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Optimal Vaccination Control and Free optimal time for a General SEIR-Epidemic Model

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Abstract. In this paper, we consider a mathematical model of a SEIR (susceptible plus exposed plus infectious plus removed populations) propagation disease. The model takes into account the total population amounts as a refrain for the illness transmission since its increase makes more difficult contacts among susceptible and infections. A control problem is formulated, we use an optimal vaccination strategies to minimize the susceptible, exposed and infected individuals and to maximize the number of recovered individuals. We presents an approach that investigates a free terminal optimal time control which give a minimum duration of a vaccination campaign. Some results concerning the existence and the characterization of the optimal control will be given. The Pontryagin's maximum principle is used to characterize the optimal control and the optimal final time. We obtained an optimality system that we sought to solve numerically by an iterative discrete shema that converges following an appropriate test similar the one related to the forward-backward sweep method. Numerical examples are given to illustrate the obtained results.

Keywords: SEIR-Epidemic model, Optimal control, Vaccination, Pontryagin's maximum principle

1 Introduction

Epidemic models study the transmission dynamics of infectious diseases in host populations. Mathematical modeling of the spread of infectious diseases has had an increasing influence on the theory and practice of disease management and control. The literature about epidemic mathematical models is exhaustive in many books and papers [3, 4, 10],[17]-[21].

Typically after the initial infection, a host stays in a latent period before becoming infectious. At the infectious stage a host may die from the disease or may recover with acquired immunity. The population can be partitioned into four compartments: susceptible, latent or exposed, infected and recovered, with size denoted by S, E, I and R respectively.

In this paper, we consider the true-mass action SEIR type epidemic model, where the model takes into account the total population amounts as a refrain for the illness transmission. It is assumed that the total population remains constant through time, so that the illness transmission is not critical. The dependence of transmission on the total population size is studied by [2, 16]. It is shown that the true mass-action approach is the correct one for modelling the transmission term.

There are many variants of the above models, for instance, including vaccination of different kinds: constant [20], impulsive [19], discrete-time, incorporating point or distributed delays [19]-[21], oscillatory behaviors [17], etc.

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A continuous-time vaccination control strategy is given in this paper. Several authors have studied the vaccination strategy of the true-mass action SEIR type epidemic model, we cite the work of [4] which have given a feedback control linearization technique to obtain a family of vaccination policies capable of asymptotically making the complete population become removed-by-immunity (immune). In [3], the control objective is the asymptotically tracking of the removed-by-immunity population to the total population while achieving simultaneously the remaining population to asymptotically converge to zero. Also the observer-based vaccination strategy is given by [5] and a stability analysis and observer design in [9] is studied for the true-mass action type epidemic model.
Optimal control theory provide a valuable tool to begin to assess the trade-offs between vaccination and treatment strategies [6–8, 10],[11]-[14]. Optimal control is a mathematical technique derived from the calculus of variation. However, the control of epidemic systems is not usually an easy task since in real situations it is rather difficult to implement the control policies suggested by the mathematical analysis.
In this paper we use optimal control strategies in the form of vaccination to control the number of susceptible individuals and infected individuals and to increase the number of recovered individuals. Consequences of providing a susceptible population with vaccination on SEIR epidemic model have been receiving much attention by researchers with their main concern being control and eradication of diseases.
However, the diseases immunization strategies are based on the conventional concept of time constant, while in practice, it is always advantageous to treat a disease as quickly as possible to minimize the negative effects of the disease on the patient's body. In addition, it is both difficult and expensive to implement vaccination for large population coverage in large time, especially while considering financial and logistical constraints. That is why we are interested to research for an optimal final time which allows us to attempt to reach the aim of those strategies with an optimal cost. In this context and as contribution in the control of the true-mass action type epidemic model, we set a characterisation of an optimal vaccination strategies that investigates a free terminal time control which give a minimum duration of vaccination campaign. The explicit expression of the optimal control and the optimal final time was obtained by using the Pontryagin's maximim principle [18].
The paper is organized as follows: In Section **??**, the model is described. In Section 3, we give some results concerning the existence of the optimal control and we use Pontryagin's maximum principle to investigate analysis of control strategies and to determine the necessary condition for the optimal control of the disease. In Section 4, we present the numerical method and the simulation results. Finally, a conclusion is summarized in Section 5.

2 SEIR epidemic model

Consider the SEIR-type epidemic model

$$\dot{S}(t) = -\mu S(t) + \omega R(t) - \beta \frac{S(t)I(t)}{N} + \mu N(1 - V(t)) \tag{1}$$

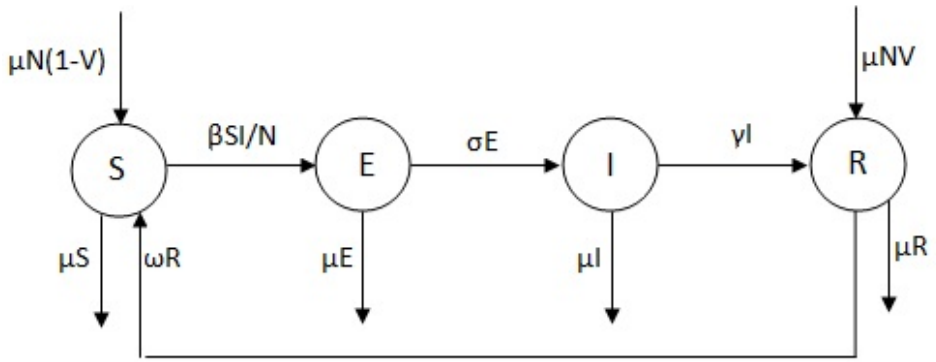
$$\dot{E}(t) = \beta \frac{S(t)I(t)}{N} - (\mu + \sigma)E(t) \tag{2}$$

$$\dot{I}(t) = -(\mu + \gamma)I(t) + \sigma E(t) \tag{3}$$

$$\dot{R}(t) = -(\mu + \omega)R(t) + \gamma I(t) + \mu N V(t) \tag{4}$$

subject to initial conditions $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$ under the vaccination constraint V: $\mathbb{R}_{0+} \longrightarrow \mathbb{R}_+$ where $\mathbb{R}_+ = \{z \in \mathbb{R} | z > 0\}$ and $\mathbb{R}_{0+} = \mathbb{R}_+ \cup \{0\}$.
In such a SEIR-model, N is the total population, μ is the rate of deaths from causes unrelated to the infection, ω is the rate of losing immunity, β is the transmission constant (with the total number of infections per unity of time at time t being $\beta \frac{S(t)I(t)}{N}$), σ^{-1} and γ^{-1} are, respectively, the average duration of latent and infective periods. All the above parameters are assumed to be nonnegative. Schematically, the flow between compartments is represented as

Assertion 1: The SEIR model (1)-(4) fulfils the constant population through time constraint, i.e.



$$N(t) = S(t) + E(t) + I(t) + R(t) = N(0) = N > 0. \tag{5}$$

Note that assertion 1 proves that the constant population through time is independent of the vaccination strategy.

In [4], the authors have discussed the positivity of the epidemic model (1)-(4) and they have given some results of vaccination free case equilibrium points and stability and they give a feedback vaccination control. In this paper, we discuss the optimal control theory of system (1)-(4) to find the vaccination control which minimize the infected and susceptible individuals and to maximize the removed individuals and this with a minimal duration of vaccination.

3 The optimal vaccination

Optimal control techniques are of great use in developing optimal strategies to control various kinds of diseases. To solve the challenges of obtaining an optimal vaccination strategy, we use optimal control theory. We consider the control variable $V(t) \in \mathcal{U}_{ad}^T$ to be the percentage of susceptible individuals being vaccinated per unit of time. Here

$$\mathcal{U}_{ad}^T = \{V \,|V(t) \text{ is measurable, } 0 \leq V(t) \leq 1, \ t \in [0,T] \ \}$$

indicates an admissible control set. Now, we consider an optimal control problem to minimize the objective functional

$$J(V,T) = \int_0^T [A_1 S(t) + A_2 I(t) - A_3 R(t) + \frac{1}{2}\tau V^2(t)]dt + \phi(T) \tag{6}$$

subject to system (1)-(4). Here A_1, A_2 and A_3 are positive constants to keep a balance in the size of $S(t)$, $I(t)$ and $R(t)$, respectively. The square of the control variable reflects the severity of the side effects of the vaccination. In the objective functional, τ is a positive weight parameter which is associated with the control $V(t)$ and ϕ is a positive increasing function such that $\lim_{t\longrightarrow+\infty}\phi(t) = +\infty$.

3.1 Existence of an optimal control

For existence, we consider a control system (1)-(4) with initial condition, The constant population constraint (5) is used in (1), (3) and (4) to eliminate the infected population $E(t)$ leading to:

$$\dot{S}(t) = -(\mu+\alpha)S(t) + \omega R(t) + (\alpha - \beta\frac{I(t)}{N})S(t) + \mu N(1-V(t)) \tag{7}$$

$$\dot{I}(t) = -(\mu+\gamma+\sigma)I(t) + \sigma(N - S(t) - R(t)) \tag{8}$$

$$\dot{R}(t) = -(\mu+\omega)R(t) + \gamma I(t) + \mu N V(t) \tag{9}$$

for any given real constant $\alpha \geq \frac{\beta}{N}\sup_{t\geq 0}\{I(t)\}$. Then we rewrite system (7)-(9) in the following form

$$\Phi_t = B\Phi + F(\Phi) \tag{10}$$

where $\Phi = [S(t)\ I(t)\ R(t)]$,

$$B = \begin{bmatrix} -(\mu+\alpha) & 0 & w \\ -\sigma & -(\mu+\gamma+\sigma) & -\sigma \\ 0 & \gamma & -(\mu+\omega) \end{bmatrix},$$

$$F(\Phi) = \begin{bmatrix} (\alpha - \beta\frac{I(t)}{N})S(t) + \mu N(1-V(t)) \\ \sigma N \\ 0 \end{bmatrix}$$

and Φ_t denote derivative of Φ with respect to time t. Equation (10) is a non-linear system with a bounded coefficient.
we set

$$D(\Phi) = B\Phi + F(\Phi)$$

We have

$$\begin{aligned} |F(\Phi_1) - F(\Phi_2)| &= |\alpha S_1 - \beta\tfrac{I_1S_1}{N} - \alpha S_1 + \beta\tfrac{I_1S_1}{N}| \\ &\leq \alpha|S_1 - S_2| + \tfrac{\beta}{N}|I_1S_1 - I_2S_2| \\ &\leq \alpha|S_1 - S_2| + \tfrac{\beta}{N}|I_1(S_1 - S_2) + S_2(I_1 - I_2)| \\ &\leq \alpha|S_1 - S_2| + \beta(|S_1 - S_2| + |I_1 - I_2|) \\ &\leq \max(\alpha,\beta)(|S_1 - S_2| + |I_1 - I_2|) \end{aligned}$$

then, we get $|D(\Phi_1) - D(\Phi_2)| \leq M|\Phi_1 - \Phi_2|$, where $M = \max(\max(\alpha,\beta), \|B\|) < \infty$. Thus, it follows that the function D is uniformly Lipschitz continuous. From the definition of the control $V(t)$ and the restriction on $S(t)$, $E(t)$, $I(t)$ and $R(t) > 0$, we see that a solution of the system (10) exists (Birkhoff and Rota, 1989, [1]).
Let us go back to the optimal control problem (6). In order to find an optimal solution, first we find the Lagrangian and Hamiltonian for the optimal control problem (6). In fact, the Lagrangian of the optimal problem is given by

$$L(S, I, R, V) = A_1S(t) + A_2I(t) - A_3R(t) + \frac{1}{2}\tau V^2(t).$$

We seek the minimal value of the Lagrangian. To accomplish this, we define the Hamiltonian H for the control problem:

$$H = L(S, I, R, V) + \lambda_1(t)\frac{dS(t)}{dt} + \lambda_2(t)\frac{dE(t)}{dt} + \lambda_3(t)\frac{dI(t)}{dt} + \lambda_4(t)\frac{dR(t)}{dt} \tag{11}$$

where λ_1, λ_2, λ_3 and λ_4 are the adjoint functions to be determined suitably.

Theorem 1. *There exists an optimal control $V^*(t)$ such that*

$$J(V^*(t), T) = \min_{u\in\mathcal{U}_{ad}^T} J(u(t), T)$$

subject to the control system (1)-(4) with initial conditions.

Proof. To prove the existence of an optimal control we use the result in (Lukes, 1982 [15]). Note that the control and the state variables are nonnegative values. In this minimizing problem, the necessary convexity of the objective functional in V(t) is satisfied.
The control space

$$\mathcal{U}_{ad}^T = \{v \mid v(t) \text{ is measurable},\ 0 \leq v(t) \leq 1,\ t \in [0, T]\}$$

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 (6), $A_1S(t) + A_2I(t) - A_3R(t) + \frac{1}{2}\tau v^2(t)$ is convex on the control $v(t)$. Also, we can easily see that, there exist a constant $\rho > 1$, positive numbers w_1 and w_2 such that $J(v(t)) \geq -w_2 + w_1(|v|^2)^{\frac{\rho}{2}}$. We conclude that there exists an optimal control.

3.2 Characterization of the optimal control

In the previous section we show the existence of an optimal control which minimize the functional (6) subject to system (1)-(4). In order to derive the necessary conditions for this optimal control, we apply Pontryagin's maximum principle to the Hamiltonian H.

Theorem 2. *Let $S^*(t)$, $E^*(t)$, $I^*(t)$ and $R^*(t)$ be optimal state solutions with associated optimal control variable $V^*(t)$ for the optimal control problem (6). Then, there exist adjoint variables λ_1, λ_2, λ_3 and λ_4, that satisfy*

$$\begin{cases} \dot{\lambda}_1 = -A_1 + \mu\lambda_1 + \beta\frac{I^*}{N}(\lambda_1 - \lambda_2) \\ \dot{\lambda}_2 = \mu\lambda_2 + (\lambda_2 - \lambda_3)\sigma \\ \dot{\lambda}_3 = -A_2 + \beta\frac{S^*}{N}(\lambda_1 - \lambda_2) + \mu\lambda_3 + \gamma(\lambda_3 - \lambda_4) \\ \dot{\lambda}_4 = A_3 + \mu\lambda_4 + \omega(\lambda_4 - \lambda_1) \end{cases} \tag{12}$$

with transversality conditions

$$\lambda_i(T) = 0, \quad i = 1, 2, 3, 4. \tag{13}$$

Furthermore, the optimal control V^* is given by

$$V^* = \max\{\min\{\frac{\mu N(\lambda_1 - \lambda_4)}{\tau}, 1\}, 0\}. \tag{14}$$

and the optimal final time is given by

$$\frac{\partial\phi}{\partial t}(T^*) = -A_1 S(T^*) - A_2 I(T^*) + A_3 R(T^*) - \frac{\tau}{2}V^2(T^*). \tag{15}$$

Proof. We use Hamiltonian (11) in order to determine the adjoint equation and the transversality conditions. From setting $S(t) = S^*(t)$, $E(t) = E^*(t)$, $I(t) = I^*(t)$ and $R(t) = R^*(t)$, and differentiating the Hamiltonian with respect to S, E, I and R, respectively, we obtain (12). And by using the optimality conditions we find

$$\frac{\partial H}{\partial v} = \tau V^*(t) - \mu N\lambda_1 + \mu N\lambda_4 = 0, \quad \text{at } v = V^*(t)$$

which gives

$$V^* = \frac{\mu N(\lambda_1 - \lambda_4)}{\tau}.$$

Using the property of the control space, we obtain

$$\begin{cases} V^* = 0 & \text{if} \quad \frac{\mu N(\lambda_1 - \lambda_4)}{\tau} \leq 0 \\ V^* = \frac{\mu N(\lambda_1 - \lambda_4)}{\tau} & \text{if} \quad 0 < \frac{\mu N(\lambda_1 - \lambda_4)}{\tau} < 1 \\ V^* = 1 & \text{if} \quad \frac{\mu N(\lambda_1 - \lambda_4)}{\tau} \geq 1. \end{cases}$$

So the optimal control is characterized as

$$V^* = \max\{\min\{\frac{\mu N(\lambda_1 - \lambda_4)}{\tau}, 1\}, 0\}.$$

The transversality condition for T to be the optimal terminal time can be stated as

$$H(T^*, S^*, I^*, R^*, V^*) + \frac{\partial\phi}{\partial t}(T^*) = 0.$$

Thus, T^* may be rewritten as in (15).

The optimal control and the state are found by solving the optimality system, which consists of the state system (1)-(4) with initial conditions at $t = 0$, the adjoint system (12) with the final conditions (13) and the characterization of the optimal control (14). So the optimality system is given by

$$\begin{cases} \dot{S}^*(t) &= -\mu S^*(t) + \omega R^*(t) - \beta \frac{S^*(t)I^*(t)}{N} + \mu N(1- \\ & \max\{\min\{\frac{\mu N(\lambda_1-\lambda_4)}{\tau}, 1\}, 0\}) \\ \dot{E}^*(t) &= \beta \frac{S^*(t)I^*(t)}{N} - (\mu+\sigma)E^*(t) \\ \dot{I}^*(t) &= -(\mu+\gamma)I^*(t) + \sigma E^*(t) \\ \dot{R}^*(t) &= -(\mu+\omega)R^*(t) + \gamma I^*(t) + \mu N \max\{\min\{\frac{\mu N(\lambda_1-\lambda_4)}{\tau}, 1\}, 0\}) \\ \dot{\lambda}_1 &= -A_1 + \mu\lambda_1 + \beta\frac{I^*}{N}(\lambda_1 - \lambda_2) \\ \dot{\lambda}_2 &= \mu\lambda_2 + \sigma(\lambda_2 - \lambda_3) \\ \dot{\lambda}_3 &= -A_2 + \beta\frac{S^*}{N}(\lambda_1 - \lambda_2) + \mu\lambda_3 + \gamma(\lambda_3 - \lambda_4) \\ \dot{\lambda}_4 &= A_3 + \mu\lambda_4 + \omega(\lambda_4 - \lambda_1) \end{cases} \tag{16}$$

with $\lambda_1(T) = 0$, $\lambda_2(T) = 0$, $\lambda_3(T) = 0$, $\lambda_4(T) = 0$, $S(0) = S_0$, $E(0) = E_0$, $I(0) = I_0$ and $R(0) = R_0$.

4 Numerical simulation

In this section we present the results obtained by solving numerically the optimality system given by theorem 2. This system consists of the state system, adjoint system, initial and final time conditions, and the control characterization.

The optimality systems is solved based on an iterative discrete scheme that converges following an appropriate test similar the one related to the Forward-Backward Sweep Method (FBSM). The state system with an initial guess is solved forward in time and then the adjoint system is solved backward in time because of the transversality conditions. Afterwards, we update the optimal control values using the values of state and adjoint variables obtained at the previous steps. Finally, we execute the previous steps till a tolerance criterion is reached.

We consider an example of an epidemic described by the SEIR model (1)-(4) with parameter values: $\mu = 0.008$ per day $(p.d.)$, $\beta = 0.454$ $p.d.$, $\omega = 0.053$ $p.d.$, $\sigma = 0.74$ $p.d.$, $\gamma = 0.4545$ $p.d.$, and a total population of $N = 10^4$. The initial condition for the individual population are given by: $S(0) = 6000$, $E(0) = 1400$, $I(0) = 2500$, $R(0) = 100$. We use $\tau = 1.4 \times 10^8$, $A_1 = 10^{-3}$, $A_1 = 1.5 \times 10^{-3}$, $A_3 = 2.5 \times 10^4$ and $\phi(t) = 1.43 \times 10^{-4}t^7$.

We can see that the optimal vaccination and treatment function have a very desirable effect upon the population of susceptible, exposed and infected which decreases while the recovered population increases for almost the entire length of therapy. The time evolution of the respective populations with and without control is displayed in Figure 1 and Figure 2 respectively.

Fig. 3 displays the time evolution of the optimal vaccination effort $V(t)$ to be applied to eradicate the disease. It can be seen that the infection would be eradicated from the population with such a vaccination practice in a relative short time period, approximately 68 days, see Fig. 4.

Fig. 4 show the effect of control by indicating that the number of susceptible individuals decreases more rapidly during the vaccination campaign.

Fig. 6 gives an example of the evolution of the number of infected individuals with and without control. We notice that in absence of control, the infected group grew to extremely high levels and in presence of the control, this group decrease greatly.

Fig. 7, show that the number of people removed with control begins to grow more than without control. In the end of the vaccination campaign, the number of recovered individuals population grew to extremely high levels.

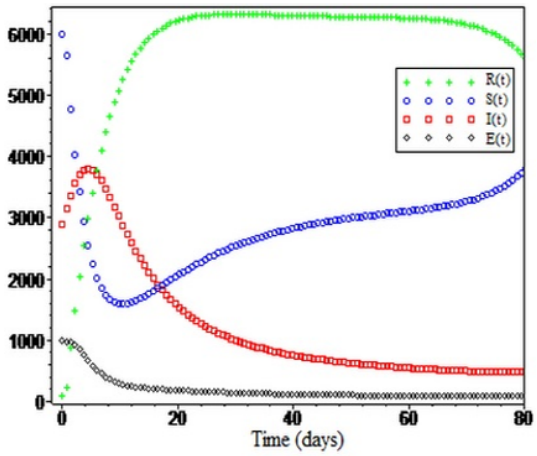


Fig. 1: Time evolution of the individual populations without vaccination

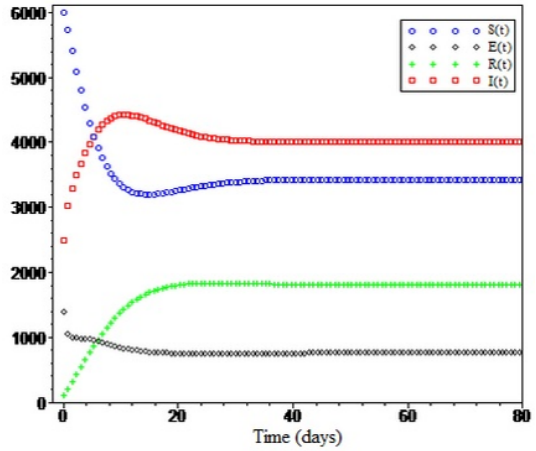


Fig. 2: Time evolution of the individual populations with vaccination

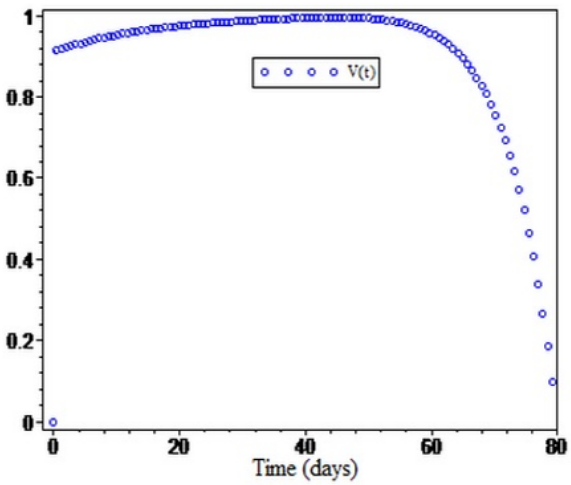


Fig. 3: Time evolution of the vaccination $V(t)$

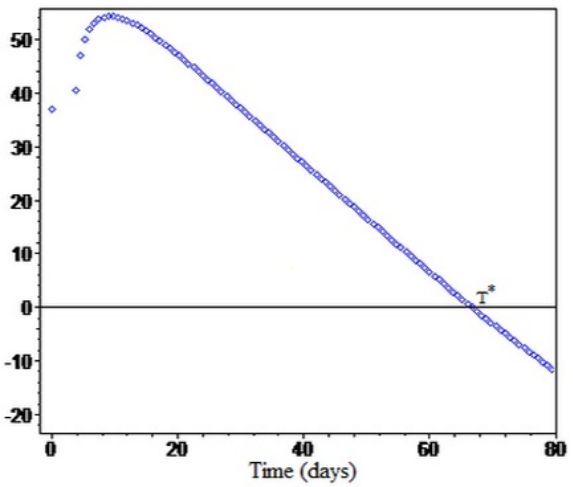


Fig. 4: The optimal final time T^*

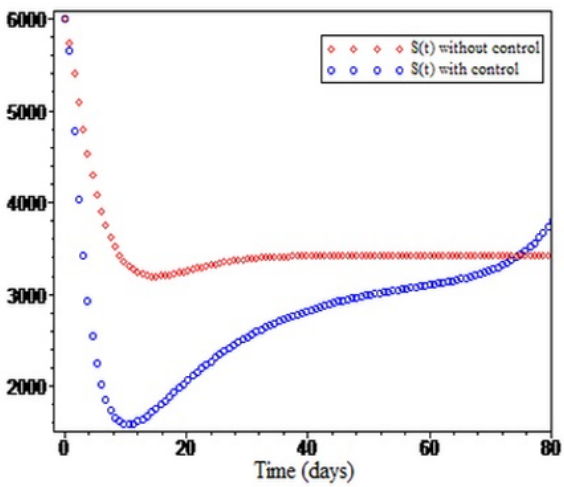


Fig. 5: The Susceptible individuals with and without controls

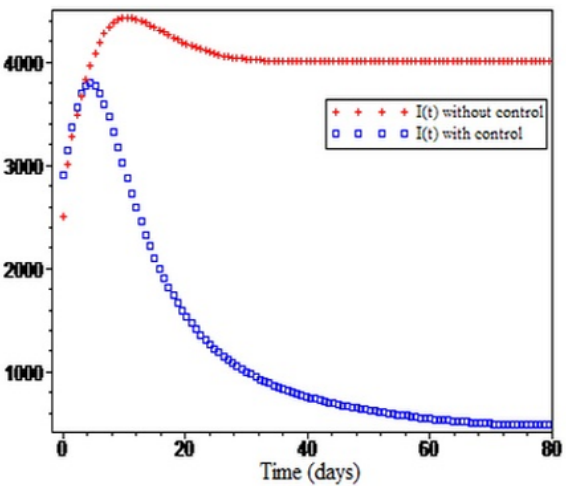


Fig. 6: The Infected individuals with and without controls

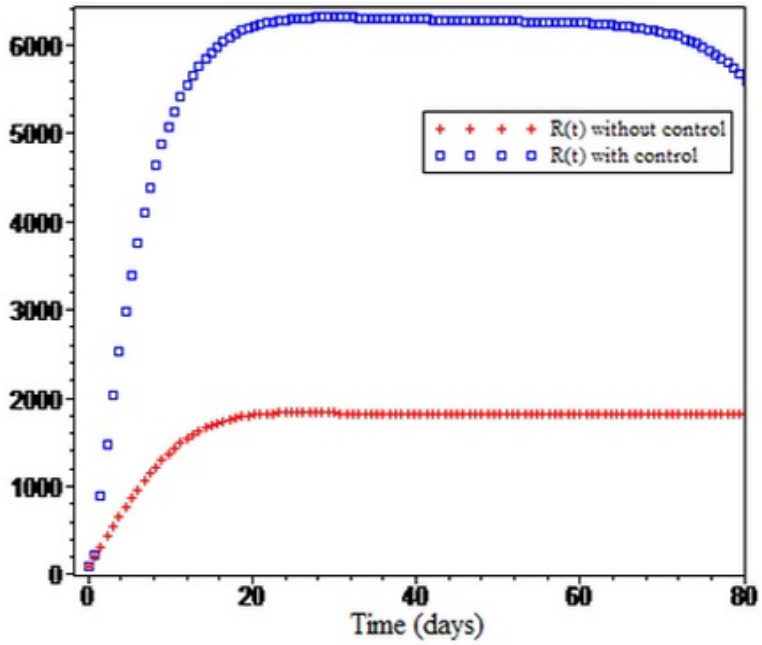


Fig. 7: The Recovered individuals with and without controls

5 Conclusion

The purpose of this work is to derive a control strategy for a true-mass action SEIR epidemic model. Our aim is to set up an optimal control problem relative to epidemic model, so it is to minimize the susceptible and the infected population and to maximize the recovered populations. A free terminal optimal time control is also investigated. By using the Pontryagin's maximum principle, the explicit expression of the optimal control and the optimal final time was obtained. A numerical simulation has been given to demonstrate the use of the obtained results. Finally, we proposes some the likely future of studies on this concept as the generalization to the case of spatiotemporal epidemic model and also the case of discrete time epidemic model.

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