CHAPTER V

ANALYTICAL EXPRESSIONS FOR STEADY-STATE CONCENTRATIONS OF SUBSTRATE, OXIDIZED AND REDUCED MEDIATOR IN AN AMPEROMETRIC BIOSensor

CHAPTER-V

ANALYTICAL EXPRESSIONS FOR STEADY-STATE

CONCENTRATIONS OF SUBSTRATE, OXIDIZED AND

REDUCED MEDIATOR IN AN AMPEROMETRIC BIOSENSOR

5.1 INTRODUCTION

In recent years, polymer membranes are widely used as carriers for immobilization of enzymes [1]. They have been utilized in biomaterials, bio-separators and biosensors [2]. The membranes provide an ideal support for the immobilization of the biocatalyst. Substrate partition at the membrane/fluid inter-phase can be used to improve the selectivity of the catalytic reaction towards the desired products [3]. Recently a new method for enzyme immobilization [4], based on a molecular recognition process has been successfully used for the building of enzymatic bio-sensors and also of a chemically active membrane [5]. In the recent three decades, much effort has been devoted to the development of various biosensors involving biologically sensitive component and transformers - devices with many field of applications [6]. Changes in membrane chemistry have been demonstrated by Robeson [7]. The better way of changing the membrane geometry aims to increase the membrane area per volume, thereby speeding the separation. This increased surface area has recently been identified as a high priority research need for membranes [8].

A two-substrate model for enzyme electrode has been devised experimentally [9, 10] where the non-linear enzyme reaction was taken into account. This model was employed to describe the behaviour of a glucose oxidize (GOx) electrode [11, 12]. It has been found that the mediators could not totally replace the natural co-substrate when both were present in the assay solution. So that here, a three-substrate model
would be required. In these cases, a complex calibration curve of the enzyme electrode was observed [13, 14].

In spite of extensive experimental investigations for the design of bio-sensor, only a few studies concerned the modeling or theoretical design of such systems. Recently Loghambal and Rajendran [15] have described the theoretical model in an amperometric oxidase enzyme-membrane electrode. Numerical solutions [16-18] were reported to a novel enzyme electrode. In those papers the enzyme electrode was modeled numerically using shooting method [17, 18] and Runge-Kutta method [16]. But in this chapter, the same system is modeled analytically. However, to the best of our knowledge, till date no general analytical results for the concentration of oxidized mediator, substrate and reduced mediator for all values of the parameters $\phi^2$, $B_o$ and $B_s$ have been reported [17]. The purpose of this chapter is to derive the closed-form of analytical expressions [19, 20] of concentrations of mediator, substrate and reduced mediator by solving the system of non-linear reaction-diffusion equations using the Adomian decomposition method (ADM) [21]. The theoretical models of enzyme electrodes give information about the mechanism and kinetics operating in the biosensor. Thus the information gained from this modeling can be useful in sensor design, optimization and prediction of the electrode’s response.

5.2 MATHEMATICAL FORMULATION AND ANALYSIS OF PROBLEMS

5.2.1 MATHEMATICAL FORMULATION

Building upon earlier work for these mechanisms, Gooding and Hall [17] presented a concise discussion and derivation of the dimensionless non-linear mass transport equation for this model, which is summarized briefly for completeness. In the enzyme-membrane geometry, the biological layer is located
between a solid substrate and an outer permeable electrode in contact with the sample. In this model the substrate and co-substrate penetrate through a permeable electrode to the enzyme layer and then reduces to the form of co-substrate which diffuses back to the electrode. The general reaction scheme for an immobilized oxidase in the presence of two oxidants can be written as follows [17]:

\[
\begin{align*}
E_{ox} + S & \underset{k_{-1}}{\overset{k_1}{\longrightarrow}} ES \overset{k_2}{\longrightarrow} E_{red} + P \\
E_{red} + O_2 & \overset{k_3}{\longrightarrow} E_{ox} + H_2O_2 \\
E_{red} + Med_{ox} & \overset{k_4}{\longrightarrow} E_{ox} + Med_{red}
\end{align*}
\]

(5.1) (5.2) (5.3)

where \( k_m \) is the rate constant for the forward direction of the \( m^{th} \) reaction and \( k_{-1} \) is the rate constant for the backward direction. If \([E_T]\) is the total enzyme concentration in the matrix then at all times,

\[
[E_T] = [E_{ox}] + [ES] + [E_{red}]
\]

(5.4)

where \([E_{ox}], [ES] \) and \([E_{red}] \) are the oxidized mediator, enzyme-substrate complex and reduced mediator enzyme concentrations respectively. At steady-state, the diffusion of a substrate into the enzyme layer is equal to the reaction rate of the substrate within the matrix. We examine a planar matrix of thickness \( y = d \), where diffusion is considered in the \( y \)-direction only (edge effects are neglected) (Fig.5.1). The corresponding governing equations in Cartesian coordinates, for the planar diffusion and reaction in the enzyme electrode are [17]:
\[
D_M \frac{d^2[\text{Med}_{\text{ox}}]}{dy^2} = k_4[\text{E}_{\text{red}}][\text{Med}_{\text{ox}}] - k_{-1}[\text{ES}] = k_2[E_T]\left(\frac{\beta_s}{[S]} + \frac{\beta_o}{[\text{Med}_{\text{ox}}]} + 1\right)^{-1}
\]  

\[5.5a\]

\[
D_S \frac{d^2[S]}{dy^2} = k_1[E_{\text{ox}}][S] - k_{-1}[\text{ES}] = k_2[E_T]\left(\frac{\beta_s}{[S]} + \frac{\beta_o}{[\text{Med}_{\text{ox}}]} + 1\right)^{-1}
\]  

\[5.5b\]

\[
D_M \frac{d^2[\text{Med}_{\text{red}}]}{dy^2} = -k_4[\text{E}_{\text{red}}][\text{Med}_{\text{ox}}] = -k_2[E_T]\left(\frac{\beta_s}{[S]} + \frac{\beta_o}{[\text{Med}_{\text{ox}}]} + 1\right)^{-1}
\]  

\[5.5c\]

where \(D_M\) is the diffusion coefficient of the oxidized and reduced forms of the mediator (assumed to be equal) and \(D_S\) is the diffusion coefficient of substrate within the enzyme layer. \([\text{Med}_{\text{ox}}], [\text{Med}_{\text{red}}]\) and \([S]\) are the concentration of oxidized mediator, reduced mediator and substrate at any position in the enzyme layer. \(\beta_s\) and \(\beta_o\) are the dimensionless rate constants (\(\beta_s = (k_{-1} + k_2)/k_1\) and \(\beta_o = k_2/k_4\)).

![Diagram of enzyme-membrane electrode geometry](image)

Fig. 5.1 Schematic representation of a typical enzyme-membrane electrode geometry [17].
We examine a planar matrix of thickness $y = d$, where diffusion is considered in the $y$-direction only (edge effects are neglected). The consumption of oxidised mediator (oxygen) and glucose, the production of hydrogen peroxide, are all related processes so there is only one independent variable for which to solve [25]

$$D_M \frac{d^2[\text{Med}_{\text{ox}}]}{dy^2} = D_S \frac{d^2[S]}{dy^2} = -D_M \frac{d^2[\text{Med}_{\text{red}}]}{dy^2} = \frac{k_2[E_+]}{[S]/[\text{Med}_{\text{ox}}]} + 1$$

where $D_M$ is the diffusion coefficient of the oxidised and reduced form of the mediator assumed to be equal) and $D_S$ is the diffusion coefficient of substrate within the enzyme layer in the bio-recognition matrix $\beta_s = (k_{1} + k_2)/k_1$ and $\beta_o = k_2/k_4$.

$[\text{Med}_{\text{ox}}]$, $[\text{Med}_{\text{red}}]$ and $[S]$ are the concentration of oxidised mediator, substrate and reduced mediator at any position in the enzyme layer.

5.2.2 BOUNDARY CONDITIONS

Eqs. (5.5a)-(5.5c) are solved for the following boundary conditions:

At the far wall, $y = 0$

$$\frac{d[\text{Med}_{\text{ox}}]}{dy} = \frac{d[S]}{dy} = \frac{d[\text{Med}_{\text{red}}]}{dy} = 0$$

At the electrode, $y = d$

$$[\text{Med}_{\text{ox}}] = [\text{Med}_{\text{ox}}]_b = K_o[\text{Med}_{\text{ox}}]_o, \quad [S] = [S]_b = K_s[S]_o, \quad [\text{Med}_{\text{red}}] = 0$$

The first boundary condition states that there is no flux of reactants and products at the far wall of the sensor. The second condition states that the substrates in the matrix are in equilibrium with the surrounding fluid at the surface of the electrode and all the hydrogen peroxide which reaches the electrode surface is oxidized. $[\text{Med}_{\text{ox}}]_b$ and $[S]_b$ are the concentration of oxidized mediator and substrate at the enzyme layer|electrode boundary, and $[\text{Med}_{\text{ox}}]_o$ and $[S]_o$ are the bulk solution
concentrations. $K_0$ and $K_s$ are the equilibrium partition coefficients for oxidized mediator and the substrate respectively.

5.2.3 NORMALISED FORM

We make the non-linear differential Eqs. (5.5a)-(5.5c) to dimensionless form by defining the following dimensionless variables,

$$ F_O = \frac{[\text{Med}_{\text{ox}}]}{[\text{Med}_{\text{ox}}]_b}, \quad F_S = \frac{[S]}{[S]_b}, \quad F_R = \frac{[\text{Med}_{\text{red}}]}{[\text{Med}_{\text{red}}]_b}, $$

$$ \chi = \frac{y}{d}, \quad B_O = \frac{[\text{Med}_{\text{ox}}]}{[\text{Med}_{\text{ox}}]_b}/\beta_O, \quad B_S = \frac{[S]}{[S]_b}/\beta_S, $$

$$ \phi_0^2 = d^2 k_2 [E_T]/D_M[\text{Med}_{\text{ox}}]_b \quad \text{and} \quad \mu_S = D_M[\text{Med}_{\text{ox}}]_b/D_S[S]_b \quad (5.8) $$

where $F_O$, $F_S$ and $F_R$ are the normalized concentration of oxidized mediator, substrate and reduced mediator in the matrix respectively and $\chi$ is the normalized distance. $B_O$ and $B_S$ are the normalized surface concentration of oxidized mediator and substrate. $\phi_0^2$ is the Thiele modulus for the oxidized mediator which governs reaction/diffusion.

The resultant expressions for the oxidized mediator, substrate and reduced mediator in non-dimensionalized form become as follows:

$$ \frac{d^2 F_O}{d\chi^2} = \phi_0^2 \left[ \frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right] \quad (5.9a) $$

$$ \frac{d^2 F_S}{d\chi^2} = \mu_S \phi_0^2 \left[ \frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right] \quad (5.9b) $$

$$ \frac{d^2 F_R}{d\chi^2} = -\phi_0^2 \left[ \frac{B_O B_S F_O F_S}{B_O F_O + B_S F_S + B_O B_S F_O F_S} \right] \quad (5.9c) $$
The consumption of oxidized mediator, substrate and reduced mediator, are all related processes. So there is only one independent variable for which to solve

\[
\frac{d^2 F_o}{d\chi^2} = \frac{1}{\mu_s} \frac{d^2 F_s}{d\chi^2} = -\frac{d^2 F_r}{d\chi^2} = \phi_o^2 \left[ \frac{B_0 F_o F_s}{B_0 F_o + B_s F_s + B_o B_s F_o F_s} \right] \tag{5.9d}
\]

The normalized boundary conditions are given by:

\[
F_o'(0) = 0 \quad F_s'(0) = 0 \quad F_r'(0) = 0 \tag{5.10}
\]

\[
F_o(l) = 1 \quad F_s(l) = 1 \quad F_r(l) = 0 \tag{5.11}
\]

From Eq. (5.9d) we get,

\[
\frac{d^2 F_o}{d\chi^2} = \frac{1}{\mu_s} \frac{d^2 F_s}{d\chi^2} \tag{5.12}
\]

and

\[
\frac{d^2 F_o}{d\chi^2} = -\frac{d^2 F_r}{d\chi^2} \tag{5.13}
\]

Integrating Eqs. (5.12) and (5.13) twice and applying the appropriate boundary conditions Eqs. (5.10) and (5.11) we get,

\[
F_s(\chi) = \mu_s (F_o(\chi) - 1) + 1 \tag{5.14}
\]

\[
F_r(\chi) = 1 - F_o(\chi) \tag{5.15}
\]

Substituting the Eq. (5.14) into Eq. (5.9a) and rearranging we get

\[
\frac{d^2 F_o}{d\chi^2} = \phi_o^2 \left[ \frac{F_o^2 + F_o [(1 - \mu_s)/\mu_s]}{F_o^2 + F_o \left( \frac{1}{B_s \mu_s} + \frac{1 - \mu_s}{B_o \mu_s} \right) + 1 - \mu_s} \right] \tag{5.16}
\]
The normalized current response is given by the following expression:

\[ I = -\left( \frac{dF_n}{d\chi} \right)_{\chi=1} \quad (5.17) \]

5.3 SOLUTIONS OF CONCENTRATION OF OXIDISED MEDIATOR, SUBSTRATE AND REDUCED MEDIATOR UNDER STEADY-STATE CONDITION

5.3.1 ANALYTICAL SOLUTION USING ADM

In this chapter, the Adomian decomposition method (see Appendix 5.A) is used to solve non-linear differential equations. The ADM [21-25] yields, without linearization, perturbation or transformation, an analytical solution in terms of a rapidly convergent infinite power series with easily computable terms. The basic principle of this method is described in Appendix 5.A and detailed derivation of dimensionless concentration of oxidized mediator \( F_0(\chi) \), from the non-linear Eq. (5.16) is described in Appendix 5.B. The analytical expression of concentration of the oxidized mediator is as follows:

\[ F_0(\chi) = 1 + \frac{1}{2(B_o + B_s + B_o B_s)} \left[ 5w_i - 1 + (1 - 6w_i)\chi^2 + w_i\chi^4 \right] \quad (5.18) \]

Where \( w_i = \frac{\phi_o^2 B_o B_s (B_s + B_o \mu_s)}{12(B_o + B_s + B_o B_s)^2} \). Using the Eq. (5.18) [or the dimensionless concentration \( F_0(\chi) \)] we can obtain the concentrations of substrate and reduced mediator from the Eqs. (5.14) and (5.15). From Eqs. (5.15), (5.17) and (5.18) we get the dimensionless current,

\[ I = \frac{\phi_o^2 B_o B_s (1 - 4w_i)}{(B_o + B_s + B_o B_s)} \quad (5.19) \]
Table 3.1 Comparison of normalized analytical steady-state concentrations of oxidized mediator $\phi_0$ (Eq. 5.13) with the numerical results when $B_o = 0.1$, $B_s = 0.01$, $\mu_s = 0.05$ and for various values of $\phi_0^2$.

| $\chi$ | $\phi_0^2 = 1$  
|        | $(d = 7.878 \text{ } \mu M)$ | $\phi_0^2 = 25$  
|        | $(d = 39.39 \text{ } \mu M)$ | $\phi_0^2 = 100$  
|        | $(d = 78.80 \text{ } \mu M)$ | $\phi_0^2 = 225$  
|        | $(d = 118.17 \text{ } \mu M)$ |
| 0 | 0.9955 | 0.9955 | 0 | 0.8889 | 0.8889 | 0 | 0.5801 | 0.5773 | 0.46 | 0.1895 | 0.1908 | 0.69 |
| 0.2 | 0.9957 | 0.9957 | 0 | 0.8933 | 0.8933 | 0 | 0.5965 | 0.5939 | 0.43 | 0.2197 | 0.2200 | 0.14 |
| 0.4 | 0.9962 | 0.9962 | 0 | 0.9066 | 0.9066 | 0 | 0.6462 | 0.6440 | 0.34 | 0.3115 | 0.3101 | 0.45 |
| 0.6 | 0.9971 | 0.9971 | 0 | 0.9288 | 0.9288 | 0 | 0.7295 | 0.7279 | 0.22 | 0.4686 | 0.4664 | 0.47 |
| 0.8 | 0.9984 | 0.9984 | 0 | 0.9599 | 0.9599 | 0 | 0.9484 | 0.8471 | 0.85 | 0.6962 | 0.6947 | 0.21 |
| 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0 |

Average deviation 0.00  
Average deviation 0.00  
Average deviation 0.38  
Average deviation 0.33  

96
5.3.2 NUMERICAL SIMULATION

The non-linear diffusion equations (Eqs. (5.9a) - (5.9c)) for the boundary conditions (Eqs. (5.10) and (5.11)) are also solved numerically. We have used the function pdex4 in Scilab numerical software to solve numerically, the initial-boundary value problems for parabolic-elliptic partial differential equations. This numerical solution is compared with our analytical results in Figs. (5.2) and (5.3) and Table 5.1. The average relative error between our analytical result (Eq. 5.18) and the numerical result of oxidized mediator concentration $F_o$ is less than 0.38% for various values of $\phi_o^2$. All possible numerical values of the dimensionless parameters used in Hall et.al [17] and in this work are given in Table 5.2. The normalized current $I$ is compared with simulation result in Table 5.3 for various values of parameters $\phi_o^2$. The average relative error is less than 3%. From the table it is also inferred that the value of the current increases when the thickness of the membrane increases.

Table 5.2 Possible numerical values for dimensionless parameters used in Hall’s et.al [17] and in this work.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Numerical values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\phi_o^2 = d^2 k_2 [E_T]/D_m [Med_{ox}]_b$</td>
<td>Hall et.al [17]: 10 - 400</td>
</tr>
<tr>
<td>$B_o = [Med_{ox}]_b/\beta_o$</td>
<td>0.00195</td>
</tr>
<tr>
<td>$B_s = [S]_b/\beta_s$</td>
<td>0.018, 0.035, 0.07, 0.14</td>
</tr>
<tr>
<td>$\mu_s = D_m [Med_{ox}]_b/D_s [S]_b$</td>
<td>0.94736</td>
</tr>
</tbody>
</table>
5.4 RESULTS AND DISCUSSION

Eqs. (5.18), (5.14) and (5.15) represent the new closed and simple approximate analytical expressions of the normalized concentrations of oxidized mediator $F_O$, substrate $F_s$ and reduced mediator $F_R$ respectively for all values of parameters $Q_0^0$, $B_O$ and $B_s$. The current response is given in Eq. (5.19).

Table 5.3 Comparison of normalized current $I$ (Eq. 5.19) with the numerical results when $B_O = 0.1$, $B_s = 0.01$, $\mu_s = 0.05$ and for various values of $Q_0^0$.

<table>
<thead>
<tr>
<th>$Q_0^0$</th>
<th>Analytical</th>
<th>Numerical</th>
<th>Error %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.009</td>
<td>0.009</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0.223</td>
<td>0.223</td>
<td>0</td>
</tr>
<tr>
<td>50</td>
<td>0.441</td>
<td>0.441</td>
<td>0</td>
</tr>
<tr>
<td>75</td>
<td>0.655</td>
<td>0.652</td>
<td>0.5</td>
</tr>
<tr>
<td>100</td>
<td>0.864</td>
<td>0.838</td>
<td>3</td>
</tr>
</tbody>
</table>

5.4.1 CONCENTRATION PROFILES

The concentration profiles for all the three species are shown in Fig. 5.2. The condition that the oxidized mediator $F_O$ (Eq. 5.18) is consumed by the enzyme reaction, as the mediator moves inwards from the electrode interface is established in the Fig. 5.2. We understand that when the substrate concentration $F_s$ (Eq. 5.14) is changed slightly across the matrix, the oxidized mediator is limiting under these
conditions rather than the substrate itself. The reduced mediator concentration $F_R$ (Eq. 5.15) has the reciprocal variation as expected from Eq. (5.9d). The maximum reduced mediator concentration is noticed at the same position in the enzyme layer, as the oxidized species becomes completely consumed.

Fig. 5.2 Dimensionless concentration of (a) oxidized mediator $F_O$ (Eq. 5.18), (b) substrate $F_S$ (Eq. 5.14) and (c) reduced mediator $F_R$ (Eq. 5.15) versus normalized distance $\chi$ for $B_O = 0.5$, $B_S = 0.0052$, $\mu_S = 0.05$ and $\phi^2_0 = 400$. Solid lines represent the analytical solution whereas the dotted lines for the numerical solution.
5.4.2 VARIATIONS IN THE THIELE MODULUS

The Thiele modulus $q_0^2$, essentially compares the reaction and diffusion in the enzyme layer. We examine the rise and downfall of concentration profiles in two cases. (a) When $q_0^2$ is less than 1, the kinetics dominate and the uptake of oxygen and substrate is kinetically controlled. The overall kinetics is governed by the total amount of active enzyme. (b) The response is under diffusion control, when the Thiele modulus is large ($q_0^2 > 1$), which is observed at high catalytic activity and great membrane thickness or low diffusion coefficient values.

In Fig. 5.3, under the consideration of lower $q_0^2$ and the sensor under kinetic control, the concentration profile varies slightly from non-enzyme linked oxygen. As $q_0^2$ increases, the oxidized mediator concentration is consumed in the enzyme reaction. Therefore the profile deviates more from the linearity. Furthermore all the oxygen within the polymer matrix is consumed well before reaching the electrode. Thus the concentration gradient nears the electrode, and hence the flux of oxygen at the electrode surface decreases. We observe that for a given layer, and hence value of $q_0^2$, the concentration profiles are also altered according to the bulk concentrations of the substrate, and co-substrate. Thus with increasing $[S]_b$ the concentration profile deviates from the response where no oxygen is consumed. Thus an increased substrate concentration $F_S$ causes a decrease in the flux to the electrode. The concentration of the reduced mediator $F_R$ increases in direct proportion to the thickness of the enzyme layer or the amount of enzyme immobilized in the matrix.
Fig. 5.3 Concentration profiles of (a) oxidised mediator $F_O$ (Eq. 5.18) (b) substrate $F_s$ (Eq. 5.14) (c) reduced mediator $F_r$ (Eq. 5.15) computed for the fixed values of $B_0 = 0.1, B_s = 0.01, \mu_s = 0.05$ and various values of Thiele modulus $\phi$. Solid lines represent the analytical solution obtained in this work whereas the dotted lines for the numerical solution.
Fig. 5.4 Concentration profiles of (a) oxidised mediator $F_o$ (Eq. 5.18) (b) substrate $F_s$ (Eq. 5.14) (c) reduced mediator $F_r$ (Eq. 5.15) for the fixed values of $B_o = 0.17$, $\mu_s = 0.5$, $\phi^2_0 = 100$ and various values of normalised surface concentration of substrate $B_s$ are plotted in accordance with the normalised distance $\chi$.
In Fig. 5.4, the concentration of the oxidized mediator, substrate and reduced mediator are shown for different substrate concentrations in the bulk electrolyte. In the absence of substrate \( B_0 \leq 0.001 \), a straight line is observed for the mediator profile. With increasing substrate concentration in the bulk electrolyte, the profile of reduced mediator bends upward as the generation of reduced mediator by the enzyme reaction increases. The profiles for oxidized mediator and substrate bend downwards.

5.4.3 CURRENT RESPONSE

The parameter of the greatest interest in an amperometric biosensor is the current. For a particular membrane, the variation in \( \phi_0^2 \) can be achieved practically, by varying the thickness of the membrane \( d \), or the loading of the enzyme \([E_+]\). As can be seen in Eq. (5.8), the thickness appears as a squared term and thus small changes will have a much more pronounced effect on the response of the enzyme electrode than the enzyme loading. The variation in current for various values of \( d \), and hence \( \phi_0^2 \) is shown in Fig. 5.5. It is evident from the figure that, the current \( I \) (Eq. 5.19) increases when \( \phi_0^2 \) increases. Furthermore when \( B_o \) and \( B_e \) is greater than 0.5, all the curves reach the steady-state value. Electroanalytical systems for high spatial resolution scanning and fabrication of micro- nano sensors need the three-dimensional study of current response. Fig. 5.6 characterizes the normalized three-dimensional steady-state current response \( I \). From this figure it is inferred that the current increases with the increasing value of the Thiele modulus \( \phi_0^2 \).
Fig. 5.5  Variation of normalised current $I$ response with (a) normalised surface concentration of oxidised mediator $B_o$ (b) normalized surface concentration of the substrate $B_s$ for various values of Thiele modulus $\phi_0^i$ is shown using Eq. (5.16).
Fig. 5.6 Plot of the three-dimensional current $I$ versus Thiele modulus $\phi_0$

(a) Normalised surface concentration of oxidized mediator $B_O$

(b) Normalised surface concentration of the substrate $B_S$ obtained via Eq. (5.16).
5.5 CONCLUSIONS

This chapter presents a theoretical treatment of an oxidized enzyme-membrane electrode in an amperometric biosensor. In this chapter, we have solved the non-linear differential equations both analytically and numerically. The approximate analytical expressions for the steady-state concentrations of oxidised mediator, substrate and reduced mediator for all values of parameters \( \rho_o^2, B_o \) and \( B_s \) at the enzyme-membrane electrode geometry are obtained using the Adomian decomposition method. A satisfactory agreement with the numerical result is noted. The analytical results obtained in this chapter can be used to analyze the effect of different parameters such as membrane thickness, type of buffer in the external solution and enzyme loading in the membrane. This theoretical result is also useful for the optimization of the bio-sensor.

5.6 APPENDIX 5.A: BASIC CONCEPT OF THE ADOMIAN DECOMPOSITION METHOD (ADM)

Adomian decomposition method [26-31] depends on decomposing the non-linear differential equation

\[
F(x, y(x)) = 0
\]

into the two components

\[
L(y(x)) + N(y(x)) = 0
\]

where \( L \) and \( N \) are the linear and the non-linear parts of \( F \) respectively. The operator \( L \) is assumed to be an invertible operator. Solving for \( L(y(x)) \) leads to

\[
L(y(x)) = -N(y(x))
\]
Applying the inverse operator \( L \) on both sides of Eq. (5.A3) yields

\[
y(x) = \phi(x) - L^{-1}\left[ N(y(x)) \right]
\]

(5.A4)

where \( \phi(x) \) is a function that satisfies the condition \( L(\phi(x)) = 0 \). Now assuming that the solution \( y \) can be represented as infinite series of the form,

\[
\sum_{n=0}^{\infty} y_n(x) = \phi(x) - L^{-1}\left( \sum_{n=0}^{\infty} A_n(x) \right)
\]

(5.A5)

where

\[
\sum_{n=0}^{\infty} y_n(x) = y(x), \quad A_n(x) = \frac{1}{n!} \left[ \frac{d^n}{d\lambda^n} N\left( \sum_{i=0}^{\infty} \lambda^i y_i(x) \right) \right]_{\lambda=0}
\]

and

\[
\sum_{n=0}^{\infty} A_n(x) = N(y(x)) \quad n \geq 0
\]

(5.A6)

Then equating the terms in the linear system of Eq. (5.A5) gives the recurrent relation

\[
y_0 = \phi(x), \quad y_{n+1} = -L^{-1}(A_n) \quad n \geq 0
\]

(5.A7)

However, in practice all the terms of series in Eq. (5.A5) cannot be determined, and the solution is approximated by the truncated series \( \sum_{n=0}^{N} y_n(x) \).

5.7 APPENDIX 5.B: ANALYTICAL SOLUTIONS OF CONCENTRATIONS OF OXIDISED MEDIATOR, SUBSTRATE AND REDUCED MEDIATOR

To solve Eq. (5.16) using the Adomian decomposition method [21-23], we write the Eq. (5.16) in the operator form,

\[
L[F_0(x)] = \phi^Z N[F_0(x)]
\]

(5.B1)

where
\[ L = \frac{d^2}{d\chi^2} \text{ and } N[F_0(\chi)] = \left[ \frac{F_0^2 + F_0 \left[ (1 - \mu_s) / \mu_s \right]}{F_0^2 + F_0 \left( \frac{1}{B_s \mu_s} + \frac{1}{B_o} + \frac{1 - \mu_s}{\mu_s} + \frac{1 - \mu_s}{\mu_s B_o} \right)} \right] \] (5.B2)

Applying the inverse operator \( L^{-1} \) on both sides of Eq. (5.B1) yields

\[ F_0(\chi) = A\chi + B + \phi^2 L^{-1} N[F_0(\chi)] \] (5.B3)

According to the ADM, the solution \( F_0(\chi) \) can be elegantly computed by using the recurrence relation

\[ F_{0,0}(\chi) = A\chi + B, \quad F_{0,n+1}(\chi) = \phi^2 L^{-1} N[F_0(\chi)] = \phi^2 L^{-1} A_n(\chi) \quad n \geq 0 \] (5.B4)

where \( A_n \) are the Adomian polynomials of \( F_{0,1}, F_{0,2}, \ldots, F_{0,n} \). We can find the first few Adomian polynomial coefficient \( A_n \) using Eq. (5.A6) as follows:

\[ A_0(\chi) = N(F_{0,0}) = \left[ \frac{F_{0,0}^2 + F_{0,0} \left[ (1 - \mu_s) / \mu_s \right]}{F_{0,0}^2 + F_{0,0} \left( \frac{1}{B_s \mu_s} + \frac{1}{B_o} + \frac{1 - \mu_s}{\mu_s} + \frac{1 - \mu_s}{\mu_s B_o} \right)} \right] \] (5.B5)

\[ A_1(\chi) = \frac{d}{d\chi} \left[ N(F_{0,0} + \lambda F_{0,1}) \right]_{\lambda=0} \]

\[ = \frac{F_{0,1,\chi}}{F_{0,0} B_o \left( \frac{1}{B_s \mu_s} + \frac{1}{B_o} + \frac{1 - \mu_s}{\mu_s} + \frac{1 - \mu_s}{\mu_s B_o} \right)} + 2 \left( \frac{1 - \mu_s}{\mu_s} \right) F_{0,0} + \left( \frac{1 - \mu_s}{\mu_s} \right)^2 \] (5.B6)

The remaining polynomials \( A_i(\chi) \) can be generated easily, using Eq. (5.A6).

Applying the following boundary conditions

\[ F_{0,0}'(0) = 0, F_{0,0}(1) = 1 \quad \text{and} \quad F_{0,i}'(0) = 0, F_{0,i}(1) = 0 \quad \text{for} \quad i \geq 1 \] (5.B7)
From Eq. (5.8.B4) and using the above conditions we obtain the following results:

\[ F_{0,0}(x) = 1 \]  
(5.B8)

\[ F_{0,1}(x) = \phi_0^3 L^{-1}[A_0(x)] = \frac{\phi_0^3 (x^2 - 1)}{2} \left( 1 + \frac{1}{B_s} + \frac{1}{B_o} \right)^{-1} \]  
(5.B9)

\[ F_{0,2}(x) = \phi_0^3 L^{-1}[A_1(x)] = \frac{\phi_0^3 (B_s + B_o \mu_2)(x^4 - 6x^2 + 5)}{24B_o B_s \left( 1 + \frac{1}{B_s} + \frac{1}{B_o} \right)} \]  
(5.B10)

Adding Eqs. (5.B8)-(5.B10), we get the concentration of oxidized mediator (Eq. (5.18)) in the text. From this solution of the oxidized mediator, the concentration profiles for the substrate and reduced mediator can be obtained using Eqs. (5.14) and (5.15).

5.8 Appendix 5.C: SCILAB PROGRAM FOR THE NUMERICAL SOLUTION OF THE SYSTEMS OF NON-LINEAR Eqs. (5.9A)-(5.9C)

```matlab
function pdex4

m = 0;
x = [0 0.2 0.4 0.6 0.8 1];
t = [0 2 4 6 8 10];
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
u3 = sol(:,:,3);
figure
plot(x,u1(end,:))
figure
plot(x,u2(end,:))
```

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ylabel('u2(x,2)')

figure

plot(x,u3(end,:))

function \([c,f,s] = \text{pdex4pde}(x,t,u,DuDx)\)

Bs=0.01;
Bo=0.1;
A=10;
us=0.05;
up=1;
c = [1;1; 1];
f = [1; 1; 1].* DuDx;

F1 =-A^2*(u(1)*u(2)/(u(1)/Bs+u(2)/Bo+(u(1)*u(2))));
F2 =-us*A^2*(u(1)*u(2)/(u(1)/Bs+u(2)/Bo+(u(1)*u(2))));
F3 =up* A^2*(u(1)*u(2)/(u(1)/Bs+u(2)/Bo+(u(1)*u(2))));
s = [F1; F2; F3];

function u0 = pdex4ic(x);

u0 = [1; 0; 1];

function [pl,ql,pr,qr] = pdex4bc(xl,ul,xr,ur,t)

pl = [0; 0; 0];
ql = [1; 1; 1];
pr = [ur(1)-1; ur(2)-1; ur(3)];
qr = [0; 0; 0];