CHAPTER – IV

VARIATIONAL ITERATION METHOD IN NONLINEAR BOUNDARY VALUE PROBLEMS IN ENZYME–SUBSTRATE REACTION–DIFFUSION PROCESSES – THE STEADY–STATE AMPEROMETRIC RESPONSE

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4.1 INTRODUCTION

The development of polymer-based materials for use as electrocatalysis and as chemical and biological sensors operating in the batch amperometric mode [1, 2] was discussed in earlier chapters. The investigation of exact solution of nonlinear equation is interesting and important. In the past several decades, many authors mainly had paid attention to study solution of nonlinear equations by using various methods, such as Backlund transformation [3], Darboux transformation [4], Inverse scattering method [5], Bilinear method [6], the tanh method [7], the sine-cosine method [8], the homogeneous balane method [9] and variational iteration method (VIM) [10,11] etc.

The variational iteration method [10-14] has been extensively worked out over a number of years by numerous authors. He [10,15] successfully applied to autonomous ordinary differential equations in [16] to nonlinear polycrystalline solids [17] and other fields. This method has been proved by many authors to be a powerful mathematical tool for various kinds of nonlinear problems. It is a promising and evolving
method. Besides its mathematical importance and its links to other branches of mathematics, it is widely used in all ramifications modern science [18]. In this method the solution procedure is very simple by means of variational theory and only few iterations lead to high accurate solutions which are valid for the whole solution domain.

The purpose of this chapter is to derive steady state analytical solution of concentration for polymer modified electrode for all values $\alpha$ and $K$ using VIM. The chosen configuration is mostly used in the design of enzymatic biosensor such as the use of polymeric matrices as an enzyme support and the mass production of biosensors by the screen printing technique [19].

4.2 MATHEMATICAL FORMULATION OF THE PROBLEM

The enzyme kinetics in biochemical systems are modeled usually by ordinary differential equations which are based only on reaction without spatial dependence of the various concentrations. Recent attention has been given to the effect of diffusion in the process of interactions [20, 21]. When this effect is taken into consideration, the various concentrations in the reaction process become spatially dependent and
the equations governing these concentrations become partial differential equations of parabolic type [20]. In an irreversible monoenzyme system the reaction scheme for free enzyme $E$ and substrate concentration $S$ may be expressed by

$$E + S \xrightleftharpoons[k_{-1}]{k_1} ES \rightarrow E + P$$

(1)

where $ES$ is the enzyme–substrate complex and $P$ is the product. Suppose that the reaction–diffusion takes place in an arbitrary $n$–dimensional medium $\Omega$ (membrane), where $\Omega$ is a bounded domain in $\mathbb{R}^n$ ($n = 1, 2, \ldots$). Then the rate of change of substrate concentration $S = S(t, \chi)$ at time $t$, position $\chi \in \Omega$ is equal to the sum of the rate due to reaction and diffusion, and is given by [20]

$$\frac{\partial S}{\partial t} = D_s \nabla (\nabla S) - \nu(t, \chi)$$

(2)

where $D_s$ is the substrate diffusion coefficient, $\nabla$ is the gradient operation and $\nu$ is the so–called initial reaction velocity.

Various models regarding the expression for $\nu$ are formulated by researchers in this field. In this chapter, we discuss some mathematical properties of the solutions for such type of models using Michaelis–
Menten hypothesis. Based on the Michaelis Menten hypothesis, the velocity function \( v \) for the simple reaction process without competitive inhibition is given by [20, 21]

\[
v(t, \chi) = k_2 E_0 S / (K_M + S)
\]

(3)

where \( E_0 \) is the total amount of enzyme and \( K_M \) is the Michaelis Menten constant. In this model, the equation for \( S \) becomes

\[
\partial S / \partial t - D \nabla \cdot (\nabla S) = -k_2 E_0 S / (K_M + S) \quad (t > 0, \chi \in \Omega).
\]

(4)

In one dimensional form equation (4) can be written as

\[
\frac{\partial S}{\partial t} = D \frac{\partial^2 S}{\partial \chi^2} - \frac{k_2 E_0 S}{K_M + S}
\]

(5)

Introducing a pseudo-first order rate constant \( K = k_2 E_0 / K_M \), we can write the above equation as

\[
\frac{\partial S}{\partial t} = D \frac{\partial^2 S}{\partial \chi^2} - \frac{KS}{1 + S/K_M}
\]

(6)

Here we consider, an initial condition of the form,

\[
S(0, \chi) = s_0(\chi) \quad (\chi \in \Omega)
\]

(7)

The system governs the substrate concentration \( S \) when there is no competitive inhibition in the reaction. We make the non-linear PDE (equation (6)) dimensionless by defining the following parameters:
\[ u = \frac{s}{k s^m}, \quad x = \chi / L, \quad \tau = D_s t / L^2, \quad K = k L^2 / D_s = \phi^2, \quad \alpha = k s^m / K_M \] \tag{8}

Where \( u \), \( x \) and \( \tau \) represent dimensionless concentrations, distance and time respectively. Here \( \alpha \) denotes a saturation parameter and \( \kappa \) denotes reaction diffusion parameter. Now the equation (6) reduces to the following dimensionless form:

\[ \frac{\partial u}{\partial \tau} = \frac{\partial^2 u}{\partial x^2} - \frac{K u}{1 + \alpha u} \quad 0 < u \leq 1 \] \tag{9}

whereas the initial condition reduces to

\[ u(x = 0) = a \quad \text{(constant)} \] \tag{10}

Lyons and co-workers [1] solved the above equations only for the limiting cases \((\alpha u << 1 \quad \text{and} \quad \alpha u >> 1)\), refer figure (1)) using Dirichlet and Neumann boundary conditions. But we wish to obtain an analytical expression for the concentration profile \( u(x) \) of substrate for all values of \( \alpha \). In steady state, \( \frac{\partial u}{\partial \tau} = 0 \).

In this case the steady state diffusion equation (9) takes the form

\[ \frac{d^2 u}{dx^2} - \frac{K u}{1 + \alpha u} = 0 \] \tag{11}

Again, this is a non-linear differential equation. Now the boundary condition (equation (10) is [1])
\begin{align}
\bar{u}(0) &= u = S_\text{ech}(\sqrt{K}) \quad \text{for} \quad \alpha \ll 1 \\
&= 1 - K/2\alpha \quad \text{for} \quad \alpha \gg 1
\end{align}

The non-linear equation (11) is solved for the above boundary conditions using variational iteration method.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{diagram}
\caption{Diagrammatic representation of saturated (zero order kinetics) and unsaturated (1st order kinetics) catalytic kinetics}
\end{figure}

The variational iteration method proposed by He [10, 15] has been successfully applied in finding the solution of differential equation in closed form. The basic concept of variational iteration method is summarized briefly here for completeness.
4.3 BASIC CONCEPTS IN THE VARIATIONAL ITERATION METHOD

To illustrate the basic concepts of variational iteration method (VIM), we consider the following nonlinear partial differential equation:

\[
L[u(x)] + N[u(x)] = g(x)
\]  
\hspace{1cm} (13)

where \( L \) is a linear operator, \( N \) is a nonlinear operator, and \( g(x) \) is a given continuous function [10,15]. According to the variational iteration method, we can construct a correct functional as follows:

\[
\tau \int_0^1 \left[ \lambda \left( L[u_n(\tau)] + N[u_n(\tau)] - g(\tau) \right) \right] d\tau
\hspace{1cm} (14)

where \( \lambda \) is a general Lagrange multiplier [10,15] which can be identified optimally via variational theory, \( u_n \) is the \( n^{\text{th}} \) approximate solution, and \( u_n \) denotes a restricted variation, i.e., \( \delta u_n = 0 \).

4.4 SOLUTION OF BOUNDARY VALUE PROBLEM

Using above variation iteration method we can write the correction functional of equation (11) as follows

\[
u_{n+1}(x) = u_n(x) + \int_0^x \lambda \left[ L[u_n(\tau)] + N[u_n(\tau)] - g(\tau) \right] d\tau
\hspace{1cm} \lambda (15)

Taking variation with respect to the independent variable \( u_n \), noticing that \( \delta u_n(0) = 0 \)
\[ \delta u_{n+1}(x) = \delta u_n(x) + \delta \int_0^x \lambda \left[ u''(s) - \frac{K u(s)}{1 + \alpha u(s)} \right] ds \]  

(16)

For all variational \( \delta u_n \) and \( \delta u_n' \), implying the following stationary conditions

\[ \delta u_n : 1 - \lambda'(s) \bigg|_{s=x} = 0 \]  

(17a)

\[ \delta u_n' : \lambda(s) \bigg|_{s=x} = 0 \]  

(17b)

\[ \delta u_n : \lambda''(s) \bigg|_{s=x} = 0 \]  

(17c)

The Lagrange multiplier can be identified as

\[ \lambda(s) = s - x \]  

(18)

Substituting the Lagrange multiplier in the iteration formula (equation (15)) we get the following approximation

\[ u_1(x) = a + \frac{K a}{(1 + \alpha a)} x^2 \]  

(19)

\[ u_2(x) = a + \frac{K x^2}{2 \alpha} + \frac{(1 + \alpha a)}{\alpha^2} \ln \left[ \frac{K a}{2(1 + \alpha a)^2} x^2 + 1 \right] \]  

(20)

\[ -\frac{\sqrt{2} K}{\alpha^{3/2} \sqrt{a}} x \tan^{-1} \left[ \frac{\sqrt{K a}}{\sqrt{2(1 + \alpha a)}} x \right] \]  

\[ u_3(x) = u_2(x) + \frac{K}{\alpha} \left[ \frac{x^2 (1 + \alpha a)}{2 \cdot 2 K \alpha a} \right] \left[ \frac{2(1 + \alpha a)^2}{(K a \alpha x^2 + 2(1 + \alpha a))^3} + \frac{3}{2} \ln \left( \frac{K a \alpha x^2}{2(1 + \alpha a)^2} + 1 \right) \right] \]  

(21)

\[ + \frac{K}{\alpha} \left[ \frac{x^2 (1 + \alpha a)}{K a \alpha x^2 + 2(1 + \alpha a)} \right] - \int_0^x (s-x) \frac{K u(s)}{1 + \alpha u(s)} ds \]  

Last term in the equation (21) is not integrated. Hence \( u_3(x) \) is not expressed in the closed form. Therefore we are taking \( u_2(x) = u(x) \).

Equation (20) represents the most general approximate expression for
the substrate concentration profiles for all values of $\alpha$ and $K$. The time
independent concentration $u(x)$ using equation (20) are represented in
Figure (2) and Figure (3) for various values of $\alpha$ and $K$.

4.5 LIMITING CASES

4.5.1 Unsaturated (First Order) Catalytic Kinetics

In this case, the substrate concentration in the film $S(\chi)$ is less than the Michaelis Menten constant $K_M$. This is explained in Figure (1).

When $\alpha u \ll 1$, the equation (11) reduces to

$$\frac{d^2u}{dx^2} - Ku = 0$$

(22)

Using the variational iteration method and boundary condition (12a), its correction functional can be written in the form

$$u_{n+1}(x) = u_n(x) + \int_a^x \lambda [u^n(s) - Ku_n(s)] ds$$

(23)

By the same manipulation, the multiplier ($\lambda(s) = s - x$) can be identified and the following iteration formula can be obtained as

$$u_{n+1}(x) = u_n(x) + \int_0^x (x-s)[u^n(s) - Ku_n(s)] ds$$

(24)

Now $u_1(x), u_2(x), u_3(x)$ becomes,
\[ u_1(x) = a \left[ 1 + \frac{Kx^2}{2} \right] \] (24a)

\[ u_2(x) = a \left[ 1 + \frac{Kx^2}{2!} + \frac{(Kx^2)^2}{4!} \right] \] (24b)

\[ u_3(x) = a \left[ 1 + \frac{Kx^2}{2!} + \frac{(Kx^2)^2}{4!} + \frac{(Kx^2)^3}{6!} \right] \] (24c)

\[ u_n(x) = a \sum_{m=0}^{n} \frac{(Kx^2)^m}{2m!} \] (24d)

\[ u(x) = a \cosh(\sqrt{K}x) \] (25)

The equation (25) derived by us is identical with equation (10) in ref [1].

4.5.2 Saturated (Zero Order) Catalytic Kinetics

In this case, the substrate concentration in the film \( S(x') \) is greater than the Michaelis Menten constant \( K_M \). (Refer Figure (1)). Hence \( au >> 1 \) reduces the equation (11) to

\[ \frac{\partial^2 u}{\partial x^2} - \frac{K}{\alpha} u = 0 \] (26)

Using He’s variational iteration method and using the boundary condition (12b), its correction functional can be written in the form

\[ u_{n+1}(x) = u_n(x) + \int_0^x \lambda[u''(s) - K / \alpha] ds \] (27)
By the same manipulation, the multiplier \((\lambda(s) = s - x)\) can be identified and the following iteration formula can be obtained as

\[
\begin{align*}
  u_{n+1}(x) &= u_n(x) + \int_0^1 (x-s)[u''(s) - K/\alpha]ds \\
  u(x) &= a + \frac{K}{2\alpha} x^2
\end{align*}
\]  

(28)

(29)

This equation is identical with equation (11) of ref [1]. These limiting case results, equation (25) (for \(\alpha << 1\)) and equation (29) (for \(\alpha >> 1\)) are compared with our main result equation (20). Table.1 and Table.2 indicates the dimensionless substrate concentration evaluated using equation (20) with the limiting case results. The average relative difference between our results (equation (20)) and limiting case results are -0.09%, -1.26%, -3.90%, -8.61%, -13.44% (for \(\alpha << 1\)) and 0, -0.11%, -0.47%, -1.27%, -3.15% (for \(\alpha >> 1\)) when \(K=0.01,1,4,9\) and 16 respectively.

4.6 ANALYSIS OF MOVING BOUNDARY

Considering the limiting situations for totally unsaturated kinetics when \(\alpha u << 1\) and saturated kinetics when \(\alpha u >> 1\). The outer part of the
region is saturated (region RII) and the inner region (region RI) remains unsaturated. This is illustrated in Figure (4).

**Fig 4. The description of two region approach used to obtain equation (32) corresponds the situation of moving boundary**

Considering a situation where the reaction kinetics is fast compared with substrate diffusion. A moving normalized distance parameter $x^*$ is defined as the boundary between regions RI and RII. The substrate $S$ diffuses into the film and a reaction front is established at $x = x^*$. When $x^* = 0$, the entire region is saturated and when $x^* = 1$, the entire region is unsaturated. In RI, $\alpha u << 1$ and in RII $\alpha u >> 1$. When $x = x^*$, $u = 1/\alpha$. Now the equation (20) becomes,
\[
\frac{1}{\alpha} = a + \frac{Kx^2}{2\alpha} + \frac{(1 + \alpha a)}{a\alpha} \ln \left[ \frac{K\alpha}{2(1 + \alpha a)^2} x^2 + 1 \right] - \frac{\sqrt{2K}}{\alpha^{3/2}} \sqrt{a} x^* \tan^{-1} \left[ \frac{\sqrt{K\alpha}}{\sqrt{2}(1 + \alpha a)} x^* \right] \tag{30}
\]

The inner region \( \text{RI} \) is unsaturated whereas the outer region \( \text{RII} \) is saturated. The line between these two regions is set at some value \( x^* \) defined in equation (32). Complete saturation occurs when \( x^* = 0 \). When \( \frac{K\alpha}{2(1 + \alpha a)^2} \) is small, we obtain,

\[
\frac{K^2 a\alpha}{12(1 + \alpha a)^3} x^{*4} - \frac{K\alpha}{2(1 + \alpha a)} x^{*2} - \alpha a + 1 = 0 \tag{31}
\]

Solving the above equation to obtain \( x^* \)

\[
x^* = \left[ \frac{3(1 + \alpha a)}{K} \left[ 1 \pm \frac{1}{\sqrt{\alpha a}} \sqrt{\frac{3\alpha^2 a^2 + 7\alpha a - 4}{3(1 + \alpha a)}} \right] \right]^{1/2} \tag{32}
\]

Equation (32) describes the position of the boundary as it moves through the film.

### 4.7 CONCLUSION

A nonlinear time independent partial differential equation has been formulated and solved using He’s variational iteration method. The primary result of this work is first accurate calculation of substrate concentration for all values of \( \alpha \) and \( K \). It gives good agreement with previous published limiting case results. The extension of the procedure
to other two dimension and three dimension geometries with various complex boundary conditions seems possible.

REFERENCES


