Introducing State Constraints in Optimal Control for Health Problems

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ITN SADCO Initial Training Network Sensitivity Analysis for Deterministic Controller Design

Introduction

SEIR models are a common way to describe the epidemics of various infectious diseases. The underlying dynamic system of multiple ordinary differential equations (ODEs) can be controlled by a vaccination strategy over time T. The resulting optimal control system is

$$(P)\quad \begin{cases} \text{Minimize } l(x(T)) + \displaystyle\int_0^T L(x(t), u(t))\, dt \\ \text{subject to} \\ \dot{x}(t) \;\; = f(x(t)) + g(x(t))u(t) \quad \text{a.e. } t \in [0,T], \\ h(x(t)) \;\; \le 0 \quad \forall t \in [0,T], \\ u(t) \;\; \in U \quad \text{a.e. } t \in [0,T], \\ x(0) \;\; = x_0, \\ x(T) \;\; \in \mathbb{R}^n, \end{cases}$$

where $x \in \mathbb{R}^n$, $U \subset \mathbb{R}^k$ (the control set), $l : \mathbb{R}^n \mathbb{R}$, $L : \mathbb{R}^n \times \mathbb{R}^k \to \mathbb{R}$, $f : \mathbb{R}^n \to \mathbb{R}^n$, $g : \mathbb{R}^n \to \mathbb{R}^n \times \mathbb{R}^k$ and $h : \mathbb{R}^n \to \mathbb{R}$. This problem, equipped with a pure state contraint (on the susceptible compartment) can be solved computationally (we use IPOPT and ICLOCS). The current work provides an analytical solution and a comparison between the analytic and computational values.

Auxiliary Definitions and Results

A *trajectory* x (an AC function) and *control* u (measurable function) comprise (x,u), an *admissable process* if it satisfies the constraints of P (esp, the *state constraint* $h(x(t)) \le 0 \,\forall t \in [0,T]$). The *solution* of P is (x^*, u^*). $[t_0^b, t_1^b] \subset [0,T]$ is a *boundary interval* if $h(x^*(t)) = 0$, $\forall t \in [t_0^b, t_1^b]$. $[t_0^i, t_1^i] \subset [0,T]$ is an *interior interval* if $h(x^*(t)) < 0$, $\forall t \in (t_0^i, t_1^i)$. If, for all $t \in [0,1]$, we have $\frac{\partial h^1}{\partial u}(x,u) = \langle \frac{\partial h}{\partial x}(x(t)), g(x(t)) \rangle \neq 0$ then the state constraint is of *order one*. $C([0,T];\mathbb{R})$ is the *space of continuous functions* and its dual is $C^*([0,T];\mathbb{R})$. $C^{\oplus}([0,T];\mathbb{R})$ is the space of nonnegative elements of C^* taken on nonnegative functions of C. (x^*, u^*) a *strong local minimum* of (P) if $\exists \varepsilon > 0$ s.t. (x^*, u^*) minimizes the cost over all admissible (x,u) with $|x(t) - x^*(t)| \le \varepsilon \,\forall t \in [0,T]$.

Let $(\hat{x}, \hat{u})$ be a reference process, $\epsilon > 0$, and the conditions (H1)-(H4) hold:

H1. the function $L(x, \cdot)$ is continuous on U for all $x \in \mathbb{R}^n$;
H2. the functions $f(\cdot)$, $g(\cdot)$, $L(\cdot, u)$ and $h(\cdot)$ are continuously differentiable on $\hat{x}(T) + \epsilon B$for all $u \in U$;
H3. the function l is Lipschitz continuous on $\hat{x}(T) + \epsilon B$;
H4. the set U is compact.

Then (P) us guaranteed to have a solution (cf. Clarke '13).

Let (x^*, u^*) be a local strong minimum. Then (cf. Vinter '00) there exists an AC function p, $\lambda \in \mathbb{R}$ and a measure $\mu \in C^{\oplus}([0,T])$ such that

(i) $(p, \lambda, \mu) \neq (0,0,0)$;
(ii) $-\dot{p}(t) = f_x^T(x^*(t))q(t) + u^*(t)g_x^T(x^*(t))q(t) - \lambda L(x^*(t), u^*(t))$;
(iii) $\langle g(x^*(t))u^*(t), q(t)\rangle - \lambda L(x^*(t), u^*(t)) \ge \langle g(x^*(t))u, q(t)\rangle - \lambda L(x^*(t), u)$, $\forall u \in [0,1]$;
(iv) $-q(T) = 0$;
(v) $supp\{\mu\} \subset \{t : \; h(x^*(t)) = 0\}$,

where q is a bounded variation function with
$q(t) = p(t) + \int_{[0,t)} \nabla h(x^*(s))\, \mu(ds)$,
$q(T) = p(T) + \int_{[0,T]} \nabla h(x^*(s))\, \mu(ds)$.

The SEIR Model

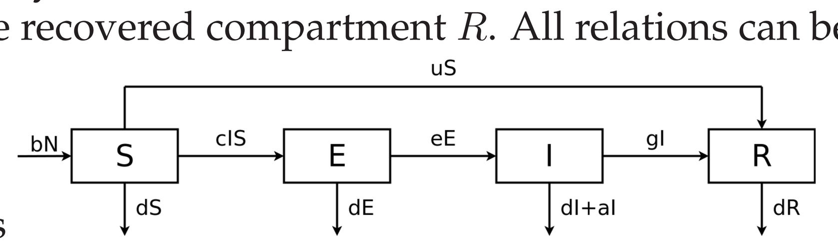
The SEIR model describes the spreading of an infectious disease among a population (N) by dividing it into four different compartments: susceptible (S), exposed, not yet infectious (E), infectious (I), recovered (R) (thus, a compartment model). $N(t) = S(t) + E(t) + I(t) + R(t)$. The dynamics of each compartment is modelled by an ODE:

$$\begin{aligned} \dot{S}(t) &= bN(t) - dS(t) - cS(t)I(t) - u(t)S(t), & S(0) &= S_0, \\ \dot{E}(t) &= cS(t)I(t) - (e+d)E(t), & E(0) &= E_0, \\ \dot{I}(t) &= eE(t) - (g+a+d)I(t), & I(0) &= I_0, \\ \dot{R}(t) &= gI(t) - dR(t) + u(t)S(t), & R(0) &= R_0, \\ \dot{N}(t) &= (b-d)N(t) - aI(t), & N(0) &= N_0, \end{aligned}$$

Meaning and values of all used parameters are given below. (cf. [3]).

Parameter	Description	Value
b	natural birth rate	0.525
d	natural death rate	0.5
c	incidence coefficient	0.001
e	exposed to infectious rate	0.5
g	recovery rate	0.1
a	disease induced death rate	0.2
A	weight parameter	0.1
T	number of years	20
S_0	initial susceptible population	1000
E_0	initial exposed population	100
I_0	initial infected population	50
R_0	initial recovered population	15
N_0	initial population	1165
W_0	initial vaccinated population	0

The system is controlled by the rate of vaccination $u(t)$ taking values in $[0,1]$. Only susceptible compartment S is vaccinated ($u(t) = 1$ means all susceptible population is vaccinated at an instant t). We also assume: every newborn is susceptible; every vaccinated individual becomes immune and proceeds to the recovered compartment R. All relations can be visualized as



The SEIR Control Problem

Preliminary observations:

- We retain the cost functional introduced in [3],
$$J(u) = \int_0^T \left(AI(t) + u^2(t) \right)\, dt.$$
- The ODE governing $\dot{R}(t)$ is substituted with the one for $\dot{N}(t)$ since $R(t) = N(t) - S(t) + E(t) + I(t)$.
- Addition of an extra variable W with $W(t) = u(t)S(t)$ counting the number of vaccinations.
- The upper bound on $S(t)$ stems from the idea that an upper bound on $I(t)$ would imply a state constraint of order > 1 otherwise. Since $\dot{E}(t)$ is determined by $cS(t)I(t)$, it can be expected that $S(t) \le S_{max}$ does the job.

The resulting SEIR control problem is

$$(P_S)\quad \begin{cases} \text{Minimize } \displaystyle\int_0^T \left(AI(t) + u^2(t)\right)\, dt \\ \text{subject to} \\ \dot{S}(t) \;\; = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t), \\ \dot{E}(t) \;\; = cS(t)I(t) - (e+d)E(t), \\ \dot{I}(t) \;\; = eE(t) - (g+a+d)I(t), \\ \dot{N}(t) \;\; = (b-d)N(t) - aI(t), \\ \dot{W}(t) \;\; = u(t)S(t), \\ S(t) \;\; \le S_{max}, \\ u(t) \;\; \in [0,1] \quad \text{for a.e. } t \in [0,T], \\ S(0) = S_0,\; E(0) = E_0,\; I(0) = I_0,\; N(0) = N_0, \\ W(0) = W_0. \end{cases}$$

The problem (P_S) corresponds exactly to (P) via the following definitions:

$$x(t) := (S(t), E(t), I(t), N(t)), \quad \tilde{A} := (0,0,A,0), \quad C := (1,0,0,0),$$

$$A_1 := \begin{bmatrix} -d & 0 & 0 & b \\ 0 & -(e+d) & 0 & 0 \\ 0 & e & -(g+a+d) & 0 \\ 0 & 0 & -a & b-d \end{bmatrix},\; B := \begin{bmatrix} -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and $l(x_0, x_1) = 0$, $L(x,u) = \langle \tilde{A}, x\rangle + u^2$, $f(x,u) = f_1(x) + g(x)u$ where $f_1(x) = A_1 x + c(-SI, SI, 0, 0)^T$, $g(x) = Bx$ and $h(x) = \langle C, x\rangle - S_{max} = S - S_{max}$ for some fixed $S_{max} > S(0)$.

Remarkably, (P_S) has free end states, a quadratic cost with respect to u and the differential equation $\dot{x}(t) = f_1(x(t)) + g(x(t))u(t)$ is affine in the control and nonlinear in the state x due to the term f_1.

Necessary Conditions for (P_S)

With the stated parameter values it can be verified that for all $t \in [0,T]$

$$\begin{aligned} 0 < L_S \le S(t) \le U_S, &\quad 0 < L_N \le N(t) \le U_N, \\ 0 \le I(t) \le U_I, &\quad\quad 0 \le E(t) \le U_E \end{aligned}$$

with some constants $U_S, L_S, U_N, L_N, U_E, U_I$. This allows us to assert conditions $(i) - (v)$ in Auxiliary Results section with $\lambda = 1$, thus the *normality* of the optimal solution. Consider $q = (q_s, q_e, q_i, q_n)$ and $p = (p_s, p_e, p_i, p_n)$.

An analysis of the Weierstrass Contition (iii) yields by looking at $u^*(t) = 0$, 1 or in $]0,1[$, respectively,

$$u^*(t) = \max\left\{0, \min\left\{1, -\frac{q_s(t)S^*(t)}{2}\right\}\right\}. \tag{1}$$

For all t in a boundary interval $[t_0^b, t_1^b]$ ($S^*(t) = S_{max}$) it holds

$$\dot{S}^*(t) = bN^*(t) - dS^*(t) - cS^*(t)I^*((t) - u^*(t)S^*(t) = 0$$

and therefore
$$u^*(t) = b\frac{N^*(t)}{S^*(t)} - d - cI^*(t). \tag{2}$$

We have $q(t) = p(t) + \int_{[0,t)} \nabla h(x^*(t))\, \mu(ds)$, $\nabla h(x^*(t)) = (1,0,0,0)$ and

$$\int_{[0,t)} (1,0,0,0)\, \mu(ds) = \left(\int_{[0,t)} \mu(ds), 0, 0, 0 \right).$$

It follows
$$q_S(t) = p_S(t) + \int_{[0,t)} \mu(ds).$$

Of main interest are the *regularity properties of the multipliers*. Results of Shvartsman & Vinter '06 allow to conclude that μ is absolutely continuous w.r.t. Lebesgue measure. This means that there exists a function $\nu \in L^1$ such that $\int_0^t \nu(s)\, ds = \int_{[0,t)} \mu(ds)$. Consequently, q is absolutely continuous on $[0,T[$ and $\dot{q}_s(t) = \dot{p}_s(t) + \nu(t)$. It can be shown that

$$\dot{q}_s(t) = (d + cI^*(t) + u^*(t))q_s(t) - \nu(t) + cI^*(t)q_e(t)$$

This allows to derive (with (1) and (2))

$$\nu(t) = -(d + cI^*(t) + u^*(t))q_s(t) - cI^*(t)q_e(t) + 2c\frac{\dot{I}^*(t)}{S_{max}} - \frac{2b\dot{N}^*(t)}{S_{max}^2}.$$

We call ν the *analytical multiplier*. The function ν is defined on $[0,T]$ but it is $\nu(t) = 0$ on any interior interval.

The results so far motivate the following numerical analysis, more precisely: to compare ν with the multiplier computed by ICLOCS, to see that q_s may have a jump when $t = T$ and that

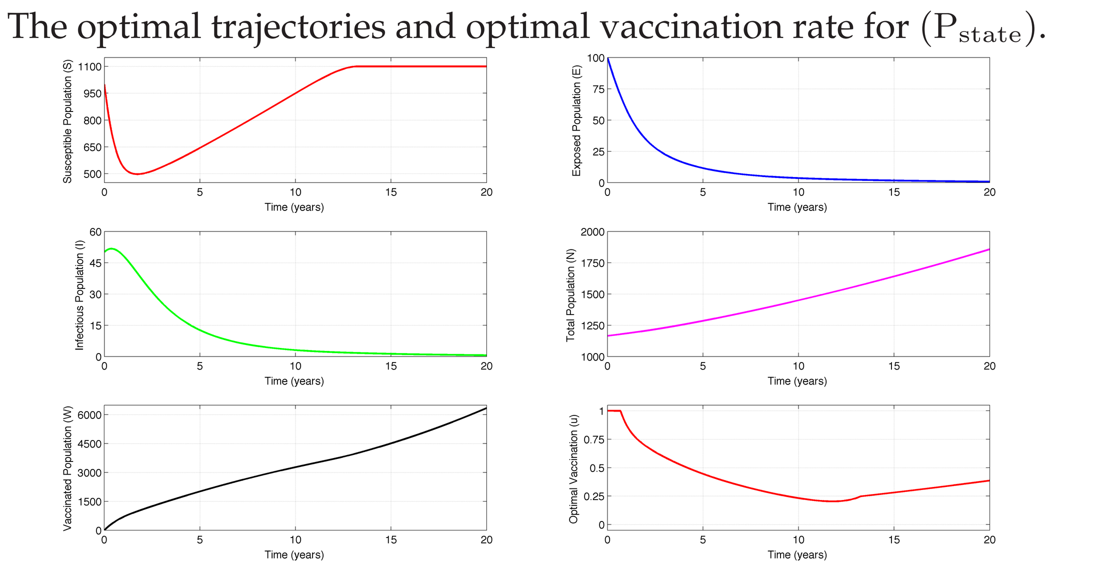
$$\begin{aligned} p_e(t) &= q_e(t), \\ p_i(t) &= q_i(t), \quad \text{and} \quad p_n(T) = p_n(T) = p_n(T) = 0. \\ p_n(t) &= q_n(t) \end{aligned}$$

Numerical results

All numerical results were obtained in [1] using the ICLOCS software (version 0.1b, cf [2]) which relies on IPOPT (Interior Point OPTimizer). We choose $u(t) \in [0, 0.9]$, the state constraint $S(t) \le S_{max}$ with $S_{max} = 1100$, $V_1 = 400$, a time interval of 20 years ($T = 20$) and a time grid with 10000 nodes. The accepted convergence tolerance at each step is $\varepsilon_{rel} = 10^{-9}$.

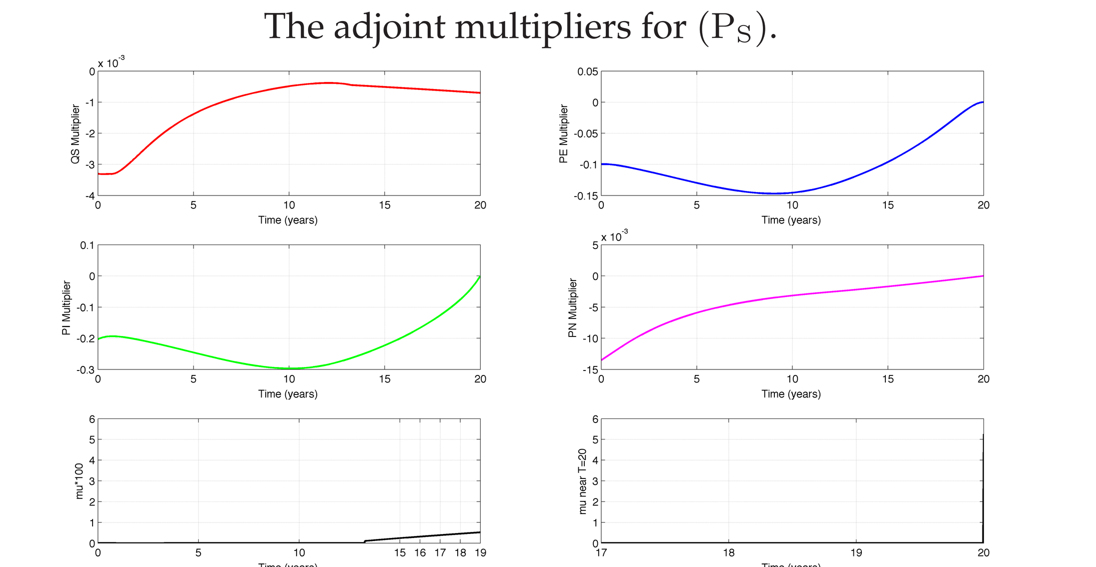
Below is the solution to (P_S) with $W = 6345$ at $t = T$. It can be observed that the state contraint is satisfied on approximately the last third of the whole time period including the end point (i.e., $S(20) = 1100$). At the same time, the control u starts to increase on the boundary interval to ensure the state constraint.

The optimal trajectories and optimal vaccination rate for (P_{state}).



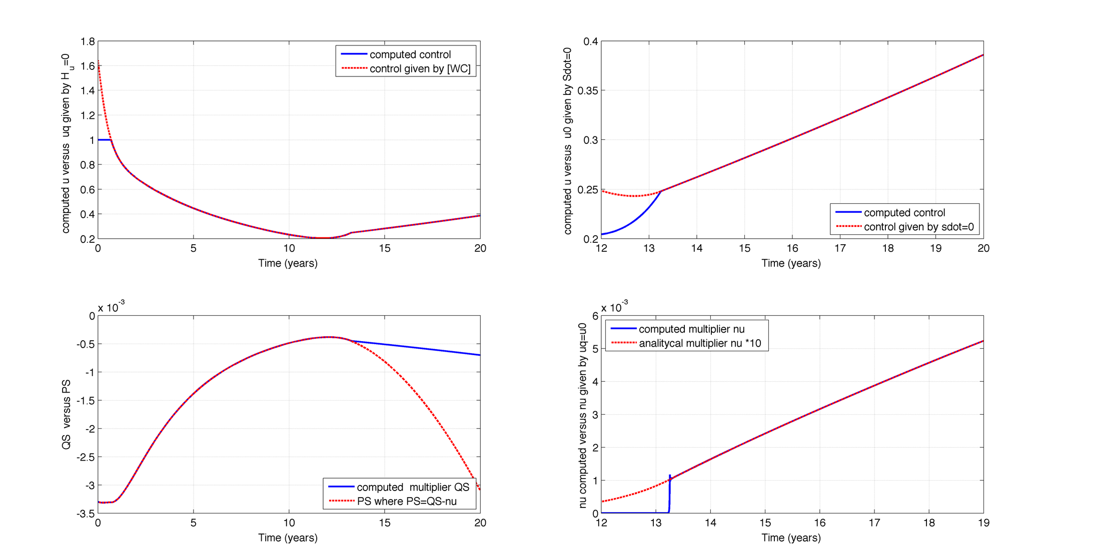
The multiplier p_s is not zero at $T = 20$ as shown below, a behaviour that fully corresponds to the visible atom hike of the measure μ at $T = 20$ (however, observe that μ is AC w.r.t. the Lebesgue measure on $[0,T[$).

The adjoint multipliers for (P_S).



Recall the analytic expressions (1) and (2) for the optimal control $u^*(t)$. The top left subgraph below showing the computed control satisfies (1) while the top right subgraph matches (2) in te case of the active state contraint.

The adjoint multipliers for (P_S).



The comparison between the multipplier computed by ICLOCS and the analytical ν is made in the bottom right subgraph below. We observe a match for all times except $t = T$ as we see in higher magnification in the bottom right graph of the middle figure.

The picture is completed by the comparison between q_s and p_s. The two start to differ on the boundary interval. However, we must have $q_s(T) = 0$ due to (iv). It follows that q_s has a jump at T due to the atom of the measure μ.

Conclusion

We studied an optimal control problem with state constraints to obtain optimal vaccination schedules and control strategies for an SEIR epidemic model of human infectious diseases. First order necessary conditions were applied to extract analytical information on the solution and multipliers of such problem that was then confronted with the computed counterparts.

The analysis allows us to verify the results on the normality of the Maximum Principle and on the regularity of multipliers and solution. It means also systematically validating solutions for an wider class of control problems.

The future questions to be investigated include e.g. calculating the begin of the boundary interval, the study of stability of the solution w.r.t. the parameters or the application of second order sufficient conditions (see Maurer '95, '02 and '13).

References

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[2] P. Falugi, E. Kerrigan and E. van Wyk. Imperial College London Optimal Control Software User Guide (ICLOCS). *Department of Electrical and Electronic Engineering, Imperial College London, UK, 2010.*

[3] R.M. Neilan and S. Lenhart. An Introduction to Optimal Control with an Application in Desease Modeling. *DIMACS Series in Discrete Mathematics, Vol. 75, 2010, pp. 67-81.*