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APPROXIMATE ANALYTICAL SOLUTION FOR NON-LINEAR REACTION DIFFUSION EQUATIONS IN A UREA BIOSENSOR INVOLVING MICHAELIS –MENTEN KINETICS

V.Ananthaswamy[1] and P Felicia Shirly[2]

[1]*PG & Research Department of Mathematics, The Madura College, Madurai, India.*

[2]*Department of Mathematics, Lady Doak College, Madurai, India.*

Corresponding author e-mail: ananthu9777@gmail.com

Abstract: In this paper, mathematical model pertaining to the dynamic behaviour of urea biosensor in non- linear zone at weak inhibition is discussed. This model is based on the system of non-linear reaction diffusion equations containing a nonlinear term related to the Michaelis-Menten kinetics. In this paper Homotopy analysis method is applied to solve the non-linear reaction diffusion equations in urea biosensor. A simple and closed-form of analytical expression for concentrations of substrate,inhibitor and product have been derived for all possible values of parameters . Furthermore, in this work, the numerical simulation of the problem is also reported using Scilab/MATLAB program. An agreement between analytical and numerical results is noted.

Keywords: Dynamic behaviour of homogeneous biosensor system for urea measuring by ion-selective electrode;Mchaelis–Mentenkinetics;System of non-linear reaction diffusion equations; Homotopy analysis method; Numerical simulation

1. Introduction

A biosensor is an analytical device that detects a chemical substance, that combines a biological component with a physicochemical detector. An ion-selectiveelectrode (ISE), is a sensor that converts the activity of a specific ion dissolved in a solution into an electrical potential.The biosensor system described depends on the property of the enzyme urease,an enzyme to be inhibited non-competitively in the presence of fluoride ions and urea. D.Katsakoset al.developed theoretical problems of an inhibitor urea biosensor with immobilized urease and base ion-selective electrode for fluoride ions. The basic differential equations describing the behavior of the inhibitor system was presented.[1] N.Stoilova et al.conducted Spectrometric measurements and determined the basic kinetic parameters of the immobilized system [2].

A *dynamic quality*'s value at one time instant depends on its values at previous time instant The mathematical modeling of dynamic measurements typically utilizes methodologies and concepts from digital signal processing. S.Stoianov et al discussed the Dynamic behavior of homogeneous biosensor system for urea measuring by ion-selective electrode (ISE) for fluoride ions.[3].Quasi-Stationary Process is a process that spreads within the system so rapidly that in the time required for it to expand to the limits of the system, its state does not have adequate time to change. It is often used in biosensor design because the basic transducer has its own inertia and as a rule the interesting

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zone of the transient process is out of the range of non-stationary behavior. Tz.Georgiev et al described the transient processes of biosensor system at homogeneous conditions by a system of ordinary non-linear differential equations.

To our knowledge no rigorous analytical solutions for the current co-ordinates substrate, inhibitor and product have been reported. In general, an analytical result is more stimulating and beneficial than the results of numerical simulation as they are amenable to various kinds of manipulation, optimization of parameter and data analysis. In this paper, we have derived an approximate analytical expressions for the current co-ordinates using Homotopy analysis method [5–10] and q homotopy analysis method [11-13].HAM contains a certain auxiliary parameter h , which provides us with a simple way to adjust and control the convergence region and rate of convergence of the series solution.Theq -HAM contains an auxiliary parameter n as well as h.q-HAM gives more chances of convergence compare to the usual HAM due to the presence of fraction factor associated with the solution. The new simple and closed-form of our approximate analytical expressionsof current co-ordinates givessatisfactory agreement with the numerical results

2.Mathematical formulation of the problem

Transient processes of biosensor system at homogeneous conditions are described by the following system of ordinary non-linear differential equations:

$$\frac{d[S]}{d\tau} = D_S \frac{d^2[S]}{d\delta^2} - \frac{V_m[S]}{K_s + r[S]} \tag{1}$$

$$\frac{d[I]}{d\tau} = D_I \frac{d^2[I]}{d\delta^2} - \frac{V_m[S]}{K_s + r[S]} \tag{2}$$

$$\frac{d[P]}{d\tau} = D_P \frac{d^2[P]}{d\delta^2} - \frac{V_m[S]}{K_s + r[S]} \tag{3}$$

where substrate [S], inhibitor [I], product [P] are the current co-ordinates , δ is the current distance and $r = 1 + \frac{[I]}{K_1}$. Following non-dimensional variables and coefficients are introduced:

$$S = \frac{[S]}{K_S}, P = \frac{[P]}{K_P}, I = \frac{[I]}{K_I}, x = \frac{\delta}{l}, \phi^2 = \frac{l^2 V_m}{DK_S}, t = \frac{D}{l^2}\tau, \lambda = \frac{D_S}{D_I}, \rho = \frac{K_S}{K_I}, \lambda_p = \frac{D_S}{D_I}, \rho_p = \frac{K_S}{K_P}$$

Here V_m is the maximum rate of the enzyme reaction without inhibition , ϕ^2 is Thiele modulus, D_S, D_I and D_P are diffusion coefficients respect to the substrate, inhibitor and product in the active membrane and K_S, K_I are Michaelis–Menten constants of the substrate and the inhibitor.

Under the assumption that the diffusion coefficients respect to the substrate, inhibitor and product in the active membrane are equal, the ratio between the constants of Michaelis for substrate and product is equal to unit, the transient processes in the inhibitory biosensor with ISE for fluoride ions is described by the following system of differential equations respect to the variable x and non-dimensional time t:

$$\frac{dS}{dt} = \frac{d^2S}{dx^2} - \frac{\phi^2}{r + 1/S} \tag{4}$$

$$\frac{dI}{dt} = \frac{d^2I}{dx^2} - \frac{\rho\phi^2}{r + 1/S} \tag{5}$$

$$\frac{dP}{dt} = \frac{d^2P}{dx^2} + \frac{\phi^2}{r + 1/S} \tag{6}$$

where $r = 1 + I$

The initial and boundary conditions are

$t = 0$, $S = 0$, $I = 1$, $P = 0$

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$$x=0,\quad \frac{dS}{dx}=0,\frac{dI}{dx}=0,\frac{dP}{dx}=0$$
$$x=1,\quad S=1,\quad I=1,\quad P=0 \tag{7}$$

3.General analytical expressions of concentration of substrate, inhibitor andproduct under steady state condition using Homotopy analysis method

Nonlinear phenomena appear in such broad scientific fields like applied mathematics, physics, and chemical engineering. Scientists in those disciplines face, constantly, with the task of finding solutions for nonlinear partial differential equations. As a matter of fact, the possibility of finding exact analytical solutions for those cases is very difficult. Liao proposed a new method in 1992, namely the Homotopy analysis method (HAM) to solve the linear andnon-linear differential equations. The main aim is to overcome the foregoing restrictions and limitations techniques, so that, it is a powerful tool to analyze strongly nonlinear problems. The HAM yields a very rapid convergence of the solution series in most cases, usually only a few iterations leading to very accurate solutions. In this paper, Homotopy analysis method and q-Homotopy analysis method are applied to solve the non-linear differential eqns. (4) - (6) under steady state. Using this method, the approximate analyticalexpressions for the dimensionless concentration of the substrate,inhibitorand product for steady state conditions are obtained as follows (AppendixA)

Under steady state condition eqns. (4) - (6). become

$$\frac{d^2S}{dx^2}=\frac{\phi^2}{r+1/S} \tag{8}$$

$$\frac{d^2I}{dx^2}=\frac{\rho\phi^2}{r+1/S} \tag{9}$$

$$\frac{d^2P}{dx^2}=-\frac{\phi^2}{r+1/S} \tag{10}$$

where $r=1+I$.

Using Homotopy Analysis Method (HAM) the approximate analytical solutions for the non-linear differential eqns. (8) - (10) are as follows:

$$S(x)=S_0-\frac{hS_0\phi^2\left(x^2-1\right)}{2}+\frac{h^2S_0\phi^2\left(hS_0\phi^2I_0+hS_0{}^2\rho\phi^2+hS_0\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}-\frac{hS_0x^2\phi^2}{2}$$
$$+\frac{5h^3S_0{}^2(\phi^2)^2I_0}{24}+\frac{5h^3S_0{}^3(\phi^2)^2\rho}{24}+\frac{5h^3S_0{}^2(\phi^2)^2}{24}+\frac{5h^2S_0\ (\phi^2)^2}{24}+\frac{hS_0\phi^2}{2} \tag{11}$$

$$I(x)=I_0-\frac{hS_0\rho\phi^2\left(x^2-1\right)}{2}+\frac{h^2S_0\rho\phi^2\left(hS_0\phi^2I_0+hS_0{}^2\rho\phi^2+hS_0\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}-\frac{hS_0x^2\rho\phi^2}{2}$$
$$+\frac{5h^3S_0{}^2\rho(\phi^2)^2I_0}{24}+\frac{5h^3S_0{}^3(\phi^2)^2\rho^2}{24}+\frac{5h^3S_0{}^2(\phi^2)^2\rho}{24}+\frac{5h^2S_0\ (\phi^2)^2\rho}{24}+\frac{hS_0\rho\phi^2}{2} \tag{12}$$

$$P(x)=\frac{hS_0\phi^2\left(x^2-1\right)}{2}-\frac{h^2S_0\phi^2\left(h\phi^2I_0+hS_0\ \rho\phi^2+h\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}+\frac{hS_0x^2\phi^2}{2} \tag{13}$$
$$-\frac{5h^3S_0\ (\phi^2)^2I_0}{24}-\frac{5h^3S_0{}^2(\phi^2)^2\rho}{24}-\frac{5h^3S_0\ (\phi^2)^2}{24}-\frac{5h^2S_0\ (\phi^2)^2}{24}-\frac{hS_0\phi^2}{2}$$

Using q-Homotopy Analysis Method (q-HAM) the approximate analytical solutions for the non-linear differential eqns. (8) - (10) are as follows:

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$$S(x)=S_0-\frac{hS_0\phi^2\left(x^2-1\right)}{2}+\frac{h^2S_0\phi^2\left(hS_0\phi^2I_0+hS_0{}^2\rho\phi^2+hS_0\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}-\frac{nhS_0x^2\phi^2}{2}$$
$$+\frac{5h^3S_0{}^2(\phi^2)^2I_0}{24}+\frac{5h^3S_0{}^3(\phi^2)^2\rho}{24}+\frac{5h^3S_0{}^2(\phi^2)^2}{24}+\frac{5h^2S_0\ (\phi^2)^2}{24}+\frac{nhS_0\phi^2}{2} \quad (14)$$

$$I(x)=I_0-\frac{hS_0\rho\phi^2\left(x^2-1\right)}{2}+\frac{h^2S_0\rho\phi^2\left(hS_0\phi^2I_0+hS_0{}^2\rho\phi^2+hS_0\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}-\frac{nhS_0x^2\rho\phi^2}{2}$$
$$+\frac{5h^3S_0{}^2\rho(\phi^2)^2I_0}{24}+\frac{5h^3S_0{}^3(\phi^2)^2\rho^2}{24}+\frac{5h^3S_0{}^2(\phi^2)^2\rho}{24}+\frac{5h^2S_0\ (\phi^2)^2\rho}{24}+\frac{nhS_0\rho\phi^2}{2} \quad (15)$$

$$P(x)=\frac{hS_0\phi^2\left(x^2-1\right)}{2}-\frac{h^2S_0\phi^2\left(h\phi^2I_0+hS_0\ \rho\phi^2+h\phi^2+\phi^2\right)\left(\frac{x^4}{12}-\frac{x^2}{2}\right)}{2}+\frac{nhS_0x^2\phi^2}{2}$$
$$-\frac{5h^3S_0\ (\phi^2)^2I_0}{24}-\frac{5h^3S_0{}^2(\phi^2)^2\rho}{24}-\frac{5h^3S_0\ (\phi^2)^2}{24}-\frac{5h^2S_0\ (\phi^2)^2}{24}-\frac{nhS_0\phi^2}{2} \quad (16)$$

where S_0 and I_0 the initial concentrations of substrate and inhibitor respectively.

4.General analytical expressions of concentration of substrate ,inhibitor and product under non-steady state condition using Homotopy Analysis Method and Laplace transform technique

Using Homotopy Analysis Method and Laplace transform method, the approximate analytical expressions of non-steady-state concentrations of substrate ,inhibitor and product (Appendix B) can be obtained as follows:

$$S(x,t)=1-\frac{hx^2k}{2}+\frac{hk}{2}+4\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-\left(\frac{(2n+1)^2\pi^2}{4}\right)t}\cos\left(\frac{(2n+1)\pi x}{2}\right)}{(2n+1)\pi}$$
$$-16hk\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-\left(\frac{(2n+1)^2\pi^2}{4}\right)t}\cos\left(\frac{(2n+1)\pi x}{2}\right)}{(2n+1)^3\pi^3} \quad (17)$$

$$I(x,t)=1-\frac{\rho\ khx^2}{2}+\frac{\rho kh}{2}+-16\rho kh\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-\left(\frac{(2n+1)^2\pi^2}{4}\right)t}\cos\left(\frac{(2n+1)\pi x}{2}\right)}{(2n+1)^3\pi^3} \quad (18)$$

$$P(x,t)=\frac{h\ x^2k}{2}-\frac{hk}{2}++16hk\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-\left(\frac{(2n+1)^2\pi^2}{4}\right)t}\cos\left(\frac{(2n+1)\pi x}{2}\right)}{(2n+1)^3\pi^3} \quad (19)$$

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where $k = \dfrac{\phi^2}{S_0 + I_0 S_0 + 1}$

4.1 Limiting cases

case 1 : $S << 1$ and $rS << 1$ (very low measuringurea concentrations with low inhibition)

The substrate equation (8) is linearized and reduce to form:

$$\frac{d^2S}{dx^2} = S\phi^2 \tag{20}$$

The exact solution of the eqn.(20) is $S(x) = \dfrac{\cosh\sqrt{\phi^2}\,x}{\cosh\sqrt{\phi^2}}$

case:2: $S >> 1$ or $1/S \approx 0$ (saturating substrateconcentrations).

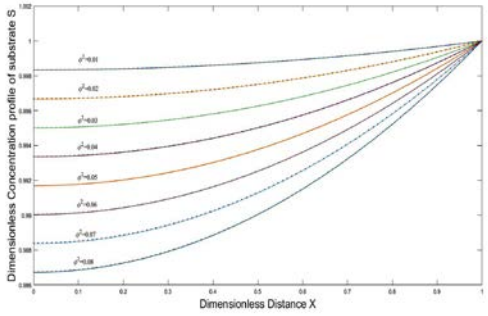
The inhibitor equation (9) is transformed in the way:

$$\frac{d^2I}{dx^2} = \frac{\rho\phi^2}{r} \tag{21}$$

The exact solution of the eqn.(21) is $I(x) = \dfrac{\rho\phi^2 x^2}{2r} + 1 - \dfrac{\rho\phi^2}{2r}$

5.Numerical simulation

In order to investigate the accuracy of the HAM solution with a finite number of terms, the system ofdifferential eqns.(4)-(6)and eqns.(8)-(10) was solved numerically. Toshow the efficiency of the present method, our results arecompared with numerical results graphically. The functionpdex4 (Euler's method) in Matlab software which is afunction of solving the boundary value problems is used tosolve eqns.(4)-(6)and eqns.(8)-(10) numerically.



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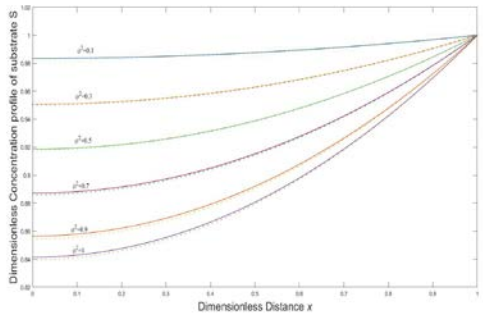

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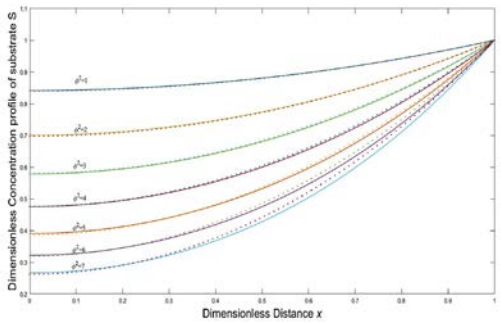
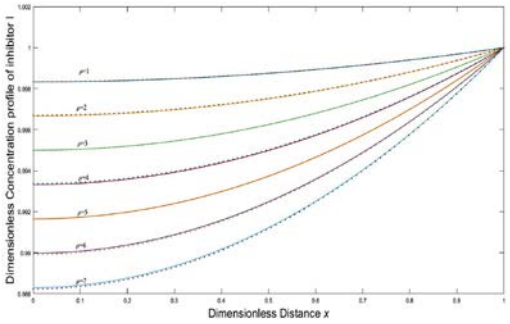


(c)

Fig.1: Plots of dimensionless concentration of substrate $S(x)$ versus dimensionless distance x for various values of parameter ϕ^2 andfor the fixed value of the parameter $\rho = 0.01$ using eqn.11. The key to the plot: (•••) represents eqn.11 and (—) represents numerical simulation



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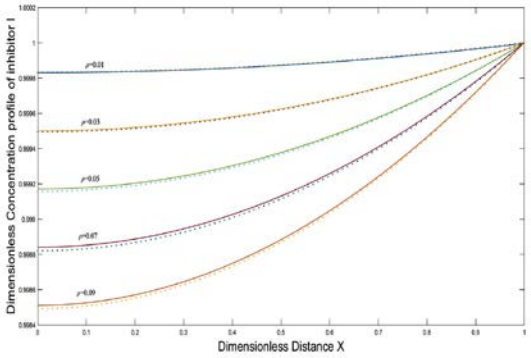

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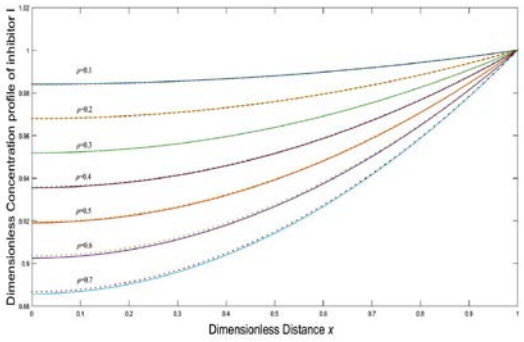

(c)

Fig.2: Plots of dimensionless concentration of inhibitor $I(x)$ versus dimensionless distance x for

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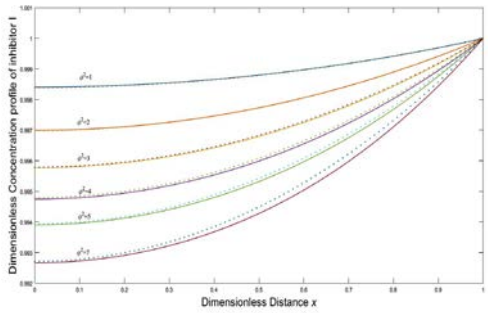
various values of parameter ρ when (a) $\phi^2 = 0.01$ (b) $\phi^2 = 0.1$(c) $\phi^2 = 1$using eqn.12. The key to the plot: (•••) represents eqn.12 and (—) represents numerical simulation



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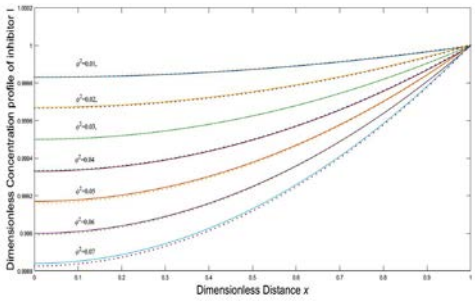

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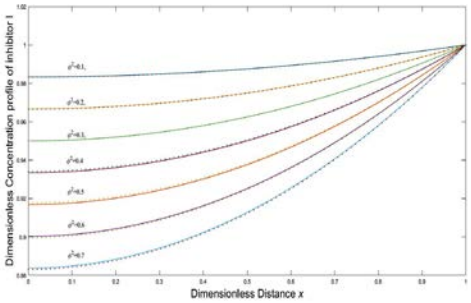
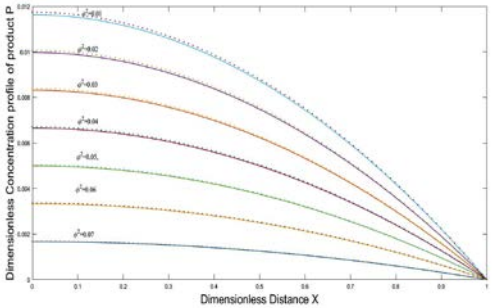


(c)

Fig.3: Plots of dimensionless concentration of inhibitor $I(x)$ versus dimensionless distance x forvarious values of parameter ϕ^2 when (a) $\rho = 0.01$ (b) $\rho = 0.1$(c) $\rho = 1$using eqn.12. The key to the plot: (•••) represents eqn.12 and (—) represents numerical simulation



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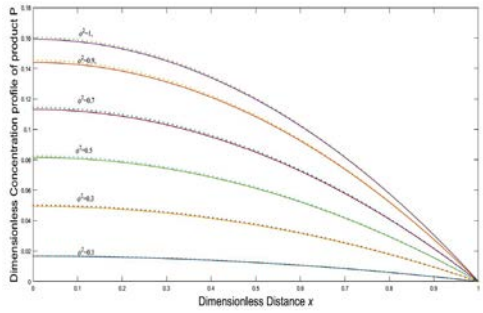

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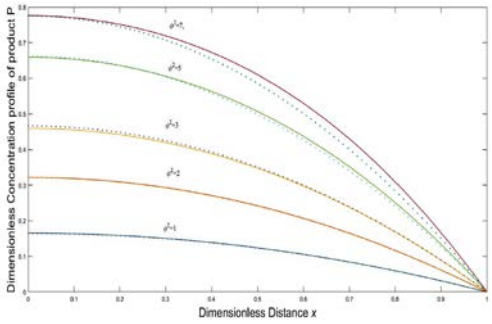

(c)

Fig.4: Plots of dimensionless concentration of product $P(x)$ versus dimensionless distance *x* for various values of parameter ϕ^2 when (a) $\rho = 0.01$ (b) $\rho = 0.1$ (c) $\rho = 1$ using eqn.13. The key to the plot: (•••) represents eqn.13 and (—) represents numerical simulation

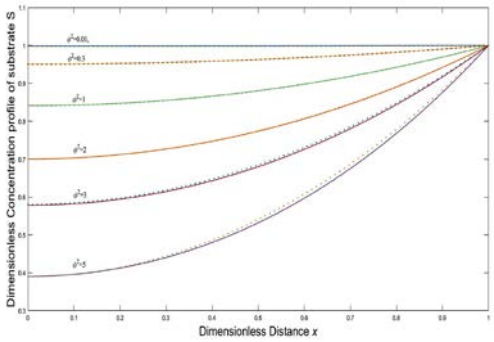

Fig.5: Plots of dimensionless concentration of substrate $S(x)$ versus dimensionless distance *x* for various values of parameter ϕ^2 andfor the fixed value of the parameter $\rho = 0.01$ eqn.14. The key to the plot: (•••) represents eqn.14 and (—) represents numerical simulation

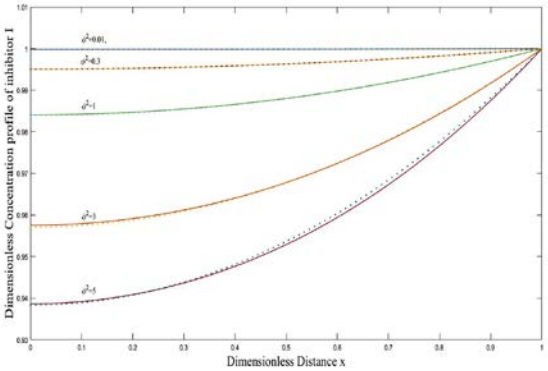

Fig.6: Plots of dimensionless concentration of inhibitor $I(x)$ versus dimensionless distance *x* for

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various values of parameter ϕ^2 andfor the fixed value of the parameter $\rho = 0.1$using eqn.15. The key to the plot: (•••) represents eqn.15 and (—) represents numerical simulation

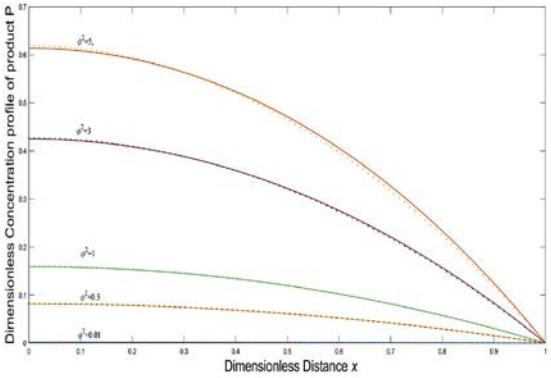

Fig.7: Plots of dimensionless concentration of product $P(x)$ versus dimensionless distance x for various values of parameter ϕ^2 andfor the fixed value of the parameter $\rho = 0.1$using eqn.16. The key to the plot: (•••) represents eqn.16 and (—) represents numerical simulation

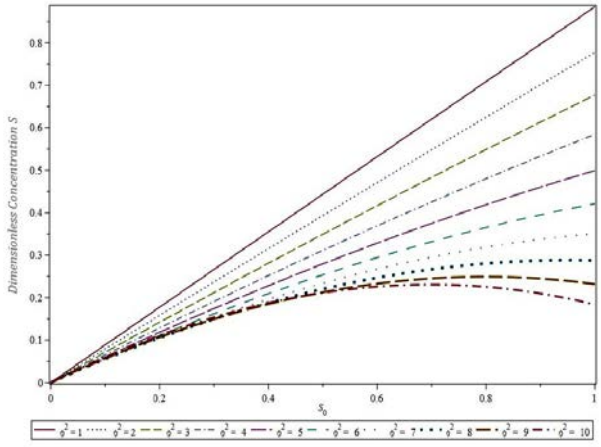

Fig.8: Plots of dimensionless concentration of substrate $S(x)$ for increased values of ϕ^2 and for the measurement range $S_0 = 1$ and for the fixed value of the parameter $\rho = 0.1$.

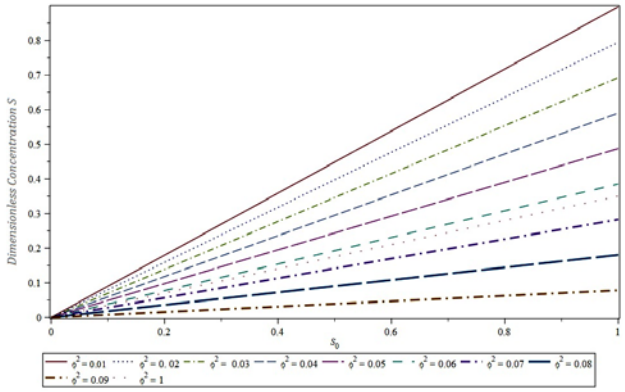

Fig.9: Plots of dimensionless concentration of substrate $S(x)$ for small values of ϕ^2 and for the measurement range $S_0 = 1$ and for the fixed value of the parameter $\rho = 0.01$.

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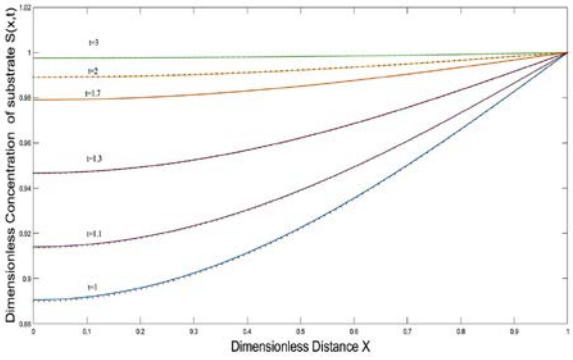

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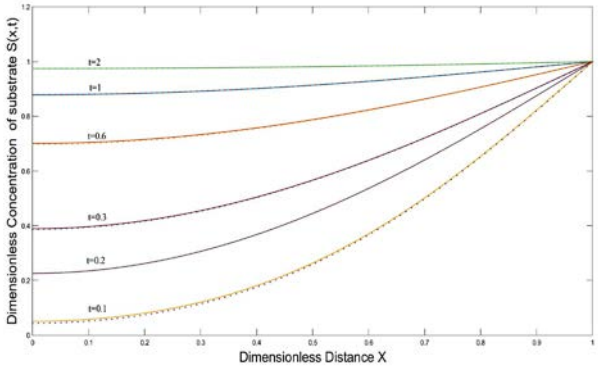

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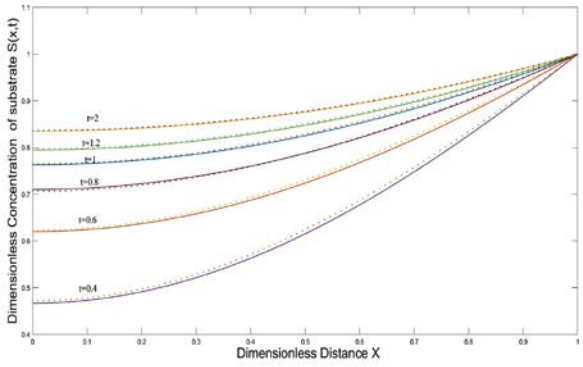

(c)

Fig.10: Plots of dimensionless substrate concentration profile $S(x,t)$ calculated using eqn.17. as a function of dimensionless distance x . Profiles are presented for the values of the parameters ϕ^2 and the dimensionless time parameter t when (a) $\phi^2 = 0.01$ (b) $\phi^2 = 0.1$ (c) $\phi^2 = 1$.

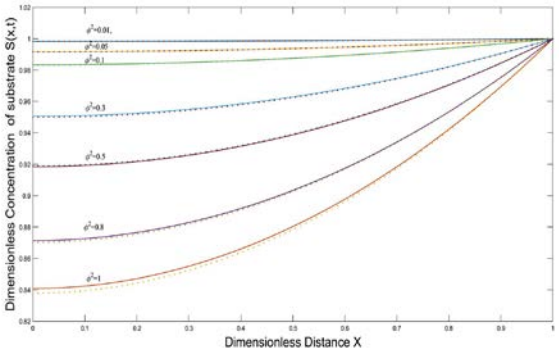

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Fig.11: Plots of dimensionless substrate concentration profile $S(x,t)$ calculated using eqn.17 as a function of dimensionless distance x . Profiles are presented for the values of the parameters ϕ^2 and the dimensionless time parameter $t = 5$

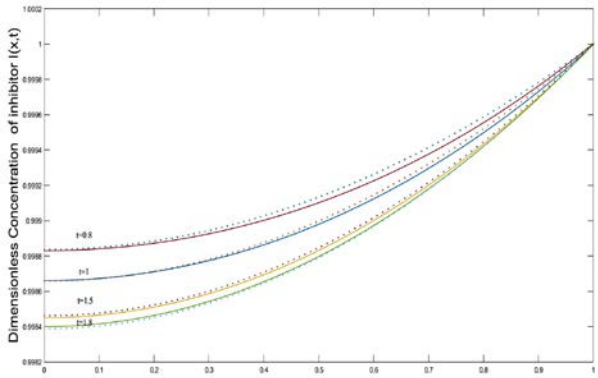
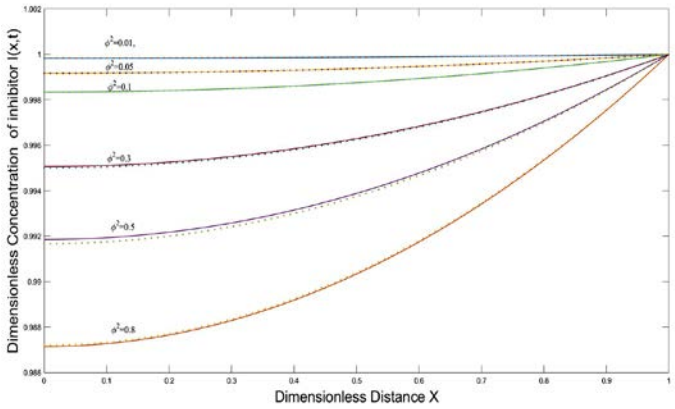
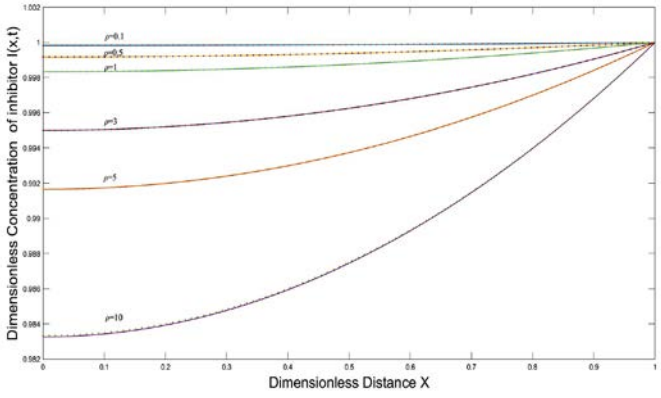


Fig.12: Plots of dimensionless inhibitor concentration profile $I(x,t)$ calculated using eqn.18 as a function of dimensionless distance x . Profiles are presented for the values of the parameters $\phi^2 = 0.1, \rho = 0.1$ and the dimensionless time parameter t



(a)



(b)

Fig13: Plots of dimensionless inhibitor concentration profile $I(x,t)$ calculated using eqn.18 as a function of dimensionless distance x. Profiles are presented for the values of the parametersand the dimensionless time parameter $t = 5$ and $\rho = 0.1$

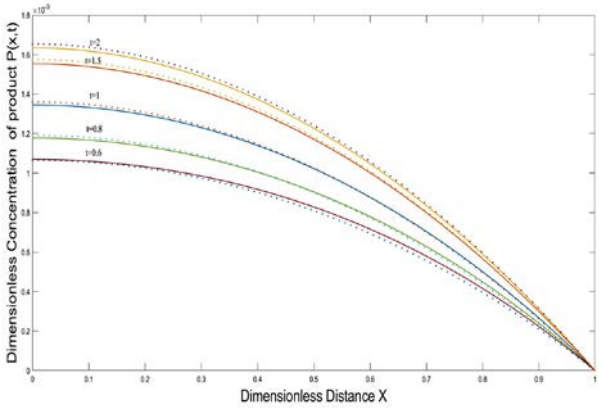


Fig14: Plots of dimensionless product concentration profile $P(x,t)$ calculated using eqn.19 as a function of dimensionless distance x . Profiles are presented for the value of the parameter $\phi^2 = 0.01$ and the dimensionless time parameter t

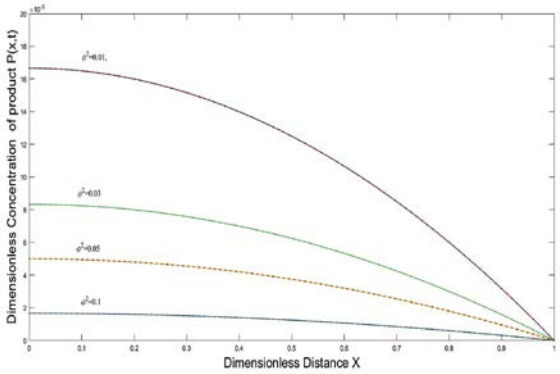
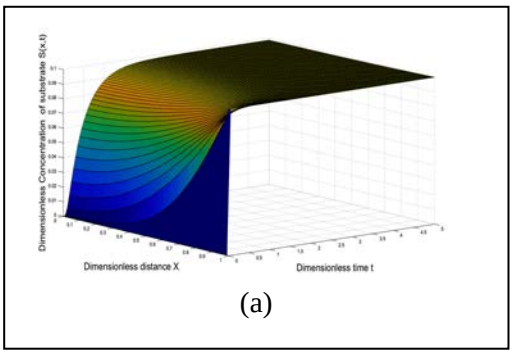
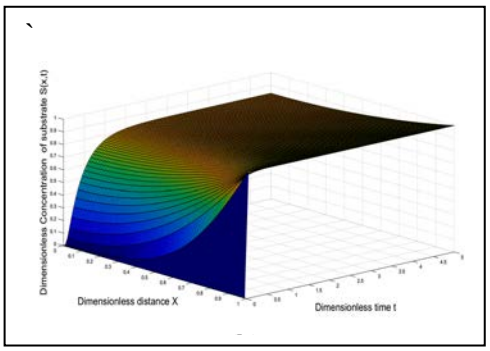


Fig15 Plots of dimensionless product concentration profile $P(x,t)$ calculated using eqn.19 as a function of dimensionless distance x . Profiles are presented for the values of the parameter ϕ^2 and the dimensionless time parameter $t = 5$ and $\rho = 0.1$



(a)



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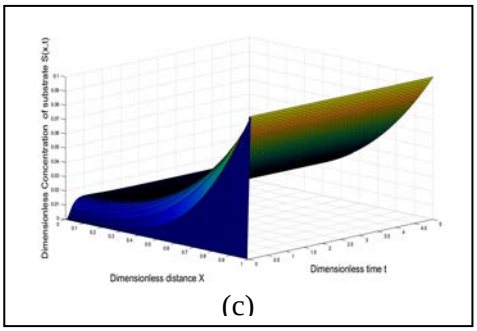
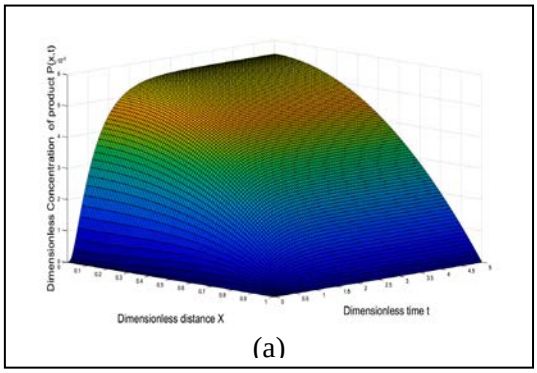
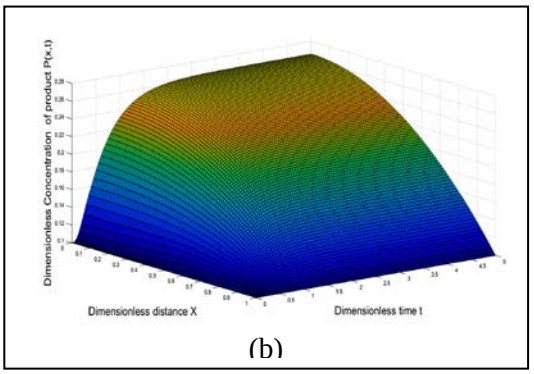


(c)

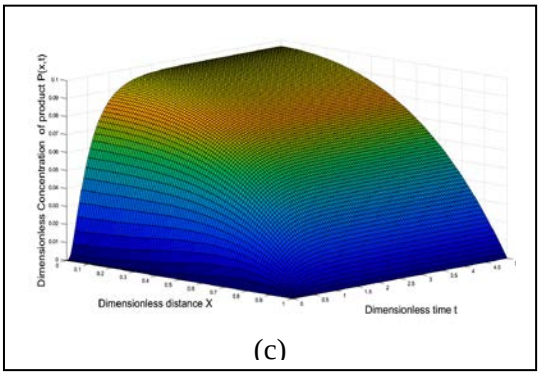
Fig16: Plot of dimensionless three dimensional non steady-state substrate concentrations S versus dimensionless distance x for various values of dimensionless time t



(a)



(b)



(c)

Fig 17: Plot of dimensionless three dimensional non steady-state product concentrations P versus dimensionless distance x for various values of dimensionless time t

6. Results and Discussions

Eqns.(4)-(6) and eqns.(8)-(10) provide simple analytical expressions for the concentration of substrate, inhibitor and the product respectively in the terms of the kinetic parameters ρ and ϕ^2 obtained using the Homotopy analysis methodTo show the efficiency of our steady state andnon-steady-state results, it is compared with numerical solution. Satisfactory agreement is noted.

In the Figs.1-7 our steady-state analytical results (eqns.(11)-(16)) are compared with simulation program for various values of the kinetic parameters ρ and ϕ^2. In the Figs.10-15 our non - steady-stateanalytical results (eqns.(17)-(19)) are compared with simulation program for various values of of the kinetic parameters ρ and ϕ^2

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The dimensionless concentration of substrate $S(x)$ versus dimensionless distance x have been depicted in Fig.1. In Figs 1(a)- 1(b) the value of ϕ^2 is varied and it can be seen that $S(x)$ increases with decrease in ϕ^2. The changes observed in dimensionless concentration of inhibitor $I(x)$ with respect to dimensionless distance x when the values of kinetic parameter ρ are varied is illustrated in Fig.2.In Figs 2(a)- 2(c) the graph depicts the variation of $I(x)$ with ρ and it is noted that both are inversely proportional. Fig.3is plotted by plotting dimensionless concentration of inhibitor $I(x)$ with respect to dimensionless distance x by varying the value of

ϕ^2 and it can also be observed that the value of $I(x)$ increases with decrease in ϕ^2.Fig.4 displays the plot of dimensionless concentration of product $P(x)$ with respect to dimensionless distance x for various value of ϕ^2. It is inferred that both are inversely related.

In Figs. 5–7the profiles of dimensionless concentrations of substrate, inhibitor and product versus dimensionless distance x have been depicted. InFigs.5,6 it is noted that dimensionless concentration of substrate $S(x)$ with respect to dimensionless distance x by varying the value of ϕ^2 and dimensionless concentration of inhibitor $I(x)$ with respect to dimensionless distance x by varying the value of ϕ^2 are inversely proportional and substrate $S(x)$, inhibitor $I(x)$ reach the value 1 when $\phi^2 = 0.01$. From Fig.7 it can also be observed that the value of $P(x)$ increases with increase in ϕ^2

The dimensionless concentration of substrate $S(x,t)$ is showcased in fig.10 and it is analysed with various values of ϕ^2.In figs.10(a)-10(c) the plot is made by providing various values to ϕ^2 and it can be stated that $S(x,t)$ increases with increase in the dimensionless time t. and it reaches the value 1 when and $t = 3, \phi^2 = 0.01$ and when and $t = 2, \phi^2 = 0.1$ respectively.

In fig.11 the value of ϕ^2 is varied and it can be observed that $S(x,t)$ value increases with decrease in ϕ^2 and reaches the value 1 when $\phi^2 = 0.01$. Fig.12 exhibits the concentration of inhibitor $I(x,t)$ when dimensionless time t is varied, it can be seen that $I(x,t)$ increases as t decreases. Fig.13 displays the plot of $I(x,t)$ for various values of ϕ^2 and ρ.It is inferred that both are inversely proportional. The dimensionless concentration of product $P(x,t)$ versus dimensionless distance x have been depicted in fig.14 and it can be observed that $P(x,t)$ value increases with increase in dimensionless time t.Fig.15 depicts the variation of $P(x,t)$ with ϕ^2 and it is noted that both are inversely proportional.

7. Conclusion

The modeling of the urea biosensor with the substrate inhibition is discussed.The analytical expressions for the concentration of substrate, inhibitor and product under steady conditions are derived using HAM and q-HAM method. The q-HAMyields a very rapid convergence of the solution series in most cases so that, it is apowerful tool to analyze strongly nonlinear problems. The analytical expressions for the concentration of substrate,inhibitor and product under non-steady conditions are obtained by using the complex inversion formula.The numerical simulation is in excellent agreement with the analytically obtained results. The influence of Thiele modulus and Michaelis–Menten constant is also investigated. Theoretical results obtained

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in this paper can also be used to analyze the effect of different parameters such as Thiele modulus and Michaelis–Menten constant.

Appendix A: Approximate analytical solution for non-linear eqn.(11) using the HomotopyAnalysis method.

The given differential equation is of the form

$$\frac{d^2S(x)}{dx^2} = \frac{\phi^2 S(x)}{S(x) + I(x)S(x) + 1} \tag{A.1}$$

In order to solve eqn.(A.1) construct the homotopy as follows

$$(1-p)\left(\frac{d^2S(x)}{dx^2}\right) = ph\left((S(x) + I(x)S(x) + 1)\frac{d^2S(x)}{dx^2} - \phi^2 S(x)\right) \tag{A.2}$$

The approximate solution of Eqn.(A.2) is as follows

$$S(x) = S_0(x) + pS_1(x) + p^2S_2(x) + \ldots \text{(A.3)}$$

Substituting Eqn.(A.3) in Eqn.(A.2) and equating the like powers of p

$$p^0 : \frac{d^2S_0(x)}{dx^2} = 0 \tag{A.4}$$

$$p^1 : \frac{d^2S_1(x)}{dx^2} - \frac{d^2S_0(x)}{dx^2} = h\left((S_0(x) + I_0(x)S_0(x) + 1)\frac{d^2S_0}{dx^2} - S_0(x)\phi^2\right) \tag{A.5}$$

$$p^2 : \frac{d^2S_2(x)}{dx^2} - \frac{d^2S_1(x)}{dx^2} = h\left((S_1(x) + I_0(x)S_1(x) + S_0(x)I_1(x) + 1)\frac{d^2S_1(x)}{dx^2} - S_0(x)\phi^2\right) \text{(A.6)}$$

The boundary conditions are as follows: $S_0(1) = S_0;\ \ S_i(1) = 0,\ i = 1,2,3.....$

$$\frac{dS_i(0)}{dx} = 0,\ i = 1,2,3..... \text{(A.7)}$$

Solving Eqns.(A.4),(A.5)and (A.6) and using the boundary conditions (A.7) we obtain the following solutions

$$S_0(x) = S_0 \text{(A.8)}$$

$$S_1(x) = -\frac{hS_0\phi^2\left(x^2 - 1\right)}{2} \text{(A.9)}$$

$$S_2(x) = \frac{h^2S_0\phi^2\left(hS_0\phi^2I_0 + hS_0{}^2\rho\phi^2 + hS_0\phi^2 + \phi^2\right)\left(\frac{x^4}{12} - \frac{x^2}{2}\right)}{2} - \frac{hS_0x^2\phi^2}{2} + \frac{5h^3S_0{}^2(\phi^2)^2I_0}{24} + \frac{5h^3S_0{}^3(\phi^2)^2\rho}{24} + \frac{5h^3S_0{}^2(\phi^2)^2}{24} + \frac{5h^2S_0\ (\phi^2)^2}{24} + \frac{hS_0\phi^2}{2} \tag{A.10}$$

Substituting eqn. (A.8) ,eqn. (A.9) and eqn.(A.10)in eqn. (A.3) and letting $p \to 1$, we get $S(x)$ which is eqn. (11) in the text.

Appendix B: To illustrate the basic ideas of the q-homotopy analysis method (q-HAM), consider the nonlinear boundary value problem

$$N[u(t)] = 0;\ t \in \eta \quad B\left(u(t), \frac{du}{dt}\right) = 0 : t \in \gamma \tag{1}$$

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where $u(t)$ defined over the region η is the function to be solved under the boundary constraints in B defined over the boundary γ of η. The q-homotopy analysis technique defines a homotopy $\phi(t,q): R \times \left[0, \frac{1}{n}\right] \to R$ so that

$$H(\phi,q) = (1-nq)\left[L(\phi(t,q)) - L(u_0)\right] - qhN\left[\phi(t,q)\right] = 0 \quad (2)$$

where $q \in \left[0, \frac{1}{n}\right], n \geq 1$ denotes the so-called embedded parameter $h \neq 0$, is an auxiliary parameter, L is a suitable auxiliary linear operator, u_0 is an initial approximation of equation (1) satisfying exactly the boundary conditions . It is obvious from equation (2) that

$$H(\phi,0) = \left[L(\phi(t,q)) - L(u_0)\right],\ H\left(\phi, \frac{1}{n}\right) = \frac{h}{n} N\left[\phi\left(t, \frac{1}{n}\right)\right]$$

The solution of equation (2) exists as a power series in q.

$$\phi(t,q) = u_0(t) + qu_1(t) + q^2 u_2(t) + ... = \sum_{k=0}^{\infty} u_k(t)\left(\frac{1}{n}\right)^k \quad (3)$$

The appreciate solutions of the coefficients $u_k(t)$ in (3) can be found from the homotopy deformation equations.Hence the approximate solution of equation (1) can be obtained as

$u(t) = \lim_{q \to \frac{1}{n}} \phi(t,q) = \sum_{k=0}^{\infty} u_k(t)\left(\frac{1}{n}\right)^k$. It was found that the auxiliary parameters *h* and *n* can adjust and control the convergence region and rate of homotopy series solutions.

Approximate analytical solution for non-linear eqn.(14) using q- Homotopy Analysis method

The given differential equation is of the form

$$\frac{d^2 S(x)}{dx^2} = \frac{\phi^2 S(x)}{S(x) + I(x)S(x) + 1} \quad (B.1)$$

In order to solve eqn.(14), construct the homotopy as follows

$$(1-nq)\left(\frac{d^2 S(x)}{dx^2}\right) = qhn\left(\left(S(x) + I(x)S(x) + 1\right)\frac{d^2 S(x)}{dx^2} - \phi^2 S(x)\right) \quad (B.2)$$

The approximate solution of eqn.(B.2) is as follows

$$S(x) = S_0(x) + qS_1(x) + q^2 S_2(x) + ... \quad (B.3)$$

Substituting eqn.(B.3) in eqn.(B.2) and equating the like powers of *q*

$$q^0 : \frac{d^2 S_0(x)}{dx^2} = 0 \quad (B.4)$$

$$q^1 : \frac{d^2 S_1(x)}{dx^2} - \frac{d^2 S_0(x)}{dx^2} = h\left(\left(S_0(x) + I_0(x)S_0(x) + 1\right)\frac{d^2 S_0}{dx^2} - S_0(x)\phi^2\right) \quad (B.5)$$

$$q^2 : \frac{d^2 S_2(x)}{dx^2} - \frac{nd^2 S_1(x)}{dx^2} = h\left(\left(S_1(x) + I_0(x)S_1(x) + S_0(x)I_1(x) + 1\right)\frac{d^2 S_1(x)}{dx^2} - S_0(x)\phi^2\right) \quad (B.6)$$

The boundary conditions are as follows: $S_0(1) = S_0;\ S_i(1) = 0, i = 1,2,3.....$

$$\frac{dS_i(0)}{dx} = 0, i = 1,2,3..... \quad (B.7)$$

Solving Eqns.(B.4),(B.5)and (B.6) and using the boundary conditions (B.7) we obtain the following solutions

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$$S_0(x) = S_0 \tag{B.8}$$

$$S_1(x) = -\frac{hS_0\phi^2\left(x^2-1\right)}{2} \tag{B.9}$$

$$S_2(x) = \frac{h^2S_0\phi^2\left(hS_0\phi^2I_0 + hS_0{}^2\rho\phi^2 + hS_0\phi^2 + \phi^2\right)\left(\frac{x^4}{12} - \frac{x^2}{2}\right)}{2} - \frac{nhS_0x^2\phi^2}{2} + \frac{5h^3S_0{}^2(\phi^2)^2I_0}{24} + \frac{5h^3S_0{}^3(\phi^2)^2\rho}{24} + \frac{5h^3S_0{}^2(\phi^2)^2}{24} + \frac{5h^2S_0\ (\phi^2)^2}{24} + \frac{nhS_0\phi^2}{2} \tag{B.10}$$

Substituting eqn. (B.8) , eqn. (B.9) and eqn.(B.10)in Eqn. (B.3) and letting $q \to 1$, we get $S(x)$ which is eqn. (14) in the text

Appendix C: Approximate analytical solution of the non- linear differential Equation (17) using Homotopy analysis method

In this appendix, we illustrate the procedure for obtaining the approximate analytical solution of eqn.(17) using the boundary conditions. In order to solve eqn.(13) ,we construct the homptopy as follows:

$$(1-p)\left[\frac{\partial^2 S}{\partial x^2} - \frac{\partial S}{\partial t}\right] = ph\left[\frac{\partial^2 S}{\partial x^2} - \frac{\partial S}{\partial t} - kS\right] \tag{C.1}$$

The approximate solution of eqn.(C1) is

$$S = S_o + S_1p + S_2p^2 + ... \tag{C.2}$$

Substituting eqn.(C.2) into an eqn.(C.1), and comparing the coefficients of like powers of p , we get

$$p0: \frac{\partial^2 S_o}{\partial x^2} - \frac{\partial S_o}{\partial t} = 0 \tag{C.3}$$

$$p^1: \frac{\partial^2 S_1}{\partial x^2} - \frac{\partial S_1}{\partial t} = -hkS_0 \tag{C.4}$$

The initial and boundary conditions in eqn.(7) become

$t = 0$, $S_o = 1$, $S_1 = -1$ $S_i = 0$, $i = 2,3,4,...$

$x = 0$, $\frac{dS_i}{dx} = 0, i = 1,2,3,...$

$x = 1$, $S_i = 1, , i = 1,2,3,4,...$ (C.5)

Now by applying Laplace transform to the eqns. (C.3)-(C.4) and to the boundary conditions in eqn.(C.5) we obtained the solution of (C.1) as

$$\bar{S}(x) = \frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}} - \frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}} + -\frac{hk}{s^2} - \frac{1}{s} \tag{C.6}$$

Now, we indicate how eqn. (C.6) can be inverted using the complex inversion formula. If $\overline{y(s)}$ represents the Laplace transform of a function $y(\tau)$, then according to the complex inversion formula we can state that

$$y(\tau) = \frac{1}{2\pi i}\oint_C \exp(s\tau)\bar{y}(s)ds \tag{C.7}$$

where the integration in eqn. (C.7) is to be performed along a line $s = c$ in the complex plane where $s = x + iy$ The real number c is chosen such that $s = c$ c lies to the right of all the singularities, but is otherwise assumed to be arbitrary. In practice, the integral is evaluated by considering the contour integral presented on the right-hand side of eqn. (C.7), which is then evaluated using the so-called Bromwich contour. The contour integral is then evaluated using the residue theorem.[14]-[17]

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In order to invert eqn.(C.6),we need to evaluate $\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)$ Now, the poles are obtained from $s\cosh\sqrt{s}=0$

Hence there is a simple pole at $s=0$ and there are infinitely many poles given by the solution of the equation $\cosh\sqrt{s}=0$

and so $s_n=-\left(\frac{(2n+1)^2\pi^2}{4}\right)$ $n=1,2,3,...$ Hence, we note that

$$\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)=\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)_{s=0}+\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)_{s=s_n} \tag{C.8}$$

The first residue in equation (C.8) is given by

$$\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)_{s=0}=1 \tag{C.9}$$

The second residue in eqn. (C.8) can be estimated as follows. It is established that if $f(z)$ can be expressed as $f(z)=\frac{g(z)}{h(z)}$ where the functions f and g are analytic at $s=s_n$ and $h(s_n)=0$ while $h'(s_n)\neq 0$ and $g(s_n)\neq 0$ then $\operatorname{Re} s\left[f(z)\right]_{s=s_n}=\sum_{n=0}^{\infty}\frac{g(s_n)e^{s\tau}}{h'(s_n)}$. Hence we can show that

$$\operatorname{Re} s\left(\frac{\cosh\sqrt{s}x}{s\cosh\sqrt{s}}\right)_{s=s_n}=4\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-A^2t}\cos(A\pi x)}{(2n+1)\pi} \tag{C.10}$$

$$\operatorname{Re} s\left(\frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}}\right)=\operatorname{Re} s\left(\frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}}\right)_{s=0}+\operatorname{Re} s\left(\frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}}\right)_{s=s_n} \tag{C.11}$$

The first residue in eqn. (C.11) is given by

$$\operatorname{Re} s\left(\frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}}\right)_{s=0}=thk+\frac{hx^2k}{2}-\frac{hk}{2} \tag{C.12}$$

The second residue in eqn. (C.11) is given by

$$\operatorname{Re} s\left(\frac{hk}{s^2}\frac{\cosh\sqrt{s}x}{\cosh\sqrt{s}}\right)_{s=s_n}=16kh\sum_{n=0}^{\infty}\frac{(-1)^{n+1}e^{-A^2t}\cos(A\pi x)}{(2n+1)^3\pi^3} \tag{C.13}$$

where $A=\frac{(2n+1)\pi}{2}$

From eqn.(C.10)-(C.14) we get $S(x,t)$ which is eqn.(14) in the text.

Appendix D: Nomenclature

Symbol	Description
S	dimensionless concentration of substrate
I	dimensionless concentration of inhibitor
P	dimensionless concentration of product
T	Dimensionless time

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ϕ^2	Thiele modulus

AppendixE: Matlab program to find numerical solutions of eqns.(4) - (6)

```
function pdex1
m=0;
x = linspace(0,1);
t = linspace(0,100);
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 t')
 figure
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,t)')
xlabel('Distance x')
ylabel('time')
figure
plot(x,u3(end,:))
title('u3(x,t)')
xlabel('Distance x')
ylabel('time')
figure
function [c,f,s] = pdex1pde(x,~,u,DuDx)
c =[1;1;1];
f =[1;1;1].*DuDx;
z=.01;z1=.1;
F=-(z*u(1))/(u(1)+u(1)*u(2)+1);
F1=-(z*z1*u(1))/(u(1)+u(1)*u(2)+1);
F2=(z*u(1))/(u(1)+u(1)*u(2)+1);
s=[F;F1;F2];

% --------------------------------------------------------------
function u0 = pdex1ic(x)
u0 =[0;1;0];
% --------------------------------------------------------------
function [pl,ql,pr,qr]=pdex1bc(xl,~,xr,ur,t)
pl = [0;0;0];
ql = [1;1;1];
pr = [ur(1)-1;ur(2)-1;ur(3)-0];
qr = [0;0;0];
```

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