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October 26, 2021

Abstract

Electro-fermentation is a novel process that consists of electrochemically controlling microbial fermentative metabolism with electrodes. In such process the electrodes act either as electron sinks or sources modifying the fermentation balance of a microbial fermentative metabolism and providing new options for the control of microbial activity. In this paper we consider a fermentative microorganism in a batch culture and we suppose that this microorganism has two metabolic pathways, each one gives rise to a corresponding fermentation product. We propose a model describing the transition between the two metabolic behaviors in response to different electrode potentials. Based on this model we study how to control the microbial ecosystem in order to maximize the production of one of the rising fermentation products.

1 Introduction

The knowledge of electroactive microorganisms has rapidly grown over the last 20 years with the development of microbial electrochemical technologies such as microbial fuel cells (MFC) and microbial electrolysis cells (MEC) for the production of electricity or hydrogen from organic matter [10]. The development of electromicrobiology has also led to several promising applications such as electro-fermentation (EF) in which the electrodes act as either electron sinks or sources modifying the fermentation balance of a microbial fermentative metabolism and providing new options for the control of microbial communities [11, 15]. EF has been successfully applied on mixed culture fermentations and pure culture fermentations and has proven efficient for increasing yields in various products such as hydrogen, acetate, propionate, butyrate, lactate, 3-hydroxypropanoic acid, ethanol, 1.3-propanediol, 2,3-butandiol, butanol or acetone [20, 18, 12, 17, 13, 4, 3, 2, 9, 8, 5, 19]. For example, a metabolic shift occurred in *Clostridium pasteurianum* when taking up electrons from an electrode poised at +0.045 V vs. SHE (Standard Hydrogen Electrode) with an increased production of reduced products such as butanol from glucose and 1.3-propanediol from glycerol [2]. From a biotechnological point of view, EF could lead to significant improvements of industrial fermentations using only a small amount of electrical power. Moreover, the use of an electrode for the triggering of the EF effect in the fermentation system introduce the possibility of a dynamic control of the fermentation. However, mathematical models describing the EF effect are currently lacking.

Here we consider a pure culture of a fermentative microorganism growing on a limiting resource in a batch culture. The EF effect is modeled by considering two microbial subpopulations producing different metabolites (f_1, f_2) giving rise to two different products (p_1, p_2). The switching between the fermentation behaviors depends on the electrodes potential V. The control parameter is simply chosen in such a way that its variation between two constants values (which correspond to two different values of V) leads to a transition between the two considered metabolic behaviors. The bioreactor equations in batch culture are simply used to establish the model [16]. Based on this model, an optimal control problem for the maximization of the production of p_2 is formulated. The Pontryagin's Maximum Principle [7, 14] is applied for the design of the optimal control strategy. The obtained results show that the optimal strategy is not trivial, in the sens that the control is not always constant (equal to that which correspond to f_2), where in some cases the metabolic behavior f_1 should be visited by the fermentative bacteria.

The paper is organized as follows. In Section 2, we give the electro-fermentation model and introduce the optimization problem. The main part of the paper is devoted to the synthesis of an optimal control strategy in two cases: case of identical growth functions in Section 3 and case of constant growth functions in Section 4. Finally, discussion and numerical simulations are given in Section 5.

2 Model description and optimization problem

In order to describe the switching between the two metabolic pathways described in the introduction, we suppose that the fermentative population is splitted into two sub-populations x_1 and x_2 in a commensalism relation to consume a substrate s. The sub-population x_1 with microbial growth rate μ_1 gives rise to a product s_1 and the sub-population x_2 with microbial growth rate μ_2 gives rise to a product s_2. We suppose that in the absence of polarized electrodes the fermentation is mainly guided by the population x_1 and when the external voltage is sufficiently large the metabolic function switch to a metabolism guided by x_2. This electro-fermentation process can be described by the following system of ordinary differential equations:

$$\begin{array}{rcl} \dot{s} & = & -\frac{1}{Y_1}\mu_1(s)x_1 - \frac{1}{Y_2}\mu_2(s)x_2 \\ \dot{x}_1 & = & \mu_1(s)x_1 - \alpha r_1 x_1 + (1-\alpha) r_2 x_2 \\ \dot{x}_2 & = & \mu_2(s)x_2 + \alpha r_1 x_1 - (1-\alpha) r_2 x_2 \end{array} \tag{1}$$

where Y_1, Y_2 are the yields coefficients, r_1, $r_2 > 0$ are positive constants and $\alpha \in [0,1]$ is the control parameter which is directly related to the external potential V and satisfies the following property:

$$\alpha = 0 \text{ if } V = 0, \quad \text{and} \quad \alpha = 1 \text{ if } V = V_0, \tag{2}$$

where $V_0 > 0$ is a threshold on the external potential over which the metabolic pathway is guided by x_2. The value of the threshold potential V_0 depends on the microorganisms x_1 and x_2. Observe that, due to the migration phenomenon between the two sub-populations, the relation between x_1 and x_2 is not simply reduced to a competition phenomenon.

The objective to maximize the total production of the sub-population x_2 over an interval of time $[0, T]$, that is the synthesis of a function $\alpha(\cdot)$ such that

$$J[\alpha(\cdot)] = \int_0^T \mu_2(s(t))x_2(t)dt, \tag{3}$$

is maximal, where $T > 0$ is fixed. This optimisation problem will be studied under the following assumption:

Assumption 1. $Y_1 = Y_2 = Y$.

Even that Assumption 1 seems very restrictive, many experimental studies show that yields are slightly different depending on V.

Note that at the price of change of units of x_1 and x_2, one can without loss of generality assume that $Y = 1$; this is conventional when dealing with chemostat type systems [6]. Therefore, we shall consider the simpler model

$$\begin{array}{rcl} \dot{s} & = & -\mu_1(s)x_1 - \mu_2(s)x_2 \\ \dot{x}_1 & = & \mu_1(s)x_1 - \alpha r_1 x_1 + (1-\alpha)r_2 x_2 \\ \dot{x}_2 & = & \mu_2(s)x_2 + \alpha r_1 x_1 - (1-\alpha)r_2 x_2, \end{array} \tag{4}$$

where $(s(0), x_1(0), x_2(0)) = (s_0, x_{10}, x_{20}) \in \mathbb{R}^3_+$.

Observe that one has $s(t) + x_1(t) + x_2(t) = s(0) + x_1(0) + x_2(0) = c > 0$ at any $t \geq 0$. Therefore, we can consider the reduced dynamics in the plane

$$\begin{array}{rcl} \dot{x}_1 & = & \mu_1(c - x_1 - x_2)x_1 - \alpha r_1 x_1 + (1-\alpha)r_2 x_2 \\ \dot{x}_2 & = & \mu_2(c - x_1 - x_2)x_2 + \alpha r_1 x_1 - (1-\alpha)r_2 x_2. \end{array} \tag{5}$$

The optimal control problem is thus reduced to (3)-(5).

3 Optimal synthesis with identical growth functions

We have the following proposition.

Proposition 1. *Assume that one has $\mu_1(s) = \mu_2(s) := \mu(s)$ for any $s > 0$. Then, the constant control $\alpha^\star = 1$ is optimal.*

Proof. Let $b = x_1 + x_2$. Then $b(\cdot)$ is the solution of

$$\dot{b} = \mu(c - b)b, \quad b(0) = x_1(0) + x_2(0) \tag{6}$$

whatever is the control $\alpha(\cdot)$. Then, the variable $X_2 = x_2/b$ is solution of

$$\dot{X}_2 = \alpha r_1(1 - X_2) - (1-\alpha)r_2 X_2, \quad X_2(0) = x_2(0)/(x_1(0) + x_2(0)). \tag{7}$$

Note that at any time t, $\dot{X}_2$ is maximal for $\alpha = 1$, whatever is $X_2 \in [0, 1]$. Let $\bar{X}_2(\cdot)$ be the solution for the control α identically equal to 1. From standard results of comparison of solutions of scalar ordinary equations, one has $X_2(t) \leq \bar{X}_2(t)$ at any t, whatever is the control $\alpha(\cdot)$. Therefore, one has

$$J[\alpha(\cdot)] = \int_0^T \mu(c - b(t))b(t)X_2(t)\,dt \leq \int_0^T \mu(c - b(t))b(t)\bar{X}_2(t)\,dt = J[1]$$

and we conclude that the constant control $\alpha^\star = 1$ is optimal. □

Proposition 1 shows that, in the case of identical growth functions, the optimal strategy in order to maximize (3) is by keeping α constantly equal to one, i.e., by keeping an external potential sufficiently larger than V_0.

4 Optimal synthesis with constant growth functions

In the case of constant (but different) growth rate functions, the optimization problem (3)-(5) is studied under the following assumption:

Assumption 2. *we assume $\mu_i(s) = k_i > 0$ for any $s \geq 0$ ($i = 1, 2$).*

The following definition will be useful in the following.

Definition 1. *Denote* $L = \frac{k_1}{k_2}$ *and* $K = \frac{r_1 - k_1}{k_2}$ *and define*

$$\tilde{\phi}(p_2) = \begin{cases} \dfrac{K + L - K(L-1)p_2 - (L+K)(p_2+1)^{-K}}{K(K+1)} & K \notin \{-1, 0\} \\ (1-L)p_2 + L\log(p_2+1) & K = 0 \\ -L + L(p_2+1) + \log(p_2+1)(1-L) & K = -1 \end{cases} \tag{8}$$

Define also, when $L > 1$*, the number*

$$\bar{\tau} := \frac{\log\left(\inf\left\{p_2 > 0;\ \tilde{\phi}(p_2) < 0\right\} + 1\right)}{k_2}. \tag{9}$$

Remark 1. *One can straightforwardly check that when* $L > 1$ *(that is when* $k_1 > k_2$*) one has*

$$\lim_{p_2 \to +\infty} \tilde{\phi}(p_2) = -\infty$$

whatever is $K > -L$ *(i.e.* $r_1 > 0$*). We deduce that* $\bar{\tau}$ *is well-defined.*

We use the Maximum Principle of Pontryagin (PMP) [14] to obtain necessary conditions. Defining the Hamiltonian

$$H(x, p, \alpha) = p_1 k_1 x_1 + (p_2 + 1)k_2 x_2 + (p_2 - p_1)(\alpha r_1 x_1 - (1-\alpha) r_2 x_2), \tag{10}$$

where $p = (p_1, p_2)$ is the adjoint vector, and denoting by x^* an optimal trajectory, the Pontryagin maximum principle provides the existence of an absolutely continuous function $p^* : [0, T] \to \mathbb{R}^2$ such that (x^*, p^*) is solution of the coupled dynamics:

$$\begin{array}{l} \dot{x}_1 = k_1 x_1 - \alpha^* r_1 x_1 + (1-\alpha^*) r_2 x_2 \\ \dot{x}_2 = k_2 x_2^* + \alpha^* r_1 x_1 - (1-\alpha^*) r_2 x_2 \\ \dot{p}_1 = -k_1 p_1 - \alpha^* r_1 (p_2 - p_1) \\ \dot{p}_2 = -k_2(p_2+1) + (1-\alpha^*) r_2 (p_2 - p_1) \end{array} \tag{11}$$

with the two-points boundary conditions $x^*(0) = x_0$, $p^*(T) = 0$, and the control $\alpha^*(\cdot)$ verifies

$$\bar{H}(x^*(t), p^*(t)) := \max_{\alpha} H(x^*(t), p^*(t), \alpha) = H(x^*(t), p^*(t), \alpha^*(t)), \quad \text{a.e. } t \in [0, T]. \tag{12}$$

In addition, the map $t \mapsto \bar{H}(x^*(t), p^*(t))$ is constant. Let

$$\phi(t) = p_2(t) - p_1(t) \tag{13}$$

be the switching function. From the maximization of the Hamiltonian, one gets

$$\alpha^*(t) = \begin{cases} 1 \text{ if } \phi(t) > 0, \\ 0 \text{ if } \phi(t) < 0, \end{cases} \quad \text{a.e. } t \text{ s.t. } \phi(t) \neq 0 \tag{14}$$

We have the following theorem.

Theorem 1. *We have the two cases:*

- *If* $k_1 \leq k_2$*, then* $\alpha^\star = 1$ *is optimal on* $[0, T]$.
- *If* $k_1 > k_2$*, then*

$$\alpha^\star(t) = \begin{cases} 1 & \text{if } t \geq \min(0, T - \bar{\tau}) \\ 0 & \text{otherwise} \end{cases}$$

  is optimal on $[0, T]$.

Proof. The adjoint equations are written

$$\begin{array}{rcl} \dot{p}_1 & = & -k_1 p_1 - \alpha r_1 (p_2 - p_1) \\ \dot{p}_2 & = & -k_2(p_2+1) + (1-\alpha) r_2 (p_2 - p_1) \end{array} \tag{15}$$

Note that system (15) is decoupled from the dynamics of x_1, x_2 and can be studied independently to the initial condition $(x_1(0), x_2(0))$. The switching function satisfies

$$\dot{\phi} = -k_2 + k_1 p_1 - k_2 p_2 + \phi\big(r_2 + \alpha(r_1 - r_2)\big). \tag{16}$$

At terminal time T, one has $\phi(T) = 0$ with $\dot{\phi}(T) = -k_2 < 0$. So we conclude about the existence of the number

$$\bar{t}_1 := \inf \{t > 0;\ \phi(\tau) > 0,\ \tau \in (t, T)\}$$

and the optimality of $\alpha = 1$ on the interval $[\bar{t}_1, T]$. On this interval, one has

$$\begin{array}{rcl} \dot{p}_2 & = & -k_2(p_2+1) \\ \dot{\phi} & = & -k_2 + (k_1 - k_2) p_2 + (r_1 - k_1)\phi \end{array} \tag{17}$$

Note that $p_2(T) = 0$ implies that one has necessarily $p_2 > 0$ on $[\bar{t}_1, T)$.

If $k_1 \leq k_2$, ϕ cannot cross 0 from below because $\phi = 0$ implies $\dot{\phi} < 0$. We deduce from (17) that ϕ is negative on $[\bar{t}_1, T)$, and thus $\bar{t}_1$ has to be equal to 0. We conclude that $\alpha^\star = 1$ is optimal on $[0, T]$.

Consider now the case $k_1 > k_2$. Let us show that an optimal solution cannot present a singular arc, i.e. a time interval on which ϕ is identically null. If not, $\dot{\phi} = 0$ and $\phi = 0$ implies from equation (16) that p_2 has to be constant on such an interval with $p_2 = k_2/(k_1 - k_2) > 0$. But from equations (15) with $\dot{p}_2 = 0$ and $p_2 = p_1$, one obtains $p_2 = -1 < 0$, and thus a contradiction. We deduce that an optimal solution is a concatenation of arcs with $\alpha = 0$ or $\alpha = 1$. Note, from equation (16), that $\dot{\phi}$ is continuous at switching times (with $\dot{\phi} = -k_2 + (k_1 - k_2)p_2 = -k_2 + (k_1 - k_2)p_1$). If $\bar{t}_1 > 0$, we consider the number

$$\bar{t}_0 := \inf \{t > 0;\ \phi(\tau) < 0,\ \tau \in (t, \bar{t}_1)\}.$$

On the interval $(\bar{t}_0, \bar{t}_1)$, $\alpha = 0$ is optimal and one has

$$\begin{array}{rcl} \dot{p}_1 & = & -k_1 p_1 \\ \dot{\phi} & = & -k_2 + (k_1 - k_2) p_1 + (r_2 - k_2)\phi. \end{array} \tag{18}$$

Note that one has $p_1(\bar{t}_1) = p_2(\bar{t}_1) > 0$, which implies $p_1(t) > p_1(\bar{t}_1)$ for $t \in [\bar{t}_0, \bar{t}_1)$. As ϕ changes its sign at $\bar{t}_1$ (from negative to positive values), one has necessarily $\dot{\phi}(\bar{t}_1) \geq 0$ (with $\phi(\bar{t}_1) = 0$). If $\bar{t}_0 > 0$, one should have $\phi(\bar{t}_0) = 0$ with $\dot{\phi}(\bar{t}_0) = -k_2 + (k_1 - k_2)p_1(\bar{t}_0) > -k_2 + (k_1 - k_2)p_1(\bar{t}_1) = \dot{\phi}(\bar{t}_1) \geq 0$, which contradicts the change of sign of ϕ at $\bar{t}_0$. We conclude that one has necessarily $\bar{t}_0 = 0$ and thus the optimal solution consists in at most one switch from $\alpha = 0$ to $\alpha = 1$.

Finally, let us consider the dynamics (17) in the backward time $\tau = T - t$:

$$\begin{array}{rcl} \dfrac{dp_2}{d\tau} & = & k_2(p_2 + 1), \quad p_2(0) = 0 \\ \dfrac{d\phi}{d\tau} & = & k_2 - (k_1 - k_2)p_2 - (r_1 - k_1)\phi, \quad \phi(0) = 0 \end{array} \tag{19}$$

Note that the map $\varphi : \tau \mapsto p_2(\tau)$ defines a diffeomorphism from $\mathbb{R}^+$ to $\mathbb{R}^+$. The solution ϕ can then be parameterized by p_2, as solution of the non-autonomous scalar differential equation

$$\frac{d\tilde{\phi}}{dp_2} = 1 - L\frac{p_2}{p_2 + 1} - K\frac{\tilde{\phi}}{p_2 + 1}, \quad \tilde{\phi}(0) = 0, \tag{20}$$

where L and K are given by Definition 1. The solution of (20) can be made explicit as given by (8). As it is underlined by Remark 1, when $L > 1$ (that is when $k_1 > k_2$) the number $\bar{\tau}$ is well-defined. Then, we have that $\phi(\bar{\tau}) = 0$ with $\phi(\tau) > 0$ for $\tau \in (0, \bar{\tau})$. Therefore, one gets $\bar{t}_1 = \max(0, T - \bar{\tau})$ and the control

$$\alpha^\star(t) = \begin{cases} 1 & \text{if } t \geq \min(0, T - \bar{\tau}) \\ 0 & \text{otherwise} \end{cases}$$

is optimal. Let us underline that when μ_i are constant functions, the optimal synthesis does not depend on the initial state.

□

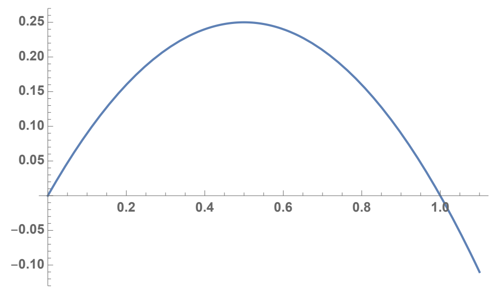

Figure 1: The plot of $\tilde{\phi}$. In this case we have $\bar{\tau} = \log(4)$.

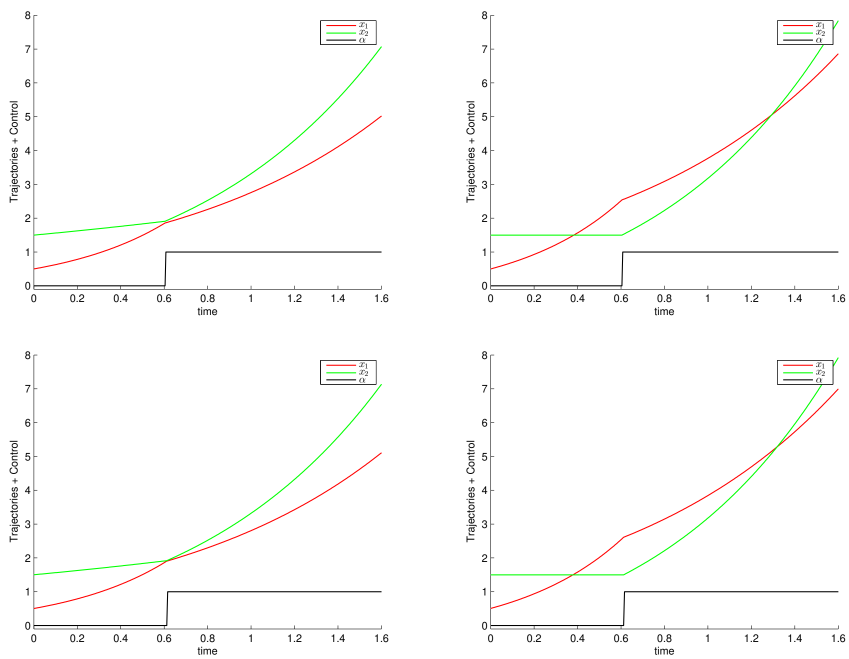

Figure 2: Exact optimal control and optimal control computed with BOCOP (top) and Matlab (bottom) for $r_2 = 0.1$ (left) and $r_2 = 0.5$ (right).

Remark 2. *It is worth noting that in the case of constant growth rate functions, the optimal control* $\alpha^\star$ *does not depend on* r_2*, the migration rate constant from population* x_2 *to population* x_1*. This is clearly recognizable from the statement of Theorem 1 and Definition 1.*

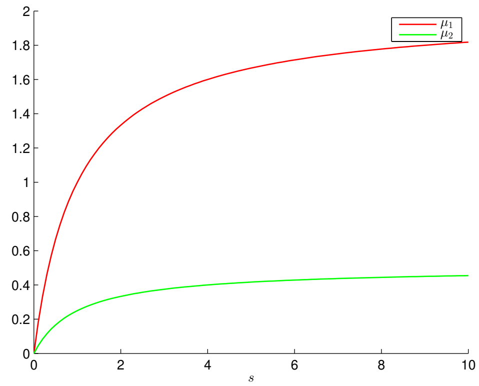

Figure 3: Kinetic rates of Monod type.

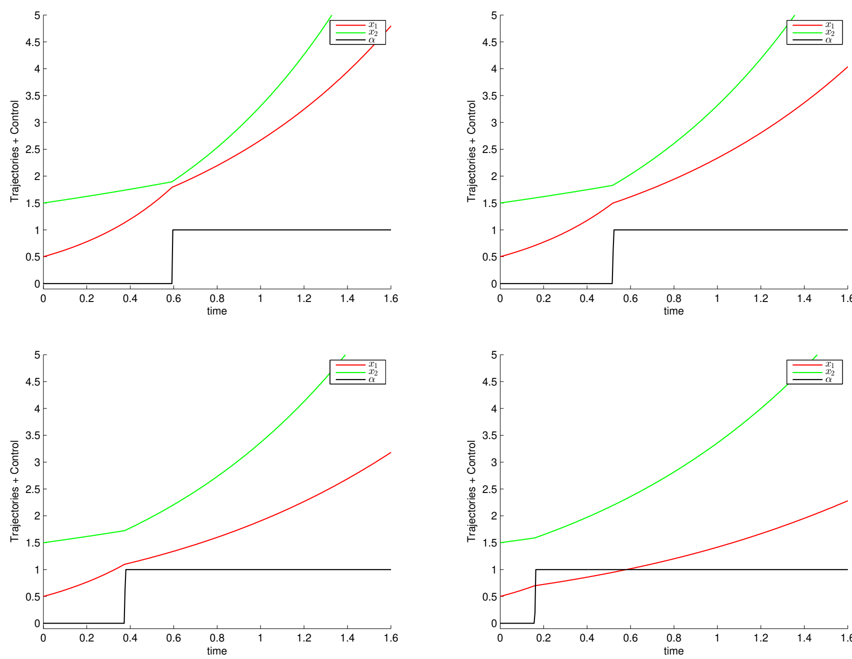

Figure 4: Optimal control computed with BOCOP for $c = 100$ (top-left), $c = 30$ (top-right), $c = 20$ (bottom-left), and $c = 15$ (bottom-right).

5 Numerical simulations and discussions

Let us consider system (5) where the growth rate functions are considered constants with values given in the following table 1. In this case the switching time $\bar{\tau}$ introduced by equation (9) is given by $\bar{\tau} = \log(4)$ and

k_1	k_2	r_1	r_2	Y_1	Y_2	T
2	1/2	1	...	1	1	2

Table 1: Numerical values of the different parameters.

the optimal control is given by

$$\alpha^\star(t) = \begin{cases} 1 & \text{if } t \geq \min(0, 2 - \log(4)) \\ 0 & \text{otherwise.} \end{cases}$$

By Figure 1 we plot the graph of $\tilde{\phi}$ given by (8). As it is underlined by Remark 1, the optimal control $\alpha^\star$ does not depend on the migration rate constant r_2. By Figure 2, using Matlab we plot the optimal control together with the optimal trajectories in two cases, $r_2 = 0.1$ (bottom-left) and $r_2 = 0.5$ (bottom-right). These plots are compared with Bocop [1] by Figure 2 (top). Bocop is a numerical optimization software which can be used to directly derive optimal solutions.

5.1 Robustness to variable kinetic rates

In this section, we consider system (5) where variable growth rate functions instead of constants ones are considered. The following Monod's type functions are considered

$$\mu_1(s) = \frac{k_1 s}{1+s}, \quad \text{and} \quad \mu_2(s) = \frac{k_2 s}{1+s}.$$

Observe that $\mu_1(s)$ and $\mu_2(s)$ are asymptotically, when s tends to $+\infty$, close to k_1 and k_2, respectively. Using Bocop, we plot in the same conditions as before with $r_2 = 0.1$ and for different values of c, the optimal control together with the optimal trajectories. We observe clearly by Figure 4 that when c is sufficiently large (i.e., for large value of s_0) the optimal trajectories are very comparable to that obtained by Theorem 1.

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