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# The Minimum Principle for Delayed Optimal Control Problems with State Constraints

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# Challenges for Optimal Control Problems **with Delays**

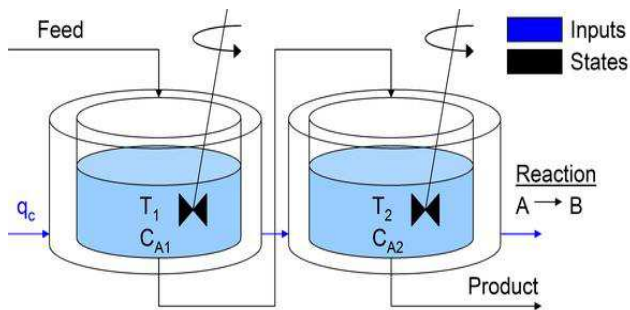
Theory and Numerics for **non-delayed** optimal control problems with control and state constraints are in a mature state-of-art:

- 1 Necessary and sufficient conditions,
- 2 Stability and sensitivity analysis,
- 3 Numerical methods: Boundary value methods, Discretization and NLP, Semismooth Newton methods,
- 4 Real-time control techniques for perturbed extremals.

**CHALLENGE:** Establish similar theoretical and numerical methods for **delayed (retarded)** optimal control problems.

- 1 **Example:** Two-stage Continuous Stirred Tank Reactor (CSTR)
- 2 Formulation of Optimal Control Problems with Delays in State and Control Variables
- 3 Minimum Principle
- 4 Numerical Treatment: Discretize and Optimize
- 5 **Example:** Optimal Control of the Innate Immune Response

# Two-Stage Continuous Stirred Tank Reactor (CSTR)



Time delays are caused by transport between the two tanks.

# Delayed Optimal Control Problem with State Constraints

State  $x(t) \in \mathbb{R}^n$ , Control  $u(t) \in \mathbb{R}^m$ , Delays  $d_x, d_u \geq 0$ .

## Dynamics and Boundary Conditions

$$\dot{x}(t) = f(x(t), x(t - d_x), u(t), u(t - d_u)), \quad \text{a.e. } t \in [0, t_f],$$

$$x(t) = x_0(t), \quad t \in [-d_x, 0],$$

$$u(t) = u_0(t), \quad t \in [-d_u, 0],$$

$$\psi(x(t_f)) = 0 \in \mathbb{R}^q, \quad (0 \leq q \leq n).$$

## Control and State Constraints

$$u(t) \in U \subset \mathbb{R}^m, \quad S(x(t)) \leq 0, \quad t \in [0, t_f] \quad (S : \mathbb{R}^n \rightarrow \mathbb{R}^k).$$

## Minimize

$$J(u, x) = g(x(t_f)) + \int_0^{t_f} f_0(x(t), x(t - d_x), u(t), u(t - d_u)) dt$$

# Literature on optimal control with time-delays

## Time delays in state variables and pure control constraints:

Kharatishvili (1961), Oguztörelı (1966), Banks (1968), Halanay (1968), Soliman, Ray (1970, chemical engineering), Warga (1972, [abstract theory, optimization in Banach spaces](#)), Guinn (1976, [transform delayed problems to standard problems](#)), Colonius, Hinrichsen (1978), Clarke, Wolenski (1991), Dadebo, Luus (1992), Mordukhovich, Wang (2003–).

## Time delays in state variables and pure state constraints:

Angell, Kirsch (1990).

## State and control delays and mixed control–state constraints:

**single delay** : Göllmann, Kern, Maurer (OCAM 2009)  
**multiple delays** : Göllmann, Maurer (JIMO 2014)

# Optimal control problems with state constraints

Use the [transformation method of Guinn \(1976\)](#) and transform an optimal control problem [with delays](#) and state constraints to a standard [non-delayed](#) optimal control problem with state constraints. Then apply the [necessary conditions for non-delayed problems](#):

- Jacobson, Lele, Speyer (1975): KKT conditions in Banach spaces.
- Maurer (1979) : Regularity of multipliers for state constraints.
- Hartl, Sethi, Thomsen (SIAM Review 1995): Survey on Maximum Principles.
- Vinter (2000): (Nonsmooth) Optimal Control

Use methodology for [mixed control-state constraints](#) in

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# The smooth case: all functions are differentiable

## Hamiltonian (Pontryagin) Function

$$H(x, y, \lambda, u, v) := \lambda_0 f_0(t, x, y, u, v) + \lambda f(t, x, y, u, v)$$

- $y$  variable with  $y(t) = x(t - d_x)$
- $v$  variable with  $v(t) = u(t - d_u)$
- $\lambda \in \mathbb{R}^n$ ,  $\lambda_0 \in \mathbb{R}$  adjoint (costate) variable

Let  $(u, x) \in \mathcal{L}^\infty([0, t_f], \mathbb{R}^m) \times \mathcal{W}^{1,\infty}([0, t_f], \mathbb{R}^n)$  be a locally optimal pair of functions. Then there exist

- an adjoint function  $\lambda \in \mathcal{BV}([0, t_f], \mathbb{R}^n)$  and  $\lambda_0 \geq 0$ ,
- a multiplier  $\rho \in \mathbb{R}^q$  (associated with terminal conditions),
- a multiplier function (measure)  $\mu \in \mathcal{BV}([0, t_f], \mathbb{R}^k)$ ,

such that the following conditions are satisfied for a.e.  $t \in [0, t_f]$ :

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# Minimum Principle

(i) **Advanced adjoint equation and transversality condition:**

$$\lambda(t) = \int_t^{t_f} (H_x(s) + \chi_{[0, t_f - d_x]}(s) H_y(s + d_x)) ds + \int_t^{t_f} S_x(x(s)) d\mu(s) \\ + (\lambda_0 g + \rho\psi)_x(x(t_f)), \quad (\text{if } S(x(t_f)) < 0)$$

where  $H_x(t)$  and  $H_y(t + d_x)$  denote evaluations along the optimal trajectory and  $\chi_{[0, t_f - d_x]}$  is the **characteristic function**.

(ii) **Minimum Condition:**

$$H(t) + \chi_{[0, t_f - d_u]}(t) H(t + d_u) \\ = \min_{w \in U} [ H(x(t), y(t), \lambda(t), w, v(t)) \\ + \chi_{[0, t_f - d_u]}(t) H(t + d_u) H(x(t + d_u), y(t), \lambda(t + d_u), u(t + d_u), w) ]$$

(iii) **Multiplier condition and complementarity condition:**

$$d\mu(t) \geq 0, \quad \int_0^{t_f} S(x(t)) d\mu(t) = 0$$

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(iii) **Multiplier condition and complementarity condition:**

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# Regularity conditions for $d\mu(t) = \eta(t)dt$ if $d_u = 0$

**Boundary arc** :  $S(x(t)) = 0$  for  $t_1 \leq t \leq t_2$ .

**Assumption** :  $u(t) \in \text{int}(U)$  for  $t_1 < t < t_2$ .

Under certain **regularity conditions** we have  $d\mu(t) = \eta(t) dt$  with a multiplier  $\eta(t)$  for all  $t_1 < t < t_2$ .

## Adjoint equation and jump conditions

$$\dot{\lambda}(t) = -H_x(t) - \chi_{[0, t_f - d_x]}(t) H_y(t + d_x) - \eta(t) S_x(x(t))$$

$$\lambda(t_k+) = \lambda(t_k-) - \nu_k S_x(x(t_k)), \quad \nu_k \geq 0$$

at each contact or junction time  $t_k$ ,  $\nu_k = \mu(t_k+) - \mu(t_k-)$

## Minimum condition on the boundary

$$H_u(t) = 0.$$

This condition allows to compute the multiplier  $\eta = \eta(x, \lambda)$ .



# Numerical Treatment: Discretize and Optimize

- 1 Choose a **suitable stepsize**  $h = t_f/N$ ,  $N \in \mathbf{N}$ , adapted to the delays  $d_x, d_y$  (commensurability). Use the implicit or explicit Euler integration scheme for the dynamic equations and define the **associated NLP** having

$$u(t_i) \approx u_i \in \mathbb{R}^m, \quad x(t_i) \approx x_i \in \mathbb{R}^n, \quad i = 0, \dots, N$$

as decision variables

- 2 Apply **NLP-Solvers** (eg. IPOPT, LOQO embedded in AMPL source code) to solve the NLP
- 3 The associated **Lagrange multipliers** ( $\hat{\lambda}_i$ ) for the discretized dynamic equations and state constraint ( $\hat{\mu}_i$ ) give a **consistent approximation of the costate and the multiplier function**

$$\hat{\lambda}(t_i) \approx \hat{\lambda}_i, \quad \hat{\eta}(t_i) \approx \frac{1}{h} \hat{\eta}_i \quad (i = 0, \dots, N), \quad \hat{v} \approx \hat{v}_N.$$

Göllmann, Kern, Maurer (2009) for two single state/control delays,  
Göllmann, Maurer (2014) for multiple delays.

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# Model of the immune response

Dynamic model of the immune response:

**Asachenko A, Marchuk G, Mohler R, Zuev S,**  
*Disease Dynamics*, Birkhäuser, Boston, 1994.

Optimal control:

**Stengel RF, Ghigliazza R, Kulkarni N, Laplace O,**  
Optimal control of innate immune response,  
*Optimal Control Applications and Methods* **23**, 91–104 (2002),

Simultaneous optimization of all control variables and delays:

**L. Göllmann, H. Maurer:** Optimal control problems with multiple  
time-delays, JIMO 2014.

Here we consider a more realistic **modified optimal control problem**.

# Innate Immune Response: state and control variables

## State variables:

- $x_1(t)$  : concentration of **pathogen**  
(=concentration of associated **antigen**)
- $x_2(t)$  : concentration of **plasma cells**,  
which are carriers and producers of antibodies
- $x_3(t)$  : concentration of **antibodies**, which kill the pathogen  
(=concentration of **immunoglobulins**)
- $x_4(t)$  : relative characteristic of a **damaged organ**  
( **0 = healthy, 1 = dead** )

## Control variables:

- $u_1(t)$  : pathogen killer
- $u_2(t)$  : plasma cell enhancer
- $u_3(t)$  : antibody enhancer
- $u_4(t)$  : organ healing factor

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# Generic dynamical model of the immune response

$$\dot{x}_1(t) = (1 - x_3(t))x_1(t) - u_1(t - d_u)x_1(t),$$

$$\dot{x}_2(t) = 3A(x_4(t))x_1(t - d_x)x_3(t - d_x) - (x_2(t) - 2) + u_2(t)x_2(t),$$

$$\dot{x}_3(t) = x_2(t) - (1.5 + 0.5x_1(t))x_3(t) + u_3(t)x_3(t),$$

$$\dot{x}_4(t) = x_1(t) - x_4(t) - u_4(t)x_4(t).$$

Immune deficiency function triggered by target organ damage

$$A(x_4) = \left\{ \begin{array}{ll} \cos(\pi x_4), & 0 \leq x_4 \leq 0.5 \\ 0 & 0.5 \leq x_4 \end{array} \right\}.$$

For  $0.5 \leq x_4(t)$  the production of plasma cells stops.

State delay  $d_x \geq 0$  in variables  $x_1$  and  $x_3$ .

Control delay  $d_u \geq 0$  in variable  $u_1$ .

Initial conditions ( $d = 0$ ):  $x_2(0) = 2$ ,  $x_3(0) = 4/3$ ,  $x_4(0) = 0$

Case 1 :  $x_1(0) = 1.5$ , decay, requires no therapy (control)

Case 2 :  $x_1(0) = 2.0$ , slower decay, requires no therapy

Case 3 :  $x_1(0) = 3.0$ , diverges without control (lethal case)

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# Optimal control model: cost functional

$L^2$ -functional quadratic in control: Stengel et al.

$$\begin{aligned} \text{Minimize } J_2(x, u) &= x_1(t_f)^2 + x_4(t_f)^2 \\ &+ \int_0^{t_f} (x_1^2 + x_4^2 + u_1^2 + u_2^2 + u_3^2 + u_4^2) dt \end{aligned}$$

Control constraints:  $0 \leq u_i(t) \leq u_{\max} = 1, i = 1, \dots, 4$

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# State Constraint

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with ceasing plasma cells production for  $0.5 \leq x_4(t)$ , we impose

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$$S(x_4(t)) := x_4(t) - \alpha \leq 0$$

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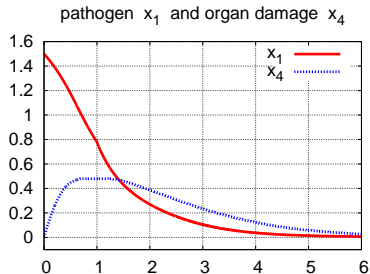
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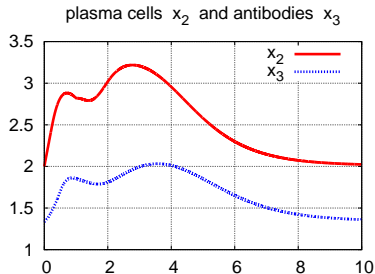
$$S(x_4(t)) := x_4(t) - \alpha \leq 0$$

# Results for $L^2$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Optimal state variables:



pathogen concentration  
organ damage

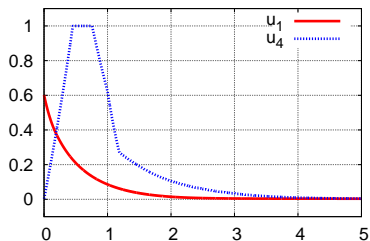


plasma cell concentration  
immunoglobulins

# Results for $L^2$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

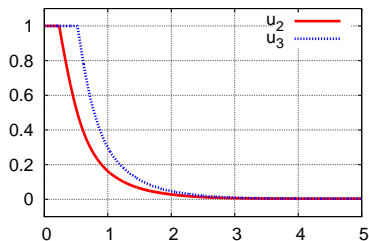
Optimal control variables:

pathogen killer  $u_1$  and organ healing factor  $u_4$



pathogen killer  
organ healing factor

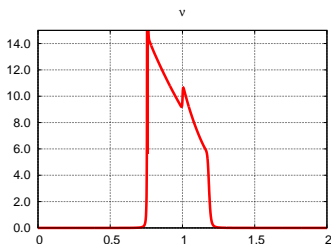
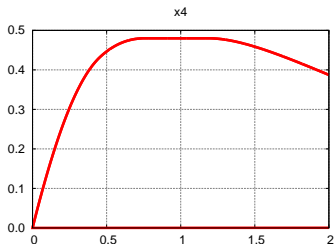
plasma cell enhancer  $u_2$ , antibody enhancer  $u_3$



plasma cell enhancer  
antibody enhancer

# Results for $L^2$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Zoom: Optimal state  $x_4$ : Boundary arc observed



organ healing factor

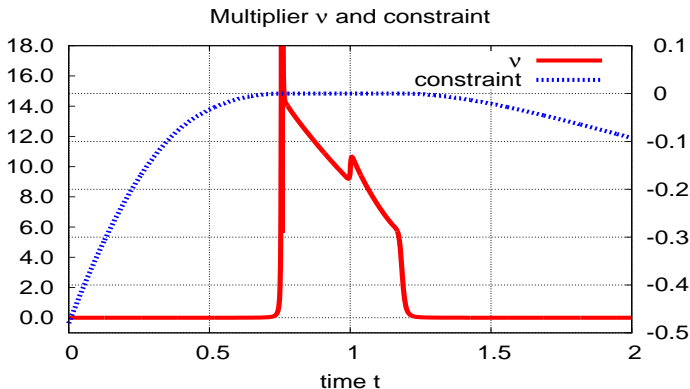
multiplier

First order necessary conditions, in particular  $H_{u_4} = 0$ , yield the multiplier on boundary arc  $x_4(t) = \alpha$  :

$$\eta(x, y, v_1, \lambda) = -2\alpha + 3\pi\lambda_2 \sin(\pi\alpha)y_1y_2 + \lambda_4 \frac{x_1}{\alpha} - \frac{2}{\alpha^2}((1-x_3)x_1 - v_1x_1)$$

# Results for $L^2$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Zoom into boundary arc  $x_4(t) = 4.8$  :



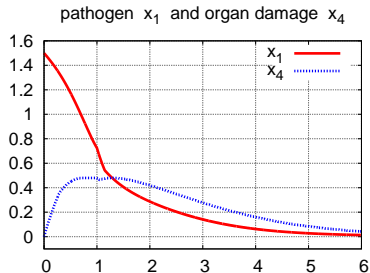
right axis: constraint  $S(x_4) - \alpha \leq 0$ .

left axis: corresponding multiplier  $\eta(t)$ .

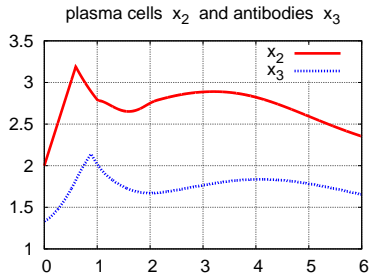


# Results for $L^1$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Optimal state variables:



pathogen concentration  
organ damage

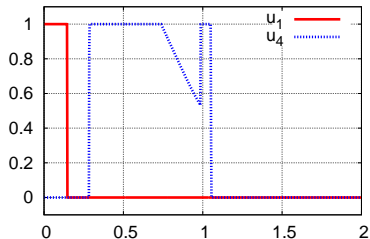


plasma cell concentration  
immunoglobulins

# Results for $L^1$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

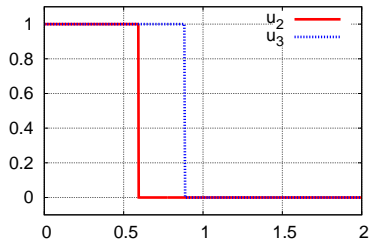
Optimal control variables:

pathogen killer  $u_1$  and organ healing factor  $u_4$



pathogen killer  
organ healing factor

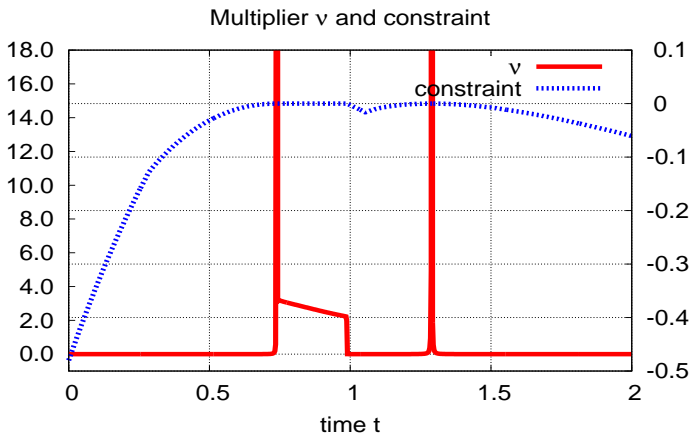
plasma cell enhancer  $u_2$ , antibody enhancer  $u_3$



plasma cell enhancer  
antibody enhancer

# Results for $L^1$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Zoom into boundary arc  $x_4(t) = 4.8$ :

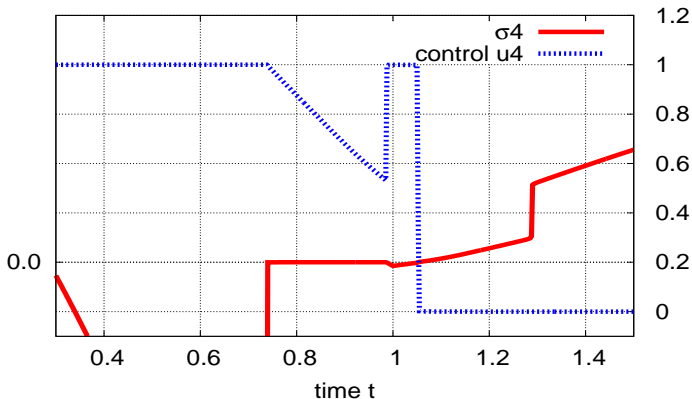


overlay: constraint  $S(x_4) - \alpha \leq 0$  (right axis)  
and corresponding multiplier  $\eta(t)$  (left axis)

# Results for $L^1$ -functional, $d_x = d_u = 1.0$ , $\alpha = 4.8$

Zoom into boundary arc  $x_4(t) = 4.8$ :

switching function  $\sigma_4$  and healing factor  $u_4$



right axis: control  $u_4$  .

left axis: corresponding switching function  $\sigma(t) = \frac{\partial H}{\partial u_4}$  .

# Further applications and future work

- 1 Optimal investment and dividend decisions of a firm
- 2 Expediting the transition from non-renewable to renewable energy (Maurer, Semmler)
- 3 Biomedical applications: optimal protocols in cancer treatment and immunology, optimal tapering of steroids
- 4 Verifiable sufficient conditions
- 5 Time and state dependent delays



**Thank you for your attention !**