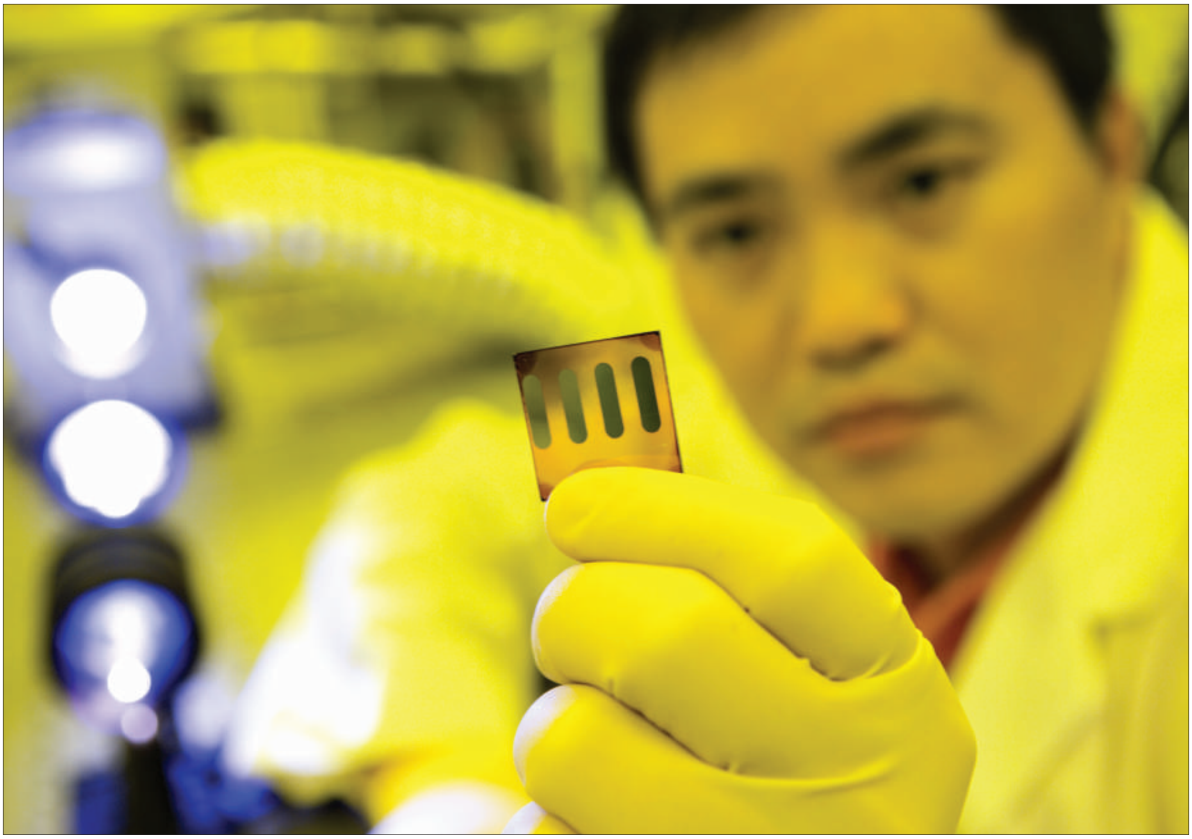

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Research Article
Mathematical Analysis of Reversible Inhibitor Biosensor Systems in Dynamic Mode

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Abstract

Background and Objectives: Biosensors are very popular and useful devices that have a very big area of use in various fields. This is the main reason due to which they are reliable, cheap and highly sensitive. The main objective of this study was to derive an approximate analytical solution for the substrate concentration, inhibitor concentration and the product concentration for the three basic types of reversible inhibitor enzyme systems and to discuss the effect of each parameter on the magnitude of concentrations. **Materials and Methods:** The mathematical model has been solved using new approach to Homotopy Perturbation Method (NHPM) and Homotopy Analysis Method (HAM). Both the solutions were compared with the numerical solution obtained using MATLAB. **Results:** It was found that, though both the solutions make a good fit with the numerical results, HAM was better of the two for this problem. **Conclusion:** The HAM was used to obtain the non-steady state expressions for substrate concentration, inhibitor concentration and product concentration profiles and have been presented in this study for the first time. The output current for biosensors in each of the cases have also been derived. The sensitivity analysis was performed for output current.

Key words: Amperometric biosensor, dynamic mode, new approach to homotopy perturbation method, homotopy analysis method, numerical simulation

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Biosensor amperometric transducers usually work in static mode and majority research papers are made in this mode[1-5]. It is known that the decay time of transient process is long for tissue biosensors and hence dynamic measurements could also be considered[6,7].

In the enzyme reactions, enzyme E and substrate S react and ES complex is formed. After that ES is transformed to a transition complex ES. Competitive inhibitors can bind to E, but not to ES. Competitive inhibition increases K_S (i.e., the inhibitor interferes with substrate binding), but does not affect V_S (the inhibitor does not hamper catalysis in ES because it cannot bind to ES). Non-competitive inhibitors have identical affinities for E and ES ($K_I = K_I'$). Non-competitive inhibition does not change K_S (i.e., it does not affect substrate binding) but decreases V_S (i.e., inhibitor binding hampers catalysis). Mixed-type inhibitors bind to both E and ES but their affinities for these two forms of the enzyme are different ($K_I \neq K_I'$). Thus mixed-type inhibitors interfere with substrate binding (increase K_S) and hamper catalysis in the ES complex (decrease V_S). All the three types of enzyme inhibitor kinetic models of biosensors in dynamic mode with competitive inhibition, non-competitive inhibition and mixed inhibition have been investigated previously[7]. The mathematical models thus framed had been solved numerically using MATLAB and no analytical solution has been reported. This study has been written to derive approximate analytical expressions for the steady state and non steady state concentrations of substrate, inhibitor and product in all the three types of enzyme inhibitor kinetic models.

The derived expressions will help to analyze the effect of the different parameters on the concentrations in all the three types of enzyme inhibitor kinetic models. Further, a parameter sensitivity analysis has been carried out to quantify the effect of each parameter. The parameter sensitivities can be used to identify where future experimental efforts should be focused on.

Non-linear mathematical models similar to the mathematical model considered here[5,6] have been previously solved only in the steady state[8,9] using the new approach to homotopy perturbation method. Till date, no non-steady state solution has been reported for this kind of a model. In this study, homotopy analysis method is proved to be a better method for solving this model when compared to the new approach to homotopy perturbation method. The non-steady state solution thus derived is presented here for the first time. The analytical solution derived here may be used to derive an approximate analytical solution for all analogous models[1-6].

The main objective of this study was to derive an approximate analytical solution for the substrate concentration, inhibitor concentration and the product concentration for the three basic types of reversible inhibitor enzyme systems and to discuss the effect of each parameter on the magnitude of concentrations.

MATERIALS AND METHODS

The mathematical model previously framed[1] has been solved analytically using two semi-analytical methods.

Study area: The mathematical analysis was carried out at the Department of Mathematics, The Madura College, Madurai, Tamil Nadu, India from April-November, 2019.

Mathematical formulation of the problem: The partial differential equations modeled for the biosensors in dynamic mode follows[1].

The governing partial differential equations for competitive inhibition are:

$$\frac{\partial S}{\partial t} = D_S \frac{\partial^2 S}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S \tag{1}$$

$$\frac{\partial I}{\partial t} = D_I \frac{\partial^2 I}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S \tag{2}$$

$$\frac{\partial P}{\partial t} = D_P \frac{\partial^2 P}{\partial x^2} + \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S \tag{3}$$

The governing partial differential equations for non-competitive inhibition are:

$$\frac{\partial S}{\partial t} = D_S \frac{\partial^2 S}{\partial x^2} - \frac{V_S}{\left(1+\frac{I}{K_I}\right)\left(K_S+S\right)} S \tag{4}$$

$$\frac{\partial I}{\partial t} = D_I \frac{\partial^2 I}{\partial x^2} - \frac{V_S}{\left(1+\frac{I}{K_I}\right)\left(K_S+S\right)} S \tag{5}$$

$$\frac{\partial P}{\partial t} = D_P \frac{\partial^2 P}{\partial x^2} + \frac{V_S}{\left(1+\frac{I}{K_I}\right)\left(K_S+S\right)} S \tag{6}$$

The governing partial differential equations for mixed inhibition are:

$$\frac{\partial S}{\partial t} = D_S \frac{\partial^2 S}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S\left(1+\frac{I}{K_I^{'}}\right)} S \qquad (7)$$

$$\frac{\partial I}{\partial t} = D_I \frac{\partial^2 I}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S\left(1+\frac{I}{K_I^{'}}\right)} S \qquad (8)$$

$$\frac{\partial P}{\partial t} = D_P \frac{\partial^2 P}{\partial x^2} + \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S\left(1+\frac{I}{K_I^{'}}\right)} S \qquad (9)$$

Subject to the following boundary conditions:

$$t = 0,\ S(x, 0) = S_0,\ I(x, 0) = I_0,\ P(x, 0) = 0 \qquad (10)$$

$$x = 0,\ S(0, t) = S_0,\ I(0, t) = I_0,\ P(0, t) = 0 \qquad (11)$$

At x = d:

$$\left.\frac{\partial S}{\partial x}\right|_{x=d} = 0,\ \left.\frac{\partial I}{\partial x}\right|_{x=d} = 0,\ P\,(d, t) = 0 \qquad (12)$$

The output current is given by:

$$I = nFAD_P \left.\frac{\partial P}{\partial x}\right|_{x=d} \qquad (13)$$

New approach to homotopy perturbation method and homotopy analysis method: Solving non-linear reaction diffusion equations play a vital role in different fields of Science and Engineering. To solve such problems, there are various analytical and numerical methods. In order to obtain an approximate analytical solution of such non-linear differential equations, semi-analytical methods such as; the Variational Iteration method[10], Adomian decomposition method[11],Homotopy analysis method[12] and Homotopy perturbation method[13-19] are applied.

The homotopy perturbation method is a powerful and efficient technique for finding solutions of nonlinear equations without the need of a linearization process. The method was first introduced in the year 1998[20-25]. Homotopy Perturbation Method (HPM) is a combination of the perturbation and homotopy methods. This method had been successfully applied to solve many nonlinear mathematical models[26-31]. Lately, a new approach to HPM[32-35] is used to solve nonlinear differential equations in zeroth iteration itself.

The homotopy analysis method is a powerful semi-analytical technique to solve nonlinear ordinary/partial differential equations. The homotopy analysis method uses the concept of the homotopy from topology to generate a convergent series solution for nonlinear systems. Homotopy Analysis Method (HAM) was first proposed in the year 1992 and has been successfully applied to solve many problems in Physics and Science[36-38]. In comparison with other perturbative and non-perturbative analytical methods, HAM offers the ability to adjust and control the convergence of a solution via the so-called convergence-control parameter. This property of the HAM has proved it to be the most effective method for obtaining analytical solutions to highly non-linear differential equations.

Approximate analytical solution to the steady state of Eq. 1-12 using new approach to homotopy perturbation method: Using new approach to homotopy perturbation method, the solution for competitive inhibition is:

$$S \approx S_0 \frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}\left(x-d\right)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)} \qquad (14)$$

$$I \approx I_0 + \frac{S_0 D_S}{D_I}\left(\frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}\left(x-d\right)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)}-1\right) \qquad (15)$$

$$P \approx -\frac{S_0 D_S}{D_P \cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}\,d\right)}\left(\begin{array}{l}\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}\left(x-d\right)\right)\\ +\left(\frac{x}{d}-1\right)\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}\,d\right)-\frac{x}{d}\end{array}\right) \tag{16}$$

The solution for non-competitive inhibition is:

$$S \approx S_0 \frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\left(x-d\right)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\,d\right)} \tag{17}$$

$$I \approx I_0 + \frac{S_0 D_S}{D_I}\left(\frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\left(x-d\right)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\,d\right)}-1\right) \tag{18}$$

$$P \approx -\frac{S_0 D_S}{D_P \cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\,d\right)}\left(\begin{array}{l}\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\left(x-d\right)\right)\\ +\left(\frac{x}{d}-1\right)\cosh\left(\sqrt{\frac{V_S}{D_S\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)}}\,d\right)-\frac{x}{d}\end{array}\right) \tag{19}$$

The solution for mixed inhibition is:

$$S \approx S_0 \frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\left(x-d\right)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,d\right)} \tag{20}$$

$$I \approx I_0 + \frac{S_0 D_S}{D_I}\left(\frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,(x-d)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,d\right)}-1\right) \tag{21}$$

$$P \approx \frac{-S_0 D_S}{D_P\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,d\right)}\left(\begin{array}{l}\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,(x-d)\right)\\ +\left(\frac{x}{d}-1\right)\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}}\,d\right)\\ -\frac{x}{d}\end{array}\right) \tag{22}$$

Approximate analytical solution to the steady state of Eq. 1-12 using homotopy analysis method: Using homotopy analysis method, the solution for competitive inhibition is:

$$S \approx S_0 + \frac{hS_0V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}x\left(d-\frac{x}{2}\right) \tag{23}$$

$$I \approx I_0 + \frac{hS_0V_S}{D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}x\left(d-\frac{x}{2}\right) \tag{24}$$

$$P \approx \frac{hS_0V_S}{2D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}x\left(x-d\right) \tag{25}$$

The solution for non-competitive inhibition is:

$$S \approx S_0 + \frac{hS_0V_S}{D_S\left(\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)\right)}x\left(d-\frac{x}{2}\right) \tag{26}$$

$$I \approx I_0 + \frac{hS_0V_S}{D_I\left(\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)\right)}x\left(d-\frac{x}{2}\right) \tag{27}$$

$$P \approx \frac{hS_0V_S}{2D_P\left(\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)\right)}x\left(x-d\right) \tag{28}$$

The solution for mixed inhibition is:

$$S \approx S_0 + \frac{hS_0V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}\times\left(d-\frac{x}{2}\right) \tag{29}$$

$$I \approx I_0 + \frac{hS_0V_S}{D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}\times\left(d-\frac{x}{2}\right) \tag{30}$$

$$P \approx \frac{hS_0V_S}{2D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}\times\left(x-d\right) \tag{31}$$

Approximate analytical solution to Eq. 1-12 using homotopy analysis method: Using homotopy analysis method and laplace transform technique, the solution for competitive inhibition in the non steady state is:

$$S = S_0 + \frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}\left(d-\frac{x}{2}\right) - \frac{16hV_S S_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2 D_S t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3 D_S} \tag{32}$$

$$I = I_0 + \frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}\left(d-\frac{x}{2}\right) - \frac{16hV_S S_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2 D_I t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3 D_I} \tag{33}$$

$$P = \frac{hV_S S_0 x}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_P}(x-d) + \frac{2hV_S S_0 d^2}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2 D_P t}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3 D_P} \tag{34}$$

The solution for non-competitive inhibition in the non steady state is:

$$S = S_0 + \frac{hV_S S_0 x}{\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)D_S}\left(d-\frac{x}{2}\right) - \frac{16hV_S S_0}{\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2 D_S t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3 D_S} \tag{35}$$

$$I = I_0 + \frac{hV_S S_0 x}{\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)D_I}\left(d-\frac{x}{2}\right) - \frac{16hV_S S_0}{\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2 D_I t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3 D_I} \tag{36}$$

$$P = \frac{hV_S S_0 x}{2\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)D_P}(x-d) + \frac{2hV_S S_0 d^2}{\left(1+\frac{I_0}{K_I}\right)(K_S+S_0)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2 D_P t}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3 D_P} \tag{37}$$

The solution for mixed inhibition in the non steady state is:

$$S = S_0 + \frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)D_S}\left(d-\frac{x}{2}\right) - \frac{16hV_S S_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2 D_S t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3 D_S} \tag{38}$$

$$I = I_0 + \frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I'}\right)\right)D_I}\left(d-\frac{x}{2}\right)$$

$$-\frac{16hV_SS_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I^{'}}\right)\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2D_It}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3D_I} \tag{39}$$

$$P=\frac{hV_SS_0x}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I^{'}}\right)\right)D_P}(x-d)$$

$$+\frac{2hV_SS_0d^2}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I^{'}}\right)\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3D_P} \tag{40}$$

Approximate analytical expression for current Eq. 13: Non steady state current for competitive inhibition is:

$$I=nFAhV_SS_0d\left(\begin{array}{l}\frac{1}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\\+\frac{2}{D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}(1-\cos(n\pi))}{n^2\pi^2}\end{array}\right) \tag{41}$$

Non steady state current for non-competitive inhibition is:

$$I=nFAhV_SS_0d\left(\begin{array}{l}\frac{1}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\\+\frac{2}{D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}(1-\cos(n\pi))}{n^2\pi^2}\end{array}\right) \tag{42}$$

Non steady state current for mixed inhibition is:

$$I=nFAhV_SS_0d\left(\begin{array}{l}\frac{1}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_{I'}}\right)\right)}\\+\frac{2}{D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_{I'}}\right)\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}(1-\cos(n\pi))}{n^2\pi^2}\end{array}\right) \tag{43}$$

Steady state current for competitive inhibition is:

$$I = \frac{nFAhV_S S_0 d}{2K_S\left(1+\frac{I_0}{K_I}\right)+2S_0} \quad (44)$$

Steady state current for non-competitive inhibition is:

$$I = \frac{nFAhV_S S_0 d}{2\left(1+\frac{I_0}{K_I}\right)\left(K_S+S_0\right)} \quad (45)$$

Steady state current for mixed inhibition is:

$$I = \frac{nFAhV_S S_0 d}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\left(1+\frac{I_0}{K_I^{'}}\right)\right)} \quad (46)$$

Numerical simulation: The nonlinear reaction diffusion Eq. 1-9 with respect to the initial and boundary conditions 10-12 are also solved numerically. The function pdex4 has been used in MATLAB software to solve the initial-boundary value problem numerically. The derived analytical results are compared with the numerical simulation.

RESULTS

The steady state approximate analytical expressions for the substrate concentration, inhibitor concentration and product concentration have been derived using the new homotopy perturbation method (Appendix A) and using homotopy analysis method (Appendix B). The two results are compared with the numerical solution obtained using MATLAB in Fig. 1-3 and parameter values which are used in graph construction of different figures are defined in Table 1. The error percentage in each figure is tabulated in Table 2-10. The non-steady state approximate analytical expressions for the substrate concentration, inhibitor concentration and product concentration have been derived using homotopy analysis method (Appendix C). The MATLAB programs for the mathematical models[1] are given in Appendix D. The sensitivity analysis was carried out for output current of the biosensor with competitive inhibition, non competitive inhibition and mixed inhibition for fixed values of parameters (Table 11).

Figure 7-9 showed the substrate concentration, inhibitor concentration and product concentration profiles for the biosensor with non-competitive inhibitions for various values of parameters. The figures indicate that substrate concentration varies directly with K_S and D_S, while inversely with V_S and K_I. A similar effect is experienced on the inhibitor concentration as well. The product concentration varies directly with V_S.

Figure 10-12 showed the substrate concentration, inhibitor concentration and product concentration profiles for biosensors with mixed inhibitions for various values of parameters. The figures clearly indicate that substrate concentration increases with increase in K_S and D_S, while decreases with increase in V_S, K_I and $K_{I'}$. The same effect is experienced on the inhibitor concentration as well. The product concentration varies as V_S.

Table 1: Parameter values used in the construction of Fig. 1-21

Parameter	S_0 (mM)	I_0 (mM)	V_S	d	n	F	A	K_S	K_I	$K_{I'}$	D_S	D_I	D_P	h
Value	5	2	2 mM sec^{-1}	1 µm	2	96.5 A.s/mmol	7.85×10^{-7} m^2	0.6 mM	0.6 mM	2 mM	2 $(µm)^2$ sec^{-1}	2 $(µm)^2$ sec^{-1}	3 $(µm)^2$ sec^{-1}	-1

S_0: Starting concentration of the measured substrate (mM), I_0: Starting concentration of the inhibitor (mM), V_S: Maximal reaction velocity (mM sec^{-1}), d: Thickness of the active membrane (µm), K_S: Reaction constant for substrate (mM), K_I: Reaction constant for inhibitor toward E (mM), K_I': Reaction constant for inhibitor toward ES (mM), D_S: Diffusion coefficient of substrate (µm^2 sec^{-1}), D_I: Diffusion coefficient of inhibitor (µm^2 sec^{-1}), D_P: Diffusion coefficient of product (µm^2 sec^{-1}), F: Faraday's number (A.s $mmol^{-1}$), A: Area of the cathode of the indicator electrode (m^2), n: Number of electrons taking part in electrochemical reaction on the electrode surface

Table 2: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 1a

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Substrate concentration (S)					
0	5	5	5	0	0
0.2	4.87962	4.88039	4.886957	0.015923	0.1504
0.4	4.78576	4.78737	4.799646	0.03371	0.290244
0.6	4.71858	4.72092	4.737607	0.049564	0.40318
0.8	4.67823	4.68105	4.700514	0.060408	0.476399
1	4.66477	4.66776	4.688171	0.064235	0.501722
Average absolute (%) error				0.037307	0.303657

Table 3: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 1b

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Concentration (I)					
0	2	2	2	0	0
0.2	1.879617764	1.880394737	1.886956704	0.041337	0.390449
0.4	1.785755160	1.787368421	1.799645518	0.090341	0.777842
0.6	1.718582334	1.720921053	1.737606706	0.136084	1.106981
0.8	1.678226590	1.681052632	1.700513605	0.168395	1.32801
1	1.664766760	1.667763158	1.688170902	0.179989	1.405851
Average absolute (%) error				0.102691	0.834855

Table 4: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 1c

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Product concentration (P)					
0	0	0	0	0	0
0.2	0.04571683802	0.04385964914	0.04035087722	4.06237	11.7374
0.4	0.06873838850	0.06578947370	0.06052631582	4.29006	11.9469
0.6	0.0688774243	0.06578947370	0.06052631582	4.48326	12.1246
0.8	0.0459934168	0.04385964914	0.04035087722	4.63929	12.2681
1	0	0	0	0	0
Average absolute (%) error				2.9125	8.01283

Table 5: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 2a

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Substrate concentration (S)					
0	5	5	5	0	0
0.2	4.961837023	4.962541209	4.963458362	0.014192	0.032676
0.4	4.932029615	4.933406593	4.935099374	0.027919	0.062241
0.6	4.910670488	4.912596154	4.914876279	0.039214	0.085646
0.8	4.897827387	4.900109890	4.902755743	0.046602	0.100623
1	4.893541588	4.895947802	4.898717785	0	0
Average absolute (%) error				0.021321	0.046864

Table 6: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 2b

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Inhibitor concentration (I)					
0	2	2	2	0	0
0.2	1.961837023	1.962912088	1.963458363	0.054799	0.082644
0.4	1.932029615	1.934065934	1.935099373	0.105398	0.158888
0.6	1.910670488	1.913461538	1.914876281	0	0
0.8	1.897827387	1.901098901	1.902755747	0	0
1	1.893541588	1.896978022	1.898717786	0.181482	0.273361
Average absolute (%) error				0.056946	0.085815

Appendix A: Approximate analytical solution for the steady state model using NHPM

Equation 1-3 in steady state become:

$$D_S \frac{\partial^2 S}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S = 0 \tag{A.1}$$

$$D_I \frac{\partial^2 I}{\partial x^2} - \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S = 0 \tag{A.2}$$

$$D_P \frac{\partial^2 P}{\partial x^2} + \frac{V_S}{K_S\left(1+\frac{I}{K_I}\right)+S} S = 0 \tag{A.3}$$

Homotopy for Eq. A1-A3 are constructed as follows:

$$(1-p)\left[\frac{\partial^2 S}{\partial x^2} - \frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} S\right] + p\left[\frac{\partial^2 S}{\partial x^2} - \frac{V_S}{D_S\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)} S\right] = 0 \tag{A.4}$$

$$(1-p)\left[\frac{\partial^2 I}{\partial x^2} - \frac{V_S}{D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} S\right] + p\left[\frac{\partial^2 I}{\partial x^2} - \frac{V_S}{D_I\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)} S\right] = 0 \tag{A.5}$$

$$(1-p)\left[\frac{\partial^2 P}{\partial x^2} + \frac{V_S}{D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} S\right] + p\left[\frac{\partial^2 P}{\partial x^2} + \frac{V_S}{D_P\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)} S\right] = 0 \tag{A.6}$$

Let the approximate solution of Eq. A4-A6 be:

$$S = S_0+pS_1+p^2S_2+ \ldots \tag{A.7}$$

$$I = I_0+pI_1+p^2I_2+ \ldots \tag{A.8}$$

$$P = P_0+pP_1+p^2P_2+ \ldots \tag{A.9}$$

The boundary conditions for the above equations becomes:

At x = 0:

$$S_0 = S_0,\ S_1 = S_2 = S_3 = \ldots = 0 \tag{A.10}$$

$$I_0 = I_0,\ I_1 = I_2 = I_3 = \ldots = 0 \tag{A.11}$$

$$P_0 = P_1 = P_2 = P_3 = \ldots = 0 \tag{A.12}$$

At x = d:

$$\left.\frac{\partial S_0}{\partial x}\right|_{x=d} = \left.\frac{\partial S_1}{\partial x}\right|_{x=d} = \left.\frac{\partial S_2}{\partial x}\right|_{x=d} = \ldots = 0 \tag{A.13}$$

$$\left.\frac{\partial I_0}{\partial x}\right|_{x=d} = \left.\frac{\partial I_1}{\partial x}\right|_{x=d} = \left.\frac{\partial I_2}{\partial x}\right|_{x=d} = \ldots = 0 \tag{A.14}$$

Appendix A: Continued

$$P_0 = P_1 = P_2 = P_3 = \ldots = 0 \tag{A.15}$$

Substituting Eq. A7-A9 in Eq. A4-A6 and equating the coefficients of p^0, the following is obtained:

$$\frac{\partial^2 S_0}{\partial x^2} - \frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}S_0 = 0 \tag{A.16}$$

$$\frac{\partial^2 I_0}{\partial x^2} - \frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}S_0 = 0 \tag{A.17}$$

$$\frac{\partial^2 P_0}{\partial x^2} + \frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}S_0 = 0 \tag{A.18}$$

Solving Eq. A16-A18 using boundary conditions A10-A15 and using the approximation $S \approx S_0$, $I \approx I_0$, $P \approx P_0$:

$$S \approx S_0 \frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}(x-d)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)}$$

$$I \approx I_0 + \frac{S_0 D_S}{D_I}\left(\frac{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}(x-d)\right)}{\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)}-1\right)$$

$$P \approx -\frac{S_0 D_S}{D_P\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)}\left(\begin{array}{c}\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}(x-d)\right)\\ +\left(\frac{x}{d}-1\right)\cosh\left(\sqrt{\frac{V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}}d\right)-\frac{x}{d}\end{array}\right)$$

The above three equations give the solution of the steady state of Eq. 1-3.

Similarly, solving the steady state of Eq. 4-6 and 7-9, the solutions given in Eq. 17-19 and 20-22 are obtained respectively.

Appendix B: Approximate analytical solution for the steady state model using HAM

The homotopy for steady state of Eq. 1-3 are framed as follows:

$$(1-p)\left[\frac{\partial^2 S}{\partial x^2}\right] = ph\left[D_S\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\frac{\partial^2 S}{\partial x^2} - V_S S\right] \quad (B.1)$$

$$(1-p)\left[\frac{\partial^2 I}{\partial x^2}\right] = ph\left[D_I\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\frac{\partial^2 I}{\partial x^2} - V_S S\right] \quad (B.2)$$

$$(1-p)\left[\frac{\partial^2 P}{\partial x^2}\right] = ph\left[D_P\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\frac{\partial^2 P}{\partial x^2} + V_S S\right] \quad (B.3)$$

Let the approximate solution of Eq. B.1-B.3 be:

$$S = S_0+pS_1+p^2S_2+ \dots \quad (B.4)$$

$$I = I_0+pI_1+p^2I_2+ \dots \quad (B.5)$$

$$P = P_0+pP_1+p^2P_2+ \dots \quad (B.6)$$

The boundary conditions for the above equations become:
At, x = 0:

$$S_0 = S_0,\ S_1 = S_2 = S_3 = \dots = 0 \quad (B.7)$$

$$I_0 = I_0,\ I_1 = I_2 = I_3 = \dots = 0 \quad (B.8)$$

$$P_0 = P_1 = P_2 = P_3 = \dots = 0 \quad (B.9)$$

At x = d:

$$\left.\frac{\partial S_0}{\partial x}\right|_{x=d} = \left.\frac{\partial S_1}{\partial x}\right|_{x=d} = \left.\frac{\partial S_2}{\partial x}\right|_{x=d} = \dots = 0 \quad (B.10)$$

$$\left.\frac{\partial I_0}{\partial x}\right|_{x=d} = \left.\frac{\partial I_1}{\partial x}\right|_{x=d} = \left.\frac{\partial I_2}{\partial x}\right|_{x=d} = \dots = 0 \quad (B.11)$$

$$P_0 = P_1 = P_2 = P_3 = \dots = 0 \quad (B.12)$$

Substituting Eq. B4-B6 in Eq. B1-B3 and equating the coefficients of p^0 and p^1, the following is obtained:

$$p^0 : \frac{\partial^2 S_0}{\partial x^2} = 0 \quad (B.13)$$

$$\frac{\partial^2 I_0}{\partial x^2} = 0 \quad (B.14)$$

$$\frac{\partial^2 P_0}{\partial x^2} = 0 \quad (B.15)$$

$$p^1 : \frac{d^2 S_1}{dx^2} - \frac{d^2 S_0}{dx^2} = h\left[D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\frac{\partial^2 S_0}{\partial x^2} - V_S S_0\right] \quad (B.16)$$

$$\frac{d^2 I_1}{dx^2} - \frac{d^2 I_0}{dx^2} = h\left[D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\frac{\partial^2 S_0}{\partial x^2} - V_S S_0\right] \quad (B.17)$$

$$\frac{d^2 P_1}{dx^2} - \frac{d^2 P_0}{dx^2} = h\left[D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\frac{\partial^2 S_0}{\partial x^2} - V_S S_0\right] \quad (B.18)$$

Solving Eq. B13-B15 using boundary conditions B7-B12:

$$S_0 = S_0,\ I_0 = I_0,\ P_0 = 0 \quad (B.19)$$

Solving Eq. B16-B18 using boundary conditions B7-B12:

$$S_1 = \frac{hS_0V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(d-\frac{x}{2}\right) \quad (B.20)$$

$$I_1 = \frac{hS_0V_S}{D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(d-\frac{x}{2}\right) \quad (B.21)$$

$$P_1 = \frac{hS_0V_S}{2D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(x-d\right) \quad (B.22)$$

Substituting Eq. B19-B22 in Eq. B4-B6:

$$S \approx S_0 + \frac{hS_0V_S}{D_S\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(d-\frac{x}{2}\right) \quad (B.23)$$

$$I \approx I_0 + \frac{hS_0V_S}{D_I\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(d-\frac{x}{2}\right) \quad (B.24)$$

$$P \approx \frac{hS_0V_S}{2D_P\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)} x\left(x-d\right) \quad (B.25)$$

The above three equations give the solution of the steady state of Eq. 1-3.

Similarly, solving the steady state of Eq. 4-6 and 7-9, the solutions given in Eq. 26-28 and 29-31 are obtained, respectively.

Appendix C: Approximate analytical solution for the non steady state model using HAM

The homotopy for Eq. 1-3 are constructed as follows:

$$(1-p)\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_S\frac{\partial^2 S}{\partial x^2}-\frac{\partial S}{\partial t}\right)\right]=ph\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_S\frac{\partial^2 S}{\partial x^2}-\frac{\partial S}{\partial t}\right)-V_S S\right] \tag{C.1}$$

$$(1-p)\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_I\frac{\partial^2 I}{\partial x^2}-\frac{\partial I}{\partial t}\right)\right]=ph\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_I\frac{\partial^2 I}{\partial x^2}-\frac{\partial I}{\partial t}\right)-V_S S\right] \tag{C.2}$$

$$(1-p)\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_P\frac{\partial^2 P}{\partial x^2}-\frac{\partial P}{\partial t}\right)\right]=ph\left[\left(K_S\left(1+\frac{I}{K_I}\right)+S\right)\left(D_P\frac{\partial^2 P}{\partial x^2}-\frac{\partial P}{\partial t}\right)+V_S S\right] \tag{C.3}$$

Let the approximate solution of Eq. C1-C3 be:

$$S = S_0+pS_1+p^2S_2+ \dots \tag{C.4}$$

$$I = I_0+pI_1+p^2I_2+ \dots \tag{C.5}$$

$$P = P_0+pP_1+p^2P_2+ \dots \tag{C.6}$$

The boundary conditions for the above equations become:
At t = 0:

$$S_0 = S_0,\ S_1 = S_2 = S_3 = \dots = 0 \tag{C.7}$$

$$I_0 = I_0,\ I_1 = I_2 = I_3 = \dots = 0 \tag{C.8}$$

$$P_0 = P_1 = P_2 = P_3 = \dots = 0 \tag{C.9}$$

At x = 0:

$$S_0 = S_0,\ S_1 = S_2 = S_3 = \dots = 0 \tag{C.10}$$

$$I_0 = I_0,\ I_1 = I_2 = I_3 = \dots = 0 \tag{C.11}$$

$$P_0 = P_1 = P_2 = P_3 = \dots = 0 \tag{C.12}$$

At x = d:

$$\left.\frac{\partial S_0}{\partial x}\right|_{x=d}=\left.\frac{\partial S_1}{\partial x}\right|_{x=d}=\left.\frac{\partial S_2}{\partial x}\right|_{x=d}=\dots=0 \tag{C.13}$$

$$\left.\frac{\partial I_0}{\partial x}\right|_{x=d}=\left.\frac{\partial I_1}{\partial x}\right|_{x=d}=\left.\frac{\partial I_2}{\partial x}\right|_{x=d}=\dots=0 \tag{C.14}$$

$$P_0 = P_1 = P_2 = P_3 = \dots = 0 \tag{C.15}$$

Substituting Eq. C4-C6 in C1-C3 and equating the coefficients of p^0 and p^1, the following is obtained:

$$p^0 : D_S\frac{\partial^2 S_0}{\partial x^2}-\frac{\partial S_0}{\partial t}=0 \tag{C.16}$$

$$D_I\frac{\partial^2 I_0}{\partial x^2}-\frac{\partial I_0}{\partial t}=0 \tag{C.17}$$

Appendix C: Continued

$$D_P\frac{\partial^2 P_0}{\partial x^2}-\frac{\partial P_0}{\partial t}=0 \tag{C.18}$$

$$p^1:\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_S\frac{d^2S_1}{dx^2}-\frac{\partial S_1}{\partial t}\right)-\left(D_S\frac{\partial^2 S_0}{\partial x^2}-\frac{\partial S_0}{\partial t}\right)\right]$$

$$=h\left[\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left(D_S\frac{\partial^2 S_0}{\partial x^2}-\frac{\partial S_0}{\partial t}\right)-V_SS_0\right] \tag{C.19}$$

$$\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_I\frac{d^2I_1}{dx^2}-\frac{\partial I_1}{\partial t}\right)-\left(D_I\frac{\partial^2 I_0}{\partial x^2}-\frac{\partial I_0}{\partial t}\right)\right]$$

$$=h\left[\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left(D_I\frac{\partial^2 I_0}{\partial x^2}-\frac{\partial I_0}{\partial t}\right)-V_SS_0\right] \tag{C.20}$$

$$\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_P\frac{d^2P_1}{dx^2}-\frac{\partial P_1}{\partial t}\right)-\left(D_P\frac{\partial^2 P_0}{\partial x^2}-\frac{\partial P_0}{\partial t}\right)\right]$$

$$=h\left[\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left(D_P\frac{\partial^2 P_0}{\partial x^2}-\frac{\partial P_0}{\partial t}\right)-V_SS_0\right] \tag{C.21}$$

Applying laplace transform to Eq. C16-C21 with respect to t:

$$D_S\frac{\partial^2\overline{S_0}}{\partial x^2}-\left(s\overline{S_0}-S_0(t=0)\right)=0 \tag{C.22}$$

$$D_I\frac{\partial^2\overline{I_0}}{\partial x^2}-\left(s\overline{I_0}-I_0(t=0)\right)=0 \tag{C.23}$$

$$D_P\frac{\partial^2\overline{P_0}}{\partial x^2}-\left(s\overline{P_0}-P_0(t=0)\right)=0 \tag{C.24}$$

$$\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_S\frac{d^2\overline{S_1}}{dx^2}-\left(s\overline{S_1}-S_1(t=0)\right)\right)\right]=h\left[-V_SS_0\right] \tag{C.25}$$

$$\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_I\frac{d^2\overline{I_1}}{dx^2}-\left(s\overline{I_1}-I_1(t=0)\right)\right)\right]=h\left[-V_SS_0\right] \tag{C.26}$$

$$\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\left[\left(D_P\frac{d^2\overline{P_1}}{dx^2}-\left(s\overline{P_1}-P_1(t=0)\right)\right)\right]=h\left[V_SS_0\right] \tag{C.27}$$

Solving Eq. C22 using boundary conditions C7-C15, $\overline{S_o(x)}=\frac{S_0}{s}$:

Taking the inverse laplace transform, $S_0(x)=S_0$ (C.28)

Appendix C: Continued

Solving Eq. C23 using boundary conditions C7-C15, $\overline{I_o(x)} = \frac{I_0}{s}$:

Taking the inverse laplace transform, $I_0(x) = I_0$ (C.29)

Solving Eq. C24 using boundary conditions C7-C15, $\overline{P_o} = 0$:

Taking the inverse laplace transform, $P_0(x) = 0$ (C.30)

Solving Eq. C25 using boundary conditions C7-C15:

$$\overline{S_1(x)} = \frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}(x-d)}{\cosh\sqrt{\frac{s}{Ds}}d}\right) \tag{C.31}$$

Now, let us invert Eq. C31 using the complex inversion formula.
In order to invert Eq. C31:

$$\operatorname{Res}\left(\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}(x-d)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right)$$

needs to be evaluated.

Now, finding the poles of $\overline{S_1}$, there is a pole at s= 0 and there are infinitely many poles given by the solution of the Eq:

$$\cosh\sqrt{\frac{s}{Ds}}d = 0$$

i.e., there are infinite number of poles at:

$$s_n = \frac{-(2n+1)^2\pi^2D_S}{4d^2}$$

where, n = 1, 2, 3, ...
Hence:

$$L^{-1}(\overline{S_1}) = \operatorname{Res}\left[\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}(x-d)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right]_{s=0}$$

$$+\operatorname{Res}\left[e^{st}\left(\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}(x-d)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right)\right]_{s=s_n} \tag{C.32}$$

Appendix C: Continued

The first residue in Eq. C32 is given by:

$$\operatorname{Res}\left[\frac{hV_S S_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}\left(x-d\right)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right]_{s=0}$$

$$=\lim_{s\to 0}\frac{d}{ds}e^{st}\left(-\frac{hV_S S_0}{K_S\left(1+\frac{I_0}{K_I}\right)+S_0}\left(\frac{\cosh\sqrt{\frac{s}{Ds}}\left(x-d\right)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right)+\frac{hV_S S_0}{K_S\left(1+\frac{I_0}{K_I}\right)+S_0}t$$

$$=-\frac{hV_S S_0 x^2}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}+\frac{dhV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}$$

$$=\frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}\left(d-\frac{x}{2}\right) \tag{C.33}$$

The second residue in Eq. C32 is given by:

$$\operatorname{Res}\left[e^{st}\left(\frac{hV_S S_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{Ds}}\left(x-d\right)}{\cosh\sqrt{\frac{s}{Ds}}d}\right)\right)\right]_{s=s_n}$$

$$=\lim_{s\to s_n}e^{st}\left[-\frac{hV_S S_0\cosh\sqrt{\frac{s}{Ds}}\left(x-d\right)}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\frac{d}{ds}\left(\cosh\sqrt{\frac{s}{Ds}}d\right)}\right]$$

$$=\frac{-16hV_S S_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{\left(-1\right)^n e^{-\frac{(2n+1)^2\pi^2 D_S t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi\left(-x+d\right)\right)d^3}{\left(2n+1\right)^3\pi^3 D_S} \tag{C.34}$$

Using the Eq. C33-C34 in Eq. C32:

$$S_1\left(x\right)=\frac{hV_S S_0 x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}\left(d-\frac{x}{2}\right)$$

$$-\frac{16hV_S S_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{\left(-1\right)^n e^{-\frac{(2n+1)^2\pi^2 D_S t}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi\left(-x+d\right)\right)d^3}{\left(2n+1\right)^3\pi^3 D_S} \tag{C.35}$$

Appendix C: Continued

Solving Eq. C26 using boundary conditions C7-C15:

$$\overline{I_1(x)} = \frac{hV_S S_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right) \tag{C.36}$$

Now, let us invert Eq. C36 using the complex inversion formula.

In order to invert Eq. C36:

$$\mathrm{Res}\left(\frac{hV_S S_0}{s^2K_S\left(1+\frac{I_0}{K_I}\right)+S_0}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right)$$

needs to be evaluated.

Now, finding the poles of $\overline{I_1}$, there is a pole at s = 0 and there are infinitely many poles given by the solution of the Eq:

$$\cosh\sqrt{\frac{s}{D_I}}d = 0$$

i.e., there are infinite number of poles at:

$$s_n = \frac{-(2n+1)^2\pi^2 D_I}{4d^2}$$

where, n = 1, 2, 3, ...

Hence:

$$L^{-1}(\overline{I_1}) = \mathrm{Res}\left[\frac{hV_S S_0}{\left(s^2K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right]_{s=0}$$

$$+\mathrm{Res}\left[e^{st}\left(\frac{hV_S S_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right)\right]_{s=s_n} \tag{C.37}$$

The first residue in Eq. C31 is given by:

$$\mathrm{Res}\left[\frac{hV_S S_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right]_{s=0}$$

$$= \underset{s\to 0}{\mathrm{lt}}\frac{d}{ds}e^{st}\left(-\frac{hV_S S_0}{K_S\left(1+\frac{I_0}{K_I}\right)+S_0}\left(\frac{\cosh\sqrt{\frac{s}{D_I}}(x-d)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right)+\frac{hV_S S_0}{K_S\left(1+\frac{I_0}{K_I}\right)+S_0}t$$

Appendix C: Continued

$$=-\frac{hV_SS_0x^2}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}+\frac{dhV_SS_0x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}$$

$$=\frac{hV_SS_0x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}\left(d-\frac{x}{2}\right) \tag{C.38}$$

The second residue in eqn. (C37) is given by:

$$\operatorname{Res}\left[e^{st}\left(\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(1-\frac{\cosh\sqrt{\frac{s}{D_I}}\left(x-d\right)}{\cosh\sqrt{\frac{s}{D_I}}d}\right)\right)\right]_{s=s_n}$$

$$=\underset{s\to s_n}{\mathrm{lt}}\, e^{st}\left[-\frac{hV_SS_0\cosh\sqrt{\frac{s}{D_I}}\left(x-d\right)}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)\frac{d}{ds}\left(\cosh\sqrt{\frac{s}{D_I}}d\right)}\right]$$

$$=\frac{-16hV_SS_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{\left(-1\right)^n e^{-\frac{(2n+1)^2\pi^2D_It}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi\left(-x+d\right)\right)d^3}{\left(2n+1\right)^3\pi^3D_I} \tag{C.39}$$

Using Eq. C38 and C39 in Eq. C37:

$$I_1\left(x\right)=\frac{hV_SS_0x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}\left(d-\frac{x}{2}\right)$$

$$-\frac{16hV_SS_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{\left(-1\right)^n e^{-\frac{(2n+1)^2\pi^2D_It}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi\left(-x+d\right)\right)d^3}{\left(2n+1\right)^3\pi^3D_I} \tag{C.40}$$

Solving Eq. C27 using boundary conditions C7-C15:

$$\overline{P_1\left(x\right)}=\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right) \tag{C.41}$$

Now, let us invert Eq. C41 using the complex inversion formula.
In order to invert Eq. C41:

Appendix C: Continued

$$\operatorname{Res}\left(\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right)\right)$$

needs to be evaluated.

Now, finding the poles of $\overline{P_1}$, there is a pole at s = 0 and there are infinitely many poles given by the solution of the Eq:

$$\sinh\sqrt{\frac{s}{D_P}}d=0$$

i.e., there are infinite number of poles at:

$$s_n=\frac{-n^2\pi^2D_P}{d^2}$$

where, n = 1, 2, 3, ...

Hence:

$$L^{-1}(\overline{P_1})=\operatorname{Res}\left[\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right)\right]_{s=0}$$

$$+\operatorname{Res}\left[\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right)\right]_{s=s_n} \tag{C.42}$$

The first residue in Eq. C42 is given by:

$$\operatorname{Res}\left[\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right)\right]_{s=0}$$

$$=\frac{hV_SS_0x}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_P}\left(x-d\right) \tag{C.43}$$

The second residue in Eq. C42 is given by:

$$\operatorname{Res}\left[e^{st}\left(\frac{hV_SS_0}{s^2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\left(\frac{\sinh\sqrt{\frac{s}{D_P}}x-\sinh\sqrt{\frac{s}{D_P}}\left(x-d\right)}{\sinh\sqrt{\frac{s}{D_P}}d}-1\right)\right)\right]_{s=s_n}$$

Appendix C: Continued

$$=\frac{2hV_SS_0d^2}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3D_P} \tag{C.44}$$

Using the Eq. C43 and C44 in Eq. C42:

$$P_1(x)=\frac{hV_SS_0x}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_P}(x-d)$$

$$+\frac{2hV_SS_0D_pd^2}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3D_P} \tag{C.45}$$

From Eq. C4-C6, $S\approx S_0+S_1$, $I\approx I_0+I_1$ and $P\approx P_0+P_1$, hence:

$$S=S_0+\frac{hV_SS_0x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_S}\left(d-\frac{x}{2}\right)$$

$$-\frac{16hV_SS_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2D_St}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3D_S} \tag{C.46}$$

$$I=I_0+\frac{hV_SS_0x}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_I}\left(d-\frac{x}{2}\right)$$

$$-\frac{16hV_SS_0}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{(2n+1)^2\pi^2D_It}{4d^2}}\cos\left(\frac{2n+1}{2d}\pi(-x+d)\right)d^3}{(2n+1)^3\pi^3D_I} \tag{C.47}$$

$$P=\frac{hV_SS_0x}{2\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)D_P}(x-d)$$

$$+\frac{2hV_SS_0d^2}{\left(K_S\left(1+\frac{I_0}{K_I}\right)+S_0\right)}\sum_{n=0}^{\infty}\frac{(-1)^n e^{-\frac{n^2\pi^2D_Pt}{d^2}}\left(\sin\left(\frac{n\pi}{d}(x-d)\right)-\sin\left(\frac{n\pi x}{d}\right)\right)}{n^3\pi^3D_P} \tag{C.48}$$

The above three equations give the solution of Eq. 1-3.

Similarly solving Eq. 4-6 and 7-9, the solutions given in Eq. 38-40 and 41-43 are obtained respectively.

Appendix D: MATLAB program to find the numerical solution

Competitive reversible inhibition system (Eq. 1-3)

```
function pdex1
m = 0;
x = linspace(0,1);
t = linspace(0,1000);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('time')
figure
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,3)')
figure
plot(x,u3(end,:))
title('u3(x,t)')
xlabel('Distance x')
ylabel('u3(x,3)')
%-----------------------------------------------------------------
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c = [1;1;1];
f = [1;1;1].*DuDx;
s0 = 5;
i0 = 2;
Vs = 2;
Ks = 0.6;
Ki = 0.4;
Kid = 2;
Ds = 2;
Di = 2;
Dp = 2;
F1 = -u(1)*Vs/(Ds*Ks*(1+u(2)/Ki)+Ds*u(1));
F2 = -u(1)*Vs/(Di*Ks*(1+u(2)/Ki)+Ds*u(1));
F3 = u(1)*Vs/(Dp*Ks*(1+u(2)/Ki)+Ds*u(1));;
s = [F1;F2;F3];
% --------------------------------------------------------------
function u0 = pdex1ic(x)
lamda = 1;
u0 = [5;2;0];
% --------------------------------------------------------------
function [pl,ql,pr,qr]=pdex1bc(xl,ul,xr,ur,t)
pl = [ul(1)-5;ul(2)-2;ul(3)-0];
ql = [0;0;0];
pr = [0;0;ur(3)-0];
qr = [1;1;0];
```

Non-competitive reversible inhibition system (Eq. 4-6)

```
function pdex1
m = 0;
x = linspace(0,1);
t = linspace(0,1000);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('time')
figure
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,3)')
figure
plot(x,u3(end,:))
title('u3(x,t)')
xlabel('Distance x')
ylabel('u3(x,3)')
%-----------------------------------------------------------------
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c =[1;1;1];
f =[1;1;1].*DuDx;
s0 = 5;
i0 = 2;
Vs = 2;
Ks = 0.6;
Ki = 0.8;
Kid = 2;
Ds = 2;
Di = 2;
Dp = 3;
F1 = -u(1)*Vs/(Ds*(1+u(2)/Ki)*(Ks+u(1)));
F2 = -u(1)*Vs/(Di*(1+u(2)/Ki)*(Ks+u(1)));
F3 = u(1)*Vs/(Di*(1+u(2)/Ki)*(Ks+u(1)));
s = [F1;F2;F3];
% --------------------------------------------------------------
function u0 = pdex1ic(x)
lamda=1;
u0 = [5;2;0];
% --------------------------------------------------------------
function [pl,ql,pr,qr]=pdex1bc(xl,ul,xr,ur,t)
pl = [ul(1)-5;ul(2)-2;ul(3)-0];
ql = [0;0;0];
pr = [0;0;ur(3)-0];
qr = [1;1;0];
```

Mixed reversible inhibition system (Eq. 7-9)

```
function pdex1
m=0;
x = linspace(0,1);
t = linspace(0,1000);
sol = pdepe(m,@pdex1pde,@pdex1ic,@pdex1bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('time')
figure
```

Appendix D: Continued

```
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,3)')
figure
plot(x,u3(end,:))
title('u3(x,t)')
xlabel('Distance x')
ylabel('u3(x,3)')
%-----------------------------------------------------------------
function [c,f,s] = pdex1pde(x,t,u,DuDx)
c = [1;1;1];
f = [1;1;1].*DuDx;
s0 = 5;
i0 = 2;
Vs = 0.5;
Ks = 0.6;
Ki = 0.6;
Kid = 2;
Ds = 2;
Di = 2;
Dp = 3;
F1 = -u(1)*Vs/(Ds*(Ks*(1+u(2)/Ki)+u(1)*(1+u(2)/Kid)));
F2 = -u(1)*Vs/(Di*(Ks*(1+u(2)/Ki)+u(1)*(1+u(2)/Kid)));
F3 = u(1)*Vs/(Dp*(Ks*(1+u(2)/Ki)+u(1)*(1+u(2)/Kid)));
s = [F1;F2;F3];
% --------------------------------------------------------------
function u0 = pdex1ic(x)
lamda = 1;
u0 = [5;2;0];
% --------------------------------------------------------------
function [pl,ql,pr,qr]=pdex1bc(xl,ul,xr,ur,t)
pl = [ul(1)-5;ul(2)-2;ul(3)-0];
ql = [0;0;0];
pr = [0;0;ur(3)-0];
qr = [1;1;0];
```

Figure 1-3 clearly showed that the solution obtained using the homotopy analysis method is the closest to the numerical solution and hence is the better of the two methods for this problem. Thus, the homotopy analysis method is used to find the non-steady state solution of the problem.

Figure 4-6 showed the substrate concentration, inhibitor concentration and product concentration profiles for biosensors with competitive inhibitions for various values of parameters. The figures clearly showed that substrate concentration increases with increase in K_S and D_S, while decreases with increase in V_S and K_I. A similar effect is experienced on the inhibitor concentration as well. That is, the inhibitor concentration increases with increase in K_S and D_I, while decreases with increase in V_S and K_I. The product concentration increases with increase in V_S.

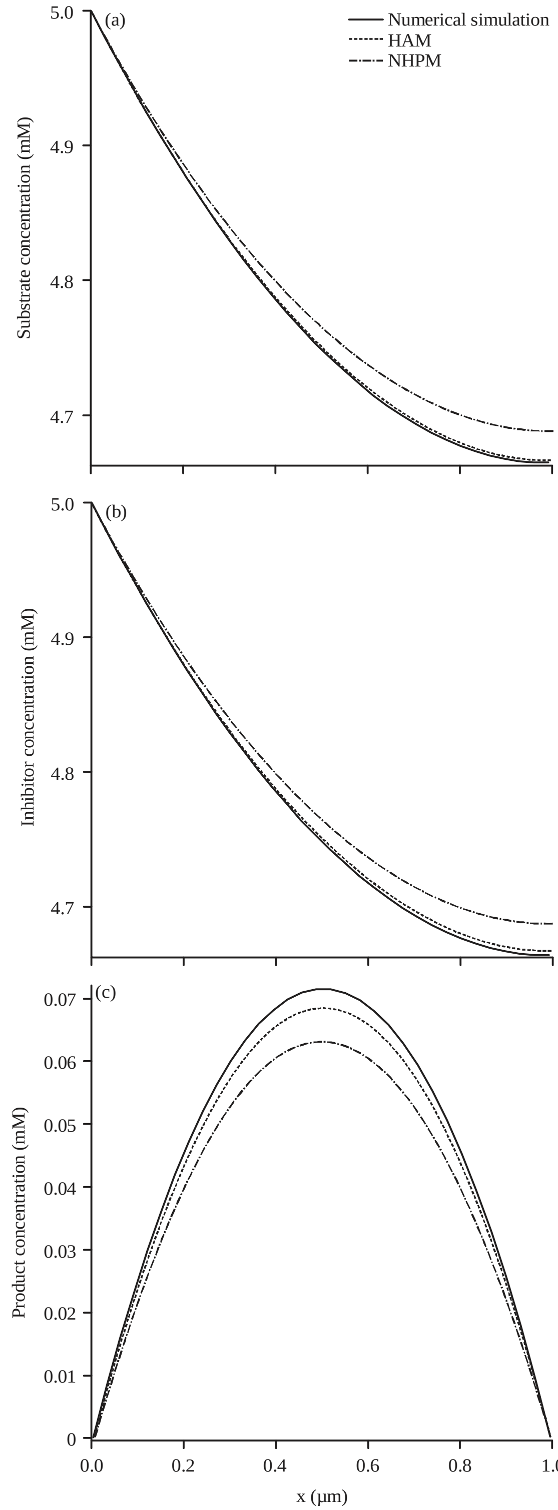

Fig. 1(a-c): Profile of the (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus distance (x) for the competitive reversible inhibition system for values of parameters given in Table 1

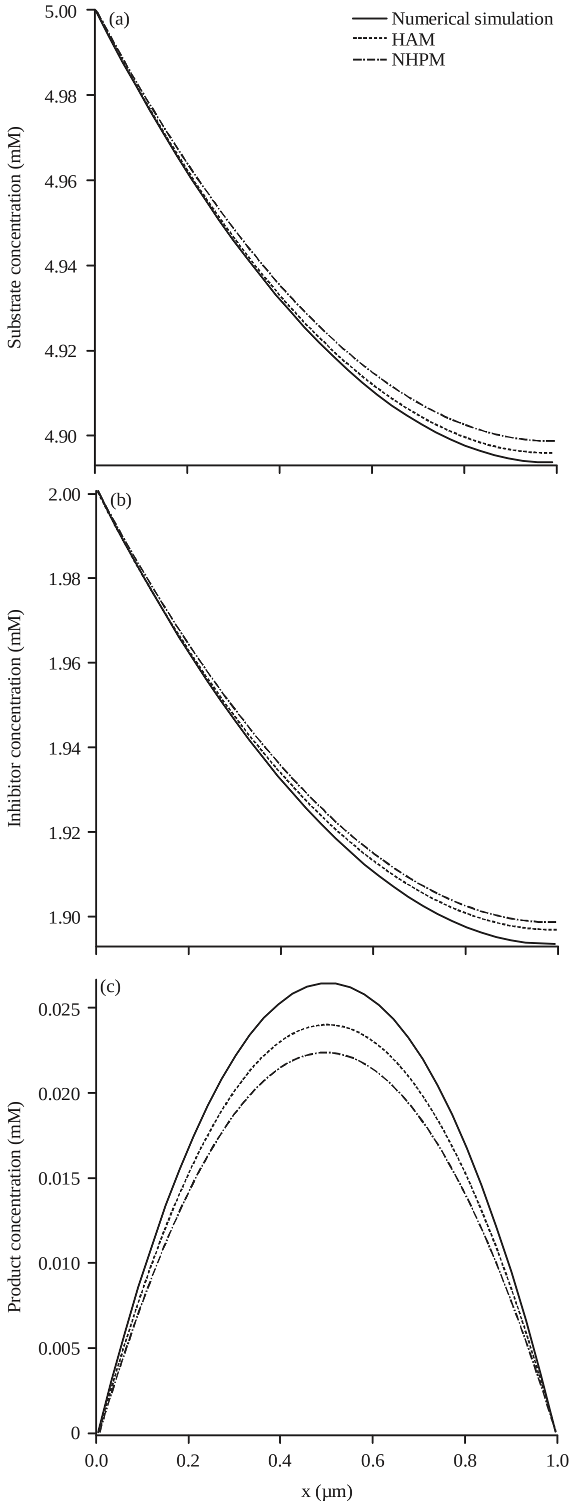

Fig. 2(a-c): Profile of the (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus distance (x) for the non-competitive reversible inhibition system for values of parameters given in Table 1

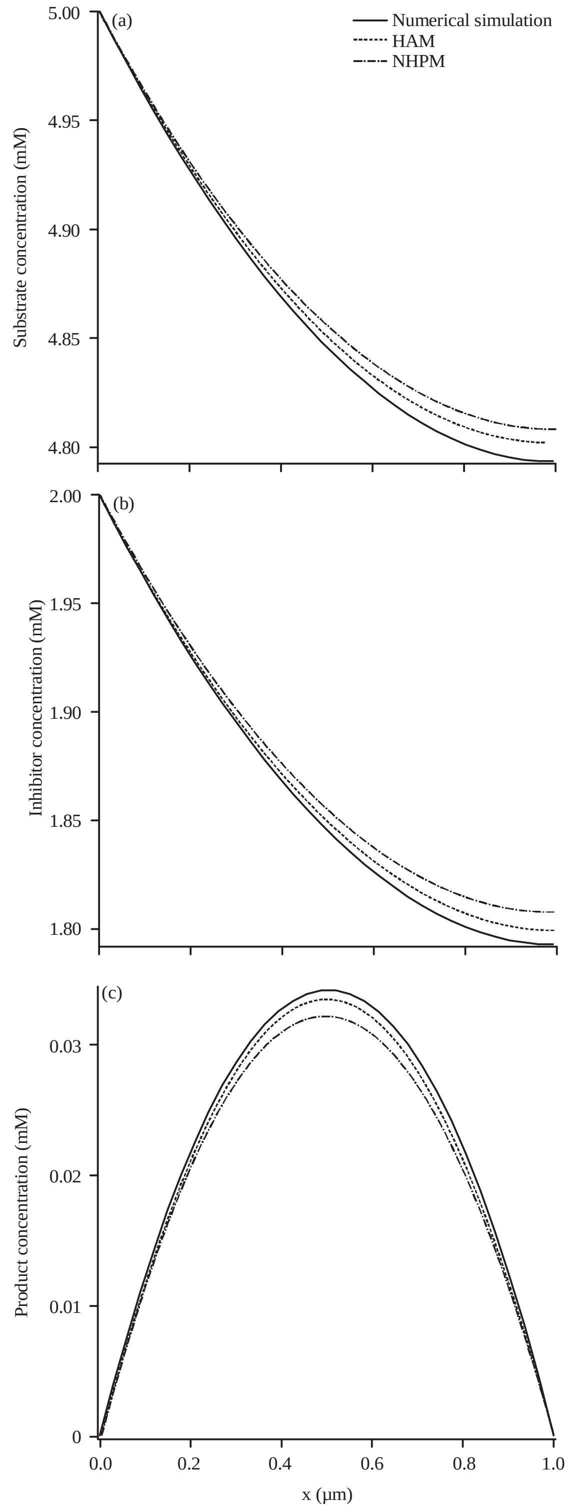

Fig. 3(a-c): Profile of the (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus distance (x) for the mixed reversible inhibition system for values of parameters given in Table 1

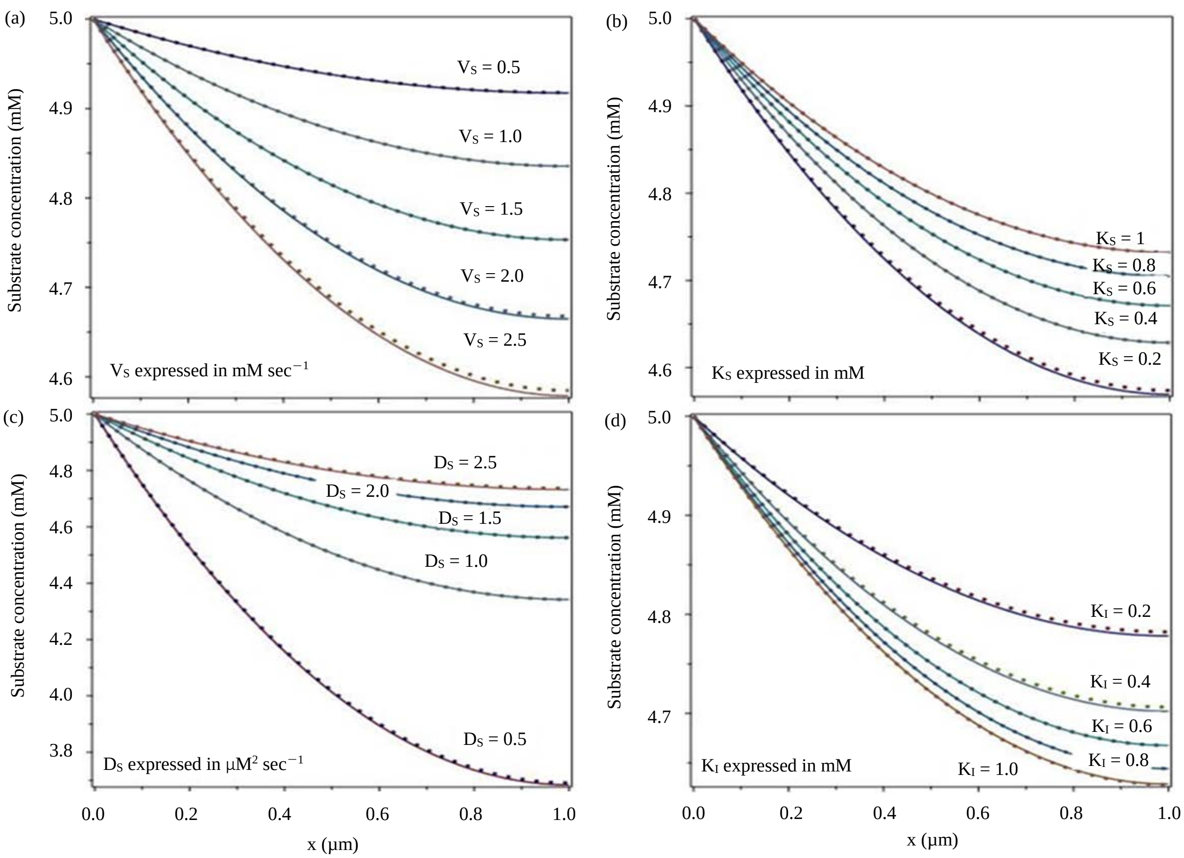

Fig. 4(a-d): Substrate concentration (S) versus distance (x) for the competitive reversible inhibition system obtained by varying one parameter and keeping all other parameters fixed
Refer parameter values given in Table 1

Table 7: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 2c

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Product concentration (P)					
0	0	0	0	0	0
0.2	0.01687097680	0.01538461538	0.01428571428	8.81017	15.3237
0.4	0.02538638454	0.02307692307	0.02142857142	0	0
0.6	0.02545351202	0.02307692307	0.02142857142	0	0
0.8	0.01700461295	0.01538461538	0.01428571428	9.52681	15.9892
1	0	0	0	0	0
Average absolute (%) error				3.05616	5.21882

Table 8: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 3a

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Substrate concentration (S)					
0	5	5	5	0	0
0.2	4.925915766	4.928571429	4.930567633	0.053912	0.094437
0.4	4.867983631	4.873015873	4.876792003	0	0
0.6	4.826433133	4.833333333	4.838502347	0	0
0.8	4.801433531	4.809523810	4.815577081	0.168497	0.294569
1	4.793088591	4.801587302	4.807943407	0.177312	0.309922
Average absolute (%) error				0.06662	0.116488

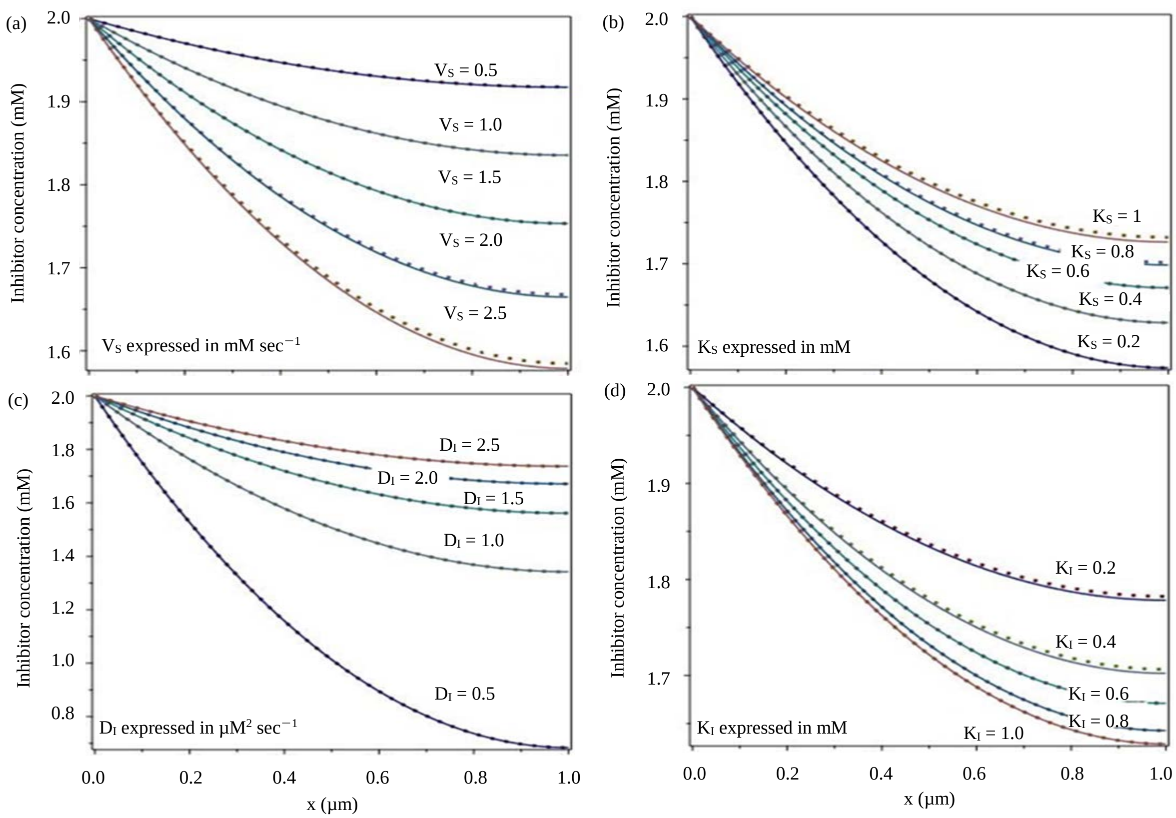

Fig. 5(a-d): Inhibitor concentration (I) versus distance (x) for the competitive reversible inhibition system, obtained by varying one parameter and keeping all other parameters fixed
Refer parameter values given in Table 1

Table 9: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 3b

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Inhibitor concentration (I)					
0	2	2	2	0	0
0.2	1.925915766	1.927857143	1.930567633	0	0
0.4	1.867983631	1.871746032	1.876792004	0.201415	0.471544
0.6	1.826433133	1.831666667	1.838502347	0	0
0.8	1.801433531	1.807619048	1.815577082	0	0
1	1.793088591	1.799603175	1.807943407	0.363316	0.828449
Average absolute (%) error				0.094122	0.216665

Table 10: Comparison between analytical values derived using homotopy analysis method and new approach to homotopy perturbation method with numerical values in Fig. 3c

Distance (x)	Numerical solution	Analytical solution using homotopy analysis method	Analytical solution using new approach to homotopy perturbation method	Absolute (%) error for homotopy analysis method	Absolute (%) error for new approach to homotopy perturbation method
Product concentration (P)					
0	0	0	0	0	0
0.2	0.02180228850	0.02137566138	0.020680699	0	0
0.4	0.03283677425	0.03206349206	0.030923573	0	0
0.6	0.03295042719	0.03206349206	0.030842465	2.69173	6.39737
0.8	0.02203040289	0.02137566138	0.020518430	2.97199	6.86312
1	0	0	0	0	0
Average absolute (%) error				0.94395	2.21008

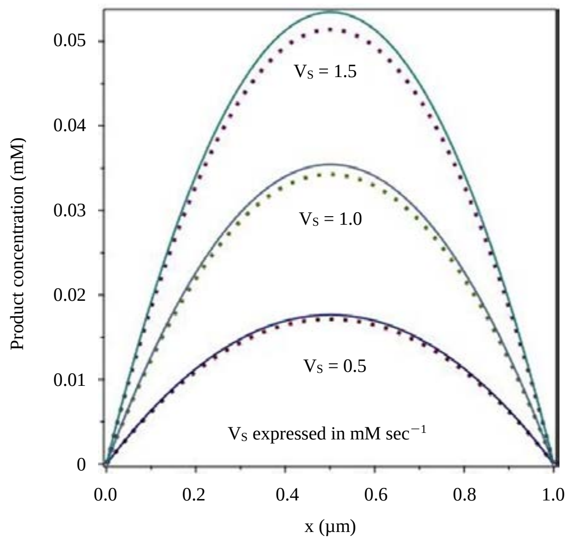

Fig. 6: Product concentration (P) versus distance (x) for the competitive reversible inhibition system, obtained by varying V_S and fixing all other parameters as in Table 1

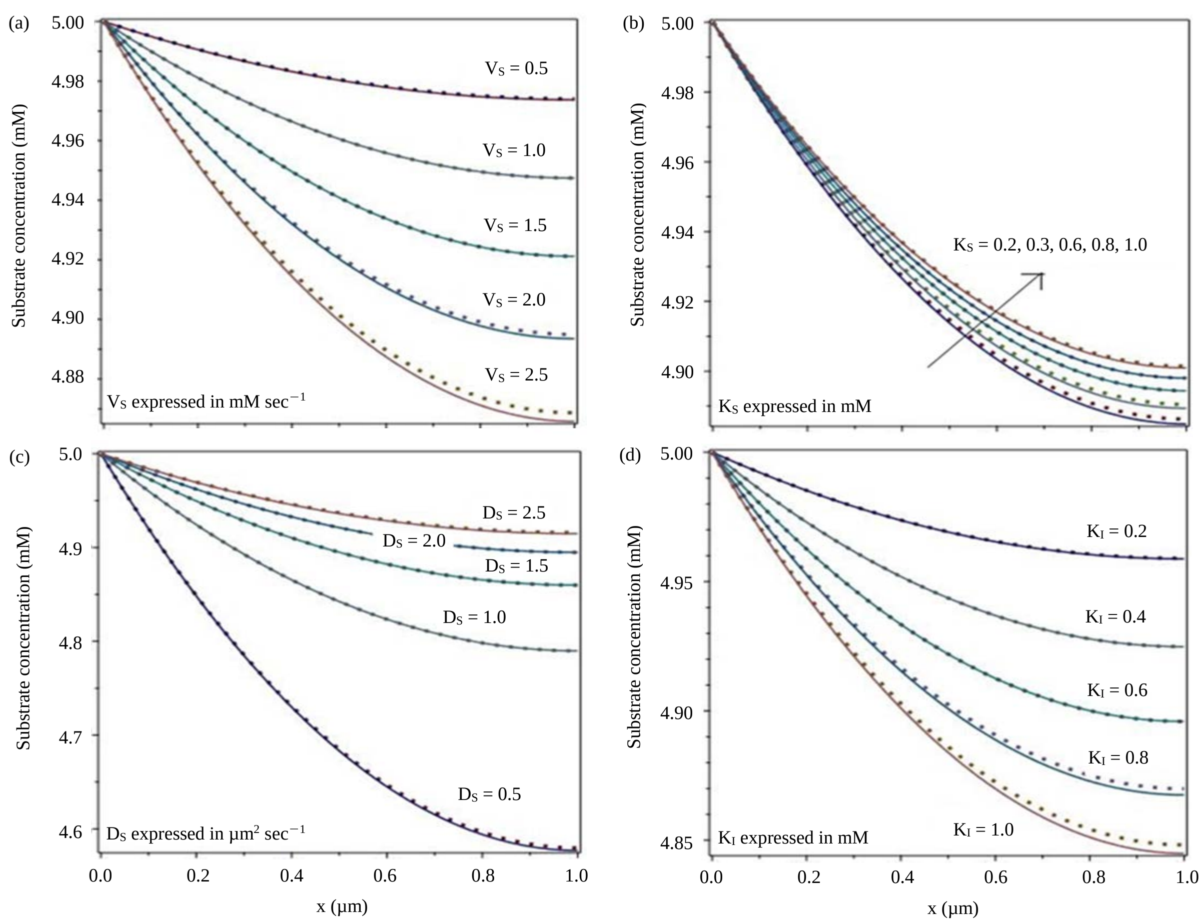

Fig. 7(a-d): Substrate concentration (S) versus distance (x) for the non-competitive reversible inhibition system, obtained by varying one parameter and keeping all other parameters fixed

Refer parameter values given in Table 1

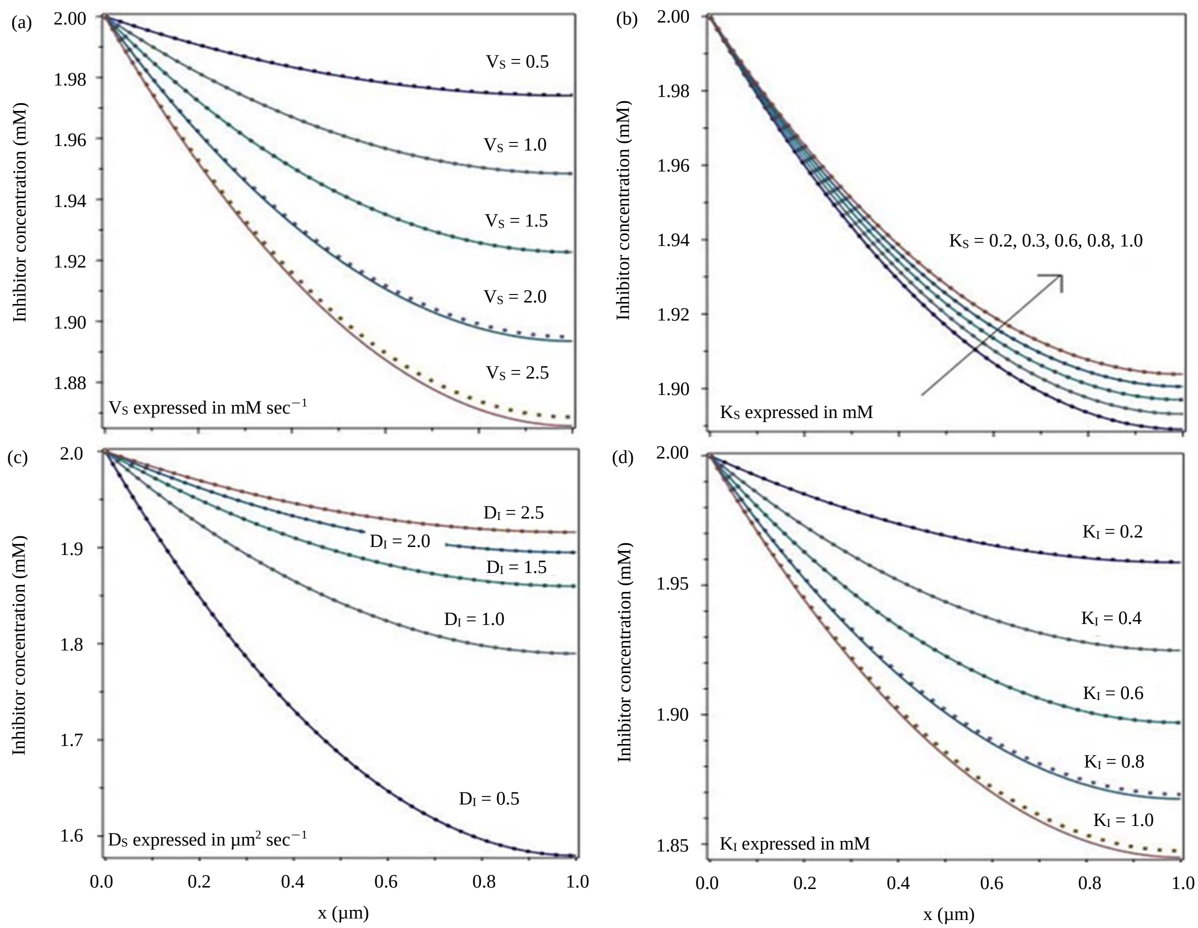

Fig. 8(a-d): Inhibitor concentration (I) versus distance (x) for the non-competitive reversible inhibition system, obtained by varying one parameter and keeping all other parameters fixed
Refer parameter values given in Table 1

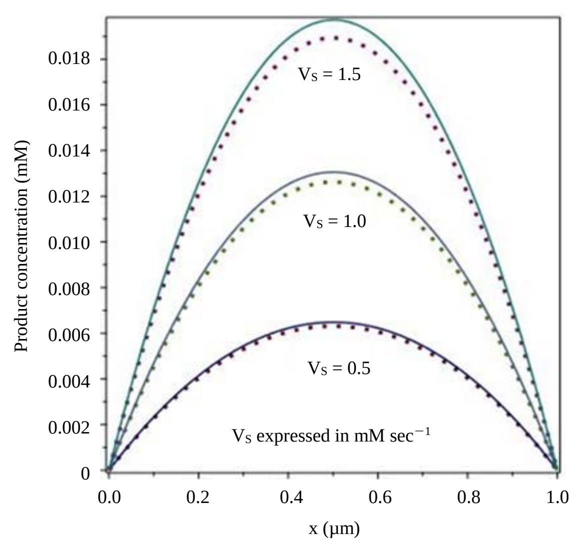

Fig. 9: Product concentration (P) versus distance (x) for the non-competitive reversible inhibition system, obtained by varying V_S and fixing all other parameters as in Table 1

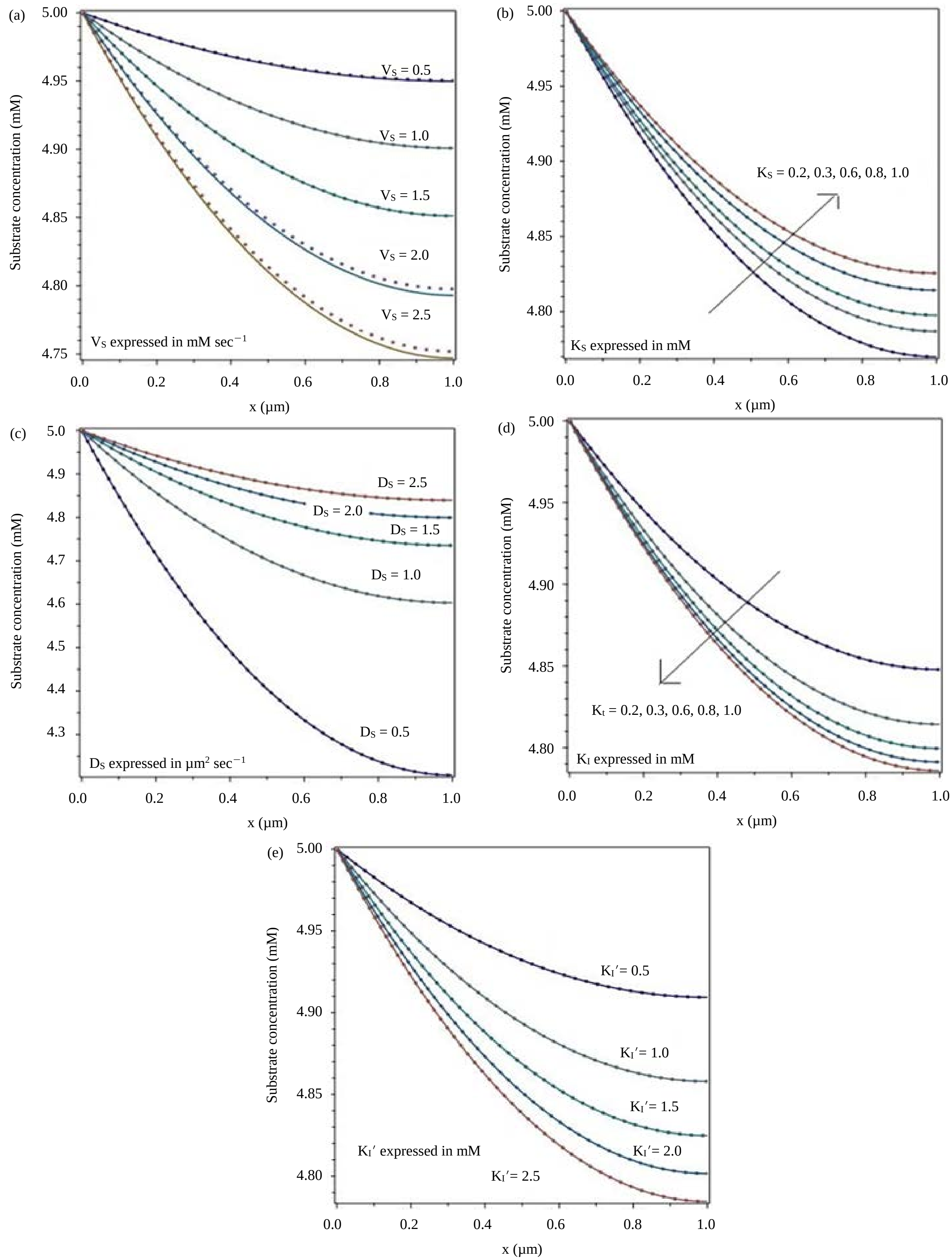

Fig.10(a-e): Substrate concentration (S) versus distance (x) for the mixed reversible inhibition system, obtained by varying one parameter and keeping all other parameters fixed

Refer parameter values given in Table 1

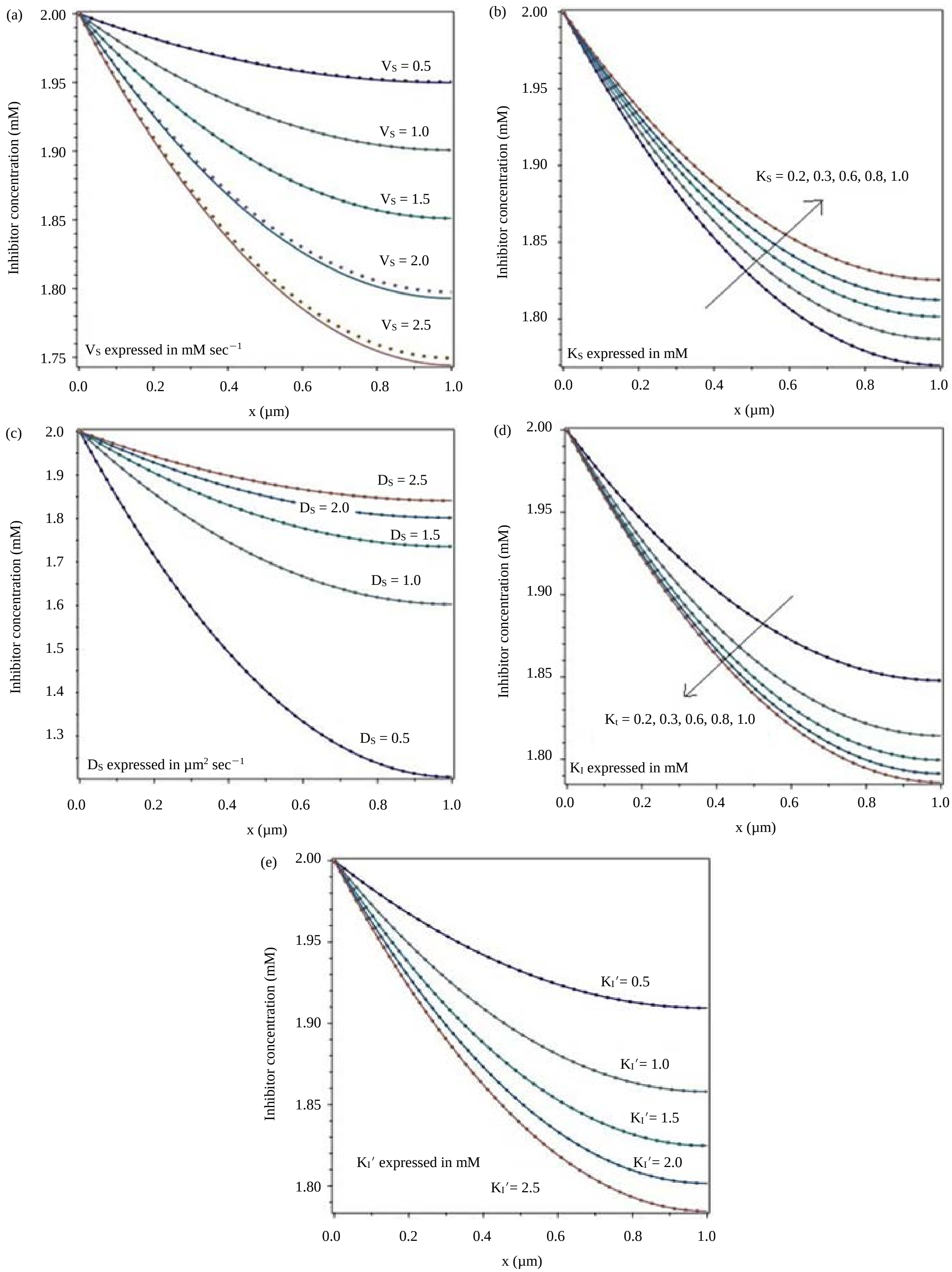

Fig. 11(a-e): Inhibitor concentration (I) versus distance (x) for the mixed reversible inhibition system, obtained by varying one parameter and keeping all other parameters fixed

Refer parameter values given in Table 1

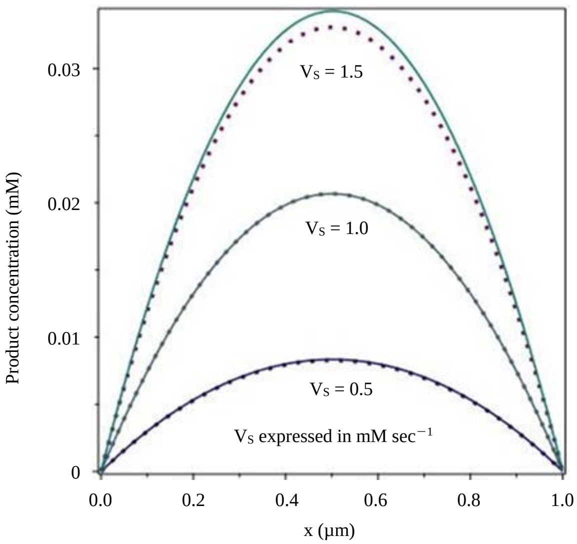

Fig. 12: Product concentration (P) versus distance (x) for the mixed reversible inhibition system, obtained by varying V_S and fixing all other parameters as in Table 1

Figure 13a depicted the substrate concentration for biosensors with competitive, non-competitive and mixed inhibition. From the figure, it is clear to observe that for fixed values of parameters the substrate concentration is the least for competitive inhibition, higher for mixed inhibition and becomes the maximum for non-competitive inhibition. From Fig. 13b, it can be seen that the same happened for inhibitor concentration also. But, from Fig. 13c, it is noted that the reverse happened for product concentration. The product concentration is maximum for competitive mixed inhibition, lower for mixed inhibition and becomes the least for non-competitive inhibition.

Figure 14-16 represented the non-steady state solutions for substrate concentration, inhibitor concentration and product concentration for biosensors with competitive, non-competitive and mixed inhibition respectively.

Figure 17a-c showed three-dimensional substrate concentration, inhibitor concentration and product concentration versus time and distance for a biosensor with competitive inhibition, while Fig. 18 and 19 represented the same for biosensors with non-competitive and mixed inhibitions respectively.

Figure 20-22 respectively showed the steady state output current of the biosensors with competitive, non-competitive and mixed inhibitions for various values of parameters. From the figures, it can be seen that for biosensors with all three inhibitions, the output current increases with increase in S_0 and V_S while decreases with increase in I_0 and K_S.

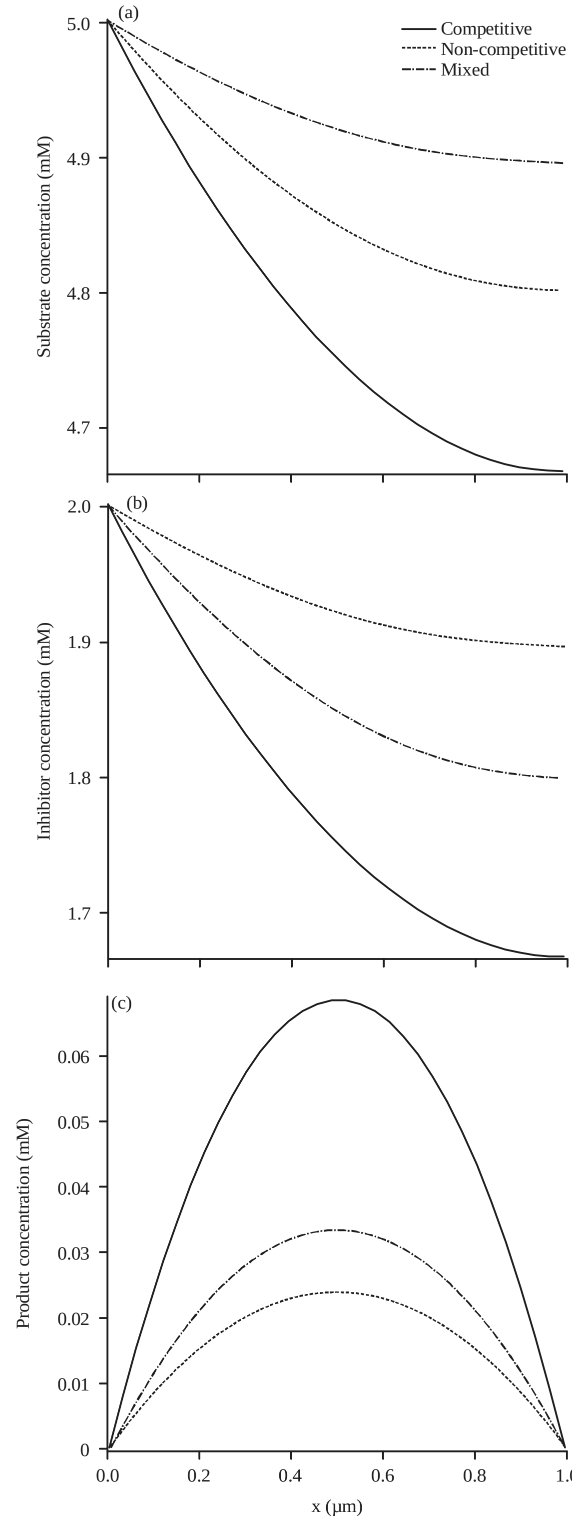

Fig. 13(a-c): (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus distance (x) for the competitive, non-competitive and mixed reversible inhibition systems for values of parameters given in Table 1

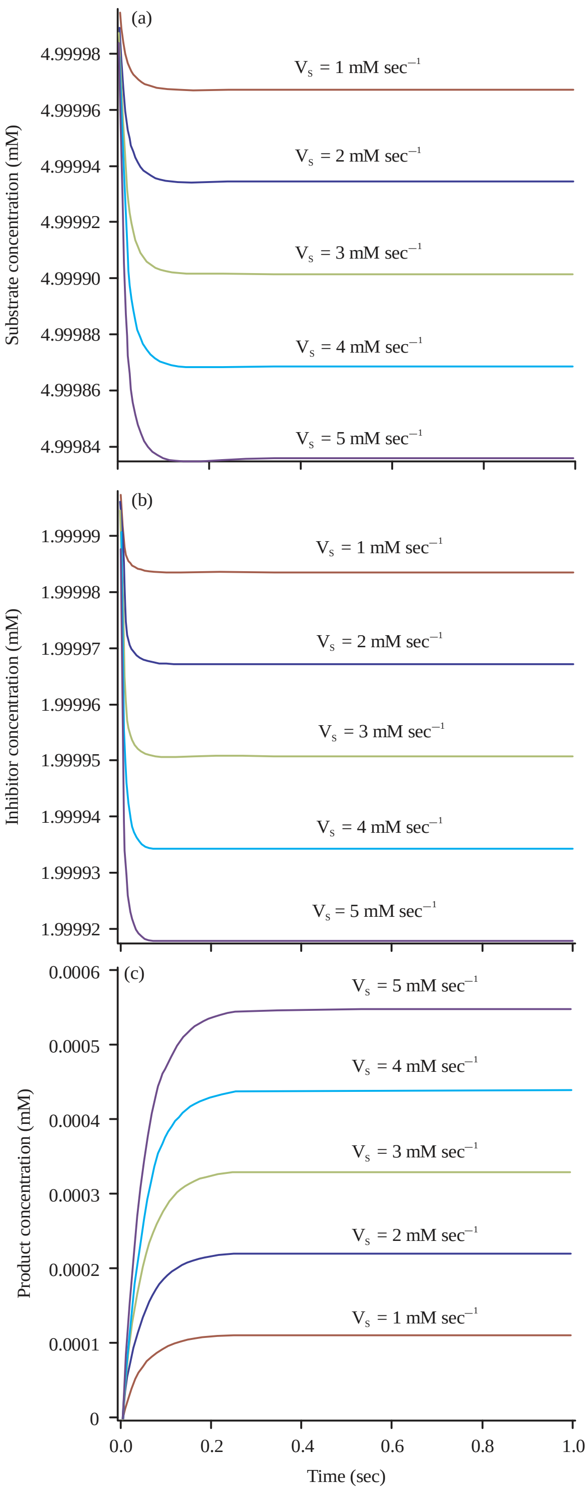

Fig. 14(a-c): Profile of the non-steady state, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus time (t) for the competitive reversible inhibition system for values of parameters given in Table 1

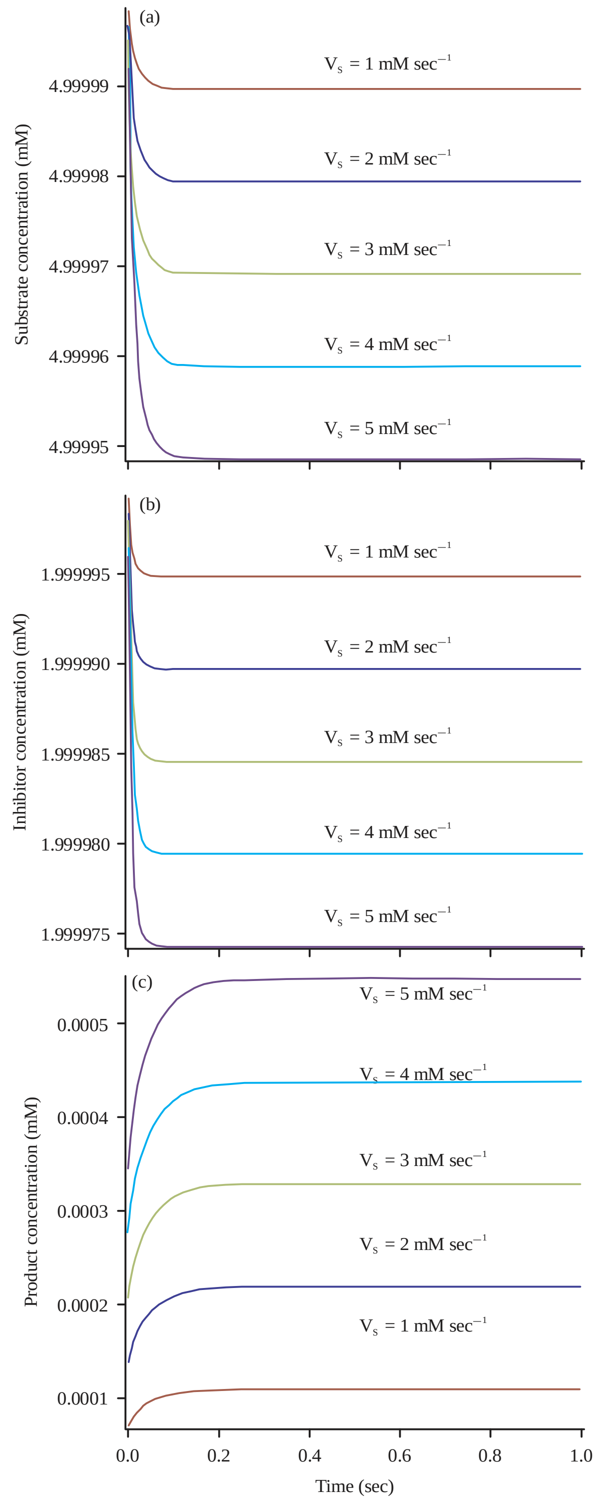

Fig. 15(a-c): Profile of the non steady state, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus time (t) for the non-competitive reversible inhibition system for values of parameters given in Table 1

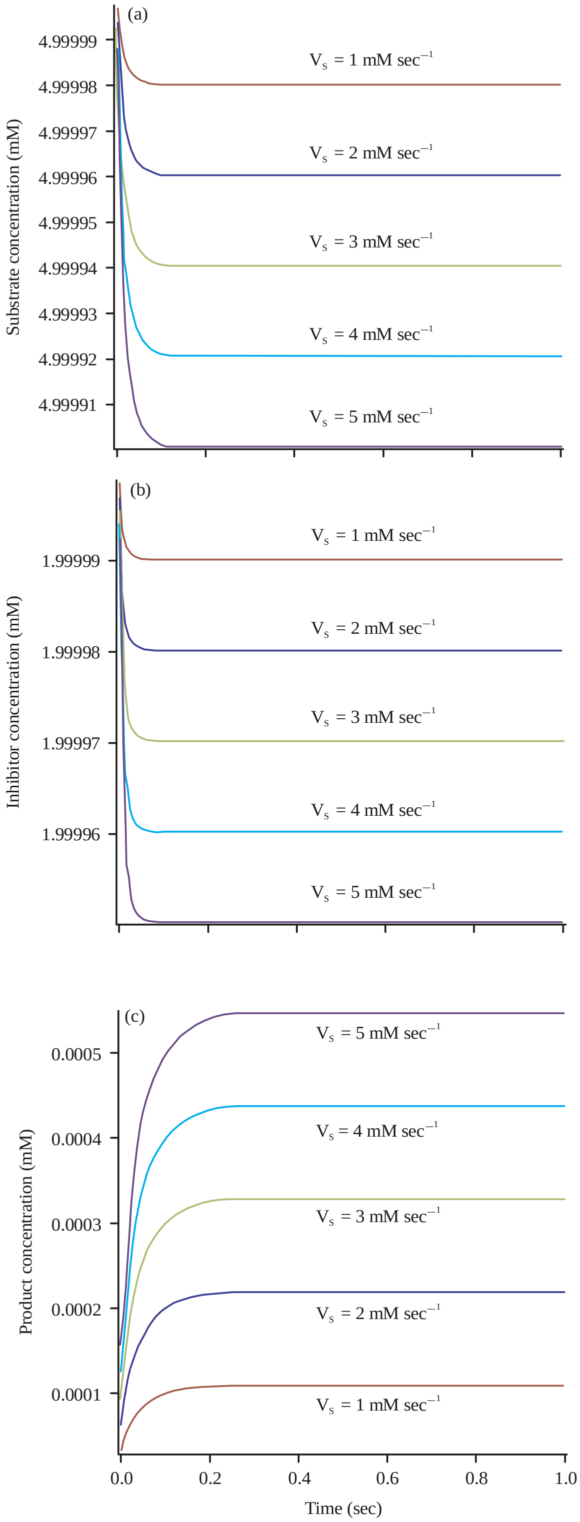

Fig. 16(a-c): Profile of the non steady state, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P) versus time (t) for the mixed reversible inhibition system for values of parameters given in Table 1

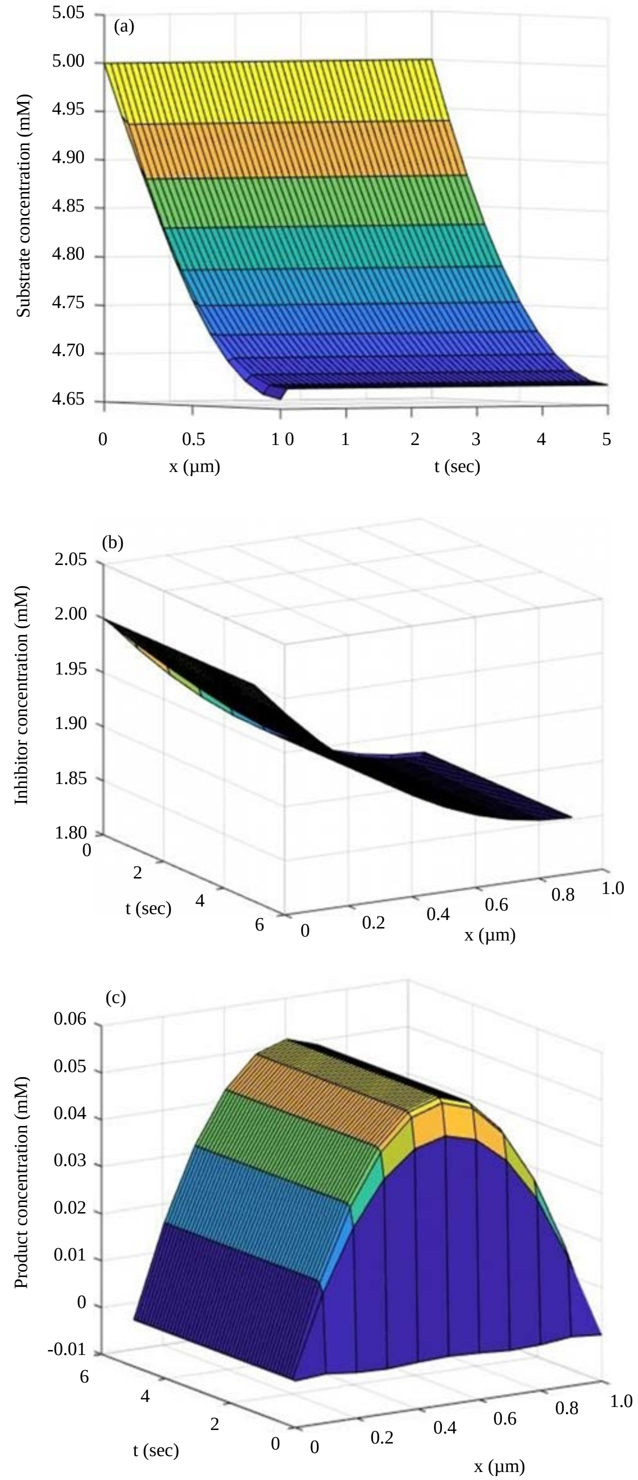

Fig. 17(a-c): Three-dimensional, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P), versus time (t) and distance (x) for the competitive reversible inhibition system for values of parameters given in Table 1

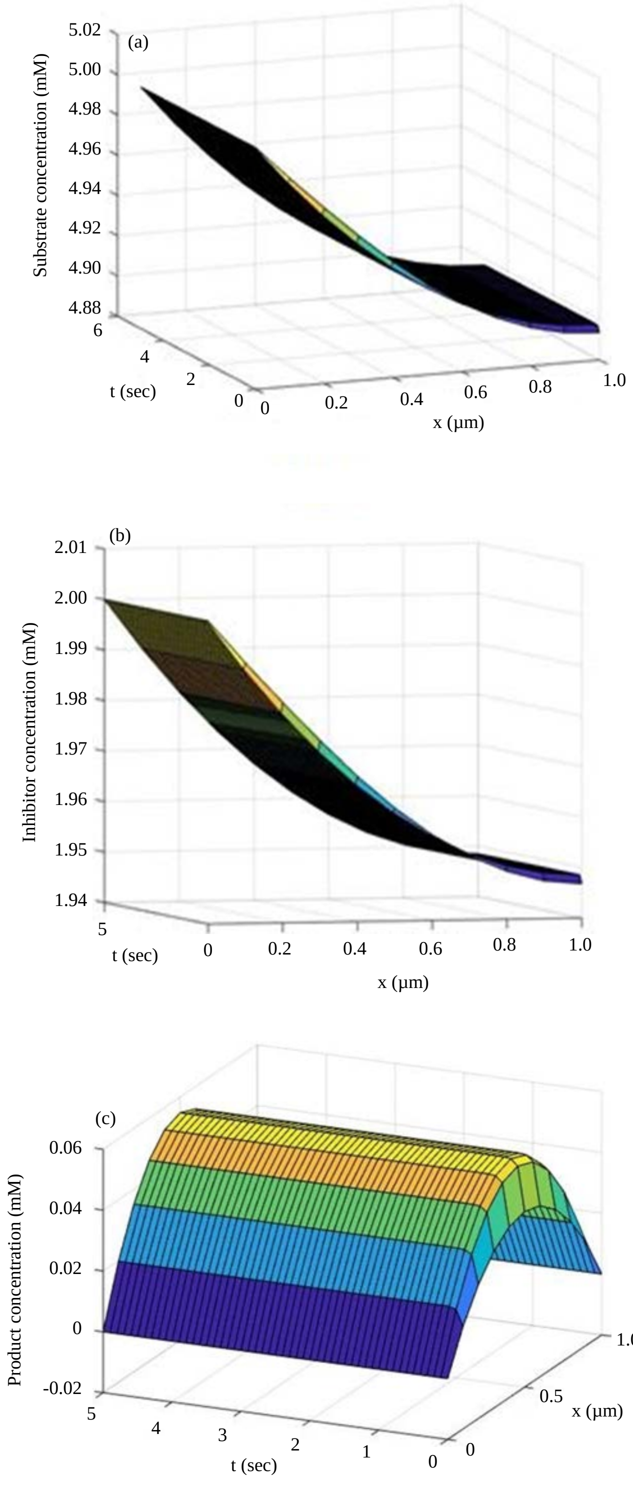

Fig. 18(a-c): Three-dimensional, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P), versus time (t) and distance (x) for the non-competitive reversible inhibition system for values of parameters given in Table 1

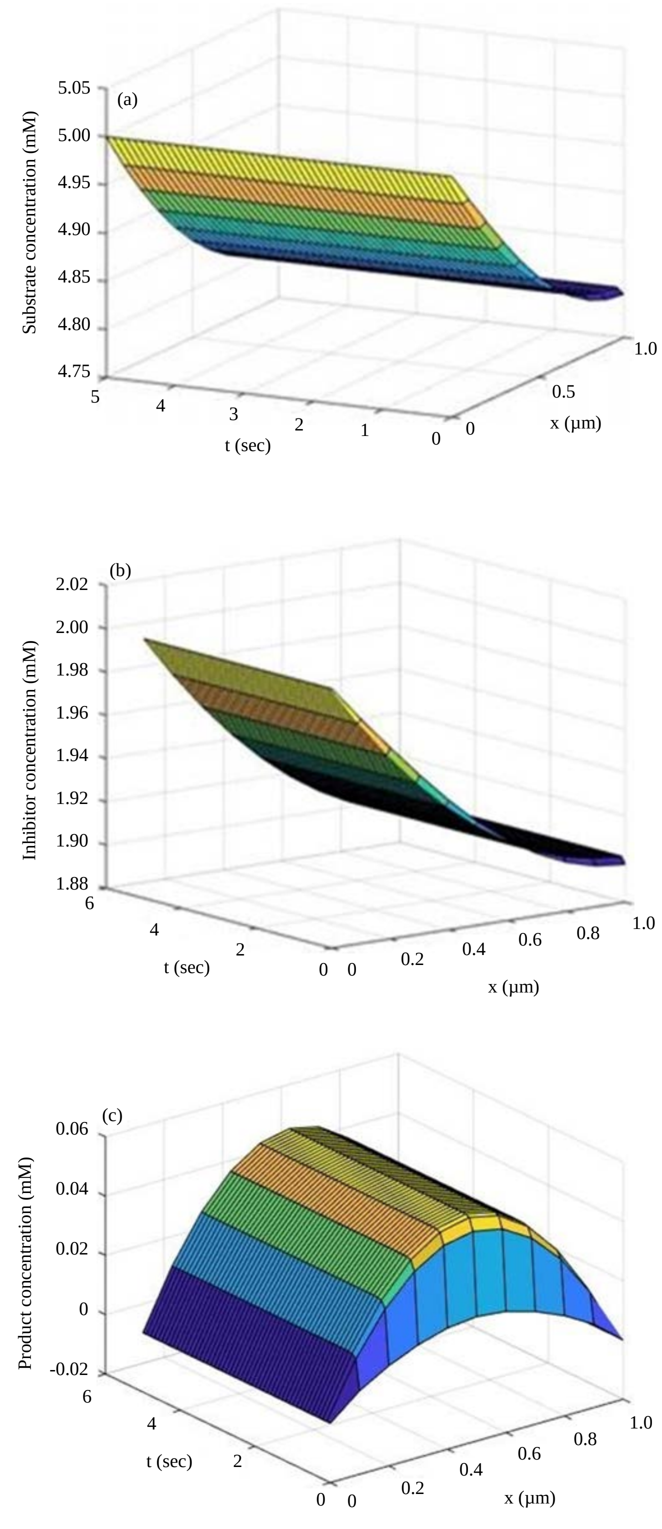

Fig. 19(a-c): Three-dimensional, (a) Substrate concentration (S), (b) Inhibitor concentration (I) and (c) Product concentration (P), versus time (t) and distance (x) for the mixed reversible inhibition system for values of parameters given in Table 1

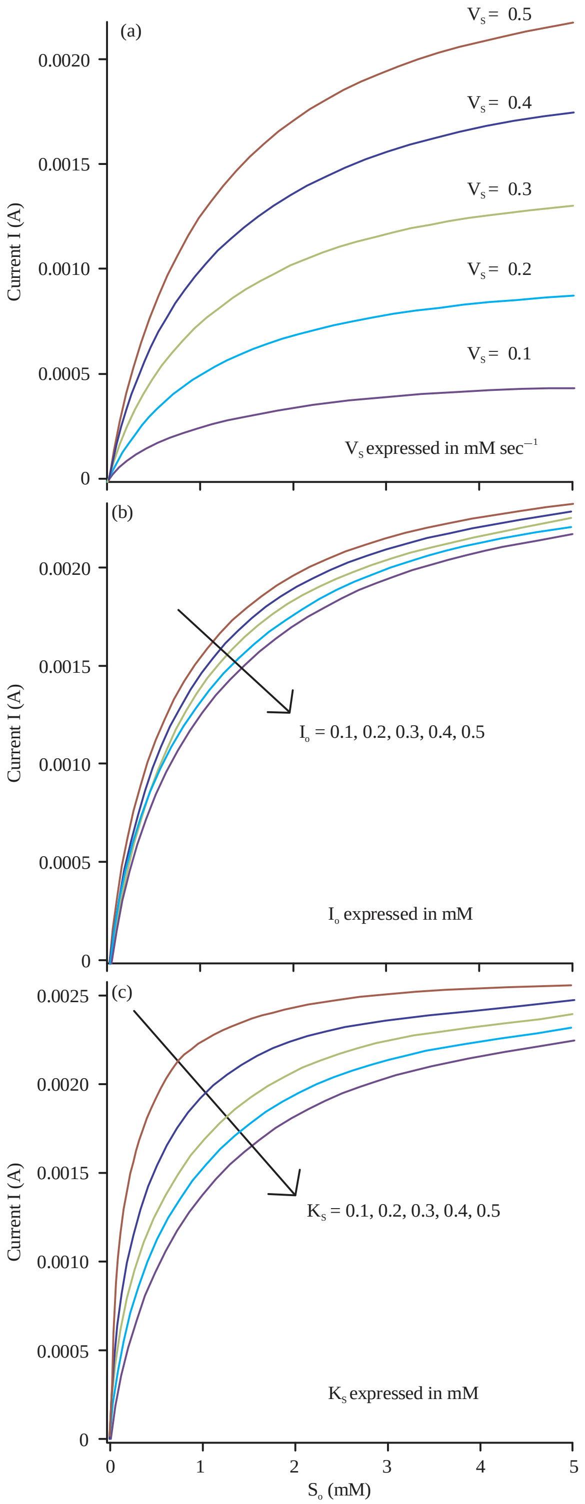

Fig. 20(a-c): Output current of the biosensor with competitive inhibition, obtained by varying one parameter and keeping all other parameters fixed

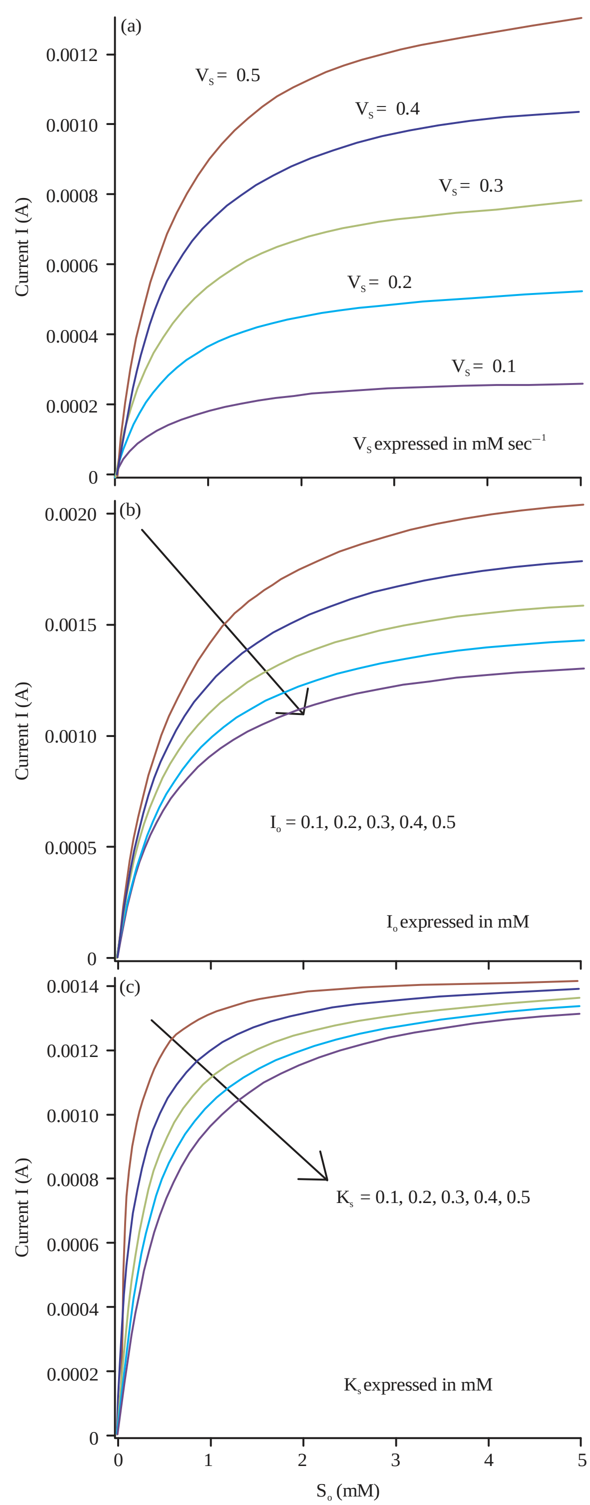

Fig. 21(a-c): Output current of the biosensor with non-competitive inhibition, obtained by varying one parameter and keeping all other parameters fixed

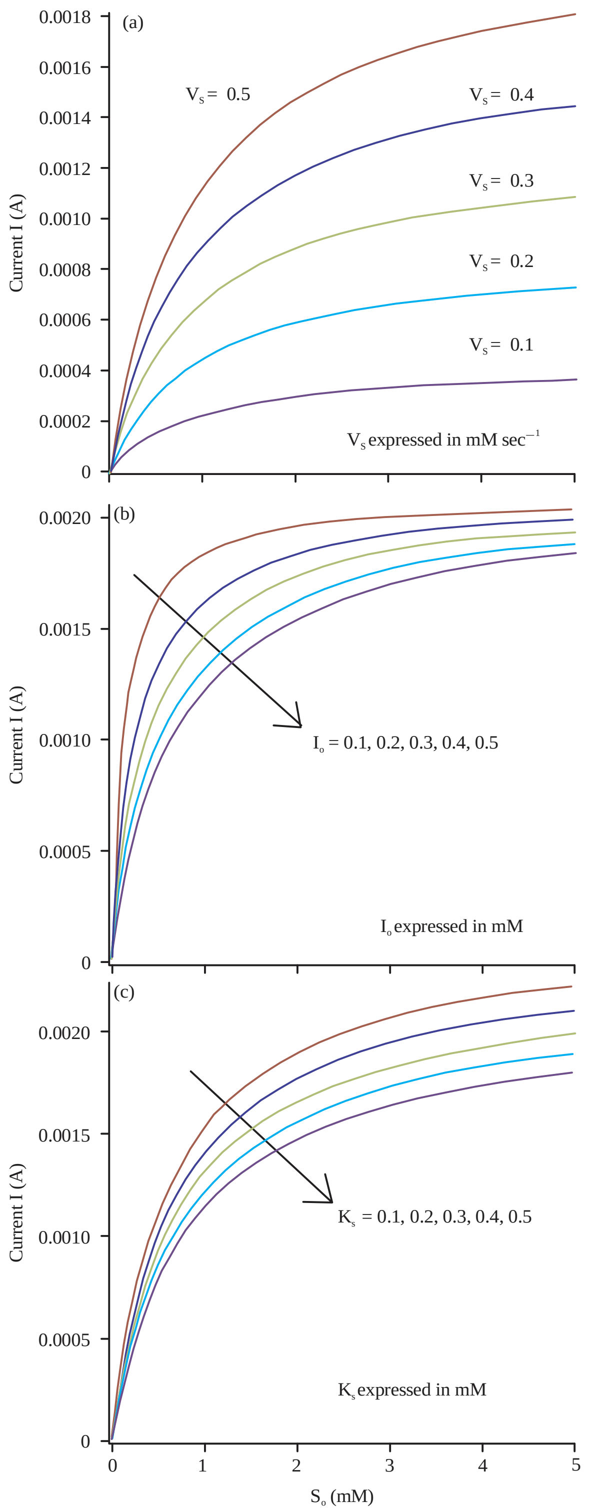

Fig. 22(a-c): Output current of the biosensor with mixed inhibition, obtained by varying one parameter and keeping all other parameters fixed

Table 11: Sensitivity analysis of parameters for output current for parameter values given in Table 1

Nature of inhibition	Parameter	Rate of change in current
Competitive	S_0	9.674627980×10^{-6}
	I_0	$-3.721010755\times10^{-6}$
	V_S	6.697819363×10^{-6}
	K_S	$-0.1612437997\times10^{-4}$
	K_I	$0.1240336920\times10^{-4}$
Non-competitive	S_0	2.608285428×10^{-6}
	I_0	$-2.675164537\times10^{-6}$
	V_S	3.477713899×10^{-6}
	K_S	$-4.347142377\times10^{-6}$
	K_I	8.917215114×10^{-6}
Mixed	S_0	5.925481030×10^{-6}
	I_0	$-3.418546752\times10^{-6}$
	V_S	5.241771696×10^{-6}
	K_S	$-9.875801698\times10^{-6}$
	K_I	7.596770547×10^{-6}

Table 1 gives the values of the parameters used in the construction of graphs. Table 2-10 showed the percentage deviation of the derived analytical results from the numerical result obtained using MATLAB. The deviation percentage is not more than 3% when the model is solved using homotopy analysis method and hence is considered to be the better choice of the two methods considered. Table 11 showed the sensitivity analysis carried out for output current of the biosensor with competitive inhibition for fixed values of parameters. The derived result showed that S_0, V_S and K_I have a positive impact on output current, while I_0 and K_S have negative impact. The sensitivity analysis for output current of the biosensors with non-competitive and mixed inhibition gave similar results. These results are also verified in Fig. 20-22.

DISCUSSION

The steady state and non-steady state solutions for the non linear mathematical model considered have been presented. This is the first time that this kind of a model is mathematically analyzed. Correlating the result derived in this study with the previous literature, it is found that the three-dimensional graphs plotted using the analytical solutions are identical to the three dimensional graphs previously simulated using MATLAB[7]. This provides evidence that the analytical solutions derived here make an excellent fit with the numerical results and hence may be accepted as an approximate analytical solution for the model[7]. Moreover, the previous result presented[7] was numerical, which is a point wise solution, while the result presented here is a general solution for any interval.

Though the analytical result derived here does make a deviation with the numerical values, the error is not a big deal. Hence, the solution derived under non-steady state will help the researchers to interpret the effect of the different parameters over the substrate concentration, product concentration, inhibitor concentration and non-steady state current. The researchers may use this result to predict the outcome of the experiments they want to perform. This will save time, money and energy.

From Table 11, the output current of the biosensor varies directly with S_0, V_S and K_I, while varies inversely with I_0 and K_S. Hence, the key drivers in increasing the output current are K_I, S_0 and V_S. Which means, an increase in either of the three results in an increased output current. On the contrary, I_0 and K_S have a negative impact on the output current. Their decrease will increase the output current.

Mathematical models developed in similar situations[1-6] have been until now been solved only in the steady state[8,9]. The solution derived here will help in deriving time dependent analytical solutions for all such similar models.

CONCLUSION

Time independent nonlinear partial differential equations (steady state) for reversible inhibitor biosensor systems in dynamic mode are solved analytically using the new homotopy perturbation method and homotopy analysis method. It is observed that the solution obtained using homotopy analysis method makes a very close approximation to the numerical solution obtained using MATLAB and hence is considered to be the better of the two methods to solve this problem. Consequently, the time dependent nonlinear partial differential equations for reversible inhibitor biosensor systems in dynamic mode are solved using homotopy analysis method. Results obtained are in excellent agreement with the steady state result. The results of this work will provide a better understanding of the non-steady state. Further, the sensitivity analysis will give a clear picture about the significance of the parameters over the output current.

To the best of our knowledge, no analytical solution has been derived for the steady and non-steady state of this mathematical model so far. The solutions presented in this study are presented for the first time.

SIGNIFICANCE STATEMENT

This study proposes the analytical expressions for the substrate concentration, product concentration and inhibitor concentration in terms of other parameters. This study will help the researchers to estimate the outcomes of an experiment, before doing it practically. The derived results could be used by researchers to extend their research and frame more relevant mathematical models.

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