



A study of nonlinear fractional-order biochemical reaction model and numerical simulations

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Abstract. This article depicts an approximate solution of systems of nonlinear fractional biochemical reactions for the Michaelis–Menten enzyme kinetic model arising from the enzymatic reaction process. This present work is concerned with fundamental enzyme kinetics utilised to assess the efficacy of powerful mathematical approaches such as the homotopy perturbation method (HPM), homotopy analysis method (HAM), and homotopy analysis transform method (HATM) to get the approximate solutions of the biochemical reaction model with time-fractional derivatives. The Caputo-type fractional derivatives are explored. The proposed method is implemented to formulate a fractional differential biochemical reaction model to obtain approximate results subject to various settings of the fractional parameters with statistical validation at different stages. The comparison results reveal the complexity of the enzyme process and obtain approximate solutions to the nonlinear fractional differential biochemical reaction model.

Keywords: fractional differential equation, nonlinear biochemical reaction model, Caputo fractional derivative, homotopy perturbation method, homotopy analysis method, homotopy analysis transform method.

1 Introduction

The theory of fractional calculus was developed primarily as an exclusively theoretical field of mathematics. Fractional calculus focuses on the investigation of derivatives and integrals of arbitrary real or complex order, which join and extend the concept of an

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integer-order derivative and integral. The triumph of the fractional methodology is acknowledged in many applications in nonlinear dynamics, complex system dynamics, and image processing. This, in turn, has led to a continuing interest in the theory of fractional differential equations (FDEs). It is identified that the integer derivative of a function is only related to its nearby points, while the fractional derivative has a connection with all the function history information. As a result, a model represented by fractional-order equations possesses memory. The integer-order differential operator is a local operator, but the fractional-order differential operator is a nonlocal operator, which means that the next state of a system depends not only on its current state but also on all its past states. This is possibly one of the most relevant features for making this fractional tool significant from an applied standpoint and innovative from a mathematical standpoint. Integrals and derivatives of integer order are the standard integrals and derivatives of analysis. But in the case of the fractional order, these ideas manifest their peculiar features. Because several alterations happen naturally in different situations, the interconnections between these alterations have to be investigated. Numerous authors have tried to model real processes using FDEs. The theory of FDEs has been broadly studied by Podlubny [28]. Miller and Ross [25] discussed that almost every field of science and engineering has the function of fractional derivatives. Significant phenomena in fluid flow, rheology, electrical networks, electromagnetics, and diffusive transport akin to diffusion, acoustics, electrochemistry, mathematical biology, viscoelasticity, and material science are well explained by FDEs.

Fractional integrals or fractional derivatives can generate more accurate fractional integrals or fractional derivatives than integrals or classical integer-order derivatives in physics and engineering. Fractional derivatives are a powerful tool for describing the memory and heredity characteristics of many materials and processes. This is the major benefit of fractional derivatives compared to classical integer-order models in which such effects are deserted without being taken into account. The benefits of fractional derivatives are obvious when simulating the mechanical and electrical characteristics of real materials, as well as when accounting for the rheological features of rocks and many other disciplines. The fractional derivative, which has nonlocal property, can be applied by many researchers [5, 22]. Nieto investigated the logistic differential equation for the generalized proportional Caputo fractional derivative in [27]. Seadawy et al. [30–33] discussed various kinds of equations to solve with numerical approaches. The mathematical modeling and simulation of systems and processes based on the classification of their properties in terms of fractional derivatives inevitably leads to FDEs and the necessity to solve such equations. However, effective general techniques for solving them cannot be found even in the most useful works on fractional derivatives and integrals. The Adomian decomposition method (ADM) [3, 14], differential transform method (DTM) [2], and HPM [8, 16] are relatively novel ways to provide analytical and approximate solutions for linear and nonlinear FDEs.

Mathematical models of biochemical reactions have been discussed for many phenomena. Now that the genome is known, there is an advanced interest in the mathematical models of the cell's biochemical reactions. Enzymes are natural, sustainable catalysts. They are biodegradable, biocompatible, and derived from organisms. Enzymes are

enormous, live, globular protein molecules that are responsible for thousands of metabolic processes that sustain life and operate as catalysts to facilitate specific chemical reactions within each cell. These reactions are required for the organism's survival. The living cell is the site of a huge amount of biological activity known as metabolism. Enzymes promote life processes in all forms of life, from viruses to people, by undergoing physical and chemical changes regularly. Enzymes operate as catalysts for life or chemicals that accelerate the rate of a chemical reaction. By reducing the activation energy necessary to activate the reaction and taking a different path through the process, the reaction rate can be dramatically increased. Enzymes do not initiate processes that would not otherwise occur, but they do allow the reaction to continue faster and at a lower temperature, as is the case in living systems. The substrate physically secures the enzyme at its active site during an enzyme-mediated reaction, transforming the substrate into new product molecules. The majority of enzymatic processes are millions of times faster than comparable uncatalyzed reactions. Enzymes are not obsessive by the reactions that are catalyzed, nor do they modify the balance of these reactions [10]. The membrane of an enzyme cell with a biochemical structure inherently possesses fractional-order electrical conductivity in biochemical reactions [9]. The goal of the fractional order, as well as significant reaction parameters on the enzymatic reaction, is to solve the fractional-order differential biochemical reaction model. Because it is difficult to find an accurate solution for every FDE, it is necessary to employ various numerical approaches [1, 11, 29]. Recently, several researchers discussed various mathematical models in [4, 26, 35]. Sen [34] investigated the ADM to analyze the short-term characteristics of a biochemical reaction model. The studies of FDEs have attracted, developed, and involved the HPM as a mathematical tool for solving ordinary and partial FDEs. HPM was introduced by He, which is the combination method of the homotopy techniques and the perturbation technique [15, 19]. HPM finds the estimated solution without any discretization or preventive assuming, and it avoids round-off errors. This method yields a closed-form power series solution with easily assessable components. The HPM has been adapted to solve fractional differential equations, which have applications in modeling anomalous diffusion, viscoelasticity, and other phenomena that exhibit fractional-order behavior. HPM has been used to solve various nonlinear differential equations in physics such as those arising in quantum mechanics, general relativity, and fluid dynamics. It allows physicists to explore the behavior of complex physical systems. HPM has been applied to a wide range of engineering problems, including heat transfer, fluid dynamics, structural analysis, and electrical circuits. Its ability to handle complex nonlinear equations has made it a valuable tool for solving practical engineering problems.

This work is organized as follows: The basic concepts of the general fractional derivative are given in Section 2. Section 3 focuses on the mathematical formulation of the Michaelis–Menten enzyme kinetics model. Section 4 discussed stability analysis for the biochemical reaction model. In Section 4.1, HPM is used for analysis of the systems of FDEs and the purpose of implementation, an efficient numerical method is proposed in Section 5. Results and discussion, as well as graphical representation, are shown in Section 6. Finally, the conclusions are given in Section 7.

2 Preliminaries

Definition 1. A real function $g(t)$, $t > 0$, is said to be in the space \mathcal{C}_μ , $\mu \in \mathbb{R}$, if there exists a real number $p > \mu$ such that $g(t) = t^p g_1(t)$, where $g_1(t) \in \mathcal{C}(0, \infty)$, and it is said to be in the space \mathcal{C}_μ^n if and only if $g^n \in \mathcal{C}_\mu$, $n \in \mathbb{N}$.

Definition 2. The Riemann–Liouville fractional integral operator \mathcal{Q}^{δ_1} of order $\delta_1 \geq 0$ of a function $f \in \mathcal{L}^1(\mathbb{R}^+)$ is defined as

$$\mathcal{Q}_{0+}^{\delta_1} g(t) = \frac{1}{\Gamma(\delta_1)} \int_0^t (t - \theta)^{\delta_1 - 1} g(\theta) d\theta, \quad \delta_1 > 0, \tag{1}$$

where $\Gamma(\delta_1)$ is the well-known gamma function. For integer $\delta_1 > 0$, Eq. (1) is known as Cauchy’s integral formula.

Riemann–Liouville function integral satisfies the following properties for suitable functions $\Phi(x)$ and $\varphi(x)$:

- (i) $\mathcal{Q}^{\delta_1}[\Phi(x) + \varphi(x)] = \mathcal{Q}^{\delta_1}\Phi(x) + \mathcal{Q}^{\delta_1}\varphi(x)$;
- (ii) $\mathcal{Q}^{\delta_1}\mathcal{Q}^{\delta_2}\Phi(x) = \mathcal{Q}^{\delta_1 + \delta_2}\Phi(x)$;
- (iii) $\mathcal{Q}^{\delta_1}\mathcal{Q}^{\delta_2}\Phi(x) = \mathcal{Q}^{\delta_2}\mathcal{Q}^{\delta_1}\Phi(x)$;
- (iv) $\mathcal{Q}^{\delta_1}t^\vartheta = (\Gamma(\vartheta + 1)/\Gamma(\delta_1 + \vartheta + 1))t^{\delta_1 + \vartheta}$, $\vartheta > -1$, $\delta_1 \geq 0$.

Definition 3. (See [20].) The Riemann–Liouville fractional derivative D^{δ_1} of order $\delta_1 \geq 0$, $n - 1 < \delta_1 < n$, $n \in \mathbb{N}$, is defined as

$$D_{0+}^{\delta_1} g(t) = D_{0+}^n \mathcal{Q}_{0+}^{n - \delta_1} g(t) = \frac{1}{\Gamma(n - \delta_1)} \left(\frac{d}{dt}\right)^n \int_0^t (t - s)^{n - \delta_1 - 1} g(s) ds,$$

where the operator D^n is the ordinary differential operator, and the function $g(t)$ has absolutely continuous derivatives up to order $n - 1$.

Definition 4. (See [7].) The Caputo fractional derivative D^{δ_1} of order $\delta_1 > 0$, $n - 1 < \delta_1 < n$, is defined by

$${}^c D_{0+}^{\delta_1} g(t) = \frac{1}{\Gamma(n - \delta_1)} \int_0^t (t - \theta)^{n - \delta_1 - 1} g^n(\theta) d\theta$$

for $n - 1 < \delta_1 \leq n$, $n \in \mathbb{N}$, $t > 0$, $h \in \mathcal{C}_{-1}^n$, where the function $g(t)$ has absolutely continuous derivatives up to order $n - 1$. If $0 < \delta_1 < 1$, then

$${}^c D_{0+}^{\delta_1} g(t) = \frac{1}{\Gamma(1 - \delta_1)} \int_0^t \frac{g'(\theta)}{(t - \theta)^{\delta_1}} d\theta,$$

where $g'(\theta) = Dg(\theta) = dg(\theta)/d\theta$.

There are two properties of the Caputo fractional derivative [13]:

- (i) Let $g \in \mathcal{C}_{-1}^n$, $n \in \mathbb{N}$. Then $D^{\delta_1}g$, $0 \leq \delta_1 \leq n$, is well defined, and $D^{\delta_1}g \in \mathcal{C}_{-1}$.
- (ii) Let $n - 1 < \delta_1 \leq n$, $n \in \mathbb{N}$, and $h \in \mathcal{C}_{\mu}^n$, $\mu \geq -1$. Then

$$(\mathcal{Q}^{\delta_1} D^{\delta_1})g(t) = g(t) - \sum_{k=0}^{n-1} g^{(k)}(0^+) \frac{t^k}{k!}.$$

The Caputo fractional derivative has better convergence properties compared to the Riemann–Liouville fractional derivative operator. This means that it can be approximated more accurately using numerical methods, which is important for numerical simulations of physical phenomena. It is a more practical, physically meaningful, and numerically efficient fractional derivative operator that is suitable for a wide range of physical phenomena involving nonsmooth functions.

3 Mathematical formulation of Michaelis–Menten enzyme kinetics model

Enzymes are proteins that function as catalysts for biochemical reactions and are called biocatalysts. Each reaction that an enzyme catalyzes consists of a very small number of reactions, frequently only one, and hence enzymes are reaction-specific catalysts. Traditional models of enzyme kinetics in biochemical systems have used ordinary and partial differential equations based purely on reactions with no spatial dependency on the various concentrations. In 1913, Michaelis and Menten [24] developed rate laws that characterise enzyme catalysed processes, utilising model reduction by time-scale separation. This became known as Michaelis–Menten kinetics.

This research focuses on a single substrate enzyme catalyzed reaction [21]



where \mathcal{E} is the enzyme, \mathcal{S} is the substrate, \mathcal{P} is the enzyme–substrate intermediate complex, and \mathcal{X} is the product. The parameters k_1 , k_{-1} , and k_2 are positive rate constants for each reaction when researching reactions in which the initial velocity was connected to the initial substrate concentration. The time evolution of scheme (2) may be calculated from the solution of the systems of coupled nonlinear ODEs [34] by using the law of mass action, which says that reaction rates are proportional to the concentration of the reactants

$$\frac{d\mathcal{S}}{dt} = -k_1\mathcal{E}\mathcal{S} + k_{-1}\mathcal{P}, \quad (3)$$

$$\frac{d\mathcal{E}}{dt} = -k_1\mathcal{E}\mathcal{S} + (k_{-1} + k_2)\mathcal{P}, \quad (4)$$

$$\frac{d\mathcal{P}}{dt} = k_1\mathcal{E}\mathcal{S} - (k_{-1} + k_2)\mathcal{P}, \quad (5)$$

$$\frac{d\mathcal{X}}{dt} = k_2\mathcal{P} \quad (6)$$

subject to the initial conditions

$$S(0) = S_0, \quad \mathcal{E}(0) = \mathcal{E}_0, \quad \mathcal{P}(0) = 0, \quad \mathcal{X}(0) = 0.$$

Since the enzyme \mathcal{E} is a catalyst, its overall concentration must remain constant. This concentration law is easily derived by adding Eqs. (4) and (5):

$$\frac{d\mathcal{E}}{dt} + \frac{d\mathcal{P}}{dt} = 0 \implies \mathcal{E}(t) + \mathcal{P}(t) = \mathcal{E}_0.$$

Furthermore, at any moment, the sum of the concentrations of the free substrate \mathcal{S} , complex \mathcal{P} , and product \mathcal{X} must be equal to the initial substrate S_0 ; that is, adding Eqs. (3), (5), and (6), it can be shown that

$$\frac{d\mathcal{S}}{dt} + \frac{d\mathcal{P}}{dt} + \frac{d\mathcal{X}}{dt} = 0 \implies S(t) + \mathcal{P}(t) + \mathcal{X}(t) = S_0.$$

These two conservation laws reduce the system of differential equations (3)–(6) to only two equations for \mathcal{S} and \mathcal{P} in dimensionless form of concentrations of substrate u and intermediate complex between enzyme and substrate v , which are provided by

$$\begin{aligned} \frac{du}{dt} &= -u + (\psi - \phi)v + uv, \\ \frac{dv}{dt} &= \frac{1}{\tau}(u - \psi v - uv) \end{aligned} \tag{7}$$

subject to the initial conditions

$$u(0) = 1, \quad v(0) = 0,$$

where ϕ , ψ , and τ are dimensionless parameters.

The integer-order models do not save memory effects on themselves (7). We convert model (7) to a fractional-order one to study the impact of memory in the above biological models. As a result, we use the general form of the Caputo fractional derivative rather than the (7) ordinary time derivatives. Additionally, to prevent dimensional mismatching [12], we change the fractional operator via the auxiliary parameter $\gamma > 0$. The new model then takes the following form:

$$\begin{aligned} \gamma^{\delta_1-1} D_t^{\delta_1} u &= -u + (\psi - \phi)v + uv, \\ \gamma^{\delta_2-1} D_t^{\delta_2} v &= \frac{1}{\tau}(u - \psi v - uv) \end{aligned} \tag{8}$$

subject to the initial conditions

$$u(0) = 1, \quad v(0) = 0.$$

In Eq. (8), it is necessary to have the same dimensions on both sides [6]. After dividing by a constant, we have the same system without the term γ^{δ_1-1} .

4 Stability analysis

The critical points are determined by reducing the right-hand side of the system of equations (8) to zero, i.e., $\gamma^{\delta_1-1} D_t^{\delta_1} u = 0$, $\gamma^{\delta_2-1} D_t^{\delta_2} v = 0$, which provides a set of algebraic expressions as

$$\begin{aligned} -u + (\psi - \phi)v + uv &= f_1(u, v), \\ \frac{1}{\tau}(u - \psi v - uv) &= f_2(u, v). \end{aligned} \quad (9)$$

Then, for $v = 0$, system (9) has equilibrium points $(0, 0)$.

Let

$$\mathcal{J}(u, v) = \begin{bmatrix} \frac{\partial f_1}{\partial u} & \frac{\partial f_1}{\partial v} \\ \frac{\partial f_2}{\partial u} & \frac{\partial f_2}{\partial v} \end{bmatrix}$$

be the variational matrix of system (9).

Then

$$\mathcal{J}(u, v) = \begin{bmatrix} -1 + v & (\phi - \psi) + u \\ \frac{1}{\epsilon}(1 - v) & \frac{1}{\epsilon}(-\phi - u) \end{bmatrix}.$$

Now the variational matrix $\mathcal{J}(\zeta_0)$ for system (9) at the critical point ζ_0 is computed as

$$\mathcal{J}(\zeta_0) = \begin{bmatrix} -1 & (\phi - \psi) \\ \frac{1}{\epsilon} & \frac{-\phi}{\epsilon} \end{bmatrix}.$$

The eigenvalues of $\mathcal{J}(\zeta_0)$ are the roots of the characteristics equation

$$\Phi(\lambda) = \lambda^2 + \left(1 + \frac{\phi}{\epsilon}\right)\lambda + \frac{\psi}{\epsilon} = 0.$$

Their are expressed as follows:

$$\lambda_1 = \frac{1}{2} \left[\left(\frac{\phi}{\epsilon} - 1 \right) + \left\{ \sqrt{\left(1 + \frac{\phi}{\epsilon} \right)^2 - 4 \frac{\psi}{\epsilon}} \right\} \right]$$

and

$$\lambda_2 = \frac{1}{2} \left[\left(\frac{\phi}{\epsilon} - 1 \right) - \left\{ \sqrt{\left(1 + \frac{\phi}{\epsilon} \right)^2 - 4 \frac{\psi}{\epsilon}} \right\} \right].$$

The equilibrium point ζ_0 is locally asymptotically stable if all of the eigenvalues λ_j of $\mathcal{J}(\zeta_0)$ satisfy the Matignon's conditions [23] as $|\arg(\lambda_j)| > \psi\pi/2$, $j = 1, 2$. The eigenvalues of $\mathcal{J}(\zeta_0)$ are both real and positive; $|\arg(\lambda_j)| = 0 < \psi\pi/2$, so the equilibrium point $\zeta_0 = (0, 0)$ is unstable.

4.1 Analysis for systems of FDEs

Many real-world applications have been represented in recent decades by systems of FDEs, which can be expressed as follows:

$$\begin{aligned}
 \gamma^{\delta_1-1} D^{\delta_1} u_1(t) &= g_1(t, u_1, u_2, \dots, u_n), \\
 \gamma^{\delta_2-1} D^{\delta_2} u_2(t) &= g_2(t, u_1, u_2, \dots, u_n), \\
 &\dots \\
 \gamma^{\delta_n-1} D^{\delta_n} u_n(t) &= g_n(t, u_1, u_2, \dots, u_n)
 \end{aligned}
 \tag{10}$$

subject to the initial conditions

$$u_r(0) = c_r, \quad r = 1, 2, \dots, n.$$

To construct the homotopy technique [15, 19],

$$\gamma^{\delta_i-1} D^{\delta_i} u_i = qg_i(t, u_1, u_2, \dots, u_n), \tag{11}$$

where $i = 1, 2, \dots, n$, and q is an embedding parameter that ranges between 0 and 1. If $q = 0$, Eq. (11) becomes the linear eqnarray $\gamma^{\delta_i-1} D^{\delta_i} u_i = 0$, and when $q = 1$, the homotopy (11) turns out to be the original systems provided in (10). We usse the parameter q to expand the solution of system (10) as follows:

$$u_i(t) = u_{i0} + \gamma^{1-\delta_i} (qu_i + q^2u_{i2} + q^3u_{i3} + q^4u_{i4} + q^5u_{i5} + q^6u_{i6} + \dots). \tag{12}$$

Substituting (12) into (11) and collecting terms with the same powers of q yields a sequence of linear equations of the form

$$\begin{aligned}
 q^0: \gamma^{\delta_i-1} D^{\delta_i} u_{i0} &= 0, \\
 q^1: \gamma^{\delta_i-1} D^{\delta_i} u_{i1} &= g_{i1}(t, u_{10}, u_{20}, \dots, u_{n0}), \\
 q^2: \gamma^{\delta_i-1} D^{\delta_i} u_{i2} &= g_{i2}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}), \\
 q^3: \gamma^{\delta_i-1} D^{\delta_i} u_{i3} &= g_{i3}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}, u_{12}, u_{22}, \dots, u_{n2}), \\
 q^4: \gamma^{\delta_i-1} D^{\delta_i} u_{i4} &= g_{i4}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}, u_{12}, u_{22}, \dots, u_{n2}, \\
 &\quad u_{13}, u_{23}, \dots, u_{n3}), \\
 &\dots,
 \end{aligned}$$

where the functions $g_{i1}, g_{i2}, g_{i3}, g_{i4}, \dots$, satisfy the following equation:

$$\begin{aligned}
 &g_i(t, u_{10} + qu_{11} + q^2u_{12} + \dots, u_{n0} + qu_{n1} + q^2u_{n2} + \dots) \\
 &= g_{i1}(t, u_{10}, u_{20}, \dots, u_{n0}) + qg_{i2}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}) \\
 &\quad + q^2g_{i3}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}, u_{12}, u_{22}, \dots, u_{n2}) \\
 &\quad + q^3g_{i4}(t, u_{10}, u_{20}, \dots, u_{n0}, u_{11}, u_{21}, \dots, u_{n1}, u_{12}, u_{22}, \dots, u_{n2}, \\
 &\quad + u_{13}, u_{23}, \dots, u_{n3}) \dots
 \end{aligned}$$

These linear equations can be readily solved by using the operator Q^{δ_i} , that is, the inverse of the operator $\gamma^{\delta_i-1} D^{\delta_i}$, which is defined by definition (2). As a result, the components

of the HPM solution u_{ir} ($r = 0, 1, 2, \dots$) can be determined. That is, by specifying $q = 1$ in (12) the HPM series solutions are completely determined, and $u_i(t) = \sum_{r=0}^{\infty} u_{ir}(t)$. The convergence and asymptotic behavior of the series are addressed in [17, 18], then the numerical computations approximate the HPM series solution, $u_i(t) = \sum_{k=0}^{\infty} u_{ir}(t)$, by the following N -term truncated series: $\phi_i N(t) = \sum_{r=0}^{N-1} u_{ir}(t)$.

5 Numerical implementation

Consider the following nonlinear fractional differential biochemical reaction model:

$$\begin{aligned}\gamma^{\delta_1-1} D_t^{\delta_1} u &= -u + (\psi - \phi)v + uv, \\ \gamma^{\delta_2-1} D_t^{\delta_2} v &= \frac{1}{\tau}(u - \psi v - uv)\end{aligned}\quad (13)$$

subject to the initial conditions

$$u(0) = 1, \quad v(0) = 0,$$

where δ_1 and δ_2 ($0 < \delta_1, \delta_2 \leq 1$) are parameters describing the order of the fractional derivative. According to (11), we construct the following homotopy technique:

$$\begin{aligned}\gamma^{\delta_1-1} D^{\delta_1} u &= q(-u + (\psi - \phi)v + uv), \\ \gamma^{\delta_2-1} D^{\delta_2} v &= q\left(\frac{1}{\tau}(u - \psi v - uv)\right).\end{aligned}\quad (14)$$

Substituting (12) into (14) and collecting terms of the same powers of q yields the following two sets of nonlinear equations:

$$\begin{aligned}q^0: \gamma^{\delta_1-1} D^{\delta_1} u_0 &= 1, \\ q^1: \gamma^{\delta_1-1} D^{\delta_1} u_1 &= -u_0 + (\psi - \phi)v_0 + u_0 v_0, \\ q^2: \gamma^{\delta_1-1} D^{\delta_1} u_2 &= -u_1 + (\psi - \phi)v_1 + u_1 v_0 + u_0 v_1, \\ q^3: \gamma^{\delta_1-1} D^{\delta_1} u_3 &= -u_2 + (\psi - \phi)v_2 + u_2 v_0 + u_1 v_1 + u_0 v_2, \\ q^4: \gamma^{\delta_1-1} D^{\delta_1} u_4 &= -u_3 + (\psi - \phi)v_3 + u_3 v_0 + u_2 v_1 + u_1 v_2 + u_0 v_3, \\ &\dots, \\ q^0: \gamma^{\delta_2-1} D^{\delta_2} v_0 &= 0, \\ q^1: \gamma^{\delta_2-1} D^{\delta_2} v_1 &= \frac{1}{\tau}(u_0 - \psi v_0 - u_0 v_0), \\ q^2: \gamma^{\delta_2-1} D^{\delta_2} v_2 &= \frac{1}{\tau}(u_1 - \psi v_1 - u_1 v_0 - u_0 v_1), \\ q^3: \gamma^{\delta_2-1} D^{\delta_2} v_3 &= \frac{1}{\tau}(u_2 - \psi v_2 - u_2 v_0 - u_1 v_1 - u_0 v_2), \\ q^4: \gamma^{\delta_2-1} D^{\delta_2} v_4 &= \frac{1}{\tau}(u_3 - \psi v_3 - u_3 v_0 - u_2 v_1 - u_1 v_2 - u_0 v_3), \\ &\dots.\end{aligned}$$

As a result of applying the operators Q^{δ_1} and Q^{δ_2} to the above sets of nonlinear equations, the first few terms of the approximate series solution for system (13) are as follows:

$$\begin{aligned}
 u_0 &= u(0) = 1, \\
 u_1 &= -\frac{t^{\delta_1}}{\Gamma(\delta_1 + 1)}, \\
 u_2 &= \frac{t^{2\delta_1}}{\Gamma(2\delta_1 + 1)} + \frac{(\psi - \phi)}{\tau} \frac{t^{\delta_1 + \delta_2}}{\Gamma(\delta_1 + \delta_2 + 1)} + \frac{1}{\tau} \frac{t^{\delta_1 + \delta_2}}{\Gamma(\delta_1 + \delta_2 + 1)}, \\
 u_3 &= -\frac{t^{3\delta_1}}{\Gamma(3\delta_1 + 1)} - \frac{(\psi - \phi)}{\tau} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} - \frac{1}{\tau} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} \\
 &\quad - \frac{(\psi - \phi)}{\tau} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} - \frac{(\psi - \phi)}{\tau^2} \frac{\psi(t^{\delta_1 + 2\delta_2})}{\Gamma(\delta_1 + 2\delta_2 + 1)} \\
 &\quad - \frac{(\psi - \phi)}{\tau^2} \frac{t^{\delta_1 + 2\delta_2}}{\Gamma(\delta_1 + 2\delta_2 + 1)} - \frac{\Gamma(\delta_1 + \delta_2 + 1)}{\tau\Gamma(\delta_1 + 1)\Gamma(\delta_2 + 1)} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} \\
 &\quad - \frac{1}{\tau} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} - \frac{\psi}{\tau^2} \frac{t^{\delta_1 + 2\delta_2}}{\Gamma(\delta_1 + 2\delta_2 + 1)} - \frac{1}{\tau^2} \frac{t^{\delta_1 + 2\delta_2}}{\Gamma(\delta_1 + 2\delta_2 + 1)}, \\
 \dots,
 \end{aligned}$$

$$\begin{aligned}
 v_0 &= v(0) = 0, \\
 v_1 &= \frac{1}{\tau} \frac{t^{\delta_2}}{\Gamma(\delta_2 + 1)}, \\
 v_2 &= -\frac{1}{\tau} \frac{t^{\delta_2 + \delta_1}}{\Gamma(\delta_2 + \delta_1 + 1)} - \frac{\psi}{\tau^2} \frac{t^{2\delta_2}}{\Gamma(2\delta_2 + 1)} - \frac{1}{\tau^2} \frac{t^{2\delta_2}}{\Gamma(2\delta_2 + 1)}, \\
 v_3 &= \frac{1}{\tau} \frac{t^{\delta_2 + 2\delta_1}}{\Gamma(\delta_2 + 2\delta_1 + 1)} + \frac{(\psi - \phi)}{\tau^2} \frac{t^{2\delta_2 + \delta_1}}{\Gamma(2\delta_2 + \delta_1 + 1)} + \frac{1}{\tau^2} \frac{t^{2\delta_2 + \delta_1}}{\Gamma(2\delta_2 + \delta_1 + 1)} \\
 &\quad + \frac{\psi}{\tau^2} \frac{t^{2\delta_2 + \delta_1}}{\Gamma(2\delta_2 + \delta_1 + 1)} + \frac{\psi^2}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2 + 1)} + \frac{\psi}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2 + 1)} \\
 &\quad + \frac{\Gamma(\delta_1 + \delta_2 + 1)}{\tau^2\Gamma(\delta_1 + 1)\Gamma(\delta_2 + 1)} \frac{t^{2\delta_2 + \delta_1}}{\Gamma(2\delta_2 + \delta_1 + 1)} + \frac{1}{\tau^2} \frac{t^{2\delta_2 + \delta_1}}{\Gamma(2\delta_2 + \delta_1 + 1)} \\
 &\quad + \frac{\psi}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2 + 1)} + \frac{1}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2 + 1)}, \\
 \dots
 \end{aligned}$$

Similarly, $u_4, u_5, u_6 \dots$, and $v_4, v_5, v_6 \dots$ can be estimated following in this manner, and the approximate series solutions are obtained as follows:

$$\begin{aligned}
 u(t) &= 1 + \gamma^{1-\delta_1} \left(-\frac{t^{\delta_1}}{\Gamma(\delta_1 + 1)} + \frac{t^{2\delta_1}}{\Gamma(2\delta_1 + 1)} + \frac{(\psi - \phi)}{\tau} \frac{t^{\delta_1 + \delta_2}}{\Gamma(\delta_1 + \delta_2 + 1)} \right. \\
 &\quad \left. + \frac{1}{\tau} \frac{t^{\delta_1 + \delta_2}}{\Gamma(\delta_1 + \delta_2 + 1)} - \frac{t^{3\delta_1}}{\Gamma(3\delta_1 + 1)} - \frac{(\psi - \phi)}{\tau} \frac{t^{2\delta_1 + \delta_2}}{\Gamma(2\delta_1 + \delta_2 + 1)} \right)
 \end{aligned}$$

$$\begin{aligned}
 & -\frac{1}{\tau} \frac{t^{2\delta_1+\delta_2}}{\Gamma(2\delta_1+\delta_2+1)} - \frac{(\psi-\phi)}{\tau} \frac{t^{2\delta_1+\delta_2}}{\Gamma(2\delta_1+\delta_2+1)} - \frac{(\psi-\phi)}{\tau^2} \\
 & \frac{\psi(t^{\delta_1+2\delta_2})}{\Gamma(\delta_1+2\delta_2+1)} - \frac{(\psi-\phi)}{\tau^2} \frac{t^{\delta_1+2\delta_2}}{\Gamma(\delta_1+2\delta_2+1)} - \frac{\Gamma(\delta_1+\delta_2+1)}{\tau\Gamma(\delta_1+1)\Gamma(\delta_2+1)} \\
 & \frac{t^{2\delta_1+\delta_2}}{\Gamma(2\delta_1+\delta_2+1)} - \frac{1}{\tau} \frac{t^{2\delta_1+\delta_2}}{\Gamma(2\delta_1+\delta_2+1)} - \frac{\psi}{\tau^2} \frac{t^{\delta_1+2\delta_2}}{\Gamma(\delta_1+2\delta_2+1)} \\
 & - \left. \frac{1}{\tau^2} \frac{t^{\delta_1+2\delta_2}}{\Gamma(\delta_1+2\delta_2+1)} - \dots \right), \\
 v(t) = & \gamma^{1-\delta_2} \left(\frac{1}{\tau} \frac{t^{\delta_2}}{\Gamma(\delta_2+1)} - \frac{1}{\tau} \frac{t^{\delta_2+\delta_1}}{\Gamma(\delta_2+\delta_1+1)} - \frac{\psi}{\tau^2} \frac{t^{2\delta_2}}{\Gamma(2\delta_2+1)} - \frac{1}{\tau^2} \frac{t^{2\delta_2}}{\Gamma(2\delta_2+1)} \right. \\
 & + \frac{1}{\tau} \frac{t^{\delta_2+2\delta_1}}{\Gamma(\delta_2+2\delta_1+1)} + \frac{(\psi-\phi)}{\tau^2} \frac{t^{2\delta_2+\delta_1}}{\Gamma(2\delta_2+\delta_1+1)} + \frac{1}{\tau^2} \frac{t^{2\delta_2+\delta_1}}{\Gamma(2\delta_2+\delta_1+1)} \\
 & + \frac{\psi}{\tau^2} \frac{t^{2\delta_2+\delta_1}}{\Gamma(2\delta_2+\delta_1+1)} + \frac{\psi^2}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2+1)} + \frac{\psi}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2+1)} \\
 & + \frac{\Gamma(\delta_1+\delta_2+1)}{\tau^2\Gamma(\delta_1+1)\Gamma(\delta_2+1)} \frac{t^{2\delta_2+\delta_1}}{\Gamma(2\delta_2+\delta_1+1)} + \frac{1}{\tau^2} \frac{t^{2\delta_2+\delta_1}}{\Gamma(2\delta_2+\delta_1+1)} \\
 & \left. + \frac{\psi}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2+1)} + \frac{1}{\tau^3} \frac{t^{3\delta_2}}{\Gamma(3\delta_2+1)} + \dots \right).
 \end{aligned}$$

6 Result and discussion

In this section, the effect of fractional order δ_1, δ_2 on the concentration of substrate and enzyme–substrate intermediate complex is investigated. The numerical simulations of the fractional-order differential biochemical reaction model through the use of HPM, HAM, and HATM consider different values of fractional order δ_1, δ_2 for dimensionless reaction parameters $\phi = 0.375, \psi = 1.0, \tau = 0.1$. Now consider that HPM at time step $\Delta t = 0.001$, HAM at $\Delta t = 0.001$, and HATM at $\Delta t = 0.001$ have been constructed.

6.1 Comparative study

In this section, a comparison study is conducted with a few existing approaches, the HAM and the HATM, to validate the solution produced by the proposed method. The results are presented in Tables 1–4 for various fractional parameter values $\delta_1 = \delta_2 = 0.25, 0.50, 0.75, 1.0$ and $\gamma = 2$. The proposed technique has great agreement with the HAM and HATM as shown in Tables 1–4. The comparison results for the four different fractional parameter values are represented in the figures. The analysis confirms that HPM can be used as a powerful mathematical tool for solving the fractional-order biochemical reaction model. Furthermore, to validate the variations, a statistical analysis has been discussed.

Table 1. Numerical results of system (13) for $\delta_1 = \delta_2 = 0.25$ and $\gamma = 2$ using HPM, HAM, and HATM.

t	$u(t)$			$v(t)$		
	HPM	HAM	HATM	HPM	HAM	HATM
0.0	0.0010	1.0000	1.0000	0	0	0
0.1	-0.1078	-44.4666	-13.2243	0.1342	0.5426	-0.5042
0.2	-0.1843	-77.3264	-24.5607	0.2286	0.9362	-0.8830
0.3	-0.2518	-106.4947	-34.8221	0.3119	1.2858	-1.2205
0.4	-0.3140	-133.4748	-44.4189	0.3886	1.6093	-1.5333
0.5	-0.3725	-158.9266	-53.5401	0.4609	1.9145	-1.8286
0.6	-0.4282	-183.2180	-62.2941	0.5297	2.2058	-2.1108
0.7	-0.4818	-206.5818	-70.7508	0.5958	2.4860	-2.3823
0.8	-0.5335	-229.1776	-78.9589	0.6596	2.7570	-2.6451
0.9	-0.5837	-251.1212	-86.9543	0.7216	3.0202	-2.9004
1.0	-0.6326	-272.5002	-94.7642	0.7819	3.2766	-3.1492
1.1	-0.6802	-293.3826	-102.4100	0.8407	3.5271	-3.3923
1.2	-0.7269	-313.8233	-109.9090	0.8983	3.7723	-3.6303
1.3	-0.7726	-333.8667	-117.2755	0.9547	4.0128	-3.8637
1.4	-0.8175	-353.5499	-124.5213	1.0101	4.2489	-4.0930
1.5	-0.8615	-372.9041	-131.6565	1.0645	4.4811	-4.3185
1.6	-0.9049	-391.9560	-138.6897	1.1180	4.7097	-4.5405
1.7	-0.9477	-410.7284	-145.6283	1.1708	4.9349	-4.7593
1.8	-0.9898	-429.2414	-152.4789	1.2228	5.1570	-4.9751
1.9	-1.0313	-447.5125	-159.2471	1.2741	5.3762	-5.1881
2.0	-1.0724	-465.5571	-165.9381	1.3247	5.5928	-5.3985

Table 2. Numerical results of system (13) for $\delta_1 = \delta_2 = 0.50$ and $\gamma = 2$ using HPM, HAM, and HATM.

t	$u(t)$			$v(t)$		
	HPM	HAM	HATM	HPM	HAM	HATM
0.0	1.0000	1.0000	1.0000	0	0	0
0.1	-0.0093	-2.9499	0.1987	0.0127	0.0460	-0.0332
0.2	-0.0296	-11.1960	-2.1279	0.0376	0.1442	-0.1234
0.3	-0.0564	-22.3805	-5.5892	0.0706	0.2778	-0.2490
0.4	-0.0885	-35.9553	-9.9821	0.1102	0.4400	-0.4030
0.5	-0.1252	-51.5992	-15.1848	0.1555	0.6272	-0.5816
0.6	-0.1661	-69.0939	-21.1137	0.2059	0.8365	-0.7820
0.7	-0.2107	-88.2786	-27.7067	0.2609	1.0662	-1.0023
0.8	-0.2588	-109.0284	-34.9154	0.3202	1.3146	-1.2410
0.9	-0.3101	-131.2424	-42.7006	0.3835	1.5807	-1.4970
1.0	-0.3646	-154.8374	-51.0299	0.4506	1.8633	-1.7691
1.1	-0.4219	-179.7426	-59.8757	0.5213	2.1616	-2.0566
1.2	-0.4820	-205.8973	-69.2143	0.5954	2.4750	-2.3588
1.3	-0.5447	-233.2485	-79.0249	0.6728	2.8027	-2.6750
1.4	-0.6100	-261.7493	-89.2891	0.7533	3.1442	-3.0047
1.5	-0.6778	-291.3582	-99.9907	0.8369	3.4990	-3.3473
1.6	-0.7480	-322.0376	-111.1150	0.9233	3.8667	-3.7025
1.7	-0.8204	-353.7536	-122.6486	1.0127	4.2468	-4.0698
1.8	-0.8951	-386.4753	-134.5795	1.1048	4.6390	-4.4488
1.9	-0.9719	-420.1746	-146.8964	1.1995	5.0429	-4.8393
2.0	-1.0509	-454.8253	-159.5893	1.2969	5.4582	-5.2410

Table 3. Numerical results of system (13) for $\delta_1 = \delta_2 = 0.75$ and $\gamma = 2$ using HPM, HAM, and HATM.

t	$u(t)$			$v(t)$		
	HPM	HAM	HATM	HPM	HAM	HATM
0.0	1.0000	1.0000	1.0000	0	0	0
0.1	0.2924	0.7550	0.9800	0.0082	0.0024	0.0028
0.2	-2.5995	-0.2723	0.8739	0.0436	0.0143	-0.0050
0.3	-8.4249	-2.5053	0.4211	0.1151	0.0406	-0.0271
0.4	-17.5938	-6.1537	-0.4877	0.2279	0.0838	-0.0656
0.5	-30.4077	-11.3669	-1.9261	0.3855	0.1458	-0.1224
0.6	-47.1097	-18.2636	-3.9503	0.5910	0.2280	-0.1987
0.7	-67.9055	-26.9430	-6.6065	0.8470	0.3315	-0.2956
0.8	-92.9746	-37.4908	-9.9338	1.1556	0.4573	-0.4142
0.9	-122.4766	-49.9831	-13.9661	1.5187	0.6065	-0.5552
1.0	-156.5563	-64.4882	-18.7341	1.9382	0.7798	-0.7196
1.1	-195.3458	-81.0686	-24.2652	2.4157	0.9779	-0.9079
1.2	-238.9675	-99.7817	-30.5843	2.9527	1.2016	-1.1209
1.3	-287.5351	-120.6808	-37.7148	3.5506	1.4515	-1.3592
1.4	-341.1551	-143.8157	-45.6780	4.2107	1.7281	-1.6234
1.5	-399.9279	-169.2332	-54.4942	4.9342	2.0321	-1.9139
1.6	-463.9485	-196.9775	-64.1821	5.7224	2.3639	-2.2313
1.7	-533.3068	-227.0905	-74.7597	6.5762	2.7242	-2.5761
1.8	-608.0886	-259.6121	-86.2438	7.4968	3.1132	-2.9488
1.9	-688.3761	-294.5802	-98.6506	8.4852	3.5316	-3.3498
2.0	-774.2476	-332.0312	-111.9954	9.5423	3.9798	-3.7794

Table 4. Numerical results of the system (13) for $\delta_1 = \delta_2 = 1.0$ and $\gamma = 2$ using HPM, HAM, and HATM.

t	$u(t)$			$v(t)$		
	HPM	HAM	HATM	HPM	HAM	HATM
0.0	1.0000	1.0000	1.0000	0	0	0
0.1	0.9242	0.9471	0.9573	0.0007	0.0004	0.0017
0.2	0.6486	0.8740	0.9830	0.0039	0.0011	0.0034
0.3	-0.1992	0.6126	1.0120	0.0141	0.0039	0.0030
0.4	-1.9914	-0.0046	0.9790	0.0360	0.0110	-0.0014
0.5	-5.1003	-1.1456	0.8188	0.0740	0.0243	-0.0117
0.6	-9.8984	-2.9782	0.4663	0.1328	0.0459	-0.0298
0.7	-16.7578	-5.6700	-0.1437	0.2169	0.0777	-0.0575
0.8	-26.0509	-9.3890	-1.0765	0.3310	0.1217	-0.0970
0.9	-38.1501	-14.3029	-2.3971	0.4795	0.1800	-0.1500
1.0	-53.4276	-20.5795	-4.1709	0.6671	0.2546	-0.2184
1.1	-72.2558	-28.3867	-6.4629	0.8983	0.3475	-0.3043
1.2	-95.0069	-37.8922	-9.3384	1.1777	0.4607	-0.4095
1.3	-122.0533	-49.2638	-12.8626	1.5098	0.5961	-0.5359
1.4	-153.7674	-62.6693	-17.1006	1.8994	0.7558	-0.6855
1.5	-190.5213	-78.2766	-22.1176	2.3508	0.9419	-0.8601
1.6	-232.6875	-96.2533	-27.9789	2.8687	1.1563	-1.0618
1.7	-280.6383	-116.7674	-34.7495	3.4577	1.4009	-1.2924
1.8	-334.7459	-139.9866	-42.4948	4.1223	1.6779	-1.5538
1.9	-395.3826	-166.0787	-51.2798	4.8671	1.9893	-1.8479
2.0	-462.9209	-195.2115	-61.1698	5.6967	2.3370	-2.1767

6.2 Statistical analysis

The statistical significance of the difference between the group of means and various values of the fractional parameter δ_1, δ_2 has been processed utilizing the t-test investigation at the 5% level of significance. The outcomes are displayed in Tables 5 and 6. The means for the $u(t)$ and $v(t)$ for various stages are significantly different at the 95% confidence interval, except since the means for the $u(t)$ and $v(t)$ are significantly different. Particularly compared to the integer-order model (when $\delta_1 = \delta_2 = 1$), the various values of the fractional parameter are significant.

The approximate results are compared with those of HAM and HATM as shown in Figs. 1, 2, 3, and 4, respectively. The above results conclude that the proposed method reveals great agreement with other existing methods such as HAM and HATM. According to the results, HPM is a relevant mathematical tool for solving the fractional differential biochemical reaction model.

Table 5. The pairwise mean difference of $u(t)$ using t-test.

t	Mean difference	95% confidence interval
$\delta_1 = \delta_2 = 1$ and 0.75	123.174890	[74.828858, 171.520923]
$\delta_1 = \delta_2 = 1$ and 0.50	-118.101976	[-183.529235, -52.674717]
$\delta_1 = \delta_2 = 1$ and 0.25	-117.918500	[-183.368224, -52.468776]
$\delta_1 = \delta_2 = 0.75$ and 0.50	-241.276867	[-353.850942, -128.702792]
$\delta_1 = \delta_2 = 0.75$ and 0.25	-241.093390	[-353.686908, -128.499873]
$\delta_1 = \delta_2 = 0.50$ and 0.25	0.183476	[0.143998, 0.222955]

Table 6. The pairwise mean difference of $v(t)$ using t-test.

t	Mean difference	95% confidence interval
$\delta_1 = \delta_2 = 1$ and 0.75	-1.519671	[-2.116654, -0.922689]
$\delta_1 = \delta_2 = 1$ and 0.50	0.946662	[0.321492, 1.571832]
$\delta_1 = \delta_2 = 1$ and 0.25	0.719667	[0.063203, 1.376130]
$\delta_1 = \delta_2 = 0.75$ and 0.50	2.466333	[1.265880, 3.666786]
$\delta_1 = \delta_2 = 0.75$ and 0.25	2.239338	[1.013404, 3.465272]
$\delta_1 = \delta_2 = 0.50$ and 0.25	-0.226995	[-0.275660, -0.178330]

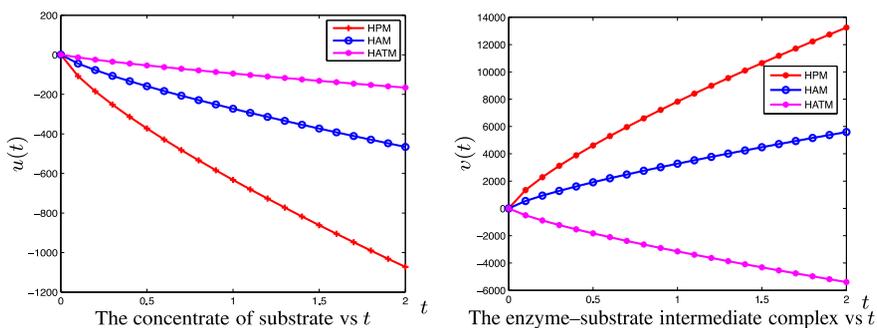


Figure 1. Graphical illustrations of system (13) with $\delta_1 = \delta_2 = 0.25$ and $\gamma = 2$.

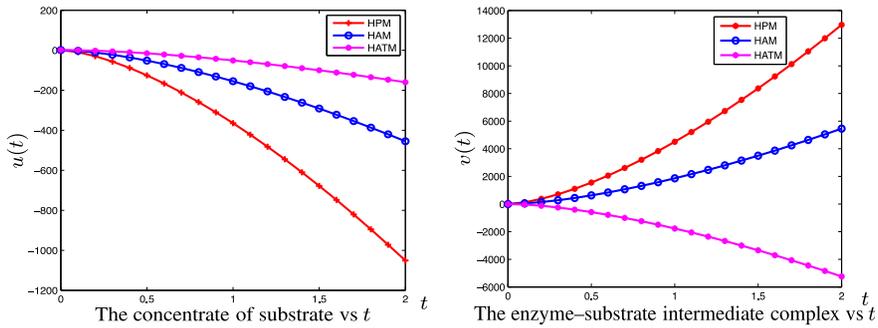


Figure 2. Graphical illustrations of system (13) with $\delta_1 = \delta_2 = 0.50$ and $\gamma = 2$.

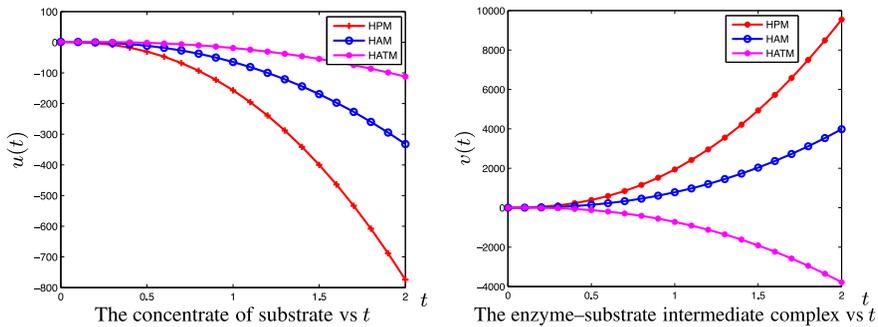


Figure 3. Graphical illustrations of system (13) with $\delta_1 = \delta_2 = 0.75$ and $\gamma = 2$.

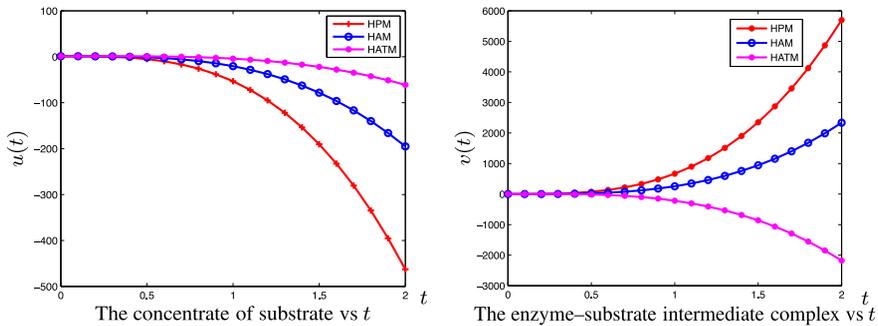


Figure 4. Graphical illustrations of system (13) with $\delta_1 = \delta_2 = 1.0$ and $\gamma = 2$.

7 Conclusion

This paper discussed an algorithm for a nonlinear fractional differential biochemical reaction model that was simulated by the HPM, HAM, and HATM. Additionally, the comparison is done between HPM, HAM, and HATM. The above-mentioned techniques can

be utilized as alternative and equivalent methods for establishing approximate solutions for the nonlinear differential biochemical reaction model with fractional-order derivatives. HAM is the generalized Taylor series technique for exploring an infinite series solution for developing the convergence region; to classify the value of h , the convergence radius of the obtained infinite series has to be determined. So HAM was not efficient for solving the nonlinear fractional differential biochemical reaction model. Similarly, HATM results are also not efficient for solving the fractional biochemical reaction model. On the other hand, HPM is a new perturbation method that searches for an asymptotic solution with few terms; no convergence theory is needed. HPM presented excellent approximate results for the nonlinear fractional differential biochemical reaction model. Hence, the proposed method HPM is a powerful mathematical technique for solving the nonlinear fractional differential biochemical reaction model. In future work, the utilization of HPM can be stretched to analyze various mathematical models, nonlinear differential equations, and fractional differential equations that emerge in the various areas of science and engineering.

Conflicts of interest. The authors declare no conflicts of interest.

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