

Dynamic flux optimization in metabolic-genetic networks

Steffen Waldherr

17th May 2013

Contents

1	A coupled metabolic-genetic reaction network	2
2	A dynamic optimization problem for a metabolic-genetic network	3
2.1	Derivation of a generic optimization problem	3
2.2	Maximum growth objective	5
2.3	Time-optimal flux dynamics	5
3	Numerical solution of the constructed optimal control problem	6
3.1	Abstract problem formulation	6
3.2	Discretization by collocation	6
3.2.1	Approximation of continuous variables	7
3.2.2	Summary of the discretization scheme	7
3.2.3	Discretization of the objective functional	8
3.2.4	Discretization of the dynamics	9
3.2.5	Discretization of the path, terminal, and integral constraints	10
3.3	Numerical solution of the discretized problem	10
3.3.1	Optimization with fixed terminal time	10
3.3.2	Optimization with free terminal time	10
3.4	Simple examples	11
3.4.1	A constrained integrator	11
3.4.2	Minimum time control of the rocket car to the origin	11
3.4.3	A minimal metabolic-genetic network	12

1 A coupled metabolic-genetic reaction network

We consider the following molecular species:

- Extracellular nutrients and / or waste $Y \in \mathbb{R}^{n_y}$
- Intracellular metabolites $X \in \mathbb{R}^{n_x}$
- Gene products $P \in \mathbb{R}^{n_p}$

The following reactions are considered:

- Exchange reactions $V_y \in \mathbb{R}^{n_{vy}}$ between the cell and the environment
- Metabolic reactions $V_x \in \mathbb{R}^{n_{vx}}$ converting one set of metabolites into another
- Gene expression reactions $V_p \in \mathbb{R}^{n_{vp}}$ generating gene products from metabolites

The network dynamics are then given by the following differential equation:

$$\begin{aligned}\dot{Y} &= -S_y^y V_y \\ \dot{X} &= S_y^x V_y + S_x^x V_x - S_p^x V_p \\ \dot{P} &= S_p^p V_p,\end{aligned}\tag{1}$$

where the S_* are the reaction stoichiometries.

From a time scale separation, we can argue that the metabolic part X of the network is in a quasi-steady state. This leads to the following simplified network:

$$\begin{aligned}\dot{Y} &= -S_y^y V_y \\ \dot{P} &= S_p^p V_p,\end{aligned}\tag{2}$$

with the metabolic flux balance constraint

$$S_y^x V_y + S_x^x V_x - S_p^x V_p = 0.\tag{3}$$

Since there are typically large difference in the molar mass' order of magnitude for metabolites versus macromolecules, it is helpful for numerical reasons to scale the system accordingly. We consider a scaling parameter α , which is an overall value for the ratio of the macromolecules' molar mass over the the metabolites' molar mass, or, equivalently, the stoichiometry of metabolites in the reactions generating macromolecules. The proposed scaling is

$$\begin{aligned}\tilde{P} &= \alpha P \\ \tilde{V}_p &= \alpha V_p.\end{aligned}\tag{4}$$

At this point, we observe that the scaling changes the quasi-steady state constraint (3) to

$$S_y^x V_y + S_x^x V_x - \alpha^{-1} S_p^x \tilde{V}_p = 0.\tag{5}$$

2 A dynamic optimization problem for a metabolic-genetic network

2.1 Derivation of a generic optimization problem

For notational convenience, we introduce the scaled molar mass vector $z = (Y, \tilde{P})$ and the scaled flux vector $v = (V_y, V_x, \tilde{V}_p)$. Define $n_v = n_{vy} + n_{vx} + n_{vp}$.

Apart from the flux balance constraint, there will typically be additional constraints on the fluxes, macromolecules, and extracellular components.

- Enzyme capacity constraints. Generally, reaction fluxes are limited by upper and lower bounds of the form

$$\left| \frac{v_1}{c_1} \right| + \dots + \left| \frac{v_m}{c_m} \right| \leq E,$$

where E is the amount of available enzyme, v_1 to v_m are the reactions catalyzed by this enzyme, and c_1 to c_m are the catalytic constants for these reactions. On the network level, this translates to the constraints

$$H_{C,y}V_y + H_{C,x}V_x + H_{C,p}\tilde{V}_p \leq H_E P, \quad (6)$$

where $H_E \in \mathbb{R}^{q_E \times n_p}$ selects the enzymatic components of the macromolecule vector P and $H_{C,\cdot} \in \mathbb{R}^{q_E \times n_v}$ contains the inverse of the catalytic constants for the corresponding fluxes. The scaled variant of this constraint is given by

$$\alpha H_{C,y}V_y + \alpha H_{C,x}V_x + H_{C,p}\tilde{V}_p \leq H_E \tilde{P}, \quad (7)$$

which we will also write shortly as $\tilde{H}_C v \leq H_E \tilde{P}$. $q_E = \sum_{i=1}^K 2^{k_i}$, where K is the number of enzymes and k_i the number of reactions catalyzed by enzyme i .

- Biomass-independent flux bounds, for example positivity of irreversible fluxes.

$$v_{min} \leq v \leq v_{max}. \quad (8)$$

Components of v_{min} and v_{max} where no bound is set may be chosen as $\pm\infty$.

- Positivity of molecular species.

$$z \geq 0. \quad (9)$$

- A set of biomass composition constraints. For example, the amount of structural cell components will put an upper bound on the feasible enzyme amount.

$$H_B \tilde{P} \leq h_B, \quad (10)$$

where $H_B \in \mathbb{R}^{q_B \times n_p}$ and $h_B \in \mathbb{R}^{q_B}$, with q_B the number of biomass composition constraints.

In terms of dynamic optimization, the constraints given above are *path constraints*, i.e., they are required to hold at any single time point during the considered time interval.

Let \mathcal{Z} be a set of desired molecular species amount, and define the set of all dynamic fluxes that take the network to the desired set at time t_f as

$$\mathcal{V}(\mathcal{Z}, z_0) = \bigcup_{t_f \geq 0} \{v \in \mathcal{M}[0, t_f] \mid z(t_f, v, z_0) \in \mathcal{Z}\}, \quad (11)$$

where $\mathcal{M}[0, t_f]$ is the set of measurable functions of appropriate dimension over the interval $[0, t_f]$, and $z(t_f, v, z_0)$ is the solution of the differential equation (2) with flux variables $v(t)$ and initial condition $z(0) = z_0$.

Given a cost functional with integral term and endpoint term, we obtain the following dynamic optimization problem:

$$\begin{aligned}
& \max_{\mathcal{V}(\mathcal{Z}, z_0)} \int_0^{t_f} \Phi(z(t), v(t)) dt + \Psi(z(t_f)) \\
& \text{s.t. } \dot{Y} = -S_y^y V_y \\
& \quad \dot{P} = S_p^p \tilde{V}_p \\
& \quad z(0) = z_0 \\
& \quad S_y^x V_y + S_x^x V_x - \alpha^{-1} S_p^x \tilde{V}_p = 0 \\
& \quad \tilde{H}_C v(t) \leq H_E P(t) \\
& \quad v_{\min} \leq v(t) \leq v_{\max} \\
& \quad z(t) \geq 0 \\
& \quad H_B \tilde{P}(t) \leq h_B.
\end{aligned} \tag{12}$$

Let us define $S = (S_y^x, S_v^x, -\alpha^{-1} S_p^x) \in \mathbb{R}^{n_x \times n_v}$. The flux balance constraint is then written as $Sv = 0$. We aim to reduce the number of optimization variables by explicitly solving for this constraint. Let $r \leq \min(n_x, n_v)$ be the rank of S . Using singular value decomposition (SVD), S can be decomposed as

$$S = S_r W^T, \tag{13}$$

with a full rank matrix $S_r \in \mathbb{R}^{n_x \times r}$ and a matrix $W \in \mathbb{R}^{n_v \times r}$ which satisfies

$$W^T W = I_r. \tag{14}$$

Also from SVD, we get a matrix $M \in \mathbb{R}^{n_v \times (n_v - r)}$ which satisfies

$$W^T M = 0. \tag{15}$$

We now substitute the optimization variable $v(t)$ by

$$v(t) = Ww(t) + Mu(t), \tag{16}$$

where $w(t) \in \mathbb{R}^r$ and $u(t) \in \mathbb{R}^{n_v - r}$. The flux balance constraint now becomes

$$Sv = S_r w = 0. \tag{17}$$

Since S_r is full rank, this implies $w = 0$, and both the flux balance constraint and the variable w can be removed from the optimization problem.

With this reduction, and by summarizing some constraints in (12), we arrive at the following general dynamic optimization problem to be solved.

$$\begin{aligned}
& \max_{\mathcal{U}(\mathcal{Z}, z_0)} \int_0^{t_f} \Phi(z(t), u(t)) dt + \Psi(z(t_f)) \\
& \text{s.t. } \dot{z} = Bu \\
& \quad z(0) = z_0 \\
& \quad G_1 z(t) \leq g_1 \\
& \quad G_2 u(t) \leq G_3 z(t) + g_2,
\end{aligned} \tag{18}$$

where

$$\begin{aligned} G_1 &= \begin{pmatrix} -I_{n_z} \\ (0, H_B) \end{pmatrix} & g_1 &= \begin{pmatrix} 0 \\ h_B \end{pmatrix} \\ G_2 &= \begin{pmatrix} -I_{n_u} \\ I_{n_u} \\ \tilde{H}_C M \end{pmatrix} & g_2 &= \begin{pmatrix} -v_{min} \\ v_{max} \\ 0 \end{pmatrix} \\ G_3 &= \begin{pmatrix} 0 \\ 0 \\ H_E \end{pmatrix} \end{aligned} \quad (19)$$

and

$$\mathcal{U}(\mathcal{Z}, z_0) = \{u \mid Mu \in \mathcal{V}(\mathcal{Z}, z_0)\}. \quad (20)$$

2.2 Maximum growth objective

A commonly used biological objective functions for metabolic fluxes is to maximize the cell's growth. In the context developed here, the objective is to maximize the biomass at the endpoint of a given time interval, given the initial biomass distribution and nutrient availability. The objective is characterized mathematically by

$$\Phi(z, u) = 0 \quad (21)$$

and

$$\Psi(z_f) = b^T p(t_f), \quad (22)$$

where $b \in \mathbb{R}^{n_p}$ is a biomass weighting vector.

2.3 Time-optimal flux dynamics

The other approach to maximize the growth rate is to minimize the time cells need to achieve a prespecified growth. In contrast to the previous approach with the maximum growth objective, the time-optimal approach requires to fix a non-trivial target set \mathcal{Z} .

One approach could be to minimize the time needed to metabolize the nutrients available at the initial time point. In order to use such an approach, we have to determine a reachable target state where all nutrients are metabolized, which may be complicated by the accumulation of waste products, or only partial availability of some sources due to a lack of required co-metabolites. With a given initial nutrient availability characterized by $y(0)$, one reasonable method could be to first try to determine the maximum achievable biomass

$$\begin{aligned} \beta^* &= \max_z & b^T p \\ \text{s.t.} & & G_c z = G_c z_0, \end{aligned} \quad (23)$$

where G_c captures all conservation relations in the metabolic-genetic network. In (23), we assume implicitly that the bounds on the fluxes are such that the corresponding target z^* is reachable by the metabolic-genetic network. In general, the constraint that z must be reachable from z_0 under the dynamics and constraints of the metabolic-genetic network should be added. Ways to check such a constraint need to be investigated. Given a solution to the optimization problem (23), the target set can then be defined as

$$\mathcal{Z} = \{z \mid b^T p \geq \beta^*\}. \quad (24)$$

An alternative approach would be to define a specific increase in biomass as the target set. Given a factor $\alpha > 1$, the target would be defined as

$$\mathcal{Z} = \{z \mid p \geq \alpha p(0)\}, \quad (25)$$

i.e., the all macromolecules will be increased by a factor of α .

For time-optimal dynamics, the objective function to be used is given by

$$\Phi(z, u) = -1 \quad (26)$$

and

$$\Psi(z_f) = 0. \quad (27)$$

3 Numerical solution of the constructed optimal control problem

3.1 Abstract problem formulation

Based on the derivations in Section 2, we consider an optimal control problem given by

$$\begin{aligned} & \max_{\mathcal{U}} \int_0^{t_f} (C(t)x(t) + D(t)u(t) + E(t))dt + Fx(t_f) \\ & \text{s.t. } \dot{x}(t) = A(t)x(t) + B(t)u(t) + u_0(t) \\ & \quad x(0) = x_0 \\ & \quad G_x(t)x(t) + G_u(t)u(t) + G_k(t) \leq 0, \quad 0 \leq t \leq t_f \\ & \quad H_x x(t_f) + H_k \leq 0 \\ & \quad \int_0^{t_f} (\tilde{C}(t)x(t) + \tilde{D}(t)u(t) + \tilde{E}(t))dt + \tilde{F}x(t_f) \leq 0 \end{aligned} \quad (28)$$

with $x(t) \in \mathbb{R}^n$, $u(t) \in \mathbb{R}^m$, and the matrices in the objective and constraints of appropriate dimension. For vector constraints, the inequalities are understood to be element-wise.

In this formulation, the final time t_f is fixed, and the set of admissible controls \mathcal{U} is the set of measurable functions on the interval $[0, t_f]$.

3.2 Discretization by collocation

The solution to the optimal control problem (28) is approximated by a collocation scheme. To this end, the time interval $[0, t_f]$ is divided into N equally sized intervals, each of length

$$h = t_f/N. \quad (29)$$

Within each interval, K collocation points are considered, using Gauss, Gauss-Radau, or Gauss-Lobatto collocation. Overall, the collocation points are given by the sequence

$$t_{1,1}, t_{1,2}, \dots, t_{1,K}, t_{2,1}, \dots, t_{N,K}. \quad (30)$$

Within each interval, the q -th collocation point is at position r_q (relative to the interval $[-1, 1]$), where r_q is determined by the collocation scheme and order. The collocation points are thus computed as

$$t_{i,q} = (i-1)h + (r_q + 1)h/2. \quad (31)$$

3.2.1 Approximation of continuous variables

The control and state derivative are discretized by the following interpolation scheme:

$$\begin{aligned} u(t) &= \sum_{q=1}^K u_{i,q} L_q\left(\frac{2t - 2t_{i-1} - h}{h}\right), & t_{i-1} \leq t \leq t_i \\ \dot{x}(t) &= \sum_{q=1}^K \dot{x}_{i,q} L_q\left(\frac{2t - 2t_{i-1} - h}{h}\right), & t_{i-1} \leq t \leq t_i, \end{aligned} \quad (32)$$

where L_q , $q = 1, \dots, K$ are suitable interpolation functions defined on the interval $(-1, 1)$. The boundaries of the time intervals are given by $t_i = ih$, $i = 1, \dots, N$ and $t_0 = 0$.

The state variable x is discretized at the boundaries of the N intervals in time, and its value within an interval is approximated by integrating over the state derivatives:

$$\begin{aligned} x(t_{i-1} + \tau) &= x_{i-1} + \int_0^\tau \dot{x}(t_{i-1} + s) ds \\ &= x_{i-1} + \sum_{q=1}^K \dot{x}_{i,q} \int_0^\tau L_q(2s/h - 1) ds \\ &= x_{i-1} + h/2 \sum_{q=1}^K \dot{x}_{i,q} \int_{-1}^{r(\tau)} L_q(s) ds, \end{aligned} \quad (33)$$

with $r(\tau) = 2\tau/h - 1$.

In the following, we will also denote

$$Q_{q,p} = \int_{-1}^{r_q} L_p(s) ds, \quad (34)$$

for $1 \leq p, q \leq K$. Then, the value of the state vector at a collocation point $t_{i,q}$ is approximated by

$$x(t_{i,q}) = x_{i-1} + \frac{h}{2} (Q_q \otimes I_n) \dot{x}_i, \quad (35)$$

where $\dot{x}_i = (\dot{x}_{i,1}, \dots, \dot{x}_{i,K})$, $Q_q = (Q_{q,1}, \dots, Q_{q,K})$ and \otimes is the Kronecker product.

3.2.2 Summary of the discretization scheme

The continuous optimization problem (28) is approximated by a discrete problem in which the optimization is done over the vector $z \in \mathbb{R}^{NK(n+m)+Nn}$, defined by

$$z = (u_{1,1}, u_{1,2}, \dots, u_{N,K}, \dot{x}_{1,1}, \dot{x}_{1,2}, \dots, \dot{x}_{N,K}, x_1, \dots, x_N), \quad (36)$$

with $u_{i,q}$, $\dot{x}_{i,q}$, and x_i , $i = 1, \dots, N$, $q = 1, \dots, K$ corresponding to the interpolation coefficients in (32) and (33).

The discrete optimization problem is written as

$$\begin{aligned} \max_z \quad & c^T z + e \\ \text{s.t.} \quad & M_e z = V_e \\ & M_i z \leq V_i, \end{aligned} \quad (37)$$

where the vector c and number e stem from the discretization of the the objective functional, the equality constraint matrix M_e and vector V_e from collocation of the differential equation and the initial condition, and the inequality constraint matrix M_i and vector V_i from the path, terminal, and integral constraints in (28). The derivation of the optimization parameters in the problem (37) from the continuous problem is discussed in the next sections 3.2.3–3.2.5.

In the following derivation of the discrete optimization problem, we will frequently denote

$$u_i = (u_{i,1}, \dots, u_{i,K}) \quad (38)$$

and

$$\dot{x}_i = (\dot{x}_{i,1}, \dots, \dot{x}_{i,K}). \quad (39)$$

3.2.3 Discretization of the objective functional

The objective functional $J(u, x, x_0) = \int_0^{t_f} (C(t)x(t) + D(t)u(t) + E(t))dt + Fx(t_f)$ is approximated by Gaussian quadrature as

$$J(u, x, x_0) \approx \frac{h}{2} \sum_{i=1}^N \sum_{q=1}^K w_q (C(t_{i,q})x(t_{i,q}) + D(t_{i,q})u(t_{i,q}) + E(t_{i,q})) + Fx(t_f), \quad (40)$$

where w_q , $q = 1, \dots, K$, are the weights of the Gaussian quadrature scheme.

Let us consider some terms individually. First, we have

$$\sum_{q=1}^K w_q C(t_{i,q})x(t_{i,q}) = WC_i(\mathbf{1}_K \otimes x_{i-1} + \frac{h}{2}(Q \otimes I_n)\dot{x}_i), \quad (41)$$

where

$$\begin{aligned} W &= (w_1 \quad \dots \quad w_K) \\ C_i &= \begin{pmatrix} C(t_{i,1}) & & 0 \\ & \ddots & \\ 0 & & C(t_{i,K}) \end{pmatrix} \\ Q &= \begin{pmatrix} Q_{1,1} & \cdots & Q_{1,K} \\ \vdots & & \vdots \\ Q_{K,1} & \cdots & Q_{K,K} \end{pmatrix}. \end{aligned} \quad (42)$$

Similarly, we have

$$\sum_{q=1}^K w_q D(t_{i,q})u(t_{i,q}) = WD_i(P \otimes I_m)u_i, \quad (43)$$

where

$$\begin{aligned} D_i &= \begin{pmatrix} D(t_{i,1}) & & 0 \\ & \ddots & \\ 0 & & D(t_{i,K}) \end{pmatrix} \\ P &= \begin{pmatrix} L_1(r_1) & \cdots & L_K(r_1) \\ \vdots & & \vdots \\ L_1(r_K) & \cdots & L_K(r_K) \end{pmatrix}. \end{aligned} \quad (44)$$

Taking the terms together, we get the following approximation of the objective functional:

$$J(u, x, x_0) \approx \tilde{J}(z) = \frac{h}{2} \sum_{i=1}^N (WC_i(\mathbf{1}_K \otimes x_{i-1} + \frac{h}{2}(Q \otimes I_n)\dot{x}_i) + WD_i(P \otimes I_m)u_i + WE_i)) + Fx_N, \quad (45)$$

where

$$E_i = \begin{pmatrix} E(t_{i,1}) \\ \vdots \\ E(t_{i,K}) \end{pmatrix}. \quad (46)$$

This approximation depends only on the optimization vector z of the discretized problem.

3.2.4 Discretization of the dynamics

A collocation scheme is used to enforce the dynamical constraint in (28), by including the differential equation evaluated at collocation points as constraint:

$$\dot{x}(t_{i,q}) = A(t_{i,q})x(t_{i,q}) + B(t_{i,q})u(t_{i,q}) + u_0(t_{i,q}) \quad (47)$$

for $i = 1, \dots, N$ and $q = 1, \dots, K$.

In the discretized optimization problems, this translates into the constraints

$$(P \otimes I_n)\dot{x}_i = A_i((\mathbf{1}_K \otimes x_{i-1}) + \frac{h}{2}(Q \otimes I_n)\dot{x}_i) + B_i(P \otimes I_m)u_i + u_{0i}, \quad (48)$$

where

$$A_i = \begin{pmatrix} A(t_{i,1}) & & 0 \\ & \ddots & \\ 0 & & A(t_{i,K}) \end{pmatrix} \quad (49)$$

$$B_i = \begin{pmatrix} B(t_{i,1}) & & 0 \\ & \ddots & \\ 0 & & B(t_{i,K}) \end{pmatrix}$$

and

$$u_{0i} = \begin{pmatrix} u_0(t_{i,1}) \\ \vdots \\ u_0(t_{i,K}) \end{pmatrix}. \quad (50)$$

Continuity constraints must be added in order to assure that the approximation to the state variable $x(t)$ is continuous at boundaries t_i of the time intervals used in the discretization. These constraints are given by

$$x_i = x_{i-1} + \frac{h}{2}(Q_0 \otimes I_n)\dot{x}_i, \quad (51)$$

where

$$Q_0 = \begin{pmatrix} \int_{-1}^1 L_1(s)ds & \cdots & \int_{-1}^1 L_K(s)ds \end{pmatrix}. \quad (52)$$

3.2.5 Discretization of the path, terminal, and integral constraints

The path constraints are approximated by enforcing them at the collocation points only:

$$G_x(t_{i,q})x(t_{i,q}) + G_u(t_{i,q})u(t_{i,q}) + G_k(t_{i,q}) \leq 0 \quad (53)$$

for $i = 1, \dots, N$ and $q = 1, \dots, K$. In terms of the optimization vector z , this is written as

$$G_x(t_{i,q})(x_{i-1} + \frac{h}{2}(Q_q \otimes I_n)\dot{x}_i) + G_u(t_{i,q})(P_q \otimes I_m)u_i + G_k(t_{i,q}) \leq 0. \quad (54)$$

The terminal constraint is simply written as

$$H_x x_N + H_k \leq 0. \quad (55)$$

The integral constraint in (28) can be approximated in the same way as the objective functional. For the discretized optimization problem, this yields the constraint

$$\frac{h}{2} \sum_{i=1}^N (W\tilde{C}_i(\mathbf{1}_K \otimes x_{i-1} + \frac{h}{2}(Q \otimes I_n)\dot{x}_i) + W\tilde{D}_i(P \otimes I_m)u_i + W\tilde{E}_i)) + \tilde{F}x_N \leq 0. \quad (56)$$

3.3 Numerical solution of the discretized problem

3.3.1 Optimization with fixed terminal time

The discretized optimization problem (37) is simply a linear program (LP), and can be solved with state-of-the-art LP solvers. From the resulting optimal vector z^* , the dynamical solution can be computed by the representations in (32) and (33).

Note that the interpolated state and control vectors $x(t)$ and $u(t)$ may violate the path constraints at points different from collocation points. Razzaghi *et al.* [1] seem to have an iterative approach to improve the constraint violation, but how they proceed is not totally clear to me.

3.3.2 Optimization with free terminal time

Optimization with free terminal time is much more difficult than with a fixed terminal time in this case. The commonly used reparametrization of the system with the terminal time introduces non-linearity in the constraints, thus impeding solution by a linear program.

A special case is a pure minimal (or maximal) time problem, where all parameters in the objective function apart from $E(t)$ are equal to zero. Since the objective functional is then monotone in the terminal time, the problem can simply be solved by bisection. Depending on whether the linear program (37) as constructed for a specific terminal time is feasible or not, the bounds on the optimal time are updated by bisection. The bisection algorithm terminates when the lower and upper bounds on the optimal value are closer than some prespecified tolerance.

If the objective functional is not monotone, one may try to do scalar optimization over the terminal time, solving the underlying LP (37) for a fixed time in each iteration. I have implemented this approach in `linopt.py`, but have no good idea how well it will work.

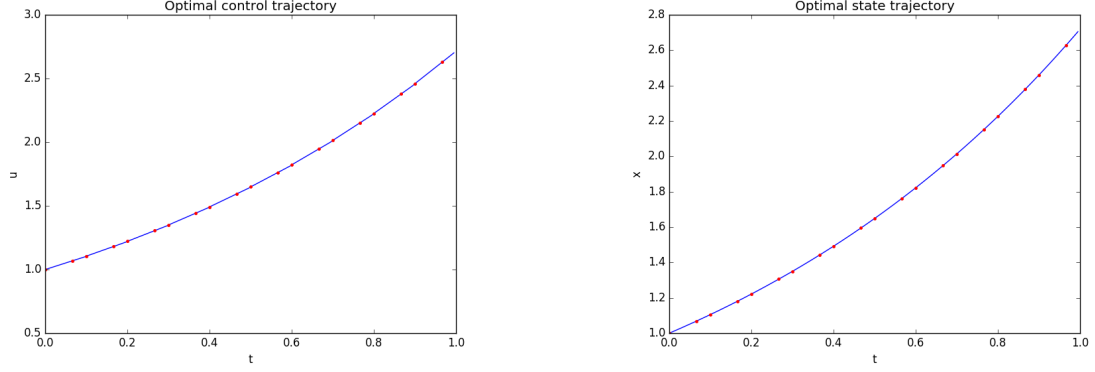


Figure 1: Numerical solution to the constrained integrator problem (57).

3.4 Simple examples

3.4.1 A constrained integrator

We consider the following optimal control problem:

$$\begin{aligned}
 & \max_{\mathcal{U}} \int_0^1 x(t) dt \\
 & \text{s.t. } \dot{x}(t) = u(t) \\
 & \quad x(0) = 1 \\
 & \quad -x(t) + u(t) \leq 0, \quad 0 \leq t \leq 1.
 \end{aligned} \tag{57}$$

Clearly, the optimal solution is

$$u^*(t) = e^t, \tag{58}$$

giving rise to the state trajectory

$$x^*(t) = e^t. \tag{59}$$

The results of a numerical solution are shown in Figure 1. For the discretization, 10 time intervals have been used, each with two collocation points in a Radau scheme. The collocation points are shown as red dots in the plots in Figure 1.

3.4.2 Minimum time control of the rocket car to the origin

The second example is the classical “rocket car” example. The control task is to steer the rocket car to a specific position (here the origin) in a minimum amount of time. The problem is formulated as follows:

$$\begin{aligned}
 & \min_{\mathcal{U}, t_f} \int_0^{t_f} 1 dt \\
 & \text{s.t. } \dot{x}_1(t) = x_2(t) \\
 & \quad \dot{x}_2(t) = u(t) \\
 & \quad x(0) = (1, 0) \\
 & \quad -1 \leq u(t) \leq 1, \quad 0 \leq t \leq t_f \\
 & \quad x(t_f) = 0.
 \end{aligned} \tag{60}$$

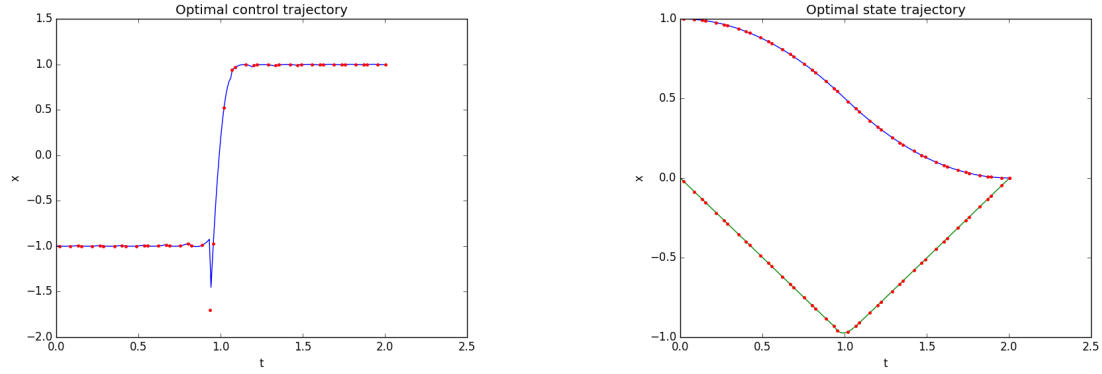


Figure 2: Numerical solution to the rocket car problem (60).

Note that the equality terminal constraint can be written as the inequality $0 \leq x(t_f) \leq 0$ to get into the framework used in the general problem (28).

The classical results show that the optimal solution is of bang-bang type. This is also seen in the numerical solution shown in Figure 2. Here, 15 time intervals with three Radau collocation points per time interval have been used.

Due to the interpolation, there is a violation of the control constraints around the switching time. This seems to be particularly severe here, because the switching time is inside one of the discrete time intervals. An alternative discretization where the switching time is at the boundary of the interval yielded a smaller violation of the control constraint.

3.4.3 A minimal metabolic-genetic network

References

- [1] M. Razzaghi, J. Nazarzadeh, and KY Nikraves. A collocation method for optimal control of linear systems with inequality constraints. *Mathematical Problems in Engineering*, 3(6):503–515, 1998.