Sufficient Conditions and Sensitivity Analysis for Optimal Bang-Bang Control Problems with State Constraints

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Abstract. Bang-bang control problems subject to a state inequality constraint are considered. It is shown that the control problem induces an optimization problem, where the optimization vector assembles the switching and junction times for bang-bang and boundary arcs. Second order sufficient conditions (SSC) for the state-constrained control problem are given which require that SSC for the induced optimization problem are satisfied and a generalized strict bang-bang property holds at switching and junction times. This type of SSC ensures solution differentiability of optimal solutions under parameter perturbations and allows to compute parametric sensitivity derivatives. A numerical algorithm is presented that simultaneously determines a solution candidate, performs the second-order test and computes parametric sensitivity derivatives. We illustrate the algorithm with two state-constrained optimal control problems in biomedicine.

1 Introduction

Second-order sufficient optimality conditions (SSC) for bang-bang controls without state constraints have been derived in Agrachev, Stefani and Zezza [1] on the basis of an induced optimization problem where the control process is optimized with respect to the unknown switching times of the bang-bang control. The equivalence of this type of SSC with a different form of SSC obtained earlier in the literature has recently been shown in [20,21,23]. Numerical methods for the verification of optimization based SSC have been developed in Maurer, Büskens, Kim and Kaya [18] using the so-called arc-parameterization method where the arc-lengths of the bang-bang arcs are optimized. Basic ideas for a sensitivity analysis of bang-bang controls may be found in Kim, Maurer [11].

The purpose of this paper is to extend the results and techniques in [18,11] to bang-bang control problems with a state constraint. In Sect. 2, we review the necessary conditions for an optimal control problem with a state constraint of order one. The regularity conditions in assumptions (A1), (A2) allow to determine the multiplier associated with the state constraint. In Sect. 3, we formulate an *induced optimization problem* where the

optimization vector assembles the switching times of bang-bang arcs, resp., the entry- and exit-times (junction times) of boundary arcs, and the free final time. The crucial point in this optimization approach is the fact that the optimal control is given in feedback form along boundary arcs.

Based on second-order sufficient conditions (SSC) for the induced optimization problem, we give SSC for the control problem which require the strict bang-bang property in assumption (A4) and the strict complementarity in (A5). In Sect. 4, the arc-parameterization method from [18] is extended to incorporate boundary arcs. The main result on sensitivity analysis is given in Sect. 5. We include a formula for the sensitivity derivatives of the switching and junction times which can be implemented into the routine NUDOCCCS developed in [4]; cf. also [5,6]. In Sect. 6, we discuss the drug displacement problem in [22] in the light of the SSC presented in Theorem 2. In Sect. 7, we determine the optimal control in a two-compartment model for cancer therapy [12], when a state constraint on the number of tumor cells is imposed.

2   Optimal Bang-Bang Control Problems with a State Constraint

Let $x(t) \in \mathbb{R}^n$ denote the state variable and $u(t) \in \mathbb{R}$ the control variable at time $t \in [0, t_f]$, where the final time $t_f > 0$ is either fixed or free. For simplicity, the control is assumed to be scalar. The following autonomous optimal control problem with control variable appearing linearly will be denoted by (OC): determine a measurable control function $u : [0, t_f] \to \mathbb{R}$ and a terminal time $t_f > 0$ such that the pair of functions $(x(\cdot), u(\cdot))$ minimizes the cost functional of Mayer type

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

subject to the constraints in the interval $[0, t_f]$,

$$\dot{x}(t) = f(x(t), u(t)) = f_0(x(t)) + f_1(x(t))u(t), \tag{2}$$
$$x(0) = x_0, \ \varphi(x(t_f), t_f) = 0, \tag{3}$$
$$u_{\min} \leq u(t) \leq u_{\max}, \tag{4}$$

and the scalar state inequality constraint

$$S(x(t)) \leq 0 \text{ for } 0 \leq t \leq t_f. \tag{5}$$

The functions $g : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}$, $f_0, f_1 : \mathbb{R}^n \to \mathbb{R}^n$, $\varphi : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^r$, $0 \leq r \leq n$, and $S : \mathbb{R}^n \to \mathbb{R}$ are assumed to be twice continuously differentiable. The state constraint is assumed to be of *order one* [9,16], i.e., the total time derivative of the function $S(x(t))$ contains the control explicitly,

$$S^1(x, u) := S_x(x)(f_0(x) + f_1(x)u) = a(x) + b(x)u, \tag{6}$$

where $b(x) = S_x(x)f_1(x) \not\equiv 0$. Here and in the sequel, partial derivatives are denoted by subscripts. A subinterval $[\tau_1, \tau_2] \subset [0, t_f]$ is called an *interior arc* if $S(x(t)) < 0$ holds on (τ_1, τ_2). The interval $[\tau_1, \tau_2]$ is called a *boundary arc* if $S(x(t)) \equiv 0$ holds for all

$t \in [\tau_1, \tau_2]$. If $[\tau_1, \tau_2]$ is maximal with this property, then τ_1 is called *entry-time* and τ_2 is called *exit-time* of the boundary arc; τ_1, τ_2 are also called *junction times*. The following assumption is a standard regularity condition for a boundary arc [9,15,17].

(**A1**) $$b(x(t)) \neq 0 \; \forall \, t \in [\tau_1, \tau_2].$$

Under this assumption, the *boundary control* on a boundary arc is determined by the equation $S^1(x,u) = a(x) + b(x)u = 0$ as the feedback expression

$$u_b(x) = -a(x)/b(x), \;\; u(t) = u_b(x(t)). \tag{7}$$

The following assumption will be needed to determine the multiplier associated with the state constraint explicitly.

(**A2**) The boundary control lies in the interior of the control region:

$$u_{\min} < u(t) = u_b(x(t)) < u_{\max} \; \forall \, t \in [\tau_1, \tau_2]. \tag{8}$$

Assumptions (A1) and (A2) allow us to formulate first order necessary conditions of Pontryagin's minimum principle in a computationally convenient form. We recall from [9,17] that the Lagrange multiplier associated with the state constraint (5) is a measure that is represented by a function μ of bounded variation. Using (A1) and (A2), it has been shown in [16,17,15,14] that the measure has a Radon-Nikodym derivative η which allows to write the following adjoint equation (11) in differential form. In the *direct adjoining approach* [9,17], the augmented Pontryagin or Hamiltonian function is defined by

$$H(x,u,\lambda,\mu) = \lambda f(x,u) + \eta S(x) = \lambda f_0(x) + \lambda f_1(x)u + \eta S(x), \tag{9}$$

where the adjoint variable $\lambda \in \mathbb{R}^n$ is a row vector and η is the multiplier associated with the state constraint.

Suppose now that $\bar{u} : [0, \bar{t}_f] \to [u_{\min}, u_{\max}]$ is an optimal control with optimal final time $\bar{t}_f$ and corresponding trajectory $\bar{x} : [0, \bar{t}_f] \to \mathbb{R}^n$. Assume that (A1), (A2) hold and the state constraint (5) is not active at $t = 0$ and $t = \bar{t}_f$,

$$S(\bar{x}(0)) < 0 \;\; \text{and} \;\; S(\bar{x}(\bar{t}_f)) < 0. \tag{10}$$

In the sequel, we will use the junction theorem in [16], Corollary 5.2 (ii), where it was shown that the adjoint variables are *continuous* at junction times provided that the state constraint is of *first order* and the control is *discontinuous* at junctions. Note that the latter property follows from (A2). Then there exist an absolutely continuous (a.c.) adjoint function $\lambda : [0, \bar{t}_f] \to \mathbb{R}^n$, a piecewise a.c. multiplier function $\eta : [0, \bar{t}_f] \to \mathbb{R}$ and a multiplier $\rho \in \mathbb{R}^r$ (row vector) such that the following conditions hold a.e. on $[0, \bar{t}_f]$:

$$\dot{\lambda}(t) = -H_x(\bar{x}(t), \bar{u}(t), \lambda(t), \eta(t)), \tag{11}$$

$$\lambda(\bar{t}_f) = l_x(\bar{x}(\bar{t}_f), \bar{t}_f, \rho), \tag{12}$$

$$H(\bar{x}(t), \bar{u}(t), \lambda(t), \eta(t))|_{t=\bar{t}_f} + l_{t_f}(\bar{x}(\bar{t}_f), \bar{t}_f, \rho) = 0, \; \text{if } t_f \text{ is free}, \tag{13}$$

$$H(\bar{x}(t), \bar{u}(t), \lambda(t), \eta(t)) = \min\{H(\bar{x}(t), u, \lambda(t), \eta(t)) \,|\, u \in [u_{\min}, u_{\max}]\}, \tag{14}$$

$$\eta(t) \geq 0, \; \eta(t) = 0, \; \text{if } S(x(t)) < 0, \tag{15}$$

where $l(x,t_f,\rho) := (g + \rho\varphi)(x,t_f)$ is the endpoint Lagrangian function. The *switching function* is defined by

$$\sigma(x,\lambda) := H_u = \lambda f_1(x), \quad \sigma(t) = \sigma(x(t),\lambda(t)). \tag{16}$$

On *interior arcs* with $S(x(t)) < 0$ the minimum condition (14) yields the control law

$$u(t) = \begin{cases} u_{\min}, & \text{if } \sigma(t) > 0, \\ u_{\max}, & \text{if } \sigma(t) < 0. \end{cases} \tag{17}$$

The switching times of the control are zeroes of the switching function. A *singular arc* occurs if the switching function $\sigma(t)$ vanishes identically on an interval $I_{\text{sing}} \subset [0,\bar{t}_f]$. In this paper, we assume that the optimal control does not contain singular arcs.

Along a *boundary arc* $[\tau_1, \tau_2]$, assumption (A2) requires that the control takes values in the interior of the control set. Hence, the minimum condition (14) implies

$$\sigma(t) = \lambda(t)f_1(x(t)) = 0 \ \forall t \in [\tau_1, \tau_2]. \tag{18}$$

This relation can be interpreted as the property that a boundary control behaves formally like a singular control, a fact that was exploited in [16] to obtain junction theorems. By differentiating (18) and using the adjoint equation (11) we find the following explicit representation of the multiplier $\eta = \eta(x,\lambda)$ in (11) (cf. [17,14]),

$$\eta(x,\lambda) = \lambda[(f_1)_x(x)f(x,u_b(x)) - f_x(x,u_b(x))f_1(x)]/b(x), \tag{19}$$

where $u_b(x(t))$ is the boundary control (7). In short, the multiplier is given by the Lie bracket $\eta(x,\lambda) = \lambda[f_1,f]$; we then set $\eta(t) = \eta(x(t),\lambda(t))$.

3 Induced Optimization Problem and Second Order Sufficient Conditions

In order to transcribe the control problem into a finite-dimensional optimization problem, we make the following assumption:

(A3) The optimal control has finitely many bang-bang and boundary arcs.

Under assumptions (A1)-(A3), the optimal control problem can be transcribed into an optimization problem in the following way. We assume that the structure of the optimal control, i.e., the sequence of finitely many bang-bang and boundary arcs, is known. Let $t_j, j = 1,\ldots,s$, be the switching and junction times which are ordered as

$$0 =: t_0 < t_1 < \ldots < t_j < \ldots < t_s < t_{s+1} := t_f. \tag{20}$$

For simplicity, assume that there exists only a single boundary arc $[\tau_1, \tau_2] = [t_k, t_{k+1}]$ with an index $1 \leq k \leq s$. Then $[0,t_k]$ and $[t_{k+1},t_f]$ are the interior arcs. By assumption, in every interval $I_j := [t_{j-1},t_j]$ there exists a function $u^j(x)$ with the property that the optimal control is given by

$$u(t) = u^j(x(t)), \ t_{j-1} \leq t \leq t_j, \ (j = 1,\ldots,s,s+1). \tag{21}$$

The interval I_{k+1} then represents the boundary arc. The function $u^j(x)$ is either the constant value of the bang-bang control on interior arcs or the boundary control $u^{k+1}(x) = u_b(x) = -a(x)/b(x)$.

Consider now the *optimization variable* $z := (t_1, \ldots, t_{s+1})^* \in \mathbb{R}^{s+1}$ with $t_{s+1} := t_f$ in case of a free final time, resp., $z := (t_1, \ldots, t_s)^* \in \mathbb{R}^s$ for fixed final time t_f, where the asterisk denotes the transpose. Denote by $x(t;z)$ the absolutely continuous solution of the ODE system

$$\dot{x}(t) = f(x(t), u^j(x(t))), \quad t_{j-1} \leq t \leq t_j, \tag{22}$$

with initial condition $x(0) = x_0$. Then the control problem (OC) can be reformulated as the following finite-dimensional optimization problem (OP) with equality constraints:

$$
\begin{aligned}
\text{Min} \quad & G(z) := g(x(t_{s+1};z), t_{s+1}) \\
\text{s.t.} \quad & \Phi(z) := \varphi(x(t_{s+1};z), t_{s+1}) = 0, \\
& \mathscr{S}(z) := S(x(t_k;z)) = 0.
\end{aligned} \tag{23}
$$

The last equation arises from the entry-condition for the boundary arc. We consider the Lagrangian for the induced optimization problem (OP) in normal form,

$$\mathscr{L}(z, \rho, \beta) = G(z) + \rho \Phi(z) + \beta \mathscr{S}(z), \tag{24}$$

with multipliers $\rho \in \mathbb{R}^r$ (row vector) and $\beta \in \mathbb{R}$. First order necessary and second order sufficient conditions (SSC) for (23) are well known in the literature. In the following theorem, we consider control problems with free final time which involve the optimization vector $z \in \mathbb{R}^{s+1}$.

Theorem 1. SSC FOR THE INDUCED OPTIMIZATION PROBLEM.
Let $\bar{z}$ be feasible for the optimization problem (23). Suppose there exist multipliers $\rho \in \mathbb{R}^r$ and $\beta \in \mathbb{R}$ such that the following three conditions hold:

(a) *rank* $[\Phi_z(\bar{z}) \, | \, \mathscr{S}_z(\bar{z})] = r + 1$,
(b) $L_z(\bar{z}, \rho, \beta) = 0$,
(c) $v^* L_{zz}(\bar{z}, \rho, \beta) v > 0$ *for all* $v \in \mathbb{R}^{s+1} \setminus \{0\}$ *with* $\Phi_z(\bar{z})v = 0$, $\mathscr{S}_z(\bar{z})v = 0$.

Then $\bar{z}$ is a strict local minimizer of the optimization problem (OP).

Arguments similar to those in [18,23] reveal that the first order conditions in part (a) and (b) of Theorem 1 are closely related to those in (11)-(13) involving the adjoint function $\lambda(t)$. Namely, using the multiplier ρ in the Lagrangian (24), we define the adjoint function $\lambda(t)$ through the transversality condition $\lambda(\bar{t}_f) = (g + \rho \varphi)_x(\bar{x}(\bar{t}_f), \bar{t}_f)$ in (12) and the adjoint equation (11) where the multiplier η is given in (19). However, on the boundary arc $[t_k, t_{k+1}]$ there exists another multiplier η^1 and an adjoint function $\lambda^1(t)$ which correspond to the so-called *indirect adjoining approach* [9,17]. Here, the Hamiltonian is defined by $H^1 = \lambda^1 f(x, u) + \eta^1 S^1(x, u)$ with the function $S^1(x, u)$ given in (6). Then the adjoint equation is $\dot{\lambda}^1 = -H_x^1$ and the multiplier η^1 is determined via the equation $H_u^1 = 0$ as $\eta^1(x, \lambda^1) = -\lambda^1 f_u(x, u_b(x))/b(x)$. The multiplier β in the Lagrangian (24) yields the jump condition $\lambda^1(t_k+) = \lambda^1(t_k-) - \beta S_x(x(t_k))$ at the entry-time t_k. Moreover, one can show the relation $\beta = \int_{t_k}^{t_{k+1}} \eta(t) dt \geq 0$.

For bang-bang control problems without state constraints, it was shown in [1,20,21,23] that one further needs the so-called *strict bang-bang property* to obtain SSC for the bang-bang control problem. The following assumption gives an extension of the strict bang-bang property to control problems with state constraints.

(A4) (a) on *interior arcs* for $j = 1, ..., k-1, k+2, ..., s$:
$$\sigma(t_j) = 0, \ \dot{\sigma}(t_j)(u(t_j^-) - u(t_j^+)) > 0, \ \sigma(t) \neq 0 \text{ for } t \neq t_j \ .$$
   (b) at the entry-time t_k and exit-time t_{k+1} of the *boundary arc*:
$$\dot{\sigma}(t_k-)(u(t_k^-) - u(t_k^+)) > 0, \ \dot{\sigma}(t_{k+1}^+)(u(t_{k+1}^-) - u(t_{k+1}^+)) > 0.$$

Finally, we need the following *strict complementarity* condition:

(A5) The multiplier $\eta(t)$ satisfies $\eta(t) > 0 \ \forall \, t \in [t_k, t_{k+1}]$.

Note that assumptions (A4) and (A5) have also been used in [13,14] to construct a local field of extremals near boundary arcs. This has enabled the authors to prove sufficient conditions (SSC) which correspond to the following form of SSC. Detailed proofs will be given elsewhere.

Theorem 2. SSC FOR THE STATE-CONSTRAINED CONTROL PROBLEM.
Let $\bar{u}$ be a feasible control for the control problem (1)-(5) which has finitely many switching and junction times $\bar{t}_j$, $j = 1, \ldots, s$, and let $\bar{x}$ be the corresponding trajectory. Suppose there exists an adjoint function $\lambda : [0, t_f] \rightarrow \mathbb{R}^n$ and a multiplier $\rho \in \mathbb{R}^r$ such that assumptions (A1)-(A5) hold with multiplier function $\eta : [0, t_f] \rightarrow \mathbb{R}$ defined by (19). Suppose further that the vector $\bar{z} = (\bar{t}_1, \ldots, \bar{t}_s, \bar{t}_{s+1})^* \in \mathbb{R}^{s+1}, \bar{t}_{s+1} = \bar{t}_f$, satisfies the SSC in Theorem 1. Then the control $\bar{u}$ provides a strict strong minimum for the control problem (OC).

4 Numerical Methods for Solving the Induced Optimization Problem

In this section, we shall extend the *arc-parameterization* method in [10,18] to solve state-constrained control problems. Instead of directly optimizing the switching and junction times t_j, $j = 1, \ldots, s$, one determines the arc-lengths (arc durations)
$$\xi_j := t_j - t_{j-1}, \ j = 1, \ldots, s, s+1, \tag{25}$$
of bang-bang and boundary arcs. Therefore, the optimization variable $z = (t_1, \ldots, t_s, t_{s+1})^*$ is replaced by the optimization variable
$$\xi := (\xi_1, \ldots, \xi_s, \xi_{s+1})^* \in \mathbb{R}^{s+1}, \ \xi_j := t_j - t_{j-1}. \tag{26}$$
The variables z and ξ are related by a linear transformation involving the regular $(s+1) \times (s+1)$-matrix R,
$$\xi = Rz, \ z = R^{-1}\xi, \ R = \begin{pmatrix} 1 & 0 & \ldots & 0 \\ -1 & 1 & \ddots & \vdots \\ & \ddots & \ddots & 0 \\ 0 & & -1 & 1 \end{pmatrix}. \tag{27}$$

In the arc-parameterization method, the time interval $[t_{j-1},t_j]$ is mapped to the fixed interval $I_j := \left[\frac{j-1}{s+1}, \frac{j}{s+1}\right]$ by the linear transformation

$$t = a_j + b_j \tau, \ \ \tau \in I_j = \left[\frac{j-1}{s+1}, \frac{j}{s+1}\right], \tag{28}$$

where $a_j = t_{j-1} - (j-1)\xi_j$, $b_j = (s+1)\xi_j$. Identifying $x(\tau) \cong x(a_j + b_j\tau) = x(t)$ in the relevant intervals, we obtain the ODE system

$$\dot{x}(\tau) = (s+1)\,\xi_j\,f(x(\tau), u^j(x(\tau))) \text{ for } \tau \in I_j. \tag{29}$$

By concatenating the solutions in the intervals I_j we get the *continuous* solution $x(t) = x(t;\xi)$ in the normalized interval $[0,1]$. When expressed via the new optimization variable ξ, the optimization problem (OP) in (23) is equivalent to the following optimization problem $(\widetilde{OP})$ with $t_f = \sum\limits_{j=1}^{s+1} \xi_j$:

$$\text{Min } \tilde{G}(\xi) := g(x(1;\xi), t_f),$$
$$\text{s.t.} \ \ \widetilde{\Phi}(\xi) := \varphi(x(1;\xi), t_f) = 0, \tag{30}$$
$$\widetilde{\mathscr{S}}(\xi) := S(x(\tfrac{k}{s+1}; \xi)) = 0.$$

The Lagrangian function is given by

$$\widetilde{\mathscr{L}}(\xi, \rho, \beta) = \widetilde{G}(\xi) + \rho\widetilde{\Phi}(\xi) + \beta\widetilde{\mathscr{S}}(\xi). \tag{31}$$

Using the linear transformation (27), it can easily be seen that the SSC for the optimization problems (OP) and $(\widetilde{OP})$ are equivalent; cf. similar arguments in [18]. To solve this optimization problem, we use a suitable adaptation of the control package NUDOCCCS in Büskens [4,6]. Then we can take advantage of the fact that this routine also provides the Jacobian of the equality constraints and the Hessian of the Lagrangian which are needed to check the second order condition in Theorem 1.

5   Sensitivity Analysis for Bang-Bang Control Problems with a State Constraint

The SSC given in Theorem 2 pave the way to stability and sensitivity analysis for *parametric* bang-bang control problems with a state constraint. Suppose that the control problem (OC) in (1)-(5) depends as well on a parameter $p \in P \subset \mathbb{R}^q$ in the following way: Minimize

$$J(x, u, t_f, p) := g(x(t_f), t_f, p) \tag{32}$$

subject to the constraints on the interval $[0, t_f]$,

$$\dot{x}(t) = f(x(t), u(t), p) = f_0(x(t), p) + f_1(x(t), p)u(t), \tag{33}$$
$$x(0) = x_0, \ \ \varphi(x(t_f), t_f, p) = 0, \tag{34}$$
$$u_{\min} \le u(t) \le u_{\max}, \tag{35}$$
$$S(x(t), p) \le 0. \tag{36}$$

All functions are supposed to be sufficiently smooth. This parametric control problem will be denoted by $(OC(p))$. For a fixed parameter $p_0 \in P$, the problem $(OC(p_0))$ is considered as the *nominal control problem*.

We shall assume that the state constraint is of order one uniformly in the parameter p, i.e., for

$$S^1(x,u,p) = S_x(x,p)(f_0(x,p) + f_1(x,p)u) = a(x,p) + b(x,p)u \tag{37}$$

we have $b(x,p) \not\equiv 0$ for all $p \in P$. Then the boundary control is given by

$$u_b(x,p) = -a(x,p)/b(x,p). \tag{38}$$

Assuming (A1)-(A5) for the nominal control problem $(OC(p_0))$, we arrive at an *induced optimization problem* (23) *in parametric form* upon inserting the parametric boundary control (38). The Lagrangian function (24) becomes

$$\mathcal{L}(z,\rho,\beta,p) = G(z,p) + \rho\,\Phi(z,p) + \beta\mathcal{S}(z,p). \tag{39}$$

Using a well-known sensitivity result for finite-dimensional parametric optimization problems (cf. [7,5,6]) we arrive at the following sensitivity result for the parametric control problem.

Theorem 3. SENSITIVITY ANALYSIS OF THE CONTROL PROBLEM $(OC(p))$.
Suppose that $\bar{u}(t) =: u(t,p_0)$ is a feasible control for the nominal control problem $(OC(p_0))$. Assume that $u(t,p_0)$ has switching and junction times $\bar{t}_j, j = 1,...,s,$ and a final time $\bar{t}_f = \bar{t}_{s+1}$ such that the SSC in Theorem 2 are satisfied. Then there exists a neighborhood $P_0 \subset P$ of the nominal parameter p_0 and functions $t_j : P_0 \to \mathbb{R}$ ($j = 1,...,s,s+1$), $\rho : P_0 \to \mathbb{R}^r$ and $\beta : P_0 \to \mathbb{R}$ with the following properties:

(1) $t_j(p_0) = \bar{t}_j, j = 1,...,s,s+1,$
(2) for every $p \in P_0$, the control $u(t,p)$ with switching and junction times $t_j(p), j = 1,...,s,$ and final time $t_f(p) = t_{s+1}(p)$ is a strict strong local minimum for $(OC(p))$. The values of $u(t,p)$ agree with those of the nominal control $\bar{u}(t)$ on every interior bang-bang interval and are determined on boundary arcs by $u(t,p) = u_b(x(t),p)$ in view of (38).

The parametric sensitivity derivatives of $z(p) := (t_1(p),...,t_s(p),t_{s+1}(p))^* \in \mathbb{R}^{s+1}$ and of $\rho(p), \beta(p)$ are given by the formula

$$\begin{pmatrix} dz/dp \\ d\rho^*/dp \\ d\beta/dp \end{pmatrix} = -\begin{pmatrix} \mathcal{L}_{zz} & (\Psi_z)^* \\ \Psi_z & \mathbf{0} \end{pmatrix}^{-1} \begin{pmatrix} \mathcal{L}_{zp} \\ \Psi_{zp} \end{pmatrix}, \tag{40}$$

where we have put

$$\Psi(z,p) = \begin{pmatrix} \Phi(z,p) \\ \mathcal{S}(z,p) \end{pmatrix}. \tag{41}$$

The right hand side in (40) is evaluated for the argument $(z(p),\rho(p),\beta(p))$.

Proof. We sketch the main ideas of the proof. Since SSC hold for the nominal induced optimization problem $(OC(p_0))$, the sensitivity theorem in [7,5,6] tells us that there exist a neighborhood $P_0 \subset P$ of p_0 and, for every $p \in P_0$, an optimal solution and multipliers

$$z(p) = (t_1(p),...,t_s(p),t_f(p)), \ \rho(p), \ \beta(p), \tag{42}$$

for the parametric problem $(OC(p))$. The triple $(z(p),\rho(p),\beta(p))$ satisfies the assumptions of Theorem 1 and is a C^1-function with respect to $p \in P_0$. We define the parametric control $u(t,p)$ in the following way. On bang-bang arcs $[t_j(p),t_{j+1}(p)]$, $j \neq k$, the control $u(t,p)$ takes the values of the nominal control on the corresponding nominal arcs $[\bar{t}_j,\bar{t}_{j+1}]$. On the boundary arc $[t_k(p),t_{k+1}(p)]$, the parametric control is defined by $u(t,p) = u_b(x(t),p)$ using the boundary control (38). Then corresponding trajectory $x(t,p)$ is determined by

$$\dot{x} = f(x,u(t,p)), \ x(0,p) = x_0. \tag{43}$$

Then the adjoint function $\lambda(t,p)$ is defined by the transversality condition

$$\lambda(t_f(p),p) := (g + \rho(p)\varphi)_x(x(t_f(p),p),t_f(p)) \tag{44}$$

and the solution to the adjoint equation

$$\dot{\lambda}(t,p) = -H_x(x(t,p),\lambda(t,p),u(t,p),\eta(t,p)), \tag{45}$$

where the multiplier $\eta(t,p)$ is given by the Lie-bracket

$$\eta(t,p) = \lambda(t,p)[f_1,f](x(t,p),u(t,p),p). \tag{46}$$

By shrinking the set P_0 if necessary, it is easy to verify that assumptions (A1)-(A5) hold for all $p \in P_0$. This proves the optimality of the triple $(x(t,p),u(t,p),\lambda(t,p))$. The sensitivity formula (40) follows from standard results in [7,5,6]. Note that Theorem 3 represents an extension of a sensitivity result for bang-bang control problems without state constraints; cf. Kim, Maurer [11]. □

We point out that the code NUDOCCCS [4] provides also the numerical evaluation of sensitivity formula (40).

6   Numerical Example: Time-Optimal Drug Displacement Problem

We consider the time-optimal control problem discussed in Bell, Katusiime [3] and Maurer, Wiegand [22]. The model simulates the interaction of the two drugs, warfarin and phenylbutazone in the human blood stream. The state variables x_1 and x_2 represent the concentration of warfarin and phenylbutazone, respectively. The problem is to control the rate of infusion (control u) of the pain-killing drug phenylbutazone such

that both drugs reach a stable steady-state in minimal time while the concentration of warfarin is bounded by a given toxic level:

$$\text{Minimize} \qquad t_f \tag{47}$$

$$\text{subject to} \qquad \dot{x}_1 = D^2(C_2(0.02 - x_1) + 46.4x_1(u - 2x_2))/C_3, \tag{48}$$

$$\dot{x}_2 = D^2(C_1(u - 2x_2) + 46.4x_2(0.02 - x_1))/C_3, \tag{49}$$

$$x_1(0) = 0.02, \quad x_2(0) = 0, \tag{50}$$

$$x_1(t_f) = 0.02, \quad x_2(t_f) = 2, \tag{51}$$

$$0 = u_{\min} \leq u(t) \leq u_{\max} = 8 \quad \forall t \in [0, t_f], \tag{52}$$

and the state constraint

$$S(x(t)) = x_1(t) - \alpha \leq 0 \qquad \forall t \in [0, t_f], \tag{53}$$

where

$$D = D(x) = 1 + 0.2x_1 + 0.2x_2, \tag{54}$$

$$C_1 = C_1(x) = D^2 + 232 + 46.4x_2, \tag{55}$$

$$C_2 = C_2(x) = D^2 + 232 + 46.4x_1, \tag{56}$$

$$C_3 = C_3(x) = C_1 C_2 - (46.4)^2 x_1 x_2. \tag{57}$$

The augmented Hamiltonian associated with the state constraint (53) is given by

$$H(x, u, \lambda, \eta) = \lambda f(x, u) + \eta S(x) = \frac{D^2}{C_3} \cdot K + \eta(x_1 - \alpha), \tag{58}$$

where

$$K := \lambda_1(C_2(0.02 - x_1) + 46.4x_1(u - 2x_2)) \\ + \lambda_2(C_1(u - 2x_2) + 46.4x_2(0.02 - x_1)). \tag{59}$$

Then the adjoint equations (11) are

$$\dot{\lambda}_1 = -H_{x_1} = -\frac{(D^2)_{x_1}C_3 - (C_3)_{x_1}D^2}{C_3^2} \cdot K - \frac{D^2}{C_3} \cdot K_{x_1} - \eta, \tag{60}$$

$$\dot{\lambda}_2 = -H_{x_2} = -\frac{(D^2)_{x_2}C_3 - (C_3)_{x_2}D^2}{C_3^2} \cdot K - \frac{D^2}{C_3} \cdot K_{x_2}, \tag{61}$$

with the following partial derivatives of K:

$$K_{x_1} = 0.02\lambda_1(C_2)_{x_1} - \lambda_1(C_2 + (C_2)_{x_1}x_1) + 46.4\lambda_1 u - 92.8x_2\lambda_1 \tag{62}$$

$$+ \lambda_2 u(C_1)_{x_1} - 2x_2\lambda_2(C_1)_{x_1} - 46.4x_2\lambda_2, \tag{63}$$

$$K_{x_2} = 0.02\lambda_1(C_2)_{x_2} - x_1\lambda_1(C_2)_{x_2} - 92.8x_1\lambda_1 + \lambda_2 u(C_1)_{x_2} \tag{64}$$

$$- 2\lambda_2(C_1 + (C_1)_{x_2}x_2) + 0.928\lambda_2 - 46.4x_1\lambda_2. \tag{65}$$

The switching function (16) is given by

$$\sigma(x,\lambda) = H_u = \frac{D^2}{C_3}(46.4x_1\lambda_1 + C_1\lambda_2). \tag{66}$$

The state constraint (53) is of order one, as the function $S^1(x,u)$ in (6) contains the control explicitly:

$$S^1(x,u) = S_x(x)f(x,u) = \frac{D^2}{C_3}(C_2(0.02 - x_1) + 46.4x_1(u - 2x_2)). \tag{67}$$

The boundary control $u_b(x)$ in (7) is determined by the feedback expression

$$u_b(x) = \frac{\alpha - 0.02}{46.4\alpha}C_2(x) + 2x_2. \tag{68}$$

Using boundary value methods it was shown in [22] that for toxic levels $0 < \alpha \leq 0.0246$ the control has the following structure with two bang-bang arcs encompassing a boundary arc:

$$u(t) = \begin{cases} 8, & \text{for } t \in [0,t_1), \\ u_b(x(t)) = \frac{\alpha - 0.02}{46.4\alpha}C_2(x(t)) + 2x_2(t), & \text{for } t \in [t_1,t_2], \\ 0, & \text{for } t \in (t_2,t_f]. \end{cases} \tag{69}$$

We choose the toxic level $\alpha = 0.024$ and compute the numerical solution using the routine IPOPT by Wächter and Biegler [27]. Using 1000 discretization points and the method of Heun for the approximation of the differential equations, IPOPT provides the solution depicted in Figs. 1-3. The final time is computed as $t_f = 358.731$ and the entry- and exit-time are $t_1 = 29.7747$ and $t_2 = 333.261$.

Now we solve the induced optimization problem (23) with optimization variables $z = (t_1,t_2,t_3)$, resp., problem (30) with variables $\xi = (\xi_1,\xi_2,\xi_3)$, where $\xi_1 = t_1$, $\xi_2 = t_2 - t_1$, $\xi_3 = t_f - t_2$. The routine NUDOCCCS [4] yields the entry-time $t_1 = 29.90806$, the exit-time $t_2 = 333.1561$ and the final time $t_f = 358.7085$. NUDOCCCS also provides the Hessian $\mathscr{L}_{\xi\xi}$ and Jacobian $\tilde{\Phi}_\xi$,
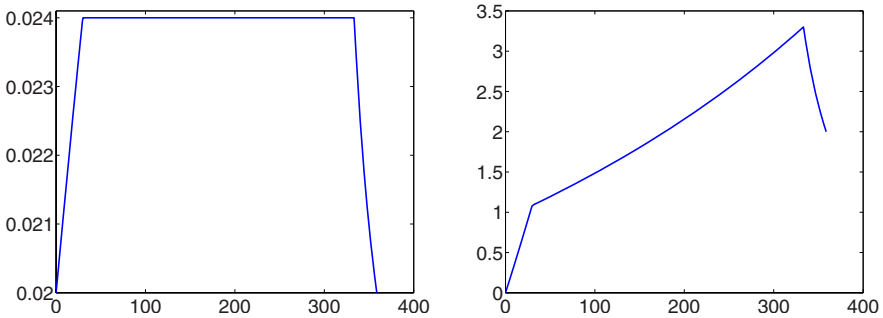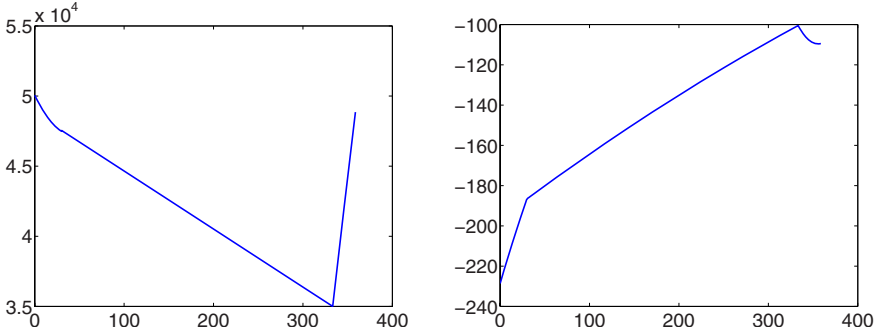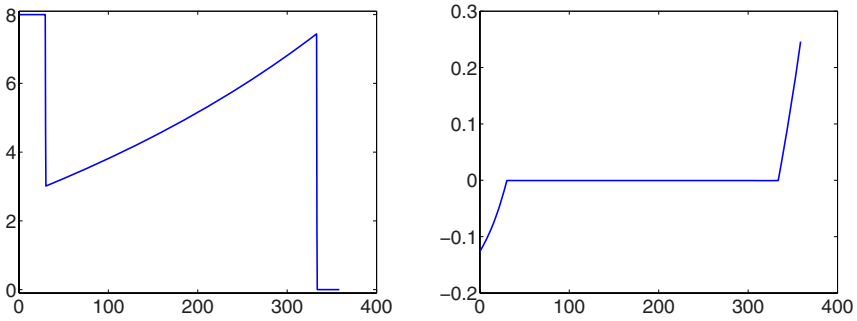

Fig. 1. Concentration of warfarin (left) and phenylbutazone (right)

Fig. 2. Adjoint variables $\lambda_1(t)$ and $\lambda_2(t)$

Fig. 3. Optimal control and switching function

$$\tilde{\mathscr{L}}_{\xi\xi} = \begin{pmatrix} -0.046251 & -0.014521 & 0.026232 \\ -0.014521 & -0.0011993 & 0.0052637 \\ 0.026232 & 0.0052637 & 0.054240 \end{pmatrix}, \tag{70}$$

$$\tilde{\Phi}_\xi = \begin{pmatrix} 0.0000000 & 0.0000000 & -0.0000954 \\ 0.0298122 & 0.0043075 & -0.0336047 \\ 0.0001245 & 0.0000000 & 0.0000000 \end{pmatrix}. \tag{71}$$

Since rank($\tilde{\Phi}_\xi$) = 3 holds, condition (*a*) of Theorem 1 is fulfilled with $s = r = 2$. Furthermore, it is clear that the first order necessary conditions hold in the induced problem, i.e., condition (b) in Theorem 1, is fulfilled. Finally, the second order condition (c) is trivially satisfied, since the matrix $\tilde{\Phi}_\xi$ is regular. Next, we check the regularity assumption (A1). The data provided by IPOPT give the following estimate:

$$b(x(t)) = 46.4 \frac{D(x(t))^2}{C_3(x(t))} x_1(t) \geq 0.23 \cdot 10^{-3}. \tag{72}$$

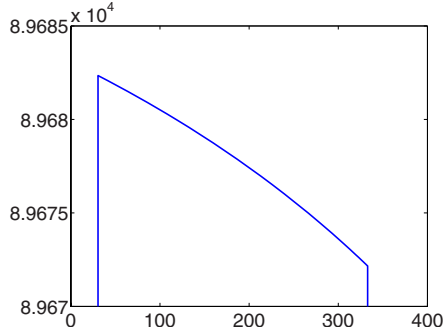Hence, (A1) is satisfied. It can be seen in Fig. 3 that also the assumptions (A2) and (A4) hold.

Fig. 4. Multiplier $\eta(t)$ from (73)

For the verification of assumption (A5), we compute the multiplier $\eta(t) = \eta(x(t), \lambda(t))$ via formula (19),

$$
\begin{aligned}
\eta(x,\lambda) =\ & \frac{2\dot{D}C_3 - D\dot{C}_3}{46.4DC_3x_1}(46.4x_1\lambda_1 + C_1\lambda_2) + \frac{1}{46.4x_1}(\dot{C}_1\lambda_2 + C_1\dot{\lambda}_2) + \frac{1}{x_1}\dot{x}_1\lambda_1 \\
& - x_3 \cdot \left(\frac{(D^2)_{x_1}C_3 - (C_3)_{x_1}D^2}{C_3^2} \cdot K + \frac{D^2}{C_3} \cdot K_{x_1} \right),
\end{aligned}
\tag{73}
$$

and insert the values of $x(t)$, $\lambda(t)$ provided by IPOPT. Note that $\eta(t) \equiv 0$ for $t \notin [t_1, t_2]$. Then Fig. 4 shows that the strict complementarity condition (A5) holds. It is noteworthy that the Lagrange multiplier for the discretized state constraint, which is provided directly by IPOPT, has the same values as the multiplier $\eta(t)$. Finally, we may conclude from Theorem 2 that the control (69) provides a strict strong minimum for the problem (47)-(53).

7   Optimal Control for a Two-Compartment Model in Cancer Chemotherapy

Ledzewicz, Schättler [12] considered a two-compartment model in cancer chemotherapy and established optimality using extremal field theory [13]. The state constraint (77) below has been studied in de Pinho, Ferreira, Ledzewicz, Schättler [24] using the methods developed in [13,14]. Here, we prove optimality on the basis of the SSC in Theorem 2 which allows us to apply the sensitivity result in Theorem 3. The description of the control model is taken from [12]: "The cell cycle is broken into two compartments of which the first combines the first growth phase G_1 and the synthesis phase S while the second contains the second growth phase G_2 and mitosis M. Let $x_i(t), i = 1, 2$, denote the number of cancer cells in the i-th compartment at time t." The control u is the drug treatment which is measured by its cell-killing effect. The control problem is to *minimize* the cost functional with *fixed* final time t_f,

$$
J(x,u) = r_1x_1(t_f) + r_2x_2(t_f) + \int_0^{t_f} u(t)dt,
\tag{74}
$$

subject to

$$\begin{aligned}
\dot{x}_1 &= -a_1 x_1 + 2(1-u)a_2 x_2, & x_1(0) &= x_{10}, \\
\dot{x}_2 &= a_1 x_1 - a_2 x_2, & x_2(0) &= x_{20}, \\
0 &\leq u(t) \leq 1 \quad \forall t \in [0, t_f].
\end{aligned} \tag{75}$$

The cost functional (74) can be transformed to a functional (1) of Mayer type by introducing the equation $\dot{x}_3 = u$, $x_3(0) = 0$, which yields

$$J(x,u) = g(x(t_f)) = r_1 x_1(t_f) + r_2 x_2(t_f) + x_3(t_f). \tag{76}$$

In addition, we consider the state constraint of order one:

$$S(x(t)) := x_1(t) + x_2(t) - \alpha \leq 0 \quad \forall t \in [0, t_f], \tag{77}$$

which imposes an upper bound on the total number of tumor cells in both compartments. The first total time derivative (6) of $S(x)$ is given by

$$S^1(x,u) = a_2 x_2 - 2a_2 x_2 u. \tag{78}$$

Obviously, assumption (A1) is satisfied since $b(x(t)) = -2a_2 x_2(t) \neq 0$ holds on $[0, t_f]$. Data for (74) and (75) are taken from [12]:

$$r_1 = 6.94, \ r_2 = 3.94, \ a_1 = 0.197, \ a_2 = 0.356, \ t_f = 10. \tag{79}$$

We choose the initial conditions $x_1(0) = x_{10} = 0.86$, $x_2(0) = x_{20} = 0.55$, which match approximately the solution in [12], where the terminal state $x(t_f)$, $i = 1,2$, was fixed and the intial state was free. The parameter α in the state constraint (77) will be assigned the value $\alpha = 1.7$ for which the state constraint becomes active. The augmented Hamiltonian (9) is given by

$$H = \lambda_1(-a_1 x_1 + 2a_2 x_2) + \lambda_2(a_1 x_1 - a_2 x_2) + \sigma u + \eta(x_1 + x_2 - \alpha), \tag{80}$$

with *switching function*

$$\sigma = \sigma(x, \lambda) = 1 - 2a_2 x_2 \lambda_1. \tag{81}$$

The adjoint equation (11) and the transversality condition (12) yield

$$\begin{aligned}
\dot{\lambda}_1 &= a_1(\lambda_1 - \lambda_2) - \eta, & \lambda_1(t_f) &= r_1, \\
\dot{\lambda}_2 &= a_2(2(u-1)\lambda_1 + \lambda_2) - \eta, & \lambda_2(t_f) &= r_2.
\end{aligned} \tag{82}$$

The *boundary control* $u_b(x)$ satisfies the equation $S^1(x, u_b(x)) \equiv 0$ which gives

$$u_b(x) \equiv \frac{1}{2}. \tag{83}$$

Hence, the boundary control lies in the interior of the control set and satisfies assumption (A2). The multiplier η for the state constraint (77) is determined by equation (19):

$$\eta(t) = a_1\lambda_1(t)\left(\frac{x_1(t)}{x_2(t)} + 1\right) - a_2\lambda_1(t) - a_1\lambda_2(t). \tag{84}$$

To determine the structure of the optimal control we first discretize the control problem with 500 gridpoints and apply the program NUDOCCCS of Büskens [4]. We find that the control has two bang-bang arcs and one *boundary arc*:

$$u(t) = \begin{cases} 0, & t \in [0, t_1), \\ u_b(x(t)) = \frac{1}{2}, & t \in [t_1, t_2], \\ 1, & t \in (t_2, t_f]. \end{cases} \tag{85}$$

Fig. 5 (left) displays the optimal control and the switching function. It clearly shows that the optimal control satisfies assumptions (A3) and (A4) since, in particular, for $k = 1$ in (A4) we have $\dot{\sigma}(t_1-) < 0$ and $\dot{\sigma}(t_2+) < 0$. Fig. 5 (right) depicts the state constrained function $x_1(t) + x_2(t)$ and the multiplier $\eta(t)$, which is seen to satisfy the *strict* complementarity condition (A5). State and adjoint variables are shown in Fig. 6, resp., Fig. 7.
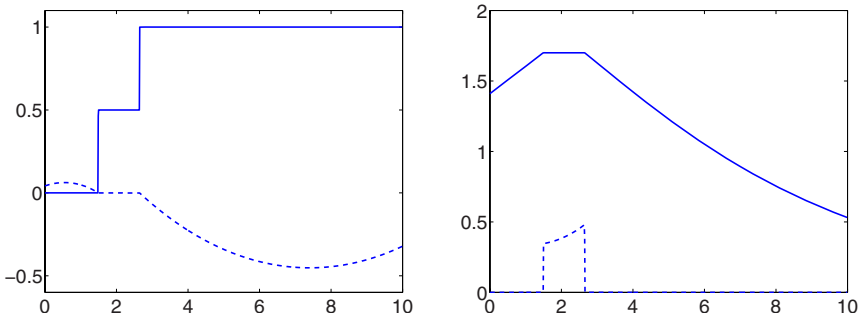
Fig. 5. Left: control with switching function (dashed); right: state constrained function $x_1(t) + x_2(t)$ with multiplier $\eta(t)$ (dashed)
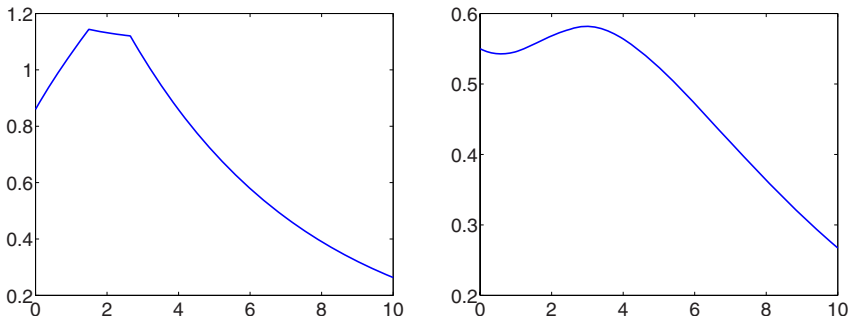
Fig. 6. State variables x_1 and x_2
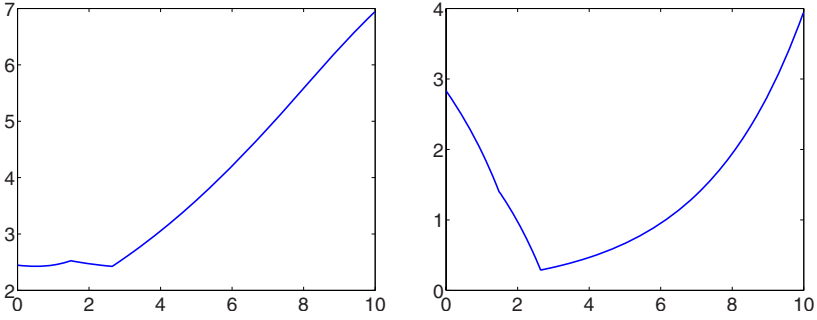
Fig. 7. Adjoint variables λ_1 and λ_2

It remains to verify the SSC in Theorem 1 for the optimization problem (30). The optimization variable is defined by (25) as

$$\xi = (\xi_1, \xi_2) = (t_1, t_2 - t_1). \tag{86}$$

Then the arc-length of the terminal time interval is given by $t_f - \xi_1 - \xi_2$ with $t_f = 10$. Since no terminal state boundary conditions are prescribed, the only equality constraint is the entry-condition of the boundary arc,

$$x_1(1/3; \xi) + x_2(1/3; \xi) = \alpha = 1.7. \tag{87}$$

The code NUDOCCCS gives the following results:

$$\begin{aligned}
t_1 &= 1.490713, \qquad t_2 = 2.653005, \\
\lambda_1(0) &= 2.44417, \quad \lambda_2(0) = 2.82883, \\
x_1(t_f) &= 0.2635156, \, x_2(t_f) = 0.2673589, \\
J(x, u) &= 10.81033.
\end{aligned} \tag{88}$$

The Hessian of the Lagrangian for (30) is computed as

$$\tilde{\mathscr{L}}_{\xi\xi} = \begin{pmatrix} 0.225319 & 0.128060 \\ 0.128060 & 0.099212 \end{pmatrix} \tag{89}$$

while the Jacobian of the equality constraint is given by $\tilde{\mathscr{S}}_\xi = (0.1979670, 0)$. Obviously, the Hessian $\tilde{\mathscr{L}}_{\xi\xi}$ is positive definite and we have rank $(\tilde{\mathscr{S}}_\xi) = 1$. Hence, we may conclude that the control (85) with data (88) satisfies the SSC in Theorem 1 and provides a strict local minimum of the optimal control problem.

Using the sensitivity result in Theorem 3 and the sensitivity formula (38), we obtain the following sensitivity derivatives for the arc-length of the first bang-bang arc and the boundary arc:

$$\begin{aligned}
d\xi_1/da_1 &= -1.513, \, d\xi_2/da_1 = 11.99, \\
d\xi_1/da_2 &= -3.350, \, d\xi_2/da_2 = 0.5165, \\
d\xi_1/dx_{10} &= -5.359, \, d\xi_1/dx_{10} = 4.421, \\
d\xi_1/dx_{20} &= -7.233, \, d\xi_1/dx_{20} = 4.077.
\end{aligned} \tag{90}$$

In particular, note the high sensitivity of the boundary arc-length with respect to a variation in the parameter a_1.

Remark. Similar numerical methods can be applied to the *three-compartment model* for cancer chemotherapy presented in Swierniak, Ledzewicz and Schättler [25]. The model involves two control variables, a blocking agent and a recruiting agent. In this problem, it is also reasonable to consider a state constraint similar to (77). Though the analogon to Theorem 2 for vector-valued control has not been fully established in the literature, one can formulate an induced optimization problem of the type (30) and check that SSC hold; cf. Goris [8]. A paper with detailed results is in preparation.

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