Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Stability analysis of the HIV model through incommensurate fractional-order nonlinear system

Bahatdin DAŞBAŞI
Kayseri University, Faculty of Applied Sciences, TR-38039, Kayseri, Turkey

ARTICLE INFO

Article history:
Received 24 February 2020
Revised 3 May 2020
Accepted 4 May 2020
Available online 11 May 2020

Keywords:
HIV mathematical model
Incommensurate fractional-order differential equation
Stability analysis
Equilibrium points
34A08
34D20
34G60
92C50
92D30

ABSTRACT

In this study, it is employed a new model of HIV infection in the form of incommensurate fractional differential equations systems involving the Caputo fractional derivative. Existence of the model’s equilibrium points has been investigated. According to some special cases of the derivative-orders in the proposed model, the asymptotic stability of the infection-free equilibrium and endemic equilibrium has been proved under certain conditions. These stability conditions related to the derivative-orders depend on not only the basic reproduction rate frequently emphasized in the literature but also the newly obtained conditions in this study. Qualitative analysis results were complemented by numerical simulations in Matlab, illustrating the obtained stability result.

© 2020 Elsevier Ltd. All rights reserved.

1. Introduction

Even though fractional-order calculus (FOC) and differential equations (FODEs) have nearly the same history as those of ordinary differential equations (ODEs), they did not attract much attention till recent decades [1]. FOC, expressed as a generalization of ordinary differentiation and integration to arbitrary non-integer order and extensively used in different fields of science recently, is a branch of mathematical analysis [2,3]. Most important feature of FOC is memory concept. If the output of a system at each time \( t \) depends only on the input at time \( t \), then such systems are said to be memoryless systems. Otherwise, if the system has to remember previous values of the input to specify the current value of the output, then such systems are called memory systems [4]. In modelling of various memory phenomena, it is mentioned that a memory process usually consists of two stages. One is short with permanent retention, and the other is governed by a simple model of fractional derivative [5]. Numerous literature has been developed on the applications of FODEs and their systems (FOSs), a new and powerful tool that has recently been employed to model complex structures with nonlinear behavior and long-term memory [6–8].

Especially, biological systems are also rich source for mathematical modeling through FOSs [9].

Considering the recent mathematical modeling process of diseases, many scientists have used FOC and FODEs to describe different variety of diseases such as Ebola [10], tuberculosis [11], hepatitis [12], dengue fever [13], MERS-Cov [14], chickenpox [15], Zika virus [16], measles [17], rubella [18], etc. Moreover, the modelling of epidemic diseases assists understanding the main mechanisms effecting the spread of the disease, so that the control strategies are proposed through the modelling process [19]. These models are combined under two main headings, as the first is modeling the spread of infected individuals in a population [20] and the second is modeling the density of the infectious pathogen such as virus, bacteria, etc. in an individual [21,22] as in this paper.

Viruses are the main cause of common human diseases such as influenza, cold, chicken pox and cold sores. Currently, there exist 21 families of viruses expressed to cause diseases in humans. Some of these diseases are very seriously infectious diseases such as AIDS (acquired immuno deficiency syndrome), Hepatitis, Herpes Simplex, Measles, avian influenza, SARS and SARS- or MERS-like coronavirus [23]. They have common features, such as they are all highly pathogenic to humans or livestock [24]. In particular AIDS, most severe stage of HIV (human immunodeficiency virus) infection, is remarkable as a fatal disease [25]. Considering the World Health Organization’s report on the global situation and HIV/AIDS trends in

https://doi.org/10.1016/j.chaos.2020.109870
0960-0779/© 2020 Elsevier Ltd. All rights reserved.
2018, there was globally about 37.9 million people living with HIV, 23.3 million people accessed antiretroviral therapy, 1.7 million people newly became infected with HIV and 770 thousand people died from AIDS-related illnesses [26]. HIV spreads only through certain body fluids such as blood, semen, pre-semenal fluids, rectal fluids, vaginal fluids, and breast milk, from an HIV-infected person. The immune response plays an important role to control the dynamics of viral infections such as HIV [21]. Mathematical models aimed to understand the host-virus interaction in case of HIV can supply non-intuitive information about the dynamics of the host response to the viruses and they can also offer new ways for the therapy. In recent years, the HIV models with cure rate has received a great deal of attention.

A general mathematical model considered the basic dynamics of virus-host cell interaction was developed by Nowak et al. in [27]. In their study, they formulated the HIV model by using the following ODEs:

\[
\begin{align*}
\frac{dx}{dt} &= \lambda - dx - \beta x v \\
\frac{dy}{dt} &= \beta x v - a y - \rho y z \\
\frac{dz}{dt} &= k y - u v \\
\frac{dw}{dt} &= c y z - b z \\
\end{align*}
\]

with positive initial conditions. In here, \(x(t), y(t), v(t),\) and \(z(t)\) are the concentrations of uninfected (susceptible) host cells, infected host cells, free viruses, and CTL cells at time \(t\), respectively. The production of uninfected cells is at a constant rate, \(\lambda\). When uninfected cells encounter with free virus particles, they become infected at a rate \(\beta x v\). \(d\) and \(b\) are rates of the natural death of uninfected cells and CTL cells, respectively. The infected cells die at an additional rate \(a y\), which is the viral caused cell death (cytopathicity or cytotoxicity). Infected cells produce new virus particles with a rate \(k y\), and the free virus particles that have been released from the cells decay with a rate \(u\). The proliferation rate of CTL cells in the presence of infected cells is \(c\). Finally, CTL cells cleans infected cells with the ratio \(\rho\) from the host. They explained the stabilities of the infection-free equilibrium and the positive equilibrium according to the basic reproduction number of the virus. Thus, they stimulated a model to work, aimed at interpreting experimental data, and led to the development of a new field of study called as viral dynamics.

Considering Eqs. (1), several nonlinear models, given in [28,29] through ODEs and [12,21,30–33] through FODEs, were studied by researchers. In this sense, they analyzed qualitatively and/or numerically their models by developing Eqs. (1) under various assumptions. Also, these models include 3-dimensional time-dependent variables, where \(T(t), I(t)\) and \(V(t)\) represents the concentration of healthy CD4 + T-cells at time \(t\), the concentration of infected CD4 + T-cells at time \(t\) and the concentration of free HIV at time \(t\), respectively.

Mascio et al. [34] also considered the effect of antiviral drugs for Eqs. (1), and so, the efficacy of these drugs was estimated by mathematical modeling for retroviruses such as HIV – 1. While a protease inhibitor causes infected cells to produce immature non-infectious virus particles, a reverse transcriptase inhibitor effectively blocks the successful infection of a cell. In this sense, they assumed that when an antiretroviral drug such as a protease inhibitor or a reverse transcriptase inhibitor are applied to a patient in steady state as the viral load falls. To model this fall, the effectiveness of the drug is introduced into the model. Therefore, the virus dynamics is reformulated to the following ODEs:

\[
\begin{align*}
\frac{dx}{dt} &= \lambda - dx - (1 - \epsilon_R) \beta x v t \\
\frac{dy}{dt} &= (1 - \epsilon_R) \beta x v t - a y \\
\frac{dz}{dt} &= (1 - \epsilon_R) k y - u v t \\
\frac{dw}{dt} &= \epsilon_R k y - u w t \\
\end{align*}
\]

with positive initial conditions. Also, \(\epsilon_R\) and \(\epsilon_P\) are the efficacies of the reverse transcriptase inhibitor and protease inhibitor, respectively, and \(v_t\) and \(v_{nt}\) denote infectious and non-infectious virions, respectively. This division of virions is because of the use of protease inhibitors. They performed stability analysis of the equilibrium points of their model. Based on Eqs. (2), several nonlinear models given in [35–37] through ODEs and [38,39] through FODEs have been developed to describe the dynamics of the HIV – 1 virus, which take into account the dynamics of the HIV infection through antiretroviral therapies with different cell populations.

According to the derivative-orders in the system, FOSs can be considered in two parts commensurate and incommensurate and commensurate FOSs is a special case of incommensurate FOSs. Therefore, studies on incommensurate FOSs as in [40–52] are increasingly included in the literature.

The proposed model in this study has the following innovations:

- It is assumed that both the infected cells and free virus particles have cleared by CTL cells and some neutralizing antibodies. Also, immune system cells have logistic growth rules.
- Model has created by using a incommensurate FOS in Caputo sense.
- In model, infected cells die at an additional rate called as the natural death rate.

In the qualitative analysis, specific conditions on the development of host cells (infected / uninfected) and viral particles (infectious / non-infectious) are obtained, which are under the pressure of the CTL response of the host and inhibitors. Additionally, the numerical simulations of the model are given as a detailed description of the dynamical behaviors of the proposed system. To do aforementioned, the rest of the paper is organized as follows.

- In Section II, some preliminary definitions related to fractional derivative operators are described. The asymptotic stability conditions of the equilibrium point not only for incommensurate but also for commensurate FOSs are given.
- The Section III presents the mathematical formulation of the proposed HIV infection model.
- The Section IV discusses biological existence of the equilibrium points for the proposed model as well as its stability analysis.
- Section V suggests numerical simulations to support the qualitative analysis results of the proposed FOS.
- In Section VI, the paper finishes with some concluding remarks.

2. Preliminaries and definitions

Definition 2.1. Based on Riemann-Liouville definition, the \(\alpha\)-th \((\alpha > 0)\) order fractional derivative of function \(f(t)\) with respect to \(t\) is given by

\[
\frac{d^\alpha f(t)}{dt^\alpha} = \frac{1}{\Gamma(m - \alpha)} \frac{d^m}{dt^m} \int_0^t (t - \tau)^{m-\alpha-1} f(\tau) d\tau, \tag{3}
\]

where \(m\) is the first integer larger than \(\alpha\) such that \(m - 1 \leq \alpha < m\) [53].

Definition 2.2. Considering the Caputo sense definition, the \(\alpha\)-th \((\alpha > 0)\) order fractional derivative of function \(f(t)\) with respect to \(t\) is described as the following:

\[
\frac{d^\alpha f(t)}{dt^\alpha} = \left\{ \frac{1}{\Gamma(m - \alpha)} \frac{d^m}{dt^m} \int_0^t \frac{f^{(m-\alpha)}(\tau)}{(t - \tau)^{m-\alpha}} d\tau \right\} \text{ for } m - 1 < \alpha < m \tag{4}
\]

where \(m\) is the first integer larger than \(\alpha\) [54].

In the rest of this paper, the notation \(\frac{d^\alpha}{dt^\alpha}\) represents the Caputo fractional derivative of order \(\alpha\).
Remark 2.1. In this paper, we have consider the following nonlinear FOS:
\[
d^2X(t) = F(t, X(t)),
\]
(5)
with suitable initial conditions \(X(0) = X_0\), where \(X(t) = [x_1(t), x_2(t), \ldots, x_n(t)]^T \in \mathbb{R}^n\) is the state vectors of Eqs (5), \(F = [f_1, f_2, \ldots, f_n] \in \mathbb{R}^n\), \(f_i : \mathbb{R} \rightarrow \mathbb{R}^n\), \(i = 1, 2, \ldots, n\), and \(\alpha = [\alpha_1, \alpha_2, \ldots, \alpha_n]^T\) is the multi-order of Eqs (5), \(\alpha \in \mathbb{R}^n\) [47]. Throughout the rest of the paper, it has been accepted that \(\alpha\) is a rational number in the interval \((0, 1)\).

Definition 2.3. In particular, if \(\alpha_1 = \alpha_2 = \ldots = \alpha_n = \alpha\), then Eqs (5) can be written as
\[
d^2X(t) = F(t, X(t)).
\]
(6)
We call Eqs (6) as the commensurate FOS, otherwise, call Eqs. (5) as incommensurate FOS [45].

Definition 2.4. The autonomous form of incommensurate FOS in Eqs. (5) is shown as
\[
d^2X(t) = F(X(t)),
\]
(7)
with initial conditions \(X(0) = X_0\). Also, the equilibrium point of Eqs. (7) is the point \(\bar{X} = (\bar{x}_1, \bar{x}_2, \ldots, \bar{x}_n)\) obtained from equations \(F(\bar{X}) = 0\).

Lemma 2.1. Eigenvalues \(\lambda_i\) for \(i = 1, 2, \ldots, m(\alpha_1 + \alpha_2 + \ldots + \alpha_n)\) of Eqs (7) are obtained from the characteristic equation given as
\[
det (\text{diag}(\lambda^{m_1}, \lambda^{m_2}, \ldots, \lambda^{m_n}) - J(\bar{X})) = 0
\]
(8)
where \(m\) is the smallest of the common multiples of the denominators of rational numbers \(\alpha_1, \alpha_2, \ldots,\) and \(J(\bar{X}) = \frac{\partial^2 F}{\partial X^T}\) are the equilibrium points. If all eigenvalues \(\lambda_i\) obtained from Eq. (8) satisfy
\[
|\arg (\lambda_i)| > \frac{\pi}{2m},
\]
then \(\bar{X}\) is asymptotically stable for incommensurate FOS in Eqs. (7) [55].

The stable and unstable regions for incommensurate and commensurate forms of Eqs. (7) are shown in Figs. 1 and 2. According to some special cases of fractional derivative orders, the stability analysis has summarized below:

i. Let \(\alpha_1 = \alpha_2 = \ldots = \alpha_n < 1\) in Eqs (7). If all eigenvalues \(\lambda_i\) for \(i = 1, 2, \ldots, n\) obtained from
\[
\text{Det} (\lambda I_{\text{comm}} - J(\bar{X})) = 0
\]
(10)
satisfies either the Routh–Hurwitz stability conditions or the following conditions:
\[
|\arg (\lambda_i)| > \frac{\alpha \pi}{2}, \quad \text{for } i = 1, 2, \ldots, n,
\]
(11)
then \(\bar{X}\) is asymptotically stable point [56]. Here, the matrix \(I_{\text{comm}}\) is an identity matrix.

Additionally, the charasteristic equation obtained from Eq. (10) can be showed by
\[
P(\lambda) = \lambda^n + a_1 \lambda^{n-1} + \ldots + a_{n-1} \lambda + a_n
\]
(12)
where coefficients \(a_i\) for \(i = 1, \ldots, n\) are real constants. The Routh-Hurwitz stability conditions for polynomial of degree \(n = 2\) and 3 can be summarized as
\[
a_1, a_2 > 0 \quad \text{for } n = 2
\]
\[
a_1, a_2 > 0 \quad \text{and } a_1 a_2 > a_3 \quad \text{for } n = 3
\]
(13)
Above mentioned criteria has supplied necessary and sufficient conditions for all roots of \(P(\lambda)\) to lie in the left half of the complex plane [57].

3. The HIV model through incommensurate FOS
In this study, the new HIV infection model in an individual based on Eqs. (1) and (2) have been analyzed by incommensurate FOS. Let us denote by \(x(t)\) population size of uninfected (or susceptible) cells of host at time \(t\), by \(y(t)\) population size of the emerged infected cells when \(x(t)\) meet free viruses at time \(t\), by \(v_f(t)\) population size of the infectious virus particles concentration at time \(t\), by \(v_n(t)\) population size of the noninfectious virus particles concentration at time \(t\) and by \(y(t)\) population size of CTL response of host at time \(t\). The recruitment of CTL responses have been classified associated with the control of HIV replication and CTL is very important for the clearance of HIV. The newly produced virus particles are separated into two parts as \(v_f(t)\) and \(v_n(t)\), to analyze the effect of protease inhibitor. Therefore, we have incommensurate FOS given by
\[
\frac{dx(t)}{dt} = \gamma - \rho x - (1 - \epsilon RT) \beta xv_f
\]
\[
\frac{dy(t)}{dt} = (1 - \epsilon RT) \beta xv_f - (\rho + \omega) y - \delta yz
\]
\[
\frac{dv_f(t)}{dt} = (1 - \epsilon RT) ky - u v_f - \sigma v_f z
\]
\[
\frac{dv_n(t)}{dt} = \epsilon p k y - u v_n - \sigma v_n z
\]
\[
\frac{dy(t)}{dt} = rz (1 - \bar{z})
\]
(14)
where \(t \geq 0, \alpha_i \in (0, 1]\) for \(i = 1, 2, \ldots, 5\) and the parameters have the properties given as
\[
\gamma, \rho, \beta, \omega, \delta, k, u, \sigma, r, C \in \mathbb{R}^+
\]
(0 < \epsilon < 1) < 1 and 0 < \epsilon < 1
(15)
We also have positive initial conditions \(x(t_0) = x_0, y(t_0) = y_0, v_f(t_0) = v_f_0, v_n(t_0) = v_n_0\) and \(z(t_0) = z_0\). The meanings of biological parameters in Eqs. (14) are given in Table 1.

The abovementioned scenario for Eqs. (14) has been graphically demonstrated in Fig. 3.
4. Qualitative analysis of the proposed HIV model

In this section, the threshold parameters given as $R_0$ and $R_1$ are first introduced to ease the qualitative analysis. Then it is discussed the existence and stability of equilibrias of the model in Eqs. (14).

**Definition 4.1.** Let

$$R_0 = \frac{\gamma \beta k (1 - \epsilon_{RT})(1 - \rho)}{\rho (\rho + \sigma C)(\rho + \omega + \delta C)}$$

and

$$R_1 = \frac{u(\rho + \omega)}{(u + \sigma C)(\rho + \omega + \delta C)}$$

for reduce the complexity of operations. Considering In Eqs. (15), it is clear that

$$0 < R_0 \text{ and } 0 < R_1 < 1.$$  \hspace{1cm} (17)

In here, the $R_0$ threshold parameter, sometimes called basic reproduction rate or basic reproductive ratio, is used to measure the transmission potential of a disease. Biologically, this parameter is the average number of newly infected cells produced by a single infected cell when almost all cells are still uninfected. Also, the parameter $R_1$ has been given only to reduce the processing complexity in the analysis.
Proposition 4.1. According to the biological existence conditions of the equilibrium points of Eqs. (14), it is obtained the following results:

i. \( E_0 \left( \frac{y}{p}, 0, 0, 0 \right) \) always exists.

ii. \( E_1 \left( \frac{y}{p}, \frac{y}{p}, \frac{y}{p}, \frac{y}{p} \right) \) exists, when \( R_0 > 1 \).

iii. \( E_2 \left( \frac{y}{p}, 0, 0, 0 \right) \) is the infection-free equilibrium point and always exists.

By the second equation of Eqs. (23), it is either \( \tilde{y} = 0 \) or \( \tilde{x} = \frac{1}{\rho u (\bar{u} + \sigma)} \) by the first equation of Eqs. (23). Therefore, we obtain the equilibrium point \( E_2 \left( \frac{y}{p}, 0, 0, 0 \right) \). This equilibrium point is the infection-free equilibrium point and it exists always according to Ineqs. (15).

Proposition 4.2. Let us consider Eqs. (14). For all \( \alpha_i \)’s for \( i = 1, 2, \ldots, 5 \) are rational numbers between 0 and 1. Assume \( m \) be the lowest common multiple of the denominators \( m_i \) of \( \alpha_i \)’s, where \( \alpha_i = \frac{m_i}{k_i^i} \), \( k_i, m_i \in \mathbb{Z}^+ \). Under aforementioned assumptions, it is provided the followings:

i. \( E_0 \) is always unstable point.

ii. When \( R_0 > R_1, E_1 \) exists. However, it is an unstable point under this condition.

iii. Let us consider infection-free equilibrium point \( E_2 \), which always exists. It is obtained the following cases:

- Let \( \alpha_2 = \alpha_3 < 1 \). If \( R_0 < 1 \) and eigenvalues obtained from

  \[ \lambda^{m(\alpha_2+\alpha_3)} = \left( u + \sigma C \right) \lambda^{m_2} + \left( \rho + \omega \right) \delta C \lambda^{m_1} \]

  + \( (u + \sigma C) \left( \rho + \omega + \delta C \right) (1 - R_0) = 0 \]

meet conditions given as \( |\arg(\lambda_n)| > \frac{\pi}{2m} \) for \( n = 1, 2, \ldots, m(\alpha_2 + \alpha_3) \), then it is asymptotically stable point for Eqs. (14).

- Let \( \alpha_2 = \alpha_3 = 0 \leq 1 \). If \( R_0 < 1 \), it is asymptotically stable point for Eqs. (14).

- Let \( \alpha_1 \neq \alpha_2 \neq \alpha_3 \). If eigenvalues obtained from

  \[ \lambda^{m(\alpha_1+\alpha_2+\alpha_3)} = \left( u + \sigma C \right) \lambda^{m(\alpha_1+\alpha_2+\alpha_3)} + \left( \rho + \omega \right) \delta C \lambda^{m(\alpha_1+\alpha_2+\alpha_3)} \]

  + \( \rho R_{0} \lambda^{m(\alpha_1+\alpha_2+\alpha_3)} + \rho R_{0} (u + \sigma C) \lambda^{m(\alpha_1+\alpha_2+\alpha_3)} \]

  + \( (u + \sigma C) \left( \rho + \omega + \delta C \right) (1 - R_0) = 0 \]

meet conditions given by \( |\arg(\lambda_n)| > \frac{\pi}{2m} \) for \( n = 1, 2, \ldots, m(\alpha_1 + \alpha_2 + \alpha_3) \), then it is asymptotically stable point for Eqs. (14).

- Let \( \alpha_1 = \alpha_2 = \alpha_3 = \alpha \leq 1 \). It is asymptotically stable point for Eqs. (14).
Proof. To perform stability analysis, the functions in Eqs. (14) are determined.

\[
\begin{align*}
\frac{dx}{dt} &= f_1(x, y, v, v_N, z) = \gamma - \rho x - (1 - f_R) \beta x v_l \\
\frac{dy}{dt} &= f_2(x, y, v, v_N, z) = (1 - \epsilon_R) \beta x y - (\rho + \alpha) y - \delta z \\
\frac{dz}{dt} &= f_3(x, y, v, v_N, z) = (1 - \epsilon_P) k y - u v_l - \sigma z v_l \\
\frac{dv}{dt} &= f_4(x, y, v, v_N, z) = \epsilon_P k y - u v_N - \sigma v_N z \\
\frac{d\tilde{z}}{dt} &= f_5(x, y, v, v_N, z) = \tau \tilde{z} (1 - \tilde{z}).
\end{align*}
\]

That jacobian matrix obtained from Eqs. (24) is

\[
J = \begin{pmatrix}
-\beta y (1 - \epsilon_R) & 0 & -\beta x (1 - \epsilon_R) & 0 & 0 \\
-\beta x (1 - \epsilon_R) & 0 & -\beta x (1 - \epsilon_R) & 0 & 0 \\
0 & k (1 - \epsilon_P) & -u & 0 & 0 \\
0 & 0 & 0 & -\sigma v_l & 0 \\
0 & 0 & 0 & r (1 - 2 \tilde{z}) & 0
\end{pmatrix}
\]

For the jacobian matrix evaluated at equilibrium point $E_j (\tilde{x}, \tilde{y}, \tilde{v}, \tilde{v}_N, \tilde{z})$ for $j = 0, 1, 2, 3$, the characteristic equation have found from

\[
(\lambda^{\alpha_4} + (u + \sigma \tilde{z})) \left( \lambda^{\alpha_5} + \tilde{z} \right) = \lambda^{\alpha_5} + (u + \sigma \tilde{z})
\]

with respect to det (diag($\lambda^{\alpha_4}, \lambda^{\alpha_5}, \lambda^{\alpha_5}, \lambda^{\alpha_4}, \lambda^{\alpha_5}) - J(E_j))$.

By Eq. (25) evaluated at $E_0 (\tilde{x}, 0, 0, 0, 0)$, some of the eigenvalues are achieved from equations given as $\lambda^{\alpha_4} = -\rho$, $\lambda^{\alpha_5} = -u$ and $\lambda^{\alpha_5} = r$ and the remaining eigenvalues are obtained from

\[
\frac{\lambda^{\alpha_5} + (u + \sigma \tilde{z})}{\lambda^{\alpha_5}} = 0
\]

such that $ciss \pi = \cos \pi + i \sin \pi = \sqrt{-1}$. Angles, $|\arg(\lambda)|$, obtained from Eq. (26) are found out as $0, 2 \pi m_5, 4 \pi m_5, \ldots$ subject to the condition of derivative-orders in Eqs (14). Clearly, these angles are not greater than $\pi m_5$ due to the definition of derivative-orders in Eqs (14). Considering Ineqs (9), the stability condition is not supplied. Therefore, $E_0$ is unstable point.

Let $R_0 > R_1$. In this case, $E_1 (\tilde{x}, 0, 0, 0, 0)$, the eigenvalues are obtained from the equations given as $\lambda^{\alpha_4} = -u$ and $\lambda^{\alpha_5} = r$ and the following determinant:

\[
\left| \begin{array}{cccc}
\lambda^{\alpha_4} + (\rho \tilde{R}_1 - 1) + \rho & 0 & -\rho \tilde{R}_1 & 0 \\
0 & \lambda^{\alpha_5} + (u + \sigma \tilde{R}_1) & -\rho \tilde{R}_1 & 0 \\
-\rho \tilde{R}_1 & 0 & \lambda^{\alpha_5} + (u + \sigma \tilde{R}_1) & -\rho \tilde{R}_1 \\
0 & 0 & -\rho \tilde{R}_1 & \lambda^{\alpha_5} + (u + \sigma \tilde{R}_1)
\end{array} \right| = 0,
\]

where $R_0$ and $R_1$ are in Eqs. (16). There is a similar state to the unstability of $E_0$, because $\lambda^{\alpha_5}$ is positive real number. In this case, $E_1$ is unstable point.

By Eq. (25) evaluated at $E_2 (\tilde{x}, 0, 0, 0, 0)$, the eigenvalues obtained from the following equations: $\lambda^{\alpha_4} = -\rho$, $\lambda^{\alpha_5} = -(u + \sigma \tilde{R}_1)$, $\lambda^{\alpha_5} = -r$ and

\[
\lambda^{m(\alpha_2 + \alpha_3)}+(u+\sigma C)\lambda^{m(\alpha_4)}+(u+\sigma C)\lambda^{m(\alpha_5)}+(u+\sigma C)
\]

\[
\times ((\rho + \omega) + \delta C)(1 - \tilde{R}_0) = 0
\]

where $R_0$ is in Eqs. (16). It is clearly that $\lambda^{m(\alpha_1)}$, $\lambda^{m(\alpha_4)}$, $\lambda^{m(\alpha_5)} \in \mathbb{R}$ in accordance with Ineqs (15). By De-Moivre formulas, we have

\[
\begin{align*}
\lambda^{\alpha_1} &= m\sqrt{\text{cis}(\frac{2n + 1}{m_4} \pi m_5)} \quad \text{for } n = 0, 1, \ldots, (m_4 - 1) \\
\lambda^{\alpha_2} &= m\sqrt{\text{cis}(\frac{2n + 1}{m_4} \pi m_5)} \quad \text{for } n = 0, 1, \ldots, (m_4 - 1) \\
\lambda^{\alpha_3} &= m\sqrt{\text{cis}(\frac{2n + 1}{m_4} \pi m_5)} \quad \text{for } n = 0, 1, \ldots, (m_5 - 1)
\end{align*}
\]

such that $\text{cis} \pi = \cos \pi + i \sin \pi$, $i = \sqrt{-1}$. Angles given as $|\arg(\lambda)| = \frac{\pi}{m_4} \frac{3 \pi}{m_5} \ldots$ so on, $|\arg(\alpha_2)| = \frac{\pi}{m_4} \frac{3 \pi}{m_5} \ldots$ so on

and $|\arg(\alpha_3)| = \frac{\pi}{m_4} \frac{3 \pi}{m_5} \ldots$ so on, are greater than $\frac{\pi}{m_4}$ due to the definition of derivative-orders in Eqs (14). In this respect, the stability conditions of $E_2$ for these eigenvalues do not deteriorate according to Ineqs (9). According to the roots of Eq. (27) must be examined. Let's remember Descartes' rule of sign [59]. If

\[
R_0 < 1
\]

then all coefficients of Eq. (27) are positive real number according in Ineqs (15) and (17). Eq. (27) has no positive root, since the sign change number of its coefficients is zero. In this sense, Eq. (27) have not positive real root, and so, the roots of this equation are composed of negative real numbers and/or complex conjugate numbers. To show the stability of $E_2$, these roots are examined according to Ineqs. (9).

As a consequence, we have the following results:

- Let $\alpha_2 \neq \alpha_3 < 1$. If eigenvalues obtained from Eq. (27) have met conditions given as $\arg(\lambda) > \frac{\pi}{2m}$ for $n = 1, 2, \ldots, m_5 (\alpha_2 + \alpha_3)$.

Ineq. (29) is satisfied, then infection-free equilibrium point $E_2 (\tilde{x}, 0, 0, 0, 0)$ is asymptotically stable.

- Let $\alpha_2 = \alpha_3 < 1$. When Eq. (27) is regulated to Eq. (12), the characteristic equation is obtained as

\[
\lambda^2 + ((\rho + \omega) + \delta C) + (u + \sigma C)\lambda + (u + \sigma C)((\rho + \omega) + \delta C)(1 - \tilde{R}_0) = 0
\]

According to $n = 2$ in Ineqs (13), it is

\[
\alpha_1 = ((\rho + \omega) + \delta C) + (u + \sigma C) \\
\alpha_2 = (u + \sigma C)((\rho + \omega) + \delta C)(1 - \tilde{R}_0)
\]

Considering Ineqs (15), if Ineq. (29) is satisfied, then it is clear that $\alpha_1 > 0$ and $\alpha_2 > 0$. The eigenvalues of Eq. (31) either are the negative real number or the complex number with negative real parts (Routh-Hurwitz Criteria). Consequently, $E_2$ is asymptotically stable in terms of Lemma 2.1-i.

Lastly, let

\[
R_0 > 1
\]
In this case, \( E_2 \neq \frac{1}{R_0} \frac{\rho \sigma (1-R_0)}{(\rho + \omega + \delta C)(\rho + \omega + \delta C)} \) exists. When Eq. (25) is evaluated at this equilibrium point, the eigenvalues are obtained from the following equation:

\[
(\lambda^{max} + (u + \sigma C))(\lambda^{max} + r)
\begin{pmatrix}
\lambda^{max} + \rho R_0 & 0 \\
-\rho (R_0 - 1) & (\lambda^{max} + ((\rho + \omega + \delta C)u + \sigma C)) \\
0 & -(1 - \epsilon_p)k
\end{pmatrix}
\]

where \( R_0 \) is in Eqs. (16). Therefore, some of the eigenvalues is acquired from \( \lambda^{max} = -(u + \sigma C) \) and \( \lambda^{max} = -r \). Considering Ineqs (15), we have \( \lambda^{max} \), \( \lambda^{max} \text{ and } \lambda^{max} \). That eigenvalues \( \lambda^{max} \) and \( \lambda^{max} \) does not influence the stability conditions of \( E_2 \) is previously stated through De-Moivre’s formulas. Accordingly, we have the following characteristic equation:

\[
\lambda^m(\alpha + \sigma C)\lambda^{m(z_2 + \sigma C)} + ((\rho + \omega + \delta C)\lambda^m(\alpha + \sigma C) + \rho R_0\lambda^{m(\sigma C) + \rho R_0(u + \sigma C)} + ((\rho + \omega + \delta C)\rho R_0\lambda^{m\sigma C}) + + \rho(R_0 - 1)(u + \sigma C))(\rho + \omega + \delta C) = 0
\]

obtained from determinant in Eq. (34). Considering Ineqs. (15), (17) and (33), the signs of the coefficients of Eq. (35) are \( + + + + + \), respectively. According to Descartes’ rule of sign, these eigenvalues are not composed of positive real numbers, since the change number of these signs is zero. Thus, eigenvalues consist of negative real numbers and/or complex conjugate numbers. To show the stability of \( E_2 \), it must be demonstrated that the eigenvalues achieved through Eq. (35) provide Ineqs (9).

Consequently, we obtain the following results:

1. Let \( \alpha_1 \neq \alpha_2 \neq \alpha_3 < 1 \). If the eigenvalues obtained from Eq. (35) meet the conditions given as

\[
|\arg(\lambda)| > \frac{\pi}{2m}
\]

for \( m = 1, 2, \ldots, m(\alpha_1 + \alpha_2 + \alpha_3) \),

then \( E_2 \) is asymptotically stable.

2. Let \( \alpha_1 = \alpha_2 = \alpha_3 = \alpha \leq 1 \). If Eq. (35) regulated with respect to Eq. (12), it is found the following characteristic equation:

\[
\lambda^3 + \alpha_1 \lambda^2 + \alpha_2 \lambda + \alpha_3 = 0
\]

where

\[
\alpha_1 = (\rho + \omega + \delta C)(\rho + \omega + \delta C), \quad \alpha_2 = \rho R_0(\rho + \omega + \delta C)(\rho + \omega + \delta C), \quad \alpha_3 = \rho R_0(\rho + \omega + \delta C)(\rho + \omega + \delta C)
\]

In Eq. (37), it is \( \alpha_1, \alpha_2, \alpha_3 > 0 \), due to Ineqs. (15), (17) and (33). On the other hand, it is

\[
\alpha_1(\alpha_2 - \alpha_3) = \rho R_0(\rho + \omega + \delta C)(\rho + \omega + \delta C)
\]

and \( \alpha_1(\alpha_2 - \alpha_3) > 0 \). In accord with \( n = 3 \) in Ineqs (13), all eigenvalues of Eq. (37) are either negative real numbers or complex numbers having negative real parts. As a result, \( E_2 \) is asymptotically stable.

The proof is accomplished. The obtained results about stability analysis sum up briefly in Table 2.

### 4.1. Qualitative analysis results and discussion

For the proposed model in this study, the possible stable equilibrium point is either infection-free equilibrium point \( E_2 \) or endemic equilibrium point \( E_2 \). Also, it is clear that these two equilibrium points are not stable under the same conditions according to Table 2. While the equilibrium point \( E_2 \) represents the state in which an individual is free of viral particles, the equilibrium point \( E_2 \) shows the state in which an individual continues to fight viral particles. In this sense, the infected individual heals or the infection continues.

Considering the derivative-orders of Eqs. (14), the rational numbers \( \alpha_1, \alpha_2, \alpha_3, \alpha_4 \) and \( \alpha_5 \) are derivative-orders in the system of time-dependent variables \( x(t), y(t), \dot{y}(t), \beta y(t), \) and \( z(t) \), respectively.

Provided that \( R_0 \) is less than one, the stability of infection-free equilibrium point varies depending on whether the derivative orders \( \alpha_2 \) and \( \alpha_3 \) are equal or not. In this sense, the infection-free status depends on the derivative-orders of equations expressing the population size of infected cells of host and the infectious viral particle concentration in the proposed model. In case of \( \alpha_2 = \alpha_3 \), infection-free equilibrium point is stable and in case of \( \alpha_2 \neq \alpha_3 \), if Eq. (27) meet Ineqs (30), it is stable.

Let’s assume that \( R_0 \) is greater than one. In this case, endemic equilibrium point \( E_3 \) exists. The stability of this point varies depending on the state \( \alpha_1 = \alpha_2 = \alpha_3 \) and \( \alpha_1 \neq \alpha_2 \neq \alpha_3 \). In this context, the endemic infection status depends on the derivative-orders of equations expressing the population sizes of uninfected and infected cells of host and the infectious viral particle concentration in the proposed model. This point is stable in case of \( \alpha_1 = \alpha_2 = \alpha_3 \) and it is stable if Eq. (35) meet Ineqs (36) in case of \( \alpha_1 \neq \alpha_2 \neq \alpha_3 \).

### 5. Numerical simulation of the proposed HIV model

To support the results of the qualitative analysis of the proposed HIV infection model in Eqs. (14), we have given numerical illustrations here. The parameter values used in model for numerical study are given in Table 3.

**Numerical Study 1:** From Table 3, the basic reproduction rate \( R_0 \) is calculated as 52.762. Also, infection-free equilibrium point and endemic equilibrium point are found as \( E_2(10^9, 0, 0, 0, 3) \) and \( E_3(1.8953e + 04, 6.3912e + 03, 2.2964e + 04, 2.6627e + 03, 3) \), respectively. It is clear that \( R_0 > 1 \). According to Table 2, \( E_3 \) ex-
Whether \( \lambda \) is the temporary trajectory of population sizes of the variables in Eqs. (14) with initial conditions \((1000, 10, 1000, 2)\) for values in Table 3.

| Notation | Value | Reference |
|----------|-------|-----------|
| \( \gamma \) | \( 10^4 \text{ ml}^{-1}\text{day}^{-1} \) | [60] |
| \( \rho \) | 0.01 day\(^{-1} \) | [60] |
| \( \beta \) | 0.000024 ml\(^{-1}\)day\(^{-1} \) | [29] |
| \( \epsilon_{RT} \) | 0.1 and 0.8** | Assumed |
| \( \epsilon_{B} \) | 0.1 and 0.8** | Assumed |
| \( \omega \) | 0.025 day\(^{-1} \) | [34,60] |
| \( \delta \) | 0.5 ml day\(^{-1} \) | [60] |
| \( k \) | 10 day\(^{-1} \) | [29] |
| \( u \) | 2.4 day\(^{-1} \) | [29] |
| \( \sigma \) | 0.0001 ml day\(^{-1} \) | Assumed |
| \( r \) | 0.6 day\(^{-1} \) | [61] |
| \( c \) | 3 ml\(^{-1} \) and 10 ml** | Assumed |
| \([\alpha_i]\) | \([\alpha_1, \alpha_2, \alpha_3, \alpha_4, \alpha_5]\) | \([\frac{1}{2}, \frac{1}{2}, \frac{1}{2}, \frac{1}{2}, \frac{1}{2}]\) | Assumed |

**: Only the used value for first numerical study.
**: Only the used value for second numerical study.
Other values are commonly used in numerical studies.

Fig. 4. According to \([\alpha_i]\) = \([\frac{1}{2}, \frac{1}{2}, \frac{1}{2}, \frac{1}{2}, \frac{1}{2}]\) for \(i = 1, 2, \ldots, 5\), the temporary trajectory of population sizes of the variables in Eqs. (14) with initial conditions \((1000, 10, 1000, 2)\) for values in Table 3.

From here, the solutions for eigenvalues are given as \(\lambda_1 = -1.0938, \lambda_2 = -0.3856, \lambda_3 = -0.3856, \lambda_4 = -0.6817 + 0.7612i, \lambda_5 = -0.6817 - 0.7612i, \lambda_6 = -0.2719 + 1.1668i, \lambda_7 = -0.2719 - 1.1668i, \lambda_8 = -0.0480 + 0.9273i, \lambda_9 = -0.0480 - 0.9273i, \lambda_{10} = 1.0688 + 0.7239i, \lambda_{11} = 1.0688 - 0.7239i, \lambda_{12} = 0.5729 + 0.7876i, \lambda_{13} = 0.5729 - 0.7876i, \lambda_{14} = 0.8458 + 0.3362i \) and \(\lambda_{15} = 0.8458 - 0.3362i \) for \( i = \sqrt{-1} \). It is satisfied ineqs (36) due to \( Re[\lambda_j] < 0 \) for \( j = 1, 2, \ldots, 9 \). Thus, eigenvalues \( \lambda_j \) do not impart the stability conditions of \( E_3 \). In addition that, \( arg[\lambda_{10}] = 33.94^\circ \), \( arg[\lambda_{11}] = 326.06^\circ \), \( arg[\lambda_{12}] = 54.19^\circ \), \( arg[\lambda_{13}] = 305.81^\circ \), \( arg[\lambda_{14}] = 21.80^\circ \) and \( arg[\lambda_{15}] = 338.20^\circ \). Considering ineqs (36), it is \( [arg(\lambda_k)] > \frac{\pi}{3} \) \( = \frac{3\pi}{10} \) for \( k = 10, 11, \ldots, 15 \). As a result, the endemic equilibrium point \( E_3 \) is asymptotically stable with respect to Table 2. This situation is observed in Fig. 5.

**Numerical Study 2:** Lastly, the values of the basic reproductive ratio and the equilibrium point are calculated as \( R_0 = 0.794 \) and \( E_2(0.10^6, 0.0, 0.10) \), respectively. Considering Table 2, \( E_3 \) is not exists due to \( R_0 < 1 \). Consequently, only the \( E_2 \) point can or not be stable according to the different states of the derivative-orders in Eqs. (14).

a) Let \([\alpha_i]\) = \([\frac{1}{2}, \frac{3}{2}, \frac{5}{2}, \frac{7}{2}, \frac{9}{2}]\) for \(i = 1, 2, \ldots, 5\). Because \( R_0 < 1 \) and \( \alpha_2 = \alpha_3 \), \( E_2 \) is asymptotically stable in terms of Table 2. This situation is shown in Figs. 6-7.

b) Lastly, let us consider as \([\alpha_i]\) = \([\frac{1}{2}, \frac{3}{2}, \frac{5}{2}, \frac{7}{2}, \frac{9}{2}]\) for \(i = 1, 2, \ldots, 5\). In here, it is \( \alpha_2 \neq \alpha_3 \). Because \( \alpha_2 = \frac{3}{2} \) and \( \alpha_3 = \frac{5}{2} \), it is \( m = 8 \).
According to \([\alpha_i] = [\frac{1}{2} 0 \frac{1}{2} \frac{1}{2} \frac{1}{2} \frac{1}{2} 0] \) for \(i = 1, 2, \ldots, 5\), the temporary trajectory of population sizes of uninfected cells in Eqs. (14) with initial conditions (1000, 10, 100, 2) for values* in Table 3.

\[
\lambda^{11} + 2.401\lambda^{6} + 5.035\lambda^{5} + 2.489 = 0. \tag{40}
\]

Therefore, we obtain that \(\lambda_1 = -0.1138 + 1.3105i, \lambda_2 = -0.1138 - 1.3105i, \lambda_3 = -1.0763 + 0.5670i, \lambda_4 = -1.0763 - 0.5670i, \lambda_5 = -0.9362, \lambda_6 = -0.2140 + 0.8523i, \lambda_7 = -0.2140 - 0.8523i, \lambda_8 = 1.1893 + 0.7449i, \lambda_9 = 1.1893 - 0.7449i, \lambda_{10} = 0.6829 + 0.4651i, \lambda_{11} = 0.6829 - 0.4651i\). Since \(\Re\{\lambda_j\} < 0\) for \(j = 1, 2, \ldots, 7\) and \(\arg(\lambda_8) = 31.88^\circ, \arg(\lambda_9) = 328.12^\circ, \arg(\lambda_{10}) = 34.65^\circ, \arg(\lambda_{11}) = 325.35^\circ\), we have \(\arg(\lambda_k) > \frac{\pi}{2m} = \frac{\pi}{2} = 11.25^\circ\) for \(k = 1, 2, \ldots, 11\). According to Table 3, \(E_2\) is asymptotically stable as seen Figs. 8–9.

5.1. Numerical simulation results and discussion

In this part, we have given some numerical simulations for the presented model in Eqs. (14). For this model, we used the values of biological parameters and derivative-orders from Table 3 (Values * and **), and so the dynamics of Eqs. (14) with different initial conditions \((x_0, y_0, y_{10}, v_{100}, z_0)\) are plotted in Figs. 4–9. Two different numerical studies have been done by using the values of Table 3. In this sense, different scenarios have been tried to be obtained.

In the first study, the values indicated by *, where \(\epsilon_{RT} = 0.1\) and \(C = 3\) ml, are used. While infection-free equilibrium point \(E_2(10^6, 0, 0, 0, 3)\) always exists, endemic equilibrium point
$E_3 (1.8953e + 04, 6.3912e + 03, 2.3964e + 04, 2.6627e + 03, 3)$ biologically exits due to $R_0 = 52.762 > 1$.

- For derivative-orders $\left[ \frac{1}{2} \ \frac{4}{5} \ \frac{4}{5} \ \frac{10}{21} \ \frac{9}{11} \right] (\alpha_1 = \alpha_2 = \alpha_3)$, $E_3$ has been shown to meet asymptotic stability conditions for Eqs. (14) according to Table 2. In this context, the Fig. 4 has drawn. Approximately at least 400 days later, the infection process will approach a positive equilibria and the disease will continue endemically.

- Eqs. (14) has been considered for derivative-orders $\left[ \frac{1}{2} \ \frac{2}{3} \ \frac{5}{8} \ \frac{19}{20} \ \frac{9}{10} \right] (\alpha_1 \neq \alpha_2 \neq \alpha_3)$. As a result of providing the related conditions in Table 2, the stability of $E_3$ was shown in Fig. 5. In this sense, it was graphically represented that this endemic case would occur after at least 600 days.

In the second study, it is used the values indicated by **, where $\epsilon_{RT} = \epsilon_{HI} = 0.8$ and $C = 10$ ml. Here, there is a situation where the efficacy of the therapy with reverse transcriptase inhibitors and reverse protease inhibitors is increased and the carrying capacity of CTL response of host is greater too. Infection-free equilibrium point and basic reproduction rate are found as $E_2 (10^6, 0.0, 0, 0, 10)$ and $R_0 = 0.794 (< 1)$, respectively.

- Let us considered the derivative-orders as $\left[ \frac{5}{8} \ \frac{5}{8} \ \frac{5}{8} \ \frac{19}{20} \ \frac{9}{10} \right] (\alpha_2 = \alpha_5)$. Taking into consideration Table 2, it is shown that $E_2$ meet asymptotic stability conditions, and thus Figs. 6–7 is drawn. In about 200 days, while infected cells and viral particles disappear, CTL response of host approaches its carrying capacity. On the other hand, it takes a long time for the uninfected cells to approach its equilibrium value.
• Derivative-orders were considered as \[ \frac{1}{2}, \frac{3}{2}, \frac{5}{2}, \frac{9}{2}, \frac{15}{2}, \frac{20}{2} \] for \( i = 1, 2, \ldots, 5 \), the temporary trajectory of population sizes of the variables in Eqs. (14) with initial conditions \((1000, 10, 1000, 100, 2)\) for values \( \alpha \) in Table 3.

6. Conclusions

In this study, we proposed the new HIV model including the five time-dependent variables: the host cells as susceptible and infected, the viral particles as infectious and noninfectious and the host’s immune system response as CTL cells. This model proposed in Eqs. (14) is the form of incommensurate fractional-order nonlinear system (FOS) with the Caputo fractional derivative. In addition, the derivative-orders of these dependent variables in the system are as follows \( \alpha_1, \alpha_2, \alpha_3, \alpha_4 \) and \( \alpha_5 \) in interval \((0, 1]\), respectively. Considering the HIV models in the literature, the main innovations in our model are as follows:

• We built the model by using incommensurate FOS consisting of five equations.
• We have assumed that CTL cells of the host have the effect of destroying both infected cells and viral particles, and CTL cells have followed the logistic growth model.

Our model exhibits two equilibria, namely, disease-free equilibrium and the endemic equilibrium points. In general, the HIV models in literature trying to explain the infection process with the ONLY parameter basic reproduction rate \( R_0 \). By qualitative analysis of our model, what we found are as follows:

• Disease-free equilibrium point always exists and is asymptotically stable,
\[
\begin{align*}
\text{If } R_0 < 1 & \quad \text{in case of } \alpha_2 = \alpha_3. \\
\text{If } R_0 < 1 \text{ and (4.12) meet conditions (4.15)} & \quad \text{in other cases.}
\end{align*}
\]

• Endemic equilibrium point exists when \( R_0 > 1 \). This point is asymptotically stable,
\[
\begin{align*}
\text{If } R_0 > 1 \text{ (also the existence condition)} & \quad \text{in case of } \alpha_1 = \alpha_2 = \alpha_3. \\
\text{If (4.20) meet conditions (4.21)} & \quad \text{in other cases.}
\end{align*}
\]

We have achieved the abovementioned stability conditions that can be seen in Table 2. To support the stability analysis results, the numerical simulations of our model have been made in the light of the parameter values taken from the literature. The obtained analysis results of model demonstrate the simplicity and the productivity of this model, when the progress of the infection is considered.

In future studies, the progress of the infection may be described better by considering such as the following factors:

• acquiring disease through gene transfer between infected and uninfected cells,
• effect of regional conditions (For example, the progression times of HIV between people living in Europe and African continent can vary considerably,) and
• different inhibitor treatment strategies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Bahatdin DAŞBAŞI: Conceptualization, Methodology, Software, Validation, Formal analysis, Writing – original draft, Writing – review & editing, Visualization, Supervision.

References

[1] Wang Z. A numerical method for delayed fractional-order differential equations. J Appl Math 2013;2013:256791.
[2] Jajarmi A, Baleanu D, Sajadi SS, Asad JH. A new feature of the fractional Euler-Lagrange equations for a coupled oscillator using a nonsingular operator approach. Front Phys 2019;7(196):1–9.
[3] Yıldız TA, Jajarmi A, Yıldız B, Baleanu D. New aspects of time fractional optimal control problems within operators with nonsingular kernel. Discrete Cont Dyn S. 2020;13(3):407–28.
[4] Matlab MA, Jamali Y. The concepts and applications of fractional order differential calculus in modelling of viscoelastic systems: a primer. Crit Rev Biomed Eng 2019;47(4):249–76.
Shi applied 04-27. Wang for from for stochastic. Baleanu 2018;15(139):1–17 Qureshi Rihan 2019;11(3):210 variable-order Xiang, Li, Hu and of modeling. Shi Ahmed. 2019;29:093111. Bat, of modeling. 2006;20(11):110506. Atangana, A. 2011;20(1):486–93. Shi, Rui L, Wang C. Dynamic analysis of a fractional-order model for hepatitis B virus with Holling II functional response. Complexity 2019;2019:1097201. Jajarmi A, Arshad S, Baleanu D. A new fractional modelling and control strategy for the outbreak of dengue fever. Physica A 2019:535:122524. Obaya I, El-Saka H, Ahmed E, Elmahdy A. ODEs on multi-strain SEIR models. J Fractal Calc Appl 2018:9(2):196–201. Qureshi S, Yusuf A. Modeling chickenpox disease with fractional derivatives: from caputo to Atangana-Baleanu. Chaos Soliton Fract 2019;122:111–18. Khan MA, Ullah S, Farhan M. The dynamics of Zika virus with Caputo fractional derivative. AMS Math. 2019;4(1):134–46. Islam MR, Peace A, Medina D, Oraby T. Integer versus fractional order SEIR deterministic and stochastic models of measles. J Environ Res Public Health 2020;17(6):2014. Atangana A, Alkahtani BST. Modeling the spread of Rubella disease using the concept of with local derivative with fractional parameter: beta-derivative. Complexity 2016;21:442–51. Huppert A, Katriel G. Mathematical modelling and prediction in infectious disease epidemiology. Clin Microbiol Infect 2013;19(11):999–1005. Angstmann CN, Henry BJ, McGann AV. A fractional-order infectivity SIR model. Physica A 2016;452:86–93. Boukhouma A, Hattaf K, Yousfi N. Dynamics of a fractional order hiv infection model with specific functional response and cure rate. Int J Differ Equ 2017;2017:8372140. Gestal MC, Dedloff MR, Torres-Sangiao E. Computational health engineering applied to model infectious diseases and antimicrobial resistance spread. Appl Sci 2019;9(12):2486. Lai X. Study of Virus Dynamics by Mathematical Models Ph.D. thesis. In: Canada: Ontario; 2014. Fan Y, Zhao K, Shi Z-L, Zhou P. Bat coronaviruses in China. Viruses 2019;11(3):310. AIDSInfo. Information on HIV/AIDS treatment, prevention and research. https://aidsinfo.nih.gov/; Accessed: 2020-04-27. WHO. Data and Statistics. http://www.who.int/hiv/data/en/; Accessed: 2020-04-27. Nowak MA, Bangham CRM. Population dynamics of immune responses to persistent viruses. Science 1996;272:528. Wang L, Liu MY. Mathematical analysis of the global dynamics of a model for HIV infection of CD4+ T cells. Math Biosci 2006;200(1):44–57. Oladotun OM, Noutchev SCO. Mathematical model for an effective management of HIV infection. Biomed Res Int 2016;2016:4217548. Ding Y, Ye H. A fractional-order differential equation model of HIV infection of CD4+ T cells. Math Comput Model 2009;50:386–92. Liu Z, Lu P. Stability analysis for HIV infection of CD4+ T-cells by a fractional differential time-delay model with cure rate. Adv Differ Equ 2014;2014:298:1–20. Cardoso LC, Dos Santos FLP, Camargo RF. Analysis of fractional-order models for hepatitis B. Comput Appl Math 2018:37:4570–86. Khader MM. The modeling dynamics of HIV and CD4+ T-cells during primary infection in fractional order: numerical simulation. Mediterr J Math 2018;15(39):1–17.