Optimal Vaccination of an Endemic Model with Variable Infectivity and Infinite Delay

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In this work, we consider a nonlinear *SEIR* (susceptible, exposed, infectious, and removed) endemic model, which describes the dynamics of the interaction between susceptible and infected individuals in a population. The model represents the disease evolution through a system of nonlinear differential equations with variable infectivity which determines that the infectivity of an infected individual may not be constant during the time after infection. To control the spread of infection and to find a vaccination schedule for an endemic situation, we use optimal control strategies which reduce the susceptible, exposed, and infected individuals and increase the total number of recovered individuals. In order to do this, we introduce the optimal control problem with a suitable control function using an objective functional. We first show the existence of an optimal control for the control problem and then derive the optimality system. Finally the numerical simulations of the model is identified to fit realistic measurement which shows the effectiveness of the model.

Key words: Variable Infectivity; Optimality; Vaccination; Numerical Simulation.
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1. Introduction

We take into account that the infectivity of an infected individual may not be constant during the time after infection. Already the variable infectivity in *SIR* (susceptible, infected, and recovered) epidemic model has been considered by Kermack and McKendrick (1927–1939). In their model with variable infectivity, I is the infected population size, not to be confused with the infectious population size, which means that it is not discriminated whether an infected individual is infectious or not. To discriminate that, the class E of exposed individuals is taken into account by several authors, see for example [1, 2].

Nowadays, due to the large mobility of people within a community or even world wide, the risk of being infected by a virus is relatively higher than several years ago. That is why it is interesting to elaborate mathematical models of the evolution of diseases in order to develop strategies to reduce the impact of the outbreak. Thus we introduce the optimal control problem with a suitable control function using an objective functional. In our control strategies, we reduce the susceptible, exposed, and infected individuals and increase the total number of recovered individuals. We first show the existence of the optimal control problem and then derive the optimum system. Finally the numerical simulations of the model are identified to fit realistic measurements which shows the effectiveness of the model.

The structure of this paper is organized as follows. The formulation of the *SEIR* endemic model is given in Section 2, which represents the dynamics of the disease. A control system for the optimum and its existence and the optimal control pairs are derived in Section 3 and in Section 4, a realistic application of our optimal control approach is given. Finally, we conclude by discussing results of the numerical simulation for our endemic model.

2. An Infection-Age Structured *SEIR* Endemic Model

In this section, we introduce another independent variable $b \geq 0$ (infection age) denoting the time that has passed since infection. The rate σ at which a susceptible individual catches the disease from an infectious individual (per unit of time) is now a function of the infection age b, i. e.,

$$\sigma = \sigma(b)\,.$$

The class of infected individuals is stratified according to infection age such that

$$i(t,b)$$

denotes the infection age density of the infected individuals at time t with infection age b. Particularly,

$$\int_{b_1}^{b_2} i(t,b)\,\mathrm{d}b$$

gives the number of infected individuals with an infection age between b_1 and b_2. Let $B(t)$ be the input into the infected class at time t. Prescribe the probability $P(b)$ of not being removed (i. e., neither yet dying nor leaving the infected stage alive) at infection age b, where $P : [0,\infty) \to [0,1]$ is the sojourn function of the infected stage [3], i. e., P is non increasing and $P(0) = 1$. Then $i(t,b)$ can be expressed as follows:

$$i(t,b) = \begin{cases} B(t-b)P(b)\,, & t > b \geq 0\,, \\ i_0(b-t)\frac{P(b)}{P(b-t)}\,, & b > t \geq 0\,, \end{cases} \tag{1}$$

where $i_0(b)$ is the age density of individuals that are in the stage at time 0. The first equation means individuals with infection age b at time $t > b$ having entered the stage at time $t-b$. The second equation means individuals with infection age b at $t < b$ and having the infection age $b-t$ at time 0.

We split up the host population into susceptible, exposed, infectious, and removed individuals whose numbers are denoted by S, E, I, and R. We consider nonfatal diseases without vertical infection and assume that the per capita mortality rate of S, E, I, and R is the same constant, denoted by $\nu > 0$. When standard incidence adopted for infection, the susceptible population size S at time t is modelled by

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \text{birth} - \nu S(t) - \frac{\int_0^\infty \sigma(b) i(t,b) S(t)\,\mathrm{d}b}{N(t)}\,,$$

where $N(t)$ is the total size of the host population ($N(t) = S(t) + E(t) + I(t) + R(t)$). Note that $I(t) = \int_0^\infty i(t,b)\,\mathrm{d}b$. The input into the exposed class is the incidence of the disease, i. e., the rate of infection, for an endemic model, is

$$\frac{\int_0^\infty \sigma(b) i(t,b) S(t)\,\mathrm{d}b}{N(t)}\,.$$

So, the exposed population size E at time t is modelled by

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{\int_0^\infty \sigma(b) i(t,b) S(t)\,\mathrm{d}b}{N(t)} - (\eta + \nu)E(t)\,,$$

where the per capita transition rate from the class E to the class I are assumed to be constant and is denoted by η.

The input $B(t)$ into the infectious class equals $\eta E(t)$. Then, by (1),

$$\frac{i(t,b)}{P(b)} = \begin{cases} \eta E(t-b)\,, & t > b \geq 0\,, \\ \frac{i_{0,(b-t)}}{P(b-t)}\,, & b > t \geq 0\,, \end{cases}$$

is differentiable for $t \neq b$ if i_0/P is differentiable, and satisfies the partial differential equation

$$\frac{\partial}{\partial t}\frac{i(t,b)}{P(b)} + \frac{\partial}{\partial b}\frac{i(t,b)}{P(b)} = 0\,,\ t \neq b\,.$$

From (1) and $P(0) = 1$, we have the boundary condition

$$i(t,0) = B(t)\,,$$

and the initial condition

$$i(0,b) = i_0(b)\,.$$

Furthermore, assume that i_0 and P are differentiable. Then i is differentiable for $t \neq b$ and

$$0 = \frac{(\partial/\partial t) i(t,b)}{P(b)} + \frac{(\partial/\partial b) i(t,b)}{P(b)} - i(t,b)\frac{P'(b)}{(P(b))^2}\,.$$

Multiplying this equation by P and assuming that the per capita rate of leaving the infected stage alive is constant and let us denoted it by μ, so we obtain

$$\frac{\partial}{\partial t}i(t,b)+\frac{\partial}{\partial b}i(t,b)+(\mu+\nu)i(t,b)=0\,,\ \ t\neq b\,,$$

because $\mu+\nu=-P'(b)/P(b)$ [3, Chapter 12], (1) can be recovered from this equation [3, Chapter 13]. Since the input of the removed stage is the output of the infected stage (i. e., the rate at which individuals leave the infected stage alive), which is $\mu I(t)$, the removed population size R at time t is modelled by

$$\frac{\mathrm{d}R}{\mathrm{d}t}=\mu I(t)-\nu R(t)\,.$$

Assuming a simplest case where the per capita birth rate equals the per capita mortality rate, we end up with the following equations:

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t}&=\nu N(t)-\nu S(t)-\frac{\int_0^\infty \sigma(b)i(t,b)S(t)\,\mathrm{d}b}{N(t)}\,,\\
\frac{\mathrm{d}E}{\mathrm{d}t}&=\frac{\int_0^\infty \sigma(b)i(t,b)S(t)\,\mathrm{d}b}{N(t)}-(\eta+\nu)E(t)\,,\\
I(t)&=\int_0^\infty i(t,b)\,\mathrm{d}b\,,\\
\frac{\partial}{\partial t}i(t,b)&+\frac{\partial}{\partial b}i(t,b)+(\mu+\nu)i(t,b)=0\,,\ \ t\neq b\,,\\
\frac{\mathrm{d}R}{\mathrm{d}t}&=\mu I(t)-\nu R(t)\,,
\end{aligned}\tag{2}$$

with the initial and boundary conditions given as

$$\begin{aligned}
&S(0)>0\,,\ \ E(0)\geq 0\,,\ \ R(0)\geq 0\,,\\
&i(t,0)=\eta E(t)\,,\ \ i(0,b)=i_0(b)\,.
\end{aligned}$$

In order to ensure the existence of solutions of (2) with the initial and boundary conditions, let

$$W(t)=\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b\,.$$

Integrating (2), we have the following system of integral equations:

$$\begin{aligned}
S(t)&=\int_0^t\left[\nu N(t-b)-\frac{S(t-b)W(t-b)}{N(t-b)}\right]\mathrm{e}^{-\nu b}\mathrm{d}b+f_1(t)\,,\\
E(t)&=\int_0^t\frac{S(t-b)W(t-b)}{N(t-b)}\,\mathrm{e}^{-(\eta+\nu)b}\,\mathrm{d}b+f_2(t)\,,\\
I(t)&=\int_0^t\eta E(t-b)\,\mathrm{e}^{-(\mu+\nu)b}\,\mathrm{d}b+f_3(t)\,,\\
W(t)&=\int_0^t\sigma(b)\eta E(t-b)\,\mathrm{e}^{-(\mu+\nu)b}\,\mathrm{d}b+f_4(t)\,,\\
R(t)&=\int_0^t\mu I(t-b)\,\mathrm{e}^{-\nu b}\,\mathrm{d}b+f_5(t)\,,
\end{aligned}\tag{3}$$

where

$$\begin{aligned}
f_1(t)&=S(0)\,\mathrm{e}^{-\nu t}\,,\ \ f_2(t)=E(0)\,\mathrm{e}^{-(\eta+\nu)t}\,,\\
f_3(t)&=\int_t^\infty i_0(b-t)\,\mathrm{e}^{-(\mu+\nu)t}\,\mathrm{d}b\,,\\
f_4(t)&=\int_t^\infty \sigma(b)i_0(b-t)\,\mathrm{e}^{-(\mu+\nu)t}\,\mathrm{d}b\,,\\
f_5(t)&=R(0)\,\mathrm{e}^{-\nu t}\,.
\end{aligned}$$

Applying standard fixed-point arguments, see for example Gripenberg et al. [4], to (3), we easily show that there exists a nonnegative solution of (3) on $[0,\infty)$ for $f_j\in L_{1,\mathrm{loc}}[0,\infty)$ $(j=1,2,3,4)$, the space of functions that are integrable on every finite interval in $[0,\infty)$. In particular, if $N(t)$ is a constant, then we see that the nonnegative solution uniquely exists, i. e., the model is well-posed.

3. Optimal Control Strategies

Optimal control deals with the problem of finding a control law for a given system such that a certain optimality criterion is achieved [5–9]. In order to get that goal, we investigate an effective strategy to control diseases cause infection on an endemic model which satisfies that the maximum number of infected individuals is not larger than that of susceptible individuals and more individuals are recovered after infection. To control both the susceptible and infected individuals, we consider the model presented in Section 2.

In system (2), we have four state variables $S(t)$, $E(t)$, $I(t)$, and $R(t)$. For the optimal control problem, we consider the control variable $u(t)\in U$ relative to the state variables $(S(t),E(t),I(t),R(t))$, where $U=\{u\in L^\infty(0,T)|0\leq u(t)\leq K<\infty,\exists K>0,t\in[0,T]\}$, says an admissible control set. The physical meaning of the control variable in this problem is that low levels of the number of infected, exposed, and susceptible individuals build. In case of no vaccination (or treatment), the number of infected and exposed individuals increases while the number of recovered individuals decreases. Prefect time of vaccination brings the number of both exposed and infected individuals to a small level, susceptible individuals begin to build again, and more individuals are recovered from infection.

The effects of infection on susceptible, exposed, and infected individuals are negative for recovered individuals around them, so we wish to minimize them. Also small amount of control variable vaccination is acceptable, therefore, we wish to penalize for amount too

large, so quadratic terms for control variable will be analyzed. Hence, our optimal control problem which minimize the objective functional, is given by

$$J(u) = \int_0^T \left(S(t) + E(t) + I(t) + \frac{A_1 u^2(t)}{2} \right) \mathrm{d}t \tag{4}$$

subject to

$$\begin{aligned}
&\frac{\mathrm{d}S}{\mathrm{d}t} = \nu N(t) - (\nu + u(t))S(t) - \frac{\int_0^\infty \sigma(b) i(t,b) S(t)\,\mathrm{d}b}{N(t)}, \\
&\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{\int_0^\infty \sigma(b) i(t,b) S(t) db}{N(t)} - (\eta + \nu)E(t), \qquad (5) \\
&\frac{\partial}{\partial t} i(t,b) + \frac{\partial}{\partial b} i(t,b) + (\mu + \nu) i(t,b) = 0, \ \ t \neq b, \\
&\frac{\mathrm{d}R}{\mathrm{d}t} = \mu I(t) - \nu R(t) + u(t) S(t),
\end{aligned}$$

where $I(t) = \int_0^\infty i(t,b)\,\mathrm{d}b$, with the initial and boundary conditions given as

$$S(0) > 0, \ \ E(0) \geq 0, \ \ R(0) \geq 0, \tag{6}$$

$$i(t,0) = \eta E(t), \ \ i(0,b) = i_0(b). \tag{7}$$

Here A_1 is a positive constant (balance factor) that represents a patient's level of acceptance of the vaccination or treatment. The aim of this work is to minimize the susceptible, exposed, and infected individuals and to maximize the total number of recovered individual by using the possible minimal control variables $u(t)$. Susceptible individuals induce an optimal control vaccination $u(t)$ before the infection.

Remark 1. In the optimal control problem, the objective functional did not explicitly depend on the state variable. However there are situations where we might wish to take it into consideration. Also there are various possibilities of fixing the position of the state at the beginning or at the end of the time interval or both but the objective functional could depend only on the final or initial position.

Theorem 1. *There exists an optimal control variable $u^* \in U$ such that*

$$J(u^*) = \min_{u \in U} J(u),$$

subject to the control system (5) with the initial and boundary conditions (6) and (7), respectively.

Proof. To prove the existence of an optimal control, we have to show the following.

1. The control and state variables are nonnegative values.
2. The control U set is convex and closed.
3. The right hand side of the state system is bounded by linear function in the state and control variables.
4. The integrand of the objective functional is concave on U.
5. There exist constants such that the integrand in (4) of the objective functional is satisfied.

In order to verify these conditions, we use a result by Lukes [10]. We note that the solutions are bounded and the set of all the control variables $u(t) \in U$ is also convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control. In addition, the integrand in the functional $S(t) + E(t) + I(t) + \frac{A_1 u^2(t)}{2}$ is convex on the control set U. Also we can easily see that there exist a constant $\sigma > 1$ and positive numbers ω_1 and ω_2 such that

$$J(u) \geq \omega_2 + \omega_1 (|u|^2)^{\sigma/2}$$

which completes the existence of an optimal control. □

To derive necessary optimality conditions, we use the Gâteaux derivative rule [11]. Given a control u, and we consider another control $u^\varepsilon = u + \varepsilon v$, where v is a variation function and $1 \geqslant \varepsilon > 0$. Let $S = S(u)$, $E = E(u)$, $I = I(u)$, $R = R(u)$, and $S^\varepsilon = S(u^\varepsilon)$, $E^\varepsilon = E(u^\varepsilon)$, $I^\varepsilon = I(u^\varepsilon)$, $R = R(u^\varepsilon)$. Then the state equations corresponding to controls u^ε is given as

$$\begin{aligned}
&\frac{\mathrm{d}S^\varepsilon(t)}{\mathrm{d}t} = \nu N(t) - (\nu + u^\varepsilon(t)) S^\varepsilon(t) \\
&\qquad - \frac{\int_0^\infty \sigma(b) i^\varepsilon(t,b) S^\varepsilon(t)\,\mathrm{d}b}{N(t)}, \qquad (8) \\
&\frac{\mathrm{d}E^\varepsilon(t)}{\mathrm{d}t} = \frac{\int_0^\infty \sigma(b) i^\varepsilon(t,b) S^\varepsilon(t)\,\mathrm{d}b}{N(t)} - (\eta + \nu) E(t), \\
&\frac{\partial}{\partial t} i(t,b) + \frac{\partial}{\partial b} i^\varepsilon(t,b) + (\nu + \mu) i^\varepsilon(t,b) = 0, \ \ t \neq b, \\
&\frac{\mathrm{d}R^\varepsilon(t)}{\mathrm{d}t} = \mu I^\varepsilon(t) - \nu R^\varepsilon(t) + u(t) S^\varepsilon(t),
\end{aligned}$$

with $I^\varepsilon(t) = \int_0^\infty i^\varepsilon(t,b)\,\mathrm{d}b$. Now, we find the difference quotient such that $\frac{S^\varepsilon - S}{\varepsilon}$ and similarly for E, I, i, and

R to get the corresponding state system for both systems (5) and (7). For a given control variable u in U_{ad} where U_{ad} represents an admissible control, fix a v in U_{ad} such that $u+\varepsilon v \in U_{ad}$ [12]. Subtracting system (5) from (7), we get

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{S^\varepsilon(t)-S(t)}{\varepsilon}\right) = -(\nu+u^\varepsilon(t))\frac{S^\varepsilon(t)-S(t)}{\varepsilon} \\
&-\frac{\int_0^\infty \sigma(b)\left(\frac{i^\varepsilon(t,b)-i(t,b)}{\varepsilon}\right)\left(\frac{S^\varepsilon(t)-S(t)}{\varepsilon}\right)\mathrm{d}b}{N(t)}, \\
&\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{E^\varepsilon(t)-E(t)}{\varepsilon}\right) = \left(\int_0^\infty \sigma(b)\left(\frac{i^\varepsilon(t,b)-i(t,b)}{\varepsilon}\right)\right. \\
&\left.\cdot\left(\frac{S^\varepsilon(t)-S(t)}{\varepsilon}\right)\mathrm{d}b\right)\Big(N(t)\Big)^{-1} - (\eta+\nu)\frac{E^\varepsilon(t)-E(t)}{\varepsilon}, \\
&\frac{\partial}{\partial t}\left(\frac{i^\varepsilon(t,b)-i(t,b)}{\varepsilon}\right) + \frac{\partial}{\partial b}\left(\frac{i^\varepsilon(t,b)-i(t,b)}{\varepsilon}\right) = \\
&-(\nu+\mu)\left(\frac{i^\varepsilon(t,b)-i(t,b)}{\varepsilon}\right), \qquad (9) \\
&\frac{\mathrm{d}}{\mathrm{d}t}\left(\frac{R^\varepsilon(t)-R(t)}{\varepsilon}\right) = \mu\frac{I^\varepsilon(t)-I(t)}{\varepsilon} - \nu\frac{R^\varepsilon(t)-R(t)}{\varepsilon} \\
&\qquad + u(t)\frac{S^\varepsilon(t)-S(t)}{\varepsilon}.
\end{aligned}$$

We assume that $\varepsilon \to 0$, $S^\varepsilon \to S$, and $\frac{S^\varepsilon-S}{\varepsilon} \to \bar{S}$, and similarly for $E(t)$, $I(t)$, $i(t,b)$, and $R(t)$, we obtain $\bar{i}$ and $\bar{R}$, respectively, and get

$$\begin{aligned}
&\frac{\mathrm{d}\bar{S}(t)}{\mathrm{d}t} = -(\nu+u(t))\bar{S}(t) - \nu(t)S(t) - \frac{\bar{S}(t)}{N(t)} \\
&\qquad\cdot\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b - \frac{S(t)}{N(t)}\int_0^\infty \sigma(b)\bar{i}(t,b)\,\mathrm{d}b, \\
&\frac{\mathrm{d}\bar{E}(t)}{\mathrm{d}t} = \frac{\bar{S}(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b \qquad (10) \\
&\qquad + \frac{S(t)}{N(t)}\int_0^\infty \sigma(b)\bar{i}(t,b)\,\mathrm{d}b - (\eta+\nu)\bar{E}(t), \\
&\frac{\partial\bar{i}(t,b)}{\partial t} + \frac{\partial\bar{i}(t,b)}{\partial b} = -(\mu+\nu)\bar{i}(t,b), \\
&\frac{\mathrm{d}\bar{R}(t)}{\mathrm{d}t} = \mu\bar{I}(t) - \nu\bar{R}(t) + u(t)\bar{S}(t) + \nu(t)S(t).
\end{aligned}$$

In order to find the adjoint equations, we can write the first equation of the above system as

$$\begin{aligned}
0 &= \left\langle \frac{\mathrm{d}\bar{S}(t)}{\mathrm{d}t} + (\nu+u(t))\bar{S}(t) + \frac{\bar{S}(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b \right. \\
&\quad \left. + \frac{S(t)}{N(t)}\int_0^\infty \sigma(b)\bar{i}(t,b)\,\mathrm{d}b + \nu(t)S(t), \lambda_1(t)\right\rangle \\
&= \left\langle \bar{S}(t), -\lambda_1'(t) + (\nu+u(t))\lambda_1(t) + \frac{\lambda_1(t)}{N(t)}\right. \qquad (11) \\
&\quad \left.\cdot\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b\right\rangle + \int_0^T\int_0^\infty \sigma(b)\bar{i}(t,b) \\
&\quad \cdot\frac{S(t)\lambda_1(t)}{N(t)}\,\mathrm{d}b\,\mathrm{d}t - \int_0^T \nu(t)S(t)\lambda_1(t)\,\mathrm{d}t,
\end{aligned}$$

where $\langle a,b\rangle = \int_0^T ab\,\mathrm{d}t$, and $'$ represents the derivative with respect to time, with

$$\begin{aligned}
&\lim_{\varepsilon\to 0}\frac{i^\varepsilon(0,b)-i(0,b)}{\varepsilon} = \bar{i}_0(b) = 0, \\
&\bar{S}_0 = 0,\ \ \lambda_1(T) = 0,\ \ \bar{I}(t) = \int_0^\infty \bar{i}(t,b)\,\mathrm{d}b.
\end{aligned} \qquad (12)$$

From the second equation, with the given boundary condition

$$\begin{aligned}
0 &= \left\langle \frac{\mathrm{d}\bar{E}(t)}{\mathrm{d}t} - \frac{\bar{S}(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b - \frac{S(t)}{N(t)}\right. \\
&\quad \left.\cdot\int_0^\infty \sigma(b)\bar{i}(t,b)\,\mathrm{d}b + (\eta+\nu)\bar{E}(t), \lambda_2(t)\right\rangle \\
&= \left\langle \bar{E}(t), -\lambda_2'(t) + (\eta+\nu)\bar{\lambda_2}(t) - \frac{\lambda_2(t)}{N(t)}\right. \qquad (13) \\
&\quad \left.\cdot\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b\right\rangle + \int_0^T\int_0^\infty \sigma(b)\bar{i}(t,b)\frac{S(t)\lambda_2(t)}{N(t)}\,\mathrm{d}b\,\mathrm{d}t,
\end{aligned}$$

From the third equation, with the boundary condition

$$\begin{aligned}
\bar{i}(t,0) &= \frac{\bar{S}(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b \\
&\quad + \frac{S(t)}{N(t)}\int_0^\infty \sigma(b)\bar{i}(t,b)\,\mathrm{d}b,
\end{aligned} \qquad (14)$$

we get

$$\begin{aligned}
0 &= \left\langle \left\langle \frac{\partial\bar{i}(t,b)}{\partial t} + \frac{\partial\bar{i}(t,b)}{\partial b} + (\mu+\nu)\bar{i}(t,b), \lambda_3(t,b)\right\rangle\right\rangle \\
&= \left\langle \left\langle \bar{i}(t,b), -\frac{\partial\lambda_3(t,b)}{\partial t} - \frac{\partial\lambda_3(t,b)}{\partial b}\right.\right. \qquad (15)
\end{aligned}$$

$$+(\mu+\nu)\lambda_3(t,b)\Big\rangle\Big\rangle - \int_0^T\int_0^\infty \left(\frac{\bar{S}(t)}{N(t)}\sigma(b)i(t,b) + \frac{S(t)}{N(t)}\sigma(b)\bar{i}(t,b)\right)\lambda_3(t,0))\,\mathrm{d}b\,\mathrm{d}t$$

with

$$\bar{i}(0,b)=0,\ \bar{i}(t,\infty)=0,\ \lambda_3(T,b)=0, \tag{16}$$

where $\langle\langle f,g\rangle\rangle = \int_0^{t_{\text{end}}}\int_0^\infty f(t,b)g(t,b)\,\mathrm{d}b\,\mathrm{d}t$. Similarly from the fourth equation of system (10), we obtain

$$\begin{aligned}0 = &\left\langle \frac{\mathrm{d}\bar{R}(t)}{\mathrm{d}t} - \int_0^\infty \bar{i}(t,b)\,\mathrm{d}b + \nu\bar{R}(t)\right.\\ &\left. - u(t)\bar{S}(t) - v(t)S(t), \lambda_4(t)\right\rangle \\ = &\left\langle \bar{R}(t), -\frac{\mathrm{d}\lambda_4(t)}{\mathrm{d}t} + \nu\lambda_4(t)\right\rangle + \left\langle \bar{S}(t), -u(t)\lambda_4(t)\right\rangle \\ &- \int_0^T\int_0^\infty \bar{i}(t,b)\lambda_4(t)\,\mathrm{d}b\,\mathrm{d}t - \int_0^T v(t)S(t)\lambda_4(t)\,\mathrm{d}t\end{aligned} \tag{17}$$

with

$$\bar{R}(0)=0,\ \lambda_4(T)=0. \tag{18}$$

We derive the Gateaux derivative of $J(u)$ as

$$0 \leqslant J'(u)v = \int_0^{t_{\text{end}}} \left(\bar{S}(t)+\bar{E}(t)+\bar{I}(t) + A_1u(t)v(t)\right)\mathrm{d}t\,. \tag{19}$$

Now we combine (12), (15), (17), and (19) with some rearrangement to obtain the adjoin system which is given by

$$\begin{aligned}\lambda_1'(t) &= (\nu+u(t))\lambda_1(t) + \frac{p(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b \\ &- \frac{\lambda_3(t,0)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b - u(t)\lambda_4(t) - 1\,, \\ \lambda_2'(t) &= (\eta+\nu)\lambda_2(t) + \frac{\lambda_1(t)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b \\ &- \frac{\lambda_3(t,0)}{N(t)}\int_0^\infty \sigma(b)i(t,b)\,\mathrm{d}b - 1\,, \\ \frac{\partial\lambda_3(t,b)}{\partial t} &+ \frac{\partial\lambda_3(t,b)}{\partial b} = (\mu+\nu)\lambda_3(t,b) \\ &+ \frac{\sigma(b)S(t)}{N}\lambda_1(t) - \frac{\sigma(b)S(t)}{N}\lambda_3(t,0) - \mu(b)\lambda_4(t) - 1\,, \\ \lambda_4'(t) &= \nu\lambda_4(t)\end{aligned} \tag{20}$$

with transversality conditions (or boundary conditions)

$$\begin{aligned}&\lambda_1(T)=0,\ \lambda_2(T)=0,\\ &\lambda_3(T,b)=0,\ \lambda_4(T)=0.\end{aligned} \tag{21}$$

Theorem 2. *If u^* in U_{ad} is an optimal control pair minimizing (4) and $(S^\star,E^\star,I^\star,R^\star)$ and $(\lambda_1,\lambda_2,\lambda_3,\lambda_4)$ are the corresponding state and adjoint variables, respectively, then*

$$u^*(t) = \min\left\{k, \max\left\{0, \frac{(\lambda_1(t)-\lambda_4(t))S^\star(t)}{A_1}\right\}\right\}.$$

Proof. Since u^* is an optimal control, so we have

$$\begin{aligned}0 &\leq \lim_{\varepsilon\to 0}\frac{J(u^\varepsilon)-J(u)}{\varepsilon} \\ &= \frac{1}{\varepsilon}\int_0^T\left(\left(S^\varepsilon(t)+E^\varepsilon(t)+I^\varepsilon(t)+\frac{A_1u^\varepsilon(t)^2}{2}\right)\right. \\ &\left.-\left(S(t)+E(t)+I(t)+\frac{A_1u^2(t)}{2}\right)\right)\mathrm{d}t \\ &= \frac{1}{\varepsilon}\int_0^T\Big((S^\varepsilon(t)-S(t))+(E^\varepsilon(t)-E(t)) \\ &+(I^\varepsilon(t)-I(t))+\frac{A_1}{2}(u^\varepsilon(t)^2-u^2(t))\Big)\mathrm{d}t \\ &= \int_0^T\left(\bar{S}(t)+\bar{E}(t)+\bar{I}(t)+A_1v(t)u(t)\right)\mathrm{d}t \\ &= \int_0^T\Big(\bar{S}(t)(-\lambda_1'(t)+(\nu+u(t))\lambda_1(t) \\ &+\frac{\lambda_1(t)}{N}\int_0^\infty\sigma(b)i(t,b)\,\mathrm{d}b - u(t)\lambda_4(t) \\ &-\frac{\lambda_3(t,0)}{N}\int_0^\infty\sigma(b)i(t,b)\,\mathrm{d}b) + \bar{E}(t)(-\lambda_2'(t) \\ &+(\eta+\nu)\bar{\lambda_2}(t) - \frac{\lambda_2(t)}{N(t)}\int_0^\infty\sigma(b)i(t,b)\,\mathrm{d}b \\ &+\int_0^T\int_0^\infty\sigma(b)\bar{i}(t,b)\frac{S(t)\lambda_2(t)}{N}\,\mathrm{d}b\,\mathrm{d}t) \\ &+\bar{I}(t)\Big(-\frac{\partial\lambda_3(t,b)}{\partial t}-\frac{\partial\lambda_3(t,b)}{\partial b}+(\mu+\nu)\lambda_3(t,b) \\ &+\frac{\sigma(b)\lambda_1(t)S(t)}{N}-\frac{1}{N}\sigma(b)S(t)\lambda_3(t,0)-\mu\lambda_4(t)\Big) \\ &-\nu\lambda_4(t)+A_1v(t)u(t))\Big)\mathrm{d}t \\ &= \int_0^{t_{\text{end}}} v(t)(S(t)(\lambda_4(t)-\lambda_1(t))+A_1u(t))\,\mathrm{d}t\,,\end{aligned} \tag{22}$$

for all $v \in U_{ad}$. We simplify further to obtain

$$\int_0^{t_{\text{end}}} v(t)(S(t)(\lambda_4(t)-\lambda_1(t))+A_1u(t))\,\mathrm{d}t \geq 0\,. \quad (23)$$

Thus on this set, in the case when $v(t) \neq 0$, the rest of the integrand must be zero so that

$$u(t) = \frac{S(t)(\lambda_1(t)-\lambda_4(t))}{A_1}\,. \quad (24)$$

Hence, by taking the upper and lower bound into account, we obtain

$$u^*(t) = \min\left\{k, \max\left\{0, \frac{(\lambda_1(t)-\lambda_4(t))S^\star(t)}{A_1}\right\}\right\}. \quad (25)$$

Here the formula (25) represents the characterization of the optimal control. □

The optimal control and the state are found by solving the optimum system, which consists of the state system (5), the adjoint system (20), boundary conditions (6) and (21), and the characterization of the optimal control (25). To solve the optimum system, we use the initial and transversality conditions together with the characterization of the optimal control variable $u^*(t)$ given by (25). By substituting the value of $u^*(t)$ in the control system (5), we get the following optimal control system:

$$\begin{aligned}
&\frac{\mathrm{d}S^*(t)}{\mathrm{d}t} = \nu N(t) - \frac{S^\star}{N(t)}\int_0^\infty \sigma(b)i^*(t,b)(t)\,\mathrm{d}b\\
&-\left(\mu+\min\left\{k,\max\left\{0,\frac{(\lambda_1(t)-\lambda_4(t))S^\star(t)}{A_1}\right\}\right\}\right)S^\star(t)\,,\\
&\frac{\mathrm{d}E^*(t)}{\mathrm{d}t} = \frac{S^\star}{N(t)}\int_0^\infty \sigma(b)i^*(t,b)(t)\,\mathrm{d}b-(\eta+\nu)E^*\\
&\frac{\partial i^*(t,b)}{\partial t}+\frac{\partial i^\star(t,b)}{\partial b} = -(\mu+\nu)i^\star(t,b)\,, \quad (26)\\
&\frac{\mathrm{d}R^*(t)}{\mathrm{d}t} = \int_0^\infty \mu(b)i^*(t,b)\,\mathrm{d}b-\nu R^\star(t)\\
&+\min\left\{k,\max\left\{0,\frac{(\lambda_1(t)-\lambda_4(t))S^\star(t)}{A_1}\right\}\right\}S^\star(t)\,.
\end{aligned}$$

To find out the optimal control and state, we will numerically solve systems (20) and (26) with the given initial and boundary conditions. In the next section, we present numerical results for the optimum system by using an iterative method.

4. Numerical Results and Discussion

In this section, we demonstrate numerically that the model formulated in terms of variable infectivity and control variable decrease the infection of diseases. To achieve this, a program is developed in MATLAB to integrate the optimum system, and the output was comprehensively verified using a detailed output from a number of runs. In this work, we obtain the optimum system from the state and adjoint equations. The optimal control problem strategy is obtained by solving the optimum system which consists of six ordinary differential equations and boundary conditions. Our choice of numerical method is the forward time/backward space finite difference method [13]. Starting with an initial guess for the adjoint variables, the state equations are solved by a forward time and backward space finite difference method. Then those state values are used to solve the adjoint equations by a backward time and forward space finite difference method because of the transversality conditions. For the convenience of the reader, we recall the scheme for the simpler case of the wave equation

$$\frac{\partial \omega}{\partial t}+\phi\frac{\partial \omega}{\partial x} = \Psi(x,t)\,, \quad (27)$$

where ϕ is a constant, and Ψ is a function depend upon space and time, t and x represent the time and space, respectively. The forward time and backward space scheme for the above problem is

$$\frac{\omega_m^{n+1}-\omega_m^n}{\Delta t}-\phi\frac{\omega_m^n-\omega_{m-1}^n}{\Delta x} = \Psi(x_m,t_n)\,, \quad (28)$$

where n denotes the time index and m the space index in the grid.

To control in both the susceptible and infected individuals, we use a control variable in the form of vaccination. We consider the treatment for 20 days because the long treatment in the form of medication has potentially harmful side effect and the best time of vaccination is the possible early stage of diseases. We use a set of parameter value $\nu = 0.25$, $\eta = 0.06$, $\sigma(0) = 0.05$, and $A_1 = 0.91$. We consider the real data used in [9, 14] for individuals $S(0) = 153$, $S(0) = 79$, and $R(0) = 68$ with $i(0,b) = 0$ and assume that $S(0) \geq L(0) = 120$ to determine the numerical simulation of the optimum system with a small time step size $\Delta t = 0.05$.

In Figure 1, we plot the susceptible individual in (2) and (5). The solid line denotes the population of susceptible individuals in (2) without control while the

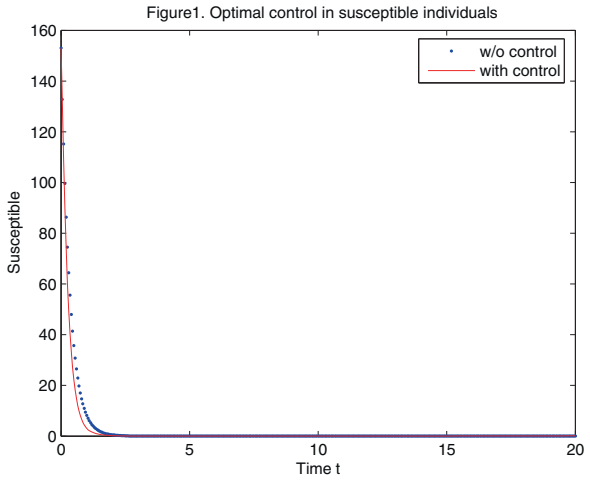

Fig. 1 (colour online). Population of susceptible individuals S with and without control.

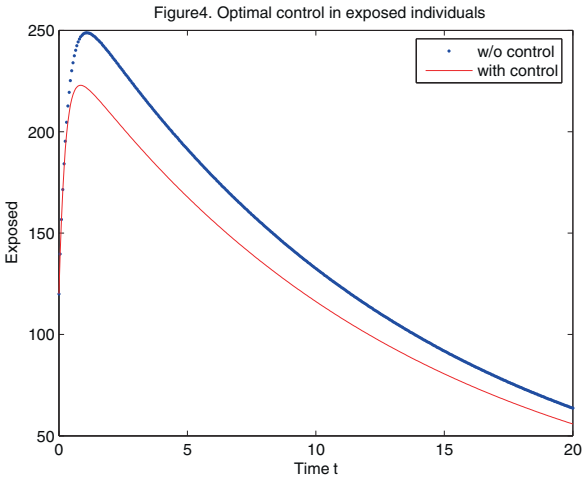

Fig. 2 (colour online). Population of exposed individuals E with and without control.

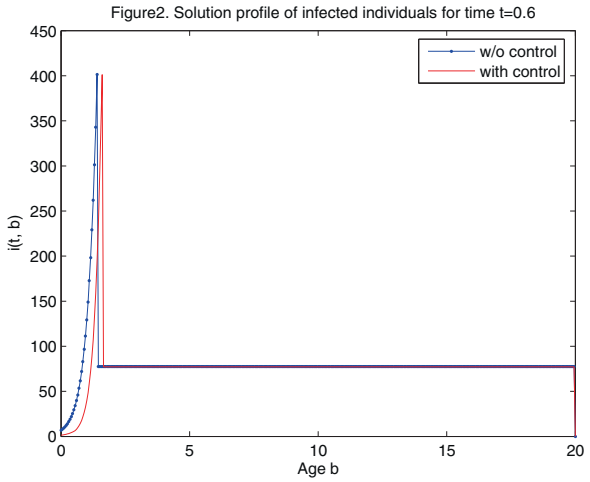

Fig. 3 (colour online). Solution profile of infected individuals with and without control for time $t = 0.6$.

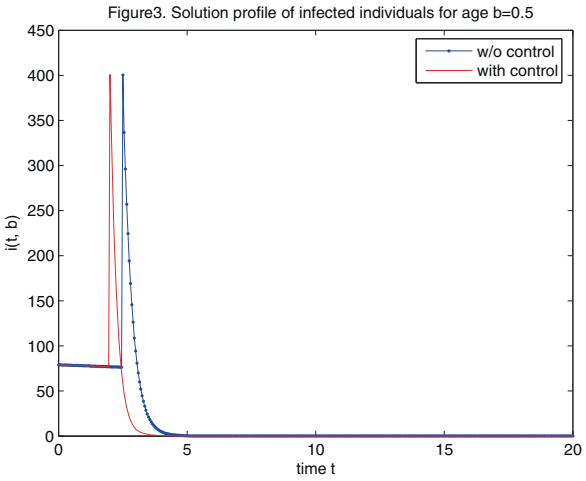

Fig. 4 (colour online). Solution profile of infected individuals with and without control for age $t = 0.5$.

plan line denotes the population of susceptible individuals in (5) with control. The population of susceptible individuals sharply decrease in the first 2 – 3 days because the maximum number of exposed and infected individuals occurs within that period of time. Figure 2 represents the exposed individuals in (2) and (5). The number of exposed individuals sharply increase at the first few days and then decreases slightly and reach at its minimum number $E = 64$ and $E^* = 56$ at the end of control. The solid line denotes that there are more exposed individuals when the control (treatment) is not implemented to the system which shows that the disease spread in a community and more susceptible individuals move to exposed individuals. Figure 3 and 4 represent solution profiles of infected individuals in (2) without control and (5) with control for time $t = 0.6$ and age $b = 0.5$, respectively. The solid line denotes that there are more infectious individuals when the control (treatment) is not implemented to the infected individuals. The solution profile of infected individuals for time $t = 0.6$ shows that the infected individuals sharply increase from the first day of infection in systems both with control (treatment) and without control (treatment) and reach at its maximum number of infected individuals $i(0.6, 2.5) = 78$ on day 2.30 and $i^*(0.6, 2.5) = 79$. After that period of time, the number

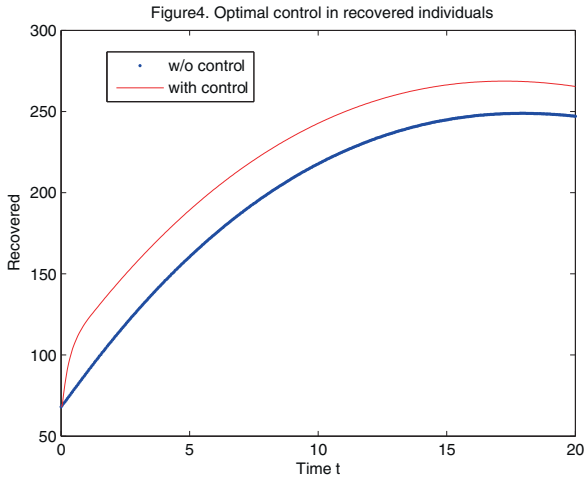

Fig. 5 (colour online). Population of recovered individuals R with and without control.

of infected individuals is stable around days 2.5 – 19 and then decrease until the control vanishes. The solution profiles in Figure 3 and 4 represent that the control is more effective in the first few days.

Figure 5 represents the recovered individuals in (2) and (5). We initiate optimal control in the form of treatment in (5). At the first day of control, about 23 recovered individuals more sharply increase than the individuals without control. Thus the rate of susceptible, exposed, and infected individuals decrease after the control (treatment) and so more individuals are recovered. The maximum number of recovered individuals at the end of control are $R = 249$ and $R^* = 268$, respectively, as can be seen in Figure 5.

In this paper, the model is identified to fit realistic measurements which represents the effectiveness of the model and shows good agrement compared to the model without time and age infectivity.

5. Concluding Remarks

In this work, we introduced a system of nonlinear differential equations with variable infectivity which determine that infected individuals may not be constant during the time after infection. To decrease the infection rate, we used optimal control theory in the form of vaccination to minimize the susceptible and infected individuals and maximize the recovered individual. New controlled models are developed from the numerical simulation of the optimum system which represents the change in each individual of the community. We also pointed out that for certain values of control rate there exists its corresponding optimal solution. Moreover we considered the time limit of the vaccination to avoid the possible harmful side effect of the long treatment. Finally, we presented the efficiency of this optimal control theory. We considered a special disease in a specific community as a realistic model, and we hope that the approach introduced in this paper will be applicable in other endemic models beyond the *SEIR* model.

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