# Optimal feeding strategy for the minimal time problem of a fed-batch bioreactor with mortality rate

Térence Bayen, Francis Mairet, Marc Mazade

# Optimal feeding strategy for the minimal time problem of a fed-batch bioreactor with mortality rate

Térence Bayen* Francis Mairet † Marc Mazade ‡

November 29, 2012

**Abstract**

We address the problem of finding an optimal feedback control for feeding a fed-batch bioreactor with one species and one substrate, from a given initial condition to a given target value in a minimal amount of time. Mortality rate for the biomass and nutrient recycling are taken into account in this work. The optimal synthesis (optimal feeding strategy) has been obtained by Moreno in 1999 when both mortality and recycling are considered negligible, in the case of Monod and Haldane growth function. This problem has been recently revisited whenever the growth function has two local maxima. Our objective is to study the effect of mortality and recycling on the optimal synthesis. Taking into account these effects does not allow to reduce the controlled system into a two-dimensional one. We provide an optimal synthesis of the problem using both Hamilton-Jacobi equation and Pontryagin maximum principle in the impulsive framework (that is when the dilution rate is allowed to take large values). We also investigate the case where the singular arc is non-necessarily controllable.

**Keywords**: Optimal Control, Minimal Time Problem, Impulsive Control, Pontryagin Maximum Principle, Bioreactor.

## 1 Introduction

This work is devoted to the study of a bioreactor which is operated in fed-batch mode. The input flow rate in the system is a key control parameter, and finding an adequate feeding strategy can significantly increase performances of the system. Such reactors have become very popular in the industry, and in particular for the wastewater treatment (see e.g. [1]).

Our objective is to find an optimal feeding strategy in order to improve the performance of the system. We are interested at studying a minimal time problem in presence of one substrate and a biomass. So, we aim at finding an optimal control that steers the system to a target in a minimal amount of time. Following [2, 3], a typical target (which has several interest in wastewater treatment) consists in reaching the maximal volume of the bioreactor with a substrate concentration less than a given value of reference (low). The novelty in this work is that we assume that the biomass has a mortality rate $k > 0$ and that nutrients can be regenerated from a fraction $\alpha \in (0, 1)$ of dead biomass with a recycling rate $k' := \alpha k < k$.

Following [3], the model that we consider is described by a three-dimensional system. When both parameters $k$ and $k'$ are zero, the system admits a conservation law (the total mass of the system), hence, it can be gathered into a two-dimensional one, see [3]. The optimal control problem becomes a minimal time problem where the underlying system is a two-dimensional quasi-affine system with one input. Finding an issue to the optimal synthesis can be performed using a combination of Greens' Theorem in the plane (see [4]) and Pontryagin maximum principle (see e.g. [5] for a large description of methods for solving the minimal time problem with target in the plane).

When the growth function is of type Monod or Haldane (see e.g. [6, 7]), and when both mortality and recycling are negligible, the optimal synthesis obtained by [3] goes as follows:

*Université Montpellier 2, Case courrier 051, 34095 Montpellier cedex 5, France ; INRA-INRIA 'MODEMIC' team, INRIA Sophia-Antipolis Méditerranée, UMR INRA-SupAgro 729 'MISTEA' 2 place Viala 34060 Montpellier (tbayen@math.univ-montp2.fr).

†INRIA 'BIOCORE' team, Sophia-Antipolis, 2004, route des Lucioles, 06902 Sophia Antipolis Cedex (francis.mairet@inria.fr).

‡Université Montpellier 2, Case courrier 051, 34095 Montpellier cedex 5, France (mmazade@math.univ-montp2.fr).

- In the case of Monod growth function, the optimal strategy is *bang-bang* (we call it also *fill and wait*) and consists in filling the reactor to the maximal volume, and then waiting until the substrate concentration is lower than the desired value.
- In the case of Haldane growth function, the optimal synthesis consists in reaching the concentration $\overline{s}$ corresponding to the maximal value of $\mu$, and keeping the substrate concentration equal to this value until reaching the maximal volume of the reactor.

Keeping constant the substrate concentration to $\overline{s}$ corresponds to a *singular arc* for the optimal control problem (therefore, this strategy is called *singular strategy*). The optimal synthesis obtained in the case of Haldane growth function has been extended in [8] to the case where the growth function has two local maxima (defining two different singular arcs), when impulsional control is allowed (see e.g. [9]). Impulsive controls for fed-batch bioreactors have been introduced in [9] and correspond to an instantaneous addition of wasted water in the reactor (that is an instantaneous dilution). The impulsional control corresponds to fed-batch reactors for which the input flow is allowed to take very large values. In this framework, the control problem becomes a minimal time problem where the underlying system is a two-dimensional quasi-affine system with two inputs and no drift (see e.g. [2, 8, 10] for a reparametrization of the time in the impulsive framework).

Our aim in this work is to find an issue to the minimal time problem when both $k$ and $k'$ can be non-zero. In this case, the total mass of the system is strictly decreasing, therefore the system cannot be reduced to a two-dimensional one as previously. It follows that it is not possible to make use of Green's Theorem to compare the cost of two distinct trajectories connecting two points (which allows to conclude on the optimality of the fill and wait or singular strategy, see [3]). One can see that when the recycling coefficient is zero, the target can always be reached by the bang-bang strategy. On the other hand, when $\alpha > 0$, the concentration of substrate is always increasing provided that it is under a certain level. Therefore, it can happen that the target is non-controllable in particular if the reference concentration is too small. So, we can infer that the system with mortality slightly differs from the system without mortality.

However, when $k$ is a very small parameter (i.e. when the mortality is small with respect to the growth), we can also expect the optimal synthesis to be close to the optimal synthesis obtained in [3]. First, notice that singular arcs for the system with both mortality and recycling coefficients should be the same as the case where $k = k' = 0$ (indeed, the definition of a singular arc only involves the derivative of the growth function, see [3]). Also, we can expect that when $k$ goes to zero, the optimal synthesis should be close to the one obtained in [3]. More precisely, our main result is Theorem 4.4 and goes as follows. When the growth function is of type Monod, then the optimal strategy is of type bang-bang (that is, fill and wait), and when the growth function is of type Haldane, then the optimal strategy is the singular arc strategy.

The paper is organized as follows. In section 2, the model without impulsive control is introduced, and we recall a standard invariance result on the system. In section 3, we make a brief review of the optimal control problem when both mortality and recycling coefficients are zero. We then investigate the case where the singular arc is not necessarily *controllable*. This means that when the volume of the reactor is above a certain level, it is not possible to maintain the substrate concentration equal to $\overline{s}$. From a mathematical point of view, this affects the optimal feedback control law as the system does not always guarantee the existence of an admissible singular control (see Propositions 3.2 and 3.3). Notice that Green's Theorem no longer applies when the singular arc is not controllable. The optimal synthesis we obtain generalizes the one which is presented in [3] when the singular arc is always controllable. In section 4, we consider the problem with mortality rate for the biomass in the impulsive framework (we first neglige the recycling coefficient), and we prove the optimality of the bang-bang strategy for Monod growth function, and the optimality of the singular arc strategy for Haldane growth function in the impulsive framework (see Theorems 4.1 and 4.3). The proof relies on Hamilton-Jacobi equation (in the Monod case) and on the exclusion of extremal trajectories via Pontryagin maximum principle (in the Haldane case). Finally, we provide the optimal synthesis of the problem with both mortality and recycling coefficients. Theorem 4.4 is a consequence of the optimality results obtained in the previous case (where only mortality is considered).

## 2 Presentation of the model

We consider the following controlled system describing a perfectly mixed reactor operated in fed-batch (see [3, 9]) with a mortality rate $k > 0$ for the biomass and a recycling rate $k' := \alpha k$, $0 < \alpha < 1$:

$$\begin{cases} \dot{x} = \left(\mu(s) - k - \frac{u}{v}\right) x, \\ \dot{s} = [-\mu(s) + k']x + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u. \end{cases} \tag{2.1}$$

Here $x$ is the concentration of biomass, $s$ the concentration of substrate, and $v$ is the volume of water in the tank. If $v_m$ is the volume of the tank, the volume $v$ is allowed to take values in $(0, v_m]$. The parameter $s_{in} > 0$ is the input concentration of substrate. The control $u$ represents the dilution rate, and the set of admissible controls is

$$\mathcal{U} = \{u : [0, \infty) \to [0, u_m] \mid u(\cdot) \text{ meas.}\},$$

where $u_m$ represents the maximum value of the dilution rate. Without any loss of generality, we can assume that $u_m = 1$. The growth function that we consider throughout the paper is either Monod or Haldane:

- For a growth function $\mu$ is of type Monod, we have: $\mu(s) = \overline{\mu}\frac{s}{k_1+s}$.
- For a growth function $\mu$ is of type Haldane, we have: $\mu(s) = \frac{h_0 s}{h_2 s^2+s+h_1}$ where $h_i > 0$ and the unique maximum of $\mu$ is achieved at $\overline{s} = \sqrt{\frac{h_1}{h_2}}$.

Next, we will assume that $k$ is small enough in order to guarantee that for certain value of the substrate concentration, the growth of biomass is possible. More precisely, we require the following assumptions on the growth function throughout the paper.

**Hypothesis 2.1.** *If $\mu$ is of type Monod, then we assume that $k$ is such that:*

$$k < \overline{\mu}. \tag{2.2}$$

In this case, we call $\tilde{s}_1$ the unique substrate concentration $s$ satisfying $\mu(\tilde{s}_1) = k'$.

**Hypothesis 2.2.** *If $\mu$ is of type Haldane, then we assume that*

$$k < \mu(\overline{s}). \tag{2.3}$$

In this case, there exist exactly two substrate concentrations $\tilde{s}'_1 < \overline{s} < \tilde{s}'_2$ such that $\mu(\tilde{s}'_1) = \mu(\tilde{s}'_2) = k'$. In the following, we assume that $\tilde{s}'_2$ satisfies:

$$\tilde{s}'_2 \geq s_{in}. \tag{2.4}$$

The next Proposition is fundamental in order to guarantee the well-posedness of solutions.

**Proposition 2.1.** *(i) In the case where $\mu$ is of type Monod, the domain*

$$E_m := \mathbb{R}^*_+ \times [\tilde{s}_1, s_{in}] \times \mathbb{R}^*_+, \tag{2.5}$$

*is invariant by* (2.1).
*(ii) In the case where $\mu$ is of type Haldane, and under assumption* (2.4)*, the set*

$$E_\alpha := \mathbb{R}^*_+ \times [\tilde{s}'_1, s_{in}] \times \mathbb{R}^*_+, \tag{2.6}$$

*is invariant by* (2.1).

Hereafter, when $\alpha = 0$ (that is $k' = 0$), we denote by $E := E_0 = \mathbb{R}^*_+ \times [0, s_{in}] \times \mathbb{R}^*_+$ the invariant set given by (2.6). The proof of the Proposition is based on the following lemma (which is a simple consequence of Gronwall's Lemma).

**Lemma 2.1.** *Consider the ordinary differential equation (ODE):*

$$\dot{y} = f(t, y), \tag{2.7}$$

*where $f : \mathbb{R} \times \mathbb{R} \to \mathbb{R}$ is a Caratheodory function local Lipschitz continuous with respect to $y$. Assume that $f(t, 0) \geq 0$ for all $t$. Then, $\mathbb{R}_+^*$ is invariant by* (2.7).

*Proof of Proposition 2.1.* For a given $u \in \mathcal{U}$, consider a trajectory $(x, s, v)$ solution of (2.1). From Cauchy-Lipschitz Theorem, we have that $x_0 > 0$ implies $x(t) > 0$ for all $t$. Now, we can write $\dot{s} = f(t, s)$, where $f(t, s) := [-\mu(s) + k']x(t) + \frac{u(t)}{v(t)}(s_{in} - s)$. So, if $\mu$ is either of type Monod or Haldane, we have $f(t, s_{in}) \leq 0$ for all $t$ (recall (2.4) in the Haldane case). Lemma 2.1 implies that we have $s(t) \leq s_{in}$ for all $t$ provided that $s(0) \leq s_{in}$. Similarly, in the case of Monod growth function, we have $f(t, \tilde{s}_1) = \frac{u(t)}{v(t)}(s_{in} - \tilde{s}_1) \geq 0$, so Lemma 2.1 implies the result. We can apply the same argument in the Haldane case which ends the proof. □

Consider now a target $\mathcal{T}$ which is defined as follows:

$$\mathcal{T} = \mathbb{R}_+^* \times [0, s_{ref}] \times \{v_m\}, \tag{2.8}$$

where $s_{ref}$ is a given reference (low) concentration. In the rest of the paper, we assume that $s_{ref}$ is such that:

- If $\mu$ is of type Monod, we assume that $s_{ref} > \tilde{s}_1$.
- If $\mu$ is of type Haldane we assume that $s_{ref} > \tilde{s}_1'$.

It follows that the target is controllable from any initial condition in $E_m$ (in the Monod case) or $E_\alpha$ (in the Haldane case). Indeed, a simple way to drive the system to the target is to let $u = 1$ until reaching $v_m$, and then we take $u = 0$ until $s_{ref}$ (if necessary). When $u = 0$, we have that $s(t)$ is strictly decreasing and converges to the equilibrium $\tilde{s}_1$ (when $\mu$ is of type Monod) or $\tilde{s}_1'$ (when $\mu$ is of type Haldane). As $s_{ref} > \tilde{s}_1$ (resp. $s_{ref} > \tilde{s}_1'$) in the case of Monod (resp. in the case of Haldane), the trajectory necessarily reaches the target in finite time.

**Remark 2.1.** *System* (2.1) *admits an implicit state constraint $v \leq v_m$. Equivalently, the control $u$ is taking values within a control restrained set $U(s, v)$ given by $U(s, v) := [0, 1]$ whenever $v < v_m$ and $U(s, v) := \{0\}$ if $v = v_m$, see e.g. [11] for a study of optimal control problems with such control constraints. One can see that whenever a trajectory satisfies $v > v_m$, then the target cannot be reached (as $u \geq 0$). Optimal trajectories will necessarily satisfy the constraint $v \leq v_m$, so we assume in the rest of the paper that at time* 0*, we have $v_0 \leq v_m$. Moreover, if $v = v_m$, then the control can only take the value* 0*.*

We are now in position to state the optimal control problem. Our aim is to minimize the amount of time $t_f(u)$ with respect to $u \in \mathcal{U}$ in order to steer (2.1) from an initial condition $(s_0, x_0, v_0)$ to the target $\mathcal{T}$:

$$\inf_{u \in \mathcal{U}} t_f(u) \text{ s.t. } (x(t_f(u)), s(t_f(u)), v(t_f(u))) \in \mathcal{T}. \tag{2.9}$$

If $k = 0$, the system (2.1) can be gathered into a two-dimensional one by considering the conserved quantity

$$M := v(x + s - s_{in}) = v_0(x_0 + s_0 - s_{in}). \tag{2.10}$$

This remark is essential in order to find an issue to the minimum time problem (see e.g. [3, 12]) by making use of Green's Theorem in the plane to compare the cost of two distinct trajectories that steer the same initial point to the same target point. When $k > 0$ and $\alpha > 0$, we have

$$\dot{M} = -k(1 - \alpha)xv < 0, \tag{2.11}$$

hence $M$ is strictly decreasing, and the same reduction is not possible for system (2.1).

# 3 Optimal synthesis without mortality

This section aims at giving an optimal feedback control to the minimum time problem in the case where no mortality is considered. The problem has been solved by [3] assuming the controllability of singular arcs. We review the result of [3] that will allow us to extend this study to the case where the singular arc is non controllable.

### 3.1 Optimal synthesis when $k = 0$ with controllability assumption

In this subsection, we present the optimal synthesis when $k = 0$ following [3]. First, (2.10) implies that $x = \frac{M}{v} + s_{in} - s$ where $M := v_0(x_0 + s_0 - s_{in})$ is given by initial conditions. Therefore the initial system can be gathered into a two-dimensional affine system with a single input $u$:

$$\begin{cases} \dot{s} = -\mu(s)(\frac{M}{v} + s_{in} - s) + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u, \end{cases} \tag{3.1}$$

where $v \leq v_m$. Initial conditions for (3.1) are taken in the domain $\mathcal{D}$ defined by:

$$\mathcal{D} := \left\{ (s, v) \in [0, s_{in}] \times (0, v_m] \quad | \quad \frac{M}{v} + s_{in} - s > 0 \right\} \tag{3.2}$$

When $M > 0$, the domain $\mathcal{D}$ coincides with $[0, s_{in}] \times [0, v_m]$, and when $M < 0$ the condition $\frac{M}{v} + s_{in} - s > 0$ ensures that $x$ remains positive. One can easily see from Lemma 2.1 that $\mathcal{D}$ is invariant by the dynamics (3.1) (under the condition that $u = 0$ whenever $v = v_m$, see Remark 2.1). As $x(t_f(u))$ is free in (2.8), the target corresponding to the two-dimensional system is $[0, s_{ref}] \times \{v_m\}$.

**Theorem 3.1.** *When $\mu$ is of type Monod, the optimal feedback control $u_M$ steering any initial condition in $\mathcal{D}$ to the target is:*

$$u_M(s, v) := \begin{cases} 1 & \text{if } v < v_m, \\ 0 & \text{if } v = v_m. \end{cases} \tag{3.3}$$

In other words, the optimal strategy is *fill and wait*, and it consists in filling the tank with maximum input flow rate until $v = v_m$, and then we let $u = 0$ until $s$ reaches the value $s_{ref}$ (if necessary). This result can be proved via Green's Theorem, see e.g. [3].

In the case where $\mu$ is of type Haldane, the optimal strategy consists in reaching as fast as possible a concentration of substrate $\overline{s}$ (for which the biomass growth rate is maximal), and to keep $s(t)$ constant equal to $\overline{s}$ until reaching the maximal volume. More precisely, the result goes as follows.

**Theorem 3.2.** *Assume that $\mu$ is of type Haldane and let $\overline{s}$ the unique maximum of $\mu$. Assume that $\overline{s} > s_{ref}$, and that*

$$\mu(\overline{s}) \left[ \frac{M}{s_{in} - \overline{s}} + v_m \right] \leq 1. \tag{3.4}$$

*Then, the optimal feedback control $u_H$ to reach the target is given by*

$$u_H(s, v) := \begin{cases} 0 & \text{if } v = v_m \quad \text{or} \quad s > \overline{s}, \\ 1 & \text{if } s < \overline{s} \quad \text{and} \quad v < v_m, \\ \bar{u}_s(v) & \text{if } s = \overline{s} \quad \text{and} \quad v < v_m, \end{cases} \tag{3.5}$$

*where*

$$\bar{u}_s(v) := \mu(\overline{s}) \left[ \frac{M}{s_{in} - \overline{s}} + v \right]. \tag{3.6}$$

This result was first proved in [3]. Here we have emphasized the controllability assumption (3.4) which is implicitly used in [3], see also [2, 8].

**Remark 3.1.** *The control $\bar{u}_s$ is called singular control and it allows to maintain the concentration of substrate equal to $\overline{s}$. It can be also written $\bar{u}_s(v) = \frac{\mu(\overline{s})x}{v(s_{in} - \overline{s})}$ so that $\bar{u}_s \geq 0$. The assumption (3.4) is essential to ensure that $\bar{u}_s(v)$ satisfies the upper bound $\bar{u}_s(v) \leq 1$ for all $v \leq v_m$.*

Our aim is now to consider the case where (3.4) is not always satisfied. This will change the optimal synthesis. When (3.4) is not satisfied, there exists $v \in (0, v_m]$ for which the control is not sufficient enough in order to keep the substrate concentration equal to $\overline{s}$.

## 3.2 Pontryagin maximum principle

In this part, we assume that $\mu$ is Haldane, and we apply Pontryagin maximum principle on (2.9) that will allow us to extend the result of Theorem 3.2 to the case where (3.4) is not satisfied (see section 3.3).

First, define the curve $v \longmapsto \gamma_{ref}(v)$ which is the unique solution of (3.1) with constant control $u = 1$ and that passes through $(s_{ref}, v_m)$. Moreover, we consider the domain:

$$\mathcal{D}' := \{(s, v) \in \mathcal{D} \mid s \geq \gamma_{ref}(v)\}. \tag{3.7}$$

When the initial point $(s_0, v_0)$ is in $\mathcal{D}\backslash\mathcal{D}'$, then Green's Theorem implies that the optimal control is $u = 1$ until $v_m$ (see e.g. [3] for more details). Hence, it is enough to consider initial conditions in $\mathcal{D}'$. Let $H := H(s, v, \lambda_s, \lambda_v, \lambda_0, r, u)$ the Hamiltonian of the system defined by:

$$H := -\lambda_s \mu(s) \left[\frac{M}{v} - (s - s_{in})\right] + u \left[\frac{\lambda_s(s_{in} - s)}{v} + \lambda_v\right] + \lambda_0.$$

If $u$ is an optimal control and $(s, v)$ the corresponding solution of (3.1), there exists $t_f > 0$, $\lambda_0 \leq 0$, and an absolutely continuous map $\lambda = (\lambda_s, \lambda_v) : [0, t_f] \to \mathbb{R}^2$ such that $(\lambda_0, \lambda) \neq 0$, $\dot{\lambda}_s = -\frac{\partial H}{\partial s}$, $\dot{\lambda}_v = -\frac{\partial H}{\partial v}$, that is:

$$\begin{cases} \dot{\lambda}_s = \lambda_s \left(\mu'(s)x - \mu(s) + \frac{u}{v}\right), \\ \dot{\lambda}_v = \lambda_s \left(\frac{-\mu(s)M + u(s_{in} - s)}{v^2}\right), \end{cases} \tag{3.8}$$

and we have the maximality condition:

$$u(t) \in \text{argmax}_{\omega \in [0,1]} H(s(t), v(t), \lambda_s(t), \lambda_v(t), \lambda_0, \omega), \tag{3.9}$$

for almost every $t \in [0, t_f]$. We call *extremal trajectory* a sextuplet $(s(\cdot), v(\cdot), \lambda_s(\cdot), \lambda_v(\cdot), \lambda_0, u(\cdot))$ satisfying (3.1)-(3.8)-(3.9), and *extremal control* the control $u$ associated to this extremal trajectory. As $t_f$ is free, the Hamiltonian is zero along an extremal trajectory. Following [8], one can prove that $\lambda_s$ is always non-zero (it is therefore of constant sign from the adjoint equation), and that $\lambda_0 < 0$ (hence we take $\lambda_0 = -1$ in the following). Next, let us define the *switching function* $\phi$ associated to the control $u$ by:

$$\phi := \frac{\lambda_s(s_{in} - s)}{v} + \lambda_v. \tag{3.10}$$

We obtain from (3.9) that any extremal control satisfies the following control law: for a.e. $t \in [0, t_f]$, we have

$$\begin{cases} \phi(t) < 0 \implies u(t) = 0 & \text{(No feeding)}, \\ \phi(t) > 0 \implies u(t) = 1 & \text{(Maximal feeding)}, \\ \phi(t) = 0 \implies u(t) \in [0, 1]. \end{cases}$$

If $\phi$ vanishes at some isolated point $t_0$ and if the control $u$ is not constant in any neighborhood of $t_0$, then we say that $t_0$ is a *switching point*. In this case, the control is *bang-bang* around $t_0$, that is $u$ switches either from 0 to 1 or from 1 to 0 at time $t_0$. Whenever $\phi$ is zero on some time interval $I \subset [0, t_f]$ (such that $\text{meas}(I) > 0$), we say that $u$ is a *singular control*, and the trajectory contains a *singular arc*. The sign of $\dot{\phi}$ is fundamental in order to obtain the optimal synthesis. By taking the derivative of $\phi$, we get:

$$\dot{\phi} = \frac{\lambda_s x(s_{in} - s)\mu'(s)}{v}. \tag{3.11}$$

Now, if an extremal trajectory contains a singular arc on some time interval $I := [t_1, t_2]$, then we have $\phi = \dot{\phi} = 0$ on $I$, hence we have $\mu'(s) = 0$ and $s = \overline{s}$ on $I$. Therefore, by solving $\dot{s} = 0$, we obtain easily the expression of the singular control given by (3.6), see e.g. [12]. Moreover, we have the following relation along a singular arc $[t_1, t_2]$:

$$t_2 - t_1 = \frac{1}{\mu(\overline{s})} \ln\left(\frac{M + v(t_2)[s_{in} - \overline{s}]}{M + v(t_1)[s_{in} - \overline{s}]}\right), \tag{3.12}$$

see e.g. [8]. By Remark 3.1 the previous expression is always positive (as $\bar{u}_s \geq 0$). If $\bar{u}_s$ is always less than 1 for $v \leq v_m$, then we say that the singular arc is *controllable*. In this case, Theorem 3.2 is a consequence of Green's Theorem that we can apply in the two sub-domains of $\mathcal{D}'$ such that $s > \overline{s}$ and $s < \overline{s}$. In these domains, we can easily compare the cost of a trajectory with the optimal one (corresponding to the feedback control (3.5)). We now investigate the case where (3.6) can be greater than 1, that is when the singular arc is not controllable.

### 3.3 Optimal synthesis without controllability of the singular arc

Let $\eta$ and $v^*$ be defined by:

$$\eta(s) := \frac{1}{\mu(s)} - \frac{M}{s_{in}-s},\ s \in (0, s_{in}),\ v^* := \eta(\overline{s}). \tag{3.13}$$

We have that the singular arc is controllable provided that $v^* \geq v_m$. We assume throughout this section that

$$v^* < v_m. \tag{3.14}$$

It follows that the singular arc is controllable for $v \in [0, v^*]$ (indeed, for $v > v^*$, (3.6) no longer defines an admissible control in $[0,1]$). Therefore, it is not possible to apply Green's Theorem to compare the cost of distinct trajectories in some parts of the domain such as when the volume is greater than $v^*$. Also, we do not have a natural candidate for the optimal feedback control. Next, we will consider the two following cases:

- Case 1: $v^* \leq 0$,
- Case 2: $0 < v^* < v_m$.

We will detail the proof of the optimal synthesis in the first case. The second case is analogous to the first one. For $v \in (0, v_m]$, consider the curve $\hat{\mathcal{C}}$ defined by $v \longmapsto \hat{\gamma}(v)$ (resp. $\check{\mathcal{C}}$ defined by $v \longmapsto \check{\gamma}(v)$), and which is the unique solution of the ODE:

$$\frac{ds}{dv} = -\mu(s)\left[\frac{M}{v} + s_{in} - s\right] + \frac{s_{in}-s}{v}, \tag{3.15}$$

and which passes through the point $(\overline{s}, v_m)$ (resp. $(\overline{s}, v^*)$). In other words, $\hat{\gamma}(v)$ and $\check{\gamma}(v)$ are solution of (3.1) backward in time with a constant control $u = 1$. These curves will play a major role in our optimal synthesis contrary to the case where the singular arc is controllable (see Figure 1 and Table 1 for parameter values). Let $\hat{v}$ (resp. $\check{v}$) the first volume value such that $\hat{\gamma}(\hat{v}) \notin (0, s_{in})$ (resp. $\check{\gamma}(\check{v}) \notin (0, s_{in})$). The next proposition is concerned with monotonicity properties of these curves in the domain $\mathcal{D}$.

**Proposition 3.1.** *(i) The curve $\hat{\gamma}$ is either decreasing on $[\hat{v}, v_m]$, either there exists a unique $v_1 \in (\hat{v}, v_m)$ such that $\hat{\gamma}(v_1) \in (0, s_{in})$ and $\frac{d\hat{\gamma}}{dv}(v_1) = 0$. Moreover, in the latter case, $\hat{\gamma}$ is increasing on $[\hat{v}, v_1]$ and is decreasing on $[v_1, v_m]$.*
*(ii) The mapping $\check{\gamma}$ is increasing on $(\check{v}, v^*]$ and decreasing on $[v^*, v_m]$.*

*Proof.* Let us first prove (i). For $v \in (\hat{v}, v_m]$, we can rewrite (3.15) as follows:

$$\frac{ds}{dv} = \frac{\mu(s)(s_{in}-s)}{v}[\eta(s) - v]. \tag{3.16}$$

When $v = v_m$, we have $\eta(\hat{\gamma}(v_m)) = \eta(\overline{s}) = v^* < v_m$, therefore, we have $\frac{d\hat{\gamma}}{dv} < 0$ in a neighborhood of $v_m$. Now, if $\hat{\gamma}$ is non-monotone on $(\hat{v}, v_m)$, then necessarily $v \longmapsto \frac{d\hat{\gamma}}{dv}$ is vanishing on $(\hat{v}, v_m]$. Assume that there exist $0 < v_2 < v_1 < v_m$ such that $\hat{\gamma}(v_1) \in (0, s_{in})$, $\hat{\gamma}(v_2) \in (0, s_{in})$ and $\frac{d\hat{\gamma}}{dv}(v_1) = \frac{d\hat{\gamma}}{dv}(v_2) = 0$. Without any loss of generality, we can assume that $\frac{d\hat{\gamma}}{dv}(v) > 0$ for $v \in (v_2, v_1)$. This gives using $\eta(\hat{\gamma}(v_2)) = v_2$:

$$\eta(\hat{\gamma}(v)) - \eta(\hat{\gamma}(v_2)) > v - v_2,\ v \in (v_2, v_1),$$

and by dividing by $v - v_2$ (with $v > v_2$), we obtain that $\frac{d}{dv}\eta(\hat{\gamma}(v))_{|v=v_2} \geq 1$. On the other hand, we find $\eta'(\hat{\gamma}(v_2))\frac{d\hat{\gamma}}{dv}(v_2) = 0$, which gives a contradiction. Therefore, there exists at most one value $v_1$ for which $\frac{d\hat{\gamma}}{dv}(v_1) = 0$, and $\hat{\gamma}(v_1) \in (0, s_{in})$. Also, by derivating (3.15) and using the fact that $\frac{d\hat{\gamma}}{dv}(v_1) = 0$ we get:

$$\frac{d^2\hat{\gamma}}{dv^2}(v_1) = -\frac{\mu(\hat{\gamma}(v_1))(s_{in} - \hat{\gamma}(v_1))}{v_1},$$

which is non-zero. In fact, we have seen that $\hat{\gamma}(v_1) > 0$. Moreover we have $\hat{\gamma}(v_1) \neq s_{in}$ from (3.15) (if $M \neq 0$, then $\frac{d\hat{\gamma}}{dv}(v_1) \neq 0$ whenever $\hat{\gamma}(v_1) = s_{in}$; if $M = 0$, then, $\hat{\gamma}(v) < s_{in}$ for all $v$ by Cauchy-Lipschitz Theorem). The conclusion of (i) follows.
Let us prove (ii). By definition of $v^*$, we have $\frac{d\check{\gamma}}{dv}(v^*) = 0$. By a similar argument as for (i), one can prove that $v^*$ is the unique zero of $v \longmapsto \frac{d\check{\gamma}}{dv}(v)$ on $(\check{v}, v_m]$. Thus $v \longmapsto \zeta(v) := \eta(\check{\gamma}(v)) - v$ has exactly one zero on $(\hat{v}, v_m]$. Moreover, we find $\frac{d\zeta}{dv}(v^*) = -1$, therefore $\zeta$ is decreasing in a neighborhood of $v^*$. It follows that $\check{\gamma}$ is increasing on $[\hat{v}, v^*]$ and decreasing on $[v^*, v_m]$, and the result follows. □

**Remark 3.2.** *From Proposition 3.1, the limits of $\hat{\gamma}(v)$ and $\check{\gamma}(v)$ when $v$ decreases to zero may be out of the domain under consideration as we deal with substrate concentration in $[0, s_{in}]$. From a mathematical point of view, determining the limit of $\hat{\gamma}$ or $\check{\gamma}$ when $v$ goes to zero is a difficult question. In view of* (3.16)*, the behavior of $\hat{\gamma}$ highly depends on the value of the parameter $M$ (which depends on initial conditions of the system). By changing $v$ into $w := -\ln v$,* (3.15) *can be gathered into a planar dynamical system. The stable manifold Theorem (see e.g. [7]) shows that $\lim_{v\to 0} \hat{\gamma}(v)$ is either finite or $\pm\infty$ (the three cases are possible and depend on the value of $M$). The study of this point is out of the scope of the paper.*

In the second case of Proposition 3.1 (i), we can prove that there exists a unique $v_* \in (0, v^*)$ such that:

$$\hat{\gamma}(v_*) = \overline{s}, \tag{3.17}$$

see Figure 1. Indeed, from (3.14), we have that $\frac{d\hat{\gamma}}{dv}(v) > 0$ for any volume value $v > v^*$ such that $\hat{\gamma}(v) = \overline{s}$. It follows that if there exists $v \in [\hat{v}, v_m]$ such that $\hat{\gamma}(v_*) = \overline{s}$, then $v_* < v^*$ (the strict follows from Cauchy-Lipschitz Theorem). The uniqueness of $v_*$ follows from the monotonicity property of $\hat{\gamma}$.

The following remark will be important in the proof of the next Proposition. We have that $\lambda_s < 0$ (see e.g. [2, 8]), and any extremal trajectory satisfies the property:

$$s(t) > \overline{s} \Longrightarrow \dot{\phi}(t) > 0 \ ; \ s(t) < \overline{s} \Longrightarrow \dot{\phi}(t) < 0.$$

In the case where $v* \leq 0$ (case 1), we have the following result (see also Fig. 1).

**Proposition 3.2.** *Assume that $v^* \leq 0$. Then, the optimal synthesis reads as follows:*

- *If $s_0 \leq \overline{s}$, then $u = 1$ on $[0, t_0]$, $u = 0$ on $[t_0, t_f]$ where $t_0$ is such that $v(t_0) = v_m$ and $s(t_f) = s_{ref}$.*
- *If $\overline{s} < s_0 < \hat{\gamma}(v_0)$, then $u = 0$ on $[0, t_0]$, $u = 1$ on $[t_0, t_1]$, $u = 0$ on $[t_1, t_f]$ where $t_0 \geq 0$, $\overline{s} < s(t_0) < \hat{\gamma}(v_0)$, $v(t_1) = v_m$, and $s(t_f) = s_{ref}$.*
- *If $s_0 \geq \hat{\gamma}(v_0)$, then $u = 0$ on $[0, t_0]$, $u = 1$ on $[t_0, t_1]$, $u = 0$ on $[t_1, t_f]$ with $t_0 > 0$, $\overline{s} < s(t_0) < \hat{\gamma}(v_0)$, $v(t_1) = v_m$, and $s(t_f) = s_{ref}$.*

*Proof.* Consider an optimal trajectory $(s(\cdot), v(\cdot), u(\cdot))$ starting at some point $(s_0, v_0) \in \mathcal{D}'$. In the present case, the control $u$ can only take the value 0 or 1 from the PMP (the singular arc is not admissible in $\mathcal{D}'$).

First, assume $s_0 \leq \overline{s}$. Combining the controllability assumption (3.14) and Lemma 2.1, we obtain $s(t) \leq \overline{s}$ for all $t$. We thus have $u = 1$ in a neighborhood of $t = 0$. Otherwise, we would have $u = 0$ together with $\phi(0) \leq 0$, and we would have for all $t$, $\phi(t) < 0$ which is not possible (as the trajectory would not reach the target). It follows that we have $u = 1$ in a neighborhood of $t = 0$. The same argument shows that the trajectory cannot switch to $u = 0$ before reaching $v_m$. This proves the first item.

Assume now that $\overline{s} < s_0 < \hat{\gamma}(v_0)$. If $\phi(0) < 0$, then we have $u = 0$, and the trajectory necessarily switches to $u = 1$ before reaching $\overline{s}$ (otherwise we would have a contradiction by the previous case). Now, we have $u = 1$ on some time interval $[t_0, t_1]$. Again, the previous case shows that the trajectory cannot switch to $u = 0$ at some time $t'$ such that $s(t') \leq \overline{s}$ with $v(t') < v_m$. As $\phi(t_0) \geq 0$ and $\dot{\phi}(t) > 0$ whenever $s(t) > \overline{s}$, we obtain that the trajectory cannot switch to $u = 0$ at some time $t''$ such that $s(t'') > \overline{s}$. Therefore, we have $u = 1$ until $v_m$, and the conclusion follows.

Now, take $s_0 > \hat{\gamma}(v_0)$. Then, we must have $u = 0$ in a neighborhood of $t = 0$ (otherwise we would have $\phi(0) > 0$ which implies that $\phi(t) > 0$ for all $t$ which is not possible). The same argument shows that the trajectory cannot switch to $u = 1$ at some substrate concentration $s(t_0) \geq \hat{\gamma}(v_0)$. Using the first item, we obtain that the trajectory necessarily switches at some time $t_0$ such that $\overline{s} < s(t_0) < \hat{\gamma}(v_0)$. By the second case, we obtain directly that $u = 1$ on some time interval $[t_0, t_1]$ with $v(t_1) = v_m$. This concludes the proof. □

**Remark 3.3.** *In the second case of proposition 3.2, the switching time $t_0$ from $u = 0$ to $u = 1$ may be zero and it can be found numerically, see section 3.4.*

Next, we consider the second case where $0 < v^* < v_m$. It is easy to see that for initial conditions such that $v_0 > v^*$, the optimal feedback control is given by proposition 3.2 (indeed, the singular arc is defined only for $v_0 \leq v^*$). Therefore, we only deal with $v_0 < v^*$. The next Proposition is illustrated on Fig. 1.

**Proposition 3.3.** *Assume $v_0 < v^*$ and that there exists $0 < v_* < v^*$ such that $\hat{\gamma}(v_*) = \overline{s}$. Then, the optimal synthesis reads as follows:*

- *If $s_0 \leq \check{\gamma}(v_0)$, then, we have $u = 1$ on $[0, t_0]$, $u = 0$ on $[t_0, t_f]$ where $t_0$ is such that $v(t_0) = v_m$.*
- *If $\check{\gamma}(v_0) < s_0 < \hat{\gamma}(v_0)$ and $s_0 \leq \overline{s}$, then we have $u = 1$ on $[0, t_0]$, $u = \bar{u}_s$ on $[t_0, t_1]$, $u = 1$ on $[t_1, t_2]$, $u = 0$ on $[t_2, t_f]$, where $s(t_0) = \overline{s}$, $t_1 - t_0 \geq 0$, $v(t_1) < v^*$, and $v(t_2) = v_m$.*
- *If $\hat{\gamma}(v_0) \leq s_0 < \overline{s}$, then we have $u = 1$ on $[0, t_0]$, $u = \bar{u}_s$ on $[t_0, t_1]$, $u = 1$ on $[t_1, t_2]$, $u = 0$ on $[t_2, t_f]$ where $s(t_0) = \overline{s}$, $v(t_1) \in (v_*, v^*)$, $v(t_2) = v_m$.*
- *If $s_0 \geq \overline{s}$ and $v_0 \leq v_*$, then we have $u = 0$ on $[0, t_0]$, $u = \bar{u}_s$ on $[t_0, t_1]$, $u = 1$ on $[t_1, t_2]$, $u = 0$ on $[t_2, t_f]$ where $s(t_0) = \overline{s}$, $v(t_1) \in (v_*, v^*)$, and $v(t_2) = v_m$.*
- *If $s_0 \geq \overline{s}$, and $v_0 > v_*$, then, the optimal control is one of the following types:*
  - *either $u = 0$ on $[0, t_0]$, $u = \bar{u}_s$ on $[t_0, t_1]$, $u = 1$ on $[t_1, t_2]$, $u = 0$ on $[t_2, t_f]$ where $s(t_0) = \overline{s}$, $t_1 - t_0 \geq 0$, $v(t_2) = v_m$,*
  - *either $u = 0$ on $[0, t_0]$, $u = 1$ on $[t_0, t_1]$, $u = 0$ on $[t_1, t_f]$ where $t_0 \geq 0$, $\overline{s} < s(t_0) < \hat{\gamma}(v_0)$, $v(t_1) = v_m$.*

*Proof.* The proof of the first item is the same as the first one of the previous Proposition. Recall also by Cauchy-Lipschitz Theorem that $v_* < v^*$.

Now, when $\check{\gamma}(v_0) < s_0 < \hat{\gamma}(v_0)$ and $s_0 \leq \overline{s}$, the trajectory cannot switch from $u = 1$ to $u = 0$ before reaching $s = \overline{s}$. Therefore, we have two cases when the trajectory reaches $s = \overline{s}$: the trajectory either crosses the singular arc, or the control becomes singular. In the second case, the trajectory switches to $u = 1$ before reaching $v^*$ (otherwise we would have $u = 0$ at the point $(\overline{s}, v^*)$ and the trajectory would not reach the target) and until $v = v_m$. Notice that $t_1 = t_0$ is possible. This means that the time interval where the trajectory is singular can be zero.

If $\hat{\gamma}(v_0) < s_0 < \overline{s}$, the proof is the same as for the second item except that the trajectory cannot leave the singular arc with $u = 1$ before $v_*$ (otherwise the trajectory reaches $v = v_m$ with $u = 1$ and $\phi > 0$, and the trajectory cannot switch to $u = 0$ at $v = v_m$ to reach the target).

The proof of the fourth item is the same as the third one except that the trajectory starts with $u = 0$ until reaching the singular arc. Similarly as in the previous item, the trajectory cannot switch to $u = 1$ before reaching $s = \overline{s}$.

The last region is given by initial conditions such that $s_0 \geq \overline{s}$, and $v_0 > v_*$. The same arguments as before can be used except that Pontryagin maximum principle is not sufficient to exclude two type of trajectories. First observe that we have $u = 0$ on some time interval $[0, t_0]$ as before (with $s(t_0) < \hat{\gamma}(t_0)$, otherwise the trajectory would not reach the target). When the trajectory crosses the curve $\hat{\gamma}$, we have two sub-cases. Either the trajectory switches to $u = 1$ before reaching $s = \overline{s}$ (as in Proposition 3.2), either the trajectory switches to the singular arc for $s = \overline{s}$. After the first switching times, the behavior of the trajectory is exactly as for the second item, and we can conclude from the other cases. □

Table 1: Parameter values (arbitrary units) of simulations for the optimal synthesis without the controllability assumption of the singular arc (see Fig. 1 and 2)

| $v_m$ | $s_{in}$ | $s_{ref}$ | $M$ | $h_0$ | $h_1$ | $h_2$ |
|---|---|---|---|---|---|---|
| 7 | 10 | 0.1 | 25 (case 1)<br>1 (case 2) | 0.5 | 1 | 0.11 |

**Remark 3.4.** *The existence of $v_* > 0$ is guaranteed by Remark 3.2 for some values of $M$. For instance, one can check that for $M = 0$, (3.15) becomes $\frac{ds}{dv} = \left[\frac{1}{v} - \mu(s)\right](s_{in} - s)$, and we have $\lim_{v \to 0} \hat{\gamma}(v) = -\infty$ as $s \longmapsto \mu(s)(s_{in} - s)$ is bounded over $\mathbb{R}$. Now, Proposition 3.1 together with this remark implies the existence of $v_* < v^*$. The optimal synthesis when $v_*$ does not exist can be obtained via Proposition 3.3 by considering only the points for which $v_0 > v_*$. We have not detailed this point for brevity.*

**Remark 3.5.** *For the last item of the previous Proposition, the optimal trajectory is either $B_0SAB_1B_0$ or $B_0B_1B_0$ where $B_0$ (resp. $B_1$) denotes an arc Bang $u = 0$ (resp. $u = 1$), and $SA$ denotes a singular arc.*

The next subsection will clarify this remark from a numerical point of view, and will provide an estimation of the switching time $t_0$ for items 2, 3, and 4 of Proposition 3.3.

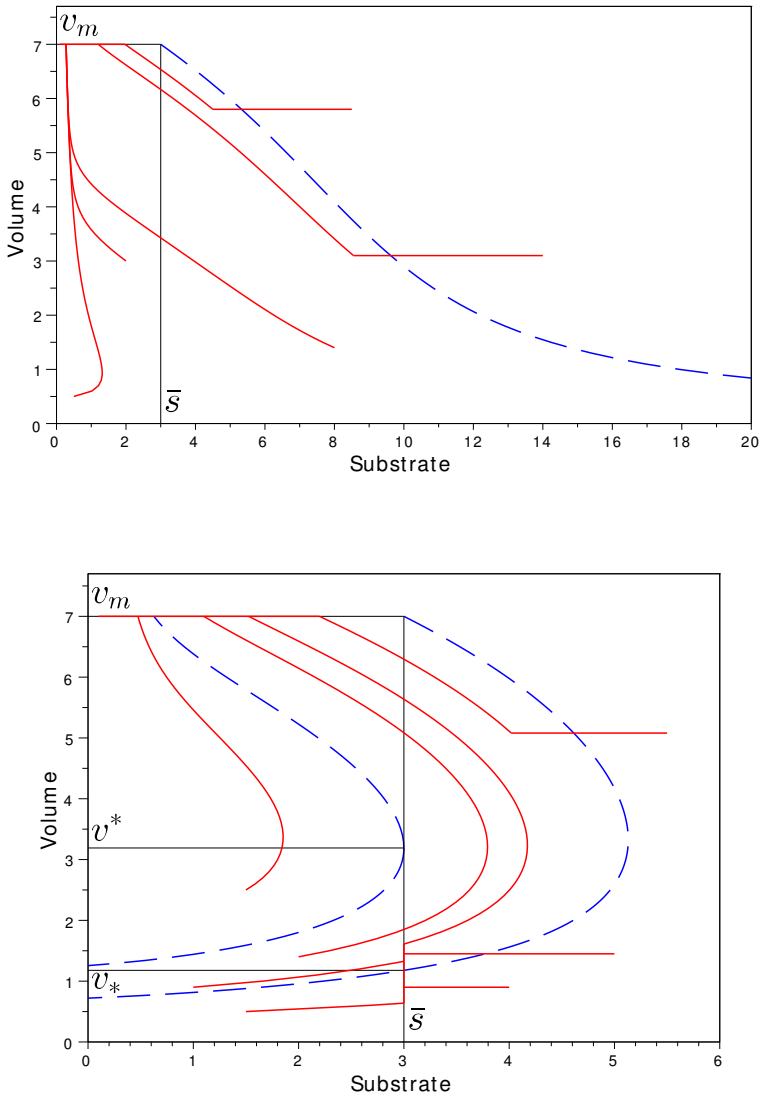


Figure 1: Optimal trajectories (in solid red lines) for various initial conditions without controllability assumption. Top: case 1 ($v^* \leq 0$), see Proposition 3.2 for the optimal synthesis; bottom: case 2 ($0 < v^* < v_m$), see Proposition 3.3. In blue dashed lines, trajectories $\hat{\mathcal{C}}$ and $\check{\mathcal{C}}$ which pass through $(\bar{s}, v^*)$ and $(\bar{s}, v_m)$.

### 3.4 Numerical computations of the switching times

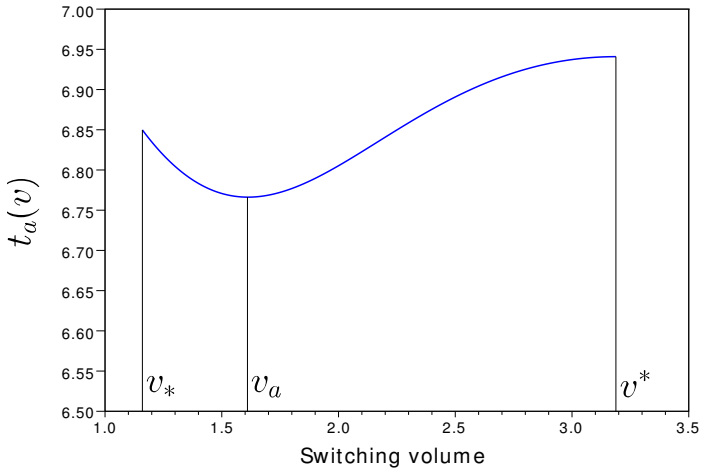


Figure 2: Time $t_a(v)$ to reach the target from $(\bar{s}, v_*)$ with the strategy: singular arc until the switching volume $v$, $u = 1$ until $v_m$, $u = 0$ until $s_{ref}$. We find that $t_a(v)$ has a unique minimum for $v = v_a$ (see Section 3.4)

Based on the optimal synthesis, optimal trajectories for various initial conditions $(s_0, v_0)$ are obtained numerically as follows:
(i) First, for various $v \in [v_*, v^*]$, we compute the time $t_a(v)$ to reach the target starting from $(\bar{s}, v_*)$ with the strategy: singular arc until $v$, $u = 1$ until $v_m$, $u = 0$ until $s_{ref}$. We find that $t_a(v)$ has a unique minimum for $v = v_a$ (see Fig. 2).
(ii) If $s_0 < \bar{s}$, the optimal trajectory starts with $u = 1$ until reaching $s = \bar{s}$ or $v = v_m$. If it reaches $s = \bar{s}$ with $v < v_a$, then it should stay on the singular arc until $v_a$, then $u = 1$ until $v_m$, and finally $u = 0$ until $s_{ref}$. Otherwise, the optimal strategy is $u = 1$ until $v_m$, and $u = 0$ until $s_{ref}$.
(iii) If $s_0 > \bar{s}$, we have three sub-cases:

- If $v_0 \geq v_a$, we search numerically $s_b \in [\bar{s}, \min(s_0, \hat{\gamma}(v_0)]$ which minimizes the time $t_b(s_b)$ to reach the target starting from $(s_0, v_0)$ with the strategy: $u = 0$ until $s_b$, $u = 1$ until $v_m$, $u = 0$ until $s_{ref}$.
- If $v_* < v_0 < v_a$, we determine $t_b(s_b)$ as above. Then, in order to determine the optimal strategy, we compare $t_b(s_b)$ with the time of the strategy $u = 0$ until $\bar{s}$, singular arc until $v_a$, $u = 1$ until $v_m$, and $u = 0$ until $s_{ref}$.
- If $v_0 < v_*$, the optimal strategy is $u = 0$ until $\bar{s}$, singular arc until $v_a$, $u = 1$ until $v_m$, and $u = 0$ until $s_{ref}$.

The numerical results (i) and (ii) answer to the question of determining the first switching time $t_0$ when the initial point is such that $s_0 < \bar{s}$. The result (iii) allows to conclude numerically which structure is optimal, either $B_0SAB_1B_0$ or $B_1B_1B_0$ whenever $s_0 > \bar{s}$ and $v_0 > v_*$ (see the last case of Proposition 3.3).

In order to determine precisely the optimal volume $v_a$ above which it is not optimal to stay on the singular arc, we can proceed as follows. For $v_0 \in [v_*, v^*]$, consider the strategy $u = \overline{u}_s$ from $v_*$ to $v_0$, $u = 1$ until $v_m$ and then $u = 0$ until $s_{ref}$. The time $\tau(v_0)$ of this strategy is (recall (3.12), see also [8]):

$$\tau(v_0) = \frac{\ln\left(\frac{M+v_0(s_{in}-\bar{s})}{M+v_*(s_{in}-\bar{s})}\right)}{\mu(\bar{s})} + v_m - v_0 + \int_{s_{ref}}^{s^\dagger(v_0)} \frac{d\sigma}{\mu(\sigma)\left(\frac{M}{v_m} + s_{in} - \sigma\right)}, \tag{3.18}$$

where $s^\dagger(v)$ is the substrate concentration when the trajectory reaches $v = v_m$. We now show that $\tau$ admits a minimum $v_a \in [v_*, v^*]$ that we will characterize hereafter. First, notice that $s^\dagger(v_0)$ is obtained after integrating

the ODE:

$$\frac{ds}{dv} = -\mu(s)\left[\frac{M}{v} + s_{in} - s\right] + \frac{s_{in}-s}{v},\ s(v_0) = \overline{s}. \tag{3.19}$$

Moreover, (3.19) can be equivalently written as $\frac{ds}{dv} = g(v,s)$ where $g$ is the right hand-side of (3.19). By the classical dependence of the solution of an ODE on parameters, we denote by $s(v,\overline{s},v_0)$ the unique solution of (3.19). It is standard that $v_0 \in \mathbb{R}_+^* \longmapsto s(v,\overline{s},v_0)$ is of class $C^1$ for all $v > 0$. It follows by composition that $v_0 \longmapsto \tau(v_0)$ is of class $C^1$ on $[v_*, v^*]$. Consequently, it admits a minimum on this interval.

By differentiating $s(v,\overline{s},v_0)$ with respect to $v_0$, we get:

$$\frac{\partial s}{\partial v_0}(v,\overline{s},v_0) = -g(v_0,\overline{s})e^{\int_{v_0}^{v}\frac{\partial g}{\partial s}(s(w,v_0,\overline{s}),w)dw},$$

hence $\frac{ds^\dagger}{dv_0}(v_0) = \frac{\partial s}{\partial v_0}(v_m,\overline{s},v_0)$. Now, we know from the PMP that $v_0 = v^*$ and $v_0 = v_*$ are not admissible (see also Proposition 3.3), hence $v_a$ necessarily satisfies $\frac{d\tau}{dv_0}(v_a) = 0$. So, if we put $\theta(v_0) := \int_{v_0}^{v_m}\frac{\partial g}{\partial s}(w,s(w,\overline{s},v_0))dw$, we obtain by taking the derivative of (3.18) with respect to $v_0$:

$$\frac{d\tau}{dv_0}(v_0) = \frac{v^*-v_0}{\frac{M}{s_{in}-\overline{s}}+v_0}\left[1 - \frac{\mu(\overline{s})(\frac{M}{v_0}+s_{in}-\overline{s})}{\mu(s^\dagger)(\frac{M}{v_m}+s_{in}-\overline{s})}e^{\theta(v_0)}\right] \tag{3.20}$$

This equation allows to obtain numerically the volume $v_a \in (v_*, v^*)$ above which extremal trajectories stop to be singular. As an example, we find $v_a \simeq 1.67$ (see Fig. 2 and Table 1 for the values of the parameters).

To conclude, we have shown that, without the controllability assumption, the optimal synthesis is quite different as the one of Theorem 3.2. Moreover, we have pointed out that it is not optimal for a trajectory to stay as long as possible on the singular arc.

# 4 Optimality results for the impulsive system

In this part, we consider the minimal time problem with an extension of (2.1) allowing impulse controls, see [8, 9]. From a practical point of view, this assumption corresponds to a maximum dilution rate $u_m \gg \sup_{s\in[0,s_{in}]}\mu(s)$. This framework allows to compute easily the value function corresponding to the different strategies ("fill and wait" and "singular arc" strategies, see Definitions 4.1 and 4.2). Our aim is to prove the following result:

- For Monod growth function, the "fill and wait" strategy is optimal.
- For Haldane growth function, the "singular arc" strategy is optimal.

The proof of these results relies on the case $\alpha = 0$. The case where $\alpha \neq 0$ is considered in the last subsection and is a simple consequence of the previous study. Therefore, we assume in this section that $\alpha = 0$ except in the subsection 4.5.

## 4.1 Statement of the problem

We first make a brief review of the impulsive framework (see e.g. [8, 9]). We consider the initial system (2.1) with an additional control $r$ which plays the role of an impulse control.

$$\begin{cases} \dot{x} = \left(r[\mu(s)-k] - \frac{u}{v}\right)x, \\ \dot{s} = -r\mu(s)x + \frac{u}{v}(s_{in}-s), \\ \dot{v} = u. \end{cases} \tag{4.1}$$

The set of admissible controls is defined as follows (the subscript $i$ is for impulsive):

$$\mathcal{U}_i = \{\mathbf{u} = (r,u) : [0,\infty[ \to \Omega \mid \text{meas.}\},$$

where $\Omega = (\{0,1\}\times[0,1]) \setminus \{(0,0)\}$. The control $u$ is the input flow rate as in (2.1) and $r$ represents an impulse control. An instantaneous addition of volume $v_+ - v_-$ (i.e. a jump from volume $v_-$ to volume $v_+$)

is achieved by taking $r = 0$ on some interval of time $[\tau_-, \tau_+]$ for system (2.1), and any measurable control $u$ satisfying the condition:

$$\int_{\tau_-}^{\tau_+} u(t)dt = v_+ - v_-, \tag{4.2}$$

see [9] for more details. In particular, there is no uniqueness of $u$ as long as integral (4.2) is equal to $v_+ - v_-$. An addition of volume $v_+ - v_-$ corresponds to a dilution of the substrate and the biomass:

$$s_+ = \frac{v_-}{v_+}s_- + \left(1 - \frac{v_-}{v_+}\right)s_{in},\ x_+ = \frac{v_-}{v_+}x_-, \tag{4.3}$$

where $s_-$, $x_-$ are the concentrations before dilution, and $s_+$, $x_+$ the ones after dilution. Hereafter, we also say that the system has an *impulse* whenever $r = 0$ on some time interval. The system (4.1) is obtained by a reparametrization of the time in (3.1), see [9]. For simplicity, the new time in (4.1) has still been denoted by $t$.

For $\xi = (s, x, v) \in E$ and a control $\mathbf{u} \in \mathcal{U}_\mathbf{i}$, let $t_\xi(\mathbf{u})$ be the first entry time in $\mathcal{T}$. In the impulsive framework, the minimum time problem, for an initial condition $\xi_0 \in E$, can be gathered into:

$$\inf_{\mathbf{u}\in\mathcal{U}_\mathbf{i}} \int_0^{t_{\xi_0}(\mathbf{u})} r(\tau)d\tau,\ \text{s.t. } (x(t_{\xi_0}(\mathbf{u})), s(t_{\xi_0}(\mathbf{u})), v(t_{\xi_0}(\mathbf{u}))) \in \mathcal{T}, \tag{4.4}$$

see [9] for more details on the reparametrization of the minimum time problem with impulsive control. Similarly as for (3.1), one can prove that the target is controllable from any initial condition in E (by making an impulse of volume $v_m - v_0$ and letting $u = 0$ until $s_{ref}$ is necessary). We can also prove by Fillipov's Theorem (see [13]) that there exists an optimal control for (4.4) in the class of *relaxed controls* taking values within the convex set $\Omega' := [0, 1] \times [0, 1]\backslash\{(0, 0)\}$. In the following, we apply Pontryagin maximum principle with control in $\Omega'$. We will see in the sections 4.3 and 4.4 that an optimal feedback control $\mathbf{u}$ satisfies $r \in \{0, 1\}$.

## 4.2 Pontryagin maximum principle in the impulsive case

In this part, we apply Pontryagin principle (PMP) on the impulsive system which gives necessary conditions on optimal trajectories. The Hamiltonian $H := H(x, s, v, \lambda_x, \lambda_s, \lambda_v, \lambda_0, r, u)$ associated to the system is:

$$H := r\left[(\lambda_x - \lambda_s)\mu(s)x - kx\lambda_x + \lambda_0\right] + u\left[\lambda_v + \frac{\lambda_s(s_{in} - s) - \lambda_x x}{v}\right]. \tag{4.5}$$

Let $\mathbf{u}$ an optimal control and $\xi := (x, s, v)$ its associated trajectory. Then, there exists $t_f > 0$, $\lambda_0 \leq 0$ and $\lambda = (\lambda_x, \lambda_s, \lambda_v) : [0, t_f] \to \mathbb{R}^3$ such that $(\lambda_0, \lambda(\cdot)) \neq 0$, $\lambda$ satisfies the adjoint equation $\dot{\lambda} = -\frac{\partial H}{\partial \xi}(\xi, \lambda, \lambda_0, \mathbf{u})$ for a.e. $t \in [0, t_f]$, that is:

$$\begin{cases} \dot{\lambda}_x = -r(\lambda_x - \lambda_s)\mu(s) + rk\lambda_x + \frac{u}{v}\lambda_x, \\ \dot{\lambda}_s = -r(\lambda_x - \lambda_s)x\mu'(s) + \frac{u}{v}\lambda_s, \\ \dot{\lambda}_v = \frac{(s_{in}-s)\lambda_s - x\lambda_x}{v^2}u, \end{cases} \tag{4.6}$$

and such that we have the maximization condition:

$$\mathbf{u}(t) \in \text{argmax}_{\mathbf{v}\in\mathbf{\Omega}'} H(\xi(t), \lambda(t), \lambda_0, \mathbf{v}), \tag{4.7}$$

for a.e. $t \in [0, t_f]$. Finally as $x(t_f)$ is free, we have the transversality condition

$$\lambda_x(t_f) = 0. \tag{4.8}$$

An extremal trajectory is a quadruplet $(\xi(\cdot), \lambda(\cdot), \mathbf{u}(\cdot), \mathbf{t_f})$ satisfying (4.1)-(4.6)-(4.7). We assume in the following that optimal trajectories are normal trajectories, that is $\lambda_0 \neq 0$, hence we take $\lambda_0 = -1$ (the fact that $\lambda_0$ cannot be zero will be discussed in the two next subsections). As we deal with a minimal time problem, the Hamiltonian is zero along an extremal trajectory:

$$H = r[(\lambda_x - \lambda_s)\mu(s)x - kx\lambda_x - 1] + u\left[\lambda_v + \frac{(s_{in} - s)\lambda_s - x\lambda_x}{v}\right] = 0, \tag{4.9}$$

Let $\phi_1$ (resp. $\phi_2$) the switching function associated to the control $r$ (resp. $u$):

$$\begin{cases} \phi_1 := (\lambda_x - \lambda_s)\mu(s)x - kx\lambda_x - 1, \\ \phi_2 := \lambda_v + \frac{(s_{in}-s)\lambda_s - x\lambda_x}{v}. \end{cases}$$

The value of an extremal control is given by the sign of $\phi_1$ and $\phi_2$. For a.e. $t \in [0, t_f]$, we have

$$\begin{cases} \phi_1 \leq 0 \text{ and } \phi_2 = 0 \Longrightarrow \ r = 0, \\ \phi_2 \leq 0 \text{ and } \phi_1 = 0 \Longrightarrow \ u = 0, \end{cases} \tag{4.10}$$

and we have also:

$$r(t)\phi_1(t) + u(t)\phi_2(t) = 0, \tag{4.11}$$

for a.e. $t \in [0, t_f]$, hence $\phi_1$ and $\phi_2$ are always negative. When $u = 0$ on some time interval, we can take without loss of generality $r = 1$ as $(r, u) \neq (0, 0)$ (see [8]). When $\phi_1 = \phi_2 = 0$ on some time interval, then, we say that the trajectory has a *singular arc*. By derivating, we obtain:

$$\begin{cases} \dot{\phi}_1 = -u\psi, \\ \dot{\phi}_2 = r\psi, \end{cases} \tag{4.12}$$

where:

$$\psi := \frac{x(s_{in} - s)}{v}(\lambda_s - \lambda_x)\mu'(s). \tag{4.13}$$

When the derivative of the growth function $\mu$ admits a zero (typically in the case where $\mu$ is of Haldane type), an optimal control can be singular. The following lemma shows that the characterization of singular arcs is essentially the same as the problem with $k = 0$ (see section 3.1).

**Lemma 4.1.** *Let $I = [t_1, t_2]$ a singular arc. Then, we have $s(t) = \overline{s}$ for $t \in [t_1, t_2]$.*

*Proof.* We have $\phi_1(t) = \phi_2(t) = 0$ for all $t \in I$. By derivating, we obtain $(\lambda_s(t) - \lambda_x(t))\mu'(s(t)) = 0$ for all $t \in I$. Let us prove that $\lambda_s - \lambda_x$ does not vanish on some time interval $J := [t_1', t_2']$. Otherwise, we would have $\lambda_s(t) - \lambda_x(t) = \dot{\lambda}_s - \dot{\lambda}_x(t) = 0$ for all $t \in J$. This condition together with the adjoint system implies that $\lambda_x(t) = 0$ for all $t \in J$. On the other hand, the expression of the Hamiltonian along the singular arc yields that $-kx\lambda_x + 1 = 0$ contradicting the fact that $\lambda_x$ is vanishing on $J$. Consequently, we have $\mu'(s(t)) = 0$ for all $t \in I$, which proves the Lemma. □

**Remark 4.1.** *Legendre-Clebsch necessary optimality condition is satisfied at the critical points of $\mu'$ which correspond to a local maximum, see e.g. [8, 14].*

To study properties of singular arcs, we define

$$\alpha := \frac{\mu(\overline{s})}{s_{in} - \overline{s}}, \ \beta := \mu(\overline{s}) - k > 0, \ \overline{x} := (s_{in} - \overline{s})\left[1 - \frac{k}{\mu(\overline{s})}\right].$$

**Proposition 4.1.** *Let us consider a singular arc with $r = 1$ on some time interval $[t_0, t_1]$ starting at some point $(x_0, \overline{s}, v_0)$. Then, the concentration of biomass, the singular control $u_s$, and the time $t(v, x_0, v_0)$ to steer (4.1) from a volume $v_0$ to $v$ are given by:*

$$x(v) = \frac{v_0}{v}x_0 + \left[1 - \frac{v_0}{v}\right]\overline{x}, \ u_s(v) = \alpha x v, \ t(v, x_0, v_0) = t_0 + \frac{1}{\beta}\ln\left(\frac{x_0 v_0 + \overline{x}[v - v_0]}{x_0 v_0}\right). \tag{4.14}$$

*Proof.* The value of the singular control is straightforward using $\dot{s} = 0$ along the singular arc. Let $\rho := xv$. By derivating, we have $\dot{\rho} = \beta\rho$ which gives $x(t)v(t) = x_0 v_0 e^{\beta(t-t_0)}$. Now we have $\dot{v} = \alpha x v = \alpha x_0 v_0 e^{\beta(t-t_0)}$, and by integrating, we obtain $v = v_0 + \frac{x_0}{\overline{x}}v_0 e^{\beta(t-t_0)} - \frac{x_0}{\overline{x}}v_0$. Combining this expression with the one of $\rho$ gives the desired expression of $x$. Finally, the expression of $\rho$ gives that $t(v, x_0, v_0) - t_0 = \frac{1}{\beta}\ln(\frac{xv}{x_0 v_0})$, and we find the desired expression of $t(v, x_0, v_0)$ by replacing $x$ by its expression. □

Next, we assume the following condition that will ensure the controllability of the singular arc with $r = 1$ for the problem with mortality (see also [2, 8]):

**Hypothesis 4.1.** *Initial conditions in $E$ are such that:*

$$\mu(\overline{s})\left[\frac{M_0}{s_{in}-\overline{s}}+v_m\right]\leq 1, \tag{4.15}$$

*where $M_0 = v_0(x_0+s_0-s_{in})$.*

Recall that along a trajectory, we have $M = v(x+s-s_{in})$, where $M$ is strictly decreasing by (2.11). Together with (4.14), we obtain for $0<v\leq v_m$:

$$u_s(v)=\alpha\left[M+v(s_{in}-s)\right]\leq \alpha[M_0+v_m(s_{in}-\overline{s})]\leq 1,$$

where the second inequality follows from Hypothesis 4.1. It follows that this hypothesis guarantees that the singular control satisfies the bound $u_s\leq 1$.

**Remark 4.2.** *(i) For given volume $0<v_0<v_1$, one can show that the mapping*

$$k\longmapsto \frac{1}{\mu(\overline{s})-k}\ln\left(1+\frac{s_{in}-\overline{s}}{x_0}\left[\frac{v_1}{v_0}-1\right]\left[1-\frac{k}{\mu(\overline{s})}\right]\right),$$

*is increasing with respect to $k$, therefore the time to steer the system from $v_0$ to $v_1$ along the singular arc is greater than the one in absence of mortality.*
*(ii). Given Hypothesis 4.1, we have $u_s(v)\in[0,1]$, for all $v\in[v_0,v_m]$, which proves that the singular arc is always controllable.*

We can also compute the time of an arc $u=0$.

**Lemma 4.2.** *Let us consider a time interval $[t_0,t_1]$ where $u=0$ and $r=1$ from $(x_0,s_0,v_0)\in E$ with $x_0>0$ to $(x_1,s_1,v_0)\in E$ with $0<s_1<s_0$. Then, we have:*

$$x_1=x_0+s_0-s+k\int_{s_0}^{s_1}\frac{d\sigma}{\mu(\sigma)},\ t_1=t_0+\int_{s_0}^{s_1}-\frac{ds}{\mu(s)(x_0+s_0-s+k\int_{s_0}^{s}\frac{d\sigma}{\mu(\sigma)})} \tag{4.16}$$

*Proof.* A straightforward computation shows that we have $\frac{dx}{ds}=\frac{k-\mu(s)}{\mu(s)}$, which gives the desired expressions after an integration (recall that if $s_0>0$ and $x_0>0$, then we have $x(t)>0$ and $s(t)>0$ for all $t$ so that the integrals are well defined). □

Also one can see immediately from (4.16) that the time of an arc $u=0$ is greater with mortality than when $k=0$.

## 4.3 Optimality result for Monod growth function

We consider in this section the case where the growth function is of type Monod and we prove that the strategy "fill and wait" (see Definition 4.1) is optimal for any value of $k>0$.

Let us first prove that $\lambda_0\neq 0$. Define the dilution curve $\mathcal{C}_0$ which passes trough the point $(s_{ref},v_m)$ by:

$$\gamma_0(s):=v_m\frac{s_{in}-s_{ref}}{s_{in}-s},\ s\in(0,s_{ref}].$$

The curve $\mathcal{C}_0$ corresponds to $\gamma_{ref}$ in the impulsive framework, and similarly as (3.7), we can define a subset $\tilde{E}\subset E$ by:

$$\tilde{E}:=\{(x,s,v)\in E\mid v\leq v_m,\ v<\gamma_0(s))\}. \tag{4.17}$$

**Proposition 4.2.** *Any optimal trajectory is such that $\lambda_0\neq 0$.*

*Proof.* Let $(x_0,s_0,v_0)\in E$, and consider an optimal trajectory starting at this point and satisfying $\lambda_0=0$. If $v_0\geq\gamma_0(s_0)$, the target $\mathcal{T}$ can be reached by a single impulse (of null cost) on some time interval $[0,t_f]$ (which is necessarily the optimal trajectory), and we have $\phi_1\leq 0$ and $\phi_2=0$ on this interval. By derivating, it follows that $\lambda_s-\lambda_x$ is zero (as $\mu'\neq 0$) which gives $\lambda_x=0$ from the adjoint equation. Now $\phi_2=0$ implies that $\lambda_v=0$, and we have a contradiction as $(\lambda(\cdot),\lambda_0)$ is non-zero.

Let us now assume that $v_0 < \gamma_0(s_0)$. There exists a time interval $I := (t_1, t_2)$ where the optimal trajectory is such that $u = 0$ and such that either $t_1$ or $t_2$ is a switching point between an impulse and an arc $u = 0$ (otherwise the trajectory would not reach the target). We have $\phi_1 = 0$ and $\phi_2 \leq 0$ on $I$, and by derivating we obtain similarly as in the case above $\lambda_s - \lambda_x = 0$ on $I$. By the adjoint equation, we obtain that $\lambda_x = \lambda_s = 0$ on $I$. Now, at the switching time, $\phi_2$ is vanishing, and so is $\lambda_v$. It follows that the pair $(\lambda(\cdot), \lambda_0)$ is zero, which contradicts the PMP. □

Following [9], we make use of the Hamilton-Jacobi equation associated to (4.4) to characterize optimal trajectories for the Monod growth function. From the expression of the Hamiltonian, the Hamilton-Jacobi equation associated to the problem reads as follows:

$$\min\left(0, 1 + x_0(\mu(s_0) - k)\frac{\partial \mathbf{v}}{\partial x_0} - x_0\mu(s_0)\frac{\partial \mathbf{v}}{\partial s_0}\right) + \min\left(0, \frac{\partial \mathbf{v}}{\partial v_0} + \frac{s_{in} - s_0}{v_0}\frac{\partial \mathbf{v}}{\partial s_0} - \frac{x_0}{v_0}\frac{\partial \mathbf{v}}{\partial x_0}\right) = 0, \tag{4.18}$$

where $(x_0, s_0, v_0) \in E$, together with the boundary condition $\mathbf{v}(x_0, s_0, v_0) = 0$ on the target $\mathcal{T}$. If $\omega : E \to \mathbb{R}$ is a given function of class $C^1$, we define:

$$\begin{cases} H_1^\omega(x_0, s_0, v_0) := 1 + x_0(\mu(s_0) - k)\frac{\partial \omega}{\partial x_0}(x_0, s_0, v_0) - x_0\mu(s_0)\frac{\partial \omega}{\partial s_0}(x_0, s_0, v_0), \\ H_2^\omega(x_0, s_0, v_0) := \frac{\partial \omega}{\partial v_0}(x_0, s_0, v_0) + \frac{s_{in} - s_0}{v_0}\frac{\partial \omega}{\partial s_0}(x_0, s_0, v_0) - \frac{x_0}{v_0}\frac{\partial \omega}{\partial x_0}(x_0, s_0, v_0), \end{cases} \tag{4.19}$$

hence (4.18) is equivalent to the two variational inequalities

$$\begin{cases} H_1^{\mathbf{v}}(x_0, s_0, v_0) \geq 0, \\ H_2^{\mathbf{v}}(x_0, s_0, v_0) \geq 0, \end{cases} \tag{4.20}$$

for any $(x_0, s_0, v_0) \in E$.

**Remark 4.3.** *We can expect that when $k$ goes to zero, the value function associated to* (4.4) *converges to the value function associated to the problem with $k = 0$ (some arguments can be found in [15]). However, such a property is not sufficient in order to deduce the optimal strategy for* (4.4) *from the case $k = 0$.*

Consider a point $(x_0, s_0, v_0)$ and let $(x_0', s_0', v_m)$ the point which is obtained by an instantaneous dilution until the maximal volume $v_m$. Recall from (4.3) that the new concentrations of biomass and substrate are given by

$$x_0' = \frac{v_0}{v_m}x_0, \;\; s_0' = \frac{v_0}{v_m}s_0 + \left(1 - \frac{v_0}{v_m}\right)s_{in}. \tag{4.21}$$

**Definition 4.1.** *From any point $(x_0, s_0, v_0) \in E$, the strategy fill and wait (FW) is $r = 0$ until $v = v_m$, and then $u = 0$ until $s \leq s_{ref}$ if $s_0' > s_{ref}$. The cost $w$ of this strategy is given by:*
*(i) If $v_0 \geq \gamma_0(s_0)$, then $w(x_0, s_0, v_0) = 0$.*
*(ii) If $v_0 < \gamma_0(s_0)$, then $w(x_0, s_0, v_0) = \int_{s_0'}^{s_{ref}} -\frac{ds}{\mu(s)[x_0' + s_0' - s + k\int_{s_0'}^{s}\frac{d\sigma}{\mu(\sigma)}]}$*

**Lemma 4.3.** *The mapping $w$ is continuous on $E$ and of class $C^1$ on $\tilde{E}$. Moreover, it satisfies:*

$$H_1^w(x_0, s_0, v_0) \geq 0, \;\; H_2^w(x_0, s_0, v_0) = 0. \tag{4.22}$$

*Proof.* For convenience, we define:

$$\rho_{\xi_0}(s) := x_0' + \int_{s_0'}^{s} \frac{k - \mu(\sigma)}{\mu(\sigma)}d\sigma, \;\; s_{ref} \leq s \leq s_0',$$

where $\xi_0 := (x_0, s_0, v_0) \in E$. Notice that we have $\rho_{\xi_0}(s) \geq x_0'$ as $s_{ref} \geq \tilde{s}_1$.

Now, one can see that we have $w = 0$ on $E \backslash \tilde{E}$, and $w > 0$ on $\tilde{E}$. Let $(x_n, s_n, v_n) \in \tilde{E}$ a sequence of points which converges to a point $(x^0, s^0, v^0) \in E$ such that $(s_0, v_0) \in \mathcal{C}_0$, i.e. $v^0 = \gamma_0(s^0)$. We have that the sequence $s_n' := \frac{v_n}{v_m}s_n + \left(1 - \frac{v_n}{v_m}\right)s_{in}$ converges to $s_{ref}$ and $s \longmapsto \frac{-1}{\mu(s)\rho_{\xi_0}(s)}$ is uniformly bounded by $\frac{1}{\mu(s_{ref})x_0'}$. So, $w(x_n, s_n, v_n)$ converges to zero, which proves the continuity of $w$ over $\mathcal{C}_0$. Moreover, by the regularity property of the integral, the function $w$ is continuous on $\tilde{E}$, which proves the continuity of $w$ in $E$.

Now, take a point $(x_0, s_0, v_0) \in \tilde{E}$, i.e. $v_0 < \gamma_0(s_0)$. Recall from (4.21) that $x_0'$ and $s_0'$ depend on $(x_0, s_0, v_0)$ in a continuously differentiable fashion. It follows from the definition of $w$ (see Definition 4.1) that it is of class $C^1$ on $\tilde{E}$.

By taking the derivative of $w$ with respect to $x_0$, $s_0$ and $v_0$ , we get:

$$\frac{\partial w}{\partial x_0}(x_0, s_0, v_0) = \frac{v_0}{v_m} \int_{s_0'}^{s_{ref}} \frac{ds}{\mu(s)\rho_{\xi_0}^2(s)} ds,$$

$$\frac{\partial w}{\partial s_0}(x_0, s_0, v_0) = \frac{v_0}{v_m} \frac{1}{x_0' \mu(s_0')} + \frac{v_0}{v_m} \left(1 - \frac{k}{\mu(s_0')}\right) \int_{s_0'}^{s_{ref}} \frac{ds}{\mu(s)\rho_{\xi_0}^2(s)} ds,$$

$$\frac{\partial w}{\partial v_0}(x_0, s_0, v_0) = \frac{1}{x_0' \mu(s_0')} \frac{s_0 - s_{in}}{v_m} + \left(\frac{x_0}{v_m} - \frac{s_0 - s_{in}}{v_m} \frac{k - \mu(s_0')}{\mu(s_0')}\right) \int_{s_0'}^{s_{ref}} \frac{ds}{\mu(s)\rho_{\xi_0}^2(s)} ds.$$

It follows that

$$H_1^w(x_0, s_0, v_0) = 1 - \frac{\mu(s_0)}{\mu(s_0')} + k x_0' \left(\frac{\mu(s_0)}{\mu(s_0')} - 1\right) \int_{s_0'}^{s_{ref}} \frac{ds}{\mu(s)\rho_{\xi_0}^2(s)} ds.$$

But, one has $\mu(s_0) \leq \mu(s_0')$ as $s_0 \leq s_0'$, and the integral above is negative as $s_0' > s_{ref}$, hence $H_1^w(x_0, s_0, v_0) \geq 0$. Moreover, a direct computation shows that $H_2^w(x_0, s_0, v_0) = 0$, and the result follows. □

**Theorem 4.1.** *The feedback control law* $\mathbf{u}_{FW}$ *given by*

$$\mathbf{u}_{FW}(s_0, x_0, v_0) := \begin{cases} (0, u), & \text{if } v_0 < v_m, \\ (1, 0), & \text{if } v_0 = v_m \text{ and } s_0 > s_{ref}, \end{cases} \tag{4.23}$$

*is optimal, and the value function associated to* (4.4) *satisfies* $\mathbf{v} = w$.

*Proof.* Lemma 4.3 allows to apply Proposition 5.4 of [9] (giving a sufficient condition for a feedback control law to be optimal). First, any solution of (4.1) with the feedback (4.23) is absolutely continuous and reaches the target in finite time. Moreover, the feedback $\mathbf{u}_{FW}$ is such that:

- The function $w$ is continuous over $E$ and of class $C^1$ on $\tilde{E}$ (the set of points where $w > 0$).
- The function $w$ fulfills (4.22) and consequently (4.18), together with the boundary condition $w = 0$ on the target $\mathcal{T}$.
- The function $w$ satisfies $r = 0$ for any point in $\tilde{E}$ such that $w = 0$.

We can conclude that this strategy is optimal. Note that in (4.29), $u$ is any measurable control taking values in $[0, 1]$ such that its integral on the period of the dilution is equal to $v_m - v_0$, see (4.2). □

## 4.4 Optimality result for Haldane growth function

We assume in this subsection that $\mu$ is of Haldane type, and that $\overline{s} > s_{ref}$. We will prove that the singular arc strategy (see Definition 4.2) is optimal for any value of $k$. The Hamilton-Jacobi equation is a direct way to prove optimality if we have a candidate for the value function which is the case here. Unfortunately the expression (4.28) provided by this strategy seems delicate to handle in this case. So, we have used Pontryagin maximum principle which allows to exclude extremal trajectories, and to prove the optimality of the singular arc strategy.

First, we can prove similarly as in the case of Monod growth function that $\lambda_0 \neq 0$ (see Proposition 4.2). The next lemma gives properties of the trajectory during an impulse of volume.

**Lemma 4.4.** *Consider an extremal trajectory starting at some point* $(x_0, s_0, v_0) \in E$ *with* $v_0 < v_m$. *Assume that we have* $r = 0$ *on some time interval* $[0, t_1]$ *where* $t_1$ *is a switching point. Then, we have:*

$$[\lambda_x^0 - \lambda_s^0][\mu(s(t_1)) - \mu(s_0)] \geq 0, \tag{4.24}$$

*where* $\lambda^0 := (\lambda_x^0, \lambda_s^0, \lambda_v^0)$ *is the initial adjoint vector.*

*Proof.* One can see that on $[0, t_1]$, we have $\dot{\lambda}_x = \frac{\dot{v}}{v}\lambda_x$, $\dot{\lambda}_s = \frac{\dot{v}}{v}\lambda_s$, thus $\lambda_x = \frac{v}{v_0}\lambda_x^0$ and $\lambda_s = \frac{v}{v_0}\lambda_s^0$. This gives

$$\phi_1 = (\lambda_x^0 - \lambda_s^0)x_0\mu(s) - 1 - kx_0\lambda_x^0. \tag{4.25}$$

As $r = 0$ on the interval $[0, t_1]$, we have $\phi_1(0) \leq 0$ and $\phi_1(t_1) = 0$ (as $t_1$ is a switching point). The lemma follows from (4.25). □

We now prove that it is not possible to have an impulse from a point in $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$ and $s_0 > \overline{s}$ to the maximal volume.

**Lemma 4.5.** *Assume that an extremal trajectory satisfies $r = 0$ from a point $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$ and $s_0 > \overline{s}$ until the maximum volume $v_m$. Then, the trajectory is not optimal.*

*Proof.* Suppose that we have $r = 0$ until $v_m$ and let $t_1$ the time where the trajectory reaches the maximal volume. We then have $u = 0$ on $[t_1, t_f]$ where $t_f > t_1$ is such that $s(t_f) = s_{ref}$ (first entry time into the target). We have $\phi_1 = 0$ on the interval $[t_1, t_f]$, therefore

$$\lambda_x - \lambda_s = \frac{1 + kx\lambda_x}{\mu(s)x}.$$

From the adjoint equation, we get that $\dot{\lambda}_x = -\frac{1}{x}$, so $\lambda_x$ is decreasing, and using (4.8), we obtain that $\lambda_x \geq 0$ on $[t_1, t_f]$. Consequently, $\lambda_x - \lambda_s$ is non-negative on $[t_1, t_f]$, thus $\lambda_x(t_1) - \lambda_s(t_1) \geq 0$. By (4.24), and from the fact that $\mu(s_0) - \mu(s(t_1)) > 0$, we obtain

$$\lambda_x^0 - \lambda_s^0 < 0,$$

where $\lambda_0 := (\lambda_x^0, \lambda_s^0, \lambda_v^0)$ is the initial adjoint vector. Recall from Lemma 4.24 that along the impulse, we have $\lambda_x - \lambda_s = \frac{v}{v_0}[\lambda_x^0 - \lambda_s^0]$. It follows that at time $t_1$, we have $\lambda_x(t_1) - \lambda_s(t_1) = \frac{v_m}{v_0}[\lambda_x^0 - \lambda_s^0] < 0$, which is a contradiction. □

**Corollary 4.1.** *Any extremal trajectory starting at some point $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$, $s_0 > \overline{s}$, and such that $s(t) > \overline{s}$ for all $t$ such that $v(t) < v_m$ is not optimal.*

*Proof.* Such a trajectory is necessarily a concatenation of arcs $u = 0$ and $u = 1$, and it contains a non-trivial impulse to the maximal volume $v_m$, and we can use Lemma 4.5 to conclude. □

Similarly, we show that a trajectory which has a switching point from an arc $u = 0$ to an impulse at a substrate concentration strictly greater than $\overline{s}$, is not optimal.

**Lemma 4.6.** *Let us consider an extremal trajectory starting at some point $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$, $s_0 > \overline{s}$. Assume that it satisfies $u = 0$ on $[0, t_0]$ and $r = 0$ on $[t_0, t_1]$ where $s(t_0) > \overline{s}$. Then, the trajectory is not optimal.*

*Proof.* As we have $\phi_2 < 0$ on $[0, t_0)$, we get that $\dot{\phi}_2(t_0) = \lim_{t \to t_0} \frac{\phi_2(t) - \phi_2(t_0)}{t - t_0} \geq 0$. We obtain from (4.13) that $\dot{\phi}_2 = \psi$, thus $\lambda_s(t_0) - \lambda_x(t_0) \leq 0$ (recall that $\mu'(s(t_0)) < 0$ as $s(t_0) > \overline{s}$). From the impulse at time $t_0$ and from Lemma 4.4, we obtain that necessarily $\lambda_x(t_0) - \lambda_s(t_0) < 0$ which is a contradiction. □

We now investigate the case where an extremal trajectory has a switching point at a substrate concentration lower than $\overline{s}$ and for a volume value strictly less than $v_m$.

**Lemma 4.7.** *Consider an extremal trajectory starting at some point $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$, $s_0 < \overline{s}$. Assume that it satisfies $u = 0$ on $[0, t_0]$ and $r = 0$ on $[t_0, t_1]$. Then, the trajectory is not optimal.*

*Proof.* We have $\phi_2 < 0$ on the interval $(0, t_0)$ and $\phi_2(t_0) = 0$, therefore $\dot{\phi}_2(t_0) \geq 0$. On the interval $[0, t_0]$, the switching function $\phi_2$ satisfies $\dot{\phi}_2 = \psi$, therefore we get $\lambda_s(t_0) - \lambda_x(t_0) \geq 0$. From Lemma 4.4, we obtain that $\lambda_x(t_0) - \lambda_s(t_0) > 0$ (because $\mu$ is increasing on $[0, \overline{s}]$), hence $\lambda_s(t_0) - \lambda_x(t_0) < 0$, which is a contradiction. □

Notice that this Lemma implies that it is not possible for an optimal trajectory to cross the singular arc with $u = 0$ at a volume $v_0 < v_m$.

We now prove that it is not optimal for a trajectory to leave the singular arc before reaching the maximal volume. Hereafter, $S_{[t_1,t_2]}$, $I_{[t_1,t_2]}$, and $NF_{[t_1,t_2]}$ denote a singular arc, an arc $r = 0$, and an arc $u = 0$ on some time interval $[t_1, t_2]$.

**Proposition 4.3.** *Consider an extremal trajectory starting at some point $(x_0, \overline{s}, v_0) \in E$ at time 0 with $v_0 < v_m$ and which contains a singular arc on some time interval $[0, t_1]$. If the trajectory is optimal, then it is singular until the maximal volume.*

*Proof.* Without any loss of generality, we may assume that the trajectory is singular until the time $t_1$ and that $v(t_1) < v_m$. From Lemma 4.7, the trajectory cannot switch to $u = 0$ at time $t_1$, therefore, if it is optimal, we necessarily have that $r = 0$ (a dilution) in a right neibourhood of $t_1$. If we have $r = 0$ until the maximal volume, we know from Lemma 4.5 that the trajectory is not optimal. Similarly, if the impulse does not reach the maximal volume, but if the extremal trajectory contains a sequence $I_{[t_1,t_2]}NF_{[t_2,t_3]}I_{[t_3,t_4]}$ with $0 < t_1 < t_2 < t_3 < t_4$, $v(t_3) < v_m$ and $s(t_3) > \overline{s}$, then we know from Lemma 4.6 that the trajectory is not optimal.

We deduce that the extremal trajectory necessarily consists of sequences of singular arcs followed by a dilution $r = 0$ and an arc $u = 0$ until $\overline{s}$. This means that there exists $t_2 > t_1$ such that $r = 0$ on $[t_1, t_2]$ with $s(t_2) > \overline{s}$, and that at time $t_2$, we have $u = 0$ until the singular arc which is reached at time $t_3$. Therefore, the only possibility for the trajectory is to contain a concatenation of sequences of type $S_{[0,t_1]}I_{[t_1,t_2]}NF_{[t_2,t_3]}$ until reaching the maximal volume $v_m$ (by a singular arc from Lemma 4.5).

We now prove that the existence of such a sequence implies a contradiction, which will prove that it is optimal for a trajectory to be singular until the maximal volume. Let $\varphi := \lambda_x - \lambda_s$.

**Claim 4.1.** *A sequence $I_{[t_1,t_2]}NF_{[t_2,t_3]}$ such that $s(t_1) = s(t_3) = \overline{s}$ satisfies $\varphi < 0$ on $[t_1, t_3]$.*

Let us prove Claim 4.1. From Lemma 4.4, we have $\varphi(t_1) < 0$ and $\varphi(t_2) < 0$. Now, as $u = 0$ on $[t_2, t_3]$, we have $\phi_1 = 0$ and $\varphi\mu(s)x = 1 + kx\lambda_x$ on this interval. Combining with the adjoint equation gives:

$$\dot{\varphi} = x\mu'(s)\varphi - \frac{1}{x}. \tag{4.26}$$

Assume that there exists $\tau \leq t_3$ such that $\varphi$ is vanishing. We can assume that $\varphi < 0$ on $[t_2, \tau)$ so that $\dot{\varphi}(\tau) \geq 0$. On the other hand, (4.26) implies that $\dot{\varphi}(\tau) = -\frac{1}{x(\tau)} < 0$, and we have a contradiction, which proves the claim.

**Claim 4.2.** *If a sequence $S_{[t_3,t_4]}$ satisfies $\varphi(t_3) < 0$, then we have $\varphi(t_4) < 0$.*

Let us prove Claim 4.2. On the interval $[t_3, t_4]$, we have $\phi_1 = \phi_2 = 0$ and $\mu'(\overline{s}) = 0$ which gives:

$$\dot{\varphi} = \frac{u_s}{v}\varphi - \frac{1}{x}, \tag{4.27}$$

where $u_s$ is the singular control (recall (4.14)). From (4.27) and Gronwall's Lemma, we obtain that $\varphi(t_3) < 0$ implies $\varphi(t_4) < 0$, as was to be proved.

To conclude the proof of the Proposition, note that from our assumption, there exists at least one sequence $S_{[0,t_1]}I_{[t_1,t_2]}NF_{[t_2,t_3]}$ as above. Combining Lemma 4.4, Claims 4.1 and 4.2, yields that $\varphi(t_1) < 0$, $\varphi(t_2) < 0$ and $\varphi(t_3) < 0$. By repeating this argument on each such sequence if necessary, we obtain that there exists a time $\overline{t} > 0$ such that $s(\overline{t}) = \overline{s}$, $v(\overline{t}) = v_m$, and $\varphi(\overline{t}) < 0$. Now, the transversality condition at the terminal time implies that

$$\varphi(t_f) = \frac{1}{\mu(s_{ref})x(t_f)} > 0,$$

which contradicts $\varphi(\overline{t}) < 0$ and Claim 4.1 (recall that Claim 4.1 together with $\varphi(\overline{t}) < 0$ implies $\varphi(t_f) < 0$). This concludes the proof. □

Let $\mathcal{C}_1$ the dilution curve which passes trough the point $(\overline{s}, v_m)$, and whose equation is given by $\gamma_1(s) := v_m \frac{s_{in}-\overline{s}}{s_{in}-s}$. The singular arc strategy is defined as follows.

**Definition 4.2.** *Let $(x_0, s_0, v_0) \in E$.*
*(i) If $v_0 \geq \gamma_1(s_0)$, the singular arc strategy coincides with the strategy fill and wait.*
*(ii) If $s_0 \leq \overline{s}$, and $v_0 < \gamma_1(s_0)$, the singular arc strategy consists of an impulse from $s_0$ to $\overline{s}$, followed by a singular arc until reaching $v = v_m$ and then an arc $u = 0$ until $s_{ref}$.*
*(iii) If $s_0 \geq \overline{s}$, the singular arc strategy consists of an arc $u = 0$ until reaching $\overline{s}$, a singular arc until $v = v_m$ and then an arc $u = 0$ until $s_{ref}$.*

**Theorem 4.2.** *For any point $(x_0, s_0, v_0) \in E$, the optimal feeding policy is the singular arc strategy.*

*Proof.* Let $(x_0, s_0, v_0) \in E$ with $v_0 < v_m$. First, assume that $s_0 < \overline{s}$. If, $v_0 > \gamma_1(s_0)$, Lemma 4.7 implies that $r = 0$ until $v_m$. In this case, the singular arc strategy coincides with the strategy fill and wait. If $v_0 < \gamma_1(s_0)$, Lemma 4.7 implies that $r = 0$ until reaching the singular arc. Otherwise, we would have a switching point to an arc $u = 0$ at some time $t_0$ with $v(t_0) < v_m$, $s(t_0) \leq \overline{s}$. As $v(t_0) < v_m$, the trajectory necessary contains a switching point to $r = 0$ at some time $t_1 > t_0$, and we can apply Lemma 4.7 to exclude this possibility. Now, Proposition 4.3 implies that the trajectory is singular until $v = v_m$.

Assume now that $s_0 > \overline{s}$. From corollary 4.1 and Lemma 4.6, we have $u = 0$ until the singular arc. From Proposition 4.3, the trajectory remains singular until $v_m$, which ends the proof. □

We now give the cost associated to this strategy. When $s_0 < \overline{s}$ and $v_0 < \gamma_1(s_0)$, we call $x_0'$ the concentration of biomass corresponding to a dilution from $s_0$ to $\overline{s}$, $v_0'$ the new volume, and $x_0''$ the biomass concentration at the end of the singular arc (at volume $v_m$):

$$x_0' = x_0 \frac{s_{in} - \overline{s}}{s_{in} - s_0}, \quad v_0' = v_0 \frac{s_{in} - s_0}{s_{in} - \overline{s}}, \quad x_0'' = \overline{x} + \frac{v_0'}{v_m}(x_0' - \overline{x}).$$

When $s_0 > \overline{s}$, we call $\tilde{x}_0'$ the concentration of biomass corresponding to an arc $u = 0$ until $\overline{s}$, and $\tilde{x}_0''$ the concentration of biomass at the end of the singular arc (at volume $v_m$):

$$\tilde{x}_0' = x_0 + s_0 - \overline{s} + k \int_{s_0}^{\overline{s}} \frac{d\sigma}{\mu(\sigma)}, \; \tilde{x}_0'' = \overline{x} + \frac{v_0}{v_m}(\tilde{x}_0' - \overline{x})$$

The cost of the singular arc strategy is:

$$\omega(x_0, s_0, v_0) = \begin{cases} w(x_0, s_0, v_0), & \text{if } v_0 \geq \gamma_1(s_0), \\ \frac{1}{\beta} \ln\left(\frac{x_0' v_0' + \overline{x}(v_m - v_0')}{x_0 v_0}\right) + \int_{\overline{s}}^{s_{ref}} \frac{-ds}{\mu(s)[x_0'' + \int_{\overline{s}}^{s} \frac{k - \mu(\sigma)}{\mu(\sigma)} d\sigma]}, & \text{if } v_0 < \gamma_1(s_0), \\ \int_{s_0}^{\overline{s}} \frac{-ds}{\mu(s)[x_0 + s_0 - s + k \int_{s_0}^{s} \frac{d\sigma}{\mu(\sigma)}]} + \frac{1}{\beta} \ln\left[\frac{\tilde{x}_0' v_0 + \overline{x}(v_m - v_0)}{\tilde{x}_0' v_0}\right] & \\ \qquad + \int_{\overline{s}}^{s_{ref}} \frac{-ds}{\mu(s)[\tilde{x}_0'' + \int_{\overline{s}}^{s} \frac{k - \mu(\sigma)}{\mu(\sigma)}]}, & \text{if } s_0 > \overline{s}. \end{cases} \tag{4.28}$$

Theorem 4.2 implies the following result.

**Theorem 4.3.** *The feedback control law $\mathbf{u}_{SA}$ given by*

$$\mathbf{u}_{SA}(s_0, x_0, v_0) := \begin{cases} (0, u), & \text{if } s_0 < \overline{s}, \; v_0 < v_m, \\ (1, u_s(v)), & \text{if } s = \overline{s}, \; v_0 < v_m, \\ (1, 0), & \text{if } v_0 = v_m \text{ or } s_0 > \overline{s}, \end{cases} \tag{4.29}$$

*is optimal, and the value function associated to* (4.4) *satisfies $\mathbf{v} = \omega$.*

*Proof.* The result is a traduction in term of feedback control of Theorem 4.2. Note that in (4.29), $u$ is any measurable control taking values in $[0, 1]$ such that its integral on the period of the dilution is equal to $v_m - v_0$ (see Defintion 4.2). □

## 4.5 Fed-batch bioreactor with mortality and recycle

In this section, we investigate the case where both coefficients $k$ and $k'$ are non-zero. So, in the impulsional framework, (2.1) becomes:

$$\begin{cases} \dot{x} = \left(r[\mu(s) - k] - \frac{u}{v}\right) x, \\ \dot{s} = r[-\mu(s) + k']x + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u. \end{cases} \tag{4.30}$$

Now, by setting $\nu(s) := \mu(s) - k'$, (4.30) becomes:

$$\begin{cases} \dot{x} = \left(r[\nu(s) - k''] - \frac{u}{v}\right) x, \\ \dot{s} = -r\nu(s)x + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u, \end{cases} \tag{4.31}$$

where $k'' = k - k' > 0$. In view of Proposition 2.1, we can apply the result of Theorem 4.1 and 4.3 to the system (4.31) on the domain $E_m \subset E$ (in the case of a Monod growth function) or $E_\alpha \subset E$ (in the case of a Haldane growth function). Indeed, both domains $E_m$ and $E_\alpha$ remain invariant for (4.31). Moreover, if $\mu$ is of type Monod, then $\nu$ is increasing on $[\tilde{s}_1, +\infty]$, and if $\mu$ is of type Haldane, $\nu$ is increasing on $[\tilde{s}'_1, \overline{s}]$, and decreasing over $[\overline{s}, s_{in}]$. So, we can apply the optimality result on these sets with $\nu$ in place of $\mu$.

**Theorem 4.4.** *(i) When $\mu$ is of type Monod, the strategy fill and wait is optimal in the domain $E_m$.*
*(ii) When $\mu$ is of type Haldane, the singular arc strategy is optimal in the domain $E_\alpha$.*

## 4.6 Numerical simulations

Finally, we have compared the cost of the optimal strategy with respect to the initial volume value and the mortality coefficient $k$ in order to measure the effect of the mortality on the system. Numerical results are depicted in tables 2,3 for $k = 0, 10^{-4}, 10^{-3}$, see also Fig. 3. As expected, the time of the optimal strategy is increasing as a function of $k$ and decreasing with respect to $v_0$. When $k$ is small and when the initial volume is close to the target, the time of the optimal trajectory is close to the optimal one with $k = 0$. Notice also that even if $k$ is small, the time to reach the target significantly differs with the one with $k = 0$ when the initial point is far from the target.

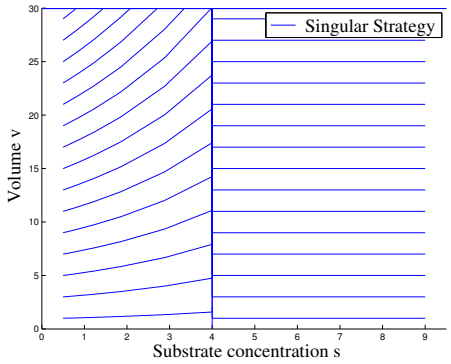


Figure 3: Plot of the projection of the singular arc strategy into the plane $(s, v)$ in the impulsional framework for different initial volume values, with a mortality coefficient $k = 10^{-4}$. Parameter values (arbitrary units) of simulations are taken as follows: $h_0 = 0.033$, $h_1 = 4$, $h_2 = \frac{1}{4}$, $s_{in} = 10$, $s_{ref} = 0.1$, $v_m = 30$, $x_0 = 13$.

Table 2: Time $t_k(v_0)$ of the singular arc strategy with $s_0 = 9$ and $k_0 = 0$, $k_1 = 10^{-4}$, $k_2 = 10^{-3}$.

| $v_0$ | 1 | 5 | 9 | 13 | 17 | 21 | 25 | 29 |
|---|---|---|---|---|---|---|---|---|
| $t_{k_0}(v_0)$ | 310.1651 | 167.2351 | 117.1540 | 86.8963 | 65.5134 | 50.3793 | 37.8862 | 21.1462 |
| $t_{k_1}(v_0)$ | 312.2648 | 168.1458 | 117.6926 | 87.2484 | 65.7451 | 50.4975 | 37.9331 | 21.1720 |
| $t_{k_2}(v_0)$ | 332.5485 | 176.9264 | 122.7791 | 90.5304 | 67.8569 | 52.8893 | 38.3771 | 21.4075 |

Table 3: Time $t_k(v_0)$ of the singular arc strategy with $s_0 = 0.5$ and $k_0 = 0$, $k_1 = 10^{-4}$, $k_2 = 10^{-3}$.

| $v_0$ | 1 | 5 | 9 | 13 | 17 | 21 | 25 | 29 |
|---|---|---|---|---|---|---|---|---|
| $t_{k_0}(v_0)$ | 314.8341 | 179.7194 | 135.5225 | 110.7341 | 93.7733 | 81.4263 | 71.9633 | 64.4641 |
| $t_{k_1}(v_0)$ | 316.9834 | 180.6965 | 136.1483 | 111.1780 | 94.1084 | 81.6887 | 72.1743 | 64.6373 |
| $t_{k_2}(v_0)$ | 338.4241 | 190.5360 | 142.9312 | 115.8383 | 97.7176 | 84.5983 | 74.5905 | 66.6930 |

# 5 Conclusions

When the singular arc is not always controllable, the optimal synthesis slightly differs from the case with controllability. In particular, it is not optimal to follow the singular arc until the maximal possible volume, which goes against the intuition. Moreover, when $k > 0$ and $k' = 0$, the optimality result of [9] can be transposed for any value of $k$ to this case. When both $k$ and $k'$ are positive, we see that our optimality result requires the reference concentration to be higher than a certain value. Also, we can conclude that the optimal feedback control law which is either Bang-Bang (for Monod growth function) or singular (for Haldane growth function) is robust in presence of mortality and recycling effects. In fact, when these parameters are not exactly known, this result shows that the optimal synthesis obtained in [3] still holds.

# Acknowledgments

The authors are grateful to A. Rapaport for helpful discussions on the paper. The authors would like to thank C. Lobry and J. Moreno for helpful discussions on the subject.

# References

[1] Betancur MJ, Moreno JA, Moreno-Andrade I, Buitrón G. Practical optimal control of fed-batch bioreactors for the waste water treatment. Internat. J. Robust Nonlinear Control 2006; **16**(3):173–190, doi: 10.1002/rnc.1046.

[2] Dochain D, Rapaport A. Minimal time control of fed-batch processes with growth functions having several maxima. IEEE Trans. Automat. Control 2011; **56**(11):2671–2676, doi:10.1109/TAC.2011.2159424.

[3] Moreno J. Optimal time control of bioreactors for the wastewater treatment. Optimal Control Appl. Methods 1999; **20**(3):145–164, doi:10.1002/(SICI)1099-1514(199905/06)20:3¡145::AID-OCA651¿3.0.CO;2-J.

[4] Miele A. Application of Green's Theorem to the extremization of linear integrals. Symp. on Vehicle Systems Optimization, Garden City: New York, 1961.

[5] Boscain U, Piccoli B. *Optimal syntheses for control systems on 2-D manifolds*, *Mathématiques & Applications (Berlin) [Mathematics & Applications]*, vol. 43. Springer-Verlag: Berlin, 2004.

[6] Monod J. Recherches sur la Croissance des Cultures Bactériennes. Hermann: Paris, 1942.

[7] Smith HL, Waltman P. The Theory of the Chemostat, Dynamics of Microbial Competition, Cambridge Studies in Mathematical Biology, vol. 13. Cambridge University Press: Cambridge, 1995, doi: 10.1017/CBO9780511530043.

[8] Bayen T, Gajardo P, Mairet F. Optimal synthesis for the minimal time control problems of fed-batch processes for growth functions with two maxima. J. Optim. Theory Appl. 2012; doi:DOI 10.1007/s10957-012-0225-0. URL `http://hal.archives-ouvertes.fr/hal-00655534/`.

[9] Gajardo P, Ramírez C, Rapaport A. Minimal time sequential batch reactors with bounded and impulse controls for one or more species. SIAM J. Control Optim. 2008; **47**(6):2827–2856, doi:10.1137/070695204.

[10] Rishel RW. An extended Pontryagin principle for control systems whose control laws contain measures. J. Soc. Indust. Appl. Math. Ser. A Control 1965; **3**:191–205.

[11] Lee J, Lee SY, Park S, Middelberg PJ. Control of fed-batch fermentations. Biotechnology advances 1999; **17**(11):29–48.

[12] Bayen T, Gajardo P, Mairet F. Minimal time control of fed-batch bioreactor with product inhibition. 20th Mediterranean Conference on Control and Automation: Barcelona, 2012. URL `http://hal.archives-ouvertes.fr/hal-00734225/`.

[13] Lee EB, Markus L. *Foundations of optimal control theory*. John Wiley & Sons Inc.: New York, 1967.

[14] Robbins HM. A generalized Legendre-Clebsch condition for the singular cases of optimal control. IBM J. of Research and Development 1967; **11**:361–372.

[15] Bardi M, Capuzzo-Dolcetta I. *Optimal control and viscosity solutions of Hamilton-Jacobi-Bellman equations*. Systems & Control: Foundations & Applications, Birkhäuser Boston Inc.: Boston, MA, 1997, doi:10.1007/978-0-8176-4755-1. With appendices by Maurizio Falcone and Pierpaolo Soravia.