APPROXIMATE SOLUTION OF NONLINEAR FRACTIONAL ORDER BIOCHEMICAL REACTION MODEL BY MULTISTAGE NEW ITERATIVE METHOD

S. K. DAMARLA, M. KUNDU

ABSTRACT. Nonlinear fractional order mathematical models usually do not have closed form solutions. Fractional order biochemical reaction model is such a model that cannot be solved analytically, hence, valid approximate solution is desired. Multistage new iterative method is proposed to acquire bounded approximate solution of fractional order biochemical reaction model. The fractional order biochemical process is simulated using the proposed method for various combinations of fractional order and dimensionless reaction parameters. The results have shown that the proposed method is reliable and computationally effective.

1. INTRODUCTION

Enzymes are responsible for all chemical reactions take place within a biological cell. Enzymes enhance rates of reactions without consuming in reactions they catalyse and do not alter equilibrium of reactions. Modeling the transient behavior of cellular processes under difficult situations like heterogeneous and in vivo conditions with classical calculus may not be realistic approach. To accurately represent such processes having inherent fractional order description, fractional derivative which has non-local property can be applied ([1] -[9]). Abdullah ([10]) employed fractional derivative to derive realistic time fractional Michaelis-Menten kinetics which describes the behaviour of macromolecules in two dimensional disordered medium in presence of obstacles. To have clear understanding regarding the role of fractional order as well as influential reaction parameters on enzymatic reaction, fractional order biochemical reaction model must be solved. It is impossible to have an exact solution for every fractional differential equation therefore it is indispensable to use numerical techniques. In this regard, Ahmed ([11]) and Molliq et al. ([12]) extended the application of multistep generalized differential transform method and modified step variational iteration method, respectively, to predict the behaviour of time-fractional enzyme kinetics in relatively large time region.

New iterative method (NIM) is an effective semi analytical technique that offers

precise approximate solutions in terms of rapidly convergent infinite series for a class of integer and non-integer order differential equations ([13] -[17]). To achieve fast convergence, revised new iterative method can be utilized ([18]). The advantage of new iterative method over widely used technique; Adomain Decomposition Method is that new iterative method does not require the computation of Adomain polynomials. However, new iterative method suffers from global convergence problem i.e. approximated solution tends to be unbounded as time domain increases. In this work, multistage new iterative method is introduced to obtain bounded and convergent approximate solutions that represent the true behaviour of fractional order biochemical reaction model in large time span. The rest of the paper is organised as follows. Basic definitions and useful properties of fractional calculus are provided in section 2. Section 3 describes nonlinear fractional order biochemical reaction model. New iterative method for solving system of fractional order differential equations is explained in section 4. Section 5 introduces multistage new iterative method. Section 6 discusses the convergence of multistage new iterative method. In section 7, new iterative method and multistage new iterative method are implemented on fractional order biochemical reaction model. Finally section 8 concludes the paper.

2. Basic Definitions and Properties

This section provides two extensively utilized definitions and some operational properties of fractional calculus ([1], [19]).

Definition 2.1 A real function $f(t)$, $t \geq 0$, is said to be in the space C_μ, $\mu \in R$ if there exists a real number $p(\geq \mu)$, such that $f(t) = t^p f_1(t)$, where $f_1(t) \in C[0, \infty)$, and it is said to be in the space C_μ^m iff $f^m \in C_\mu$, $m \in N$.

Definition 2.2 The Riemann-Liouville fractional integral of order $\alpha(> 0)$ of function $f(t) \in C_\mu$, $\mu > -1$ is defined as

$$J^\alpha f(t) = \frac{1}{\Gamma(\alpha)} \int_{t_0}^t (t - \tau)^{\alpha - 1} f(\tau) \, d\tau, \; t > t_0 \qquad (1)$$

The Riemann-Liouville fractional derivative is

$$_{t_0}D_t^\alpha f(t) = D^m J^{m-\alpha} f(t) = \frac{1}{\Gamma(m - \alpha)} \frac{d^m}{dt^m} \int_{t_0}^t (t - \tau)^{m-\alpha-1} f(\tau) d\tau, \; t > t_0 \quad (2)$$

where α is a non-integer that satisfies the relation $m - 1 < \alpha \leq m, m \in N$.

We mention here few properties of Riemann-Liouville fractional integral operator, J^α, which will be utilized in next sections.

For function $f(t) \in C_\mu$, $\mu > -1$, $\alpha, \beta > 0$ and $\gamma > -1$

     2.2.1 $J^\alpha J^\beta f(t) = J^{\alpha+\beta} f(t)$

     2.2.2 $J^\alpha J^\beta f(t) = J^\beta J^\alpha f(t)$

     2.2.3 $J^\alpha t^\gamma = \frac{\Gamma(\gamma+1)}{\Gamma(\alpha+\gamma+1)} t^{\alpha+\gamma}$

Definition 2.3 The fractional derivative of function $f(t)$ in the Caputo sense is defined as

$$_{t_0}D_*^\alpha f(t) = \frac{1}{\Gamma(m - \alpha)} \int_{t_0}^t (t - \tau)^{m-\alpha-1} f^m(\tau) \, d\tau, \; t > t_0 \qquad (3)$$

Although the Riemann-Liouville fractional derivative is mathematically rigorous, it cannot be applied to model a physical process since it requires the evaluation of fractional derivatives and integrals at the initial time $t_0 = 0$. Yet these fractional initial conditions do not have meaningful physical explanation and impossible to determine. But the Caputo fractional derivative needs only the values of function $f(t)$ and its $m-1$ integer order derivatives at the initial time $t_0 = 0$. The Riemann-Liouville fractional derivative performs first fractional integration and then integer order differentiation to achieve derivative of order α whereas the Caputo fractional derivative computes in reverse manner. However, both the definitions will coincide for homogeneous initial conditions.

3. NONLINEAR FRACTIONAL ORDER BIOCHEMICAL REACTION MODEL

In this paper, we consider nonlinear fractional order biochemical reaction model which is generalization of classical model proposed by Meena et al. ([20]) to describe single substrate-enzyme reaction scheme:

$$E + S \leftrightarrow ES \rightarrow E + P \tag{4}$$

where E is the enzyme, S is the substrate, ES is the enzyme-substrate intermediate complex and P is the product. The reaction mechanism given in equation (4) implies that the target molecules i.e. substrates are bind to enzymes' active site to form enzyme-substrate intermediate complex, which in turn, decomposes irreversibly into the original enzyme and product. The reversible reaction can occur between enzyme-substrate intermediate complex and reactants when the concentration of reactants and ES achieve equilibrium stage.

Let s, e, c and p be the concentrations of S, E, ES and P, respectively. From the law of mass action, we get the following biochemical reaction model comprises system of nonlinear ordinary differential equations.

$$\frac{ds}{dt} = -k_1 es + k_{-1} c \tag{5a}$$

$$\frac{de}{dt} = -k_1 es + (k_2 + k_{-1})c \tag{5b}$$

$$\frac{dc}{dt} = k_1 es - (k_1 + k_2)c \tag{5c}$$

$$\frac{dp}{dt} = k_2 c \tag{5d}$$

with initial conditions;

$$s(0) = s_0, e(0) = e_0, c(0) = 0, p(0) = 0 \tag{6}$$

The parameters k_1, k_{-1} and k_2 in the above model are positive rate constants for each reaction.

Combining equations (5b) and (5c) and using initial conditions (equation (6)) leads to

$$e(t) + c(t) = e_0 \tag{7}$$

Using the above algebraic equation and the system of differential equations given in equations (5a) to (5d), the following two equations for s and c can be obtained.

$$\left. \begin{array}{l} \frac{ds}{dt} = -k_1 e_0 s + (k_1 s + k_{-1})c \\ \frac{dc}{dt} = k_1 e_0 s - (k_1 s + k_{-1} + k_2)c \end{array} \right\} \tag{8}$$

The initial conditions for this system are $s(0) = s_0$ and $c(0) = 0$.
Substitution of parameters presented in equation (9) in equations (6) and (8) results in dimensionless model provided by equations (10) and (11).

$$\tau = \frac{k_1 e_0 t}{\epsilon}, u(\tau) = \frac{s(t)}{s_0}, v(\tau) = \frac{c(t)}{e_0}, w(\tau) = \frac{p(t)}{e_0}, \lambda = \frac{k_2}{k_1 s_0}, k = \frac{k_{-1} + k_2}{k_1 s_0}, \epsilon = \frac{e_0}{s_0} \Bigg\}$$

$$(9)$$

$$\left.\begin{aligned}
\frac{du}{d\tau} &= -u\epsilon + \epsilon(u + k - \lambda)v \\
\frac{dv}{d\tau} &= u - (u + k)v \\
\frac{dw}{d\tau} &= \lambda v
\end{aligned}\right\}$$

$$(10)$$

$$\left.\begin{aligned}
u(0) &= 1 \\
v(0) &= 0 \\
w(0) &= 0
\end{aligned}\right\}$$

$$(11)$$

By introducing non-integer order into the above classical model, fractional order biochemical reaction model is obtained as

$$\left.\begin{aligned}
D_*^{\alpha_1} u(\tau) &= -u\epsilon + \epsilon(u + k - \lambda)v \\
D_*^{\alpha_2} v(\tau) &= u - (u + k)v \\
D_*^{\alpha_3} w(\tau) &= \lambda v
\end{aligned}\right\}$$

$$(12)$$

$$\left.\begin{aligned}
u(0) &= 1 \\
v(0) &= 0 \\
w(0) &= 0
\end{aligned}\right\}$$

$$(13)$$

where α_1, α_2 and α_3 are non-integer orders satisfying the relation $0 < \alpha_1, \alpha_2, \alpha_3 \leq 1$ and D_* is Caputo fractional derivative. The fractional orders α_1, α_2 and α_3 will be altered together and independently to analyze their impact on the fractional order biochemical reaction model.

4. NEW ITERATIVE METHOD (NIM)

Let us consider the following general form of system of fractional order differential equations:

$$D_*^{\alpha_1} x_i(t) = L_i(t, x_1, x_2, \ldots, x_n) + N_i(t, x_1, x_2, \ldots, x_n) + g_i(t), \ i = 1, 2, \ldots, n, \ t \in [0, T]$$

$$(14)$$

where $D_*^{\alpha_i}$ is the Caputo fractional derivative of order α_i satisfies the relation $0 < \alpha_i \leq 1$, L_i is a linear operator, N_i is a nonlinear operator and $g_i(t)$ is a given function.
The initial conditions for the aforementioned system are

$$x_i(0) = a_i \tag{15}$$

Multiplication with the inverse operator J^{α_i} on both sides of equation (14) yields

$$x_i(t) = x_i(0) + J^{\alpha_i}(L_i(t, x_1, x_2, \ldots, x_n)) + J^{\alpha_i}(N_i(t, x_1, x_2, \ldots, x_n)) + J^{\alpha_i}(g_i(t))$$

$$(16)$$

According to new iterative method, solution $x_i(t)$ can be approximated by the infinite series:

$$x_i(t) = \sum_{m=0}^{\infty} x_{im}(t) \tag{17}$$

The non-linear term $N_i(t, x_1, x_2, \ldots, x_n)$ in equation (16) can be decomposed as

$$N_i\left(t, \sum_{m=0}^{\infty} x_{1m}, \ldots, \sum_{m=0}^{\infty} x_{nm}\right) = N_i(t, x_{10}, \ldots, x_{n0}) + \sum_{m=1}^{\infty}(N_{i1} - N_{i2}) \quad (18)$$

where $N_{i1} = N_i\left(t, \sum_{j=0}^{m} x_{1j}, \ldots, \sum_{j=0}^{m} x_{nj}\right)$

$\qquad N_{i2} = N_i\left(t, \sum_{j=0}^{m-1} x_{1j}, \ldots, \sum_{j=0}^{m-1} x_{nj}\right)$

Replacing $x_i(t)$ and nonlinear term $N_i(t, x_1, x_2, \ldots, x_n)$ in equation (16) with equations (17) and (18), respectively, leads to

$$\sum_{m=0}^{\infty} x_{im} = x_i(0) + J^{\alpha_i}(L_{i1}) + J^{\alpha_i}(N_{i0}) + J^{\alpha_i}\left(\sum_{m=1}^{\infty}(N_{i1} - N_{i2})\right) + J^{\alpha_i}(g_i(t)) \quad (19)$$

where $N_{i0} = N_i(t, x_{10}, \ldots, x_{n0})$

$\qquad N_{i1} = N_i\left(t, \sum_{j=0}^{m} x_{1j}, \ldots, \sum_{j=0}^{m} x_{nj}\right)$

$\qquad N_{i2} = N_i\left(t, \sum_{j=0}^{m-1} x_{1j}, \ldots, \sum_{j=0}^{m-1} x_{nj}\right)$

$\qquad L_{i1} = L_i\left(t, \sum_{m=0}^{\infty} x_{1m}, \ldots, \sum_{m=0}^{\infty} x_{nm}\right)$

From the following recurrence relations, components of series solution can be determined.

$$x_{i0} = x_i(0) + J^{\alpha_i}(g_i(t)) \quad (20)$$

$$x_{i1} = J^{\alpha_i}(L_i(t, x_{10}, \ldots, x_{n0}) + N_i(t, x_{10}, \ldots, x_{n0})) \quad (21)$$

$$x_{im+1} = J^{\alpha_i}(L_i(t, x_{1m}, \ldots, x_{nm})) + J^{\alpha_i}(N_{i1} - N_{i2}), m \geq 1 \quad (22)$$

where $N_{i1} = N_i\left(t, \sum_{j=0}^{m} x_{1j}, \ldots, \sum_{j=0}^{m} x_{nj}\right)$

$\qquad N_{i2} = N_i\left(t, \sum_{j=0}^{m-1} x_{1j}, \ldots, \sum_{j=0}^{m-1} x_{nj}\right)$

Truncating the series solution rendered in equation (17) to N finite terms gives practical solution.

5. MULTISTAGE NEW ITERATIVE METHOD (MNIM)

As we shall notice in section 7, new iterative method can provide valid approximate solution only in the neighborhood of initial time. This drawback prevents its application to real processes. To overcome this difficulty, multistage strategy is applied to new iterative method. This multistage approach makes new iterative method capable of predicting the behaviour of any kind of fractional order process in arbitrary time interval. The steps of multistage new iterative method are as follows. Divide the time interval $[0, T]$ into M subintervals i.e. $[t_0, t_1], [t_1, t_2], \ldots, [t_{M-1}, t_M = T]$ with constant step size $h = \frac{T}{M}$. At each stage, a set of differential equations of fractional order will be solved using new iterative method with arbitrary initial conditions. In order to compute approximate solution in each stage, we need to know arbitrary initial conditions at the left end point of every subinterval. Usually we do not have these information except at the initial time $t_0 = 0$. Therefore, knowledge of a process at initial time $t_0 = 0$ is used to calculate approximate solution in first subinterval $[t_0, t_1]$ and this solution serves as initial condition for next subinterval $[t_1, t_2]$. Likewise, we can obtain approximate solution in every subinterval and this procedure will continue untill desired time span is reached. The number of terms (N) of series solution and the step size, h, greatly influence the efficiency of multistage new iterative method. As h decreases, convergence quickly achieves. It is to be noted that very small step size causes high computational time.

6. ANALYSIS OF CONVERGENCE

In this section, we show the convergence of multistage new iterative method prior to its implementation on fractional order biochemical reaction model.

For simplicity, we consider system of nonlinear fractional order differential equations of the form

$$D_*^{\alpha_i} x_i(t) = F_i(t, x_1, \ldots, x_n); \quad i = 1, 2, \ldots, n, \quad 0 < \alpha_i \leq 1, \quad t \in [0, T] \quad (23)$$

subject to initial conditions; $x_i(0) = a_i$.

From sections 4 and 5, the solution $x_i(t)$ can be approximated in any time interval by the infinite series:

$$x_i(t) = \sum_{m=0}^{\infty} x_{im}(t) \quad (24)$$

whose components are

$$x_{i0}(t) = x_i(t^*) \quad (25)$$

$$x_{i1} = \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} F_i(\tau, x_{10}, x_{20}, \ldots, x_{n0}) \, d\tau \quad (26)$$

$$x_{im+1}(t) = \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} \left((t - \tau)^{\alpha_i - 1} (F_{i1} - F_{i2}) \right) d\tau, m \geq 1 \quad (27)$$

where $F_{i1} = (\tau, \sum_{k=0}^{m} x_{1k}, \ldots, \sum_{k=0}^{m} x_{nk})$, $F_{i2} = (\tau, \sum_{k=0}^{m-1} x_{1k}, \ldots, \sum_{k=0}^{m-1} x_{nk})$

We now prove that the series solution $\sum_{m=0}^{\infty} x_{im}$ converges to $x_i(t)$, the exact solution of given initial value problem.

Let us consider

$$M = \left| F_i \left(\tau, \sum_{k=0}^{m} x_{1k}, \ldots, \sum_{k=0}^{m} x_{nk} \right) \right|, \quad m \geq 0, \quad i \in [1, n] \quad (28)$$

$$K = \left| \left(\frac{\partial F_i \left(\tau, \sum_{k=0}^{m} x_{1k}, \ldots, \sum_{k=0}^{m} x_{nk} \right)}{\partial \left(\sum_{k=0}^{m} x_{jk} \right)} \right)_{\sum_{l=0}^{m-1} x_{1l}, \ldots, \sum_{l=0}^{m-1} x_{nl}} \right|, m \geq 1, i, j \in [1, n] \quad (29)$$

From equations (26) and (27),

$$\left. \begin{aligned} |x_{i1}(t)| &= \left| \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} F_i(\tau, x_{10}, \ldots, x_{n0}) \, d\tau \right| \\ &\leq \left| \frac{1}{\Gamma(\alpha_i)} \right| \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} |F_i(\tau, x_{10}, \ldots, x_{n0})| \, d\tau \\ &\leq \frac{M}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} \, d\tau \\ &\leq \frac{M(t - t^*)^{\alpha_i}}{\Gamma(\alpha_i + 1)} \end{aligned} \right\} \quad (30)$$

$$\left. \begin{aligned} |x_{i2}(t)| &= \left| \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} (F_{i1} - F_{i0}) \, d\tau \right| \\ &\leq \left| \frac{1}{\Gamma(\alpha_i)} \right| \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} |F_{i1} - F_{i0}| \, d\tau \\ &\leq \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t - \tau)^{\alpha_i - 1} \left| F_{i0} + \sum_{j=1}^{n} (DF) x_{j1} - F_{i0} \right| d\tau \\ &\leq \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} \left((t - \tau)^{\alpha_i - 1} \sum_{j=1}^{n} |(DF)| |x_{j1}| \right) d\tau \\ &\leq \frac{nK}{\Gamma(\alpha_i)} \int_{t^*}^{t} \left((t - \tau)^{\alpha_i - 1} \frac{M(\tau - t^*)^{\alpha_i}}{\Gamma(\alpha_i + 1)} \right) d\tau \\ &\leq \frac{nKM(t - t^*)^{2\alpha_i}}{\Gamma(2\alpha_i + 1)} \end{aligned} \right\} \quad (31)$$

where $F_{i0} = (\tau, x_{10}, x_{20}, \ldots, x_{n0})$

$F_{i1} = (\tau, x_{10} + x_{11}, \ldots, x_{n0} + x_{n1})$

$DF = \left(\frac{\partial F_{i1}}{\partial (x_{j0} + x_{j1})} \right)_{x_{10}, x_{20}, \ldots, x_{n0}}$

$$\vdots$$
$$\vdots$$
$$\vdots$$

$$
\left.
\begin{aligned}
|x_{im+1}(t)| &= \left| \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t-\tau)^{\alpha_i - 1} (F_{im} - F_{im1}) \, d\tau \right| \\
&\leq \left| \frac{1}{\Gamma(\alpha_i)} \right| \int_{t^*}^{t} (t-\tau)^{\alpha_i - 1} |F_{im} - F_{im1}| \, d\tau \\
&\leq \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t-\tau)^{\alpha_i - 1} \left| F_{im1} + \sum_{j=1}^{n} (DF) x_{jm} - F_{im1} \right| \, d\tau \\
&\leq \frac{1}{\Gamma(\alpha_i)} \int_{t^*}^{t} (t-\tau)^{\alpha_i - 1} \sum_{j=1}^{n} |DF| \, |x_{jm}| \, d\tau \\
&\leq \frac{(Kn)^m M (t-t^*)^{(m+1)\alpha_i}}{\Gamma(1+(m+1)\alpha_i)}
\end{aligned}
\right\}
\qquad (32)
$$

where $F_{im} = F_i(\tau, \sum_{k=0}^{m} x_{1k}, \ldots, \sum_{k=0}^{m} x_{nk})$
$$F_{im1} = F_i(\tau, \sum_{k=0}^{m-1} x_{1k}, \ldots, \sum_{k=0}^{m-1} x_{nk})$$
$$DF = \left(\frac{\partial F_{im}}{\partial \left(\sum_{k=0}^{m} x_{jk} \right)} \right)_{\sum_{l=0}^{m-1} x_{1l}, \ldots, \sum_{l=0}^{m-1} x_{nl}}$$

It is known that the series $\sum_{m=0}^{\infty} \frac{(Kn)^m M (t-t^*)^{(m+1)\alpha_i}}{\Gamma(1+(m+1)\alpha_i)}$ is convergent for entire solution domain $t \in [0, \infty)$, hence, the series solution; $\sum_{m=0}^{\infty} x_{im}(t)$ is absolutely and uniformly convergent in any large time domain.

7. APPLICATION OF NIM AND MNIM

The fractional order biochemical reaction model bestowed in equations (12) and (13) can be written in form of system of second kind Volterra integral equations as

$$u(\tau) = u(0) + J^{\alpha_1} \left(-u\epsilon + \epsilon (u + k - \lambda) \right) \qquad (33)$$

$$v(\tau) = v(0) + J^{\alpha_2} \left(u - (u + k) v \right) \qquad (34)$$

$$w(\tau) = w(0) + J^{\alpha_3} (\lambda v) \qquad (35)$$

with initial conditions; $u(0) = 1$, $v(0) = 0$ and $w(0) = 0$.

As per new iterative method discussed in section 4 and using the initial approximations; $u_0 = 1, v_0 = 0, w_0 = 0$, we get the following analytical expressions for normalized concentration of substrate (u), enzyme-substrate intermediate complex (v) and product (w).

$$u(\tau) = 1 - \epsilon \frac{\tau^{\alpha_1}}{\Gamma(\alpha_1 + 1)} + \epsilon^2 \frac{\tau^{2\alpha_1}}{\Gamma(2\alpha_1 + 1)} + \epsilon (k - \lambda) \frac{\tau^{\alpha_1 + \alpha_2}}{\Gamma(\alpha_1 + \alpha_2 + 1)} - \cdots \cdots \quad (36)$$

$$v(\tau) = \frac{\tau^{\alpha_2}}{\Gamma(\alpha_2 + 1)} - \epsilon \frac{\tau^{\alpha_1 + \alpha_2}}{\Gamma(\alpha_1 + \alpha_2 + 1)} - k \frac{\tau^{2\alpha_2}}{\Gamma(2\alpha_2 + 1)} + \cdots \cdots \cdots \cdots \quad (37)$$

$$w(\tau) = \lambda \frac{\tau^{\alpha_2 + \alpha_3}}{\Gamma(\alpha_2 + \alpha_3 + 1)} - \epsilon\lambda \frac{\tau^{\alpha_1 + \alpha_2 + \alpha_3}}{\Gamma(\alpha_1 + \alpha_2 + \alpha_3 + 1)} - \lambda k \frac{\tau^{2\alpha_2 + \alpha_3}}{\Gamma(2\alpha_2 + \alpha_3 + 1)} + \cdots \cdots$$
$$(38)$$

For special case of $\alpha_1 = \alpha_2 = \alpha_3 = 1$, normalized concentrations of substrate (u), enzyme-substrate intermediate complex (v) and product (w) obtained using the NIM are plotted in figure 1. From figure 1, it can be observed that the concentration of substrate, enzyme-substrate intermediate complex and product are unbounded. By employing the multistage new iterative method with $N = 3$ and $h = 0.1$, we get bounded approximate solutions which are in good agreement with solutions obtained by Runge-Kutta method (fourth order) as illustarted in figure 2.

In comparison to new iterative method, the multistage new iterative method exhibited superior performance in representing the real transient behaviour of fractional order biochemical reaction model. Hence, the multistage new iterative method with $N = 3$ will be utillized for further analysis of time fractional enzyme kinetics for three different sets of dimensionless reaction parameters and for various values of fractional orders; α_1, α_2 and α_3.

We now assume that the fractional orders; α_1, α_2 and α_3 are equal $(\alpha_1 = \alpha_2 = \alpha_3 = 1)$. The fractional order biochemical reaction model is simulated using MNIM for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and for different values of α $(0.97, 0.9, 0.8, 0.7)$. The response of normalized concentration of substrate, enzyme-substrate intermediate complex and product are shown in figure 3. For each value of α, normalized concentration of substrate and enzyme-substrate intermediate complex are slowly decreasing from their initial values to approach zero. On the other hand, normalized product concentration is slowly increasing and eventually attains constant value. Figure 4 displays the effect of increased dimensionless reaction parameters; $k_3 = 2, \lambda = 1, \epsilon = 0.5$ and fractional order, α, on time fractional enzymatic kinetics. The increase in dimensionless reaction parameters increases the product concentration and decreases the maximum value of concentration of enzyme-substrate intermediate complex. The response of concentration of u, v and w for $k_3 = 5, \lambda = 3, \epsilon = 0.8$ and $\alpha = \{0.97, 0.9, 0.80.7\}$ are depicted in figure 5. The additional increase in dimensionless reaction parameters has significant impact on the process variables; u, v and w. As the value of α decreasing, the normalized concentration of substrate and enzyme-substrate intermediate complex are quickly approaching zero. The profile of normalized product concentration follows same trend for each value of α and achieves lowest steady state value 1.250 at $\tau \geq 13$.

In order to investigate the individual effect of fractional orders; α_1, α_2 and α_3 on the concentration of substrate, enzyme-substrate intermediate complex and product, we consider different values of α_1, α_2 and α_3 for dimensionless reaction parameters; $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$. The response of fractional order biochemical reaction model to $\alpha_1 = 0.87$, $\alpha_2 = 0.97$ and $\alpha_3 = 0.75$ is shown in figure 6. The unequal fractional orders cause product concentration to reach highest value of 2.265. At $\tau \geq 9.6$, the substrate concentration is constant at minimum value of 4.0209×10^{-7}. The concentration of enzyme-substrate intermediate complex reaches maximum value of 0.3592 at $\tau = 1.4$ after that slowly reduces to 0.0047. Figures 7 and 8 show the response of normalized process variables; u, v and w for two different sets of fractional orders. It is again noticed that low value of fractional order induces process variables; u and v to reach their respective steady states quickly and gives highest product concentration for normal values of dimensionless reaction parameters.

The inference can be derived from this analysis that the approximate solutions are continuously depending on fractional order. When the value of α tend to 1, the approximate solutions are converging to the exact solutions. As the value of α diminishing, the concentrations of substrate and enzyme-substrate intermediate complex are quickly coming close to zero and the product concentration reaches to its highest value.
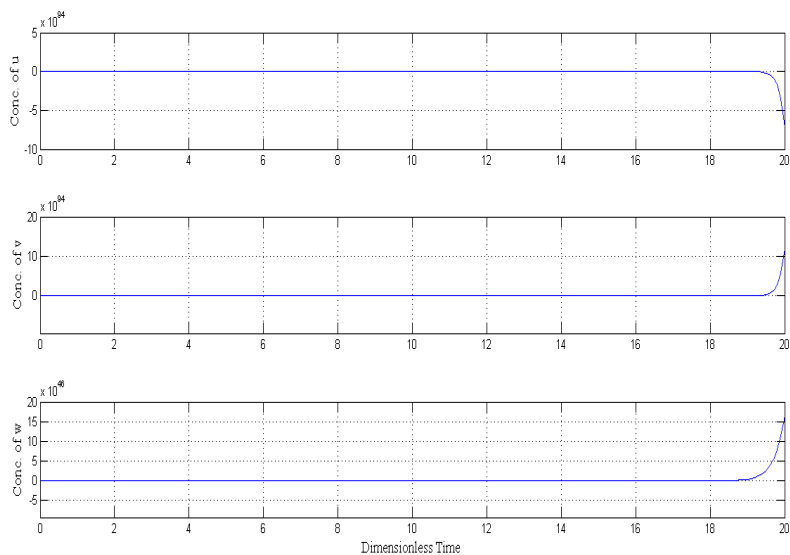
FIGURE 1. Approximate solutions obtained by New Iterative Method for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and $\alpha_1 = \alpha_2 = \alpha_3 = 1$
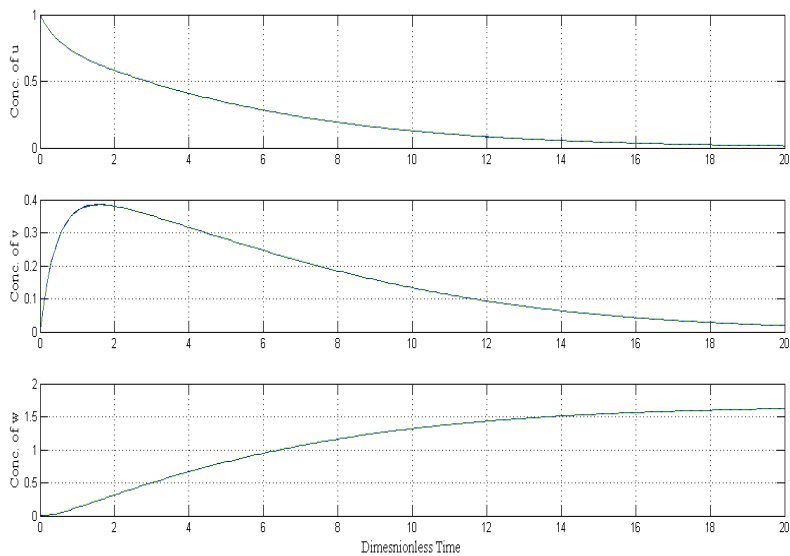

FIGURE 2. Comparison between Multistage New Iterative Method (dashed line) and Runge-Kutta Method (solid line) for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and $\alpha_1 = \alpha_2 = \alpha_3 = 1$
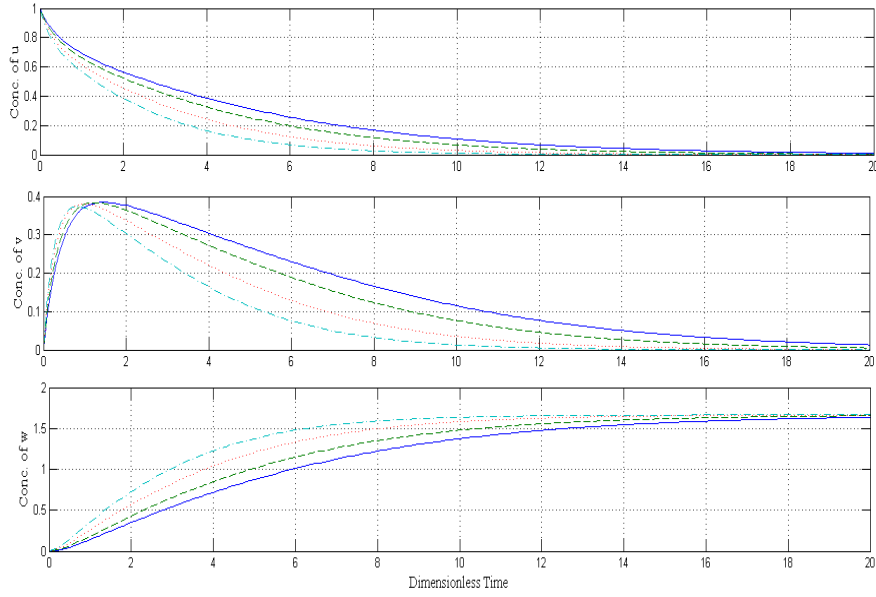
FIGURE 3. Profiles of u, v and w for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and
for $\alpha = 0.97$ (solid), 0.9 (dashed), 0.8 (dotted), 0.7 (dashed-dotted)
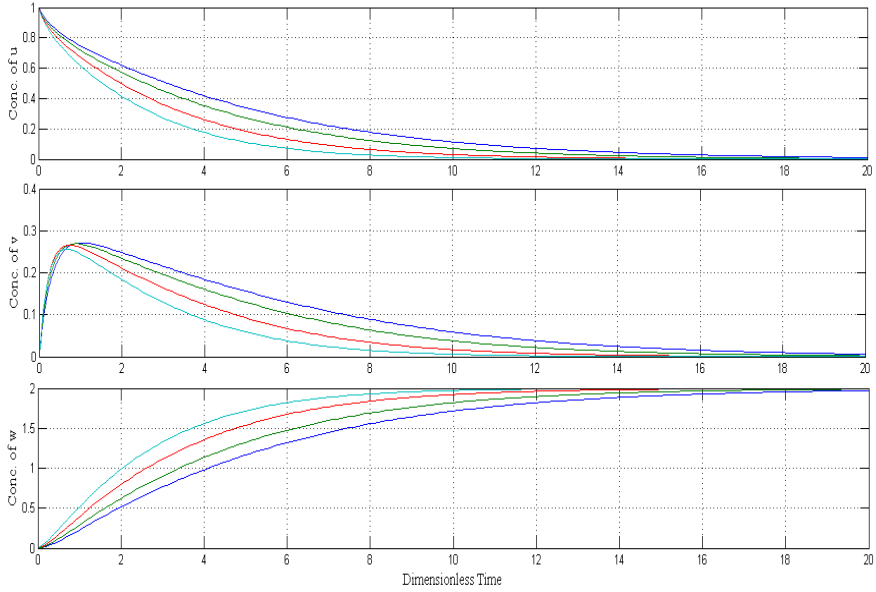
FIGURE 4. Profiles of u, v and w for $k_3 = 2, \lambda = 1, \epsilon = 0.5$ and for
$\alpha = 0.97$ (solid), 0.9 (dashed), 0.8 (dotted), 0.7 (dashed-dotted)
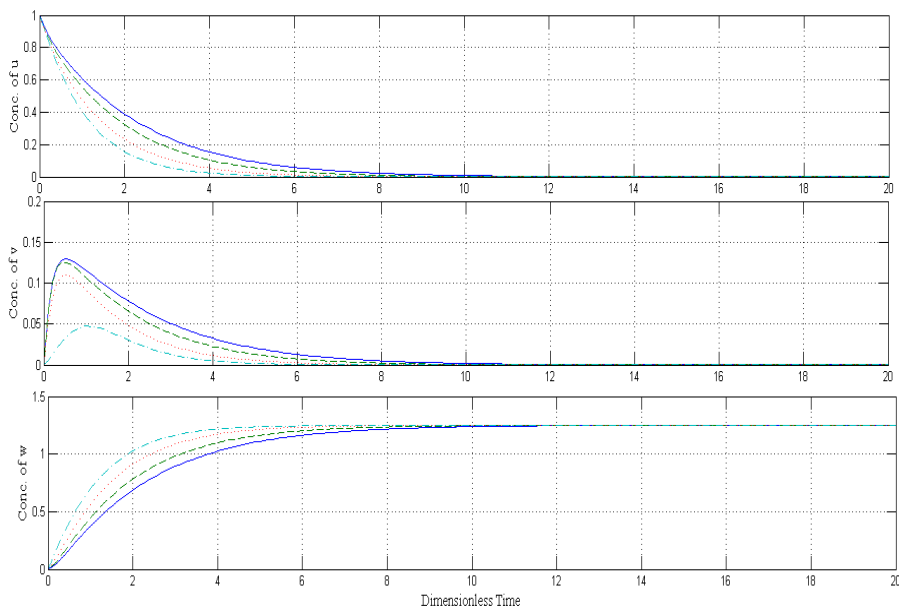
FIGURE 5. Profiles of u, v and w for $k_3 = 5, \lambda = 3, \epsilon = 0.8$ and for $\alpha = 0.97$ (solid), 0.9 (dashed), 0.8 (dotted), 0.7 (dashed-dotted)
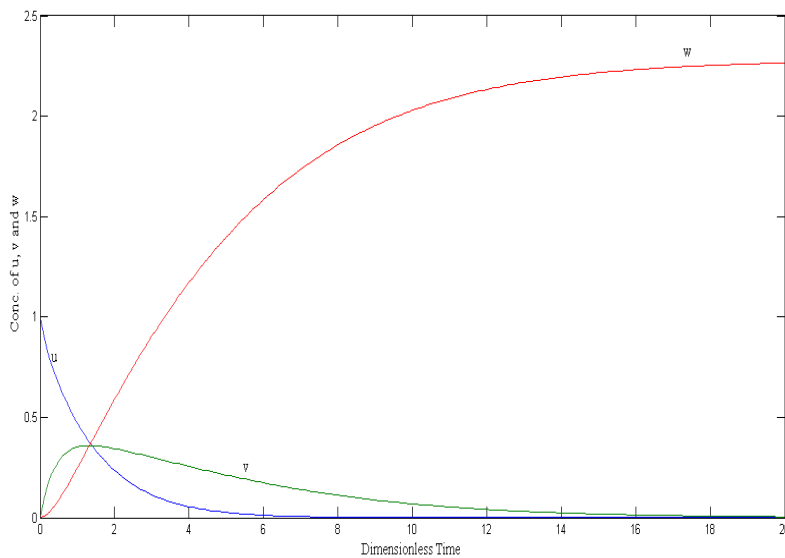

FIGURE 6. Approximate solutions obtained by multistage new iterative method for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and for $\alpha_1 = 0.87, \alpha_2 = 0.97, \alpha_3 = 0.75$
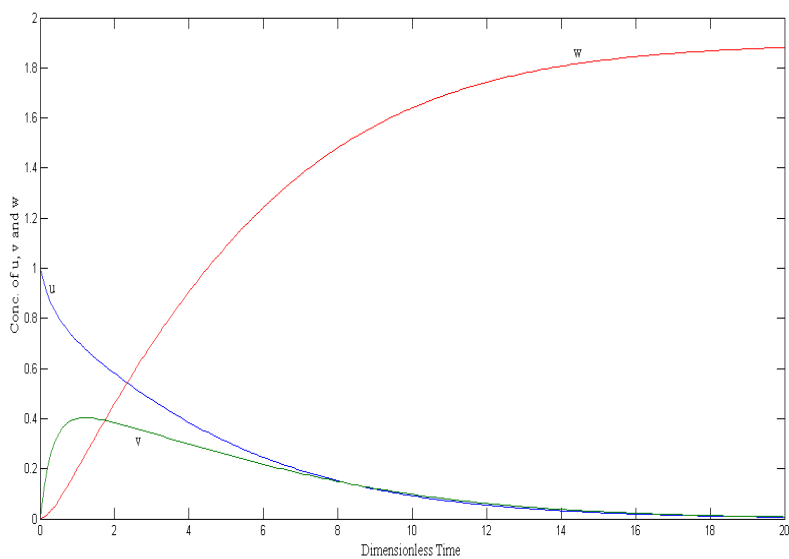
FIGURE 7. Approximate solutions obtained by multistage new iterative method for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and for $\alpha_1 = 0.95, \alpha_2 = 0.85, \alpha_3 = 0.9$
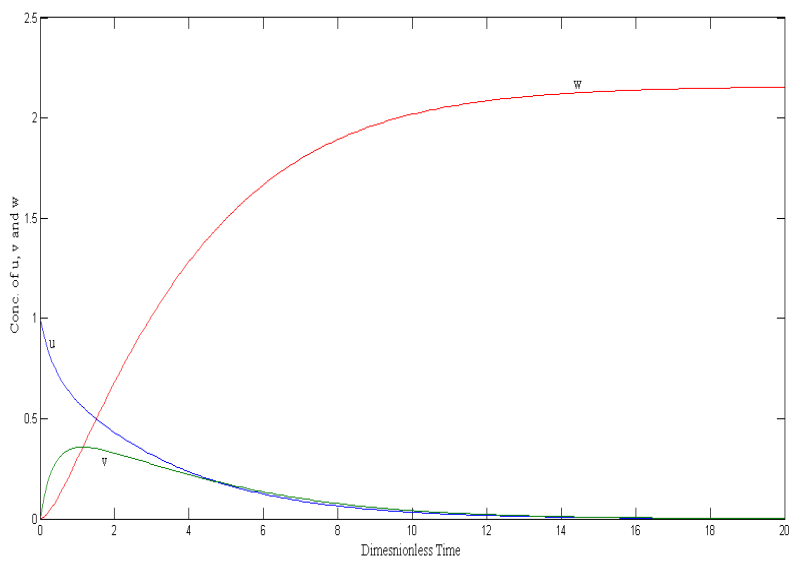

FIGURE 8. Approximate solutions obtained by multistage new iterative method for $k_3 = 1, \lambda = 0.5, \epsilon = 0.6$ and for $\alpha_1 = 0.8, \alpha_2 = 0.9, \alpha_3 = 0.7$

8. CONCLUSIONS

The nonlinear fractional order biochemical reaction model is simulated by using multistage strategy with new iterative method. Comparison between approximate solutions obtained by multistage new iterative and Runge-Kutta method shows that the proposed method is reliable. The approximate solutions derived using MNIM for various combinations of fractional order and dimensionless reaction parameters could represent the true behaviour of fractional order biochemical reaction model in large time domain. However, NIM method failed to achieve the solution for this real process over large time span. The real process was assumed as a multistage process of equal time span and each stage was assumed to contain a set of non-integer order differential equations. The solutions we got here as analytical solution in discrete form over each and every stage of the process. This study reveals that this method takes few terms and less time to compute approximate solution and recommends its application as a powerful alternative to a wide variety of real processes.

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S. K. Damarla
Department of Chemical Engineering, National Institute of Technology Rourkela, Odisha, India
    E-mail address: seshu.chemical@gmail.com, 511ch113@nitrkl.ac.in

M. Kundu
Department of Chemical Engineering, National Institute of Technology Rourkela, Odisha, India
    E-mail address: mkundu@nitrkl.ac.in