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Optimal Control Design of the In-vivo HIV Fractional Model

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Abstract

HIV is a leading cause of death, in particular, in Sub-Saharan Africa. In this paper, a fractional differential system in vivo deterministic models for HIV dynamics is presented and analyzed. The main roles played by different HIV treatment methods are investigated using fractional optimal control theory. We use three treatment regimens as system control variables to determine the best strategies for controlling the infection. The optimality system is numerically solved using the fractional Adams-Bashforth technique.

Keywords: Fractional optimal control, HIV, Pontryagin's maximum principle, Fractional Adams-Bashforth method.

تصميم التحكم الأمثل للنموذج الكسري لفيروس نقص المناعة البشرية داخل الجسم الحي

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قسم الرياضيات , كلية العلوم , جامعة البصرة , البصرة , العراق

الخلاصة

فيروس نقص المناعة البشرية هو سبب رئيسي للوفاة ، لا سيما في أفريقيا جنوب الصحراء الكبرى. في هذا البحث ، تم تقديم وتحليل نظام معادلات تفاضلية كسرية في النماذج الحتمية في الجسم الحي لديناميكيات فيروس نقص المناعة البشرية. يتم التحقيق في الأدوار الرئيسية التي تلعبها طرق علاج فيروس نقص المناعة البشرية المختلفة باستخدام نظرية التحكم الأمثل الكسري. نستخدم ثلاثة أنظمة علاجية كمتغيرات للتحكم في النظام لتحديد أفضل الاستراتيجيات للسيطرة على العدوى. تم حل نظام الأمثلية عددياً باستخدام تقنية Adams-Bashforth الكسرية.

1. Introduction

HIV is an abbreviation for human immunodeficiency virus. HIV is a virus that remains in the body indefinitely. Unlike other viruses that cause the common cold or flu, which only stay in the body for a few days. Memory is associated with the process of evolution and epidemic control in human societies. There should be a correlation between people's prior knowledge of disease spread and their response; for example, if people know that a specific disease has occurred in their area, they may take precautionary measures like vaccinations [1]. On the other hand, memory effects are a significant feature of fractional-order derivatives that do not exist in integer-order derivatives. In contrast to the local behavior of integer order derivatives, these derivatives are non-local. In other words, the next state of a fractional system is determined by

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all of its historical states as well as its current state [2].

Over time, mathematical modeling has played an important role in analyzing the dynamics of diseases such as tuberculosis, malaria and acquired immune deficiency syndrome (AIDS). Where it played an important role in the comprehension of the epidemiological patterns of disease treatment [3, 4, 5]. Also, the optimal control theory is a very important and effective tool in disease modeling as it provides strategies that are appropriate for the prevention and control of diseases [6, 7, 8, 9].

Since fractional-order behavior is dependent on memory, fractional optimal control problems (FOCPs) are now being applied to epidemiological models for faster and more precise disease control. As a result, FOCPs can become one of the most versatile methods for modeling memory-related epidemiological and biological systems [10]. Sun as well et al [11] also presented a comparison that was between the derivative of an integer and a fractional derivative of a fixed order, as well as two types of fractional derivatives that were of variable order in describing the effect of memory in systems. For biological systems with memory, Rehan [12] presented a class of differential models with the fractional arrangement, an example being tumor-immune system dynamics and T-cell dynamics of HIV infection, so Rayhan proposed a stable, unconditioned method using the fractional Caputo derivative of ordering α and Euler's approximation implicit to find a numerical solution to the resulting systems. Sun et al. suggest the existence of the term noise in the partial order in the random order partial differential equation model [13]. By surveying three new methodologies for modeling fractional derivatives, Chen et al. [14] have demonstrated that these new methodologies are useful mathematical tools for describing complex physical behaviors. Fractional optimal control problems are a generalization of classical optimal control problems, we note that the differential equations are fractional differential equations [15]. Agrawal (2004) [16] formulated a generalization of FOCPs in terms of partial Riemann-Liouville derivatives (R-LFDs) and presented a numerical method for solving FOCPs. Using the fractional Grunwald-Letnikov derivative, Agrawal formulated FOCPs and used numerical techniques to solve a set of equations [17].

Sweilam et al. [18] used two numerical methods to solve FOCP for the fractional multi-strain tuberculosis model. By using fractional optimal control, Ding et al. [19] studied the HIV-Immune system model and used a forward-backward algorithm to solve the FOCP. The authors obtained optimality conditions for all FOCPs by expressing the co-state and state equations in terms of right and left fractional derivatives.

The rest of this article is organized as follows. Section two provides preliminaries and concepts that are used throughout this work. In section three, we give a general formulation of the HIV model' fractional optimal control problem. In section four, we used the maximal Pontryagin principle to infer the necessary conditions. In section five, we discussed the numerical results. Finally, section six summarizes the conclusions.

2. Preliminary

Fractional order derivatives are defined in a variety of ways, including Riemann-Liouville, Caputo, Grunwald Letnikov, Atangana-Baleanu, Caputo-Fabrizio, and others. For more information about fractional order definitions with applications, see, for example, [20, 21] and the references therein. Throughout the article, we have used Caputo's definition.

Definition 2.1 [22] Let $f \in C^n, a > 0$ and $\alpha, a, b, t \in \mathbb{R}$. Then the left (right) Caputo fractional derivative of order $m-1 < \alpha < m \in \mathbb{N}$ of f are given by

$${}^c D_t^\alpha f(t) = \frac{1}{\Gamma(m-\alpha)} \int_a^t (t-\xi)^{m-\alpha-1} f^{(m)}(\xi) d\xi \quad (1)$$

$${}^c D_b^\alpha f(t) = \frac{(-1)^m}{\Gamma(m-\alpha)} \int_t^b (\xi-t)^{m-\alpha-1} f^{(m)}(\xi) d\xi \quad (2)$$

where $m-1 < \alpha < m, m \in \mathbb{N}$ and $\Gamma(-)$ is the Gamma function.

3. Model Formulation

In order to conduct fractional optimum control procedures, we need to develop a model that explains the fundamental interaction between the body's immune system and HIV virions. We create a mathematical model for HIV in-host infection using three-drug combinations. Seven variables are included in the model, which are (T) susceptible, (I) infected, (I_l) latently infected, (V) HIV infectious virions, (V_n) non-infectious HIV virions, (Z) CD^+8 T-cells, and (Z_a) activated CD^+8 T-cells. Table 1 describes the model's parameter variables inside the host.

Table 1-Parameters used in HIV in-vivo and their meaning

Parameter	Description
λ_T	The rate of production of non-infected $CD4^+$ T cells.
μ_T	The rate of dissolution of non-infected $CD4^+$ T-cells.
χ	The viral infection rate of $CD4^+$ T-cells.
μ_I	The death rate of the infected $CD4^+$ T-cells.
μ_{I_l}	Latently infected $CD4^+$ T-cell death rate.
ε_V	The rate in which HIV virions are produced from the infected $CD4^+$ T-cells.
μ_V	The infectious virus's mortality rate.
μ_{V_n}	The non-infectious virus's mortality rate.
γ	The rate at which activated $CD8^+$ T-cells kill infected cells.
λ_Z	The rate of production of $CD8^+$ T-cells.
μ_z	The rate at which T-cells die.
β	The rate at which the virus activates $CD8^+$ T-cells and infects $CD4^+$ T-cells.
μ_{Z_a}	Activated defense cell decay rate.

In order to explain the in vivo dynamics of HIV, we construct the following system of fractional differential equations:

$$\begin{aligned}
 {}^c D_t^\alpha T &= \lambda_T - \mu_T T - (1-u_1(t))\chi TV, \\
 {}^c D_t^\alpha I &= (1-u_2(t))\chi TV - \mu_I I - \gamma IZ_a, \\
 {}^c D_t^\alpha I_l &= u_2(t)\chi TV - \mu_{I_l} I_l, \\
 {}^c D_t^\alpha V &= (1-u_3(t))\varepsilon_V \mu_I I - \mu_V V, \\
 {}^c D_t^\alpha V_n &= u_3(t)\varepsilon_V \mu_I I - \mu_{V_n} V_n, \\
 {}^c D_t^\alpha Z &= \lambda_Z - \mu_z Z - \beta ZI, \\
 {}^c D_t^\alpha Z_a &= \beta ZI - \mu_{Z_a} Z_a,
 \end{aligned} \quad (3)$$

$$\begin{aligned}
H(T(t), I(t), I_1(t), V(t), V_n(t), Z(t), Z_a(t), \lambda(t), u(t), t) = & (A_1 T + A_2 Z - A_3 V - B_1 u_1^2 - B_2 u_2^2 - B_3 u_3^2) \\
& + \lambda_1 (\lambda_T - \mu_T T - (1 - u_1(t)) \chi TV) \\
& + \lambda_2 ((1 - u_2(t)) \chi TV - \mu_1 I - \gamma I Z_a) \\
& + \lambda_3 (u_2(t) \chi TV - \mu_{I_1} I_1) \\
& + \lambda_4 ((1 - u_3(t)) \varepsilon_V \mu_1 I - \mu_V V) \\
& + \lambda_5 (u_3(t) \varepsilon_V \mu_1 I - \mu_{V_n} V_n) \\
& + \lambda_6 (\lambda_z - \mu_z Z - \beta Z I) \\
& + \lambda_7 (\beta Z I - \mu_{Z_a} Z_a) \\
& + v_{11} u_1(t) + v_{12} (1 - u_1(t)) + v_{21} u_2(t) \\
& + v_{22} (1 - u_2(t)) + v_{31} u_3(t) + v_{32} (1 - u_3(t))
\end{aligned} \tag{8}$$

where $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7) \in \mathbb{R}^7$ is the adjoint variable, $u = (u_1, u_2, u_3)$ is the control variable and $v_{ij} \geq 0$ are the penalty multipliers that incorporate the boundedness of the control variables and fulfill the following criteria

$$\begin{aligned}
v_{11} u_1(t) + v_{12} (1 - u_1(t)) &= 0 \quad \text{at } t_i \\
v_{21} u_2(t) + v_{22} (1 - u_2(t)) &= 0 \quad \text{at } t_i \\
v_{31} u_3(t) + v_{32} (1 - u_3(t)) &= 0 \quad \text{at } t_i
\end{aligned} \tag{9}$$

Now, we compute the necessary conditions of the model (3).

$${}_0^c D_t^\alpha T = \lambda_T - \mu_T T - (1 - u_1(t)) \chi TV = \frac{\partial H}{\partial \lambda_1} \tag{10}$$

$${}_0^c D_t^\alpha I = (1 - u_2(t)) \chi TV - \mu_1 I - \gamma I Z_a = \frac{\partial H}{\partial \lambda_2} \tag{11}$$

$${}_0^c D_t^\alpha I_1 = u_2(t) \chi TV - \mu_{I_1} I_1 = \frac{\partial H}{\partial \lambda_3} \tag{12}$$

$${}_0^c D_t^\alpha V = (1 - u_3(t)) \varepsilon_V \mu_1 I - \mu_V V = \frac{\partial H}{\partial \lambda_4} \tag{13}$$

$${}_0^c D_t^\alpha V_n = u_3(t) \varepsilon_V \mu_1 I - \mu_{V_n} V_n = \frac{\partial H}{\partial \lambda_5} \tag{14}$$

$${}_0^c D_t^\alpha Z = \lambda_z - \mu_z Z - \beta Z I = \frac{\partial H}{\partial \lambda_6} \tag{15}$$

$${}_0^c D_t^\alpha Z_a = \beta Z I - \mu_{Z_a} Z_a = \frac{\partial H}{\partial \lambda_7} \tag{16}$$

$$\begin{aligned}
{}_t^c D_{T_f}^\alpha \lambda_1 = & A_1 - \lambda \mu_T - \lambda \chi V + \lambda u_1(t) \chi V + \lambda \chi Y - \lambda u_2(t) \chi V \\
& + \lambda_3 u_2(t) \chi V = \frac{\partial H}{\partial T}
\end{aligned} \tag{17}$$

$$\begin{aligned}
{}_t^c D_{T_f}^\alpha \lambda_2 = & -\lambda_2 \mu_1 - \lambda \chi Z_a + \lambda \varepsilon_V \mu_1 - \lambda u_4(t) \varepsilon_V \mu_1 + \lambda u_5(t) \varepsilon_V \mu_1 \\
& - \lambda_6 \beta Z + \lambda_7 \beta Z = \frac{\partial H}{\partial I}
\end{aligned} \tag{18}$$

$${}^c D_{T_f}^\alpha \lambda_3 = -\lambda_3 \mu_{I_1} = \frac{\partial H}{\partial I_1} \quad (19)$$

$${}^c D_{T_f}^\alpha \lambda_4 = -A_3 - \lambda \chi T + \lambda u_1 (\psi) \chi T + \lambda \chi_2 T - \lambda u_2 \epsilon_2 \chi T + \lambda_3 u_2(t) \chi T - \lambda \mu_V = \frac{\partial H}{\partial V} \quad (20)$$

$${}^c D_{T_f}^\alpha \lambda_5 = -\lambda_5 \mu_{V_n} = \frac{\partial H}{\partial V_n} \quad (21)$$

$${}^c D_{T_f}^\alpha \lambda_6 = A_2 - \lambda \mu_z - \lambda \beta I + \lambda \beta I = \frac{\partial H}{\partial Z} \quad (22)$$

$${}^c D_{T_f}^\alpha \lambda_7 = -\lambda \gamma I - \lambda \mu_{Z_a} = \frac{\partial H}{\partial Z_a} \quad (23)$$

Where $\lambda_i(T_f) = 0, i=1,2,\dots,7$ are the transversely conditions.

Theorem 4.1 The optimal controls (u_1^*, u_2^*, u_3^*) that maximize the objective function given by Eq. (4) over the invariant area are presented by

$$u_1^* = \max(0, \min(1, \frac{\lambda_1 \chi TV}{2B_1}))$$

$$u_2^* = \max(0, \min(1, \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2}))$$

$$u_3^* = \max(0, \min(1, \frac{-\lambda_4 \epsilon_V \mu_I I + \lambda_5 \epsilon_V \mu_I I}{2B_3}))$$

Proof: In the Pontryagin's maximum principle of the model (3), the optimal controls u_1^*, u_2^* and u_3^* achieve the following conditions:

$$\frac{\partial H}{\partial u_1} = 0 \quad (24)$$

$$\frac{\partial H}{\partial u_2} = 0 \quad (25)$$

$$\frac{\partial H}{\partial u_3} = 0 \quad (26)$$

From Eq. (8) differentiating the Hamiltonian function with respect to u_1 on the set $U: t|u_1 \in [0,1]$, we can get the following optimality equation

$$\frac{\partial H}{\partial u_1} = -2B_1 u_1 + \lambda \chi TV + v_{11} - v_{12} = 0 \quad (27)$$

Put $u_1 = u_1^*$ in Eq.(27). Then we get u_1^* as follows

$$u_1^* = \frac{\lambda_1 \chi TV + v_{11} - v_{12}}{2B_1} \quad (28)$$

From the conditions given by Eq. (9), we can get the following distinct three cases:

1. On the set $(t|u_1^* \in (0,1))$, in Eq.(28) we assume $v_{11} = v_{12} = 0$. Then u_1^* is given by

$$u_1^* = \frac{\lambda_1 \chi TV}{2B_1} \quad (29)$$

2. Likewise, on the set $(t|u_1^* = 1)$ put $v_{11} = 0$ and $v_{12} \geq 0$, then from Eq.(28), we get

$$u_1^* = 1 = \frac{\lambda_1 \chi TV - v_{12}}{2B_1} \quad (30)$$

Eq.(30) we can rewrite it as follows:

$$u_1^* = 1 \leq \frac{\lambda_1 \chi TV}{2B_1} \quad (31)$$

Accordingly, for the set $(t|u_1^* = 1)$, we have

$$u_1^* = \min\left(\frac{\lambda_1 \chi TV}{2B_1}\right) \quad (32)$$

3. On the set $(t|u_1^* = 0)$, put $v_{11} \geq 0$ and $v_{12} = 0$ then from Eq.(28) we will get

$$u_1^* = 0 = \frac{\lambda_1 \chi TV + v_{11}}{2B_1} \quad (33)$$

which implies that

$$u_1^* = 0 \geq \frac{\lambda_1 \chi TV}{2B_1} \quad (34)$$

From Eq. (29), Eq. (32), and Eq. (34), we get u_1^* , as follows:

$$u_1^* = \begin{cases} \frac{\lambda_1 \chi TV}{2B_1} & \text{if } 0 < \frac{\lambda_1 \chi TV}{2B_1} < 1 \\ 0 & \text{if } \frac{\lambda_1 \chi TV}{2B_1} \leq 0 \\ 1 & \text{if } \frac{\lambda_1 \chi TV}{2B_1} \geq 1 \end{cases} \quad (35)$$

The control u_1^* is formulated as follows:

$$u_1^* = \max\left(0, \min\left(\frac{\lambda_1 \chi TV}{2B_1}\right)\right) \quad (36)$$

On the set $U : t|u_2 \in [0,1]$. From Eq. (8) differentiating the Hamiltonian function with respect to u_2 we can get the following optimality equation

$$\frac{\partial H}{\partial u_2} = -2B_2 u_2 - \lambda_2 \chi TV + \lambda_3 \chi TV + v_{21} - v_{22} = 0 \quad (37)$$

Put $u_2 = u_2^*$ in Eq.(37). Then we get the optimal control as follows:

$$u_2^* = \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV + v_{21} - v_{22}}{2B_2} \quad (38)$$

From the conditions given by Eq. (9), we can get the following distinct three cases

1. On the set $(t|u_2^* \in (0,1))$, in Eq.(38) we assume $v_{21} = v_{22} = 0$. Then u_2^* is given by

$$u_2^* = \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} \quad (39)$$

2. Likewise, on the set $(t|u_2^* = 1)$ put $v_{21} = 0$ and $v_{22} \geq 0$, then from Eq.(38) we get

$$u_2^* = 1 = \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV - v_{22}}{2B_2} \quad (40)$$

Eq.(40) we can rewrite it as follows

$$u_2^* = 1 \leq \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} \quad (41)$$

Accordingly, for the set $(t|u_2^* = 1)$, we have

$$u_2^* = \min\left(1, \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2}\right) \quad (42)$$

3. On the set $(t|u_2^* = 0)$, put $v_{21} \geq 0$ and $v_{22} = 0$ then from Eq.(38) we will get

$$u_2^* = 0 = \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV + \frac{v_{21}}{2}}{2B_2} \quad (43)$$

which implies that

$$u_2^* = 0 \geq \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} \quad (44)$$

Now, from Eq. (40), Eq. (42), and Eq. (44) we can get u_2^* , as follow

$$u_2^* = \begin{cases} \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} & \text{if } 0 < \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} < 1 \\ 0 & \text{if } \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} \leq 0 \\ 1 & \text{if } \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2} \geq 1 \end{cases} \quad (45)$$

The control u_2^* is formulated as follows

$$u_2^* = \max\left(0, \min\left(1, \frac{-\lambda_2 \chi TV + \lambda_3 \chi TV}{2B_2}\right)\right) \quad (46)$$

On the set $U : t|u_3 \in [0,1]$ We can derive the following optimality equation from Eq. (8) by differentiating the Hamiltonian function with respect to u_3 .

$$\frac{\partial H}{\partial u_3} = -2B_3 u_3 - \lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I + v_{31} - v_{32} = 0 \quad (47)$$

Put $u_3 = u_3^*$ in Eq.(47). Then we get the optimal control as follows

$$u_3^* = \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I + v_{31} - v_{32}}{2B_3} \quad (48)$$

From the conditions given by Eq. (9), we can obtain the three distinct cases listed below.

1. On the set $(t|u_3^* \in (0,1))$, in Eq.(48) we assume $v_{31} = v_{32} = 0$. Therefore, the optimal control u_3^* is given by

$$u_3^* = \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} \quad (49)$$

2. Likewise, on the set $(t|u_3^* = 1)$ put $v_{31} = 0$ and $v_{32} \geq 0$, then from Eq.(48), we get

$$u_3^* = 1 = \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I - v_{32}}{2B_3} \quad (50)$$

Eq.(50) we can rewrite it as follows

$$u_3^* = 1 \leq \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} \tag{51}$$

Accordingly, for the set $(t|u_3^* = 1)$, we have

$$u_3^* = \min(1, \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3}) \tag{52}$$

3. On the set $(t|u_3^* = 0)$, put $v_{31} \geq 0$ and $v_{32} = 0$ then from Eq.(48) we will get

$$u_3^* = 0 = \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I + v_{31}}{2B_3} \tag{53}$$

which implies that

$$u_3^* = 0 \geq \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} \tag{54}$$

From Eq. (49), Eq. (52), and Eq. (54), we can get u_3^* as follow

$$u_3^* = \begin{cases} \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} & \text{if } 0 < \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} < 1 \\ 0 & \text{if } \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} \leq 0 \\ 1 & \text{if } \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3} \geq 1 \end{cases} \tag{55}$$

The control u_3^* is formulated as follows

$$u_3^* = \max(0, \min(1, \frac{-\lambda_4 \varepsilon_V \mu_1 I + \lambda_5 \varepsilon_V \mu_1 I}{2B_3})) \tag{56}$$

5. Discussion of the Numerical Results

In this part, we use the fractional Adams-Bashforth technique on the optimality scheme to explore the influence of optimal strategy on HIV. This method offers numerical solutions over a long time interval. For the simulations with the initial conditions and parameters, we use the MAPEL software. We will continue iterating until convergence is achieved. This problem is a fractional problem, with discrete boundary conditions at times $a = 0$. The T_f represents the time in months when treatment is discontinued. Moreover, we will take the values of the weight functions as $B_1 = B_2 = B_3 = 0.01$. We use the parameter values mentioned in Table 2 to obtain the numerical solution of the in vivo model.

The main results have been graphically illustrated using numerical simulation results. Also, we discussed the numerical solutions to the optimality system described by Eq. (11) of the FOCP (10). The fractional Adams-Bashforth method is a good way to find numerical solutions to fractional ordinary differential equations. It can be used to solve both linear and nonlinear problems. In this section, the primary goal is to explain how the combination of controls u_1, u_2 and u_3 affects the proposed model in relation to the relative weights of the controls used. The derivative order α has an effect on the values of the controls, as it is shown in Figure 8, Figure 9, and Figure 10. This is related to the memory characteristic of fractional derivatives. When α is increased to 1, the maximum levels of the controls are reduced. However, when α is increased to 1, the fractional derivative memory effect is diminished.

Table 2-The parameters and controls for the HIV model

Parameter	Value	Reference
λ_T	$10\text{cell} / \text{mm}^3 / \text{day}$	[23]
μ_T	10^{-2}day^{-1}	[24]
χ	$24 \times 10^{-6}\text{mm}^3\text{vir}^{-1}\text{day}^{-1}$	[25]
μ_I	0.5day^{-1}	[26]
μ_{I_1}	0.5day^{-1}	[26]
ε_V	$100\text{vir.cell}^{-1}\text{day}^{-1}$	Assessment
μ_V	2day^{-1}	[28]
μ_{V_n}	3day^{-1}	Assessment
γ	$2 \times 10^{-2}\text{day}^{-1}$	[28]
λ_Z	$20\text{cell}/\text{mm}^3/\text{day}$	[28]
μ_z	$4 \times 10^{-2}\text{day}^{-1}$	[28]
β	$4 \times 10^{-3}\text{day}^{-1}$	[28]
μ_{Z_a}	$4 \times 10^{-3}\text{day}^{-1}$	[28]
u_1	0–1	Assessment
u_2	0–1	Assessment
u_3	0–1	Assessment

Table 3- Shows the initial values of variables for the HIV model.

Variables	Initial values
$T(t)$	$T(0) = 500\text{cell} / \text{mm}^3$
$I(t)$	$I(0) = 100\text{cell} / \text{mm}^3$
$I_1(t)$	$I_1(0) = 0\text{cell} / \text{mm}^3$
$V(t)$	$V(0) = 100\text{virion} / \text{mm}^3$
$V_n(t)$	$V_n(0) = 0\text{virion} / \text{mm}^3$
$Z(t)$	$Z(0) = 100\text{cell} / \text{mm}^3$
$Z_a(t)$	$Z_a(0) = 10\text{cell} / \text{mm}^3$

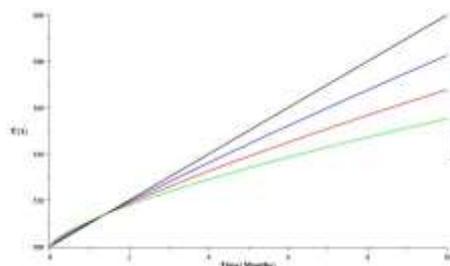


Figure 1- $T(t)$ with $0 < \alpha \leq 1$

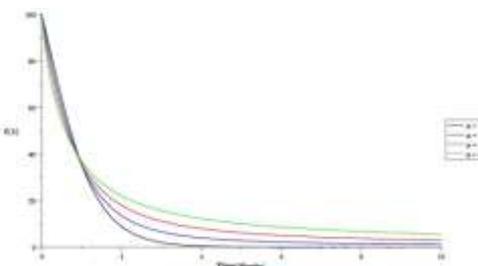


Figure 2- $I(t)$ with $0 < \alpha \leq 1$

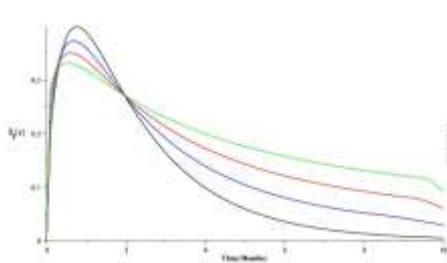


Figure 3- $I_l(t)$ with $0 < \alpha \leq 1$

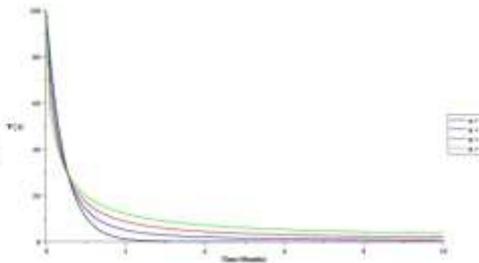


Figure 4- $V(t)$ with $0 < \alpha \leq 1$

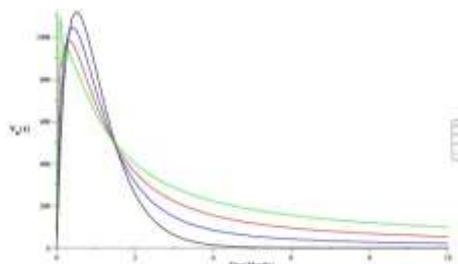


Figure 5- $V_n(t)$ with $0 < \alpha \leq 1$

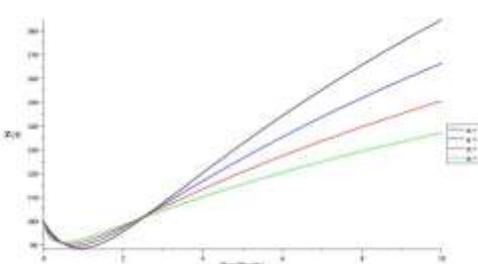


Figure 6- $Z(t)$ with $0 < \alpha \leq 1$

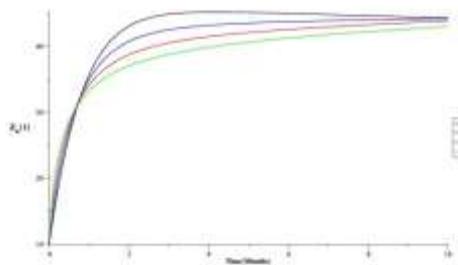


Figure 7- $Z_a(t)$ with $0 < \alpha \leq 1$

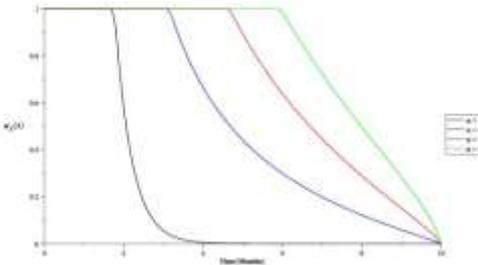


Figure 8- $u_1(t)$ with $0 < \alpha \leq 1$

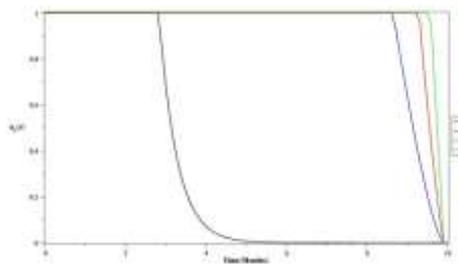


Figure 9- $u_2(t)$ with $0 < \alpha \leq 1$

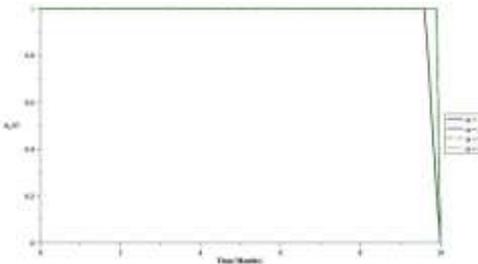


Figure 10- $u_3(t)$ with $0 < \alpha \leq 1$

6. Conclusion

In this paper, we presented a fractional optimum control issue for the in-vivo HIV fractional model. The Pontryagin maximum principle has been used to derive the fractional-order optimal necessary conditions. Then, we used the fractional Adams-Bashforth method to transform the given problem into an optimization problem. The numerical simulation was done by using the optimization technique in Maple 16 to study the behavior of how the combination of controls u_1, u_2 and u_3 affects the proposed model depending on relative weights. Also, we studied the effect of the order of the fractional derivative (the memory property of fractional derivatives) on this model. However, if we do not take the memory property of the in-vivo HIV model into account, i.e., $\alpha = 1$, one can see that our result is consistent with the work in [29]. That is to say, our study in this paper is an extension of the study in [29].

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