CHAPTER – III

MATHEMATICAL MODELING OF
DIFFUSION AND KINETICS IN
AMPEROMETRIC IMMOBILIZED ENZYME
ELECTRODES*

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3.1 INTRODUCTION

Recently, there has been much interest in the development of amperometric enzyme electrodes [1, 2]. Rahamathunissa and Rajendran [3] obtained the analytical solutions for substrate concentration and transient current for both steady-state and non-steady-state amperometric polymer-modified electrodes using Danckwerts' relation. Andrieux et al. [4] and Albery and Hillman [5] analyzed the kinetics of reactions at polymer-modified electrodes. During these reactions, species from the solution react with a mediator that was bound in a film at the electrode surface. The approximate analytical solutions can be obtained for limiting cases by linearizing the non-linear term [6]. In the case of an immobilized enzyme, the problem is further complicated by the non-linear enzyme kinetics. For the enzyme kinetics problem, approximate analytical solutions have been developed by Blaedel et al. [7], Kulys et al. [8] and Bartlett and Whitaker [9] for the only the limiting cases (saturated and unsaturated). The applications of numerical and approximate analytical methods can be seen by Bartlett and Pratt [10]. The numerical simulation can be found by Bartlett et al. [11]. Senthamarai and Rajendran derived the approximate analytical expressions for the substrate, mediator concentrations and current for the non-linear Michaelis-Menten kinetic scheme in a system of coupled non-linear reaction-diffusion processes at conducting polymer-modified ultramicroelectrodes [12] using the variational iteration method. In this chapter, we present the approximate analytical expressions for the concentrations of the mediator and substrate. These concentrations were determined using homotopy perturbation method (HPM) [13,14]. The current was...
determined corresponding to all possible values of the parameters $a_e, \kappa, \gamma, \eta$ and $\mu$.

These parameters are explained below in Equation (3.10).

### 3.2 MATHEMATICAL FORMULATION OF THE PROBLEM AND ANALYSIS

#### 3.2.1 MATHEMATICAL FORMULATION

Fig. 3.1 shows the general kinetic scheme for an enzyme-membrane/electrode. $A$ and $B$ are the oxidized and reduced forms of the mediator. $E_1$ and $E_2$ are the oxidized and reduced forms of the enzyme. $S$ and $P$ are the substrate and the product of the enzymatic reaction, respectively. Diffusion of mediator $A$ and substrate $S$ occurs within the film with diffusion coefficients $D_A$ and $D_S$, respectively. Partition of the substrate between the film and the bulk solution is described by the partition coefficient $K_S$. The mediator partition is described by $K_A$. The reactions that occur within the film (Fig. 3.1) in the kinetic scheme can be written as follows:

$$A + E_2 \xrightarrow{k_E} B + E_1 \quad (3.1)$$

$$E_1 + S \xrightarrow{k_E} E_2 + P \quad (3.2)$$

and the reaction at the electrode is $B \rightarrow A$. Here, $k_E$ and $k_A$ are second-order rate constants that describe the reaction between the enzyme and the substrate and between the enzyme and the mediator, respectively. According to Michaelis-Menten kinetics, the following is true:

$$k_E = \frac{k_{cat}}{K_M + [S]} \quad (3.3)$$
Fig. 3.1 Schematic representation of a typical enzyme-membrane-electrode showing the processes considered in the model. The homogenous enzyme kinetics that occurs throughout the film is described by Eqs. (3.1)-(3.3).

where $k_{\text{cat}}$ denotes the catalytic rate constant, and $K_M$ denotes the Michaelis-Menten constant. The homogenous enzyme kinetics described by Eqs. (3.1-3.3) occurs throughout the film from $x = 0$ to $x = l$, where $l$ is the thickness of the membrane. We consider a situation in which the mediator is entrapped within the film. This situation does not include a separate soluble redox mediator that is re-oxidized on a conducting entrapment matrix. Here, the rate constants for a heterogeneous reaction on the supporting matrix must be considered. The differential equations that quantify the diffusion and reaction within the film may be written as follows [6]:

---
\[
\frac{\partial [A]}{\partial t} = D_A \frac{\partial^2 [A]}{\partial x^2} - k_d [E]_z [A] \tag{3.4}
\]

\[
\frac{\partial [S]}{\partial t} = D_S \frac{\partial^2 [S]}{\partial x^2} - \frac{k_{cat} [E]_z [S]}{K_M + [S]} \tag{3.5}
\]

\[
\frac{\partial [E]_z}{\partial t} = k_d [A] [E]_z - \frac{k_{cat} [E]_z [S]}{K_M + [S]} \tag{3.6}
\]

Assuming that the enzyme is bound within the film, is not free to diffuse and is in the steady-state \(\frac{d[E]_z}{dt} = 0\), Eq. (3.6) leads to the following:

\[
[E]_z = \frac{k_{cat} [E]_z [S]}{k_d [A] (K_M + [S]) + k_{cat} [S]} \tag{3.7}
\]

where \([E]_z = [E]_z + [E]_z\) denotes the total concentration of the immobilized enzyme.

Then, in the steady-state, Eqs. (3.4) and (3.5) are reduced to the following:

\[
D_A \frac{d^2 [A]}{dx^2} = \frac{k_d k_{cat} [A] [S] [E]_z}{k_d [A] (K_M + [S]) + k_{cat} [S]} \tag{3.8}
\]

\[
D_S \frac{d^2 [S]}{dx^2} = \frac{k_d k_{cat} [A] [S] [E]_z}{k_d [A] (K_M + [S]) + k_{cat} [S]} \tag{3.9}
\]

Equations (3.8) and (3.9) are solved for the following boundary conditions:

\[
x = l, \quad [S] = [S]_o K_s \tag{3.9a}
\]

\[
x = 0, \quad d[S]/dx = 0 \tag{3.9b}
\]

\[
x = 0, \quad [A] = [A]_e \tag{3.9c}
\]

and

\[
x = l, \quad d[A]/dx = 0 \tag{3.9d}
\]

We make the non-linear differential Equations (3.8) and (3.9) dimensionless by defining the following parameters:
where \( a \) is the dimensionless concentration of the mediator and \( s \) is the dimensionless concentration of the substrate. \( \chi \) is the normalized distance from the electrode/membrane interface. \( \kappa \) describes the equilibrium constant between the diffusion of \( B \) within the film and its reaction with the enzyme. \( \eta \) denotes the relative amount of depletion of the substrate and oxidized mediator within the film. The parameter \( \gamma \) represents the equilibrium constant between the two forms of the enzyme. The ratio of the substrate concentration within the film to the Michaelis constant is described by \( \mu \). The subscript \( \infty \) denotes the concentration in the bulk solution. \( a \) and \( s \) are normalized with respect to the total concentrations \( K_A[B_\Sigma]_\infty \) and \( K_S[S]_\infty \) of the two species within the film, where \( [B_\Sigma] = [A] + [B], \; K_A[B_\Sigma]_\infty = [B_\Sigma] \), and \( K_S[S]_\infty = [S] + [P] \). When \( \kappa \ll 1 \), \( B \) can diffuse across the film before it reacts with the enzyme. For \( \eta \ll 1 \), consumption of the substrate is greater than mediator reduction, and for \( \eta \gg 1 \), the mediator reduction is greater than consumption of the substrate. For \( \gamma \ll 1 \), all of the enzymes are in the \( E_1 \) form. For unsaturated Michaelis-Menten kinetics, \( \mu \ll 1 \). For saturated kinetics, \( \mu \gg 1 \). Eqs. (3.8) and (3.9) reduce to the following dimensionless forms:

\[
\frac{d^2a}{d\chi^2} = \frac{\kappa^2as}{\gamma a(1 + \mu s) + s} \quad (3.11)
\]

\[
\frac{d^2s}{d\chi^2} = \frac{\gamma \eta^{-1} \kappa^2as}{\gamma a(1 + \mu s) + s} \quad (3.12)
\]

The dimensionless boundary conditions for Eqs. (3.11) and (3.12) are as follows:
\[ \chi = 0, \, ds / d\chi = 0 \quad (3.12b) \]

\[ \chi = 0, \, a = a_c \quad (3.12c) \]

and

\[ \chi = 1, \, da / d\chi = 0. \quad (3.12d) \]

The parameter \( \varepsilon \) is the dimensionless potential, which can be defined as

\[ \varepsilon = (E - E^0)nF / RT \quad (3.13) \]

where \( E \) is the potential of an electrode, \( E^0 \) is the standard potential of an electrode, \( n \) is the number of electrons, \( F \) is the Faraday constant, \( R \) is the universal gas constant and \( T \) is the absolute temperature. Combining the Nernst equation

\[ E = E^0 + (RT / nF) \ln ([A]_0 / [B]_0) \]

and Eq. (3.13) gives the dimensionless oxidized mediator concentration \( a_c \) at the electrode surface:

\[ a_c = 1 / [1 + \exp(-\varepsilon)] \quad (3.14) \]

Here \([A]_0\) and \([B]_0\) denote the concentration of the two forms of the mediator at the electrode surface. Eq. (3.14) gives the boundary condition for \( a \) at the electrode surface. The dimensionless flux of substrate (\( J_s \)) consumed at the electrode is considered as the following:

\[ J_s = \frac{l_j_s}{D_A [B]_{x_0} K_A} = \frac{\eta}{\gamma} \left( \frac{ds}{d\chi} \right)_{\chi=1} = \left( \frac{da}{d\chi} \right)_{\chi=1} - \left( \frac{da}{d\chi} \right)_{\chi=0}, \quad (3.15) \]

and that of the mediator (\( J_{obs} \)) measured at the electrode is as follows:

\[ J_{obs} = \frac{l_j_{obs}}{D_A [B]_{x_0} K_A} = \left( \frac{da}{d\chi} \right)_{\chi=0}. \quad (3.16) \]

With respect to the boundary condition, the flux of the substrate reacting within the film is equal to the observed flux: \( J_{obs} = J_s \).
3.2.2 SOLUTION OF BOUNDARY VALUE PROBLEM USING THE HPM

Recently, many authors have applied the HPM to various problems and demonstrated the efficiency of the HPM for handling non-linear structures and solving various physics and engineering problems [15-18]. This method is a combination of homotopy in topology and classic perturbation techniques. Ji-Huan He used the HPM to solve the Lighthill equation [19], the Duffing equation [20] and the Blasius equation [21]. The idea has been used to solve non-linear boundary value problems [22], integral equations [23-25], Klein–Gordon and Sine–Gordon equations [26], Emden–Flower type equations [27] and many other problems. This wide variety of applications shows the power of the HPM to solve functional equations. The HPM is unique in its applicability, accuracy and efficiency. The HPM [28] uses the imbedding parameter $\rho$ as a small parameter, and only a few iterations are needed to search for an asymptotic solution. Using this method (see Appendix 3.B), we can obtain the following solution to Eq. (3.11):

$$a(\chi) = W_1 \cosh \kappa [\cosh(2\kappa(1-\chi)) - 3] + \cosh(\kappa(1-\chi))[W_2 + W_4(3 - \cosh 2\kappa)] - W_3 (W_4 + W_5 + W_6)(2\chi - \chi^2)$$

(3.17)

where

$$W_1 = \frac{\mu^2 (1 + \mu)}{6 \cosh^3 \kappa}, \quad W_2 = \frac{a_e}{\cosh \kappa}, \quad W_3 = \frac{(\kappa \gamma)^2 a_e^3}{2(e^{2\kappa} + 1)\eta}, \quad W_4 = 1 - 2e^\kappa + \kappa + \eta,$$

$$W_5 = (1 + e^{2\kappa})\eta\mu(2 + \mu), \quad W_6 = e^{2\kappa}(1 - \kappa + \eta).$$

(3.18)

Equation (3.17) represents the analytical expression of the mediator concentration for all values of the parameters $\kappa$, $\gamma$, $\eta$, $\mu$ and $a_e$. Eq. (3.17) satisfies the boundary conditions at $\chi = 0, a = a_0$ and at $\chi = 1, da/d\chi = 0$. In the thin film approximation case in which $\kappa^2/\eta < 1$ and the substrate can diffuse much further than the thickness
of the film before it reacts with the enzyme, the result is $s \approx 1$. Therefore, the expression of the mediator concentration becomes the following:

$$a(\chi) = W_1 \cosh \kappa [\cosh(2\kappa(1-\chi)) - 3] + \cosh(\kappa(1-\chi))[W_2 + W_4(3 - \cosh 2\kappa)]$$

(3.19)

The solution to Eq. (3.12) is as follows:

$$s(\chi) = 1 - W_8(1 + \kappa \sinh \kappa) + W_7(1 + 2\kappa \sinh 2\kappa) + 6W_7\kappa^2 + [W_6 \kappa \sinh \kappa - 2W_7 \kappa \sinh 2\kappa] \chi - 6\kappa^2W_7 \chi^2 + W_8 \cosh(\kappa(1-\chi)) - W_7 \cosh(2\kappa(1-\chi))$$

(3.20)

where

$$W_7 = \frac{W_7 \gamma \cosh \kappa}{2\eta}, \quad W_8 = \frac{\gamma}{\eta} [W_4(3 - \cosh 2\kappa) + W_2]$$

(3.21)

Equation (3.20) represents the analytical expression of the substrate concentration for all values of the parameters $\kappa$, $\gamma$, $\eta$, $\mu$ and $a_c$. Eq. (3.20) satisfies the boundary conditions at $\chi = 1$, $s = 1$ and $\chi = 0$, $ds/d\chi = 0$. From Eqs. (3.15) and (3.19), we can obtain the dimensionless flux, which is as follows:

$$J_s = J_{obs} = \frac{\eta}{\gamma} (W_7 \sinh \kappa - 2W_7, \sinh 2\kappa - 12W_7 \kappa)$$

(3.22)

where $W_7$ and $W_8$ are given by Eq. (3.21). Eq. (3.17) and Eq. (3.20) are the closed forms of the approximate analytical expressions of the concentrations of the mediator and substrate for all values of the parameters $\kappa$, $\gamma$, $\eta$, $\mu$ and $a_c$. Eq. (3.22) is the new approximate expression of the flux.
<table>
<thead>
<tr>
<th>Limiting cases</th>
<th>Pratt et al. work</th>
<th>Fig no.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
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<tr>
<td><strong>Mediator-limited</strong></td>
<td>$a = a_e \left[ \cosh(\chi) - \tanh(\chi) \sinh(\chi) \right]$</td>
<td></td>
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<tr>
<td>Kinetics</td>
<td>(Eq. 3.23)</td>
<td></td>
</tr>
<tr>
<td>$\frac{a}{s} &lt; \frac{1}{\gamma (1 + \mu s)}$</td>
<td>$a$</td>
<td>$a &lt; \frac{1}{\gamma (1 + \mu s)}$</td>
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<tr>
<td></td>
<td>$s$</td>
<td>$s$</td>
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<td></td>
<td>Fig. 3.2 ($\kappa &lt; 1$)</td>
<td>(Eq. 3.17 &amp; 3.23)</td>
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<tr>
<td></td>
<td>$\kappa = 0.1, \gamma = 0.001, \eta = 10, \mu = 0.001, a_e = 1$</td>
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</tr>
<tr>
<td></td>
<td>$\kappa = 0.1, \gamma = 0.01, \eta = 0.1, \mu = 0.1, a_e = 1$</td>
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<td></td>
<td>Fig. 3.3 ($\kappa &gt; 1$)</td>
<td>(Eq. 3.20)</td>
</tr>
<tr>
<td></td>
<td>$\kappa = 5, \gamma = 0.001, \eta = 10, \mu = 0.001, a_e = 1$</td>
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<tr>
<td></td>
<td>$\kappa = 10, \gamma = 0.01, \eta = 0.1, \mu = 0.1, a_e = 1$</td>
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<tr>
<td><strong>Substrate-limited</strong></td>
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<tr>
<td>Kinetics</td>
<td>$s = \frac{\cosh(\chi / \eta^{1/2})}{\cosh(\chi / \eta^{1/2})}$</td>
<td></td>
</tr>
<tr>
<td>$\frac{a}{s} &gt; \frac{1}{\gamma (1 + \mu s)}$</td>
<td>$s$</td>
<td>$s$</td>
</tr>
<tr>
<td></td>
<td>Fig. 3.5 ($\kappa &lt; 1$)</td>
<td>(Eq. 3.17)</td>
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<tr>
<td></td>
<td>$\kappa = 0.1, \gamma = 2, \eta = 4, \mu = 0.001, a_e = 1$</td>
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</tr>
<tr>
<td></td>
<td>$\kappa = 0.1, \gamma = 100, \eta = 10^5, \mu = 0.01, a_e = 0.01$</td>
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<tr>
<td></td>
<td>Fig. 3.6 ($\kappa &gt; 1$)</td>
<td>(Eq. 3.20 &amp; 3.24)</td>
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<tr>
<td></td>
<td>$\kappa = 5, \gamma = 2, \eta = 4, \mu = 0.001, a_e = 1$</td>
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</tr>
<tr>
<td></td>
<td>$\kappa = 5, \gamma = 100, \eta = 10^5, \mu = 0.01, a_e = 0.01$</td>
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</tbody>
</table>
Table 3.2 Expression for the concentration of the mediator in the thin film approximation (Pratt et al. [6]).

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Pratt et al work for thin film approximation</th>
<th>Fig no.</th>
</tr>
</thead>
</table>
| $\frac{\kappa^2}{\eta} < 1$ and $s = 1$ | $a = \left[a_e + \gamma(1 + \mu)\right]\left\{\cosh\left[\frac{\chi\kappa}{1 + \gamma(1 + \mu)}\right] \right. - \left. \tanh\left[\frac{\kappa}{1 + \gamma(1 + \mu)}\right] \sinh\left[\frac{\chi\kappa}{1 + \gamma(1 + \mu)}\right]\right\} - \gamma(1 + \mu)$ | Fig. 3.8 ($\kappa < 1$)  
(Eq. 3.19 & 3.25)  
$\kappa = 0.1, \gamma = 10^{-5}$,  
$\mu = 0.1, a_e = 1$ |
| $\kappa = 5, \gamma = 10^{-5}$,  
$\mu = 0.1, a_e = 1$ | | Fig. 3.8 ($\kappa > 1$)  
(Eq. 3.19 & 3.25)  
$\kappa = 10, \gamma = 10^{-5}$,  
$\mu = 0.1, a_e = 1$ |
Table 3.3 Various expressions of the dimensionless current (Pratt et al. [6]).

<table>
<thead>
<tr>
<th>Limiting cases</th>
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<th>Fig no.</th>
</tr>
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<tbody>
<tr>
<td>Mediator-limited kinetics</td>
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<tr>
<td>$a/s &lt; 1/\gamma (1 + \mu s)$</td>
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<td></td>
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<tr>
<td>$J_{obs} = \kappa a_e \tanh(\kappa)$</td>
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<td></td>
</tr>
<tr>
<td>$J_{obs} = \kappa^2 a_e$ for $\kappa &lt; 1$</td>
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<td></td>
</tr>
<tr>
<td>$J_{obs} = \kappa a_e$ for $\kappa &gt; 1$</td>
<td>(Eq. 3.26)</td>
<td>Fig. 3.9 (a) (Eq. 3.22 &amp; 3.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\kappa = 0.01, \gamma = 0.001,$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\eta = 0.1, \mu = 0.01$</td>
</tr>
</tbody>
</table>

| Substrate-limited kinetics               |                  |                                  |
| $a/s > 1/\gamma (1 + \mu s)$             |                  |                                  |
| $J_{obs} = \eta^{1/2} \kappa \tanh \left[ \frac{\kappa}{\eta^{1/2} (1 + \mu)} \right]$ | (Eq. 3.27)       | Fig. 3.9 (b) (Eq. 3.22 & 3.27)   |
| $J_{obs} = \frac{\kappa^2}{\gamma (1 + \mu)}$ for $\kappa < \eta^{1/2} (1 + \mu)$ |                  | $\gamma = 10, \eta = 0.01,$     |
| $J_{obs} = \frac{\eta^{1/2} \kappa}{\gamma}$ for $\kappa > \eta^{1/2} (1 + \mu)$ |                  | $\mu = 0.01, a_e = 0.01$        |

| Thin film approximation                   |                  |                                  |
| $\frac{\kappa^2}{\eta} < 1$              |                  |                                  |
| $J_{obs} = \frac{\kappa [a_e + \gamma (1 + \mu)]}{1 + \gamma (1 + \mu)} \tanh \left[ \frac{\kappa}{1 + \gamma (1 + \mu)} \right]$ | (Eq. 3.28)       | Fig. 3.9 (c) (Eq. 3.22 & 3.28)   |
|                                          |                  | $\kappa = 0.01, \gamma = 0.01,$|
|                                          |                  | $\eta = 0.1, a_e = 1$           |
3.3 RESULTS AND DISCUSSION

Pratt et al. [6] derived the approximate analytical solutions of the mediator and the substrate concentrations and the current for different limiting cases. Various analytical expressions for the concentration of the mediator and substrate for $a/s < 1/\gamma (1 + \mu s)$ and $a/s > 1/\gamma (1 + \mu s)$ are given in Table 3.1. The analytical expression for the thin film approximation is given in Table 3.2. The analytical expressions for the dimensionless current derived by Pratt et al. [6] for various limiting cases are given in Table 3.3.

![Graph](image_url)

**Fig. 3.2** Plot of the two-dimensional comparative case diagram of the mediator concentration $a$ versus the normalized distance $\chi$ when $\gamma a < s/(1 + \mu s)$ for $\gamma = 0.001, \eta = 10, \mu = 0.001$ and $a_e = 1$ and various values of $\kappa$. The plot is according to Eq. (3.17), and $\bullet \bullet \bullet \bullet$ is plotted according to Eq. (3.23).
3.3.1 COMPARISON WITH THE WORK OF PRATT ET AL. [6]

3.3.1.1 MEDIATOR-LIMITED KINETICS. \[ a/s < 1/(1 + \mu s) \]

In this case, the mediator-enzyme reaction is the rate-determining step. Figs.
3.2 and 3.3 represent the concentration profiles of the mediator and the substrate for
various values of the parameters \( \kappa, \gamma, \eta, \mu \) and \( a_e \), respectively. The concentration
of the mediator \( a \) is closer to unity when the values of all of the parameters are less
than 0.4. The concentration of the substrate \( s \) is equal to unity when the values of all
of the parameters are less than 1. When \( \kappa > 1 \), the concentration of the mediator \( a \)
decreases quickly when \( \chi < 0.5 \), and \( a \) reaches the steady-state value zero when \( \chi \geq 0.5 \)
(Fig. 3.2).

![Graph](image)

Fig. 3.3 Plot of the two-dimensional diagram of the substrate concentrations
versus the normalized distance \( \chi \) when \( \gamma a < s/(1 + \mu s) \) for
\( \gamma = 0.01, \eta = 0.1, \mu = 0.1 \) and \( a_e = 1 \) and various values of \( \kappa \). — is
plotted according to Eq. (3.20).
However, the concentration of the substrate increases gradually (Fig. 3.3). Fig. 3.4 shows the normalized mediator concentration profiles of $a$ for various values of $\kappa$ and $\chi$. This data confirm that the concentration profiles of the mediator $a$ decrease when $\kappa$ increases for all values of distance $\chi$.

**Fig. 3.4** The normalized three-dimensional mediator concentration profiles of $a$ calculated using Eq. (3.17) for $\kappa$ in the range of 0 to 100.

### 3.3.1.2 SUBSTRATE-LIMITED KINETICS. ($ a/s > 1/\gamma (1 + \mu s) $)

In this case, the enzyme-substrate kinetics is rate limiting. When $\kappa$ is small, the concentrations of the mediator and the substrate are always close to 1 (Fig. 3.5).
Fig. 3.5 Plot of the two-dimensional diagram of the mediator concentration $a$ versus the normalized distance $\chi$ when $\gamma a > s/(1 + \mu s)$ for $\gamma = 2, \eta = 4, \mu = 0.001$ and $a_c = 1$ and various values of $\kappa$. is plotted according to Eq. (3.17).

When $\kappa > 1$ and $\chi \geq 0.5$, the concentration of the mediator $a$ reaches the steady-state value. When $\kappa > 1$, the concentration of the substrate increases slowly and reaches the steady-state value 1 (Fig. 3.6). Fig. 3.7 shows the three-dimensional concentration profile of the substrate in $\chi$ and $\kappa$ space calculated using Eq. (3.20). This figure shows that the concentration of the substrate is inversely proportional to $\kappa$. 
Fig. 3.6 Plot of the two-dimensional comparative case diagram of the substrate concentration $s$ versus the normalized distance $Y$ when $\gamma a > s / (1 + \mu s)$ for $\gamma = 100, \eta = 10^5, \mu = 0.01$ and $a_e = 0.01$ and various values of $\kappa$.

---

3.3.1.3 THIN FILM APPROXIMATION

In this case, $\kappa^2 / \eta < 1$ and $s = 1$. The concentration of the mediator is equal to 1 when $\kappa$ and $\gamma$ are both less than 1 (Fig. 3.8). When $\kappa$ or $\gamma$ increases, the concentration of the mediator slowly decreases. Figs. 3.9 (a) – 3.9 (c) show the dimensionless current for various values of $\kappa$, $\gamma$, $\eta$, $\mu$ and $a_e$. 
Fig. 3.7 The normalized three-dimensional substrate concentration profiles $s$ calculated using Eq. (3.20) for $\kappa$ in the range of 0 to 100.

The current increases as $\varepsilon$ increases in the region $-4 < \varepsilon < 2$, and a steady-state appears when $\varepsilon > 2$ and $\varepsilon < -4$ (Fig. 3.9 (a)). The value of the current increases in direct proportion to the values of $\kappa$ (Fig. 3.9 (b)). The value of the current increases in indirect proportion to the value of $\mu$ (Fig. 3.9 (c)). The mediator concentration $a$ (Eq. (3.17)) and the substrate concentration $s$ (Eq. (3.20)) are compared with Pratt’s work.
in Tables 3.4 and 3.5. For the thin film approximation, the comparison of the mediator concentration $a$ (Eq. (3.19)) with Pratt’s result [6] is given in Table 3.6. In all the cases, the average relative error is less than 0.03%.

Fig. 3.8 Plot of the two-dimensional comparative case diagram of the mediator concentration $a$ versus the normalized distance $\chi$ for the thin film approximation for $\gamma = 10^{-5}, \mu = 0.1$ and $a_c = 1$ and various values of $\kappa$. $- - -$ is plotted according to Eq.(3.19), and $\ast \ast \ast$ is plotted according to Eq. (3.25).
Fig. 3.9 Comparison of the dimensionless current against (a) $\varepsilon$ (b) $\kappa$ (c) $\mu$ in the range of $10^{-1}$ to 10. — is plotted according to Eq. (3.22), and • • • is plotted according to Pratt’s work [6].
Table 3.4 Comparison of the mediator concentration $a$ for various values of $\chi$ and $\kappa$ when $\gamma = 0.001, \eta = 10, \mu = 0.001$ and $a_e = 1$

<table>
<thead>
<tr>
<th>$\chi$</th>
<th>$\kappa = 0.1$</th>
<th>$\kappa = 5$</th>
<th>$\kappa = 10$</th>
</tr>
</thead>
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<tr>
<td></td>
<td>This work</td>
<td>Pratt et al</td>
<td>This work</td>
</tr>
<tr>
<td></td>
<td>Eq. (3.17)</td>
<td>work Eq. (3.23) deviation of Eq. (3.17)</td>
<td>work Eq. (3.17) deviation of Eq. (3.17)</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.2</td>
<td>0.9982</td>
<td>0.9982</td>
<td>0</td>
</tr>
<tr>
<td>0.4</td>
<td>0.9968</td>
<td>0.9968</td>
<td>0</td>
</tr>
<tr>
<td>0.6</td>
<td>0.9958</td>
<td>0.9958</td>
<td>0</td>
</tr>
<tr>
<td>0.8</td>
<td>0.9952</td>
<td>0.9952</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0.9950</td>
<td>0.9950</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Average deviation</td>
<td>0</td>
<td>Average deviation</td>
</tr>
</tbody>
</table>
Table 3.5 Comparison of the substrate concentration $s$ for various values of $\chi$ and $\kappa$ when $\gamma = 100, \eta = 10^3, \mu = 0.01$ and $\sigma = 0.01$

<table>
<thead>
<tr>
<th>$\chi$</th>
<th>$\kappa = 0.1$</th>
<th>$\kappa = 5$</th>
<th>$\kappa = 10$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>This work Eq. (3.20)</td>
<td>Pratt et al work Eq. (3.24)</td>
<td>% deviation of Eq. (3.20)</td>
</tr>
<tr>
<td>0</td>
<td>0.9999</td>
<td>0.9999</td>
<td>0.9998</td>
</tr>
<tr>
<td>0.2</td>
<td>0.9999</td>
<td>0.9999</td>
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</tr>
<tr>
<td>0.4</td>
<td>0.9999</td>
<td>0.9999</td>
<td>0.9998</td>
</tr>
<tr>
<td>0.6</td>
<td>0.9999</td>
<td>0.9999</td>
<td>0.9999</td>
</tr>
<tr>
<td>0.8</td>
<td>0.9999</td>
<td>0.9999</td>
<td>0.9999</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Average deviation</td>
<td>0.01</td>
<td>Average deviation</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Table 3.6 Comparison of the mediator concentration $a$ for the thin film approximation for various values of $\chi$ and $\kappa$ when $\gamma = 10^{-5}, \mu = 0.1$ and $a_c = 1$

<table>
<thead>
<tr>
<th>$\chi$</th>
<th>$\kappa = 0.1$</th>
<th>$\kappa = 5$</th>
<th>$\kappa = 10$</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td>Pratt et al work Eq. (3.25)</td>
<td>% deviation of Eq. (3.19)</td>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.2</td>
<td>0.9982</td>
<td>0.9982</td>
<td>0</td>
</tr>
<tr>
<td>0.4</td>
<td>0.9968</td>
<td>0.9968</td>
<td>0</td>
</tr>
<tr>
<td>0.6</td>
<td>0.9958</td>
<td>0.9958</td>
<td>0</td>
</tr>
<tr>
<td>0.8</td>
<td>0.9952</td>
<td>0.9952</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0.9950</td>
<td>0.9950</td>
<td>0</td>
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<tr>
<td>Average deviation</td>
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<td>Average deviation</td>
<td>0</td>
</tr>
</tbody>
</table>
3.4 CONCLUSIONS

A non-linear time-independent differential equation for the polymer-modified electrodes has been formulated and solved using the HPM. The primary result of this work is an approximate calculation of the concentration and current profiles of the mediator and substrate for various values of the parameters $\kappa$, $\gamma$, $\eta$, $\mu$ and $a_z$. Our results agree well with the previous limiting case results. This result is very useful for determining the behavior of the system. The extension of the procedure to systems such as the redox hydrogel systems [29, 30], in which the mediator and the enzymes are entrapped in a uniform film at the electrode surface, and a study of the effects of mass transport in the bulk solution both seem possible. The analytical result presented here can be used with the approximate analytical formulae to optimize enzyme electrodes. The model may be used to optimize the design of a sensor system by making rational changes to the enzyme loading, film thickness, choice and concentration of the mediator and film properties.

3.5 APPENDIX 3.A: BASIC CONCEPTS OF THE HPM

The HPM method has overcome the limitations of traditional perturbation methods. It can take full advantage of the traditional perturbation techniques, so a considerable deal of research has been conducted to apply the homotopy technique to solve various strong non-linear equations [13,14]. To explain this method, let us consider the following function:

\[ f(x) = x^2 - 2x + 1 \]
\[ D_\circ(u) - f(r) = 0, \quad r \in \Omega \] \hspace{1cm} (3.A1)

with the boundary conditions of

\[ B_\circ(u, \frac{\partial u}{\partial n}) = 0, \quad r \in \Gamma \] \hspace{1cm} (3.A2)

where \( D_\circ \) is a general differential operator, \( B_\circ \) is a boundary operator, \( f(r) \) is a known analytical function and \( \Gamma \) is the boundary of the domain \( \Omega \). Generally speaking, the operator \( D_\circ \) can be divided into a linear part \( L \) and a non-linear part \( N \). Eq. (3.A1) can therefore be written as

\[ L(u) + N(u) - f(r) = 0 \] \hspace{1cm} (3.A3)

By the homotopy technique, we construct a homotopy \( v(r, p): \Omega \times [0,1] \rightarrow \mathbb{R} \) that satisfies

\[ H(v, p) = (1 - p)[L(v) - L(u_0)] + p[D_\circ(v) - f(r)] = 0. \] \hspace{1cm} (3.A4)

\[ H(v, p) = L(v) - L(u_0) + pL(u_0) + p[N(v) - f(r)] = 0. \] \hspace{1cm} (3.A5)

where \( p \in [0,1] \) is an embedding parameter, and \( u_0 \) is an initial approximation of Eq. (3.A1) that satisfies the boundary conditions. From Eqs. (3.A4) and (3.A5), we have

\[ H(v, 0) = L(v) - L(u_0) = 0 \] \hspace{1cm} (3.A6)

\[ H(v, 1) = D_\circ(v) - f(r) = 0. \] \hspace{1cm} (3.A7)

When \( p = 0 \), Eq. (3.A4) and Eq. (3.A5) become linear equations. When \( p = 1 \), they become non-linear equations. The process of changing \( p \) from zero to unity is that of \( L(v) - L(u_0) = 0 \) to \( D_\circ(v) - f(r) = 0 \). We first use the embedding parameter \( p \) as a "small parameter" and assume that the solutions of Eqs. (3.A4) and (3.A5) can be written as a power series in \( p \) :
\[ v = v_0 + pv_1 + p^2v_2 + \ldots \]  
\[ (3.A8) \]

Setting \( p = 1 \) results in the approximate solution of Eq. (3.A1):

\[ u = \lim_{p \to 1} v = v_0 + v_1 + v_2 + \ldots \]  
\[ (3.A9) \]

This is the basic idea of the HPM.

### 3.6 APPENDIX 3.B: APPROXIMATE ANALYTICAL SOLUTIONS OF THE MEDIATOR AND SUBSTRATE

Using the HPM, we construct a homotopy for Eqs. (3.11) and (3.12) as follows:

\[ (1 - p) \left( \frac{d^2a}{d \chi^2} - \kappa^2 a \right) + p \left( \frac{d^2a}{d \chi^2} + \gamma a \frac{d^2a}{d \chi^2} (1/s + \mu) - \kappa^2 a \right) = 0 \]  
\[ (3.B1) \]

and

\[ (1 - p) \left( \frac{d^2s}{d \chi^2} \right) + p \left( \frac{d^2s}{d \chi^2} + \gamma a \frac{d^2s}{d \chi^2} (1/s + \mu) - \gamma \eta^{-1} \kappa^2 a \right) = 0 \]  
\[ (3.B2) \]

The approximate solution of (3.B1) is

\[ a = a_0 + pa_1 + p^2a_2 + \ldots \]  
\[ (3.B3) \]

and the approximate solution of (3.B2) is

\[ s = s_0 + ps_1 + p^2s_2 + \ldots \]  
\[ (3.B4) \]

Subs. Eq. (3.B3) into Eq. (3.B1) and arranging the coefficients of \( p \) powers, we have
\[ p^0: \frac{d^2 a_0}{d\chi^2} - \kappa^2 a_0 = 0 \]  
(3.B5)

\[ p^1: \frac{d^2 a_1}{d\chi^2} - \kappa^2 a_1 + \gamma a_0 \frac{d^2 a_0}{d\chi^2} (1/s_0 + \mu) = 0 \]  
(3.B6)

\[ p^2: \frac{d^2 a_2}{d\chi^2} - \kappa^2 a_2 + \gamma a_1 \frac{d^2 a_1}{d\chi^2} (1/s_0 + \mu) + \gamma a_0 \frac{d^2 a_0}{d\chi^2} (1/s_0 + \mu) - \gamma \frac{d^2 a_0}{d\chi^2} a_0 \frac{s_1}{s_0} = 0 \]  
(3.B7)

Substituting Eq. (3.B4) into Eq. (3.B2) and arranging the coefficients of \( p \) powers, we have

\[ p^0: \frac{d^2 s_0}{d\chi^2} = 0 \]  
(3.B8)

\[ p^1: \frac{d^3 s_1}{d\chi^2} - \gamma \eta^{-1} \kappa^2 a_0 + \gamma a_0 \frac{d^2 s_0}{d\chi^2} (1/s_0 + \mu) = 0 \]  
(3.B9)

\[ p^2: \frac{d^2 s_2}{d\chi^2} - \gamma \eta^{-1} \kappa^2 a_1 + \gamma a_1 \frac{d^2 s_1}{d\chi^2} (1/s_0 + \mu) + \gamma a_0 \frac{d^2 s_0}{d\chi^2} (1/s_0 + \mu) - \gamma a_0 \frac{d^2 s_0}{d\chi^2} \frac{s_1}{s_0} = 0 \]  
(3.B10)

The initial approximations are as follows:

\[ a_0(0) = a_c, \quad a_0'(0) = 0, \quad a_i'(1) = 0 \text{ for all } i=1,2,3,... \]  
(3.B11)

\[ s_0(0) = 1, \quad s_0'(0) = 0, \quad s_i'(0) = 0 \text{ for all } i=1,2,3,... \]  
(3.B12)

From Eq. (3.B5) we get

\[ a_0(\chi) = W_2 \cosh(\kappa(1-\chi)) . \]  
(3.B13)

From Eq. (3.B8) we get

\[ s_0 = 1. \]  
(3.B14)
subs. Eq. (3.B13) and Eq. (3.B14) into Eq. (3.B6), we obtain the solution to Eq. (3.B6):

\[ a_1(\chi) = W_1 \left[ \cosh \kappa (\cosh(2\kappa(1 - \chi)) - 3) + (3 - \cosh 2\kappa) \cosh(\kappa(1 - \chi)) \right]. \quad (3.B15) \]

Using Eq. (3.B13), Eq. (3.B14) and Eq. (3.B15) in Eq. (3.B9) and then solving we get

\[ s_1(\chi) = \frac{r W_2}{\eta} \left[ - (1 + \kappa \sinh \kappa) + (\kappa \sinh \kappa) \chi + \cosh(\kappa(1 - \chi)) \right]. \quad (3.B16) \]

Using Eq. (3.B13) to Eq. (3.B16) and Eq. (3.B7) we get

\[ a_2(\chi) = W_3(W_4 + W_5 + W_6)(-2\chi + \chi^2). \quad (3.B17) \]

Using Eq. (3.B13) to Eq. (3.B16) in Eq. (3.B10) and then solving Eq. (3.B10) we obtain

\[ s_2 = \frac{r W_1}{2\eta} \left[ \frac{2(\cosh 2\kappa - 3)[1 + (\kappa \sinh \kappa)(1 - \chi) - \cosh(\kappa(1 - \chi))] + \cosh \kappa [1 + (1 - \chi)(2\kappa \sinh 2\kappa - 6\kappa^2(\chi + 1)) - \cosh(2\kappa(1 - \chi))] }{\cosh \kappa [1 + (1 - \chi)(2\kappa \sinh 2\kappa - 6\kappa^2(\chi + 1)) - \cosh(2\kappa(1 - \chi))]} \right]. \quad (3.B18) \]

Adding Eqs. (3.B13), (3.B15) and (3.B17), we get Eq. (3.17) (the concentration of the mediator, \( a \)) in the text. Similarly, by adding Eqs. (3.B14), (3.B16) and (3.B18) we get Eq. (3.20) (the concentration of the substrate, \( s \)) in the text.