Optimal Control for Infectious Diseases
(L1 case)

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Aim

Control of infectious diseases via vaccination!!!

Work based on
Optimal control of epidemiological SEIR models with $L_1$-objectives
and control and state constraints
by Maurer and dP (submitted)

and
Optimal control of Infectious Diseases involving
Normalized SEIR Models
by Nogueira, Maurer and dP (working paper, to be submitted)

A special thanks to Urszula Ledzewicz and Heinz Schättler
for numerous discussions on this work
Outline

1. SEIR Model
2. Brief Review of Optimal Control for SEIR Model
   • with L1 cost
   • with constraints and L1 cost
3. Optimal Control SEIR Model with periodic incidence rate
4. Normalized Model and Optimal Control
   • a first choice of cost
   • comparison
   • how to translate constraints
5. FUTURE WORK
Everyone is assumed to be susceptible,

Susceptible individuals become infected through horizontal transmission with infected individuals,

Infected People can either die or recover completely,

All recovered individuals (vaccinated or recovered from infection) are immune.

**Horizontal transmission**: from one individual to another by direct contact (touching, biting), or indirect contact air (cough or sneeze).
1. SEIR MODEL

ODE's

\begin{align*}
\dot{S}(t) &= bN(t) - dS(t) - c \frac{S(t)I(t)}{N(t)}, \\
\dot{E}(t) &= c \frac{S(t)I(t)}{N(t)} - (f + d)E(t), \\
\dot{I}(t) &= fE(t) - (g + a + d)I(t), \\
\dot{R}(t) &= gI(t) - dR(t), \\
\dot{N}(t) &= (b - d)N(t) - aI(t),
\end{align*}

with initial values

\begin{align*}
S(0) &= S_0, \\
E(0) &= E_0, \\
I(0) &= I_0, \\
R(0) &= R_0, \\
N(0) &= N_0.
\end{align*}

- $S(t)$: number of Susceptible individual.
- $E(t)$: number of Exposed, ind.
- $I(t)$: number of Infectious ind
- $R(t)$: number of Recovered ind.
- $N(t)$: total number of population

$N(t) = S(t) + E(t) + I(t) + R(t)$
Introducing Vaccination

Let $u$ be the rate of vaccination.

Only Susceptible Individuals are vaccinated.

How to define Vaccination Policies?
2. Optimal Control L1

**L\(^1\) cost Problem**

Minimize \( \int_0^T (AI(t) + Bu(t)) \, dt \)

subject to

\[
\begin{align*}
\dot{S}(t) &= bN(t) - dS(t) - c \frac{S(t)I(t)}{N(t)} - S(t)u(t), \\
\dot{E}(t) &= c \frac{S(t)I(t)}{N(t)} - (f + d)E(t), \\
\dot{I}(t) &= fE(t) - (g + a + d)I(t), \\
\dot{W}(t) &= S(t)u(t), \\
\dot{N}(t) &= (b - d)N(t) - aI(t), \\
u(t) &\in [0, 1] \text{ a.e. } t,
\end{align*}
\]

Counting number of vaccines

Minimize \( \int_0^T (Ax(t) + Bu(t)) \, dt \)

subject to

\[
\begin{align*}
\dot{x}(t) &= f(x(t)) - g(x(t))u(t), \\
u(t) &\in [0, 1] \text{ a.e. } t,
\end{align*}
\]

x(0) = x\(_0\).
2. Optimal Control L1

$\text{L}^1 \text{ Cost: Optimal Controls}$

Bang- Bang and Bang- Singular- Bang
2. Optimal Control

Optimal Control Problems solved by Direct Method:

discretize the problem and solve the optimization problem with NLSolvers

Interface with NLP Solver used:

ICLOCS developed by Paola Falugi, Eric Kerrigan and Eugene van Wyk

AMPL developed by Robert Fourer, David Gay and Brian Kerrighan at Bell Laboratories

With AMPL and ICLOCS the NLS solver used is IPOPT.

Mostly 2000 or 10000 grid points and Implicit Euler Scheme with error tolerance $10^{-9}$

NOTE: $L^2$ case vs $L^1$ case

$L^1$ case exhibits bang-bang controls and bang-singular-bang controls
whereas $L^2$ does not.

- ICLOCS was unable to determine the singular controls (chattering)
- AMPL has not problem with singular controls
Both AMPL and ICLOCS provide the numerical multipliers.

In all the above cases we validate numerical solutions using necessary and sufficient conditions.

• For $L^1$ problems, when control is bang-bang, verification of SSC and determination of switching times following Maurer, Buskens, Kim, and Kaya (2005) using the code
  • NUDOCCCS;
  • Implementation of Induced Optimization Problem with AMPL.

• For $L^1$ problems, with singular controls, analytical expression tested numerically.
2. Optimal Control

Validation of numerical solutions

![Graph showing optimal control over time](image)

- $u$
- $u$ singular
- $\phi$

Time [years]
3. Periodic Incidence Rate

Suppose that
- Incidence rate is periodic being 0 in the warmer months (e.g.)
- Susceptible individuals get exposed by contact with outside world.

\[
\begin{align*}
\dot{S}(t) &= bN(t) - (d + \gamma(t))S(t) - c(t) \frac{S(t)I(t)}{N(t)}, \\
\dot{E}(t) &= c(t) \frac{S(t)I(t)}{N(t)} + \gamma(t)S(t) - (f + d)E(t), \\
\dot{I}(t) &= fE(t) - (g + a + d)I(t), \\
\dot{R}(t) &= gI(t) - dR(t), \\
\dot{N}(t) &= (b - d)N(t) - aI(t).
\end{align*}
\]
3. Periodic Incidence Rate

where

\[
\begin{align*}
    c(t) &= \max \{ c_0(1 + \delta \sin(2\pi t - \pi/2), c_0 \} - c_0 \\
    \gamma(t) &= \gamma_0(1 + \sin(2\pi t - \pi/2))
\end{align*}
\]
### 3. Periodic Incidence Rate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$b$</td>
<td>natural birth rate</td>
<td>0.012</td>
</tr>
<tr>
<td>$d$</td>
<td>natural death rate</td>
<td>0.009</td>
</tr>
<tr>
<td>$c_0$</td>
<td>&quot;incidence&quot; coefficient</td>
<td>0.004</td>
</tr>
<tr>
<td>$\delta$</td>
<td>&quot;incidence&quot; coefficient</td>
<td>0.28</td>
</tr>
<tr>
<td>$\gamma_0$</td>
<td>&quot;incidence&quot; coefficient</td>
<td>0.002</td>
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<tr>
<td>$e$</td>
<td>exposed to infectious rate</td>
<td>0.8</td>
</tr>
<tr>
<td>$g$</td>
<td>recovery rate</td>
<td>0.15</td>
</tr>
<tr>
<td>$a$</td>
<td>disease induced death rate</td>
<td>0.01</td>
</tr>
<tr>
<td>$T$</td>
<td>number of years</td>
<td>20</td>
</tr>
<tr>
<td>$S_0$</td>
<td>initial susceptible population</td>
<td>1165</td>
</tr>
<tr>
<td>$E_0$</td>
<td>initial exposed population</td>
<td>0</td>
</tr>
<tr>
<td>$I_0$</td>
<td>initial infected population</td>
<td>0</td>
</tr>
<tr>
<td>$R_0$</td>
<td>initial recovered population</td>
<td>0</td>
</tr>
<tr>
<td>$N_0$</td>
<td>initial population</td>
<td>1165</td>
</tr>
<tr>
<td>$W_0$</td>
<td>initial vaccinated population</td>
<td>0</td>
</tr>
</tbody>
</table>

DISEASE PARAMETERS ARE NOT CLINICAL VALUES

~European values

For $t=0$ population free of disease
3. Periodic Incidence Rate

Without Control

N(20) = 1226

I(20) > 150
Minimize $\int_0^T (AI(t) + Bu(t)) \, dt$

subject to

$$\dot{S}(t) = bN(t) - (d + \gamma(t))S(t) - c(t) \frac{S(t)I(t)}{N(t)} - u(t)S(t),$$

$$\dot{E}(t) = c(t) \frac{S(t)I(t)}{N(t)} + \gamma(t)S(t) - (f + d)E(t),$$

$$\dot{I}(t) = fE(t) - (g + a + d)I(t),$$

$$\dot{N}(t) = (b - d)N(t) - aI(t),$$

$$u(t) \in [0, 1] \text{ a.e. } t,$$

$$x(0) = x_0.$$
3. Periodic Incidence Rate

OCP with $A=1$ and $B=2$

$N(20)=1236 > 1226.$
3. Periodic Incidence Rate

OCP with $A=1$ and $B=2$

Cost: 32
$W(20)\sim 130$, $N(20)\sim 1237$, $I(20)=1$

\[ 0 \leq u \leq 1 \]
3. Periodic Incidence Rate

OCP with $0 \leq u \leq 0.2$

Recall that treatment of infected people is expensive

Cost: $110$ (vs 32)
$I(20) = 4$
4. Normalized SEIR Model

S, E, I and R represent number of people. They are INTEGERS.

So ... how to interpret \( I(t) = 1.5 \)?

No big problem if the population is large, but for small populations... should we consider *Mixed Integer Programming*?

Well, we believe that the spreading of any infectious diseases mainly based on the distribution of the population by compartments. And with fraction we can work with continuous variables.
4. Normalized SEIR Model

**Idea:** Normalization of the population.

\[
\begin{align*}
    s(t) &= \frac{S(t)}{N(t)}, \\
    e(t) &= \frac{E(t)}{N(t)}, \\
    i(t) &= \frac{I(t)}{N(t)}, \\
    r(t) &= \frac{R(t)}{N(t)},
\end{align*}
\]

and

\[
s(t) + e(t) + i(t) + r(t) = 1 \text{ for all } t.
\]

Now \( s, e, i \) and \( r \) denote the **PERCENTAGE** of the total population in compartments \( S, E, I \) and \( R \).

Size of the total population is ignored.
4. Normalized SEIR Model

\[
\begin{align*}
\dot{s}(t) &= b - cs(t)i(t) - bs(t) + ai(t)s(t) - u(t)s(t), \\
\dot{e}(t) &= cs(t)i(t) - (f + b)e(t) + ai(t)e(t), \\
\dot{i}(t) &= fe(t) - (g + a + b)i(t) + ai^2(t), \\
\dot{r}(t) &= gi(t) - rb(t) + ai(t)r(t) + u(t)s(t).
\end{align*}
\]
How to define the $L^1$ cost for the Normalized SEIR Model?

In the SEIR model cost is

$$J_1(x,u) = \int_0^T AI(t) + Bu(t) \, dt = B \int_0^T \frac{A}{B} I(t) + u(t) \, dt.$$ 

Thus minimizing $J_1$ turns up minimizing

$$\int_0^T \beta I(t) + u(t) \, dt, \quad \beta = \frac{A}{B}.$$ 

In the Normalized SEIR Model $i$ is a percentage. So ”similar cost” would be

$$\int_0^T \rho i(t) + u(t) \, dt, \quad \rho = \frac{A \pi}{B},$$

where $\pi$ is roughly approximated to the average of TOTAL population in $T$ years.
### 4. Normalized SEIR Model

#### Parameters

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<tr>
<td>b</td>
<td>Natural birth rate</td>
<td>0.011</td>
</tr>
<tr>
<td>d</td>
<td>Death rate</td>
<td>0.009</td>
</tr>
<tr>
<td>c</td>
<td>Incidence coefficient in ((P))</td>
<td>1.1</td>
</tr>
<tr>
<td>f</td>
<td>Exposed to infectious rate</td>
<td>0.5</td>
</tr>
<tr>
<td>g</td>
<td>Recovery rate</td>
<td>0.1</td>
</tr>
<tr>
<td>a</td>
<td>Disease induced death rate</td>
<td>0.2</td>
</tr>
<tr>
<td>A</td>
<td>Weight of infected population</td>
<td>3</td>
</tr>
<tr>
<td>B</td>
<td>Weight of the vaccination effort</td>
<td>10</td>
</tr>
<tr>
<td>ρ</td>
<td>Weight parameter</td>
<td>300</td>
</tr>
<tr>
<td>T</td>
<td>Number of years</td>
<td>20</td>
</tr>
<tr>
<td>s₀</td>
<td>Initial susceptible population</td>
<td>0.858</td>
</tr>
<tr>
<td>e₀</td>
<td>Initial exposed population</td>
<td>0.086</td>
</tr>
<tr>
<td>i₀</td>
<td>Initial infected population</td>
<td>0.043</td>
</tr>
</tbody>
</table>

In the above table we have \(s₀ = S₀/N₀\), \(e₀ = E₀/N₀\) and \(i₀ = I₀/N₀\) where \(N₀ = 1165\), \(S₀ = 1000\), \(I₀ = 50\) and \(E₀ = 100\) are the values used in M&dP 15 and L&N10.
3. Normalized SEIR Model

Susceptible population

Infective population

Susceptible population

Infectious population

Deadly!
4. Normalized SEIR Model

**Not Normalized Problem**

Minimize \( \int_0^T (AI(t) + Bu(t)) \, dt \)

subject to

\[
\begin{align*}
\dot{S}(t) &= bN(t) - dS(t) - c \frac{S(t)I(t)}{N(t)} - u(t)S(t), \\
\dot{E}(t) &= c \frac{S(t)I(t)}{N(t)} - (f + d)E(t), \\
\dot{I}(t) &= fE(t) - (g + a + d)I(t), \\
\dot{N}(t) &= (b - d)N(t) - aI(t), \\
u(t) &\in [0, 1] \quad \text{for } a.e. \ t \in [0, T], \\
x(0) &= x_0 = (S_0, E_0, I_0, N_0).
\end{align*}
\]

**Normalized Problem**

Minimize \( \int_0^T (\rho i(t) + u(t))) \, dt \)

subject to

\[
\begin{align*}
\dot{s}(t) &= b - cs(t)i(t) - bs(t) + ai(t)s(t) - u(t)s(t), \\
\dot{e}(t) &= cs(t)i(t) - (f + b)e(t) + ai(t)e(t), \\
\dot{i}(t) &= fe(t) - (g + a + b)i(t) + a\tilde{i}^2(t), \\
u(t) &\in [0, 1] \quad \text{for } a.e. \ t \in [0, T], \\
x(0) &= (s(0), e(0), i(0)) = (s_0, e_0, i_0).
\end{align*}
\]
4. Normalized SEIR Model

Comparison of Problems

Classical Model: $A=3$, $B=10$

Normalized Model: $\rho=300$
4. Normalized SEIR Model

Classical Model: $A=3, B=10$

Normalized Model: $\rho=300$

Comparison of Problems
4. Normalized SEIR Model

Normalized model does not depend on the death rate. But THE CLASSICAL model does, right??? YES!!!

Classical Model: $A=3, B_{10}, d=0.0099$

Classical Model: $A=3, B_{10}, d=0.0005$
4. Normalized SEIR Model

Normalized model does not depend on the death rate. But classical model does. **DOES IT?????**

Classical Model: $A=3$, $B=10$, $d=0.0099$

![Normalized model graph](image1)

Classical Model: $A=3$, $B=10$, $d=0.0005$

![Classical model graph](image2)

Control $u$
Do the optimal controls coincide? The answer is NO.

Classical Model: $A=3$, $B=10$, $d=0.0099$

Classical Model: $A=3$, $B=10$, $d=0.0005$
4. Normalized SEIR Model

Comparison of Problems

Classical Model: Different death rates gives us different optimal controls.

This DOES NOT discard the NORMALIZED SEIR MODEL!

It does put the pressure on the criterious choice of $\rho$ in the cost.

Indeed, to compare Classical models with Normalized models we should have

$$\rho(t) = \frac{A \ast N(t)}{B}.$$ 

We use instead $\pi$ as a rough approximation $\pi$ of the average population $N(t)$:

$$\rho = \frac{A \ast \pi}{B}.$$
This comparison between models raises the question:

**WHAT IS THE APPROPRIATE COST FOR OPTIMAL CONTROL INVOLVING NORMALIZED MODELS?**

**Idea: Multi-objective cost?**
5. Future Work

For any of the mentioned models
• For specific disease with “real” parameters ....
• Introduction of delays. How???

For the Periodic Incidence Rate
• Can we treat the case of flu?? Subdivision of S
• compartment -old or children??

For the Normalized Case
• Multi-objective cost
• New and meaningful constraints

Also, sensitivity analysis w.r.t. the parameters.
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Procedia Technology, 2014
Thank you for your attention