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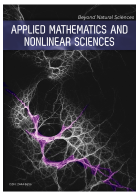

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System Analysis of HIV Infection Model with $CD4^{+}T$ under Non-Singular Kernel Derivative

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Abstract

Infectious diseases have caused the death of many people throughout the world for centuries. For this purpose, many researchers have investigated these diseases for establishing new treatment and protective measures. The most important of these is HIV disease. In this study, an HIV infection model of $CD4^{+}T$ cells is handled comprehensively with the newly defined Atangana-Baleanu (AB) fractional derivative. The existence and uniqueness of the solutions for fractionalized HIV disease model with the new derivative by considering the Arzela-Ascoli theorem.

Keywords: Atangana-Baleanu (AB) derivative, HIV infection model, Arzela-Ascoli theorem, existence and uniqueness.
AMS 2010 codes: 34A08, 47H10, 34A34.

1 Introduction

Over the past 50 years, the Human Immunodeficiency Virus (HIV) has become a lethal disease that affects the world in a global sense. HIV is a virus that generates infection by targeting immune system cells and causes fatal consequences if infection progresses. According to the researches conducted by the World Health Organization (WHO) worldwide, approximately 35 million people were affected by this disease, 940000 people died from HIV-related causes at the end of 2017. These statistics are inevitably increasing in spite of all the precaution taken over the years.

For this reason, many scientists worldwide are doing various researches in order to prevent such deadly diseases. Mathematical modeling is the most important part of these researches. With the help of mathematical models, researchers obtain very crucial information about the spread of diseases and measures to be taken [1–3].

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On the other hand, fractional calculus has become a very important tool in mathematical modeling as in many other fields in recent years [4–20].

Furthermore, there are many studies in the literature, which are modeled by the fractional concept related to diseases and bad habits [21–28].

In this paper, by the above motivation, we will handle an HIV infection model of $CD4^{+}T$ cells, considered in [1], for investigating the system components under the effect of non-singular kernel derivative which is defined in [12].

For this purpose, the rest of the paper is divided into 4 Sections. In Section 2, some basic necessary definitions and theorem for Atangana-Baleanu (AB) derivative, which is also named as non-singular Mittag-Leffler kernel derivative, are given. Section 3 is devoted to the model construction. In Section 4, the existence and uniqueness of the solutions for the HIV infection model in the frame of the AB fractional derivative are given. Finally, in Section 5, our results are briefly summarized.

2 Basic definitions and preliminaries

Definition 1. Let $f \in H^1(a,b)$, $a<b$ be a function and $\upsilon \in [0,1]$. The Atangana-Baleanu derivative in Caputo type of order υ of f is given by [12]:

$$ {}_{a}^{ABC}D_{t}^{\upsilon}\left[f(t)\right] = \frac{B(\upsilon)}{1-\upsilon}\int_{a}^{t} f'(x)\,E_{\upsilon}\left[-\upsilon\frac{(t-x)^{\upsilon}}{1-\upsilon}\right]dx. \tag{1} $$

Definition 2. Let $g \in H^1(a,b)$, $a<b$ be a function and $\upsilon \in [0,1]$. The Atangana-Baleanu derivative in Riemann-Liouville type of order υ of f is defined by [12]:

$$ {}_{a}^{ABR}D_{t}^{\upsilon}\left[f(t)\right] = \frac{B(\upsilon)}{1-\upsilon}\frac{d}{dt}\int_{a}^{t} g(x)\,E_{\upsilon}\left[-\upsilon\frac{(t-x)^{\upsilon}}{1-\upsilon}\right]dx. \tag{2} $$

Definition 3. The fractional integral related to the fractional derivative is given by [12]:

$$ {}_{a}^{AB}I_{t}^{\upsilon}\left[f(t)\right] = \frac{1-\upsilon}{B(\upsilon)}f(t) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_{a}^{t} f(\lambda)(t-\lambda)^{\upsilon-1}\,d\lambda. \tag{3} $$

3 Model description

In this section, the fractional order HIV infection model of $CD4^{+}T$ cells by the AB fractional derivative is constructed according to the reference in [1].

This system can be modeled by the three fractional order nonlinear differential equations as follow:

$$ \begin{aligned} {}_{0}^{ABC}D_{t}^{\upsilon}(T(t)) &= q-\overline{\upsilon}T(t)+rT(t)\left(1-\frac{T(t)+I(t)}{T_{\max}}\right)-kV(t)T(t), \\ {}_{0}^{ABC}D_{t}^{\upsilon}(I(t)) &= kV(t)T(t)-\beta I(t), \\ {}_{0}^{ABC}D_{t}^{\upsilon}(V(t)) &= \mu\beta I(t)-\gamma V(t), \end{aligned} \tag{4} $$

where, $T(t)$ is the number of healty $CD4^{+}T$ cells at time t, $I(t)$ is the concentration of infected $CD4^{+}T$ cells by the HIV viruses at time t, $V(t)$ is the number of HIV viruses at time t and $\overline{\upsilon}$, r, $T_{\max}$, k, β, μ and γ are the estimated data from real world applications.

4 Existence and uniqueness of the solutions

In this section, the existence and uniqueness of the solutions to the model (4) is described and proved under the effect of AB fractional derivative.

For this purpose, first of all, we apply AB fractional integral in Eq. (3) on both sides of the system and we get

$$
\begin{aligned}
&T(t)-T(0)=\frac{1-\upsilon}{B(\upsilon)}\left\{q-\overline{\upsilon}T(t)+rT(t)\left(1-\frac{T(t)+I(t)}{T_{\max}}\right)-kV(t)T(t)\right\}\\
&+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}\left\{q-\overline{\upsilon}T(y)+rT(y)\left(1-\frac{T(y)+I(y)}{T_{\max}}\right)-kV(y)T(y)\right\}dy,\\
&I(t)-I(0)=\frac{1-\upsilon}{B(\upsilon)}\{kV(t)T(t)-\beta I(t)\}+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}\{kV(y)T(y)-\beta I(y)\}dy,\\
&V(t)-V(0)=\frac{1-\upsilon}{B(\upsilon)}\{\mu\beta I(t)-\gamma V(t)\}+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}\{\mu\beta I(y)-\gamma V(y)\}dy.
\end{aligned}
\tag{5}
$$

We can choose our kernels $s(t,T(t))$, $s(t,I(t))$, $s(t,V(t))$ for simplifying the demonstration of the equation (5) as follows,

$$
\begin{aligned}
s(t,T(t))&=q-\overline{\upsilon}T(t)+rT(t)\left(1-\frac{T(t)+I(t)}{T_{\max}}\right)-kV(t)T(t),\\
s(t,I(t))&=kV(t)T(t)-\beta I(t),\\
s(t,V(t))&=\mu\beta I(t)-\gamma V(t).
\end{aligned}
$$

At first, we need to be able to identify an operator. We will then show that this operator is compact. Now, we consider the operator $K:H\to H$ and then we get

$$
\begin{aligned}
KT(t)&=\frac{1-\upsilon}{B(\upsilon)}s(t,T(t))+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}s(y,T(y))dy,\\
KI(t)&=\frac{1-\upsilon}{B(\upsilon)}s(t,I(t))+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}s(y,I(y))dy,\\
KV(t)&=\frac{1-\upsilon}{B(\upsilon)}s(t,V(t))+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t(t-y)^{\upsilon-1}s(y,V(y))dy.
\end{aligned}
\tag{6}
$$

Lemma 1. *Let $M\subset H$ be bounded in this way, we can find $n,r,l>0$ such that*

$$
\begin{aligned}
\|T(t_2)-T(t_1)\|&\le n\|t_2-t_1\| \text{ for every } T\in M,\\
\|I(t_2)-I(t_1)\|&\le r\|t_2-t_1\| \text{ for every } I\in M,\\
\|V(t_2)-V(t_1)\|&\le l\|t_2-t_1\| \text{ for every } V\in M.
\end{aligned}
$$

Then $\overline{K(M)}$ is compact.

Proof. Let $N = \max\left\{\frac{1-\upsilon}{B(\upsilon)} + s(t,T(t))\right\}$ and $0 \le T(t) \le P$. For $T(t) \in M$, then we have the followings

$$\begin{aligned}\|KT(t)\| &= \left\|\frac{1-\upsilon}{B(\upsilon)}s(t,T(t)) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t (t-y)^{\upsilon-1}s(y,T(y))\,dy\right\| \\ &\le \frac{1-\upsilon}{B(\upsilon)}N + \frac{\upsilon}{B(\upsilon)}N\frac{t^{\upsilon}}{\Gamma(\upsilon+1)}. \end{aligned} \tag{7}$$

Let $R = \max\left\{\frac{1-\upsilon}{B(\upsilon)} + s(t,I(t))\right\}$ and $0 \le I(t) \le Q$. For $I(t) \in M$

$$\begin{aligned}\|KI(t)\| &= \left\|\frac{1-\upsilon}{B(\upsilon)}s(t,I(t)) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t (t-y)^{\upsilon-1}s(y,I(y))\,dy\right\| \\ &\le \frac{1-\upsilon}{B(\upsilon)}R + \frac{\upsilon}{B(\upsilon)}R\frac{t^{\upsilon}}{\Gamma(\upsilon+1)}. \end{aligned} \tag{8}$$

In a similar way, $S = \max\left\{\frac{1-\upsilon}{B(\upsilon)} + s(t,V(t))\right\}$ and $0 \le V(t) \le S$. For $V(t) \in M$

$$\begin{aligned}\|KV(t)\| &= \left\|\frac{1-\upsilon}{B(\upsilon)}s(t,V(t)) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t (t-y)^{\upsilon-1}s(y,V(y))\,dy\right\| \\ &\le \frac{1-\upsilon}{B(\upsilon)}S + \frac{\upsilon}{B(\upsilon)}S\frac{t^{\upsilon}}{\Gamma(\upsilon+1)}. \end{aligned} \tag{9}$$

From the Eqs. (7)-(9), the function K is bounded.

Now, we will consider $t_1 < t_2$ and $T(t) \in M$. For $\varepsilon > 0$, if $|t_2 - t_1| < \delta$ then we obtain

$$\begin{aligned}\|KT(t_2) - KT(t_1)\| &= \left\|\frac{1-\upsilon}{B(\upsilon)}s(t_2,T(t_2)) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^{t_2} (t_2-y)^{\upsilon-1}s(y,T(y))\,dy\right. \\ &\left. -\frac{1-\upsilon}{B(\upsilon)}s(t_1,T(t_1)) - \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^{t_1} (t_1-y)^{\upsilon-1}s(y,T(y))\,dy\right\| \\ &\le \frac{1-\upsilon}{B(\upsilon)}\|s(t_2,T(t_2)) - s(t_1,T(t_1))\| \\ &+ \left\|\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^{t_2}(t_2-y)^{\upsilon-1}s(y,T(y))\,dy - \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^{t_1}(t_1-y)^{\upsilon-1}s(y,T(y))\,dy\right\| \\ &\le \frac{1-\upsilon}{B(\upsilon)}\|s(t_2,T(t_2)) - s(t_1,T(t_1))\| \\ &+ \frac{\upsilon P}{B(\upsilon)\Gamma(\upsilon)}\left\{\int_0^{t_2}(t_2-y)^{\upsilon-1}\,dy - \int_0^{t_1}(t_1-y)^{\upsilon-1}\right\}, \end{aligned} \tag{10}$$

and then

$$\begin{aligned}\int_0^{t_2}(t_2-y)^{\upsilon-1}\,dy - \int_0^{t_1}(t_1-y)^{\upsilon-1}\,dy &= \int_0^{t_1}\left\{(t_1-y)^{\upsilon-1} - (t_2-y)^{\upsilon-1}\right\}dy + \int_{t_1}^{t_2}(t_2-y)^{\upsilon-1}\,dy \\ &= 2\frac{(t_2-t_1)^{\upsilon}}{\upsilon}. \end{aligned} \tag{11}$$

Now, we will investigate the following:

$$\begin{aligned}\|s(t_2,T(t_2))-s(t_1,T(t_1))\| &\leq \|T(t_2)-T(t_1)\|(\overline{\upsilon}+ra+k(b+c))\\ &\leq F_1 n\|t_2-t_1\|\\ &\leq A\|t_2-t_1\|. \end{aligned} \tag{12}$$

Putting Eqs. (11) and (12) in Eq. (10), we have

$$\begin{aligned}\|KT(t_2)-KT(t_1)\| &\leq \frac{1-\upsilon}{B(\upsilon)}A\|t_2-t_1\|+\frac{\upsilon P}{B(\upsilon)\Gamma(\upsilon)}2\frac{\|t_2-t_1\|^{\upsilon}}{\upsilon}\\ &\leq \frac{1-\upsilon}{B(\upsilon)}A\|t_2-t_1\|+\frac{2\upsilon P}{B(\upsilon)\Gamma(\upsilon+1)}\|t_2-t_1\|.\end{aligned}$$

Let $\delta_1=\frac{\varepsilon}{\frac{1-\upsilon}{B(\upsilon)}A+\frac{2\upsilon P}{B(\upsilon)\Gamma(\upsilon+1)}}$ and then we find

$$\|KT(t_2)-KT(t_1)\|<\varepsilon.$$

With the same rule step by step, we can obtain the following for other two equations. For each $\varepsilon>0$, we can find $\delta_2=\frac{\varepsilon}{\frac{1-\upsilon}{B(\upsilon)}B+\frac{2\upsilon Q}{B(\upsilon)\Gamma(\upsilon+1)}}$, $\delta_3=\frac{\varepsilon}{\frac{1-\upsilon}{B(\upsilon)}C+\frac{2\upsilon V}{B(\upsilon)\Gamma(\upsilon+1)}}$ such that

$$\|KI(t_2)-KI(t_1)\|\leq \frac{1-\upsilon}{B(\upsilon)}B\|t_2-t_1\|+\frac{2\upsilon Q}{B(\upsilon)\Gamma(\upsilon+1)}\|t_2-t_1\|$$

and

$$\|KV(t_2)-KV(t_1)\|\leq \frac{1-\upsilon}{B(\upsilon)}C\|t_2-t_1\|+\frac{2\upsilon V}{B(\upsilon)\Gamma(\upsilon+1)}\|t_2-t_1\|.$$

Consequently,

$$\|KI(t_2)-KI(t_1)\|<\varepsilon \text{ and } \|KV(t_2)-KV(t_1)\|<\varepsilon$$

are satisfied. So $T(M)$ is equicontinuous and using Arzelo-Ascoli Theorem, $\overline{T(M)}$ is compact. □

Theorem 2. *$S:[a,b]\times[0,\infty)\to[0,\infty)$ be a continuous function and $S(t,.)$ increasing for each t in $[a,b]$. Let us assume that one can find v,w satisfying $M(D)v\leq S(t,v)$, $M(D)w\geq S(t,w)$ for $0\leq v(t)\leq w(t)$ and $a\leq t\leq b$. Then our new equation has a positive solution.*

Proof. We should consider the fixed point of the operator K. We know that the operator $K:H\to H$ is completely continuous. Let $T_1\leq T_2$, $I_1\leq I_2$ and $V_1\leq V_2$ then we get

$$\begin{aligned}KT_1(t) &\leq \frac{1-\upsilon}{B(\upsilon)}s(t,T_1(t))+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t (t-y)^{\upsilon-1}\|s(y,T_1(y))\|dy\\ &\leq KT_2(t).\end{aligned}$$

By a similar way, we obtain

$$\begin{aligned}KI_1(t) &\leq \frac{1-\upsilon}{B(\upsilon)}s(t,I_1(t))+\frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)}\int_0^t (t-y)^{\upsilon-1}\|s(y,I_1(y))\|dy\\ &\leq KI_2(t),\end{aligned}$$

and

$$\begin{aligned} KV_1(t) &\leq \frac{1-\upsilon}{B(\upsilon)} s(t, V_1(t)) + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)} \int_0^t (t-y)^{\upsilon-1} \|s(y, V_1(y))\| \, dy \\ &\leq KV_2(t). \end{aligned}$$

Hence K is increasing operator. By the help of conjecture, we have $Km \geq m$ and $Kn \leq n$. So, the operator $K : \langle n,m \rangle \to \langle n,m \rangle$ is compact and continuous from Lemma 1. In that case, H is a normal cone. □

To obtain uniqueness of the solutions, we begin the following steps.

$$\begin{aligned} \|KT_1(t) - KT_2(t)\| &\leq \frac{1-\upsilon}{B(\upsilon)} \|s(t, T_1(t)) - s(t, T_2(t))\| \\ &\quad + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)} \int_0^t (t-y)^{\upsilon-1} \|s(y, T_1(y)) - s(y, T_2(y))\| \, dy \\ &\leq \frac{1-\upsilon}{B(\upsilon)} F_1 \|T_1(t) - T_2(t)\| \\ &\quad + \frac{\upsilon}{B(\upsilon)\Gamma(\upsilon)} F_1 \int_0^t (t-y)^{\upsilon-1} \|T_1(y) - T_2(y)\| \, dy, \end{aligned} \tag{13}$$

which yields

$$\|KT_1(t) - KT_2(t)\| \leq \left\{ \frac{1-\upsilon}{B(\upsilon)} F_1 + \frac{\upsilon F_1 b^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} \right\} \|T_1(t) - T_2(t)\|. \tag{14}$$

For the other components of the model, we find

$$\|KI_1(t) - KI_2(t)\| \leq \left\{ \frac{1-\upsilon}{B(\upsilon)} F_2 + \frac{\upsilon F_2 b^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} \right\} \|I_1(t) - I_2(t)\|, \tag{15}$$

and

$$\|KV_1(t) - KV_2(t)\| \leq \left\{ \frac{1-\upsilon}{B(\upsilon)} F_3 + \frac{\upsilon F_3 c^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} \right\} \|V_1(t) - V_2(t)\|. \tag{16}$$

Therefore, if the following conditions hold

$$\begin{aligned} \frac{1-\upsilon}{B(\upsilon)} F_1 + \frac{\upsilon F_1 b^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} &< 1, \\ \frac{1-\upsilon}{B(\upsilon)} F_2 + \frac{\upsilon F_2 b^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} &< 1, \\ \frac{1-\upsilon}{B(\upsilon)} F_3 + \frac{\upsilon F_3 c^{\upsilon}}{B(\upsilon)\Gamma(\upsilon+1)} &< 1, \end{aligned}$$

the mapping K is a contraction, which implies fixed point and thus the model has a unique positive solution.

5 Concluding remarks

In this work, we have examined the system response of the HIV infection model in [1] by modeling the AB fractional derivative in Caputo sense. The theoretical studies have shown that the solution of the discussed model in Eq. (4) is exist and unique under the AB fractional derivative.

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