Numerical Methods for optimal control

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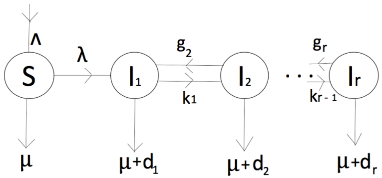
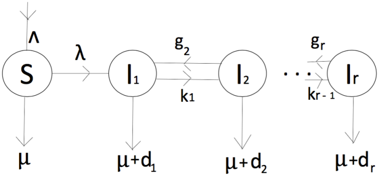

Λ
λ
S
I1
g2
k1
I2
gr
kr - 1
Ir
μ
μ+d1
μ+d2
μ+dr

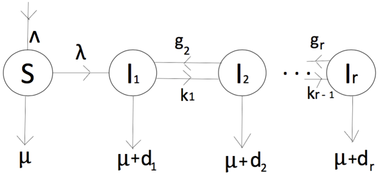


- $bN = \Lambda$: All recruitment in the population is in the susceptible compartment.
- $k_m I_m$: The transition rate from the class I_m to I_{m+1} .
- $g_{m+1} I_{m+1}$: The transition rate of I_{m+1} to I_m.
- μ : The natural death rate, d_m the over-mortalities due at the infection.
- $\lambda = c\beta_m \dfrac{I_m(t)}{N(t)}$: The force of infection associated of the model.
- β_m : The probability that contact between an infected of the class I_m and a susceptible to result in infection.
- c : The number of contacts for a susceptible per unit time.

$$
\begin{cases}
\dot{S}(t) &= \Lambda - \mu S(t) - \displaystyle\sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t); \\
\dot{I}_1(t) &= \displaystyle\sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t) - (k_1 + \mu + d_1) I_1 + g_2 I_2; \\
\dot{I}_2(t) &= k_1 I_1(t) - (k_2 + g_2 + \mu + d_2) I_2(t) + g_3 I_3(t); \\
 & \vdots \\
\dot{I}_r(t) &= k_{r-1} I_{r-1}(t) - (k_r + g_r + \mu + d_r) I_r(t) + g_{r+1} I_{r+1}(t);
\end{cases}
\tag{1}
$$

$$
N = S + \sum_{m=1}^{r} I_m
$$

Antiretroviral therapy (ART) medecines for HIV infection



- Antiretroviral therapy (ART) is the use of HIV medicines to treat HIV infection. It can help an individual of class I_k, $k = 2, ..., r$ to have a rate of CD4 Cell $\geq$ 500 cells/μL and to come back to class I_1.
- A finite intervalle of treatment is necessary since we assume HIV has the ability to mutate at such a fast pace that it is able to build up resistance to the drug treatment after a finite time.
- We seek to minimize population of infective groups while also keeping the cost of the treatments low.

$$\begin{cases} \dot{S}(t) &=& \Lambda - \mu S(t) - \sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t); \\ \dot{I}_1(t) &=& \sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t) - (k_1 + \mu + d_1) I_1 + g_2 I_2 + u(t) \sum_{s=2}^{r} a_s Is; \\ \dot{I}_2(t) &=& k_1 I_1(t) - (k_2 + g_2 + \mu + d_2) I_2(t) + g_3 I_3(t) - a_2 u(t) I_2; \\ \dot{I}_3(t) &=& k_2 I_2(t) - (k_3 + g_3 + \mu + d_3) I_3(t) + g_4 I_4(t) - a_3 u(t) I_3; \end{cases} \quad (2)$$

Optimal intervention strategies

A control scheme is assumed to be optimal if it minimizes the objective functional (minimize population of infective groups while also keeping the cost of the treatments low):

$$J(u) = \int_{t_0}^{t_f} \sum_{m=1}^{3} A_i I_i(t) + Bu^2(t)dt. \qquad (3)$$

where B is balancing cost factor due to size and importance of parts of the objective functional. A_i denote weights that balance the size of the terms I_i.

Existence of the optimal control

We seek to find an optimal control u^*, such that:

$$J(u^*) = \min_{u \in \Omega} J(u). \tag{4}$$

where $\Omega = \Big\{ u \in L^1(t_0, t_f) \mid 0 \leq u \leq 1 \Big\}$.

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Consider the control problem with system equations. There exists $u^* \in \Omega$ such that

$$\min_{u \in \Omega} J(u) = J(u^*) \tag{5}$$

Hamiltonian terms for the control constraints

$$\mathcal{H}\Big(S(t), I_1(t), ..., I_r(t), N(t), u(t)\Big) = \sum_{m=1}^{r} A_i I_i(t) + Bu^2(t) +$$
$$\lambda_1(t)\Big[\Lambda - \mu S(t) - \sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t)\Big] +$$
$$\lambda_2(t)\Big[\sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t) - (k_1 + \mu + d_1)I_1 + g_2 I_2 + u(t)\sum_{s=2}^{r} a_s Is] +$$
$$\lambda_3(t)\Big[-(k_2 + g_2 + \mu + d_2)I_2(t) + g_3 I_3(t) - a_2 u(t) I_2\Big] +$$
$$\lambda_4(t)\Big[-(k_3 + g_3 + \mu + d_3)I_3(t) + g_4 I_4(t) - a_3 u(t) I_3\Big]$$

with mixed control-state constraints

There exists optimal control u^* and solutions S^*, I_1^*, ..., I_r^* to the corresponding state system (6), there exists adjoint functions $\lambda_1(t)$, $\lambda_2(t)$,..., $\lambda_{r+1}(t)$ such that

$$
\begin{aligned}
\dot{\lambda}_1(t) &= -\frac{\partial \mathcal{H}}{\partial S} = \lambda_1(t)\left(\mu + \sum_{m=1}^{r} c\beta_m \frac{I_m^*(t)\Big(I_1^*(t) + I_2^* + \dots + I_r^*(t)\Big)}{N^{*2}(t)}\right) \\
&- \lambda_2(t)\sum_{m=1}^{r} c\beta_m \frac{I_m^*(t)\Big(I_1^*(t) + I_2^*(t) + \dots + I_r^*(t)\Big)}{N^{*2}(t)} \\
\dot{\lambda}_2(t) &= -A_1 + \lambda_1(t)\sum_{m=1}^{r} \frac{cS^*(t)(\beta_1 - \beta_m)I_m^*(t)}{N^{*2}(t)} \\
&- \lambda_2(t)\left(\sum_{m=1}^{r} \frac{cS^*(t)(\beta_1 - \beta_m)I_m^*(t)}{N^{*2}(t)} + k_1 + \mu + d_1\right) \\
\dot{\lambda}_{r+1}(t) &= -A_r + \lambda_1(t)\sum_{m=1}^{r} \frac{cS^*(t)(\beta_r - \beta_m)I_m^*(t)}{N^{*2}(t)} \\
&- \lambda_2(t)\left(\sum_{m=1}^{r} \frac{cS^*(t)(\beta_r - \beta_m)I_m^*(t)}{N^{*2}(t)} + a_r u^*(t)\right) \\
&- g_r\lambda_r(t) + \lambda_{r+1}\Big(k_r + \mu + d_r + g_r + a_r u(t)\Big)
\end{aligned}
$$

$$\begin{cases} \dot{S}(t) &= \Lambda - \mu S(t) - \sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t); \\ \dot{I}_1(t) &= \sum_{m=1}^{r} c\beta_m \frac{I_m(t)}{N(t)} S(t) - (k_1 + \mu + d_1) I_1 + g_2 I_2 + u(t) \sum_{s=2}^{r} a_s Is; \\ \dot{I}_2(t) &= k_1 I_1(t) - (k_2 + g_2 + \mu + d_2) I_2(t) + g_3 I_3(t) - a_2 u(t) I_2; \\ \dot{I}_3(t) &= k_2 I_2(t) - (k_3 + g_3 + \mu + d_3) I_3(t) + g_4 I_4(t) - a_3 u(t) I_3; \end{cases} \quad (6)$$

with transversality conditions

$$\lambda_i(t_f) = 0, \quad i = 1, ..., 5$$

and $N^* = S^* + I_1^* + ... + I_r^*$. The optimal control is given by

$$u^* = \min\left\{\max\left\{a, \frac{1}{2B}\sum_{s=2}^{r}(\lambda_{s+1} - \lambda_2)a_s I_s\right\}, b\right\} \quad (7)$$

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- Using Pontryagin's Maximum Principle for optimal control problem
- The optimality equation is $\dfrac{\partial \mathcal{H}}{\partial u} \quad = \quad 2Bu^* + \sum_{s=2}^{r}(\lambda_2 - \lambda_{s+1})a_s I_s \ \ at \ \ u^*$
- According to standard control arguments involving the bounds on the control, we obtain the characterization of u^*.

Backward

We use Euler's scheme adapt it to our case as following:

$$
\left\{
\begin{array}{lcl}
\dfrac{S^{i+1}-S^{i}}{h} & = & \Lambda-\mu S^{i+1}-\displaystyle\sum_{m=1}^{r} c\beta_m \frac{I_m^i}{N^i} S^{i+1};\\
\dfrac{I_1^{i+1}-I_1^{i}}{h} & = & \displaystyle\sum_{m=1}^{r} c\beta_m \frac{I_m^i}{N^i} S^{i}-(k_1+\mu+d_1)I_1^{i+1}+g_2 I_2^i;\\
 & \vdots &
\end{array}
\right.
$$

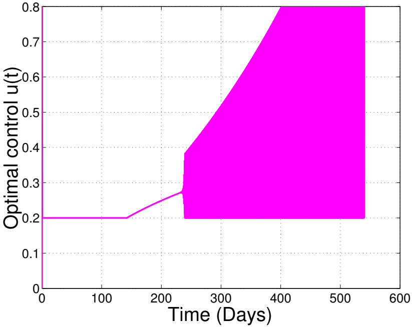
NFDS scheme ?
ODE45 ?

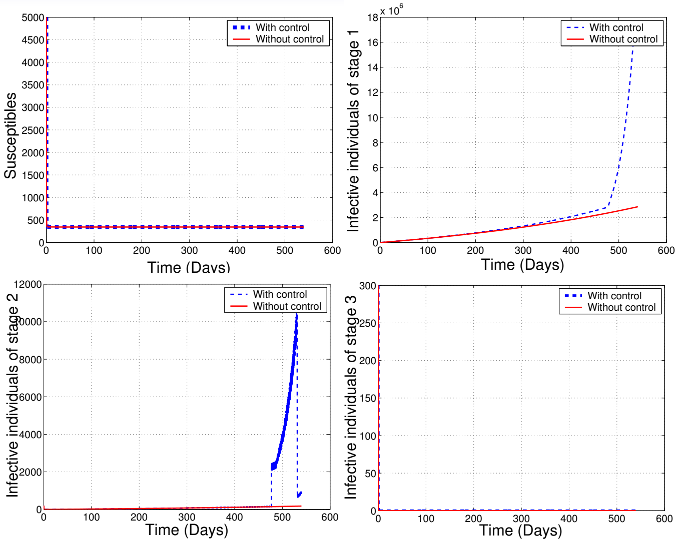
By using a similar technique, we approximate the time derivative of the adjoint variables by their first-order backward-difference and we use the appropriated scheme as follows:

$$\left\{ \begin{array}{lcl} \dfrac{\lambda_1^{n-i} - \lambda_1^{n-i-1}}{h} & = & \Lambda - \mu \lambda_1^{n-i-1} - \sum_{m=1}^{r} c\beta_m \dfrac{I_m^{n-i}}{N^{n-i}} \lambda_1^{n-i-1}; \\ & \vdots & \end{array} \right.$$

Hence an algorithm resulting from the above, to solve the optimality system and then to compute the optimal control pair is

- Step 1 : $\lambda(t_n) = 0, S^0 = S_0, ...$
- Step 2 : for $i = 1, ..., n$ compute $S^i, I_r^i, r = 1, 2, 3.$ simulataneously $\lambda_s^{n-i}, s = 1, 2, 3, 4.$ and u_i


Optimal control u(t)
Time (Days)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0
100
200
300
400
500
600


Susceptibles
Time (Days)
With control
Without control
Infective individuals of stage 1
x 10^6
Time (Days)
With control
Without control
Infective individuals of stage 2
Time (Days)
With control
Without control
Infective individuals of stage 3
Time (Days)
With control
Without control