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Research Article

# Theoretical Analysis of Pre-Steady State Behaviour of Non-Linear Double Intermediate Enzymatic Reaction

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**Abstract:** This paper explores the mathematical modelling of a non-linear double intermediate enzymatic reaction, focusing on its pre-steady state behaviour. Using homotopy perturbation and Taylor's series methods, an approximate analytical solution is derived for the concentrations of substrate, the first enzyme-substrate complex, and the second enzyme-substrate complex. The model is applicable in scenarios where the initial substrate concentration dramatically exceeds that of the enzyme and when they are comparable. Comparisons between analytical and numerical solutions are made, highlighting the efficacy of the proposed model. Additionally, an improved understanding is achieved by comparing results obtained from Matlab simulations with analytical solutions. Moreover, sensitivity analysis on parameters affecting the concentrations is conducted. This mathematical model enhances comprehension of biochemical reactions in living organisms.

***Keywords*:** homotopy perturbation method, Taylor's series method, pre-steady state, double intermediate, non-linear equations

**MSC:** 34A34, 34B15, 34B18, 34B60

## 1. Introduction

The majority of chemical conversion in biochemistry, the food industry, chemical reactions, and biological processes take place with the help of proteins called enzymes [1]. Enzymes are made up of amino acids. It is used as a catalyst in the chemical reaction to speed up the reaction rate without being altered in the process between reactants and products. A particular enzyme is used to increase the reaction rate of a specific reaction. During the enzymatic reaction, the enzyme communicates with the substrate and changes shape. When the catalysis begins, the substrate is completely secured inside the enzyme in an accurate position like a lock and key. This model is called as lock and key model. It was first proposed in 1894 [2]. The pre-steady state kinetics studies the reaction in which no products and intermediates are formed after an enzyme is mixed with the substrate.

In biochemistry, many proteins are connected with the Michaelis-Menten model [3], which makes sense of the playful way of behaving in enzyme response. It depends on the understanding that Enzyme (E) responds with the Substrate (S)


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to frame a catalyst-substrate complex (ES) by the reversible response. The complex (ES) is isolated into Product (P), invigorating the catalyst.

$$E + S \underset{r_{-1}}{\overset{r1}{\longleftrightarrow}} ES \overset{r2}{\leftrightarrow} E + P$$

Where $r_1$, $r_{-1}$ and $r_2$ are the rate constants of reaction.

## 1.1 *Related works*

Effective mathematical modelling serves as a valuable tool for elucidating enzymatic reaction processes. Since direct analytical solutions are unavailable for many non-linear enzymatic reaction equations, employing approximate analytical methods such as the variational iteration method (VIM) [4, 5], Akbari Ganji method (AGM) [6, 7], differential transform method (DTM) [8, 9], homotopy perturbation method (HPM) [10, 11], and homotopy analysis method (HAM) [12, 13] becomes essential for obtaining analytical solutions. Most realistic models across chemistry, engineering, biology, and physics exhibit nonlinearity, making obtaining analytical solutions for such systems impractical. Non-linear partial differential equations (PDEs) typically require numerical solution methods, as they lack analytical solutions. Consequently, numerical solutions offer a significant advantage in efficiently tackling non-linear PDEs. However, the effectiveness of numerical solutions hinges upon crucial factors such as consistency, stability, convergence, and accuracy, which are essential characteristics that must be met.

Over the last two decades, researchers have created numerous mathematical models to study non-linear enzymatic reaction processes [14]. Syed Ibrahim and colleagues [15] constructed a mathematical model for non-linear enzyme reaction processes employing the variational iteration method. Mary and co-authors [16] formulated and analyzed a mathematical model for non-linear enzyme catalyst reaction processes employing the homotopy perturbation method. Thangapandi et al. [17] utilized the homotopy perturbation method to address the non-linear boundary value problem concerning enzyme-substrate chemical reactions.

## 1.2 *Innovative contribution*

Frenzen and Maini [18] developed a mathematical model for enzyme kinetics with two intermediates in an enzymatic reaction. To our knowledge, no rigorous analytical expression for pre-steady-state substrate concentrations, the first enzyme-substrate complex, and the second enzyme-substrate complex has been reported in previous studies. This is the first attempt to solve this mathematical model analytically. To determine the accuracy and efficiency of the proposed methods, we compare our analytical results to the numerical simulation results obtained by the MATLAB software. Generally, most mathematical models involve the reaction with single intermediates, but this is the first to calculate the analytical expressions for the double intermediates.

The primary objective is to illustrate the application of these concepts to a biological reaction involving two intermediates, especially when the conventional formulation is inadequate, such as when the initial substrate concentration is minimal. These challenges are particularly relevant in vivo, where the ratio frequently approaches unity. The transformation of one molecule into another within a cell constitutes a biological process often facilitated by enzymes.

In this study, we introduce a simple and approximate polynomial equation for the concentrations. Despite two intermediate phases in the reaction, the methodology employed in this study can also be extrapolated to other biochemical reactions. We employ homotopy perturbation and Taylor's series method to examine the dynamics of the reaction-diffusion and rate constant parameters. Below are listed some characteristics of the HPM:

- Researchers and practitioners can use HPM because it is comparatively simple.
- It can be used to solve various kinds of science and engineering issues, including integral, partial, and linear and nonlinear equations.

• In contrast to strictly numerical approaches, the homotopy perturbation approach offers analytical approximations that can shed light on the behaviour of the system under study.

• The approach enables a step-by-step solution process by following a methodical technique that includes building a homotopy and the perturbation series.

• The homotopy perturbation approach applies to a broader range of problems than standard perturbation methods since it does not necessitate a small parameter assumption.

• Compared to purely numerical approaches, it can produce correct results with comparatively few repetitions, potentially lowering processing effort.

The Key characteristics of the Taylor series method are:

• The mathematical idea of expanding a function into an infinite sum of terms serves as the foundation for the Taylor series approach.

• It uses derivatives of the function at that place to create a local approximation of a function around that point.

• The degree of approximation accuracy is contingent upon the number of terms contained in the series expansion and the distance between the expansion point and the point of interest.

• The behaviour of the function and its derivatives determines the radius of convergence, within which the convergence of the Taylor series approach is assured.

• It can be used for a variety of tasks and issues, such as differential equation solutions that are both analytical and numerical.

• Using the method's error analysis feature, practitioners can determine the accuracy of the approximation and modify the expansion accordingly.

• Implementing Taylor series expansions, particularly for low-order and simple functions, can be easy.

• Partial derivatives can extend the Taylor series method to multivariate functions, allowing it to be used for multidimensional issues.

This paper focuses on non-linear ordinary differential equations of double intermediate in an enzymatic reaction. Analytical expressions for the concentrations of substrate, first enzyme-substrate complex, and second enzyme-substrate complex under pre-steady state conditions are performed using HPM and TSM for different parameter values. A better understanding is noted in examining numerical solutions obtained by MATLAB software and mathematical recreation. Furthermore, sensitivity analysis for the concentrations of substrate, first enzyme-substrate complex and second enzyme-substrate complex are also obtained for reaction-diffusion and rate constant parameters. Since the initial enzyme-to-substrate concentration ratio is frequently ordered as one, this mathematical model may be helpful for biochemical reactions that occur in living organisms.

## 2. Mathematical formulation of the problem

Consider a double intermediate enzyme-catalyst reaction [18, 19]

$$E + S \underset{k_{-1}}{\overset{k_1}{\longleftrightarrow}} Y \xrightarrow{k_2} Z \xrightarrow{k_3} E + P$$

Here an Enzyme (E) binds with the Substrate (S) by a reversible reaction to form an intermediate first Enzyme-Substrate complex (Y). Again, the complex Y is converted into a second Enzyme-Substrate complex (Z) by the irreversible transformation, which in turn splits up into the original Enzyme (E) and Product (P). $k_1, k_{-1}, k_2,$ and $k_3$ represents the rate constants of the reaction. By our assumption, the rate constants of $k_{-2}$ Z and $k_{-3}$P are small compared to other reaction rates, so these steps are taken as irreversible.

The law of mass action describes the reaction as the following differential equation:

$$\frac{dS}{dt} = -k_1SE + k_{-1}Y \tag{1}$$

$$\frac{dE}{dt} = -k_1SE + k_{-1}Y + k_3Z \tag{2}$$

$$\frac{dY}{dt} = k_1SE - k_{-1}Y - k_2Y \tag{3}$$

$$\frac{dZ}{dt} = k_2Y - k_3Z \tag{4}$$

$$\frac{dP}{dt} = k_3Z \tag{5}$$

With condition,

$$E(0) = E_0,\ S(0) = S_0,\ Y(0) = 0,\ Z(0) = 0,\ P(0) = 0. \tag{6}$$

The conservation equations for the system (1, 2, 3, 4, 5) with initial conditions (6) are as follows:

$$E + Y + Z = E_0,\ S + Y + Z + P = S_0 \tag{7}$$

By adding (4) and (5), we get

$$\frac{dZ}{dt} + \frac{dP}{dt} = k_2Y \tag{8}$$

Following the pre-steady state period, the reaction rate of the combination $p+2$ stabilizes, resulting in an approximately constant concentration of the first enzyme-substrate complex (y).

Therefore, we get $\frac{dY}{dt} = 0$ By using $\frac{dY}{dt} = 0$ and (7), we get $Y$ in terms of $S$ and $Z$ as

$$Y = \frac{(E_0 - Z)S}{(K + S)} \tag{9}$$

Where,

$$K = \frac{(k_{-1} + k_2)}{k_1} \tag{10}$$

As per (9), the variable reaches a steady state concerning the present values of $s$ and $z$. (1) and (4) dictate $s$ and $z$'s evolution. However, maintaining the heuristic argument presented above becomes difficult due to uncertainty about

the relative magnitudes of different variables in these equations. In specific scenarios, $z$ might be disregarded since it is expected to be considerably smaller than the (9) expression. Utilizing (9) in conjunction with Eqn (1) yields.

$$\frac{dS}{dt} = -\frac{k_2 E_0 S}{(K+S)} \tag{11}$$

We can employ the initial conditions $S(0) = S_0$ and (11) to ascertain $S$, under the presumption of a slight fluctuation in substrate concentration during the pre-steady state phase. The course of action when comparing $Z$ to $E_0$ is still under consideration. It's important to note that $Z$ should exhibit a rapid increase from its initial value of zero during the pre-steady state phase, as the sum of $P+Z$, when combined with (4) and (5), is proportional to $Y$. To progress systematically, the system needs to be nondimensionalized at this stage. Simplifying the problem into a set of differential equations is crucial to eliminate $E$ by utilizing 7 and to determine $P$ if $Z$ is known, as indicated in (4).

$$\frac{dS}{dt} = -k_1 S(E_0 - Y - Z) + k_{-1} Y. \tag{12}$$

$$\frac{dY}{dt} = -k_1 S(E_0 - Y - Z) - (k_{-1} + k_2) Y. \tag{13}$$

$$\frac{dZ}{dt} = k_2 Y - k_3 Z \tag{14}$$

With initial conditions,

$$S(0) = S_0, Y(0) = 0, Z(0) = 0. \tag{15}$$

(12)-(14) were made dimensionless form by using the following parameters:

$$S = \alpha s, Y = \lambda y, Z = \pi z, t = y\tau, \pi = E_0, \alpha = S_0, \lambda = \frac{(E_0 S_0)}{S_0 + K}, \eta = \frac{S_0}{K}, k = \frac{k_{-1}}{k_2}, \beta = k_3 k_{-1} + k_2 \tag{16}$$

The system of (12)-(14) in dimensionless form becomes as follows:

$$\frac{ds}{dt} = -\mu s(\tau) + \frac{\eta}{1+\eta}\mu s(\tau) y(\tau) + \mu s(\tau) z(\tau) + \frac{\mu k}{(1+k)(1+\eta)} y(\tau) \tag{17}$$

$$\frac{dy}{dt} = s(\tau) - \frac{\eta}{1+\eta} s(\tau) y(\tau) - s(\tau) z(\tau) - \frac{1}{(1+\eta)} y(\tau) \tag{18}$$

$$\frac{dz}{dt} = \frac{\eta}{(1+\eta)^2 (1+k)} y(\tau) - \frac{\beta}{(1+\eta)} z(\tau), \tag{19}$$

With conditions

$$s(0) = 1, y(0) = 0, z(0) = 0 \tag{20}$$

## 3. Homotopy Perturbation Method (HPM)

HPM is a dynamical and well-organized method for determining the solutions of both linear and non-linear ordinary/ partial differential equations. It was proposed by He [20]. The Homotopy Perturbation Method (HPM) combines elements of traditional perturbation methods with concepts from homotopy theory in topology. Unlike traditional perturbation methods, HPM doesn't necessitate a small parameter in equations. This characteristic grants it a notable advantage, as it can furnish analytical approximations for various non-linear problems encountered in applied sciences.

In contrast to many other numerical techniques, HPM does not require the linearization of the non-linear equations before solving. This streamlines the solution procedure while maintaining the equations' original form. The primary benefit of HPM is its capacity to yield precise analytical approximations for non-linear problems with minimum processing overhead, rendering it an invaluable instrument in scientific investigations and engineering contexts. Nowadays, HPM is used for solving time-dependent problems [21] and several non-linear equations, such as the Blasius equation, duffing equation [22], boundary value problems [23], and Lane Emden equation [24] etc... In recent years, many authors have contributed more to solving non-linear equations by utilizing HPM [25, 26]. Noeiaghdam et al. [27] introduced a dynamic approach based on the homotopy perturbation method for solving second-kind integral equations, employing the CESTAC method. Samad Noeiaghdam and collaborators [28] examined the error estimation of the homotopy perturbation method for solving second-kind Volterra integral equations featuring piecewise smooth kernels, utilizing the CADNA Library.

By employing this HPM, the following solution can be obtained for the concentrations of substrate, the first enzyme-substrate complex, and the second enzyme-substrate complex:

Substrate

$$(1-p)\left(\frac{ds}{d\tau} + \mu s(\tau)\right) + p\left(\frac{ds}{d\tau} + s(\tau)\mu - \frac{\eta}{1+\eta}s(\tau)y(\tau)\mu - s(\tau)z(\tau)\mu - \frac{k\mu y(\tau)}{(1+k)(1+\eta)}\right) = 0 \tag{21}$$

First enzyme-substrate complex

$$(1-p)\left(\frac{dy}{d\tau} + \frac{y(\tau)}{1+\eta}\right) + p\left(\frac{dy}{d\tau} + \frac{y(\tau)}{1+\eta} - s(\tau) + \frac{\eta}{1+\eta}s(\tau)y(\tau) + s(\tau)z(\tau)\right) = 0 \tag{22}$$

Second enzyme-substrate complex

$$(1-p)\left(\frac{dz}{d\tau} + \frac{\beta z(\tau)}{(1+\eta)}\right) + p\left(\frac{dz}{d\tau} + \frac{\beta z(\tau)}{(1+\eta)} - \frac{\eta y(\tau)}{(1+k)(1+\eta)^2}\right) = 0 \tag{23}$$

The initial conditions are as follows:

$$s(0) = 1, y(0) = 0, z(0) = 0 \tag{24}$$

The approximate solutions of (21)-(23) are

$$s = s_0 + ps_1 + p^2 s_2 + p^3 s_3 + , \tag{25}$$

$$y = y_0 + py_1 + p^2 y_2 + p^3 y_3 + , \tag{26}$$

$$z = z_0 + pz_1 + p^2 z_2 + p^3 z_3 + , \tag{27}$$

substituting (25)-(27) in (21)-(23) and equating the coefficients of powers of $p$, we get,

For substrate concentration ($s$)

$$p^0: \frac{ds_0}{d\tau} + \mu s_0(\tau) = 0$$

$$p^1: \frac{ds_1}{d\tau} + \mu s_1(\tau) - \frac{\eta}{1+\eta} s_0(\tau) y_0(\tau)\mu - s_0(\tau) z_0(\tau)\mu - \frac{k\mu y_0(\tau)}{(1+k)(1+\eta)} = 0$$

$$p^2: \frac{ds_2}{d\tau} + \mu s_1(\tau) - \frac{\eta}{1+\eta} s_0(\tau) y_1(\tau)\mu - s_0(\tau) z_1(\tau)\mu - \frac{k\mu y_1(\tau)}{(1+k)(1+\eta)} = 0 \tag{28}$$

For first enzyme-substrate complex ($y$)

$$p^0: \frac{dy_0}{d\tau} + \frac{y_0(\tau)}{1+\eta} = 0$$

$$p^1: \frac{dy_1}{d\tau} + \frac{y_1(\tau)}{1+\eta} - s_0(\tau) + \frac{\eta}{1+\eta} s_0(\tau) y_0(\tau) + s_0(\tau) z_0(\tau) = 0$$

$$p^2: \frac{dy_2}{d\tau} + \frac{y_1(\tau)}{1+\eta} - s_1(\tau) + \frac{\eta}{1+\eta} s_0(\tau) y_1(\tau) - s_0(\tau) z_1(\tau) = 0 \tag{29}$$

For second enzyme-substrate complex ($z$)

$$p^0: \frac{dz_0}{d\tau} + \frac{\beta z_0(\tau)}{1+\eta} = 0$$

$$p^1: \frac{dz_1}{d\tau} + \frac{\beta z_1(\tau)}{1+\eta} - \frac{\eta y_0(\tau)}{(1+\eta)^2(1+k)} = 0$$

$$p^2: \frac{dy_2}{d\tau} + \frac{\beta z_2(\tau)}{1+\eta} - \frac{\eta y_1(\tau)}{(1+\eta)^2(1+k)} = 0 \tag{30}$$

Solving (28)-(30) by using conditions (24), we get

$$s_0(\tau) = e^{-\mu\tau},$$

$$s_1(\tau) = 0,$$

$$s_2(\tau) = \frac{k(\mu+\mu^2)}{(1+k)(\mu\eta+\eta-1)(\mu^2+\mu-1)}\left[e^{\frac{\tau(\mu^2+\mu-1)}{\mu+1}-t\mu} - e^{-\mu t}\right] - \frac{\eta(\mu+\mu^2)}{\mu\eta+\mu-1}\left[e^{-\mu t} - e^{t(-\mu)}\right.$$

$$\left. - \frac{t}{\mu+1}\right] + \frac{\eta}{\mu\eta+\mu-1}\left[e^{-2\mu t} - e^{-\mu t}\right] - \frac{tk\mu e^{-\mu t}}{(1+k)(\mu\eta+\mu-1)},$$

$$y_0(\tau) = 0$$

$$y_1(\tau) = \frac{\eta+1}{\mu\eta+\mu-1}\left[e^{-\frac{\tau}{(\mu+1)}} - e^{-\mu\tau}\right],$$

$$y_2(\tau) = \frac{2\eta^2+2\eta-\eta/\mu}{(\mu\eta+\mu-1)(2(\eta+1)\mu-1)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right]$$

$$- \frac{\eta^2+\eta}{(\eta\mu+\mu-1)(2(\eta+1)\mu-1)}\left[e^{\tau(\frac{1}{\eta+1}-\mu)} - e^{\frac{\tau}{(\tau+1)}}\right]$$

$$z_0(\tau) = 0,$$

$$z_1(\tau) = 0,$$

$$z_2(\tau) = \frac{\eta(1+\eta+\mu+\eta\mu)}{(1+\eta)(k+1)(\mu\eta+\mu-1)(-\eta+\eta\mu+\mu-\beta)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right],$$

$$+ \frac{\eta^2+\eta}{(1+\eta)(k+1)(\mu\eta+\mu-1)(\eta\mu+\mu-\beta)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right] \tag{31}$$

By HPM, we can deduce that

$$s(\tau) = lim_{p\to 1}s(\tau) = s_0 + s_1 + s_2 + , \tag{32}$$

$$y(\tau) = lim_{p\to 1}y(\tau) = y_0 + y_1 + y_2 + , \tag{33}$$

$$z(\tau) = lim_{p\to 1}z(\tau) = z_0 + z_1 + z_2 + , \tag{34}$$

### 3.1 *An approximate analytical expressions of substrate concentration, first enzyme-substrate complex, second enzyme-substrate complex by using Homotopy Perturbation Method (HPM)*

$$s(\tau) = e^{-\mu\tau} + \frac{k(\mu+\mu^2)}{(1+k)(\mu\eta+\eta-1)(\mu^2+\mu-1)}\left[e^{\frac{\tau(\mu^2+\mu-1)}{\mu+1}-t\mu} - e^{-\mu t}\right] - \frac{\eta(\mu+\mu^2)}{\mu\eta+\mu-1}\left[e^{-\mu t} - e^{t(-\mu)-\frac{t}{\mu+1}}\right]$$

$$+ \frac{\eta}{\mu\eta+\mu-1}\left[e^{-2\mu t} - e^{-\mu t}\right] - \frac{tk\mu e^{-\mu t}}{(1+k)(\mu\eta+\mu-1)}, \tag{35}$$

$$y_2(\tau) = \frac{\eta+1}{\mu\eta+\eta-1}\left[e^{\tau/(\mu+1)} - e^{\mu\tau}\right] + \frac{2\eta^2+2\eta-\eta/\mu}{(\mu\eta+\mu-1)(2(\eta+1)\mu-1)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right]$$

$$- \frac{\eta^2+\eta}{(\eta\mu+\mu-1)(2(\eta+1)\mu-1)}\left[e^{\tau(\frac{1}{\eta+1}-\mu)} - e^{\frac{\tau}{(\tau+1)}}\right] \tag{36}$$

$$z_2(\tau) = \frac{\eta(1+\eta+\mu+\eta\mu)}{(1+\eta)(k+1)(\mu\eta+\mu-1)(-\eta+\eta\mu+\mu-\beta)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right],$$

$$+ \frac{\eta^2+\eta}{(1+\eta)(k+1)(\mu\eta+\mu-1)(\eta\mu+\mu-\beta)}\left[e^{\tau}(-\frac{1}{\eta+1}\mu) - \tau(\frac{1}{\eta+1}+\mu) - e^{-\tau/(\eta+1)}\right] \tag{37}$$

(35)-(37) addresses the mathematical expressions for the non-dimensional concentrations of substrate $s(\tau)$, first $y(\tau)$ and second $z(\tau)$ enzyme-substrate complex.

### 3.2 *Taylor's series method*

The system of non-linear differential equations is tackled using Taylor's series technique. This method represents the terms as an infinite sum of series centered at a specific derivative point of the function. Taylor's series method is a potent means of approximating functions and resolving equations. It can readily transform any intricate sum into a simpler one. It furnishes precise analytical expressions that facilitate understanding mathematical models across diverse scientific and engineering domains. Utilizing the Taylor series can produce a differentiable approximate solution, which can then be substituted with the initial or boundary conditions into the equation. This approach allows for a direct assessment of the solution's accuracy. In recent years, there has been a notable rise in the application of Taylor's series method to address a variety of non-linear problems, encompassing fractional Bratu-type equations, third-order boundary value problems, non-linear oscillator problems, and non-linear ordinary and fractional differential equations such as Lane-Emden [29–32].

Taylor's Series method can be used to find the solutions to (17)-(19). The solutions are represented as follows:

$$s(\tau) = s(0) + \tau s(0) + \frac{\tau^2}{2}s(0) + \frac{\tau^3}{3!}s(0) + \frac{\tau^4}{4!}s^{iv}(0) + , \tag{38}$$

$$y(\tau) = y(0) + \tau y(0) + \frac{\tau^2}{2}y(0) + \frac{\tau^3}{3!}y(0) + \frac{\tau^4}{4!}y^{iv}(0) + , \tag{39}$$

$$z(\tau) = z(0) + \tau z(0) + \frac{\tau^2}{2}z(0) + \frac{\tau^3}{3!}z(0) + \frac{\tau^4}{4!}z^{iv}(0) + , \tag{40}$$

Given that,

$$s(0) = 1, y(0) = 0, z(0) = 0, \tag{41}$$

By putting $\tau = 0$ (17)-(19) and using (20), we get

$$s(0) = -\mu, y(0) = 1, z(0) = 0 \tag{42}$$

By differentiating (17)-(19) with respect to $\tau$ we get

$$\begin{aligned} s''(0) =& \mu^2 + \frac{\eta}{1+\eta}\mu + \frac{\mu k}{(1+k)(1+\eta)}, \\ y''(0) =& -\mu - \frac{\eta}{1+\eta} + \frac{1}{1+\eta} \\ z''(0) =& \frac{\eta}{(1+k)(1+\eta)^2}, \end{aligned} \tag{43}$$

Similarly, by repeating the same procedure, we get,

$$s'''(0) = -\mu^3 - \frac{\eta\mu^2}{(1+\eta)} + \frac{\mu^2 k}{(1+k)(1+\eta)} - \frac{\eta\mu^2 + \mu^2\eta^2 + \eta^2\mu + \eta\mu}{(1+\eta)^2} + \frac{\mu\eta}{(1+\eta)^2(1+k)} - \frac{\mu^2 k - \mu^2\eta k}{(1+k)(1+\eta)^2},$$

$$y'''(0) = \mu^2 + \frac{\mu k}{(1+k)(1+\eta)} + \frac{3\eta\mu}{1+\eta} - \frac{\eta}{(1+\eta)^2(1+k)} - \frac{\eta(-\mu\eta - \eta - \mu - 1)}{(1+\eta)^2} - \frac{(-\mu\eta - \eta - \mu - 1)}{(1+\eta)^2},$$

$$z'''(0) = \frac{\eta}{(1+\eta)^2(1+k)}\left(-\mu - \frac{\eta}{1+\eta} - \frac{1}{1+\eta}\right) - \frac{\beta}{1+\eta}\left(\frac{\eta}{(1+\eta)^2(1+k)}\right) \tag{44}$$

By substituting (41)-(44) in (38)-(40), we get the analytical expressions for the concentrations.

Using Taylor's series approach, an approximation of the analytical expressions of substrate concentration, the first enzyme-substrate complex, and the second enzyme-substrate complex are as follows:

$$s(\tau) = 1 - \mu\tau + (\mu^2 + \frac{\eta}{1+\eta}\mu + \frac{\mu k}{(1+k)(1+\eta)})\frac{\tau^2}{2!} - \frac{\tau^3}{3!}(-\mu^3 - \frac{\eta\mu}{(1+\eta)} + \frac{\mu^2 k}{(1+k)(1+\eta)} -$$

$$\frac{\eta\mu^2 + \mu^2\eta^2 + \eta^2\mu + \eta\mu}{(1+\eta)^2} + \frac{\mu\eta}{(1+\eta)^2(1+k)} - \frac{\mu^2 k - \mu^2\eta k + \mu\eta k + \mu k}{(1+k)(1+\eta)^2}) + , \tag{45}$$

$$y(\tau) = \tau + (-\mu - \frac{\eta}{1+\eta} + \frac{1}{1+\eta})\frac{\tau^2}{2!} + \frac{\tau^3}{3!}(\mu^2 + \frac{\mu k}{(1+k)(1+\eta)} + \frac{3\eta\mu}{1+\eta} - \frac{\eta}{(1+\eta)^2(1+k)} -$$

$$\frac{\eta(-\mu\eta - \eta - \mu - 1)}{(1+\eta)^2} - \frac{(-\mu\eta - \eta - \mu - 1)}{(1+\eta)^2}) + , \tag{46}$$

$$z(\tau) = (\frac{\eta}{(1+k)(1+\eta)^2})\frac{\tau^2}{2!} + (\frac{\eta}{(1+\eta)^2(1+k)}(-\mu - \frac{\eta}{1+\eta} - \frac{1}{1+\eta}) - \frac{\beta}{1+\eta}(\frac{\eta}{(1+\eta)^2(1+k)}))\frac{\tau^3}{3!} + \tag{47}$$

(45)-(47) are the mathematical expressions for the dimensionless concentration of substrate $s(\tau)$, first $y(\tau)$ and second $z(\tau)$ enzyme-substrate complex obtained by using TSM.

## 4. Comparison of analytical results with numerical simulation

The validity and dependability of the offered analytical approaches are assessed in this section using numerical simulations. This study's analytical expressions were compared to the numerical solution obtained by the Matlab programme, which handles initial value problems for ordinary differential equations [33]. Tables (1, 2, 3) present a comparison between the analytical results (HPM, TSM) generated in this study and the numerical results obtained using MATLAB software in Appendix A. This comparison encompasses various values of the reaction-diffusion parameter $\mu$, focusing on the concentration of substrate, first enzyme-substrate complex, and second enzyme-substrate complex. Notably, the HPM results exhibit a more substantial agreement with the numerical results compared to the TSM results. The highest average percentage of variation between HPM and TSM is 0.62% and 1.26% for the concentration of substrate, 0.65% and 1.25% for first enzyme-substrate complex, and second enzyme-substrate complex are observed as 0.63%, 0.68%, respectively.

**Table 1.** Comparing a numerical solution for various experimental values of the parameter with an approximative analytical solution for the concentration of the substrate $s(\tau)$ using (35) and (45)

| $\tau$ | | | $\mu = 2$ | | | | | $\mu = 3$ | | | | | $\mu = 5$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Num | HPM Eqn(35) | Error % of HPM | TSM Eqn(45) | Error % of TSM | Num | HPM Eqn(35) | Error % of HPM | TSM Eqn(45) | Error % of TSM | Num | HPM Eqn(35) | Error % of HPM | TSM Eqn(45) | Error % of TSM |
| 0 | 1 | 1 | 0.00 | 1 | 0.00 | 1.0000 | 1.0000 | 0.00 | 1 0.00 | 1.0000 | 1.0000 | 0.00 | 1 | 0 | |
| 0.2 | 0.5935 | 0.5915 | 0.34 | 0.5904 | 0.50 | 0.5324 | 0.5426 | 1.92 | 0.5309 | 0.28 | 0.4504 | 0.4577 | 1.62 | 0.4489 | 0.33 |
| 0.4 | 0.3792 | 0.3795 | 0.08 | 0.3778 | 0.36 | 0.2808 | 0.2835 | 0.96 | 0.2789 | 0.68 | 0.1917 | 0.1928 | 0.57 | 0.1901 | 0.83 |
| 0.6 | 0.2333 | 0.2336 | 0.13 | 0.2311 | 0.94 | 0.1463 | 0.1452 | 0.75 | 0.1450 | 0.89 | 0.0878 | 0.0879 | 0.10 | 0.0859 | 2.16 |
| 0.8 | 0.1418 | 0.1430 | 0.84 | 0.1401 | 1.20 | 0.0753 | 0.0763 | 1.27 | 0.0744 | 1.12 | 0.0388 | 0.0393 | 1.31 | 0.0372 | 4.12 |
| 1 | 0.0827 | 0.0833 | 0.73 | 0.0810 | 2.05 | 0.0413 | 0.0414 | 0.29 | 0.0403 | 2.42 | 0.0188 | 0.0187 | 0.32 | 0.0179 | 4.79 |
| | Error | | 0.35 | 0.84 | Error % | 0.88 | | 0.90 | Error % | 0.65 | | 2.04 | | | |

**Table 2.** Comparison of an approximate analytical solution of first enzyme-substrate concentration $y(\tau)$ with numerical simulation using (36) and (46) for different values of $\mu$

| $\tau$ | | | $\mu = 10$ | | | | | $\mu = 20$ | | | | | $\mu = 35$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM |
| 0 | 0.0000 | 0.0000 | 0.00 | 0.0000 | 0.00 | 0.0000 | 0.0000 | 0.00 | 0.000 | 0.00 | 0.0000 | 0.0000 | 0.00 | 0.0000 | 0.00 |
| 0.2 | 0.0756 | 0.0763 | 0.90 | 0.0742 | 1.85 | 0.0492 | 0.0499 | 1.38 | 0.0480 | 2.43 | 0.0399 | 0.0402 | 0.85 | 0.0384 | 3.76 |
| 0.4 | 0.0830 | 0.0833 | 0.33 | 0.0824 | 0.72 | 0.0504 | 0.0505 | 0.36 | 0.0495 | 1.98 | 0.0403 | 0.0403 | 0.05 | 0.0399 | 0.99 |
| 0.6 | 0.0842 | 0.0843 | 0.12 | 0.0832 | 1.19 | 0.0506 | 0.0504 | 0.45 | 0.0500 | 1.19 | 0.0405 | 0.0401 | 0.84 | 0.0400 | 1.23 |
| 0.8 | 0.0846 | 0.0847 | 0.05 | 0.0839 | 0.83 | 0.0508 | 0.0502 | 1.26 | 0.0503 | 0.98 | 0.0407 | 0.0405 | 0.42 | 0.0403 | 0.98 |
| 1 | 0.0849 | 0.0849 | 0.05 | 0.0840 | 1.06 | 0.0510 | 0.0499 | 2.20 | 0.0508 | 0.39 | 0.0408 | 0.0398 | 2.52 | 0.0396 | 2.94 |
| | Error | | 0.24 | 0.94 | Error % | 0.94 | | 1.16 | Error % | 0.78 | | 1.65 | | | |

**Table 3.** Comparison of a numerical solution for the parameter $z(\tau)$ for various experimental values $\mu$ with an approximative analytical solution obtained using (37) and (47)

| $\tau$ | | | $\mu = 10$ | | | | | $\mu = 20$ | | | | | $\mu = 35$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM | Num | HPM Eqn(36) | Error % of HPM | TSM Eqn(46) | Error % of TSM |
| 0 | 0.0000 | 0.0000 | 0.00 | 0.0000 | 0.00 | 0.0000 | 0.0000 | 0.00 | 0.000 | 0.00 | 0.0000 | 0.0000 | 0.00 | 0.0000 | 0.00 |
| 0.2 | 2.71E-05 | 2.72E-05 | 0.44 | 2.68E-05 | 1.10 | 2.07E-05 | 2.12E-05 | 2.42 | 2.02E-05 | 0.70 | 1.71E-05 | 1.72E-05 | 0.88 | 1.68E-05 | 0.94 |
| 0.4 | 5.50E-05 | 5.47E-05 | 0.55 | 5.43E-05 | 1.27 | 4.25E-05 | 4.24E-05 | 0.26 | 4.20E-05 | 0.55 | 3.45E-05 | 3.43E-05 | 0.55 | 3.40E-05 | 0.58 |
| 0.6 | 7.93E-05 | 7.91E-05 | 0.18 | 7.90E-05 | 0.38 | 6.14E-05 | 6.07E-05 | 1.14 | 6.03E-05 | 1.17 | 5.03E-05 | 4.99E-05 | 0.87 | 4.92E-05 | 0.93 |
| 0.8 | 1.00E-04 | 1.00E-04 | 0.00 | 0.99E-05 | 1.00 | 8.01E-05 | 8.01E-05 | 0.02 | 7.98E-05 | 0.11 | 6.44E-05 | 6.42E-05 | 0.31 | 6.39E-05 | 1.02 |
| 1 | 1.20E-04 | 1.23E-04 | 2.50 | 1.18E-05 | 1.20 | 9.53E-05 | 9.45E-05 | 0.84 | 9.40E-05 | 0.89 | 7.79E-05 | 7.76E-05 | 0.39 | 7.73E-05 | 0.43 |
| | Error | | 0.61 | 0.73 | Error % | 0.78 | | 0.57 | Error % | 0.50 | | 0.65 | | | |

## 5. Results and discussion

We notice that utilizing the HPM and TSM yields new and straightforward polynomial expressions for the substrate concentration and the concentrations of the first and second enzyme-substrate complexes, as described in (35) to (37) and (45) to (47).

Figures 1 (a-b) depict the substrate concentration plotted against dimensionless time using Equation (35). In Figure 1 (a), the plot is generated for constant values of $\eta = k = 0.001$, where $\eta$ and $k$ denote the reaction-diffusion parameters. These parameters regulate the balance between chemical reaction rates and substance diffusion velocities within the system, influencing how substances disperse relative to their reaction rates. With increasing $\mu$, the dimensionless substrate concentration gradually diminishes. The graph illustrates this trend for varying values of $\mu$, reaching a steady state when $\tau \geq 0.6$ where $\mu$ represents the reaction-diffusion parameter governing the initial substrate and enzyme concentration dynamics.

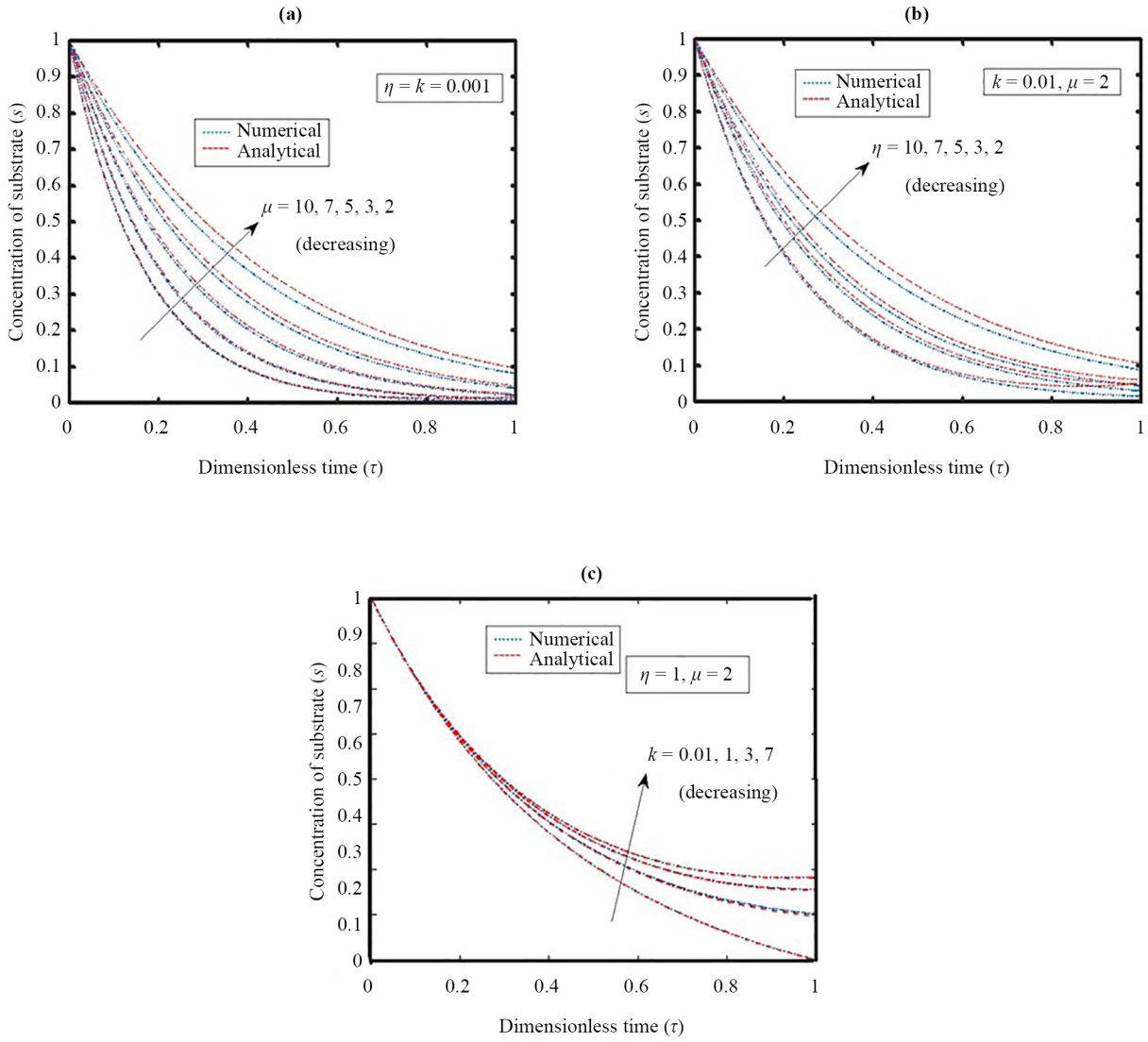


**Figure 1.** Comparison of the substrate concentration $s(\tau)$ derived from Eqn (35) with numerical outcomes across various values of reaction-diffusion parameters

In Figure 1 (b), the reaction-diffusion parameter $\eta$ for the substrate is depicted for different values, with fixed values of $k = 0.01$ and $\mu = 2$. The substrate concentration declines as $\eta$ increases, elucidating how the initial substrate concentration reacts with the enzyme and diffuses. The system reaches a steady state condition when $\tau \geq 0.8$.

Figure 1 (c) shows the reaction-diffusion parameter $k$ for the substrate across various values while maintaining $\eta = 1$ and $\mu = 2$ constants. As k rises, the substrate concentration also increases, revealing the backwards-to-forward reaction ratio when the substrate interacts with the enzyme to produce the first enzyme-substrate complex. A steady state is achieved in the system when $\tau = 0.8$

Figures 2 (a-b) potrays graphs illustrating the concentration of the first enzyme-substrate complex $y$ plotted against dimensionless time $\tau$. Figure 2 (a) shows that for fixed values of $\mu = k = 100$, the dimensionless concentration of the first enzyme-substrate complex declines as the value of increases, reaching a steady state when $\tau \geq 0.4$. This observation suggests that as the initial substrate concentration reacts with the enzyme, it reduces the concentration of intermediate complexes to form the product.

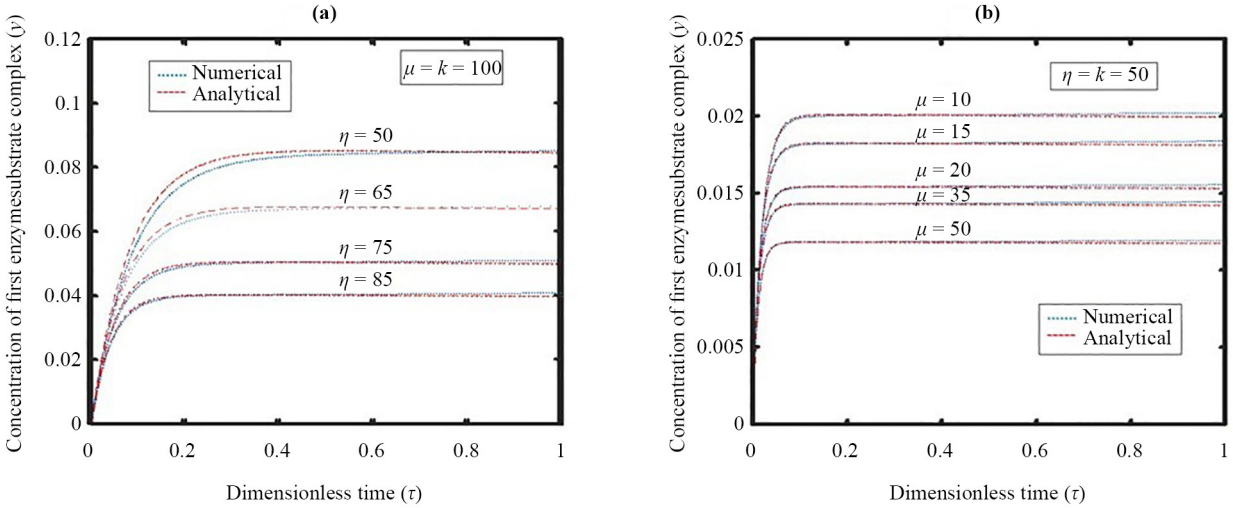


**Figure 2.** The concentration of the first enzyme-substrate complex y versus dimensionless time $(\tau)$ for different values of parameters can be obtained by utilizing (36)

Figure 2 (b) illustrates the graph drawn for fixed values of $\eta = k = 50$ and varying values of $\mu$. It demonstrates that the concentration of the first enzyme-substrate complex $y$ decreases as increases. A steady state is attained when $\tau \geq 0.2$.

Figures 3 (a-b) illustrates the evolution of the second-enzyme substrate complex $z$ over dimensionless time $\tau$ across various reaction-diffusion parameter values. In Figure 3 (a), the plot encompasses various $\mu$ values while maintaining fixed values of $\eta = \beta = 20$ and $k = 5$. As $\mu$ increases, the second enzyme-substrate complex $z$ concentration decreases.

In Figure 3 (b), the graph is plotted for varying $k$ values while keeping $\mu$ fixed at 50 and maintaining $\eta = \beta = 20$. The concentration of the second enzyme-substrate complex diminishes as the value of $k$ increases. Figure 3 (c-d) shows a graph illustrating different values of $\eta$ and $\beta$. The graph shows that as both $\eta$ and $\beta$ increase, the concentration of the second enzyme-substrate complex $z$ decreases. $\beta$ is the ratio of rate constant reactions. Rate constants denote the correlation between the molar concentration of reactants and the speed of a chemical reaction.

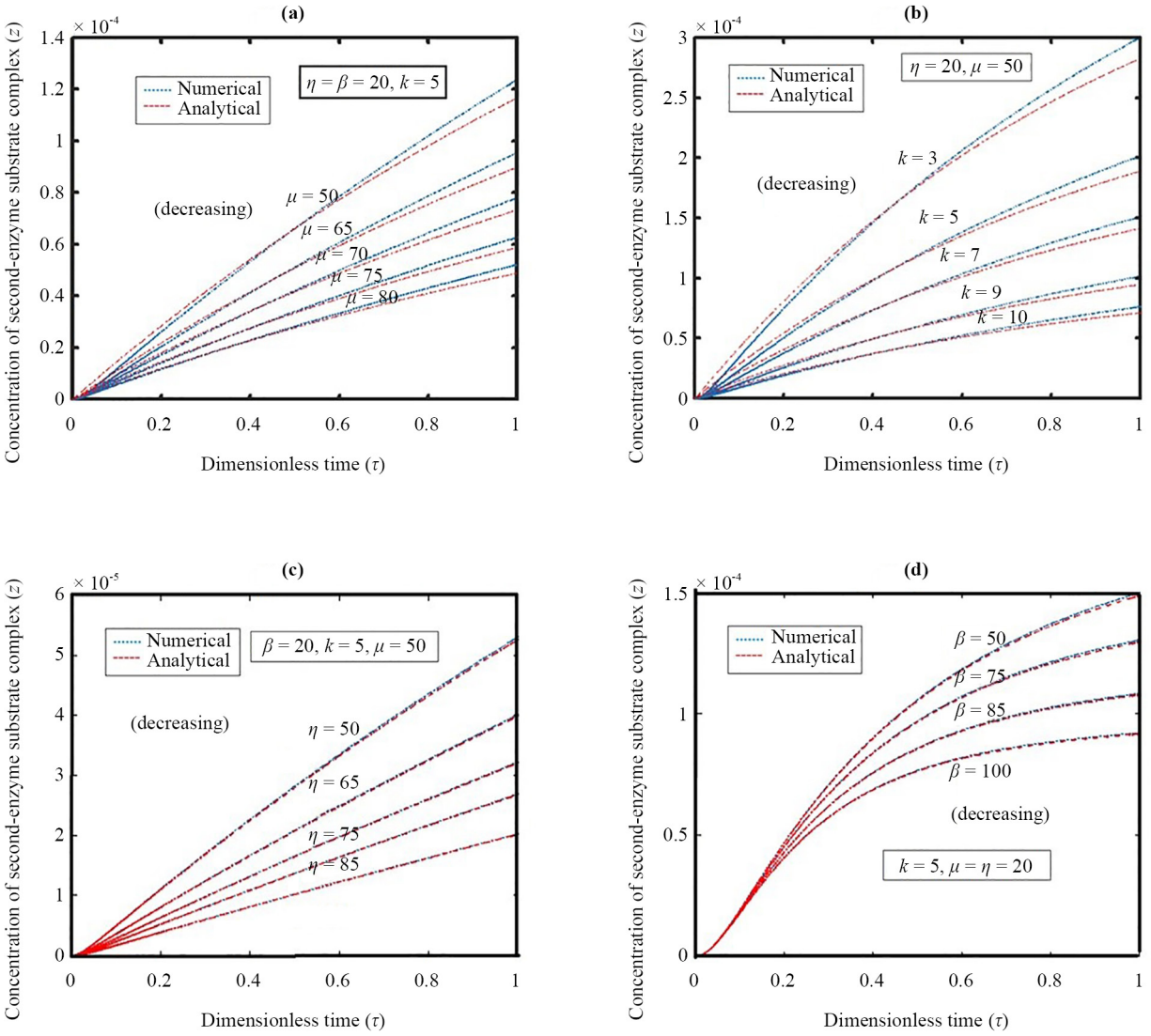


**Figure 3.** Plot of non-dimensional concentration of second enzyme substrate complex $z(\tau)$ for different qualities of parameters by using (37)

The preceding Figures show that the graph is plotted across different values of reaction-diffusion parameters $\mu$, $\eta$, $\beta$, and $k$. Reaction-diffusion parameters play a crucial role in dictating the dynamics of chemical reactions and the propagation of substances within a medium. These parameters determine the rate at which reactants transform into products and govern the dispersion of substances across both temporal and spatial dimensions. Manipulating these parameters empowers researchers to manage the speed and scope of reactions and diffusion phenomena across diverse systems, including biological tissues, chemical reactors, and environmental contexts. The concentrations of substrate $s$, first intermediate complex $y$, and second intermediate complex $z$ decrease across all values of the reaction-diffusion parameters $(\mu, \eta, \beta)$. For various values of $k$, the concentration of substrate increases, the first enzyme-substrate complex remains stable, and the second-enzyme substrate complex decreases. This phenomenon is observed in various chemical reactions occurring in living organisms and within the clinical industry, where substrate and enzyme-substrate complex concentration decreases as they react to yield a product.

## 5.1 *Analyzing parameter differentials for sensitivity*

A differential sensitivity analysis identifies the model parameters that influence model outcomes most. From Figure 4, it can be deduced that the reaction and diffusion parameters and exhibit a more significant influence on the concentrations of substrate, the first enzyme-substrate complex, and the second enzyme-substrate complex when varied. Conversely, the parameter contributes only minimally to changes in the concentrations of substrate, the first enzyme-substrate complex, and the second enzyme-substrate complex. solely affects the concentration of the second enzyme-substrate complex.

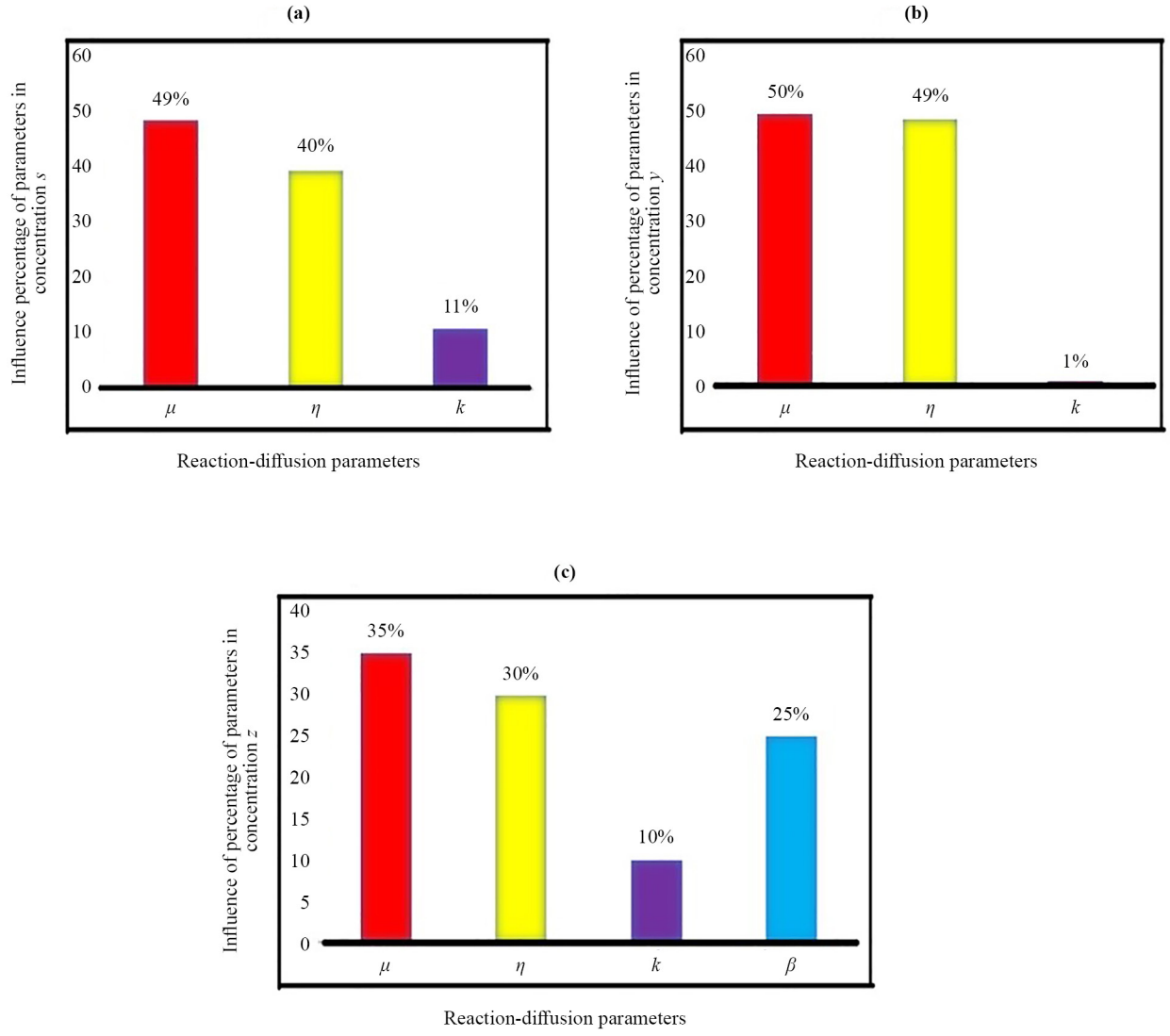


**Figure 4.** Conducting sensitivity analysis to assess the impact of parameters on the concentrations of (a) substrate $s(\tau)$ utilizing equation (35), (b) the first enzyme-substrate complex $y(\tau)$ employing equation (36), and (c) the second enzyme-substrate complex $z(\tau)$ using equation (37)

# 6. Conclusion

This article discusses a mathematical model focused on the pre-steady state behaviour of a non-linear double intermediate enzymatic reaction. Approximate analytical expressions for the concentrations of substrate, first enzyme-substrate complex, and second enzyme-substrate complex are derived using the homotopy Perturbation and Taylor's

series methods. Efficient discussion has been conducted on the impact of various parameters on the concentrations. The presented methodology's accuracy was effectively showcased by comparing the analytical and numerical results obtained using MATLAB software. Among them, the homotopy perturbation method exhibits remarkable performance and superior accuracy compared to Taylor's series method. HPM and TSM are crucial in resolving mathematical challenges across various fields. Their utilization extends to science, engineering, economics, and other disciplines, addressing the imperative for precise mathematical modelling and analysis. Although both techniques can deliver approximate solutions for specific issues, their effectiveness may diminish for intricate or highly non-linear systems. Enhancing accuracy in Taylor's series expansions often necessitates incorporating higher-order terms, a practice that can substantially escalate computational complexity. Moreover, this theoretical model can encompass steady-state and non-steady-state behaviours, accommodating higher-order and intricate boundary conditions in future research.

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## Conflict of interest

The authors declare no competing financial interest.

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# Appendix A

```
function graphmain3
options= odeset('RelTol',1e-6,'stats','on');
X0=[1;0;0];
tspan=[0,1];
tic
toc
figure
hold on
%plot(t,X(:,1),'*');
%plot(t,X(:,2),'.');
%plot(t,X(:,3),'+');
legend('x1','x2','x3','x4')
ylabel('x')
xlabel('t')
return
function [dx_dt]=TestFunction(t,x)
w=20;r=20;k=5;s=90.5;
dx_dt(1)=w*(-x(1)+(r/(1+r))*x(1)*x(2)+x(1)*x(3)+((k*x(2))/((1+k)*(1+r))));
dx_dt(2)=x(1)-(1*(r/(1+r))*x(1)*x(2)-x(1)*x(3)-(x(2)/(1+r)));
dx_dt(3)=((r*x(2))/((1+r)2*(1+k)))-(s/(1+r))*x(3);
dx_dt = dx_dt';
return
```