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THEORY AND APPLICATIONS OF OPTIMAL CONTROL PROBLEMS WITH MULTIPLE TIME-DELAYS

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Abstract. In this paper we study optimal control problems with multiple time delays in control and state and mixed type control-state constraints. We derive necessary optimality conditions in the form of a Pontryagin type Minimum Principle. A discretization method is presented by which the delayed control problem is transformed into a nonlinear programming problem. It is shown that the associated Lagrange multipliers provide a consistent numerical approximation for the adjoint variables of the delayed optimal control problem. We illustrate the theory and numerical approach on an analytical example and an optimal control model from immunology.

1. **Introduction.** Dynamic systems with delays in both state and control variables play an important role in the modeling of real-life phenomena in chemical and biological processes, in economics and mechanics and various other fields, cf. [4, 5, 6, 18, 19]. There is an extensive literature on the necessary optimality conditions for retarded optimal control problems with either pure control constraints or pure state constraints; cf. [1, 3, 6, 7, 11, 13, 15, 16, 17, 21, 23, 26, 27, 28, 35]. In particular, Warga [35] presents a general approach for deriving necessary optimality conditions which is based on optimization theory in function spaces. We must admit that we could not translate the necessary conditions of Warga [35] in the presence of a practical example like the one in Section 6. Despite the impressive amount of theoretical work, only a few numerical examples may be found in the literature, notably in chemical engineering, cf. [8, 24, 26, 27, 28]. But usually no attempt has been made to verify the necessary conditions accurately by providing adjoint variables.

In [10], we have presented a Minimum (Maximum) Principle for delayed optimal control with mixed control-state constraints and have illustrated the theory on several numerical examples. In this paper, we consider optimal control problems with multiple time-delays and mixed control-state constraints (Section 2) and extend the approach in [10] to derive a Minimum Principle (Section 3). Again,

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we use the transformation technique introduced in Guinn [11] to convert the delayed control problem into a higher-dimensional undelayed control problem. This approach requires a commensurability condition for the delays which is also crucial for discretization and optimization methods to solve the delayed control problem (Section 4). The analysis is restricted to Euler's method but can be generalized to higher-order Runge–Kutta methods. We show that the Lagrange multipliers of the finite-dimensional optimization problems can be identified with the discretized adjoint (costate) variables thus enabling us to verify all conditions of the Minimum Principle. Section 5 presents an academic example which possesses an analytical solution. This allows to test the accuracy of the numerical solution for various step sizes. Finally, in Section 6 we treat an optimal control problem modeling the innate immune response which was introduced by Stengel et al. [29, 30]. For cost functionals of L^2–type and L^1–type, optimal controls are determined simultaneously in all control components both in the undelayed and delayed case. In addition, we introduce a mixed control-state constraint to reduce the state variable representing the damage of an organ.

2. **Optimal control problems with multiple time-delays in state and control.**

We consider constrained optimal control problems with multiple time-delays in state and control variables. The control problem is subject to mixed control-state inequality constraints. Let $x(t) \in \mathbb{R}^n$ denote the state variable and $u(t) \in \mathbb{R}^m$ the control variable at time $t \in [0, T]$ with fixed terminal time $T > 0$. The positive time-delays in the state and control variables are given by a constant vector $(r_1, \ldots, r_d) \in \mathbb{R}^d$ satisfying

$$0 =: r_0 < r_1 < \ldots < r_d.$$

Thus r_0 represents the nondelayed variables. We shall study the following multiple time-delayed optimal control problem (MDOCP) with mixed control-state constraints which is given as MAYER form:

Minimize

$$J(u, x) = g(x(T)) \tag{1}$$

subject to the retarded differential equation, boundary conditions and mixed control-state inequality constraints

$$\dot{x}(t) = f(t, x(t - r_0), \ldots, x(t - r_d), u(t - r_0), \ldots, u(t - r_d)), \quad \text{a.e. } t \in [0, T], \tag{2}$$

$$x(t) = x_0(t), \quad t \in [-r_d, 0], \tag{3}$$

$$u(t) = u_0(t), \quad t \in [-r_d, 0), \tag{4}$$

$$\psi(x(T)) = 0, \tag{5}$$

$$C(t, x(t - r_0), \ldots, x(t - r_d), u(t - r_0), \ldots, u(t - r_d)) \le 0, \quad \text{a.e. } t \in [0, T]. \tag{6}$$

The functions $g : \mathbb{R}^n \to \mathbb{R}, f : [0, T] \times \mathbb{R}^{(d+1)\cdot n} \times \mathbb{R}^{(d+1)\cdot m} \to \mathbb{R}^n, \psi : \mathbb{R}^n \to \mathbb{R}^q, \quad 0 \le q \le n$, and $C : [0, T] \times \mathbb{R}^{(d+1)\cdot n} \times \mathbb{R}^{(d+1)\cdot m} \to \mathbb{R}^p$ are assumed to be continuously differentiable, while the functions $x_0 : [-r_d, 0] \to \mathbb{R}^n, u_0 : [-r_d, 0] \to \mathbb{R}^m$ only need to be continuous.

In the following, we shall use the placeholder variables $y_0, y_1, \ldots, y_d$ for the retarded state variables, i.e., $y_\delta(t) = x(t - r_\delta)$ for $\delta = 0, 1, \ldots, d$, and the placeholder variables $v_0, v_1, \ldots, v_d$ for the retarded control variables, i.e., $v_\delta(t) = u(t - r_\delta)$ for

$\delta = 0, 1, \ldots, d$. Note that the case of an unequal number of delays in state and control is included as we admit that

$$\frac{\partial h}{\partial y_\delta} = 0 \quad \text{or} \quad \frac{\partial h}{\partial v_\delta} = 0, \quad h \in \{f, C\}, \quad \text{and some} \quad \delta \in \{0, \ldots, d\}$$

A cost functional of Bolza form,

$$J(u,x) = g(x(T)) + \int_0^T L(t, x(t-r_0), \ldots, x(t-r_d), u(t-r_1), \ldots, u(t-r_d))\,\mathrm{d}t \quad (7)$$

with a C^1-function $L : [0,T] \times \mathbb{R}^{(d+1)\cdot n} \times \mathbb{R}^{(d+1)\cdot m} \to \mathbb{R}$ can be transformed to a cost functional in Mayer form by introducing the additional state variable x_{n+1} defined by the retarded equation

$$\dot{x}_{n+1} = L(t, x(t-r_0), \ldots, x(t-r_d), u(t-r_0), \ldots, u(t-r_d)), \quad x_{n+1}(0) = 0. \quad (8)$$

Then the objective (7) can be rewritten in Mayer form as $J(\tilde{x}, u) = g(x(T)) + x_{n+1}(T)$ with the augmented state variable $\tilde{x} = (x, x_{n+1}) \in \mathbb{R}^{n+1}$.

A pair of functions $(u,x) \in L^\infty([0,T], \mathbb{R}^m) \times W^{1,\infty}([0,T], \mathbb{R}^n)$ is called an *admissible pair* for problem (MDOCP), if the state x and control u satisfy the restrictions (2)–(6). An admissible pair $(\hat{u}, \hat{x})$ is called a *locally optimal pair* or *weak minimum* for (MDOCP), if

$$J(\hat{u}, \hat{x}) \leq J(u, x)$$

holds for all admissible (u,x) in a neighborhood of $(\hat{u}, \hat{x})$ with $\|x(t) - \hat{x}(t)\|$, $\|u(t) - \hat{u}(t)\| < \varepsilon$ for all $t \in [0,T]$ and $\varepsilon > 0$ sufficiently small. Instead of considering a *weak minimum*, we could also work with the more general notion of a *Pontryagin minimum*; cf. Milyutin, Osmolovskii [20].

3. Necessary optimality conditions for time-delayed optimal control problems with mixed control-state constraints.

In [10], we have derived a Pontryagin-type Minimum Principle for optimal control problems with two independent delays and nondelayed mixed control-state constraints using a transformation technique introduced by Guinn [11]. The following analysis generalizes this approach to the optimal control problem (MDOCP). Guinn's approach consists in transforming the *delayed* optimal control to a higher-dimensional *nondelayed* problem and requires the following commensurability condition. We note that this condition will be indispensable for the numerical discretization techniques presented in Section 3. However, strictly speaking the commensurability condition is not needed in derivation of the (local) Minimum Principle when one applies the theory of necessary conditions for optimization problems in Banach spaces.

Assumption 1 (Commensurability Condition)**.** *Assume that there exist a constant* $h > 0$ *and integers* $k_1, \ldots, k_d, N$ *with*

$$r_\delta = k_\delta h \quad (\delta = 1, \ldots, d) \quad \textit{and} \quad T = N\,h. \quad (9)$$

In view of $0 = r_0 < r_1 < \ldots < r_d$ we have $0 < k_1 < \ldots < k_d$. In analogy to the nondelayed case we define a free Hamiltonian (or Pontryagin) function by

$$H(t, y_0, \ldots, y_d, v_0, \ldots, v_d, \lambda) := \lambda^* f(t, y_0, \ldots, y_d, v_0, \ldots, v_d), \quad \lambda \in \mathbb{R}^n, \quad (10)$$

and an *augmented* Hamiltonian function involving the mixed control-state constraint (6) by

$$\begin{aligned} \mathcal{H}(t, y_0, \ldots, y_d, v_0, \ldots, v_d, \lambda, \mu) :=& H(t, y_0, \ldots, y_d, v_0, \ldots, v_d) \\ &+ \mu^* C(t, y_0, \ldots, y_d, v_0, \ldots, v_d), \end{aligned} \quad (11)$$

where $\lambda \in \mathbb{R}^n$ and $\mu \in \mathbb{R}^p$. Similar to the nondelayed case we need a supplementary regularity condition for the active control-state constraints

Assumption 2 (Regularity Condition)**.** *For a locally optimal pair $(\hat{u}, \hat{x})$ and $t \in [0, T]$ let*

$$J_0(t) := \{j \in \{1, \ldots, p\} \,|\, C_j(t, \hat{x}(t - r_0), \ldots, \hat{x}(t - r_d), \hat{u}(t - r_0), \ldots, \hat{u}(t - r_d)) = 0\}$$

denote the set of active indices for the inequality constraints (6). Assume that the gradients

$$\frac{\partial C_j(t, \hat{x}(t - r_0), \ldots, \hat{x}(t - r_d), \hat{u}(t - r_0), \ldots, \hat{u}(t - r_d))}{\partial(v_0, \ldots, v_d)}, \quad j \in J_0(t) \tag{12}$$

are linearly independent.

Together with the commensurability condition, which can be guaranteed in practice for any numerical discretization based method, we obtain the following set of first order necessary optimality conditions for (MDOCP).

Theorem 3.1 (Minimum Principle for Multiple Delayed Optimal Control Problems)**.** *Let $(\hat{u}, \hat{x})$ be locally optimal for (MDOCP) with delays satisfying Assumptions 1 and 2. Then there exist a adjoint (costate) function $\hat{\lambda} \in W^{1,\infty}([0, T], \mathbb{R}^n)$, a number $\lambda_0 \geq 0$, a multiplier function $\hat{\mu} \in L^\infty([0, T], \mathbb{R}^p)$ and a multiplier $\hat{\nu} \in \mathbb{R}^q$, such that the following conditions hold for a.e. $t \in [0, T]$:*

1. *Adjoint Differential Equation: For a.e. $t \in [0, T]$:*

$$\dot{\hat{\lambda}}(t)^* = -\sum_{\delta=0}^{d} \chi_{[0, T - r_\delta]}(t) \hat{\mathcal{H}}_{y_\delta}(t + r_\delta), \tag{13}$$

   where $\hat{\mathcal{H}}_{y_\delta}(t)$ denotes the evaluation of the partial derivatives $\mathcal{H}_{y_\delta}$ at $(t, \hat{x}(t - r_0), \ldots, \hat{x}(t - r_d), \hat{u}(t - r_0), \ldots, \hat{u}(t - r_d), \hat{\lambda}(t), \hat{\mu}(t))$,

2. *Transversality Condition:*

$$\hat{\lambda}(T)^* = \lambda_0 g_x(\hat{x}(T)) + \hat{\nu}^* \psi_x(\hat{x}(T)); \tag{14}$$

3. *Minimum Condition for the Free Hamiltonian Function:*

$$\begin{aligned}
&\sum_{\delta=0}^{d} \chi_{[0, T - r_\delta]}(t) \hat{H}(t + r_\delta) \\
&\leq H(t, \ldots, u, \hat{u}(t - r_1), \ldots, \hat{u}(t - r_d)) \\
&\quad + \sum_{\delta=1}^{d-1} \chi_{[0, T - r_\delta]}(t) H(t + r_\delta, \ldots, \hat{u}(t + r_\delta - r_{\delta-1}), u, \hat{u}(t + r_\delta - r_{\delta+1}), \ldots) \\
&\quad + \chi_{[0, T - r_d]}(t) H(t + r_d, \ldots, \hat{u}(t + r_d - r_1), \ldots, \hat{u}(t + r_d - r_{d-1}), u)
\end{aligned} \tag{15}$$

   for all $u \in \mathbb{R}^m$ satisfying

$$\begin{aligned}
&C(t, \hat{x}(t - r_0), \ldots, \hat{x}(t - r_d), \\
&\qquad \hat{u}(t - r_0), \ldots, \hat{u}(t - r_{\delta-1}), u, \hat{u}(t - r_{\delta+1}), \ldots, \hat{u}(t - r_d)) \\
&\leq 0 \qquad \text{for} \quad \delta = 0, \ldots, d,
\end{aligned}$$

   where $\hat{H}(t)$ denotes the evaluation of the free Hamiltonian H at $(t, \hat{x}(t - r_0), \ldots, \hat{x}(t - r_d), \hat{u}(t - r_0), \ldots, \hat{u}(t - r_d), \hat{\lambda}(t), \hat{\mu}(t))$,

4. *Local Minimum Condition for the Augmented Hamiltonian Function*

$$\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t)\hat{\mathcal{H}}_{v_\delta}(t+r_\delta) = 0. \tag{16}$$

5. *Non-negativity of Multiplier and Complementarity Condition:*

$$\hat{\mu}(t) \geq 0 \quad \textit{and} \quad \hat{\mu}_i(t)C_i(t,\hat{x}(t-r_0),\ldots,\hat{u}(t-r_d)) = 0, \quad i = 1,\ldots,p. \tag{17}$$

Remark. When the cost functional is given in Bolza form (7), the free Hamiltonian (10) becomes

$$\begin{aligned} H(t,y_0,y_1,\ldots,y_d,u_0,u_1,\ldots,u_d) \quad &= \quad \lambda_0 L(t,x_0,\ldots,x_d,u_0,\ldots,u_d) \\ &\quad\; +\lambda^* f(t,x_0,\ldots,x_d,u_0,\ldots,u_d). \end{aligned} \tag{18}$$

The augmented Hamiltonian $\mathcal{H}$ agrees with the one defined in (11).

Proof. The proof of Theorem 3.1 uses the transformation technique suggested by Guinn [11] who derived first order necessary conditions for unconstrained optimal control problems with a single time-delay in the state variable. Now we apply a further extension of this transformation method to the multiple delayed problem (MDOCP). In view of the commensurability condition (9), there exists a constant $h > 0$ and integers $k_1,\ldots,k_d$ such that with $k_0 := 0$ we can rewrite the delays as

$$r_\delta = k_\delta h, \qquad \delta = 0,\ldots,d.$$

The time interval $[0,h]$ will be considered as the base time interval for the transformed (augmented) control problem assigned to (MDOCP).

We introduce the state variable $\Xi^* = (\xi_0^*,\ldots,\xi_{N-1}^*) \in \mathbb{R}^{N\cdot n}$, $\xi_i \in \mathbb{R}^n$, and control variable $\Theta^* = (\theta_0^*,\ldots,\theta_{N-1}^*) \in \mathbb{R}^{N\cdot m}$, $\theta_i \in \mathbb{R}^m$, which are defined by

$$\xi_i(t) := x(t+ih), \quad \theta_i(t) := u(t+ih), \quad \text{for} \quad t\in[0,h], \quad i = 0,\ldots,N-1. \tag{19}$$

The continuity of the state $x(t)$ in $[0,T]$ implies the following boundary conditions for the augmented state $\Xi(t)$,

$$\xi_i(h) = \xi_{i+1}(0), \qquad i = 0,\ldots,N-2,$$

which can be written as

$$V_i(\xi_{i+1}(0),\xi_i(h)) := \xi_i(h) - \xi_{i+1}(0) = 0, \qquad i = 0,\ldots,N-2. \tag{20}$$

In terms of the new state and control variables Ξ and Θ, the multiple delayed optimal control problem (MDOCP) is equivalent to the following nondelayed optimal control problem on the basic time interval $[0,h]$:

$$\text{Minimize} \qquad J(\Theta,\Xi) = g(\xi_{N-1}(h)) \tag{21}$$

subject to

$$\begin{aligned} &\dot{\xi}_i(t) = f(t+ih,\xi_{i-k_0}(t),\ldots,\xi_{i-k_d}(t),\theta_{i-k_0}(t),\ldots,\theta_{i-k_d}(t)), \quad t\in[0,h], \\ &\qquad i = 0,\ldots,N-1, \end{aligned} \tag{22}$$

$$\begin{aligned} V_i(\xi_{i+1}(0),\xi_i(h)) &= 0, \quad i = 0,\ldots,N-2, \\ V_{N-1}(\xi_{N-1}(h)) := \psi(\xi_{N-1}(h)) &= 0, \end{aligned} \tag{23}$$

$$\begin{aligned} &C(t+ih,\xi_{i-k_0}(t),\ldots,\xi_{i-k_d}(t),\theta_{i-k_0}(t),\ldots,\theta_{i-k_d}(t)) \leq 0, \quad t\in[0,h], \\ &\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad i = 0,\ldots,N-1. \end{aligned} \tag{24}$$

The fixed initial value profiles (3) and (4) are included in this notation by considering the variables $\xi_{-k_d}, \dots, \xi_{-1}$ and $\theta_{-k_d}, \dots, \theta_{-1}$ defined by

$$\begin{aligned} \xi_i(t) &:= x_0(t+ih) \\ \theta_i(t) &:= u_0(t+ih) \end{aligned} \qquad i = -k_d, -k_d-1, \dots, -1, \quad t \in [0,h].$$

Introducing adjoint variables and multipliers for the augmented delayed problem (21)–(24) by

$$\Lambda = (\Lambda_0, \dots, \Lambda_{N-1})^* \in \mathbb{R}^{N\cdot n}, \quad M = (M_0, \dots, M_{N-1})^* \in \mathbb{R}^{N\cdot p},$$

the Hamiltonians (10) and (11) for the augmented control problem become

$$K(t,\Xi,\Theta,\Lambda) = \sum_{i=0}^{N-1} \Lambda_i^* f(t+ih, \xi_{i-k_0}, \dots, \xi_{i-k_d}, \theta_{i-k_1}, \dots, \theta_{i-k_d}), \tag{25}$$

$$\begin{aligned} \mathcal{K}(t,\Xi,\Theta,\Lambda,M) = {} & K(t,\Xi,\Theta,\Lambda)+ \\ & + \sum_{i=0}^{N-1} M_i^* C(t+ih, \xi_{i-k_0}, \dots, \xi_{i-k_d}, \theta_{i-k_0}, \dots, \theta_{i-k_d}) \end{aligned} \tag{26}$$

Thus in analogy to (19), every locally optimal pair $(\hat{u}(\cdot), \hat{x}(\cdot))$ for (MDOCP) defines a pair

$$(\hat{\Theta}(\cdot), \hat{\Xi}(\cdot)) = (\hat{\theta}_0, \dots, \hat{\theta}_{N-1}, \hat{\xi}_0, \dots, \hat{\xi}_{N-1})$$

by

$$\hat{\xi}_i(t) := \hat{x}(t+ih), \quad \hat{\theta}_i(t) := \hat{u}(t+ih), \quad \text{for} \quad t \in [0,h], \quad i = 0, \dots, N-1, \tag{27}$$

which is a minimizer to the augmented problem (21)–(24). Note that the assumed regularity condition (12) ensures a corresponding regularity condition for the mixed control-state constraints (24) of the augmented problem.

Pontryagin's Minimum Principle for delayed optimal control problems cf. [14, 20, 22, 25] assures the existence of a adjoint (costate) function $\hat{\Lambda} \in W^{1,\infty}([0,h], \mathbb{R}^{N\cdot n})$, a multiplier $\lambda_0 \geq 0$, a multiplier function $\hat{M} \in L^\infty([0,h], \mathbb{R}^{N\cdot p})$ and a vector $\hat{\nu} \in \mathbb{R}^{(N-1)\cdot n+q}$, $\hat{\nu} = (\hat{\nu}_0^*, \dots, \hat{\nu}_{N-2}^*, \hat{\nu}_{N-1}^*)^*$ where $\hat{\nu}_0, \dots \hat{\nu}_{N-2} \in \mathbb{R}^n$ and $\hat{\nu}_{N-1} \in \mathbb{R}^q$, such that the following conditions hold for almost every $t \in [0,h]$:

1. *Adjoint differential equation:*
$$\frac{\mathrm{d}}{\mathrm{d}t}\hat{\Lambda}(t)^* = -\mathcal{K}_\Xi(t, \hat{\Xi}(t), \hat{\Theta}(t), \hat{\Lambda}(t), \hat{M}(t)); \tag{28}$$
2. *Transversality condition:*
$$\hat{\Lambda}(0)^* = -\nu^* V_{\Xi^\alpha}(\hat{\Xi}(0), \hat{\Xi}(h)) \tag{29}$$
$$\hat{\Lambda}(h)^* = \lambda_0 \Gamma_{\Xi^\beta}(\hat{\Xi}(h)) + \nu^* V_{\Xi^\beta}(\hat{\Xi}(0), \hat{\Xi}(h)) \tag{30}$$

   where
$$\begin{aligned} V(\Xi^\alpha, \Xi^\beta) &= \Big(V_0(\xi_0^\beta, \xi_1^\alpha), \dots, V_{N-2}(\xi_0^\beta, \xi_1^\alpha),\, V_{N-1}(\xi_{N-1}^\beta)\Big)^* \\ &= \Big(\xi_0^\beta - \xi_1^\alpha,\, \xi_1^\beta - \xi_2^\alpha, \dots, \xi_{N-2}^\beta - \xi_{N-1}^\alpha,\, \psi(\xi_{N-1}^\beta)\Big)^* \end{aligned}$$
   denotes the function defining the boundary constraints, and
$$\Gamma(\Xi^\beta) = g(\xi_{N-1}^\beta).$$
   Herein
$$\Xi^\alpha = (\xi_0^\alpha, \dots, \xi_{N-1}^\alpha), \quad \Xi^\beta = (\xi_0^\beta, \dots, \xi_{N-1}^\beta)$$

represent placeholder variables for the boundary states $\Xi(0)$ and $\Xi(h)$. For the components Λ_i of the adjoint variable Λ, the transversality condition becomes

$$\hat{\Lambda}_i(0)^* = -\sum_{j=0}^{N-1} \hat{\nu}_j^* \frac{\partial}{\partial \xi_i^\alpha} V_j(\hat{\xi}_{j+1}(0), \hat{\xi}_j(h))$$

$$\hat{\Lambda}_i(h)^* = \lambda_0 \frac{\partial}{\partial \xi_i^\beta} \Gamma(\hat{\Xi}(h)) + \sum_{j=0}^{N-1} \hat{\nu}_j^* \frac{\partial}{\partial \xi_i^\beta} V_j(\hat{\xi}_{j+1}(0), \hat{\xi}_j(h)),$$

for $i = 0, \ldots, N-1$ [1]. In particular this gives the following explicit boundary conditions:

$$\hat{\Lambda}_i(0) = \hat{\nu}_{i-1}, \quad i = 1, \ldots, N-1, \tag{31}$$

$$\hat{\Lambda}_i(h) = \hat{\nu}_i, \quad i = 0, \ldots, N-2, \tag{32}$$

$$\hat{\Lambda}_{N-1}(h)^* = \lambda_0 g_x(\hat{\xi}_{N-1}(h)) + \hat{\nu}_{N-1}^* w_x(\hat{\xi}_{N-1}(h)). \tag{33}$$

3. *Minimum condition for the free Hamiltonian:*

$$K(t, \hat{\Xi}(t), \hat{\Theta}(t), \hat{\Lambda}(t)) \leq K(t, \hat{\Xi}(t), \Theta, \hat{\Lambda}(t)) \tag{34}$$

for all admissible $\Theta = (\theta_0^*, ..., \theta_{N-1}^*)^* \in \mathbb{R}^{Nm}$ satisfying

$$C(t + ih, \hat{\xi}_{i-k_0}(t), \ldots, \hat{\xi}_{i-k_d}(t), \theta_0, \ldots, \theta_d) \leq 0$$

for $i = 0, \ldots, N-1$.

4. *Local minimum condition for the augmented Hamiltonian:*

$$\mathcal{K}_\Theta(t, \hat{\Xi}(t), \hat{\Theta}(t), \hat{\Lambda}(t), M(t)) = 0. \tag{35}$$

5. *Non-negativity of multiplier and complementarity condition:*

$$\begin{aligned} &\hat{M}(t) \geq 0, \quad t \in [0, h] \\ &\hat{M}_i(t)^* C(t + ih, \hat{\xi}_{i-k_0}(t), \ldots, \hat{\xi}_{i-k_d}(t), \hat{\theta}_{i-k_0}(t), \ldots, \hat{\theta}_{i-k_d}(t)) = 0, \ t \in [0, h], \\ &i = 0, \ldots, N-1. \end{aligned} \tag{36}$$

Let us first evaluate the adjoint equations for the components $\hat{\Lambda}_j$ with $j = 0, 1, N-1-k_d$:

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t} \hat{\Lambda}_j(t)^* = -\hat{\mathcal{K}}_{\xi_j}(t) \\ &= -\sum_{\delta=0}^{d} \Big[\hat{\Lambda}_{k_\delta+j}(t)^* f_{y_\delta}(t + (k_\delta + j)h, \hat{\xi}_{k_\delta+j-k_0}(t), \ldots, \underbrace{\hat{\xi}_{k_\delta+j-k_\delta}}_{j}(t), \ldots, \hat{\xi}_{k_\delta+j-k_d}(t), \ldots) \\ &\quad + \hat{M}_{k_\delta+j}(t)^* C_{y_\delta}(t + (k_\delta + j)h, \hat{\xi}_{k_\delta+j-k_0}(t), \ldots, \underbrace{\hat{\xi}_{k_\delta+j-k_\delta}}_{j}(t), \ldots, \hat{\xi}_{k_\delta+j-k_d}(t), \ldots) \Big] \end{aligned}$$

Note that for $j > N-1-k_d$ the number of state variables ξ_j appearing in the augmented Hamiltonian (26) is reduced due to index shifting by $k_0, \ldots, k_d$. In detail, we summarize up the occurrence of variables ξ_j within $\mathcal{K}$ depending on j:

[1] Actually for $j = N-1$, the component $V_j(\hat{\xi}_{j+1}(0), \hat{\xi}_j(h)) = V_{N-1}(\hat{\xi}_{N-1}(h))$ does not involve the variable $\hat{\xi}_N(0)$. We do not refer to this fact in the sums for reasons of readability.

for $0 \le j \le N-1-k_d$:	every ξ_j occurs $d+1$-times in $\mathcal{K}$
for $N-1-k_d < j \le N-1-k_{d-1}$:	every ξ_j occurs d-times in $\mathcal{K}$
$\vdots$	$\vdots$
for $N-1-k_2 < j \le N-1-k_1$:	every ξ_j occurs twice in $\mathcal{K}$
for $N-1-k_1 < j \le N-1-k_0$:	every ξ_j occurs once in $\mathcal{K}$
for $N-1-k_0 < j$:	component ξ_j does not occur in $\mathcal{K}$

Taking this fact into account, we are able to rewrite the adjoint equations for every component $\hat{\Lambda}_j$, $0 \le j \le N-1$ in a compact form:

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\hat{\Lambda}_j(t)^* = -\hat{\mathcal{K}}_{\xi_j}(t)\\
&= -\sum_{\delta=0}^{d} \chi_\delta^j \Big[\hat{\Lambda}_{k_\delta+j}(t)^* f_{y_\delta}(t+(k_\delta+j)h, \hat{\xi}_{k_\delta+j-k_0}(t), \ldots, \hat{\xi}_j(t), \ldots, \hat{\xi}_{k_\delta+j-k_d}(t), \ldots)\\
&\quad + \hat{M}_{k_\delta+j}(t)^* C_{x_\delta}(t+(k_\delta+j)h, \hat{\xi}_{k_\delta+j-k_0}(t), \ldots, \hat{\xi}_j(t), \ldots, \hat{\xi}_{k_\delta+j-k_d}(t), \ldots)\Big],
\end{aligned}$$

where

$$\chi_\delta^j := \chi_{\{0,\ldots,N-1-k_\delta\}}(j)$$

denotes the characteristic function of the index set $\{0, \ldots, N-1-k_\delta\}$. As for $j > N-1-k_0$, the variables ξ_j do not appear in $\mathcal{K}$, i.e.

$$\hat{\mathcal{K}}_{\xi_j} = 0, \quad j > N-1-k_0,$$

we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\hat{\Lambda}_j(t) = 0, \quad j > N-1-k_0, \quad t \in [0,h]. \tag{37}$$

Thus, the adjoint variable $\hat{\Lambda}_j$ is constant for $j > N-1-k_0$.

Now we are able to define the adjoint function $\hat{\lambda} \in W^{1,\infty}([0,T],\mathbb{R}^n)$ and multiplier function $\hat{\mu} \in L^\infty([0,T],\mathbb{R}^p)$ for the multiple delayed optimal control problem (MDOCP) in the following way. For $t \in [0,T]$ there exists $0 \le j \le N-1$ with $jh \le t \le (j+1)h$. This gives $\chi_\delta^j = \chi_{\{0,\ldots,N-1-k_\delta\}}(j) = \chi_{[0,T-r_\delta]}(t)$ as

$$j \in \{0,\ldots,N-1-k_\delta\} \quad \iff \quad t \in [0,(N-1-k_\delta+1)h] = [0, Nh-k_\delta h] = [0, T-r_\delta].$$

We now put

$$\hat{\lambda}(t) := \hat{\Lambda}_j(t-jh), \quad \hat{\mu}(t) := \hat{M}_j(t-jh) \tag{38}$$

and obtain from the previous adjoint equation:

$$\begin{aligned}
&\dot{\hat{\lambda}}(t) = \frac{\mathrm{d}}{\mathrm{d}t}\hat{\Lambda}_j(t-jh)\\
&= -\sum_{\delta=0}^{d} \chi_\delta^j \Big[\hat{\Lambda}_{k_\delta+j}(t-jh)^* f_{y_\delta}(t+k_\delta h, \hat{x}(t+(k_\delta-k_0)h), \ldots\\
&\qquad\qquad \ldots, \hat{x}(t), \ldots, \hat{x}(t+(k_\delta-k_d)h), \ldots)\\
&\qquad + \hat{M}_{k_\delta+j}(t-jh)^* C_{y_\delta}(t+k_\delta h, \hat{x}(t+(k_\delta-k_0)h), \ldots\\
&\qquad\qquad \ldots, \hat{x}(t), \ldots, \hat{x}(t+(k_\delta-k_d)h), \ldots)\Big]
\end{aligned}$$

$$
\begin{aligned}
&= -\sum_{\delta=0}^{d} \chi_\delta^j \Big[\hat{\lambda}(t+k_\delta h)^* f_{y_\delta}(t+k_\delta h, \hat{x}(t+(k_\delta-k_0)h), \ldots \\
&\qquad\qquad\qquad\qquad \ldots, \hat{x}(t), \ldots, \hat{x}(t+(k_\delta-k_d)h), \ldots) \\
&\qquad + \hat{\mu}(t+k_\delta h)^* C_{y_\delta}(t+k_\delta h, \hat{x}(t+(k_\delta-k_0)h), \ldots \\
&\qquad\qquad\qquad\qquad \ldots, \hat{x}(t), \ldots, \hat{x}(t+(k_\delta-k_d)h), \ldots)\Big] \\
&= -\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t) \Big[\hat{\lambda}(t+r_\delta)^* f_{y_\delta}(t+r_\delta, \hat{x}(t+r_\delta-r_0), \ldots \\
&\qquad\qquad\qquad\qquad \ldots, \hat{x}(t), \ldots, \hat{x}(t+r_\delta-r_d), \ldots) \\
&\qquad + \hat{\mu}(t+r_\delta)^* C_{y_\delta}(t+r_\delta, \hat{x}(t+r_\delta-r_0), \ldots, \hat{x}(t), \ldots, \hat{x}(t+r_\delta-r_d), \ldots)\Big] \\
&= -\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t) \mathcal{H}_{y_\delta}(t+r_\delta, \hat{x}(t+r_\delta-r_0), \ldots, \hat{x}(t), \ldots, \hat{x}(t+r_\delta-r_d), \ldots) \\
&= -\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t) \hat{\mathcal{H}}_{y_\delta}(t+r_\delta)
\end{aligned}
$$

Thus we have found the adjoint equation (13). The transversality condition (33) for Λ_{N-1},

$$\hat{\Lambda}_{N-1}(h)^* = \lambda_0 g_x(\hat{\xi}_{N-1}(h)) + \hat{\nu}_{N-1}^* \psi_x(\hat{\xi}_{N-1}(h)),$$

gives the desired transversality condition (14) for (MDOCP) in view of $T = Nh$:

$$\hat{\lambda}(Nh) = \lambda_0 g_x(\hat{x}(Nh)) + \hat{\nu}^* \psi_x(\hat{x}(Nh)), \quad \hat{\nu} := \hat{\nu}_{N-1} \in \mathbb{R}^q.$$

Evaluation of transversality conditons (31) and (32)

$$\hat{\lambda}((ih)^-) = \hat{\Lambda}_{i-1}(h) \overset{(32)}{=} \hat{\nu}_{i-1} \overset{(31)}{=} \hat{\Lambda}_i(0) = \hat{\lambda}((ih)^+)$$

for $i = 1, \ldots, N-1$ ensures the continuity of the costate $\hat{\lambda}$ in $t = ih$ for $i = 1, \ldots, N-1$. To verify the minimum condition for the Hamiltonian H, we consider $t \in [0,T]$ and the corresponding index $j \in \{0, \ldots, N-1\}$ with $jh \le t \le (j+1)h$. Putting $t' := t - jh \in [0,h]$, the minimum condition (34) gives

$$K(t', \hat{\Xi}(t'), \hat{\Theta}(t'), \hat{\Lambda}(t')) \le K(t', \hat{\Xi}(t'), \Theta, \hat{\Lambda}(t')), \tag{39}$$

for all $\Theta \in \mathbb{R}^{Nm}$ satisfying

$$C(t'+ih, \hat{\xi}_{i-k_0}(t'), \ldots, \hat{\xi}_{i-k_d}(t'), \theta_{i-k_0}, \ldots, \theta_{i-k_d}) \le 0, \quad i = 0, \ldots, N-1.$$

The local minimum condition (35) yields $\mathcal{K}_\Theta(t') = 0$. Now we define a particular control policy $\Theta = (\theta_0^*, ..., \theta_{N-1}^*)^* \in \mathbb{R}^{N \cdot m}$ by

$$\theta_i := \left\{ \begin{array}{ll} \hat{u}(t'+ih), & i \ne j \\ u, & i = j \end{array} \right., \quad i = 0, \ldots, N-1,$$

where the control vector $u \in \mathbb{R}^m$ is satisfies

$$C(t, \hat{x}(t-r_0), \ldots, \hat{x}(t-r_d), \hat{u}(t-r_0), \ldots, \hat{u}(t-r_{\delta-1}), u, \hat{u}(t-r_{\delta+1}), \ldots, \hat{u}(t-r_d)) \le 0,$$

for $\delta = 0, \ldots, d$. Evaluating the inequality (39) for this vector Θ and removing identical expressions on both sides, we get for the remaining terms associated with

$j + k_\delta$ for $\delta = 0, \ldots, d$:

$$\sum_{\delta=0}^{d} \chi_\delta^j \Big[\hat{\Lambda}_{k_\delta+j}(t')^* f(t' + (j+k_\delta)h, \ldots, \hat{\theta}_{j+k_\delta-k_0}(t'), \ldots, \hat{\theta}_j(t'), \ldots, \hat{\theta}_{j+k_\delta-k_d}(t'))\Big]$$
$$\leq$$
$$\sum_{\delta=0}^{d} \chi_\delta^j \Big[\hat{\Lambda}_{k_\delta+j}(t')^* f(t' + (j+k_\delta)h, \ldots, \hat{\theta}_{j+k_\delta-k_0}(t'), \ldots, \theta_j = u, \ldots, \hat{\theta}_{j+k_\delta-k_d}(t'))\Big]$$

Redefining the adjoint and multiplier function in (38) with $t' = t - jh$, we obtain

$$\sum_{\delta=1}^{d} \chi_{[0,T-r_\delta]}(t) \Big[\hat{\lambda}(t+r_\delta)^* f(t+r_\delta, \ldots, \hat{u}(t+r_\delta-r_1), \ldots, \hat{u}(t), \ldots, \hat{u}(t+r_\delta-r_d))\Big]$$
$$\leq$$
$$\sum_{\delta=1}^{d} \chi_{[0,T-r_\delta]}(t) \Big[\hat{\lambda}(t+r_\delta)^* f(t+r_\delta, \ldots, \hat{u}(t+r_\delta-r_1), \ldots, u, \ldots, \hat{u}(t+r_\delta-r_d))\Big]$$

and hence the desired minimum condition (15) for the Hamiltonian H,

$$\begin{aligned} &\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t) \hat{H}(t+r_\delta) \\ \leq\ &\sum_{\delta=0}^{d} \chi_{[0,T-r_\delta]}(t) H(t+r_\delta, \ldots, \hat{u}(t+r_\delta-r_1), \ldots, u, \ldots, \hat{u}(t+r_\delta-r_d)) \end{aligned}$$

resp., the local minimum condition (16) for the augmented Hamiltonian. Condition (36) immediately implies the multiplier and complementarity condition (17) in view of (38). □

Remark. A feasible pair $(\hat{u}, \hat{x})$ that satisfies the necessary conditions in Theorem 3.1 is called an *extremal*. An extremal is called *normal*, if the multiplier λ_0 in Theorem 3.1 is nonzero and, hence, can be normalized to $\lambda_0 = 1$. It is easy to show that any extremal for a control problem with free terminal state is normal; cf. the examples in Sections 5 and 6.

4. **Discretization, optimization and consistency of adjoint equations.** We have assumed that the cost functional for the multiple delayed control problem (MDOCP) is given in Mayer form

$$J(u, x) = g(x(T)).$$

Any cost functional given in Bolza form (7) can be transformed to Mayer form by using the additional ODE (8). As in the case of nondelayed differential equations, there exist standard integration schemes of Euler or Runge–Kutta type for the delay differential equation

$$\dot{x}(t) = f(t, x(t-r_0), \ldots, x(t-r_d), u(t-r_0), \ldots, u(t-r_d)).$$

Using a uniform step size $h > 0$, it is crucial to match the positive delays $r_1, \ldots, r_d$. This can be guaranteed by the commensurability condition (9). Then any integer fraction of h can be chosen in order to refine the discretization grid. For this purpose, let $h > 0$ be a step size satisfying (9), i.e.

$$r_\delta = k_\delta h, \quad \delta = 0, \ldots, d, \qquad T = Nh.$$

with integers $0 = k_0 < k_1 < \ldots < k_d$ and N. This defines an equidistant discretization mesh with grid points $t_i = ih$, $i = 0, 1, ..., N$. In the following, we consider only the Euler integration scheme. Using the approximations $x(t_i) \approx x_i \in \mathbb{R}^n$, $u(t_i) \approx u_i \in \mathbb{R}^m$, we obtain the following nonlinear programming problem (NLP):

$$\text{Minimize} \qquad J(u,x) = g(x_N) \tag{40}$$

subject to

$$x_i - x_{i+1} + hf(t_i, x_{i-k_0}, \ldots, x_{i-k_d}, u_{i-k_1}, \ldots, u_{i-k_d}) = 0, \quad i = 0, .., N-1, \tag{41}$$

$$\psi(x_N) = 0, \tag{42}$$

$$C(t_i, x_{i-k_0}, \ldots, x_{i-k_d}, u_{i-k_0}, \ldots, u_{i-k_d}) \le 0, \quad i = 0, .., N-1. \tag{43}$$

Herein the initial value profiles x_0 and u_0 provide the values

$$x_{-i} := x_0(-ih), \quad i = 0, .., k_d, \tag{44}$$

$$u_{-i} := u_0(-ih), \quad i = 1, .., k_d. \tag{45}$$

The optimization variable in (NLP) is defined by the vector

$$z := (u_0, x_1, u_1, x_2, ..., u_{N-1}, x_N) \in \mathbb{R}^{N(m+n)}.$$

Assuming normality, the Lagrangian function for (NLP) is given by

$$\begin{aligned}\mathcal{L}(z, \lambda, \mu, \nu_N) := {}& g(x_N) + \nu_N^* \psi(x_N) \\ & + \sum_{i=0}^{N-1} \lambda_i^* (x_i - x_{i+1} + hf(t_i, x_{i-k_0}, \ldots, x_{i-k_d}, u_{i-k_0}, \ldots, u_{i-k_d})) \\ & + \sum_{i=0}^{N-1} \mu_i^* C(t_i, x_{i-k_0}, \ldots, x_{i-k_d}, u_{i-k_0}, \ldots, u_{i-k_d}),\end{aligned} \tag{46}$$

with Lagrange multipliers $\lambda = (\lambda_0, \lambda_1, \ldots, \lambda_{N-1}) \in \mathbb{R}^{n \cdot N}$, $\lambda_i \in \mathbb{R}^n$ $(i = 0, \ldots, N-1)$, for equations (41), $\mu = (\mu_0, \mu_1, \ldots, \mu_{N-1}) \in \mathbb{R}^{p \cdot N}$, $\mu_i \in \mathbb{R}^p$ $(i = 0, \ldots, N-1)$, for the inequality constraints (43), and $\nu_N \in \mathbb{R}^q$ for the boundary condtion (42). Note that the variables x_{-i} $(i = 0, \ldots, k_d)$ and u_{-i} $(i = 1, \ldots, k_d)$ appearing in the Lagrangian have fixed values in view of the initial conditions (44) and (45). For an optimal solution $\bar{z}$, the Karush-Kuhn-Tucker (KKT) necessary optimality conditions for (NLP) then imply the existence of Lagrange multipliers $(\bar{\lambda}, \bar{\mu}, \bar{\nu}_N)$ satisfying the equations

$$\frac{\partial \mathcal{L}}{\partial x_i}(\bar{z}, \bar{\lambda}, \bar{\mu}, \bar{\nu}_N) = 0 \quad (i = 1, ..., N), \qquad \frac{\partial \mathcal{L}}{\partial u_i}(\bar{z}, \bar{\lambda}, \bar{\mu}, \bar{\nu}_N) = 0 \quad (i = 0, ..., N-1).$$

For indices $i = 1, \ldots, N-1$, the first set of equations yields the relations

$$\begin{aligned} 0 = {}& -\bar{\lambda}_{i-1}^* + \bar{\lambda}_i^* \\ & + \sum_{\delta=1}^{d} \chi_\delta^j \Big[h \bar{\lambda}_{i+k_\delta}^* f_{y_\delta}(t_{i+k_\delta}, \bar{x}_{i+k_\delta-k_0}, \ldots, \bar{x}_{i+k_\delta-k_d}, \bar{u}_{i+k_\delta-k_1}, \ldots, \bar{u}_{i+k_\delta-k_d}) \\ & + \bar{\mu}_{i+k_\delta}^* C_{y_\delta}(t_{i+k_\delta}, \bar{x}_{i+k_\delta-k_0}, \ldots, \bar{x}_{i+k_\delta-k_d}, \bar{u}_{i+k_\delta-k_1}, \ldots, \bar{u}_{i+k_\delta-k_d}) \Big]. \end{aligned} \tag{47}$$

Recall that we used the variables $y_0, y_1, \ldots, y_d \in \mathbb{R}^n$ and $u_0, y_1, \ldots, u_d \in \mathbb{R}^m$ as placeholders for the delayed state and control variables. Finally, for the index

$i = N$ we get the boundary condition

$$0 = -\bar{\lambda}_{N-1} + g_x(\bar{x}_N) + \bar{\nu}_N^* \psi_x(\bar{x}_N). \tag{48}$$

Rearranging the preceding equations, we find

$$\begin{aligned} &\bar{\lambda}_i^* - \bar{\lambda}_{i-1}^* \\ &= -h \sum_{\delta=1}^{d} \chi_\delta^j \Big[\bar{\lambda}_{i+k_\delta}^* f_{y_\delta}(t_{i+k_\delta}, \bar{x}_{i+k_\delta-k_0}, \ldots, \bar{x}_{i+k_\delta-k_d}, \bar{u}_{i+k_\delta-k_0}, \ldots, \bar{u}_{i+k_\delta-k_d}) \\ &\quad + \frac{1}{h} \bar{\mu}_{i+k_\delta}^* C_{y_\delta}(t_{i+k_\delta}, \bar{x}_{i+k_\delta-k_0}, \ldots, \bar{x}_{i+k_\delta-k_d}, \bar{u}_{i+k_\delta-k_0}, \ldots, \bar{u}_{i+k_\delta-k_d}) \Big], \end{aligned} \tag{49}$$

for $i = 1, \ldots, N-1$.

Furthermore, the KKT conditions imply the non-negativity of the multipliers $\bar{\mu}_i$ and the complementarity conditions:

$$\bar{\mu}_i \geq 0, \quad \bar{\mu}_i C(t_i, \bar{x}_{i-k_0}, \ldots, \bar{x}_{i-k_d}, \bar{u}_{i-k_0}, \ldots, \bar{u}_{i-k_d}) = 0 \quad \text{for} \quad i = 0, ..., N-1. \tag{50}$$

Introducing *scaled* multipliers μ_i/h, equations (49) can be identified as the Euler discretization of the advanced adjoint equation (13) with boundary condition (14). Hence, the Lagrange multipliers provide the approximations

$$\hat{\lambda}(t_i) \approx \bar{\lambda}_i \in \mathbb{R}^n, \quad \hat{\mu}(t_i) \approx \bar{\mu}_i/h \in \mathbb{R}^p \quad (i = 0, ..., N-1). \tag{51}$$

Then the first order conditions $\partial\mathcal{L}/\partial u_i = 0$, $i = 0, ..., N-1$, represent the discretized local minimum condition (16) for the augmented Hamiltonian.

To solve the optimization problem (NLP) in (40) – (43) numerically, we employ the programming language AMPL developed by Fourer, Gay and Kernighan [9] in conjunction with the optimization solvers LOQO by Vanderbei [31, 32] or IPOPT by Wächter et al. [33, 34]. Both solvers also provide the Lagrange multipliers and thus yield the discretized adjoint variables and the multiplier function for the control problem (MDOCP) according to (51). This gives the opportunity to test numerical solutions for necessary optimality conditions given by Theorem 3.1. In particular we are able to check the Complementarity Condition (17) for mixed control-state-contrained problems. For problems with control functions appearing linearly in the dynamics and in the objective functional, the minimum condition for the free Hamiltonian (15) provides switching conditions for the optimal control. We will employ these results to subsequently check the numerical solutions obtained by IPOPT and LOQO for the examples in the following sections.

Note that instead of Euler's discretization scheme we may also use higher-order Runge–Kutta integration methods, e.g., Heun's second-order method or the implicit Euler method. For nondelayed optimal control problems, Hager [12] has given a detailed analysis of consistency and convergence for higher order Runge-Kutta schemes. A similar study should be be undertaken for retarded control problems which, however, is beyond the scope of this paper.

For notational convenience in the following examples, we omit the "hat" to denote optimal solutions.

5. **Analytical example.**

We consider the following optimal control problem in Bolza form (7) with the delay $r = 1$ in the state and $s = 2$ in the control variable:

$$\text{Minimize} \quad \int_0^3 (x^2(t) + u^2(t))\, \mathrm{d}t \tag{52}$$

subject to

$$\dot{x}(t) = x(t-1)x(t-2)u(t-2), \quad t \in [0,3], \tag{53}$$

$$x(t) = 1, \quad t \in [-2,0], \tag{54}$$

$$u(t) = 0, \quad t \in [-2,0). \tag{55}$$

In the general form of the control problem (MDOCP) with a Bolza cost functional we find $d = 2$ and the delays

$$r_0 = 0, \quad r_1 = 1, \quad r_2 = 2.$$

A control-state constraint will be imposed later. For simplicity, let us keep the notation x and u for the nondelayed state and control variable and denote by y_k, resp., v_k $(k = 1,2)$ the delayed state and control variables. Then the Hamiltonian (10) is given by

$$H(t,x,y_1,y_2,u,v_1,v_2,\lambda) = x^2 + u^2 + \lambda\, y_1 y_2 v_2\,. \tag{56}$$

For an optimal pair (u,x), the adjoint equation (13) and transversality condition (14) in Theorem 3.1 yield

$$\begin{aligned}
\dot{\lambda}(t) &= -\mathcal{H}_x(t,x(t),x(t-1),x(t-2),u(t),u(t-1),u(t-2),\lambda(t)) \\
&\quad - \chi_{[0,2]}(t)\mathcal{H}_{y_1}(t+1,x(t+1),x(t),x(t-1),u(t+1),u(t),u(t-1),\lambda(t+1)) \\
&\quad - \chi_{[0,1]}(t)\mathcal{H}_{y_2}(t+2,x(t+2),x(t+1),x(t),u(t+2),u(t+1),u(t),\lambda(t+2)) \\
&= -2x(t) - \chi_{[0,2]}(t)\lambda(t+1)x(t-1)u(t-1) - \chi_{[0,1]}(t)\lambda(t+2)x(t+1)u(t), \\
\lambda(3) &= 0.
\end{aligned}$$

It immediately follows from (53)–(55) that

$$x(t) = 1 \quad \text{for} \quad t \in [0,2].$$

The state variable can only be influenced by the control $u(t-2)$ on the terminal interval $[2,3]$. Hence, it suffices to determine the optimal control $u(t)$ on the interval $[0,1]$. The minimum condition (15) requires the minimization of the expression

$$\begin{aligned}
&H(t,x(t),x(t-1),x(t-2),u,u(t-1),u(t-2)) \\
&\quad + \chi_{[0,2]}(t)H(t+1,x(t+1),x(t),x(t-1),u(t+1),u,u(t-1)) \\
&\quad + \chi_{[0,1]}(t)H(t+2,x(t+2),x(t+1),x(t),u(t+2),u(t+1),u)
\end{aligned}$$

with respect to the control variable $u \in \mathbb{R}$ for $t \in [0,3]$. As H does not depend on v_1, the middle term $H(t+1,x(t+1),x(t),x(t-1),u(t+1),u,u(t-1))$ can be deleted in the preceding sum. Hence, the function

$$\begin{aligned}
&H(t,x(t),x(t-1),x(t-2),u,u(t-1),u(t-2)) \\
&\quad + \chi_{[0,1]}(t)H(t+2,x(t+2),x(t+1),x(t),u(t+2),u(t+1),u) \\
&= (x(t))^2 + u^2 + \lambda(t)x(t-1)x(t-2)u(t-2) \\
&\quad + \chi_{[0,1]}(t)((x(t+2))^2 + (u(t+2))^2 + \lambda(t+2)x(t+1)x(t)u)
\end{aligned}$$

has to be minimized with respect to u for $t \in [0,3]$. Therefore, the gradient of this expression with respect to u vanishes:

$$2u(t) + \chi_{[0,1]}(t)\lambda(t+2)x(t+1)x(t) = 0. \tag{57}$$

For $t \in [0,1]$, we obtain the control

$$u(t) = -\frac{1}{2}\,\lambda(t+2)x(t+1) = -\frac{1}{2}\,\lambda(t+2), \quad t \in [0,1].$$

On the interval $[1,3]$, we immediately get from (57)

$$u(t) = 0 \quad \text{for} \quad t \in [1,3].$$

Then on $[2,3]$, the adjoint and the state equation become

$$\dot{\lambda}(t) = -2x(t), \quad \dot{x}(t) = x(t-1)x(t)u(t-2) = u(t-2) = -\frac{1}{2}\lambda(t).$$

This yields a second-order differential equation for λ,

$$\ddot{\lambda}(t) = -2\dot{x}(t) = \lambda(t), \quad \text{for} \quad t \in [2,3],$$

which has the general solution

$$\lambda(t) = Ae^t + Be^{-t}, \quad x(t) = -\frac{1}{2}\left(Ae^t - Be^{-t}\right).$$

The constants A and B can be determined from the transversality condition (14) and the continuity of the state $x(t)$ at $t=2$,

$$\lambda(3) = 0, \quad x(2) = 1,$$

from which we find

$$A = \frac{-2e^{-2}}{e^2+1}, \qquad B = \frac{2e^4}{e^2+1}.$$

Then the control u on the first segment $[0,1]$ is given by

$$u(t) = \frac{e^{-2}}{e^2+1}e^{t+2} - \frac{e^4}{e^2+1}e^{-(t+2)} \quad \text{for} \quad t \in [0,1].$$

Now we evaluate the costate on the second interval $[1,2]$. The advanced differential equation

$$\begin{aligned}\dot{\lambda}(t) &= -2x(t) - \lambda(t+1)x(t-1)u(t-1) = -2 + \frac{1}{2}(\lambda(t+1))^2 \\ &= -2 + \frac{1}{2}\left(\frac{-2e^{-2}}{e^2+1}e^{t+1} + \frac{2e^4}{e^2+1}e^{-(t+1)}\right)^2\end{aligned}$$

and the continuity of the costate, $\lambda(2^-) = \lambda(2^+) = \frac{2(e^2-1)}{e^2+1} \approx 1.523188312$, yield the explicit solution

$$\begin{aligned}\lambda(t) &= \lambda(2^+) + \int_2^t \left(-2 + \frac{1}{2}(\lambda(\tau+1))^2\right) \mathrm{d}\tau \\ &= \frac{e^{2t-2} - e^{6-2t}}{(e^2+1)^2} - t \cdot \left(\frac{4e^2}{(e^2+1)^2} + 2\right) + \frac{4(e^2-1)}{(e^2+1)^2} + 6 \quad \text{for} \quad t \in [1,2].\end{aligned}$$

Similarly, we can compute $\lambda(t)$ on the first interval $[0,1]$. Since $x(t) = 1$ and $u(t) = 0$ on $[0,1]$, the adjoint equation reduces to

$$\begin{aligned}\dot{\lambda}(t) &= -2x(t) - \lambda(t+1)x(t-1)u(t-1) - \lambda(t+2)x(t+1)u(t) \\ &= -2 - \lambda(t+2)u(t) \\ &= 2\left(\frac{e^{2-t} - e^t}{(e^2+1)^2} - 1\right).\end{aligned}$$

Then the continuity of λ in $t=1$, $\lambda(1^-) = \lambda(1^+) = \frac{2(e^2-1)}{(e^2+1)^2} + 3 \approx 3.181568498$, leads to the following representation

$$\lambda(t) = \frac{e^{2t} - (2e^4 + 8e^2 - 2)t + 5e^4 + 16e^2 + 3 - e^{4-2t}}{(e^2+1)^2} \quad \text{for} \quad t \in [0,1].$$

Summing up our findings, we have obtained the optimal solution (x, u, λ):

$$\begin{aligned}
\text{for } t \in [0,1]: \quad & x(t) = 1, \quad u(t) = \frac{e^{-2}}{e^2+1} e^{t+2} - \frac{e^4}{e^2+1} e^{-(t+2)}, \\
& \lambda(t) = \frac{e^{2t} - (2e^4 + 8e^2 - 2)t + 5e^4 + 16e^2 + 3 - e^{4-2t}}{(e^2+1)^2}, \\
\text{for } t \in [1,2]: \quad & x(t) = 1, \quad u(t) = 0, \\
& \lambda(t) = \frac{e^{2t-2} - e^{6-2t}}{(e^2+1)^2} - t \cdot \left(\frac{4e^2}{(e^2+1)^2} + 2 \right) + \frac{4(e^2-1)}{(e^2+1)^2} + 6, \\
\text{for } t \in [2,3]: \quad & x(t) = \frac{e^{-2}}{e^2+1} e^{t} + \frac{e^4}{e^2+1} e^{-t}, \quad u(t) = 0, \\
& \lambda(t) = \frac{-2e^{-2}}{e^2+1} e^{t} + \frac{2e^4}{e^2+1} e^{-t}.
\end{aligned}$$

The analytical optimal solution allows us to determine the optimal performance index explicitly after some lengthy computations:

$$J = \int_0^3 (x^2(t) + u^2(t))\,\mathrm{d}t = 3 - \frac{2}{e^2+1} \approx 2.761594156\,.$$

Let us now compare the analytical solution with the numerical results. We solve the nonlinear optimization problem (40)–(45) obtained by Euler discretization and use the interior point code IPOPT developed by Wächter et al. [33, 34] and the LOQO algorithm by Vanderbei [31, 32].

In both cases we apply an error tolerance tol $=10^{-10}$. The starting solution is $x(t) \equiv 1$ and $u(t) \equiv 0$. Starting with a rather coarse discretization of $N = 600$ grid points, we find the following results for both codes

grid size	IPOPT	LOQO
$N = 600$	$J = 2.763044$	$J = 2.763044$
	CPU: 0.003s	CPU: 0.003s
$N = 60000$	$J = 2.761609$	$J = 2.761609$
	CPU: 0.406s	CPU: 0.414s
$N = 480000$	$J = 2.761596$	$J = 2.761596$
	CPU: 3.724s	CPU: 3.940s

Compared with the analytically determined value of $J = 2.761594156$, the numerically obtained performance index $J(x, u) = 2.763044158$ for the rather coarse grid of $N = 600$ points gives a deviation of about 0.05% from the analytical value $J = 2.761594156$. The extremely fine discretization with $N = 480000$ grid points yields an objective functional of $J(x, u) = 2.761596$ which is correct in 6 decimals. Fig. 1 displays the numerical solution for a mesh of $N = 600$ grid points, which visually is identical with the solution determined analytically.

Now we impose a mixed type control-state constraint with a delay in the control variable:

$$x(t) + u(t-2) \geq 0.5. \tag{58}$$

In terms of the (MDOCP) this implies a the constraint

$$C(t, x, y_1, y_2, u, v_1, v_2) = 0.5 - x - v_2 \leq 0. \tag{59}$$

The regularity condition (2) in Assumption 2 is satisfied in view of

$$\frac{\partial C}{\partial(u, v_1, v_2)} = (0, 0, -1) \neq 0.$$

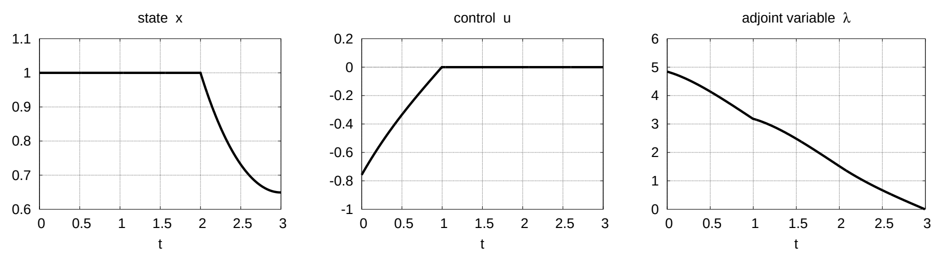

FIGURE 1. Optimal state $x(t)$, control $u(t)$ and adjoint $\lambda(t)$ determined numerically ($N = 600$).

The augmented Hamiltonian (11) is given by

$$\mathcal{H}(t, x, y_1, y_2, u, v_1, v_2, \lambda, \mu) = x^2 + u^2 + \lambda y_1 y_2 v_2 + \mu(0.5 - x - v_2).$$

The adjoint equation (13) yields

$$\dot{\lambda}(t) = -2x(t) - \chi_{[0,2]}(t)\lambda(t+1)x(t-1)u(t-1) - \chi_{[0,1]}(t)\lambda(t+2)x(t+1)u(t) + \mu(t).$$

On a boundary arc $[t_1, t_2]$ with $0 \le t_1 < t_2 \le 3$ we have $x(t) + u(t-2) = 0.5$. The multiplier $\mu(t)$ can be computed by the local minimum condition (16) which gives

$$\mathcal{H}_u(t) + \chi_{[0,1]}(t)\mathcal{H}_{v_2}(t+2) = 2u(t) + \chi_{[0,1]}(t)(\lambda(t+2)x(t+1)x(t) - \mu(t+2)) = 0.$$

Hence, on a boundary arc with $x(t) + u(t-2) = 0.5$ for $t \in [t_1, t_2] \subset [2, 3]$, the

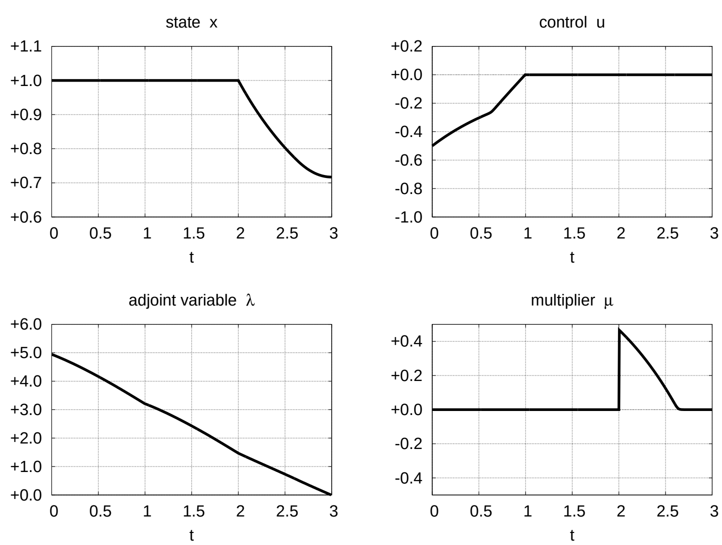

FIGURE 2. Numerical solution of the constrained problem ($N = 600$). *Top row*: state $x(t)$ and control $u(t)$. *Bottom row*: adjoint variable $\lambda(t)$ and multiplier μ for the constraint $x(t)+u(t-2) \ge 0.5$.

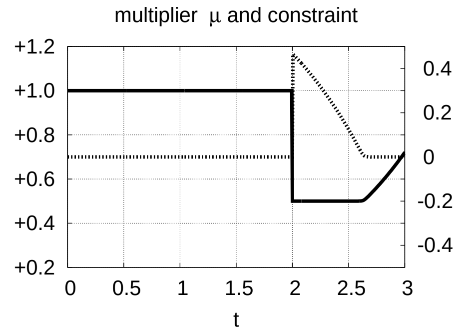

FIGURE 3. Constraint $x(t)+u(t-2)$ (solid line, left scale) and associated multiplier $\mu(t)$ (dashed line, right scale) for the constrained problem determined numerically ($N = 600$).

multiplier μ is computed as a function of the state and adjoint variable:

$$\mu(t) = 2u(t-2) + \lambda(t)x(t-1)x(t-2) = 2u(t-2) + \lambda(t).$$

For this constraint, we are not able to determine an analytical solution. Therefore, we apply the LOQO code with $N = 600$ grid points and obtain $J = 2.779208$ which gives a slightly higher objective functional than that of the unconstrained problem. Fig. 2 displays the computed state, control and adjoint variable as well as the constraint and associated multiplier μ. The mixed control-state constraint (58) becomes active in the interval $[2, 2.6]$. In particular Fig. 3 confirms that the multiplier μ satisfies the non-negativity and the multiplier condition (17) as expected by the necessary conditions.

6. **Example: Control of the innate immune response.** Delays in the dynamics of a control system frequently occur in models where significant transportation times of state and control data arise. In biomedicine, the development and treatment of a disease can be considered as a paradigm for delayed dynamic systems, since it usually takes some time for a drug to become effective. Moreover, the biological reaction to a pathological situation, e.g., to a virus attack, can be significantly delayed.

In this section, we investigate optimal control strategies in a model of the innate immune response suggested by Stengel et al. [29, 30]. The underlying dynamic model was developed by Asachenkov et al. [2]. Stengel et al. [29, 30] propose to introduce delays in the control model, but investigate only the nondelayed system. The authors determine optimal solutions for each control component separately, but fail to present optimal solutions where all components are optimized simultaneously.

The state variable of the optimal control model has four components:

x_1 : concentration of pathogen
(i.e. concentration of associated antigen)
x_2 : concentration of plasma cells,
which are carriers and producers of antibodies

x_3 : concentration of antibodies, which kill the pathogen (i.e. concentration of immunoglobulins)

x_4 : relative characteristic of a damaged organ (0 = healthy, 1 = dead).

A therapy treatment involves four (idealized) therapeutic control agents:

u_1 : pathogen killer

u_2 : plasma cell enhancer

u_3 : antibody enhancer

u_4 : organ healing factor.

The four nonlinear ODEs of the dynamic model are taken from Stengel et al. [29] with concrete parameter values. Possible delays are as follow: delays r_{x1} in the pathogen concentration x_1 and r_{x3} in the antibody concentration x_3, and a delay r_{u1} in the control variable u_1 (pathogen killer). The delays r_{x1} and r_{x3} cause a delayed plasma cell production.

$$\dot{x}_1(t) = (1 - x_3(t))x_1(t) - u_1(t - r_{u1}), \tag{60}$$

$$\dot{x}_2(t) = 3A(x_4(t))x_1(t - r_{x1})x_3(t - r_{x3}) - (x_2(t) - 2) + u_2(t), \tag{61}$$

$$\dot{x}_3(t) = x_2(t) - (1.5 + 0.5x_1(t))x_3(t) + u_3(t), \tag{62}$$

$$\dot{x}_4(t) = x_1(t) - x_4(t) - u_4(t). \tag{63}$$

We choose the delays

$$r_{x1} = 1.0, \quad r_{x2} = 1.5, \quad r_{u1} = 2.0,$$

which gives the following delays with $d = 2$ in the setting of the control problem (MDOCP):

$$0 = r_0 < r_1 := r_{x1} = 1.0 < r_2 := r_{x3} = 1.5 < r_3 := r_{u1} = 2.0.$$

The initial values and functions are given as follows

$$\begin{array}{lll} u_1(t) = 0, & -r_{u1} = -2.0 \le t < 0, & \\ x_1(t) = 0, & -r_{x1} = -1.0 \le t < 0, & x_1(0) = 3, \\ x_3(t) = 4/3, & -r_{x3} = -1.5 \le t \le 0, & \\ x_2(0) = 2, & x_4(0) = 0. & \end{array} \tag{64}$$

Note that the initial function for x_1 is *discontinuous* at $t = 0$. The idea behind this choice of initial function is that plasma cells can take notice of a pathogen attack and start production of antibodies only after a delay time r_{x1}. Stengel et al. [29] showed that the initial value $x_1(0)$ of the pathogen represents the lethal case, since the pathogen $x_1(t)$ diverges without control. The final state $x(T)$ is free though some components may be prescribed as well. The immune deficiency function $A(x_4)$ in (61) triggered by target organ damage is given by

$$A(x_4) = \left\{ \begin{array}{lll} \cos(\pi x_4) & \text{for} & 0 \le x_4 \le 0.5 \\ 0 & \text{for} & 0.5 \le x_4 \end{array} \right\}. \tag{65}$$

Note that the function $A(x_4)$ is not differentiable at $x_4 = 0.5$, so that the control problem has a nonsmooth dynamics. In order to avoid the non-differentiability of the function $A(x_4)$ at $x_4 = 0.5$, we shall consider the following mixed control-state constraint without delays:

$$C(x(t), u(t)) = 0.1u_4(t) + x_4(t) \le \alpha \le 0.5 \quad \text{for all} \quad t \in [0, T] \tag{66}$$

The regularity condition $C_u(x(t), u(t)) = (0, 0, 0, 0.1) \ne (0, 0, 0, 0)$ is obviously satisfied.

In the sequel, we study two types of cost functionals that can be roughly classified as a L^2–functional and L^1–functional. Stengel et al. [29] consider a L^2–type functional, where large values of pathogen concentration, poor organ health, and high doses of therapeutic agents are penalized *quadratically*. For simplicity, we chose all penalty weights as ones. Hence, optimal control functions $u_i \in L^\infty([0,T])$, $i = 1,..,4$, are to be determined that minimize the cost functional

$$J_2(x,u) = x_1^2(T) + x_4^2(T) + \int_0^T (x_1^2(t) + x_4^2(t) + u_1^2(t) + u_2^2(t) + u_3^2(t) + u_4^2(t))\,\mathrm{d}t \quad (67)$$

under the constraints (60)–(66). Here, $x = (x_1, x_2, x_3, x_4)$ denotes the state and $u = (u_1, u_2, u_3, u_4)$ the control variable. It can easily be seen that optimal control functions $u_i(\cdot)$ are *continuous*. In contrast to L^2–functionals, we will also consider the following L^1–functional that is linear in the control variables:

$$J_1(x,u) = x_1^2(T) + x_4^2(T) + \int_0^T (x_1^2(t) + x_4^2(t) + u_1(t) + u_2(t) + u_3(t) + u_4(t))\,\mathrm{d}t\,. \quad (68)$$

For this L^1–functional, it will be crucial to impose bounds for the control variables:

$$0 \le u_i(t) \le u_i^{\max} = 2 \quad \text{for all} \quad t \in [0,T], \quad i = 1,2,3,4. \quad (69)$$

Then the control variable u appears linearly in the Hamiltonian and, hence, optimal controls will be of bang-bang or singular type.

Optimal control for the L^2–functional (67). For notational purpose we introduce the following set of variables representing the delayed variables: y_1 stands for $x_1(t - r_{x1}) = x(t - r_1)$, y_3 stands for $x_3(t - r_{x3}) = x(t - r_2)$, and v_1 represents $u_1(t - r_{u1}) = u_1(t - r_3)$. We keep the notation $x = (x_1, x_2, x_3, x_4)$ and $u = (u_1, u_2, u_3, u_4)$ for the nondelayed state and control variables. Then the Hamiltonian (10) for the delayed control problem (60)–(67) with L^2–functional (67) is given by

$$\begin{aligned} H(x, y_1, y_3, u, v_1, \lambda) = {} & x_1^2 + x_4^2 + u_1^2 + u_2^2 + u_3^2 + u_4^2 \\ & + \lambda_1((1 - x_3)x_1 - v_1) + \lambda_2(3A(x_4)\, y_1\, y_3 + u_2 - (x_2 - 2)) \\ & + \lambda_3(x_2 - (1.5 + 0.5x_1)x_3) + u_3) + \lambda_4(x_1 - x_4 - u_4), \end{aligned} \quad (70)$$

where $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)$ denotes the adjoint variable (costate). Taking into account the mixed control–state constraint (66), the *augmented Hamiltonian* (11) becomes

$$\mathcal{H}(t, x, y_1, y_3, u, v_1, \lambda, \mu) = H(t, x, y_1, y_3, u, v_1, \lambda) + \mu\,(0.1u_4 + x_4 - \alpha) \quad (71)$$

with a scalar multiplier μ. The adjoint equations (13) yield the following advanced equations:

$$\begin{aligned} \dot\lambda_1(t) = & -2x_1(t) - \lambda_1(t)(1 - x_3(t)) + 0.5\lambda_3(t)x_1(t) - \lambda_4(t) \\ & - \chi_{[0,T-r_{x1}]}(t) \cdot 3\lambda_2(t + r_{x1}) \cdot A(x_4(t + r_{x1}))x_3(t + r_{x1} - r_{x3}) \\ \dot\lambda_2(t) = & \lambda_2(t) - \lambda_3(t) \\ \dot\lambda_3(t) = & \lambda_1(t)x_1(t) + \lambda_3(t)(1.5 + 0.5x_1(t)) \\ & - \chi_{[0,T-r_{x3}]}(t) \cdot 3\lambda_2(t + r_{x3}) \cdot A(x_4(t + r_{x3}))x_1(t + r_{x3} - r_{x1}) \\ \dot\lambda_4(t) = & -2x_4(t) - 3\lambda_2(t)A'(x_4(t))x_1(t - r_{x1})x_3(t - r_{x3}) + \lambda_4(t) - \mu(t) \end{aligned} \quad (72)$$

The transversality condition (14) gives

$$\lambda_1(T) = 2x_1(T), \quad \lambda_2(T) = 0, \quad \lambda_3(T) = 0, \quad \lambda_4(T) = 2x_4(T). \tag{73}$$

Let us now evaluate the local minimum condition (16) for the augmented Hamiltonian with respect to the control components. Since no bounds are prescribed for the control variables, the minimum condition yields the following 4 equations:

$$\begin{aligned}
\mathcal{H}_{u_1}[t] + \chi_{[0,T-r_{u1}]}(t)\mathcal{H}_{v_1}[t+r_{u1}] = 2u_1(t) - \chi_{[0,T-r_{u1}]}(t)\lambda_1(t+r_{u1}) &= 0, &(74)\\
\mathcal{H}_{u_2}[t] = 2u_2(t) + \lambda_2(t) &= 0, &(75)\\
\mathcal{H}_{u_3}[t] = 2u_3(t) + \lambda_3(t) &= 0, &(76)\\
\mathcal{H}_{u_4}[t] = 2u_4(t) - \lambda_4(t) + 0.1\mu(t) &= 0. &(77)
\end{aligned}$$

For interior arcs with $0.1u_4(t) + x_4(t) < 0$ we have $\mu(t) = 0$ and thus obtain the control law

$$\begin{aligned}
&u_1(t) = \left\{ \begin{array}{lll} \lambda_1(t+r_{u1})/2 & \text{for} & 0 \le t < T - r_{u1} \\ 0 & \text{for} & T - r_{u1} \le t \le T \end{array} \right\} , \quad u_2(t) = -\lambda_2(t)/2, \\
&u_3(t) = -\lambda_3(t)/2 \qquad\qquad\qquad\qquad\qquad\qquad\quad , \quad u_4(t) = \lambda_4(t)/2.
\end{aligned} \tag{78}$$

When the mixed control-state constraint (69) is active, i.e., $0.1\,u_4(t) + x_4(t) = \alpha$ holds on an interval $[t_1, t_2] \subset [0, T]$, we obtain the *boundary control* $u_4(t) = 10(\alpha - x_4(t))$. Then equation (77) yields the multiplier

$$\mu(t) = 10(\lambda_4(t) - 2u_4(t)) = 10(\lambda_4(t) - 20(\alpha - x_4(t))). \tag{79}$$

as a function of the state and adjoint variable.

To obtain a numerical solution, we apply the Euler-discretization approach as presented in the Section 4. The delays are $r_0 = 0$, $r_1 = r_{x1} = 1.0$, $r_2 = r_{x3} = 1.5$, $r_3 = r_{u1} = 2.0$ and the final time is $T = 10.0$.

First, we compute the solution to the nondelayed control problem without the mixed control-state constraint (66). For $N = 10000$ grid points we get the following functional value and terminal values $x_1(T)$ and $x_4(T)$:

$$J_2(x,u) = 7.14246, \quad x_1(T) = 5.034 \times 10^{-9},\ x_4(T) = 4.2855 \times 10^{-6}$$

The transversality condition (73) yields the terminal costate

$$\lambda(T) = (2x_1(T), 0.0, 0.0, 2x_4(T)).$$

The state and control variables are displayed in Fig. 4. The simultaneous action of the controls efficiently kills the pathogen within a short period of time. Hence, state and control variables are shown only on the reduced time interval $[0, 6]$. The adjoint variable $\lambda_4(t)$ and, hence, the control $u_4(t)$ are differentiable everywhere except at $t_1 = 0.736$ and $t_2 = 1.44$, where we have $x_4(t_k) = 0.5$ for $k = 1, 2$, cf. Fig. 4, left column.

Next, we study the optimal solution with delays $r_1 = r_{x1} = 1.0$, $r_2 = r_{x3} = 1.5$, $r_3 = r_{u1} = 2.0$. The Euler discretization with $N = 2000$ grid points gives the following results:

$$J_2(x,u) = 16.5357, \quad x_1(T) = 1.5325 \times 10^{-5},\ x_4(T) = 1.2157 \times 10^{-4},$$

which provides the adjoint variable $\lambda(T) = (2x_1(T), 0.0, 0.0, 2x_4(T))$.

Optimal state and control variables are displayed in Fig. 5 which clearly shows the delayed antibody production of plasma cells. The initial high peak of x_2 in the nondelayed solution is replaced by two smaller peaks appearing after the delay time $r_{x1} = 1$. The organ is severely damaged with values $x_4(t) \ge 0.5$ on the rather

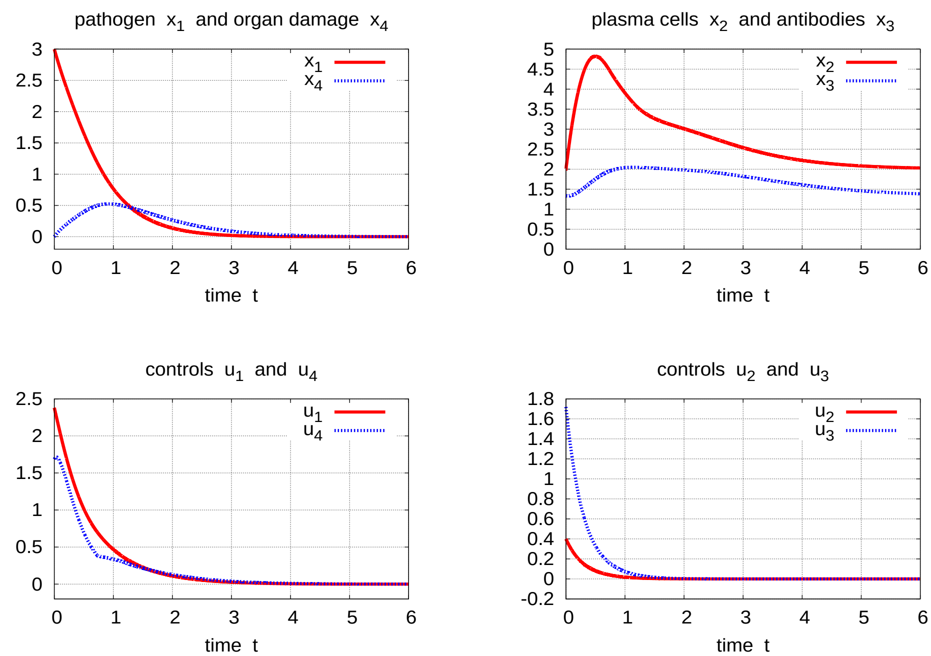

FIGURE 4. L^2-functional (67): nondelayed solution without mixed control-state constraint (66). *Top row*: (a) pathogen x_1 and organ damage x_4; (b) plasma cells x_2 and antibodies x_3. *Bottom row*: (a) pathogen killer u_1 and organ healing factor u_4; (b) plasma cells enhancer u_2 and antibody enhancer u_3.

large interval $[0.267, 2.64]$ with a peak value of $x_4(\tau) = 0.9196$ at $\tau = 1.04$. This strongly motivates to consider the mixed control-state (66), $0.1u_4(t) + x_4(t) \le \alpha$, with $\alpha < 0.5$.

For $\alpha = 0.3$ we obtain the optimal solution shown in Fig 6. It takes a bit longer to reduce the pathogen to small values, but the organ damage shrinks to a maximum value of 0.286. There is only one high peak of plasma cells x_2 for $t \ge 1$. The numerical results obtained for $N = 2000$ grid points are

$$J_2(x, u) = 18.9443, \quad x_1(T) = 1.0506 \times 10^{-4},\ x_4(T) = 4.7795 \times 10^{-5}.$$

Optimal solutions for the L^1–functional (68). Let us study now the L^1–functional

$$J_1(x, u) = x_1^2(T) + x_4^2(T) + \int_0^T (x_1^2(t) + x_4^2(t) + u_1(t) + u_2(t) + u_3(t) + u_4(t))\,\mathrm{d}t\,,$$

for which the Hamiltonian becomes a linear function of the control variables. The adjoint equations and transversality condition agrees with those in (72) and (73).

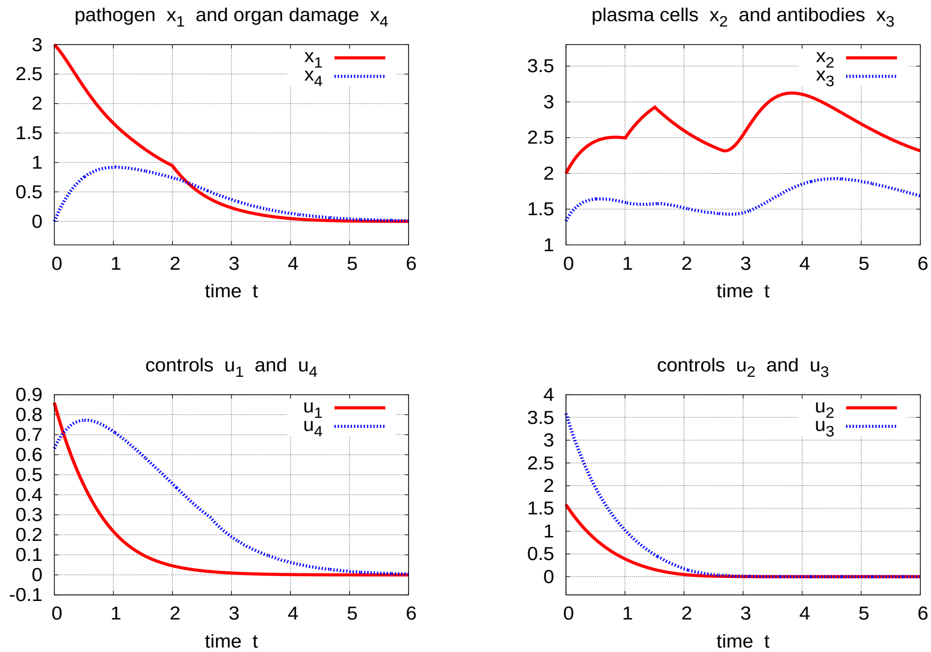

FIGURE 5. L^2-functional (67): optimal solution with delays $r_{x1} = 1.0$, $r_{x3} = 1.5$, $r_{u1} = 2.0$ but without mixed control-state constraint (66). *Top row*: (a) pathogen x_1 and organ damage x_4; (b) plasma cells x_2 and antibodies x_3. *Bottom row*: (a) pathogen killer u_1 and organ healing factor u_4; (b) plasma cells enhancer u_2 and antibody enhancer u_3.

The evaluation of the minimum condition (15) leads to the switching functions

$$\begin{array}{lclcl} \sigma_1(t) & = & H_{u_1}[t] + \chi_{[0,T-r_{u1}]}(t)\, H_{v_1}[t + r_{u1}] & = & 1 - \chi_{[0,T-r_{u1}]}(t)\, \lambda_1(t + r_{u1}), \\ \sigma_2(t) & = & H_{u_2}[t] & = & 1 + \lambda_2(t), \\ \sigma_3(t) & = & H_{u_3}[t] & = & 1 + \lambda_3(t), \\ \sigma_4(t) & = & H_{u_4}[t] & = & 1 - \lambda_4(t), \end{array} \tag{80}$$

which determine the minimizing controls according to

$$u_k(t) = \left\{ \begin{array}{lll} 2 & \text{if} & \sigma_k(t) < 0 \\ 0 & \text{if} & \sigma_k(t) > 0 \\ \text{singular} & \text{if} & \sigma_k(t) = 0 \quad \text{in} \quad I_s \subset [0,T] \end{array} \right\}, k = 1, \ldots, 4. \tag{81}$$

The following computations show that optimal controls are bang-bang in the nondelayed control problem, whereas in the delayed problem, the control u_4 has singular subarcs. It is interesting to note that the control u_4 along an active arc of the mixed constraint (66) behaves like a singular arc as long as it stays in the interior of the control set $[0, 2]$.

First, the state and control variables are computed for the nondelayed control problem omitting the constraint (66). Using $N = 4000$ grid points, the Euler

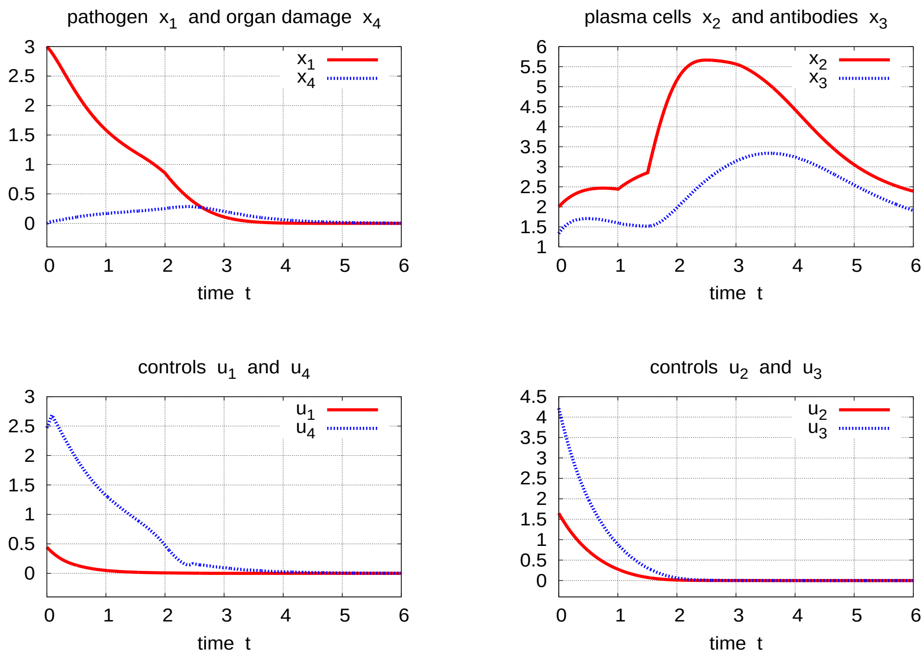

FIGURE 6. L^2-functional (67): optimal solution with delays $r_{x1} = 1.0$, $r_{x3} = 1.5$, $r_{u1} = 2.0$ and constraint $0.1u_4 + x_4 \leq 0.3$. *Top row*: (a) pathogen x_1 and organ damage x_4; (b) plasma cells x_2 and antibodies x_3. *Bottom row*: (a) pathogen killer u_1 and organ healing factor u_4; (b) plasma cells enhancer u_2 and antibody enhancer u_3.

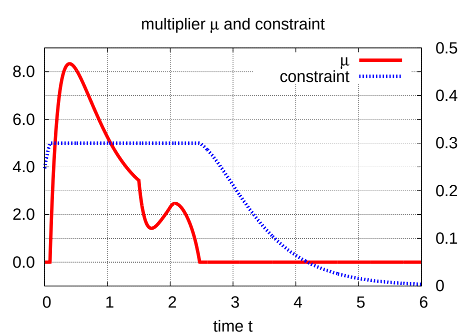

FIGURE 7. L^2-functional (67) and delays $r_{x1} = 1.0$, $r_{x3} = 1.5$, $r_{u1} = 2.0$: constrained function $0.1u_4(t) + x_4(t)$ (right scale) and multiplier $\mu(t)$ (left scale).

discretization furnishes the numerical results

$$J_1(x, u) = 6.03717, \quad x_1(T) = 9.18314 \times 10^{-4}, \quad x_2(T) = 1.54738 \times 10^{-3}.$$

The state variables are depicted in Fig. 8 on the reduced time interval $[0, 6]$ as well as the control variables, resp. the switching functions (80) on the time intervals $[0, 1.5]$, resp. $[0, 2]$. The control u_2 is identically zero, whereas the controls u_1, u_3, u_4 are bang-bang with only one switch at t_k from $u_k = 2$ to $u_k = 0$: $t_1 = 0.668$, $t_3 = 0.238$, $t_4 = 0.430$. Fig. 8 clearly demonstrates that the switching conditions (81) for the minimizing controls are perfectly satisfied. Drugs u_1, u_3, u_4 have to be given in full doses before discontinuing abruptly at separate switching times.

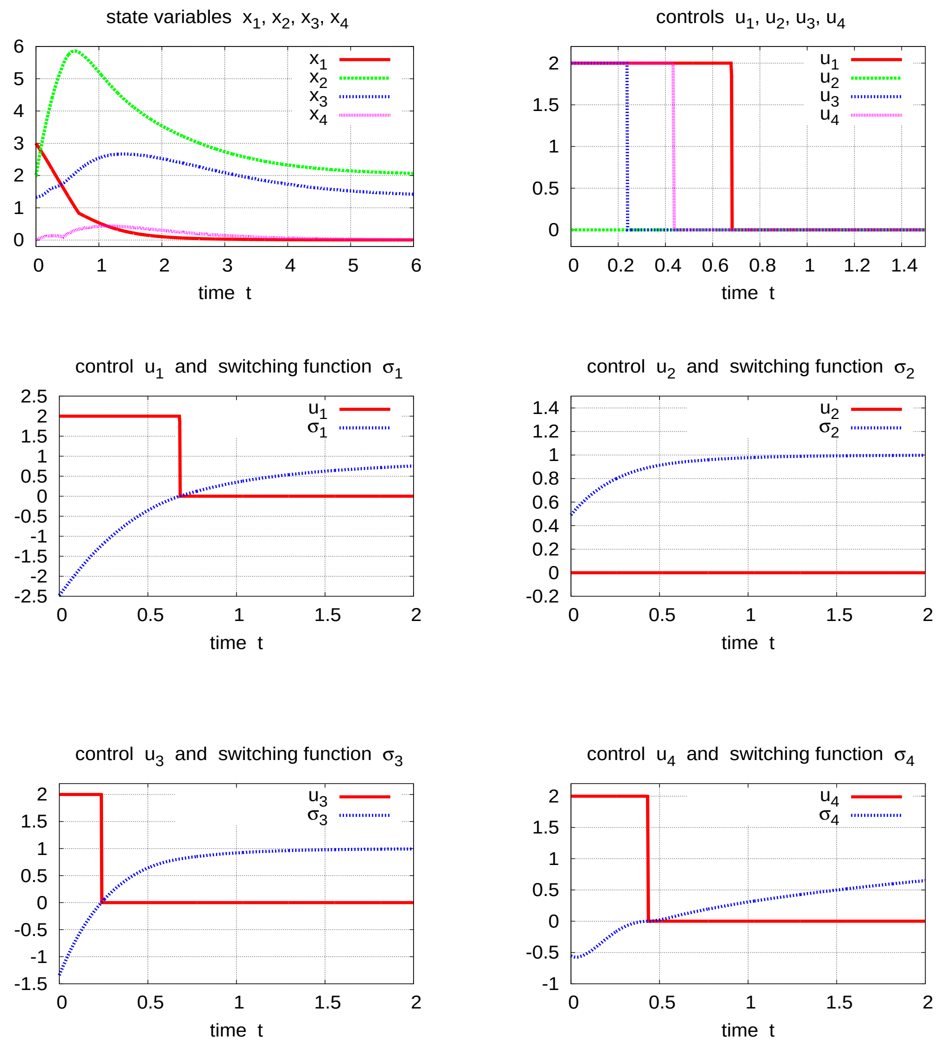

FIGURE 8. L^1-functional (68): optimal solution without delays and mixed control-state constraint (66). *Top row*: (a) state variables $x_k, k = 1, 2, 3, 4$, control variables $u_k, k = 1, 2, 3, 4$; *Middle row*: control u_1, resp. u_2 and switching function σ_1, resp. σ_2; *Bottom row*: control u_3, resp. u_4 and switching function σ_3, resp. σ_4.

Now, we compute the optimal solution with delays $r_1 = r_{x1} = 1.0$, $r_2 = r_{x3} = 1.5$, $r_3 = r_{u1} = 2.0$ and get the following results with $N = 1000$ grid points:

$$J_1(x,u) = 14.6579, \quad x_1(T) = 2.29399 \times 10^{-4}, \quad x_2(T) = 8.41865 \times 10^{-4}.$$

Optimal state control and control variables are displayed in Fig. 9. It is surprising that the pathogen killer u_1 is identically zero. The controls u_2 and u_3 are bang-bang with only one switch, while the organ healing factor u_4 is a rather complicated control composed by several bang-bang and singular arcs. The bottom of Fig. 9 exhibits the controls u_3 and u_4 and its associated switching functions σ_3 and σ_4 on the reduced interval $[0, 3]$ to demonstrate more clearly that the control law (81) is satisfied numerically.

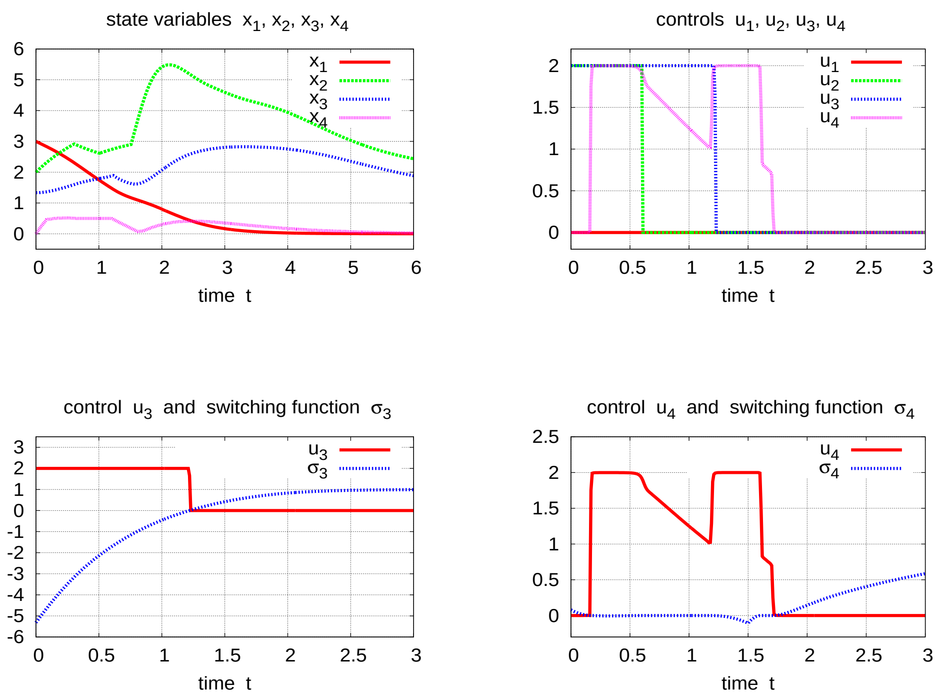

FIGURE 9. L^1-functional (68): optimal solution with delays $r_{x1} = 1.0$, $r_{x2} = 1.5$, $r_{u1} = 2.0$ but without constraint (66). *Top row*: (a) state variables $x_k, k = 1, 2, 3, 4$, (b) control variables $u_k, k = 1, 2, 3, 4$; *Bottom row*: (a) control u_3 and switching function σ_3, (b) control u_4 and switching function σ_4.

Finally, we consider the control problem with delays and impose the mixed control-state constraint $0.1u_4(t) + x_4(t) \leq 0.5$ as for the L^2–functional. Here, for $N = 2000$ grid points we get the results

$$J_1(x,u) = 14.6632, \quad x_1(T) = 2.4058 \times 10^{-4}, \quad x_2(T) = 8.6099 \times 10^{-4}.$$

Fig. 10 shows optimal controls that are similar to those in Fig. 9: the pathogen killer u_1 is identically zero, the controls u_2 and u_3 are bang-bang with one switch, and the control u_4 has bang-bang and boundary arcs. Here, it is noteworthy that the initial bang-bang arc with $u_4 = 2$ is followed by a boundary arc with active constraint $0.1u_4(t) + x_4(t) = 0.5$.

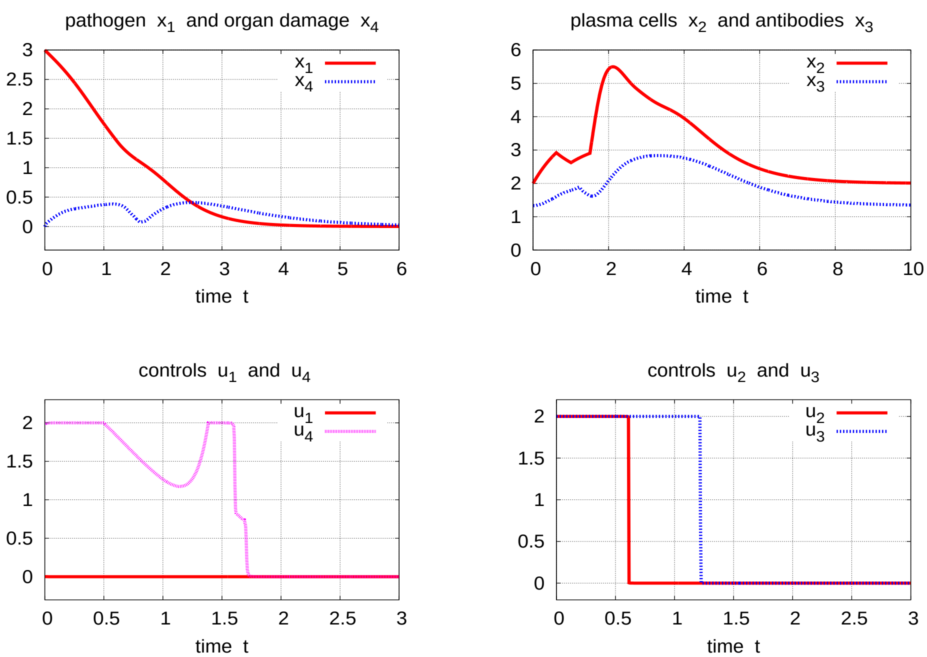

FIGURE 10. L^1–functional (68) with delays $r_{x1} = 1.0$, $r_{x2} = 1.5$, $r_{u1} = 2.0$ and constraint $0.1u_4 + x_4 \leq 0.5$. *Top row*: (a) state variables x_1 and x_4, (b) state variables x_2 and x_3. *Bottom row*: control variables u_1 and u_4, (b) control variables u_2 and u_3.

Fig. 11 displays the constraint function $0.1u_4(t) + x_4(t)$ and the associated multiplier μ.

7. **Conclusion.** We have derived necessary optimality conditions in the form of a Pontryagin Minimum Principle for optimal controls problems with multiple time-delays and mixed control-state constraints. The transformation technique in [11, 10] has been used to transform the delayed control problem into an augmented non-delayed control problem to which the standard Minimum Principle can be applied. A special feature of the Minimum Principle for delayed control problems is that the adjoint equations for the costate variable involve advanced times. The proof of the Minimum Principle involves a commensurability assumption for the time-delays, which is also of importance in the numerical approach. We discuss the Euler discretization of the dynamic equations by which the optimal control problem is transcribed into a high-dimensional nonlinear programming problem (NLP). It is shown that the Lagrange multipliers for this NLP correspond to the discretized costate variables and the multipliers associated to the mixed control-state constraint.

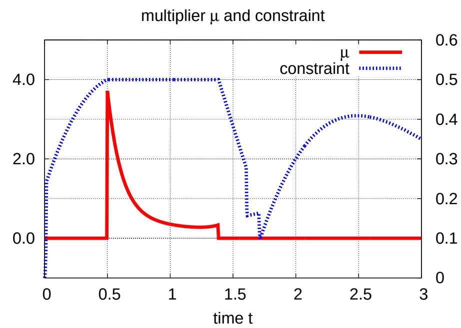

FIGURE 11. L^1-functional and delays $r_{x1} = 1.0$, $r_{x3} = 1.5$, $r_{u1} = 2.0$: constrained function $0.1u_4 + x_4$ (right scale) and multiplier $\mu(t)$ (left scale).

The Minimum Principle and the numerical approach is illustrated on two examples. First, we present an academic example that has an analytical solution when no constraints are present. The comparison of the analytical and numerical solution demonstrates the excellent performance of the NLP approach. Then we discuss the optimal control of the innate immune response, where the dynamic model is taken from previous work by Stengel et al. [29, 30]. In this model, we introduce additional time delays since the antigen and antibody concentration affects the plasma cell production after significant duration. Also, a delayed action of the applied drug is involved as it usually takes some time for an agent to become effective. In the numerical analysis we consider objective functionals of L_2- and L_1-type. In the latter case bang-bang-controls can result from L_1-type functionals that are easier to realize in medical attendance.

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