

## Research Article

# Mathematical analysis of immobilized enzyme with reaction-generated pH change on the kinetics using Asymptotic methods

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### Abstract

A mathematical model to describe the effects of electrostatic interaction with reaction-generated pH change on the kinetics of immobilized enzyme has been developed. This model contains a non-linear term related to Michaelis-Menten kinetics. Analytical expressions pertaining to the substrate concentration and hydrogen ion concentration were reported for all values of Thiele module  $W$  and  $\Gamma_1, \Gamma_2, S, X, s_0/h_0$ . In this work, we report the theoretically evaluated steady state effectiveness factor for immobilized enzyme systems. These analytical results were found to be in good agreement with numerical results. Moreover, herein we employ "Homotopy analysis method" (HAM) to solve non-linear reaction/diffusion equations.

## Introduction

Most of the authors have been studied immobilization of different enzymes on various carriers and examined the effectiveness of the immobilization method by comparing the kinetic properties of soluble and immobilized enzymes [1-3]. With the recent development of immobilization techniques, interesting potential applications of enzymes as catalysts have been proposed in fields as diverse as medicine, sewage treatment, and industrial processing. Since enzymes depend upon specific three dimensional conformations of their molecules for activity, any physical influence of the matrix or chemical modification of the enzyme might alter its properties. Indeed, a number of recent have reported altered properties of enzymes after immobilization. However, it has not always been taken into consideration that the apparent change in the chemical properties are not entirely due to the physical influence of the matrix or chemical modification of the enzyme. External and internal diffusion effects can considerably alter the Michaelis-Menten constant, the activity, and the thermal sensitivity. For engineering purposes, better understanding is needed of immobilized enzyme kinetics and

the factors that influence the rate of the reaction. Ramachandran et al. [3] have presented glucose oxidase on nonporous glass beads by covalent bonding and its kinetics studied under well-defined reactor geometry and flow conditions.

Goldstein et al. [2] were the first to consider these electrostatic effects in immobilized enzyme systems in terms of the apparent Michaelis-Menten constant. Shuler et al. [4] have examined the combined effects of external diffusional resistance and electrostatic field for a non-porous immobilized enzyme system. Kobayashi and Laidler [5] have been considered the electrostatic and external diffusional effects for various types of enzyme kinetics. The effect of both internal and external diffusional resistances together with electrostatic interaction for the small pore case and large pore case were considered by Gupta and Ramachandran [6]. They developed an expression for the overall effectiveness factor in order to evaluate quantitatively the effect of partitioning of charged substrate in and outside the carrier on the overall reaction rate.

Only numerical solutions were available for all the above said models since substrate concentration rate is a non-linear function of the substrate and hydrogen ion concentrations. More often finite differences [7] and orthogonal collocation [1,8-10] methods were used to solve the boundary value problems. Here as in enzymatic kinetics, the result is non-linear equations system whenever the mass balance equations are non-linear. Recently Ramachandran et al. [11] presented the effect of interaction between charged carrier and the hydrogen ion, including

both internal and external resistance for both small pore and large pore cases. However, to the best of author's knowledge, no general analytical results of substrate and hydrogen ion concentrations and effectiveness factor for immobilized enzyme on kinetics have been published. The purpose of this article is to derive steady state analytical expressions of substrate, hydrogen ion concentration, the effectiveness factor and to describe the reduced equilibrium rate constants using Homotopy analysis method.

**2. Formulation of the boundary value problem and analysis**

Let us consider the enzyme catalyses reaction scheme as follows [11]:



The effect of hydrogen ion concentration equation is given by [11]

$$r(s, g) = \frac{V_m s}{s + K_m} \frac{1}{1 + \frac{g}{K_1} + \frac{K_2}{g}} \tag{2}$$

where  $K_1$  and  $K_2$  are the equilibrium constants,  $s$  and  $g$  are the substrate and hydrogen ion concentration respectively.  $V_m$  defines maximum rate of reaction,  $K_m$

denote Michaelis-Menten constant. The dimension non-linear reaction diffusion equations are as follows[11]

$$D_{es} \frac{d^2 s}{dx^2} = \frac{V_m s}{s + K_m} \frac{1}{1 + \frac{g}{K_1} + \frac{K_2}{g}} \tag{3}$$

$$D_{eh} \frac{d^2 g}{dx^2} = - \frac{V_m s}{s + K_m} \frac{1}{1 + \frac{g}{K_1} + \frac{K_2}{g}} \tag{4}$$

and the boundary conditions are

$$\frac{ds}{dx} = 0 \quad \text{at } x = 0 \tag{5}$$

$$D_{es} \frac{ds}{dx} = k_s (s_0 - s) \quad \text{at } x = L \tag{6}$$

$$\frac{dg}{dx} = 0 \quad \text{at } x = 0 \tag{7}$$

$$D_{eh} \frac{dg}{dx} = M k_h \left( h_0 - \frac{g}{P} \right) \quad \text{at } x = L \tag{8}$$

where  $D_{es}$  and  $D_{eh}$  are the effective diffusion constant,  $x$  denotes the distance from the centre of the pore,  $M$  is dimensionless electrostatic potential modifier,  $P$  defines

$$M^{-1} = \frac{1 + Ei(\cdot) - e - \ln|\cdot|}{Ku} \tag{9}$$

and

$$\cdot = \frac{Z_n F \Phi_0}{RT} \tag{10}$$

$$P = e^{-\cdot} \tag{11}$$

We make the non-linear differential equations outlined (3) and (4) dimensionless quantities the above equations can be written as

$$\frac{d^2 S}{dX^2} = \frac{wS}{1+\chi S} \frac{1}{1+r_1 H + \frac{1}{r_2 H}} \tag{12}$$

$$\frac{d^2 H}{dX^2} = -\frac{D_{es}}{D_{eh}} \frac{s_0}{h_0} \frac{wS}{1+\chi S} \frac{1}{1+r_1 H + \frac{1}{r_2 H}} \tag{13}$$

where  $S = s/s_0$  is the dimensionless substrate concentration,  $H = g/h_0$  is the dimensionless hydrogen ion concentration,  $X = x/L$  denotes dimensionless

$$\frac{dS}{dX} = \frac{dH}{dX} = 0 \quad \text{at } X = 0 \tag{14}$$

$$\frac{dS}{dX} = S_s(1-S) \quad \text{at } X = 1 \tag{15}$$

$$\frac{dH}{dX} = M S_s \frac{D_{es}}{D_{eh}} \frac{k_h}{k_s} \left(1 - \frac{H}{P}\right) \quad \text{at } X = 1 \tag{16}$$

where  $S_s = kL/D$  denotes Sherwood number,  $r_1 = h_0/K_1$  and  $r_2 = h_0/K_2$  are reduced equilibrium

partition coefficient,  $L$  represents the length of pore,  $k_s$  and  $k_h$  are the external mass transfer coefficient of substrate and hydrogen ion concentration. Also

length,  $\chi$  is dimensionless Michaelis-Menten constant. The corresponding boundary conditions are

rate constant. The Thiele modulus  $W$  is defined as follows [11]:

$$W = \frac{V_m L^2}{D_{es} K_M} \tag{17}$$

The effectiveness factor  $\gamma$  is

$$\gamma = \frac{1}{W} (1 + \chi) \left( 1 + r_1 + \frac{1}{r_2} \right) \left( \frac{dS}{dX} \right)_{X=1} \tag{18}$$

and reaction rate of equation  $V$  is

$$V = \left( \frac{dS}{dX} \right)_{X=1} \tag{19}$$

### 3. Homotopy Analysis Method (HAM)

Liao [12] proposed a powerful analytical method for nonlinear problems, namely the Homotopy analysis method (see Appendix A). Different from all reported perturbation and non-perturbative techniques, the Homotopy analysis method [13-19] itself provides us with a convenient way to control and adjust the convergence region and rate of approximation series, when necessary. Briefly speaking, the Homotopy analysis method has the following advantages: It

is valid even if a given nonlinear problem does not contain any small/large parameters at all; It can be employed to efficiently approximate a nonlinear problem by choosing different sets of base functions. In this paper we employ HAM to give approximate analytical solutions of coupled non-linear reaction/diffusion Eq.(12) and (13). Using Homotopy analysis method (see Appendix –A and B) we can obtain the following new approximate substrate concentration and hydrogen ion concentration, we’ve

$$S(X) = 1 - hW \left( \frac{1}{S_s} + \frac{1}{2} - \frac{X^2}{2} \right) + A \left( \frac{1}{S_s} + \frac{1}{2} - \frac{X^2}{2} \right) - B \left( \frac{1}{S_s} + \frac{1}{4} + \frac{X^4}{4} \right) \tag{20}$$

where

$$A = hW + h^2W(1 + \chi) \left( r_1 P^2 + P + \frac{1}{r_2} \right) - \frac{(D_{es} / D_{eh}) (s_0 / h_0) P W^2 h^2}{2} - \frac{h^2 P^2 W^2 (s_0 / h_0)}{M S_s (k_h / k_s)} + \frac{h^2 W^2 P}{2} + \frac{h^2 W^2 P}{S_s}$$

$$\text{and } B = \frac{h^2 P W^2}{6} - \frac{(D_{es} / D_{eh}) (s_0 / h_0) P W^2 h^2}{6}$$

$$H(X) = P + \frac{D_{es} / D_{eh} s_0 / h_0 P W}{2} (X^2 - 1) - \frac{P^2 W s_0 / h_0}{M S_s k_h / k_s} + Q \left( \frac{X^2}{2} - \frac{1}{2} \right) - W \left( \frac{1}{4} - \frac{X^4}{4} \right) - \frac{P}{M S_s k_h / k_s D_{es} / D_{eh}} (Q + W) \tag{21}$$

where

$$Q = (D_{es} / D_{eh}) (s_0 / h_0) P W \left( 1 + h(1 + \chi) \left( r_1 P^2 + P + \frac{1}{r_2} \right) + h^2 W \left( \frac{1}{2} + \frac{1}{S_s} \right) \right) - \frac{((D_{es} / D_{eh}) (s_0 / h_0))^2 P W^2 h}{2} - \frac{h D_{es} / D_{eh} (s_0 / h_0)^2 P^2 W^2}{M S_s (k_h / k_s)}$$

$$W = \frac{(D_{es} / D_{eh} s_0 / h_0)^2 P W^2 h^2}{6} - \frac{h^2 W^2 P D_{es} / D_{eh} s_0 / h_0}{6}$$

From Eqs. (18)-(20), we can obtain the dimensionless reaction rate of equation  $V$  and effectiveness factor  $y$ , which is as follows:

$$V = -hW \left( 2 + h(1+x)(r_1 P^2 + P + \frac{1}{r_2}) \right) + s_0 / h_0 P W^2 h^2 \left( \frac{D_{es} / D_{eh}}{2} + \frac{P}{M S_s k_h / k_s} \right) - h^2 W^2 P \left( \frac{1}{2} + \frac{1}{S_s} \right) + J \tag{22}$$

$$y = \left( \frac{1}{W} \right) (1+x) \left( 1 + r_1 + \frac{1}{r_2} \right) V \tag{23}$$

**Appendix A**

**Basic idea of Homotopy analysis Method**

Consider the following differential equation [17]:

$$N[u(t)] = 0 \tag{A1}$$

where,  $N$  is a nonlinear operator,  $t$  denotes an independent variable,  $u(t)$  is an unknown function. For simplicity, we ignore all boundary or initial conditions, which can be treated in the similar way. By means of generalizing the conventional homotopy method, Liao constructed the so-called zero-order deformation equation as:

$$(1 - p)L[\{ (t; p) - u_0(t) \}] = phH(t)N[\{ (t; p) \}] \tag{A2}$$

where  $p \in [0,1]$  is the embedding parameter,  $h \neq 0$  is a nonzero auxiliary parameter,  $H(t) \neq 0$  is an auxiliary function,  $L$  is an auxiliary linear operator,  $u_0(t)$  is an initial guess of  $u(t)$  and  $\{ (t; p) \}$  is an unknown function. It is

$$\{ (t;0) = u_0(t) \text{ and } \{ (t;1) = u(t) \tag{A3}$$

important, that one has great freedom to choose auxiliary unknowns in HAM. Obviously, when  $p = 0$  and  $p = 1$ , it holds:

respectively. Thus, as  $p$  increases from 0 to 1, the solution  $\{ (t; p) \}$  varies from the initial guess  $u_0(t)$  to the solution have:

$u(t)$ . Expanding  $\{ (t; p) \}$  in Taylor series with respect to  $p$ , we

$$\{ (t; p) = u_0(t) + \sum_{m=1}^{+\infty} u_m(t) p^m \tag{A4}$$

where

$$u_m(t) = \frac{1}{m!} \frac{\partial^m \{ (t; p) \}}{\partial p^m} \Big|_{p=0} \tag{A5}$$

If the auxiliary linear operator, the initial guess, the auxiliary parameter  $h$ , and the auxiliary function are so properly chosen, the series Eq. (A.4) converges at  $p=1$  then we have:

$$u(t) = u_0(t) + \sum_{m=1}^{+\infty} u_m(t) . \tag{A6}$$

Define the vector

$$\vec{u}_n = \{u_0, u_1, \dots, u_n\} \tag{A7}$$

Differentiating Eq. (A.2) for  $m$  times with respect to the embedding parameter  $p$ , and then setting  $p = 0$  and finally

dividing them by  $m!$ , we will have the so-called  $m^{\text{th}}$ -order deformation equation as:

$$L[u_m - \mathfrak{t}_m u_{m-1}] = hH(t)\mathfrak{R}_m(\vec{u}_{m-1}) \tag{A8}$$

where

$$\mathfrak{R}_m(\vec{u}_{m-1}) = \frac{1}{(m-1)!} \frac{\partial^{m-1} N[\{ (t; p) \}]}{\partial p^{m-1}} \Big|_{p=0} \tag{A9}$$

and

$$\mathfrak{t}_m = \begin{cases} 0, & m \leq 1, \\ 1, & m > 1. \end{cases} \tag{A10}$$

Applying  $L^{-1}$  on both side of equation (A.8), we get

$$u_m(t) = \mathfrak{t}_m u_{m-1}(t) + hL^{-1}[H(t)\mathfrak{R}_m(\vec{u}_{m-1})] \tag{A11}$$

In this way, it is easily to obtain  $u_m$  for  $m \geq 1$ , at  $M^{\text{th}}$  order, we have

$$u(t) = \sum_{m=0}^M u_m(t)$$

When  $M \rightarrow +\infty$ , we get an accurate approximation of the original equation (A.1). For the convergence of the above method we refer the reader to Liao [17]. If equation (A.1)

admits unique solution, then this method will produce the unique solution. If equation (A.1) does not possess unique solution, the HAM will give a solution among many other (possible) solutions.

**Appendix B.**

**Approximate analytical solutions of the system of Equations (3-8) using Homotopy Analysis Method**

The given differential equations are of the form as:

$$\frac{d^2\check{S}}{dX^2} = \frac{1}{1+\chi\check{S}} \frac{w\check{S}}{1+r_1\check{<} + \frac{1}{r_2\check{<}}} \tag{B1}$$

$$\frac{d^2\check{<}}{dX^2} = -\frac{D_{es}}{D_{eh}} \frac{s_0}{h_0} \frac{1}{1+\chi\check{S}} \frac{w\check{S}}{1+r_1\check{<} + \frac{1}{r_2\check{<}}} \tag{B2}$$

The boundary conditions are

$$\frac{d\check{S}}{dX} = \frac{d\check{<}}{dX} = 0 \quad \text{at } X = 0 \tag{B3}$$

$$\frac{d\check{S}}{dX} = S_s(1-\check{S}) \quad \text{at } X = 1 \tag{B4}$$

$$\frac{d\check{<}}{dX} = MS_s \frac{D_{es}}{D_{eh}} \frac{k_h}{k_s} \left(1 - \frac{\check{<}}{P}\right) \quad \text{at } X = 1 \tag{B5}$$

In order to solve Eqs. (B1) and (B2) by means of the HAM, we first construct the Zeroth-order deformation equation by taking  $H(t) = 1$ ,

$$(1-p)\left(\frac{d^2\check{S}}{dX^2}\right) = ph\left(\left\{\left(\check{<} + r_1\check{<}^2 + \frac{1}{r_2}\right)(1+\chi\check{S})\frac{d^2\check{S}}{dX^2}\right\} - w\check{S}\check{<}\right) \tag{B6}$$

$$(1-p)\left(\frac{d^2\check{<}}{dX^2}\right) = ph\left(\left\{\left(\check{<} + r_1\check{<}^2 + \frac{1}{r_2}\right)(1+\chi\check{S})\frac{d^2\check{<}}{dX^2}\right\} + \frac{D_{es}}{D_{eh}} \frac{s_0}{h_0} w\check{S}\check{<}\right) \tag{B7}$$

Subject to the initial condition  $\{(0; p) = 0$ , where  $p \in [0,1]$  is an embedding parameter and  $h = 0$  is the so-called convergence control parameter. When  $p = 0$

$$p^0 : \frac{d^2 \check{\mathcal{S}}_0}{dX^2} = 0 \tag{B8}$$

$$p^0 : \frac{d^2 \check{\langle}_0}{dX^2} = 0 \tag{B9}$$

From (B8) and (B9), we get

$$\check{\mathcal{S}}_0 = 1 \tag{B10}$$

$$\check{\langle}_0 = 1 \tag{B11}$$

When  $p = 1$  the Eqs. (B6) and (B7) are equivalent to (B1) and (B2), thus it holds

$$\check{\mathcal{S}}(x;1) = \check{\mathcal{S}}(x) \tag{B12}$$

$$\check{\langle}(x;1) = \check{\langle}(x) \tag{B13}$$

Expanding  $\check{\mathcal{S}}(x; p)$  and  $\check{\langle}(x; p)$  in Taylor series with respect to the embedding parameter  $p$ , we have,

$$\check{\mathcal{S}}(x; p) = \check{\mathcal{S}}_o(x) + \sum_{m=1}^{\infty} \check{\mathcal{S}}_m(x) p^m \tag{B14}$$

$$\check{\langle}(x; p) = \check{\langle}_o(x) + \sum_{m=1}^{\infty} \check{\langle}_m(x) p^m \tag{B15}$$

$$\text{where } \check{\mathcal{S}}_o(x) = \check{\mathcal{S}}(x;0) \text{ and } \check{\langle}_o(x) = \check{\langle}(x;0) \tag{B16}$$

and  $\check{\mathcal{S}}_m(x)$  and  $\check{\langle}_m(x)$  [ $m = 1, 2, \dots$ ] will be determined later. Note that the above series contains the convergence

control parameter  $h$ . Assuming that  $h$  is chosen so properly that the above series is convergent at  $p = 1$ . We have the solution series as

$$\check{\mathcal{S}}(x) = \check{\mathcal{S}}_o(x) + \sum_{m=1}^{\infty} \check{\mathcal{S}}_m(x) p^m \tag{B17}$$

$$\check{\langle}(x) = \check{\langle}_o(x) + \sum_{m=1}^{\infty} \check{\langle}_m(x) p^m \tag{B18}$$



$$\text{where } \check{S}_m(x) = \frac{1}{m!} \frac{\partial^m \check{S}(x; p)}{\partial p^m} \Big|_{p=0} \text{ and } \check{\kappa}_m(x) = \frac{1}{m!} \frac{\partial^m \check{\kappa}(x; p)}{\partial p^m} \Big|_{p=0} \quad (\text{B19})$$

Equating the like the co-efficient of the like powers of  $p$  we have,

$$p^1 : \frac{d^2 \check{S}_1}{dX^2} + hW = 0 \quad (\text{B20})$$

$$p^1 : \frac{d^2 \check{\kappa}_1}{dX^2} - h \frac{D_{es} s_0 W \check{S}_0 \check{\kappa}_0}{D_{eh} h_0} = 0 \quad (\text{B21})$$

$$p^2 : \left( \frac{d^2 \check{S}_2}{dX^2} - \frac{d^2 \check{S}_1}{dX^2} \right) - \left[ h \left( (\check{\kappa}_0 + r_1 \check{\kappa}_0^2 + \frac{1}{r_2})(1 + \chi \check{S}_0) \frac{d^2 \check{S}_1}{dX^2} \right) \right] + hW \check{S}_0 \check{\kappa}_1 + hW \check{\kappa}_0 \check{S}_1 = 0 \quad (\text{B22})$$

$$p^2 : \frac{d^2 \check{\kappa}_2}{dX^2} - \frac{d^2 \check{\kappa}_1}{dX^2} - h \frac{D_{es} s_0 W \check{S}_1 \check{\kappa}_0}{D_{eh} h_0} - h \frac{D_{es} s_0 W \check{S}_0 \check{\kappa}_1}{D_{eh} h_0} - h \left( (\check{\kappa}_0 + r_1 \check{\kappa}_0^2 + \frac{1}{r_2})(1 + \chi \check{S}_0) \frac{d^2 \check{\kappa}_1}{dX^2} \right) = 0 \quad (\text{B23})$$

From Eqs. (B19-22) we get

$$\check{S}_1 = -\frac{hWX^2}{2} + \frac{hW}{2} + \frac{hW}{s_s} \quad (\text{B24})$$

$$\check{S}_2 = N \left( \frac{1}{s_s} + \frac{1}{2} - \frac{X^2}{2} \right) - J \left( \frac{1}{s_s} + \frac{1}{4} + \frac{X^4}{4} \right) \quad (\text{B25})$$

where

$$N = hW + h^2 W (1 + \chi) \left( r_1 P^2 + P + \frac{1}{r_2} \right) - \frac{D_{es} / D_{eh} s_0 / h_0 P W^2 h^2}{2} - \frac{h^2 P^2 W^2 s_0 / h_0}{MS_s k_h / k_s} + \frac{h^2 W^2 P}{2} + \frac{h^2 W^2 P}{s_s}$$

$$\text{and } J = \frac{h^2 P W^2}{6} - \frac{D_{es} / D_{eh} s_0 / h_0 P W^2 h^2}{6}$$

$$\langle_1 = \frac{D_{es} / D_{eh} s_0 / h_0 P W}{2} (1 - X^2) - \frac{P^2 W s_0 / h_0}{M S_s k_h / k_s} \tag{B26}$$

$$\langle_2 = Q \left( \frac{X^2}{2} - \frac{1}{2} \right) - W \left( \frac{1}{4} - \frac{X^4}{4} \right) - \frac{P}{M S_s k_h / k_s D_{es} / D_{eh}} (Q + W) \tag{B27}$$

where

$$Q = D_{es} / D_{eh} s_0 / h_0 P W \left( 1 + h(1 + \chi)(r_1 P^2 + P + \frac{1}{r_2}) + h^2 W \left( \frac{1}{2} + \frac{1}{S_s} \right) \right) - \frac{(D_{es} / D_{eh} s_0 / h_0)^2 P W^2 h}{2} - \frac{h D_{es} / D_{eh} (s_0 / h_0)^2 P^2 W^2}{M S_s k_h / k_s}$$

$$\text{and } W = \frac{(D_{es} / D_{eh} s_0 / h_0)^2 P W^2 h^2}{6} - \frac{h^2 W^2 P D_{es} / D_{eh} s_0 / h_0}{6}$$

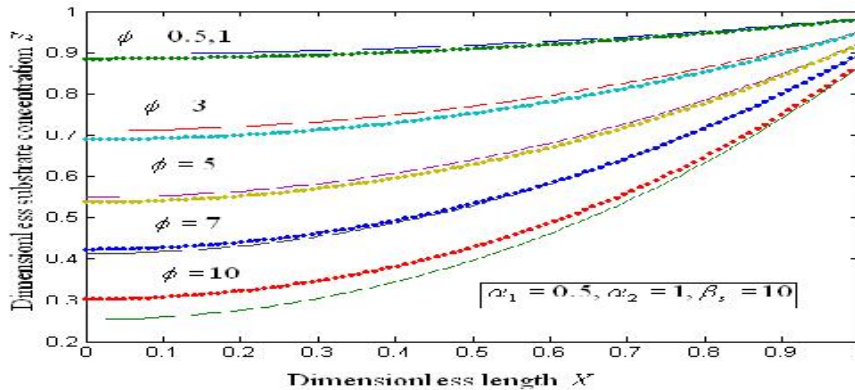
Adding Eqs. (B10) and (B24-25) and Eqs. (B11) and (B26-27), we get Eqs. (20) and (21) in the text.

### 4. Results and Discussion

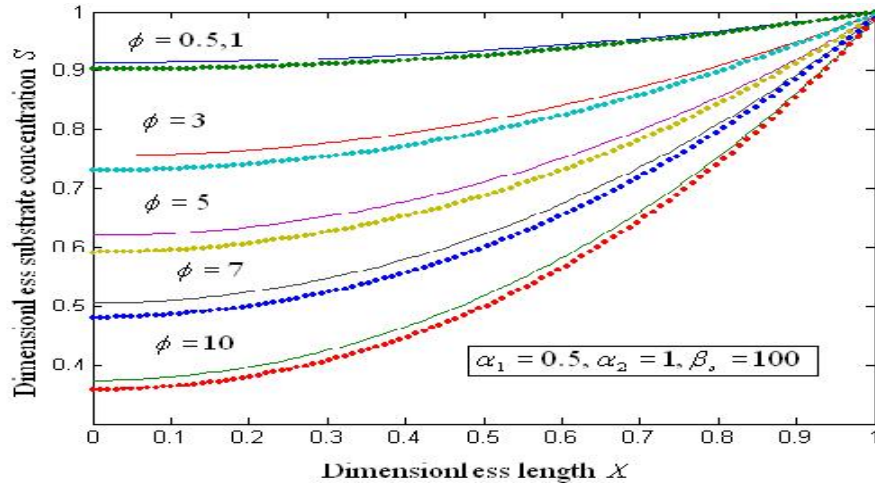
Eqs. (12) and (13) represent the analytical solutions of the concentration of substrate, hydrogen ion and effectiveness factor respectively. The Thiele modulus  $W$  can be varied by changing either the particle radius or the amount of concentration of substrate and hydrogen ion. This parameter describes the relative importance of diffusion and reaction in the particle radius. When  $W$  is small, the kinetics are the dominant resistance; the overall uptake of substrate, hydrogen ion and in the enzyme matrix is kinetically controlled. Under these conditions, the substrate and hydrogen ion concentration profile across the membrane is essentially uniform. In contrast, when the Thiele modulus  $W$  is large, diffusion limitations are the principal determining factor.

#### 4.1 Comparison of analytical and numerical results

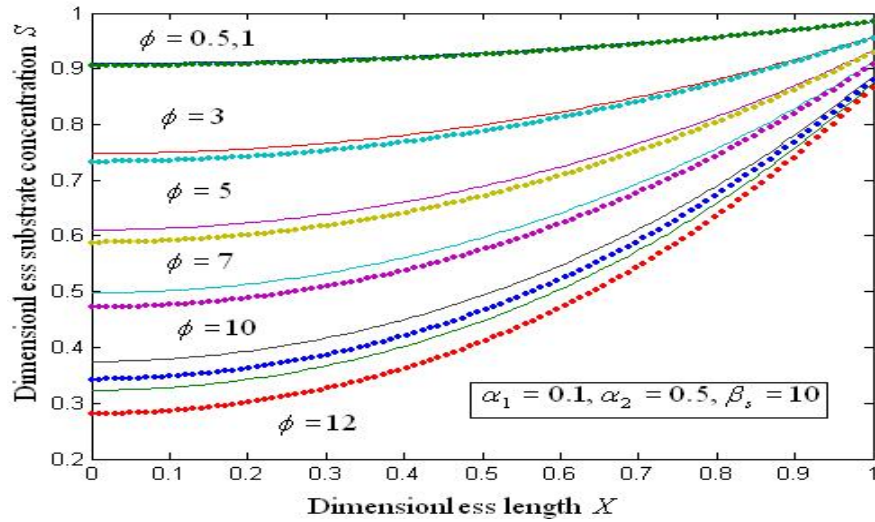
Figs. 1a-c show the dimensionless steady-state substrate concentration for the different values of  $W$  calculated using Eq. (20). From these figures, we can see that the value of the concentration decreases when Thiele modulus  $W$  increases. The concentration of substrate  $S(X)$  increases slowly and rises abruptly when  $X \geq 0.1$  and all values of  $W$ . When  $W < 1$  and  $r_1 \leq 0.5, r_2 \leq 1$ , the concentration of substrate  $S(X) \approx 1$  (steady-state value). When  $W$  is small, the overall uptake of substrate in the enzyme matrix is kinetically controlled and the substrate concentration profile across the membrane is identical.



**Fig.1a.** The Thiele modulus  $W$  on the dimensionless substrate concentration  $S$  obtained from our analytical solution presented in this work (Eq. (20)) for  $r_1 = 0.5, r_2 = 1, S_s = 10$ .



**Fig.1b.**The Thiele modulus  $W$  on the dimensionless substrate concentration  $S$  obtained from our analytical solution presented in this work (Eq. (20)) for  $r_1 = 0.5, r_2 = 1, S_s = 100$ .



**Fig.1c.**The Thiele modulus  $W$  on the dimensionless substrate concentration  $S$  obtained from our analytical solution presented in this work (Eq. (20)) for  $r_1 = 0.1, r_2 = 0.5, S_s = 10$ .

Figs. 2a-c show the dimensionless steady-state hydrogen ion concentration for the different values of  $W$  calculated using Eq. (21). From these figures, we can see that the value of the concentration increases when Thiele modulus  $W$  increases. The concentration of hydrogen ion  $H(X)$  decreases slowly and rises abruptly when

$X \geq 0.1$  and all values of  $W$ . When  $W < 1$  and  $r_1 \leq 0.5, r_2 \leq 1$ , the concentration of hydrogen ion reaches the steady-state value. When  $W$  is small, the overall uptake of hydrogen ion in the enzyme matrix is kinetically controlled and the hydrogen ion concentration profile across the membrane is identical.

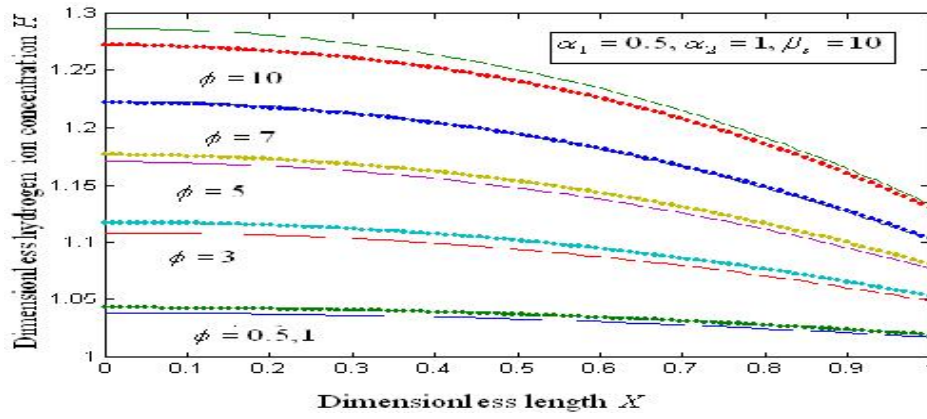


Fig.2a. The Thiele modulus  $W$  on the dimensionless hydrogen ion concentration  $H$  obtained from our analytical solution presented in this work (Eq. (21)) for  $\Gamma_1 = 0.5, \Gamma_2 = 1, S_s = 10$ .

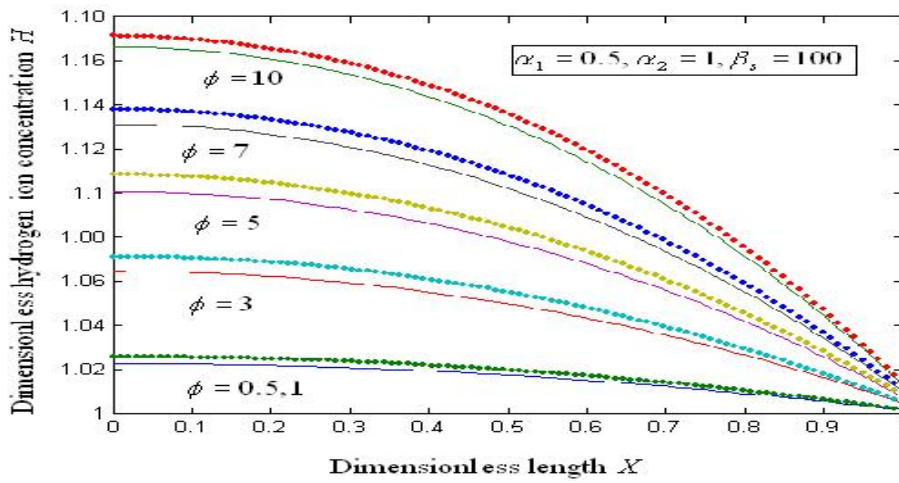


Fig.2b. The Thiele modulus  $W$  on the dimensionless hydrogen ion concentration  $H$  obtained from our analytical solution presented in this work (Eq. (21)) for  $\Gamma_1 = 0.5, \Gamma_2 = 1, S_s = 100$ .

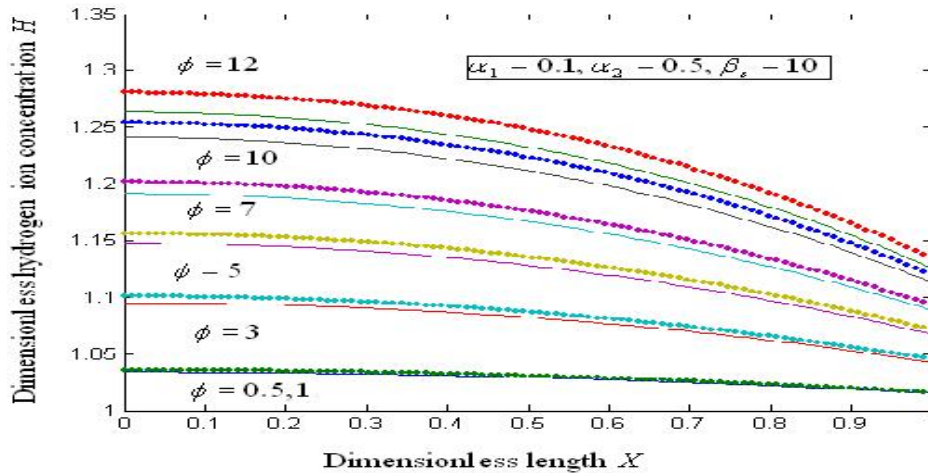
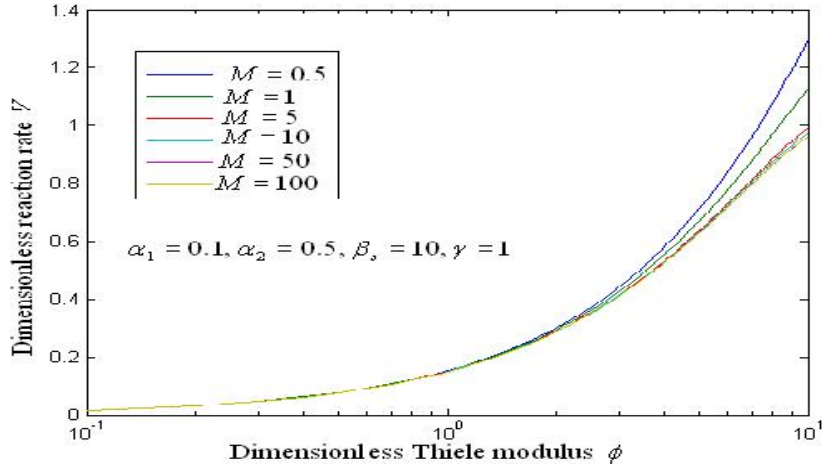


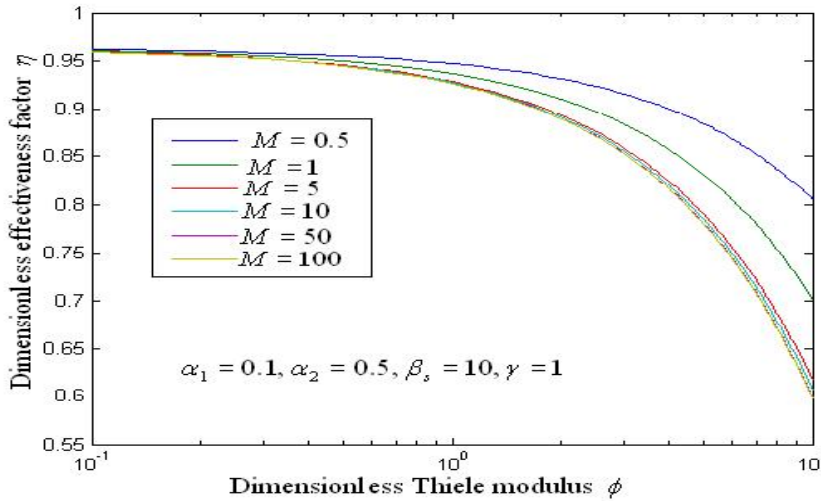
Fig.2c. The Thiele modulus  $W$  on the dimensionless hydrogen ion concentration  $H$  obtained from our analytical solution presented in this work (Eq. (21)) for  $\Gamma_1 = 0.1, \Gamma_2 = 0.5, S_s = 10$ .

Figs. 3(a-b). represent the dimensionless reaction rate  $V$  and effectiveness factor  $\eta$  versus dimensionless Thiele modulus  $W$  for different values of dimensionless module  $M$ . From these figures, it is inferred that, the reaction rate and effectiveness factor decreases quite rapidly as dimensionless module  $W$  increases, approaching zero at

high values, which corresponds to internal diffusion controlled processes. Moreover, it is also well known that, a constant value of dimensionless module  $W$ , the effectiveness factor increases for  $\Gamma_1 = 0.1, \Gamma_2 = 0.5, S_s = 10, \chi = 1$ .



**Fig.3a.** Plot of dimensionless reaction rate  $V$  versus Thiele modulus  $W$  for various values of  $M$  and the fixed value of  $\Gamma_1 = 0.1, \Gamma_2 = 0.5, S_s = 10, \chi = 1$ . Reaction rate is calculated using the equation (22).



**Fig. 3b.** Plot of dimensionless effectiveness factor  $\eta$  versus Thiele modulus  $W$  for various values of  $M$  and the fixed value of  $\Gamma_1 = 0.1, \Gamma_2 = 0.5, S_s = 10, \chi = 1$ . Effectiveness factor is calculated using the equation (23).

4.2 Effect of reduced equilibrium rate constants

Dimensionless reduced equilibrium rate constants  $\Gamma_1, \Gamma_2$  are defined as the ratio of hydrogen ion concentration to the equilibrium constants. These parameters can be varied from  $5 \times 10^{-5}$  to  $30 \times 10^{-5} M$ . Fig. 4(a-b) illustrates the dimensionless substrate concentration as a function of dimensionless length for

various values of reduced equilibrium rate constants. However, in fig. 4a the dimensionless substrate concentration increases rapidly when the value of equilibrium constant  $K_1$  decreases at the same time fig. 4b the value of substrate concentration increases when equilibrium constant  $K_2$  increases.

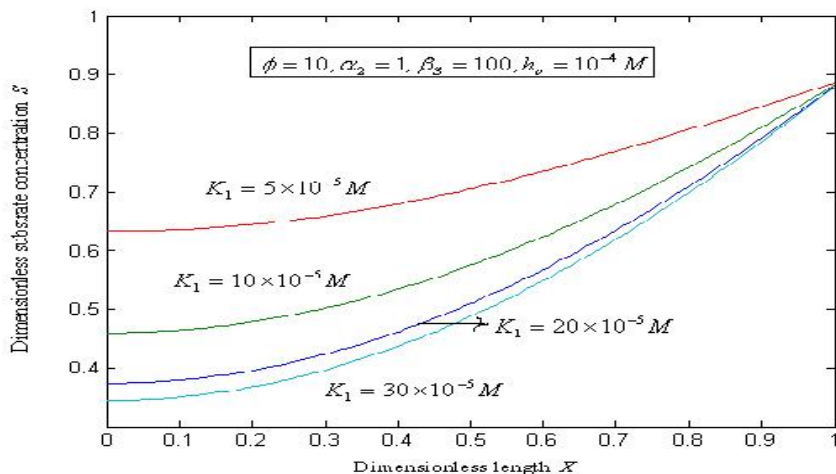


Fig. 4a: The equilibrium constant  $K_1$  on the dimensionless substrate concentration  $S$  obtained from our analytical solution presented in this work (Eq. (20)) for  $W = 10, h_o = 10^{-4} M, r_2 = 1, S_s = 100$ .

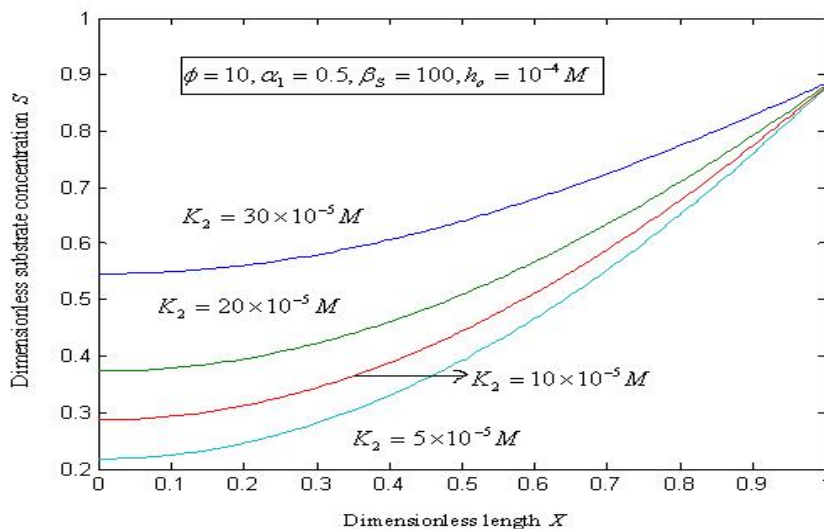
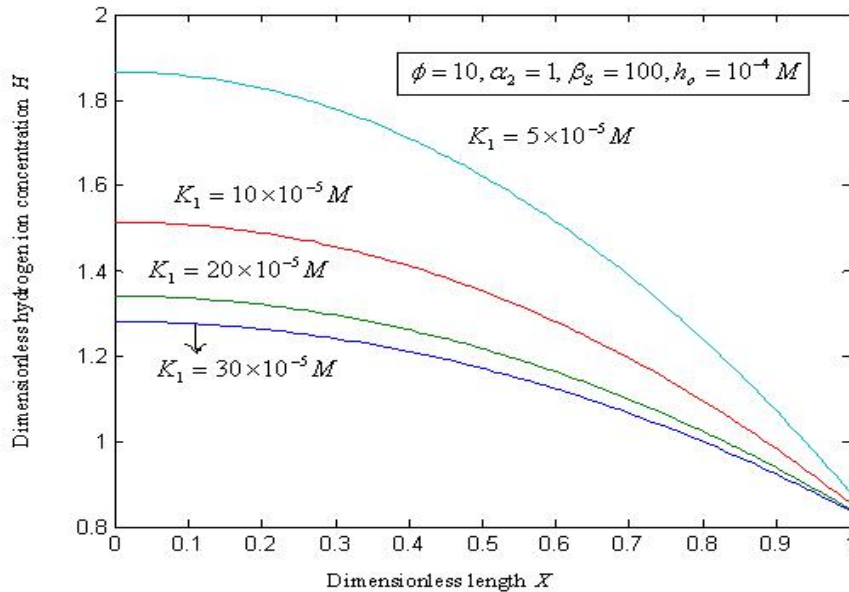


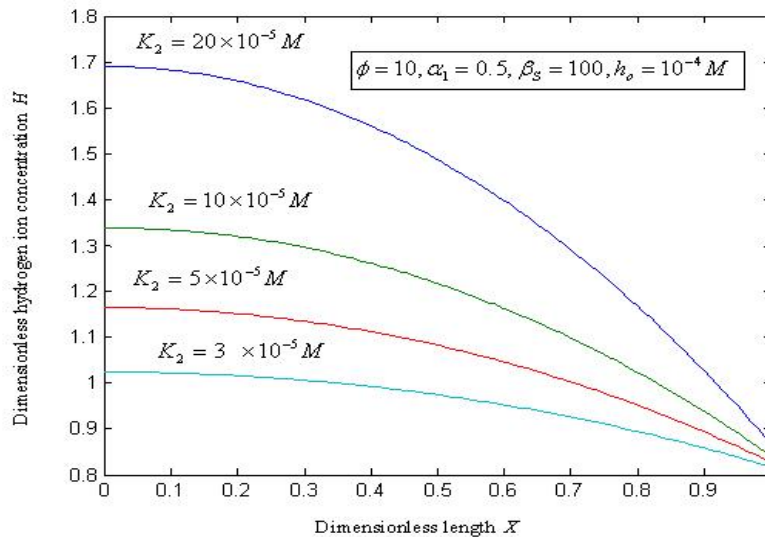
Fig. 4b: The equilibrium constant  $K_2$  on the dimensionless substrate concentration  $S$  obtained from our analytical solution presented in this work (Eq. (20)) for  $W = 10, h_o = 10^{-4} M, r_1 = 0.5, S_s = 100$ .

Dimensionless reduced equilibrium rate constants  $\Gamma_1, \Gamma_2$  are defined as the ratio of hydrogen ion concentration to the equilibrium constants. The value of  $K_1, K_2$  is varied from  $3 \times 10^{-5}$  to  $30 \times 10^{-5} M$ . Fig. 5(a-b) represents the concentration of hydrogen ion as a function of dimensionless length for different values of equilibrium

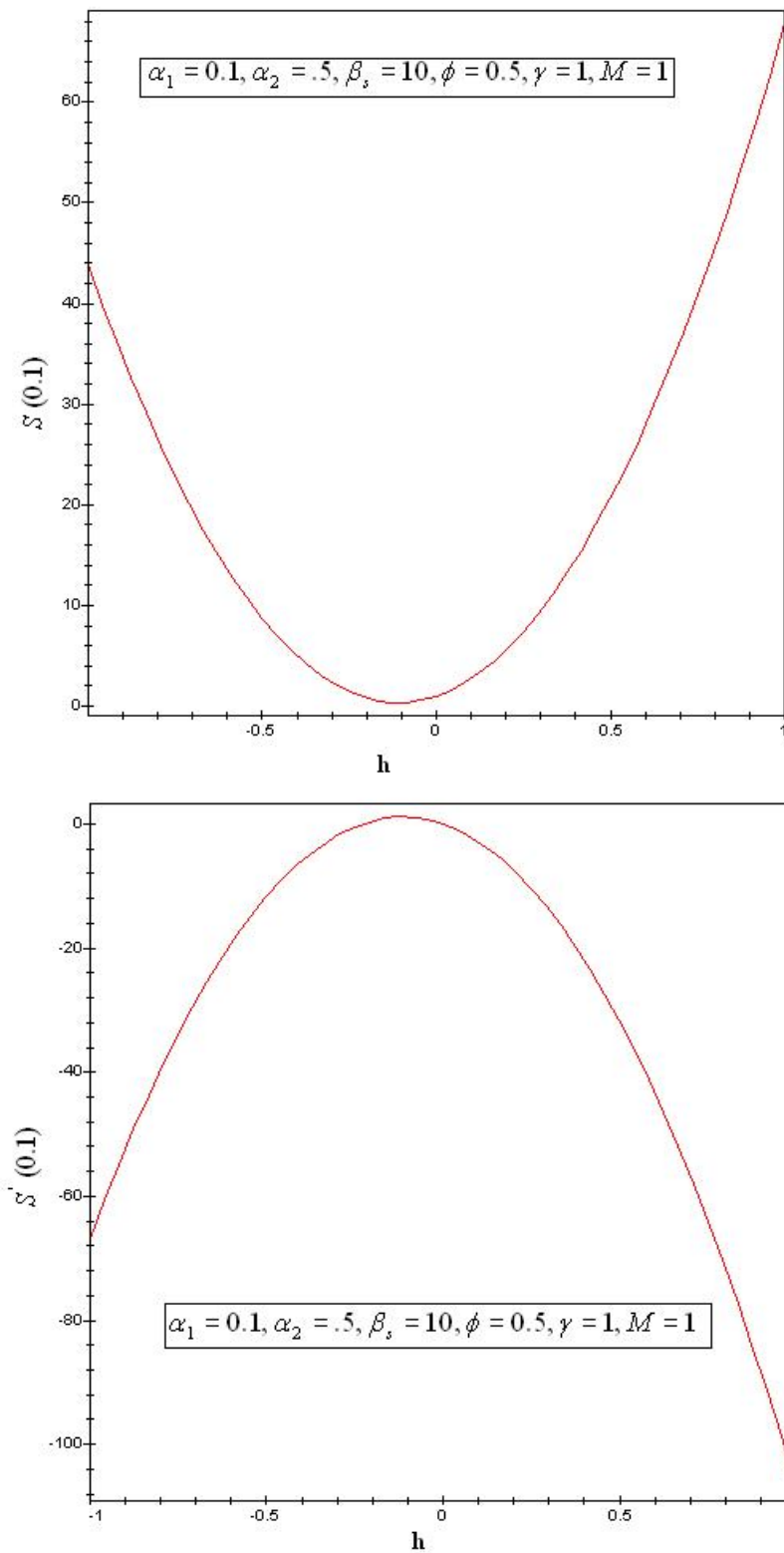
constants  $K_1, K_2$ . In this fig. 5a, it is inferred that, the value of the concentration for hydrogen ion increases strongly with decreasing  $K_1$  seeing that fig. 5b hydrogen ion decreases when decreasing  $K_2$  for the fixed value of  $\Gamma_1 = 0.5, \Gamma_2 = 1, w = 10, S_s = 100, h_o = 10^{-4} M$ .



**Fig. 5a:** The equilibrium constant  $K_1$  on the dimensionless hydrogen ion concentration  $H$  obtained from our analytical solution presented in this work (Eq. (21)) for  $w = 10, h_o = 10^{-4} M, \Gamma_2 = 1, S_s = 100$ .



**Fig. 5b:** The equilibrium constant  $K_2$  on the dimensionless hydrogen ion concentration  $H$  obtained from our analytical solution presented in this work (Eq. (21)) for  $w = 10, h_o = 10^{-4} M, \Gamma_1 = 0.5, S_s = 100$ .



**Fig.6:** The  $h$  curves to indicate the convergence region for  $r_1 = 0.1, r_2 = 0.5, S_s = 10, w = 0.5, x = 1, M = 1$ .



**5. Numerical simulation**

The HAM provides an analytical solution in terms of an infinite power series. However, there is a practical need to evaluate this solution and to obtain numerical values from the infinite power series. The consequent series truncation and the practical procedure conducted to accomplish this task, together transforms the otherwise analytical results into an exact solution, which is evaluated to a finite degree of accuracy. In order to investigate the accuracy of the

HAM solution with a finite number of terms, the system of differential equation were solved. To show the efficiency of the present method for our problem in comparison with the numerical solution (SCILAB program) we report our results graphically. The SCILAB program is also given in Appendix C. The numerical solution is compared with our analytical result in Table 1 and 2. The numerical values of parameters employed in Ramachandran et al. [11] and in this study are given in Table 3.

**Appendix C**

```
function pdex4
m = 0;
x = linspace(0,1);
t=linspace(0,100000);
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,1);
u2 = sol(:,2);
figure
plot(x,u1(end,:))
title('u1(x,t)')
xlabel('Distance x')
ylabel('u1(x,2)')
figure
%-----
plot(x,u2(end,:))
title('u2(x,t)')
xlabel('Distance x')
ylabel('u2(x,2)')
% -----
function [c,f,s] = pdex4pde(x,t,u,DuDx)
c = [1; 1];
f = [1; 1] .* DuDx;
phi=5;
y=1;
alpha1=0.1;
alpha2=0.5;
a=0.25;
q=10^(-4);
r=10^(-4);
F=- (phi*u(1)*u(2))/(1+y*u(1))*(1/(u(2)+alpha1*u(2)^2+1/(alpha2)));
F1=a*q/r*(phi*u(1)*u(2))/(1+y*u(1))*(1/(u(2)+alpha1*u(2)^2+1/(alpha2)));
s=[F; F1];
% -----
function u0 = pdex4ic(x); %create a initial conditions
u0 = [1; 0];
% -----
function [pl,ql,pr,qr]=pdex4bc(xl,ul,xr,ur,t) %create a boundary conditions
K=10;
M=1;
a=0.25;
b=1;
P=1;
pl = [0; 0];
ql = [1; 1];
pr = [-K*(1-ur(1)); -M*K*a*b*(1-ur(2))];
qr = [1; 1];
```

**Table1:** Comparison of normalized substrate concentration  $S$  Eq. (20) and numerical simulation for various values of Thiele modulus  $W$  and  $r_1 = 0.5, r_2 = 1, S_s = 100, h = -0.13$ .

$x$	Concentration of $S$								
	$S$ (when $W=1$ )			$S$ (when $W=5$ )			$S$ (when $W=10$ )		
	This work	Simulation	Error %	This work	Simulation	Error %	This work	Simulation	Error %
0	0.9132	0.9121	0.1206	0.6195	0.5933	4.4159	0.3732	0.3575	4.3916
0.2	0.9166	0.9158	0.0874	0.6342	0.6179	2.6379	0.396	0.3792	4.4304
0.4	0.927	0.9175	1.0354	0.6779	0.6664	1.7257	0.459	0.4476	2.5469
0.6	0.9432	0.9371	0.6509	0.7498	0.7359	1.8888	0.5657	0.5679	0.3874
0.8	0.9668	0.9645	0.2385	0.8487	0.8476	0.1298	0.7088	0.7212	1.7194
1	0.9972	0.9981	0.0902	0.9659	0.9699	0.4124	0.981	0.9858	0.4869
	Average		0.3705	Average		1.8684	Average		2.3271

**Table2:** Comparison of normalized hydrogen ion concentration  $H$  Eq. (21) and numerical simulation for various values of Thiele modulus  $W$  and  $r_1 = 0.5, r_2 = 1, S_s = 100, h = -0.13$ .

$x$	Concentration of $H$								
	$H$ (when $W=1$ )			$H$ (when $W=5$ )			$H$ (when $W=10$ )		
	This work	Simulation	Error %	This work	Simulation	Error %	This work	Simulation	Error %
0	1.021	1.026	0.4873	1.1001	1.109	0.8025	1.165	1.171	0.5124
0.2	1.030	1.025	0.4878	1.1003	1.105	0.4253	1.159	1.166	0.6003
0.4	1.020	1.022	0.1957	1.099	1.093	0.5489	1.150	1.149	0.0870
0.6	1.015	1.017	0.1967	1.084	1.073	1.0252	1.115	1.119	0.3575
0.8	1.01	1.01	0.0000	1.053	1.044	0.8621	1.083	1.073	0.9319
1	1.002	1.002	0.0000	1.006	1.008	0.1984	1.013	1.1014	8.0268
	Average		0.2279	Average		0.6437	Average		1.7527

Dimensionless parameters

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Sherwood number	$S = kL/D$
reduced equilibrium rate constant	$r_1 = h_o/K_1, r_2 = h_o/K_2$
Thiele modulus	$W = \frac{V_m L^2}{D_{es} K_M}$
Effectiveness factor	$\eta = \frac{1}{W} (1+x) \left( 1+r_1 + \frac{1}{r_2} \right) V$
Dimensionless Michaelis-Menten constant	$X$

---

**Table 3: Range/values of parameters in Ramachandran et al. [11] and this work**

Parameters	Range of parameters in Ref [11]	Value of the parameter in this work if $h = -0.13$						
		Fig 1(a-c)	Fig. 2(a-c)	Fig. 3(a-b)	Fig 4a	Fig 4b	Fig 5a	Fig 5b
$K_1 (M)$	$5 \times 10^{-2}$				$5-30 \times 10^{-2} M$		$5-30 \times 10^{-2} M$	
$K_2 (M)$	$10^{-2}$					$5-30 \times 10^{-2} M$		$5-30 \times 10^{-2} M$
$K_M (M)$	$10^{-2}$							
$k_i/k_e$	1	1	1	1	1	1	1	1
$D_{ai}/D_{ei}$	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
$s_0 (M)$	$10^{-4}, 10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$
$h_0 (M)$	$10^{-4} - 10^{-7}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$	$10^{-4}$
$M$		1	1	0.5-100	1	1	1	1
$P$		1	1	1	1	100	1	100
$\beta_s$	10,100,1000, $\infty$	10,100	10,100	10	100	0.5	100	0.5
$\alpha_1$	0.02-2	0.1, 0.5	0.1, 0.5	0.1	0.33-2	0.33-2	1	0.5-3.33
$\alpha_2$	0.01-10	0.5, 1	0.5, 1	0.5	1	1	1	1
$\gamma$		1	1	1	1	10	1	10
$\phi$	4,40-1000	0.5-12	0.5-12	1	1	10	10	1
$\eta$					10			

## Conclusion

A non-linear time independent equation has been formulated and solved analytically using Homotopy analysis method. The primary result of this work is the first approximate calculations of substrate concentrations and hydrogen ion concentration and effectiveness factor for non-linear Michaelis-Menten kinetic scheme. A simple closed form of analytical expressions of steady-state substrate, hydrogen ion concentrations and are given. Furthermore, on the basis of the outcome of this work, it is possible to calculate the approximate amounts of effectiveness factor used for immobilized enzyme on kinetics for all possible values of the parameters. This method is an extremely simple method and it is also a promising method to solve other non-linear equations. This theoretical analysis is useful for enzyme immobilized on very small particles the analysis shows that depending on the charge of the carrier the bulk pH can be optimally chosen to increase the overall rate of reaction. Determination of  $h$  is also given in Appendix D.

## Appendix D

### Determining the region of $h$ for validity

The analytical solution should converge. It should be noted that the auxiliary parameter  $h$  controls the convergence and accuracy of the solution series. The analytical solution represented by Eq. (20) contains the auxiliary parameter  $h$ , which gives the convergence region and rate of approximation for the homotopy analysis method. In order to define region such that the solution series is independent of  $h$ , a multiple of  $h$ -curves are plotted. The region where the distribution of  $S$  and  $S'$  versus  $h$  is a horizontal line is known as the convergence region for the corresponding function. The common region among the  $S(X)$  and its derivatives are known as the overall convergence region. To study the influence of  $h$  on the convergence of solution, the  $h$ -curves of  $S(0.1)$  and  $S'(0.1)$  are plotted in Fig. 6 respectively, for  $\{ =0.5$  and  $\{ =0.5$  and  $r_1 = 0.1, r_2 = 0.5, S_s = 10$ . These figures clearly indicate that the valid region of  $h$  is about  $-1 < h < -0.8$ . Similarly we can find the value of the convergence control parameter  $h$  for different values of constant parameters.

## Appendix E

### Nomenclature

$K_1, K_2$  equilibrium constants  
 $s$  substrate concentration  
 $V_m$  maximum rate of reaction  
 $K_m$  Michaelis-Menten constant  
 $D$  diffusivity  
 $D_{es}, D_{ek}$  effective diffusivity  
 $x$  distance from the centre of the pore  
 $M$  dimensionless electrostatic potential modifier  
 $P$  partition coefficient  
 $L$  length of pore  
 $e$  Euler's constant (0.5772)  
 $E_i(x)$  exponential integral  
 $F$  Faraday's constant  
 $h$  hydrogen ion concentration  
 $k_s, k_h$  external mass transfer coefficient  
 $S$   $s/s_0$ , dimensionless substrate concentration  
 $H$   $h/h_0$ , dimensionless hydrogen ion concentration  
 $X$   $x/L$ , dimensionless length  
 $N$  flux  
 $r(s, a)$  rate of the reaction

$R$  gas constant  
 $T$  temperature  
 $Z$  valency of hydrogen ion

#### Greek letters

$X$  dimensionless Michaelis-Menten constant  
 $S$   $kL/D$ , Sherwood number  
 $\Gamma_1, \Gamma_2$   $h_o/K_1, h_o/K_2$ , reduced equilibrium rate constant  
 $U$  thickness of diffusion layer  
 $k$  Debye-Hickal reciprocal length  
 $\}$  dimensionless surface potential  
 $W$  Thiele modulus  
 $\gamma$  effectiveness factor  
 $\Phi_o$  surface potential on the membrane

#### Subscripts

$O$  bulk conditions  
 $h$  hydrogen ion  
 $s$  substrate

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