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GLOBAL DYNAMICS OF A MULTI-STAGE FRACTIONAL HIV-INFECTED MODEL WITH GENERAL INCIDENCE RATE AND DRUG EFFICACY

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Abstract. For several decades researchers have been studying global dynamics of viral infection models to prevent wide outbreak of scattered virus both in population and vivo such as Dengue fever, SARS-COV2, HRSV, and immunodeficiency diseases. In this paper, our main aim is obtaining sufficient conditions for the global stability of equilibria of a Caputo fractional derivative order system with general incidence functional response by using Lyapunov's method and LaSalle's invariance principle. We prove the global stability of stationary points by the values of the basic reproduction number (R_0) and we consider this threshold as a strong index for our sensitivity analysis. We confirm theoretical results through numerical simulations.

Keywords: viral infection; multi-stage infection; Caputo fractional derivative; Lyapunov functional; stability.
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1. INTRODUCTION

Fractional calculus has many use in engineering and medical sciences such as time-fractional vibration equations (TFVEs) especially for large membrane [4, 12, 16], and epidemic models [5, 14, 20]. Fractional derivatives (FD) have high efficacy in modeling biological infections,

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real adaptive systems, and cure and control theories. Clearly, infected mathematical models have biological importance to study short and long dynamics of invading viruses such as HIV, HBV, HCV, SARS-COV2,...[13, 18, 3, 7, 11, 15] as disturbing factors in vivo. many researchers have modeled HIV infection both in population and cellular cases to get better understanding of virus proliferations[9, 11, 19]. As general incidence rate concludes vast range of cases in modeling the viral infections [1, 6], we proposed a Caputo FDE multi-stage model due to DNA formation and integration process in a copied infected cell. Moreover, HIV drug treatments appeared through three inhibitors to analyze HIV progress completely. Non-local memory-dependent trait of Caputo fractional operator will content us about considered past scenario and optimality [2, 10]. To get the desire, the next section presents some preliminaries, our model formulation, determined the threshold parameter as basic reproduction number. Basically, this threshold alarms us to take effective approaches after well recognition such as getting highly active antiretroviral therapy (HAART) diet and HIV medicines and services to direct HIV patients on time. To continue, we set equilibria of our fractional model, and discussed well-posedness of solutions. Section 3 establishes the global stability of the equilibria which has vital importance in facing to chaotic system to minimize damaging immune system and AIDS pathogenesis develepement. Moreover, to prevent HIV transmission from mother to child during pregnancy or sex partner. To examine the robustness of the model, in section 4 we use basic reproduction number as a sensitive index and present numerical simulations for various orders of derivative to demonstrate the efficacy of analytical outcomes. Finally section 5 draws some deductions.

2. Model Formulation and Preliminary Results

In this section, we introduce a fractional-order viral infection model formulated using the Caputo fractional derivative. The model aims to describe the interactions between uninfected target cells, infected cells at different stages of infection, and viral particles.

We begin by defining the state variables of the model. The variable $T(t)$ denotes the population of uninfected target cells. The variables $I_1(t)$, $I_2(t)$, and $I_3(t)$ represent infected cells that have completed reverse transcription, productively infected cells, and infected cells with failed DNA integration, respectively. The variable $L(t)$ denotes the population of latently infected cells.The quantities $V_I(t)$ and $V_{NI}(t)$ correspond to infectious and non-infectious viral particles.

Next, we describe the parameters governing the biological processes involved. The parameter s represents the production rate of uninfected cells, while d and d_1 denote the natural death rates of uninfected cells and I_1-infected cells, respectively. The parameters k_1 and k_2 describe the transition rates from I_1 to I_2 and I_3. The parameter p denotes the fraction of infected cells entering latency. The parameters δ, d_3, and d_L represent the death rates of productively infected cells, I_3-infected cells, and latently infected cells, respectively, whereas a is the activation rate of latently infected cells. The quantity $N\delta$ denotes the rate of viral production per infected cell, and c is the viral clearance rate. Finally, ε_{RT}, ε_{II}, and ε_{PI} denote the efficacies of reverse transcriptase, integrase, and protease inhibitors, respectively.

To account for the infection mechanism, we incorporate a general incidence function. The function $f\big(T(t),V_I(t)\big)$ represents a general incidence rate describing the interaction between uninfected target cells and infectious viral particles. This general formulation allows for a wide class of nonlinear infection mechanisms. Throughout this work, the incidence function $f(T,V_I)$ is assumed to be continuously differentiable and to satisfy

$$f(0,V_I) = f(T,0) = 0, \qquad f(T,V_I) > 0 \text{ for all } T > 0,\ V_I > 0,$$

and to be non-decreasing with respect to both arguments.

Under the above assumptions, the dynamics of the model are governed by the following fractional-order system:

$$\text{(1)} \quad \begin{cases} D^{\alpha}T(t) = s - dT(t) - (1-\varepsilon_{RT}) f\big(T(t),V_I(t)\big) V_I(t), \\ D^{\alpha}I_1(t) = (1-\varepsilon_{RT}) f\big(T(t),V_I(t)\big) V_I(t) - d_1 I_1(t) - (1-\varepsilon_{II}) k_1 I_1(t) - k_2 I_1(t), \\ D^{\alpha}I_2(t) = (1-p)(1-\varepsilon_{II}) k_1 I_1(t) - \delta I_2(t) + aL(t), \\ D^{\alpha}I_3(t) = k_2 I_1(t) - d_3 I_3(t), \\ D^{\alpha}L(t) = p(1-\varepsilon_{II}) k_1 I_1(t) - d_L L(t) - aL(t), \\ D^{\alpha}V_I(t) = (1-\varepsilon_{PI}) N\delta I_2(t) - cV_I(t), \\ D^{\alpha}V_{NI}(t) = \varepsilon_{PI} N\delta I_2(t) - cV_{NI}(t). \end{cases}$$

The system (1) is supplemented with nonnegative initial conditions:

$$T(0)=T_0\geq 0,\quad I_1(0)=I_{1,0}\geq 0,\quad I_2(0)=I_{2,0}\geq 0,\quad I_3(0)=I_{3,0}\geq 0,\quad L(0)=L_0\geq 0,$$

$$V_I(0)=V_{I,0}\geq 0,\quad V_{NI}(0)=V_{NI,0}\geq 0.$$

Since the model is formulated in the sense of the Caputo fractional derivative, only classical initial conditions are required.

2.1. Well-posedness.

Theorem 1. *All solutions of System* (1) *with non-negative initial conditions exist uniquely for all $t>0$ and remain bounded and non-negative.*

Proof. Obviously, the dynamics of the Model (1) can be studied without considering I_3 and V_{NI} equations so for the following system we have

$$\left\{\begin{array}{rcl} D^{\alpha}T(t) &=& s-\mu_1 T-(1-\varepsilon_{RT})f\big(T(t),V_I(t)\big)V_I(t),\\ D^{\alpha}I_1(t) &=& (1-\varepsilon_{RT})f\big(T(t),V_I(t)\big)V_I(t)-d_1I_1-(1-\varepsilon_{II})k_1I_1-k_2I_1,\\ D^{\alpha}I_2(t) &=& (1-p)(1-\varepsilon_{II})k_1I_1-\delta I_2+aL,\\ D^{\alpha}L(t) &=& p(1-\varepsilon_{II})k_1I_1-d_LL-aL,\\ D^{\alpha}V_I(t) &=& (1-\varepsilon_{PI})N\delta I_2-cV_I. \end{array}\right. \tag{2}$$

Since

$$D^{\alpha}T(t)\big|_{T=0}=s\geq 0,$$

$$D^{\alpha}I_1(t)\big|_{I_1=0}=(1-\varepsilon_{RT})\,f(T(t),V_I(t))\,V_I(t),\quad \text{for all } T,V_I\geq 0,$$

$$D^{\alpha}I_2(t)\big|_{I_2=0}=(1-p)(1-\varepsilon_{II})k_1I_1+aL,\quad \text{for all } I_1,L\geq 0,$$

$$D^{\alpha}L(t)\big|_{L=0}=p(1-\varepsilon_{II})k_1I_1,\quad \text{for all } I_1\geq 0,$$

$$D^{\alpha}V_I(t)\big|_{V_I=0}=(1-\varepsilon_{PI})N\delta I_2,\quad \text{for all } I_2\geq 0,$$

it follows that the solutions of the System (2) remain nonnegative for all $t\geq 0$.

Now consider the following function:

$$M(t)=T(t)+I_1(t)+I_2(t)+L(t)+\frac{1}{2(1-\varepsilon_{PI})N}V_I(t).$$

We have

$$D^{\alpha}M(t) = s - \mu_1 T(t) - (d_1+k_2)I_1(t) - \frac{\delta}{2}I_2(t) - d_L L(t) - \frac{c}{2(1-\varepsilon_{PI})N}V_I(t) \leq s - \zeta M(t),$$

where $\zeta = \min\left\{\mu_1, d_1+k_2, \frac{\delta}{2}, d_L, c\right\}$.

Hence,

$$\limsup_{t\longrightarrow+\infty} M(t) \leq \frac{s}{\zeta}.$$

Therefore, $T(t), I_1(t), I_2(t), L(t), V_I(t)$ are finally bounded.

Through summing up the equations of the System (2) and multiplying the both sides by $e^{\mu_1(t)}$ we have

$$\begin{aligned} s\,e^{\mu_1 t} &= D^{\alpha}T(t)e^{\mu_1(t)} + \mu_1 T(t)e^{\mu_1(t)} + D^{\alpha}I_1(t)e^{\mu_1(t)} + (d_1+k_2)I_1(t)e^{\mu_1(t)} + D^{\alpha}I_2(t)e^{\mu_1(t)} \\ &\quad + \delta I_2(t)e^{\mu_1(t)} + D^{\alpha}L(t)e^{\mu_1(t)} + d_L L(t)e^{\mu_1(t)}. \end{aligned}$$

Through integrating simultaneously on both sides of the equations we have

$$\begin{aligned} \int_0^t se^{\mu_1(x)}dx &= \int_0^t \left\{D^{\alpha}T(x)e^{\mu_1(x)} + \mu_1 T(x)e^{\mu_1(x)}\right\}dx + \int_0^t \left\{D^{\alpha}I_1(x)e^{\mu_1(x)} + (d_1+k_2)I_1(x)e^{\mu_1(x)}\right\}dx \\ &\quad + \int_0^t \left\{D^{\alpha}I_2(x)e^{\mu_1(x)} + \delta I_2(x)e^{\mu_1(x)}\right\}dx + \int_0^t \left\{D^{\alpha}L(x)e^{\mu_1(x)} + d_L L(x)e^{\mu_1(x)}\right\}dx. \end{aligned}$$

Hence,

$$\begin{aligned} \frac{s}{\mu_1}(e^{\mu_1(t)} - 1) &= T(t)e^{\mu_1(t)} + I_1(t)e^{\mu_1(t)} + I_2(t)e^{\mu_1(t)} + L(t)e^{\mu_1(t)} - T_0 - I_{10} - I_{20} - L_0 \\ &\quad - (\mu_1 - (d_1+k_2))\int_0^t I_1(x)e^{\mu_1(x)}dx - (\mu_1 - \delta)\int_0^t I_2(x)e^{\mu_1(x)}dx \\ &\quad - (\mu_1 - d_L)\int_0^t L(x)e^{\mu_1(x)}dx. \end{aligned}$$

Through multiplying the both sides of the equation by $e^{-\mu_1(t)}$ we have

$$\begin{aligned} \frac{s}{\mu_1}(1 - e^{-\mu_1(t)}) &= T(t) + I_1(t) + I_2(t) + L(t) - (T_0 - I_{10} - I_{20} - L_0 e^{-\mu_1(t)}) \\ &\quad - (\mu_1 - (d_1+k_2))\int_0^t I_1(x)e^{(x-t)\mu_1}dx - (\mu_1 - \delta)\int_0^t I_2(x)e^{(x-t)\mu_1}dx \\ &\quad - (\mu_1 - d_L)\int_0^t L(x)e^{(x-t)\mu_1}dx. \end{aligned}$$

According to Lemma 3.3 in [15] , we have

$$\frac{s}{\mu_1} \geq \limsup_{t\longrightarrow+\infty} T(t) + \frac{d_1+k_2}{\mu_1}\limsup_{t\longrightarrow+\infty} I_1(t) + \frac{\delta}{\mu_1}\limsup_{t\longrightarrow+\infty} I_2(t) + \frac{d_L}{\mu_1}\limsup_{t\longrightarrow+\infty} L(t),$$

$$\frac{s}{\mu_1} \geq \liminf_{t\longrightarrow+\infty} T(t) + \frac{d_1+k_2}{\mu_1} \liminf_{t\longrightarrow+\infty} I_1(t) + \frac{\delta}{\mu_1} \liminf_{t\longrightarrow+\infty} I_2(t) + \frac{d_L}{\mu_1} \liminf_{t\longrightarrow+\infty} L(t).$$

Through subtracting we have

$$\begin{aligned} 0 \geq \limsup_{t\longrightarrow+\infty} T(t) - \liminf_{t\longrightarrow+\infty} T(t) + \frac{d_1+k_2}{\mu_1}\left(\limsup_{t\longrightarrow+\infty} I_1(t) - \liminf_{t\longrightarrow+\infty} I_1(t)\right) \\ + \frac{\delta}{\mu_1}\left(\limsup_{t\longrightarrow+\infty} I_2(t) - \liminf_{t\longrightarrow+\infty} I_2(t)\right) + \frac{d_L}{\mu_1}\left(\limsup_{t\longrightarrow+\infty} L(t) - \liminf_{t\longrightarrow+\infty} L(t)\right). \end{aligned}$$

Then,

$$\limsup_{t\to+\infty} T(t) = \liminf_{t\to+\infty} T(t), \quad \limsup_{t\to+\infty} I_1(t) = \liminf_{t\to+\infty} I_1(t),$$

$$\limsup_{t\to+\infty} I_2(t) = \liminf_{t\to+\infty} I_2(t), \quad \limsup_{t\to+\infty} L(t) = \liminf_{t\to+\infty} L(t).$$

Hence, the limit of $T(t), I_1(t), I_2(t), L(t)$ exist when $t \longrightarrow \infty$.

Clearly,

$$V_I(t) = V_{10}e^{-ct} + (1-\varepsilon_{PI})N\delta \int_0^t I_2(x)x^{(x-t)c}dx,$$

Then,

$$\limsup_{t\longrightarrow+\infty} V_I(t) \leq \frac{(1-\varepsilon_{PI}N\delta)}{c} \limsup_{t\longrightarrow+\infty} I_2(t),$$

$$\liminf_{t\longrightarrow+\infty} V_I(t) \leq \frac{(1-\varepsilon_{PI}N\delta)}{c} \liminf_{t\longrightarrow+\infty} I_2(t).$$

Through using the quality above, we get

$$\limsup_{t\longrightarrow+\infty} V_I(t) - \liminf_{t\longrightarrow+\infty} V_I(t) \leq 0.$$

Thus,

$$\limsup_{t\longrightarrow+\infty} V_I(t) = \liminf_{t\longrightarrow+\infty} V_I(t).$$

Hence, the limit of $V_I(t)$ exists when $t \longrightarrow \infty$. □

2.2. Equilibria and threshold parameters. We now investigate the existence of equilibria of system (2) and introduce the basic reproduction number R_0.

Proposition 1. *System* (2) *always admits an infection-free equilibrium given by*

$$E_0 = \left(\frac{s}{\mu_1}, 0, 0, 0, 0\right).$$

Proof. Setting

$$D^{\alpha}T = D^{\alpha}I_1 = D^{\alpha}I_2 = D^{\alpha}L = D^{\alpha}V_I = 0$$

in system (2) and assuming the absence of infection, that is, $I_1 = I_2 = L = V_I = 0$, the first equation reduces to

$$0 = s - \mu_1 T,$$

which yields $T = \frac{s}{\mu_1}$. Hence, the infection-free equilibrium E_0 exists for all parameter values. □

We now seek an endemic equilibrium E_1 corresponding to the persistence of infection, for which $V_I^* \neq 0$.

At equilibrium, setting $D^{\alpha}I_1 = 0$ in system (2) gives

$$(1-\varepsilon_{RT})f(T^*,V_I^*)V_I^* = \big(d_1 + (1-\varepsilon_{II})k_1 + k_2\big)I_1^*,$$

which implies

$$I_1^* = \frac{s - \mu_1 T^*}{d_1 + (1-\varepsilon_{II})k_1 + k_2}.$$

From the equilibrium equations $D^{\alpha}I_2 = 0$ and $D^{\alpha}L = 0$, we obtain

$$I_2^* = \frac{(1-\varepsilon_{II})k_1(s-\mu_1 T^*)(ap + (1-p)(a+d_L))}{\delta(a+d_L)(d_1 + (1-\varepsilon_{II})k_1 + k_2)},$$

and

$$L^* = \frac{p(1-\varepsilon_{II})k_1(s-\mu_1 T^*)}{(a+d_L)(d_1 + (1-\varepsilon_{II})k_1 + k_2)}.$$

Moreover, setting $D^{\alpha}V_I = 0$ yields

$$V_I^* = \frac{(1-\varepsilon_{PI})N\delta I_2^*}{c}.$$

Substituting the above expressions into the equilibrium equation $D^{\alpha}T = 0$ leads to the scalar equation

$$(1-\varepsilon_{RT})f\left(T^*, \frac{(1-\varepsilon_{PI})N(1-\varepsilon_{II})k_1(s-\mu_1 T^*)(ap+(1-p)(a+d_L))}{(d_1+(1-\varepsilon_{II})k_1+k_2)c(a+d_L)}\right)$$

$$\times\left(\frac{(d_1+(1-\varepsilon_{II})k_1+k_2)c(a+d_L)}{(1-\varepsilon_{PI})N(1-\varepsilon_{II})k_1(ap+(1-p)(a+d_L))}\right) = 0,$$

which implicitly defines T^*.

Linearizing system (2) around the infection-free equilibrium E_0 and applying the next-generation matrix method, the basic reproduction number is given by

$$R_0 = \frac{(1-\varepsilon_{RT})f\left(\frac{s}{\mu_1},0\right)(1-\varepsilon_{PI})N(1-\varepsilon_{II})k_1(ap+(1-p)(a+d_L))}{(d_1+(1-\varepsilon_{II})k_1+k_2)c(a+d_L)}.$$

If $R_0 > 1$, the above scalar equation admits a unique solution

$$T^* \in \left(0, \frac{s}{\mu_1}\right),$$

which guarantees the existence of a unique endemic equilibrium

$$E_1 = (T^*, I_1^*, I_2^*, L^*, V_I^*).$$

The above analysis leads to the following result, which summarizes the existence of equilibria of system (2).

Theorem 2. *If $R_0 \leq 1$, system* (2) *admits only the infection-free equilibrium E_0. If $R_0 > 1$, system* (2) *admits a unique endemic equilibrium E_1.*

Remark 1. Theorem 2 highlights the threshold role of the basic reproduction number R_0. When $R_0 \leq 1$, the infection dies out and only the infection-free equilibrium exists, whereas the condition $R_0 > 1$ ensures the persistence of the infection through the emergence of a unique endemic equilibrium.

3. GLOBAL DYNAMICS

Clearly, the corresponding ordinary differential equations (ODEs) of System (2) is given by

$$\dot{u} = f(u), \tag{3}$$

where $u = \begin{bmatrix} T \\ I_1 \\ I_2 \\ L \\ V_I \end{bmatrix}$ and $f(u) = \begin{bmatrix} s - dT - (1-\varepsilon_{RT})f(T(t),V_I(t))V_I(t) \\ (1-\varepsilon_{RT})f(T(t),V_I(t))V_I(t) - d_1I_1 - (1-\varepsilon_{II})k_1I_1 - k_2I_1 \\ (1-p)(1-\varepsilon_{II})k_1I_1 - \delta I_2 + aL \\ p(1-\varepsilon_{II})k_1I_1 - d_LL - aL \\ (1-\varepsilon_{PI})N\delta I_2 - cV_I \end{bmatrix}.$

Hence, System (2) can be written as

$$D_t^{\alpha}u = f(u),$$

where D_t^α is the fractional derivative in the Caputo sense of order $\alpha \in (0,1]$. For $\alpha = 1$, we get the ODE Model (3).

The Jacobian matrix of reduced Model (2) at E_0 is given by

$$J = \begin{bmatrix} -\mu_1 & 0 & 0 & 0 & -(1-\varepsilon_{RT})f(\frac{s}{\mu_1},0) \\ 0 & -(d_1+(1-\varepsilon_{II})k_1+k_2) & 0 & 0 & (1-\varepsilon_{RT})f(\frac{s}{\mu_1},0) \\ 0 & (1-p)(1-\varepsilon_{II})k_1 & -\delta & a & 0 \\ 0 & p(1-\varepsilon_{II})k_1 & 0 & -a-d_L & 0 \\ 0 & 0 & (1-\varepsilon_{PI})N\delta & 0 & -c \end{bmatrix}.$$

Obviously, it has an eigenvalue $\lambda = -\mu_1$, then consider

$$y(\lambda) = \lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0 \tag{4}$$

As

$$y(0) = b_4 = (d_1+(1-\varepsilon_{II})k_1+k_2)cd\delta(1-R_0)$$

If $R_0 > 1$, we have

$$y(0) < 0,$$

and

$$\lim_{\lambda \longrightarrow +\infty} y(\lambda) = +\infty$$

Thus, (4) has at least one positive eigenvalue. Hence, E_0 is unstable if $R_0 > 1$.

Theorem 3. *If $R_0 \leq 1$, then E_0 is globally asymptotically stable.*

Proof. We define Lyapunov functional as follows

$$L_0(u) = T - T_0 - \int_{T_0}^{T} \frac{f(T_0,0)}{f(\tau,0)}d\tau + I_1 + \frac{d(d_1+(1-\varepsilon_{II})k_1+k_2)}{(1-\varepsilon_{II})k_1\Big(ap+(1-p)d\Big)}I_2$$
$$+ \frac{a(d_1+(1-\varepsilon_{II})k_1+k_2)}{(1-\varepsilon_{II})k_1\Big(ap+(1-p)d\Big)}L + \frac{d(d_1+(1-\varepsilon_{II})k_1+k_2)}{(1-\varepsilon_{PI})N(1-\varepsilon_{II})k_1\Big(ap+(1-p)d\Big)}V_I.$$

Based on the results of [17], we deduce that L_0 is a Lyapunov functional at E_0 when $R_0 \leq 1$. Moreover, we have

$$D_t^\alpha L_0(u) \leq \nabla L_0(u).f(u).$$

By using Theorem 1 (i) in [8], we conclude that L_0 is also a Lyapunov functional for FDE Model (2) at E_0 when $R_0 \leq 1$. Therefore, E_0 is globally asymptotically stable when $R_0 \leq 1$. □

Theorem 4. *If $1 < R_0$, then E_1 is globally asymptotically stable.*

Proof. We consider the following Lyapunov functional

$$\begin{aligned} L_1(u) = & \frac{\left(\frac{ap}{a+d_L}+1-p\right)(1-\varepsilon_{II})k_1}{(d_1+(1-\varepsilon_{II})k_1+k_2)}\left(T-T^*-\int_{T^*}^{T}\frac{f(T^*,V_I^*)}{f(\tau,V_I^*)}d\tau\right) \\ & + \frac{\left(\frac{ap}{a+d_L}+1-p\right)(1-\varepsilon_{II})k_1}{(d_1+(1-\varepsilon_{II})k_1+k_2)}\left(I_1-I_1^*-I_1^* ln\frac{I_1}{I_1^*}\right)+\left(I_2-I_2^*-I_2^* ln\frac{I_2}{I_2^*}\right) \\ & + \frac{a}{a+d_L}\left(L-L^*-L^* ln\frac{L}{L^*}\right)+\frac{1}{N(1-\varepsilon_{PI})}\left(V_I-V_I^*-V_I^* ln\frac{V_I}{V_I^*}\right). \end{aligned}$$

By means of [17], we get that L_1 is a Lyapunov functional at E_1 when $R_0 > 1$. Furthermore, we have

$$D_t^{\alpha} L_1(u) \leq \nabla L_1(u).f(u).$$

By applying Theorem 1 (i) of [8], we deduce that L_1 is also a Lyapunov functional for FDE Model (2) at E_1 when $R_0 > 1$. Thus, E_1 is globally asymptotically stable when $R_0 > 1$. □

4. Numerical Simulations and Discussion

In this section, we present numerical simulations to illustrate the theoretical results. We consider several values of the fractional order, namely $\alpha = 0.7, 0.8, 0.9$, and 1, and we use the parameter values listed in Table 1.

When the parameter values given in the second column of Table 1 are adopted, the basic reproduction number is computed as $R_0 = 0.05 \leq 1$. In this case, System (1) admits the infection-free equilibrium (IFE) E_0. According to Theorem 3, the solution of System (1) converges to E_0 (see Figs. 1–7). In particular, Fig. 1 shows that the population of uninfected cells increases, whereas the densities of the infected cell populations and viral loads decrease significantly and tend to zero. Consequently, the virus is cleared from the host and the infection is eliminated.

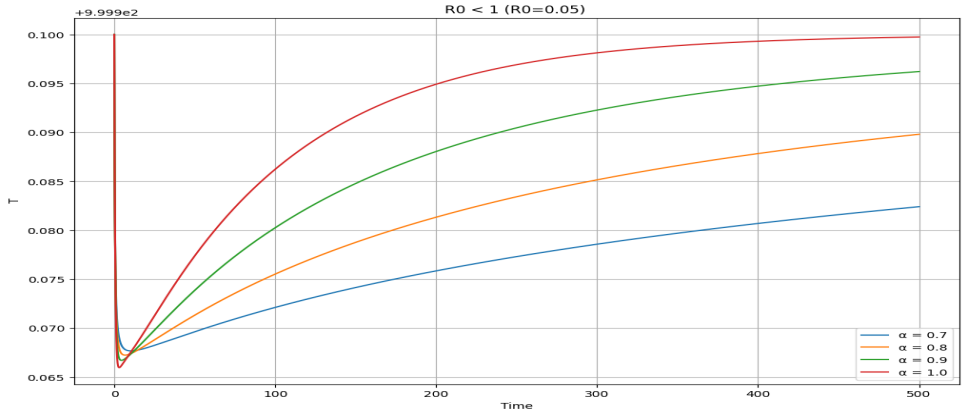

FIGURE 1. Stable inclination of plots towards the IFE E_0 for T using distinct values of α related to System (1).

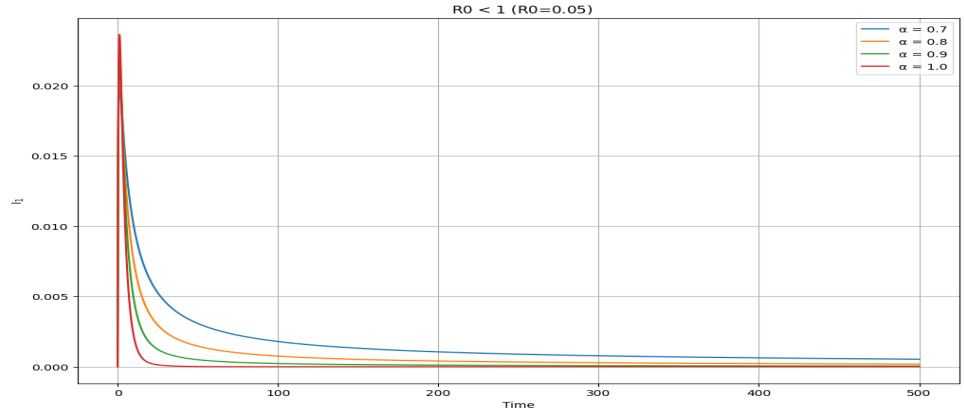

FIGURE 2. Stable inclination of plots towards the IFE E_0 for I_1 using distinct values of α related to System (1).

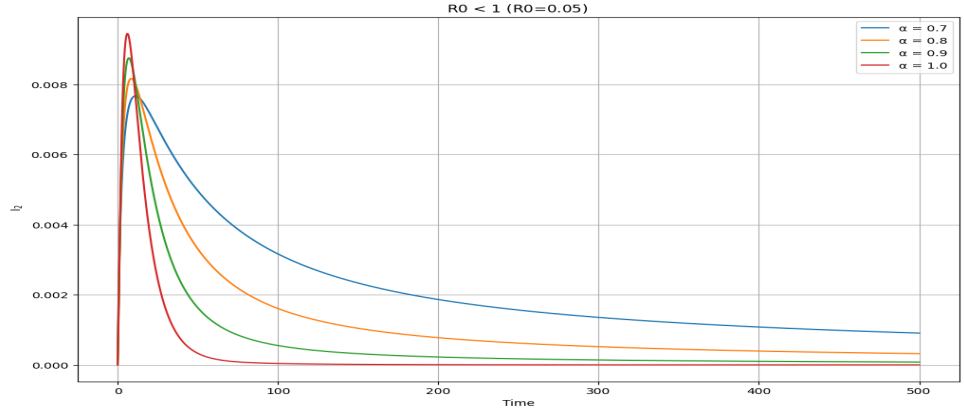

FIGURE 3. Stable inclination of plots towards the IFE E_0 for I_2 using distinct values of α related to System (1).

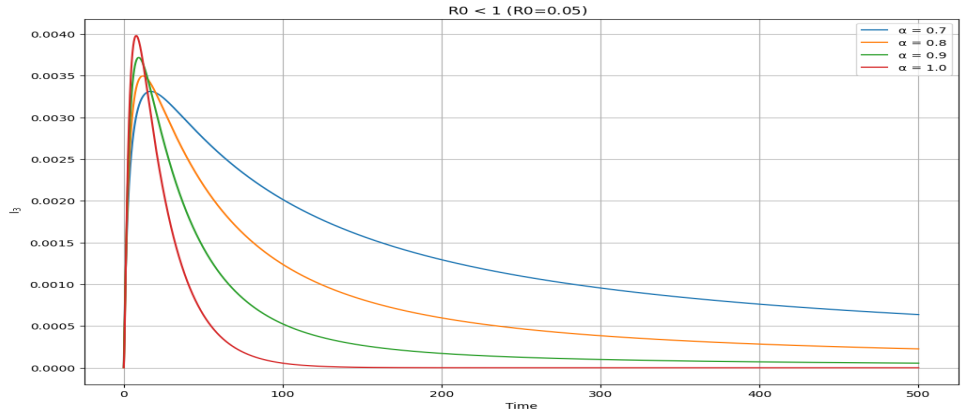

FIGURE 4. Stable inclination of plots towards the IFE E_0 for I_3 using distinct values of α related to System (1).

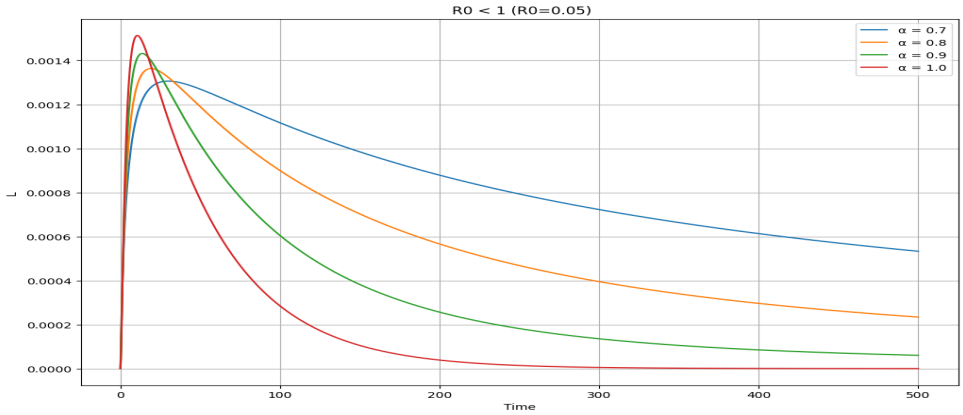

FIGURE 5. Stable inclination of plots towards the IFE E_0 for L using distinct values of α related to System (1).

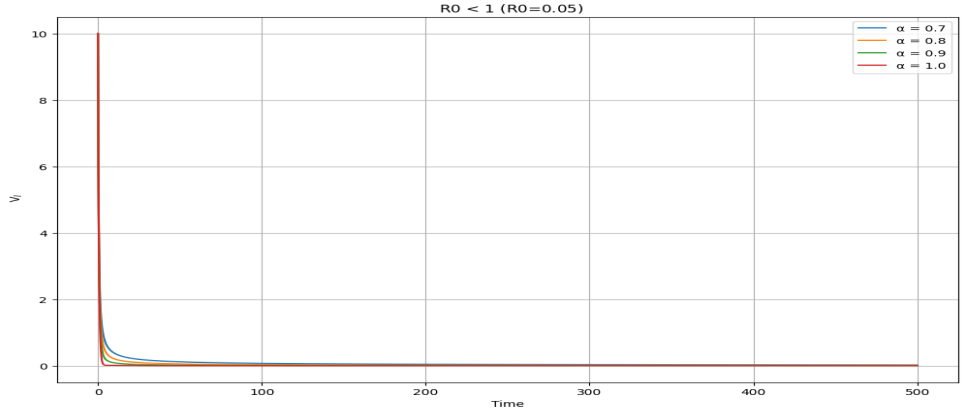

FIGURE 6. Stable inclination of plots towards the IFE E_0 for V_I using distinct values of α related to System (1).

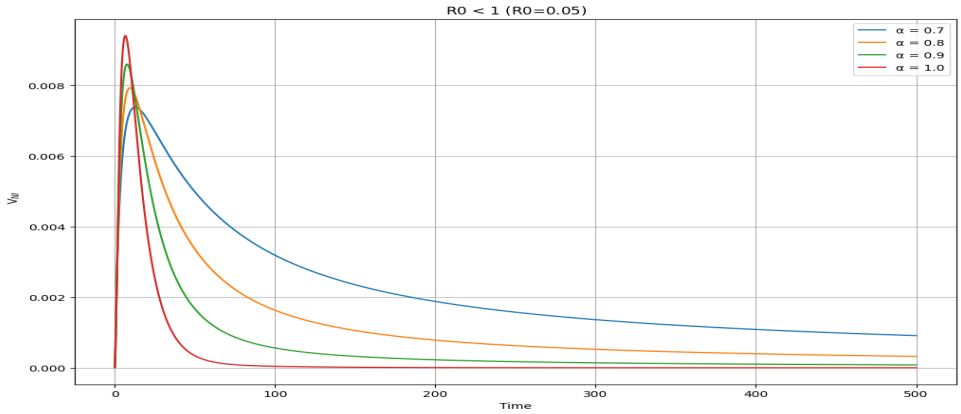

FIGURE 7. Stable inclination of plots towards the IFE E_0 for V_{NI} using distinct values of α related to System (1).

When the parameter values reported in the third column of Table 1 are considered, the basic reproduction number is computed as $R_0 = 7.07 > 1$. In this case, the endemic equilibrium E_1 is globally asymptotically stable, indicating that the virus persists in the host and the infection evolves into a chronic state. According to Theorem 4, the solution of System (1) converges to E_1, as illustrated in Figs. 8–14.

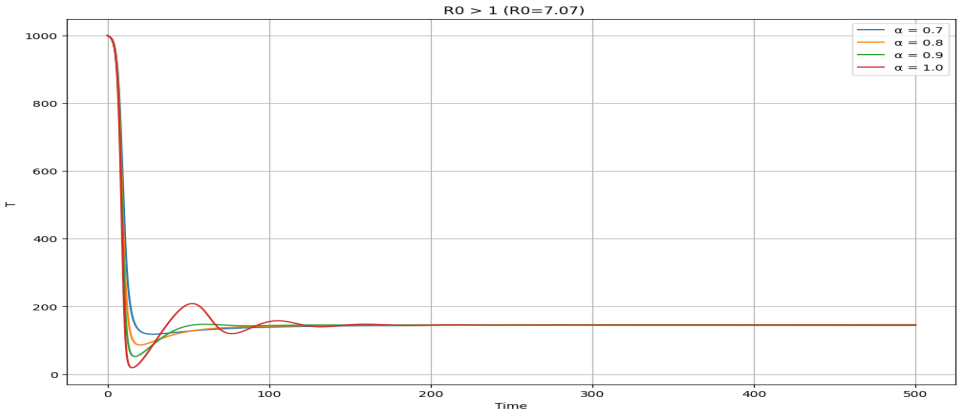

FIGURE 8. Stable inclination of plots towards the IE E_1 for T using distinct values of α related to System (1).

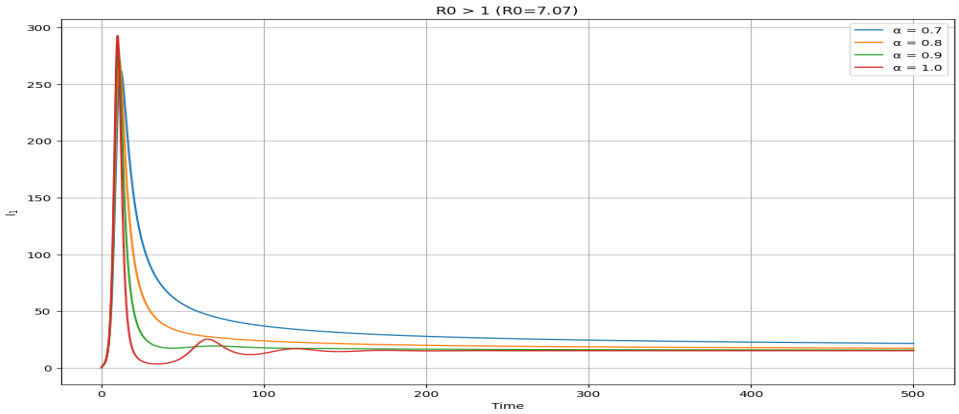

FIGURE 9. Stable inclination of plots towards the IE E_1 for I_1 using distinct values of α related to System (1).

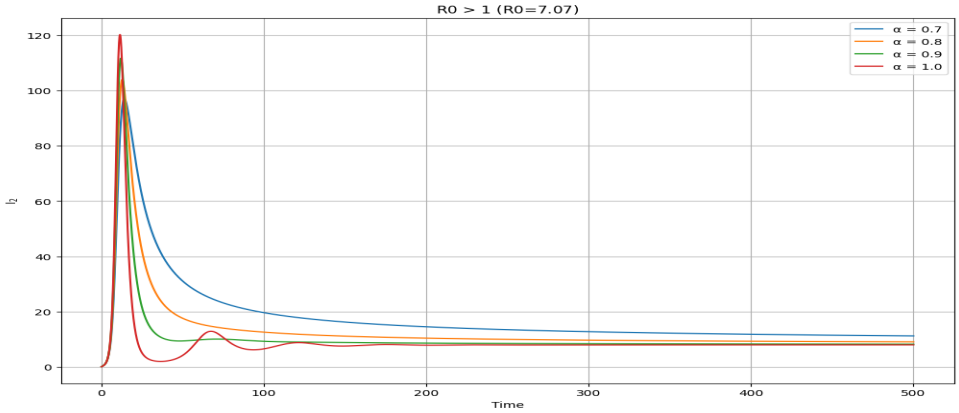

FIGURE 10. Stable inclination of plots towards the IE E_1 for I_2 using distinct values of α related to System (1).

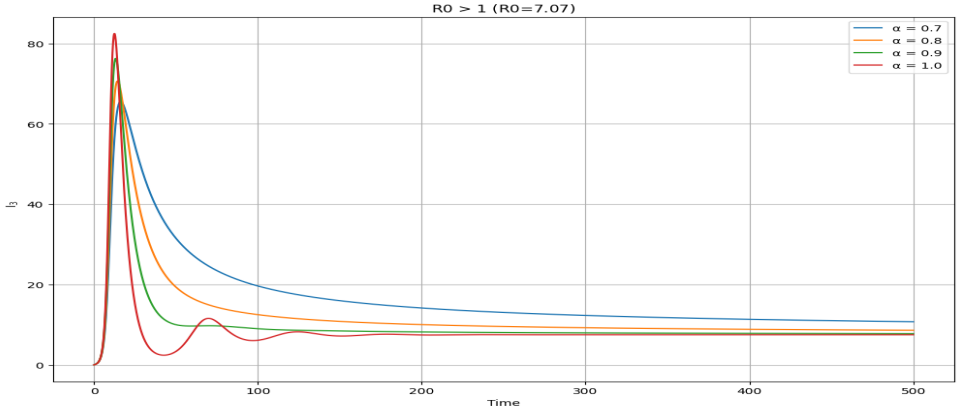

FIGURE 11. Stable inclination of plots towards the IE E_1 for I_3 using distinct values of α related to System (1).

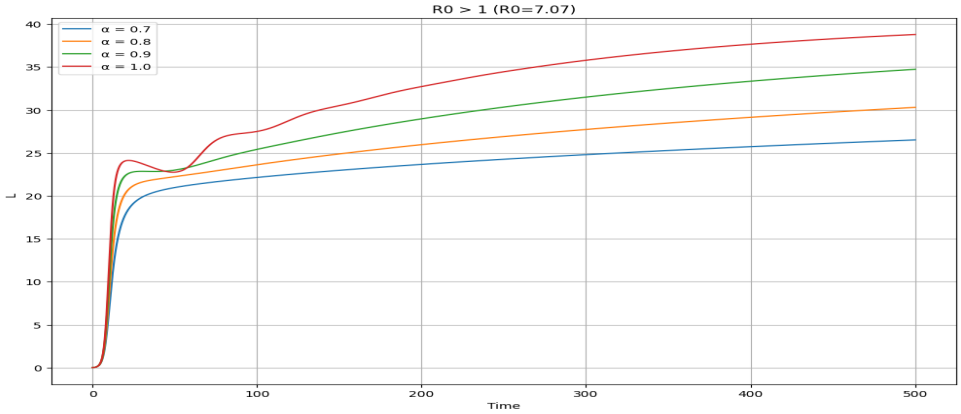

FIGURE 12. Stable inclination of plots towards the IE E_1 for L using distinct values of α related to System (1).

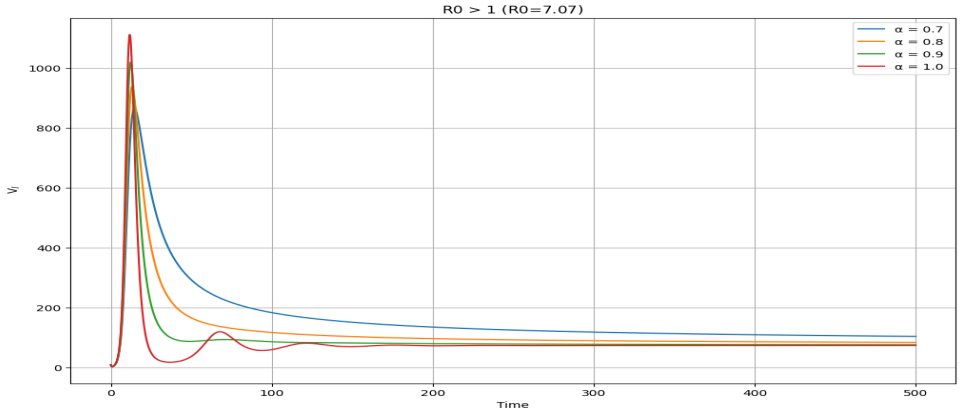

FIGURE 13. Stable inclination of plots towards the IE E_1 for V_I using distinct values of α related to System (1).

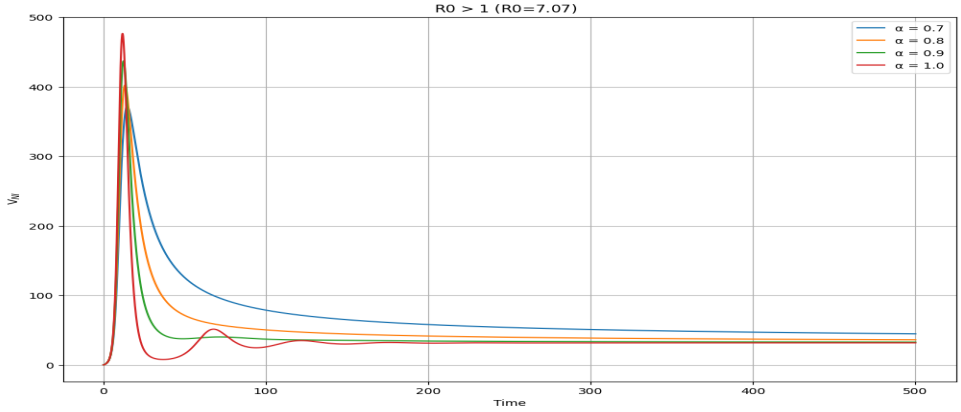

FIGURE 14. Stable inclination of plots towards the IE E_1 for V_{NI} using distinct values of α related to System (1).

TABLE 1. Parameter values used in numerical simulations

Parameters	$R_0 < 1$	$R_0 > 1$	**Units**
s	10.0	10.0	cells·day^{-1}
d	0.01	0.01	day^{-1}
β	0.001	0.001	virion^{-1}·day^{-1}
d_1	0.1	0.2	day^{-1}
k_1	0.2	0.3	day^{-1}
k_2	0.05	0.1	day^{-1}
p	0.1	0.05	dimensionless
δ	0.1	0.5	day^{-1}
d_3	0.05	0.2	day^{-1}
d_L	0.01	0.002	day^{-1}
a	0.01	0.003	day^{-1}
$N\delta$	50.0	80.0	virions·day^{-1}
c	2.0	3.0	day^{-1}
ε_{RT}	0.6	0.2	dimensionless
ε_{II}	0.5	0.1	dimensionless
ε_{PI}	0.7	0.3	dimensionless

TABLE 2. Viral loads for different values of α

α	$R_0 < 1$		$R_0 > 1$	
	V_I	V_{NI}	V_I	V_{NI}
0.7	866.654011	371.345382	866.65	371.35
0.8	938.659662	402.240109	938.66	402.24
0.9	1020.019972	437.134412	1020.02	437.13
1.0	1112.011758	476.576468	1112.01	476.58

We compare the peaks of the viral loads V_I and V_{NI} for different values of α, as reported in Table 2. The results indicate that both viral loads increase as α increases. Larger values of α reduce memory effects in the system, leading to higher infectious and non-infectious viral loads. This highlights the crucial role of memory effects in moderating viral replication dynamics.

5. CONCLUSION

In this parer, we have proposed a fractional HIV infected model with seven main compartments that are target host cells, infectious cells that have finished the process of reverse transcription, infected cells which can produce new infectious viruses, infected cells that fail the DNA integration, latently infected cells, non-infectious viral particles owning the efficacy of protease inhibitors, and infectious viral particles. We used specific incidence rate of type Bilinear as functional response. We derived one threshold parameter, the primary infection reproductive number R_0 . Under defined presumptions, it is shown that the proposed model has a bounded and nonnegative response as desired in any population dynamics. By using stability analysis of Caputo fractional derivative order system, we have proved that if the primary reproductive number $R_0 \leq 1$, then the uninfected steady state is GAS for all $\alpha \in (0, 1]$. consequently the viruses are unable to invade the target cells and be cleared. Hence, using antiviral drug treatment can control and prevent the infection. If $1 < R_0$, then the E_1 is GAS. In this stage, viruses have strong ability to invade the host and weaken the immune system. To stop replicating the viruses in the body, HIV medicines and medical devices are essential approaches to fight HIV. Based on the above theoretical analysis, we realize that the global dynamics of the model are completely determined by computations of the reproductive number R_0. Furthermore, we observe that the fractional α does not affect on our model related to global dynamics, but it can affect the time for reaching the steady states (see the figures).

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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