

Numerical Solution of a Fractional Order Model of HIV Infection of CD4⁺T Cells Using Müntz-Legendre Polynomials

Mojtaba Rasouli Gandomani, M. Tavassoli Kajani*

Department of Mathematics
Isfahan (Khorasgan) Branch, Islamic Azad University
Isfahan, Iran
E-mails: mojtabamath@yahoo.com, tavassoli_k@yahoo.com

*Corresponding author

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Abstract: In this paper, the model of HIV infection of CD4⁺T cells is considered as a system of fractional differential equations. Then, a numerical method by using collocation method based on the Müntz-Legendre polynomials to approximate solution of the model is presented. The application of the proposed numerical method causes fractional differential equations system to convert into the algebraic equations system. The new system can be solved by one of the existing methods. Finally, we compare the result of this numerical method with the result of the methods have already been presented in the literature.

Keywords: HIV infection model, Fractional ODE, Müntz-Legendre polynomials, Collocation Method.

Introduction

The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) which has a roughly spherical shape and a diameter of about 120 nm (about 60 times smaller than the dimension of red blood cell). It attacks the immune system of the body. Without a strong immune system, the body can not fight against cancers or other infectious diseases effectively. HIV infects and destroys certain white blood cells called CD4⁺T cells which are an important part of the immune system. If too many CD4⁺ cells are destroyed, the body is not perfectly capable of defending against infection. The fact is that the early and timely treatment can slow or stop progress of HIV infection. The medicines can help the immune system return to a healthier condition. The number of infected and uninfected CD4⁺T cells is important to measure HIV progress and to get best treatment and cure [5, 12].

Recently, different mathematical models are presented to examine the dynamics of CD4⁺T cells. The model in [27] is one of them with a system of differential equations as follows:

$$\begin{cases} \frac{dT(t)}{dt} = q - \eta T(t) + rT(t) \left(1 - \frac{T(t) + 1}{T_{\max}}\right) - kV(t)T(t) \\ \frac{dI(t)}{dt} = kV(t)T(t) - \beta I(t) \\ \frac{dV(t)}{dt} = \mu \beta I(t) - \gamma V(t) \\ T(0) = T_0, \quad I(0) = I_0, \quad V(0) = V_0 \end{cases}, \quad 0 \leq t \leq R < \infty. \quad (1)$$

Each parameter in this model is explained in Table 1. Recently, many mathematicians have examined this model and present lots of different numerical methods to solve it. For example,

Table 1. List of variables and parameters [2, 19, 21, 27]

Parameters and variables	Meaning
$T(t)$	The concentration of uninfected CD4 ⁺ T in the blood
$I(t)$	The concentration of infected CD4 ⁺ T in the blood
$V(t)$	The concentration of HIV virus particle in the blood
η	Turnover rate of uninfected CD4 ⁺ T cells
β	Turnover rate of infected CD4 ⁺ T cells
γ	Turnover rate of HIV virus particles
$1 - \frac{T+1}{T_{\max}}$	Logistic growth indicator of uninfected CD4 ⁺ T cells
k	The infection rate of CD4 ⁺ T cells by HIV virus
kVT	The incident of HIV infection of healthy CD4 ⁺ T
μ	The number of virus particles produced by each infected CD4 ⁺ T cell during its life time
q	The generation rate of uninfected CD4 ⁺ T cells in the body
$\mu\beta$	The generation rate of virions through infected CD4 ⁺ T cells
T_{\max}	The maximal concentration of CD4 ⁺ T cells in the blood
r	Tate of cells' duplication through the process of mitosis when they are stimulated by antigen and mitogen

Ongum [20] has solved it by using Adomian Laplace decomposition. Srivastava et al. [23] have presented an accurate approximate solution of the differential equations system with a numerical method based on DTM. Yuzbasi [28] employs Bessel polynomials to find a numerical method for approximating the solution of the differential equations.

In recent years, the application of fractional differential equations has been found in different fields of sciences as well as in many scientific and practical models [10, 15]. Fractional differential equations are applied in many natural phenomena in which case these equations have more validity and adaptation to the natural phenomena. Biological systems have fractal structures and they have very close ties with fractional differential equations [24, 25, 26]. Thus using fractional differential equations for these systems can produce more natural results. For instances, by using fractional differential equations, Arafa et al. [1] examined the impact of antiretroviral drugs and Erturk et al. [8] considered a model of kind of human virus which can infect CD4⁺T cells. Other applications of fractional differential equations are demonstrated in [6, 14, 22].

In this paper we consider the presented model in Eq. (1) as a form of fractional differential equations so the model changes as follows:

$$\begin{cases} D_*^{\alpha_1} T(t) = q - \eta T(t) + rT(t) \left(1 - \frac{T(t)+1}{T_{\max}}\right) - kV(t)T(t), \\ D_*^{\alpha_2} I(t) = kV(t)T(t) - \beta I(t), \\ D_*^{\alpha_3} V(t) = \mu\beta I(t) - \gamma V(t), \\ T(0) = T_0, \quad I(0) = I_0, \quad V(0) = V_0, \end{cases} \quad \begin{matrix} 0 \leq t \leq R < \infty, \\ 0 < \alpha_1, \alpha_2, \alpha_3 \leq 1, \end{matrix} \quad (2)$$

where we adopt Caputo's formula to obtain fractional derivative as follows:

$$D_*^\alpha y(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t (t - \tau)^{-\alpha} y'(\tau) d\tau.$$

The application of the different numerical methods to solve of fractional differential equations has attracted a lot of interest of mathematicians. For example, Chen et al. [4] used an algorithm based on wavelets as well as Jafari and Daftardar-Gejji [11] applied Adomian decomposition and Zurigat et al. [30] also took advantage of analysis homotopy to approximate fractional

differential equations. For more details one can read [7, 13, 18, 29].

In this paper, our aim is to solve fractional differential equations (2) system with a collocation method based on the Müntz-Legendre polynomials. Since fractional derivative from a polynomial with integer order is not necessarily a polynomial with integer order so it is better to use collocation method based on polynomials with fractional order. The main advantage of using the Müntz-Legendre polynomials is that they have fractional order and actually their fractional derivative is also a Müntz-Legendre polynomial with the result that the use of the Müntz-Legendre polynomials in collocation method seems logical. Esmaeili et al. [9] used the Müntz-Legendre polynomials to solve fractional differential equations.

The paper is organized as follows: Section 2 is devoted to preliminaries. In fact this section contains two subsections. In the first one we introduce Jacobi polynomials. The second one is related to Müntz-Legendre polynomials. The collocation method to solve fractional differential equations system is presented in section 3. In section 4, the results are compared. Section 5 concludes the paper.

Preliminaries

Jacobi polynomials

The Jacobi polynomials are extensively used for solving fractional differential equations. They are orthogonal on the interval $[-1, 1]$ with respect to the weight function

$$w^{(\alpha, \beta)}(t) = (1-t)^\alpha (1+t)^\beta,$$

where $\alpha, \beta > -1$.

These polynomials can be obtained through the following recurrent relation:

$$\begin{aligned} J_0^{(\alpha, \beta)}(t) &= 1, & J_1^{(\alpha, \beta)}(t) &= \frac{1}{2}((\alpha - \beta) + (\alpha + \beta + 2)t), \\ a_k^{(\alpha, \beta)} J_{k+1}^{(\alpha, \beta)}(t) &= b_k^{(\alpha, \beta)}(t) J_k^{(\alpha, \beta)}(t) - c_k^{(\alpha, \beta)} J_{k-1}^{(\alpha, \beta)}(t), \\ a_k^{(\alpha, \beta)} &= 2(k+1)(k + \alpha + \beta + 1)(2k + \alpha + \beta), \\ b_k^{(\alpha, \beta)}(t) &= (2k + \alpha + \beta + 1)((2k + \alpha + \beta)(2k + \alpha + \beta + 2)t + \alpha^2 - \beta^2), \\ c_k^{(\alpha, \beta)} &= 2(k + \alpha)(k + \beta)(2k + \alpha + \beta + 2). \end{aligned} \tag{3}$$

The initial derivative of the Jacobi polynomials can be obtained as follows:

$$\frac{d}{dt} J_k^{(\alpha, \beta)}(t) = \frac{1}{2}(k + \alpha + \beta + 1) J_{k-1}^{(\alpha+1, \beta+1)}(t). \tag{4}$$

Müntz-Legendre polynomials

Let $\Lambda_n = \{\lambda_1, \lambda_2, \dots, \lambda_n\}$ be under condition $\text{Re}(\lambda_k) > -\frac{1}{2}$ such that Müntz-Legendre polyno-

mials on the interval $(0, 1]$ are defined as follows [3, 17]:

$$L_n(t) = L(\Lambda_n, t) = \sum_{k=0}^n C_{n,k} t^{\lambda_k}, \quad C_{n,k} = \frac{\prod_{v=0}^{n-1} (\lambda_k + \bar{\lambda}_v + 1)}{\prod_{v=0, v \neq k}^n (\lambda_k - \lambda_v)}. \quad (5)$$

Basic properties of the Müntz-Legendre polynomials:

$$\begin{aligned} (L_n, L_m) &= \int_0^1 L_n(t) L_m(t) dt = \frac{\delta_{mn}}{\lambda_n + \bar{\lambda}_n + 1}, \\ L_n(1) &= 1, \\ L'_n(1) &= \lambda_n + \sum_{k=0}^{n-1} (\lambda_k + \bar{\lambda}_k + 1). \end{aligned} \quad (6)$$

Here, all λ_k are chosen so that $\lambda_k = \alpha k$ (α is a positive real number), the shifted Müntz-Legendre polynomials on the interval $I = [0, R)$ are defined as follows :

$$L_{I,n}(t : \alpha) = \sum_{k=0}^n C_{n,k} \left(\frac{t}{R}\right)^{\alpha k}, \quad C_{n,k} = \frac{(-1)^{n-k}}{\alpha^n k! (n-k)!} \prod_{v=0}^{n-1} ((k+v)\alpha + 1). \quad (7)$$

Some of the shifted Müntz-Legendre polynomials' properties according to [3] are:

$$L_{I,n}(R : \alpha) = 1, \quad L'_{I,n}(R : \alpha) = \frac{\alpha n + \sum_{k=0}^{n-1} (2\alpha k + 1)}{R}.$$

Regarding Eq. (6), we have:

$$\int_0^R L_{I,n}(t) L_{I,m}(t) dt = \frac{R \delta_{mn}}{1 + 2\alpha n}.$$

Furthermore, following [13] a stable recurrence relation can be obtained for shifted Müntz-Legendre polynomials via the Jacobi polynomials, as follows:

$$\begin{aligned} L_{I,0}(t : \alpha) &= 1, \quad L_{I,1}(t : \alpha) = \left(\frac{1}{\alpha} + 1\right) \left(\frac{t}{R}\right)^{\alpha} - \frac{1}{\alpha}, \\ a_{I,n} L_{I,n+1}(t : \alpha) &= b_{I,n}(t) L_{I,n}(t : \alpha) - c_{I,n} L_{I,n-1}(t : \alpha), \\ a_{I,n} &= a_n^{(0, \frac{1}{\alpha} - 1)}, \quad b_{I,n}(t) = b_n^{(0, \frac{1}{\alpha} - 1)} \left(2 \left(\frac{t}{R}\right)^{\alpha} - 1\right), \quad c_{I,n} = c_n^{(0, \frac{1}{\alpha} - 1)}. \end{aligned} \quad (8)$$

In addition, according to [17] fractional derivative of these polynomials can also be obtained with the following equation:

$$D_*^{\alpha} L_{I,n}(t : \alpha) = \frac{1 + \alpha n}{\alpha \Gamma(1 - \alpha) R^{\alpha}} \int_0^R (1 - \tau^{\frac{1}{\alpha}})^{-\alpha} J_{n-1}^{(1, \frac{1}{\alpha})} \left(2 \left(\frac{t}{R}\right)^{\alpha} \tau - 1\right) d\tau. \quad (9)$$

Method of solution

This section is devoted to presentation of the numerical method for evaluating fractional differential equations system. Assume $\alpha_1 = \alpha_2 = \alpha_3 = \alpha$. We approximate the unknown functions of $T(t)$, $I(t)$, $V(t)$, by using a linear combination of the shifted Müntz-Legendre function as follows:

$$\begin{aligned}
 T(t) &\approx T_n(t) = \sum_{j=0}^N c_j L_{I,j}(t : \alpha), \\
 I(t) &\approx I_n(t) = \sum_{j=0}^N d_j L_{I,j}(t : \alpha), \\
 V(t) &\approx V_n(t) = \sum_{j=0}^N e_j L_{I,j}(t : \alpha),
 \end{aligned} \tag{10}$$

where coefficients $c_j, d_j, e_j, j = 0, 1, 2, \dots, N$ are unknown. Now substituting Eq. (10) into the fractional differential equations system Eq. (2) gives the following results:

$$\left\{ \begin{aligned}
 &\sum_{j=0}^N c_j D_*^{\alpha_1} L_{I,j}(t : \alpha) = q - \eta \sum_{j=0}^N c_j L_{I,j}(t : \alpha) \\
 &\quad + r \sum_{j=0}^N c_j L_{I,j}(t : \alpha) \left(1 - \frac{\sum_{j=0}^N c_j L_{I,j}(t : \alpha) + 1}{T_{\max}} \right) \\
 &\quad - k \sum_{j=0}^N e_j L_{I,j}(t : \alpha) \sum_{j=0}^N c_j L_{I,j}(t : \alpha), \\
 &\sum_{j=0}^N d_j D_*^{\alpha_2} L_{I,j}(t : \alpha) = k \sum_{j=0}^N e_j L_{I,j}(t : \alpha) \sum_{j=0}^N c_j L_{I,j}(t : \alpha) - \beta \sum_{j=0}^N d_j L_{I,j}(t : \alpha), \\
 &\sum_{j=0}^N e_j D_*^{\alpha_3} L_{I,j}(t : \alpha) = \mu \beta \sum_{j=0}^N d_j L_{I,j}(t : \alpha) - \gamma \sum_{j=0}^N e_j L_{I,j}(t : \alpha), \\
 &\sum_{j=0}^N c_j L_{I,j}(0 : \alpha) = T_0, \quad \sum_{j=0}^N d_j L_{I,j}(0 : \alpha) = I_0, \quad \sum_{j=0}^N e_j L_{I,j}(0 : \alpha) = V_0.
 \end{aligned} \right. \tag{11}$$

The fractional derivative of the above Legendre functions is obtained via Eq. (9).

Now, the collocation points $\theta_i, i = 1, 2, \dots, n$ should be substitute into Eq. (11). It is a fact, that the best and simplest choice for the collocation points θ_i is Chebyshev points associated with the interval $[0, R]$ which is defined as follows:

$$\theta_i = \frac{R}{2} - \frac{R}{2} \cos\left(\frac{\pi i}{n}\right), \quad i = 1, 2, \dots, n.$$

Hence, the Eq. (11) is converted:

$$\left\{ \begin{array}{l}
 \sum_{j=0}^N c_j D_*^{\alpha_1} L_{I,j}(\theta_i : \alpha) = q - \eta \sum_{j=0}^N c_j L_{I,j}(\theta_i : \alpha) \\
 \quad + r \sum_{j=0}^N c_j L_{I,j}(\theta_i : \alpha) \left(1 - \frac{\sum_{j=0}^N c_j L_{I,j}(\theta_i : \alpha) + 1}{T_{\max}} \right) \\
 \quad - k \sum_{j=0}^N e_j L_{I,j}(\theta_i : \alpha) \sum_{j=0}^N c_j L_{I,j}(\theta_i : \alpha), \\
 \sum_{j=0}^N d_j D_*^{\alpha_2} L_{I,j}(\theta_i : \alpha) = k \sum_{j=0}^N e_j L_{I,j}(\theta_i : \alpha) \sum_{j=0}^N c_j L_{I,j}(\theta_i : \alpha) - \beta \sum_{j=0}^N d_j L_{I,j}(\theta_i : \alpha), \\
 \sum_{j=0}^N e_j D_*^{\alpha_3} L_{I,j}(\theta_i : \alpha) = \mu \beta \sum_{j=0}^N d_j L_{I,j}(\theta_i : \alpha) - \gamma \sum_{j=0}^N e_j L_{I,j}(\theta_i : \alpha), \\
 \sum_{j=0}^N c_j L_{I,j}(0 : \alpha) = T_0, \quad \sum_{j=0}^N d_j L_{I,j}(0 : \alpha) = I_0, \quad \sum_{j=0}^N e_j L_{I,j}(0 : \alpha) = V_0,
 \end{array} \right. \quad (12)$$

Finally, Eq. (12) generates a system of $3n + 3$ algebraic equations with $3n + 3$ unknown coefficients which can be solved by one of the existing methods and unknown coefficients $c_j, d_j, e_j, j = 0, 1, 2, \dots, n$ should be obtained. Substituting these coefficients in Eq. (10), we obtain $T_n(t), I_n(t)$ and $V_n(t)$.

Numerical results

We employed Maple 16 software to find approximate solution.

In this section, we use the presented numerical method to solve the fractional differential equations system Eq. (2). Besides, we consider the initial values and the explained parameters of the model as follows:

$$T_0 = 0.1, \quad I_0 = 0, \quad V_0 = 0.1, \quad q = 0.1, \quad \eta = 0.02, \quad \beta = 0.3, \\
 r = 3, \quad \gamma = 2.4, \quad k = 0.00027, \quad T_{\max} = 1500, \quad \mu = 10.$$

First, we use the presented method for $\alpha = 1$ and then we compare the obtained results with those of previous methods (See Tables 2, 3 and 4).

Table 2. Numerical comparison for $T(t)$.

t	LADM-Pade [20]	Method in [28]	VIM [16]	RK4	Present Method
0.0	0.1	0.1	0.1	0.1	0.1
0.2	0.2088072731	0.2038616561	0.2088073214	0.2088080833	0.208808084
0.4	0.4061052625	0.3803309335	0.4061346587	0.4062405393	0.406240543
0.6	0.7611467713	0.6954623767	0.7624530350	0.7644238890	0.766442390
0.8	1.3773198590	1.2759624442	1.3978805880	1.4140468310	1.414046852
1.0	2.3291697610	2.3832277428	2.5067466690	2.5915948020	2.591559480

Figs. 1, 2 and 3, respectively demonstrate $T(t), I(t)$ and $V(t)$ using proposed method for $N = 15$ and $\alpha = 0.80, 0.85, 0.90, 0.95, 0.99, 1$.

Table 3. Numerical comparison for $I(t)$.

t	LADM-Pade [20]	Method in [28]	VIM [16]	RK4	Present Method
0.0	0	0	0	0	0
0.2	0.603270728e-5	0.6247872100e-5	0.6032634366e-5	0.6032702150e-5	0.603270224e-5
0.4	0.131591617e-4	0.1293552225e-4	0.1314878543e-4	0.1315834073e-4	0.131583409e-4
0.6	0.212683688e-4	0.2035267183e-4	0.2101417193e-4	0.2122378506e-4	0.212237854e-4
0.8	0.300691867e-4	0.2837302120e-4	0.2795130456e-4	0.3017741955e-4	0.301774201e-4
1.0	0.398736542e-4	0.3690842367e-4	0.2431562317e-4	0.4003781468e-4	0.400378155e-4

Table 4. Numerical comparison for $V(t)$

t	LADM-Pade [20]	Method in [28]	VIM [16]	RK4	Present Method
0.0	0.1	0.1	0.1	0.1	0.1
0.2	0.06187996025	0.06187991856	0.06187995314	0.06187984331	0.061879843
0.4	0.03831324883	0.03829493490	0.03830820126	0.03829488788	0.038294888
0.6	0.02439174349	0.02370431860	0.02392029257	0.02370455014	0.023704550
0.8	0.009967218934	0.01467956982	0.01621704553	0.01468036377	0.014680364
1.0	0.003305076447	0.02370431861	0.01608418711	0.009100845043	0.0091008450

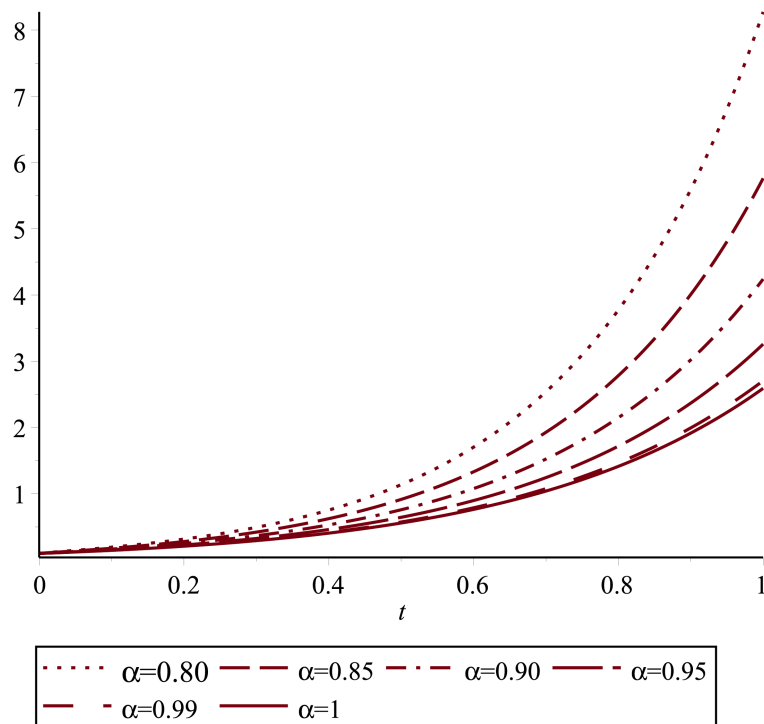


Fig. 1 The approximate solutions $T(t)$ for $N = 15$

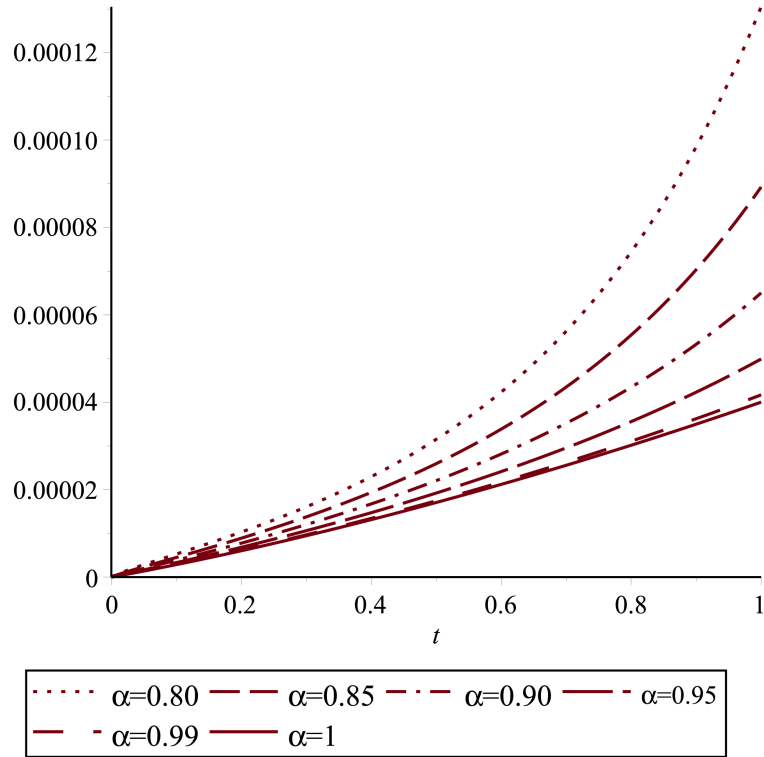


Fig. 2 The approximate solutions $I(t)$ for $N = 15$

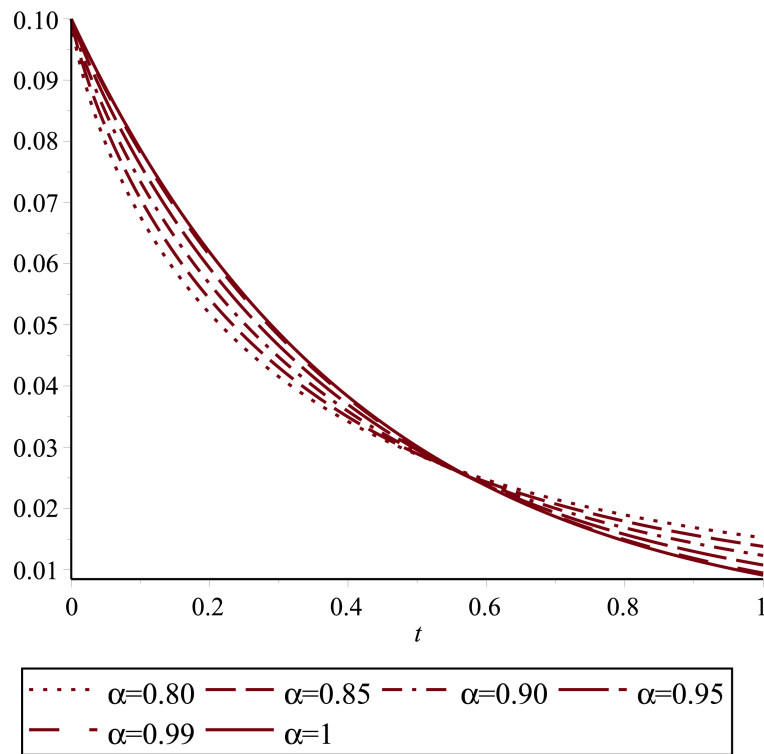


Fig. 3 The approximate solutions $V(t)$ for $N = 15$

Tables 5, 6 and 7 show the values of $T(t)$, $I(t)$ and $V(t)$, for $N = 15$, $\alpha = 0.75, 0.80, 0.85, 0.90, 0.95, 0.98$.

Table 5. The values of $T(t)$ for $N = 15$

t	$\alpha = 0.75$	$\alpha = 0.80$	$\alpha = 0.85$	$\alpha = 0.90$	$\alpha = 0.95$	$\alpha = 0.98$
0.0	0.1	0.1	0.1	0.1	0.1	0.1
0.2	0.3670560	0.3165184	0.2790315	0.2501158	0.2272514	0.2157344
0.4	0.9419131	0.7540629	0.6246844	0.5309877	0.4606339	0.4264249
0.6	2.2858520	1.7039759	1.3317891	1.0784967	0.8979687	0.8133480
0.8	5.4360892	3.7737946	2.7836259	2.1489168	1.8178109	1.5242915
1.0	12.784070	8.2742007	5.7619568	4.2409152	3.2590105	2.8300579

Table 6. The values of $I(t)$ for $N = 15$

t	$\alpha = 0.75$	$\alpha = 0.80$	$\alpha = 0.85$	$\alpha = 0.90$	$\alpha = 0.95$	$\alpha = 0.98$
0.0	0	0	0	0	0	0
0.2	1.2151979e-5	1.0315362e-5	8.9043994e-6	7.7692349e-6	6.8290042e-6	6.3363901e-6
0.4	2.8204527e-5	2.2989039e-5	1.9385818e-5	1.6753726e-5	1.4746964e-5	1.3753198e-5
0.6	5.5742298e-5	4.2343235e-5	3.3864401e-5	2.8164952e-5	2.4155672e-5	2.2294605e-5
0.8	1.0695931e-4	7.4433150e-5	5.5403434e-5	4.3464569e-5	3.5585428e-5	3.2111872e-5
1.0	2.0660978e-4	1.3048453e-4	8.9263409e-5	6.5030221e-5	4.9905893e-5	4.3511235e-5

Table 7. The values of $V(t)$ for $N = 15$

t	$\alpha = 0.75$	$\alpha = 0.80$	$\alpha = 0.85$	$\alpha = 0.90$	$\alpha = 0.95$	$\alpha = 0.98$
0.0	0.1	0.1	0.1	0.1	0.1	0.1
0.2	0.0496485	0.0518676	0.0542264	0.0567019	0.0592643	0.0608295
0.4	0.0335988	0.0342057	0.0349582	0.0358789	0.0369869	0.0377472
0.6	0.0251079	0.0246948	0.0243227	0.0240146	0.0237983	0.0237253
0.8	0.0199388	0.0189386	0.0179038	0.0168397	0.0157587	0.0151098
1.0	0.0165367	0.0151977	0.0137958	0.0123158	0.0107509	0.0097708

Conclusion

This paper proposed a model based on performance of HIV virus for in faction of $CD4^+T$ cells. We formulated the model as a fractional differential equations system. The model was solved by collocation and Müntz-Legendre polynomials. Since the real solution is unknown, we compare obtained results for $\alpha = 1$, with those published in the literature. Further, we show results for different values of α . Our findings demonstrate that the proposed method has a high accuracy compared to other methods. Besides, the presented method is simple and can be applied for solving the fractional cases.

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Mojtaba Rasouli Gandomani, M.Sc.

E-mail: mojtabamath@yahoo.com



He was born on May 13, 1986 in Isfahan, Iran. He received the B.Sc. degree in Applied Mathematics from the Islamic Azad University, Mobarakeh Branch, Isfahan, Iran, in 2010 and a M.Sc. degree in Applied Mathematics from Islamic Azad University, Isfahan (Khorasgan) Branch, Isfahan, Iran, in 2015.

Majid Tavassoli Kajani, Ph.D.

E-mail: mtavassoli@khuisf.ac.ir



He was born on December 26, 1974 in Isfahan, Iran. He received the Ph.D. degree in Applied Mathematics (Numerical Analysis, Integral Equation) from the Science and Research Branch, Islamic Azad University, Tehran, Iran, on September 2003. He has also been a member of the Faculty of Basic Sciences with the Islamic Azad University, Isfahan (Khorasgan) Branch, Isfahan, Iran. He has authored or coauthored more than 60 papers in international journals such as the Applied Mathematical Modelling, the Journal of Computational and Applied Mathematics, the Mathematical Problems in Engineering, Applied Mathematics and Computation, etc.