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Dynamical Analysis of a Fractional-order HIV Model

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Abstract: A fractional-order model for the immunological and therapeutic control of HIV is studied qualitatively. The equilibria are found and their local stability are investigated. Also the global stability of the infection-free equilibrium is established. The optimal efficacy level of anti-retroviral therapy needed to eradicate HIV from the body of an HIV-infected individual is obtained.

Keywords: HIV, Fractional-order, Basic reproductive number, Equilibria, Stability, Anti-retroviral therapy.

1 Introduction

Mathematical and computer modeling has been found numerous applications in a variety of growing fields such as finite element modeling of thin layers [Givoli (2004)], multiscale crystal plasticity modeling [Hasebe (2006)], acoustic waveguide modeling [Lu and Zhu (2007)], aerodynamic hysteresis modeling of an airfoil [Cui, Liao, and Yu (2009)] and so on. Referring to modeling of HIV infection, many models are based on ordinary differential equations (ODEs), typically of order four or less. [Nowak and Bangham (1996)] proposed an ODE model which describes the interaction between a replicating virus population and immune responses. Their model has been important in the field of mathematical modeling of HIV infection [Nowak and May (2000); Gumel and Moghadas (2004); Iwami, Nakaoka, and Takeuchi (2006)]. Recently, [Iwami, Nakaoka, and Takeuchi (2006)] developed the model by introducing frequency dependence. However, the abovementioned models do not take into account the fractional-order derivatives that have been extensively applied in many fields. Many mathematicians and applied researchers have tried to model real processes using fractional ordinary differential equations (FODEs) (for example, [Kilbas, Srivastava, and Trujillo (2006); Ahmed, El-Sayed, and El-Saka (2007); El-Sayeda, El-Mesiryb, and El-Saka (2007); Hilfer

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(2000); Podlubny (1999); Ahmed and Elgazzar (2007)]). More recently, [Ding and Ye (2009)] introduced fractional-order into a model of HIV infection of $CD4^+$ T-cells and carried out a detailed analysis on stability of equilibrium. In [Ye and Ding (2009)], the chaotic behaviors produced from a fractional-order HIV model with viral diversity were presented. In [Kou, Yan, and Liu (2009)], local asymptotical stability analysis for a fractional-order model of HIV-1 was also given.

Particular emphasis is that fractional-order models possess memory [Ahmed and Elgazzar (2007); Hilfer (2000)], while the main features of immune response involve memory [Velasco-Hernandez, Garcia, and Kirschner (2001)]. Hence, a fractional order HIV model with cytotoxic T lymphocyte (CTL) immune response is proposed in this paper. Our aim of this paper is to offer a generalization of the dynamical model [Iwami, Nakaoka, and Takeuchi (2006))] (one-virus model). The generalization is obtained by permitting the state dynamics of the model to assume fractional-order and incorporating antiretroviral therapy.

To do so, we consider a four-dimensional fractional-order model which monitors the temporal dynamics of uninfected CD4+T cells (x(t)), infected CD4+T cells (y(t)), free virus (v(t)) and CTLs (z(t)). The new system is described by the following FODEs:

$$\begin{cases} D^{\alpha}x = s - \beta'(1-\tau)xv - \mu_1 x, \\ D^{\alpha}y = \beta'(1-\tau)xv - \mu_2 y - pz\frac{y}{x+y}, \\ D^{\alpha}v = ky - \mu_3 v, \\ D^{\alpha}z = cz\frac{y}{x+y} - \mu_4 z. \end{cases} \tag{1}$$

Here s is the source of CD4+ T cells (from the thymus), β' is the infection rate, τ models the effectiveness of anti-retroviral therapy, p is the clearance rate of infected cells by CTLs, k is the number of HIV virions produced per infected cell, and c is the production rate of CTLs. The parameters μ_1, μ_2, μ_4 are the natural death terms of the x, y and z populations, respectively. The clearance rate of the virus is μ_3.

Time derivatives of any continuous function $f(t)$ on the left-hand side of system (1) are the Caputo fractional derivative of order $0 < \alpha \leq 1$ and are represented as [Kilbas, Srivastava, and Trujillo (2006); Podlubny (1999)]

$$D^{\alpha}f(t) = \begin{cases} I^{1-\alpha}Df(t), & , \quad 0 < \alpha < 1, \\ Df(t) = \frac{d}{dt}f(t) & , \quad \alpha = 1. \end{cases}$$

The fractional integral of order $\alpha > 0$ of a continuous function $f : R^+ \to R$ is given by

$$I^{\alpha}f(t) = \frac{1}{\Gamma(\alpha)}\int_0^t (t-\tau)^{\alpha-1}f(\tau)d\tau.$$

To simplify the model, it is reasonable to assume that this system describes the qualitative dynamics of the asymptomatic phase of HIV infection. Thus, we may introduce as a good approximation that the virus is in steady state (i.e., $D^\alpha v = 0$) and hence $v = ky/\mu_3$ (see [Iwami, Nakaoka, and Takeuchi (2006)]). This leads to the following simplified system of FODEs:

$$\begin{cases} D^\alpha x = s - \beta(1-\tau)xy - \mu_1 x, \\ D^\alpha y = \beta(1-\tau)xy - \mu_2 y - pz\frac{y}{x+y}, \\ D^\alpha z = cz\frac{y}{x+y} - \mu_4 z. \end{cases} \tag{2}$$

Here we define $\beta = k\beta'/\mu_3$ and we always assume that c is larger than μ_4, i.e., $c > \mu_4$. Note that $D^\alpha z < 0$ always holds true if $c \leq \mu_4$. By generalized mean value theorem [Odibat and Shawagfeh (2007)], we get $z(t)$ is decreasing if $c \leq \mu_4$.

This paper is organized as follows. In the next section we show that the fractional-order model (2) possesses a unique non-negative solution as desired in any population dynamics. A detailed analysis on local asymptotic stability of equilibrium and global asymptotic stability of E_0 are carried out in Section 3 and Section 4, respectively. In Section 5, optimal efficacy of anti-retroviral therapy is given. In Section 6, numerical simulations are provided to verify the analytical results. Conclusions in Section 7 close the paper.

2 Non-negative solution

Denote $R^3_+ = \{(x,y,z) \in R^3 \mid x(t) \geq 0, y(t) \geq 0, z(t) \geq 0\}$.

Theorem 1. For any initial value $(x(0),y(0),z(0))^T$ in Int R^3_+, there is a unique solution to Eq(2) on $t \geq 0$ and the solution will remain in R^3_+, where IntR^3_+ is the interior of R^3_+.

Proof. By applying Theorem 3.1 and Remark 3.2 of [Lin (2007)] and noticing that the system (2) is autonomous, we know that there is a unique solution to Eq(2) on $t \geq 0$.

Next, we show that the solution with $(x(0),y(0),z(0))^T \in$ Int R^3_+ is always positive whenever the solution exists. Suppose that if fails, i.e. there exists $t^* > 0$ at which, at least, one of the elements of the solution becomes "0" and until which all elements of the solution are positive. There are three possibilities as follows.

Case 1. If $x(t^*) = 0$ holds, then $D^\alpha x(t^*) \leq 0$. But the first equation of Eq(2) implies $D^\alpha x(t^*) = s > 0$ which is a contradiction. Thus we always have $x(t) \geq 0, t \geq 0$.

Case 2. If $z(t^*) = 0$ holds, then $x(t) > 0, y(t) > 0$ when $t \in [0,t^*]$ and $z(t) > 0$ when $t \in [0,t^*)$. By the third equation of Eq(2), we have

$$D^\alpha z \geq -\mu_4 z, \qquad t \in [0,t^*],$$

which implies

$$z(t) \geq z(0)E_\alpha(-\mu_4 t^\alpha), \qquad z \in [0,t^*].$$

Since $z(0) > 0$, we obtain $z(t^*) > 0$ which is a contraction.

Case 3. If $y(t^*) = 0$ holds, then $x(t) > 0, z(t) > 0$ when $t \in [0,t^*]$ and $y(t) > 0$ when $t \in [0,t^*)$. Let $M_1 = \max_{t\in[0,t^*]} z(t), m = \min_{t\in[0,t^*]} x(t) > 0$. By the second equation of Eq(2), we have

$$D^\alpha y \geq (-\mu_2 - \frac{pM_1}{m})y, \qquad t \in [0,t^*],$$

which implies

$$y(t) \geq y(0)E_\alpha[(-\mu_2 - \frac{pM_1}{m})t^\alpha], \qquad t \in [0,t^*].$$

Since $y(0) > 0$, we have $y(t^*) > 0$ which is a contraction.

Therefore, the solution with $(x(0), y(0), z(0)) \in \text{Int}R^3_+$ is always positive.

3 Local asymptotic stability analysis

In this section, we present the results of local asymptotic stability analysis of the equilibrium points.

3.1 Infection-free equilibrium, E_0

To evaluate the equilibria, let

$$\begin{cases} D^\alpha x = 0, \\ D^\alpha y = 0, \\ D^\alpha z = 0. \end{cases}$$

Then the infection-free equilibrium of system (2) is $E_0 = (\frac{s}{\mu_1}, 0, 0)$. The Jacobian matrix $J(E_0)$ for system (2) evaluated at E_0 is given by

$$J(E_0) = \begin{pmatrix} -\mu_1 & -\beta(1-\tau)\frac{s}{\mu_1} & 0 \\ 0 & \beta(1-\tau)\frac{s}{\mu_1} - \mu_2 & 0 \\ 0 & 0 & -\mu_4 \end{pmatrix}.$$

E_0 is locally asymptotically stable (LAS) if all of the eigenvalues λ of the Jacobian matrix $J(E_0)$ satisfy the following condition [Ahmed, El-Sayed, and El-Saka (2007); Matignon (1996)]:

$$|arg(\lambda)| > \frac{\alpha\pi}{2}. \tag{3}$$

The eigenvalues of $J(E_0)$ are $-\mu_1, \beta(1-\tau)\frac{s}{\mu_1} - \mu_2$ and $-\mu_4$.
Let

$$R_0 = \frac{\beta(1-\tau)s}{\mu_1\mu_2}.$$

It is clear that E_0 is LAS if $R_0 < 1$ and is unstable if $R_0 > 1$. The quantity R_0 is called the basic reproductive number of infection[Nowak and May (2000)].

3.2 Boundary equilibrium, E_1

Assuming $R_0 > 1$; it follows that the system (2) has a unique boundary equilibrium $E_1 = (x_1^*, y_1^*, 0)$, where

$$x_1^* = \frac{\mu_2}{\beta(1-\tau)} = \frac{s}{\mu_1 R_0}, \qquad y_1^* = \frac{s\beta(1-\tau) - \mu_1\mu_2}{\beta(1-\tau)\mu_2} = \frac{s(R_0-1)}{\mu_2 R_0}.$$

The Jacobian matrix $J(E_1)$ for system (2) evaluated at E_1 is given by

$$J(E_1) = \begin{pmatrix} -\mu_1 R_0 & -\mu_2 & 0 \\ \mu_1(R_0-1) & 0 & -\frac{p\mu_1(R_0-1)}{\mu_2+\mu_1(R_0-1)} \\ 0 & 0 & \frac{c\mu_1(R_0-1)}{\mu_2+\mu_1(R_0-1)} - \mu_4 \end{pmatrix}. \tag{4}$$

For $J(E_1)$ given by Eq(4), the characteristic equation becomes

$$[\lambda^2 + \mu_1 R_0\lambda + \mu_1\mu_2(R_0-1)](\lambda - \frac{c\mu_1(R_0-1)}{\mu_2+\mu_1(R_0-1)} + \mu_4) = 0 \tag{5}$$

and hence all the eigenvalues are

$$\lambda_{1,2} = \frac{-\mu_1 R_0 \pm \sqrt{(\mu_1 R_0)^2 - 4\mu_1\mu_2(R_0-1)}}{2},$$

$$\lambda_3 = \frac{c\mu_1(R_0-1)}{\mu_2+\mu_1(R_0-1)} - \mu_4.$$

If $R_0 > 1$, then $\lambda_{1,2}$ have negative real parts. Furthermore, let

$$R_0^* = \frac{\mu_2\mu_4}{\mu_1(c-\mu_4)} + 1.$$

If $1 < R_0 < R_0^*$, then $\lambda_3 < 0$ and E_1 is LAS. If $R_0 > R_0^*$, then $\lambda_3 > 0$ and E_1 is unstable.

The analytical results of Section 3.1 and 3.2 are summarized in the following theorem.

Theorem 2.

(i) E_0 always exists in R^3_+. If $R_0 > 1$, then E_1 exists in R^3_+.

(ii) E_0 is locally asymptotically stable (LAS) if $R_0 < 1$ and is unstable if $R_0 > 1$. E_1 is LAS if $1 < R_0 < R_0^*$ and is unstable if $R_0 > R_0^*$.

3.3 Endemic equilibrium, E_2

It can be shown that the system (2) has a unique endemic equilibrium $E_2 = (x_2^*, y_2^*, z_2^*)$, if $R_0 > R_0^*$, where

$$x_2^* = \frac{-\mu_1 + \sqrt{(\mu_1)^2 + 4\hat{\beta}s}}{2\hat{\beta}}, \qquad y_2^* = \frac{\mu_4}{c-\mu_4}x_2^*,$$

$$z_2^* = \frac{cx_2^*}{p(c-\mu_4)}(\beta(1-\tau)x_2^* - \mu_2), \qquad \hat{\beta} = \frac{\mu_4(1-\tau)}{c-\mu_4}\beta.$$

To discuss the local stability of the endemic equilibrium E_2, we consider the linearized system of (2) at E_2. The Jacobian matrix at E_2 is given by

$$J(E_2) = \begin{pmatrix} -\beta(1-\tau)y_2^* - \mu_1 & -\beta(1-\tau)x_2^* & 0 \\ \beta(1-\tau)y_2^* + pz_2^*\frac{y_2^*}{(x_2^*+y_2^*)^2} & \beta(1-\tau)x_2^* - \mu_2 - pz_2^*\frac{x_2^*}{(x_2^*+y_2^*)^2} & -p\frac{y_2^*}{x_2^*+y_2^*} \\ -cz_2^*\frac{y_2^*}{(x_2^*+y_2^*)^2} & cz_2^*\frac{x_2^*}{(x_2^*+y_2^*)^2} & c\frac{y_2^*}{x_2^*+y_2^*} - \mu_4 \end{pmatrix}.$$

For notational convenience, we denote $x_2^* = x, y_2^* = y$ and $z_2^* = z$. Since

$$s - \beta(1-\tau)xy - \mu_1 x = 0, \quad \beta(1-\tau)x - \mu_2 - pz\frac{1}{x+y} = 0, \quad \frac{cy}{x+y} = \mu_4$$

and

$$\frac{x}{x+y} = \frac{c-\mu_4}{c},$$

we can rewrite $J(E_2)$ in the following form:

$$J(E_2) = \begin{pmatrix} -\beta(1-\tau)y - \mu_1 & -\beta(1-\tau)x & 0 \\ \beta(1-\tau)y + \frac{\mu_4}{c}(\beta(1-\tau)x - \mu_2) & \frac{\mu_4}{c}(\beta(1-\tau)x - \mu_2) & -\frac{p\mu_4}{c} \\ -\frac{\mu_4}{p}(\beta(1-\tau)x - \mu_2) & \frac{c-\mu_4}{p}(\beta(1-\tau)x - \mu_2) & 0 \end{pmatrix}.$$

Then the characteristic equation of the linearized system of (2) is

$$\Phi(\lambda) = \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{6}$$

where

$$\begin{aligned}
a_1 &= \beta(1-\tau)(y-\frac{\mu_4}{c}x)+\mu_1+\frac{\mu_2\mu_4}{c},\\
a_2 &= \frac{\beta(1-\tau)\mu_4}{c}(\beta(1-\tau)x-\mu_2)(x-y)+\frac{\mu_4(c-\mu_1-\mu_4)}{c}(\beta(1-\tau)x-\mu_2)\\
&\quad +\beta^2(1-\tau)^2xy,\\
a_3 &= \frac{\mu_4}{c}(\beta(1-\tau)x-\mu_2)[\beta(1-\tau)\mu_4x-(c-\mu_4)((\beta(1-\tau)y-\mu_1)].
\end{aligned}$$

Thus, we have the following theorem.

Theorem 3.

(i) If $R_0 > R_0^*$, then E_2 exists in IntR_+^3, where IntR_+^3 is the interior of R_+^3.

(ii) The endemic equilibrium E_2 is LAS if all of the eigenvalues λ of $J(E_2)$ satisfy $|arg(\lambda)| > \frac{\alpha\pi}{2}$ [Ahmed, El-Sayed, and El-Saka (2007); Matignon (1996)].

Denote

$$\begin{aligned}
D(\Phi) &= -\begin{vmatrix} 1 & a_1 & a_2 & a_3 & 0\\ 0 & 1 & a_1 & a_2 & a_3\\ 3 & 2a_1 & a_2 & 0 & 0\\ 0 & 3 & 2a_1 & a_2 & 0\\ 0 & 0 & 3 & 2a_1 & a_2 \end{vmatrix}\\
&= 18a_1a_2a_3+(a_1a_2)^2-4a_3a_1^3-4a_2^3-27a_3^2.
\end{aligned}$$

Furthermore, using the results of Ref.[Ahmed and Elgazzar (2007)], we have

Theorem 4. We assume that E_2 exists in IntR_+^3.

(i) If the discriminant of $\Phi(\lambda), D(\Phi)$ is positive and Routh-Hurwitz conditions are satisfied, i.e.,

$$D(\Phi) > 0 \quad and \quad a_1 > 0, a_3 > 0, a_1a_2 > a_3,$$

then the endemic equilibrium E_2 is LAS.

(ii) If $D(\Phi) < 0, a_1 \geq 0, a_2 \geq 0, a_3 > 0, \alpha < 2/3$, then the endemic equilibrium E_2 is LAS.

(iii) If $D(\Phi) < 0, a_1 > 0, a_2 > 0, a_1a_2 = a_3, \alpha \in [0,1)$, then the endemic equilibrium E_2 is LAS.

(iv) If $D(\Phi) < 0, a_1 < 0, a_2 < 0, \alpha > 2/3$, then the endemic equilibrium E_2 is unstable.

4 Global asymptotic stability of E_0

In this section, we first give sufficient conditions for the global asymptotic stability of equilibrium which generalize the result for ODEs. Then we show the global asymptotic stability of E_0.

Suppose Ω is an open subset of R^n. Consider the autonomous system

$$D^{\alpha}X = f(X), \tag{7}$$

where $f \in C(\Omega, R^n), 0 < \alpha \leq 1$.

If $V \in C^1(\Omega, R)$, we define the $\alpha-$order derivative of $V(X)$ along the solution of Eq(7) as following form; namely

$$D^{\alpha}V = \frac{d^{\alpha}V}{dt^{\alpha}}|_{(7)} = I^{1-\alpha}DV = I^{1-\alpha}(\frac{dV}{dX}\cdot\frac{dX}{dt}).$$

Definition 1. We say $V(X)$ is a Liapunov function on a set Ω in R^n relative to Eq(7) if $V \in C^1(\Omega, R)$ and $D^{\alpha}V \leq 0$ on Ω.

Let

$$E = \{X \in CL\Omega \mid D^{\alpha}V = 0\}$$

and

M=largest set in E which is invariant with respect to Eq(7),

where CL Ω is the closure of Ω.

To prove the main theorem we put forward an important lemma.

Lemma 1. Assume that

(i) V is a Liapunov function on Ω;

(ii) V is a positive definite function;

(iii)$V(X) \to +\infty$ when $\| X \| \to +\infty$;

(iv) $M = \{X^* \mid f(X^*) = 0\}$.

Then equilibrium X^* is globally asymptotic stable (GAS).

The proof of this lemma is similar to the proof of Theorem 1 in [Zhang, L, and Chen (2005)].

We now prove the main theorem.

Theorem 5. If $R_0 < 1$, then the infection-free equilibrium E_0 is globally asymptotically stable (GAS).

Proof. We note from Theorem 2 that E_0 is the only equilibrium of system (2) whenever $R_0 < 1$. We now show the stronger result that E_0 is GAS.

Consider the following positive definite function:

$V = y$.

The $\alpha-$order derivative of V along the solution of the system (2) can be written as

$$\begin{aligned} D^{\alpha}V &= I^{1-\alpha}(\frac{dV}{dy}\cdot\frac{dy}{dt}) = I^{1-\alpha}(\frac{dy}{dt}) = D^{\alpha}y \\ &= \beta(1-\tau)xy - \mu_2 y - pz\frac{y}{x+y} \\ &\leq y[(\beta(1-\tau)x - \mu_2]. \end{aligned}$$

In fact, in the absence of virus, the healthy T-cell population (x) has a steady state value $x_0 = \frac{s}{\mu_1}$. Since the presence of HIV only decreases the T-cell population, we know $x \leq x_0 = \frac{s}{\mu_1}$, if $x(0) \leq x_0$. From the first equation of (2), we also find this. Thus,

$$D^{\alpha}V \leq y[(\beta(1-\tau)\frac{s}{\mu_1} - \mu_2] \leq 0,$$

when $R_0 < 1$. Note that $D^{\alpha}V = 0$ if and only if $y = 0$. Then Lemma 1 implies that $y \to 0$ as $t \to \infty$.

If $y = 0$, then the system (2) for x and z reduces to a following system,

$$\begin{cases} D^{\alpha}x = s - \mu_1 x, \\ D^{\alpha}z = -\mu_4 z, \end{cases} \tag{8}$$

whose solution is

$$\begin{cases} x(t) = (-\frac{s}{\mu_1} + x(0))E_{\alpha}(-\mu_1 t^{\alpha}) + \frac{s}{\mu_1}, \\ z(t) = z(0)E_{\alpha}(-\mu_4 t^{\alpha}). \end{cases} \tag{9}$$

So the solution of Eq(8) approach $(\frac{s}{\mu_1}, 0)$ as $t \to \infty$. Therefore, the infection-free equilibrium E_0 is GAS.

5 Optimal efficacy of anti-retroviral therapy

The epidemiological implication of global stability of E_0 (when $R_0 < 1$) is that the number of the infected cells (y) vanish in time (and, consequently, the disease is eradicated in vivo) [Gumel and Moghadas (2004)]. Note that

$$R_0 = \frac{\beta(1-\tau)s}{\mu_1\mu_2};$$

this indicates that R_0 is dependent on the treatment parameter τ and R_0 is a decreasing function of τ. We refer to the efficacy of anti-retroviral therapy, which corresponds to $R_0 = 1$ as the 'critical efficacy' (τ_c). Thus,

$$\tau_c = 1 - \frac{\mu_1 \mu_2}{\beta s}.$$

This means that $R_0(\tau_c) = 1$ and $R_0 < 1$ for $\tau > \tau_c$.

Hence, optimal treatment: If $\tau \geq \tau_c$, then HIV can be eliminated in vivo.

6 Numerical simulation

In this section, we carry out numerical simulations for system (2) with parameters $s = 1, \mu_1 = 0.01, \mu_2 = \mu_4 = 0.05, \beta = 0.005$ and $p = c = 1$. Most of the parameters are set according to [Nowak and May (2000)]. The remaining parameters are chosen to be consistent with biological plausibility. With these parameter values, $\tau_c = 0.9, E_0 = (100, 0, 0)$ and $R_0^* = 1.2632$. The effect of anti-retroviral therapy (τ) is monitored by using various values of τ in the simulations. The results, tabulated in Table 1, clearly show that higher values of τ leads to corresponding decrease in R_0 and , ultimately, to disease eradication.

Table 1

The results of numerical simulation

τ	R_0	E_1	E_2	Comment
0	10	(10, 18, 0)	(45.51, 2.40, 8.50)	$0 < \alpha < 0.9761, E_2$ is LAS
				$0.9761 \leq \alpha \leq 1, E_2$ is unstable
0.4	6	(16.67, 16.67, 0)	(53.98, 2.84, 6.36)	$0 < \alpha < 0.9781, E_2$ is LAS
				$0.9781 \leq \alpha \leq 1, E_2$ is unstable
0.8	2	(50, 10, 0)	(72.41, 3.81, 1.71)	$0 < \alpha < 0.9949, E_2$ is LAS
				$0.9949 \leq \alpha \leq 1, E_2$ is unstable
0.88	1.2	(83.33, 3.33, 0)	Does not exist	E_1 is LAS
0.9	1	Does not exist	Does not exist	E_0 is GAS
$0.9 \leq \tau \leq 1$	$0 \leq R_0 \leq 1$	Does not exist	Does not exist	E_0 is GAS

For $\tau = 0.4 < \tau_c$, when $\alpha = 0.9$, numerical simulations show that trajectories of system (2) approach to the endemic equilibrium E_2 (see Figure 1(A1)-(A2)). However, when $\alpha = 1$ (that is the case of classical integer-order), E_2 is unstable by the Routh-Hurwitz criterion (see Figure 2(B1)-(B2)).

For the case where $\tau = 0.95 > \tau_c$, $\alpha = 0.9$ and $\alpha = 1$, respectively, simulation results show that trajectories of system (2) approach to the infection-free equilibrium, E_0 (see Figure 3(C1)-(C2)). Clearly, the above simulation results confirm the theoretical results in this paper.

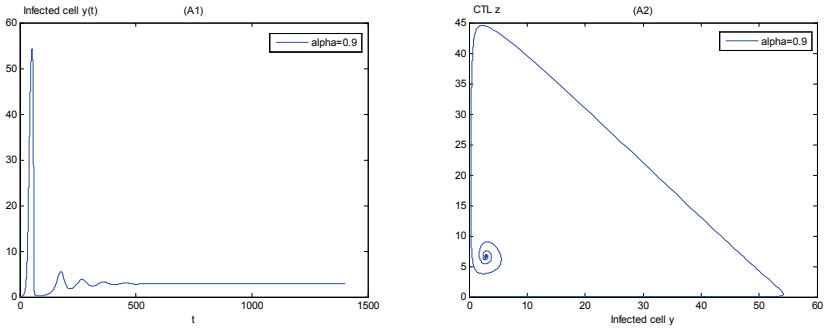

Figure 1: Numerical solutions of fractional-order model: in (A1)-(A2) $\tau = 0.4,\ \alpha = 0.9$. The plots show that trajectories of system (2) approach to the endemic equilibrium.

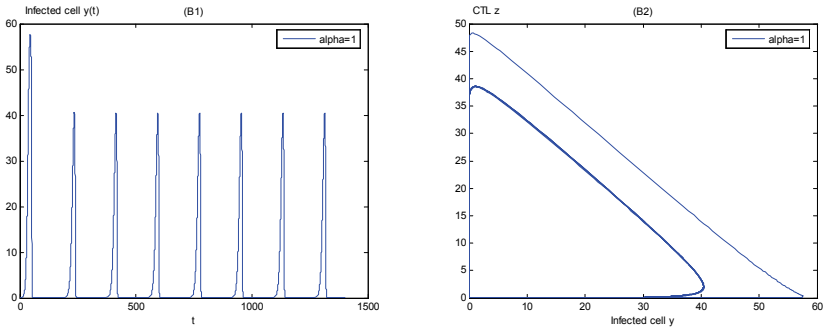

Figure 2: Numerical solutions of fractional-order model: in (B1)-(B2) $\tau = 0.4,\ \alpha = 1$. The plots show that the endemic equilibrium is unstable.

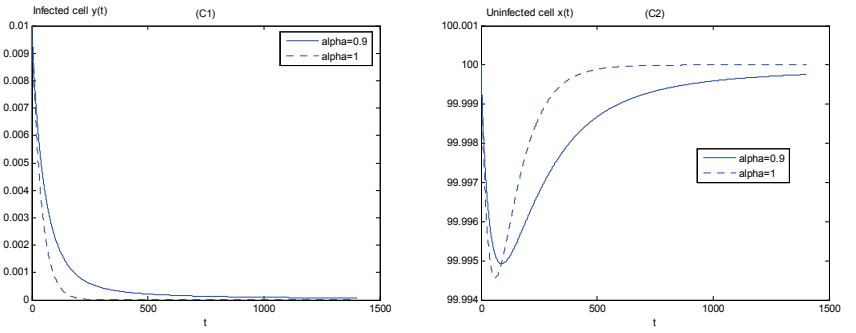

Figure 3: Numerical solutions of fractional-order model: in (C1)-(C2) $\tau = 0.95,\ \alpha = 0.9$ and $\alpha = 1$, respectively. The plots show that trajectories of system (2) approach to the infection-free equilibrium.

7 Conclusions

In this paper, we proposed a fractional-order HIV model as a generalization of an integer-order model by permitting the state dynamics of the model to assume fractional-order and incorporating antiretroviral therapy.We showed the fractional-order model (2) possessed a unique non-negative solution. By using stability analysis on fractional-order system, we obtained sufficient conditions on the parameters for the local stability of the equilibria. Also we gave some sufficient conditions for the global asymptotic stability of equilibrium which generalized the result for ODEs. Our analysis implied that higher values of τ leads to corresponding decrease in R_0 and , ultimately, to disease eradication, where τ was the effectiveness of antiretroviral therapy. An Adams-type predictor-corrector method [Diethelm, Ford, and Freed (2002);Diethelm, Ford, and Freed (2004)] was used for the numerical solutions of the fractional-order system (2).

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