Stability analysis and optimal control of a fractional HIV-AIDS epidemic model with memory and general incidence rate

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Abstract. We investigate the celebrated mathematical SICA model but using fractional differential equations in order to better describe the dynamics of HIV-AIDS infection. The infection process is modelled by a general functional response and the memory effect is described by the Caputo fractional derivative. Stability and instability of equilibrium points are determined in terms of the basic reproduction number. Furthermore, a fractional optimal control system is formulated and the best strategy for minimizing the spread of the disease into the population is determined through numerical simulations based on the derived necessary optimality conditions.

Key words. HIV-AIDS infection; Fractional calculus; Fractional differential equations; Stability.

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1 Introduction

Acquired Immune Deficiency Syndrome (AIDS) is a chronic infectious disease caused by the human immunodeficiency virus (HIV). The virus attack and destruct the immune response system, which plays a crucial role to defend the human body against viral pathogens. The last statistics of The Joint United Nations Programme on HIV and AIDS (UNAIDS) show that 36.9 million people were living with HIV, where 21.7 million individuals were accessing anti-retro-viral therapy (ART) and 1.8 million became newly infected with HIV [1]. Therefore, the world is now facing huge challenges and should be committed to provide appropriate preventive strategies in order to control the AIDS epidemic process.

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In the course of history, mathematical modelling of natural phenomena, described by ordinary differential equations (ODE), has proven valuable in analysing various diseases dynamics, such as HIV/AIDS, Malaria, and Tuberculosis, and also plays an important role in better understanding the global behaviour of epidemiological models. However, memory has a crucial role in the evolution and control of any epidemic process. The experience or knowledge of people about the spread of a disease in the past, affects their response. If people know about the history of a certain disease in their environment, then they may use different precautions, such as vaccination and treatment. Consequently, incorporating memory seems very appropriate to study such epidemic models. This is done here through the use of fractional differentiation.

Fractional derivatives, which provide a generalization of the integer order derivative to an arbitrary order, has become an adequate mathematical tool to characterize the memory effect of complex systems. This particular property is neglected by integer order derivatives, which explains why fractional calculus is nowadays widely applied to model various dynamical processes in different fields of science and engineering, such as mechanics, image processing, viscoelasticity, bioengineering, finance, psychology, and biology. The advantage of using systems of fractional differential equations (FDE) over ODE systems is that they provide an excellent tool for the description of memory and hereditary properties. Indeed, the fractional derivative is a non-local operator, in contrast with the integer derivative, which means that if we want to compute a fractional derivative at some point \( t = t_1 \), we need all its history from the starting point \( t = t_0 \) up to the point \( t = t_1 \). Furthermore, another feature of FDE is that their stability region is larger than ODE, which can help to reduce errors arising from the neglected parameters in modelling real-life problems.

Since modelling of dynamic systems by ODE cannot precisely describe experimental and measurement data, FDE are now being extensively applied to study and control the dynamics of infectious diseases. In [13], Rihan et al. analyse a fractional model for HCV dynamics in presence of interferon-α (IFN) treatment. According to numerical simulations and the real data, they also confirm that the FDE are better descriptors of HCV systems than ODE. In the study of Arafa et al. [14], the authors compared between the results of the fractional order model, the results of the integer model, and the measured real data obtained from 10 patients during primary HIV infection, and they proved that the results of the fractional order model give better predictions to the plasma virus load of the patients than those of the integer order model. In the work of Wojtak et al. [15], the authors investigate the uniform asymptotic stability of the unique endemic equilibrium for a Caputo fractional-order tuberculosis (TB) model. They confirm that the proposed fractional-order model provides richer and more flexible results when compared with the corresponding integer-order TB model. In [16], the authors propose a non-linear fractional-order model to explain and understand the outbreaks of influenza A (H1N1) worldwide. They show that the fractional-order model gives wider peaks and leads to better approximations for the real epidemic data. The authors in [17] propose a fractional-order model and show, through numerical simulations, that the fractional models fit better the first dengue epidemic recorded in the Cape Verde islands off the coast of West Africa when compared with ODE models. For fractional optimal control problems (FOCP), we can cite the work of Sweilam et al., where a fractional optimal control model for tuberculosis infection, including the impact of diabetes and resistant strains, is studied [18]. Also, we mention the study of Rosa and Torres, where optimal control of a fractional order epidemic model with application to human respiratory syncytial virus infection is proposed and studied [19]. In the case of HIV/AIDS infection, Kheiri and Jafari propose and analyse a fractional optimal control of an HIV/AIDS epidemic model with random testing and contact tracing [20]. On the other hand, a fractional malaria transmission model is investigated by Pinto and Tenreiro Machado [21] on the basis of optimal control techniques. Other works can be found in [18/21/22].

From all this biological and mathematical considerations, here we are interested to investigate the transmission process of HIV-AIDS infection, taking into account the memory effect that exists in most dynamical systems. The infection process is modelled by a general incidence rate which covers, under some hypothesis, the most functional response existing in the literature. Using Lyapunov functionals and the fractional invariance principal, we prove that the global dynamics of the model is determined by the basic reproduction number. Furthermore, in order to minimize the spread of the disease into the population, a fractional optimal control is formulated and numerically solved based on Moroccan data.

We organized the paper as follows. In Section 2, some properties of the solutions are given and existence conditions of the equilibrium points are discussed. The stability analysis of the equilibria is studied in Section 3 while in Section 4 the fractional optimal control of the model is investigated. An application of our analysis to Morocco data is given in Section 5. We end with Section 6 of conclusions.

2 Well-possessedness of the model

In this section, we propose a fractional SICA epidemic model with general incidence rate (Section 2.2) and give some preliminary but fundamental results that include the well-possessedness of the model and existence conditions of the possible equilibria (Section 2.2).
2.1 Mathematical model

Taking into consideration the memory effect presented by Caputo fractional derivatives, we propose the following SICA epidemic model with general incidence rate:

\[
\begin{align*}
\frac{d^\alpha S(t)}{dt^\alpha} &= A - \mu S(t) - f(S(t), I(t)) I(t), \\
\frac{d^\alpha I(t)}{dt^\alpha} &= f(S(t), I(t)) I(t) - (\rho + \phi + \mu) I(t) + \sigma A(t) + \omega C(t), \\
\frac{d^\alpha C(t)}{dt^\alpha} &= \phi I(t) - (\omega + \mu) C(t), \\
\frac{d^\alpha A(t)}{dt^\alpha} &= \rho I(t) - (\sigma + \mu + d) A(t),
\end{align*}
\]

where \( \frac{d^\alpha}{dt^\alpha} \) represents the Caputo fractional derivative of order \( 0 < \alpha \leq 1 \) defined for an arbitrary function \( \varphi \) \(^{(27)}\) by

\[
\frac{d^\alpha}{dt^\alpha} \varphi(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{\varphi'(x)}{(t-x)^\alpha} dx.
\]

Note that when \( \alpha \to 1 \) system \(^{(1)}\) becomes a classical system of ODEs.

**Remark 1** The Caputo derivative is a good choice in order to include long-term memory effects. Indeed, the power-law function \( (t-x)^{-\alpha} \), that appears in its definition, exhibits a slow decay and the state of the system at quite early times also contribute to the evolution of the system. This type of kernel guarantees the existence of scaling features as it is often intrinsic in natural phenomena. Hence, fractional derivatives, when introducing a convolution integral with a power-law memory kernel, are useful to describe memory effects in dynamical systems. The decaying rate of the memory kernel (a time-correlation function) depends on \( \alpha \). A lower value of \( \alpha \) corresponds to more slowly-decaying time-correlation functions (long memory). In some sense, the strength of the memory is controlled by \( \alpha \). As \( \alpha \to 1 \), the influence of memory decreases: the system tends toward a memoryless system. While modeling various memory phenomena, one observes that memory processes usually consist of two stages. One is short with permanent retention, while the other is governed by a simple model of fractional derivative. It has been shown that fractional models perfectly fits the test data of memory phenomena in different disciplines, for example in mechanics, but also in biology and psychology. The interested reader in these issues is referred to \(^{(28)}\).

The variables \( S, I, C \) and \( A \) represent individuals, respectively, susceptible, HIV infected with no clinical symptoms of AIDS, HIV infected under ART treatment, with a viral load remaining low, and HIV infected with AIDS clinical symptoms. The susceptible population is increased by the recruitment of individuals at a rate \( A \), while \( \mu \) is the natural death rate of all individuals. Susceptible individuals acquire HIV infection at a rate \( f(S, I) \) by following effective contact with those in the class \( I \). HIV-infected individuals with no AIDS symptoms \( I \) progress to the class \( C \) at a rate \( \phi \) and, if they do not follow treatment, to the class \( A \) at a rate \( \rho \). HIV-infected individuals with AIDS symptoms are treated for HIV at rate \( \sigma \). Individuals in the class \( C \) that do not maintain treatment, leave to the class \( I \) at a rate \( \omega \). We assume that only HIV-infected individuals with AIDS symptoms \( A \) suffer from an AIDS induced death rate, denoted by \( d \). As in \(^{(29)}\), the general incidence function \( f(S, I) \) is assumed to be continuously differentiable in the interior of \( \mathbb{R}_+^2 \) and to satisfy the following hypotheses:

\[
\begin{align*}
&f(0, I) = 0, \quad \text{for all } I \geq 0, \quad (H_1) \\
&\frac{\partial f}{\partial S}(S, I) > 0, \quad \text{for all } S > 0 \text{ and } I \geq 0, \quad (H_2) \\
&\frac{\partial f}{\partial I}(S, I) \leq 0, \quad \text{for all } S \geq 0 \text{ and } I \geq 0. \quad (H_3)
\end{align*}
\]

Biologically, the three hypotheses \( H_1, H_2 \) and \( H_3 \) are reasonable. Indeed, the first means that the incidence function is equal to zero if there are no susceptible individuals. The second one signifies that the incidence rate is increasing when the number of infected individuals is constant and the number of susceptible individuals increases. This means that the higher the number of susceptible individuals, the higher the average number of individuals infected over time. The last hypothesis means that the higher the number of infected individuals, the lower the average number of infected individuals over time.

2.2 Preliminary results

Since model \(^{(1)}\) describes the evolution of population, we need to prove that the solutions are non-negative and bounded for all time. These properties imply the global existence of solutions. For biological considerations, we assume that the initial conditions satisfy

\[
S(0) = S_0 \geq 0, \quad I(0) = I_0 \geq 0, \quad C(0) = C_0 \geq 0, \quad A(0) = A_0 \geq 0.
\]
Theorem 1 For any initial conditions satisfying (2), system (1) has a unique solution on \([0, +\infty)\). Moreover, this solution remains non-negative and bounded for all \(t \geq 0\). In addition, we have

\[
N(t) \leq N(0) + \frac{A}{\mu}
\]

where \(N(t) = S(t) + I(t) + C(t) + A(t)\).

Proof First, system (1) can be written as follows:

\[
\frac{C_0}{D_t^\alpha} X(t) = F(X),
\]

where

\[
X(t) = \begin{pmatrix} S(t) \\ I(t) \\ C(t) \\ A(t) \end{pmatrix} \quad \text{and} \quad F(X) = \begin{pmatrix} A - \mu S(t) - f(S(t), I(t)) I(t) \\ f(S(t), I(t)) I(t) - (\rho + \phi + \mu) I(t) + \sigma A(t) + \omega C(t) \\ \phi I(t) - (\omega + \mu) C(t) \\ \rho I(t) - (\sigma + \mu + d) A(t) \end{pmatrix}.
\]

Clearly, function \(F\) satisfies the conditions given in [30]. Then, there exists a unique local solution of the initial value problem (3). Now, we show that the non-negative orthant \(\mathbb{R}_+^4 = \{X \in \mathbb{R}^4 : X \geq 0\}\) is a positively invariant set. We denote by \(t^*\) the first time at which at least one of the variables is equal to zero:

\[
t^* = \min\{t > 0 : S(t)I(t)C(t)A(t) = 0\}.
\]

We discuss four cases. (i) If \(S(t^*) = 0\), then it follows that \(I(t) \geq 0, C(t) \geq 0\) and \(A(t) \geq 0\) when \(t \in [0, t^*)\). From the first equation of system (1), we have

\[
\frac{C_0}{D_t^\alpha} S(t)_{t=t^*} = \Lambda > 0.
\]

By the generalized mean value theorem [31], \(S(t)\) is a non-decreasing function for \(t \in (t^* - \epsilon, t^*)\), where \(\epsilon\) is sufficiently small. So, \(S(t) < 0\) for \(t \in (t^* - \epsilon, t^*)\), which is a contradiction with \(S(t) > 0\) when \(t \in (0, t^*)\). (ii) Let \(I(t^*) = 0\). In this case, we have \(S(t) \geq 0, C(t) \geq 0\) and \(A(t) \geq 0\) when \(t \in [0, t^*)\). From the second equation of system (1), we have

\[
\frac{C_0}{D_t^\alpha} I(t)_{t=t^*} = \sigma A(t) + \omega C(t) \geq 0.
\]

Hence, function \(I(t)\) is non-decreasing for \(t \in (t^* - \epsilon, t^*)\), where \(\epsilon\) is sufficiently small. Thus, \(I(t) \leq 0\) for \(t \in (t^* - \epsilon, t^*)\). This is in contradiction with \(I(t) > 0\) when \(t \in (0, t^*)\). (iii) Let \(C(t^*) = 0\). Then, \(S(t) \geq 0, I(t) \geq 0\) and \(A(t) \geq 0\) when \(t \in [0, t^*)\). From the third equation of system (1), we have

\[
\frac{C_0}{D_t^\alpha} C(t)_{t=t^*} = \phi I(t) \geq 0.
\]

Therefore, function \(C(t)\) is non-decreasing for \(t \in (t^* - \epsilon, t^*)\), where \(\epsilon\) is sufficiently small. So \(C(t) \leq 0\) for \(t \in (t^* - \epsilon, t^*)\). That is a contradiction with \(C(t) > 0\) when \(t \in (0, t^*)\). (iv) Let \(A(t^*) = 0\). Hence, \(S(t) \geq 0, I(t) \geq 0\) and \(C(t) \geq 0\) when \(t \in [0, t^*)\). From the last equation of system (1), we have

\[
\frac{C_0}{D_t^\alpha} A(t)_{t=t^*} = \rho I(t) \geq 0.
\]

As a result, function \(A(t)\) is non-decreasing for \(t \in (t^* - \epsilon, t^*)\), where \(\epsilon\) is sufficiently small. So \(A(t) \leq 0\) for \(t \in (t^* - \epsilon, t^*)\), which is in contradiction with \(A(t) > 0\) when \(t \in (0, t^*)\).

Next, we prove the boundedness of solutions. By adding together all the equations of system (1), one has that

\[
\frac{C_0}{D_t^\alpha} N(t) \leq A - \mu N(t).
\]

Hence,

\[
N(t) \leq N(0)E_\alpha(-\mu t^\alpha) + \frac{A}{\mu}[1 - E_\alpha(-\mu t^\alpha)].
\]

Since \(0 \leq E_\alpha(-\mu t^\alpha) \leq 1\), we obtain

\[
N(t) \leq N(0) + \frac{A}{\mu}.
\]

Consequently, the solutions of system (1) are bounded for \(t \geq 0\). Finally, the existence and uniqueness of solution for the initial value problem (3) in \([0, +\infty)\) is deduced from [30] Theorem 3.1 and Remark 3.2. \(\square\)
Now, we investigate the existence of equilibria of (1). It is easy to see that system (1) has a disease-free equilibrium of the form

$$E_f = \left( \frac{A}{\mu}, 0, 0, 0 \right).$$

Therefore, the basic reproduction number $R_0$ of system (1) is given by

$$R_0 = \frac{f \left( \frac{A}{\mu}, 0 \right) \xi_2 \xi_3}{\mathcal{D}},$$

where

$$\xi_2 = \omega + \mu,$$

$$\xi_3 = \sigma + \mu + d,$$

$$\mathcal{D} = \mu [\xi_2 (\xi_3 + \rho) + \phi \xi_3 + \rho d] + \rho \omega d.$$

Biologically, this number represents the average of new infected individuals produced by a single HIV-infected/AIDS individual on contact in a completely susceptible population.

The other equilibria satisfy the following system:

$$\begin{align*}
A - \mu S(t) - f(S(t), I(t)) I(t) &= 0, \\
f(S(t), I(t)) I(t) - \xi_1 I(t) + \sigma A(t) + \omega C(t) &= 0, \\
\phi I(t) - \xi_2 C(t) &= 0, \\
\rho I(t) - \xi_3 A(t) &= 0,
\end{align*}$$

where $\xi_1 = \rho + \phi + \mu$.

Since FDEs have the same equilibrium points as ODEs counterparts, then we have the following direct result from [32].

**Theorem 2**

(i) If $R_0 \leq 1$, then system (1) has a unique disease-free equilibrium of form (4).

(ii) If $R_0 > 1$, then the disease-free equilibrium is still present and system (1) has a unique endemic equilibrium of the form $E^* = (S^*, I^*, C^*, A^*)$ with $S^* \in \left( 0, \frac{A}{\mu} \right)$, $I^* > 0$, $C^* > 0$, and $A^* > 0$.

### 3 Global stability

The aim of this section is to establish the global stability of equilibria of (1) by using the fractional La-Salle’s invariance principle and an important lemma presented in [33,34]. Firstly, we have the following global stability result for the infection-free equilibrium $E_f$.

**Theorem 3** The disease-free equilibrium $E_f$ is globally asymptotically stable if $R_0 \leq 1$.

**Proof** For the global stability of $E_f$, we construct the following Lyapunov functional:

$$V_1(S, I, C, A) = S - S_0 - \int_{S_0}^S \frac{f(S_0, 0)}{f(X, 0)} dX + I + \frac{\omega}{\xi_2} C + \frac{\sigma}{\xi_3} A,$$

where $S_0 = \frac{A}{\mu}$. Obviously, functional $V_1$ is non-negative. Computing the fractional time derivative of $V_1$ along the solution of (1), we get

$$\frac{D_t^\alpha}{0} V_1 = \frac{D_t^\alpha}{0} \left( S - S_0 - \int_{S_0}^S \frac{f(S_0, 0)}{f(X, 0)} dX + \frac{\omega}{\xi_2} D_t^\alpha C + \frac{\sigma}{\xi_3} D_t^\alpha A \right) + \frac{C}{0} D_t^\alpha I.$$

We start by proving that

$$\frac{C}{0} D_t^\alpha \left( S - S_0 - \int_{S_0}^S \frac{f(S_0, 0)}{f(X, 0)} dX \right) \leq \left( 1 - \frac{f(S_0, 0)}{f(S, 0)} \right) \frac{C}{0} D_t^\alpha S. \quad (6)$$
Hence, the inequality (7) can be written as

\[ C_0 \alpha D_t^\alpha S(t) - f(S,0)_0C_0 \alpha D_t^\alpha \left[ \int_{S_0}^S \frac{1}{f(X,0)} dX \right] \leq 0. \]  

(7)

Using the definition of the Caputo fractional derivative, we have

\[ C_0 \alpha D_t^\alpha S(t) = \frac{1}{\Gamma(1-\alpha)} \int_t^t S'(y) (t - y)^{\alpha-1} dy \]

and

\[ C_0 \alpha D_t^\alpha \left[ \int_{S_0}^S \frac{1}{f(X,0)} dX \right] = \frac{1}{\Gamma(1-\alpha)} \int_t^t S'(y) (t - y)^{\alpha-1} f(S,y) dX. \]

Consequently, the inequality (7) can be written as

\[ \frac{1}{\Gamma(1-\alpha)} \int_t^t S'(y) (t - y)^{\alpha-1} \left( 1 - \frac{f(S(t),0)}{f(S,y),0} \right) dy \leq 0. \]  

(8)

Now, we show that inequality (8) holds. Denoting

\[ \Psi(t) = \frac{1}{\Gamma(1-\alpha)} \int_t^t S'(y) (t - y)^{\alpha-1} \left( 1 - \frac{f(S(t),0)}{f(S,y),0} \right) dy, \]

we integrate by parts defining

\[ v(y) = \frac{(t - y)^{-\alpha}}{\Gamma(1-\alpha)}, \quad v'(y) = \frac{\alpha(t - y)^{-(\alpha+1)}}{\Gamma(1-\alpha)} \]

and

\[ w'(y) = S'(y) \left( 1 - \frac{f(S(t),0)}{f(S,y),0} \right), \quad w(y) = S(y) - S(t) - \int_{S(t)}^{S(y)} \frac{f(S(t),0)}{f(X,0)} dX, \]

to obtain

\[ \Psi(t) = \left[ \frac{(t - y)^{-\alpha}}{\Gamma(1-\alpha)} \left( S(y) - S(t) - \int_{S(t)}^{S(y)} \frac{f(S(t),0)}{f(X,0)} dX \right) \right] |_{y=t} - \left[ \frac{(t - t_0)^{-\alpha}}{\Gamma(1-\alpha)} \left( S(t_0) - S(t) - \int_{S(t)}^{S(t_0)} \frac{f(S(t),0)}{f(X,0)} dX \right) \right] - \int_{t_0}^t \alpha(t - y)^{-(\alpha+1)} \left( S(y) - S(t) - \int_{S(t)}^{S(y)} \frac{f(S(t),0)}{f(X,0)} dX \right) dy. \]  

(9)

We can easily see that the first term in (9) is undefined \( \left( \frac{0}{0} \right) \). We analyse the corresponding limit. By Hôpital’s rule, we get

\[ \lim_{y \to t} \frac{(t - y)^{-\alpha}}{\Gamma(1-\alpha)} \left( S(y) - S(t) - \int_{S(t)}^{S(y)} \frac{f(S(t),0)}{f(X,0)} dX \right) = \lim_{y \to t} \frac{S'(y) \left( 1 - \frac{f(S(t),0)}{f(S,y),0} \right)}{-\alpha \Gamma(1-\alpha)(t - y)^{\alpha-1}} = 0. \]

Hence,

\[ \Psi(t) = - \left[ \frac{(t - t_0)^{-\alpha}}{\Gamma(1-\alpha)} \left( S(t_0) - S(t) - \int_{S(t)}^{S(t_0)} \frac{f(S(t),0)}{f(X,0)} dX \right) \right] - \int_{t_0}^t \frac{\alpha(t - y)^{-(\alpha+1)}}{\Gamma(1-\alpha)} \left( S(y) - S(t) - \int_{S(t)}^{S(y)} \frac{f(S(t),0)}{f(X,0)} dX \right) dy. \]  

(10)
Then,
\[
\psi(t) = \frac{1}{\Gamma(1-\alpha)} \int_{t_0}^{t} \frac{S'(y)}{(t-y)^\alpha} \left( 1 - \frac{f(S(t), 0)}{f(S(y), 0)} \right) dy \leq 0.
\] (11)

As a result, the inequality (8) is satisfied. Consequently,
\[
\frac{C}{\alpha} D_0^\alpha V_1(t) \leq \left( 1 - \frac{f(S_0, 0)}{f(S, 0)} \right) \left( \frac{C}{\alpha} D_0^\alpha S + \frac{C}{\alpha} D_0^\alpha I + \frac{\omega}{\xi_2} \frac{C}{\alpha} D_0^\alpha C + \frac{\sigma}{\xi_3} \frac{C}{\alpha} D_0^\alpha A \right)
\]
\[
\leq \mu \left( 1 - \frac{f(S_0, 0)}{f(S, 0)} \right) (S_0 - S) + D \xi_2 \xi_3 I \left( \frac{f(S, I)}{f(S, 0)} R_0 - 1 \right)
\]
\[
\leq \mu \left( 1 - \frac{f(S_0, 0)}{f(S, 0)} \right) (S_0 - S) + \xi_2 \xi_3 I (R_0 - 1).
\]

Since \( f \) is an increasing function with respect to \( S \), we have
\[
1 - \frac{f(S_0, 0)}{f(S, 0)} \geq 0 \quad \text{for} \quad S \geq S_0,
\]
\[
1 - \frac{f(S_0, 0)}{f(S, 0)} < 0 \quad \text{for} \quad S < S_0.
\]

We finally get
\[
\left( 1 - \frac{f(S_0, 0)}{f(S, 0)} \right) (S_0 - S) \leq 0.
\]

Under the assumption \( R_0 \leq 1 \), it follows that \( \frac{C}{\alpha} D_0^\alpha V_1 \leq 0 \). Moreover, the largest compact invariant set in \( \{ (S, I, C, A) \in \mathbb{R}^4 : \frac{C}{\alpha} D_0^\alpha V_1 \leq 0 \} \) is the singleton \( E_f \). Accordingly, by LaSalle invariance principle, the infection-free equilibrium \( E_f \) is globally asymptotically stable when \( R_0 \leq 1 \).

Now, we focus on the stability of the endemic equilibrium \( E^* \). For that, we assume that the function \( f \) satisfies the following condition:
\[
\left( 1 - \frac{f(S, I)}{f(S, I^*)} \right) \left( \frac{f(S, I^*)}{f(S, I)} - \frac{I}{I^*} \right) \leq 0, \quad \text{for all} \quad S, I > 0.
\] (H4)

**Theorem 4**

(i) If \( R_0 > 1 \), then \( E_f \) becomes unstable.

(ii) If \( R_0 > 1 \) and (H4) holds, then the endemic equilibrium \( E^* \) is globally asymptotically stable.

**Proof** The proof of the instability of \( E_f \) is based on the computation of the Jacobian matrix of system (1), which is given at any equilibrium point \( E(S, I, C, A) \) by
\[
\begin{pmatrix}
-\mu - \frac{\partial f}{\partial S} I - f(S, I) & 0 & 0 \\
\frac{\partial f}{\partial I^*} I + f(S, I) & \omega & \sigma \\
0 & \phi & -\xi_2 \\
0 & \rho & -\xi_3
\end{pmatrix}.
\] (12)

We recall that \( E \) is locally asymptotically stable if all the eigenvalues \( \lambda \) of (12) satisfy the following condition (35):
\[
|\arg(\lambda)| > \frac{\alpha \pi}{2}
\]

From (12), the characteristic equation at \( E_f \) is given by
\[
g(\lambda) = \lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3 = 0,
\] (13)

where
\[
a_1 = \xi_1 + \xi_2 + \xi_3 - f(S_0, 0),
a_2 = \xi_1 \xi_2 + \xi_1 \xi_3 + \xi_2 \xi_3 - (\xi_2 + \xi_3) f(S_0, 0) - \phi \omega - \rho \sigma,
a_3 = (1 - R_0) D.
\]
Since the arithmetic mean is greater than or equal to the geometric mean, it is clear that $\lambda^* > 0$ and $g(\lambda^*) = 0$. In addition, we have $|\arg(\lambda^*)| = 0 < \frac{\alpha \pi}{2}$. Consequently, $E_f$ is unstable when $R_0 > 1$.

We define the Lyapunov functional $V_2$ for $E^*$ as follows:

$$V_2(S, I, C, A) = S - S^* - \int_{S^*}^{S} f(S^*, I^*) \, dX + I - I^* \ln \left( \frac{I^*}{I} \right) + \frac{\omega}{\xi_2} (C - C^* - C^* \ln \left( \frac{C}{C^*} \right)) + \frac{\sigma}{\xi_3} (A - A^* - A^* \ln \left( \frac{A}{A^*} \right)).$$

The fractional time derivative of $V_2$ along the positive solutions of system (11) satisfies

$$\frac{D_t^\alpha}{\alpha} V_2 \leq \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right) \frac{D_t^\alpha}{\alpha} S + \left(1 - \frac{I^*}{I} \right) \frac{D_t^\alpha}{\alpha} I + \frac{\omega}{\xi_2} \left(1 - \frac{C}{C^*} \right) \frac{D_t^\alpha}{\alpha} C + \frac{\sigma}{\xi_3} \left(1 - \frac{A}{A^*} \right) \frac{D_t^\alpha}{\alpha} A.$$

Applying the equalities $A = \mu S^* + f(S^*, I^*)$ and $\xi_1 I^* = f(S^*, I^*) I^* + \omega C^* + \sigma A^*$, we get

$$\frac{D_t^\alpha}{\alpha} V_2 \leq \mu (S^* - S) \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right) + f(S^*, I^*) \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right)$$

$$+ \frac{f(S^*, I^*) f(S, I^*)}{f(S, I^*)} \left(1 - \frac{C I^*}{C^* I} \right) + \frac{\sigma}{\xi_3} \left(1 - \frac{A I^*}{A^* I} \right) - f(S, I) I_1 - \xi I +$$

$$+ \frac{\omega}{\xi_2} \left(1 - \frac{C^* I}{C^* I^*} \right) + \frac{\sigma}{\xi_3} \left(1 - \frac{A^* I}{A^* I} \right) - f(S, I) I_1 - \xi I +$$

$$+ \frac{\omega}{\xi_2} \left(1 - \frac{C^* I}{C^* I^*} \right) + \frac{\sigma}{\xi_3} \left(1 - \frac{A^* I}{A^* I} \right) - f(S, I) I_1 - \xi I$$

$$\leq \mu (S^* - S) \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right) + \omega C^* \left(2 - \frac{C^* I}{C^* I^*} \right)$$

$$+ \sigma A^* \left(2 - \frac{A^* I}{A^* I} - \frac{A^* I}{A^* I^*} \right) + 2f(S^*, I^*) I^* + \frac{f(S^*, I^*) f(S, I)}{f(S, I^*)}$$

$$- \frac{f(S^*, I^*) f(S^*, I^*)}{f(S, I^*)} - f(S^*, I^*) I - f(S, I) I^*$$

$$\leq \mu (S^* - S) \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right) + \omega C^* \left(2 - \frac{C^* I}{C^* I^*} \right)$$

$$+ \sigma A^* \left(2 - \frac{A^* I}{A^* I} - \frac{A^* I}{A^* I^*} \right) + f(S^*, I^*) I^* \left[1 - \frac{f(S, I)}{f(S, I^*)} - \frac{f(S^*, I^*)}{f(S^*, I^*)} - \frac{I}{I^*} + \frac{f(S, I)}{f(S, I^*)} \right]$$

$$\leq \mu (S^* - S) \left(1 - \frac{f(S^*, I^*)}{f(S, I^*)} \right) + \omega C^* \left(2 - \frac{C^* I}{C^* I^*} \right)$$

$$+ \sigma A^* \left(2 - \frac{A^* I}{A^* I} - \frac{A^* I}{A^* I^*} \right) + f(S^*, I^*) I^* \left[1 - \frac{f(S, I)}{f(S, I^*)} - \frac{f(S^*, I^*)}{f(S^*, I^*)} - \frac{I}{I^*} + \frac{f(S, I)}{f(S, I^*)} \right].$$

Since the arithmetic mean is greater than or equal to the geometric mean, it is clear that

$$2 - \frac{C^* I}{C^* I^*} - \frac{C^* I}{C^* I^*} \leq 0,$$

$$2 - \frac{A^* I}{A^* I} - \frac{A^* I}{A^* I^*} \leq 0,$$

$$3 - \frac{f(S^*, I^*)}{f(S, I^*)} - \frac{f(S^*, I^*)}{f(S^*, I^*)} - \frac{f(S, I)}{f(S, I^*)} \leq 0,$$
and the equalities hold only for $S = S^*$, $I = I^*$, $C = C^*$ and $A = A^*$. Note that
\[
1 - \frac{f(S^*, I^*)}{f(S, I)} \geq 0 \quad \text{for} \quad S \geq S^*
\]
and
\[
1 - \frac{f(S^*, I^*)}{f(S, I)} < 0 \quad \text{for} \quad S < S^*.
\]
This leads to
\[
(S^* - S) \left(1 - \frac{f(S^*, I^*)}{f(S, I)}\right) \leq 0.
\]
Therefore, $\frac{d}{dt} V_2 \leq 0$. Further, the largest invariant set in $\{(S, I, C, A) \in \mathbb{R}^4 : \frac{d}{dt} V_2 \leq 0\}$ is the singleton $E^*$. The global stability of $E^*$ follows from LaSalle’s invariance principle.

4 Fractional optimal control of the model

In this section, our main aim is to minimize the number of HIV infected individuals and, simultaneously, to reduce the cost associated with such strategies. This is achieved by introducing public education into communities, as a preventive measure time dependent control $v_1(t)$, to start ART treatment, and move $I$ individuals to the $C$ compartment, while control $v_2(t)$ is designed to provide effective treatment to infected individuals with AIDS symptoms. Thus, we consider the following fractional optimal control problem:

\[
\min J(I(t), v_1(t), v_2(t)) = \int_0^{t_f} \left[ I(t) + A(t) + B_1 \delta v_1^2(t) + B_2 \delta v_2^2(t) \right] dt
\]

subject to the fractional control system

\[
\begin{align*}
\frac{D_t^\alpha S(t)}{D_t^\alpha} &= A - \mu S(t) - f(S(t), I(t)) I(t), \\
\frac{D_t^\alpha I(t)}{D_t^\alpha} &= f(S(t), I(t)) I(t) - (\rho + v_1(t) + \mu)I(t) + v_2(t)A(t) + \omega C(t), \\
\frac{D_t^\alpha C(t)}{D_t^\alpha} &= v_1(t)I(t) - (\omega + \mu)C(t), \\
\frac{D_t^\alpha A(t)}{D_t^\alpha} &= \rho I(t) - (v_2(t) + \mu + \delta)A(t),
\end{align*}
\]

with given initial conditions

\[
S(0) = S_0 \geq 0, \quad I(0) = I_0 \geq 0, \quad C(0) = C_0 \geq 0, \quad A(0) = A_0 \geq 0.
\]

Remark 2 While it is not necessary to use quadratic controls in the cost functional \[14\], this is the most common way to penalize the use of controls: see, e.g., [36] or [37].

The parameters $0 < B_1, B_2 < \infty$ are positive weights, $\delta$ is the maximum number of infectious individuals for the problem without control, $B_i \delta v_i^2(t)$, $i = 1, 2$, is the cost of applying control effort $v_i$, and $t_f$ is the duration of the control program. The set of admissible control functions is

\[
U = \{(v_1(\cdot), v_2(\cdot)) \in L^\infty(0, t_f) : 0 \leq v_i(t) \leq v_{i\text{max}}, 1 = 1, 2, \forall t \in [0, t_f]\}.
\]

To obtain the necessary optimality conditions for our fractional optimal control problem, we define the Hamiltonian function as follows:

\[
H = I + A + B_1 \delta v_1^2(t) + B_2 \delta v_2^2(t) + \xi_1 (A - \mu S(t) - f(S(t), I(t)) I(t)) + \xi_2 (f(S(t), I(t)) I(t) - (\rho + v_1(t) + \mu)I(t) + v_2(t)A(t) + \omega C(t)) + \xi_3 (v_1(t)I(t) - (\omega + \mu)C(t)) + \xi_4 (\rho I(t) - (v_2(t) + \mu + \delta)A(t)).
\]
Furthermore, the optimal controls $v_t$ in Section 4, in the classical (\textit{The Pontryagin Maximum Principle is used to numerically solve the optimal control problem (14)–(17), as discussed in Section 5. Applications and numerical simulations}) supplemented with the adjoint system

\[
\begin{aligned}
C D_t^\alpha \xi_1(t') &= -\rho \xi_1(t') + \frac{\partial f}{\partial S} I(t')(\xi_2(t') - \xi_1(t')),
C D_t^\alpha \xi_2(t') &= 1 - \left(\frac{\partial f}{\partial I} I(t') + f(S, I)\right) \xi_1(t') + \xi_3(t') v_1(t') + \rho \xi_4(t') + \left(\frac{\partial f}{\partial I} I(t') + f(S, I) - \rho - v_1(t') - \mu\right) \xi_2(t'),
C D_t^\alpha \xi_3(t') &= \omega \xi_2(t') - (\omega + \mu) \xi_3(t'),
C D_t^\alpha \xi_4(t') &= 1 + v_2(t') \xi_2(t') - (v_2(t') + \mu + d) \xi_4(t'),
\end{aligned}
\]  

with $t' = t_f - t$, the initial and transversality conditions

\[
\begin{aligned}
S(0) &= S_0 \geq 0, \quad I(0) = I_0 \geq 0, \quad C(0) = C_0 \geq 0, \quad A(0) = A_0 \geq 0, \\
\xi_1(t_f) &= \xi_2(t_f) = \xi_3(t_f) = \xi_4(t_f) = 0.
\end{aligned}
\]

Furthermore, the optimal controls $v_1^*$ and $v_2^*$ are given by

\[
\begin{aligned}
v_1^* &= \min \left( v_{1\text{max}}, \max \left( 0, \frac{\xi_2 - \xi_1}{2 B_1 \delta} \right) \right),
\end{aligned}
\]

\[
\begin{aligned}
v_2^* &= \min \left( v_{2\text{max}}, \max \left( 0, \frac{\xi_4 - \xi_2}{2 B_2 \delta} \right) \right),
\end{aligned}
\]  

\section{5 Applications and numerical simulations}

The Pontryagin Maximum Principle is used to numerically solve the optimal control problem (14)–(17), as discussed in Section 4. In the classical ($\alpha = 1$) and fractional ($\alpha < 1$) cases, the predict-evaluate-correct-evaluate (PECE) method of Adams–Basforth–Moulton is implemented in MATLAB. First, we solve system (14) by the PECE procedure with initial values for the state variables based on Moroccan data:

\[
S_0 = (N_0 - (2 + 9))/N_0, \quad I_0 = 2/N_0, \quad C_0 = 0, \quad A_0 = 9/N_0,
\]

with $N_0=23023935$ and a guess for the control over the time interval $[0, t_f]$, thereby obtaining the values of the state variables $S$, $I$, $C$ and $A$. As in [20], a change of variable is applied to the adjoint system and to the transversality conditions, obtaining the fractional initial value problem (19)–(20). Such IVP is also solved with the PECE procedure, and the values of the co-state variables $\xi_i$, $i = 1, \ldots, 4$, are obtained. The controls are then updated by a convex combination of the previous controls and the current values computed according to (21). This procedure is repeated iteratively until the values of all the variables and the values of the controls are very close to the ones of the previous iteration. The solutions of the classical model were successfully confirmed by a classical forward-backward scheme, also implemented in MATLAB.

Solving the initial system (14) with $\alpha = 1$ (classical derivatives), we notice that the maximum number of $I$ individuals, $\delta$, is $1.24 \times 10^{-7}$. This value is the one we use in numerical experiments. We also use $v_{1\text{max}} = v_{2\text{max}} = 1$, $B_1 = B_2 = 2.5$, and the other parameters are fixed according to Table 1 (see [32]), where $\beta$ is the effective transmission rate.

\begin{table}[h]
\centering
\caption{Parameter values of system (14).}
\begin{tabular}{|c|c|c|}
\hline
parameter & description & value \\
\hline
$\mu$ & Natural death rate & $1/74.02$ \\
$\lambda$ & Recruitment rate & $2.19\mu$ \\
$\beta$ & HIV transmission rate & 0.755 \\
$\phi$ & HIV treatment rate for $I$ individuals & 1 \\
$\rho$ & Default treatment rate for $I$ individuals & 0.1 \\
$\sigma$ & AIDS treatment rate & 0.33 \\
$\omega$ & Default treatment rate for $C$ individuals & 0.09 \\
$d$ & AIDS induced death rate & 1 \\
\hline
\end{tabular}
\end{table}
Because the World Health Organization (WHO) goals for most diseases are usually fixed for five years periods, we considered $t_f = 5$.

Without loss of generality, in what follows we consider the incidence function to be

$$f(S, I) = \beta S.$$  

This function is chosen because, when compared with other incidence functions, this was the one that better fitted to real data [32].

In order to perceive the effect of the derivative order on the variation of the variables of the problem, we considered, as in [40], some fractional order derivatives, namely $\alpha = 1.0, 0.85, 0.70$ and 0.3. In Figure 1, 2a, and 2b, we have the solutions of the fractional optimal control problem (FOCP) for that values of $\alpha$. We observe that a change in the derivative order corresponds to variations of the state variables and of the first control, $v_1$. On the other hand, the second control, $v_2$, does not vary with that change, remaining null. Treatment of AIDS individuals was considered cheaper, i.e., smaller values for $B_2$ (weight of $v_2$ in the cost functional) were considered but $v_2$ has not changed. This means that treating people with AIDS symptoms is useless when we can act over infected people with ART treatment.

The existence of an endemic situation ($R_0 = 7.534 > 1$ [32]), the existence of a high percentage of susceptible individuals and a control that vanishes at the end of the time interval motivates that, in the end of the time interval, the number of $I$ individuals exceeds its initial value. Other values of $\alpha$, lower than one, were also tested, but the results do not changed qualitatively. According with Figure 11 decreasing the derivative order, $\alpha$, means that, after a certain value of time, it decreases the number of individuals of compartments $S$ and $C$ while increasing the value of individuals in compartment $A$. We note that the variation of $\alpha$ has little impact in the variation of infected individuals, $I$.

Remark 3 Solutions of adjoint variables can be easily included in numerical simulations: see, e.g., [41]. While in [41] the inclusion of the adjoint variables is important, because of the non-regularity of the control variable, which is obviously explained by those variables, here, however, the inclusion of the adjoint variables do not bring new insights:
the nonzero control $v_1$ has a classical evolution, starting at its maximum, one, after it decreases and vanishes at the end of the time interval. This behaviour is common to many known examples and the adjoint variables, in turn, follow qualitatively this evolution, with different magnitudes.

![Graphs showing optimal controls $v_1$, $v_2$, and efficacy function $F(t)$](image)

**Fig. 2:** Control functions $v_1(t)$ and $v_2(t)$ associated to the FOCP (14)–(21) with values from Table I weights $B_1 = B_2 = 2.5$, and the fractional order derivatives $\alpha = 1.0, 0.85, 0.7$ and $0.3$.

The efficacy function [42] is defined by

$$F(t) = \frac{i(0) - i^*(t)}{i(0)} = 1 - \frac{i^*(t)}{i(0)},$$

(22)

where $i^*(t) = I^*(t) + A^*(t)$ is the optimal solution of the fractional optimal control and $i(0) = I(0) + A(0)$ is the corresponding initial condition. This function measures the proportional variation in the number of infected individuals, HIV infected or infected with AIDS, after the application of the controls $\{v^*_1, v^*_2\}$, by comparing the number of infectious individuals at time $t$ with the initial value $i(0)$. In Figure 2c, the efficacy function is exhibited for the three considered values of $\alpha$. Interestingly, the classical model is the most effective.

Some summary measures are presented to evaluate the cost and the effectiveness of the proposed fractional control measures during the intervention period. The total cases averted by the intervention during the time period $t_f$ is defined in [42] by

$$AV = i(0)i_f - \int_0^{t_f} i^*(t) \, dt,$$

(23)

where $i^*(t) = I^*(t) + A^*(t)$ is the optimal solution corresponding to the fractional optimal controls $\{v^*_1, v^*_2\}$ and $i(0) = I(0) + A(0)$ is the corresponding initial condition.

Effectiveness is defined as the proportion of cases averted on the total cases possible under no intervention [42]:

$$\overline{F} = \frac{AV}{i(0)t_f} = 1 - \frac{\int_0^{t_f} i^*(t) \, dt}{i(0)t_f}.$$

(24)
The total cost associated with the intervention is defined in \[42\] by
\[
TC = \int_0^T C_1 v_1(t)I^*(t) + C_2 v_2(t)A^*(t) \, dt, \tag{25}
\]
where \(C_i\) corresponds to the per person unit cost of the two possible interventions: (i) detection and treatment of HIV infected individuals \((C_1)\); (ii) and detection and treatment of HIV infected individuals with AIDS \((C_2)\). Following \[42\], the average cost-effectiveness ratio is given by
\[
ACER = \frac{TC}{AV}. \tag{26}
\]

Table 2: Summary of cost-effectiveness measures for classical \((\alpha = 1)\) and fractional \((0 < \alpha < 1)\) HIV-AIDS disease optimal control problem. Parameters according to Table 1 and \(C_1 = C_2 = 1\).

| \(\alpha\) | \(AV\) | \(TC\) | \(ACER\) | \(F\) |
|---|---|---|---|---|
| 1.0 | 1.55815e-06 | 2.21066e-07 | 0.141877 | 0.652268 |
| 0.85 | 1.46382e-06 | 2.37665e-07 | 0.16236 | 0.612779 |
| 0.70 | 1.36489e-06 | 2.54213e-07 | 0.186252 | 0.571365 |
| 0.30 | 1.09485e-06 | 2.94279e-07 | 0.268786 | 0.458322 |

In Table 2, the cost-effectiveness measures, for our fractional optimal control problem, are summarized. Those results show the effectiveness of the control \(v_1\) to reduce HIV infectious individuals and the superiority of the classical model \((\alpha = 1)\).

The impact of the variation of the weight \(B_1\) over the cost functional value \(J\) (left) and on the effectiveness measure \(F\) (right) for the fractional order derivatives \(\alpha = 1.0, 0.85, 0.7\) and 0.3.

The fractional model is more effective when treatment is expensive, i.e., hard to implement. To illustrate this behaviour, we considered \(B_1 = 40\) and determined the derivative order with the best effectiveness measure. The highest value of effectiveness, 0.309505, was attained with \(\alpha = 0.30\), a quite low value. The respective value for the classical model \((\alpha = 1)\) is 0.269456. Figures 4 and 5 compare the fractional solution with the classical one. When compared with the classical model, the variables \(S\) and \(C\), of the fractional model, behave analogously to above cases with \(B_1 = 2.5\) and other values of \(\alpha\), but move further apart. With respect to \(I + A\) individuals, we see that, in average, the fractional solution is lower than the classical solution. We also notice that the first control of the fractional model is more intense than the one of the classical model in most part of the time interval. Such behaviour of control \(v_1\) can be the reason of the higher effectiveness of such model. The second control is not exhibited because it remains null. The efficacy function, presented in Figure 5b, confirms that the fractional model is the best choice in this case.
Fig. 4: State variables of the FOCP (14)–(21), with values from Table 1, weights $B_1 = B_2 = 40$, and the fractional order derivatives $\alpha = 1.0$ and 0.30.

Fig. 5: Control function $v_1(t)$ and efficacy function $F(t)$ associated to the FOCP (14)–(21), with values from Table 1, weights $B_1 = B_2 = 40$, and the fractional order derivatives $\alpha = 1.0$ and 0.30.

6 Conclusion

We investigated the dynamics involved in HIV-AIDS infection by means of a fractional SICA model with Caputo’s fractional derivatives. Besides determining the points of stability of the system, we also applied fractional optimal control to virtualize determined scenarios and choose a strategy that minimizes the spreading of the disease.

The infection process was modelled by a general functional response. This general incidence function $f(S, I)$ was used to compute the basic reproduction number under biologically reasonable hypothesis. Under such hypothesis,
function \( f \) covers many types of incidence functions existing in the literature, such as the bilinear incidence rate, saturated incidence rate, Beddington–DeAngelis, Crowley–Martin, and Hattaf–Yousfi functional responses. In numerical simulations, we have chosen the bilinear incidence rate \( f(S, I) = \beta S \), which has shown a better fitting to real data of Morocco.

Stability and instability of equilibrium points were determined in terms of the basic reproduction number. Then, a fractional optimal control system was formulated and the best strategy for minimizing the spread of the disease into the population was determined through numerical simulations based on the derived necessary optimality conditions.

Application of optimal control to the fractional SICA model shows that HIV treatment is effective on the reduction of infected individuals. Also, our results show that treating people with AIDS symptoms is useless when we can act over infected people with ART treatment. The modification of the value of the fractional derivative order, \( \alpha \), corresponds to variations of solutions to the fractional optimal control problem. When treatment becomes expensive, the fractional model (\( \alpha < 1 \)) is more appropriated due to its effectiveness and because it provides control measures not as expensive as the ones given by the classical model.

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