Controlling Influenza A (H1N1) Through the Fractional SIR Model With Time Delay

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ABSTRACT

The objective of this article is to formulate a mathematical model to make a vaccination strategy to reduce outbreaks of influenza A (H1N1) via a fractional model, taking into account the time it takes for the vaccine to be active. For this purpose, the SIR model is modified by using the Caputo fractional derivative, unifying the unit of time on both sides of each equation, and adding the control variable with a time delay (the vaccine variable). Meanwhile, the theory of optimal control is used to construct an algorithm that enables us to determine the optimal vaccination strategy. The forward and backward Euler method has been used to find the optimal solutions numerically. The numerical simulation is based on data from Morocco's experience with influenza A (H1N1).

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1. Introduction

In recent years, epidemiology has become an increasingly important part of modern life. In fact, the mathematical modeling that provided a connection between mathematics and epidemiology has become an active field of study [1-4]. Mathematical models are frequently used to investigate the dynamics of infectious disease transmission, spread control, vaccinations strategies, and the asymptotic behavior of epidemiological models [5-6]. Control theory plays a important role in the development of epidemiology. Indeed, controlling the spread of viruses has become a vital subject today [7-9]. More specifically, the applications of optimal control theory appear clearly in a variety of fields, such as therapy design, animal disease control, the best tuberculosis prevention strategy, and so on. [10-11]. Beside optimal control theory, fractional calculus introduces wonderful tools to describe more complete real-life models. This is due to three main reasons: The first is that the fractional derivative is nonlocal. The second, the stability region of the system described by a fractional differential equation (FDE), is larger than the system described by an ordinary differential equation (ODE). Finally, fractional derivatives carry more historical information than the classical derivative [12-16]. When a physical system relies on past data, a generalization of the ODE known as the delay differential equation (DDE) can be applied [17]. The solution of DDEs required not only knowledge of the status at current time but also knowledge of the status in previous time. DDEs have verity of applications in many fields including: the mathematical modeling physiological, chemical kinetics, pharmaceutical kinetics, ship, spacecraft navigational control, population dynamics, and infectious diseases. Several papers have been published in the last decade on the numerical solution of delay differential equations [18, 20]. As a result, various numerical methods have been developed and applied to provide approximate solutions [21]. The fractional DDE is a non-integer order version of the DDE. Several papers have been published in the last decade on the numerical solution of fractional delay differential equations. The exact solutions to the majority of fractional DDEs are unknown. As a result, various numerical methods [20-23] for providing approximate solutions have been developed and applied. Yang and Cao [24] used fixed point theory to investigate the solvability of initial value problems for nonlinear fractional DDEs. Wang [25] approximated fractional DDEs using a combination of the Adams Bashforth Moulton and linear interpolation methods. The main sections of this article are as follows: The second section focuses on developing and designing the optimal control strategy for the considered model using the time delay fractional-order SIR

epidemic model. While Section 3 focuses on introducing a numerical simulation to clarify our main results using a practical case from Morocco's experience with influenza A (H1N1), Section 4 provides a short summary and conclusions.

2. The design of an optimal vaccination strategy

The theory of fractional optimum control is a popular way for obtaining the extreme value of a dynamically changeable objective function. This section utilizes fractional optimal control theory to determine the optimal pharmacological treatments as a function of time. During an epidemic, the aim of government health care is to minimize losses by reducing the number of susceptible S, and preventing the infected number of people I meanwhile increasing the people number of recovery R. Mathematically, the problem is to minimize the cost function for a fixed terminal time t_f. There are many interesting definitions of fractional derivatives in fractional calculus [26], but for this purpose, we will use the famous Caputo derivatives due to their advantage on initial value problems.

Definition 1 [26] The fractional integral of order $0<\alpha<1,\ t>0$ is defined by

$$J^{\alpha} f(t)=\frac{1}{\Gamma(\alpha)}\int_0^t \frac{f(x)}{(t-x)^{1-\alpha}}\,dx \tag{1}$$

Definition 2 [26] Let $n-1<\alpha<n$, the Caputo fractional derivative of order α is given by

$${}^{C}D^{\alpha} f(t)=\frac{1}{\Gamma(\mathrm{n}-\alpha)}\int_0^t \frac{f^{n}(x)}{(t-x)^{\alpha+1-n}}\,dx \tag{2}$$

Consider the cost function as follow

$$\Im(u)=\int_0^{t_f}[AS(t)+BI(t)-CR(t)+\frac{D}{2}u^2(t)]dt \tag{3}$$

Where $A,B,C,D\geq 0$ weights that equalize the scale of the words are indicated. That is, we are looking for finding $u^*(t)$ which satisfy the following:

$$\Im(u^*(t))=\min\left\{\Im(u(t)):0\leq u\leq 1,\ 0\leq t\leq t_f,\ \text{such that the state equations are satisfied}\right\},$$

subject to the Caputo fractional equations as following

$$
\begin{aligned}
{}_0^C D_t^\alpha S(t) &= \Lambda^\alpha - \beta^\alpha \frac{S(t)I(t)}{S(t)+I(t)+R(t)} - d^\alpha S(t) - u(t-\tau)S(t-\tau),\\
{}_0^C D_t^\alpha I(t) &= \beta^\alpha \frac{S(t)I(t)}{S(t)+I(t)+R(t)} - (\gamma^\alpha + d^\alpha + \varepsilon^\alpha) I(t),\\
{}_0^C D_t^\alpha R(t) &= \gamma^\alpha I(t) - d^\alpha R(t) + u(t-\tau)S(t-\tau).
\end{aligned} \tag{4}
$$

Now, the first step is constructing the following Hamiltonian function:

$$
\tilde{H}(S,I,R,u,t) = AS(t) + BI(t) - CR(t) + \frac{D}{2}u^2(t) + \sum_{j=1}^{3} p_j({}_0^C D_t^\alpha S(t) + {}_0^C D_t^\alpha I(t) + {}_0^C D_t^\alpha R(t)). \tag{5}
$$

After that, we derive the necessary conditions from Eq. (5) as follows:

$$
{}_t^C D_{t_f}^\alpha p_1(t) = \frac{\partial \tilde{H}(t)}{\partial S(t)} + \hbar_{[0,t_f-\tau]}(t) \frac{\partial \tilde{H}(t+\tau)}{\partial S(t-\tau)}, \tag{6}
$$

$$
{}_t^C D_{t_f}^\alpha p_2(t) = \frac{\partial \tilde{H}(t)}{\partial I(t)}, \tag{7}
$$

$$
{}_t^C D_{t_f}^\alpha p_3(t) = \frac{\partial \tilde{H}(t)}{\partial R(t)}, \tag{8}
$$

where

$$
\hbar_{[0,t_f-\tau]}(t) = \begin{cases} 1, & t \in [0, t_f - \tau] \\ 0, & otherwise \end{cases}. \tag{9}
$$

And $p_1(t_f) = p_2(t_f) = p_3(t_f) = 0$ are the Lagrange multipliers.

Theorem 1 Consider u^* is optimal control with the corresponding state S^*, I^* and R^* then there exist p_1, p_2 and p_3 satisfies the following:

$$
\begin{aligned}
{}_t^C D_{t_f}^\alpha p_1(t) = A &- p_1(t)d^\alpha - (p_1(t) - p_2(t))\beta^\alpha \frac{I^*(t)}{S(t)+I(t)+R(t)} \\
&+ \hbar_{[0,t_f-\tau]}(p_3(t+\tau) - p_1(t+\tau))u^*(t)
\end{aligned} \tag{10}
$$

$$
\begin{aligned}
{}_t^C D_{t_f}^\alpha p_2(t) = B &- (p_1(t) - p_2(t))\beta^\alpha \frac{S^*(t)}{S^*(t)+I^*(t)+R^*(t)} \\
&- (d^\alpha + \gamma^\alpha + \varepsilon^\alpha) p_2(t) + \gamma^\alpha \, p_3(t)
\end{aligned} \tag{11}
$$

$$
{}_t^C D_{t_f}^\alpha p_3(t) = -C - d^\alpha p_3(t) \tag{12}
$$

With transversality conditions

$$p_1(t_f) = p_2(t_f) = p_3(t_f) = 0 \tag{13}$$

Hence, u^* has the following formula:

$$u^*(t) = \max(0, \min(1, \frac{(p_1(t+\tau) - p_3(t+\tau)}{D} \hbar_{[0,t_f-\tau]}(t) S^*(t))) \tag{14}$$

Proof: By definition the Hamiltonian function $\tilde{H}$, we get

$$\begin{aligned} \tilde{H}(S^*, I^*, R^*, u^*, t) = AS^*(t) + BI^*(t) - CR^*(t) + \frac{D}{2}u^{*2}(t) \\ + p_1 {}_0^C D_t^\alpha S^*(t) + p_2 {}_0^C D_t^\alpha I^*(t) + p_3 {}_0^C D_t^\alpha R^*(t). \end{aligned} \tag{15}$$

Then

$$\begin{aligned} \tilde{H}(S^*, I^*, R^*, u^*, t) = AS^*(t) + BI^*(t) - CR^*(t) + \frac{D}{2}u^{*2}(t) \\ + p_1(\Lambda^\alpha - \beta^\alpha \frac{S^*(t)I^*(t)}{S^*(t)+I^*(t)+R^*(t)} - d^\alpha S^*(t) - u^*(t-\tau)S^*(t-\tau)) \\ + p_2(\beta^\alpha \frac{S^*(t)I^*(t)}{S^*(t)+I^*(t)+R^*(t)} - (\gamma^\alpha + d^\alpha + \varepsilon^\alpha)I^*(t)) \\ + p_3(\gamma^\alpha I^*(t) - d^\alpha R^*(t) + u^*(t-\tau)S^*(t-\tau)). \end{aligned} \tag{16}$$

By using Pontryagin's minimum principle with delay we can get

$$\begin{aligned} {}_t^C D_{t_f}^\alpha p_1(t) &= \frac{\partial \tilde{H}(t)}{\partial S^*(t)} + \hbar_{[0,t_f-\tau]}(t) \frac{\partial \tilde{H}(t+\tau)}{\partial S^*(t-\tau)} \\ &= A - p_1(t)d^\alpha - (p_1(t) - p_2(t))\beta^\alpha \frac{I^*(t)}{S^*(t)+I^*(t)+R^*(t)} \\ &\quad + \hbar_{[0,t_f-\tau]}(p_3(t+\tau) - p_1(t+\tau))u^*(t). \end{aligned} \tag{17}$$

$$\begin{aligned} {}_t^C D_{t_f}^\alpha p_2(t) &= \frac{\partial \tilde{H}(t)}{\partial I^*(t)} \\ &= B - (p_1(t) - p_2(t))\beta^\alpha \frac{S^*(t)}{S^*(t)+I^*(t)+R^*(t)} \\ &\quad - (d^\alpha + \gamma^\alpha + \varepsilon^\alpha)p_2(t) + \gamma^\alpha p_3(t) \end{aligned} \tag{18}$$

$${}_t^C D_{t_f}^\alpha p_3(t) = \frac{\partial \tilde{H}(t)}{\partial R^*(t)} = -C - d^\alpha p_3(t) \tag{19}$$

And the transversality conditions $p_1(t_f) = p_2(t_f) = p_3(t_f) = 0$, and u^* can be obtained as follows:

$$\frac{\partial \tilde{H}(t)}{\partial u^*(t)} + \hbar_{[0,t_f-\tau]}(t)\frac{\partial \tilde{H}(t+\tau)}{\partial u^*(t-\tau)} = 0, \tag{20}$$

$$Du^*(t) + \hbar_{[0,t_f-\tau]}(t)(p_3(t-\tau) - p_1(t-\tau))S^*(t) = 0, \tag{21}$$

$$u^*(t) = \frac{(p_1(t-\tau) - p_3(t-\tau))}{D}\hbar_{[0,t_f-\tau]}(t)\,S^*(t). \tag{22}$$

Since $0 \le u \le 1$ then we can rewrite u^* in the Eq. (22) as follow

$$u^*(t) = \max(0, \min(1, \frac{(p_1(t+\tau) - p_3(t+\tau)}{D}\hbar_{[0,t_f-\tau]}(t)\,S^*(t))). \tag{23}$$

3 Numerical Simulations

In this section, we investigate the effect of optimal strategy on the delay fractional SIR model using the forward and backward fractional Euler method. This method provides a numerical solution for any specific time interval. The MAPLE 2020 software has been used to make this simulation. Here, all computations are performed by implemeenting real data based on influenza A (H1N1) in Morocco as described in Table 1 and Table 2.

Table 1: model parameters and control

Parameters	Value	Reference
β	0.3059	[27]
Λ	1174.14	[27]
d	3.9139×10^{-5}	[27]
γ	0.2	[27]
ε	0.0063	[28]
τ	10	[28]
u	$0-1$ variable	Assessment

Table 2: The initial conditions for the variables for SIR model

Variable	**Initial values**
$S(t)$	$S(0)=30\times10^{6}$
$I(t)$	$I(0)=30$
$R(t)$	$R(0)=28$

Using numerical simulation results, the key outcomes have been graphically presented. The main results of the above analysis can be summarized by drawing some figures to explain the effect of the optimal vaccination strategy. Indeed, Figure 1 and Figure 2 show that in the case of control, the number of susceptible individuals S decreases more rapidly at the end of the vaccination period than with no vaccination process. However, the infected number of individuals I with and without control is depicted in Figure 3 and Figure 4. It demonstrates that when the optimal vaccination strategy has been used, the number of infected individuals I decreases dramatically, whereas, in the without of control, the infected number of individuals I increases. Also, the removed R number with and without control is depicted in Figure 5 and Figure 6. It demonstrates that when the optimal vaccination strategy has been used, the removed number R of people will be increased dramatically, whereas, in the without control, the removed number R of people will be increased slowly. The process of the proposed method is depicted in the algorithm below.

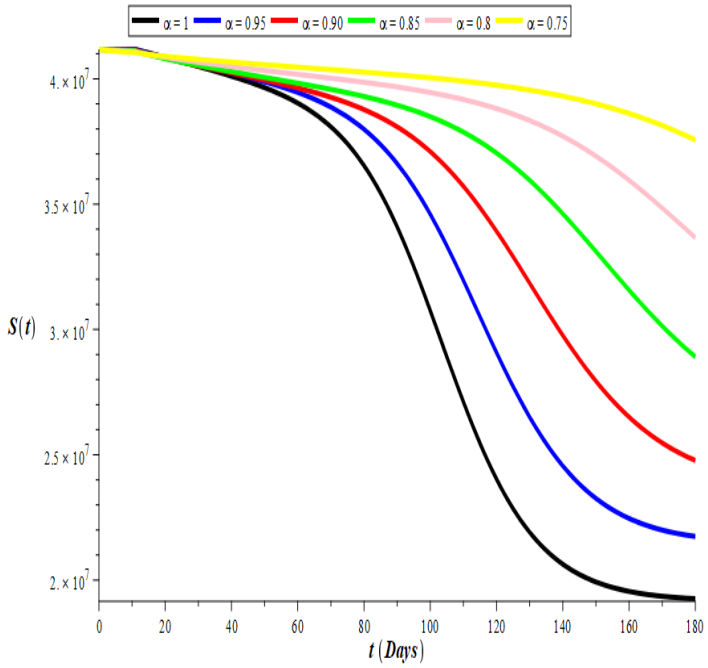

Figure 1: Represents the Susceptible with control.

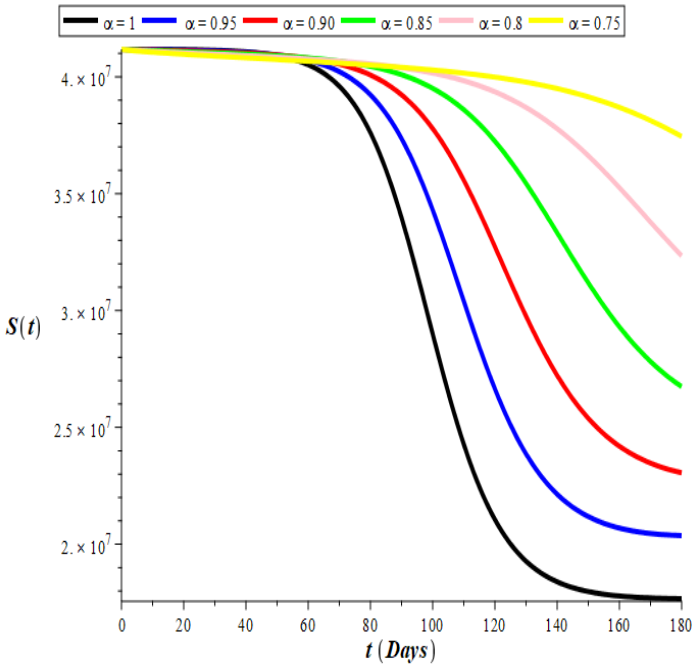

Figure 2: Represents the Susceptible without control.

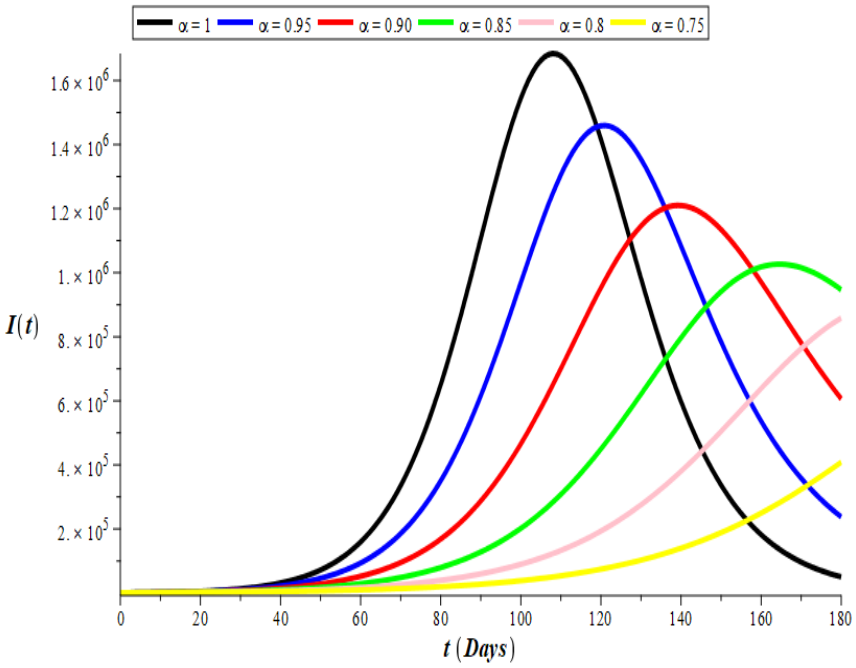

Figure 3: Represents the Infected with control.

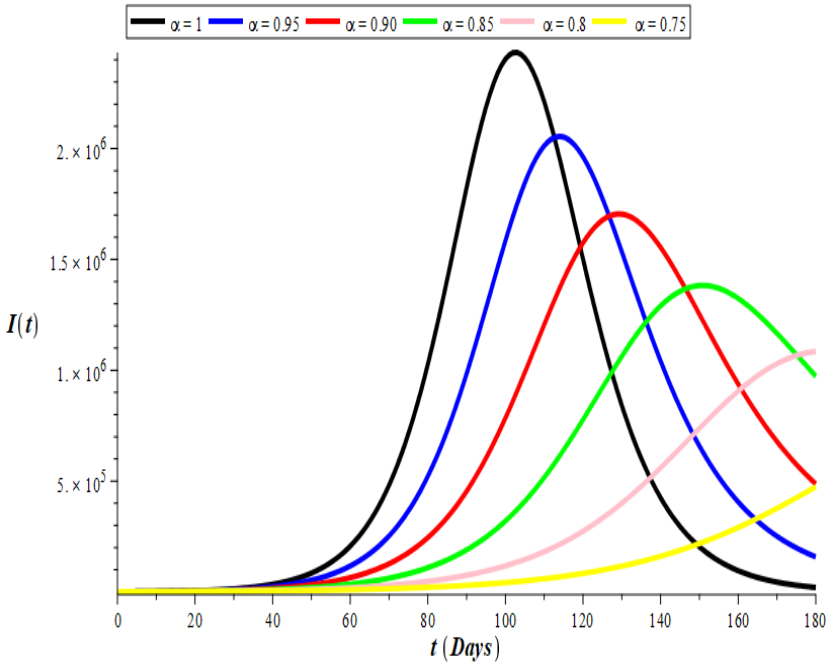

Figure 4: Represents the Infected without control.

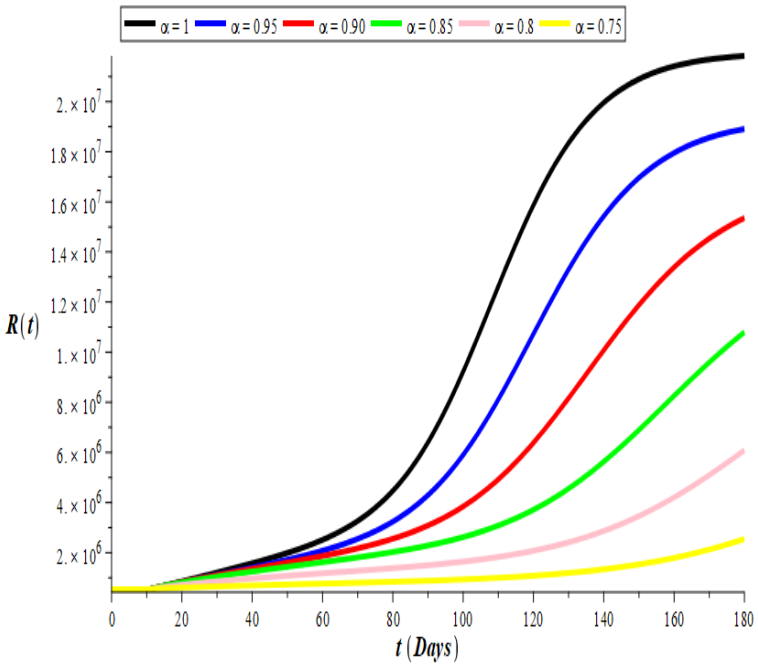

Figure 5: Represents the Removed with control.

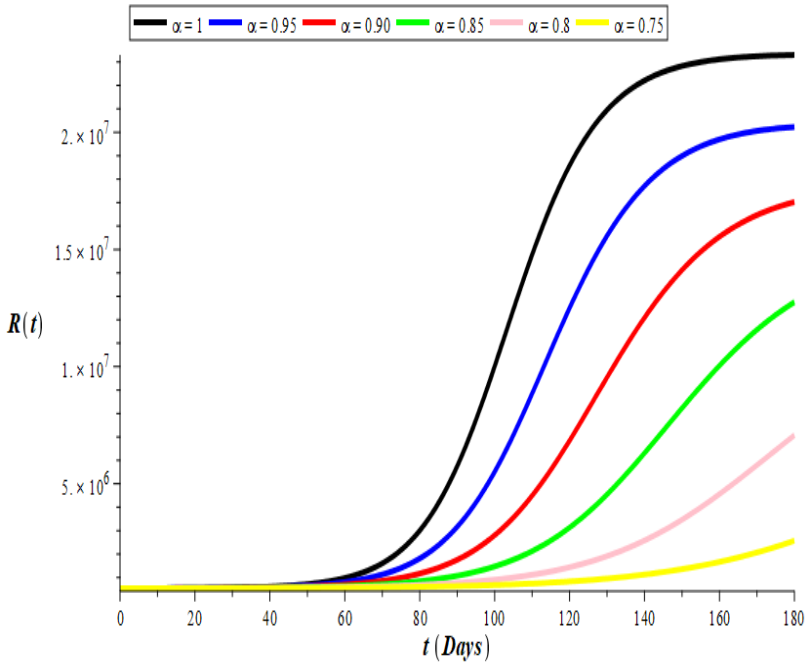

Figure 6: Represents the Removed without control.

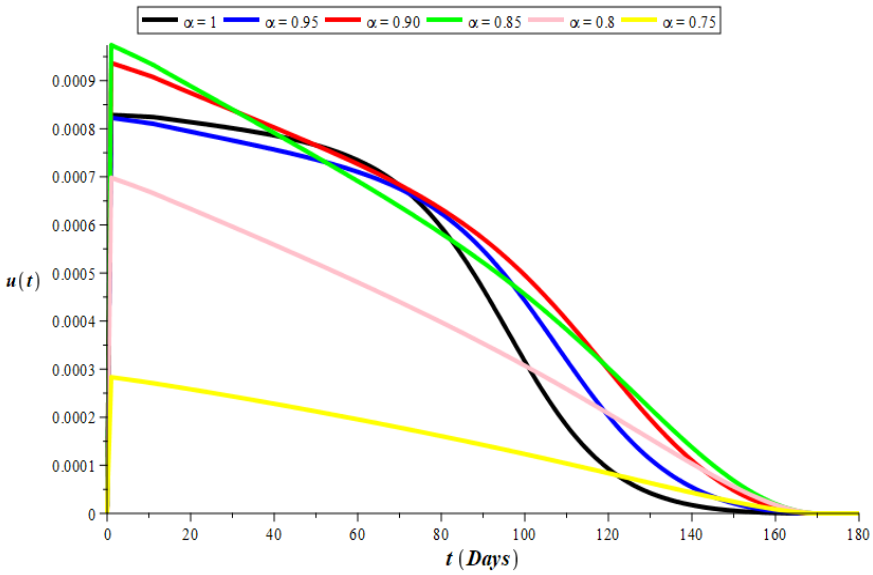

Figure 7: Represents the optimal control.

4 Conclusions

This study presents a Caputo fractional SIR epidemiological model that incorporates a time delay representing the amount of time necessary for individuals to transition from the susceptible class to the recovered class after receiving vaccination. The goal of this paper is to build an algorithm for solving the fractional SIR model with time delay. Also, the fractional-order optimal necessary conditions were derived using the Pontryagin minimum principle. We used the forward and backward Euler method to get the optimal solution. The numerical simulation was carried out by making use of the optimization method in Maple 20. The purpose of this was to investigate the behavior of the proposed model and how the combination of control u affects it. In addition to this, we investigated how this model is affected by the memory property of fractional derivatives, which is represented by the order of the fractional derivative.

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السيطرة على الأنفلونزا A (H1N1) من خلال نموذج SIR الكسري مع تأخير الوقت

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المستخلص

الهدف من هذه المقالة هو صياغة نموذج رياضي لعمل إستراتيجية تطعيم من أجل السيطرة على تفشي الأنفلونزا A (H1N1) عبر نموذج كسري ، مع الأخذ في الاعتبار الوقت الذي يستغرقه اللقاح ليكون نشطًا. لهذا الغرض ، تم تعديل نموذج SIR باستخدام مشتقة كابوتو الكسرية ، وتوحيد الزمن على جانبي كل معادلة ، وإضافة متغير التحكم (متغير اللقاح) مع تأخير زمني. وفي الوقت نفسه ، تم استخدام نظرية التحكم الأمثل لبناء خوارزمية تمكننا من تحديد استراتيجية التطعيم المثلى. ثم استخدامت طريقة أويلر الامامية والخلفية لإيجاد الحل الامثل عدديًا. اعتمدت المحاكاة العددية على بيانات من تجربة المغرب مع الأنفلونزا A (H1N1).