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Original Article

Single and Multiobjective Optimal Control of Epidemic Models Involving Vaccination and Treatment

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ABSTRACT

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Introduction: A rigorous multiobjective optimal control strategy (that does not require the use of weighting functions) of the epidemic models that consider vaccination and treatment strategies is presented. Modifications of the standard susceptible-infectious-removed, susceptible-exposed-infectious-removed, and the modified susceptible-infectious-removed models are dynamically optimized to minimize the number of infected individuals while, controlling the rate at which the individuals are vaccinated and treated.

Method: The optimization program, Pyomo , where the differential equations are automatically converted to a Nonlinear Program using the orthogonal collocation method is used for performing the dynamic optimization calculations. The Lagrange-Radau quadrature with three collocation points and 10 finite elements are chosen. The resulting nonlinear optimization problem was solved using the solver BARON 19.3, accessed through the Pyomo-GAMS27.2 interface.

Results: The computational results how that the multiobjective optimal control profiles generated by this strategy are very similar to those produced when weighting functions are used.

Conclusion: The main conclusion of this work is to demonstrate that one can perform a rigorous dynamic optimization of epidemic models without the use of weighting functions that have the potential to produce some uncertainty and doubt in the results, in addition to dealing with unnecessary additional variables.

Introduction

Epidemiological models that simulate the spread of infectious diseases, are necessary to understand the dynamics of the spreading of the infection and to take steps that will result in the minimization of the number of infected people. In order to minimize the spreading of the infections one must perform dynamic optimization calculations and computationally obtain the parameters that will result in the minimum value of the number of infected subjects.

Epidemiological models have been developed by many researchers to enable the understanding of the dynamics of these diseases. Ronald Ross (1) (1908) demonstrated that mosquitoes transmit malaria and developed the first mathematical model for malaria transmission. After the Second World War, Macdonald picked up where Ross left off and focused on developing a highly applied theory to complement the global public health rollout of Dichloro Diphenyl Trichlorethane (DDT). The state of mathematical theory was solidified by Macdonald(2) and in the 1960s by Garrett-Jones (3, 4).This work has motivated the use of mathematical methods (5, 6) to quantitatively understand issues pertaining to biology, medicine and infectious diseases. Other significant work concerning dynamic models was conducted by considered a general model(7-19), with the population of susceptible and infectious human's assumed constant, and facing only one virus. Esteva and Varga (16-19) also proposed models that considered the effects of the exponential growth of the human population, a constant disease rate, and two serotypes of the virus. Additionally, significant work pertaining to epidemiological modeling was done (20, 21). A lot of work on epidemic models was done by Hethcote and co-workers (22-25) where the effects of the variation of parameters was studied. Optimal control of epidemiological models was performed by a few researchers (15, 26, 27). Brauer (28) considered epidemic models involving asymptomatic, quarantined, and isolated individuals and discusses the compromise between vaccination and treatment. Gaff et al (29) performed multiobjective optimal control using weighting functions for SIR (susceptible-infectious-removed) SEIR (susceptible-exposed-infectious-removed, and SIRS (modified susceptible-infectious-removed) epidemiological models that included terms that account for vaccinations and treatment. S represents susceptible individuals, E and I represent the exposed and infected individuals while R represents the removed individuals who have overcome and have immunity from the infection. In this work, rigorous multiobjective optimal control without using weighting functions for these models is performed and it is shown that the resulting profiles are very similar to those obtained by Gaff et al (29). Gaff et al (29) perform a single objective optimal control lumping all the objective functions using weighting functions. The aim of this paper is to perform a multiobjective optimal control where no weighting functions are used. In this paper, a single objective optimal control problem is initially solved for each objective function to generate a utopia point and the Euclidean distance from this point is minimized subject to all the constraints.

This paper is organized as follows. First the SIR, SEIR and the SIRS models will be described. The multiobjective optimal control strategy is then presented. This will be followed by the results, discussion and conclusions.

Epidemic models (Model Equations)

The SIR model consists of the equations

$$\frac{dS}{dt} = \mu N - \beta \frac{SI}{N} - \nu S - \mu \frac{NS}{K} \quad (1)$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - (\gamma + \tau + \delta) I - \mu \frac{NI}{K} \quad (2)$$

$$\frac{dR}{dt} = (\gamma + \tau) I + \nu S - \mu \frac{NR}{K} \quad (3)$$

Where N = S+I+R. The SEIR model equations are

$$\frac{dS}{dt} = \mu N - \beta \frac{SI}{N} - \nu S - \mu \frac{NS}{K} \quad (4)$$

$$\frac{dE}{dt}=\beta\frac{SI}{N}-\varepsilon E-\mu\frac{NE}{K} \tag{5}$$

$$\frac{dI}{dt}=\varepsilon E-(\gamma+\tau+\delta)I-\mu\frac{NI}{K} \tag{6}$$

$$\frac{dR}{dt}=(\gamma+\tau)I+\nu S-\mu\frac{NR}{K} \tag{7}$$

While the SIRS (here it is assumed that after a time period $\frac{1}{\omega}$ subjects in the removed class return to the susceptible class) model is represented by the equations

$$\frac{dS}{dt}=\mu N-\beta\frac{SI}{N}-\nu S-\mu\frac{NS}{K}+\omega R \tag{8}$$

$$\frac{dI}{dt}=\beta\frac{SI}{N}-(\gamma+\tau+\delta)I-\mu\frac{NI}{K} \tag{9}$$

$$\frac{dR}{dt}=(\gamma+\tau)I+\nu S-\mu\frac{NR}{K}-\omega R \tag{10}$$

All three models are discussed in Gaff et al[29]. Details and values of the parameters are given in table 1

Table 1. Parameter values (Obtained from Gaff[29])

Name	Description	Value
S_0	Susceptible population at t=0	4500
E_0	Exposed population at t=0	498
I_0	Infected population at t=0	499 (for SEIR model 1)
R_0	Removed population at t=0	1
K	Capacity	5000
μ	Growth rate	0.00004
δ	Death rate	0-0.1/day
β	Incidence rate	0.05-0.55/day
γ	Infect time	0.1/day
ω	Rate of waning	0.001/day
ε	Rate of transition	0.1/day
B_1	Weighting function for I	1
B_2	Weighting function for vaccination	1000
B_3	Weighting function for treatment	1000
ν_{max}	Maximum vaccination rate	0.1
τ_{max}	Maximum treatment rate	0.6

Multiobjective optimal control (MOOC)Strategy

Gaff et al (29) use weighting parameters minimizing the number of people who become infected while at the same time controlling effort involved in vaccinating and treating the population. The functions that were part of the objective function were

$$\sum_0^{t_f} I(t), \quad \sum_0^{t_f} \tau^2(t) \quad \text{and} \quad \sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 .$$

The function that was minimized was

$$B_1\sum_0^{t_f} I(t) + B_2 \sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 + B_3\sum_0^{t_f} \tau^2(t)$$

.

In this paper no weighting functions are used. A single objective optimal control problem is initially solved for each objective function (30, 31) to generate a utopia point and the Euclidean distance from this point is minimized subject to all the constraints.

For a multiobjective optimal control problem

$$\begin{aligned} &\min \Phi(x,u) = (\phi_1, \phi_2, \phi_3, \phi_4, \phi_5 ....\phi_n) \\ &\textit{subject to } \frac{dx}{dt} = \Psi(x,u) \\ &h(x,u) \le 0 \\ &x^L \le x \le x^U \\ &u^L \le u \le u^U \end{aligned} \tag{11}$$

the single objective optimization problems are solved independently minimizing each ϕ_i (i=1,2,3…n) individually. This will lead to minimized values ϕ_i^* (i=1,2,3,..n) . Then the problem that will be solved is

$$\begin{aligned} &\min \sqrt{\{\sum_{i=1}^{n} (\phi_i - \phi_i^*)^2\}} \\ &\textit{subject to } \frac{dx}{dt} = \mathrm{K}(x,u) \\ &h(x,u) \le 0 \\ &x^L \le x \le x^U \\ &u^L \le u \le u^U \end{aligned} \tag{12}$$

The optimization program, Pyomo (32), where the differential equations are automatically converted to a Nonlinear Program (NLP) using the orthogonal collocation method(33) is used for performing the dynamic optimization calculations. The Lagrange-Radau quadrature with three collocation points and 10 finite elements are chosen. The resulting nonlinear optimization problem was solved using the solver BARON 19.3 (34), accessed through the Pyomo-GAMS27.2 (35) interface. BARON implements a Branch-and-reduce strategy and provides a guaranteed global optimal solution. This procedure does not involve the use of weighting functions not does it impose additional parameters or additional constraints on the problem unlike the epsilon correction method (36). (A comparison is made with the weighting function methods and it is observed that although the objective function values are different the profiles of the optimized variables are very similar.

Results

For the SIR model, when $\sum_0^{t_f} I(t)$, $\sum_0^{t_f} \tau^2(t)$ and $\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2$ were individually minimized, the minimized objective values were 453.636, 0.3272 and 0, For the weighted sum method, the minimized objective function was

$$B_1\sum_0^{t_f} I(t) + B_2 \sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 + B_3\sum_0^{t_f} \tau^2(t)$$

the minimized objective value was 780.909
In this work, the objective function that was minimized was

$$\sqrt{(\sum_0^{t_f} I(t) - 453.636)^2 + (\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 - 0)^2 + (\sum_0^{t_f} \tau^2(t) - 0.3272)^2}$$

and the minimized objective function value was 41.24. The values of the minimized objective value are presented in Table 2.

Table 2. Objective Values for SIR model

Objective function	Minimized value of Objective
$\sum_0^{t_f} I(t)$	453.636
$\sum_0^{t_f} \tau^2(t)$	0.3272
$\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2$	0
MOOC Method in this article	41.24
Weighted function method	780.909

For the SEIR model, when $\sum_0^{t_f} I(t)$, $\sum_0^{t_f} \tau^2(t)$ and $\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2$ were individually minimized, the minimized objective values were 0.9090, 0.3272 and 0, For the weighted sum method, the minimized objective function was

$$B_1\sum_0^{t_f} I(t) + B_2 \sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 + B_3\sum_0^{t_f} \tau^2(t)$$

and the minimized objective function value was 328.181 In this work , the objective function that was minimized was

$$\sqrt{(\sum_0^{t_f} I(t) - 0.9090)^2 + (\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 - 0)^2 + (\sum_0^{t_f} \tau^2(t) - 0.3272)^2}\ .$$

and the minimized objective function value was 0.0879. The values of the minimized objective value are presented in Table 3

Table 3. Objective Values for SEIR model

Objective function	Minimized value of Objective
$\sum_0^{t_f} I(t)$	0.9090
$\sum_0^{t_f} \tau^2(t)$	0.3272
$\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2$	0
MOOC Method in this article	0.0879
Weighted function method	328.181

For the SIRS model, when $\sum_0^{t_f} I(t)$, $\sum_0^{t_f} \tau^2(t)$ and $\sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2$ were individually minimized, the minimized objective values were 453.636, 0.3272 and 0, For the weighted sum method, the minimized objective function was

$$B_1\sum_0^{t_f} I(t) + B_2 \sum_0^{t_f} (\frac{R(t)}{k})^{10}\{\nu(t)\}^2 + B_3\sum_0^{t_f}\tau^2(t)$$

the minimized objective value was 780.909 In this work , the objective function that was minimized was

$$\sqrt{(\sum_0^{t_f} I(t) - 453.636)^2 + (\sum_0^{t_f}(\frac{R(t)}{k})^{10}\{\nu(t)\}^2 - 0)^2 + (\sum_0^{t_f}\tau^2(t) - 0.3272)^2}$$

and the minimized objective function value was 41.24. The values of the minimized objective value are presented in Table 4. The values of the minimized objective function were the same as in the SIR model.

Table 4. Objective Values for SIRS model

Objective function	Minimized value of Objective
$\sum_0^{t_f} I(t)$	453.636
$\sum_0^{t_f}\tau^2(t)$	0.3272
$\sum_0^{t_f}(\frac{R(t)}{k})^{10}\{\nu(t)\}^2$	0
MOOC Method in this article	41.24
Weighted function method	780.909

Discussion

Figures 1a-1i, are profiles for the SIR model, 2a-2i are for the SEIR model and 3a-3i for the SIRS model. Figures 1(a-c), 2(a-c) and 3(a-c) are the single objective optimal control profiles where the minimized objective functions were $\sum_0^{t_f} I(t)$, $\sum_0^{t_f}\tau^2(t)$ and $\sum_0^{t_f}(\frac{R(t)}{k})^{10}\{\nu(t)\}^2$ for the three models. A comparison of the figures 1d and 1e, 1f and 1g, 1h and 1i, 2d and 2e, 2f and 2g, 2h and 2i, 3d and 3e, 3f and 3g, 3h and 3i, demonstrates an insignificant difference between the profiles generated by the weighted function method and the MOOC method used in this paper. Hence it is shown that one can avoid the use of unnecessary weight functions to generate optimal profiles. This strategy enables us to control more than one parameter and be as effective as a single objective optimal control strategy.

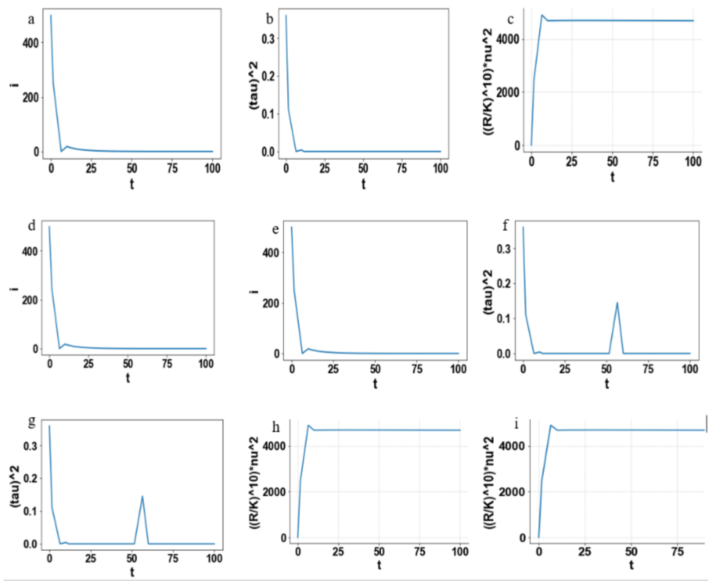

Figure 1. 1a – 1i

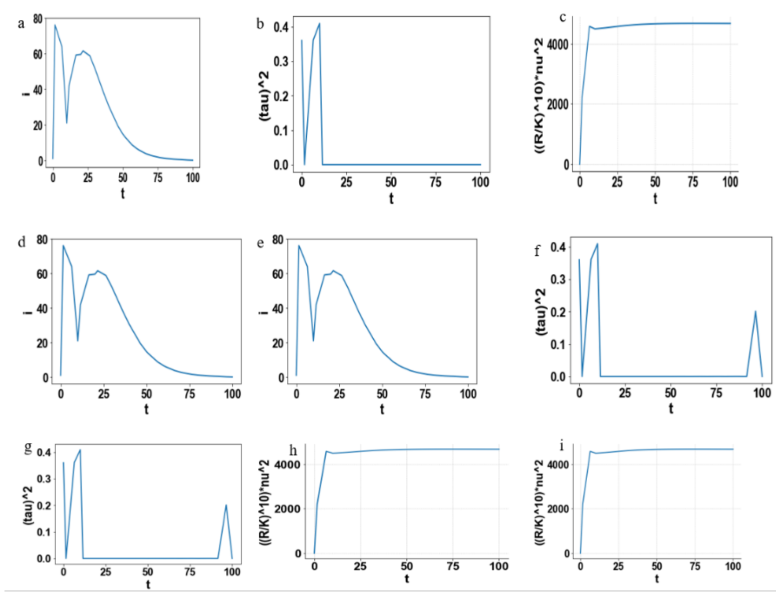

Figure 2. 2a-2i

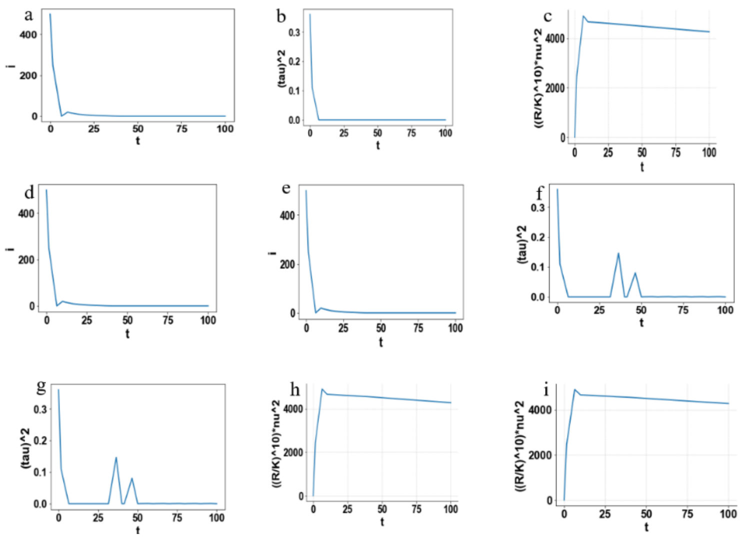

Figure 3. 3a-3i

Conclusions

The main conclusion of this work is to demonstrate that one can perform a rigorous dynamic optimization of epidemic models without the use of weighting functions that have the potential to produce some uncertainty and doubt in the results, in addition to dealing with unnecessary additional variables. This strategy will definitely be helpful when there are a large number of variables that need to be optimized.

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