefficients for substrate, co-substrate and product. K_i denotes the reaction constant for concentration profiles ($i = S, P, C$), respectively. V_m is the enzyme rate and δ represents the coordinate distance. And the l represents the thickness of active membrane, ϕ^2 is the thiele Module, λ is diffusion coefficient of product, μ is the diffusion coefficient of co-substrate and ρ is reaction rate constant for co-substrate. The diagnosis of the biosensor system depends on the enzyme kinetics and the enzyme reaction as well as on the basic transducer. The kinetics is distinguished in to two kinetics as follows:

Michaelis-Menten kinetics	Ping-Pong kinetics
$\vartheta(S,C) = \frac{\varphi^2 S}{1+S}$ (3)	$\vartheta(S,C) = \frac{\varphi^2 S}{1+\frac{1}{S}+\frac{1}{C}}$ (4)

The two types of biosensors can be described with the following system of differential equations:

Inhibitor	Michaelis-Menten kinetics	Ping-Pong kinetics
Substrate	$\frac{d^2S}{dx^2} - \frac{\varphi^2 S}{1+S} = 0$ (5)	$\frac{d^2S}{d^2x} - \frac{\varphi^2}{1+1/S+1/C} = 0$ (8)
Product	$\frac{1}{\lambda}\frac{d^2P}{dx^2} + \frac{\varphi^2 S}{1+S} = 0$ (6)	$\frac{1}{\lambda}\frac{d^2P}{d^2x} + \frac{\varphi^2}{1+1/S+1/C} = 0$ (9)
Co Substrate	$\frac{1}{\mu\,\rho}\frac{d^2C}{dx^2} - \frac{\varphi^2 S}{1+S} = 0$ (7)	$\frac{1}{\mu\,\rho}\frac{d^2C}{d^2x} - \frac{\varphi^2}{1+1/S+1/C} = 0$ (10)

Eqs. (5) - (10) are subjected to the following boundary conditions:

$$x = 0,\ S(x) = S_{in},\ P(x) = 0,\ C(x) = C_{in},\ x = l,\ \frac{dS}{dx} = 0,\ P(x) = 0,\ C(x) = 0 \tag{11}$$

The initial current of the biosensor system is recorded normally in substrate, product and co-substrate concentrations at the electrode and are as follows:

$$Is = \pm\, nFAD_S\left(\frac{dS}{dx}\right)_{x=0} \tag{12}$$

$$Ip = \pm\, nFAD_P\left(\frac{dP}{dx}\right)_{x=0} \tag{13}$$

$$Ic = \pm\, nFAD_C\left(\frac{dC}{dx}\right)_{x=0} \tag{14}$$

where n is the number of electrons taking part in electrochemical reaction, F is the Faraday's number, and A is the area of the electrode surface [m^2].

3. ANALYTICAL SOLUTIONS OF CONCENTRATIONS OF SUBSTRATE, PRODUCT AND CO-SUBSTRATE UNDER STEADY-STATE CONDITION USING THE NEW HOMOTOPY PERTURBATION METHOD

Recently many nonlinear equations are solved by using a method called Homotopy perturbation method. The benefit of the method is that it does not need small parameter in the system, and it leads to wide application in nonlinear wave equations [13]. Recently, many authors have used HPM to solve various nonlinear engineering problems [14-19]. This method is a combination of Homotopy in topology and classic perturbation techniques. The HPM has uniqueness in its applicability, accuracy, and efficiency. Recently, a new approach of HPM has been used to solve the nonlinear problem. In this method simple approximate solutions are obtained in the zeroth iteration. In this work, a new approach to Homotopy perturbation method is used (Appendix A) to solve the nonlinear differential equations (5) – (10). Using this method, the analytical expression of the concentration of substrate $S(x)$, product $P(x)$ and co-substrate $C(x)$ can be obtained as follows:

Michaelis – Menten kinetics:

Inhibitors	Concentrations	Steady State Current
Substrate	$S(x)=\frac{S_{in}\,[\mathrm{Cosh}\,\alpha_0\,(1-x)]}{\mathrm{Cosh}\,\alpha_0}$ (15)	$\psi_{S_2}=\left\lvert\frac{I_S\,l}{nFAD_S}\right\rvert=\alpha_0\,S_{in}\,\tanh\alpha_0$ (18)
Product	$P(x)=\frac{\lambda C_{in}}{\mu\beta}\left[1-\frac{\mathrm{Sinh}\,\beta_0\,(1-x)}{\mathrm{Sinh}\,\beta_0}-x\right]$ (16)	$\psi_{P_2}=\left\lvert\frac{I_P\,l}{nFAD_P}\right\rvert=\frac{\lambda C_{in}}{\mu\beta}\left[\mathrm{Coth}\,\beta_0-1\right]$ (19)
Co substrate	$C(x)=\frac{C_{in}\ \mathrm{Sinh}\,\beta_0\,(1-x)}{\mathrm{Sinh}\,\beta_0}$ (17)	$\psi_{C_2}=\left\lvert\frac{I_C\,l}{nFAD_C}\right\rvert=C_{in}\,\beta_0\,\coth\beta_0$ (20)

$$* \quad \alpha_0^2=\frac{\phi^2}{1+S_{in}},\quad \beta_0^2=\frac{\mu_i\,\rho\,\phi^2}{1+S_{in}} \tag{21}$$

Ping - Pong kinetics:

Inhibitors	Concentrations	Steady State Current
Substrate	$S(x)=\frac{S_{in}\left[\cos h\,\alpha(1-x)\right]}{\mathrm{Cos}\,h\,(\alpha)}$ (22)	$\psi_{S_3}=\left\lvert\frac{I_S\,l}{nFAD_S}\right\rvert=\alpha\,S_{in}\,\tanh\alpha$ (25)
Product	$P(x)=\frac{\lambda}{\mu\rho}\left(C_{in}-\frac{C_{in}\ \mathrm{Sin}\,h\,\beta(1-x)}{\mathrm{Sin}\,h\,\beta}-C_{in}\,x\right)$ (23)	$\psi_{P_3}=\left\lvert\frac{I_P\,l}{nFAD_P}\right\rvert=\frac{\lambda}{\mu\rho}\left[C_{in}\left[\mathrm{Coth}\,\beta-1\right]\right]$ (26)
Co substrate	$C(x)=\frac{C_{in}}{\mathrm{Sin}\,h\,\beta}\mathrm{Sin}\ h\,\beta(1-x)$ (24)	$\psi_{C_3}=\left\lvert\frac{I_C\,l}{nFAD_C}\right\rvert=C_{in}\ \beta\ \mathrm{Coth}\,\beta$ (27)

$$* \quad \alpha^2=\frac{C_{in}\ \phi^2}{S_{in}\ C_{in}\ +C_{in}\ +S_{in}},\quad \beta^2=\frac{\mu\rho\ \phi^2\ S_{in}C_0}{S_{in}\ C_{in}\ +C_{in}\ +S_{in}} \tag{28}$$

4. NUMERICAL SIMULATION

The non- linear differential Eqns. (5)-(10) with boundary conditions (11) have been solved numerically using Scilab software. A respective script pdex4 is provided in Appendix C. The numerical solutions are compared with the analytical results in Fig 4. The comparison reveals that the analytical and numerical results are satisfactory with agreement.

5. RESULTS AND DISCUSSION

The normalized non- linear differential equations are solved using a new Homotopy perturbation method. Eqs. (15-17) and (22-24) represent the analytical expression of the concentrations of substrate, product and co-substrate for various values of Thiele modulus ϕ^2 and the dimensionless parameters, for Michaelis-Menten and Ping-Pong kinetics respectively. The analytical results are compared with the numerical results in Figs (1-3).

In Fig. (1) dimensionless concentration of the substrate $S(x)$ versus dimensionless distance x is plotted for the Michaelis-Menten kinetics are calculated using Eqn.(15), for different values of the thiele modulus ϕ^2. From the figure, it is inferred that concentration substrate decreases when ϕ^2 increases.

Fig.(2) reprsents the concentration of the product $P(x)$ versus dimensionless distance x for the Michaelis-Menten kinetics are calculated using Eqn.(16), for different values of the thiele modulus ϕ^2, diffusion coefficient λ, reaction rate constant for co-substrate μ, and diffusion coefficient of co-substrate ρ. From the fig. it is inferred that concentration of product increases gradually and reaches the maximum value at $x = 0.5$ and then decreases. Also, concentration of product increases when λ and ϕ^2 increases and μ and ρ decreases.

Fig. (3) dimensionless concentration of the co-substrate $C(x)$ versus dimensionless distance x is plotted for the Michaelis-Menten kinetics are calculated using Eqn.(17), from this fig. it is noted the concentration of co-substrate increases when ϕ^2 and ρ decrease.

Fig. (4-6) represent concentrations of substrate, product and co-substrate for various values of parameters for Ping-Pong kinetics. The influence of the parameters ϕ^2, μ, ρ and λ in Ping-Pong kinetics is same as Michaelis-Menten kinetics.

6. CONCLUSIONS

In this work, a mathematical model that describes the steady-state response of a two parameters diagnostic of biosensor is discussed. New homotopy perturbation method is applied to solve the system of steady-state non-linear differential equations in different dynamic models for two types of kinetics. Analytical expressions corresponding to substrate, product and co-substrate concentrations are derived as the function of dimensionless parameters. Our analytical results for the concentration of substrate product and co-substrate are compared with simulation results satisfactory agreement is noted.

ACKNOWLEDGEMENT

This work was supported by the Department of Science and Technology, SERB-DST (EMR/2015/002279) Government of India. Also the authors thanks to Mr. S. Mohamed Jaleel, the Chairman and Dr. A. Senthil Kumar, the Principal, Sethu Institute of Technology, Kariapatti, India for their constant encouragement.

Appendix-A: Analytical solution of concentrations C, S and P by solving equations (5-7) for Michaelis-Menten kinetics.

Equations (5-7) can be written as follows:

$$\frac{d^2S}{dx^2} - \frac{\phi^2 S}{1+S} = 0 \tag{A1}$$

$$\frac{1}{\lambda}\frac{d^2P}{dx^2} + \frac{\varphi^2 S}{1+S} = 0 \tag{A2}$$

$$\frac{1}{\mu\rho}\frac{d^2C}{dx^2} - \frac{\varphi^2 S}{1+S} = 0 \tag{A3}$$

Now the boundary condition becomes

$$x = 0, \quad S(x) = S_{in}, \quad P(x) = 0, \quad C(x) = C_{in} \tag{A4}$$

$$x = 1, \quad \frac{dS}{dx} = 0, \quad P(x) = 0, \quad C(x) = C_{in} \tag{A5}$$

Equation (A1) and (A3) can be written as,

$$\frac{d^2s}{dx^2} - \frac{\varphi^2 S}{1+S} = 0 \tag{A6}$$

$$\frac{d^2P}{dx^2}+\lambda\frac{\varphi^2 S}{1+S}=0 \tag{A7}$$

$$\frac{d^2C}{dx^2}-\mu\rho\frac{\varphi^2 S}{1+S}=0 \tag{A8}$$

Homotopy for the above equation can be constructed as follows:

$$(1-p)\left[\frac{d^2S}{dx^2}-\frac{\phi^2 S}{1+S(x=0)}\right]+p\left[(1+S)\frac{d^2S}{dx^2}-\phi^2 S\right]=0 \tag{A9}$$

$$(1-p)\left[\frac{d^2P}{dx^2}-\lambda\frac{\phi^2 S}{1+S(x=0)}\right]+p\left[(1+S)\frac{d^2P}{dx^2}-\lambda\phi^2 S\right]=0 \tag{A10}$$

$$(1-p)\left[\frac{d^2C}{dx^2}-\mu\rho\frac{\phi^2 S}{1+S(x=0)}\right]+p\left[(1+S)\frac{d^2C}{dx^2}-\mu\rho\phi^2 S\right]=0 \tag{A11}$$

The approximation solution of the equations (A1) and (A3) are,

$$S=S_0+pS_1+p^2S_2+p^3S_3+\ldots\ldots \tag{A12}$$

$$P=P_0+pP_1+p^2P_2+p^3P_3+\ldots\ldots \tag{A13}$$

$$C=C_0+pC_1+p^2C_2+p^3C_3+\ldots\ldots \tag{A14}$$

Substituting Eqn. (A12 - A14) in Eqn. (A9 - A11) and comparing the coefficients of like powers of p , we obtain the following equations:

$$p^0:\frac{d^2S_0}{dx^2}-\frac{\phi^2 S_0}{1+S_{in}}=0 \tag{A15}$$

$$p^0:\frac{d^2P_0}{dx^2}+\lambda\frac{\phi^2 S_0}{1+S_{in}}=0 \tag{A16}$$

$$p^0:\frac{d^2C_0}{dx^2}-\mu\rho\frac{\phi^2 S_0}{1+S_{in}}=0 \tag{A17}$$

The boundary conditions are,

$$x=0,\quad S_0=S_{in},\quad P_0=0,\quad C_0=C_{in} \tag{A18}$$

$$x=1,\quad \frac{dS}{dx}=0,\quad P_0=0,\quad C_0=C_{in} \tag{A19}$$

Solving the Eqns. (A15-A17) using the boundary conditions (A18) and (A19), we can find the following results

$$S_0(x)=A\cosh\sqrt{A_1}(x)+B\sinh\sqrt{A_1}(x) \tag{A20}$$

where, $$A_1=\frac{\phi^2 S_0}{1+S_0},\quad A=S_{in},\quad B=-S_{in}\frac{\sinh\sqrt{A_1}}{\cosh\sqrt{A_1}} \tag{A21}$$

Equation (A20) can be written as,

$$S_0(x)=S_{in}\frac{\cosh(\sqrt{A_1}(x-1))}{\cosh\sqrt{A_1}} \tag{A22}$$

Substituting eqn (A22) in (A16) and (A17) and solving eqn (A16) and (A17) using this boundary condition (A18) and (A19) we get the eqn (16) and (17) in the text.

Appendix-B: Relation between P and C

Equation (9) and (10) can be written as,

$$\frac{1}{\lambda}\frac{d^2P}{dx^2}+\frac{\varphi^2}{1+\frac{1}{S}+\frac{1}{C}}=0 \tag{B1}$$

$$\frac{1}{\mu\rho}\frac{d^2C}{dx^2}-\frac{\varphi^2}{1+\frac{1}{S}+\frac{1}{C}}=0 \tag{B2}$$

Now boundary conditions are,

$$\begin{aligned} x=0,\quad & P(x)=0,\ C(x)=C_{in} \\ x=1,\quad & P(x)=0,\ C(x)=0 \end{aligned} \tag{B3}$$

Using (B1) and (B2),

$$\frac{1}{\lambda}\frac{d^2P}{dx^2}=-\frac{1}{\mu\rho}\frac{d^2C}{dx^2}=0 \tag{B4}$$

Integrating on both sides of the equation we get,

$$\frac{1}{\lambda}\frac{dP}{dx}=-\frac{1}{\mu\rho}\frac{dC}{dx}+c_1=0 \tag{B5}$$

Once again integrating on both sides of the above equation we get,

$$\frac{1}{\lambda}P(x)=-\frac{1}{\mu\rho}C(x)+c_1x+c_2=0 \tag{B6}$$

Using the boundary conditions (B3), we get

$$c_2=\frac{1}{\mu\rho}C_{in} \text{ and } c_1=-\frac{1}{\mu\rho}C_{in} \tag{B7}$$

Eqn (B6) becomes,

$$\begin{aligned} \frac{1}{\lambda}P(x)&=-\frac{1}{\mu\rho}C(x)-\frac{1}{\mu\rho}C_{in}x+\frac{1}{\mu\rho}C_{in} \\ \frac{1}{\lambda}P(x)&=\frac{1}{\mu\rho}\left(-C(x)-C_{in}x+C_{in}\right) \\ P(x)&=\frac{\lambda}{\mu\rho}\left(C_{in}-C(x)-C_{in}x\right) \end{aligned} \tag{B8}$$

Appendix-C: Analytic solution of Eqn(10) (Ping-Pong mechanism):

$$\frac{1}{\mu\rho}\frac{d^2C}{dx^2}-\frac{\varphi^2}{1+\frac{1}{S}+\frac{1}{C}}=0 \tag{C1}$$

Homotopy for the above equation can be constructed as follows

$$(1-p)\left[\frac{d^2C}{dx^2}-\frac{\mu\ \rho+S_{in}\ \varphi^2\ C}{S_{in}\ C_{in}+C_{in}+S_{in}}\right]+p\left[\left(S\ C+C+S\right)\frac{d^2C}{dx^2}+\mu\ S_{in}\ \varphi^2\ S\ C\right]=0 \tag{C2}$$

The approximation solution of the above equation (8) and (9) are,

$$S = S_0 + pS_1 + p^2S_2 + p^3S_3 + \ldots\ldots\ldots$$
$$C = C_0 + pC_1 + p^2C_2 + p^3C_3 + \ldots\ldots\ldots \quad \text{(C3)}$$

Substituting eqn (C3) in (C2) and equating the co-efficient of p on both sides we get

$$p_0 : \frac{d^2C_0}{dx^2} - \frac{\mu\rho\ S_{in}\ C_0\varphi^2}{S_{in}\ C_{in} + C_{in} + S_{in}} = 0 \quad \text{(C4)}$$

The above equation can be written as

$$\frac{d^2C_0}{dx^2} - \beta^2\ C_0 = 0, \quad \text{(C5)}$$

$$where\ \ \beta^2 = \frac{\mu\ \rho\ \varphi^2\ S_{in}\ C_0}{S_{in}\ C_{in} + C_{in} + S_{in}} \quad \text{(C6)}$$

The boundary conditions are,

$$x = 0, \quad C_0(x) = C_{in}$$
$$x = 1, \quad C_0(x) = 0 \quad \text{(C7)}$$

The solution of the eqn (C5) is

$$C_0(x) = \frac{C_{in}}{\text{Sin}\, h\ \beta}\text{Sin}\ h\beta\left(1-x\right) \quad \text{(C8)}$$

Considering the first iteration, we get,

$$C(x) \approx C_0(x) \quad \text{(C9)}$$

Appendix D: Analytic solution of concentration S using eqn (8)

Eqn (8) for Ping-Pong kinetic is,

$$\frac{d^2S}{dx^2} - \frac{\varphi^2\ S\ C}{S\,C + C + S} = 0 \quad \text{(D1)}$$

Homotopy for the above equation can be constructed as follows:

$$\left(1-p\right)\left[\frac{d^2S}{dx^2} - \frac{C_{in}\ \varphi^2\ S}{S_{in}\ C_{in} + C_{in} + S_{in}}\right] + p\left[\left(S\ C + C + S\right)\frac{d^2S}{dx^2} - \varphi^2\ S\,C\ \right] = 0 \quad \text{(D2)}$$

The approximation solution of the equations (8) and (10) are,

$$S = S_0 + pS_1 + p^2S_2 + p^3S_3 + \ldots\ldots\ldots$$
$$C = C_0 + pC_1 + p^2C_2 + p^3C_3 + \ldots\ldots\ldots \quad \text{(D3)}$$

Substituting eqn (D3) in (D2) and equating the like co-efficient of p on both sides we get

$$p_0 : \frac{d^2S_0}{dx^2} - \frac{C_{in}\ \varphi^2\ S_0}{S_{in}\ C_{in} + C_{in} + S_{in}} = 0 \quad \text{(D4)}$$

The above equation can be written as

$$\frac{d^2S_0}{dx^2} - \alpha^2\ S_0 = 0, \quad \text{(D5)}$$

$$where\ \ \alpha^2 = \frac{C_{in}\ \varphi^2}{S_{in}\ C_{in} + C_{in} + S_{in}} \quad \text{(D6)}$$

Boundary conditions are,

$$x = 0, \quad S_0(x) = S_{in}, \qquad x = 1, \quad \frac{dS}{dx} = 0 \tag{D7}$$

The solution of eqn. (A5) is

$$S_0(x) = A\,\mathrm{Co}\,h(\alpha x) + B\,\mathrm{Sin}\,h(\alpha x) \tag{D8}$$

Using the boundary conditions we get,

$$S_0(x) = \frac{S_{in}\left[\cos h\,\alpha(1-x)\right]}{\mathrm{Cos}\,h(\alpha)} \tag{D9}$$

Considering first iteration, we get,

$$S(x) \approx S_0(x) \tag{D10}$$

Appendix-E: Scilab program to find the numerical solution of the Eqns. (5-7)

```
function pdex4
m = 0;
x = linspace(0,1);
t=linspace(0,100000);
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('u1(x,2)')
%------------------------------------------------------------------
figure
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,2)')
% ------------------------------------------------------------
figure
plot(x,u3(end,:))
title('u3(x,t)')
xlabel('Distance x')
ylabel('u3(x,2)')
 %------------------------------------------------------------
function [c,f,s] = pdex4pde(x,t,u,DuDx)
c = [1; 1; 1];
f = [1; 1; 1] .* DuDx;
l=0.1;mu=1;q=1;p=1;a=1;
F=-(q*u(1))/(1+u(1));
F1=(a*q*u(1))/(1+u(1));
F2=-(mu*p*q*u(1))/(1+u(1));
s=[F; F1; F2];
% ------------------------------------------------------------
function u0 = pdex4ic(x);
u0 = [1; 1; 1];
% ------------------------------------------------------------
function [pl,ql,pr,qr]=pdex4bc(xl,ul,xr,ur,t)
pl = [ul(1)-1;ul(2)-0;ul(3)-1];
ql = [0; 0; 0];
pr = [0; ur(2)-0;ur(3)-0];
qr = [1;0; 0];
```


NOMENCLATURE

$S(x)$ - Concentrations of substrate
$P(x)$ - Concentrations of product
$C(x)$ - Concentrations of co-substrate
D_S - Diffusion coefficients for substrate
D_C - Diffusion coefficients for co-substrate
D_P - Diffusion coefficients for product.
V_m - Enzyme rate
δ - Coordinate distance.
l - Thickness of active membrane,
ϕ^2 - Thiele Module,
λ - Diffusion coefficient of product,
μ - Diffusion coefficient of co-substrate
ρ - Reaction rate constant for co-substrate.
n - Number of electrons taking part in electrochemical reaction
F - Faraday's number,
A - Area of the electrode surface [m^2].

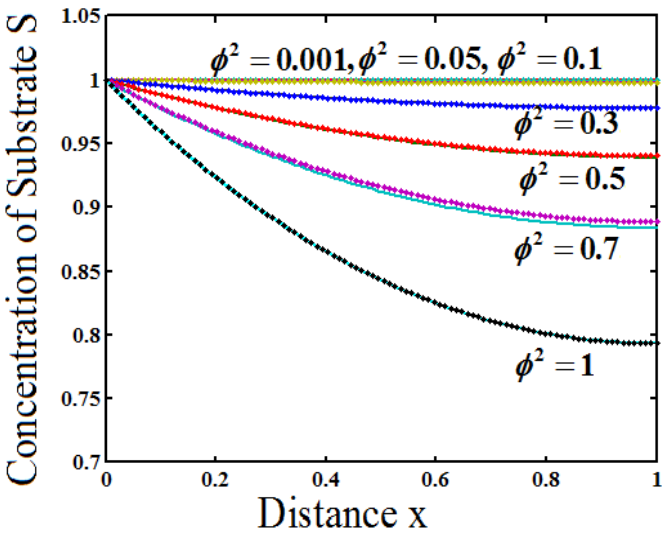

Figure-1: Plot of dimensionless concentration of the substrate $S(x)$ versus dimensionless distance x for the Michaelis-Menten kinetics calculated using Eqn. (15), for different values of the thiele modulus ϕ^2 .

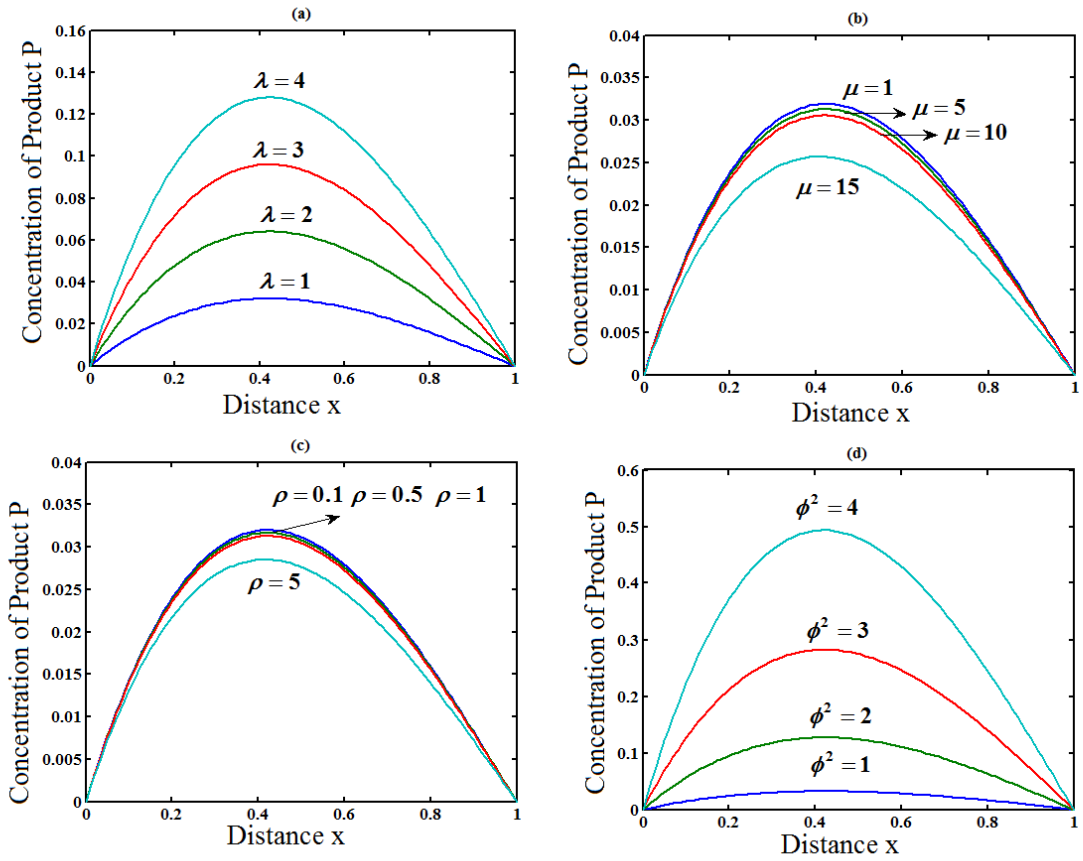

Figure-2: Plot of dimensionless concentration of the product $P(x)$ versus dimensionless distance x for the Michaelis-Menten kinetics calculated using Eqn. (16), for different values of the thiele modulus ϕ^2, diffusion coefficient λ, reaction rate constant for co-substrate μ, and diffusion coefficient of co-substrate ρ.

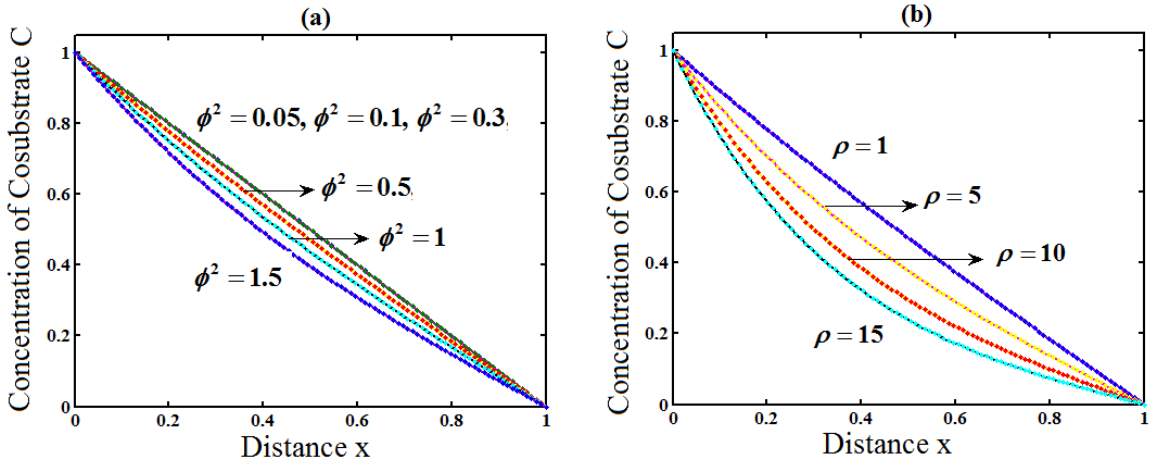

Figure-3: Plot of dimensionless concentration of the co-substrate $C(x)$ versus dimensionless distance x for the Michaelis-Menten kinetics calculated using Eqn.(17), for different values of the thiele modulus ϕ^2 and diffusion coefficient of co-substrate ρ.

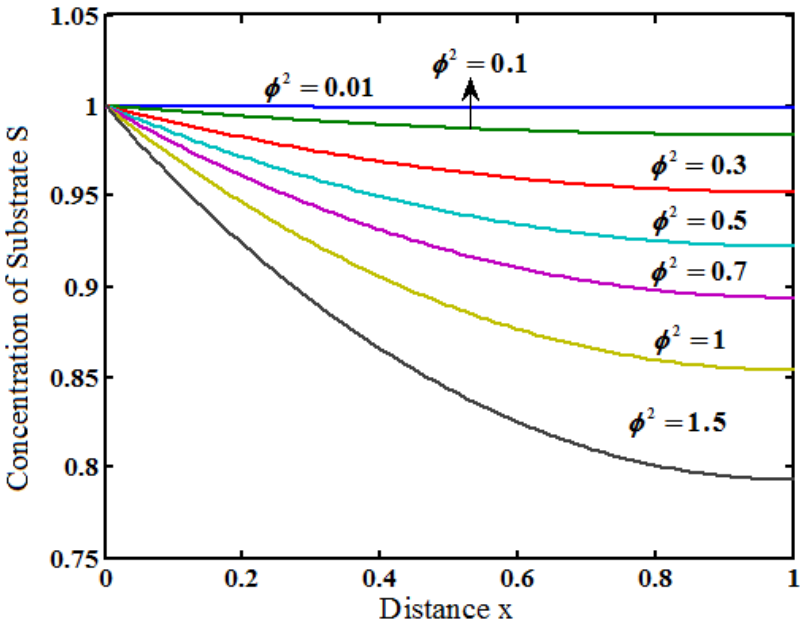

Figure-4: Plot of dimensionless concentration of the substrate $S(x)$ versus dimensionless distance x for the Ping-Pong kinetics calculated using Eqn. (22) for different values of the thiele modulus ϕ^2.

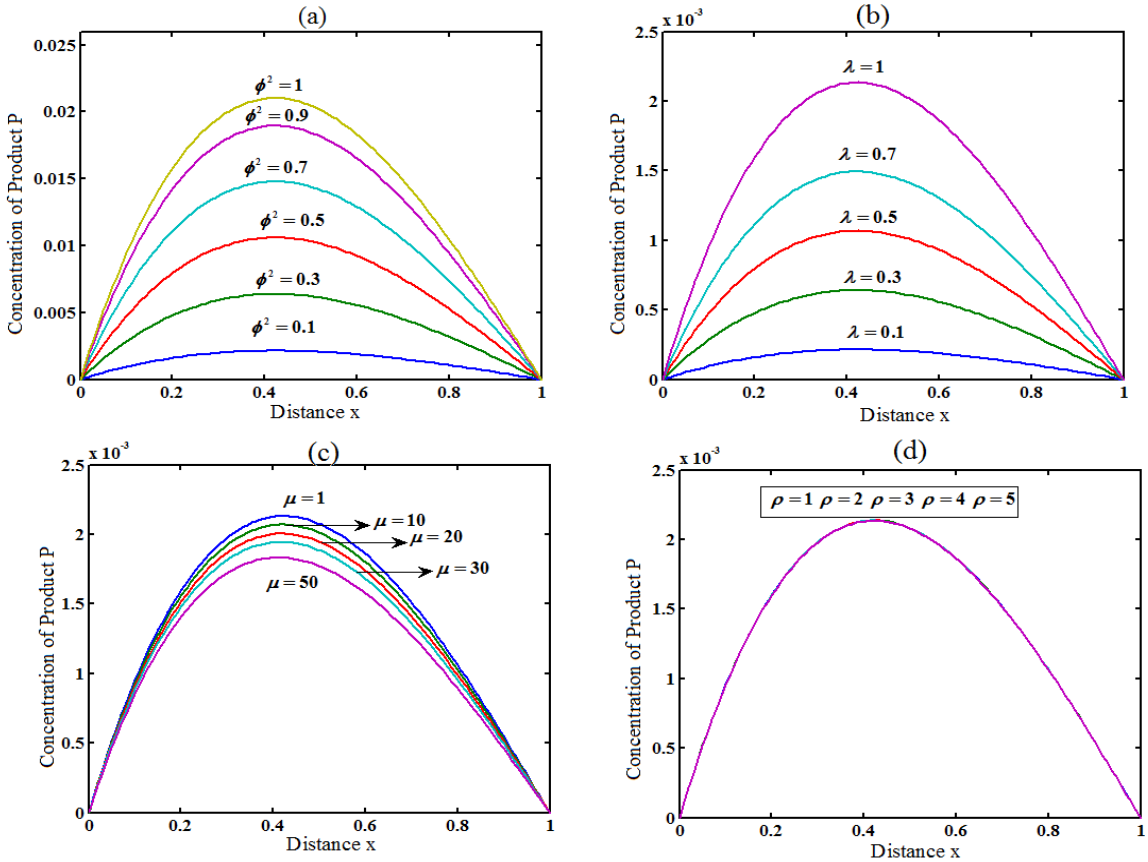

Figure-5: Plot of dimensionless concentration of the product $P(x)$ versus dimensionless distance x for the Ping-Pong kinetics calculated using Eqn. (23), for different values of the Thiele modulus ϕ^2, diffusion coefficient λ, reaction rate constant for co-substrate μ, and diffusion coefficient of co-substrate ρ.

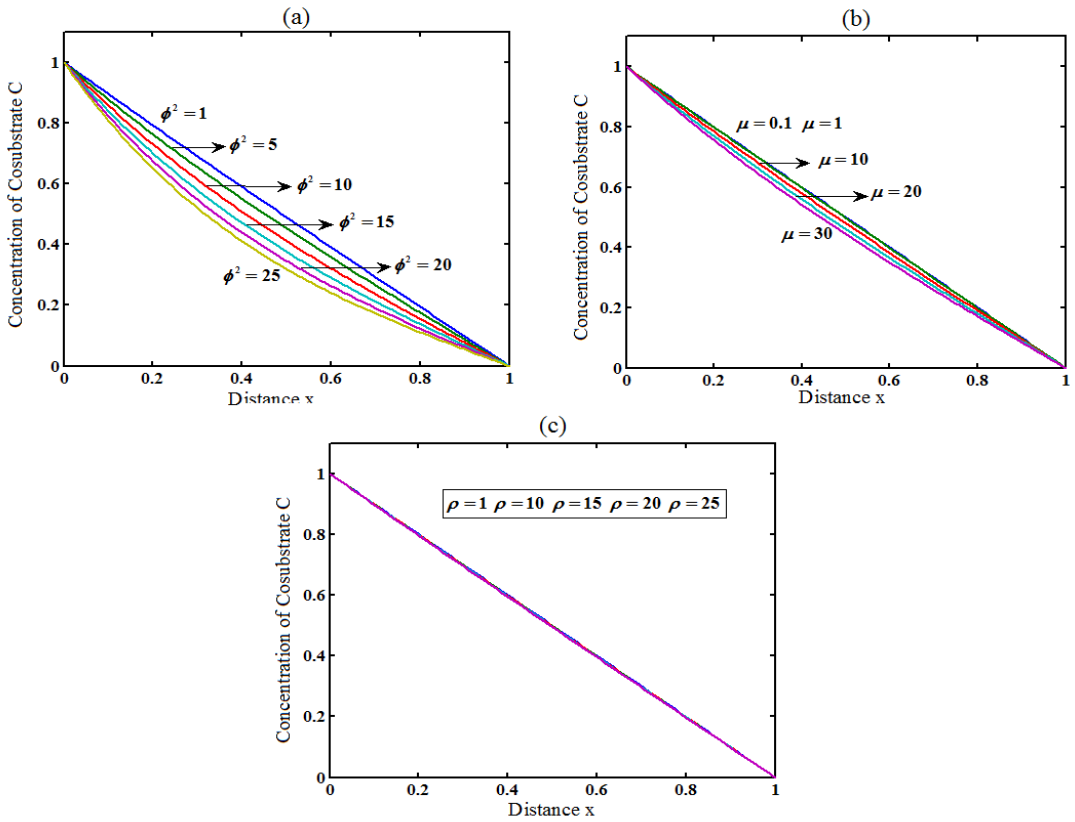

Figure-6: Plot of dimensionless concentration of the co-substrate $C(x)$ versus dimensionless distance x for the Ping-Pong kinetics calculated using Eqn.(24), for different values of the Thiele modulus ϕ^2 and diffusion coefficient of co-substrate ρ .

REFERENCES

1. Scheller, F., Schubert, F. Biosensors, vol. 7, Elsevier, Amsterdam., (1988).
2. Wollenberger, U., Lisdat, F., Scheller, F.W. Enzymatic Substrate Recycling Electrodes. Frontiers in Biosensorics. B and II, Practical Applications, Birkhauser Verlag, Basel, (1997)., pp. 45-70.
3. T. Schulmeister, Mathematical modeling of the dynamic behavior of amperometric enzyme electrodes, Selective Electrode Rev., 12 (1990)., pp. 203-260.
4. A.J. Baeumner, C. Jones, C.Y.Wong, A. Price, A generic sandwich-type biosensor with nanomolar detection limits, Anal. Bioanal. Chem., 378 (2004)., pp.1587-1593.
5. R. Baronas, F. Ivanauskas, J. Kulys, The inuence of the enzyme membrane thickness on the response of amperometric biosensors, Sensors., 3 (2003)., pp. 248-262.
6. Rajendran, L. Chemical Sensors Simulation and Modeling, Electrochemical Sensors. In: Korotchenkov, G., Ed(2013).
7. R. Baronas, et al., Mathematical Modeling of Biosensors: An Introduction for Chemists and Mathematicians. Springer (2010).
8. R. Aris, The Mathematical Theory of Diffusion and Reaction in Permeable Catalysts. The Theory of the Steady State, Clarendon Press, Oxford., (1975)., p.26.
9. L.K. Bieniasz, D. Britz, Recent developments in digital simulation of electro analytical experiments, Pol. J. Chem., 78 (2004)., pp.1195-1219.
10. P. Manimozhi, A. Subbiah, L. Rajendran, Solution of steady-state substrate concentration in the action of biosensor response at mixed enzyme kinetics, Sensors and Actuators B., 147 (2010)., pp.290-297.
11. M.Razzagi, S.Yousefi, Legendre wavelets method for the solution of nonlinear problems in the calculus of variations. Math. Comput. Model., 34, (2001)., pp.45-54.
12. P. Katzarova, V. Rangelova & S. Kuneva, Two parameters diagnostic of biosensor transducers, Biotechnology & Biotechnological Equipment., 20:1 (2006)., pp.190-194.
13. T. Ozis¸ and A. Yildirim, "A comparative study of He's Homotopy perturbation method for determining frequency-amplituderelation of a nonlinear oscillator with discontinuities," International Journal of Nonlinear Sciences and Numerical Simulation, vol. 8, no. 2, (2007) pp. 243–248.

14. M. M. Mousa and S. F. Ragab, "Application of the homotopy perturbation method to linear and nonlinear schr¨odinger equations," Zeitschrift fur Naturforschung-A Journal of Physical Sciences, vol. 63, no. 3-4, (2008)., pp. 140–144,.
15. J. H. He, "Homotopy perturbation technique," Computer Methods in AppliedMechanics and Engineering, vol. 178., (1999)., pp. 257–262,.
16. L. Rajendran, S. Anitha, Reply to 'Comments on analytical solution of amperometric enzymatic reactions based onHPM', Electrochimica Acta., 102, (2013)., pp. 474–476.
17. V. Meena , K. Indira , Sunil Kumar , L. Rajendran , A new mathematical model for effectiveness factors in biofilm under toxic conditions, Alexandria Engineering Journal., (2014) 53., pp.917–928
18. A. Meena, L. Rajendran, Mathematical modeling of amperometric and potentiometric biosensors and system of nonlinear equations homotopy perturbation approach, Journal of Electroanalytical Chemistry., 644, 1, (2010)., pp.50–59.
19. P. Manimozhi, A. Subbiah, L. Rajendran, Solution of steady-state substrate concentration in the action of biosensor response at mixed enzyme kinetics, Sensors and Actuators, B: Chemical, 147, no. 1, (2010)., pp.290–297.

Source of support: Department of Science and Technology,
SERB-DST (EMR/2015/002279) Government of India, Conflict of interest: None Declared.