



## Brief paper

Optimization of the separation of two species in a chemostat<sup>☆</sup>Térence Bayen<sup>a,b,1</sup>, Francis Mairet<sup>c</sup><sup>a</sup> Université Montpellier 2, Case courrier 051, 34095 Montpellier Cedex 5, France<sup>b</sup> INRA-INRIA 'MODEMIC' team, INRIA Sophia-Antipolis Méditerranée, UMR INRA-SupAgro 729 'MISTEA' 2 place Viala 34060 Montpellier, France<sup>c</sup> Inria BIOCORE, BP93, 06902 Sophia-Antipolis Cedex, France

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## ABSTRACT

In this work, we study a two species chemostat model with one limiting substrate, and our aim is to optimize the selection of the species of interest. More precisely, the objective is to find an optimal feeding strategy in order to reach in minimal time a target where the concentration of the first species is significantly larger than the concentration of the other one. Thanks to the Pontryagin Maximum Principle, we introduce a singular feeding strategy which allows to reach the target, and we prove that the feedback control provided by this strategy is optimal whenever initial conditions are chosen in the invariant attractive manifold of the system. The optimal synthesis of the problem in presence of more than one singular arc is also investigated.

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## 1. Introduction

Selection of species has been widely used in agriculture and biotechnology in order to improve productivity. For microorganisms, the selection process can be based on genetic tools. Another way to proceed is to drive the competition between species in a chemostat. In this case, a control strategy should be defined adequately in order to select species according to a given criteria (see e.g. Masci, Bernard, and Grogard (2008) and Masci et al. (2009)). Here, we consider a two species chemostat limited by one substrate with Monod-like growth functions (see Smith and Waltman (1995)). The following property known as the *competitive exclusion principle* is standard in the theory of chemostat (see Smith and Waltman (1995)): given a constant dilution rate, the species which can grow at a rate equal to the dilution with the smallest substrate concentration survives whereas the other one disappears as time goes to infinity. This approach can be used in order to select asymptotically one of the two species provided that the dilution rate is adequately chosen.

In this paper, we propose an alternative approach based on optimal control theory in order to reach in finite time a certain

target where the concentration of a given species is significantly larger than the other one. More precisely, our aim is to find an optimal feeding strategy in order to steer the system to this target in minimal time. To characterize optimal trajectories, we proceed as follows. We assume that initial conditions are in the invariant attractive set of the system (see Smith and Waltman (1995)), so that it can be put into a two-dimensional affine controlled system with a single input. Thanks to the Pontryagin Maximum Principle and cooperatively properties of the adjoint system, we show that it is not optimal for a trajectory to have a switching point before reaching either the target or the singular arc. This leads to a complete description of optimal trajectories in the case where initial conditions are taken in the invariant attractive set. Theorem 1 is our main result and states that the optimal strategy is singular. In other words, the optimal feedback control corresponds to a most rapid approach (see Cartigny and Rapaport (2004)) to a singular arc (if it is reached).

The paper is organized as follows. Section 2 is devoted to the statement of the optimal control problem. In Section 3, we apply the Pontryagin Maximum Principle in order to derive necessary conditions on optimal trajectories. In Section 4, we introduce the singular arc strategy, and we prove that it is optimal for reaching the target (Theorem 1). The last section discusses the problem in presence of more than one singular arc (which may happen with Haldane-like growth functions).

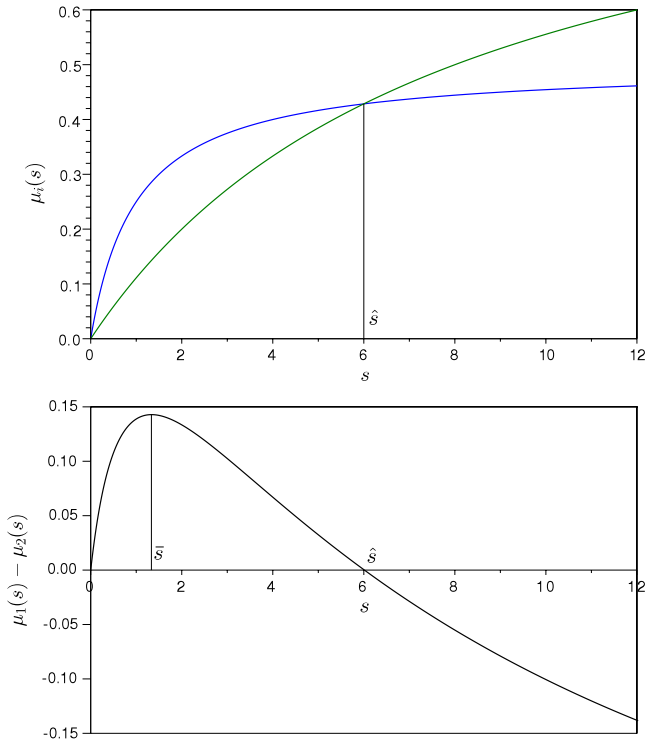
## 2. Statement of the problem

A chemostat model with one limited resource, two species, and adimensioned yield coefficients can be modeled as follows

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**Fig. 1.** Top: plot of the growth functions  $\mu_1$  (in blue) and  $\mu_2$  (in green) satisfying Hypothesis 1. Bottom: plot of  $s \mapsto \mu_1(s) - \mu_2(s)$ . (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

(see Smith and Waltman (1995)):

$$\begin{cases} \dot{x}_1 = [\mu_1(s) - u]x_1, \\ \dot{x}_2 = [\mu_2(s) - u]x_2, \\ \dot{s} = -\mu_1(s)x_1 - \mu_2(s)x_2 + u[s_{in} - s]. \end{cases} \quad (1)$$

Here,  $x_1$  (resp.  $x_2$ ) is the concentration of the first (resp. second) species in the reactor,  $s$  is the concentration of substrate,  $s_{in}$  is the input substrate concentration,  $u$  is the dilution rate, and  $\mu_i$  are the growth functions of the two species. In the following, we suppose that the specific growth rates of both species  $\mu_i$ ,  $i = 1, 2$  are nonnegative increasing  $C^1$  functions with  $\mu_i(0) = 0$ . We will also impose that the first species grows faster than the second one when substrate is scarce, and vice versa (see e.g. Fig. 3A in Norberg (2004) for a collection of data from several studies on silica-limited diatoms which illustrate such tradeoff between substrate affinity and maximum growth rate).

**Hypothesis 1.** The growth functions of the two species fulfill the following conditions:

- there exists a unique  $\hat{s} > 0$  such that  $\mu_1(\hat{s}) = \mu_2(\hat{s})$
- the function  $s \mapsto \mu_1(s) - \mu_2(s)$  is increasing on  $(0, \bar{s})$ , and decreasing on  $(\bar{s}, +\infty)$ , with  $\bar{s} < \hat{s}$ .

For example, Hypothesis 1 is fulfilled for two growth rates of Monod type (see Fig. 1):

$$\mu_1(s) := \frac{\bar{\mu}_1 s}{k_1 + s}, \quad \mu_2(s) := \frac{\bar{\mu}_2 s}{k_2 + s} \quad (2)$$

with  $\bar{\mu}_1 k_2 > \bar{\mu}_2 k_1$  and  $\bar{\mu}_1 < \bar{\mu}_2$ .

Our aim is to find an adequate feeding strategy in order to reach in finite time a target set where the concentration of the first species is significantly larger than the other one. In order to simplify the system, we will make the following requirements. Let  $M := x_1 + x_2 + s$  denote the total mass of the system, which satisfies:

$$\dot{M} = u(s_{in} - M). \quad (3)$$

From (3), it is standard that the set

$$F := \{(x_1, x_2, s) \in \mathbb{R}_+^* \times \mathbb{R}_+^* \times \mathbb{R}_+^* \mid x_1 + x_2 + s = s_{in}\},$$

is invariant and attractive for system (1), see Smith and Waltman (1995). From now on, we assume that initial conditions are in the set  $F$ , so that the triple  $(x_1, x_2, s)$  satisfies  $x_1 + x_2 + s = s_{in}$ . System (1) becomes a two-dimensional affine system with one input  $u$ :

$$\begin{cases} \dot{x}_1 = [\mu_1(s) - u]x_1, \\ \dot{x}_2 = [\mu_2(s) - u]x_2, \end{cases} \quad (4)$$

where  $s = s_{in} - x_1 - x_2$ . The set of admissible controls for (4) is given by:

$$\mathcal{U} := \{u : [0, +\infty] \rightarrow [0, u_{\max}] \mid \text{meas.}\},$$

where  $u_{\max}$  denotes the maximum dilution rate. As  $s$  is positive, initial conditions are in the set

$$E := \{(x_1, x_2) \in \mathbb{R}_+^* \times \mathbb{R}_+^* \mid x_1 + x_2 < s_{in}\},$$

which is invariant with respect to (4). We are now in position to state the optimal control problem. Let  $\varepsilon > 0$  be a small parameter. In order to select the first species, we consider a target  $\mathcal{T}$  defined as follows:

$$\mathcal{T} := \{(x_1, x_2) \in E \mid x_2 \leq \varepsilon x_1\}.$$

The optimal control problem reads as follows. Given  $x_0 := (x_1^0, x_2^0) \in E$ , our aim is to find an admissible control  $u \in \mathcal{U}$  steering the solution  $x(\cdot)$  of (4) from  $x_0$  to the target in minimal time:

$$\inf_{u \in \mathcal{U}} t(u) \text{ s.t. } x(t(u)) \in \mathcal{T}, \quad (5)$$

where  $t(u)$  is the first entry time in the target.

**Remark 1.** From a practical point of view, it is important to ensure that  $x_1(t(u))$  is also over a certain threshold. For sake of simplicity, we do not add this constraint. We will see in the optimal synthesis that this is actually not necessary.

Without any loss of generality, we may assume that  $u_{\max} = 1$ . The next assumption is standard and means that the maximum value of the input flow rate can be larger than the growth of microorganisms (see e.g. Bayen, Gajardo, and Mairet (2013) and Gajardo, Ramirez, and Rapaport (2008)):

**Hypothesis 2.** The growth function  $\mu_1$  and  $\mu_2$  satisfy:

$$\max_{s \in [0, s_{in}]} (\mu_1(s), \mu_2(s)) < 1. \quad (6)$$

The next assumption means that the input substrate concentration has been chosen large enough such that both species can win the competition.

**Hypothesis 3.** The input substrate concentration satisfies  $s_{in} > \hat{s}$ .

**Remark 2.** For any initial condition  $x^0 \in E$ , there exists a control  $u \in \mathcal{U}$  steering (4) to the target  $\mathcal{T}$ . Indeed, one can apply the competitive exclusion principle (see Smith and Waltman (1995)) with a constant control  $u < \mu_1(\hat{s})$  in order to select the first species. By the previous remark, the compactness of the control set, and the linearity of (4) with respect to  $u$ , one can apply Fillipov's Theorem (see e.g. Vinter (2000)) in order to prove the existence of an optimal control for (5).

We now introduce subsets of  $E$  that will play a major role in the optimal synthesis of the problem (see Section 4). Let us write (4) as a two-dimensional affine system with a drift:

$$\dot{x} = f(x) + ug(x),$$

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