EUROPEAN JOURNAL OF PURE AND APPLIED MATHEMATICS
2025, Vol. 18, Issue 1, Article Number 5670
ISSN 1307-5543 – ejpam.com
Published by New York Business Global

Modeling the Response of the Immune System to HIV-Tumor Interaction via a Fractional Framework

Rashid Jan[1,2], Mansoor Alsulami[3,*], Normy Norfiza Abdul Razak[1]

[1] *Institute of Energy Infrastructure (IEI), Department of Civil Engineering, College of Engineering, Universiti Tenaga Nasional (UNITEN), Putrajaya Campus, Jalan IKRAM-UNITEN, 43000 Kajang, Selangor, Malaysia*
[2] *Mathematics Research Center, Near East University TRNC, Mersin 10, Nicosia 99138, Turkey*
[3] *Department of Mathematics, Faculty of Science, King Abdulaziz University, P. O. Box 80203, Jeddah 21589, Saudi Arabia*

Abstract. The interaction between cancer and HIV underscores the paramount significance of immune response mechanisms in both diseases, illuminating the necessity for tailored management and treatment approaches to address cancer in individuals living with HIV. In this study, a mathematical model is formulated to conceptualize the interaction between HIV and tumors in relation to the immune system's response. The basic theory and concepts of the Caputo-Fabrizio operator are presented to analyze the recommended dynamics. The dynamics of HIV and tumor interactions in the context of immune response are systematically investigated. A numerical scheme has been developed to analyze the proposed system and evaluate the impact of various input factors on its dynamics. The numerical findings highlight the key parameters driving the intricate interactions between HIV, tumors, and immune dynamics, providing valuable insights to guide public health interventions and treatment strategies.

2020 Mathematics Subject Classifications: 92D25, 92D30

Key Words and Phrases: Fractional calculus, HIV-tumor dynamics, Immune response, Numerical results, Dynamical behavior

1. Introduction

The progression of HIV in the presence of a tumor involves a complex interplay between viral dynamics, immune suppression, and cancer biology [8]. HIV targets CD4+ T cells, leading to significant immunosuppression, which weakens the body's ability to detect and combat cancerous cells. This compromised immune system allows tumors to

*Corresponding author.
DOI: https://doi.org/10.29020/nybg.ejpam.v18i1.5670

Email addresses: rashid_ash2000@yahoo.com (R. Jan), maalsulami2@kau.edu.sa (M. Alsulami), normy@uniten.edu.my (N. N. A. Razak)

grow more aggressively and evade immune surveillance more easily. Chronic inflammation caused by HIV further alters the tumor microenvironment, promoting tumor growth and metastasis. The introduction of antiretroviral therapy (ART) has improved the immune function of HIV-positive individuals, reducing the incidence of AIDS-defining cancers [10]. However, the increased life expectancy due to ART has led to a higher prevalence of non-AIDS-defining cancers, which can be more challenging to manage in the presence of HIV. The interaction between ART and cancer therapies, coupled with the underlying immunosuppression, complicates treatment strategies and can adversely affect the prognosis. As such, managing the progression of HIV in the presence of a tumor requires a multidisciplinary approach that addresses both the viral infection and the cancer while navigating the challenges posed by drug interactions and immune recovery.

HIV still affects millions of people worldwide, making it a serious global health problem [23]. HIV continues to place a heavy financial and health burden on afflicted individuals and communities even in the face of tremendous advancements in antiretroviral therapy, which have changed the status of the infection. HIV disproportionately affects marginalized populations, exacerbating social and economic inequalities. Consequently, HIV remains not just a medical issue but a complex social and public health challenge that demands sustained global efforts and resources [29]. Mathematical modeling is crucial for understanding and managing viral infections because it allows researchers to simulate the spread and progression of viruses within individuals and across populations [17, 24]. These models provide insights into key factors such as transmission dynamics, immune response, and the impact of interventions like vaccination or antiviral treatments [6, 28]. By capturing the complex interactions between a virus and its host, as well as the broader population, mathematical models enable the prediction of disease outcomes, the assessment of potential public health strategies, and the optimization of treatment protocols [11]. Even though HIV is still a serious worldwide health concern, current studies and developments in biomathematics present encouraging opportunities for enhancing the management and treatment of this fatal illness.

The intricate phenomena of the HIV viruses and $CD4^+$ T-cells have been studied previously using mathematical modeling, as mentioned in [25]. By clarifying the relationship between HIV and host cells, these findings contribute to our understanding of the effects on immune response, depletion of $CD4^+$ T-cells, and viral replication rates. Several clinical aspects of HIV, such as the decrease in $CD4^+$ T-cells, lower amounts of free virus, and the extended latency period inside the patients, are successfully captured by the work introduced by Perelson and Nelson [26]. First of all, the model was presented by Perelson et al. [26] which was then examined by the authors in their work [7]. They presented the interaction of T cells and HIV in more precious way. This streamlined formulation enhances the understanding of HIV dynamics. In [4], the authors investigated the stability of the equilibria of HIV model. The research by Bushnaq and his friend [4] enhanced the existing models by including memory related factor in the dynamics. Later studies by other researchers [22, 30] used a variety of techniques and approaches to look at the progression of HIV. This study focuses on the progression of HIV in the presence of a tumor, aiming to elucidate the interactions between HIV, the tumor, and the immune system.

Fractional calculus is employed to model the dynamics of infectious diseases with greater precision and accuracy [14, 16]. This approach allows the model to capture memory effects and non-local interactions, which are often present in biological systems but are not well-represented by traditional integer-order models [9, 13]. Fractional epidemic models provide a more comprehensive and accurate framework for modeling the dynamics of vector-borne infections [15]. They incorporate memory effects, capture complex and heterogeneous dynamics, and offer better fits to real-world data. These advantages make fractional models a powerful tool for understanding, predicting, and controlling vector-borne diseases, ultimately leading to more effective public health interventions and better outcomes [3]. Recent advancements in the theory of fractional calculus have significantly expanded its mathematical foundations as well as its applications [1, 20, 21]. The ability of FO derivatives is to incorporate memory effects and non-local interactions provides a more accurate representation of the complexities inherent in the transmission and progression of HIV and tumor in the response of immune. The fractional framework provides a more effective means of capturing the intricate dynamics of diseases compared to traditional integer-order models, enabling improved predictions and the development of more effective control strategies. In this study, we employ fractional derivatives to investigate the in-vivo dynamics of HIV progression and its interaction with the immune system, influenced by the presence of a tumor.

This study is arranged as: In Section 2, we formulate the dynamics of HIV-tumor interaction in the response of immune. Section 3 presents the key concepts and idea of Caputo-Fabrizio derivative. A numerical method has been outlined in Section 4 for the model analysis. In Section 4, the impact of input factors has been investigated. The conclusion and final remarks are stated in Section 5.

2. HIV and tumor-immune dynamics

Here, we have structured a mathematical model to represent the progression of HIV in the presence of tumor to immune response. Numerous studies [2, 19, 30, 31] have significantly advanced the understanding of the intricate dynamics governing HIV infection. These models have examined diverse facets of HIV pathogenesis, identifying various factors that contribute to the infection's progression. Notably, the work in [30] provided detailed insights into the dynamics of HIV as:

$$\begin{cases} \frac{d\mathrm{T}}{dt} = s - \eta_T \mathrm{T} + r\mathrm{T}(1 - \frac{\mathrm{T}+\mathrm{I}}{T_{\max}}) - k\mathrm{V}\mathrm{T}, \\ \frac{d\mathrm{I}}{dt} = k\mathrm{V}\mathrm{T} - \eta_I \mathrm{I}, \\ \frac{d\mathrm{V}}{dt} = N\eta_I \mathrm{I} - \eta_V \mathrm{V}, \end{cases}$$

where particles of HIV, uninfected and infected T-cells, indicated by V, T, and I, respectively. In addition, the factor s represents the addition of new T-cells, whereas η_T measures the rate of T-cell death. Within the framework given, k indicates the infection rate, whereas r represents the proliferation rate of healthy $CD4^+$ T-cell. The dynamics of HIV with saturated incidence that was first put forward by Perelson and Nelson [27]

looks like this mathematically:

$$\begin{cases} \frac{d\mathrm{T}}{dt} = r\mathrm{T}(1-\frac{\mathrm{T}}{T_{\max}}) - \frac{\beta \mathrm{VT}}{1+\alpha \mathrm{V}}, \\ \frac{d\mathrm{I}}{dt} = \frac{\beta \mathrm{VT}}{1+\alpha \mathrm{V}} - \eta_I \mathrm{I}, \\ \frac{d\mathrm{V}}{dt} = N\eta_I \mathrm{I} - \eta_V \mathrm{V}. \end{cases}$$

Additionally, we have considered the case where $CD4^+$ T-cells that are not yet infected can infect previously infected T-cells; this is denoted by the mass infection terms αTI. Furthermore, α is supposed to equal the recovery rate. Consequently, the dynamics of HIV in light of the above described factors can be stated as follows:

$$\begin{cases} \frac{d\mathrm{T}}{dt} &= s - \eta_T \mathrm{T} + r\mathrm{T}(1-\frac{\mathrm{T}}{T_{\max}}) - k\mathrm{VT} - \alpha \mathrm{IT}, \\ \frac{d\mathrm{I}}{dt} &= k\mathrm{VT} + \alpha \mathrm{IT} - \eta_I \mathrm{I}, \\ \frac{d\mathrm{V}}{dt} &= N\eta_I \mathrm{I} - \eta_V \mathrm{V} - k\mathrm{VT}, \end{cases}$$

where ν denotes the protease inhibitor's efficiency and α indicates the rate of cellular infection. Fractional epidemic models have attracted interest in recent years because they effectively capture the intricate dynamics involved in the transmission of infectious diseases [12]. These models serve as a robust and adaptable approach for analyzing and forecasting the transmission of infectious diseases, offering benefits that enhance and broaden the capabilities of traditional integer-order models. Here, we assume tumor cells, health T cells, infected T cells and HIV particles by T, H, I and V, respectively. Then, the dynamics of HIV and tumor in the presence of immune response is as:

$$\begin{cases} {}_0^{CF}D_t^{\xi}\mathrm{T}(t) &= \hbar + r\mathrm{T}(1-\frac{\mathrm{T}}{\aleph}) - k_1\mathrm{TH}, \\ {}_0^{CF}D_t^{\xi}\mathrm{H}(t) &= s - k_1\mathrm{HT} - k_2\mathrm{HI} - k_3\mathrm{HV} + r_1\mathrm{H}(1-\frac{\mathrm{H}}{\mathrm{H}_{max}}) - \delta_H\mathrm{H}, \\ {}_0^{CF}D_t^{\xi}\mathrm{I}(t) &= k_2\mathrm{HI} + k_3\mathrm{HV} - \delta_I\mathrm{I}, \\ {}_0^{CF}D_t^{\xi}\mathrm{V}(t) &= Nc\mathrm{I} - k\mathrm{HV} - \delta_V\mathrm{V}, \end{cases} \tag{1}$$

where ${}_0^{CF}D_t^{\xi}$ denotes the Caputo-Fabrizio operator which is a relatively new concept. Its unique properties make it more attractive for modeling real-world phenomena.

3. Fractional theory and results

Here, we present the following concepts and ides of Caputo-Fabrizio (CF) operator to investigate our model.

Definition 1. *Consider $g \in H^1(a,b)$, then the CF fractional operator [5] with normality $\mathcal{W}(\hbar)$ can be stated as*

$$D_k^{\hbar}(g(k)) = \frac{\mathcal{W}(\hbar)}{1-\hbar}\int_a^k g'(x)\exp\left[-\hbar\frac{k-x}{1-\hbar}\right]dx, \tag{2}$$

where $b > a$ and $\hbar \in [0,1]$, additionally, $\mathcal{W}(\hbar)$ represents normalization function with $\mathcal{W}(0) = \mathcal{W}(1) = 1$. If $g \notin H^1(a,b)$, then we get

$$D_k^{\hbar}(g(k)) = \frac{\hbar\mathcal{W}(\hbar)}{1-\hbar}\int_a^k (g(k)-g(x))\exp\left[-\hbar\frac{k-x}{1-\hbar}\right]dx. \tag{3}$$

Remark 1. *If* $\sigma = \frac{1-\hbar}{\hbar} \in [0, \infty)$ *and* $\hbar = \frac{1}{1+\sigma} \in [0, 1]$*, then from (3), one can get*

$$D_k^{\hbar}(g(k)) = \frac{M(\sigma)}{\sigma} \int_a^k g'(x) e^{[-\frac{k-x}{\sigma}]} dx, \tag{4}$$

furthermore, the below is obtained

$$\lim_{\sigma \longrightarrow 0} \frac{1}{\sigma} \exp\Big[- \frac{k-x}{\sigma} \Big] = \delta(x-k), \tag{5}$$

where $\sigma \in [0, \infty]$ *and* $M(\sigma)$ *is the normalized term of* $\mathcal{W}(\hbar)$ *with* $M(0) = M(\infty) = 1$*. Moreover,* $\sigma \to 0$ *as* $\hbar \to 1$*.*

Definition 2. *[18], Integral for the above fractional operator can be stated as*

$$I_k^{\hbar}(g(k)) = \frac{2(1-\hbar)}{(2-\hbar)\mathcal{W}(\hbar)} g(k) + \frac{2\hbar}{(2-\hbar)\mathcal{W}(\hbar)} \int_0^k g(u) du, \ k \geq 0, \tag{6}$$

with the order $\hbar$ *and* $0 < \hbar < 1$*.*

Remark 2. *From the above Definition (2), we have*

$$\frac{2(1-\hbar)}{(2-\hbar)\mathcal{W}(\hbar)} + \frac{2\hbar}{(2-\hbar)\mathcal{W}(\hbar)} = 1, \tag{7}$$

where $\mathcal{W}(\hbar) = \frac{2}{2-\hbar}$*. From [18], we have*

$$D_k^{\hbar}(g(k)) = \frac{1}{1-\hbar} \int_0^k g'(x) \exp\Big[\hbar \frac{k-x}{1-\hbar}\Big] dx, \ k \geq 0. \tag{8}$$

4. Numerical scheme for the dynamics

Here, we will present the dynamics of the recommended through a numerical method to analyze the significance of different scenario. We use the Adams-Bashforth technique of two step for solution of the model. For the first equation of the model, we have

$$y_1(t) - y_1(0) = \frac{1-\xi}{\mathscr{U}(\xi)} \mathscr{H}_1(t, y_1) + \frac{\xi}{\mathscr{U}(\xi)} \int_0^t \mathscr{H}_1(\vartheta, y_1) d\vartheta. \tag{9}$$

In the next step, by take $t = t_{m+1}, m = 0, 1, \ldots,$, we have

$$y_1(t_{m+1}) - y_1(0) = \frac{1-\xi}{\mathscr{U}(\xi)} \mathscr{H}_1(t_m, y_1(t_m)) + \frac{\xi}{\mathscr{U}(\xi)} \int_0^{t_{m+1}} \mathscr{H}_1(t, y_1) dt. \tag{10}$$

and

$$y_1(t_m) - y_1(0) = \frac{1-\xi}{\mathscr{U}(\xi)} \mathscr{H}_1(t_{m-1}, y_1(t_{m-1})) + \frac{\xi}{\mathscr{U}(\xi)} \int_0^{t_m} \mathscr{H}_1(t, y_1) dt. \tag{11}$$

Next, the difference of successive terms are

$$y_{1_{m+1}} - y_{1_m} = \frac{1-\xi}{\mathscr{U}(\xi)}\Big(\mathscr{H}_1(t_m, y_{1_m}) - \mathscr{H}_1(t_{m-1}, y_{1_{m-1}})\Big) + \frac{\xi}{\mathscr{U}(\xi)}\int_m^{t_{m+1}} \mathscr{H}_1(t, y_1)dt. \quad (12)$$

Here, the function $\mathscr{H}1(t, y_1)$ is approximated over $[t_k, tk+1]$ using an interpolation polynomial, yielding

$$\mathscr{P}_k(t) \cong \frac{\mathscr{H}_1(t_k, y_k)}{h}(t - t_{k-1}) - \frac{\mathscr{H}_1(t_{k-1}, y_{k-1})}{h}(t - t_k), \quad (13)$$

where $h = t_m - t_{m-1}$ is the time spent. Moreover, $\mathscr{P}_k(t)$ is utilized to evaluate the below integral

$$\begin{aligned}\int_m^{t_{m+1}} \mathscr{H}_1(t, y_1)dt &= \int_m^{t_{m+1}} \left(\frac{\mathscr{H}_1(t_m, y_{1_m})}{h}(t - t_{m-1}) - \frac{\mathscr{H}_1(t_{m-1}, y_{1_{m-1}})}{h}(t - t_m)\right)dt, \\ &= \frac{3h}{2}\mathscr{H}_1(t_m, y_{1_m}) - \frac{h}{2}\mathscr{H}_1(t_{m-1}, y_{1_{m-1}}). \quad (14)\end{aligned}$$

Now, put (14) into (12), we have

$$\begin{aligned} y_{1_{m+1}} &= y_{1_m} + \left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{3\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_1(t_m, y_{1_m}) \\ &- \left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_1(t_{m-1}, y_{1_{m-1}}), \quad (15)\end{aligned}$$

which is the necessary scheme for the first equation of the model (1). By following a similar procedure, the corresponding schemes for other equations of (1) of HIV-tumor can also be determined, as given by

$$\begin{aligned} y_{2_{m+1}} &= y_{2_m} + \left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{3\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_2(t_m, y_{2_m}) \\ &-\left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_2(t_{m-1}, y_{2_{m-1}}), \quad (16)\end{aligned}$$

$$\begin{aligned} y_{3_{m+1}} &= y_{3_m} + \left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{3\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_3(t_m, y_{3_m}) \\ &-\left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_3(t_{m-1}, y_{3_{m-1}}), \quad (17)\end{aligned}$$

and

$$\begin{aligned} y_{4_{m+1}} &= y_{4_m} + \left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{3\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_4(t_m, y_{4_m}) \\ &-\left(\frac{1-\xi}{\mathscr{U}(\xi)} + \frac{\xi h}{2\mathscr{U}(\xi)}\right)\mathscr{H}_4(t_{m-1}, y_{4_{m-1}}). \quad (18)\end{aligned}$$

This approach uses an exponential decay rule for the CF operator.

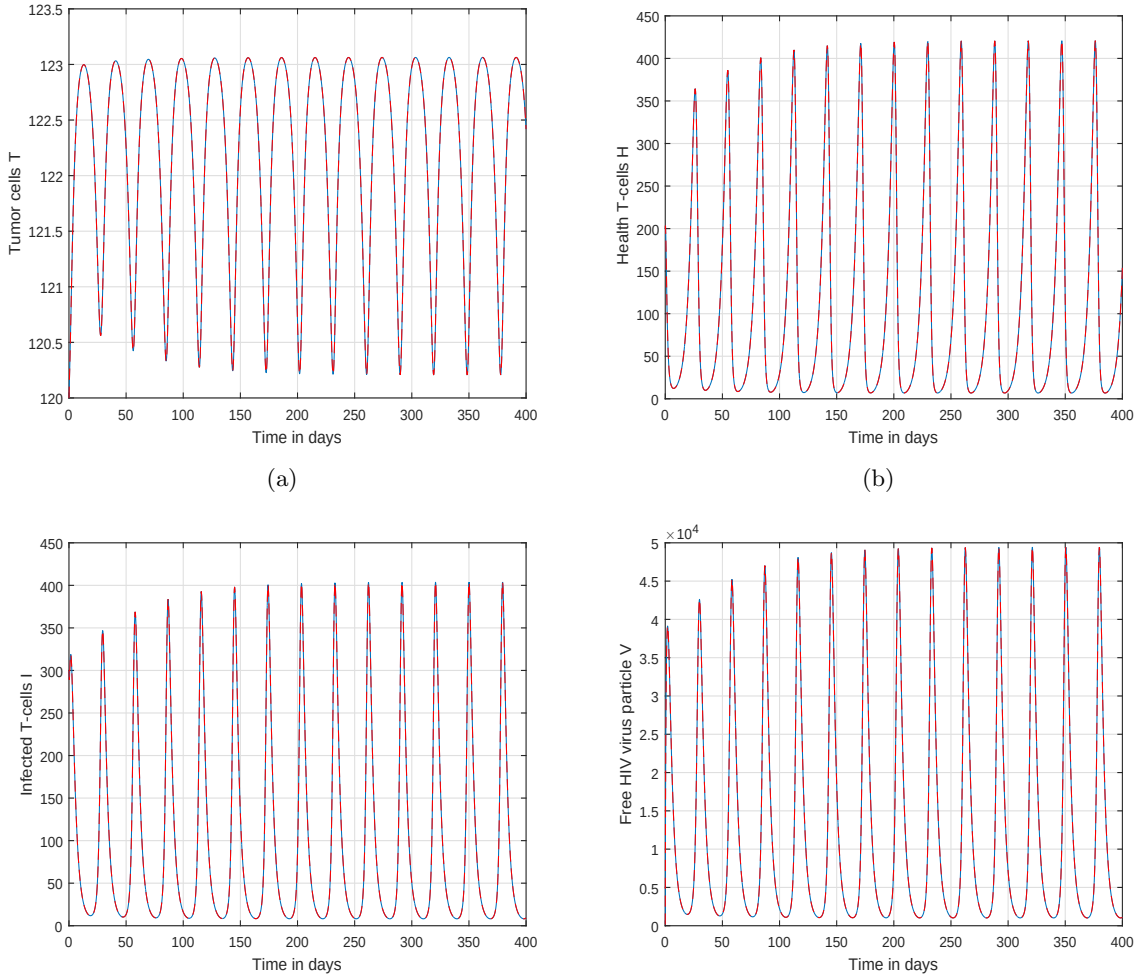

Figure 1: Time series analysis of the model (1) HIV and tumor in the response of immune system by taking $\hbar = 1$, $r = 0.3$ and $\xi = 1.00$.

5. Results and discussions

The significance of analyzing the progression of HIV in the presence of a tumor using a fractional approach lies in the ability to model complex interactions between the immune system, viral load, and tumor dynamics more accurately. HIV and tumor cells both impact the immune system, particularly $CD4^+$ T-cells. Traditional integer-order models may fall short in capturing the long-term memory and hereditary properties inherent in biological systems. By applying fractional calculus, especially with non-singular kernels like Atangana-Baleanu operator, the intricate feedback loops and interactions between HIV, immune cells, and tumors can be better represented. This offers a more realistic simulation of the disease progression, accounting for the time-dependent changes in immune system

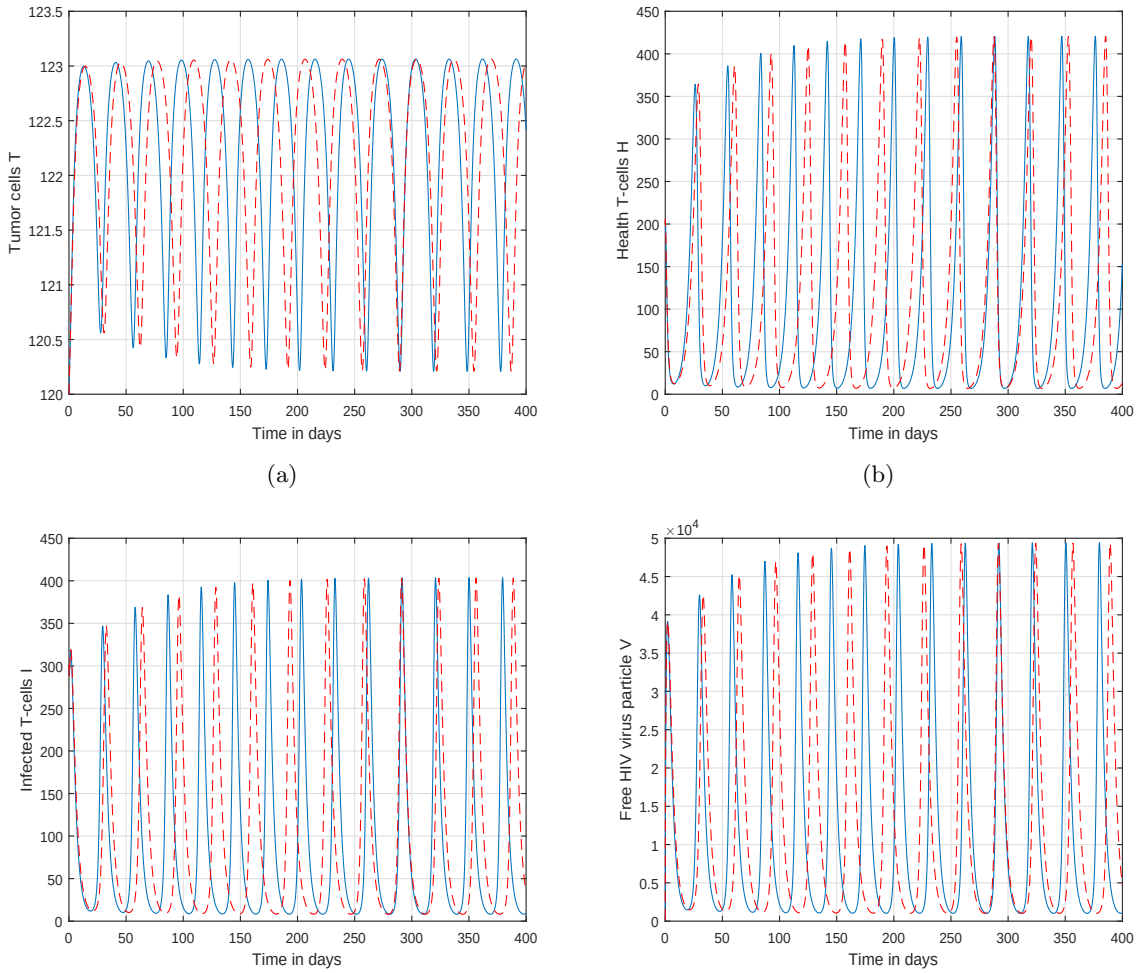

Figure 2: Time series analysis of the model (1) HIV and tumor in the response of immune system by taking $\hbar = 1$, $r = 0.3$, $s = 1$ and $\xi = 0.90$.

efficacy and viral load, which are vital for designing effective treatment strategies.

Moreover, a fractional approach to immune response dynamics allows researchers to explore the oscillatory and potentially chaotic behaviors observed in the immune system under the dual pressure of HIV infection and tumor growth. This mathematical framework provides deeper insights into how both HIV and tumor cells may exploit the immune system's vulnerabilities, causing destabilization in immune function. Such modeling is not only significant for understanding the co-progression of HIV and cancer but also for optimizing therapeutic interventions. It enables the development of combined treatment strategies that take into account both infections, targeting not just the viral load or tumor growth individually but considering the overall immune system dynamics, leading to improved patient outcomes in co-infection scenarios.

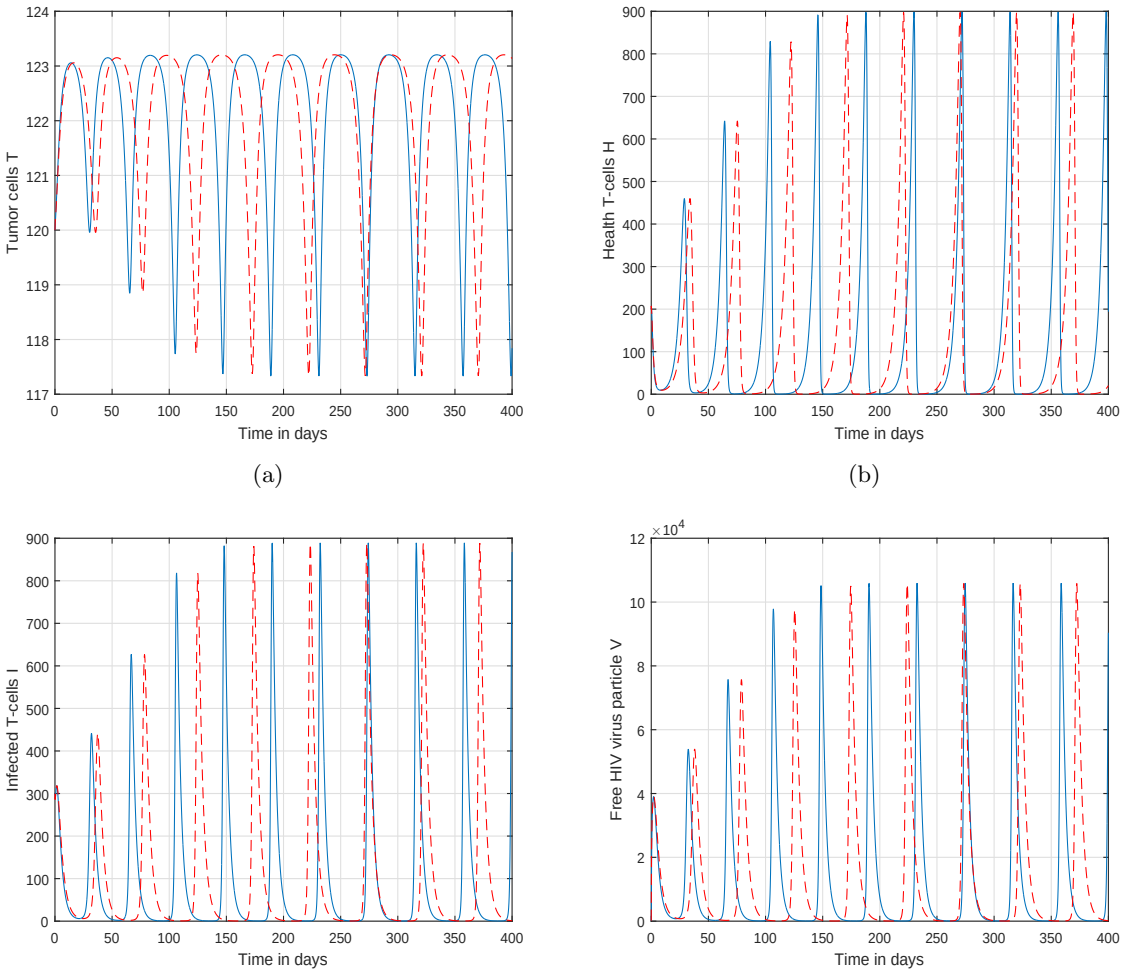

Figure 3: Representation of the tracking paths of the proposed system (1) by taking the value of $s = 0.1$, $\xi = 0.85$ and $r = 0.3$.

Here, various simulations are performed to conceptualize the intricate phenomena of the dynamics of HIV and tumor with the response of immune. For simulation purposes, we assumed the values T = 120, H = 200, I = 300 and V = 150. We conducted various simulations to demonstrate the influence of various factors on the tracking paths of the system and its chaotic behavior. In the first simulation, we set the parameter values to $\hbar = 1.00$, $s = 1$, and $r = 0.3$, while the value of ξ is assumed to be 1.00 in Figure 1 and 0.90 in Figure 2. We observed the influence of the fractional order on the solution pathways. The simulation outcomes clearly reveal the substantial effect of the fractional order on the infection dynamics. Importantly, υ shows potential as an effective instrument for controlling the infection spread. Consequently, we advise policymakers to undertake a more thorough examination of this fractional parameter to obtain a better knowledge of

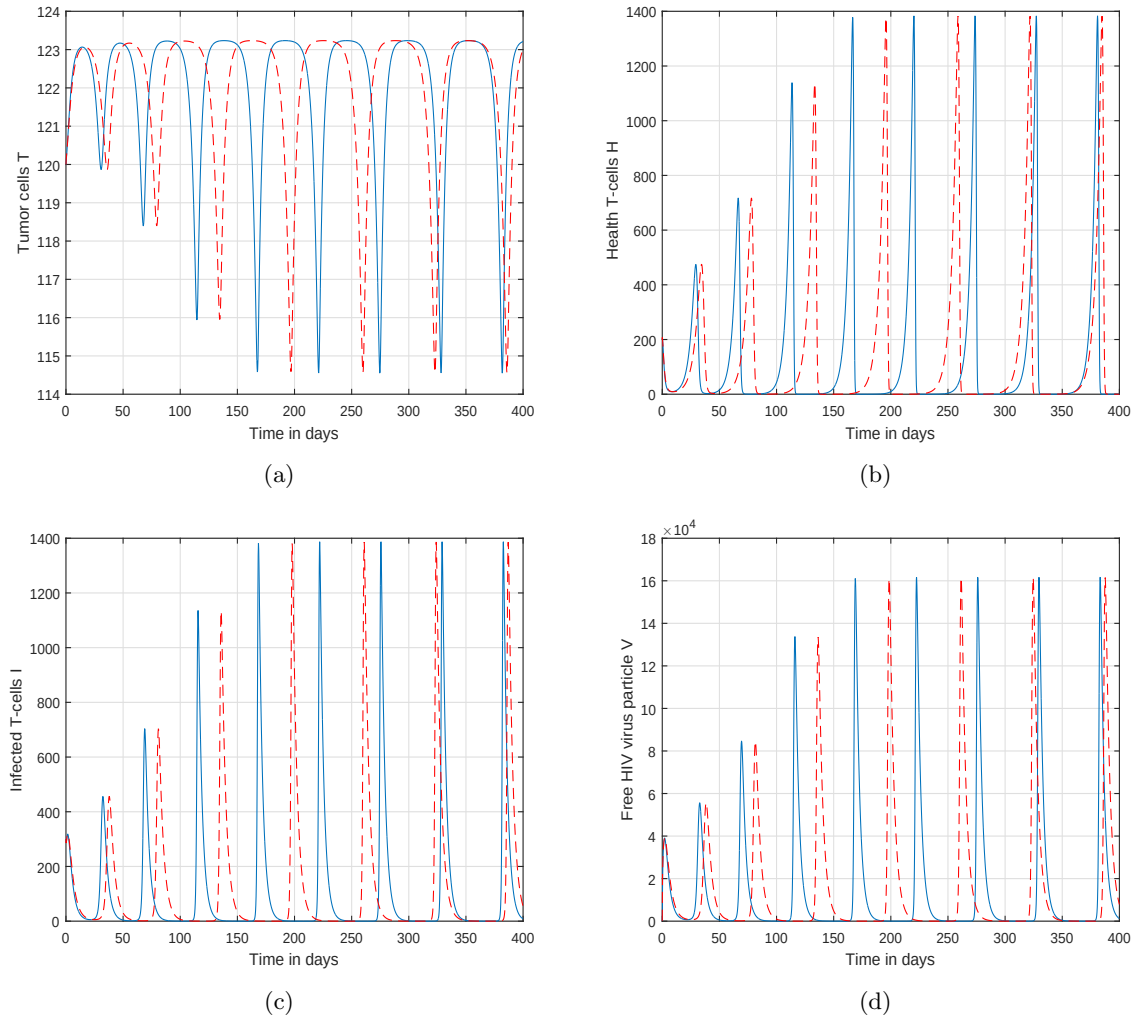

Figure 4: Visualization of the tracking paths of the proposed system (1) by taking the value of $s = 0.01$, $\xi = 0.85$ and $r = 0.3$.

its ability to mitigate the infection. This thorough examination could provide important insights for developing focused policies for infection prevention and control.

In the second simulation, shown in Figures 3 and 4, we illustrate the effect of the CD4$^+$ T-cell source term on solution pathways of the recommended system. In Figure 3, the source term is set to $s = 0.1$, while in Figure 4, the value of s is reduced to 0.01. The variation in the oscillatory behavior of the system has been noticed with the variation of the source term of the CD4$^+$ T-cell. CD4$^+$ T-cells influence the tumor microenvironment, promoting anti-tumor immunity by activating macrophages and other immune cells that can inhibit tumor growth. An increased source term of CD4$^+$ T-cells leads to a stronger immune response, potentially reducing tumor growth. CD4$^+$ T-cells are the primary target of HIV, and the progressive depletion of these cells leads to immune system failure.

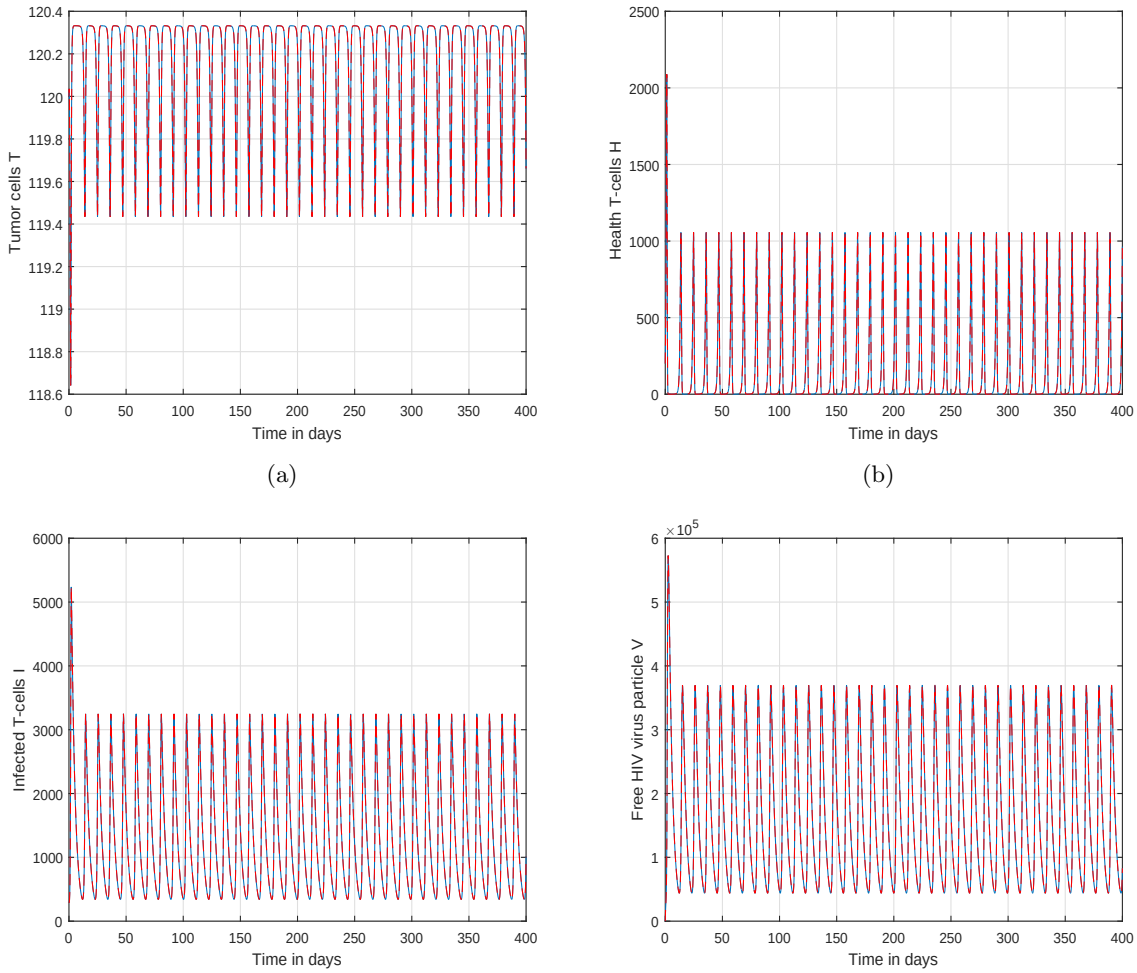

Figure 5: Graphical view analysis of the time series of the proposed system (1) by taking the value of $r_1 = 3$, $\xi = 0.85$ and $s = 1$.

The source term reflects the replenishment rate of $CD4^+$ T-cells, which is critical for maintaining immune function in HIV-positive individuals. The source term of $CD4^+$ T-cells is essential for maintaining a robust immune response, and its modulation can have significant therapeutic implications for both tumor reduction and HIV management.

In Figure 5, we illustrate the effect of tumor growth rate on the dynamics of HIV-tumor interactions in response to the immune system. In this simulation, the tumor growth rate r is varied from 0.3 to 3.0 to highlight the resulting changes in the system's time series. The results indicate that this input parameter amplifies oscillatory behavior within the system, thereby increasing the risk of infection. The chaotic nature of HIV and tumor dynamics in the presence of an immune response is characterized by complex, unpredictable behavior that arises from the nonlinear interactions between viral replication, tumor growth, and

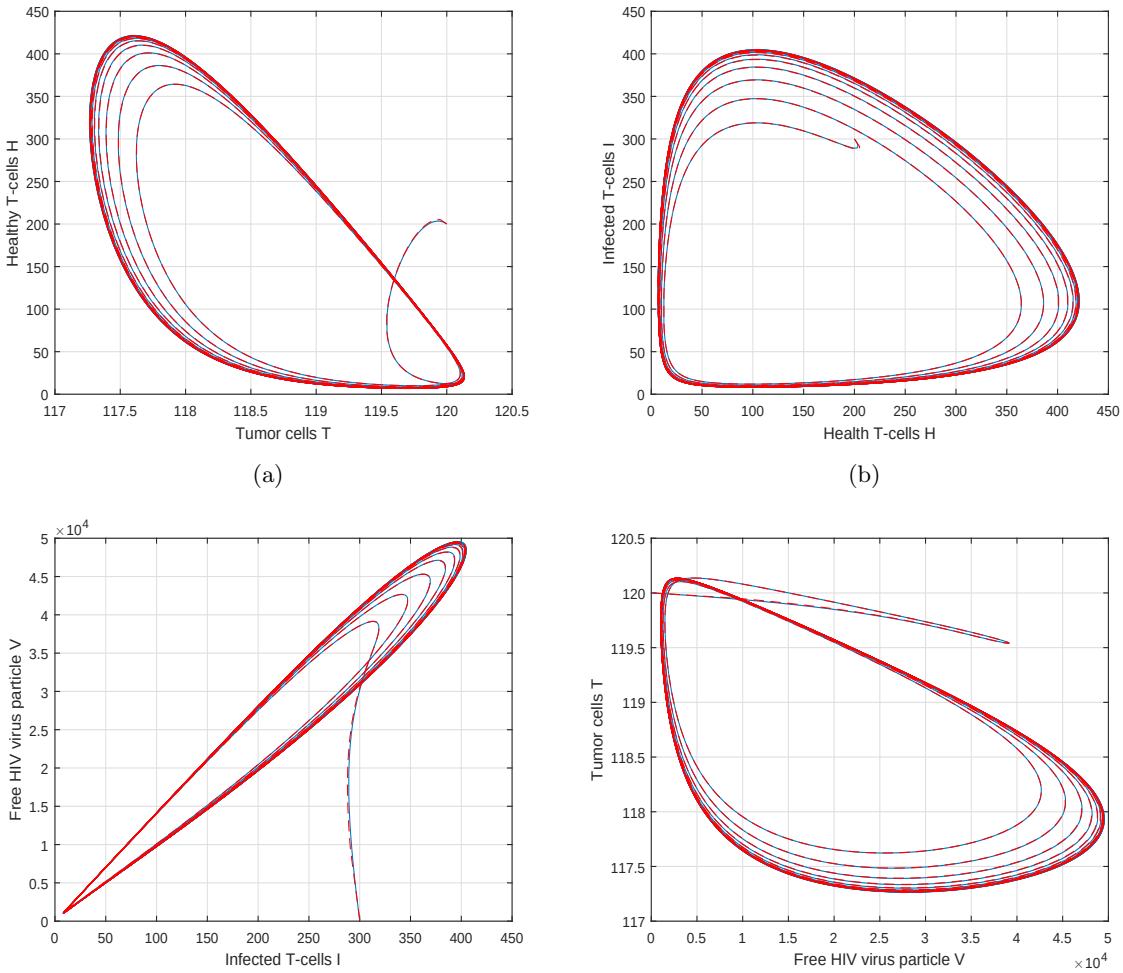

Figure 6: Chaotic nature of the recommended model (1) of the HIV and tumor in the response of immune by considering the input values $\xi = 0.9$, $\hbar = 0.1$, $s = 1.00$ and $r_1 = 0.35$.

the body's immune defense. In Figures 6-8, the chaotic behavior of the proposed system is depicted. In Figure 6, the parameters are set to $\xi = 0.90$, $\hbar = 0.1$, $s = 1.0$, and $r = 0.3$ to demonstrate the system's chaotic dynamics. We assume $N = 2000$, $H_{max} = 1000$, $r = 0.3$ and 0.85 in Figure 7 while the value of $\hbar = 0.1$, $s = 2.0$ and $k_1 = k1 = 1 * 10^{(-5)}$ in Figure 8 to conceptualize the chaotic behavior of the system.

The interactions between HIV, tumor cells, and immune components exhibit nonlinear feedback loops. These feedback mechanisms can lead to sensitive dependence on initial conditions, where small variations in the system's parameters or state can result in vastly different outcomes over time. Chaotic dynamics often manifest as irregular oscillations in viral load, tumor cell populations, and immune cell levels. These oscillations are driven by the immune system's efforts to control HIV and tumor growth, as well as the adaptive

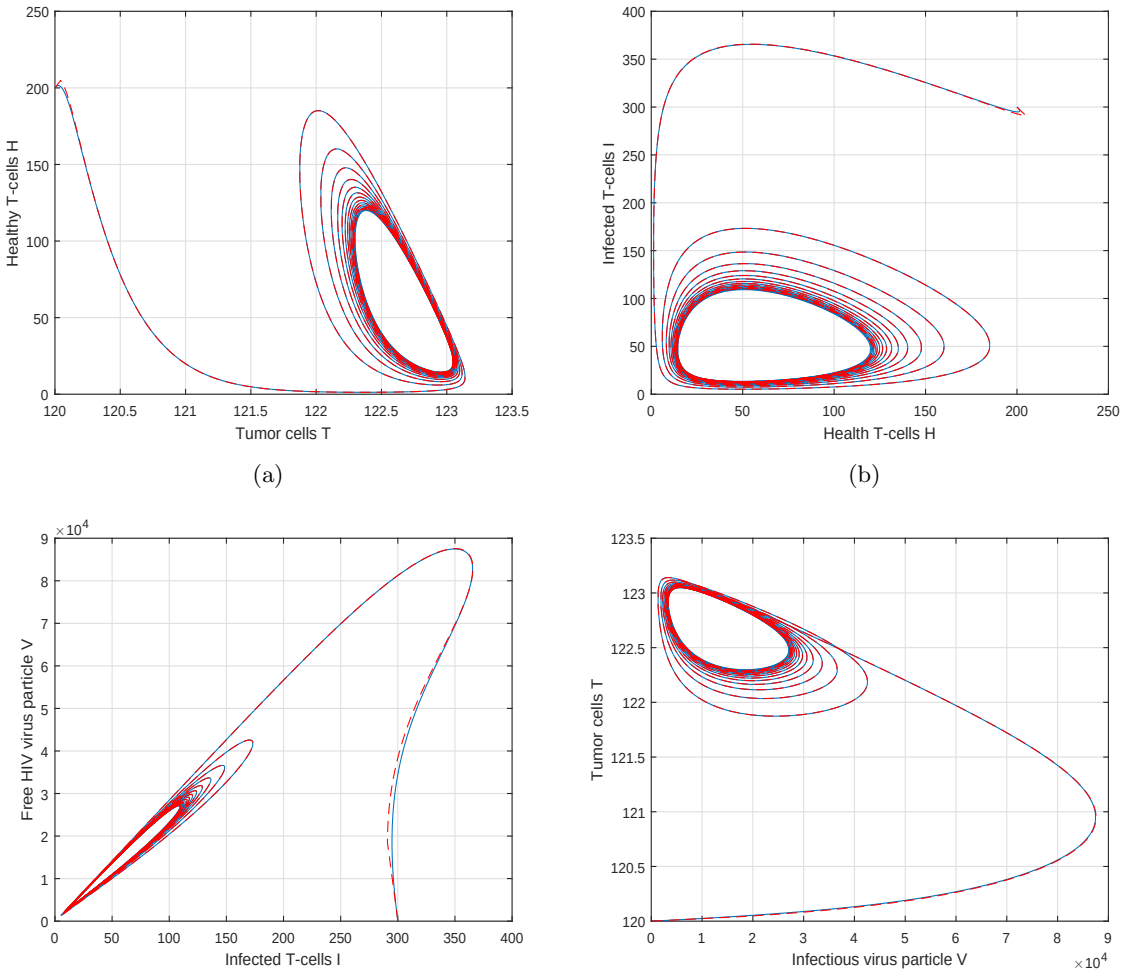

Figure 7: Dynamical behavior of the model (1) of HIV and tumor in the response of immune by considering the input values $N = 2000$, $r = 0.3$, $H_{max} = 1000$ and $\xi = 0.85$ to visualize the chaotic nature of the system.

strategies of the virus and tumor to evade immune detection. Moreover, HIV weakens the immune response by infecting $CD4^+$ T-cells, while tumors can evade immune surveillance through various mechanisms, such as altering antigen expression or promoting an immunosuppressive microenvironment. This dual interference from HIV and tumors can lead to complex and chaotic dynamics, where the immune system's response becomes highly variable and unpredictable. The chaotic nature of these dynamics presents challenges for treatment strategies, as the system may respond in unexpected ways to interventions like antiretroviral therapy, immunotherapy, or chemotherapy. Effective treatment must account for the potential for sudden shifts in the behavior of the system due to the sensitivity of chaotic dynamics.

We demonstrated distinct patterns in HIV viral load and tumor growth in response to

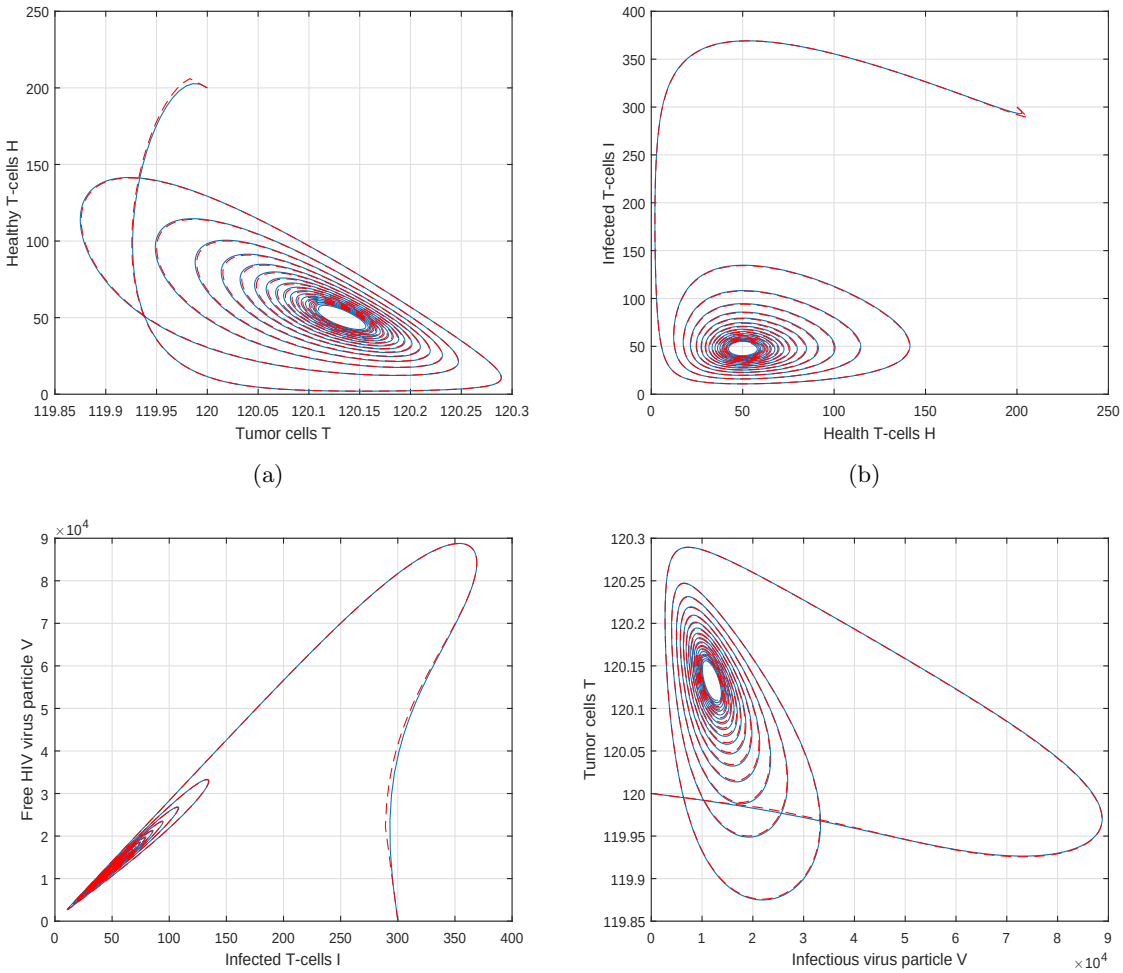

Figure 8: Dynamical behavior of the model (1) of HIV and tumor in the response of immune by considering the input values $s = 2$, $\hbar = 0.1$, $H_{max} = 1000$ and $k_1 = 1 * 10^{(-5)}$ to visualize the chaotic nature of the system.

variations in immune system dynamics. Specifically, changes in immune response parameters led to observable shifts in both HIV and tumor trajectories, highlighting the sensitivity of these dynamics to immune modulation. Variations in $CD4^+$ T-cell dynamics, such as changes in the source term and growth rate, influenced the system's stability and oscillatory behavior. Higher source terms for $CD4^+$ T-cells were associated with a more robust immune response, which in turn impacted both HIV control and tumor growth. The system exhibited chaotic behavior under certain parameter settings, as evidenced by irregular oscillations in HIV viral load and tumor cell populations. This chaos was attributed to the complex interactions between HIV, tumor cells, and the immune response. Numerical simulations revealed sensitive dependence on initial conditions and parameter values, underscoring the importance of precise and adaptive treatment strategies. Future

research directions should aim to refine mathematical models, explore novel therapeutic approaches, integrate diverse data sources, and address global health challenges to advance our understanding and treatment of HIV and tumors in the context of immune responses.

6. Concluding Remarks

The study on HIV and tumor dynamics within the framework of immune responses holds substantial importance. It deepens our understanding of the intricate interactions between these diseases, facilitates the optimization of treatment strategies, enhances disease management, and guides public health policies. This comprehensive approach not only contributes to better patient outcomes but also drives advancements in scientific knowledge. In this study, a mathematical model was developed to conceptualize the interaction between HIV and tumors in relation to the immune system's response. The foundational theory and concepts of the Caputo-Fabrizio derivative were presented to investigate the proposed dynamics. The dynamics of HIV-tumor interactions in the context of immune response were systematically explored. We presented a numerical scheme to conceptualize the dynamics through numerical results. Numerical results are presented to illustrate the impact of various parameters on the infection dynamics. The system's trajectories have been analyzed numerically, revealing distinct patterns in HIV viral load and tumor growth under varying immune system dynamics. Specifically, alterations in immune response parameters resulted in notable shifts in both HIV and tumor progression, underscoring the sensitivity of these dynamics to immune modulation. Our findings highlight key parameters that critically influence system behavior, offering valuable insights for designing targeted therapeutic interventions.

References

[1] Sultan Alyobi and Rashid Jan. Qualitative and quantitative analysis of fractional dynamics of infectious diseases with control measures. *Fractal and Fractional*, 7(5):400, 2023.

[2] Sadia Arshad, Dumitru Baleanu, Weiping Bu, and Yifa Tang. Effects of hiv infection on cd4+ t-cell population based on a fractional-order model. *Advances in Difference Equations*, 2017:1–14, 2017.

[3] Abdon Atangana and Sania Qureshi. Mathematical modeling of an autonomous nonlinear dynamical system for malaria transmission using caputo derivative. *Fractional order analysis: Theory, methods and applications*, pages 225–252, 2020.

[4] SAMIA Bushnaq, Sajjad Ali Khan, Kamal Shah, and Gul Zaman. Existence theory of hiv-1 infection model by using arbitrary order derivative of without singular kernel type. *J. Math. Anal*, 9(1):16–28, 2018.

[5] Michele Caputo and Mauro Fabrizio. A new definition of fractional derivative without singular kernel. *Progress in Fractional Differentiation & Applications*, 1(2):73–85, 2015.

[6] Anil Chavada, Nimisha Pathak, and Sagar R Khirsariya. A fractional mathematical model for assessing cancer risk due to smoking habits. *Math. Model. Control*, 4(3):246–259, 2024.

[7] Rebecca V Culshaw and Shigui Ruan. A delay-differential equation model of hiv infection of cd4+ t-cells. *Mathematical biosciences*, 165(1):27–39, 2000.

[8] Dima Dandachi and Fanny Morón. Effects of hiv on the tumor microenvironment. *Tumor Microenvironment: State of the Science*, pages 45–54, 2020.

[9] Ihtisham Ul Haq, Nigar Ali, and Shabir Ahmad. A fractional mathematical model for covid-19 outbreak transmission dynamics with the impact of isolation and social distancing. *Math. Model. Control*, 2:228–242, 2022.

[10] Corrilynn O Hileman and Nicholas T Funderburg. Inflammation, immune activation, and antiretroviral therapy in hiv. *Current Hiv/aids reports*, 14:93–100, 2017.

[11] Rashid Jan, Salah Boulaaras, Hussain Ahmad, Muhammad Jawad, Sulima Zubair, and Mohamed Abdalla. A robust study of tumor-immune cells dynamics through non-integer derivative. *Fractal and Fractional*, 7(2):164, 2023.

[12] Rashid Jan, Salah Boulaaras, Asma Alharbi, and Normy Norfiza Abdul Razak. Nonlinear dynamics of a zoonotic disease with control interventions through fractional derivative. *European Journal of Pure and Applied Mathematics*, 17(4):3781–3800, 2024.

[13] Rashid Jan, Salah Boulaaras, Mohammad Alnegga, and Farah Aini Abdullah. Fractional-calculus analysis of the dynamics of typhoid fever with the effect of vaccination and carriers. *International Journal of Numerical Modelling: Electronic Networks, Devices and Fields*, 37(2):e3184, 2024.

[14] Rashid Jan, Salah Boulaaras, Sultan Alyobi, and Muhammad Jawad. Transmission dynamics of hand–foot–mouth disease with partial immunity through non-integer derivative. *International Journal of Biomathematics*, 16(06):2250115, 2023.

[15] Rashid Jan, Salah Boulaaras, Sultan Alyobi, Karthikeyan Rajagopal, and Muhammad Jawad. Fractional dynamics of the transmission phenomena of dengue infection with vaccination. *Discrete Contin. Dyn. Syst. Ser. S*, 2022.

[16] Rashid Jan, Normy Norfiza Abdul Razak, Salah Boulaaras, Ziad Ur Rehman, and Salma Bahramand. Mathematical analysis of the transmission dynamics of viral infection with effective control policies via fractional derivative. *Nonlinear Engineering*, 12(1):20220342, 2023.

[17] Rashid Jan, Normy Norfiza Abdul Razak, Sania Qureshi, Imtiaz Ahmad, and Salma Bahramand. Modeling rift valley fever transmission: insights from fractal-fractional dynamics with the caputo derivative. *Mathematical Modelling and Control*, 4(2):163–177, 2024.

[18] Jorge Losada and Juan J Nieto. Properties of a new fractional derivative without singular kernel. *Progr. Fract. Differ. Appl*, 1(2):87–92, 2015.

[19] Bobisa Mobisa, GO Lawi, and JK Nthiiri. Modelling in vivo hiv dynamics under combined antiretroviral treatment. *Journal of Applied Mathematics*, 2018(1):8276317, 2018.

[20] Pshtiwan Othman Mohammed, Ravi P Agarwal, Majeed A Yousif, Eman Al-Sarairah,

Alina Alb Lupas, and Mohamed Abdelwahed. Theoretical results on positive solutions in delta riemann–liouville setting. *Mathematics*, 12(18):2864, 2024.

[21] Pshtiwan Othman Mohammed, Alina Alb Lupas, Ravi P Agarwal, Majeed A Yousif, Eman Al-Sarairah, and Mohamed Abdelwahed. Theoretical investigation of fractional estimations in liouville–caputo operators of mixed order with applications. *Axioms*, 13(8):570, 2024.

[22] Mevlüde Yakit Ongun. The laplace adomian decomposition method for solving a model for hiv infection of cd4+ t cells. *Mathematical and Computer Modelling*, 53(5-6):597–603, 2011.

[23] Abhishek Pandey and Alison P Galvani. The global burden of hiv and prospects for control. *The Lancet HIV*, 6(12):e809–e811, 2019.

[24] Bengisen Pekmen and Ummuhan Yirmili. Numerical and statistical approach on chemotaxis-haptotaxis model for cancer cell invasion of tissue. *Mathematical Modelling and Control*, 4(2):195–207, 2024.

[25] Alan S Perelson, Denise E Kirschner, and Rob De Boer. Dynamics of hiv infection of cd4+ t cells. *Mathematical biosciences*, 114(1):81–125, 1993.

[26] Alan S Perelson and Patrick W Nelson. Mathematical analysis of hiv-1 dynamics in vivo. *SIAM review*, 41(1):3–44, 1999.

[27] Alan S Perelson and Patrick W Nelson. Mathematical analysis of hiv-1 dynamics in vivo. *SIAM review*, 41(1):3–44, 1999.

[28] Tao-Qian Tang, Zahir Shah, Rashid Jan, Wejdan Deebani, and Meshal Shutaywi. A robust study to conceptualize the interactions of cd4+ t-cells and human immunodeficiency virus via fractional-calculus. *Physica Scripta*, 96(12):125231, 2021.

[29] Marta Trapero-Bertran and Juan Oliva-Moreno. Economic impact of hiv/aids: a systematic review in five european countries. *Health economics review*, 4:1–16, 2014.

[30] H Vazquez-Leal, L Hernandez-Martinez, Y Khan, VM Jimenez-Fernandez, U Filobello-Nino, A Diaz-Sanchez, AL Herrera-May, R Castaneda-Sheissa, A Marin-Hernandez, F Rabago-Bernal, et al. Multistage hpm applied to path tracking damped oscillations of a model for hiv infection of cd4+ t cells. *British Journal of Mathematics & Computer Science*, 4(8):1035–1047, 2014.

[31] Xueyong Zhou, Xinyu Song, and Xiangyun Shi. A differential equation model of hiv infection of cd4+ t-cells with cure rate. *Journal of Mathematical Analysis and Applications*, 342(2):1342–1355, 2008.