

Theory of the Transient Current Response for the Homogeneous Mediated Enzyme Catalytic Mechanism at the Rotating Disc Electrode

B Manimegalai¹, L Rajendran¹, MEG Lyons^{2,*}

¹ Department of Mathematics, AMET Deemed to be University, Kanathur, Chennai-603112.

² School of Chemistry & AMBER National Centre, University of Dublin, Trinity College Dublin, Dublin 2, Ireland.

*E-mail: melyons@tcd.ie (MEG Lyons)

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This paper presents the approximate analytical expression for transient and steady-state concentration profiles of enzymes, mediator, substrate and current. The transport and kinetics of the reaction in the diffusion layer with a rotating disc electrode are described using closed-form solutions of homogeneous systems. These new approximate analytical expressions are valid for all values of parameters. Furthermore, in this work, the numerical simulation is also presented using the Matlab program. The analytical results are compared with simulation results, and satisfactory agreement is noted.

Keywords: Nonlinear reaction kinetics; Rotating-disc electrode; Transient conditions; Amperometric response of Homogeneous mediated enzyme catalysis.

1. INTRODUCTION

Nonlinear differential equations are used in many fields such as rotating disc electrode [1-7], biosensors [8-12], biofuel cells [13-16], biofilms [17-18], bioreactors [19], biofilters [20] and ultramicroelectrodes [21-22] etc. It is very important to solve the nonlinear equations, but exact solutions for such equations are not available [23]. So we can use some asymptotic methods like homotopy perturbation method [24-28], Adomian decomposition method [29-30], variational iteration method [31-34], Taylor series method [35], Akbari Ganji's method [36-37], Pade approximant method [7,9] to solve nonlinear equations.

Nonlinear equation occurs in the homogeneous mediated enzyme reaction mechanism. Albery and coworkers [38] presented a comprehensive theoretical treatment for an amperometric enzyme electrode that uses a mediator interacting in a homogeneous solution to transfer the electrons. Bartlett

and Pratt [39] presented the results of a study of the glucose, glucose oxidase, ferrocene monocarboxylic acid system using the rotating disc electrode. The limiting current during the anodic dissolution of tungsten rotating disk electrode in alkaline solutions, as well as the distribution of ionic concentrations, partial currents, and potential near the anode, are all numerically solved by Volgin *et al.* [40]. Schwartz and coworkers [41] investigated the nonlinear behaviour of a sinusoidally modulated rotating disk electrode to determine the flow and concentration field interactions that trigger resonance and nullification conditions in the system's electrochemical response. Using the variational iteration method, Loghambal and Rajendran [42] proposed an approximate analytical solution of steady-state nonlinear differential equations describing the transport and kinetics of the enzyme and mediator in the diffusion layer of the electrode. Saravanakumar *et al.* [43] provided an approximate analytical expression of current for the non-steady-state convection-diffusion equation of the rotating disk electrode for all time.

Saravanakumar and coworkers [44] derived an analytical expression of concentration and current by solving the reaction convection-diffusion equations for the EC' and ECE reaction mechanism. Chitra Devi *et al.* [45] solved a system of convection-diffusion equations in the pseudo-first-order EC-catalytic mechanism at a rotating disk electrode. Visuvasam *et al.* [46] studied the analytical and numerical solution of nonlinear diffusion equations for the chronoamperometric limiting current generated from the electrochemical reaction in a rotating disk electrode for second-order ECE reactions when the chemical step is irreversible.

Albery and coworkers [38], Bartlett and Pratt [39] analysed the comprehensive theoretical treatment for an amperometric enzyme electrode that uses a mediator interacting in a homogeneous solution to transfer the electrons at the rotating disc electrode for steady-state conditions. However, to the best of our knowledge, there was ~~the~~ no rigorous analytical expression corresponding to the concentrations and current for non-steady-state conditions reported. In this communication, the approximate analytical expressions of the enzyme, mediator, substrate concentrations and transient and steady-state current are derived.

2. MATHEMATICAL FORMULATION OF THE PROBLEM

The homogeneous kinetics of mediated enzyme reactions which describe overall two-electron processes are expressed by [38,39]:



where $k_E = k_{cat}S_{\infty}/(K_m + S_{\infty})$ and S_{∞} is the substrate concentration in the bulk solution. Substrate present to regenerate reduced form of the enzyme, E' . Building upon earlier work for these mechanisms, Albery *et al.* [38] and Bartlett *et al.* [39] presented a concise discussion and derivation of the mass transport equation for these mechanisms for non-steady-state condition, which is summarized briefly for completeness. The following schematic diagram depicts the reaction system.

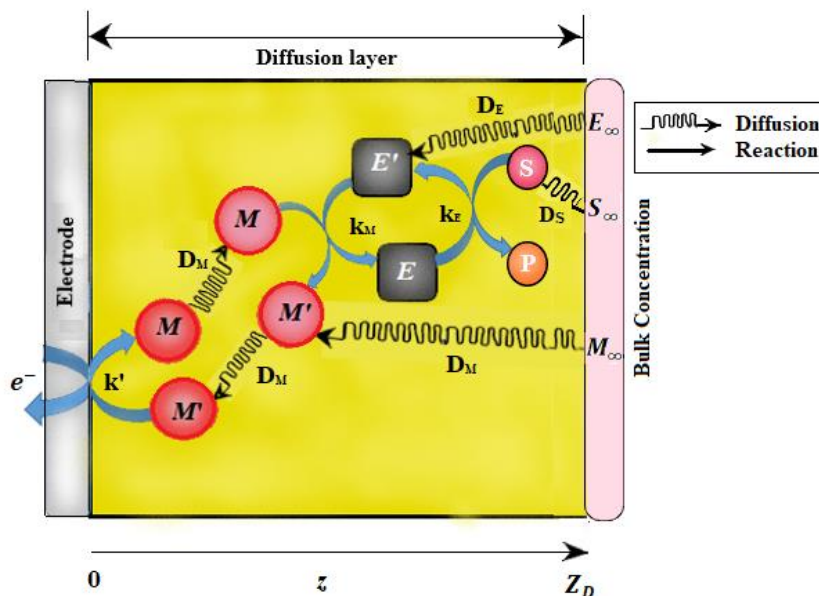


Figure 1. A schematic diagram of the homogeneous system.

The oxidized and reduced forms of the mediator species are represented by M and M' , respectively. The oxidized and reduced enzyme species are E and E' . k_M is a bimolecular rate constant and k_E a pseudo-first-order rate constant for the reaction between E and S . When the substrate concentration is high enough, the enzyme becomes saturated and k_E equals k_{cat} . Nonlinear reaction diffusion-reaction equations for the four species [38,39] can be written as follows:

$$\frac{\partial m(z,t)}{\partial t} = D_M \frac{\partial^2 m(z,t)}{\partial z^2} - k_M e'(z,t) m(z,t) \tag{4}$$

$$\frac{\partial m'(z,t)}{\partial t} = D_M \frac{\partial^2 m'(z,t)}{\partial z^2} + k_m e'(z,t) m(z,t) \tag{5}$$

$$\frac{\partial e'(z,t)}{\partial t} = D_E \frac{\partial^2 e'(z,t)}{\partial z^2} - k_m e'(z,t) m(z,t) + k_E e(z,t) \tag{6}$$

$$\frac{\partial e(z,t)}{\partial t} = D_E \frac{\partial^2 e(z,t)}{\partial z^2} + k_m e'(z,t) m(z,t) - k_E e(z,t) \tag{7}$$

In the above analysis, the only diffusion of enzyme and mediator is examined. We assume that substrate is present in excess, so the reaction-diffusion of S may be neglected. If not, the further reaction-diffusion equation must be considered, and the equation of the substrate is as follows:

$$\frac{\partial S(z,t)}{\partial t} = D_S \frac{\partial^2 S(z,t)}{\partial z^2} - \frac{k_{cat} e_{\Sigma} S(z,t)}{K_m + S(z,t)} \tag{8}$$

where m , m' and e, e' are the concentrations of oxidized and reduced form mediator and enzyme. S is the concentration of substrate. D_M and D_E are the diffusion coefficients of species M, M' and E, E' respectively. D_S is the diffusion coefficients of the substrate. The concentration of total enzyme e_{Σ} in the solution is considered to be uniform. This means that the oxidized and reduced forms of the enzyme

have the same diffusion coefficients. Then at any place and any time in the solution $e + e' = e_{\Sigma}$. Assuming that the diffusion coefficients of the oxidized and reduced forms of the mediator are equal and that the mediator is totally reduced in bulk solution. i.e $m + m' = m_{\Sigma} = m'_{\infty} = m_0$. Here m_{Σ} is the total concentration of the mediator, m'_{∞} is the bulk concentration of the reduced mediator. m_0 is the concentration of M at the electrode surface. The initial and boundary conditions are [38,39]

$$\text{At } t = 0, m = m' = m_{\Sigma}, e = e' = e_{\Sigma}, \text{ and } S = S_{\infty} \tag{9}$$

$$\text{At } z = Z_D, m = 0, m' = m_{\Sigma}, e = 0, e' = e_{\Sigma} \text{ and } S = S_{\infty} \tag{10}$$

$$\text{At } z = 0, m = m_{\Sigma}, m' = 0, \frac{\partial e}{\partial z} = 0, \frac{\partial e'}{\partial z} = 0 \text{ and } \frac{\partial S}{\partial z} = 0 \tag{11}$$

The current I is calculated from the flux of mediator reacting at the electrode:

$$I = -nFAD_M \left(\frac{\partial m}{\partial z} \right)_{z=0} \tag{12}$$

The following dimensionless variables are used in this model.

$$u = \frac{m}{m_{\Sigma}}, u' = \frac{m'}{m_{\Sigma}}, v = \frac{e}{e_{\Sigma}}, w = \frac{S}{S_{\infty}}, \chi = \frac{z}{Z_D}, \tau = \frac{D_M t}{Z_D^2}, \gamma = \frac{m_{\Sigma}}{e_{\Sigma}}, \tag{13}$$

$$\xi = \frac{D_E}{D_M}, \xi' = \frac{D_S}{D_M}, \beta = \frac{S_{\infty}}{K_M}, \kappa_M = \frac{k_M Z_D^2 e_{\Sigma}}{D_M}, \kappa_E = \frac{k_E Z_D^2}{D_E}, \kappa_S = \frac{k_{cat} Z_D^2 e_{\Sigma}}{K_M D_M}$$

Here Z_D is the Levich diffusion layer thickness given by

$$Z_D = 0.64 \nu^{1/6} D_M^{1/3} / \sqrt{W} \tag{14}$$

where ν is the kinematic viscosity and W (Hz) is the rotation speed. Now the Eq. (4), Eq. (6) and Eq. (8) are reduced in dimensionless form as follows:

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} - \kappa_M u(\chi, \tau) v(\chi, \tau) \tag{15}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \xi \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} - \kappa_E [\gamma u(\chi, \tau) v(\chi, \tau) + \xi(1 - v(\chi, \tau))] \tag{16}$$

$$\frac{\partial w(\chi, \tau)}{\partial \tau} = \xi' \frac{\partial^2 w(\chi, \tau)}{\partial \chi^2} - \frac{\kappa_S w(\chi, \tau)}{1 + \beta w(\chi, \tau)} \tag{17}$$

The corresponding initial and boundary conditions for the above two equations are given by,

$$\tau = 0, u = 1, v = 1, w = 1 \tag{18}$$

$$\chi = 1, u = 0, v = 1, w = 1 \tag{19}$$

$$\chi = 0, u = 1, \frac{\partial v}{\partial \chi} = 0, \frac{\partial w}{\partial \chi} = 0 \tag{20}$$

In dimensionless terms the current becomes [39]

$$\psi = \frac{I Z_D}{nFAD_M m_{\Sigma}} = - \left(\frac{\partial u}{\partial \chi} \right)_{\chi=0} \tag{21}$$

3. ANALYTICAL EXPRESSION OF CONCENTRATION OF THE SPECIES USING NEW APPROACH OF HOMOTOPY PERTURBATION METHOD (HPM)

Solving systems of nonlinear equations, which is one of the most fundamental problems in mathematics, can be used to solve several applied problems. In the physical and chemical sciences, novel methods have recently been used to solve nonlinear problems [23]. HPM is a common method used to solve a differential equation.

The HPM was proposed by He in 1999 [24]. This approach has recently been used in nanotechnology to solve nonlinear oscillator problems [25-26]. This method is also applied to solve coupled nonlinear differential equations in the microelectromechanical system [27], and axial vibration system [28], etc. Using the new approach of HPM, the approximate analytical expressions for the concentration of the mediator, enzyme and substrate are obtained (Appendix-A) as follows:

$$u(\chi, \tau) = \frac{\sinh((1-\chi)\sqrt{\eta\kappa_M})}{\sinh(\sqrt{\eta\kappa_M})} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta\kappa_M \sinh((\chi-1)n\pi)}{\eta\kappa_M + (n\pi)^2} - \sinh(n\pi\chi) \right\} e^{-(\eta\kappa_M + (n\pi)^2)\tau} \tag{22}$$

$$v(\chi, \tau) \approx \frac{\cosh\left(\chi\sqrt{\kappa_E\left(1+\frac{\lambda\gamma}{\xi}\right)}\right)}{\cosh\left(\sqrt{\kappa_E\left(1+\frac{\lambda\gamma}{\xi}\right)}\right)} + \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)} \frac{e^{-(f_1(n))\tau/4} \kappa_E (\xi f_1(n) + 4(\xi + \lambda\gamma)) \cos(\chi(2n+1)\pi/2)}{f_1(n)} \tag{23}$$

$$w(\chi, \tau) \approx \frac{\cosh(\chi\sqrt{\varphi})}{\cosh(\sqrt{\varphi})} + \frac{1}{\pi \xi'} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)} \frac{e^{-(f_2(n))\tau/4} (4\varphi\xi' - (\xi'-1)f_2(n)) \cos(\chi(2n+1)\pi/2)}{f_2(n)} \tag{24}$$

The dimensionless current is given as follows:

$$\psi = \sqrt{\eta\kappa_M} \coth(\sqrt{\eta\kappa_M}) - 2 \sum_{n=1}^{\infty} (-1)^n \left\{ \frac{\eta\kappa_M (-1)^n}{\eta\kappa_M + (n\pi)^2} - 1 \right\} e^{-(\eta\kappa_M + (n\pi)^2)\tau} \tag{25}$$

Where,

$$f_1(n) = \pi^2(2n+1)^2 \xi + 4\kappa_E(\xi + \lambda\gamma), f_2(n) = 4\varphi + \pi^2(2n+1)^2, \varphi = \frac{\kappa_S}{\xi'(1+\beta)} \text{ and } \eta = \operatorname{sech}\left(\sqrt{\kappa_E\left(1+\frac{\lambda\gamma}{\xi}\right)}\right) \tag{26}$$

4. LIMITING CASES

Here we have derived the concentration of the mediator, enzyme and corresponding expression of current for various special cases.

4.1. Limiting case 1: Enzyme-mediator kinetics and high reaction rate

We begin by considering the case where $\xi = 1$, $\gamma \ll 1$ (enzyme-mediator reaction is rate limiting) and $\kappa_E \ll 1$ (the most E will escape from the diffusion layer before regenerated to E'). The rate of reaction is sufficiently high ($\kappa_M \gg 1$ and M will be more likely to react than escape). Since both u and v are less than unity, the term $\gamma \kappa_M u(\chi, \tau)v(\chi, \tau)$ and $\kappa_E \xi(1-v(\chi, \tau))$ are neglected. In this situation the Eqs. (15) and (16) becomes as follows:

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} - \kappa_M u(\chi, \tau)v(\chi, \tau) \tag{27}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} \tag{28}$$

Using the initial and boundary conditions (18-20), we can solve Eqs. (27) and (28) to obtain exact analytical expressions for mediator and enzyme concentrations (Appendix B).

$$u(\chi, \tau) = \frac{\sinh((1-\chi)\sqrt{\kappa_M})}{\sinh(\sqrt{\kappa_M})} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left[\frac{\kappa_M (\sin((\chi-1)n\pi))}{\kappa_M + (n\pi)^2} - \sin(n\pi\chi) \right] e^{-(\kappa_M + (n\pi)^2)\tau} \tag{29}$$

$$v(\chi, \tau) = 1 \tag{30}$$

The current becomes

$$\psi = \sqrt{\kappa_M} \coth(\sqrt{\kappa_M}) - 2 \sum_{n=1}^{\infty} (-1)^n \left[\frac{(-1)^n \kappa_M}{\kappa_M + n^2 \pi^2} - 1 \right] e^{-(\kappa_M + n^2 \pi^2)\tau} \tag{31}$$

The steady-state current $\psi_{ss} = \sqrt{\kappa_M}$ when $\gamma \ll 1$ and $\kappa_E \ll 1$. This is the limiting case I result of Bartlett et al. [39].

4.2. Limiting case 2: Enzyme-substrate kinetics and high rate of reaction

When the rate of reaction is sufficiently high ($\kappa_M \gg 1$ and M will be more likely to react than escape) and $\kappa_E \ll 1$ (the most E will escape from the diffusion layer before regenerated to E'), and $\gamma \gg 1$ (enzyme-substrate reaction is the rate limiting step), $\xi = 1$ (equal diffusion coefficients of enzyme and mediator), the nonlinear reaction diffusion equations (15-16) becomes as follows:

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} - \kappa_M u(\chi, \tau)v(\chi, \tau) \tag{32}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} - \gamma u(\chi, \tau)v(\chi, \tau) \tag{33}$$

The approximate expressions of mediator and enzyme concentrations are obtained by solving the above two equations with the boundary conditions (18-20).

$$u(\chi, \tau) \approx \frac{\sinh((1-\chi)\sqrt{\eta_0 \kappa_M})}{\sinh(\sqrt{\eta_0 \kappa_M})} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta_0 \kappa_M \sinh((\chi-1)n\pi)}{\eta_0 \kappa_M + (n\pi)^2} - \sinh(n\pi\chi) \right\} e^{-(\eta_0 \kappa_M + (n\pi)^2)\tau} \tag{34}$$

$$v(\chi, \tau) \approx \frac{\cosh(\chi\sqrt{\lambda\gamma})}{\cosh(\sqrt{\lambda\gamma})} + \frac{16\lambda\gamma}{\pi^3} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)^3} \left(1 + \frac{4\lambda\gamma}{f_3(n)}\right) \cos\left(\frac{(2n+1)\pi\chi}{2}\right) e^{-(f_3(n))\tau/4} \tag{35}$$

The current is

$$\psi = \sqrt{\eta_0\kappa_M} \coth(\sqrt{\eta_0\kappa_M}) - 2 \sum_{n=1}^{\infty} (-1)^n \left\{ \frac{\eta_0\kappa_M (-1)^n}{\eta_0\kappa_M + (n\pi)^2} - 1 \right\} e^{-(\eta_0\kappa_M + (n\pi)^2)\tau} \tag{36}$$

where $f_3(n) = \pi^2(2n+1)^2 + 4\lambda\gamma$, $\eta_0 = \operatorname{sech}(\sqrt{\gamma})$, $\lambda = \frac{\sinh(\sqrt{\eta_0\kappa_M}/2)}{\sinh(\sqrt{\eta_0\kappa_M})}$ (37)

When κ_M is very large and the maximum value of $\eta_0 = \operatorname{sech}(\sqrt{\gamma})=1$, from the Eq. (36) we get $\psi_{ss} = \sqrt{\kappa_M}$.

4.3. Limiting case 3: Enzyme-mediator kinetics and low reaction rate

When the rate of reaction is sufficiently low ($\kappa_M \ll 1$ and the most M escapes from the diffusion layer without reacting) and $\kappa_E \ll 1$ (the most E will escape from the diffusion layer before regenerated to E'), $\gamma \ll 1$ (enzyme-mediator reaction is rate limiting), the reaction diffusion equations (15-16) becomes

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} \tag{38}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} \tag{39}$$

Using the initial and boundary conditions (18-20), we get exact solution as follows:

$$u(\chi, \tau) = 1 - \chi - \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \sin(n\pi\chi) e^{-(n\pi)^2\tau} \tag{40}$$

$$v(\chi, \tau) = 1 \tag{41}$$

The current is

$$\psi = 1 + 2 \sum_{n=1}^{\infty} (-1)^n e^{-[n^2\pi^2]\tau} \tag{42}$$

When both $\gamma < 1$, $\kappa_M < 1$, the current for steady-state $\psi_{ss} = 1$. This result is also confirmed in Bartlett et al. [39]. Approximate analytical expressions of dimensionless concentrations and current for the above different limiting cases is also given Table. 1.

5. RESULT AND DISCUSSION

Equations (22), (23) and (24) are the new, general and simple analytical expressions of concentration profiles for the mediator (u), enzyme (v) and substrate (S) for transient conditions. Albery and co-workers [38], Bartlett and Pratt [39] derived the different approximate solutions for various limiting cases for steady-state only. Logambal and Rajendran [42] applied He's variational iteration

method to find an approximate analytical solution of steady-state nonlinear differential equations describing the transport and kinetics of the enzyme and of the mediator in the diffusion layer of the electrode. But in this method, it is very difficult to find the unknown parameter in the concentration.

We have also derived analytical expressions of concentration of mediator, enzyme and current for transient conditions for the three main limiting cases such as (i) Enzyme-mediator kinetics and high reaction rate, (ii) Enzyme-substrate kinetics and high rate of reaction, (iii) Enzyme-mediator kinetics and low reaction rate. Approximate analytical expressions of concentration of mediator and current are also validated with the numerical results and limiting case result in Tables 2-3 and Fig. 2. A satisfactory agreement is noted. Also, from the Table, it is observed that when the distance from the electrode surface increases, the concentration of mediator decreases.

Table 2. Comparison of dimensionless concentration of mediator, $u(\chi, \tau)$ (Eq.(25)) with simulation results for $\kappa_M = 1, \kappa_E = 1, \xi = 1, \gamma = 0.1$.

χ	$\tau = 0.05$			$\tau = 0.1$			$\tau = 5$				
	Num	Ana Eq. (25)	Error %	Num	Ana Eq. (25)	Error %	Num	Ana Eq. (25)	Error %		
0	1	1	0	1	1	0	1	1	0		
0.25	0.94	0.96	2.13	0.86	0.88	2.32	0.7	0.71	1.43		
0.5	0.84	0.85	1.11	0.67	0.69	2.98	0.44	0.46	4.54		
0.75	0.55	0.56	1.82	0.39	0.4	2.56	0.22	0.23	4.55		
1	0	0	0	0	0	0	0	0	0		
Average Error %			1.03	Average Error %			1.57	Average Error %			2.1

Table 3. Comparison of dimensionless concentration of mediator, $u(\chi, \tau)$ (Eq. (25)) with simulation results for $\kappa_M = 10, \kappa_E = 0.1, \xi = 1, \gamma = 0.1$.

χ	$\tau = 0.05$			$\tau = 0.1$			$\tau = 5$				
	Num	Ana Eq. (25)	Error %	Num	Ana Eq. (25)	Error %	Num	Ana Eq. (25)	Error %		
0	1	1	0	1	1	0	1	1	0		
0.25	0.68	0.69	1.47	0.54	0.54	1.85	0.45	0.45	0		
0.5	0.55	0.56	1.82	0.33	0.34	3.12	0.19	0.20	5.3		
0.75	0.35	0.36	2.86	0.17	0.18	5.88	0.075	0.08	6.7		
1	0	0	0	0	0	0	0	0	0		
Average Error %			1.23	Average Error %			2.2	Average Error %			2.4

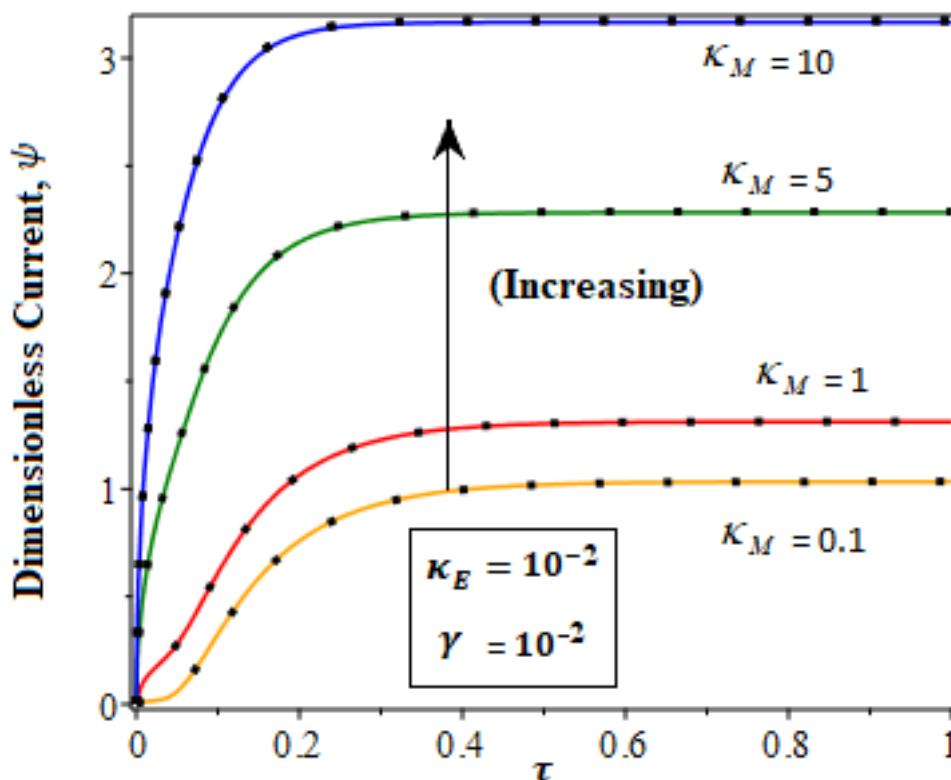


Figure 2. Comparison of dimensionless current, ψ (Eq. (25)) (solid line) with limiting current (Eq. (36)) (dotted line) versus dimensionless time, τ for all values of the parameter $\kappa_E = 10^{-2}$, $\gamma = 10^{-2}$, $\xi = 1$ and for different values of parameter κ_M .

Eq. (25) is the new expression of transient expression of current for all time in terms of parameter κ_M, κ_E, ξ , and γ . The parameter κ_M in these equations represents the chance of the mediator M escaping from the diffusion layer before reacting with the enzyme. If $\kappa_M > 1$, M is more likely to respond rather than escape. If $\kappa_M = 1$, the majority of M exits the diffusion layer without reacting.

Similarly, the κ_E describes the chance of enzyme E being converted to E' by substrate inside the diffusion layer. If $\kappa_E > 1$, the majority of E formed in the diffusion layer is transformed back to E' inside the layer. If $\kappa_E < 1$ is valid, the maximum of E will leave the diffusion layer before being regenerated to E' .

The local steady-state between the two enzyme forms at the electrode surface is defined by the parameter γ . If γ is less than unity ($\kappa_M < \kappa_E$), the predominant form E' at the electrode surface is the same as the bulk form. If γ is greater than unity, the predominant form at the electrode surface will be E ; somewhere in the diffusion layer, the predominant form will switch from E to E' if the kinetics are quick enough to maintain the steady-state. The transient current profiles for different values of the chemical reaction parameter κ_M, κ_E, ξ , and γ are displays in the Figs. 3(a-d). From Figures 3(a-d), it is inferred that, the value of the current increases when κ_M (dimensionless rate constant of mediator) and ξ (ratio of diffusion coefficients of the enzyme to the mediator) increases. It is also notice that an

increase in κ_E (dimensionless rate constant of enzyme) and γ (ratio of total concentration of the mediator to the enzyme) leads to decrease current values. Also the current reaches the steady-state value when $\tau > 0.5$ for all values of other parameters. The three-dimension plot (Fig.4(a-c)) of current versus other parameters also confirm this results.

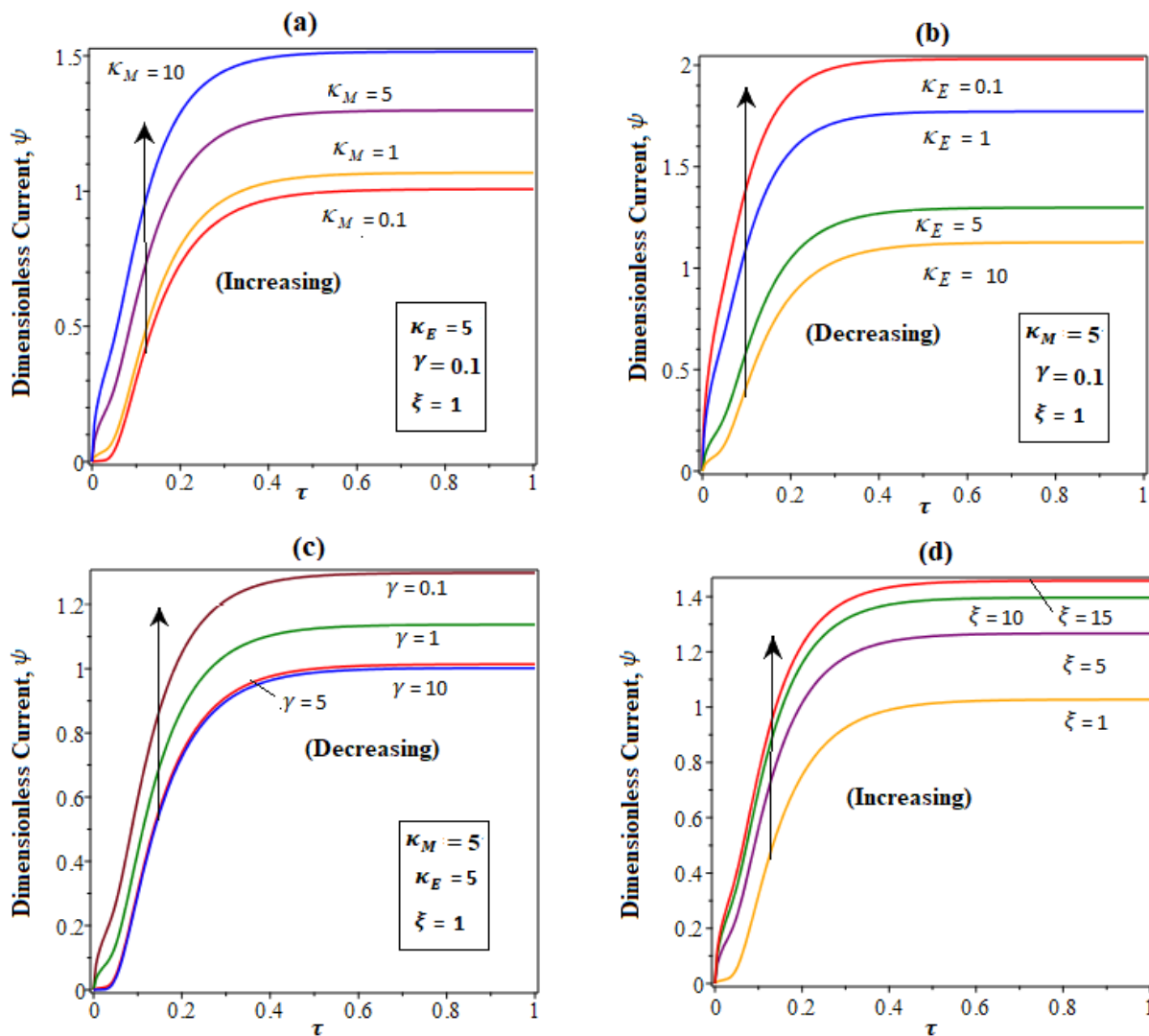


Figure 3. Dimensionless current, ψ (Eq.(25)) versus dimensionless time, τ for various values of the parameter (a) $\kappa_E = 5, \gamma = 0.1, \xi = 1$, and for different values of parameter κ_M . (b) $\kappa_M = 5, \gamma = 0.1, \xi = 1$, and for different values of parameter κ_E . (c) $\kappa_E = 5, \kappa_M = 5, \xi = 1$, and for different values of parameter γ . (d) $\kappa_M = 10, \kappa_E = 5, \gamma = 5$, and for different values of parameter κ_M .

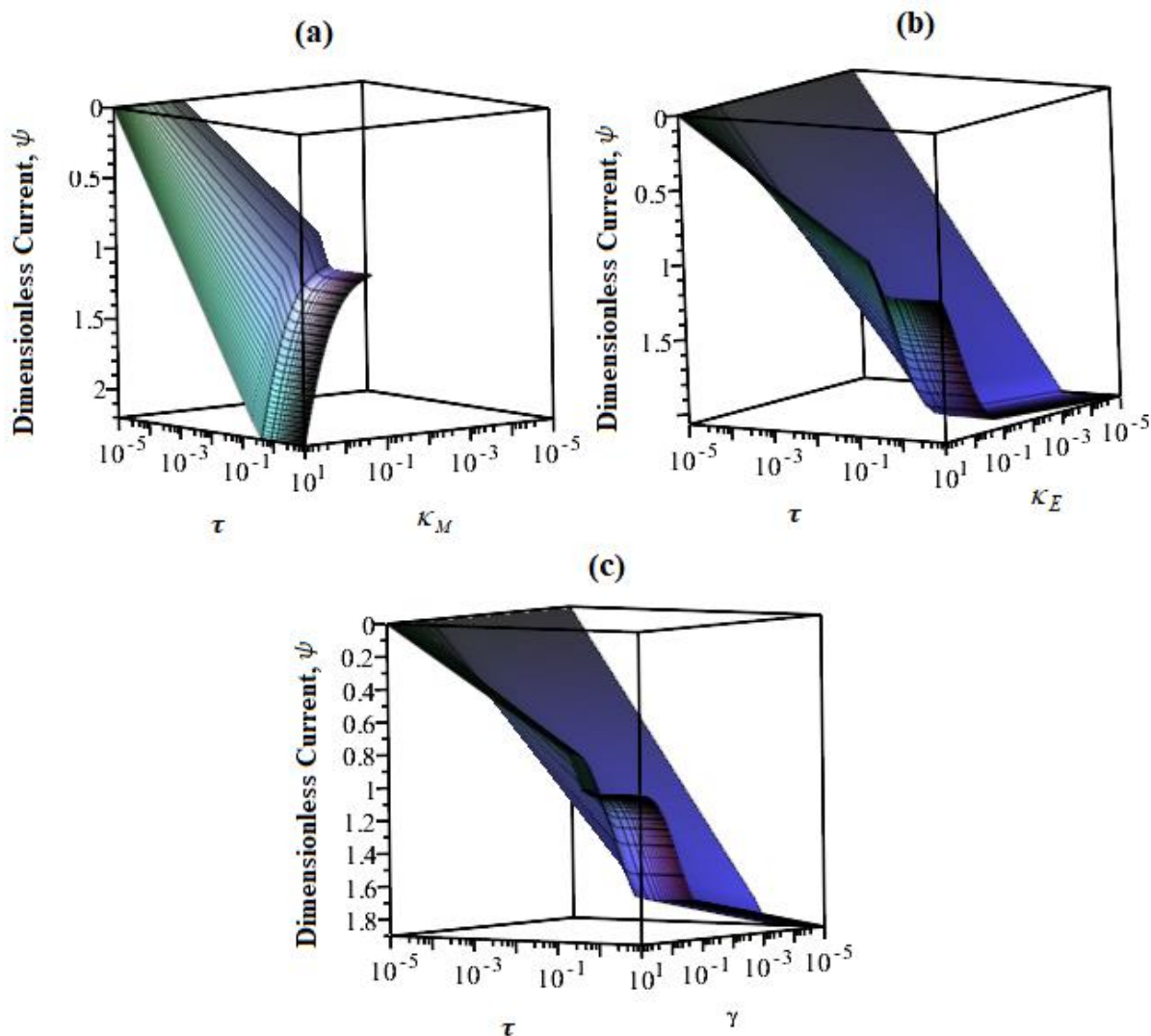


Figure 4. Three dimensionless plot of current (Eq. (25)) versus (a) κ_M and τ for $\kappa_E = 1, \xi = 1, \gamma = 0.1$. (b) κ_E and τ for $\kappa_M = 5, \xi = 1, \gamma = 0.1$. (c) γ and τ for $\kappa_E = 1, \xi = 1, \kappa_M = 5$.

6. CONCLUSIONS

The approximate solutions of a second-order system of nonlinear differential equations describing the transport and kinetics of the enzyme and the mediator in the diffusion layer of the electrode are derived. The exact (Limiting case-1 and 3) and approximate (Limiting case-2) analytical solutions of the diffusion-reaction equations for transient conditions are also provided. The simple closed-form of expressions of concentrations of mediator, enzyme and current are derived for all values of parameters. The numerical and analytical results are compared for some of the experimental value of the parameter. The Tables and figures show that analytical results are in good agreement with the simulation result.

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1. Analytical expressions of dimensionless concentrations and current for different cases.

Cases	Dimensionless concentration of mediator, $u(\chi, \tau)$	Dimensionless concentration of enzyme, $v(\chi, \tau)$	Dimensionless current, ψ
For all values of parameters	$\frac{\sinh\left(\frac{(1-\chi)\sqrt{\eta\kappa_M}}{\sqrt{\eta\kappa_M}}\right)}{\sinh\left(\frac{\sqrt{\eta\kappa_M}}{\sqrt{\eta\kappa_M}}\right)} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta\kappa_M \sinh((\chi-1)n\pi)}{\eta\kappa_M + (n\pi)^2} - \sinh(n\pi\chi) \right\} e^{-(\eta\kappa_M + (n\pi)^2)\tau}$	$\frac{\cosh\left(\chi \sqrt{\kappa_E} \left(1 + \frac{\lambda\gamma}{\xi}\right)\right)}{\cosh\left(\sqrt{\kappa_E} \left(1 + \frac{\lambda\gamma}{\xi}\right)\right)} + \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)} e^{-\frac{(f_1(n)\tau)^2}{4}} \frac{\kappa_E \left(\xi f_1(n) + 4(\xi + \lambda\gamma)\right) \cos\left(\frac{\chi(2n+1)\pi}{2}\right)}{f_1(n)}$	$\sqrt{\eta\kappa_M} \coth\left(\frac{\sqrt{\eta\kappa_M}}{\sqrt{\eta\kappa_M}}\right) - 2 \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta\kappa_M^{(-1)^n}}{\eta\kappa_M + (n\pi)^2} - 1 \right\} e^{-(\eta\kappa_M + (n\pi)^2)\tau}$
Limiting case 1 $\gamma \ll 1$, $\kappa_E \ll 1$, $\kappa_M \gg 1$, $\xi = 1$	$\frac{\sinh\left(\frac{(1-\chi)\sqrt{\kappa_M}}{\sqrt{\kappa_M}}\right)}{\sinh\left(\frac{\sqrt{\kappa_M}}{\sqrt{\kappa_M}}\right)} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left[\frac{\kappa_M \sin((\chi-1)n\pi)}{\kappa_M + (n\pi)^2} - \sin(n\pi\chi) \right] e^{-\left(\kappa_M + (n\pi)^2\right)\tau}$	1	$\sqrt{\kappa_M} \coth\left(\frac{\sqrt{\kappa_M}}{\sqrt{\kappa_M}}\right) - 2 \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left[\frac{\kappa_M^{(-1)^n}}{\kappa_M + n^2\pi^2} - 1 \right] e^{-\left(\kappa_M + n^2\pi^2\right)\tau}$
Limiting case 2 $\kappa_E \ll 1$, $\kappa_M \gg 1$, $\gamma \gg 1$, $\xi = 1$	$\frac{\sinh\left(\frac{(1-\chi)\sqrt{\eta_0\kappa_M}}{\sqrt{\eta_0\kappa_M}}\right)}{\sinh\left(\frac{\sqrt{\eta_0\kappa_M}}{\sqrt{\eta_0\kappa_M}}\right)} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta_0\kappa_M \sinh((\chi-1)n\pi)}{\eta_0\kappa_M + (n\pi)^2} - \sinh(n\pi\chi) \right\} e^{-(\eta_0\kappa_M + (n\pi)^2)\tau}$	$\frac{\cosh\left(\chi \sqrt{\lambda\gamma}\right)}{\cosh\left(\sqrt{\lambda\gamma}\right)} + \frac{16\lambda\gamma}{\pi^3} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)^3} \left(1 + \frac{4\lambda\gamma}{f_3(n)}\right) \cos\left(\frac{(2n+1)\pi\chi}{2}\right) e^{-\frac{(f_3(n)\tau)^2}{4}}$	$\sqrt{\eta_0\kappa_M} \coth\left(\frac{\sqrt{\eta_0\kappa_M}}{\sqrt{\eta_0\kappa_M}}\right) - 2 \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta_0\kappa_M^{(-1)^n}}{\eta_0\kappa_M + (n\pi)^2} - 1 \right\} e^{-(\eta_0\kappa_M + (n\pi)^2)\tau}$
Limiting case 3 $\gamma \ll 1$, $\kappa_M \ll 1$, $\kappa_E \ll 1$	$1 - \chi - \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \sin(n\pi\chi) e^{-(n\pi)^2\tau}$	1	$1 + 2 \sum_{n=1}^{\infty} \frac{(-1)^n}{n} e^{-\left[n^2\pi^2\right]\tau}$

where,

$$f_1(n) = \pi^2(2n+1)^2\xi + 4\kappa_E(\xi + \lambda\gamma), f_3(n) = \pi^2(2n+1)^2 + 4\lambda\gamma, \varphi = \frac{\kappa_S}{\xi'(1+\beta)}, \eta = \sec h\left(\sqrt{\kappa_E} \left(1 + \frac{\gamma}{\xi}\right)\right), \eta_0 = \sec h(\sqrt{\gamma}), \lambda = \frac{\sinh\left(\frac{\sqrt{\eta_0\kappa_M}}{\sqrt{\eta_0\kappa_M}}/2\right)}{\sinh\left(\frac{\sqrt{\eta_0\kappa_M}}{\sqrt{\eta_0\kappa_M}}\right)}$$

Table 4. Previous results of current by Bartlett et al. [39] for all limiting cases:

Limiting case	Dimensionless current	Dimension current
Case I : $\gamma \ll 1, \kappa_E \ll 1$ (Limiting case-1)	$\sqrt{\kappa_M}$	$nFAm_\Sigma \sqrt{D_M k_M e_\Sigma}$
Case IV: $\kappa_E \ll 1, \kappa_M \gg 1$	$\kappa_M / \gamma \kappa_E$	$nFAD_E e_\Sigma / Z_D$
Case VI: $\gamma \ll 1, \kappa_E \gg 1$	$\sqrt{2\kappa_M / \gamma}$	$nFA\sqrt{2D_M m_\Sigma k_E e_\Sigma}$
Case VII: $\kappa_E > 1, \kappa_M \gg 1$	$\kappa_M / \gamma \sqrt{\kappa_E}$	$nFAe_\Sigma \sqrt{D_E k_M}$
Case VIII: $\gamma < 1, \kappa_M < 1$ (Limiting case-3)	1	$nFAD_M m_\Sigma / Z_D$

NOMENCLATURE:

Parameter	Meaning	Units
M and M'	Mediator in oxidized and reduced form	-
E and E'	Enzyme in oxidized and reduced form	-
m and m'	Concentration of mediator in oxidized and reduced form	$mol\ cm^{-3}$
e and e'	Concentration of enzyme in oxidized and reduced form	$mol\ cm^{-3}$
S	Concentration of substrate	$mol\ cm^{-3}$
t	Time	s
k_M, k_E, k_{cat}	Rate constants	s^{-1}
D_M	Diffusion coefficients of species M, M'	$cm^2\ s^{-1}$
D_E	Diffusion coefficients of species E, E' .	$cm^2\ s^{-1}$
D_S	Diffusion coefficients of substrate	$cm^2\ s^{-1}$
m_Σ, e_Σ	Total concentration of mediator and enzyme	$mol\ cm^{-3}$
K_M	Michaelis–Menten constant	$mol\ cm^{-3}$
S_∞	Substrate concentration in the bulk solution	$mol\ cm^{-3}$
m'_∞	Concentration of reduced mediator in the bulk solution	$mol\ cm^{-3}$
m_0	Concentration of M at the electrode surface	$mol\ cm^{-3}$
Z_D	Levich diffusion layer thickness	m
ν	Kinematic viscosity	$cm^2\ s^{-1}$
W	Rotation speed	Hz
I	Current	μA
F	Faraday constant	$C\ mol^{-1}$
A	Universal gas constant	$J\ K^{-1}\ mol^{-1}$
u	Dimensionless concentration of the mediator	None
v	Dimensionless concentration of the enzyme	None
w	Dimensionless concentration of the substrate	None
χ	Dimensionless distance from the electrode/membrane interface	None
τ	Dimensionless time	None
γ	Ratio of the rates of the enzyme-substrate and	None

	enzyme-mediator reactions at the electrode surface	
ξ	Diffusion coefficient ratio of the enzyme to the mediator	None
ξ'	Diffusion coefficient ratio of the substrate to the mediator	None
κ_M	Dimensionless rate constant of the mediator	None
κ_E	Dimensionless rate constant of the enzyme	None
ψ	Dimensionless current	None

Appendix-A

We can construct the homotopy [17] for the equations (15-16) are as follows:

$$(1-p) \left[\frac{\partial u(\chi, \tau)}{\partial \tau} - \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} + \kappa_M u(\chi, \tau) v(x=0, \tau = \infty) \right] + p \left[\frac{\partial u(\chi, \tau)}{\partial \tau} - \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} + \kappa_M u(\chi, \tau) v(\chi, \tau) \right] = 0 \tag{A1}$$

$$(1-p) \left[\frac{\partial v(\chi, \tau)}{\partial \tau} - \xi \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} + \gamma \kappa_E u(\chi=1/2, \tau = \infty) v(\chi, \tau) - \kappa_E \xi (1-v(\chi, \tau)) \right] + p \left[\frac{\partial v(\chi, \tau)}{\partial \tau} - \xi \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} + \gamma \kappa_E u(\chi, \tau) v(\chi, \tau) - \kappa_E \xi (1-v(\chi, \tau)) \right] = 0 \tag{A2}$$

The approximate solution of Eq. (15) and Eq. (16) are

$$u = u_0 + pu_1 + p^2u_2 + \dots \tag{A3}$$

$$v = v_0 + pv_1 + p^2v_2 + \dots \tag{A4}$$

Substituting equations (A3) and (A4) into equations (A1) and (A2) and equating the coefficients of like powers of p , we get

$$p^0 : \frac{\partial^2 u_0(\chi, \tau)}{\partial \chi^2} - \frac{\partial u_0(\chi, \tau)}{\partial \tau} + \kappa_M u_0(\chi, \tau) v_0(0, \tau = \infty) = 0 \tag{A5}$$

$$p^0 : \frac{\partial^2 v_0(\chi, \tau)}{\partial \chi^2} - \frac{1}{\xi} \frac{\partial v_0(\chi, \tau)}{\partial \tau} - \frac{\gamma}{\xi} \kappa_E u\left(\frac{1}{2}, \tau = \infty\right) v_0(\chi, \tau) + \kappa_E (1-v_0(\chi, \tau)) = 0 \tag{A6}$$

For solving the above equations, we need to take Laplace transformation. Therefore, Eqs. (A5) and (A6) becomes,

$$\frac{d^2 \bar{u}_0(\chi, s)}{d\chi^2} - \eta \bar{u}_0(\chi, s) = -1 \tag{A7}$$

$$\frac{d^2 \bar{v}_0(\chi, s)}{d\chi^2} - \left(\frac{1}{\xi} (s + \lambda \gamma \kappa_E) + \kappa_E \right) \bar{v}_0(\chi, s) = -\frac{1}{\xi} - \kappa_E \tag{A8}$$

The corresponding boundary conditions are

$$\chi = 0, \bar{u}(0) = 1/s, \frac{d\bar{v}_0}{d\chi} = 0 \tag{A9}$$

$$\chi = 1, \bar{u}(1) = 0, \bar{v}_0 = 1/s \tag{A10}$$

where s is the Laplace variable and an over bar indicates a Laplace-transformed quantity, $\eta = v_0(0, \tau = \infty)$ and $\lambda = u_0(1/2, \tau = \infty)$ Solving the Eq. (A8), and using the boundary conditions and (A9) and (A10) we can find the following results

$$\bar{v}_0(\chi, s) = \left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right] \frac{\cosh\left(\left[\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right] \chi\right)}{\cosh\left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E}\right)} + \frac{1 + \kappa_E \xi}{s + \kappa_E \xi + \lambda \gamma \kappa_E} \tag{A11}$$

Now, we indicate how Eq. (A11) can be inverted using the complex inversion formula. If $\bar{y}(s)$ represents the Laplace transform of a function $y(\tau)$, then according to the complex inversion formula we can state that

$$y(\tau) = \frac{1}{2\pi \int_{c-i\infty}^{c+i\infty} \exp[s\tau] \bar{y}(s) ds} = \frac{1}{2\pi i} \oint_c \exp[s\tau] \bar{y}(s) ds \tag{A12}$$

where the integration in Eq. (A12) is to be performed along a line $s = c$ in the complex plane where $s = x + iy$. The real number c is chosen such that $s = c$ lies to the right of all the singularities, but is otherwise assumed to be arbitrary. In practice, the integral is evaluated by considering the contour integral presented on the right-hand side of Eq. (A12), which is then evaluated using the so-called Bromwich contour. The contour integral is then evaluated using the residue theorem which states for any analytic function $F(z)$.

$$\oint_c F(z) dz = 2\pi i \sum_n \text{Re } s[F(z)]_{z=z_0} \tag{A13}$$

where the residues are computed at the poles of the function $F(z)$. Hence from Eq. (A13), we note that

$$y(\tau) = \sum_n \text{Re } s[\exp[s\tau] \bar{y}(s)]_{s=s_0} \tag{A14}$$

From the theory of complex variables we can show that the residue of a function $F(z)$ at a simple pole at $z = a$ is given by

$$\text{Re } s[F(z)]_{z=a} = \lim_{z \rightarrow a} \{(z - a)F(z)\} \tag{A15}$$

Hence, in order to invert Eq. (A11), we need to evaluate

$$\text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right] + \text{Res} \left[\frac{1 + \kappa_E \xi}{s + \kappa_E \xi + \lambda \gamma \kappa_E} \right] \quad (\text{A16})$$

The poles are obtained from $s(s + \kappa_E \xi + \lambda \gamma \kappa_E) = 0$ and $\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right) = 0$. Hence there is

a simple pole at $s = 0$, $s = -(\kappa_E \xi + \lambda \gamma \kappa_E)$ and there are infinitely many poles given by the solution of

the equation $\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right) = 0$ and so $s_n = \frac{-\pi^2 (2n+1)^2 \xi}{4} - (\kappa_E \xi + \lambda \gamma \kappa_E)$ where $n = 0, 1, 2, \dots$. Hence we note that

$$\begin{aligned} & \text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s=0} \\ &= \text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \kappa_E \gamma) \lambda \gamma \kappa_E} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right] \\ &+ \text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s=-(\kappa_E \xi + \lambda \gamma \kappa_E)} + \text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \kappa_E \gamma}{s(s + \kappa_E \xi + \kappa_E \gamma)} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s=s_n} \end{aligned} \quad (\text{A17})$$

$$\begin{aligned} & \text{Res} \left[\frac{\left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right] \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s=0} \\ &= \lim_{s \rightarrow 0} \left(\frac{(s-0)e^{s\tau} (\kappa_E \xi (1-s) + \lambda \gamma \kappa_E) \cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E) \cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right) \\ &= \frac{\cosh \left(\chi \sqrt{\frac{\lambda \gamma \kappa_E}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{\lambda \gamma \kappa_E}{\xi} + \kappa_E} \right)} \end{aligned} \quad (\text{A18})$$

$$\begin{aligned}
 & \text{Res} \left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s = -(\kappa_E \xi + \lambda \gamma \kappa_E)} \\
 &= \lim_{s \rightarrow -(\kappa_E \xi + \lambda \gamma \kappa_E)} \left(\frac{(s + \kappa_E \xi + \lambda \gamma \kappa_E) e^{s\tau} (\kappa_E \xi (1-s) + \lambda \gamma \kappa_E) \cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E) \cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right) \\
 &= -e^{-(\kappa_E \xi + \lambda \gamma \kappa_E)\tau} (1 + \kappa_E \xi) \tag{A19}
 \end{aligned}$$

$$\begin{aligned}
 & \text{Res} \left[\frac{\kappa_E \xi (1-s) + \lambda \gamma \kappa_E}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \frac{\cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{\cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right]_{s = s_n} \\
 &= \lim_{s \rightarrow s_n} \left(\frac{(s - s_n) e^{s\tau} (\kappa_E \xi (1-s) + \lambda \gamma \kappa_E) \cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{s(s + \kappa_E \xi + \lambda \gamma \kappa_E) \cosh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right) \tag{A20}
 \end{aligned}$$

Applying L-Hospital rule in the above equation,

$$\begin{aligned}
 &= \lim_{s \rightarrow s_n} \left(2 \frac{e^{s\tau} (\kappa_E \xi (1-s) + \lambda \gamma \kappa_E) \cosh \left(\chi \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)}{s \sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \sinh \left(\sqrt{\frac{(s + \lambda \gamma \kappa_E)}{\xi} + \kappa_E} \right)} \right) \\
 &= \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)} \frac{e^{-(f_1(n))\tau/4} (\kappa_E \xi f_1(n) + 4(\kappa_E \xi + \lambda \gamma \kappa_E)) \cos(\chi (2n+1)\pi/2)}{f_1(n)} \tag{A21}
 \end{aligned}$$

$$\begin{aligned}
 \text{Res} \left[\frac{1 + \kappa_E \xi}{s + \kappa_E \xi + \lambda \gamma \kappa_E} \right]_{s = -(\kappa_E \xi + \lambda \gamma \kappa_E)} &= \lim_{s \rightarrow -(\kappa_E \xi + \lambda \gamma \kappa_E)} \left(\frac{(s + \kappa_E \xi + \lambda \gamma \kappa_E) e^{s\tau} (1 + \kappa_E \xi)}{(s + \kappa_E \xi + \lambda \gamma \kappa_E)} \right) \\
 &= e^{-(\kappa_E \xi + \lambda \gamma \kappa_E)\tau} (1 + \kappa_E \xi) \tag{A22}
 \end{aligned}$$

$$v(\chi, \tau) \approx \frac{\cosh \left(\sqrt{\frac{\lambda \gamma \kappa_E}{\xi} + \kappa_E} \chi \right)}{\cosh \left(\sqrt{\frac{\lambda \gamma \kappa_E}{\xi} + \kappa_E} \right)} + \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{(2n+1)} \frac{e^{-(f_1(n))\tau/4} (\kappa_E \xi f_1(n) + 4(\kappa_E \xi + \lambda \gamma \kappa_E)) \cos(\chi (2n+1)\pi/2)}{f_1(n)}$$

$$(A23)$$

Where, $f_1(n) = \pi^2(2n+1)^2 \xi + 4(\kappa_E \xi + \lambda \gamma \kappa_E)$

Using Eq. (A23), Eq. (A7) can be written as follows

$$\frac{d^2 \bar{u}_0(\chi)}{d\chi^2} - (s + \eta \kappa_M) \bar{u}_0(\chi) = -1 \tag{A24}$$

Where $\eta = \frac{1}{\cosh\left(\sqrt{\kappa_E \left(1 + \frac{\gamma}{\xi}\right)}\right)}$ (A25)

On solving Eq. (A24), we get

$$\bar{u}_0(\chi, \tau) = \frac{1}{s + \eta \kappa_M} - \frac{\eta \kappa_M \sinh\left((\chi - 1)\sqrt{s + \eta \kappa_M}\right)}{s(s + \eta \kappa_M) \sinh\left(\sqrt{s + \eta \kappa_M}\right)} - \frac{\sinh\left(\chi \sqrt{s + \eta \kappa_M}\right)}{(s + \eta \kappa_M) \sinh\left(\sqrt{s + \eta \kappa_M}\right)} \tag{A26}$$

Applying the complex inversion formula for the above equation similar to Eq. (A11) we get,

$$u(\chi, \tau) \approx \frac{\sinh\left((1 - \chi)\sqrt{\eta \kappa_M}\right)}{\sinh\left(\sqrt{\eta \kappa_M}\right)} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left\{ \frac{\eta \kappa_M \sinh\left((\chi - 1)n\pi\right)}{\eta \kappa_M + (n\pi)^2} - \sinh(n\pi\chi) \right\} e^{-(\eta \kappa_M + (n\pi)^2)\tau} \tag{A27}$$

Appendix B:

For the limiting case 1 (Enzyme-mediator kinetics and low reaction rate), the equation for the concentration of mediator and enzyme are given by

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} - \kappa_M u(\chi, \tau) v(\chi, \tau) \tag{B1}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} \tag{B2}$$

with boundary conditions

$$\tau = 0, \quad u = 1, \quad v = 1 \tag{B3}$$

$$\chi = 1, \quad u = 0, v = 1 \tag{B4}$$

$$\chi = 0, \quad u = 1, \quad \frac{\partial v}{\partial \chi} = 0 \tag{B5}$$

The Laplace transformation for the Eq. (B2) is as follows:

$$\frac{d^2 \bar{v}(\chi, s)}{d\chi^2} - s \bar{v}(\chi, s) = -1 \tag{B6}$$

The corresponding boundary conditions are

$$\left. \frac{d\bar{v}}{d\chi} \right|_{\chi=0} = 0, \quad \bar{v}(1) = 1/s \tag{B7}$$

On solving Eq. (B6) with respect to the boundary conditions (B7), we get

$$\bar{v}(\chi, s) = 1/s \tag{B8}$$

Using the complex inversion formula, Eq. (B8) becomes

$$v(\chi, \tau) = 1 \tag{B9}$$

Substituting Eq. (B9) in Eq. (B1) we get the following equation,

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} - \kappa_M u(\chi, \tau) \tag{B10}$$

The Laplace transformation for the above equation is as follows:

$$\frac{d^2 \bar{u}(\chi, s)}{d\chi^2} - (s + \kappa_M) \bar{u}(\chi, s) = -1 \tag{B11}$$

With the corresponding boundary condition

$$\bar{u}(0) = 1/s, \quad \bar{u}(1) = 0 \tag{B12}$$

On solving Eq. (B11) with respect to the boundary condition (B12), we get

$$\bar{u}(\chi, \tau) = \frac{1}{s + \kappa_M} - \frac{\kappa_M \sinh((\chi - 1)\sqrt{s + \kappa_M})}{s(s + \kappa_M) \sinh(\sqrt{s + \kappa_M})} - \frac{\sinh(\chi\sqrt{s + \kappa_M})}{(s + \kappa_M) \sinh(\sqrt{s + \kappa_M})} \tag{B13}$$

Applying the complex inversion formula for the above equation we get,

$$u(\chi, \tau) = \frac{\sinh((1 - \chi)\sqrt{\kappa_M})}{\sinh(\sqrt{\kappa_M})} + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \left[\frac{\kappa_M (\sin((\chi - 1)n\pi))}{\kappa_M + (n\pi)^2} - \sin(n\pi\chi) \right] e^{-(\kappa_M + (n\pi)^2)\tau} \tag{B14}$$

For the limiting case 3 (Enzyme-mediator kinetics and high reaction rate), the equation for the concentration of mediator and enzyme are given by

$$\frac{\partial u(\chi, \tau)}{\partial \tau} = \frac{\partial^2 u(\chi, \tau)}{\partial \chi^2} \tag{B15}$$

$$\frac{\partial v(\chi, \tau)}{\partial \tau} = \frac{\partial^2 v(\chi, \tau)}{\partial \chi^2} \tag{B16}$$

The Laplace transformation for the above equations are as follows:

$$\frac{d^2 \bar{u}(\chi, s)}{d\chi^2} - s \bar{u}(\chi, s) = -1 \tag{B17}$$

$$\frac{d^2 \bar{v}(\chi, s)}{d\chi^2} - s \bar{v}(\chi, s) = -1 \quad (\text{B18})$$

The boundary conditions are as follows:

$$\bar{u}(0) = 1/s, \quad \bar{u}(1) = 0 \quad (\text{B19})$$

$$\left. \frac{d\bar{v}}{d\chi} \right|_{\chi=0} = 0, \quad \bar{v}(1) = 1/s \quad (\text{B20})$$

On solving Eq. (B17) and Eq. (B18) with respect to the above boundary conditions, we get

$$\bar{u}(\chi, s) = \frac{1}{s} - \frac{\sinh(\chi\sqrt{s})}{s \sinh(\sqrt{s})} \quad (\text{B21})$$

$$\bar{v}(\chi, s) = 1/s \quad (\text{B22})$$

Using the complex inversion formula, the above two equations becomes,

$$u(\chi, \tau) = 1 - \chi - \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{(-1)^n}{n} \sin(n\pi\chi) e^{-(n\pi)^2 \tau} \quad (\text{B23})$$

$$v(\chi, \tau) = 1 \quad (\text{B24})$$

Appendix C. Illustrative Matlab code.

Matlab coding for Eq. (15) and Eq. (16):

```
function pdex4
m = 0;
x = linspace(0,1);
t = linspace(0,10);
sol = pdepe(m,@pdex4pde,@pdex4ic,@pdex4bc,x,t);
u1 = sol(:,:,1);
u2 = sol(:,:,2);
figure
plot(x,u1(end,:))
% cftool(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;
```

```

km=10;
r=5;
ke=0.1;
e=1;
F1 = -km*u(1)*u(2);
F2 = -r*ke*u(1)*u(2)+ke*e*(1-u(2));
s = [F1;F2];
function u0 = pdex4ic(x)
u0 = [1; 1];
function [pl,ql,pr,qr] = pdex4bc (xl,ul,xr,ur,t)
pl = [ul(1)-1;0];
ql = [0;1];
pr = [ur(1);ur(2)-1];
qr = [0; 0];

```

Matlab coding for Eq. (22):

```

function umani
x=linspace(0,1);
km =10; % parameter
gamma=5;
ke=0.1;
e=1;
t = 0.1;
s = 0; % initial sum
N = 100;% number of terms
for n = 1: N;
L = 1/cosh((gamma*ke/e+ke)^(1/2));
s = s+((-1)^n)/n*((L*km)*(sin((x-1)*n*pi))/(L*km+(n*pi)^2)-sin(n*pi*x))*exp(-
t*(L*km+(n*pi)^2));
u = sinh((1-x)*((L*km)^(1/2)))/sinh((L*km)^(1/2))+2/pi*s;
plot(x,u);
end

```

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