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Numerical analysis of fractional order model of HIV-1 infection of CD4^+ T-cells

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Abstract In this article, we present a fractional order HIV-1 infection model of $CD4^+$ T-cell. We analyze the effect of the changing the average number of the viral particle N with initial conditions of the presented model. The Laplace Adomian decomposition method is applying to check the analytical solution of the problem. We obtain the solutions of the fractional order HIV-1 model in the form of infinite series. The concerned series rapidly converges to its exact value. Moreover, we compare our results with the results obtained by Runge-Kutta method in case of integer order derivative.

Keywords. Infectious diseases models, Fractional Derivatives, Laplace transform, Adomian decomposition method, Analytical solution.

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1. Introduction

Human immune deficiency virus (HIV) is a lenti virus that causes acquired immune deficiency syndrome (AIDS). This serious disease destroys the immune system of human being which produce life-threatening opportunistic infections in the body. In human immune system HIV infects primary cell such as helper T-cell, dendritic cells and macrophages. When $CD4^+$ T-cell numbers decline below a critical level, cell-mediated immunity is lost and the body become more progressively susceptible to

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opportunistic infections. HIV epidemic disease is the most dangerous health disease of the modern time. HIV continuously spreading all over the world and there have been few sources to continuous it. This is a clear advances in our knowledge of the molecular biology of the virus and its effect on the human bodies. This is a major dangerous discoveries in the second decade of the epidemic. HIV infections transfer from a fatal illness into a chronic conditions. This has led to dramatic change in mobility and mortality from illness. Moreover,despite these advances on the biomedical front, the epidemic continues to spread and treatment remains unavailable to the overwhelming majority of those who require it. It due to destroy millions of peoples and expenditure of enormous amount of money in health care and research. Although on the medical frontier there have been many advances, but still is no vaccine available for HIV. A mathematical model is determined the transmission dynamics of HIV-1 disease and explain technics to control these disease. In [18], Perelson was introduced a simple mathematical model for the primary infection with HIV. This model is important in the field of mathematical models of HIV infection and also many other models have been proposed, which takes this model as their inspiration. Perelson extended this model and presented behavior of the model and also consider four category of the models, uninfected CD4$^+$ T-cell, latently infected CD4$^+$ T-cell, productively infected CD4$^+$ T-cell and virus population. Rong et al.[3], modified the model further to study the evaluation of drug resistance. Sadegh Zebai et al. presented the model of HIV-1 infected T-cell and presented stability of the model.
The classical order model provided in [2] is given by

$$\begin{cases} \dfrac{dT}{dt} = \beta - kVT - dT + bT^{'}, \\ \dfrac{dT^{'}}{dt} = kVT - (b+\delta)T^{'}, \\ \dfrac{dV}{dt} = N\delta T^{'} - cV, \end{cases} \tag{1.1}$$

with given initial conditions, $T(0) = T_0, T^{'}(0) = T_0^{'}, V(0) = V_0$. In this article, we consider the following fractional order extension of the given model as suggested in [2]. Thus the new fractional order epidemic model is given by

$$\begin{cases} {}^cD^{\alpha_1}T = \beta - kVT - dT + bT^{'}, \\ {}^cD^{\alpha_2}T^{'} = kVT - (b+\delta)T^{'}, \\ {}^cD^{\alpha_3}V = N\delta T^{'} - cV, \end{cases} \tag{1.2}$$

with given initial conditions, $T(0) = T_0,\ T^{'}(0) = T_0^{'},\ V(0) = V_0$, where $0 < \alpha_i \leq 1$ for $i = 1, 2, 3$. The initial conditions are independent on each other and satisfy the relation $N(0) = T + T^{'} + V$ where N is the total number of the individuals in the population, T, $T^{'}$ and V denote the uninfected CD4$^+$ cells, infected CD4$^+$ T-cells and free HIV virus particles in the blood respectively, d is the natural death rate, k represent rate of infection T-cells, δ represents death rate of infected T-cells, b represent rate of those infected cells which return to uninfected class, c represent death rate of virus and N is the average number of viral particles produced by an infected

cells. For the given model of fractional order the numerical solutions are studied by using Adomian decomposition method coupled with Laplace transform. For the verification of our procedure results, we assigned random values to the initial conditions and parameters.
In 1980 Adomian decomposition method (ADM) was introduced by Adomian, which is an effective method for finding numerical and explicit solution of a wide class of differential equations representing physical problems. This method works efficiently for both initial value problems as well as for boundary value problem, for partial and ordinary differential equations, for linear and non-linear equations and also for stochastic system as well [20]. In this method no perturbation or linearization is required. LADM has been done extensive work to provide analytical solution of non-linear equations as well as solving frictional order differential equations. In this paper, we operate Laplace transform method, which is a powerful techniques in engineering and applied mathematics. With the help of this method we transform fractional differential equations into algebraic equations, then solved this algebraic equations by ADM.

2. Preliminaries

Here, in this section we recall some fundamental definitions and results from fractional calculus. For further detailed study, we refer to [5, 10, 23, 12, 14].

Definition 2.1. The fractional integral of Riemann-Liouville type of order $\alpha \in \mathbb{R}_+$ of a function $f : (0, \infty) \to \mathbb{R})$ is defined as

$$I^{\alpha}_{0+} f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} f(s)\, ds,$$

provided that the integral on the right side is pointwise defined on $(0, \infty)$.

Definition 2.2. The Caputo fractional order derivative of a function f on the interval $[0, T]$ is defined by

$${}^{c}D^{\alpha}_{0+} f(t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t (t-s)^{n-\alpha-1} f^{(n)}(s)\, ds,$$

provided that the integral on the right side is pointwise defined on $(0, \infty)$. Further $n = [\alpha] + 1$ and $[\alpha]$ represents the integer part of α.

Lemma 2.3. *The following result holds for fractional differential equations*

$$I^{\alpha}[{}^{c}D^{\alpha} h](t) = h(t) + \sum_{i=0}^{n-1} \frac{h^{(i)}(0)}{i!} t^i,$$

for arbitrary $\alpha > 0, \quad i = 0, 1, 2, \ldots, n-1,$ *where* $n = [\alpha] + 1$ *and* $[\alpha]$ *represents the integer part of* α.

Proof. For the proof of Lemma 2.3, see [11]. □

Definition 2.4. We recall the definition of Laplace transform of Caputo derivative as

$$\mathcal{L}\{{}^{c}D^{\alpha}y(t)\} = s^{\alpha}h(s) - \sum_{k=0}^{n-1} s^{\alpha-i-1}y^{(k)}(0),\ n-1<\alpha<n, n\in N.$$

for arbitrary $c_i \in \mathbb{R}$, $\quad i = 0, 1, 2, \dots, n-1$, where $n = [\alpha]+1$ and $[\alpha]$ represents the integer part of α.

3. The Laplace Adomian Decomposition Method

In this section, we discuss the general procedure of the model (1.2) with given initial conditions. Applying Laplace transform on both side of the model (1.2) as,

$$\begin{cases} \mathcal{L}\{{}^{c}D^{\alpha_1}T\} = \mathcal{L}\{\beta - kVT - dT + bT^{'}\}, \\ \mathcal{L}\{{}^{c}D^{\alpha_2}T^{'}\} = \mathcal{L}\{kVT - (b+\delta)T^{'}\}, \\ \mathcal{L}\{{}^{c}D^{\alpha_3}V\} = \mathcal{L}\{N\delta T^{'} - cV\}, \end{cases} \tag{3.1}$$

which implies that

$$\begin{cases} s^{\alpha_1}\mathcal{L}\{T\} - s^{\alpha_1-1}T(0) = \mathcal{L}\{\beta - kVT - dT + bT^{'}\}, \\ s^{\alpha_2}\mathcal{L}\{T^{'}\} - s^{\alpha_2-1}T^{'}(0) = \mathcal{L}\{kVT - (b+\delta)T^{'}\}, \\ s^{\alpha_3}\mathcal{L}\{V\} - s^{\alpha_3-1}V(0) = \mathcal{L}\{N\delta T^{'} - cV\}. \end{cases} \tag{3.2}$$

Now using initial conditions and taking inverse Laplace transform in model (3.2), we have

$$\begin{cases} T = T_0 + \mathcal{L}^{-1}\left[\dfrac{1}{s^{\alpha_1}}\mathcal{L}\{\beta - kVT - dT + bT^{'}\}\right], \\ T^{'} = T_0^{'} + \mathcal{L}^{-1}\left[\dfrac{1}{s^{\alpha_1}}\mathcal{L}\{kVT - (b+\delta)T^{'}\}\right], \\ V = V_0 + \mathcal{L}^{-1}\left[\dfrac{1}{s^{\alpha_1}}\mathcal{L}\{N\delta T^{'} - cV\}\right]. \end{cases} \tag{3.3}$$

Assuming that the solutions, $T, T^{'}, V$ in the form of infinite series given by

$$T = \sum_{n=0}^{\infty} T_n,\ T^{'} = \sum_{n=0}^{\infty} T_n^{'},\ V = \sum_{n=0}^{\infty} V_n, \tag{3.4}$$

and the nonlinear term VT involved in the model is decompose by Adomian polynomial as

$$VT = \sum_{n=0}^{\infty} P_n, \tag{3.5}$$

where P_n are Adomian polynomials defined as

$$P_n = \frac{1}{\Gamma(n+1)}\frac{d^n}{d\lambda^n}\left[\sum_{k=0}^{n}\lambda^k V_k \sum_{k=0}^{n}\lambda^k T_k\right]|_{\lambda=0}\ . \tag{3.6}$$

Using (3.5),(3.6) and (3.4) in model (3.3), we have

$$\begin{cases} \mathcal{L}(T_0) = \dfrac{T_0}{s},\ \mathcal{L}(T_0^{'}) = \dfrac{T_0^{'}}{s}\ \ \mathcal{L}(V_0) = \dfrac{V_0}{s}, \\ \mathcal{L}(T_1) = \dfrac{\beta}{s^{\alpha_1+1}} + \dfrac{-k}{s^{\alpha_1}}\mathcal{L}\{P_0\} - \dfrac{d}{s^{\alpha_1}}\mathcal{L}\{T_0\} + \dfrac{b}{s^{\alpha_1}}\mathcal{L}\{T_0^{'}\}, \\ \mathcal{L}(T_1^{'}) = \dfrac{-k}{s^{\alpha_2}}\mathcal{L}\{P_0\} - \dfrac{(b+\delta)}{s^{\alpha_2}}\mathcal{L}\{T_0^{'}\},\ \mathcal{L}(V_1) = \dfrac{N\delta}{s^{\alpha_3}}\mathcal{L}\{T_0^{'}\} - \dfrac{c}{s^{\alpha_3}}\mathcal{L}\{V_0\}, \\ \mathcal{L}(T_2) = \dfrac{-k}{s^{\alpha_1}}\mathcal{L}\{P_1\} - \dfrac{d}{s^{\alpha_1}}\mathcal{L}\{T_1\} + \dfrac{b}{s^{\alpha_1}}\mathcal{L}\{T_1^{'}\}, \\ \mathcal{L}(T_2^{'}) = \dfrac{-k}{s^{\alpha_2}}\mathcal{L}\{P_1\} - \dfrac{(b+\delta)}{s^{\alpha_2}}\mathcal{L}\{T_1^{'}\},\ \ \mathcal{L}(V_2) = \dfrac{N\delta}{s^{\alpha_3}}\mathcal{L}\{T_1^{'}\} - \dfrac{c}{s^{\alpha_3}}\mathcal{L}\{V_1\}, \\ \qquad\vdots \\ \mathcal{L}(T_{n+1}) = \dfrac{-k}{s^{\alpha_1}}\mathcal{L}\{P_n\} - \dfrac{d}{s^{\alpha_1}}\mathcal{L}\{T_n\} + \dfrac{b}{s^{\alpha_1}}\mathcal{L}\{T_n^{'}\}, \\ \mathcal{L}(T_{n+1}^{'}) = \dfrac{-k}{s^{\alpha_2}}\mathcal{L}\{P_n\} - \dfrac{(b+\delta)}{s^{\alpha_2}}\mathcal{L}\{T_n^{'}\},\ \ \mathcal{L}(V_{n+1}) = \dfrac{N\delta}{s^{\alpha_3}}\mathcal{L}\{T_n^{'}\} - \dfrac{c}{s^{\alpha_3}}\mathcal{L}\{V_n\}. \end{cases} \tag{3.7}$$

Taking laplace inverse of (3.7) on both side, we get

$$\begin{cases} T_0 = T_0,\ T_0^{'} = T_0^{'},\ V_0 = V_0, \\ T_1 = \dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)} + (-kV_0T_0 - T_0 + T_0^{'})\dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)},\ T_1^{'} = (kV_0T_0 - (b+\delta)T_0^{'})\dfrac{t^{\alpha_2}}{\Gamma(\alpha_2+1)}, \\ V_1 = (\delta NT_0^{'} - cV_0)\dfrac{t^{\alpha_3}}{\Gamma(\alpha_3+1)}, \\ T_2 = (-kV_0T_0 - T_0 + T_0^{'})(-kV_0 - d)\dfrac{t^{2\alpha_1}}{\Gamma(2\alpha_1+1)} - kT_0(\delta NT_0 - cV_0)\dfrac{t^{\alpha_3+\alpha_1}}{\Gamma(\alpha_3+\alpha_1)} \\ -k(\delta NT_0 - cV_0)\dfrac{t^{\alpha_3+2\alpha_1}}{\Gamma(\alpha_3+2\alpha_1+1)} + b(kV_0T_0 - (b+\delta)T_0^{'})\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)}, \\ T_2^{'} = kV_0(-kV_0T_0 - T_0 + T_0^{'})\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)} + k(T_0\delta NT_0^{'} - cV_0)T_0\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} \\ +(\delta NT_0^{'} - cV_0)\dfrac{\alpha_3+\alpha_2}{\Gamma(\alpha_3+\alpha_2+1)} + (\delta NT_0 - cV_0)\dfrac{t^{\alpha_3+\alpha_1}}{\Gamma(\alpha_3+\alpha_1+1)} \\ -(b+\delta)(kV_0T_0 - (b+\delta)T_0^{'})\dfrac{t^{2\alpha_2}}{2\alpha_2+1}, \\ V_2 = \delta N(kV_0T_0 - (b+\delta)T_0^{'})\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} - c(\delta NT_0^{'} - cV_0)\dfrac{t^{2\alpha_3}}{\Gamma(2\alpha_3+1)}. \end{cases} \tag{3.8}$$

On the above fashion, we can obtain the remaining terms similarly. Finally, we get the solution in the form of infinite series is given by

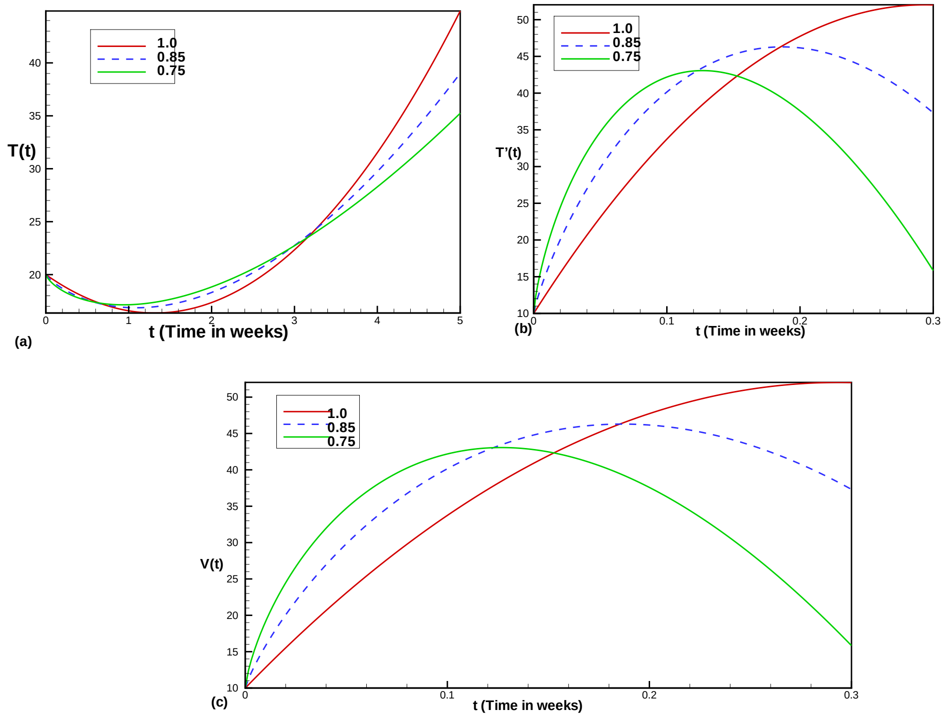
$$
\begin{aligned}
T(t) &= T_0 + T_1 + T_2 + T_3 + \dots = \sum_{i=0}^{\infty} T_i, \\
T^{'}(t) &= T_0^{'} + T_1^{'} + T_2^{'} + \dots = \sum_{i=0}^{\infty} T_i^{'}, \\
V(t) &= V_0 + V_1 + V_2 + V_3 + \dots = \sum_{i=0}^{\infty} V_i.
\end{aligned}
\tag{3.9}
$$

4. Numerical Simulation

In this section we find numerical simulation of the considered problem (1.2), using values of the parameter $N = 100,\ \delta = 0.16,\ k = 0.0024,\ V_0 = 10,\ T_0^{'} = 20,\ T_0 = 70,\ b = 0.2,\ c = 3.4,\ \beta = 1$, then after some simplification, we can write the solution of proposed model (1.2) after three terms as

$$
\begin{cases}
T_0 = 70,\ T_0^{'} = 20,\ V_0 = 10, \\
T_1 = \dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)} - 51.68\dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)},\ T_1^{'} = -5.52\dfrac{t^{\alpha_2}}{\Gamma(\alpha_2+1)},\ V_1 = 286\dfrac{t^{\alpha_3}}{\Gamma(\alpha_3+1)}, \\
T_2 = 1.36\dfrac{t^{2\alpha_1}}{\Gamma(2\alpha_1+1)} - 48.04\dfrac{t^{\alpha_3+\alpha_1}}{\Gamma(\alpha_3+\alpha_1)} - 182.44\dfrac{t^{\alpha_3+2\alpha_1}}{\Gamma(\alpha_3+2\alpha_1+1)} \\
\qquad - 2.60\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)}, \\
T_2^{'} = -1.24\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)} + 50.73\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} - 29.20\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} \\
\qquad - 17.20\dfrac{\alpha_3+\alpha_1}{\Gamma(\alpha_3+\alpha_1+1)} + 1.11\dfrac{t^{2\alpha_2}}{\Gamma(2\alpha_2+1)}, \\
V_2 = -0.88\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} - 972.40\dfrac{t^{2\alpha_3}}{\Gamma(2\alpha_3+1)}.
\end{cases}
\tag{4.1}
$$

FIGURE 1. The plot shows the dynamics of $T(t)$, $T^{'}(t)$ and $V(t)$ for various values of $\alpha_i(i=1,2,3)=1$ via LADM.

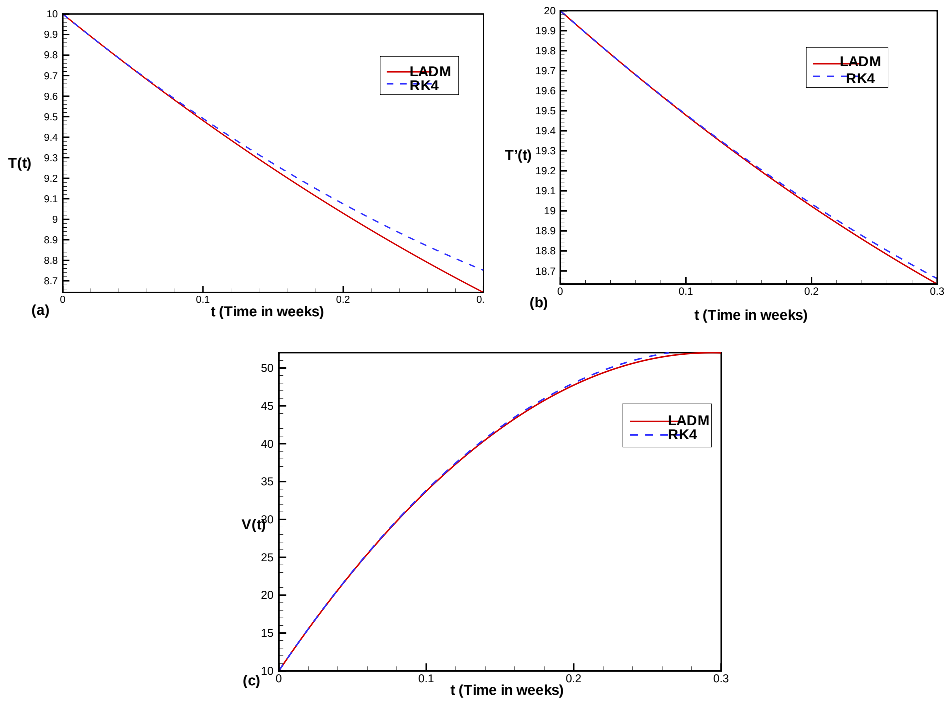


After, three terms the solutions become

$$
\begin{cases}
T = 70 + \dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)} - 51.68\dfrac{t^{\alpha_1}}{\Gamma(\alpha_1+1)} + 1.36\dfrac{t^{2\alpha_1}}{\Gamma(2\alpha_1+1)} - 48.04\dfrac{t^{\alpha_3+\alpha_1}}{\Gamma(\alpha_3+\alpha_1)} \\
\qquad - 182.44\dfrac{t^{\alpha_3+2\alpha_1}}{\Gamma(\alpha_3+2\alpha_1+1)} - 2.60\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)}, \\
T^{'} = 20 - 5.52\dfrac{t^{\alpha_2}}{\Gamma(\alpha_2+1)} - 1.24\dfrac{t^{\alpha_2+\alpha_1}}{\Gamma(\alpha_2+\alpha_1+1)} + 50.73\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} \\
\qquad - 29.20\dfrac{t^{\alpha_3+\alpha_2}}{\Gamma(\alpha_3+\alpha_2+1)} - 17.20\dfrac{\alpha_3+\alpha_1}{\Gamma(\alpha_3+\alpha_1+1)} + 1.11\dfrac{t^{2\alpha_2}}{\Gamma(2\alpha_2+1)}, \\
V = 10 + 286\dfrac{t^{\alpha_3}}{\Gamma(\alpha_3+1)} - 0.88\dfrac{t^{\alpha_3+\alpha_2+1}}{\Gamma(\alpha_3+\alpha_2+1)} - 972.40\dfrac{t^{2\alpha_3}}{\Gamma(2\alpha_3+1)}.
\end{cases}
\tag{4.2}
$$

From Figure 1, one can see that fractional order produces freedom in growing or decaying of various cells in the given models. Clearly from the plot, we observed that

FIGURE 2. The comparison between the solutions via $RK4$ and LADM method at classical order $\alpha_i(i = 1, 2, 3) = 1$.



fractional order has the great effect on the behavior of dynamics of various cells in the proposed model. From the Figure 2, we see that our scheme provides close agreement between the solutions obtained by RK4 method and proposed method. Our method is better than RK4 because it has no need of predefined step size and neither required discretization of data.

5. Convergence Analysis

The above solution in the form of series, which is rapidly convergent and converges uniformly to the exact solution. To check the convergence of the series (4.2), we use classical techniques, (see [1, 22]). For sufficient conditions of convergence of this method , we give the following theorem by using idea [7, 16].

Theorem 5.1. *Let $\mathcal{B}$ and $\mathcal{B}$ be two Banach spaces and $\mathcal{T} : \mathcal{B} \to \mathcal{B}$ be a contractive nonlinear operator such that for all $x, x^{'} \in \mathcal{B}, ||\mathcal{T}(x) - \mathcal{T}(x^{'})|| \leq k||x - x^{'}||, 0 < k < 1$. Then by using of Banach contraction principle, $\mathcal{T}$ has a unique point x such that $\mathcal{T}x = x$, where $x = (T, T^{'}, V)$. The series given in (4.2) can be written by applying*

Adomian decomposition method as

$$x_n = \mathcal{T}x_{n-1}, x_{n-1} = \sum_{i=1}^{n-1} x_i, n = 1, 2, 3, \ldots,$$

and assume that $x_0 = x_0 \in \mathcal{S}_r(x)$ *where* $\mathcal{S}_r(x) = \{x^{'} \in \mathcal{B} : ||x^{'} - x|| < r\}$*, then, we have*

(*i*) $x_n \in \mathcal{S}_r(x)$;

(*ii*) $\lim\limits_{n\to\infty} x_n = x$.

Proof. : For (i), using mathematical induction for $n = 1$, we have

$$||x_0 - x|| = ||\mathcal{T}(x_0) - \mathcal{T}(x)|| \leq k||x_0 - x||.$$

Let the result is true for $n - 1$, then

$$||x_0 - x|| \leq k^{n-1}||x_0 - x||.$$

we have

$$||x_n - x|| = ||\mathcal{T}(x_{n-1}) - \mathcal{T}(x)|| \leq k||x_{n-1} - x|| \leq k^n||x_0 - x||.$$

Hence using (i) we, have

$$||x_n - x|| \leq k^n||x_0 - x|| \leq k^n r < r,$$

which implies that $x_n \in \mathcal{S}_r(x)$.
(ii) Since $||x_n - x|| \leq k^n||x_0 - x||$ and as $\lim_{n\to\infty} k^n = 0$.
So, we have $\lim_{n\to\infty} ||x_n - x|| = 0 \Rightarrow \lim_{n\to\infty} x_n = x$. □

6. Conclusion

With the help of Laplace transform coupled with Adomain decomposition method, we have developed an easy numerical scheme to compute the numerical solutions of nonlinear model of HIV-1 of fractional order. The dynamics of the various cells involved in the model have been displayed using Matlab. Also the comparison of the dynamics of the corresponding cells via RK4 method and proposed method has also displayed for classical order in the last Figure 2. From the above analysis, we conclude that the proposed method is an efficient method and many nonlinear problems of fractional order as well as classical order differential and integral equations can easily be solved for their numerical solutions, where the exact solution is impossible or difficult to calculate.

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