



Optimal control for variable order fractional HIV/AIDS and malaria mathematical models with multi-time delay



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Abstract In this article, optimal control for variable order fractional multi-delay mathematical model for the co-infection of HIV/AIDS and malaria is presented. This model consists of twelve differential equations, where the variable order derivative are in the sense of Caputo. Three control variables are presented in this model to minimize the number of the co-infected individuals showing no symptoms of AIDS, the infected individuals with malaria, and the individuals asymptotically infected with HIV/AIDS. Necessary conditions for the control problem are derived. The Grünwald-Letnikov nonstandard finite difference scheme is constructed to simulating the proposed optimal control system. The stability of the proposed scheme is proved. In order to validate the theoretical results numerical simulations and comparative studies are given.

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1. Introduction

Malaria and AIDS caused by the human immunodeficiency virus(HIV), are two main universal health problems of our time. Recently, increased research efforts are made to get an

efficient vaccine to halt the progression and transmission of malaria, for more details see [2–4].

Mickens [40,41] proposed the nonstandard finite difference method (NSFDM), which can be easy to contract [40], for improving the discretizations of some terms in the differential equations, such that depending on the denominator function and the specific discretization this method be more accurate and more stable than standard method [34,37]. This technique applied in the fields of physics, chemistry, engineering [39,42,43,30]. Especially, the most attractive applications are in mathematical biology and ecology [31,35]. In addition, the NSFDM are well performed in solving fractional-order

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system, such as the fractional order neuron system [32] and the fractional Hodgkin-Huxley model [33].

Nowadays, mathematical models can be considered as a successfully powerful tool to test hypotheses, confirm experiments, and simulate the dynamics of complex systems.

In the mean time, fractional calculus can be considered as a hot topic of research work in many scientific fields especially in mathematics and engineering, it is a generalization of the integer order differentiation and integration to non-integer order. Applications of fractional calculus have taken off in the last few decades, after centuries of small advancements. This is due to the fact that fractional-order models provide more accurate description of memory and hereditary properties of the system, compared with models of integer-order [52–55]. To understand the physical meaning of the fractional models, we refer to some articles explaining fractional calculus geometrically, see for examples [56–58] and the references cited therein.

Naturally, time-delay or memory is an unavoidable factor in dynamics of most of real life phenomena. Examples of fractional order derivatives with time delay can be found in a variety of scientific areas: engineering, biology, epidemiology, amongst others [5–10,49].

Pontryagin's maximum principle of optimal control problems with time-delay is based on differential equations with delay. This topic is discussed in the sixties of the last century for more details see [60–62]. Recently Sweilam and et al. in [47] extended this principle to the fractional order. Some interesting real-life models of fractional optimal control problems (FOCP) have been presented in [11,17–21,48,50,51]. Moreover, a useful and interesting contributions in the development of the Lagrange multipliers and the fractal variational principles in fractal space are given in [58,59].

Moreover, the variable-order fractional (VOF) derivatives is a powerful tool for describing the effects of the long variable memory of systems which changes with time and the constant-order fractional derivative depicts the long memory of systems while the integer order derivative can be used to characterize the short memory. The advantage of using variable order in the fractional differential equations is appeared in some papers such as [22–24].

One of the new topics in mathematics is the variable order fractional optimal control problems (VOFOCP) [25,26], which it development as extension to the FOCP.

The main contribution of this work is to investigate the effect of the optimal control of the variable order for HIV/AIDS and Malaria mathematical models with multi-time delay and develop an efficient numerical algorithm to approximate the solutions of the proposed model. Three control variables are presented in this model to reduce the number of the infected individuals of malaria and HIV/AIDS. Comparative studies between Grünwald-Letnikov nonstandard finite difference method (GL-NSFDM) and Grünwald-Letnikov standard finite difference method (GL-SFDM) are presented. Numerical simulations for the obtained variable order fractional system are presented.

The article is organized as follows: In Section 2, the variable order fractional calculus and the preliminaries of GL-NSFDM are introduced. In Section 3, variable order fractional mathematical model of HIV/AIDS and malaria is given. In Section 4, formulation of VOFOCP is presented. In Section 5, numerical methods for VOFOCP are presented. In Section 6, numerical

simulations are given to show the efficiency and applicability of the GL-NSFDM, also, the stability analysis of the proposed method are proved. Finally, the conclusions are given in Section 7.

2. Notations and preliminaries

In this section, we recall some important definitions of the variable order fractional calculus which are used thought out the remaining sections of this paper.

2.1. Variable order fractional calculus

The general form of the variable order fractional differential equation is given as follows [29]:

$${}^C D_t^{\alpha(t)} x(t) = f(t, x(t)), \quad x(0) = x_0, \quad 0 < \alpha(t) \leq 1. \quad (1)$$

The Liouville-Caputo fractional derivative with variable order $\alpha(t)$ is defined as follows:

$${}^C D_t^{\alpha(t)} f(t) = \frac{1}{\Gamma(1-\alpha(t))} \int_0^t (t-\tau)^{-\alpha(t)} f'(\tau) d\tau, \quad 0 < \alpha(t) \leq 1. \quad (2)$$

3. The model problem

In the following, the variable order fractional mathematical model for HIV/AIDS and the co-infection malaria with multi-time delay is considered. This model proposed by Pinto and Carvalho in [27] as fractional order and it is given by Arfa et. al., in [28] as variable order. The definitions of all variables of the proposed model given in Table 1. Also, the parameters and their interpretation of the proposed model are introduced in Table 2. Three control variables G_n , G_m and G_h are added in order to health care for the infected individuals such as give them the treatments soothing regularly. These controls are introduced to reduce the number of the I_h , I_{mhiv} and I_{hiv} . The modified model is then represented by a system of variable order fractional differential equations as follows:

Table 1 The variables of the proposed model [28].

Variable	Definition
N_h	The population of human
S_h	The susceptible individuals
V_h	The individuals vaccinated against malaria
I_h	The individuals infected with malaria
I_{mhiv}	The co-infected humans showing no symptoms of AIDS
I_{hiv}	The humans asymptotically infected with HIV/AIDS
Y_h	The humans infected and anti-malaria vaccinated
A_{mhiv}	The co-infected individuals displaying signs of AIDS
A_{hiv}	The humans infected with HIV and showing symptoms of AIDS
N_m	The mosquitoes population
S_m	The susceptible mosquitoes
I_m	The infectious mosquitoes

Table 2 The parameters of the proposed model [28].

Parameter	Definition	Value
$A_h^{z(t)}$	The proportion of susceptible individuals get within the human population	$0.05^{z(t)}$
$p^{z(t)}$	The rate of people successfully vaccinated	$0.4^{z(t)}$
$\sigma^{z(t)}$	The rate of Vaccinated individuals may become susceptible	$0.009^{z(t)}$
$B_h^{z(t)}$	The possibility that a bite of an infectious mosquito leads to the infection of a susceptible people	$0.04^{z(t)}$
$\eta_{HM}^{z(t)}$	Infectiousness to malaria of co-infected people displaying signs and symptoms of AIDS	$1.5030^{z(t)}$
$c^{z(t)}$	The proportion of female mosquitoes bites	$0.5^{z(t)}$
$A_m^{z(t)}$	The rate of recruited of the susceptible mosquitoes	$6^{z(t)}$
$\phi_2^{z(t)}$	The proportion of recovery of the I_{mhiv}	$0.002^{z(t)}$
$\phi_3^{z(t)}$	The rate of recovery of $A_{mhiv}(t)$ from malaria	$0.0005^{z(t)}$
$b^{z(t)}$	The rate of people within the community	$0.3^{z(t)}$
$z^{z(t)}$	The efficacy of adopted strategies for people protection	$0.9^{z(t)}$
$r_h^{z(t)}$	The charge of recuperation of human beings inflamed with malaria and getting to the inclined magnificence	$0.0005^{z(t)}$
$\alpha_{h1}^{z(t)}$	The proportion of death of people infected with malaria	$0.0004^{z(t)}$
$\alpha_{h2}^{z(t)}$	The rate of development of I_{hiv} to AIDS	$0.0004^{z(t)}$
$B_m^{z(t)}$	The possibility that a mosquito's chunk at some point of a malaria inflamed human has a tendency to infection of the mosquito	$0.83^{z(t)}$
$\epsilon_2^{z(t)}$	The proportion of decrease in sexual intercourse due to malaria disease	$0.8^{z(t)}$
$\delta_H^{z(t)}$	The speed of death from AIDS	$0.000913^{z(t)}$
$\mu_h^{z(t)}$	The speed of the natural death for all human	$0.0000391^{z(t)}$
$\gamma^{z(t)}$	The efficacy of the preerythrocytic vaccine	$0.64^{z(t)}$
$c^{z(t)}$	shows the rate of reducing of transmission from vaccinated humans to susceptible mosquitoes	$0.86^{z(t)}$
$\tau_h^{z(t)}$	The avrage of time after it susceptible individuals enter the category I_h	$14^{z(t)}$
$\tau_m^{z(t)}$	The time after it the exposed mosquitoes turn infectious	$12^{z(t)}$
$\mu_m^{z(t)}$	The speed of natural death of mosquitoes	$0.04^{z(t)}$
τ	The speed of rised malaria mortality of people co-infected with HIV	1.001
$\psi^{z(t)}$	indicates the growth in HIV mortality thanks to the co-infection with malaria	$1.002^{z(t)}$
θ_1	The impact of the preerythrocytic vaccine within the reducing of mortality thanks to disease	4.1
θ_2	The effect of the preerythrocytic vaccine within the raising of the recovery	0.06
v_1	The supposed upward thrust in sensibility to malaria as impacts of HIV infection	1.002
v_2	The speed of increase in sensibility to malaria of humans of $A_{hiv}(t)$	1.5
$\eta_A^{z(t)}$	The price of accelerating mortality thanks to the presence of the parasite within the frame	$1.4^{z(t)}$
$\alpha_m^{z(t)}$	The speed of accelerating mortality thanks to the presence of the parasite within the body	$0.01^{z(t)}$
$\zeta^{z(t)}$	Defines the ones co-infected individuals increase to AIDS quicker than the ones infected most effective with HIV	$1.002^{z(t)}$
$B_H^{z(t)}$	The rate of HIV infection	$0.001^{z(t)}$

$$\begin{aligned} {}_0^C D_t^{z(t)} N_h(t) &= A_h^{z(t)} \\ &- \alpha_{h1}^{z(t)} \left(I_h(t) + I_h(t) Q_1^{z(t)} G_m(t) + (1 - \theta_2) Y_h(t) \right) \\ &- \tau \alpha_{h1}^{z(t)} I_{mhiv}(t) - (\tau \alpha_{h1}^{z(t)} + \psi \delta_H^{z(t)}) A_{mhiv}(t) \\ &- \delta_H^{z(t)} A_{hiv} - \mu_h^{z(t)} N_h(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{z(t)} S_h(t) &= (1 - p) A_h^{z(t)} - f_h(t) S_h(t) - B_{hiv}(t) S_h(t) \\ &+ r_h^{z(t)} (I_h(t) + \theta_1 Y_h(t)) + \sigma^{z(t)} V_h(t) - \mu_h^{z(t)} S_h(t), \end{aligned}$$

$${}_0^C D_t^{z(t)} V_h(t) = p A_h^{z(t)} - f_h(t) (1 - \gamma) V_h(t) - V_h(t) (\sigma^{z(t)} + \mu_h^{z(t)}),$$

$$\begin{aligned} {}_0^C D_t^{z(t)} I_h(t) &= f_h(t - \tau_h) S_h(t - \tau_h) e^{-\mu_h^{z(t)} \tau_h} - \epsilon_2 B_{hiv}(t) I_h(t) \\ &- (r_h^{z(t)} + \alpha_{h1}^{z(t)} + \mu_h^{z(t)} + Q_1^{z(t)} G_m(t)) I_h(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{z(t)} I_{mhiv}(t) &= v_1 f_h(t - \tau_h) I_{hiv}(t - \tau_h) e^{-\mu_h^{z(t)} \tau_h} + \epsilon_2 B_{hiv}(t) I_h(t) \\ &- (\zeta^{z(t)} \alpha_{h2}^{z(t)} + \phi_2^{z(t)} + \tau \alpha_{h1}^{z(t)} + \mu_h^{z(t)} + Q_2^{z(t)} G_n(t)) I_{mhiv}(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{z(t)} I_{hiv}(t) &= S_h(t) B_{hiv}(t) + \phi_2^{z(t)} I_{mhiv}(t) + Q_2^{z(t)} G_n(t) I_{mhiv}(t) \\ &- v_1 f_h(t) I_{hiv}(t) \\ &- (\alpha_{h2}^{z(t)} + \mu_h^{z(t)} + Q_3^{z(t)} G_h(t)) I_{hiv}(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{z(t)} Y_h(t) &= f_h(t - \tau_h) (1 - \gamma) V_h(t - \tau_h) e^{-\mu_h^{z(t)} \tau_h} \\ &- (\theta_1 r_h^{z(t)} + (1 - \theta_2) \alpha_{h1}^{z(t)} + \mu_h^{z(t)}) Y_h(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{z(t)} A_{mhiv}(t) &= \zeta \alpha_{h2}^{z(t)} I_{mhiv}(t) + v_2 f_h(t - \tau_h) A_{hiv}(t - \tau_h) e^{-\mu_h^{z(t)} \tau_h} \\ &- (\mu_h^{z(t)} + \phi_3^{z(t)} + \tau \alpha_{h1}^{z(t)} + \psi \delta_H^{z(t)}) A_{mhiv}(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} A_{hiv}(t) &= \alpha_{h2}^{\alpha(t)} I_{hiv}(t) + I_{hiv}(t) Q_3^{\alpha(t)} G_h(t) + \phi_3^{\alpha(t)} A_{mhiv}(t) \\ &\quad - v_2 f_h(t) A_{hiv}(t) - (\mu_h^{\alpha(t)} + \delta_H^{\alpha(t)}) A_{hiv}(t), \\ {}_0^C D_t^{\alpha(t)} N_m(t) &= A_m^{\alpha(t)} - \alpha_m^{\alpha(t)} I_m(t) - \mu_m^{\alpha(t)} N_m(t), \end{aligned}$$

$${}_0^C D_t^{\alpha(t)} S_m(t) = A_m^{\alpha(t)} - S_m(t) f_m(t) - \mu_m^{\alpha(t)} S_m(t),$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} I_m(t) &= S_m(t - \tau_m) f_m(t - \tau_m) e^{-\mu_m^{\alpha(t)} \tau_m} \\ &\quad - (\mu_m^{\alpha(t)} + \alpha_m^{\alpha(t)}) I_m(t), \end{aligned} \quad (3)$$

where,

$$f_h = B_h^{\alpha(t)} c^{\alpha(t)} \left(1 - b^{\alpha(t)} z^{\alpha(t)} \right) \frac{I_m(t)}{N_h(t)},$$

$$B_{hiv}(t) = \frac{B_H^{\alpha(t)} \left(I_{hiv}(t) + \eta_{HM}^{\alpha(t)} I_{mhiv}(t) + \eta_A^{\alpha(t)} \left(A_{hiv}(t) + \eta_{HM}^{\alpha(t)} A_m^{\alpha(t)} \right) \right)}{N_h(t)},$$

and

$$\begin{aligned} F_m &= B_m^{\alpha(t)} c^{\alpha(t)} \left(1 - b^{\alpha(t)} z^{\alpha(t)} \right) \\ &\quad \times \frac{(I_h(t) + I_{mhiv}(t) + (1 - \epsilon^{\alpha(t)}) Y_h + A_{mhiv}(t))}{N_h(t)}, \end{aligned}$$

where, the parameters $Q_1^{\alpha(t)}$, $Q_2^{\alpha(t)}$ and $Q_3^{\alpha(t)}$ are the weight factors. It is important to notice that the parameters depend on the variable-order $\alpha(t)$ to make the system consistent in the physical sense and more consistent the reality, we must make sure that the right-hand sides of these equations have the same dimensions for more details see [44,45,47]. Concerning the equilibrium point of a dynamical model is proved in details in [28]. The basic reproduction number of the model (3) is given as follows [27]:

$$R_0 = \max\{R_m, R_{hiv}\}, \quad (4)$$

where

$$\begin{aligned} R_m &= \left(\frac{\mu_h^{\alpha(t)} \beta_h^{\alpha(t)} A_m^{\alpha(t)} e^{-\mu_h^{\alpha(t)} \tau_h^{\alpha(t)}} e^{-\mu_m^{\alpha(t)} \tau_m^{\alpha(t)}} c^2 \left(1 - b^{\alpha(t)} z^{\alpha(t)} \right)^2}{(\alpha_m^{\alpha(t)} + \mu_m^{\alpha(t)}) \mu_m^{\alpha(t)} A_h^{\alpha(t)} (\sigma^{\alpha(t)} + \mu_h^{\alpha(t)})} \right) \\ &\quad \times \left(\frac{\sigma^{\alpha(t)} + \mu_h^{\alpha(t)} (1 - P^{\alpha(t)})}{r_h^{\alpha(t)} + \mu_h^{\alpha(t)} + a_{h1}^{\alpha(t)}} + \frac{(1 - \epsilon^{\alpha(t)}) (1 - \epsilon^{\alpha(t)}) \mu_h^{\alpha(t)} P^{\alpha(t)}}{\theta_1 r_h^{\alpha(t)} + (1 - \theta_2) a_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)}} \right), \\ R_{hiv} &= \left(\frac{\beta_H^{\alpha(t)} (\mu_h^{\alpha(t)} + \delta_H^{\alpha(t)} + \eta_A^{\alpha(t)} a_{h2}^{\alpha(t)} (1 - P^{\alpha(t)}))}{(\alpha_{h2}^{\alpha(t)} + \mu_h^{\alpha(t)}) (\mu_h^{\alpha(t)} + \delta_H^{\alpha(t)})} \right), \end{aligned}$$

where R_m is the basic reproduction number of malaria model and R_{hiv} is the basic reproduction of HIV model. If $R_0 > 1$, this mean that the infection will be able to spread in a population. But if $R_0 < 1$, the infection will disappear.

4. Formulation of VOFOCP

Consider the variables in the system (3) belongs to R^{12} , let $\Omega = \{G_m(\cdot), G_n(\cdot), G_h(\cdot) | G_m, G_n, G_h \text{ are Lebesgue measurable on } [0, 1], 0 \leq G_m(\cdot), G_n(\cdot), G_h(\cdot) \leq 1, \forall t \in [0, T_f]\}$, is the set of admissible control functions.

The goal is to minimize the following cost functional:

$$\begin{aligned} J(G_m, G_n, G_h) &= \int_0^{T_f} \left(I_h + I_{hiv} + I_{mhiv} + \frac{1}{2} B_1 G_m^2 + \frac{1}{2} B_2 G_n^2 + \frac{1}{2} B_3 G_h^2 \right) dt, \end{aligned} \quad (5)$$

where B_1, B_2, B_3 are the weight coefficients. Subjected to the following constraints:

Let us denoting the state vector by

$$X := (N_h, S_h, V_h, I_h, I_{mhiv}, I_{hiv}, Y_h, A_{mhiv}, A_{hiv}, N_m, S_m, I_m, G_m, G_n, G_h, t), \quad i = 1, \dots, 12,$$

$$Y := X(t - d_\tau) : d_\tau = \{\tau_h, \tau_m\},$$

$$G = (G_m, G_n, G_h)$$

The dynamical system (3) can be written as:

$${}_0^C D_t^{\alpha(t)} X = f(X, Y, G), \quad (6)$$

and satisfying these initial conditions.

$$\begin{aligned} N_h(\vartheta) &= \psi_1(\vartheta), S_h(\vartheta) = \psi_2(\vartheta), V_h(\vartheta) = \psi_3(\vartheta), I_h(\vartheta) \\ &= \psi_4(\vartheta), I_{mhiv}(\vartheta) = \psi_5(\vartheta), I_{hiv}(\vartheta) = \psi_6(\vartheta), Y_h(\vartheta) \\ &= \psi_7(\vartheta), A_{mhiv}(\vartheta) = \psi_8(\vartheta), A_{hiv}(\vartheta) = \psi_9(\vartheta), N_m(\vartheta) \\ &= \psi_{10}(\vartheta), S_m(\vartheta) = \psi_{11}(\vartheta) \text{ and } I_m(\vartheta) = \psi_{12}(\vartheta), \text{ where } \vartheta \in [-d_\tau, 0]. \end{aligned}$$

The modified cost functional takes the form:

$$\tilde{J} = \int_0^{T_f} [H(X, Y, G, \lambda) - \lambda f(X, Y, G)] dt, \quad (7)$$

where $\lambda = \lambda_i$, $i = 1, 2, 3, \dots, 12$, and $H(X, Y, G, \lambda)$ is the Hamiltonian functional of the form

$$\begin{aligned} H(X, Y, G, \lambda) &= \left(I_h + I_{hiv} + I_{mhiv} + \frac{1}{2} B_1 G_m^2 + \frac{1}{2} B_2 G_n^2 + \frac{1}{2} B_3 G_h^2 \right) \\ &\quad + \lambda f(X, Y, G). \end{aligned} \quad (8)$$

The necessary conditions can be obtained by extension the conditions in [11] to variable order fractional as [25] with time delay [47]. These can be derived from (7) and (8) as follows:

$${}_0^C D_t^{\alpha(t)} \lambda = H_X[t] + X_{[0, T_f - d_\tau]} H_Y(t + d_\tau), \quad (9)$$

where

$$X_{[0, T_f - d_\tau]} = \begin{cases} 1, & t \in [0, T_f - d_\tau], \quad d_\tau = h, m, \\ 0, & \text{otherwise,} \end{cases} \quad (10)$$

and it is required that:

$$\lambda(T_f) = 0, \quad (11)$$

where λ is the Lagrange multipliers.

$$H_G[t] = 0. \quad (12)$$

Also,

$${}_0^C D_t^{\alpha(t)} X = H_\lambda[t], \quad (13)$$

Theorem 4.1. Let G_m^* , G_n^* and G_h^* be the optimal controls with corresponding state variables X^* then there exist adjoint variables λ^* , satisfies the following:(i) Co-state equations:

$${}_C D_t^{\alpha(t)} \lambda^* = H_{X^*}[t] + X_{[0, T_f - d_t]} H_{Y^*}(t + d_t), \quad (14)$$

(ii) with transversality conditions

$$\lambda^*(T_f) = 0, \quad (15)$$

(iii) optimality condition:

$$H(X, Y, G, \lambda) = \min_{0 \leqslant G_m, G_n, G_h \leqslant 1} H(X^*, Y^*, G^*, \lambda^*). \quad (16)$$

Furthermore, the control functions G_m , G_n , G_h are given by:

$$G_m^* = \min \left(1, \max \left(0, \frac{I_h^* \lambda_4^* Q_1^{\alpha(t)} - I_h^* \lambda_2^* Q_1^{\alpha(t)}}{B1} \right) \right), \quad (17)$$

$$G_n^* = \min \left(1, \max \left(0, \frac{\lambda_5^* I_{mhiv}^* Q_2^{\alpha(t)} - \lambda_6^* I_{mhiv}^* Q_2^{\alpha(t)}}{B2} \right) \right), \quad (18)$$

$$G_h^* = \min \left(1, \max \left(0, \frac{\lambda_6^* I_{hiv}^* Q_3^{\alpha(t)} - \lambda_9^* I_{hiv}^* Q_3^{\alpha(t)}}{B3} \right) \right). \quad (19)$$

Proof. Using the conditions (9), We can get the Eq. (14), where the Hamiltonian H_a^* is given by:

$$H^* = \frac{1}{2} B_1 G_m^{*2} + \frac{1}{2} B_2 G_n^{*2} + \frac{1}{2} B_3 G_h^{*2} + {}_0^C D_t^{\alpha(t)} f(X^*, Y^*, G^*). \quad (20)$$

Moreover, the transversality conditions $\lambda^*(T_f) = 0$ hold and the optimal controls (17)–(19) can be claimed from the minimization condition (16). By substituting the values of G_m^* , G_n^* , G_h^* in the control system (3), we get the state system as follows:

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} N_h^*(t) &= A_h^{\alpha(t)} - \alpha_{h_1}^{\alpha(t)} \left(I_h^*(t) + I_h(t) Q_1^{\alpha(t)} G_m^*(t) + (1 - \theta_2) Y_h^*(t) \right) \\ &\quad - \tau \alpha_{h_1}^{\alpha(t)} I_{mhiv}^*(t) - \left(\tau \alpha_{h_1}^{\alpha(t)} + \psi \delta_H^{\alpha(t)} \right) A_{mhiv}^*(t) - \delta_H^{\alpha(t)} A_{hiv}^*(t) \\ &\quad - \mu_h^{\alpha(t)} N_h^*(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} S_h^*(t) &= A_h^{\alpha(t)} (1 - p) - f_h(t) S_h^*(t) - B_{hiv}(t) S_h^*(t) \\ &\quad + r_h^{\alpha(t)} (I_h^*(t) + \theta_1 Y_h^*(t)) + \sigma^{\alpha(t)} V_h^*(t) - \mu_h^{\alpha(t)} S_h^*(t), \end{aligned}$$

$${}_0^C D_t^{\alpha(t)} V_h^*(t) = p A_h^{\alpha(t)} - f_h(t) (1 - \gamma) V_h^*(t) - V_h^*(t) \left(\sigma^{\alpha(t)} + \mu_h^{\alpha(t)} \right),$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} I_h^*(t) &= f_h(t - \tau_h) S_h^*(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} - \epsilon_2 B_{hiv}(t) I_h^*(t) \\ &\quad - \left(r_h^{\alpha(t)} + \alpha_{h_1}^{\alpha(t)} + \mu_h^{\alpha(t)} + Q_1^{\alpha(t)} G_m \right)^* (t) I_h^*(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} I_{mhiv}^*(t) &= v_1 f_h(t - \tau_h) I_{hiv}^*(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} + \epsilon_2 B_{hiv}(t) I_h^*(t) \\ &\quad - \left(\zeta^{\alpha(t)} \alpha_{h_2}^{\alpha(t)} + \phi_2^{\alpha(t)} + \tau \alpha_{h_1}^{\alpha(t)} + \mu_h^{\alpha(t)} + Q_2^{\alpha(t)} G_n^*(t) \right) I_{mhiv}^*(t), \end{aligned}$$

$$\begin{aligned} {}_0^C D_t^{\alpha(t)} I_{hiv}^*(t) &= S_h^*(t) B_{hiv}(t) + \phi_2^{\alpha(t)} I_{mhiv}^*(t) + Q_2^{\alpha(t)} G_n^*(t) I_{mhiv}^*(t) \\ &\quad - v_1 f_h(t) I_{hiv}^*(t) \\ &\quad - \left(\alpha_{h_2}^{\alpha(t)} + \mu_h^{\alpha(t)} + Q_3^{\alpha(t)} G_h^*(t) \right) I_{hiv}^*(t), \\ {}_0^C D_t^{\alpha(t)} Y_h^*(t) &= f_h(t - \tau_h) (1 - \gamma) V_h^*(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} \\ &\quad - \left(\theta_1 r_h^{\alpha(t)} + (1 - \theta_2) \alpha_{h_1}^{\alpha(t)} + \mu_h^{\alpha(t)} \right) Y_h^*(t), \\ {}_0^C D_t^{\alpha(t)} A_{mhiv}^*(t) &= \zeta \alpha_{h_2}^{\alpha(t)} I_{mhiv}^*(t) + v_2 f_h(t - \tau_h) A_{hiv}^*(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} \\ &\quad - \left(\mu_h^{\alpha(t)} + \phi_3^{\alpha(t)} + \tau \alpha_{h_1}^{\alpha(t)} + \psi \delta_H^{\alpha(t)} \right) A_{mhiv}^*(t), \\ {}_0^C D_t^{\alpha(t)} A_{hiv}^*(t) &= \alpha_{h_2}^{\alpha(t)} I_{hiv}^*(t) + I_{hiv}^*(t) Q_3^{\alpha(t)} G_h^*(t) + \phi_3^{\alpha(t)} A_{mhiv}^*(t) \\ &\quad - v_2 f_h(t) A_{hiv}^*(t) - \left(\mu_h^{\alpha(t)} + \delta_H^{\alpha(t)} \right) A_{hiv}^*(t), \\ {}_0^C D_t^{\alpha(t)} N_m^*(t) &= A_m^{\alpha(t)} - \alpha_m^{\alpha(t)} I_m^*(t) - \mu_m^{\alpha(t)} N_m^*(t), \\ {}_0^C D_t^{\alpha(t)} S_m^*(t) &= A_m^{\alpha(t)} - f_m(t) S_m^*(t) - \mu_m^{\alpha(t)} S_m^*(t), \\ {}_0^C D_t^{\alpha(t)} I_m^*(t) &= f_m(t - \tau_m) S_m^*(t - \tau_m) e^{-\mu_m^{\alpha(t)} \tau_m} - \left(\mu_m^{\alpha(t)} + \alpha_m^{\alpha(t)} \right) I_m^*(t). \end{aligned} \quad (21)$$

5. Numerical methods for solving VOFOCP

In this section we consider two methods for solving VOFOCP. These methods are GL-SFDM [38] and GL-NSFDM [34,37] and for more details about the rules for the construction of NSFDM see [40]. Concerning the convergence of the NSFDM, we refer to this reference [46].

The nonstandard differences approximation of Caputo operator in (1) is given by the Grünwald-Letinkov's approach as follows:

$${}_0^C D_t^{\alpha(t)} x(t)|_{t=t_n} = \frac{1}{(\phi(\Delta t))^{\alpha(t)}} \left(x_{n+1} - \sum_{i=1}^{n+1} w_i x_{n+1-i} - q_{n+1} x_0 \right), \quad (22)$$

where

$$w_i = (-1)^{i-1} \binom{\alpha(t)}{i}, w_1 = \alpha(t),$$

$$q_i = \frac{t_i^{-\alpha(t)}}{\Gamma(1 - \alpha(t))}, i = 1, 2, 3, \dots, n+1.$$

The coordinate of each mesh point is:

$$t_n = n \Delta t, \quad n = 0, 1, 2, 3, \dots, N,$$

where

$$h := \Delta t = \frac{t_{final}}{N},$$

where N is a natural number, t_{final} is the final time and h is represented the step size.

Now by using the relation (22) we obtain the following GL-NSFDM [37,34] for system (3). Since each of these equations is linear in $N_{h_{n+1}}$, $S_{h_{n+1}}$, $V_{h_{n+1}}$, $I_{h_{n+1}}$, $I_{mhiv_{n+1}}$, $I_{hiv_{n+1}}$, $A_{mhiv_{n+1}}$, $A_{hiv_{n+1}}$, $N_{m_{n+1}}$, $S_{m_{n+1}}$ and $I_{m_{n+1}}$, after some simple calculations, we have the following explicit solutions:

$$\begin{aligned}
N_{h_{n+1}} &= \frac{1}{\left(1 + \phi(h)^{\alpha(t)} \mu_h^{\alpha(t)}\right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(A_h^{\alpha(t)} - \alpha_{h1}^{\alpha(t)} \left(I_{h_n} + I_{h_n} Q_1^{\alpha(t)} G_m - (1 - \theta_2) Y_{h_n} \right) \right. \right. \\
&- \tau \alpha_{h1}^{\alpha(t)} I_{mhiv_n} - \left(\tau \alpha_{h1}^{\alpha(t)} + \psi \delta_H^{\alpha(t)} \right) A_{mhiv_n}(t) - \delta_H^{\alpha(t)} A_{hiv_n}(t) \Big) \\
&+ \sum_{i=1}^{n+1} w_i N_{h_{n+1-i}} + q_{n+1} N_h(0),
\end{aligned}$$

$$\begin{aligned}
S_{h_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\mu_h^{\alpha(t)} + B_{hiv_n}(t) + F_{h_n} \right)}(t) \\
&\times \left(\phi(h)^{\alpha(t)} \left((1 - P) A_h^{\alpha(t)} + r_h^{\alpha(t)} (I_{h_n}(t) + \theta_1 Y_{h_n}(t)) + \sigma^{\alpha(t)} V_{h_n}(t) \right) \right. \\
&+ \sum_{i=1}^{n+1} w_i S_{h_{n+1-i}} + q_{n+1} S_h(0) \Big),
\end{aligned}$$

$$\begin{aligned}
V_{h_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\sigma^{\alpha(t)} + \mu_h^{\alpha(t)} + f_h(t)(1 - \gamma) \right)} \\
&\times \left(\phi(h)^{\alpha(t)} P A_h^{\alpha(t)} + \sum_{i=1}^{n+1} w_i V_{h_{n+1-i}} + q_{n+1} V_h(0) \right),
\end{aligned}$$

$$\begin{aligned}
I_{h_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\epsilon_2 B_{hiv_n}(t) + \left(r_h^{\alpha(t)} + \alpha_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)} \right) + Q_1^{\alpha(t)} G_m \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(f_{h_n}(t - \tau_h) S_{h_n}(t - \tau_h) \times e^{-\mu_h^{\alpha(t)} \tau_h} \right) + \sum_{i=1}^{n+1} w_i I_{h_{n+1-i}} + q_{n+1} I_h(0) \right),
\end{aligned}$$

$$\begin{aligned}
I_{mhiv_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\zeta^{\alpha(t)} \alpha_{h2}^{\alpha(t)} + \phi_2^{\alpha(t)} + \tau \alpha_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)} + Q_2^{\alpha(t)} G_n \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(v_1 f_{h_n}(t - \tau_h) \times I_{hiv_n}(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} + \epsilon_2 B_{hiv_n}(t) I_h(t) \right) \right. \\
&+ \sum_{i=1}^{n+1} w_i I_{mhiv_{n+1-i}} + q_{n+1} I_{mhiv}(0) \Big),
\end{aligned}$$

$$\begin{aligned}
I_{hiv_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(v_1 f_{h_n}(t) + \alpha_{h2}^{\alpha(t)} + \mu_h^{\alpha(t)} + Q_3^{\alpha(t)} G_h \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(B_{hiv_n}(t) S_{h_n}(t) + \phi_2^{\alpha(t)} I_{mhiv_n}(t) + Q_2^{\alpha(t)} G_n I_{mhiv_n} \right) \right. \\
&+ \sum_{i=1}^{n+1} w_i I_{hiv_{n+1-i}} + q_{n+1} I_{hiv}(0) \Big),
\end{aligned}$$

$$\begin{aligned}
Y_{h_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\theta_1 r_h^{\alpha(t)} + (1 - \theta_2) \alpha_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)} \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(f_{h_n}(t - \tau_h) (1 - \gamma) V_{h_n}(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} \right) \right. \\
&+ \sum_{i=1}^{n+1} w_i Y_{h_{n+1-i}} + q_{n+1} Y_h(0) \Big),
\end{aligned}$$

$$\begin{aligned}
A_{mhiv_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\mu_h^{\alpha(t)} + \phi_3^{\alpha(t)} + \tau \alpha_{h1}^{\alpha(t)} + \psi \delta_H^{\alpha(t)} \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(\zeta \alpha_{h2}^{\alpha(t)} I_{mhiv_n}(t) + v_2 f_{h_n}(t - \tau_h) \right. \right. \\
&\times A_{hiv_n}(t - \tau_h) e^{-\mu_h^{\alpha(t)} \tau_h} - \mu_h^{\alpha(t)} \Big) \\
&+ \sum_{i=1}^{n+1} w_i A_{mhiv_{n+1-i}} + q_{n+1} A_{mhiv}(0) \Big), \\
A_{hiv_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(v_2 f_{h_n}(t) + \mu_h^{\alpha(t)} + \delta_H^{\alpha(t)} \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(\alpha_{h2}^{\alpha(t)} I_{hiv_n}(t) + Q_3^{\alpha(t)} G_h I_{hiv_n}(t) + \phi_3^{\alpha(t)} A_{mhiv_n}(t) \right) \right. \\
&+ \sum_{i=1}^{n+1} w_i A_{hiv_{n+1-i}}(t) + q_{n+1} A_{hiv}(0) \Big), \\
N_{m_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \mu_m^{\alpha(t)}} \\
&\times \left(\phi(h)^{\alpha(t)} \left(A_m^{\alpha(t)} - \alpha_m^{\alpha(t)} I_{m_n}(t) \right) + \sum_{i=1}^{n+1} w_i N_{m_{n+1-i}}(t) + q_{n+1} N_m(0) \right), \\
S_{m_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(f_{m_n}(t) + \mu_m^{\alpha(t)} \right)} \\
&\times \left(\phi(h)^{\alpha(t)} A_m^{\alpha(t)} + \sum_{i=1}^{n+1} w_i S_{m_{n+1-i}}(t) + q_{n+1} S_m(0) \right), \\
I_{m_{n+1}} &= \frac{1}{1 + \phi(h)^{\alpha(t)} \left(\mu_m^{\alpha(t)} + \alpha_m^{\alpha(t)} \right)} \\
&\times \left(\phi(h)^{\alpha(t)} \left(f_{m_n}(t - \tau_m) S_{m_n}(t - \tau_m) e^{-\mu_m^{\alpha(t)} \tau_m} \right. \right. \\
&+ \sum_{i=1}^{n+1} w_i I_{m_{n+1-i}}(t) + q_{n+1} I_m(0) \Big),
\end{aligned} \tag{23}$$

5.1. Stability of GL-NSFD

In this section we will prove that the GL-NSFD approximation is stable. Let us consider a test problem in the following form:

$${}_0^C D_t^{\alpha(t)} y(t) = E_0 y(t) + E_1 y(t - d_\tau), \quad t > 0, \tag{24}$$

$$E_1 < E_0, \quad y(t) = \theta(t), \quad t \in [-d_\tau, 0], \quad y(0) = y_0,$$

such that $0 < \alpha(t) \leq 1$, $E_0 < 0$ is a constant and $\theta(t)$, is continuous and bounded function.

Theorem 5.1. The GL-NSFD (22) is stable and consistent when applied to the test Problem (24) for all $t \geq 0$.

We assume that the approximate solution of (24) is of the form $y(t_n) \approx y_n \equiv \xi_n$, then (24) can be reduced to

$$\frac{1}{h^{\alpha(t)}} \left(\xi_{n+1} - \sum_{i=1}^{n+1} \mu_i \xi_{n+1-i} - q_{i+1} \xi_0 \right) = E_0 \xi_n + E_1 \xi_{n-\tau},$$

or

$$\xi_{n+1} = h^{\alpha(t)} E_0 \xi_n + h^{\alpha(t)} E_1 \xi_{n-\tau} + \sum_{i=1}^{n+1} \mu_i \xi_{n+1-i} + q_{i+1} \xi_0, \quad n \geq 1.$$

Since

$$\mu_1 = \alpha(t) < 1, \quad E_0 < 0,$$

and

$$0 < q_{i+1} < q_i < \dots < q_1 = \frac{1}{\Gamma(1 - \alpha(t))},$$

then

$$\xi_1 \leq \xi_0, \quad (25)$$

$$\xi_{n+1} \leq h^{\alpha(t)} E_0 + h^{\alpha(t)} E_1 \xi_{n-\tau} + \xi_n + \sum_{i=1}^{n+1} \mu_i \xi_{n+1-i}, \quad n \leq 1. \quad (26)$$

Thus, for $n = 1$, the inequality (26) implies

$$\begin{aligned} \xi_2 &\leq \alpha(t) E_0 \xi_1 + h^{\alpha(t)} E_1 \xi_{n-\tau} + \mu_1 \xi_1 + \mu_2 \xi_0 \\ &\leq (\alpha(t) E_0 + \mu_1) \xi_1 + \mu_2 \xi_0. \end{aligned}$$

Using the relation (25) and the positivity of the coefficients E_0, μ_2, μ_1 and $\alpha(t)$ we get

$$\xi_2 \leq \xi_1, \quad (27)$$

Repeating the process, we have from (26)

$$\xi_{n+1} \leq h^{\alpha(t)} E_0 \xi_n + h^{\alpha(t)} E_1 \xi_{n-\tau} + \sum_{i=1}^{n+1} \mu_i \xi_{n+1-i} \leq \xi_n. \quad (28)$$

Thus,

$$\xi_{n+1} \leq \xi_n \leq \xi_{n-1} \leq \xi_{n-2} \leq \dots \leq \xi_0,$$

with the assumption that

$$\xi_{n+1} = |\gamma^{n+1}| \leq \xi_0 = |\gamma^0|.$$

which entails $\|\gamma^{n+1}\| \leq \|\gamma^0\|$, so that we have stability.

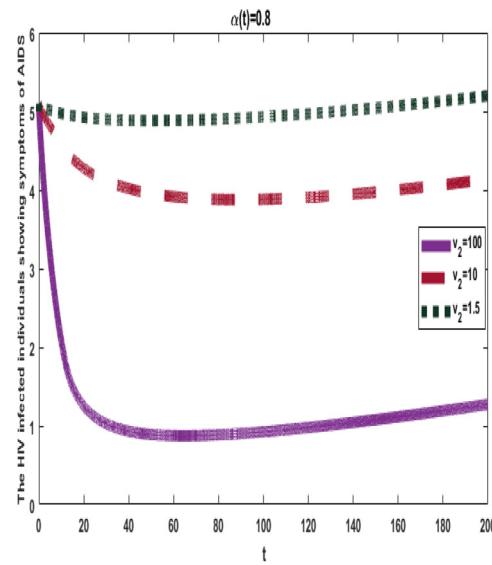
6. Numerical Simulations

In the following, numerical simulations of the proposed model (3) with and without optimal control are presented. All values of the parameters are given in Table 2. Throughout this section we used different values of $\alpha(t)$ and $\phi(h)$. The initial conditions are given as follows: $N_h = 430, S_h(0) = 300, V_h(0) = 100, I_h(0) = 5, I_{mhiv}(0) = 5, I_{hiv}(0) = 5, Y_h(0) = 5, A_{mhiv}(0) = 5, A_{hiv}(0) = 5, N_m(0) = 450, S_m(0) = 430, I_m(0) = 20$ two methods;

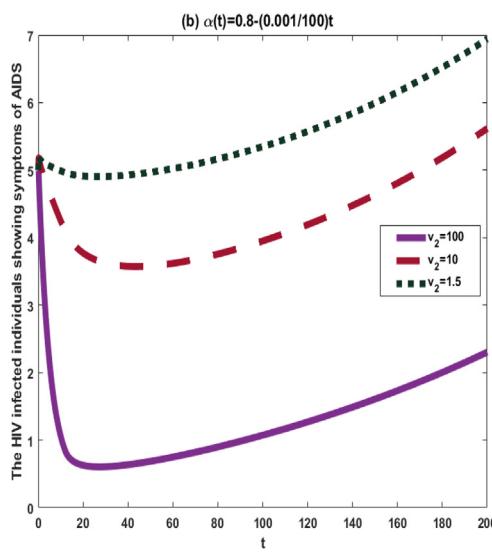
GL-NSFDM and GL-SFDM are used to solve the state system (21). Then by using the implicit finite difference method [36] we will solve the co-state Eqs. (29) with transversality

Table 4 Comparison between the values of the cost functional using GL-NSFDM with and without controls cases and $T_f = 100$ with $\phi(h) = e^h - 1$.

$\alpha(t)$	$J(G_n^*, G_m^*, G_h^*)$ with three control	$J(G_n^*, G_m^*, G_h^*)$ without control	Reduction
0.7-(0.001) t	1.4163e + 04	3.0360e + 04	53.35%
0.7-(0.008) t	1.5872e + 04	4.6042e + 04	65.53%
0.7-(0.002) t	3.4657e + 03	4.1867e + 04	91.72%
0.9-(0.008) t	3.7568e + 03	7.1097e + 04	94.72%
0.7-(0.003) t	5.1003e + 03	5.2077e + 04	90.21%



(a)



(b)

Fig. 1 Numerical simulations of A_{hiv} at (a) $\alpha(t) = 0.8$ and (b) $\alpha(t) = 0.8 - (0.001/100)t$ with $B_h = 0.01$ and $G_m = G_n = G_h = 0$ using GL-NSFDM..

Table 3 Comparison between GL-NSFDM and GL-SFDM when $t_{final} = 1000$ for different value of h and $\alpha(t) = 0.8 - 0.0001t$.

h	GL-NSFDM	GL-SFDM
0.1	Convergent	Convergent
1	Convergent	Convergent
2	Convergent	Divergent
10	Convergent	Divergent
20	Convergent	Divergent
50	Convergent	Divergent

conditions (11). **Table 3** reports the convergence behavior of the solution by using GL-NSFDM and GL-SFDM when $\alpha(t) = 0.8 - 0.0001t$. We can conclude from this table that GL-NSFDM is convergent for large h while GL-SFDM converges only when h is small. So, GL-NSFDM can save the

computational time. **Table 4** shows the comparison between the values of objective functional using GL-NSFDM with and without controls cases and $T_f = 100$.

We show in **Fig. 1** in uncontrolled case that, the effect of the parameter v_2 which is the susceptibility to malaria of

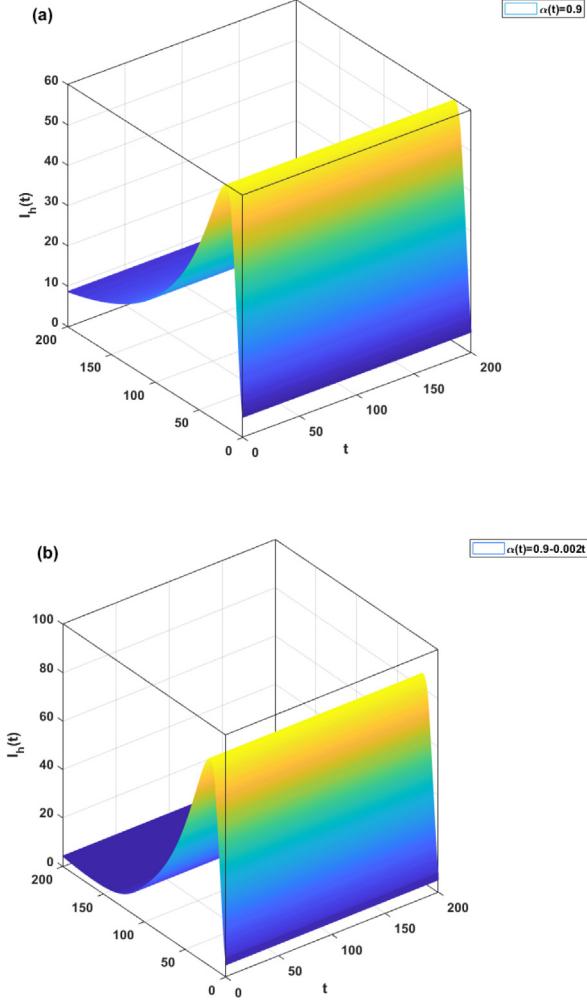


Fig. 2 The individuals infected with malaria with $B_h = 0.05$, $v_2 = 100$, $G_m, G_n, G_h = 0$ at (a) $\alpha(t) = 0.9$, (b) $\alpha(t) = 0.9 - 0.002t$ using GL-NSFDM..

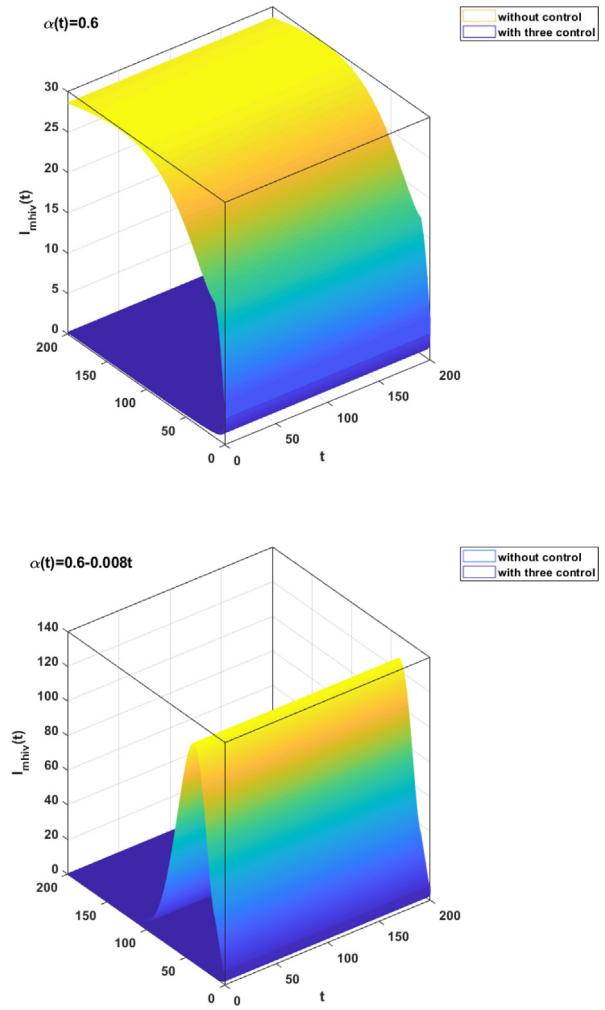


Fig. 4 Numerical simulations of I_{mhiv} with $\psi = 2$ and $B_h = 0.05$ at (a) $\alpha(t) = 0.6$ (b) $\alpha(t) = 0.6 - 0.008t$ using GL-NSFDM..

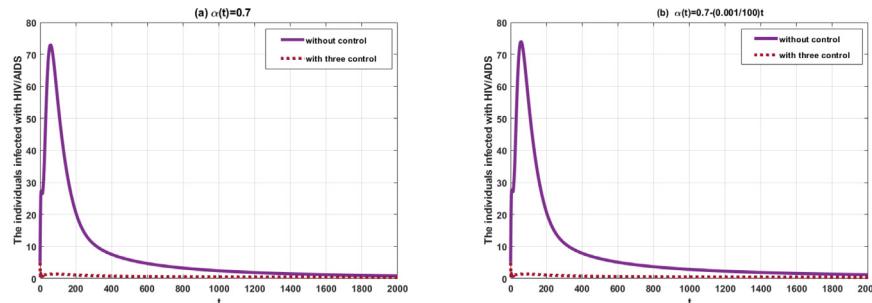


Fig. 3 Numerical simulations of the individuals infected with HIV/AIDS with $\psi = 3$ and $B_h = 0.05$, $v_2 = 100$ at (a) $\alpha(t) = 0.7$, (b) $\alpha(t) = 0.7 - (0.01/100)t$, using GL-NSFDM..

individuals showing symptoms of AIDS. It is shown that when v_2 increases; the number of HIV infected individuals showing symptoms of AIDS decreases. Also, when we use the variable order fractional $\alpha(t) = 0.8 - (0.01/100)t$ means the memory in the model is described by a decreasing function so the model behavior is slower with time. Fig. 2, explains how the behavior of A_{hiv} is changing at $\alpha(t) = 0.9$, $\alpha(t) = 0.9 - 0.002t$ using the proposed method in uncontrolled case. Also, we noted that when we use the variable order fractional $\alpha(t) = 0.9 - (0.002)t$ the memory is described by a decreasing function so the model behavior is slower with time. Figs. 3–7, shows the behavior of I_h , I_{hiv} and I_{mhiv} in cases of control and without control at different values of $\alpha(t)$. These figures demonstrate that in case of without control, the number of the population of infected and asymptotically infected are increasing, while the number of these population are decreasing in controlled case. Fig. 8, show the behavior of I_h , I_{hiv} and I_{mhiv} in the control case with different values of $\alpha(t)$. Fig. 9, shows the behavior of approximate solutions for the control variables at $\alpha(t) = 0.7 - (0.001)t$. Table 5 reports the values of objective functional using GL-NSFDM and GL-SFDM, we noted that the result which obtain by GL-NSFDM is better than the result which obtain by GL-SFDM. Moreover, Table 6 shows the comparison between

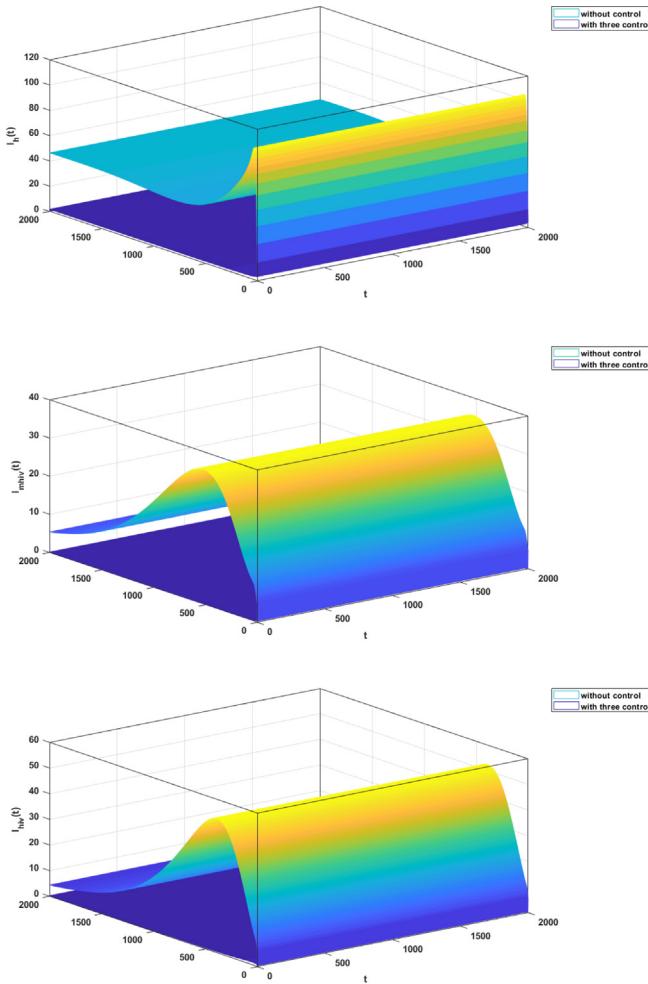


Fig. 5 Numerical simulations of I_h , I_{mhiv} , I_{hiv} with $\psi = 3$, $B_h = 0.05$ at $\alpha(t) = 0.8 - 0.01\sin(\pi t)$ using GL-NSFDM..

the values of objective functional using different $\phi(h)$ and $\alpha(t)$, we noted that the results which are obtained by $\phi(h) = 3(e^h - 1)$ is the best results.

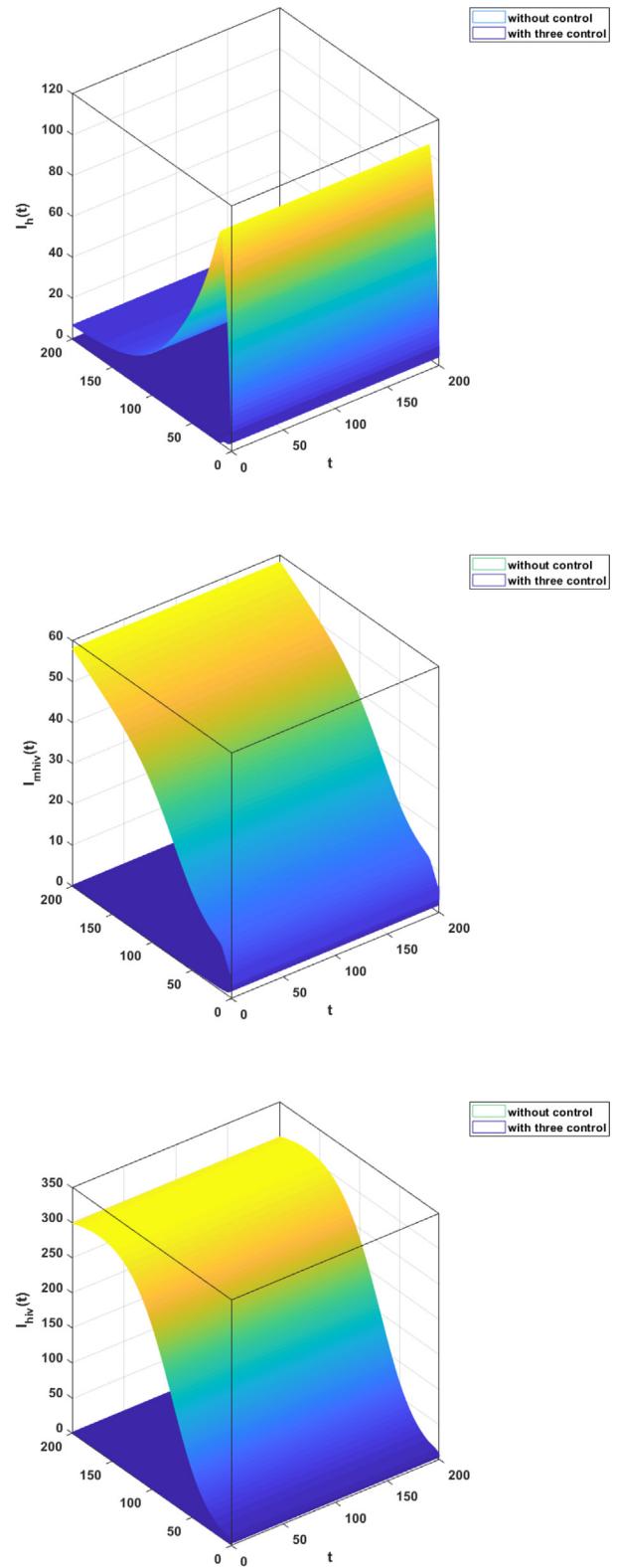


Fig. 6 Numerical simulations of I_h , I_{mhiv} , I_{hiv} with $\psi = 3$, $B_h = 0.05$ and $\alpha(t) = 0.7 - (0.001)t$ using GL-NSFDM..

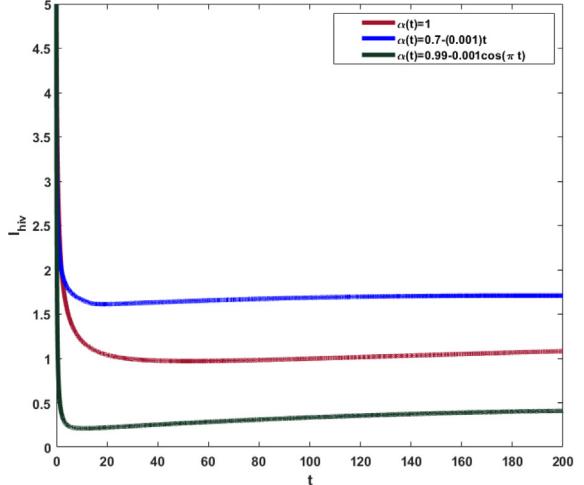
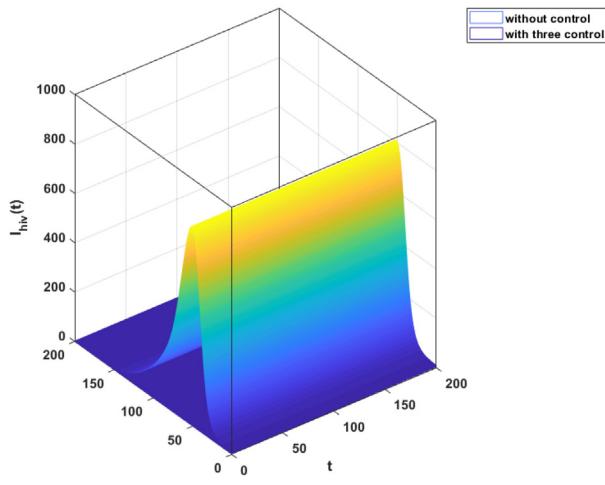
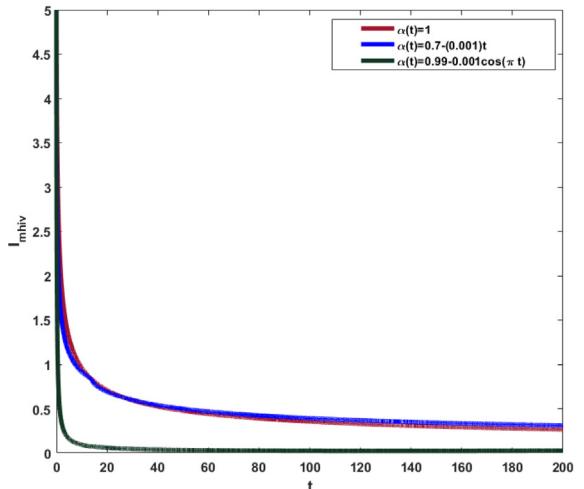
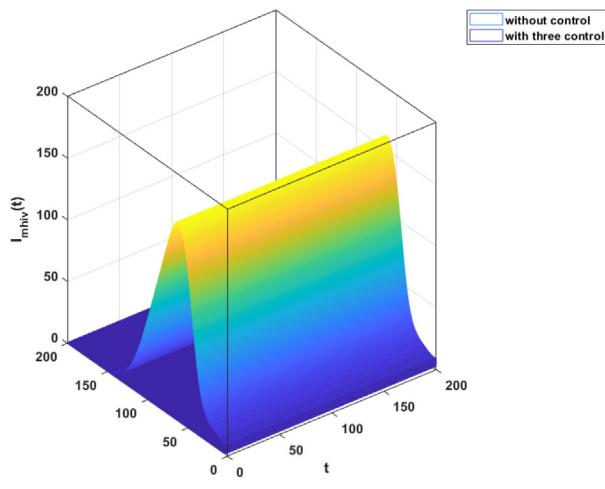
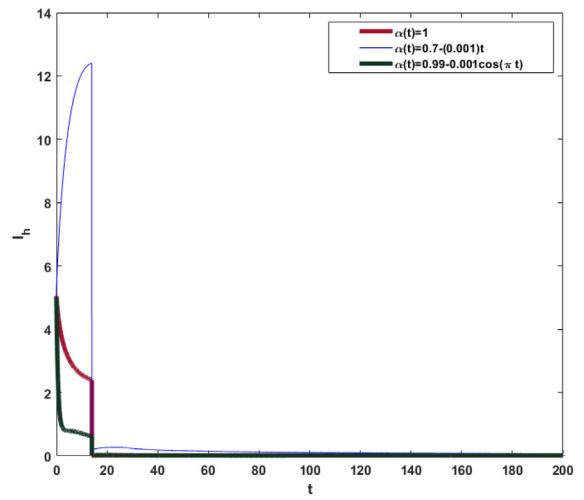
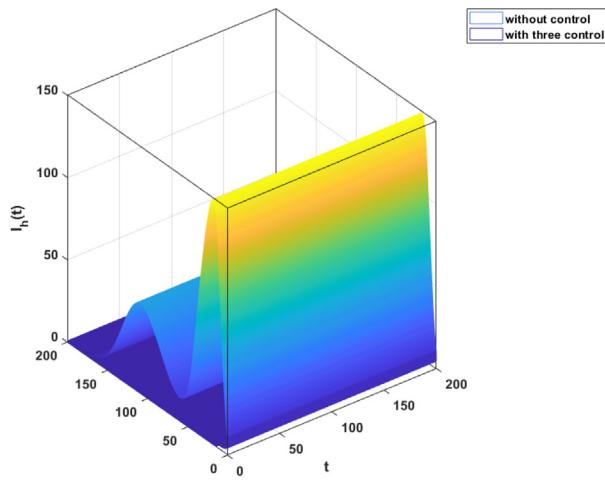


Fig. 7 Numerical simulations of I_h, I_{mhiv}, I_{hiv} with $\psi = 2, B_h = 0.05$ and $\alpha(t) = 0.9 - (0.008)t$ using GL-NSFDM..

Fig. 8 Numerical simulations of I_h, I_{mhiv}, I_{hiv} using GL-NSFDM at different $\alpha(t)$ in the control case..

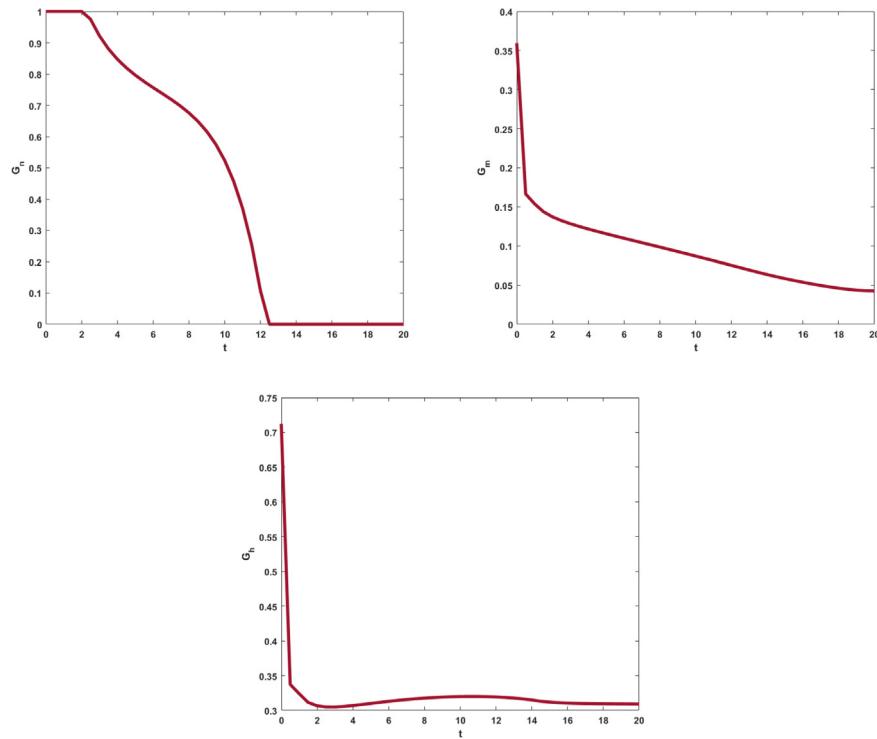


Fig. 9 Numerical simulations of the control variables at $\alpha(t) = 0.7 - (0.001)t$ using GL-NSFDM..

Table 5 Comparison between the value of cost functional using GL-NSFDM and GL-SFDM with $T_f = 50$ with $\phi(h) = 0.0001(e^h - 1)$.

$\alpha(t)$	GL-SFDM	GL-NSFDM
1	1.3490e + 04	8.3440e + 03
0.99-(0.001) cos(πt)	1.3124e + 04	7.0247e + 03
0.7-(0.001) t	1.5837e + 04	1.6399e + 03
0.7-(0.003) t	1.8194e + 04	5.9756e + 03
0.9-(0.008) t	2.5034e + 04	5.4049e + 03

7. Conclusions

In this paper, optimal control of HIV/AIDS and malaria mathematical model with variable order fractional operator and multi-delays time is presented. Three control variables

are presented in this model to minimize the number of I_h , I_{hiv} and I_{mhiv} . Necessary optimality conditions are derived. GL-NFDM is constructed to study the behavior of the proposed model. Special attention is given to study the stability of the proposed method. It was shown that this method has good stability properties. Some simulations are presented to support our theoretical findings. It is concluded that, the proposed dynamical model is more suitable and more general to describe the biological phenomena with memory than the integer and fractional order model. Also, the combination of variable order fractional derivative with time-delay and optimal control in the model improves the dynamics and increases complexity of the model. Moreover, GL-NFDM can be applied to solve such variable order fractional optimality systems simply and effectively.

Declaration of Competing Interest

None.

Table 6 Comparison between GL-SFDM and GL-NSFDM with different $\phi(h)$, $T_f = 200$.

$\alpha(t)$	GL-SFDM	GL-NSFDM	GL-NSFDM	GL-NSFDM
	$\phi(h) = (e^h - 1)$		$\phi(h) = 3(e^h - 1)$	$\phi(h) = 0.0001(e^h - 1)$
1	2.0099e + 04	1.4661e + 04	9.9821e + 03	1.2685e + 04
0.99 - 0.001cos(πt)	2.0722e + 04	1.6621e + 04	9.0524e + 03	1.2700e + 04
1 - 0.1sin(0.008t)	1.9277e + 04	1.6509e + 04	8.3037e + 03	1.2717e + 04
0.98 - 0.01cos(πt)	1.5019e + 04	1.3107e + 04	7.3999e + 03	1.2740e + 04
0.99 - 0.005cos(πt)	2.0894e + 04	1.8938e + 04	8.6873e + 03	1.2707e + 04
0.98 - (0.0002/100)t	1.8923e + 04	1.6497e + 04	8.2780e + 03	1.2719e + 04

Appendix A. Appendix

The adjoint (co-state) equations given as follows:

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_1^* = & \left(-\lambda_1^* \mu_h^{\alpha(t)} \right. \\ & + \frac{\lambda_2^* S_h^* B_h^{\alpha(t)} (I_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} I_{mhiv}^*(t) + \eta_A^{\alpha(t)} (A_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} A_{mhiv}^*(t)))}{N_h^{*2}(t)} \\ & - \frac{\lambda_3^* (1 - \gamma^{\alpha(t)}) V_h^*(t) B_h^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} I_m^*(t)}{N_h^{*2}(t)} \\ & - \frac{\lambda_4^* S_h^*(t) B_h^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} I_m^*(t)}{N_h^{*2}(t)} \\ & - \frac{\lambda_5^* \epsilon_2^{\alpha(t)} I_h^*(t) B_h^{\alpha(t)} (I_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} I_{mhiv}^*(t) + \eta_A^{\alpha(t)} (A_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} A_{mhiv}^*(t)))}{N_h^{*2}(t)} \\ & - \frac{\lambda_6^* B_h^{\alpha(t)} (I_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} I_{mhiv}^*(t) + \eta_A^{\alpha(t)} (A_{hiv}^*(t) + \eta_{HM}^{\alpha(t)} A_{mhiv}^*(t)))}{N_h^{*2}(t)} \\ & - \frac{\lambda_7^* (1 - \gamma^{\alpha(t)}) B_h^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} I_m^* V_h^*(t)}{N_h^{*2}(t)} \\ & - \frac{\lambda_8^* v_2^{\alpha(t)} A_{hiv}^*(t) B_h^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} I_m^*(t)}{N_h^{*2}(t)} \\ & \left. - \frac{\lambda_9^* v_2^{\alpha(t)} B_h^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} I_m^*(t)}{N_h^{*2}(t)} \right), \end{aligned}$$

$${}_{T_f}^C D_t^{\alpha(t)} \lambda_2^* = \left(-\lambda_2^* (B_{hiv}(t) + \mu_h^{\alpha(t)} - f_h(t) \lambda_2^* (\lambda_4^* f_h(t) + \lambda_6^* B_{hiv}(t))) \right),$$

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_3^* = & \left(\lambda_2^* \sigma^{\alpha(t)} - \lambda_3^* (1 - \gamma^{\alpha(t)}) f_h(t) - \lambda_3^* (\sigma^{\alpha(t)} + \mu_h^{\alpha(t)}) \right. \\ & \left. + \lambda_7^* f_h(t) (1 - \gamma^{\alpha(t)}) e^{-\mu_h^{\alpha(t)} \tau_h} \right), \end{aligned}$$

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_4^* = & \left(1 - \alpha_{h1}^{\alpha(t)} \lambda_1^* + r_h^{\alpha(t)} \lambda_2^* - \left(r_h^{\alpha(t)} + \alpha_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)} \right) \lambda_4^* \right. \\ & + \epsilon_2^{\alpha(t)} B_{hiv}(t) \lambda_5^* + \frac{\lambda_{11}^* S_m^*(t) B_m^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)}}{N_h^*(t)} \\ & \left. + \lambda_{12}^* X_{[0, T_f - \tau_h]} S_m^*(t) - Q_1^{\alpha(t)} G_m \lambda_4^* + Q_1^{\alpha(t)} G_m \lambda_2^* \right), \end{aligned}$$

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_5^* = & \left(1 - \tau^{\alpha(t)} \alpha_{h1}^{\alpha(t)} \lambda_1^* - \lambda_2^* \frac{S_h^*(t) B_H^{\alpha(t)} \eta_{HM}^{\alpha(t)}}{N_h^*(t)} + \frac{\lambda_4^* \epsilon_2^{\alpha(t)} I_h^*(t) B_H^{\alpha(t)} \eta_{HM}^{\alpha(t)}}{N_h^*(t)} \right. \\ & + \frac{\lambda_5^* \epsilon_2^{\alpha(t)} I_h^*(t) B_H^{\alpha(t)} \eta_{HM}^{\alpha(t)}}{N_h^*(t)} - \left(\alpha_{h2}^{\alpha(t)} + \phi_2 + \tau \alpha_{h1} + m u_h \right) \lambda_5^* \\ & + \phi_2 \lambda_6^* + \lambda_8^* \alpha_{h2} \\ & + \frac{S_h^*(t) B_H^{\alpha(t)} \eta_{HM}^{\alpha(t)} \lambda_6^*}{N_h^*(t)} - \frac{\lambda_{11}^* B_m^{\alpha(t)} (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} S_m^*(t)}{N_h^*(t)} \\ & - \lambda_{12}^* X_{[0, T_f - \tau_h]} S_m^*(t) B_m^{\alpha(t)} \times (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} \frac{1}{N_h^*(t)} \\ & \left. - Q_2^{\alpha(t)} G_n \lambda_5^* + Q_2^{\alpha(t)} G_n \lambda_6^* \right), \end{aligned}$$

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_6^* = & \left(1 + \lambda_5^* v_1^{\alpha(t)} f_h(t) + \lambda_6^* S_h^*(t) \frac{B_H^{\alpha(t)}}{N_h^*(t)} - \lambda_6^* v_1^{\alpha(t)} f_h(t) \right. \\ & \left. - \left(\alpha_{h2}^{\alpha(t)} + \mu_h^{\alpha(t)} \right) \lambda_6^* + \lambda_9^* \alpha_{h2}^{\alpha(t)} - Q_3^{\alpha(t)} G_h \lambda_6^* + Q_2^{\alpha(t)} G_h \lambda_9^* \right), \end{aligned}$$

$$\begin{aligned} {}_{T_f}^C D_t^{\alpha(t)} \lambda_7^* = & \left(-\alpha_{h1}^{\alpha(t)} \lambda_1^* (1 - \theta_2^{\alpha(t)}) + \lambda_2^* \theta_1^{\alpha(t)} \right. \\ & - \lambda_7^* \left(\theta_1^{\alpha(t)} r_h^{\alpha(t)} + (1 - \theta_2^{\alpha(t)}) \alpha_{h1}^{\alpha(t)} + \mu_h^{\alpha(t)} \right) \\ & - \lambda_{11}^* S_m^*(t) \frac{1 - \epsilon_1^{\alpha(t)}}{N_h^*(t)} + \lambda_{12}^* X_{[0, T_f - \tau_h]} B_m^{\alpha(t)} \\ & \times (1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} S_m^*(t) \frac{1 - \epsilon_2^{\alpha(t)}}{N_h^*(t)} \Bigg), \\ {}_{T_f}^C D_t^{\alpha(t)} \lambda_9^* = & \left(-\delta_H^{\alpha(t)} \lambda_1^* - \frac{\lambda_2^* S_h^*(t) B_H^{\alpha(t)} \eta_A^{\alpha(t)}}{N_h^*(t)} - \frac{\lambda_4^* \epsilon_2^{\alpha(t)} I_h^*(t) \eta_A^{\alpha(t)} B_H^{\alpha(t)}}{N_h^*(t)} \right. \\ & + \epsilon_2^{\alpha(t)} I_h^*(t) \lambda_5^* \frac{\eta_A^{\alpha(t)} B_H^{\alpha(t)}}{N_h^*(t)} + \frac{\lambda_6^* S_h^* \eta_A^{\alpha(t)} B_H^{\alpha(t)}}{N_h^*(t)} + \lambda_8^* v_2^{\alpha(t)} f_h(t) \\ & \left. - \lambda_9^* v_2^{\alpha(t)} f_h(t) - (\mu_h^{\alpha(t)} + \delta_H^{\alpha(t)}) \lambda_9^* \right), \\ {}_{T_f}^C D_t^{\alpha(t)} \lambda_{10}^* = & (\lambda_{10}^* \mu_m^{\alpha(t)}), \\ {}_{T_f}^C D_t^{\alpha(t)} \lambda_{11}^* = & \left(-\lambda_1^* f_m^*(t) - \lambda_{11}^* \mu_m^{\alpha(t)} + \lambda_{12}^* X_{[0, T_f - \tau_m]} f_m^*(t) \right), \\ {}_{T_f}^C D_t^{\alpha(t)} \lambda_{12}^* = & \left(1 - (\mu_m^{\alpha(t)} + \sigma_m^{\alpha(t)}) \lambda_{10}^* - \lambda_2^* S_h^*(t) \frac{(1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)} B_h^{\alpha(t)}}{N_h^*(t)} \right. \\ & - \frac{\lambda_3^* (1 - \gamma^{\alpha(t)}) V_h^*(t) B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \\ & + \frac{\lambda_4^* S_h^*(t) B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \\ & + \frac{v_1^{\alpha(t)} \lambda_5^* I_{hiv}^*(t) B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \\ & - \frac{v_1^{\alpha(t)} \lambda_6^* I_{hiv}^*(t) B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \\ & + \frac{\lambda_7^* (1 - \gamma^{\alpha(t)}) V_h^*(t) B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \\ & \left. + \lambda_8^* v_2^{\alpha(t)} A_{hiv}^* - \frac{\lambda_9^* A_{hiv}^* v_2^{\alpha(t)} B_h^{\alpha(t)} ((1 - b^{\alpha(t)} z^{\alpha(t)}) c^{\alpha(t)})}{N_h^*(t)} \right), \quad (29) \end{aligned}$$

References

- [2] G.V. Brown, Progress in the development of malaria vaccines: context and constraints, *Parasitologia* 41 (1999) 429–432.
- [3] L.H. Miller, P.H. David, T.J. Hadley, R.R. Freeman, Perspectives for malaria vaccination, *Philos. Trans. Roy. Soc. B: Biol. Sci.* 304 (2) (1984) 99–115.
- [4] D. Kazmin, H.I. Nakaya, E.K. Lee et al., Systems analysis of protective immune responses to RTS, S malaria vaccination in humans, *Proceedings of the National Academy of Sciences of the United States of America*, 114(9), 2425–2430, (2017).
- [5] R. Caponetto, G. Dongola, L. Fortuna, *Fractional-order systems: modeling and control applications*, World Scientific, London, 2010.
- [6] A.R.M. Carvalho, C.M.A. Pinto, Non-integer order analysis of the impact of diabetes and resistant strains in a model for TB infection, *Commun Nonlinear Sci. Numer. Simulat* 61 (2018) 104–126.

- [7] A.M.A. El-Sayed, A.E.M. El-Mesiry, H.A.A. El-Saka, On the fractional-order logistic equation, *Appl. Math. Lett.* 20 (2007) 817–823.
- [8] J.A.T. Machado, Fractional-order derivative approximations in discrete-time control systems, *Syst. Anal. Model. Simul.* 34 (1999) 419–434.
- [9] N.H. Sweilam, S.M. AL-Mekhlafi, On the optimal control for fractional multi-strain TB model, *Optim. Control Appl. Meth.* 37 (2016) 1355–1374.
- [10] H. Xu, Analytical approximations for a population growth model with fractional-order, *Commun. Nonlinear Sci. Numer. Simul.* 14 (2009) 1978–1983.
- [11] O.P. Agrawal, A general formulation and solution scheme for fractional optimal control problems, *Nonlinear Dynam.* 38 (2004) 323–337.
- [12] N.H. Sweilam, S.M. AL-Mekhlafi, Optimal control for a time delay multi-strain tuberculosis fractional model: A numerical approach, *IMA J. Math. Control Inform.* 36 (2019) 317–340.
- [13] N.H. Sweilam, S.M. AL-Mekhlafi, Optimal control for a nonlinear mathematical model of tumor under immune suppression: A numerical approach, *Optim. Control Appl. Meth.* 39 (2018) 1581–1596.
- [14] A. Jajarmi, S. Arshad, D. Baleanu, A new fractional modelling and control strategy for the outbreak of dengue fever, *Physica A* 535 (2019), <https://doi.org/10.1016/j.physa.2019.122524>.
- [15] D. Baleanu, A. Jajarmi, S.S. Sajjadi, et al., A new fractional model and optimal control of a tumor-immune surveillance with non-singular derivative operator, *Chaos, Solitons, and Fractals* 29 (8), 083127, (2019), doi: 10.1063/1.5096159.
- [16] T. Akman Yildiz, A fractional dynamical model for honeybee colony population, *Int. J. Biomath.* 11 (2018) 1–23.
- [17] J.E. Solís-Pérez, J.F. Gómez-Aguilar, Novel numerical method for solving variable-order fractional differential equations with power, exponential and Mittag-Leffler laws, *Chaos, Solitons, and Fractals* 14 (2018) 175–185.
- [18] H. Zhang, F. Liu, M.S. Phanikumar, M.M. Meerschaert, A novel numerical method for the time variable fractional order mobile-immobile advection-dispersion model, *Comput. Math. Appl.* 66 (5) (2013) 693–701.
- [19] H. Sun, A. Chang, Y. Zhang, W. Chen, A review on variable-order fractional differential equations: Mathematical foundations, Physical Models, and its Applications, *Fract. Calc. Appl. Anal.* 22 (1) (2019) 27–59.
- [20] N.H. Sweilam, S.M. AL-Mekhlafi, A.S. Alshomrani, D. Baleanu, Comparative study for optimal control nonlinear variable-order fractional tumor model, *Chaos, Solitons and Fractals* 136 (2020), <https://doi.org/10.1016/j.chaos.2020.109810>.
- [21] G.M. Bahaa, Fractional optimal control problem for variable-order differential systems, *Fract. Calc. Appl. Anal.* 20 (6) (2018) 1447–1470.
- [22] A. Carvalho, C.M.A. Pinto, A Delay fractional order model for the co-infection of malaria and HIV/AIDS, *Journal of Int. J. Dynam. Control* 5 (2017) 168–186.
- [23] A.A.M. Arafa, M. Khalil, A. Sayed, A non-integer variable order mathematical model of human immunodeficiency virus and malaria co-infection with time delay, *J. Hindawi Complexity* (2019) 4291017.
- [24] B.P. Moghaddam, S. Yaghoobi, J.T. Machado, An extended predictor-corrector algorithm for variable-order fractional delay differential equations, *J. Comput. Nonlinear Dyn.* 1 (2016) 1–11.
- [25] S. Banerjee, J.B. Cole, T. Yatagai, Calculation of diffraction characteristics of sub wavelength conducting gratings using a high accuracy nonstandard finite-difference time-domain method, *Opt. Rev.* 12 (4) (2005) 274–280.
- [26] S. Elsheikh, R. Ouifki, K.C. Patidar, A non-standard finite difference method to solve a model of HIV-Malaria co-infection, *J. Diff. Eq. Appl.* 20 (3) (2014) 354–378.
- [27] K. Moaddy, A.G. Radwan, K.N. Salama, S. Momani, I. Hashim, The fractional-order modeling and synchronization of electrically coupled neuron systems, *Comput. Math. Appl.* 64 (10) (2012) 3329–3339.
- [28] A. Nagy, N.H. Sweilam, An efficient method for solving fractional Hodgkin-Huxley model, *Phys. Lett. A* 378 (30) (2014) 1980–1984.
- [29] A.J. Arenas, G. González-Parra, B.M. Chen-Charpentier, Construction of nonstandard finite difference schemes for the SI and SIR epidemic models of fractional order, *Math. Comput. Simul.* 121 (2016) 48–63.
- [30] S. Moghadas, M. Alexander, B. Corbett, A non-standard numerical scheme for a generalized Gause-type predator-prey model, *Physica D* 188 (1) (2004) 134–151.
- [31] N.H. Sweilam, S.M. AL-Mekhlafi, Optimal control for a time delay multi-strain tuberculosis fractional model: a numerical approach, *IMA J. Math. Control Inform.* 36 (2019) 317–340.
- [32] Z. Iqbal, N. Ahmed, D. Baleanu, W. Adel, M. Rafiq, M.A. Rehman, A.S. Alshomrani, Positivity and boundedness preserving numerical algorithm for the solution of fractional nonlinear epidemic model of HIV/AIDS transmission, *Chaos, Solitons and Fractals Nonlinear Sci., Nonequilibrium and Complex Phenom.* 134 (2020) 109706.
- [33] R. Scherer, S.L. Kalla, Y. Tang, J. Huang, The Grünwald-Letnikov method for fractional differential equations, *Comput. Math. Appl.* 62 (3) (2011) 902–917.
- [34] N.H. Sweilam, A.T. Assiri, M.M. Abou Hasan, Numerical solutions of nonlinear fractional Schrödinger equations using nonstandard discretizations, *Numer. Methods Partial Differ. Eqs.* 33 (5) (2016) 1399–1419.
- [35] R.E. Mickens, Nonstandard finite difference models of differential equations, World Scientific, Singapore, 1994.
- [36] R.E. Mickens, Exact solutions to a finite-difference model of nonlinear reaction advection equation: implications for numerical analysis, *Numer. Methods Partial Differential Eq.* 5 (4) (1989) 313–325.
- [37] D. Zhu, S. Kinoshita, D. Cai, J.B. Cole, Investigation of structural colors in Morpho butterflies using the nonstandard-finite-difference time-domain method: Effects of alternately stacked shelves and ridge density, *Phys. Rev. E* 80 (5) (2009).
- [38] K. Moaddy, S. Momani, I. Hashim, The non-standard finite difference scheme for linear fractional PDEs in fluid mechanics, *Comput. Math. Appl.* 61 (4) (2011) 1209–1216.
- [39] A. Dabiri, B.P. Moghaddam, J.A. Tenreiro Machado, Optimal variable-order fractional PID controllers for dynamical systems, *J. Comput. Appl. Math.* 339 (2018) 40–48.
- [40] Behrouz Parsa Moghaddam, Arman Dabiri and José António Tenreiro Machado, Application of variable-order fractional calculus in solid mechanics, *Handbook of Fractional Calculus with Applications, Volume 7 Applications in Engineering, Life and Social Sciences, Part A*, Edited by: Dumitru Baleanu and António Mendes Lopes, De Gruyter, (2019). <https://doi.org/10.1515/9783110571905>.
- [41] J.M.S. Lubuma, K.C. Patidar, Uniformly convergent non-standard finite difference methods for self-adjoint singular perturbation problems, *J. Comput. Appl. Math.* 191 (2) (2006) 228–238.
- [42] N.H. Sweilam, F.A. Rihan, S.M. AL-Mekhlafi, A fractional-order delay differential model with optimal control for cancer treatment based on synergy between anti-angiogenic and immune cell therapies, *Discr. Continuous Dynam. Syst. Ser. B* 13 (9) (2020) 2403–2424.
- [43] F.A. Rihan, S. Lakshmanan, H. Maurer, Optimal Control of Tumour-Immune Model with Time-Delay and Immuno-Chemotherapy, *Appl. Math. Comput.* 353 (7) (2019) 147–165.
- [44] F.A. Rihan, G. Velmurugan, Dynamics of Fractional-Order Delay Differential Model for Tumor-Immune System, *Chaos, Solitons and Fractals* 132 (3) (2020) 109592.

- [50] A. Jajarmi, M. Hajipour, E. Mohammadzadeh, D. Baleanu, A new approach for the nonlinear fractional optimal control problems with external persistent disturbances, *J. Franklin Inst.* 335 (9) (2018) 3938–3967.
- [51] A. Jajarmi, D. Baleanu, Suboptimal control of fractional-order dynamic systems with delay argument, *J. Vib. Control* 24 (12) (2018) 2430–2446.
- [52] A. Atangana, Z. Hammouch, G. Mophou, K.M. Owolabi, Focus point on modelling complex real-world problems with fractal and new trends of fractional differentiation, *Eur. Phys. J. Plus* 133 (8) (2018) 315.
- [53] Q.M. Al-Mdallal, On fractional-Legendre spectral Galerkin method for fractional Sturm-Liouville problems, *Chaos, Solitons & Fractals* 116 (2018) 261–267.
- [54] Q.M. Al-Mdallal, A.S. Abu Omer, Fractional-order Legendre-collocation method for solving fractional initial value problems, *Appl. Math. Comput.* 321 (2018) 74–84.
- [55] Mohamed A. Hajji, Qasem Al-Mdallal, Numerical simulations of a delay model for immune system-tumor interaction, *Sultan Qaboos University Journal for Science [SQUJS]* 23 (1) (2018) 19–31.
- [56] J.H. He, A Tutorial review on fractal space time and fractional calculus, *Int J Theor Phys.* 53(11)(2014).
- [57] J.H. He, S.K. Elagan, Z.B. Li, Geometrical explanation of the fractional complex transform and derivative chain rule for fractional calculus, *Phys. Lett. A* 376 (4) (2012) 257–259.
- [58] J.H. He, Fractal calculus and its geometrical explanation, *Results Phys.* 10 (2018) 272–276.
- [59] J.H. He, Lagrange crisis and generalized variational principle for 3D unsteady flow, *Int. J. Numer. Meth. Heat Fluid Flow* 30 (3) (2019) 1189–1196.
- [60] D.H. Chyung, E.B. Lee, Linear optimal systems with time delays, *SIAM J. Control* 4 (3) (1966) 548–575.
- [61] M.R. Hestenes, On variational theory and optimal control theory, *SIAM J. Control* 3 (1) (1968) 23–48.
- [62] G.L. Kharatishvili, *Optimal Control Processes with Time-Delay* [in Russian], Tbilisi (1961).

Further reading

- [1] A. Baradaji, B. Sigauquw, S. Sanz, et al, Impact of malaria at the end of pregnancy on infant mortality and morbidity, *J. Infect. Dis.* 203 (5) (2011) 691–699.
- [12] D. Baleanu, K. Diethelm, E. Scalas and J.J. Trujillo, *Fractional calculus: models and numerical methods*, Series on Complexity, Nonlinearity and Chaos, 3. World Scientific Publishing Co., Pte. Ltd., Hackensack, NJ, (2012).
- [13] A.H. Bhrawy, M.A. Zaky, Shifted fractional-order Jacobi orthogonal functions: Application to a system of fractional differential equations, *Appl. Math. Model.* 40 (2016) 832–845.
- [14] R. Denysiuk, C.J. Silva, D.F.M. Torres, Multi objective optimization to a TB-HIV/AIDS co-infection optimal control problem, *Comp. Appl. Math.* 37 (2018) 2112–2128.
- [15] A. Khan, G. Zaman, Optimal control strategy of SEIR endemic model with continuous age-structure in the exposed and infectious classes, *Optim. Control Appl. Meth.* 39 (2018) 1716–1727.
- [16] A.B. Salati, M. Shamsi, D.F.M. Torres, Direct transcription methods based on fractional integral approximation formulas for solving nonlinear fractional optimal control problems, *Commun. Nonlinear Sci. Numer. Simul.* 67 (2019) 334–350.