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Optimal Control for Infectious Diseases
(L1 case)

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OCHERA

COMPETE PROGRAMA OPERACIONAL FACTORES DE COMPETITIVIDADE

QREN

FEDER

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA

Aim

Control of infectious diseases via vaccination!!!

Work based on

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

by Maurer and dP (submitted)

and

Optimal control of Infectious Diseases involving Normalized SEIR Models

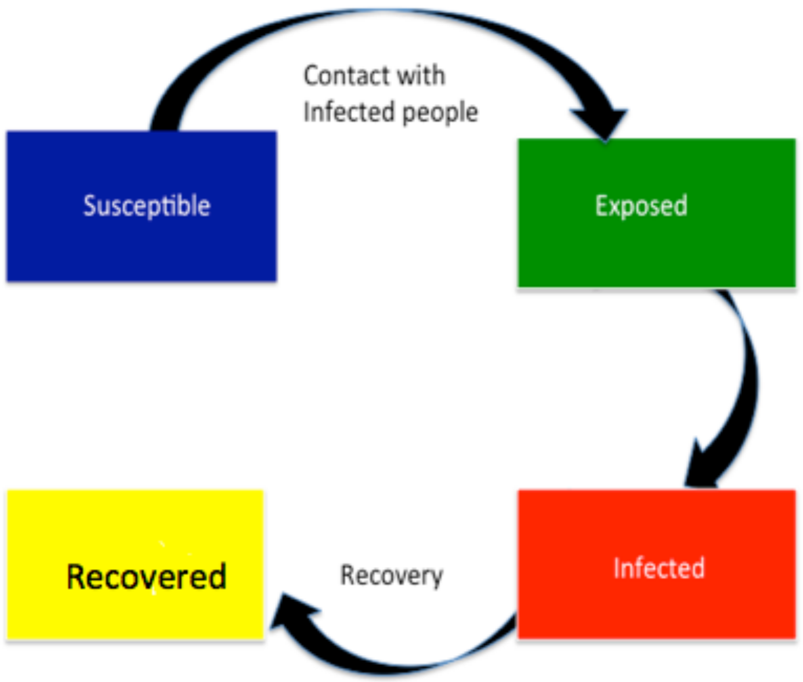
by Nogueira, Maurer and dP (working paper, to be submitted)

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

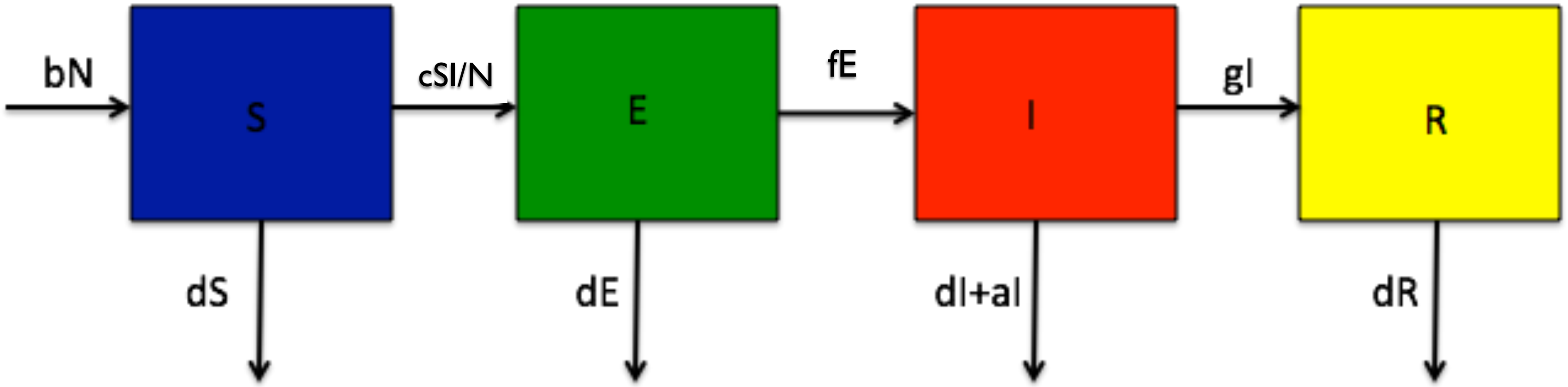
Outline

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

1. SEIR MODEL



- 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).

I. SEIR MODEL

ODE's

$$
\begin{cases}
\dot{S}(t) = bN(t) - dS(t) - c\dfrac{S(t)I(t)}{N(t)}, \\
\dot{E}(t) = c\dfrac{S(t)I(t)}{N(t)} - (f+d)E(t), \\
\dot{I}(t) = fE(t) - (g+a+d)I(t), \\
\dot{R}(t) = gI(t) - dR(t), \\
\dot{N}(t) = (b-d)N(t) - aI(t), \\
\text{with initial values} \\
S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ R(0) = R_0,\ N(0) = N_0.
\end{cases}
$$

vs. $\tilde{c}S(t)I(t) \quad (\tilde{c} = c/\tilde{N})$.

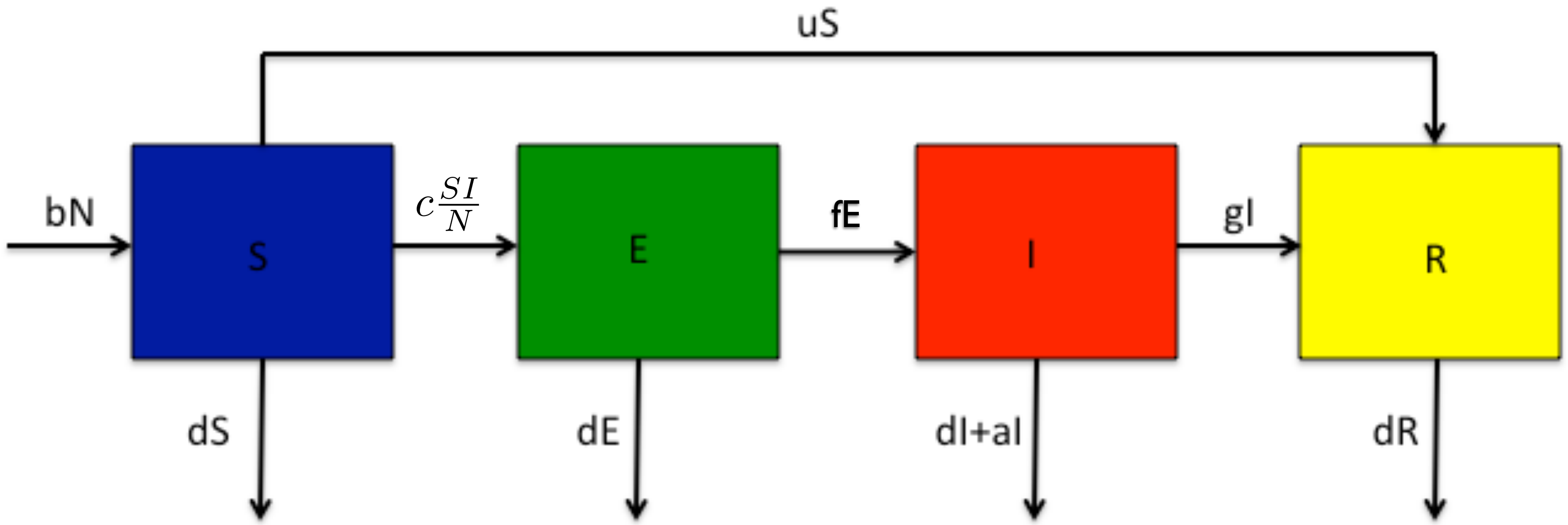
N(t)=S(t)+E(t)+I(t)+R(t)

- 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

Introducing Vaccination

Let u be the rate of vaccination.

Only Susceptible Individuals are vaccinated.



How to define Vaccination Policies?

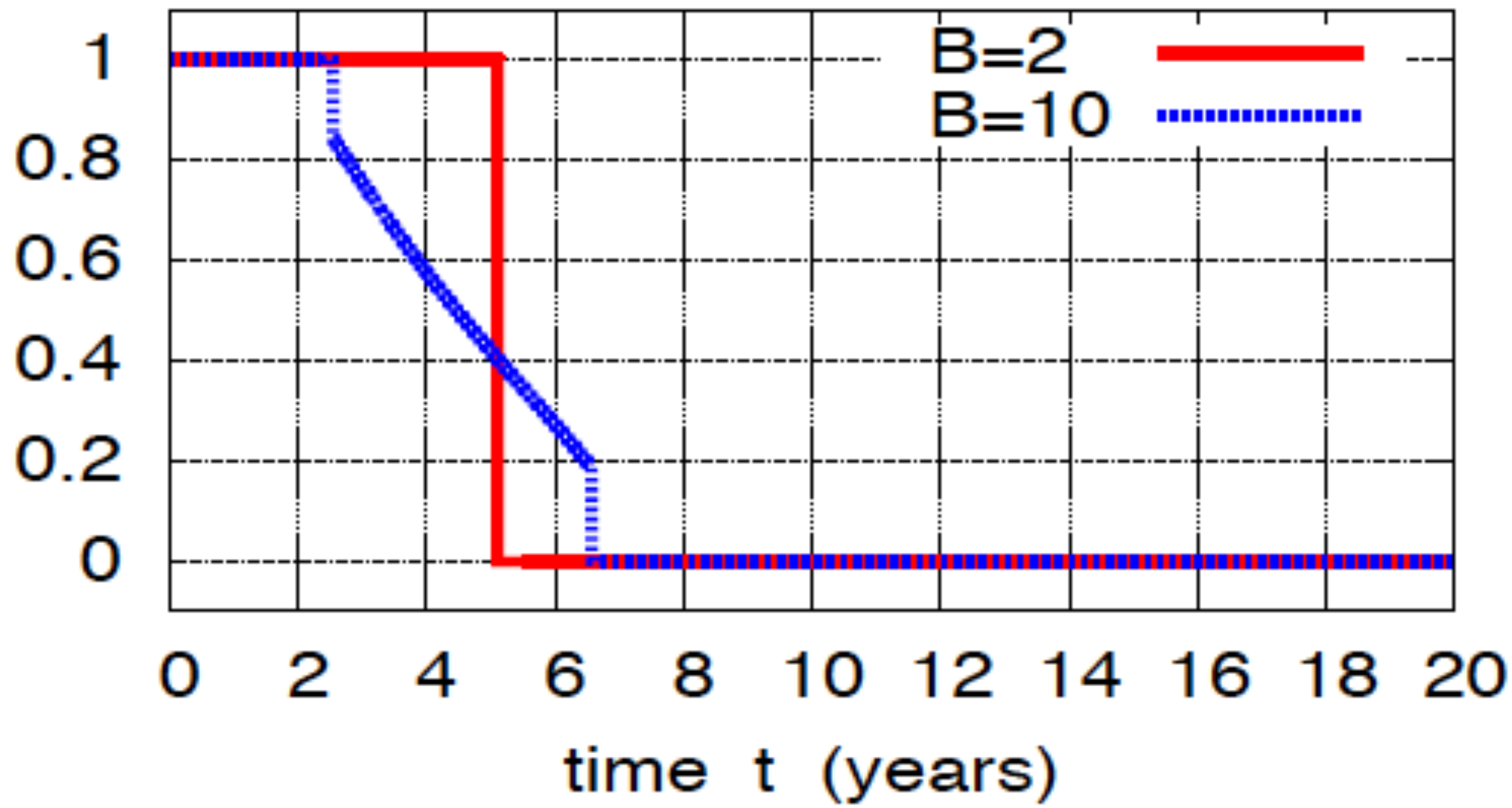
L^1 cost Problem

$$
\left\{
\begin{aligned}
&\text{Minimize } \int_0^T (AI(t) + Bu(t))\,dt \\
&\text{subject to} \\
&\dot{S}(t) = bN(t) - dS(t) - c\frac{S(t)I(t)}{N(t)} - S(t)u(t), \\
&\dot{E}(t) = c\frac{S(t)I(t)}{N(t)} - (f+d)E(t), \\
&\dot{I}(t) = fE(t) - (g+a+d)I(t), \\
&\dot{W}(t) = S(t)u(t), \\
&\dot{N}(t) = (b-d)N(t) - aI(t), \\
&u(t) \in [0,1] \text{ a.e. } t, \\
&x(0) = x_0.
\end{aligned}
\right.
$$

Counting number of vaccines ($\dot{W}(t) = S(t)u(t)$)

$$
\begin{aligned}
&\text{Minimize } \int_0^T (Ax(t) + Bu(t))\,dt \\
&\text{subject to} \\
&\dot{x}(t) = f(x(t)) - g(x(t))u(t), \\
&u(t) \in [0,1] \text{ a.e. } t, \\
&x(0) = x_0.
\end{aligned}
$$

L^1 Cost: Optimal Controls



Bang- Bang and Bang- Singular- Bang

Numerical Software

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*

Validation of numerical solutions

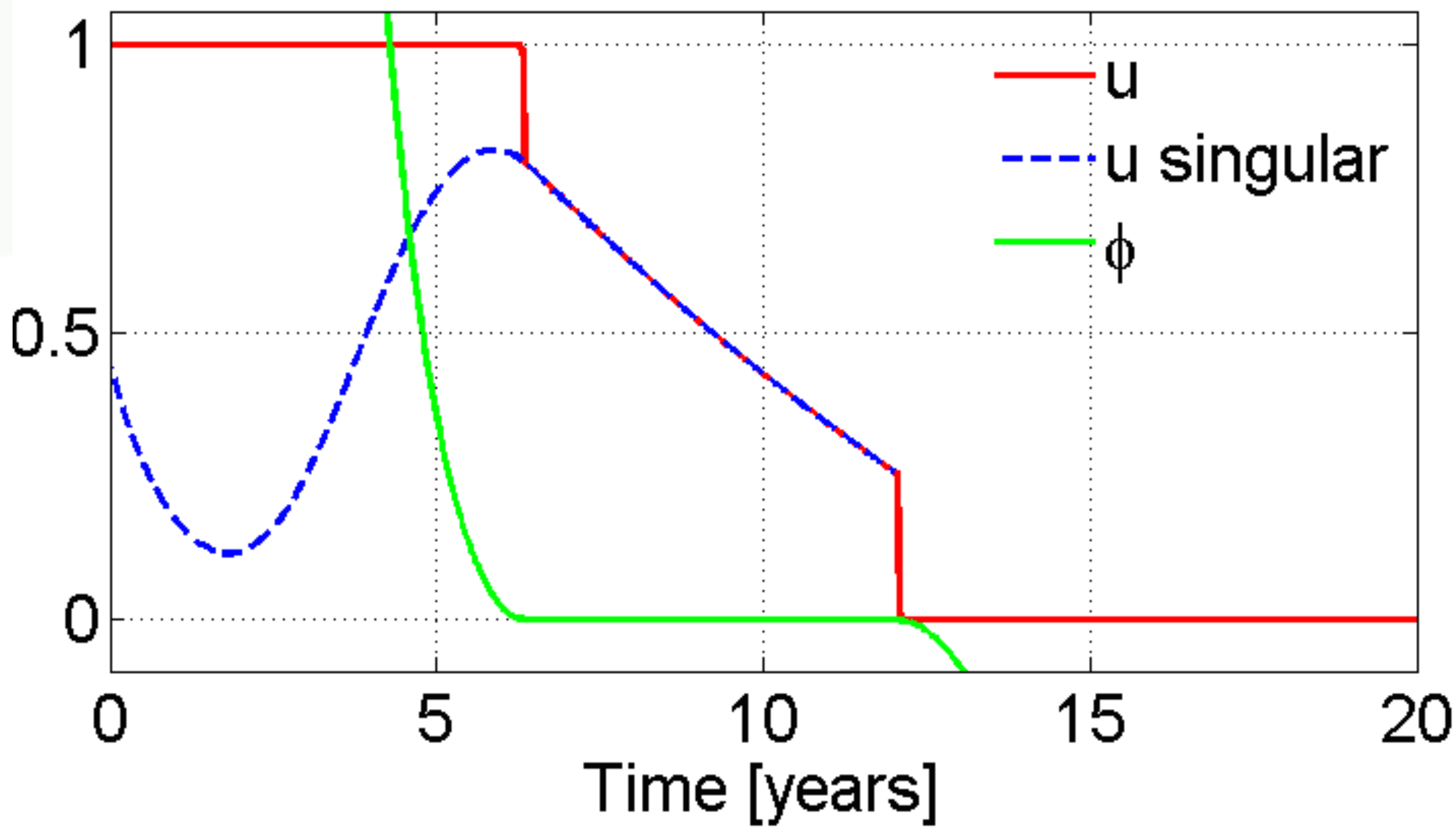
Both AMPL and **ICLOCS** provide the numerical multipliers.

In all the above cases we validate numerical solutions using necesary 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.**

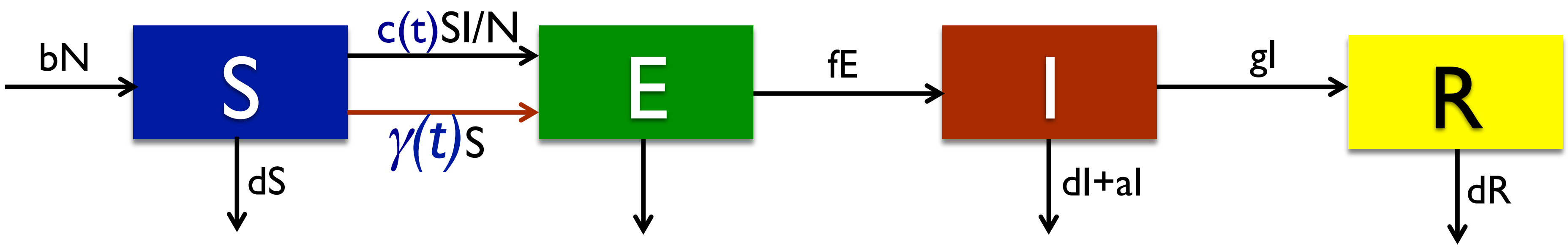
Validation of numerical solutions



3. Periodic Incidence Rate

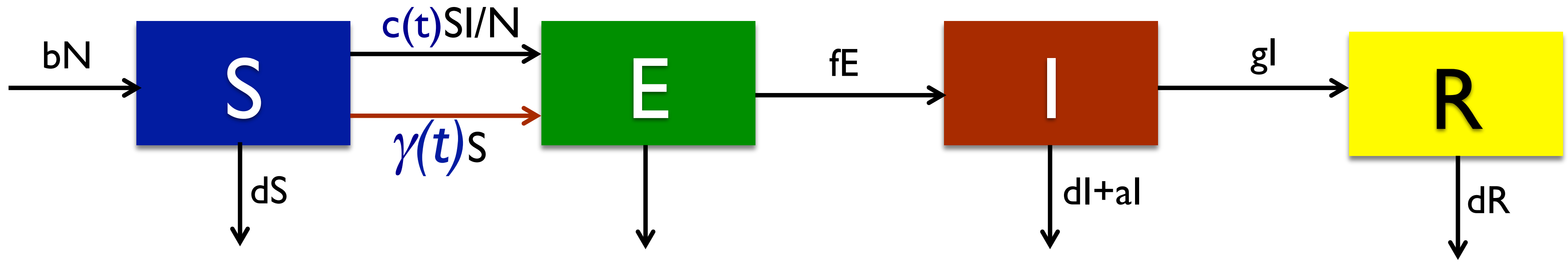
Suppose that

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



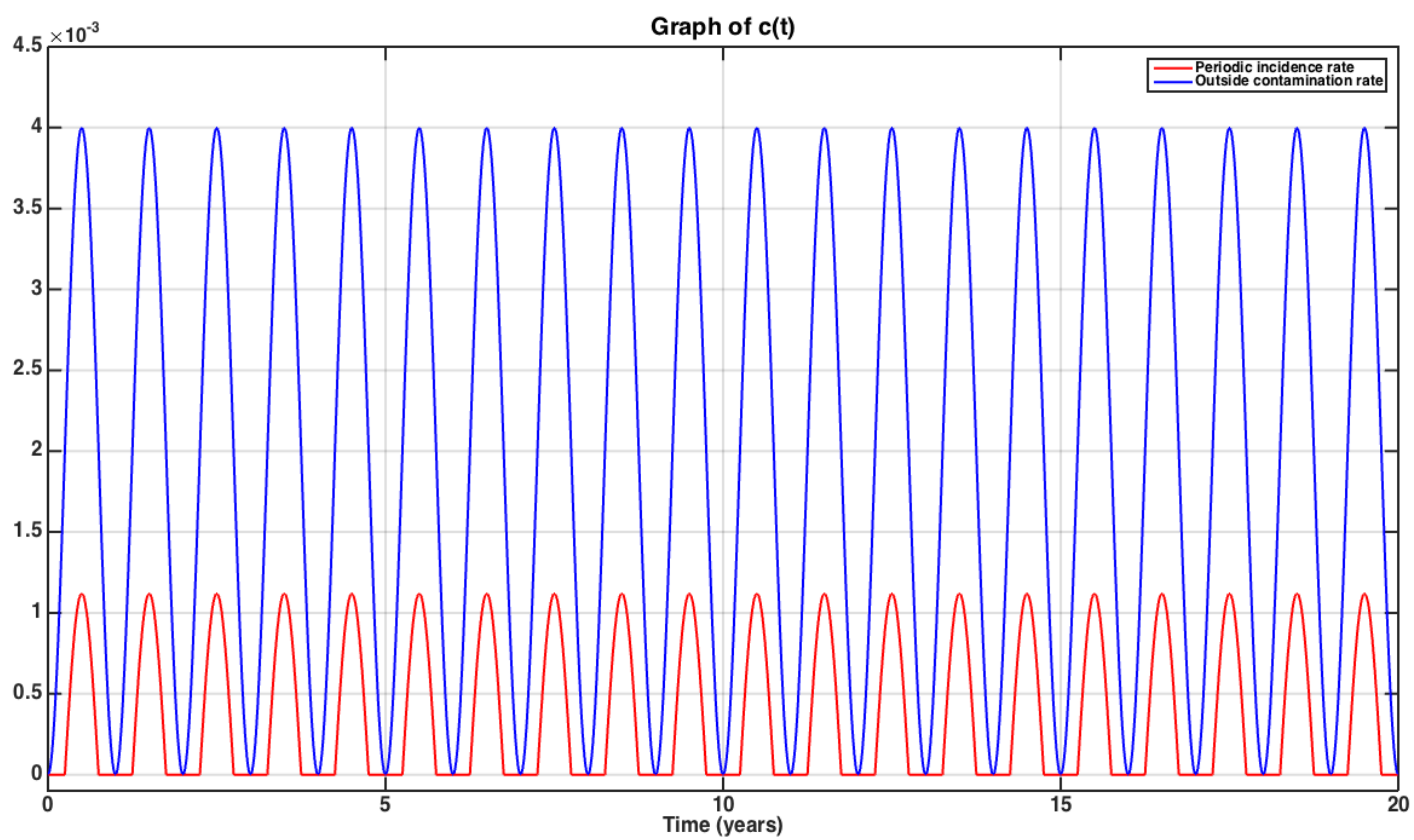
$$\begin{cases} \dot{S}(t) = bN(t) - (d + \gamma(\mathbf{t}))S(t) - \mathbf{c}(\mathbf{t})\dfrac{S(t)I(t)}{N(t)}, \\ \dot{E}(t) = \mathbf{c}(\mathbf{t})\dfrac{S(t)I(t)}{N(t)} + \gamma(\mathbf{t})S(t) - (f + d)E(t), \\ \dot{I}(t) = fE(t) - (g + a + d)I(t), \\ \dot{R}(t) = gI(t) - dR(t), \\ \dot{N}(t) = (b - d)N(t) - aI(t). \end{cases}$$

3. Periodic Incidence Rate



where

$$\begin{cases} c(t) = max\,\{c_0(1+\delta\sin(2\pi t-\pi/2), c_0\} - c_0 \\ \gamma(t) = \gamma_0(1+\sin(2\pi t-\pi/2)) \end{cases}$$



3. Periodic Incidence Rate

Parameter	Description	Value
b	natural birth rate	0.012
d	natural death rate	0.009
c_0	"incidence" coefficient	0.004
δ	"incidence" coefficient	0.28
γ_0	"incidence" coefficient	0.002
e	exposed to infectious rate	0.8
g	recovery rate	0.15
a	disease induced death rate	0.01
T	number of years	20
S_0	initial susceptible population	1165
E_0	initial exposed population	0
I_0	initial infected population	0
R_0	initial recovered population	0
N_0	initial population	1165
W_0	initial vaccinated population	0

~~European values

For t=0 population free of disease

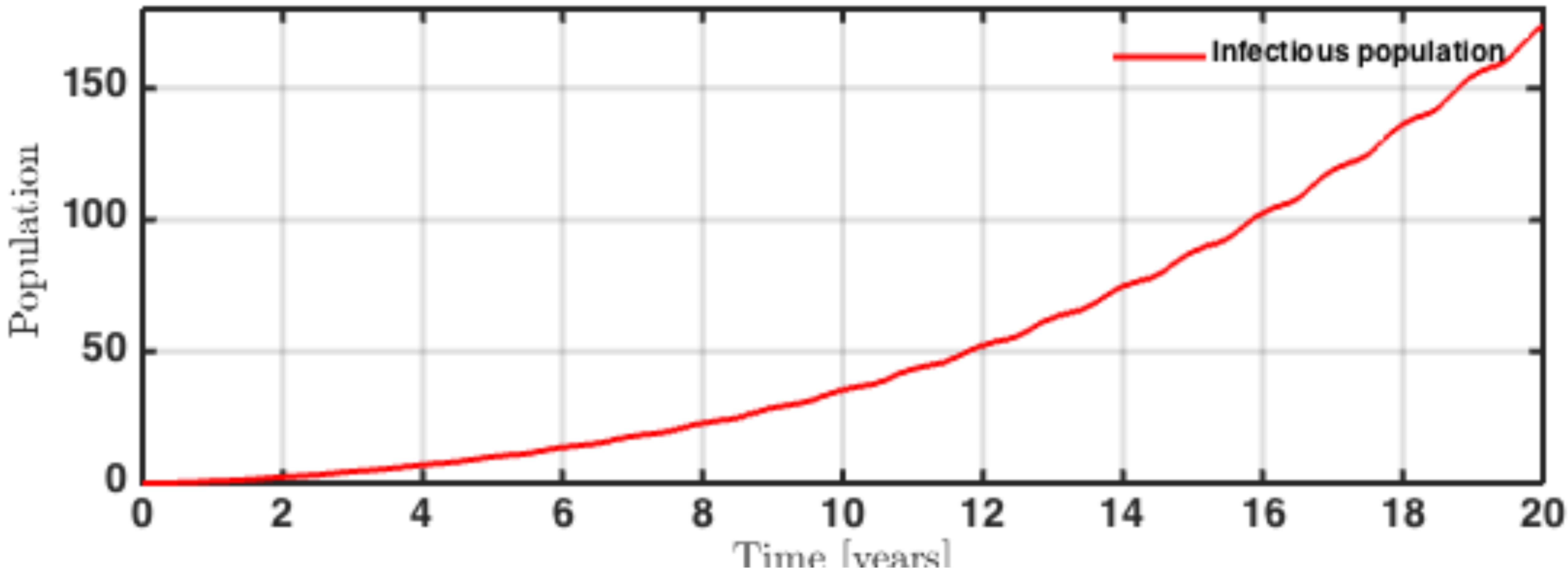
DISEASE PARAMETERS ARE NOT **CLINICAL VALUES**

3. Periodic Incidence Rate

Without Control

N(20)=1226

I(20)> 150



OCP with A=1and B=2

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

subject to

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

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

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

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

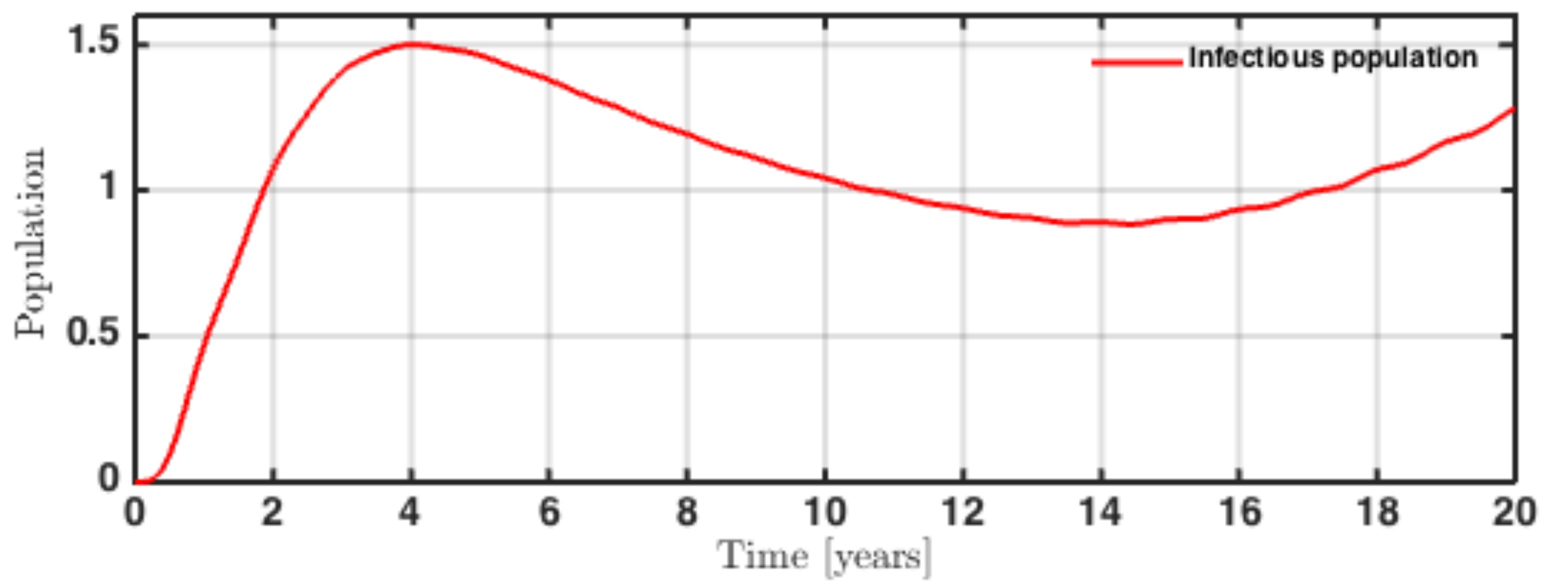
$$u(t) \in [0, 1] \text{ a.e. } t,$$

$$x(0) = x_0.$$

3. Periodic Incidence Rate

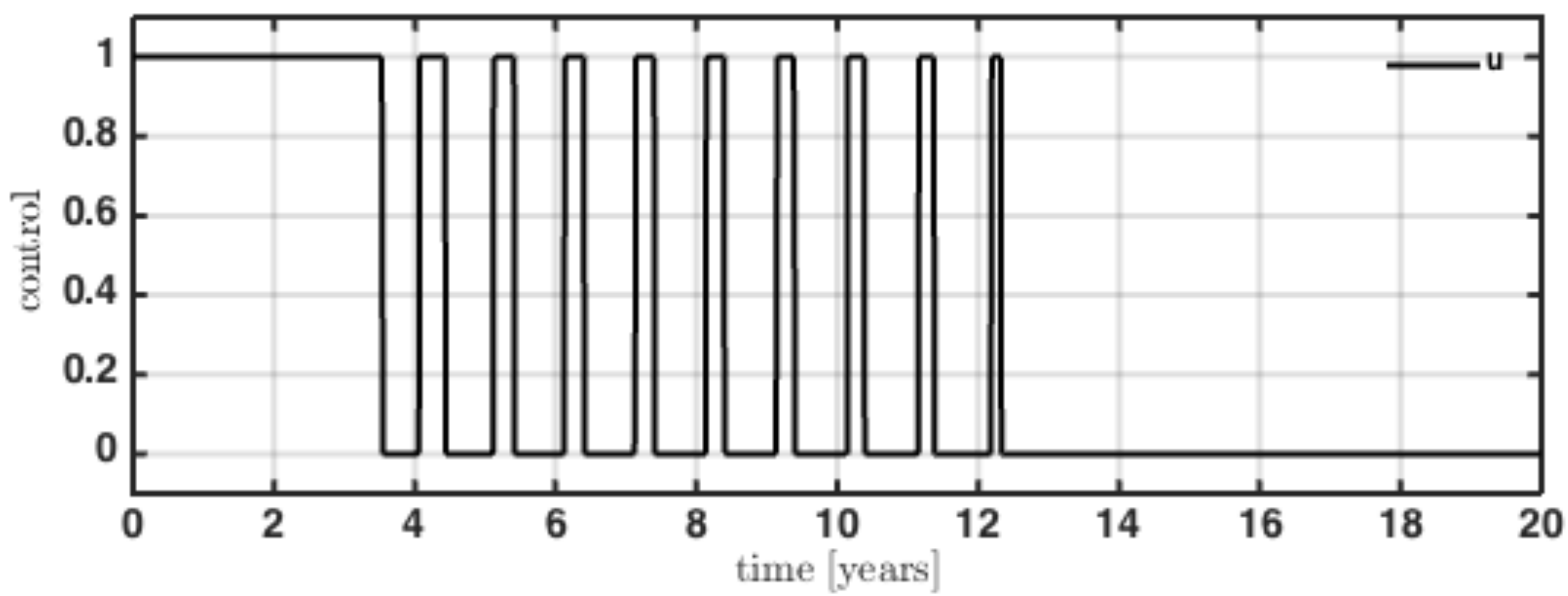
OCP with A=1and B=2

Infected I



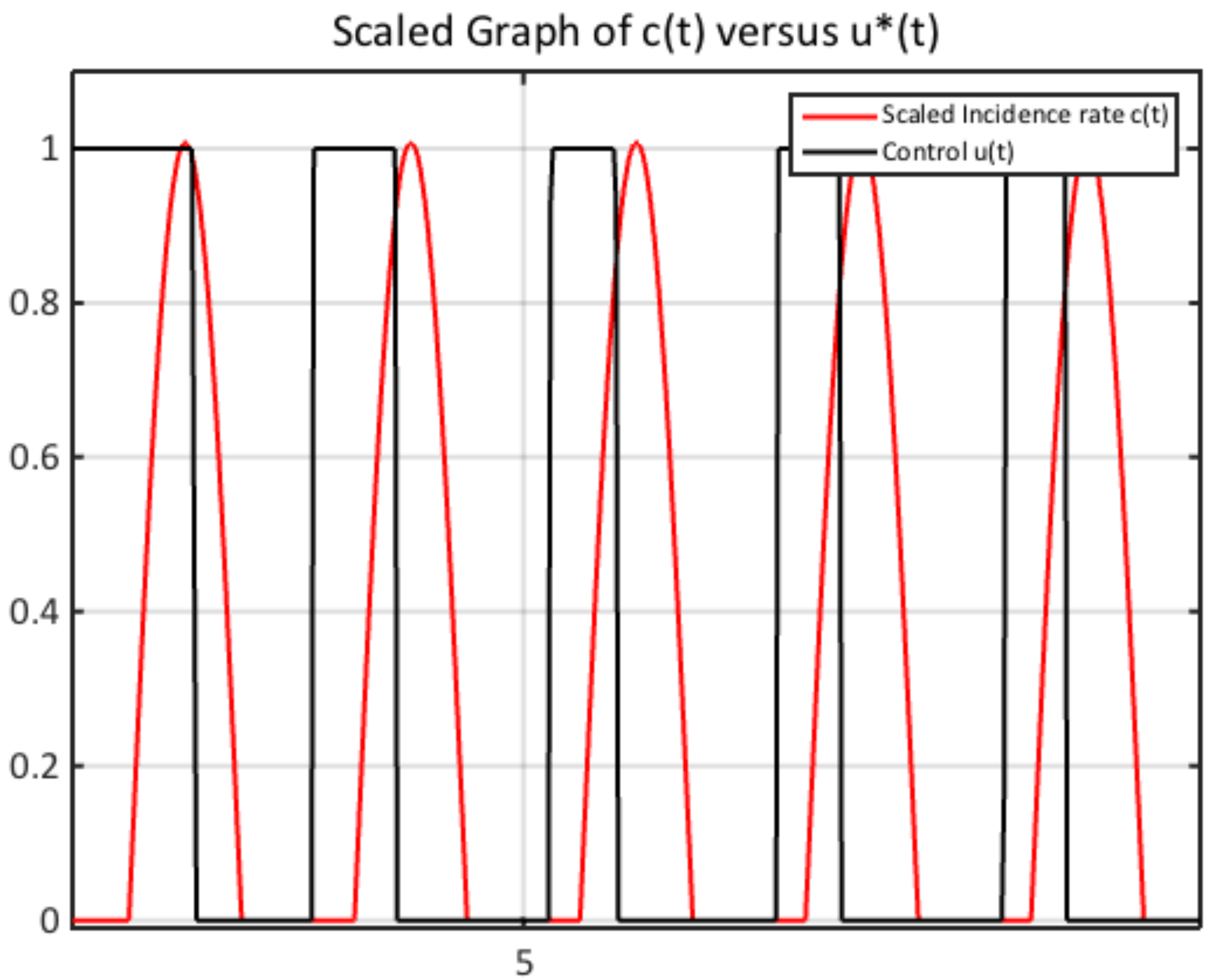
N(20)=1236>1226.

Control u



3. Periodic Incidence Rate

OCP with A=1and B=2

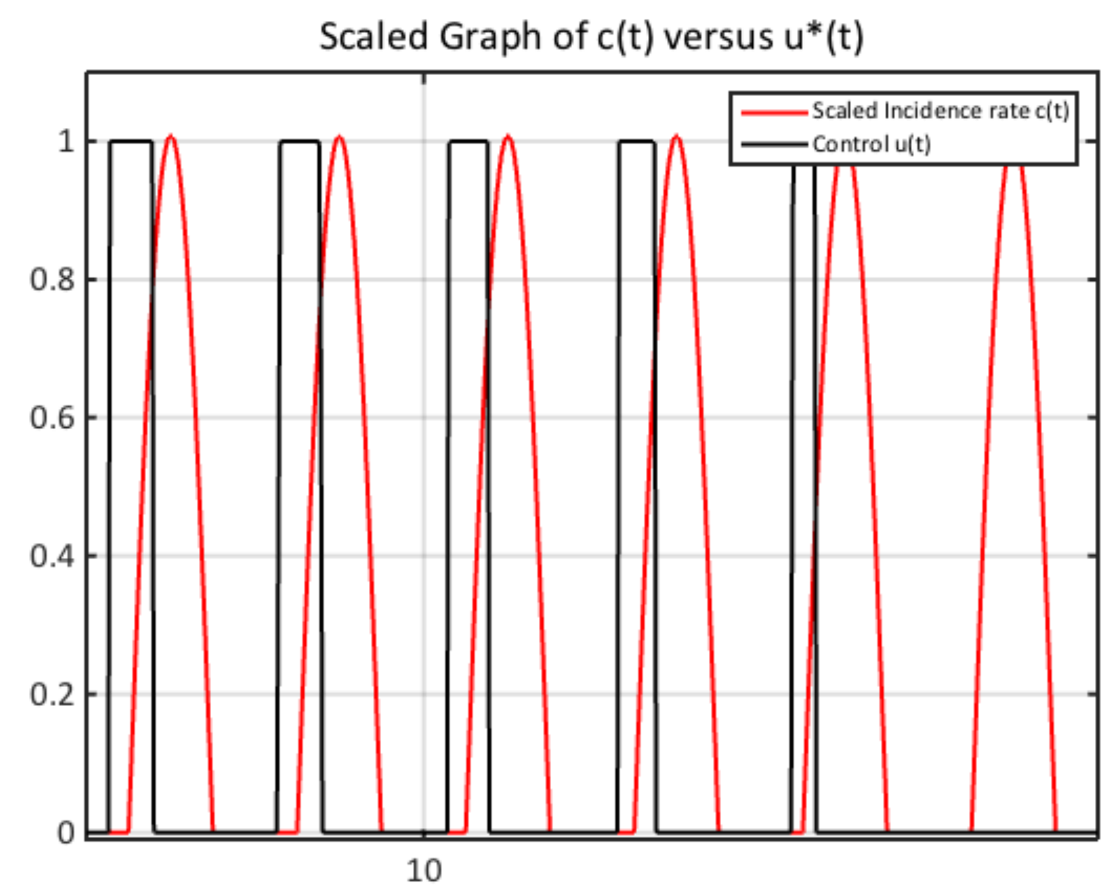


Cost: **32**

W(20)~130,

N(20)~1237,

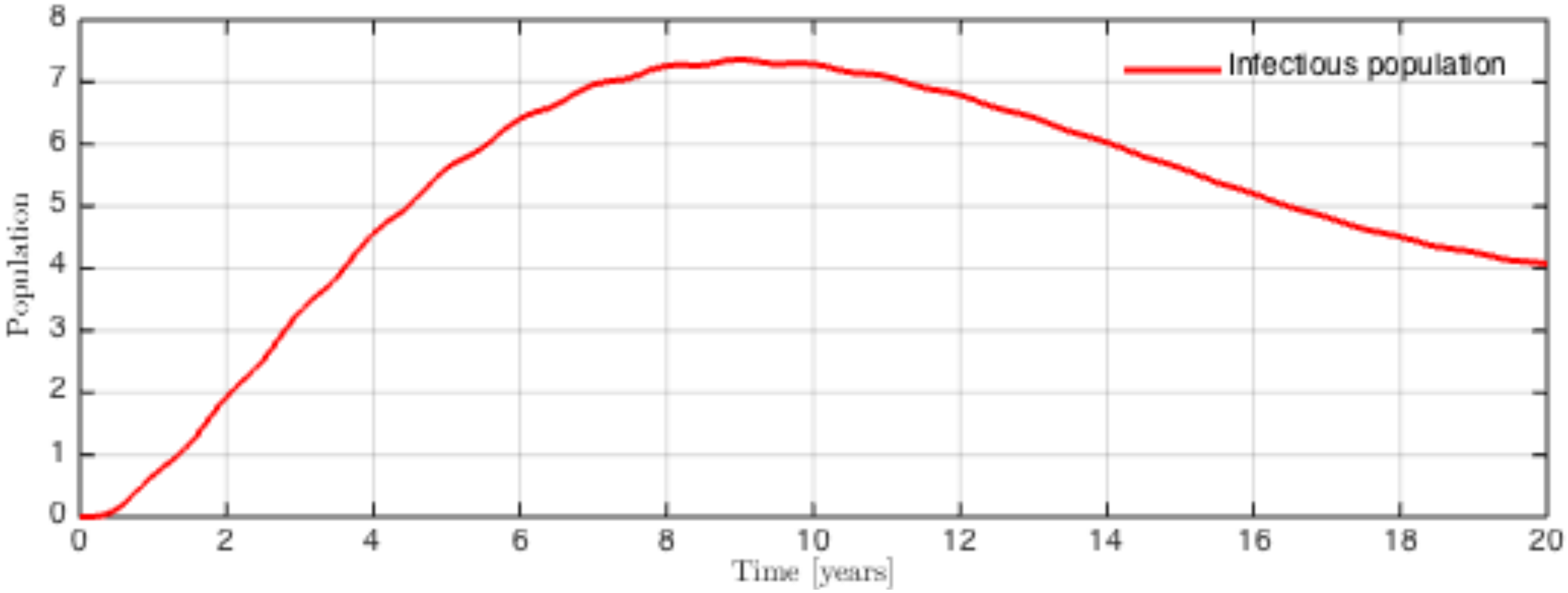
I(20)=1



$$0 \leq u \leq 1$$

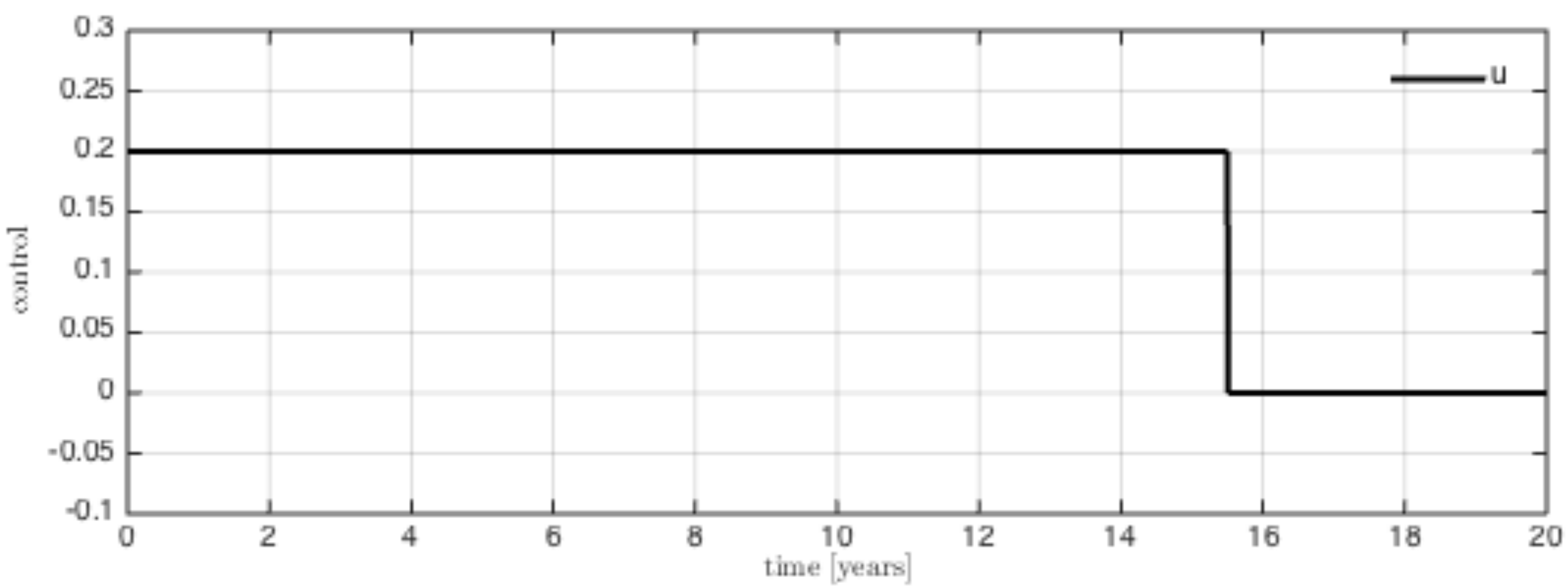
3. Periodic Incidence Rate

$$\text{OCP with } 0 \leq u \leq 0.2$$



Cost: **110** (vs 32)

I(20)=4



Recall that treatment of infected people is expensive

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.

Idea: Normalization of the population.

$$s(t) = \frac{S(t)}{N(t)}, \quad e(t) = \frac{E(t)}{N(t)}, \quad i(t) = \frac{I(t)}{N(t)}, \quad r(t) = \frac{R(t)}{N(t)},$$

and

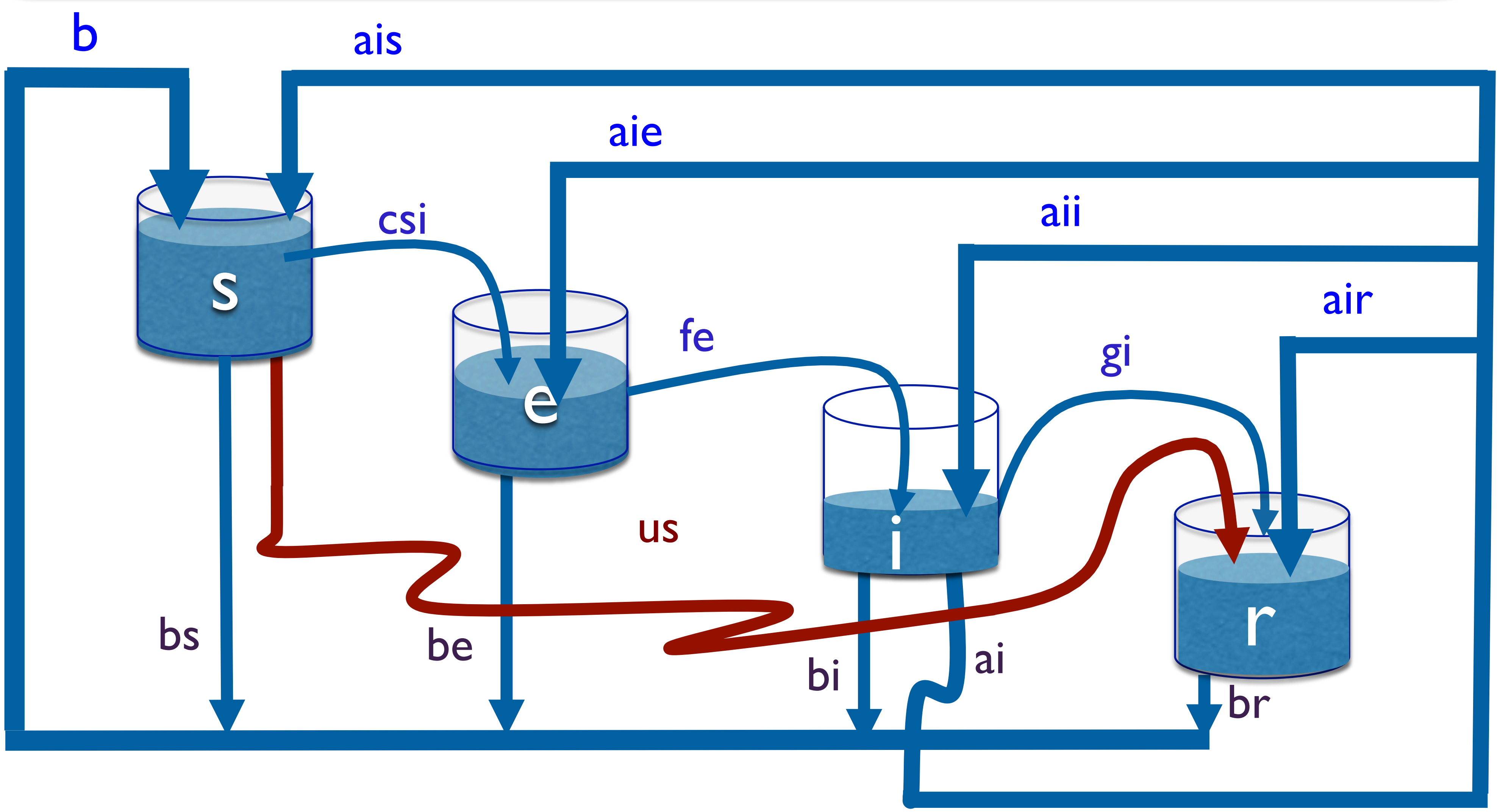
$$s(t) + e(t) + i(t) + r(t) = 1 \text{ for all } t.$$

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

$$
\begin{aligned}
\dot{s}(t) =& b - cs(t)i(t) - bs(t) + ai(t)s(t) - u(t)s(t),\\
\dot{e}(t) =& cs(t)i(t) - (f+b)e(t) + ai(t)e(t),\\
\dot{i}(t) =& fe(t) - (g+a+b)i(t) + ai^2(t),\\
\dot{r}(t) =& gi(t) - rb(t) + ai(t)r(t) + u(t)s(t).
\end{aligned}
$$



Choice of Cost

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 minimzing

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

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 π is *roughly* approximated to the average of TOTAL population in T years.

4. Normalized SEIR Model

Parameters

Parameter	Description	Value
b	Natural birth rate	0.011
d	Death rate	0.009
c	Incidence coefficient in (P)	1.1
f	Exposed to infectious rate	0.5
g	Recovery rate	0.1
a	Disease induced death rate	0.2
A	weight of infected population	3
B	weight of the vaccination effort	10
ρ	Weight parameter	300
T	Number of years	20
s_0	Initial susceptible population	0.858
e_0	Initial exposed population	0.086
i_0	Initial infected population	0.043

Very high

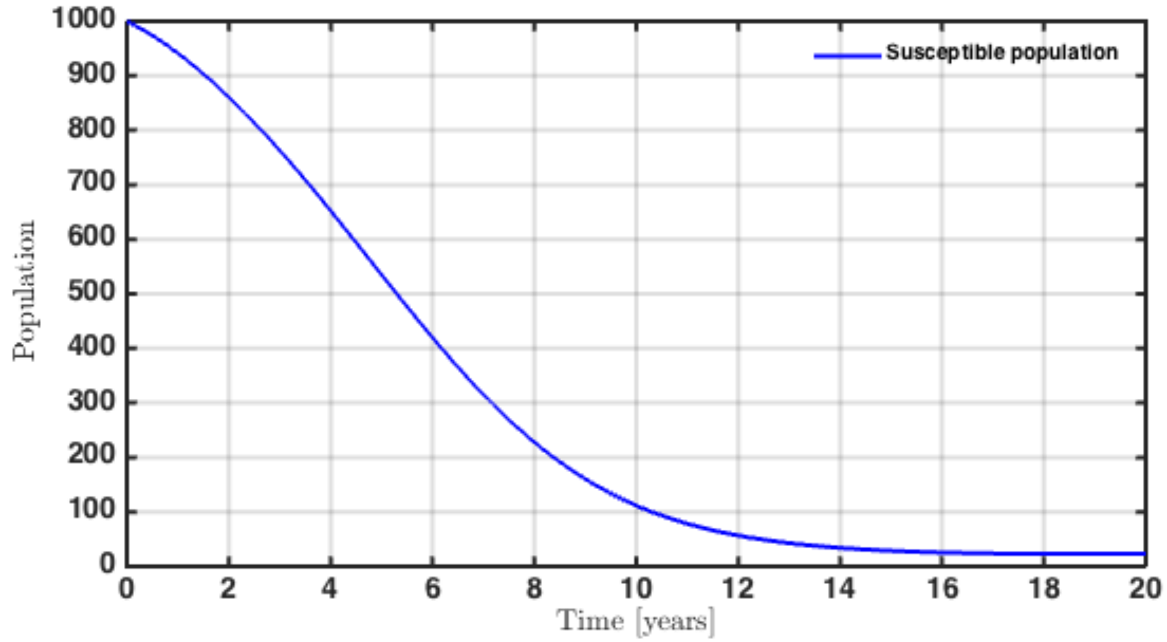
$(A = 3, B = 10, \pi = 1000)$

In the above table we have $s_0 = S_0/N_0$, $e_0 = E_0/N_0$ and $i_0 = I_0/N_0$ where $N_0 = 1165$, $S_0 = 1000$, $I_0 = 50$ and $E_0 = 100$ are the values used in M&dP 15 and L&N10.

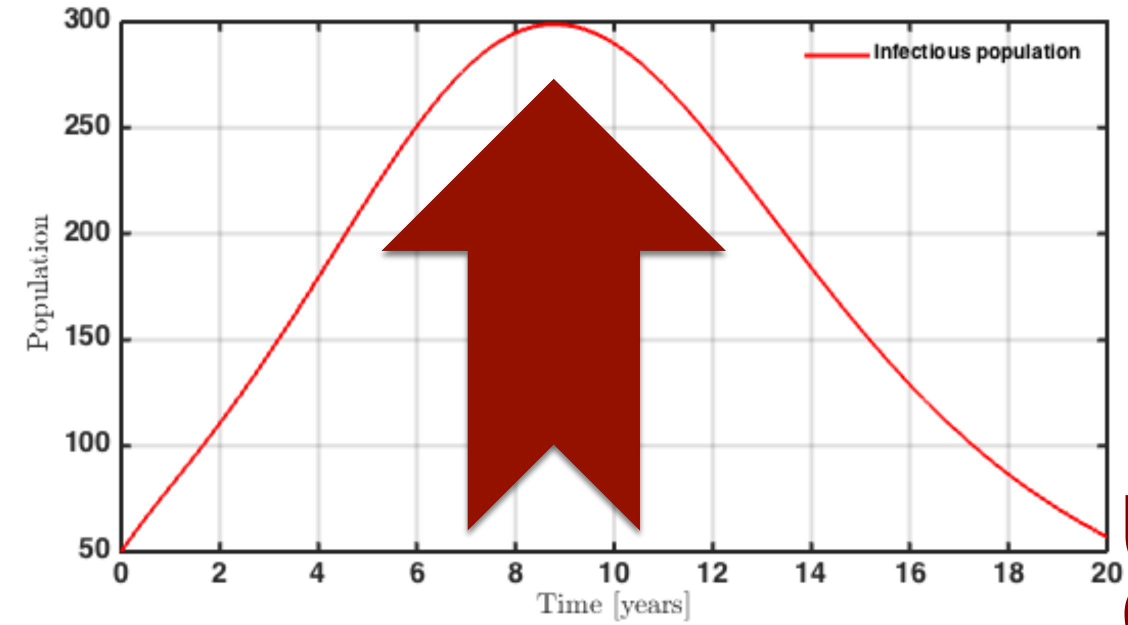
3. Normalized SEIR Model

Systems with **NO control**

Susceptible population

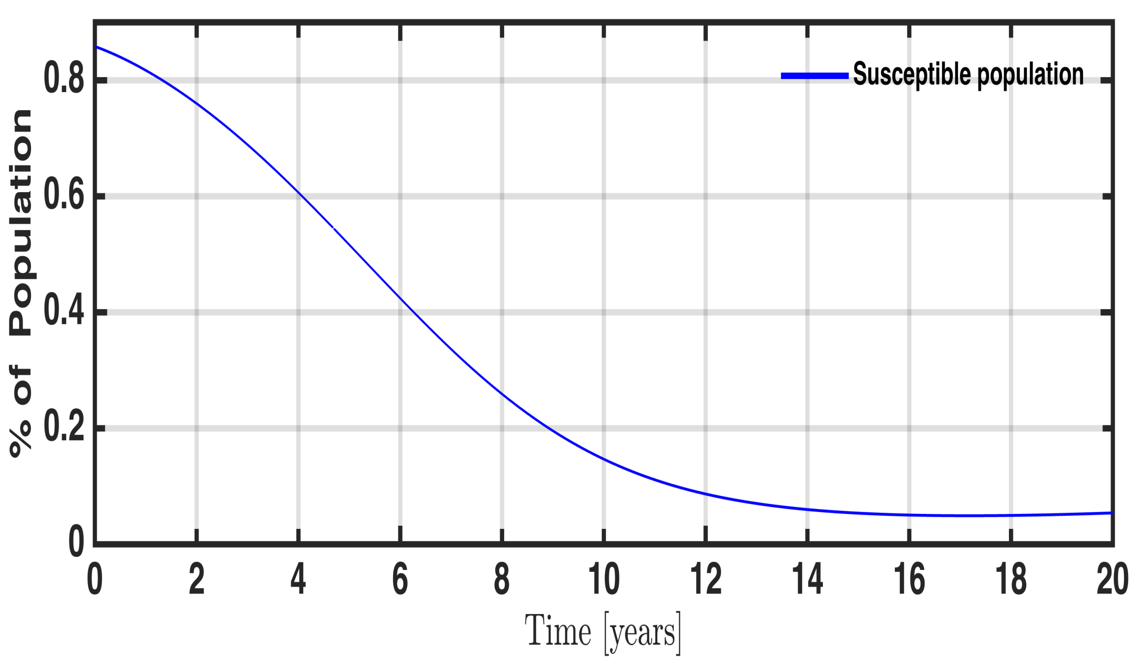


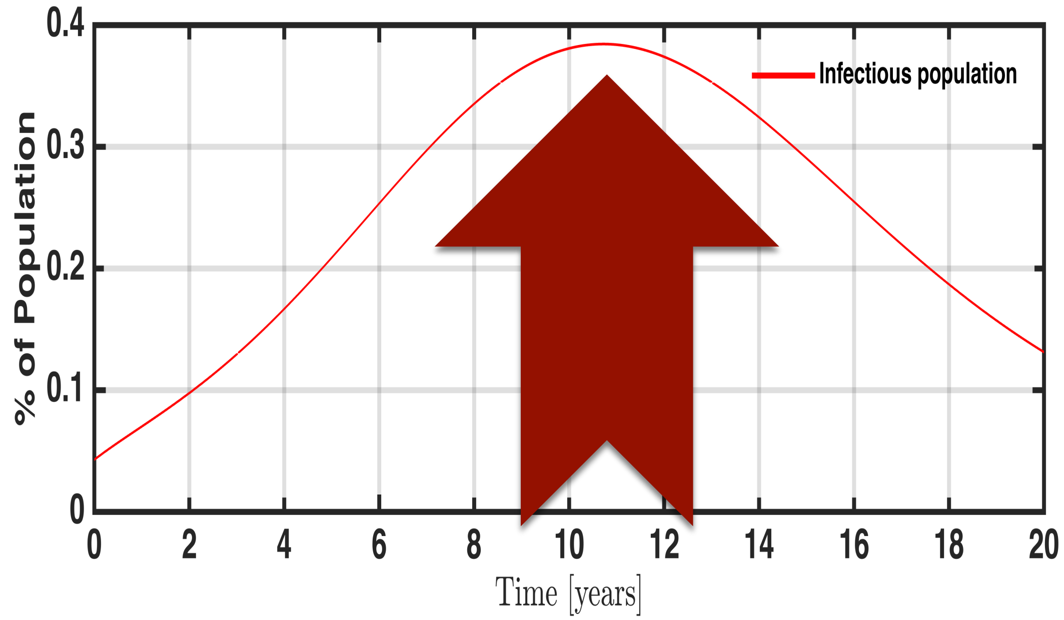
Infected population



Deadly!

NORMALIZED





Comparison of Problems

Not Normalized Problem

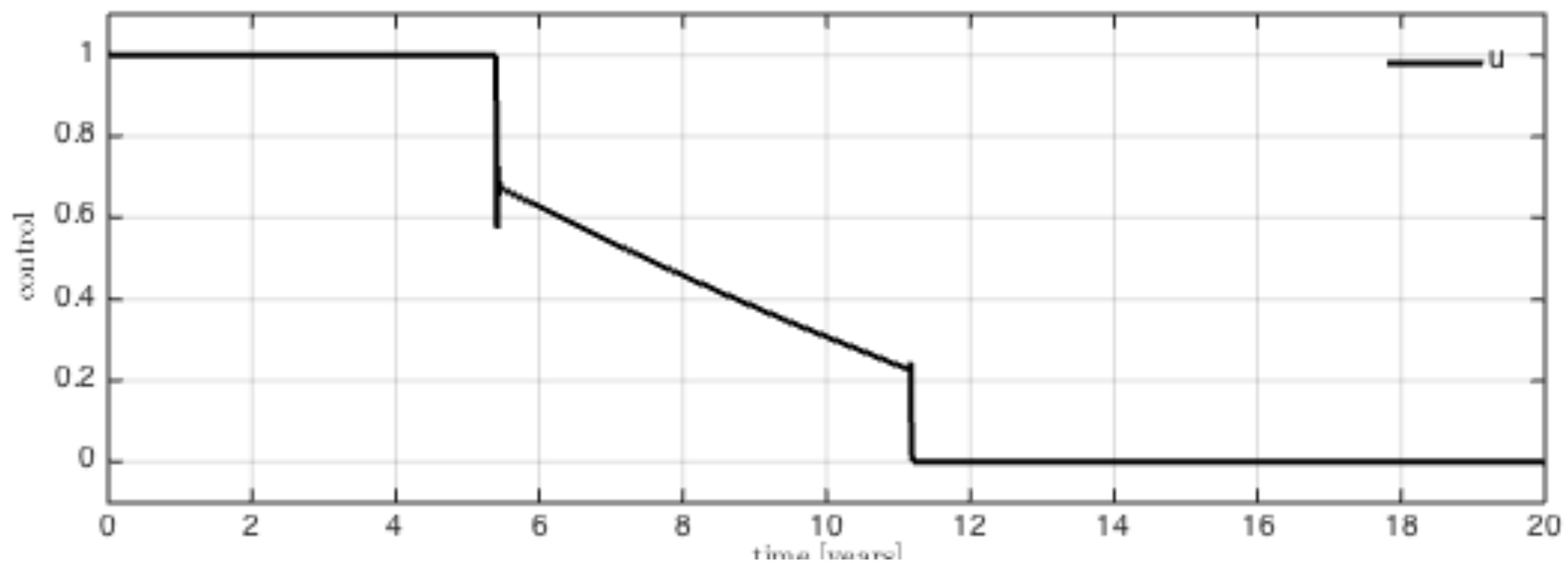
$$\begin{cases} \text{Minimize} \quad \int_0^T (AI(t) + Bu(t))\, dt \\ \text{subject to} \\ \quad \dot{S}(t) = bN(t) - dS(t) - c\frac{S(t)I(t)}{N(t)} - u(t)S(t), \\ \quad \dot{E}(t) = c\frac{S(t)I(t)}{N(t)} - (f+d)E(t), \\ \quad \dot{I}(t) = fE(t) - (g+a+d)I(t), \\ \quad \dot{N}(t) = (b-d)N(t) - aI(t), \\ \quad u(t) \in [0,1] \quad \text{for æ} \quad t \in [0,T], \\ \quad x(0) = x_0 = (S_0, E_0, I_0, N_0). \end{cases}$$

Normalized Problem

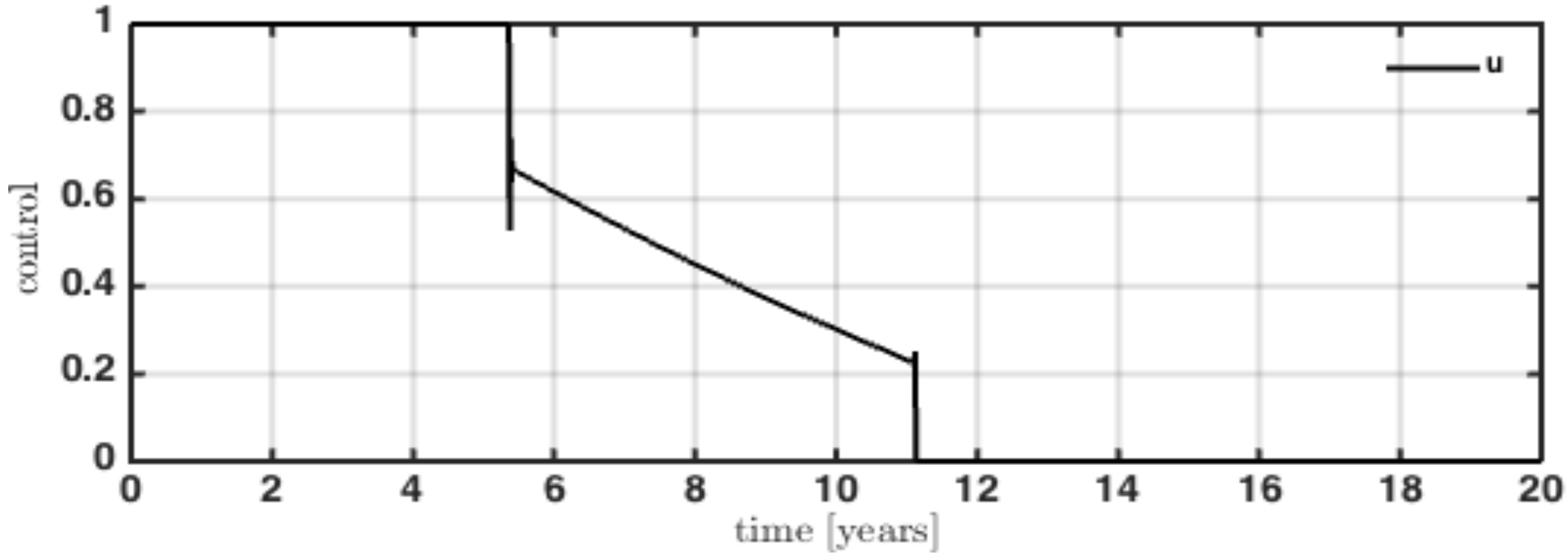
$$\begin{cases} \text{Minimize} \quad \int_0^T (\rho i(t) + u(t)))\, dt \\ \text{subject to} \\ \quad \dot{s}(t) = b - cs(t)i(t) - bs(t) + ai(t)s(t) - u(t)s(t), \\ \quad \dot{e}(t) = cs(t)i(t) - (f+b)e(t) + ai(t)e(t), \\ \quad \dot{i}(t) = fe(t) - (g+a+b)i(t) + ai^2(t), \\ \quad u(t) \in [0,1] \quad \text{for a. e.} \quad t \in [0,T], \\ \quad x(0) = (s(0), e(0), i(0)) = (s_0, e_0, i_0). \end{cases}$$

Comparison of Problems

Classical Model: A=3, B=10



Normalized Model: ρ=300

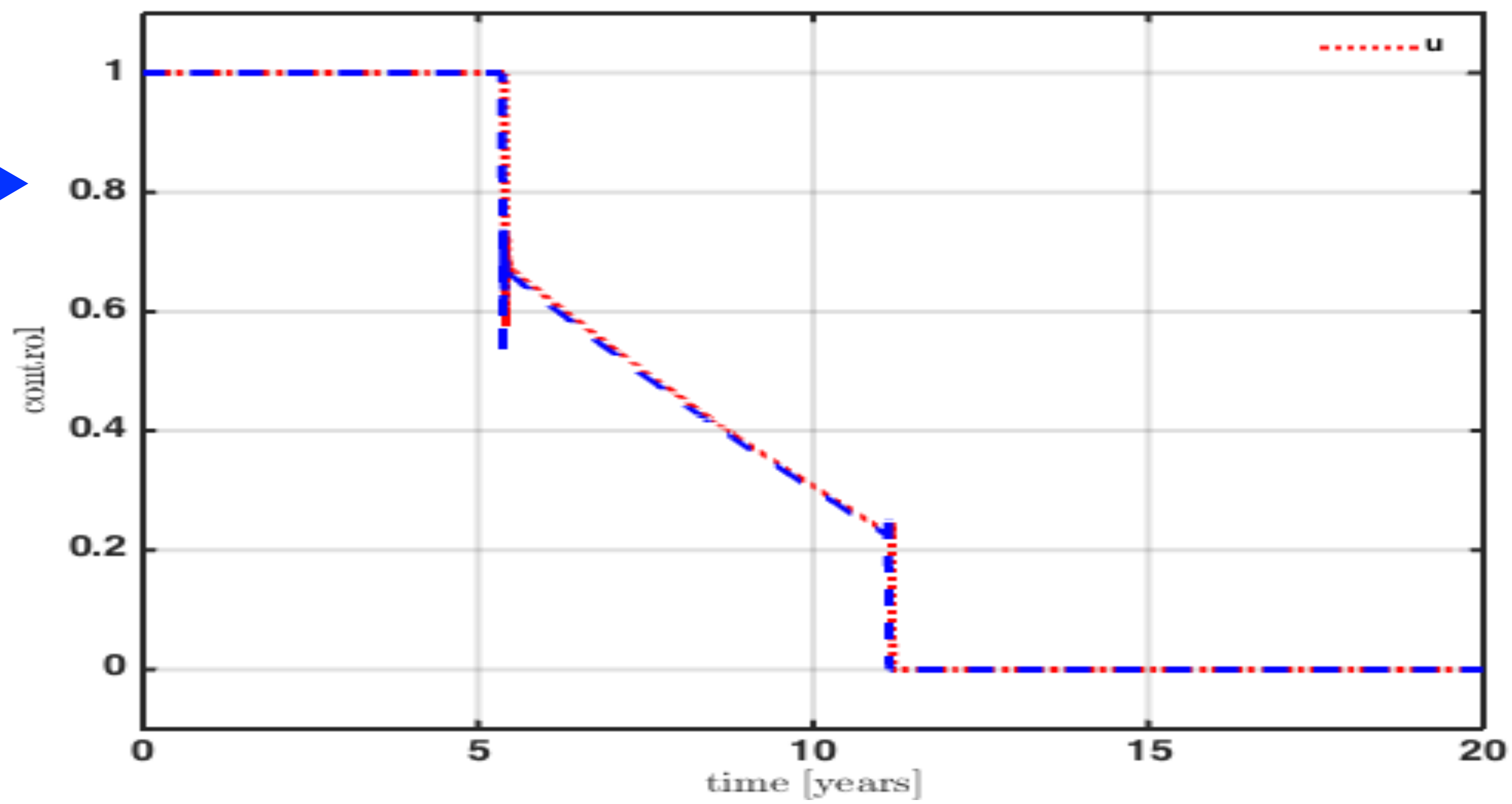


4. Normalized SEIR Model

Comparison of Problems

Classical Model: A=3, B=10

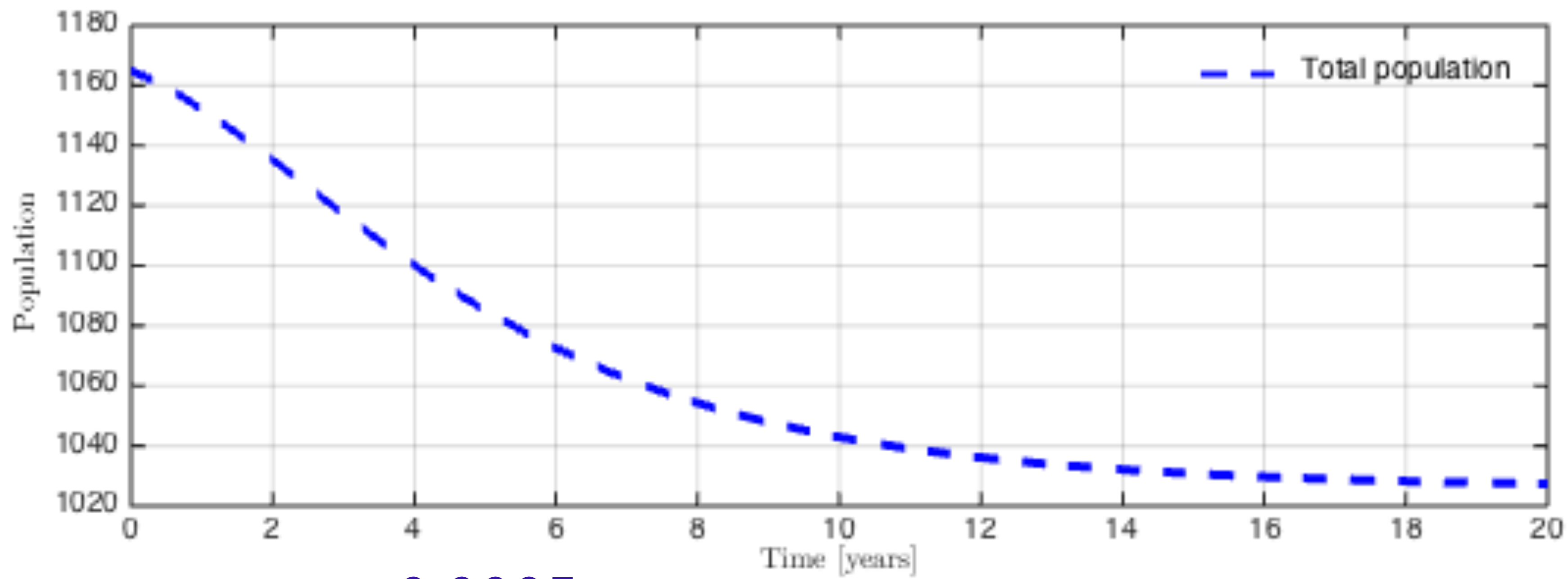
Normalized Model: ρ=300



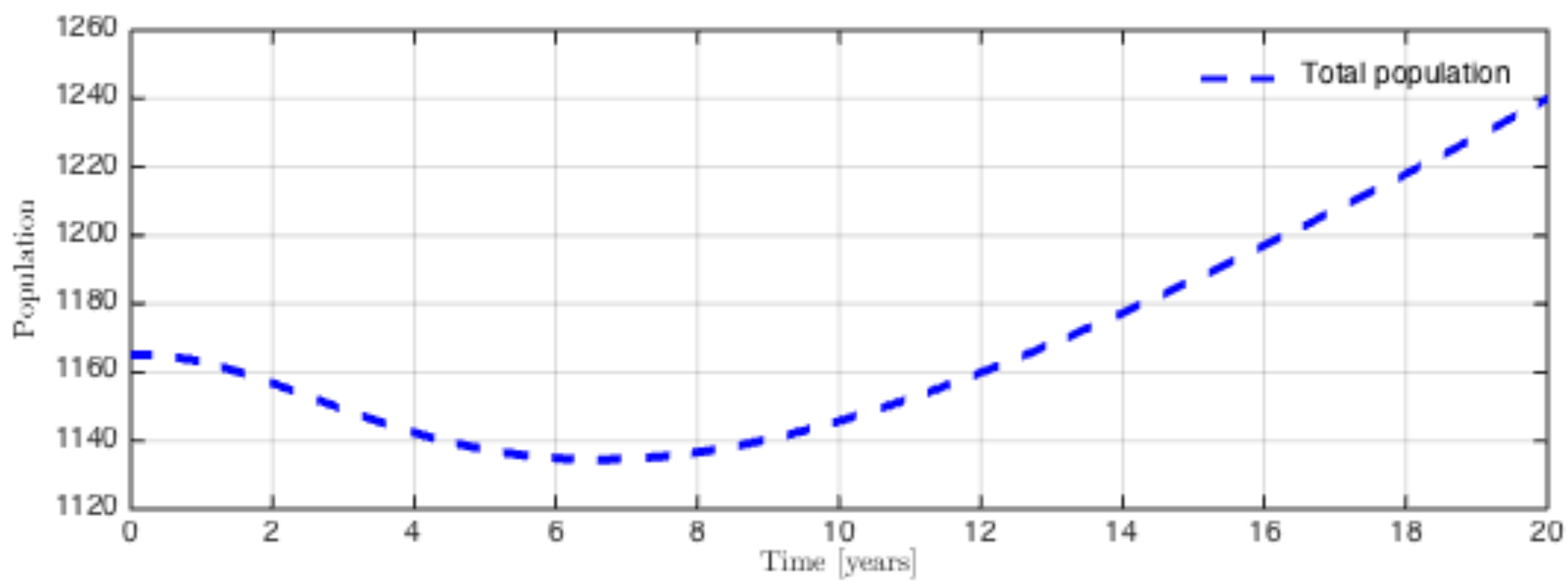
4. Normalized SEIR Model

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

Classical Model: A=3, B10, d=0.0099



Classical Model: A=3, B10, d=0.0005

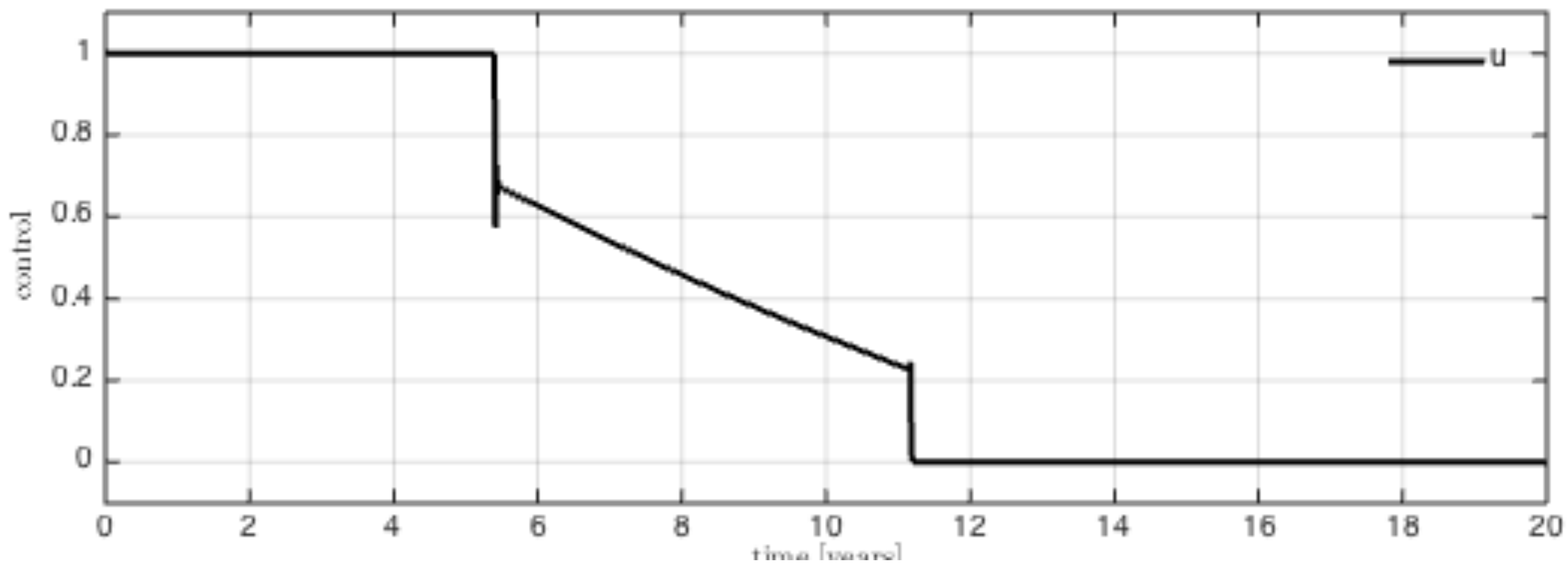


Total population

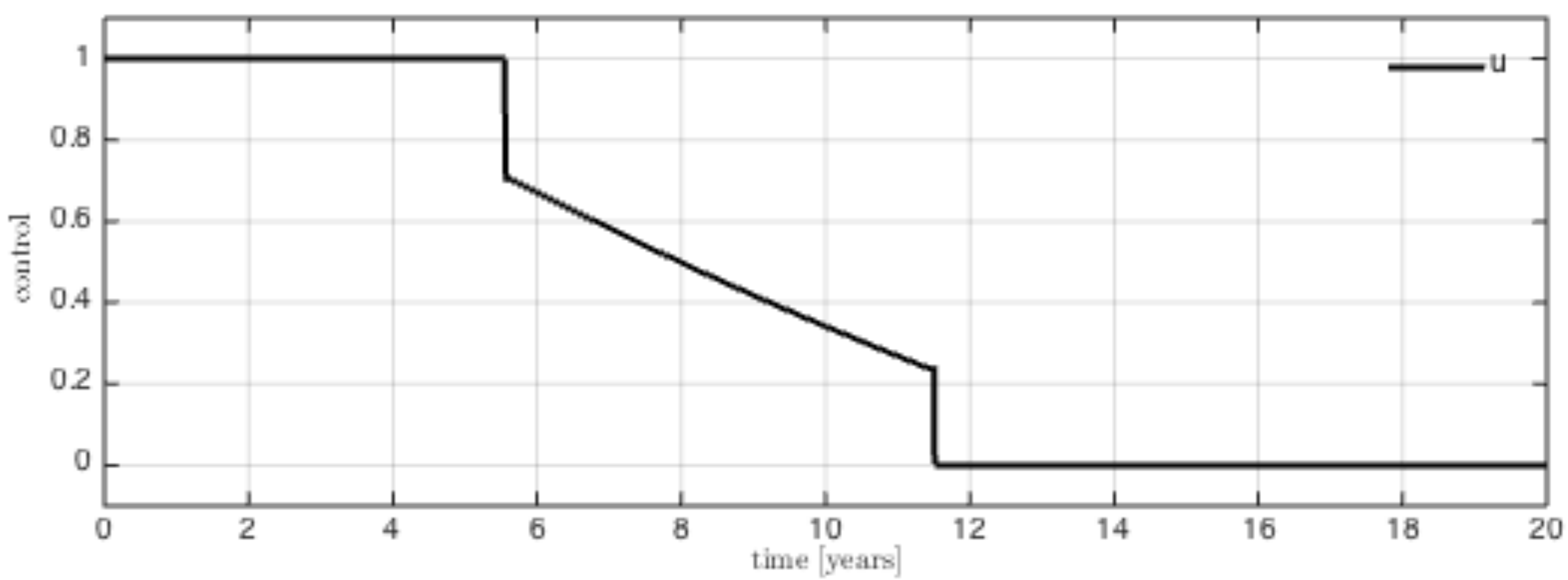
4. Normalized SEIR Model

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

Classical Model: A=3, B10, d=0.0099



Classical Model: A=3, B10, d=0.0005



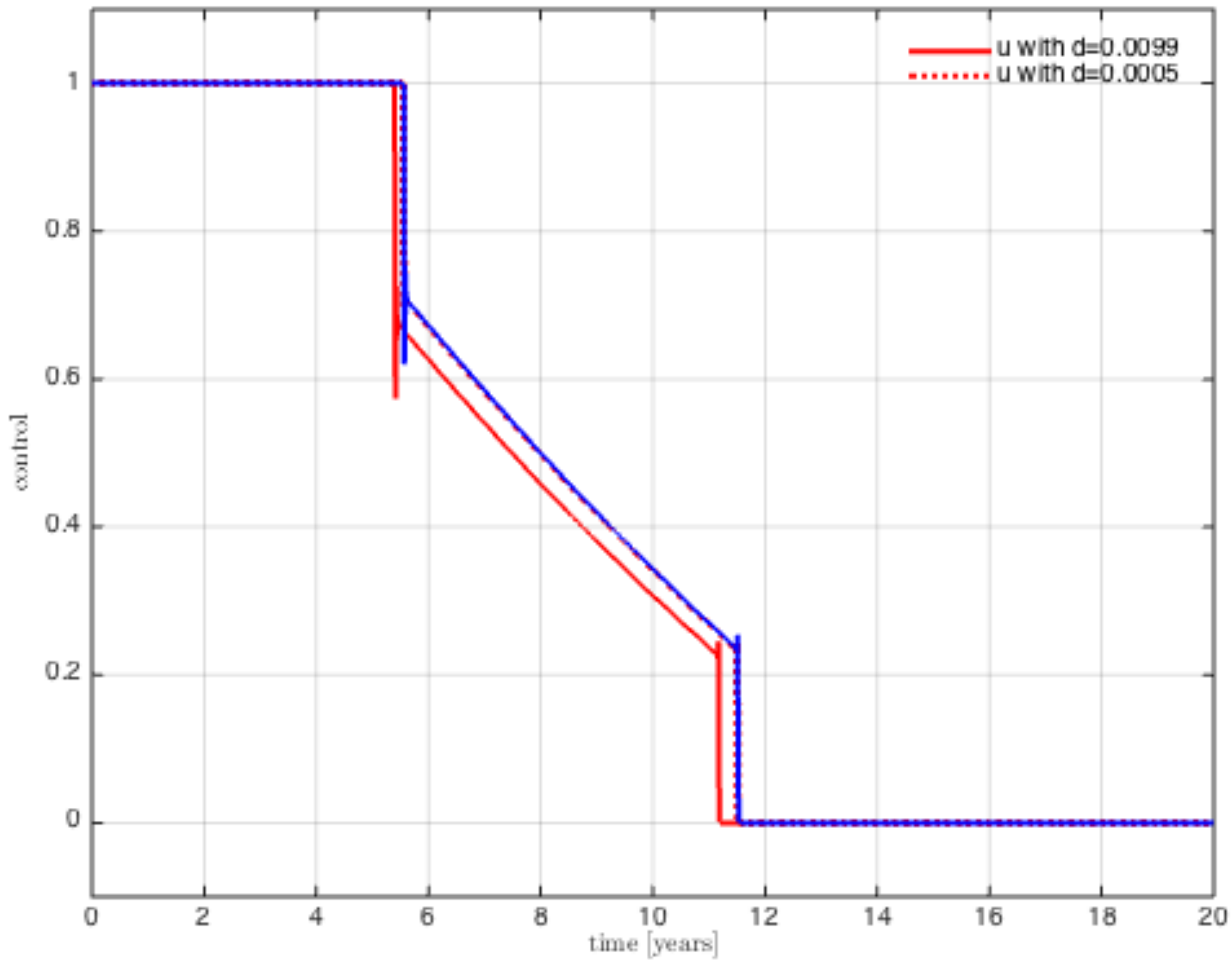
Control u

Comparison of Problems

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**



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 ρ in **the cost**.

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

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

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

$$\rho = \frac{A * \pi}{B}.$$

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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Thank you for your attention