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Mathematical modeling in amperometric oxidase enzyme–membrane electrodes

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ABSTRACT

The theoretical analysis of the steady-state amperometric oxidase enzyme–membrane electrode is developed. The model is based on diffusion equations containing a non-linear term related to Michaelis–Menten kinetics of the enzymatic reaction. We employ the homotopy perturbation method (HPM) to solve the system of coupled non-linear diffusion equations for the steady-state condition. Simple and approximate polynomial expressions of concentration of oxygen (mediator), substrate and flux are derived for all possible values of parameters ϕ (Theiele modulus), B_O (normalized surface concentration of mediator), and B_S (normalized surface concentration of substrate). Furthermore, in this work the numerical solution of the problem is also reported using SCILAB program. The analytical results are compared with the numerical results and found to be in good agreement.

1. Introduction

Problems of coupled diffusion and non-linear chemical reactions are found in practical situation [1–3]. In such systems the diffusion of the chemical species into a phase is accompanied by a chemical reaction either with species already presents in the phase, or catalysed by species within the phase. Examples include diffusion and reaction in immobilized enzyme membranes [4–6], diffusion into living cells and micro-organisms, and chemical reactions in high polymer substances.

Biosensors, particularly enzyme-based amperometric sensors, have been studied extensively because of their scientific significance and commercial potential in both academic and applied fields [7,8]. In the first generation, enzymes were immobilized via membrane silica–gel (SiO_2 + gelatin). This membrane creates a flexible matrix, negligible swelling in aqueous solution and thermal stability on the electrode [1]. In the second generation, glucose oxidases (GODs) were immobilized through a polyvinyl alcohol (PVA) layer and a Prussian blue (PB) mediator. In the last generation, GOD immobilization influence was also studied for the selfassembled monolayers (SAMs) of cysteamine onto the platinum surface [3].

The general principle of enzyme electrodes was introduced about three decades ago by Clark and Lyons [9]. Since then, many biosensors based on electrochemical enzyme electrodes have been described, the majority of these devices operating in an amperometric mode. The development of models for enzyme electrodes provides a better understanding of the individual processes influencing the response of the device, and this information may be used as a guide for directions for improvement of the sensor design. Mathematical models can explain such regularities. The general features of amperometric response were analyzed in the publications of Mell and Maloy [10,11]. There have been many reports on models for enzyme electrodes.

Schulmeister [12,13] has described models for multilayer and multienzyme electrodes; these models assumed operation of the electrode under diffusion control, such as the enzyme kinetics are linear with substrate. This allows the reaction and diffusion system to be described by a parabolic differential equation with linear inhomogeneities. A model for a two substrate enzyme electrode has been devised by Leypoldt and Gough [14] where the non-linear enzyme reaction was taken into account. The information gained from modeling can be useful in sensor design, optimization and prediction of the electrode's response. However till date few of the models proposed for enzyme electrodes [15–19] have been presented with a specific view to electrode design.

Cambiaso et al. [20] numerically obtained the transient behaviour of the electrode current in amperometric enzyme sensor for 4 different substrate concentrations using C language. Mackey et al. [21] compared the behaviour of an electrochemical enzyme biosensor with a theoretical analysis based on mathematical model and numerical simulation by the implicit Crank–Nicolson technique [22]. Jobst et al. [23] developed an implicit difference scheme for the simulation of the steady state and transient behaviour of multi-membrane multi-enzyme sensors. Some of the numerous algebraic solutions and simulations known to the literature

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describe the coupling of reaction and mass transport very versatile [24–26]. Sorochinskii and Kurganov analyzed the non-linear kinetics of cyclic conversions of the substrate in amperometric bienzyme sensors [27].

The transient kinetics of the biosensors was studied by Kulys et al. [28]. Rigorous analytical and numerical solution was reported by Manimozhi et al. [29] for a steady-state substrate concentration at the biosensor at mixed enzyme kinetics and external diffusion limitation in the case of substrate inhibition. Flexer et al. [30] applied relaxation and simplex mathematical algorithms to the study of steady-state electrochemical response of immobilized enzyme biosensors. Mathematical models for the description of the concentration profile measured by a single-layer, single-enzyme electrode placed in a single-line flow-injection system were developed by Kolev [31]. Also Kolev obtained the analytical solution in both the Laplace and the time domains for the special case of pseudo-first-order kinetics. Baronas et al. [32] analyzed a plate-gap model of a porous enzyme doped electrode covered by a porous inert membrane using finite-difference technique.

Earlier, the response of an amperometric oxidase enzyme electrode, monitored by the consumption of oxygen, was numerically modeled using a two substrate model by Gooding and Hall [15]. However, to the best of our knowledge, till date no general analytical results for the concentration of mediator and substrate for all values of the parameters ϕ, B_O and B_S have been reported [15]. The purpose of this communication is to derive analytical expressions for concentration of the mediator (oxygen) and substrate in amperometric oxidase enzyme electrode.

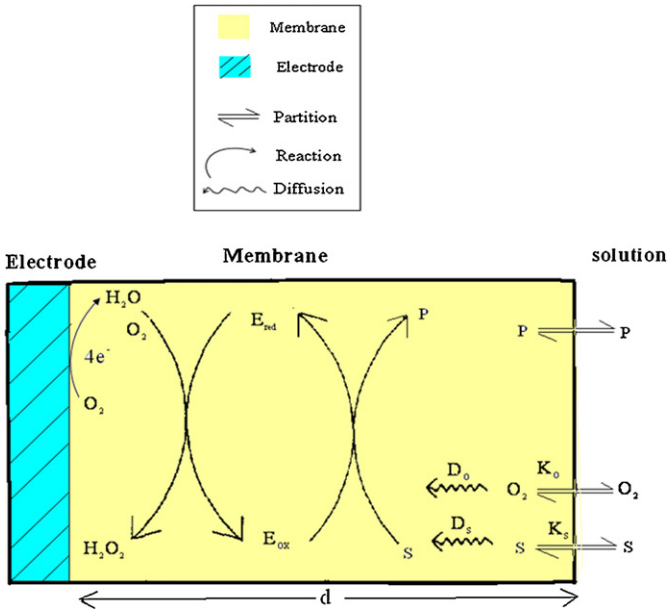

Fig. 1. Schematic representation of a typical enzyme–membrane|electrode showing the processes is considered in the model. The model describes the mechanism by which an oxidase enzyme moves from the fully oxidised state to the fully reduced form and back to an oxidised state in a catalytic cycle as shown in the scheme in the text.

2. Mathematical formulation of analysis and problems

2.1. Mathematical formulation

Building upon earlier work of this electrode, Gooding and Hall [15] presented a concise discussion and the derivation of mass transport equation for an amperometric enzyme electrode, which is summarized briefly for completeness. The model presented in this article is derived from a model developed by Parker and Schwartz [33] for a potentiometric sensor. This model is extended by Martens and Hall [18] for mediated amperometric sensors and Gooding and Hall [15] for oxidase enzyme electrode. The following assumptions include: steady-state conditions apply, diffusion in the matrix obeys Fick's laws, the matrix is homogeneous, the reaction is isothermal and the rate constants of the immobilized glucose oxidase are the same as the soluble enzyme.

2.1.1. Schematic representation

The model describes the mechanism by which an oxidase enzyme moves from the fully oxidised state to the fully reduced form and back to an oxidised state in a catalytic cycle which may be written as follows (see Fig. 1):

$$E_{OX} + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E_{red} + P$$

$$E_{red} + O_2 \xrightarrow{k_3} E_{OX} + H_2O_2$$

where k_m is the rate constant for the forward direction of the mth reaction and k_{-1} is the rate constant for the backward direction. The total enzyme concentration $[E_T]$ at all times is,

$$[E_T] = [E_{OX}] + [ES] + [E_{red}] \quad (1)$$

where $[E_{OX}]$, $[E_S]$ and $[E_{red}]$ are the oxidised, substrate and reduced mediator enzyme concentrations respectively. The diffusion of a substrate into the enzyme layer at steady-state is equal to the reaction rate of the substrate within the matrix. Thus the material balance of oxygen and substrate, within the thickness of matrix may be written as [15] follows:

$$D_O \frac{d^2[O_2]}{dy^2} = k_3[E_{red}][O_2] = \frac{k_2 k_1}{k_{-1} + k_2}[E_{OX}][S] = \frac{k_2[E_T]}{(\beta_S/[S]) + (\beta_O/[O_2]) + 1} \quad (2)$$

and

$$D_S \frac{d^2[S]}{dy^2} = k_1[E_O][S] - k_{-1}[ES] = \left(k_1 - \frac{k_{-1}k_1}{k_{-1} + k_2}\right)[E_{OX}][S] = \frac{k_2[E_T]}{(\beta_S/[S]) + (\beta_O/[O_2]) + 1} \quad (3)$$

where D_O and D_S are the diffusion coefficients of oxygen and the substrate within the enzyme layer. $[O_2]$ and $[S]$ are the concentration of the mediator (oxygen) and substrate at any position in the enzyme layer. Following the nomenclature of Athinson and Lester [34], we can write $\beta_S = (k_{-1} + k_2)/k_1$ and $\beta_O = k_2/k_3$. It is important to observe that, from Eqs. (2) and (3), we get

$$D_O \frac{d^2[O_2]}{dy^2} = D_S \frac{d^2[S]}{dy^2} \quad (4)$$

The implication of Eq. (4) is that there is only one independent variable which must be solved to obtain the concentration of the other species. We examine a planar matrix of thickness $y = d$ where diffusion is considered in the y-direction only (edge effects are neglected).

2.1.2. Boundary conditions

At the polymer/solution interface, $y = d$:

$$[O_2] = [O_2]_b = K_O[O_2]_\infty$$

$$[S] = [S]_b = K_S[S]_\infty \quad (5)$$