Optimal Control Problems
for the
Control of Infectious Diseases
(L1 case)

Helmut Maurer and Maria do Rosário de Pinho

ITN SADCO
Initial Training Network
Sensitivity Analysis for Deterministic Controller Design
FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA
COMPETE
PROGRAMA OPERACIONAL FACTORES DE COMPETITIVIDADE
QREN
FEDER

Aim

Control of infectious diseases via vaccination!!!

We replace L2 costs by L1 costs in existent SEIR compartmental models and we validate the numerical solutions.

Work based on

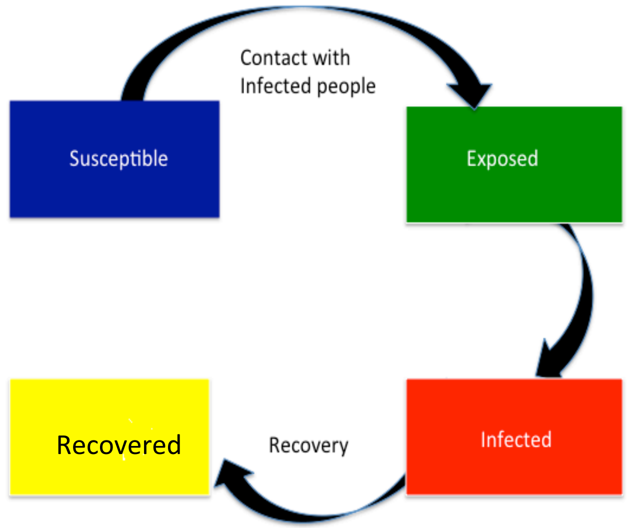
Optimal control of epidemiological SEIR models with L1-objectives and control and state constraints

by Maurer and dP (submitted)

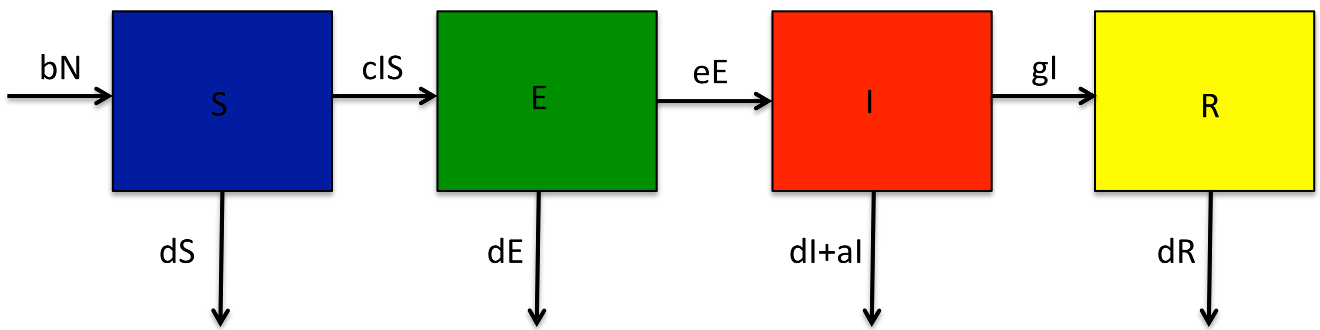
Outline

- SEIR Model
- Optimal Control for SEIR Model
  - previous models with L2 cost
  - with L1 cost
- Case i: Unlimited Number of vaccines
- Case ii: Limited Number of vaccines
- Case iii: Mixed Constraints
- Case iv: ....State Constraints.... next time......

I. SEIR MODEL



- Everyone is assumed to be susceptible,
- **Susceptible individuals become infected through <u>horizontal transmission</u> with infected individuals**,
- Infected People can either **die** or **recover** completely,
- All **recovered** individuals (vaccinated or recovered from infection) are immune.

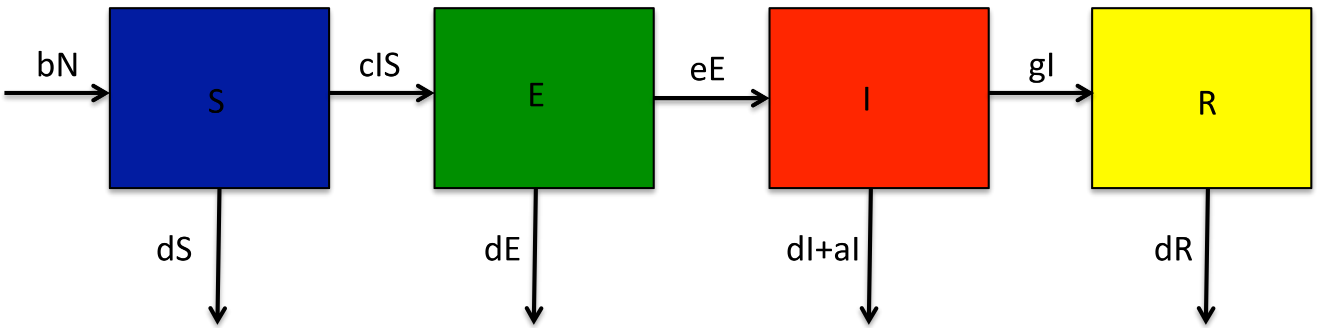


Horizontal transmission: from one individual to another by direct contact (touching, biting), or indirect contact air (cough or sneeze).

Parameters

b: natural exponential birth rate,
d: natural exponential death rate over time.
e: rate at which the exposed individuals become infected,
g: rate at which infectious individuals recover,
a: death rate due to the disease in an infected individual,
c: incidence coefficient of horizontal transmission,

cS(t)I(t): the rate of transmission



ODE's

$$\begin{cases} \dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) \\ \dot{E}(t) = cS(t)I(t) - (e+d)E(t) \\ \dot{I}(t) = eE(t) - (g+a+d)I(t) \\ \dot{R}(t) = gI(t) - dR(t) \\ \dot{N}(t) = (b-d)N(t) - aI(t) \\ \text{with the boundary conditions} \\ S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ R(0) = R_0,\ N(0) = N_0. \\ S(T),\ E(T),\ I(T),\ R(T),\ \ N(T) \in R \end{cases}$$

in other models $\eta \frac{S(t)I(t)}{N(t)}$

$$\boxed{N(t)=S(t)+E(t)+I(t)+R(t)}$$

- 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

Parameters

(in Neilan & Lenhart)

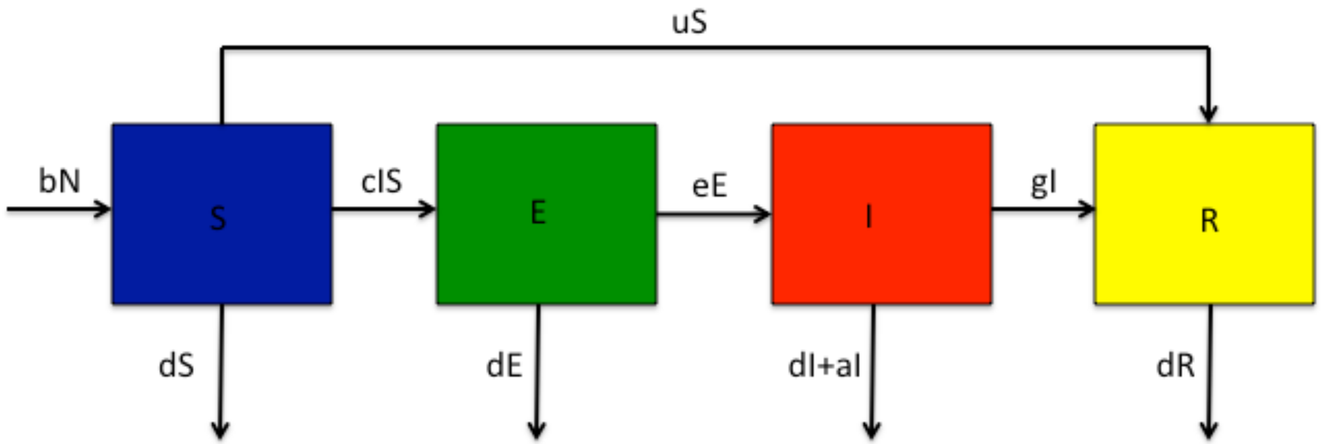
Parameters	Definition of Parameters	Values
b	natural birth rate	0.525
d	natural death rate	0.5
c	incidence coefficient	0.001
e	exposed to infectious rate	0.5
g	recovery rate	0.1
a	disease induced death rate	0.2
T	number of years	20
S_0	initial susceptible population	1000
E_0	initial exposed population	100
I_0	initial infected population	50
R_0	initial recovered population	15
N_0	initial population	1165

where in the world?

Introducing Vaccination

Let u be the rate of vaccination.

Only Susceptible Individuals are vaccinated.



How to define Vaccination Policies?

2. Optimal Control L2

Neilan & Lenhart Problem 2010

$$
\begin{cases}
\text{Minimize } \int_0^T (0.1I(t) + u^2(t))dt \\
\text{s.t} \\
\dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t) \\
\dot{E}(t) = cS(t)I(t) - (e+d)E(t) \\
\dot{I}(t) = eE(t) - (g+a+d)I(t) \\
\dot{W}(t) = u(t)S(t) \\
\dot{N}(t) = (b-d)N(t) - aI(t) \\
u(t) \in [0,1] \qquad \text{control constraints} \\
S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ W(0) = W_0,\ N(0) = N_0
\end{cases}
$$

L^2 cost

Counting number of vaccines

$$
\begin{aligned}
&\text{Minimize} \quad \int_0^T (\langle A, x(t)\rangle + u^2(t))dt \\
&\text{subject to} \\
&\dot{x}(t) = f(x(t)) + g(x(t))u(t) \\
&u(t) \in [0,1] \\
&x(0) = 0
\end{aligned}
$$

- ★ Control is scalar
- ★ Control set is convex and compact
- ★ Dynamic is affine wrt control
- ★ Cost is strongly convex wrt control
- ★ End state free

2. Optimal Control L2

Biswas, Kornienko, Paiva, dP 2014

Mixed Constraints

$$\text{Minimize } \int_0^T (AI(t) + u^2(t))\, dt$$

subject to

$$\dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) - S(t)u(t),$$
$$\dot{E}(t) = cS(t)I(t) - (e + d)E(t),$$
$$\dot{I}(t) = eE(t) - (g + a + d)I(t),$$
$$\dot{N}(t) = (b - d)N(t) - aI(t),$$
$$S(t)u(t) - V_0 \leq 0 \quad \text{a.e. } t,$$
$$u(t) \in [0, 1] \text{ a.e. } t,$$
$$x(0) = x_0.$$

State Constraints

$$\text{Minimize } \int_0^T (AI(t) + u^2(t))\, dt$$

subject to

$$\dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) - S(t)u(t),$$
$$\dot{E}(t) = cS(t)I(t) - (e + d)E(t),$$
$$\dot{I}(t) = eE(t) - (g + a + d)I(t),$$
$$\dot{N}(t) = (b - d)N(t) - aI(t),$$
$$S(t) - S_{max} \leq 0 \quad \text{for all } t,$$
$$u(t) \in [0, 1] \text{ a.e. } t,$$
$$x(0) = x_0.$$

and with both mixed and state constraints

but........

Are L2 costs appropriate?

No!

What about L1 costs?

L1 Mixed Constrained case previously appeared
in
Kornienko, dP, Maurer
conference paper 2014

Numerical Software

We solve our problems by Direct Method

Interface with NLP Solver:

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

and

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

With AMPL and ICLOCS **IPOPT** is used.

Mostly 10000 or 20000 grid points

and

Implicit Euler Scheme with error tolerance $\leq 10^{-8}$

Also, we use

NUDOCCCS developed by C. Buskens.

Unlimited Vaccines (UV)

Unlimited Vaccines (UV)

Simplest Case:

$$
(OCP) \quad \begin{cases}
\text{Minimize} \quad J(x,u) = \int_0^T (I(t) + Bu(t))\, dt \\
\text{subject to} \\
\quad \dot{S}(t) = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t), \quad S(0) = S_0, \\
\quad \dot{E}(t) = cS(t)I(t) - (e+d)E(t), \quad E(0) = E_0, \\
\quad \dot{I}(t) = eE(t) - (g+a+d)I(t), \quad I(0) = I_0, \\
\quad \dot{N}(t) = (b-d)N(t) - aI(t), \quad N(0) = N_0, \\
\quad u(t) \in [0,1] \quad \text{for æ } t \in [0,T],
\end{cases}
$$

B will be 2 or 10.

Necessary Conditions for UV

- adjoint variables: $p_S, \; p_E, \; p_I, \; p_N, \; \lambda = 1$
- gives us optimal control: Bang- bang and singular arcs
- numerics show singular arcs may occur

$$u_*(t) = \begin{cases} 1 & , \quad \text{if} \quad \phi(t) > 0 \\ 0 & , \quad \text{if} \quad \phi(t) < 0 \\ \text{singular} & , \quad \text{if} \quad \phi(t) = 0 \;\; \forall \, t \in [t_1, t_2] \subset [0, T] \end{cases}$$

where $\phi(x, p) = H_u(x, u, p) = -B - p_S\, S$ is the switching function.

N. C. & Singular Control for UV

Using

$$\boxed{\dot{\phi} = p_E\, c\, I\, S - p_S\, b\, N = 0}$$

and the explicit formula from NCO we show that:

- the strict Generalized Legendre-Clebsch Condition

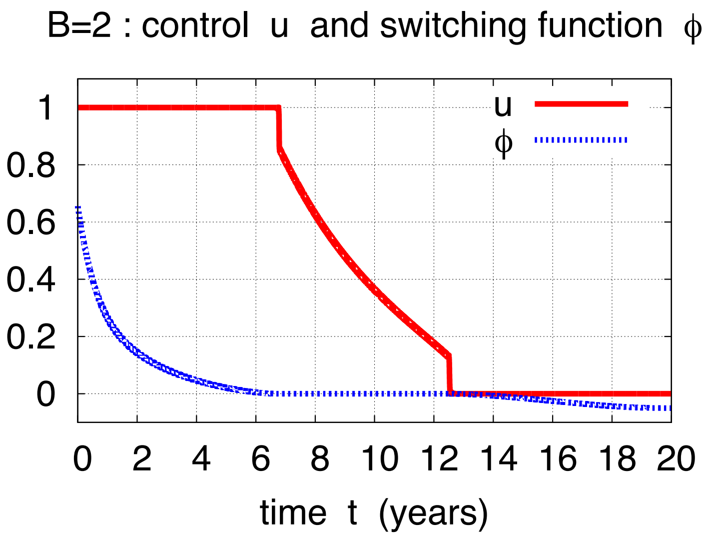
$$\frac{\partial \ddot{\phi}}{\partial u} = -p_E\, 2\, c\, I\, S\ > 0\,.$$

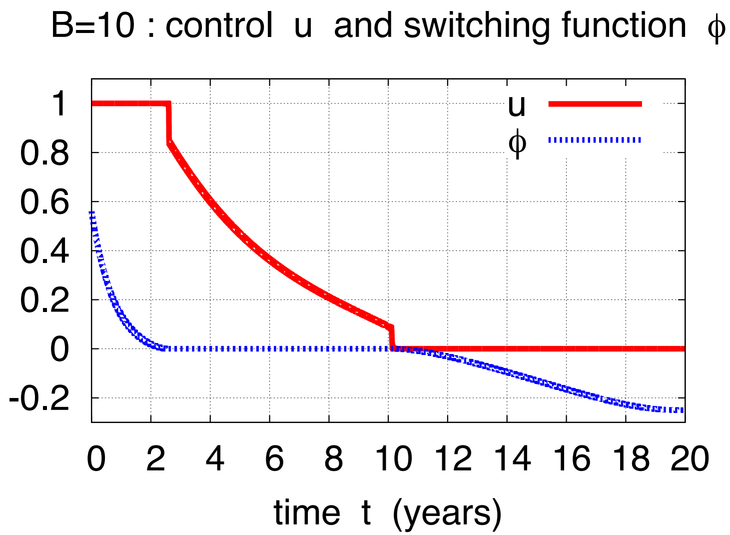
- and we get the formula for the singular control

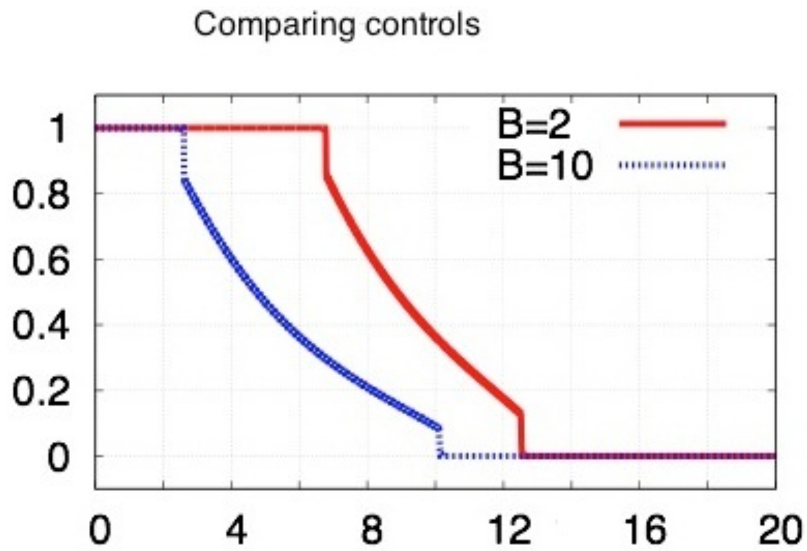
$$\boxed{\begin{aligned} u_{sing}(x,p) = \quad & B\, b\,((b-d)N - aI)/(\,p_E cI2S^2\,) + 0.5\,(e+d) - 0.5\, e\, p_I/p_E \\ & + 0.5(e\, E/I - (g+a+d)) + bN/S - d - cI\,. \end{aligned}}$$

2. Optimal Control L1-(i)

Numerics: control for UV







In both cases,
B=2 and B=10,
numeric singular control
agrees with
analytical singular control.

Control Structure: Bang- Singular-Bang

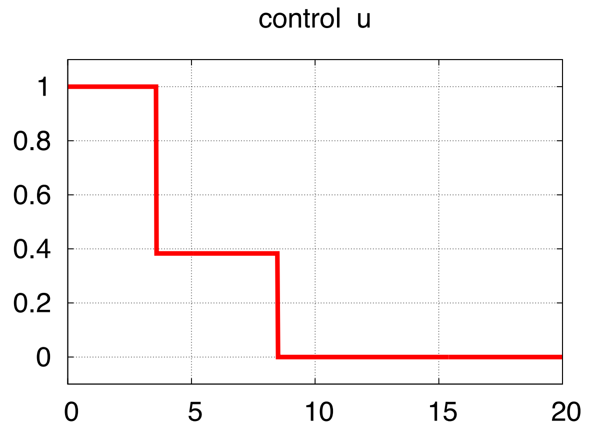
2. Optimal Control L1-(i)

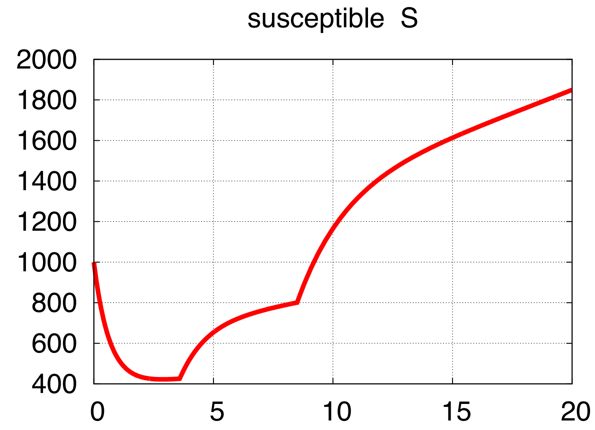
Approximation

For B=10

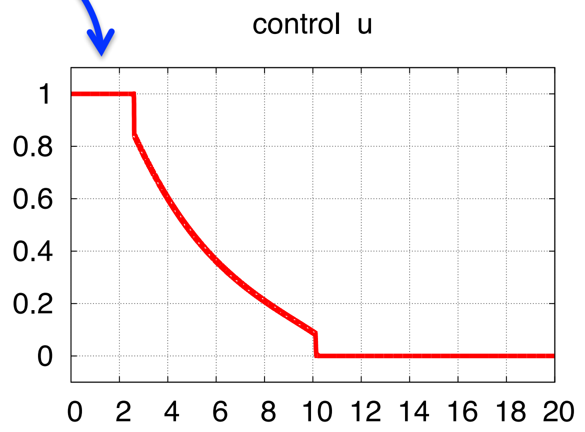
$$u(t) = \begin{cases} 1 & \text{for} \quad 0 \le t < t_1 \\ u_c & \text{for} \quad t_1 \le t \le t_2 \\ 0 & \text{for} \quad t_2 < t \le T \end{cases}$$

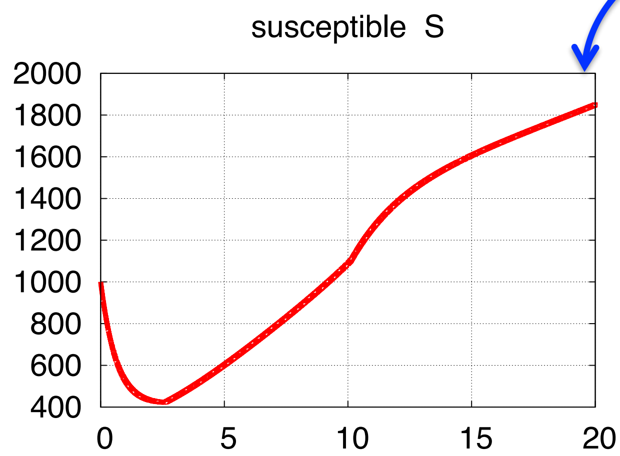
u_c optimized.





Using the arc parametrization method implemented with NUDOCCC





Limited Vaccines
(UV)

Limited Vaccines (LV)

$$(OCP\!-\!LV)\quad \begin{cases} \text{Minimize} \quad J(x,u) = \displaystyle\int_0^T (I(t) + Bu(t))\; dt \\ \text{subject to} \\ \quad \dot{S}(t) \quad = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t), \qquad S(0) = S_0, \\ \quad \dot{E}(t) \quad = cS(t)I(t) - (e+d)E(t), \qquad E(0) = E_0, \\ \quad \dot{I}(t) \quad = eE(t) - (g+a+d)I(t), \qquad I(0) = I_0, \\ \quad \dot{W}(t) \quad = u(t)S(t), \qquad W(0) = 0,\; W(T) = 2500, \\ \quad \dot{N}(t) \quad = (b-d)N(t) - aI(t), \qquad N(0) = N_0, \\ \quad u(t) \quad \in [0,1] \quad \text{for æ} \quad t \in [0,T], \end{cases}$$

In the previous case we get W(T)= 4880.123...

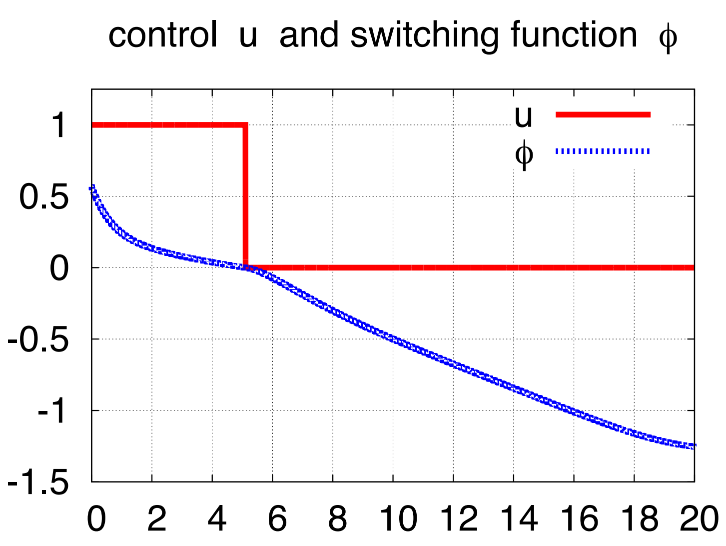
2. Optimal Control L1-(ii) Limited Vaccines (LV)

Again the control law

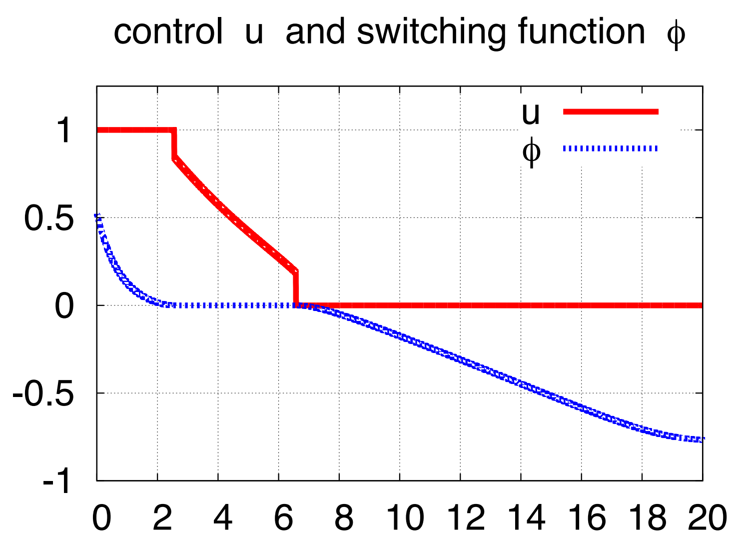
$$u_*(t) = \begin{cases} 1 & , \quad \text{if} \quad \phi(t) > 0 \\ 0 & , \quad \text{if} \quad \phi(t) < 0 \\ \text{singular} & , \quad \text{if} \quad \phi(t) = 0 \ \forall\, t \in [t_1, t_2] \subset [0, T] \end{cases}$$

where $\phi(x,p) = H_u(x,u,p)$.

B=2: Bang-Bang



B=10: Bang-Singular-Bang



2. Optimal Control L1-(ii) Limited Vaccines (LV)

For B=2

Induced Optimization Problem (IOP):

$$\begin{array}{ll} \text{Minimize} & J_1(z) := J(x,u) \\ \text{wrt} & z = t_1 \end{array}$$

Numerical Results: $J_1(z) = 226,71703$ and $t_1 = 5,105562.$

SSC hold for IOP: $\text{Hessian}(J_1)_{zz} > 0$ is positive-definite

SSC hold for the control problem: Strict bang bang property holds.

Pointwise Limited Vaccines (Mixed Constraints)

2. Optimal Control L1-(iii) Pointwise Limited Vaccines (MC)

$$
(OCP\!-\!MC)\quad \left\{\begin{array}{lll}
\text{Minimize} & J(x,u) = \int_0^T (I(t) + Bu(t))\,dt & \\
\text{subject to} & & \\
\dot{S}(t) & = bN(t) - dS(t) - cS(t)I(t) - u(t)S(t), & S(0) = S_0, \\
\dot{E}(t) & = cS(t)I(t) - (e+d)E(t), & E(0) = E_0, \\
\dot{I}(t) & = eE(t) - (g+a+d)I(t), & I(0) = I_0, \\
\dot{W}(t) & u(t)S(t), & W(0) = 0, \\
\dot{N}(t) & = (b-d)N(t) - aI(t), & N(0) = N_0, \\
S(t)u(t) & \leq 125, & \\
u(t) & \in [0,1] \quad \text{for æ} \;\; t \in [0,T], &
\end{array}\right.
$$

Mixed Constraint

Necessary Conditions:

Augmented Hamiltonian: $\mathcal{H}(x,p,q,u) = \langle p, f(x) + g(x)u\rangle - qSu$

We now have a multiplier **q** associated with the mixed constraint

Necessary conditions yield

$$u_*(t) = \begin{cases} 125/S_*(t) & , \quad \text{if} \quad \phi(t) > 0 \\ 0 & , \quad \text{if} \quad \phi(t) < 0. \end{cases}$$

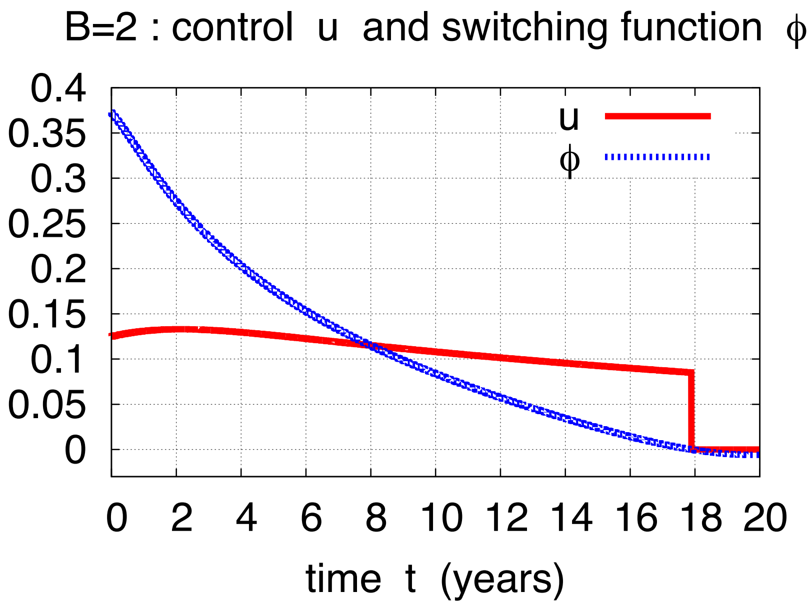
and

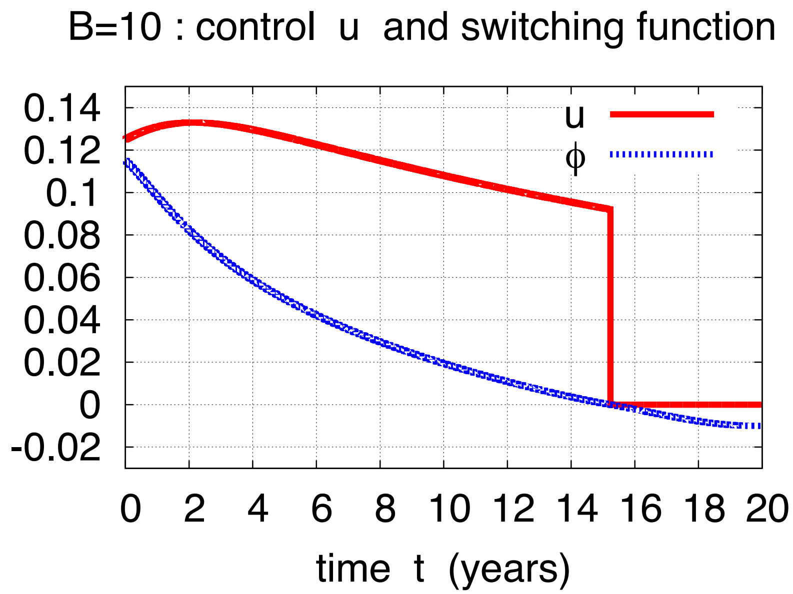
$$\boxed{q(t) = \begin{cases} -\dfrac{B}{S_*(t)} - p_s(t) = \phi(t)/S_*(t) & , \quad \text{if} \quad u_*(t) = 125/S_*(t) \\ 0 & , \quad \text{if} \quad u_*(t) < 125/S_*(t) \end{cases}}$$

Here $\phi(x, p) = -B - p_S\, S$ is the *switching function.*

2. Optimal Control L1-(iii)

Pointwise Limited Vaccines (MC)





Strict Bang bang property holds

$$\phi(t) > 0 \quad \text{for} \;\; 0 \le t < t_1, \quad \dot{\phi}(t_1) < 0, \quad \phi(t) < 0 \quad \text{for} \;\; t_1 < t \le T.$$

Pointwise Limited Vaccines (MC)

Let $v = Su$.

$$\begin{cases} \text{Minimize} \quad \displaystyle\int_0^T \left(I(t) + \frac{B}{S(t)}\, v(t) \right) dt \\ \text{subject to} \\ \dot{x}(t) = f(x(t)) + g(x(t))v(t) \\ v(t) \in [0, 125] \\ x(0) = 0 \end{cases}$$

Then

$$S_*(t)u_*(t) = v^*(t) = \begin{cases} 125 \quad , \quad \text{if} \quad \phi(t) > 0 \\ 0 \quad , \quad \text{if} \quad \phi(t) < 0. \end{cases}$$

We then show we have a strict strong minimum for the (MC) problem.

State Constraints (ST)? NO!

Next time….perhaps…

References

H. Maurer, C. Buskens, J.-H.R. Kim, and Y. Kaya,
Optimization methods for the verification of second-order sufficient conditions for bang-bang controls,
Optimal Control Methods and Applications, 26, (2005).

N. P. Osmolovskii and H. Maurer,
Applications to Regular and Bang-Bang Control: Second-Order Necessary and Sufficient Optimality Conditions in Calculus of Variations and Optimal Control,
SIAM Advances in Design and Control, 24, SIAM Publications, Philadelphia, 2013.

dP, Igor Kornienko and Helmut Maurer
Optimal Control of a SEIR Model with Mixed Constraints and L^1 *Control*
CONTROLO'2014 -Lecture Notes in Electrical Engineering 321

Biswas, Paiva & de Pinho
A SEIR model for control of infectious diseases with constraints,
Mathematical Biosciences and Engineering, 11, No. 4, (2014).

Igor Kornienko, LT Paiva, dP
Introducing State Constraints in Optimal Control for Health Problems
Procedia Technology, 2014

Thank you for your attention