Optimal control and stabilization of a SEITR epidemic model with vaccination and treatment

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Outline

1. Introduction
   - Background
   - Our aim

2. SEITR epidemic model

3. Basic reproduction number

4. Stabilization of the equilibrium points

5. Optimal control
   - Sufficient condition
   - Necessary condition for the optimal pair

6. Numerical simulation

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Background

Mathematical models have become important tools in epidemiology in understanding epidemiological patterns of diseases. The most important concern for mathematical models in epidemiology is qualitative analysis. Mathematical analysis can provide valuable information about how to control infectious disease outbreaks best.
Background

- Mathematical Models
  
  SI, SIR, SIRS, SEIR, SEIRS, SVITR, SEITR.

- Main Concerns
  
  Stabilization and Optimal Control.
Analysis

- Construct the SEITR epidemic model,
- Compute the reproduction number $R_0$.
- Stabilization at the Equilibrium points.
- Optimal control.
- Numerical simulation.
Our aim

To construct an epidemic model in accordance with the actual situation. Based on the fact that the vaccination and treatment can affect the spread of the disease, we introduce the corresponding control variables into the model. Try to find the lowest (optimal) cost. Use MATLAB to run the numerical simulations.
Optimal control problem of SEITR model

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Epidemic Model with controls

S: Susceptible population
I: Infective population
R: Recovered population
E: Exposed population
T: Infective population in treatment

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Meanings of the parameters:

\( b \): The rate at which new individual enter the population (Birth rate)
\( p \): A fraction of \( b \) which is vaccinated (rate of the vaccinated new-born baby)
\( \alpha \): Effective contact rate (rate people get sick)
\( \theta \): Natural recovery rate
\( \mu \): Natural death rate
\( \delta_1 \): Disease induced death rate of infective population without treatment
\( \delta_2 \): Disease induced death rate of infective population with treatment
\( \beta \): The proportion of exposed class who become infective
\( \gamma \): Treatment rate
\( \sigma \): Recovery rate due to treatment
\( \rho \): Rate of immunity loss
Epidemic model with controls

\[
\begin{align*}
\dot{S}(t) &= (1 - p)b - \alpha S(t)I(t) + \rho R(t) - \mu S(t) \\
\dot{E}(t) &= \alpha S(t)I(t) - (\beta + \mu)E(t) \\
\dot{I}(t) &= \beta E(t) - (\gamma + \delta_1 + \mu + \theta)I(t) \\
\dot{T}(t) &= \gamma I(t) - (\sigma + \delta_2 + \mu)T(t) \\
\dot{R}(t) &= pb + \sigma T(t) - (\mu + \rho)R(t) + \theta I(t)
\end{align*}
\]  

(1)

Initial data:

\[S(0) > 0, E(0) \geq 0, I(0) > 0, T(0) \geq 0, R(0) > 0\]
We introduce two controls in the epidemic model: Control of vaccination $u_1$, control of treatment $u_2$. $u_1$ represents the fraction of susceptible individuals being vaccinated per unit time $t$, $u_2$ represents the rate of infective individuals entering in the treatment per unit time at time $t$. $u_1(t), u_2(t)$ are the levels of controls on vaccination and treatment.
Epidemic model with controls

\begin{align*}
\dot{S}(t) &= (1 - p)b - \alpha S(t)I(t) + \rho R(t) - (\mu + u_1(t))S(t) \\
\dot{E}(t) &= \alpha S(t)I(t) - (\beta + \mu)E(t) \\
\dot{I}(t) &= \beta E(t) - (u_2(t) + \delta_1 + \mu + \theta)I(t) \\
\dot{T}(t) &= u_2(t)I(t) - (\sigma + \delta_2 + \mu)T(t) \\
\dot{R}(t) &= pb + \sigma T(t) - (\mu + \rho)R(t) + \theta I(t) + u_1(t)S(t)
\end{align*}

Initial data:

\[ S(0) > 0, E(0) \geq 0, I(0) \geq 0, T(0) \geq 0, R(0) > 0 \]
Admissible set of the controls:

\[ U = \{ (u_1, u_2) : u_i(t) \in [0, 1], t \in [0, t_f], i = 1, 2 \mid u_i \text{ is measurable} \} \]

The cost can include funds needed for control implementation, hospitalization and lost of many hours of work due to illness. More often the cost of implementing a control would be nonlinear. It is reasonable to use a quadratic function for measuring the control cost:

\[
J(u_1, u_2) = \int_0^{t_f} \left[ E(t) + I(t) + B_1 u_1(t)^2 + B_2 u_2(t)^2 \right] dt.
\]

Here \( B_1 \) and \( B_2 \) are weights. We are seeking for controls \((u_1^*(t), u_2^*(t))\) minimizing \( J(u_1(t), u_2(t)) \). The performance specification involves minimizing the number of population with flu, as well as the costs for applying controls on vaccination and treatment.
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The basic reproduction number $R_0$ is arguably the most important quantity in infectious disease epidemiology. It is among the quantities most urgently estimated for emerging infectious diseases in outbreak situations.

Generally, in the epidemic model, there are two equilibrium points: Disease-free equilibrium (DFE) and Endemic equilibrium. The stability of these equilibrium is decided by $R_0$. When $R_0 < 1$, the DFE is stable and the disease can be eliminated by effective controls.

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The basic reproduction number can be seen as the average number of new cases of an infection caused by one typical infected individual, in a population consisting of susceptible only.
Basic reproduction number

- Basic reproduction number of (1):
  \[ R_0 = \frac{\alpha \beta b[(1 - p)\mu + \rho]}{\mu(\mu + \rho)(\beta + \mu)(\gamma + \delta_1 + \mu + \theta)} \]

- Basic reproduction number of (2):
  \[ R_0' = \frac{\alpha \beta b[(1 - p)\mu + \rho]}{\mu(\beta + \mu)(\mu + u_1 + \rho)(u_2 + \delta_1 + \mu + \theta)} \]
Basic reproduction number

- Basic reproduction number of (1):
  \[ R_0 = \frac{\alpha \beta b[(1 - p)\mu + \rho]}{\mu(\mu + \rho)(\beta + \mu)(\gamma + \delta_1 + \mu + \theta)} \]

- Basic reproduction number of (2):
  \[ R'_0 = \frac{\alpha \beta b[(1 - p)\mu + \rho]}{\mu(\beta + \mu)(\mu + u_1 + \rho)(u_2 + \delta_1 + \mu + \theta)} \]
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Stabilization of the equilibrium point:
System (1) has two equilibrium points:

1. **Disease-free equilibrium (DFE):** $E_0 : \left( \frac{b[\mu(1-p)+\rho]}{\mu(\mu+\rho)}, 0, 0, 0, \frac{bp}{\mu+\rho} \right)$.

2. **When $R_0 > 1$, system (1) has an endemic equilibrium:** $E_1 : (\bar{S}, \bar{E}, \bar{I}, \bar{T}, \bar{R})$. 
Stabilization of the equilibrium points

1. Local stabilization
   - When $R_0 < 1$, system (1) is locally asymptotically stable at DFE $E_0$.
   - When $R_0 > 1$, system (1) is locally asymptotically stable at Endemic equilibrium $E_1$.

2. Global stabilization
   - When $R_0 \leq 1$, system (1) is globally asymptotically stable at DFE $E_0$. 

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It is easy to check that system (2) satisfies:

1. Admissible control set $U$ is non-empty.
2. $U$ is convex and closed.
3. The right hand side of system (2) is continuous and

\[
\left\| \frac{d\vec{X}}{dt} \right\| \leq \|\vec{A}\| + w_1\|\vec{X}\| + w_2\|(u_1, u_2)^\top\|
\]

$w_1, w_2$ is determined by the parameters of the system.
4. The integral $J(u_1(\cdot), u_2(\cdot))$ is convex in $U$.
5. There exist constant $q > 1$ and positive numbers $w_1, w_2$ satisfying $E(t) + I(t) + B_1u_1(t)^2 + B_2u_2(t)^2 \geq w_2 + w_1(u_1^2 + u_2^2)^{\frac{q}{2}}$ due to the boundedness of the state variables.

Hence there exists a pair $(u_1^*, u_2^*)$ such that

\[
J(u_1^*, u_2^*) = \min_{(u_1, u_2) \in U} \{J(u_1, u_2)\}.
\]
Define a Hamiltonian:

\[
H(S, E, I, T, R, u_1, u_2, \lambda_i, t) = E + I + B_1 u_1^2 + B_2 u_2^2 + \lambda_1 [(1 - p)b - \alpha SI + \rho R - (\mu + u_1)S] + \lambda_2 [\alpha SI - (\beta + \mu)E] \\
+ \lambda_3 [\beta E - (u_2 + \delta_1 + \mu + \theta)I] + \lambda_4 [u_2 I - (\sigma + \delta_2 + \mu)T] \\
+ \lambda_5 [pb + \sigma T - (\mu + \rho)R + \theta I + u_1 S].
\]

where \( \lambda(i), i = 1, 2, 3, 4, 5 \) are the adjoint function of \( S, E, I, T, R \).
**Theorem** Assume that $S^*, E^*, I^*, T^*, R^*$ is the solution of (2) corresponding to the optimal control pair $(u_1^*, u_2^*)$. Then $\lambda(i)$, $i = 1, 2, 3, 4, 5$ satisfy:

\[
\begin{align*}
\dot{\lambda}_1(t) &= (\lambda_1 - \lambda_2)\alpha I^* + \lambda_1(\mu + u_1) - \lambda_5 u_1 \\
\dot{\lambda}_2(t) &= -1 + \lambda_2(\beta + \mu) - \lambda_3 \beta \\
\dot{\lambda}_3(t) &= -1 + (\lambda_1 - \lambda_2)\alpha S^* + \lambda_3(u_2 + \delta_1 + \mu + \theta) - \lambda_4 u_2 - \lambda_5 \theta \\
\dot{\lambda}_4(t) &= \lambda_4(\sigma + \delta_2 + \mu) - \lambda_5 \sigma \\
\dot{\lambda}_5(t) &= \lambda_5(\mu + \rho) - \lambda_1 \rho
\end{align*}
\]

where

\[
\lambda_i(t_f) = 0 \quad \text{for} \quad i = 1, 2, 3, 4, 5.
\]

\[
u_1^* = \min\{\max\{0, \frac{(\lambda_1 - \lambda_5)S^*}{2B_1}\}, 1\}. \\
u_2^* = \min\{\max\{0, \frac{(\lambda_3 - \lambda_4)I^*}{2B_2}\}, 1\}.
\]
The adjoint system of (2) is:

\[
\begin{align*}
\dot{S}^*(t) &= (1 - p)b - \alpha S^* I^* + \rho R^* - (\mu + \min \{\max \{0, \frac{(\lambda_1 - \lambda_5)S^*}{2B_1}\}, 1\})S^* \\
\dot{E}^*(t) &= \alpha S^* I^* - (\beta + \mu) E^* \\
\dot{I}^*(t) &= \beta E^* - (\min \{\max \{0, \frac{(\lambda_3 - \lambda_4)I^*}{2B_2}\}, 1\} + \delta_1 + \mu + \theta) I^* \\
\dot{T}^*(t) &= \min \{\max \{0, \frac{(\lambda_3 - \lambda_4)I^*}{2B_2}\}, 1\} I^* - (\sigma + \delta_2 + \mu) T^* \\
\dot{R}^*(t) &= pb + \sigma T^* - (\mu + \rho) R^* + \theta I^* + \min \{\max \{0, \frac{(\lambda_1 - \lambda_5)S^*}{2B_1}\}, 1\} S^* \\
\dot{\lambda}_1(t) &= (\lambda_1 - \lambda_2)\alpha I^* + \lambda_1 \mu + (\lambda_1 - \lambda_5)\min \{\max \{0, \frac{(\lambda_1 - \lambda_5)S^*}{2B_1}\}, 1\} \\
\dot{\lambda}_2(t) &= -1 + \lambda_2(\beta + \mu) - \lambda_3 \beta \\
\dot{\lambda}_3(t) &= -1 + (\lambda_1 - \lambda_2)\alpha S^* + (\lambda_3 - \lambda_4)\min \{\max \{0, \frac{(\lambda_3 - \lambda_4)I^*}{2B_2}\}, 1\} \\
&\quad + \lambda_3(\delta_1 + \mu + \theta) - \lambda_5 \theta \\
\dot{\lambda}_4(t) &= \lambda_4(\sigma + \delta_2 + \mu) - \lambda_5 \sigma \\
\dot{\lambda}_5(t) &= \lambda_5(\mu + \rho) - \lambda_1 \rho
\end{align*}
\]
We first run the program with MATLAB by means of the following parameters. Here $R_0 = 0.6823 < 1$.

**Table:** Parameters when $R_0 < 1$.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$p$</th>
<th>$b$</th>
<th>$\alpha$</th>
<th>$\beta$</th>
<th>$\rho$</th>
<th>$\gamma$</th>
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<td>2.5</td>
<td>0.1</td>
<td>0.1</td>
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<tr>
<td>Parameter</td>
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<td>$\sigma$</td>
<td>$\theta$</td>
<td>$\delta_1$</td>
<td>$\delta_2$</td>
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</tr>
<tr>
<td>Value</td>
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<td>0.2</td>
<td>0.2</td>
<td>0.35</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>
Numerical simulation

Figure: When $R_0 < 1$, Numbers of the population with different initial data.
The diagrams show that: When $R_0 < 1$, $(\bar{S})$ and $(\bar{R})$ reach to a fixed value. $(E)$, $(I)$ and $(T')$ tend to zero. It verifies that when $R_0 < 1$, DFE is locally asymptotical stable.
We first run the program with MATLAB by means of the following parameters. Here $R_0 = 1.097 > 1$.

**Table:** Parameters when $R_0 > 1$.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>$p$</th>
<th>$b$</th>
<th>$\alpha$</th>
<th>$\beta$</th>
<th>$\rho$</th>
<th>$\gamma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
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<td>1.5</td>
<td>0.4</td>
<td>0.3</td>
<td>0.4</td>
<td>0.45</td>
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</table>

<table>
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<tr>
<th>Parameter</th>
<th>$\mu$</th>
<th>$\sigma$</th>
<th>$\theta$</th>
<th>$\delta_1$</th>
<th>$\delta_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>0.15</td>
<td>0.4</td>
<td>0.45</td>
<td>0.35</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Numerical simulation

Figure: When $R_0 = 1.097$, Numbers of the population with different initial data.
The diagrams show that: When $R_0 = 1.097$, $(\bar{S})$ and $(\bar{R})$, $(E)$, $(I)$ and $(T)$ reach to a fixed value. It verifies that when $R_0 > 1$, DFE is locally asymptotical stable.
We use the following parameters. The weights in the cost functional are given by $B_1 = 30$, $B_2 = 5$. We draw the numbers of the population in four diagrams: 1) with two controls; 2) only with vaccination; 3) only with treatment; 4) Without controls.

Table: Parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>$p$</td>
<td>0.5</td>
</tr>
<tr>
<td>$b$</td>
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<tr>
<td>$\alpha$</td>
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<tr>
<td>$\delta_1$</td>
<td>0.35</td>
</tr>
<tr>
<td>$\delta_2$</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Figure: Population in four different strategies.
Numerical simulation

The exposed population (E) and infective population (I) levels obtained by means of both controls (vaccination and treatment) are lower than the level obtained using only one control (vaccination or treatment) or no control. The recovered population (R) level obtained via both controls is much higher than the level with only one control (vaccination or treatment) or without any control. So we can conclude that ” intervention practices that involving both vaccination and treatment controls yields a relatively better result”. 
Figure: Vaccination ($u_1$) and treatment ($u_2$).

The above diagrams conclude: we should give full effort in vaccination and treatment in the beginning of the disease. This means that vaccination and treatment both are very important in the beginning of disease outbreak than when the disease prevails.
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THANK YOU!

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