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An approximate solution of a fractional order differential equation model of human T-cell lymphotropic virus I (HTLV-I) infection of CD4$^+$ T-cells

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ABSTRACT

In this paper, a fractional order differential system for modeling human T-cell lymphotropic virus I (HTLV-I) infection of CD4$^+$ T-cells is studied and its approximate solution is presented using a multi-step generalized differential transform method. The method is only a simple modification of the generalized differential transform method, in which it is treated as an algorithm in a sequence of small intervals (i.e. time step) for finding accurate approximate solutions to the corresponding systems. The solutions obtained are also presented graphically.

1. Introduction

Most people are not familiar with fractional calculus. Indeed, it is three centuries old, as old as the traditional calculus. The research of the theory of fractional differential equations has only been begun considerably recently [1,2]. At this time, the applications of fractional differential equations to physics, biology and engineering are a recent focal of interest [2,3]. Numerous systems are known to exhibit fractional order dynamics, such as viscoelastic systems [4], robotic manupulators [5], gear transmissions [6] and vibration systems [7]. More lately, many mathematicians and scientists worked on the problem of finding the qualitative characteristics and numerical solutions of biological models of fractional order [8–10]. There are variant approaches of modeling diverse biological systems, e.g. ordinary differential equations, difference equations and partial differential equations. In these studies mentioned above, differential equations of fractional order are used. The major reason is that fractional differential equations are innately reference to systems with memory, which stands in most biological systems.

The human T-cell lymphotropic virus-I (HTLV-I) is a retrovirus with a single-stranded RNA virus containing reverse transcriptase (RT) activity and has been implicated in two significant human diseases like adult T-cell leukemia (ATL) and HTLV-I associated myelopathy/tropical spastic paralysis (HAM/TSP). HTLV-I is transmitted in various ways including by sex, blood transfusion, infected needle sharing and vertically from mother to baby. The virus primarily infects CD4^4 T cells and once the infection has taken place spreading to naive cells is through cell-to-cell infection.

There has been an enormous effort made in the mathematical modeling of HTLV-I since the 1990s (see Refs. [11–17]). In Ref. [18], the authors proposed a modified model that describes the T-cell dynamics of human T-cell lymphotropic virus I

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(HTLV-I) infection and the development of adult T-cell leukemia (ATL). The model is given by:

$$T' = \lambda - \mu_T T - \kappa T_A T, \tag{1}$$

$$T_L' = \kappa_1 T_A T - (\mu_L + \gamma) T_L, \tag{2}$$

$$T_A' = \gamma\, T_L - (\mu_A + \rho) T_A, \tag{3}$$

$$T_M' = \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{M_{\max}}}\right) - \mu_M T_M, \tag{4}$$

under the initial values:

$$T(0) = c_1, \qquad T_L(0) = c_2, \qquad T_A(0) = c_3, \qquad T_M(0) = c_4, \tag{5}$$

where T, T_L and T_A denote the numbers of uninfected, latent infected, actively infected $CD4^+$ cells, and T_M the number of leukemia cells, respectively. The parameters λ, λ, μ_T, κ and κ_1, κ and λ, μ_T, κ and κ_1 are the source of $CD4^+$ T-cells from precursors, the natural death rate of $CD4^+$ T-cells, the rate at which uninfected cells are contacted by actively infected cells, the rate of infection of T-cells with a virus from actively infected cells, respectively. μ_L, μ_A and μ_M are blanket death terms for latently infected, actively infected and leukemic cells. Additionally, γ and ρ represent the rates at which latently infected and actively infected cells become actively infected and leukemic, respectively. The rate β determines the speed at which the saturation level for leukemia cells is reached. $T_{M_{\max}}$ is the maximal value that adult T-cell leukemia can reach.

Now we study the fractional-order into the model of HTLV-I infection of $CD4^+$ T-cells [18]. The new system is described by the following set of fractional differential equation

$$D^\alpha T = \lambda - \mu_T T - \kappa T_A T, \tag{6}$$

$$D^\alpha T_L = \kappa_1 T_A T - (\mu_L + \gamma) T_L, \tag{7}$$

$$D^\alpha T_A = \gamma T_L - (\mu_A + \rho) T_A, \tag{8}$$

$$D^\alpha T_M = \rho T_A + \beta T_M \left(1 - \frac{T_M}{T_{M_{\max}}}\right) - \mu_M T_M, \tag{9}$$

where α is a parameter describing the order of the fractional time-derivative in the Caputo sense and $0 < \alpha < 1$, subject to the same initial conditions given in Eq. (5). The general response expression contains a parameter describing the order of the fractional derivatives that can be varied to obtain various responses. Obviously, the integer-order system can be viewed as a special case from the fractional-order system by putting the time-fractional order of the derivative equal to unity. In other words, the ultimate behavior of the fractional system response must converge to the response of the integer order version of the equation.

According to our knowledge, this work represents the first available numerical solution for a model of differential equations of HTLV-I of fractional order. For this reason, we intend to obtain the approximate solution of the problems (5)–(9) via a reliable algorithm based on an adaptation of the generalized differential transform method (GDTM) [19–22], called the multi-step generalized differential transform method (MSGDTM). It can be found that the corresponding numerical solutions obtained by using GDTM is valid only for a short time while the ones obtained by using the MSGDTM is more valid and accurate during a long time.

This paper is organized as follows. In Section 2, we present some necessary definitions and notations related to fractional calculus. In Section 3, the proposed method is described. In Sections 4 and 5, the method is applied to the problems (5)–(9) and numerical simulations are presented graphically, respectively. Finally, the conclusions are given in Section 6.

2. Preliminaries

For the concept of the fractional derivative we will adopt Caputo's definition which is a modification of the Riemann–Liouville definition and has the advantage of dealing properly with initial value problems in which the initial conditions are given in terms of the field variables and their integer order which in the case in most physical processes.

Definition 1. A function $f(x)$ $(x > 0)$ is said to be in the space C_α $(\alpha \in R)$ if it can be written as $f(x) = x^p f_1(x)$ for some $p > \alpha$ where $f_1(x)$ is continuous in $[0, \infty)$, and it is said to be in the space C_α^m if $f^{(m)} \in C_\alpha,\ m \in N$.

Definition 2. The Riemann–Liouville integral operator of order $\alpha > 0$ with $a \geq 0$ is defined as

$$(J_a^\alpha f)(x) = \frac{1}{\Gamma(\alpha)} \int_a^x (x-t)^{\alpha-1} f(t)\mathrm{d}t, \quad x > a, \tag{10}$$

$$(J_a^0 f)(x) = f(x). \tag{11}$$

Properties of the operator can be found in [23]. We only need here the following: For $f \in C_\alpha$, $\alpha, \beta > 0$, $a \geq 0$, $c \in R$ and $\gamma > -1$, we have

$$(J_a^\alpha J_a^\beta f)(x) = (J_a^\beta J_a^\alpha f)(x) = (J_a^{\alpha+\beta} f)(x), \tag{12}$$

$$J_a^\alpha x^\gamma = \frac{x^{\gamma+\alpha}}{\Gamma(\alpha)} B_{\frac{x-a}{x}}(\alpha, \gamma+1), \tag{13}$$

where $B_\tau(\alpha, \gamma+1)$ is the incomplete beta function which is defined as

$$B_\tau(\alpha, \gamma+1) = \int_0^\tau t^{\alpha-1}(1-t)^\gamma \mathrm{d}t, \tag{14}$$

$$J_a^\alpha \mathrm{e}^{cx} = \mathrm{e}^{ac}(x-a)^\alpha \sum_{k=0}^{\infty} \frac{[c(x-a)]^k}{\Gamma(\alpha+k+1)}. \tag{15}$$

The Riemann–Liouville derivative has certain disadvantages when trying to model real-world phenomena with fractional differential equations. Therefore, we shall introduce a modified fractional differential operator D_a^α proposed by Caputo in his work on the theory of viscoelasticity.

Definition 3. The Caputo fractional derivative of $f(x)$ of order $\alpha > 0$ with $a \geq 0$ is defined as

$$(D_a^\alpha f)(x) = (J_a^{m-\alpha} f^{(m)})(x) = \frac{1}{\Gamma(m-\alpha)} \int_a^x \frac{f^{(m)}(t)}{(x-t)^{\alpha+1-m}} \mathrm{d}t, \tag{16}$$

for $m-1 < \alpha \leq m,\ m \in N, x \geq a, f(x) \in C_{-1}^m$.

The Caputo fractional derivative was investigated by many authors, for $m-1 < \alpha \leq m, f(x) \in C_\alpha^m$ and $\alpha \geq -1$, we have

$$(J_a^\alpha D_a^\alpha f)(x) = J^m D^m f(x) = f(x) - \sum_{k=0}^{m-1} f^{(k)}(a) \frac{(x-a)^k}{k!}. \tag{17}$$

For mathematical properties of fractional derivatives and integrals one can consult the mentioned references.

3. MSGDTM algorithm

In this section we present the multi-step generalized differential transform method (MSGDTM) that we have developed for the numerical solution of systems of fractional differential equations. For this purpose, we consider the following initial value problem for systems of fractional differential equations

$$\begin{aligned} D_*^{\alpha_1} y_1(t) &= f_1(t, y_1, y_2, \ldots, y_n), \\ D_*^{\alpha_2} y_2(t) &= f_1(t, y_1, y_2, \ldots, y_n), \\ &\vdots \\ D_*^{\alpha_n} y_n(t) &= f_1(t, y_1, y_2, \ldots, y_n), \end{aligned} \tag{18}$$

subject to the initial conditions

$$y_i(t_0) = c_i, \quad i = 1, 2, \ldots, n, \tag{19}$$

where $D_*^{\alpha_i}$ is the Caputo fractional derivative of order α_i, where $0 < \alpha_i \leq 1$, for $i = 1, 2, \ldots, n$. Let $[t_0, T]$ be the interval over which we want to find the solution of the initial value problems (18)–(19). In actual applications of the generalized differential transform method (GDTM), the Kth-order approximate solution of the initial value problems (18)–(19) can be expressed by the finite series

$$y_i(t) = \sum_{i=0}^{K} Y_i(k)(t-t_0)^{k\alpha_i}, \quad t \in [t_0, T], \tag{20}$$

where $Y_i(k)$ satisfied the recurrence relation

$$\frac{\Gamma((k+1)\alpha_i + 1)}{\Gamma(k\alpha_i + 1)} Y_i(k+1) = F_i(k, Y_1, Y_2, \ldots, Y_n). \tag{21}$$

$Y_i(0) = c_i$, $F_i(k, Y_1, Y_2, \ldots, Y_n)$ is the differential transform of function $f_i(t, y_1, y_2, \ldots, y_n)$ for $i = 1, 2, \ldots, n$. The basics steps of the GDTM can be found in [19–22].

Assume that the interval $[t_0, T]$ is divided into M subintervals $[t_{m-1}, t_m]$, $m = 1, 2, \ldots, M$ of equal step size $h = (T - t_0)/M$ by using the nodes $t_m = t_0 + mh$. The main ideas of the MSGDTM are as follows:

First, we apply the GDTM to the initial value problems (18)–(19) over the interval $[t_0, t_1]$, we will obtain the approximate solution $y_{i,1}(t)$, $t \in [t_0, t_1]$, using the initial condition $y_i(t_0) = c_i$, for $i = 1, 2, \ldots, n$. For $m \geq 2$ and at each subinterval $[t_{m-1}, t_m]$ we will use the initial condition $y_{i,m}(t_{m-1}) = y_{i,m-1}(t_{m-1})$ and apply the GDTM to the initial value problems (18)–(19) over the interval $[t_{m-1}, t_m]$. The process is repeated and generates a sequence of approximate solutions $y_{i,m}(t)$, $m = 1, 2, \ldots, M$, for $i = 1, 2, \ldots, n$. Finally the MSGDTM assumes the following solution

$$y_i(t) = \begin{cases} y_{i,1}(t), & t \in [t_0, t_1] \\ y_{i,2}(t), & t \in [t_1, t_2] \\ \vdots \\ y_{i,M}(t), & t \in [t_{M-1}, t_M]. \end{cases} \tag{22}$$

The new algorithm, MSGDTM, is simple for computational performance for all values of h. As we will see in the next section, the main advantage of the new algorithm is that the obtained solution converges for wide time regions.

4. Solving the systems (6)–(9) using the multi-step generalized differential transform method (MSGDTM)

In Ref. [24], it has been shown that MSDTM is a very accurate and efficient method for solving integer order non-chaotic or chaotic systems and the results have shown remarkable performance compared with the RK4 method. In this section, this method is applied to the fractional order system given in Eqs. (6)–(9).

Applying the MSGDTM Algorithm to Eqs. Using (6)–(9) gives

$$\begin{cases} T_T(k+1) = \dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left(\lambda\delta(k) - \mu_T T_T(k) - \kappa\displaystyle\sum_{l=0}^{k} T_{AA}(l)T_T(k-l)\right), \\ T_{LL}(k+1) = \dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left(\kappa_1\displaystyle\sum_{l=0}^{k} T_{AA}(l)T_T(k-l) - (\mu_L+\gamma)T_{LL}(k)\right), \\ T_{AA}(k+1) = \dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left[\gamma T_{LL}(k) - (\mu_A+\rho)T_{AA}(k)\right], \\ T_{MM}(k+1) = \dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left[\rho T_{AA}(k) + \beta\left(T_{MM}(k) - \dfrac{1}{T_{M_{\max}}}\displaystyle\sum_{l=0}^{k} T_{MM}(l)T_{MM}(k-l)\right) - \mu_M T_{MM}(k)\right], \end{cases} \tag{23}$$

where $T_T(k), T_{LL}(k), T_{AA}(k)$ and $T_{MM}(k)$ are the differential transformation of $T(t), T_L(t), T_A(t)$ and $T_M(t)$, respectively and $\delta(k)$ equals 1 when $k = 0$ and equals 0 otherwise. The differential transform of the initial conditions are given by $T_T(0) = c_1, T_{LL}(0) = c_2, T_{AA}(0) = c_3, T_{MM}(0) = c_4$. In view of the differential inverse transform, the differential transform series solution for the systems (6)–(9) can be obtained as

$$\begin{cases} T(t) = \displaystyle\sum_{n=0}^{N} T_T(n)t^{\alpha n}, \\ T_L(t) = \displaystyle\sum_{n=0}^{N} T_{LL}(n)t^{\alpha n}, \\ T_A(t) = \displaystyle\sum_{n=0}^{N} T_{AA}(n)t^{\alpha n}, \\ T_M(t) = \displaystyle\sum_{n=0}^{N} T_{MM}(n)t^{\alpha n}. \end{cases} \tag{24}$$

Now, according to the multi-step generalized differential transform method, the series solution for the systems (6)–(9) is suggested by

$$T(t) = \begin{cases} \displaystyle\sum_{n=0}^{K} T_{T_1}(n)t^{\alpha n}, & t \in [0, t_1] \\ \displaystyle\sum_{n=0}^{K} T_{T_2}(n)(t-t_1)^{\alpha n}, & t \in [t_1, t_2] \\ \vdots \\ \displaystyle\sum_{n=0}^{K} T_{T_M}(n)(t-t_{M-1})^{\alpha n}, & t \in [t_{M-1}, t_M], \end{cases} \tag{25}$$

$$T_L(t)=\begin{cases}\sum_{n=0}^{K} T_{LL_1}(n)t^{\alpha n}, & t\in[0,t_1]\\ \sum_{n=0}^{K} T_{LL_2}(n)(t-t_1)^{\alpha n}, & t\in[t_1,t_2]\\ \vdots & \\ \sum_{n=0}^{K} T_{LL_M}(n)(t-t_{M-1})^{\alpha n}, & t\in[t_{M-1},t_M],\end{cases} \tag{26}$$

$$T_A(t)=\begin{cases}\sum_{n=0}^{K} T_{AA_1}(n)t^{\alpha n}, & t\in[0,t_1]\\ \sum_{n=0}^{K} T_{AA_2}(n)(t-t_1)^{\alpha n}, & t\in[t_1,t_2]\\ \vdots & \\ \sum_{n=0}^{K} T_{AA_M}(n)(t-t_{M-1})^{\alpha n}, & t\in[t_{M-1},t_M],\end{cases} \tag{27}$$

$$T_M(t)=\begin{cases}\sum_{n=0}^{K} T_{MM_1}(n)t^{\alpha n}, & t\in[0,t_1]\\ \sum_{n=0}^{K} T_{MM_2}(n)(t-t_1)^{\alpha n}, & t\in[t_1,t_2]\\ \vdots & \\ \sum_{n=0}^{K} T_{MM_M}(n)(t-t_{M-1})^{\alpha n}, & t\in[t_{M-1},t_M],\end{cases} \tag{28}$$

where $T_{T_i}(n)$, $T_{LL_i}(n)$, $T_{AA_i}(n)$ and $T_{MM_i}(n)$ for $i=1,2,\dots,M$ satisfy the following recurrence relations

$$\begin{cases} T_{T_i}(k+1)=\dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left(\lambda\delta(k)-\mu_T T_{T_i}(k)-\kappa\sum_{l=0}^{k}T_{AA_i}(l)T_{T_i}(k-l)\right),\\ T_{LL_i}(k+1)=\dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left(\kappa_1\sum_{l=0}^{k}T_{AA_i}(l)T_{T_i}(k-l)-(\mu_L+\gamma)T_{LL_i}(k)\right),\\ T_{AA_i}(k+1)=\dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\left[\gamma\, T_{LL_i}(k)-(\mu_A+\rho)T_{AA_i}(k)\right],\\ T_{MM_i}(k+1)=\dfrac{\Gamma(\alpha k+1)}{\Gamma(\alpha(k+1)+1)}\Bigg[\rho T_{AA_i}(k)+\beta\left(T_{MM_i}(k)-\dfrac{1}{T_{M_{\max}}}\sum_{l=0}^{k}T_{MM_i}(l)T_{MM_i}(k-l)\right)\\ \qquad -\mu_M T_{MM_i}(k)\Bigg],\end{cases} \tag{29}$$

such that $T_{T_i}(0)=T_{T_{i-1}}(0)$, $T_{LL_i}(0)=T_{LL_{i-1}}(0)$, $T_{AA_i}(0)=T_{AA_{i-1}}(0)$ and $T_{MM_i}(0)=T_{MM_{i-1}}(0)$.

Finally, we start with $T_{T_0}(0)=c_1$, $T_{LL_0}(0)=c_2$, $T_{AA_0}(0)=c_3$ and $T_{MM_0}(0)=c_4$, using the recurrence relation given in Eq. (29), then we can obtain the multi-step solution given in Eqs. (25)–(28).

5. Numerical results

We take the parameters

$$\lambda=6/\text{day},\quad \mu_T=0.6/\text{day},\quad \kappa=\kappa_1=0.1\text{mm}^3\text{day}^{-1},\quad \mu_L=0.006/\text{day},\quad \gamma=0.0004/\text{day},$$
$$\mu_A=0.05/\text{day},\quad \rho=0.00004/\text{day},\quad \beta=0.0003/\text{day},\quad T_{M_{\max}}=2200/\text{mm}^3 \quad\text{and}$$
$$\mu_M=0.0005/\text{day}$$

and the initial conditions

$$T_T(0)=1000/\text{mm}^3,\quad T_{LL}(0)=250/\text{mm}^3,\quad T_{AA}(0)=1.5/\text{mm}^3\quad\text{and}\quad T_{MM}(0)=0/\text{mm}^3.$$

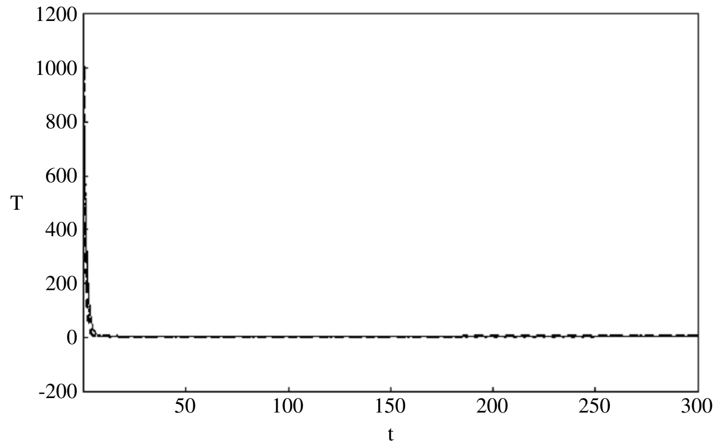

Fig. 1. $T(t)$ versus t: (Solid line) $\alpha = 1.0$, (Dotted line) $\alpha = 0.95$, (Dashed line) $\alpha = 0.85$.

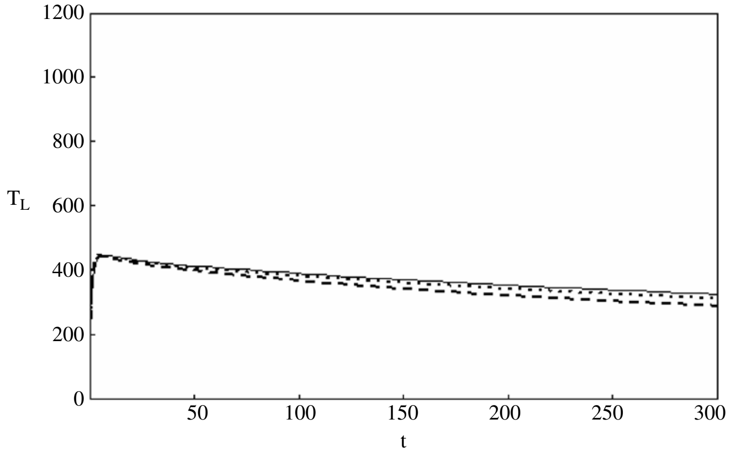

Fig. 2. $T_L(t)$ versus t: (Solid line) $\alpha = 1.0$, (Dotted line) $\alpha = 0.95$, (Dashed line) $\alpha = 0.85$.

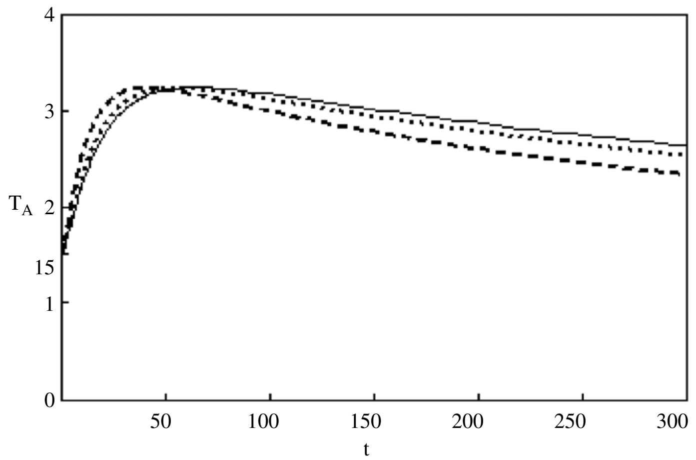

Fig. 3. $T_A(t)$ versus t: (Solid line) $\alpha = 1.0$, (Dotted line) $\alpha = 0.95$, (Dashed line) $\alpha = 0.85$.

Figs. 1–4 show the approximate solutions for T, T_L, T_A and T_M obtained for different values of α using the multi-step generalized differential transform method. From the numerical results in Figs. 1–4, it is clear that the approximate solutions depend continuously on the time-fractional derivative α. It is to be noted that the step size 0.05 was used in evaluating

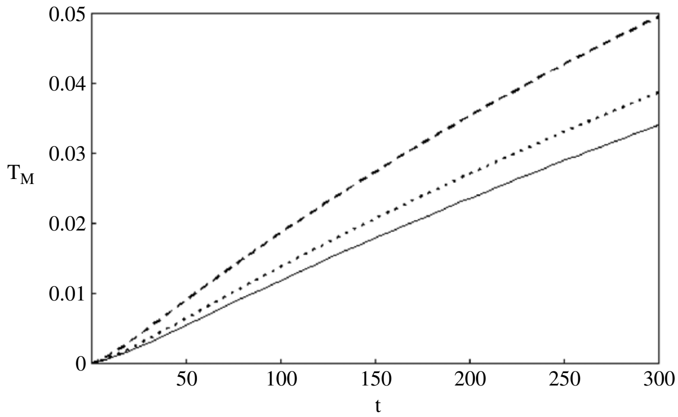

Fig. 4. $T_M(t)$ versus t: (Solid line) $\alpha = 1.0$, (Dotted line) $\alpha = 0.95$, (Dashed line) $\alpha = 0.85$.

the approximate solutions in Figs. 1–4. It is evident that the efficiency of this approach can be dramatically enhanced by decreasing the step size and computing further terms or further components of T, T_L, T_A and T_M.

6. Conclusions

In this paper, a fractional order differential system for modeling a human T-cell lymphotropic virus I (HTLV-I) infection of $CD4^+$ T-cells is studied and its approximate solution is presented using a multi-step generalized differential transform method. The approximate solutions obtained by MSGDTM are highly accurate and valid for a long time. The reliability of the method and the reduction in the size of the computational domain give this method a wider applicability. Finally, the recent appearance of nonlinear fractional differential equations as models in some fields such as mathematical medicine and biology makes it necessary to investigate the method of solutions for such equations and we hope that this work is a step in this direction.

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