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Optimal control of an epidemiological model with multiple time delays

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ABSTRACT

In this paper, we consider an optimal control model governed by a system of delay differential equations representing an SIR model. We extend the model of Kaddar (2010) by incorporating the suitable controls. We consider two control strategies in the optimal control model, namely: the vaccination and treatment strategies. The model has three time delays that represent the incubation period, and the times taken by the vaccine and treatment to be effective. We derive the first-order necessary conditions for the optimal control and perform numerical simulations to show the effectiveness as well as the applicability of the model for different values of the time delays. These numerical simulations show that the model is more sensitive to the delays representing the incubation period and the treatment delay, whereas the delay associated with the vaccine is not significant.

1. Introduction

Epidemiological models are often used to describe the dynamics of epidemic diseases in populations. There have been many variations of such classical epidemiological models [13,14]. These models are based on the standard Susceptible-Infectious-Susceptible, Susceptible-Infectious-Recovered and Susceptible-Exposed-Infectious-Recovered models, which are determined according to the difference on the method of transmission, nature of the disease, e.g., those with short/long incubation period, killer/curable diseases, etc, and the response of the individuals to it, for instance, gaining transient/permanent immunity, dying from the disease, etc. [7,23,29]. The main purpose of formulating a such epidemiological model is to understand the long-term behavior of the epidemic disease and to determine the possible strategies to control it.

Differential equations, whether they are ordinary, delay, partial or stochastic, are one of the main mathematical tools being used to formulate many epidemiological models. The focus in such epidemiological models has been on the incidence rate at which people move from the class of susceptible individuals to the class of infective individuals. These incidence rates have been modeled mostly by using bilinear and Holling type of functional responses [12,15,20,27,28].

On the other hand, optimal control has extensively been used as a strategy to control the epidemic outbreaks [9]. The main idea behind using the optimal control in epidemics is to search for, among the available strategies, the most effective strategy that reduces the infection rate to a minimum level while optimizing the cost of deploying a therapy or a preventive

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vaccine that is used for controlling the disease progression (see, for example, [30]). In terms of epidemic diseases, such strategies can include therapies, vaccines, isolation and educational campaigns [3,6,9,17].

Recently, many optimal control models pertaining to epidemic diseases have appeared in the literature. They include, but not limited to, delayed SIRS epidemic model [18] (where Laarbi et al. proposed an optimal control model governed by a delayed SIRS model with a single time delay representing the incubation period), delayed SIR model [1] (where Abta et al. formulated an optimal control model to optimize the costs of vaccination and treatment on a delayed SIR model with a single delay representing the incubation period and a saturated incidence rate), tuberculosis model [25] (where Silva and Torres proposed optimal control strategies to minimize the cost of interventions using data from Angola), HIV model [11] (where Hattaf and Yousfi used optimal controls to represent the efficiency of drug treatment in inhibiting viral production and preventing new infections), swine flu [5] (where Boklund et al. studied epidemiological and economic consequences of some control strategies in a classical swine flu epidemic under Danish conditions with respect to herd demographics and geography and investigated the effect of extra biosecurity measures on farms) and dengue fever [2] (where Aldila et al. designed an optimal control problem using four different control parameters and discussed some results about epidemic prevention and outbreak reduction strategies).

An important class of optimal control problems, is the class of problems characterized by delay differential equations. The existence theorems and the derivation of the first order optimality conditions for optimal control problem governed by delay differential equations have been discussed by many authors [4,8,10,19]. Barati [4] introduced a new approach based on embedding method for finding an approximate solution for a wide range of nonlinear optimal control problems with delays in state and control variables subject to mixed-control state constraints. In [8], Frankena considered a general optimal control problem involving ODEs with delayed arguments and a set of equality and inequality restrictions on state and control variables. Using variational techniques, she presented a maximum principle in pointwise form and then from this maximum principle, she derived necessary conditions for the existence of the optimal controls. Göllmann et al. [10] derived necessary optimality conditions in the form of Pontryagin's minimum principle for optimal control problems with delays in state and control variables. In [19], Nababan derived a Filippov-type lemma for functions involving delays. He then used this lemma to prove the existence of an optimal control for a class of nonlinear control processes with delays appearing in both state and control variables.

In this paper, we consider an optimal control problem governed by a system of delay differential equations with multiple time delays. The governing state equations of the optimal control model are described in a SIR framework with a saturated incidence rate and a time delay representing the incubation period. This model is found in [16]. Furthermore, we consider two additional time delays in the optimal control model. These delays represent the times taken by the vaccine and therapy before each of these two strategies become effective. Then we derive first-order necessary conditions for existence of the optimal control and develop a numerical method for solving them.

The rest of this paper is organized as follows. In Section 2, we give the statement of the optimal control problem. We derive the necessary conditions for existence of the optimal control in Section 3. In Section 4, we describe the numerical method and present the resulting numerical simulations. Finally, we discuss these results in Section 5 along with some concluding remarks.

2. Statement of the optimal control problem

Given the initial state of the population (S_0, I_0, R_0), our goal is to compute the optimal pair of vaccination and treatment strategies (u, v) that would maximize the recovered population and minimize both the infected and susceptible populations; and at the same time minimize the costs of applying the vaccination and treatment strategies. To achieve this goal, optimal control is an appropriate choice for expressing the above problem mathematically. Therefore, we consider in this paper an optimal control problem of the form

$$\min_{(u,v)\in\mathbb{U}} J(u(t), v(t)) = S(T) + I(T) - R(T) + \int_0^T \big(C_1 u^2(t) + C_2 v^2(t) + S(t) + I(t) - R(t)\big)dt, \tag{2.1}$$

subject to the state equations

$$\dot{S}(t) = \Omega - \frac{\beta S(t) I(t)}{1 + \alpha_1 S(t) + \alpha_2 I(t)} - \mu S(t) - u(t) S(t), \tag{2.2}$$

$$\dot{I}(t) = \frac{\beta S(t-\tau) I(t-\tau)}{1 + \alpha_1 S(t-\tau) + \alpha_2 I(t-\tau)} - (\mu + \alpha + \gamma) I(t) - v(t) I(t), \tag{2.3}$$

$$\dot{R}(t) = \gamma I(t) + u(t-\sigma) S(t-\sigma) + v(t-\delta) I(t-\delta) - \mu R(t), \tag{2.4}$$

and history data

$$S(\theta) = \varphi_S(\theta), \theta \le 0, \tag{2.5}$$

$$I(\theta) = \varphi_I(\theta), \theta \leq 0, \tag{2.6}$$

$$R(\theta) = \varphi_R(\theta), \theta \leq 0, \tag{2.7}$$

where $\varphi_S(\theta)$, $\varphi_I(\theta)$ and $\varphi_R(\theta)$ are the history functions associated with the susceptible, infected and recovered populations, respectively. The two functions $u(t)$ and $v(t)$ represent vaccination and treatment strategies. These control functions are assumed to be $L^\infty(0, T)$ functions, belonging to a set of admissible controls

$$\mathbb{U} = \{(u, v) : u_{min} \leq u(t) \leq u_{max}, v_{min} \leq v(t) \leq v_{max}\},$$

where $0 \leq u_{min} < u_{max} \leq 1$ and $0 \leq v_{min} < v_{max} \leq 1$. The two constants C_1 and C_2 are weighted costs associated with the use of the controls $u(t)$ and $v(t)$, respectively. The state equations are formulated from an SIR model with a saturated incidence rate with a time delay τ, where $S(t)$, $I(t)$ and $R(t)$ are the numbers of susceptible, infected and recovered individuals at time t, respectively. The parameters Ω is the recruitment rate, β is the transmission rate, α_1 and α_2 are parameters measuring the inhibitory effect, μ is the natural death rate, α is the death rate due to the disease and γ is the recovery rate of the infective individuals. The time delay τ represents the incubation period. That is to say, only susceptible individuals who got infected at time $t - \tau$ are able to communicate the disease at time t.

In the above optimal control model, we assume that only susceptible individuals who are vaccinated at time $t - \sigma$ and infected individuals who are treated at time $t - \delta$ can recover at time t. Therefore, the two time delays $\sigma > 0$ and $\delta > 0$ refer to the times taken by the vaccination and treatment strategies before the controls become effective.

When the two controls $u(t)$ and $v(t)$ are set to zero for all $t \in [-\max\{\tau, \sigma, \delta\}, T]$, we obtain the SIR model (with a time delay and saturated incidence rate) as seen in [16]:

$$\dot{S}(t) = \Omega - \frac{\beta S(t) I(t)}{1 + \alpha_1 S(t) + \alpha_2 I(t)} - \mu S(t), \tag{2.8}$$

$$\dot{I}(t) = \frac{\beta S(t-\tau) I(t-\tau)}{1 + \alpha_1 S(t-\tau) + \alpha_2 I(t-\tau)} - (\mu + \alpha + \gamma) I(t), \tag{2.9}$$

$$\dot{R}(t) = \gamma I(t) - \mu R(t). \tag{2.10}$$

The delay differential equation model described by Eqs. (2.8)–(2.10) has two equilibrium points: a disease-free equilibrium E_0 given by

$$E_0 = \left(\frac{\Omega}{\mu}, 0, 0\right)$$

and an endemic equilibrium $E^* = (S^*, I^*, R^*)$ where,

$$S^* = \frac{\Omega((\mu + \alpha + \gamma) + \alpha_2 \Omega)}{\mu\left((\mu + \alpha + \gamma)\widetilde{R} + \alpha_2 \Omega\right)},$$

$$I^* = \frac{\Omega(\widetilde{R} - 1)}{(\mu + \alpha + \gamma)\widetilde{R} + \alpha_2 \Omega},$$

$$R^* = \frac{\gamma \Omega(\widetilde{R} - 1)}{\mu((\mu + \alpha + \gamma)\widetilde{R} + \alpha_2 \Omega)},$$

with

$$\widetilde{R} = \frac{\Omega(\beta - \alpha_1(\mu + \alpha + \gamma))}{\mu(\mu + \alpha + \gamma)}.$$

The basic reproduction number of (2.8)–(2.10) is given by

$$R_0 = \frac{\beta \Omega}{(\mu + \alpha + \gamma)(\alpha_1 \Omega + \mu)}.$$

In [16], it was proven that if $R_0 < 1$, then the disease-free equilibrium is asymptotically stable and if $R_0 > 1$ then it is unstable.

It was also proven that for $\tau = 0$, the steady state E^* is locally asymptotically stable if and only if $R_0 > 1$. Moreover, E^* is locally asymptotically stable for all $\tau \geq 0$ if and only if $R_0 > 1$.

On the other-hand, the disease-free equilibrium for system (2.2)–(2.4) is given by

$$E_0^c = \left(\frac{\Omega}{u + \mu}, 0, \frac{\Omega}{\mu(u + \mu)}\right), \tag{2.11}$$

whereas the endemic equilibrium E_c^* is given by

$$E_c^* = \left(\frac{\Omega(\kappa + \alpha_2\Omega)}{(\mu+u)(\kappa\widetilde{R} + \alpha_2\Omega)}, \frac{\Omega(\widetilde{R}-1)}{\kappa\widetilde{R} + \alpha_2\Omega}, \frac{1}{\mu}\left(\frac{u\Omega(K + \alpha_2\Omega)}{(\mu+u)(\kappa\widetilde{R} + \alpha_2\Omega)} + \frac{\Omega(\gamma+\nu)(\widetilde{R}-1)}{\kappa\widetilde{R} + \alpha_2\Omega} \right) \right),$$

where $\kappa = \mu + \nu + \alpha + \nu$ and $\widetilde{R} = \Omega(\kappa + \alpha_2\Omega)/(\kappa(\mu+u))$.

The basic reproduction number R_c of system (2.2)–(2.4) is given by

$$R_c = \frac{\beta S^*}{(1+\alpha_1 S^*)(\mu+\alpha+\gamma+\nu)} = \frac{\beta\Omega}{(\alpha_1\Omega + \mu + u)(\alpha+\gamma+\mu+\nu)}, \tag{2.12}$$

and it is clear that when $u \to 0$ and $\nu \to 0$ then $R_c \to R_0$.

3. Existence and characterization of the optimal control

In this section, we discuss the existence of the optimal control and then construct the Hamiltonian of the optimal control problem to derive the first order necessary conditions for the optimal control.

3.1. Existence of optimal control

To show the existence of the optimal control for the problem under consideration, we notice that the set of admissible controls $\mathbb{U}$ is, by definition, closed and bounded. It is also convex because $[u_{min}, u_{max}] \times [\nu_{min}, \nu_{max}]$ is convex in $\mathbb{R}^2$. It is obvious that there is an admissible pair $((u(t), \nu(t)), (S(t), I(t), R(t)))$ for the problem. For example, one can select $u(t) = u_{min}$ and $\nu(t) = \nu_{max}$ for all $t \in [0, T]$ and solve the resulting delay differential Eqs. (2.2)–(2.4) to obtain the corresponding solution of the system. Moreover, the solution is bounded, since the state variables and the history functions are continuous and the domain is bounded. Also, the objective function is convex in the controls $u(t)$ and $\nu(t)$. Hence, the existence of the optimal control comes as a direct result from the Filippove–Cesari theorem [19,24]. We therefore, have the following result.

Theorem 3.1. *Consider the optimal control problem (2.1) subject to (2.2)–(2.7). Then there exists an optimal pair of controls (u^*, ν^*) and a corresponding optimal states (S^*, I^*, R^*) that minimizes the objective function $J(u, \nu)$ over the set of admissible controls $\mathbb{U} = \{(u, \nu) : u_{min} \le u(t) \le u_{max}, \nu_{min} \le \nu(t) \le \nu_{max}\}$.*

3.2. Characterization of optimal control

In this subsection, we derive the first order necessary conditions for the existence of optimal control, by constructing the Hamiltonian H and then applying the Pontryagin's maximum principle.

To simplify the notations we write $\mathbf{x}(t) = [S(t), I(t), R(t)]^T$, $\mathbf{u}(t) = [u(t), \nu(t)]^T$ and $\boldsymbol{\lambda}(t) = [\lambda_1(t), \lambda_2(t), \lambda_3(t)]^T$. We also define $\mathbf{u}_\sigma := \mathbf{u}(t-\sigma)$, $\mathbf{u}_\delta := \mathbf{u}(t-\delta)$, $\mathbf{x}_\tau := \mathbf{x}(t-\tau)$, $\mathbf{x}_\sigma := \mathbf{x}(t-\sigma)$ and $\mathbf{x}_\delta := \mathbf{x}(t-\delta)$. We denote by $f(\mathbf{u}(t), \mathbf{x}(t))$ the integrand part of the objective function (2.1) and by f_1, f_2 and f_3 the right-hand sides of the state Eqs. (2.2)–(2.4). With these notations and terminologies, the Hamiltonian is given by

$$\begin{aligned} H &= H(\mathbf{u}(t), \mathbf{x}(t), \boldsymbol{\lambda}(t), \mathbf{u}_\sigma(t), \mathbf{u}_\delta(t), \mathbf{x}_\tau(t), \mathbf{x}_\sigma(t), \mathbf{x}_\delta(t)), \\ &= f(\mathbf{u}(t), \mathbf{x}(t)) + \boldsymbol{\lambda}^T(t)\dot{\mathbf{x}}(t), \\ &= C_1u^2 + C_2\nu^2 + S + I - R + \lambda_1\left(\Omega - \frac{\beta SI}{1+\alpha_1 S + \alpha_2 I} - (\mu+u)S\right) \\ &\quad + \lambda_2\left(\frac{\beta S_\tau I_\tau}{1+\alpha_1 S_\tau + \alpha_2 I_\tau} - (\mu+\alpha+\gamma+\nu)I\right) + \lambda_3(\gamma I + u_\sigma S_\sigma + \nu_\delta I_\delta - \mu R). \end{aligned} \tag{3.1}$$

Let $\chi_{[a,b]}(t)$ be the characteristic function defined by

$$\chi_{[a,b]}(t) = \begin{cases} 1, & \text{if } t \in [a, b], \\ 0, & \text{otherwise.} \end{cases} \tag{3.2}$$

Let $\mathbf{u}^*(t) = [u^*(t), \nu^*(t)]^T$ be the optimal control and $\mathbf{x}^*(t) = [S^*(t), I^*(t), R^*(t)]^T$ be the corresponding optimal trajectory. Then there exists $\boldsymbol{\lambda}(t) \in \mathbb{R}^3$ such that the first order necessary conditions for the existence of optimal control are given by the equations

$$0 = \left[\frac{\partial H}{\partial \mathbf{u}}(t) + \chi_{[0,T-\sigma]}(t)\left[\frac{\partial H}{\partial \mathbf{u}_\sigma}(t)\right]_{t=t+\sigma} + \chi_{[0,T-\delta]}(t)\left[\frac{\partial H}{\partial \mathbf{u}_\delta}(t)\right]_{t=t+\delta} \right]_{\mathbf{u}=\mathbf{u}^*}, \tag{3.3}$$

$$\frac{d\mathbf{x}}{dt} = \frac{\partial H}{\partial \boldsymbol{\lambda}}, \tag{3.4}$$

$$\frac{d\boldsymbol{\lambda}}{dt} = -\left[\frac{\partial H}{\partial \mathbf{x}}(t) + \chi_{[0,T-\tau]}(t)\left[\frac{\partial H}{\partial \mathbf{x}_\tau}(t)\right]_{t=t+\tau} + \chi_{[0,T-\sigma]}(t)\left[\frac{\partial H}{\partial \mathbf{x}_\sigma}(t)\right]_{t=t+\sigma}\right]_{\mathbf{x}=\mathbf{x}^*} + \chi_{[0,T-\delta]}(t)\left[\left[\frac{\partial H}{\partial \mathbf{x}_\delta}(t)\right]_{t=t+\delta}\right]_{\mathbf{x}=\mathbf{x}^*} \tag{3.5}$$

In the componentwise form, the above conditions are expressed as

1. The optimality conditions:

$$\left[\frac{\partial H}{\partial u(t)} + \chi_{[0,T-\sigma]}(t)\frac{\partial H}{\partial u_\sigma}\bigg|_{t=t+\sigma}\right]_{u(t)=u^*(t)} = 0 \tag{3.6}$$

$$\left[\frac{\partial H}{\partial v(t)} + \chi_{[0,T-\delta]}(t)\frac{\partial H}{\partial v_\delta}\bigg|_{t=t+\delta}\right]_{v(t)=v^*(t)} = 0. \tag{3.7}$$

Simplifying Eqs. (3.6) and (3.7), we obtain

$$2C_1u^*(t) - \lambda_1(t)S(t) + \chi_{[0,T-\sigma]}(t)\lambda_3(t+\sigma)S(t) = 0 \tag{3.8}$$

$$2C_2v^*(t) - \lambda_2(t)I(t) + \chi_{[0,T-\delta]}(t)\lambda_3(t+\delta)I(t) = 0. \tag{3.9}$$

Further simplification of (3.8) and (3.9) yields

$$u^*(t) = \begin{cases} \max\left\{u_{min}, \min\left\{u_{max}, \frac{(\lambda_1(t)-\lambda_3(t+\sigma))S(t)}{2C_1}\right\}\right\}, & 0 \le t \le T-\sigma, \\ \max\left\{u_{min}, \min\left\{u_{max}, \frac{\lambda_1(t)S(t)}{2C_1}\right\}\right\}, & T-\sigma \le t \le T, \end{cases} \tag{3.10}$$

and

$$v^*(t) = \begin{cases} \max\left\{v_{min}, \min\left\{v_{max}, \frac{(\lambda_2(t)-\lambda_3(t+\delta))I(t)}{2C_2}\right\}\right\}, & 0 \le t \le T-\delta, \\ \max\left\{v_{min}, \min\left\{v_{max}, \frac{\lambda_2(t)I(t)}{2C_2}\right\}\right\}, & T-\delta \le t \le T. \end{cases} \tag{3.11}$$

2. The state equations: given by the forms (2.2), (2.3) and (2.4).
3. The co-state equations:

$$\frac{d\lambda_1(t)}{dt} = -\left[\frac{\partial H}{\partial S} + \chi_{[0,T-\tau]}(t)\frac{\partial H}{\partial S_\tau}\bigg|_{t=t+\tau} + \chi_{[0,T-\sigma]}(t)\frac{\partial H}{\partial S_\sigma}\bigg|_{t=t+\sigma}\right]_{(\mathbf{u}(t),\mathbf{x}(t))=(\mathbf{u}^*(t),\mathbf{x}^*(t))},$$

$$\frac{d\lambda_2(t)}{dt} = -\left[\frac{\partial H}{\partial I} + \chi_{[0,T-\tau]}(t)\frac{\partial H}{\partial I_\tau}\bigg|_{t=t+\tau} + \chi_{[0,T-\delta]}(t)\frac{\partial H}{\partial I_\delta}\bigg|_{t=t+\delta}\right]_{(\mathbf{u}(t),\mathbf{x}(t))=(\mathbf{u}^*(t),\mathbf{x}^*(t))},$$

$$\frac{d\lambda_3(t)}{dt} = -\left[\frac{\partial H}{\partial R}\right]_{(\mathbf{u}(t),\mathbf{x}(t))=(\mathbf{u}^*(t),\mathbf{x}^*(t))},$$

which when simplified, lead to

$$\begin{aligned}\frac{d\lambda_1(t)}{dt} &= \left[\frac{\beta I(1+\alpha_2 I)}{(1+\alpha_1 S+\alpha_2 I)^2}\right]\left(\chi_{[0,T-\tau]}(t)\lambda_2(t+\tau) - \lambda_1(t)\right) \\ &\quad + (\mu + u(t))\lambda_1(t) + \chi_{[0,T-\sigma]}(t)\lambda_3(t+\sigma)u(t),\end{aligned} \tag{3.12}$$

$$\begin{aligned}\frac{d\lambda_2(t)}{dt} &= 1 + \left[\frac{\beta S(t)(1+\alpha_1 S(t))}{(1+\alpha_1 S(t)+\alpha_2 I(t))^2}\right]\left(\chi_{[0,T-\tau]}(t)\lambda_2(t+\tau) - \lambda_1(t)\right) \\ &\quad - (\mu+\alpha+\gamma+v(t))\lambda_2(t) + \gamma\lambda_3(t) + \chi_{[0,T-\delta]}(t)\lambda_3(t+\delta)v(t),\end{aligned} \tag{3.13}$$

$$\frac{d\lambda_3(t)}{dt} = -1 - \mu\lambda_3(t). \tag{3.14}$$

4. The transversality conditions:

$$\lambda_1(T) = 1, \tag{3.15}$$

$$\lambda_2(T) = 1, \tag{3.16}$$

$$\lambda_3(T) = -1. \tag{3.17}$$

Remark 3.1. It is worth noting that

1. The Hamiltonian function H is strongly convex in the control variables.
2. The right-hand sides of the state and co-state equations are Lipshitz continuous.
3. The set of the admissible controls $\mathbb{U}$ is convex.

Hence, by the theorems found in [21,22], the solution of the optimal control problem described by Eqs. (2.1)–(2.7) is unique.

4. Numerical simulations

In this section, we discuss the discretization of the optimal control problem described by Eqs. (2.1)–(2.7), and present the numerical results obtained through our simulations.

For the discretization of the optimal control problem, we used the control parameterization technique [26]. The state variables are evaluated at discrete points $t_0 = 0 < t_1 < \ldots, t_N = T$, where $h = t_{j+1} - t_j = T/N$, whereas the control variables are evaluated at switching points $s_0 = 0 < s_1 < \ldots < s_{N_C} = T$, where $h_{N_C} = s_{j+1} - s_j = T/N_C$ and $N = Q \cdot N_C$ for some positive integer Q. The controls u and v are dealt with as piecewise constants, within the switching intervals $[s_j, s_{j+1})$. At each quadrature point t_j, the control variables $u(t)$ and $v(t)$ are evaluated as $u_j \approx u(t_j) = u(s(\lfloor j/Q \rfloor))$ and $v_j \approx v(t_j) = v(s(\lfloor j/Q \rfloor))$.

For the discrtization of the objective function (2.1), we used the Simpson's quadrature formula. The discrete version of the objective function therefore takes the form

$$J(u,v) \approx S_N + I_N - R_N + \frac{h}{3}\left(f(\mathbf{x}_0, \mathbf{u}_0) + f(\mathbf{x}_N, \mathbf{u}_N) + 4\sum_{j=1}^{\lfloor N/2 \rfloor} f(\mathbf{x}_{2j-1}, \mathbf{u}_{2j-1}) + 2\sum_{j=1}^{\lfloor N/2 \rfloor} f(\mathbf{x}_{2j}, \mathbf{u}_{2j}) \right), \tag{4.1}$$

where $f(\mathbf{x}(t), \mathbf{u}(t)) = C_1 u^2(t) + C_2 v^2(t) + S(t) + I(t) - R(t)$ is the integrand part of the objective function and $\mathbf{x}_j$ and $\mathbf{u}_j$ are the numerical approximations of $\mathbf{x}(t_j)$ and $\mathbf{u}(t_j)$, respectively.

For the discretization of the state equations, we use the classical Crank-Nicholson's method. Under this discretization scheme, the state equations become equality constraints of the form

$$\mathbf{x}_{j+1} - \mathbf{x}_j - \frac{h}{2}\left(\mathbf{f}(\mathbf{x}_j, \mathbf{u}_j, \mathbf{x}_{\tau j}, \mathbf{u}_{\tau j}) + \mathbf{f}(\mathbf{x}_{j+1}, \mathbf{u}_{j+1}, \mathbf{x}_{\tau j+1}, \mathbf{u}_{\tau j+1})\right) = 0;\ j = 0, \ldots, N-1, \tag{4.2}$$

where $\mathbf{f}(\mathbf{x}_j, \mathbf{u}_j, \mathbf{x}_{\tau j}, \mathbf{u}_{\tau j})$ is the vector of the right hand sides of Eqs. (2.2)–(2.4) evaluated at the point t_j.

The initial conditions become equality constraints of the form

$$\mathbf{x}_0 - [S_0, I_0, R_0]^T = 0. \tag{4.3}$$

The controls box constraints take the form

$$\mathbf{u}_{min} - \mathbf{u}_j \le 0;\ j = 0, \ldots, N, \tag{4.4}$$

$$\mathbf{u}_j - \mathbf{u}_{max} \le 0;\ j = 0, \ldots, N, \tag{4.5}$$

Using Matlab's optimization toolbox, we finally simulate the nonlinear programming problems (4.1)–(4.5). For the numerical simulations, we set $\Omega = 0.95$, $\alpha_1 = \alpha_2 = 0.25$, $\beta = 0.08$, $\mu = 0.01$, $\alpha = 0.1$ and $\gamma = 0.005$. This set parameters gives the basic reproduction number of the delay differential equation model described by Eqs. (2.8)–(2.10) as $R_0 \approx 2.7814$. Since $R_0 > 1$, the unique asymptotically stable endemic equilibrium is given by

$$E^* \approx (444.0000, 787.4783, 393.7391).$$

The dynamic of the model for $\tau = 6$ is shown in Fig. 1. We start from $\varphi_S(t) = 50, \varphi_I(t) = 10$ and $\varphi_R(t) = 0$, for $t \le 0$.

To solve the optimal control model described by Eqs. (2.1)–(2.7), we consider the per-unit cost of the vaccine $C_1 = 10$ and the per-unit cost of the therapy $C_2 = 5$.

We start the simulations from the equilibrium state (444.0000, 787.4783, 393.7391). We consider the following five cases for the time delays of the model

1. $\tau = \sigma = \delta = 0$ in which we ignore the time delays.
2. $\tau = 6$, $\sigma = \delta = 0$.
3. $\tau = 2$, $\sigma = 0$ and $\tau = 6$.
4. $\tau = 0$, $\sigma = 6$ and $\tau = 0$.
5. $\tau = 6$, $\sigma = 3$ and $\tau = 4$.

The computed optimal controls and the corresponding optimal states that we obtained are explained through Figs. 2–11 and will be discussed in the next section.

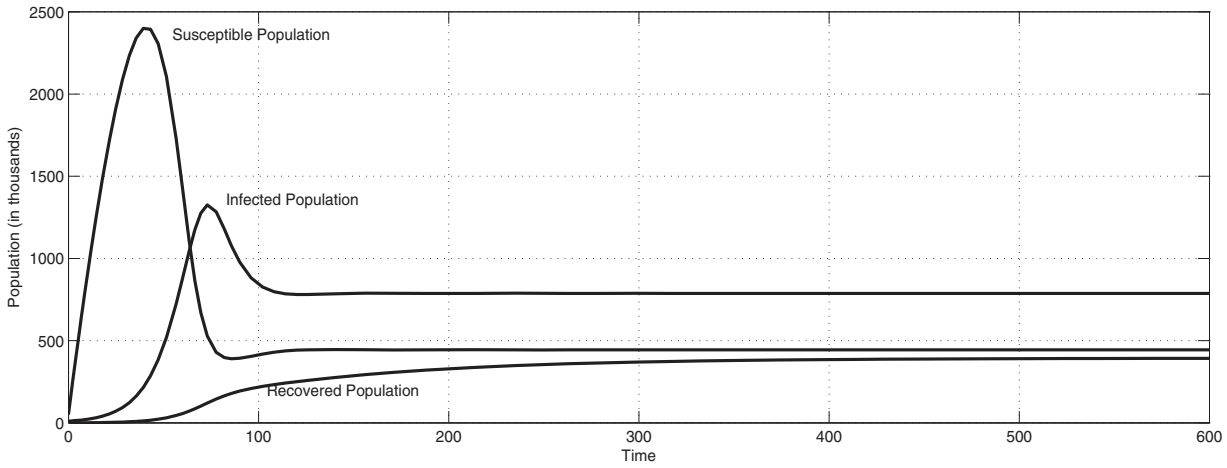

Fig. 1. The dynamics of the delayed SIR model.

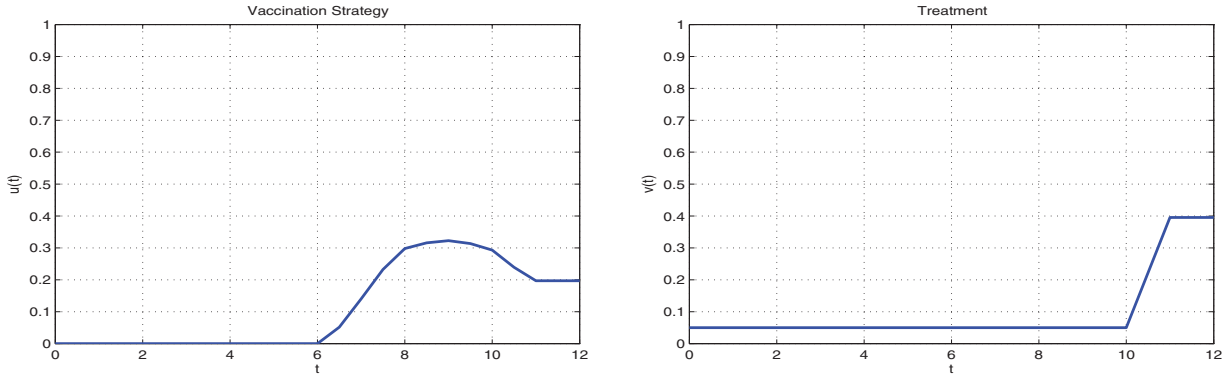

Fig. 2. The optimal controls for $\tau = \sigma = \delta = 0$.

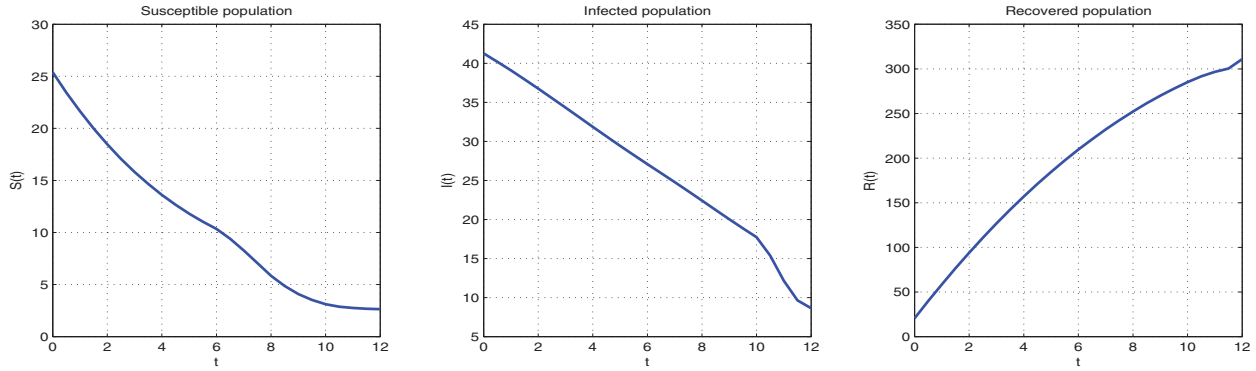

Fig. 3. The optimal states for $\tau = \sigma = \delta = 0$.

5. Discussions and concluding remarks

In this paper, we considered an optimal control formulation SIR model with a time delay (representing the incubation period) and a saturated incidence rate. The two control functions $u(t)$ and $v(t)$, which represent the vaccination and treatment strategies, are subject to time delays before being effective. Then we formulated the objective function of the optimal control problem. We discussed the existence of the optimal control and then derived the first order necessary conditions for the optimal control through constructing the Hamiltonian and using the Pontryagin's maximum principle.

For the numerical simulations we considered several cases. The first case was when all the time delays are zeros (see Figs. 2 and 3) which showed that low levels of vaccines and treatments can steer the disease to decay. The next case is with

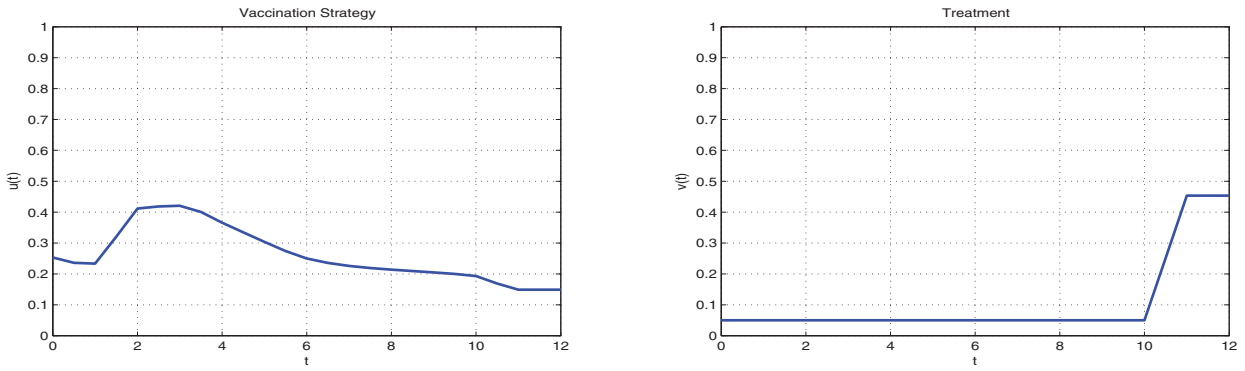

Fig. 4. The optimal controls for $\tau = 6$, $\sigma = \delta = 0$.

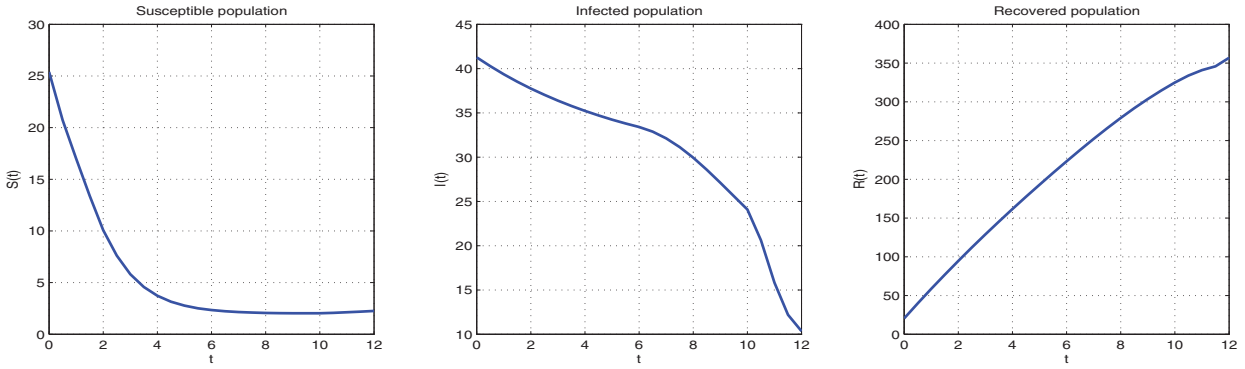

Fig. 5. The optimal states for $\tau = 6$, $\sigma = \delta = 0$.

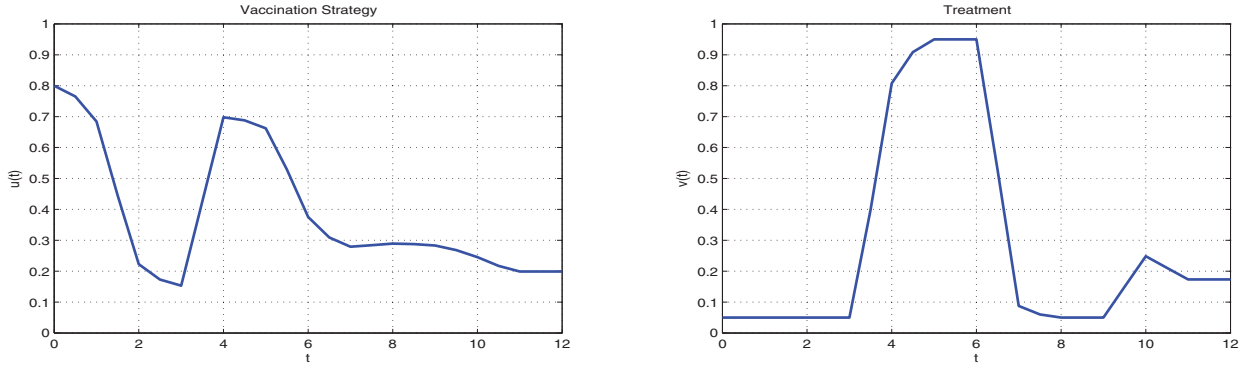

Fig. 6. The optimal controls for $\tau = 2$, $\sigma = 0$, $\delta = 6$.

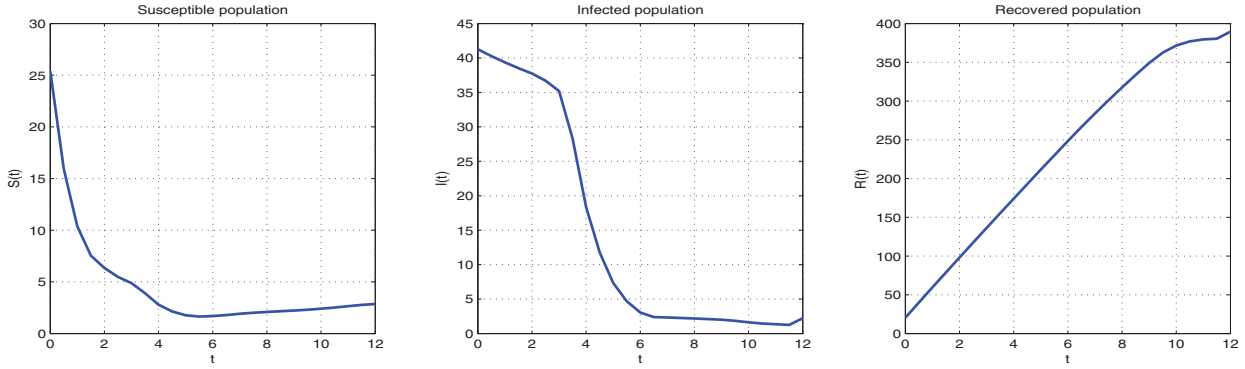

Fig. 7. The optimal states for $\tau = 2$, $\sigma = 0$, $\delta = 6$.

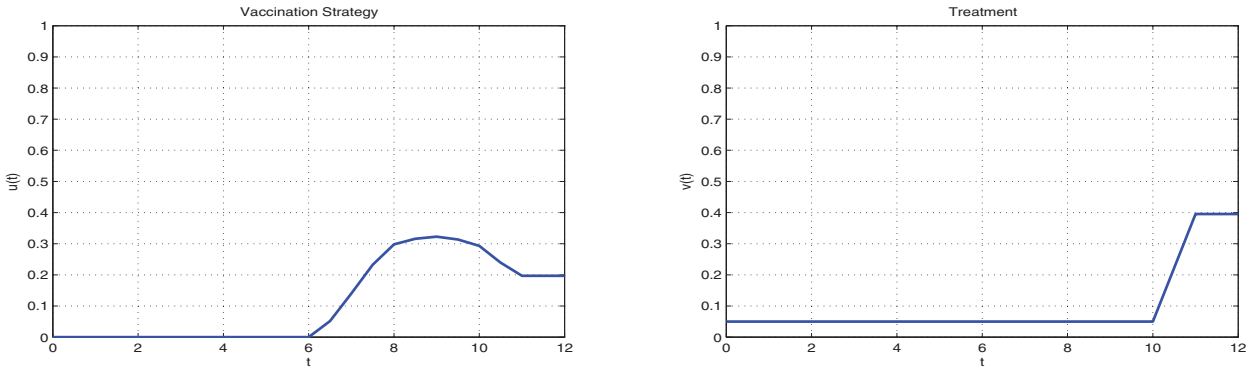

Fig. 8. The optimal controls for $\tau = 0$, $\sigma = 6$ and $\delta = 0$.

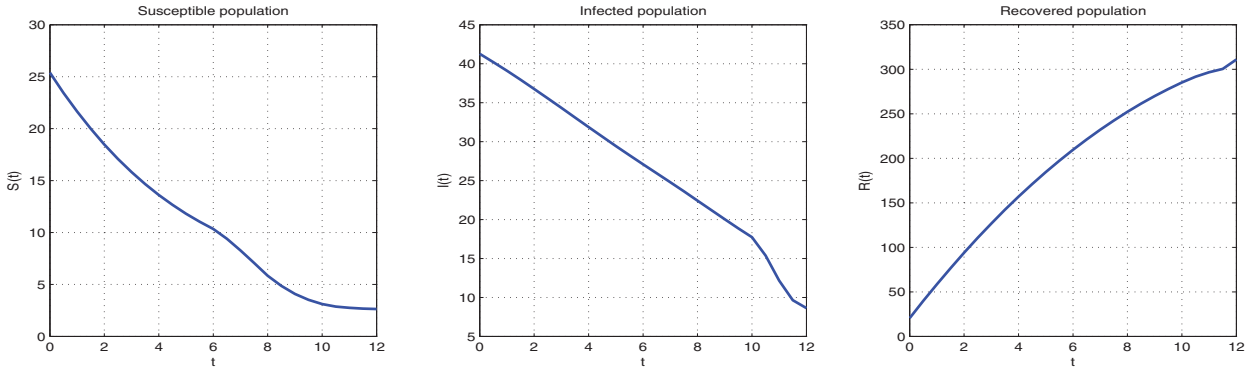

Fig. 9. The optimal states for $\tau = 0$, $\sigma = 6$ and $\delta = 0$.

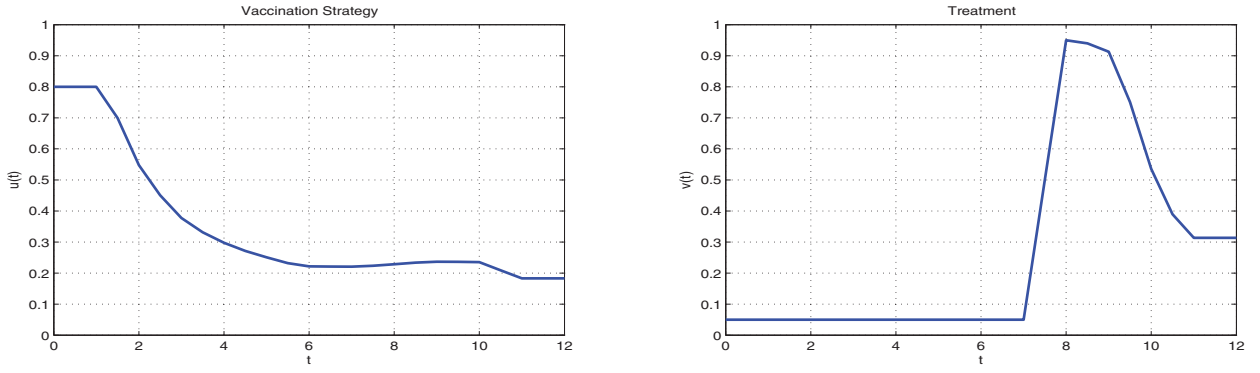

Fig. 10. The optimal controls for $\tau = 6$, $\sigma = 3$ and $\delta = 4$.

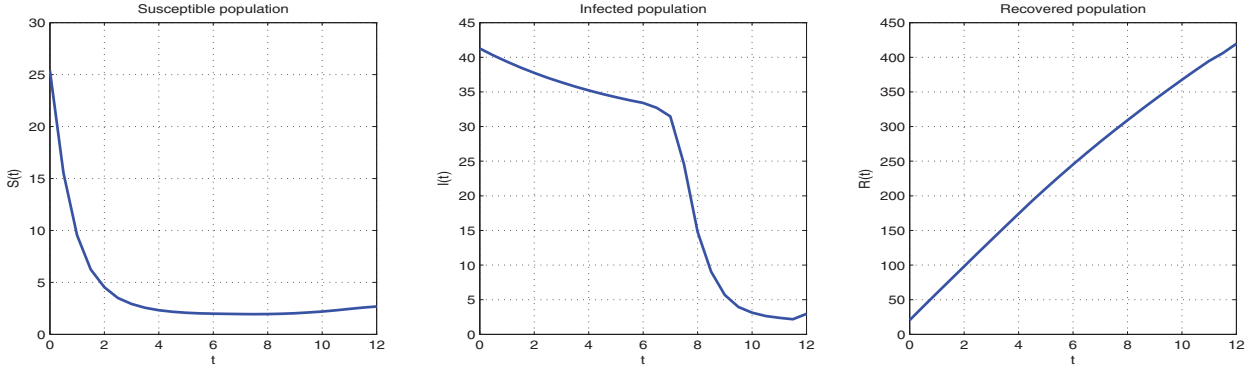

Fig. 11. The optimal states for $\tau = 6$, $\sigma = 3$ and $\delta = 4$.

the delay $\tau = 6$, and without delays in the vaccination and treatment controls (Figs. 4 and 5) showed the necessity of using the vaccination strategy all the time. When the delay taken by the treatment is considered larger than the incubation period (Figs. 6 and 7), maximum levels of vaccines and treatment are needed to control the disease. The case when the incubation period and the treatment delay are ignored ($\tau = \delta = 0$), while the delay in the vaccine is considered (Figs. 8 and 9), did not show a difference from the case when all the time delays of the model where ignored. Finally, in the two last two cases we considered the three time delays, again the maximum levels of vaccination and treatment are seen.

Further numerical simulations, which we have not shown in this paper, showed that the vaccination delay is not really significant. Only the delays of the incubation period and the treatment count in the model.

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