



Interactive Fuzzy Fractional Differential Equation: Application on HIV Dynamics

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Abstract. This work presents an application of interactive fuzzy fractional differential equation, with Caputo derivative, to an HIV model for seropositive individuals under antiretroviral treatment. The initial condition of the model is given by a fuzzy number and the differentiability is given by a fuzzy interactive derivative. A discussion about the model considering these notions are presented. Finally, a numerical solution to the problem is provided, in order to illustrate the results.

Keywords: Fuzzy fractional differential equation · Interactive arithmetic · F-correlated fuzzy process · HIV dynamics

1 Introduction

Fractional Differential Equations (FDE) can be seen as a generalization of Ordinary Differential Equations (ODE) to arbitrary non-integer order [14]. The concept of Fuzzy Fractional Differential Equation (FFDE) was introduced by Agarwal *et al.* in [1]. There are several papers that solve FFDEs, for example [26, 35].

Here we consider the Fuzzy Fractional Differential Equations (FFDE) under the interactive derivative of Caputo, that is, the differentiability is given by an interactive derivative, as proposed by Santo Pedro *et al.* [26]. We use the fractional interactive derivative to describe a viral dynamics in seropositive individuals under antiretroviral treatment (ART). An HIV population dynamics has already been considered as a process with memory. In this case, it was described by a system of delay-differential equations associated mainly to pharmacological delay, defined as the time interval required to absorption, distribution and penetration of the drug in the target cells of the virus [16].

The dynamics of biological systems usually evolve with some uncertainty, which may be inherent in the phenomenon or result from environmental variation. It seems pertinent modeling a biological system as a process with memory, so it cannot depend on instant time alone. For these reasons, the fractional differential equation is used [2,3].

Our goal in this work is to provide new insight into well-known models of HIV. For this, we will use fractional differential equations, which are used to treat processes with memories [2,3], and the interactive derivative, which considers both correlated processes and variability at the initial condition [5,27]. Current studies consider interactivity in the modeling of biological processes, in particular, in the dynamics of HIV, when assuming the existence of a memory coefficient [15].

This work is structured as follows. Section 2 presents preliminary concepts about fuzzy set theory, as well as the fuzzy derivative for autocorrelated processes. Section 3 presents fuzzy interactive fractional derivatives. Section 4 presents the fuzzy interactive fractional differential equation under the Caputo derivative. Section 5 presents HIV dynamics under Caputo derivative and Sect. 6 presents the final comments.

2 Preliminary

A fuzzy subset A of \mathbb{R}^n is described by its membership function $\mu_A : \mathbb{R}^n \rightarrow [0, 1]$, where $\mu_A(u)$ means the degree in which u belongs to A . The r -levels of the fuzzy subset A are classical subsets defined as:

$$[A]_r = \{u \in \mathbb{R}^n : \mu_A(u) \geq r\} \text{ for } 0 < r \leq 1 \text{ and} \\ [A]_0 = \overline{\{u \in \mathbb{R}^n : \mu_A(u) > 0\}}.$$

The fuzzy subset A of \mathbb{R} is a fuzzy number if its r -levels are closed and nonempty intervals of \mathbb{R} and the support of A , $\text{supp}(A) = \{u \in \mathbb{R} : \mu_A(u) > 0\}$, is limited [4]. The family of the fuzzy subsets of \mathbb{R}^n with nonempty compact and convex r -levels is denoted by $\mathbb{R}_{\mathcal{F}}^n$, while the family of fuzzy numbers is denoted by $\mathbb{R}_{\mathcal{F}}$.

The Pompeiu-Hausdorff distance $d_\infty : \mathbb{R}_{\mathcal{F}}^n \times \mathbb{R}_{\mathcal{F}}^n \rightarrow \mathbb{R}_+ \cup \{0\}$, is defined by

$$d_\infty(A, B) = \sup_{0 \leq r \leq 1} d_H([A]_r, [B]_r), \quad (1)$$

where d_H is the Pompeiu-Hausdorff distance for compact subsets of \mathbb{R}^n . If A and B are fuzzy numbers, that is, $A, B \in \mathbb{R}_{\mathcal{F}}$, then (1) becomes

$$d_\infty(A, B) = \sup_{0 \leq r \leq 1} \max\{|a_r^- - b_r^-|, |a_r^+ - b_r^+|\}.$$

From now on, the continuity of a fuzzy function is associated with the metric d_∞ . The symbols $+$ and $-$ stands for the traditional (Minkowski) sum and difference between fuzzy numbers, which can be also defined via Zadeh's extension principle [19].

Let $A, B \in \mathbb{R}_{\mathcal{F}}$ and $J \in \mathcal{F}_J(\mathbb{R}^2)$. The fuzzy relation J is a joint possibility distribution of A and B if, [8]

$$\max_v \mu_J(u, v) = \mu_A(u) \text{ and } \max_u \mu_J(u, v) = \mu_B(v), \forall u, v \in \mathbb{R}.$$

In this case, A and B are called marginal possibility distributions of J .

The fuzzy numbers A and B are said to be *non-interactive* if, and only if, its joint possibility distribution J is given by $\mu_J(u, v) = \min\{\mu_A(u), \mu_B(v)\}$ for all $u, v \in \mathbb{R}$. Otherwise, the fuzzy numbers are said to be *interactive* [8, 10].

Let A and B be fuzzy numbers with joint possibility distribution J and $f : \mathbb{R}^2 \rightarrow \mathbb{R}$. The extension of f with respect to J , applied to the pair (A, B) , is the fuzzy subset $f_J(A, B)$ with membership function defined by [7]

$$\mu_{f_J(A, B)}(u) = \begin{cases} \sup_{(w, v) \in f^{-1}(u)} \mu_J(w, v) & \text{if } f^{-1}(u) \neq \emptyset \\ 0 & \text{if } f^{-1}(u) = \emptyset \end{cases}, \quad (2)$$

where $f^{-1}(u) = \{(w, v) : f(w, v) = u\}$.

If J is given by the minimum t-norm, then $f_J(A, B)$ is the Zadeh's extension principle of f at A and B [7].

Theorem 1 [7, 12]. *Let $A, B \in \mathbb{R}_{\mathcal{F}}$, J be a joint possibility distribution whose marginal possibility distributions are A and B , and $f : \mathbb{R}^2 \rightarrow \mathbb{R}$ a continuous function. In this case, $f_J : \mathbb{R}_{\mathcal{F}} \times \mathbb{R}_{\mathcal{F}} \rightarrow \mathbb{R}_{\mathcal{F}}$ is well-defined and*

$$[f_J(A, B)]_r = f([J]_r) \text{ for all } r \in [0, 1]. \quad (3)$$

Let $A \in \mathbb{R}_{\mathcal{F}}$. The length of the r -level set of A is defined by

$$\text{len}([A]_r) = a_r^+ - a_r^-, \text{ for all } r \in [0, 1].$$

If $r = 0$, then $\text{len}([A]_0) = \text{diam}(A)$.

A strongly measurable and limited integrable fuzzy function is called integrable. The fuzzy integral of Aumann of $x : [a, b] \rightarrow \mathbb{R}_{\mathcal{F}}$, with $[x(t)]_r = [x_r^-(t), x_r^+(t)]$ is defined by [13]

$$\begin{aligned} \left[\int_a^b x(t) dt \right]_r &= \int_a^b [x(t)]_r dt = \int_a^b [x_r^-(t), x_r^+(t)] dt \\ &= \left\{ \int_a^b y(t) dt \mid y : [a, b] \rightarrow \mathbb{R} \text{ is a measurable selection for } [x(\cdot)]_r \right\}, \end{aligned} \quad (4)$$

for all $r \in [0, 1]$, provided (4) define a fuzzy number.

Let us focus on the special relationship called interactivity. There are several types of joint possibility distributions that generate different interactivities. This manuscript studies the interactivity called linear correlation, which is obtained as follows.

Let $A, B \in \mathbb{R}_{\mathcal{F}} \setminus \mathbb{R}$ and a function $F: \mathbb{R} \rightarrow \mathbb{R}$. The fuzzy numbers A and B are called F -correlated if its joint possibility distribution is given by [8]

$$\mu_J(x, y) = \chi_{\{(u, v=F(u))\}}(x, y) \mu_A(x) = \chi_{\{(u, v=F(u))\}}(x, y) \mu_B(y) \quad (5)$$

Note that the fuzzy number B coincides with the Zadeh's extension principle of the function F evaluated at the fuzzy number A . If F is invertible, then $A = F^{-1}(B)$ and, in this case,

$$[J]_r = \{(u, F(u)) \in \mathbb{R}^2 | u \in [A]_r\} = \{(F^{-1}(v), v) \in \mathbb{R}^2 | v \in [B]_r\}. \quad (6)$$

Also, if F is a continuous function, then the r -levels of B are given by [4]

$$[B]_r = F([A]_r).$$

The fuzzy numbers are called linearly correlated (or linearly interactive), if the function F is given by $F(u) = qu + r$. Let A and B be F -correlated fuzzy numbers. The operation $B \otimes_F A$ is defined by [7],

$$\mu_{B \otimes_F A}(w) = \begin{cases} \sup_{u \in \Phi_{\otimes}^{-1}(w)} \mu_A(u) & \text{if } \Phi_{\otimes}^{-1}(w) \neq \emptyset \\ 0 & \text{if } \Phi_{\otimes}^{-1}(w) = \emptyset \end{cases}, \quad (7)$$

where $\Phi_{\otimes}^{-1}(w) = \{u | w = u \otimes v, v = F(u)\}$, and $\otimes \in \{+, -, \times, \div\}$.

From Theorem 1, the four arithmetic operations of F -correlated fuzzy numbers, for all $r \in [0, 1]$, are given by

$$[B +_F A]_r = \{F(w) + w \in \mathbb{R} | w \in [A]_r\}; \quad (8)$$

$$[B -_F A]_r = \{F(w) - w \in \mathbb{R} | w \in [A]_r\}; \quad (9)$$

$$[B \cdot_F A]_r = \{wF(w) \in \mathbb{R} | w \in [A]_r\}; \quad (10)$$

$$[B \div_F A]_r = \{F(w) \div w \in \mathbb{R} | w \in [A]_r\}, \quad 0 \notin [A]_0. \quad (11)$$

Moreover, the scalar multiplication of λB , with $B = F(A)$, is given by $[\lambda B]_r = \{\lambda F(w) \in \mathbb{R} | w \in [A]_r\}$.

Proposition 1 [27]. Let A and B be F -correlated fuzzy numbers, i.e., $[B]_r = F([A]_r)$, with F monotone differentiable, $[A]_r = [a_r^-, a_r^+]$ and $[B]_r = [b_r^-, b_r^+]$, thus, for all $r \in [0, 1]$,

$$1) [B -_F A]_r = \{F(w) - w | w \in [A]_r\} =$$

$$\begin{cases} i. [b_r^- - a_r^-, b_r^+ - a_r^+] \text{ if } F'(z) > 1, \quad \forall z \in [A]_r \\ ii. [b_r^+ - a_r^+, b_r^- - a_r^-] \text{ if } 0 < F'(z) \leq 1, \quad \forall z \in [A]_r; \\ iii. [b_r^- - a_r^+, b_r^+ - a_r^-] \text{ if } F'(z) \leq 0, \quad \forall z \in [A]_r \end{cases} \quad (12)$$

$$2) [B +_F A]_r = \{F(w) + w | w \in [A]_r\} =$$

$$\begin{cases} i. [b_r^- + a_r^-, b_r^+ + a_r^+] \text{ if } F'(z) > 0, \quad \forall z \in [A]_r \\ ii. [b_r^+ + a_r^-, b_r^- + a_r^+] \text{ if } -1 < F'(z) \leq 0, \quad \forall z \in [A]_r. \\ iii. [b_r^- + a_r^+, b_r^+ + a_r^-] \text{ if } F'(z) \leq -1, \quad \forall z \in [A]_r \end{cases} \quad (13)$$

In the first case (12)-i., we have $\text{len}([A]_r) < \text{len}([B]_r)$, and $-_F$ coincides with Hukuhara difference [13], while in (12)-ii., we have $\text{len}([A]_r) > \text{len}([B]_r)$ and, $-_F$ coincides with generalized Hukuhara difference [6, 34]. In fact, the generalized Hukuhara and Hukuhara differences are particular cases of an interactive difference [34]. Additionally, $-_F$ coincides with standard difference when $F'(z) \leq -1$, and $+_F$ coincides with standard sum when $F'(z) > 0$.

Assuming A and B linearly correlated fuzzy numbers, that is $F(u) = qu + r$, and $[B]_r = q[A]_r + r$, with $[A]_r = [a_r^-, a_r^+]$ and $[B]_r = [b_r^-, b_r^+]$, (12) and (13) becomes

$$[B -_L A]_r = \begin{cases} i. [b_r^- - a_r^-, b_r^+ - a_r^+] & \text{if } q \geq 1 \\ ii. [b_r^+ - a_r^+, b_r^- - a_r^-] & \text{if } 0 < q < 1 \\ iii. [b_r^- - a_r^+, b_r^+ - a_r^-] & \text{if } q < 0 \end{cases} \quad (14)$$

and

$$[B +_L A]_r = \begin{cases} i. [b_r^- + a_r^-, b_r^+ + a_r^+] & \text{if } q > 0 \\ ii. [b_r^+ + a_r^-, b_r^- + a_r^-] & \text{if } -1 \leq q < 0. \\ iii. [b_r^- + a_r^+, b_r^+ + a_r^-] & \text{if } q < -1 \end{cases} \quad (15)$$

It is worth to notice that $+_L$ coincides with standard sum when q is positive, and $-_L$ coincides with standard difference when q is negative [11]. Moreover, $-_L$ coincides with generalized Hukuhara difference [6] when q is positive and when $q > 1$ it coincides with Hukuhara difference [13]. It is interesting to mention that the authors of [25] used linearly interactive fuzzy numbers to fit an HIV dataset.

2.1 Autocorrelated Fuzzy Processes

Autocorrelated fuzzy processes are similar to autocorrelated statistical processes [5, 11, 27, 28]. These types of fuzzy processes have been carried out in areas such as, epidemiology [30, 33] and population dynamics [27, 29].

Let $L([a, b], \mathbb{R}_{\mathcal{F}})$ be the set of all Lebesgue integrate functions from the bounded interval $[a, b]$ into $\mathbb{R}_{\mathcal{F}}$, and $AC([a, b], \mathbb{R}_{\mathcal{F}})$ be the set of all absolutely continuous functions from $[a, b]$ into $\mathbb{R}_{\mathcal{F}}$. A fuzzy process x is defined by a fuzzy-number-valued function $x : [a, b] \rightarrow \mathbb{R}_{\mathcal{F}}$. Considering $[x(t)]_r = [x_r^-(t), x_r^+(t)]$, for all $r \in [0, 1]$, the process x is δ -locally F -autoregressive at $t \in (a, b)$ (F -autoregressive for short) if there exists a family of real functions $F_{t,h}$ such that, for all $0 < |h| < \delta$ [27],

$$[x(t+h)]_r = F_{t,h}([x(t)]_r), \quad \forall r \in [0, 1]. \quad (16)$$

If $x : [a, b] \rightarrow \mathbb{R}_F$ is a F -autoregressive fuzzy process, then the function x is F -correlated differentiable (F -differentiable for short) at $t_0 \in [a, b]$ if there exists a fuzzy number $x'_F(t_0)$ such that [27]

$$x'_F(t_0) = \lim_{h \rightarrow 0} \frac{x(t_0+h) -_F x(t_0)}{h}, \quad (17)$$

where the above limit exists and it is equal to $x'_F(t_0)$ (using the metric d_{∞}). If x'_F exists, for all $t \in [a, b]$, then we say that x is F -differentiable.

Next theorem provides a characterization of the F derivative by means of r -levels.

Theorem 2 [27]. Let $x : [a, b] \rightarrow \mathbb{R}_{\mathcal{F}}$ be F -differentiable at $t_0 \in [a, b]$, with $[x(t)]_r = [x_r^-(t), x_r^+(t)]$, where the corresponding family of functions $F_{t_0, h} : I \rightarrow \mathbb{R}$ is monotone continuously differentiable for each h , for $r \in [0, 1]$ and $F_{t, h}$, $\forall t \in [a, b]$. Then,

$$[x'_F(t_0)]_r = \begin{cases} [(x_r^-)'(t_0), (x_r^+)'(t_0)] & \text{if } F'_{t, h}(w) > 1 \\ [(x_r^+)'(t_0), (x_r^-)'(t_0)] & \text{if } 0 < F'_{t, h}(w) \leq 1 \\ \{(x_r^-)'(t_0)\} = \{(x_r^+)'(t_0)\} & \text{if } F'_{t, h}(w) \leq 0 \end{cases}$$

for each $0 < |h| < \delta$, $\delta > 0$, and $\forall w \in [x(t)]_r$.

The process x is called expansive if, the diameter of $x(t)$ is a non-decreasing function at t , and equivalently, x is called contractive if, the diameter of $x(t)$ is a non-increasing function at t .

Theorem 3 [26]. Let $x \in AC([a, b], \mathbb{R}_{\mathcal{F}})$ be F -differentiable, where $[x(t)]_r = [x_r^-(t), x_r^+(t)]$.

- I. Suppose x is expansive, that is, $\text{len}([x(t)]_r)$ is an increase function on $[a, b]$. If function x'_F is Aumann integrable then $(x_r^-)'(t)$ and $(x_r^+)'(t)$ are integrable on $t \in [a, b]$, and

$$\left[\int_a^t x'_F(s) ds \right]_r = \left[\int_a^t (x_r^-)'(s) ds, \int_a^t (x_r^+)'(s) ds \right].$$

- II. Suppose x is contractive, that is, $\text{len}([x(t)]_r)$ is a decrease function on $[a, b]$. If function x'_F is Aumann integrable then $(x_r^-)'(t)$ and $(x_r^+)'(t)$ are integrable on $t \in [a, b]$, and

$$\left[\int_a^t x'_F(s) ds \right]_r = \left[\int_a^t (x_r^+)'(s) ds, \int_a^t (x_r^-)'(s) ds \right].$$

2.2 Fuzzy Fractional Integral and Fuzzy Fractional Derivative

The Riemann-Liouville fractional integral $I_{a+}^{\alpha} f$ of a function $f \in (L[a, b], \mathbb{R})$, of order $\alpha \in (0, 1]$ is defined by [31],

$$(I_{a+}^{\alpha} f)(t) = \frac{1}{\Gamma(\alpha)} \int_a^t (t-s)^{\alpha-1} f(s) ds, \quad \text{for } t > a \quad (18)$$

where $\Gamma(\alpha)$ is the gamma function. If $\alpha = 1$, we have $(I_{a+}^1 f)(t) = \int_a^t f(s) ds$.

The Riemann-Liouville derivative of order $\alpha \in (0, 1]$, is defined by [31]

$$(D^{\alpha} f)(t) = \frac{d}{dt} I^{1-\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \frac{d}{dt} \int_a^t (t-s)^{-\alpha} f(s) ds, \quad (19)$$

for $t > a$.

Definition 1 [31]. The Riemann-Liouville derivative of order $\alpha \in (0, 1]$, is defined by

$$({}^{RL}D_{a+}^{\alpha}f)(t) = \frac{d}{dt}I_{a+}^{1-\alpha}f(t) = \frac{1}{\Gamma(1-\alpha)} \frac{d}{dt} \int_a^t (t-s)^{-\alpha} f(s) ds, \text{ for } t > a. \quad (20)$$

Definition 2 [31]. Let $f \in (L[a, b], \mathbb{R})$ and suppose there exists ${}^{RL}D_{a+}^{\alpha}f$ on $[a, b]$. The Caputo fractional derivative ${}^CD_{a+}^{\alpha}f$ is defined by

$$({}^CD_{a+}^{\alpha}f)(t) = \left({}^{RL}D_{a+}^{\alpha}[f(\cdot) - f(a)] \right)(t), \text{ for } t \in (a, b]. \quad (21)$$

Besides that, if $f \in AC([a, b], \mathbb{R})$, then

$$({}^CD_{a+}^{\alpha}f)(t) = \frac{1}{\Gamma(1-\alpha)} \int_a^t (t-s)^{-\alpha} f'(s) ds, \quad \forall t \in (a, b] \quad (22)$$

and

$$({}^{RL}D_{a+}^{\alpha}f)(t) = ({}^CD_{a+}^{\alpha}f)(t) + \frac{(t-a)^{-\alpha}}{\Gamma(1-\alpha)} f(a), \quad \forall t \in (a, b]. \quad (23)$$

The next section considers the fuzzy process x in the above definitions, instead of the deterministic function f . The idea is to use the concepts of fuzzy integral and fuzzy F -correlated derivative.

3 Fuzzy Interactive Fractional Derivative

The fuzzy integral fractional Riemann-Liouville, of order $\alpha > 0$, of x is defined by

$$[(I_{a+}^{\alpha}x)(t)]_r = \frac{1}{\Gamma(\alpha)} \left[\int_a^t (t-s)^{\alpha-1} x_r^-(s) ds, \int_a^t (t-s)^{\alpha-1} x_r^+(s) ds \right], \quad t > a. \quad (24)$$

For fuzzy fractional derivative consider $x \in L([a, b], \mathbb{R}_{\mathcal{F}})$ and the fuzzy process

$$x_{1-\alpha}(t) = \int_a^t \frac{(t-s)^{-\alpha}}{\Gamma(1-\alpha)} x(s) ds, \quad \text{for all } t \in (a, b], \quad (25)$$

where $x_{1-\alpha}(a) = \lim_{t \rightarrow a+} x_{1-\alpha}(t)$ in the sense of Pompeiu-Hausdorff metric. Recall that for all $0 < \alpha \leq 1$, the fuzzy function $x_{1-\alpha} : (a, b] \rightarrow \mathbb{R}_{\mathcal{F}}$ defines a fuzzy number.

Definition 3 [26]. The fuzzy Riemann-Liouville fractional derivative of order $0 < \alpha \leq 1$ of x with respect to F -derivative is defined by

$$({}^{RLF}D_{a+}^{\alpha}x)(t) = \frac{1}{\Gamma(1-\alpha)} \left(\int_a^t (t-s)^{-\alpha} x(s) ds \right)'_F = (x_{1-\alpha}(t))'_F, \quad (26)$$

where $\int_a^t (t-s)^{-\alpha} x(s) ds$ is a F -correlated fuzzy process, F -differentiable for all $t \in (a, b]$.

It is important to highlight that, $\int_a^t (t-s)^{-\alpha} x(s) ds$ can be an expansive or contractive fuzzy process. However, it is expansive if $x(\cdot)$ is expansive [31]. So, if $x_{1-\alpha}(\cdot)$ or $x(\cdot)$ is expansive, then

$$[\text{RL}_F D_{a+}^{\alpha} x(t)]_r = \frac{1}{\Gamma(1-\alpha)} \left[\frac{d}{dt} \int_a^t (t-s)^{-\alpha} x_r^-(s) ds, \frac{d}{dt} \int_a^t (t-s)^{-\alpha} x_r^+(s) ds \right]. \quad (27)$$

Thus,

$$[\text{RL}_F D_{a+}^{\alpha} x(t)]_r = \begin{cases} i. [D_{a+}^{\alpha} x_r^-(t), D_{a+}^{\alpha} x_r^+(t)] & \text{if } x_{1-\alpha}(\cdot) \text{ or } x(\cdot) \text{ is expansive} \\ ii. [D_{a+}^{\alpha} x_r^+(t), D_{a+}^{\alpha} x_r^-(t)] & \text{if } x_{1-\alpha}(\cdot) \text{ is contractive} \end{cases}. \quad (28)$$

Definition 4. Let x be a F -correlated fuzzy process. The fuzzy Caputo fractional derivative ${}^C F D_{a+}^{\alpha} x$ with respect to F -derivative is defined by

$$({}^C F D_{a+}^{\alpha} x)(t) = \left({}^{RL}_F D_{a+}^{\alpha} [x(\cdot) -_F x(a)] \right)(t), \text{ for } t \in (a, b]. \quad (29)$$

Thus,

$$({}^C F D_{a+}^{\alpha} x)(t) = \frac{1}{\Gamma(1-\alpha)} \left(\int_a^t (t-s)^{-\alpha} (x(s) -_F x(a)) ds \right)'_F. \quad (30)$$

From (26) if $x_{1-\alpha}(\cdot)$ is contractive, then

$$[({}^C F D_{a+}^{\alpha} x)(t)]_r = \begin{cases} [({}^C D_{a+}^{\alpha} x_r^-(t), {}^C D_{a+}^{\alpha} x_r^+(t))] & \text{if } x(\cdot) \text{ is expansive} \\ [({}^C D_{a+}^{\alpha} x_r^+(t), {}^C D_{a+}^{\alpha} x_r^-(t))] & \text{if } x(\cdot) \text{ is contractive} \end{cases}. \quad (31)$$

Theorem 4 [26]. Let $x \in AC([a, b], \mathbb{R}_{\mathcal{F}})$ be a F -correlated fuzzy process, F -differentiable with $[x(t)]_r = [x_r^-(t), x_r^+(t)]$, for $r \in [0, 1]$, and $0 < \alpha \leq 1$. In this case, $[({}^C F D_{a+}^{\alpha} x)(t)]_r =$

$$\begin{cases} \left[\int_a^t \frac{(t-s)^{-\alpha}}{\Gamma(1-\alpha)} (x_r^-)'(s) ds, \int_a^t \frac{(t-s)^{-\alpha}}{\Gamma(1-\alpha)} (x_r^+)'(s) ds \right] & \text{if } x \text{ is expansive} \\ \left[\int_a^t \frac{(t-s)^{-\alpha}}{\Gamma(1-\alpha)} (x_r^+)'(s) ds, \int_a^t \frac{(t-s)^{-\alpha}}{\Gamma(1-\alpha)} (x_r^-)'(s) ds \right] & \text{if } x \text{ is contractive} \end{cases}, \quad (32)$$

for $t \in [a, b]$.

In the fuzzy fractional calculus the derivative that the researchers usually used is the generalized Hukuhara derivative (gH). Our results via F -correlated derivative are similar to those obtained via gH. However, the domains of arithmetic operations via F -correlated process and via gH are different as can be seen in (8)–(11). Although the difference (9) coincides with the difference gH, the multiplication and division operations F -correlated do not coincide with standard arithmetic operations, which are used with gH. These facts imply that the solutions of fuzzy differential equations via gH and via F can be different. For example via numerical simulations [32].

4 Fuzzy Interactive Fractional Differential Equations

Consider the following fuzzy fractional initial value problem given by the F -correlated fractional Caputo derivative of order $\alpha \in (0, 1]$

$$\begin{aligned}({}^C F D_{a+}^{\alpha} x)(t) &= f(t, x(t)), \\ x(a) &= x_0 \in \mathbb{R}_{\mathcal{F}},\end{aligned}\tag{33}$$

where $f : (a, b] \times \mathbb{R}_{\mathcal{F}} \rightarrow \mathbb{R}_{\mathcal{F}}$ is fuzzy continuous function on Pompeiu-Hausdorff metric. The F -correlated fuzzy process $x : [a, b] \rightarrow \mathbb{R}_{\mathcal{F}}$ is said to be a solution of (33) if $x \in C([a, b], \mathbb{R}_{\mathcal{F}})$, $x(a) = x_0$ and $({}^C F D_{a+}^{\alpha} x)(t) = f(t, x(t))$, for all $t \in (a, b]$.

For all $r \in [0, 1]$, consider $[x_0]_r = [x_{0r}^-, x_{0r}^+]$ and

$$[f(t, x)]_r = [f_r^-(t, x_r^-(t), x_r^+(t)), f_r^+(t, x_r^-(t), x_r^+(t))].$$

Thus, for all $r \in [0, 1]$, the solutions $x(\cdot)$ of (33) satisfy [26]

– if x is expansive on $[a, b]$

$$\begin{aligned}({}^C F D_{a+}^{\alpha} x_r^-)(t) &= f_r^-(t, x_r^-(t), x_r^+(t)); \quad x_r^-(a) = x_{0r}^- \\({}^C F D_{a+}^{\alpha} x_r^+)(t) &= f_r^+(t, x_r^-(t), x_r^+(t)); \quad x_r^+(a) = x_{0r}^+\end{aligned}\tag{34}$$

– if x is contractive on $[a, b]$

$$\begin{aligned}({}^C F D_{a+}^{\alpha} x_r^+)(t) &= f_r^-(t, x_r^-(t), x_r^+(t)); \quad x_r^-(a) = x_{0r}^- \\({}^C F D_{a+}^{\alpha} x_r^-)(t) &= f_r^+(t, x_r^-(t), x_r^+(t)); \quad x_r^+(a) = x_{0r}^+.\end{aligned}\tag{35}$$

The Fuzzy Fractional Initial Value Problems (FFIVPs) given by (34) and (35) boil down to classical Fractional Initial Value Problems. Hence, numerical solution for the FFIVP can be provided by the method proposed by [22], which is based on the modified trapezoidal rule and the fractional Euler's method, for Caputo fractional derivative. The generalization of this method for FFIVPs can be founded in [17].

Consider a fractional initial (classical) value problem given by

$${}^C D_{a+}^{\alpha} x(t) = f(t, x(t)), \quad x(0) = x_0.$$

Let $[0, a]$ be an interval divided in k subintervals $[t_i, t_{i+1}]$ with equal size h . Then the solution $x(t_j)$, for each $t_j \in [0, a]$, is given by

$$\begin{aligned}x(t_j) &= x_0 + M((j-1)^{\alpha+1} - (j-\alpha-1)j^{\alpha})f(t_0, x(t_0)) \\&+ M \sum_{i=1}^{j-1} ((j-i+1)^{\alpha+1} - 2(j-i)^{\alpha+1} + (j-i-1)^{\alpha+1})f(t_i, x(t_i)) \\&+ M(f(t_j, x(t_{j-1})) + Nf(t_{j-1}, x(t_{j-1}))),\end{aligned}\tag{36}$$

where

$$M = \frac{h^{\alpha}}{\Gamma(\alpha+2)} \quad \text{and} \quad N = \frac{h^{\alpha}}{\Gamma(\alpha+1)}.$$

Next an application of this method is applied in a HIV model that describes the viral dynamics of individuals, under antiretroviral treatment.

5 Viral Dynamics for Seropositive Individuals Under Antiretroviral Treatment (ART)

Data obtained in various studies [20,24] suggests that the virus concentration decay in bloodstream is approximately exponential after the patient was placed on a potent antiretroviral drug. One of the simplest models of viral dynamics consider the effect of antiretroviral as Eq. (37)

$$\frac{dv}{dt} = P - cv, \quad (37)$$

where P is the rate of virus production, c is the clearance rate and $v = v(t)$ is the virus concentration. This model assumes that the treatment is initiated at $t = 0$ and that the efficiency of the treatment is partial when $P > 0$, once the drug could not instantly block all viral production [23].

Although Eq. (37) describes the viral dynamics considering the effect of the drugs, the classical differential equation does not take some behaviours of this dynamic into account. For instance, there is a time interval between the infection of the cell and the release of new infectious viral particles, called *virions*. This means that there exists an intracellular delay, which can be modeled by a system of delay differential equation [9]. For this reason consider the gamma distribution. According to Mittler et al. [18] the gamma distribution can be used to describe the delay presented in the HIV dynamic, because the curves of the gamma distribution are more realistic than the curves of normal distribution, since some cells may take a long time to release virus.

The gamma distribution is widely used to deal with fractional differential equations. Due to the well-established fractional calculus theory, here we adopt the Caputo derivative. To this end, consider the intracellular delay given by the difference $t - s$, where $0 < s < t$. The Caputo derivative of v of order $\alpha \in [0, 1]$ is given by

$$D_C^\alpha v(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t v'(s)(t-s)^{-\alpha} ds, \quad (38)$$

which can be rewritten as

$$D_C^\alpha v(t) = \int_0^t [f(t-s)e^{t-s}] v'(s) ds, \quad (39)$$

where $f(t-s)$ is the gamma distribution of $t-s$, that is, for $0 < s < t$ and $\alpha \in [0, 1]$,

$$f(t-s) = \frac{(t-s)^{-\alpha} e^{-(t-s)}}{\Gamma(1-\alpha)}. \quad (40)$$

Therefore, as a non local operator, the Caputo derivative provides the effect of intracellular delay at the virus concentration. In this case, it is weighted by the exponential function e^{t-s} , which assign more weight to a shorter delay, as depicted in Fig. 1.

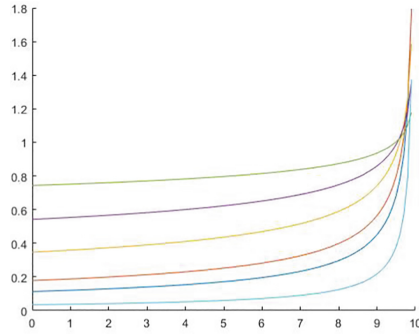


Fig. 1. Representation of wheighted gamma distribution of intracellular delay.

Now, since the initial value of the virus concentration is usually uncertain, the initial condition to this model is described by a fuzzy number, which gives raise to the following Fuzzy Fractional Differential Equation with Caputo derivative

$$\begin{cases} ({}^C D^\alpha v)(t) + cv(t) = P, \\ v(0) = V_0 \in \mathbb{R}_{\mathcal{F}} \end{cases} \quad (41)$$

where $c, P \in \mathbb{R}^+$.

Here we consider two cases for this dynamic. The first one is when the fuzzy process is expansive i.e, the diameter of the process is a non-decreasing function at t , and the second one is when the fuzzy process is contractive, i.e, the diameter of the process is a non-increasing function at t . So, the function $f(t_i, x(t_i))$ that appears in the formula (36) must be adapted for each case, using the formulas (34) and (35).

Figure 2 illustrates the numerical solution for the FFIVP considering different fuzzy processes. In the case where one expects that uncertainty increases over time, then we must take an expansive process into account, as Subfigure (a) of Fig. 2 depicts. On the other hand, in the case where one expects that uncertainty decreases over time, then we must take a contractive process into account, as Subfigure (b) of Fig. 2 depicts.

Note that the numerical solution for the expansive process assumes negative values. Since we are dealing with the number of infected individuals, the numerical solution obtained from the expansive process is not consistent. This implies that only the contractive process is appropriated for this model. Now, we can still interpret the expansive process for this case. Although it assumes negative values, we verify that the evolution of the disease increases over time. In addition, its width increases, illustrating a chaotic scenario with increasing uncertainty.

Also observe that, in both cases, there is an oscillation in the beginning of the solutions. This is a typical behavior of problems involving FDEs.

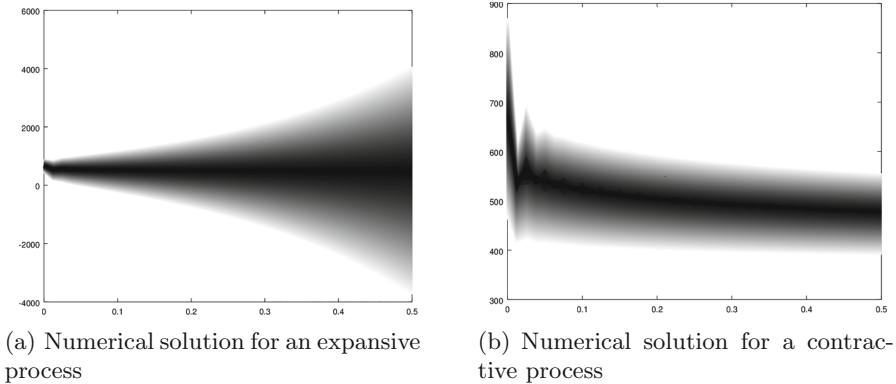


Fig. 2. Numerical solution to the HIV model given by (41). The gray lines represent the r -levels of the fuzzy solutions, where their endpoints for r varying from 0 to 1 are represented respectively from the gray-scale lines varying from white to black. The initial condition is given by $v_0 = (470; 670; 870)$, $h = 0.125$ and $\alpha = 0.3$.

6 Final Comments

In this manuscript, we present an HIV viral dynamics model for individuals under antiretroviral treatment. The modeling was done by considering Interactive Fuzzy Fractional Differential Equations (IFFDE), that considers an underlying interactivity in the process and its use is justified by the fact that biological processes have memories in their dynamics [2, 3].

Viral load, as an autocorrelated process, considers that there is a memory coefficient in its modeling, this means that the instant of time t is associated to the previous instant time $t - 1$. Specifically, the Caputo fractional derivative allows us to take the intracellular delay as a non fixed value into account, by means of the gamma distribution. This distribution assigns more weight to a lower intracellular delay and it carries biological informations, in contrast to the classical derivatives. The FFIVP via Caputo derivative provides solutions related to the value of $\alpha \in [0, 1]$, once the bigger the value of α , the faster the viral load decays.

The uncertainty in the number of viral particles produced by each infected cell suggests that the viral load can be represented as a fuzzy number. Through IFFDE, it was possible to describe the phenomenon from two points of view: expansive process (the diameter of the solution is a non-decreasing function in t) and contractive process (the diameter of the solution is a non-increasing function in t), in contrast to other methods given in the literature.

Finally, we present a numerical solution to illustrate the obtained results. In both cases, a decrease in plasma viremia in the bloodstream is obtained, which corroborates the data presented in the literature [21].

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References

1. Agarwal, R.P., Lakshmikantham, V., Nieto, J.J.: On the concept of solution for fractional differential equations with uncertainty. *Nonlinear Anal.: Theory Methods Appl.* **72**(6), 2859–2862 (2010)
2. Arafa, A.A.M., Rida, S.Z., Khalil, M.: Fractional modeling dynamics of HIV and CD4+ T-cells during primary infection. *Nonlinear Biomed. Phys.* **6**(1), 1 (2012)
3. Arafa, A.A.M., Rida, S.Z., Khalil, M.: Fractional-order model of HIV infection with drug therapy effect. *J. Egypt. Math. Soc.* **22**(3), 538–543 (2014)
4. Barros, L.C., Bassanezi, R.C., Lodwick, W.A.: *A First Course in Fuzzy Logic, Fuzzy Dynamical Systems, and Biomathematics*, 1st edn. Springer, Heidelberg (2017). <https://doi.org/10.1007/978-3-662-53324-6>
5. Barros, L.C., Santo Pedro, F.: Fuzzy differential equations with interactive derivative. *Fuzzy Sets Syst.* **309**, 64–80 (2017)
6. Bede, B.: *Mathematics of Fuzzy Sets and Fuzzy Logic*. Springer, Heidelberg (2013). <https://doi.org/10.1007/978-3-642-35221-8>
7. Cabral, V.M., Barros, L.C.: Fuzzy differential equation with completely correlated parameters. *Fuzzy Sets Syst.* **265**, 86–98 (2015)
8. Carlsson, C., Fullér, R., Majlender, P.: Additions of completely correlated fuzzy numbers. In: *Proceedings of 2004 IEEE International Conference on Fuzzy Systems*, vol. 1, pp. 535–539 (2004)
9. Culshaw, R.V., Ruan, S.: A delay-differential equation model of HIV infection of CD4+ T-cells. *Math. Biosci.* **165**(1), 27–39 (2000)
10. Dubois, D., Prade, H.: Additions of interactive fuzzy numbers. *IEEE Trans. Autom. Control* **26**(4), 926–936 (1981)
11. Esmi, E., Santo Pedro, F., Barros, L.C., Lodwick, W.A.: Fréchet derivative for linearly correlated fuzzy function. *Inf. Sci.* **435**, 150–160 (2018)
12. Fullér, R.: *Fuzzy reasoning and fuzzy optimization*. Turku Centre for Computer Science (1998)
13. Kaleva, O.: Fuzzy differential equations. *Fuzzy Sets Syst.* **24**, 301–317 (1987)
14. Kilbas, A.A.A., Srivastava, H.M., Trujillo, J.J.: *Theory and Applications of Fractional Differential Equations*, vol. 204. Elsevier Science Limited, Amsterdam (2006)
15. Laiate B., Santo Pedro, F., Esmi E., Barros L.C.: HIV dynamics under antiretroviral treatment with interactivity. In: Lesot, M.-J., et al. (eds.) *IPMU 2020. CCIS*, vol. 1239, pp. 212–225. Springer, Heidelberg (2020)
16. Laiate, B., Jafelice, R.M., Esmi, E., Barros, L.C.: An interpretation of the fuzzy measure associated with choquet calculus for a HIV transference model. In: Kearfott, R.B., Batyrshin, I., Reformat, M., Ceberio, M., Kreinovich, V. (eds.) *IFSA/NAFIPS 2019*. AISC, vol. 1000, pp. 306–317. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-21920-8_28
17. Mazandarani, M., Kamyad, A.V.: Modified fractional Euler method for solving fuzzy fractional initial value problem. *Commun. Nonlinear Sci. Numer. Simul.* **18**, 12–21 (2013)
18. Mittler, J.E., Sulzer, B., Neumann, A.U., Perelson, A.S.: Influence of delayed viral production on viral dynamics in HIV-1 infected patients. *Math. Biosci.* **152**, 143–163 (1998)
19. Mizumoto, M., Tanaka, K.: Bounded-sum or bounded-difference for fuzzy sets. *Trans. IECE (D)* **59**, 905–912 (1976)
20. Nelson, P.W., Mittler, J.E., Perelson, A.S.: Effect of drug efficacy and the eclipse phase of the viral life cycle on estimates of HIV viral dynamic parameters. *J. Acquir. Immune Defic. Syndr.* **26**, 405–412 (2001)

21. Notermans, D.W., Goudsmit, J., Danner, S.A., DeWolf, F., Perelson, A.S., Mittler, J.: Rate of HIV-1 decline following antiretroviral therapy is related to viral load at baseline and drug regimen. *Aids* **12**(12), 1483–1490 (1998)
22. Odibat, Z.M., Momani, S.: An algorithm for the numerical solution of differential equations of fractional order. *J. Appl. Math. Inf.* **26**, 15–27 (2008)
23. Perelson, A.S., Nelson, P.W.: Mathematical analysis of HIV-1 dynamics in vivo. *Soc. Ind. Appl. Math.* **41**(1), 3–44 (1999)
24. Perelson, A.S., et al.: Decay characteristics of HIV-1-infected compartments during combination therapy. *Nature* **387**(6629), 188–191 (1997)
25. Pinto, N.J.B., Esmi, E., Wasques, V.F., Barros, L.C.: Least square method with quasi linearly interactive fuzzy data: fitting an HIV dataset. In: Kearfott, R., Batyrshin, I., Reformat, M., Ceberio, M., Kreinovich, V. (eds.) *IFSA/NAFIPS 2019*. *Advances in Intelligent Systems and Computing*, vol. 1000, pp. 177–189. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-21920-8_17
26. Santo Pedro, F., Martins, M. M., Wasques, V. F., Esmi, E., Barros, L. C.: Fuzzy fractional under interactive derivative. *Fuzzy Sets Syst.* (submitted)
27. Santo Pedro, F., Barros, L.C., Esmi, E.: Population growth model via interactive fuzzy differential equation. *Inf. Sci.* **481**, 160–173 (2019)
28. Santo Pedro, F., Esmi, E., Barros, L.C.: Calculus for linearly correlated fuzzy function using Fréchet derivative and Riemann integral. *Inf. Sci.* **512**, 219–237 (2020)
29. Santo Pedro, F., Barros, L.C., Esmi, E.: Measure of interactivity on fuzzy process autocorrelated: malthusian model. In: Kearfott, R., Batyrshin, I., Reformat, M., Ceberio, M., Kreinovich, V. (eds.) *FSA/NAFIPS 2019*. *Advances in Intelligent Systems and Computing*, vol. 1000, pp. 567–577. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-21920-8_50
30. Santo Pedro, F., Barros, L.C., Esmi, E.: Interactive fuzzy process: an epidemiological model. In: Barreto, G., Coelho, R. (eds.) *NAFIPS 2018. Communications in Computer and Information Science*, vol. 831, pp. 108–118. Springer, Cham (2019). https://doi.org/10.1007/978-3-319-95312-0_10
31. Van Ngo, H., Lupulescu, V., O'Regan, D.: A note on initial value problems for fractional fuzzy differential equations. *Fuzzy Sets Syst.* **347**, 54–69 (2018)
32. Wasques, V.F., Esmi, E., Barros, L.C., Bede, B.: Comparison between numerical solutions of fuzzy initial-value problems via interactive and standard arithmetics. In: Kearfott, R.B., Batyrshin, I., Reformat, M., Ceberio, M., Kreinovich, V. (eds.) *IFSA/NAFIPS 2019*. *AISC*, vol. 1000, pp. 704–715. Springer, Cham (2019). https://doi.org/10.1007/978-3-030-21920-8_62
33. Wasques, V.F., Esmi, E., Barros, L.C., Sussner, P.: Numerical solutions for bidimensional initial value problem with interactive fuzzy numbers. In: Barreto, G., Coelho, R. (eds.) *NAFIPS 2018. Communications in Computer and Information Science*, vol. 831, pp. 84–95. Springer, Cham (2018). https://doi.org/10.1007/978-3-319-95312-0_8
34. Wasques, V.F., Esmi, E., Barros, L.C., Sussner, P.: The generalized fuzzy derivative is interactive. *Inf. Sci.* **519**, 93–109 (2020)
35. Zahra, A., Dumitru, B., Babak, S., Guo-Cheng, W.: Spline collocation methods for systems of fuzzy fractional differential equations. *Chaos Solit. Fractals* **131**, 109510 (2020)