Fed-batch bioreactor with mortality rate

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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. Our objective is to study the effect of mortality and recycling on the optimal synthesis. We provide an optimal synthesis of the problem using Pontryagin maximum principle, which extends the result of Moreno in the impulsive framework with mortality and recycling effect.

Keywords: Waste treatment, Optimal Control, Minimum time control, Singular control, Impulse.

1. INTRODUCTION

Our objective in this work is to find an optimal feeding strategy for the minimal time problem of a fed-batch bioreactor. The novelty 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 Moreno [1999], 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 Moreno [1999]. Finding an issue to the optimal synthesis can be performed using a combination of Greens' Theorem in the plane (see Miele [1961]) and Pontryagin maximum principle (see e.g. Boscain and Piccoli [2004]). When the growth function μ is of type Monod or Haldane, and when both mortality and recycling are negligible, the optimal synthesis obtained by Moreno [1999] goes as follows. In the case of Monod growth function, the optimal strategy is *bang-bang* (we call it also *fill and wait*). In the case of Haldane growth function, the optimal synthesis consists in reaching the concentration $\overline{s}$ corresponding to the maximal value of μ, and keeping the substrate concentration equal to this value until reaching the maximal volume of the reactor (singular arc). The previous results have been extended in the impulsive framework to the case where the growth function is of type Monod or Haldane (see Gajardo et al. [2008]), and to the case where the growth function has two local maxima defining two different singular arcs (see Bayen et al. [2012]).

Our aim in this work is to find an issue to the minimal time problem when both parameters k and k' can be nonzero. 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, which will significantly change the analysis in comparison with Gajardo et al. [2008], Bayen et al. [2012]. When k is a very small parameter (i.e. when the mortality is small with respect to the growth), we can expect the optimal synthesis to have similarities to the one obtained in Moreno [1999]. Actually, our main result is Theorem 15 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), see Theorem 14, and when the growth function is of type Haldane, then the optimal strategy is the singular arc strategy, see Theorem 13.

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 consider the problem with mortality rate in the impulsive framework (we first neglige the recycling coefficient), and we prove the optimality of the singular arc strategy for Haldane growth function. As a consequence, we obtain that the bang-bang strategy is optimal for Monod growth function (see Theorems 13 and 14). Finally, we provide the optimal synthesis of the problem with both mortality and recycling coefficients, which is a consequence of the previous results (where only mortality is considered).

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2. PRESENTATION OF THE MODEL

We consider the following controlled system describing a perfectly mixed reactor operated in fed-batch (see Moreno [1999], Gajardo et al. [2008]) with a mortality rate $k > 0$ for the biomass and a recycling rate $k' := \alpha k$ $(0 < \alpha < 1)$ of the substrate:

$$\begin{cases} \dot{x} = \left(\mu(s) - k - \frac{u}{v}\right) x, \\ \dot{s} = [-\mu(s) + k']x + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u. \end{cases} \tag{1}$$

Here x is the concentration of biomass, s the concentration of substrate, and v 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 input flow 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 input flow 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 μ of type Monod, we have: $\mu(s) = \overline{\mu}\frac{s}{k_1+s}$.
- For a growth function μ 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 μ 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 μ is of type Monod, then we assume that k is such that:

$$k < \overline{\mu}. \tag{2}$$

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

Hypothesis 2.2. If μ is of type Haldane, then we assume that k is such that:

$$k < \mu(\overline{s}). \tag{3}$$

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 also assume (in the case of Haldane) that the input substrate concentration s_{in} satisfies:

$$\tilde{s}'_2 \geq s_{in}. \tag{4}$$

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

Proposition 1. (i) In the case where μ is of type Monod, the domain

$$E_m := \mathbb{R}^*_+ \times [\tilde{s}_1, s_{in}] \times \mathbb{R}^*_+, \tag{5}$$

is invariant by (1).
(ii) In the case where μ is of type Haldane, and under assumption (4), the set

$$E_\alpha := \mathbb{R}^*_+ \times [\tilde{s}'_1, s_{in}] \times \mathbb{R}^*_+, \tag{6}$$

is invariant by (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 (6). The proof of the Proposition is based on the following lemma (which is a simple consequence of Gronwall's Lemma).

Lemma 2. Consider the ordinary differential equation (ODE):

$$\dot{y} = f(t, y), \tag{7}$$

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 (7).

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

$$\mathcal{T} := \mathbb{R}^*_+ \times [0, s_{ref}] \times \{v_m\}, \tag{8}$$

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

- If μ is of type Monod, we assume that $s_{ref} > \tilde{s}_1$.
- If μ 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_α (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 μ is of type Monod) or $\tilde{s}'_1$ (when μ 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.
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 (1) from an initial condition $(x_0, s_0, v_0) \in \mathbb{R}^*_+ \times \mathbb{R}^*_+ \times \mathbb{R}^*_+$ to the target $\mathcal{T}$:

$$\inf_{u \in \mathcal{U}} t_f(u) \text{ s.t. } (x(t_f(u)), s(t_f(u)), v(t_f(u))) \in \mathcal{T}. \tag{9}$$

If $k = 0$, the system (1) can be gathered into a two-dimensional one (see e.g. Moreno [1999], Bayen et al. [2013]) by considering the conserved quantity

$$M := v(x + s - s_{in}) = v_0(x_0 + s_0 - s_{in}). \tag{10}$$

When $k > 0$ and $\alpha > 0$, we cannot reduce the system into a two-dimensional system. Indeed, we have:

$$\dot{M} = -k(1 - \alpha)xv < 0, \tag{11}$$

hence M is strictly decreasing, and the same reduction is not possible for system (1).

3. OPTIMALITY RESULTS FOR THE IMPULSIVE SYSTEM

Following Bayen et al. [2012], Gajardo et al. [2008], we consider an extension of the minimal time problem both with mortality and recycling coefficients allowing impulse controls in (1). From a practical point of view, this assumption corresponds to a maximum input flow rate $u_m \gg \sup_{s \in [0, s_{in}]} \mu(s)$. This framework allows also to compute easily the value function corresponding to the different strategies, and also to split the biological part and the dilution part in (1). We will 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 essentially on the case $\alpha = 0$ (see subsection 3.5 when $\alpha \neq 0$).

3.1 Statement of the problem

We first make a brief review of the impulsive framework (see e.g. Bayen et al. [2012], Gajardo et al. [2008]). We consider the initial system (1) with an additional control r which plays the role of an impulse control:

$$\begin{cases} \dot{x} = \left(r[\mu(s) - k] - \frac{u}{v}\right)x, \\ \dot{s} = -r\mu(s)x + \frac{u}{v}(s_{in} - s), \\ \dot{v} = u. \end{cases} \tag{12}$$

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 (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 (1), and any measurable control u satisfying the condition:

$$\int_{\tau_-}^{\tau_+} u(t)dt = v_+ - v_-, \tag{13}$$

see Gajardo et al. [2008] for more details. In particular, there is no uniqueness of u as long as integral (13) is equal to $v_+ - v_-$. An addition of volume $v_+ - v_-$ corresponds to a *dilution* of the substrate and the biomass:

$$s_+ = \frac{v_-}{v_+}s_- + \left(1 - \frac{v_-}{v_+}\right)s_{in}, \; x_+ = \frac{v_-}{v_+}x_-, \tag{14}$$

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. For $\xi = (x, s, v) \in E$ 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:

$$\inf_{\mathbf{u} \in \mathcal{U}_\mathbf{i}} \int_0^{t_{\xi_0}(\mathbf{u})} r(\tau)d\tau, \tag{15}$$
$$\text{s.t. } (x(t_{\xi_0}(\mathbf{u})), s(t_{\xi_0}(\mathbf{u})), v(t_{\xi_0}(\mathbf{u}))) \in \mathcal{T},$$

see Gajardo et al. [2008] for more details on the parametrization of the minimum time problem with impulsive controls. Similarly as for (**??**), 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} if necessary). We can also prove by Fillipov's Theorem (see Lee and Markus [1967]) that there exists an optimal control for (15) in the class of *relaxed controls* taking values within the convex set $\Omega' := [0,1] \times [0,1] \setminus \{(0,0)\}$. In the following, we apply Pontryagin maximum principle with control in Ω'. We will see in the sections 3.4 and 3.3 that an optimal feedback control $\mathbf{u}$ necessarily satisfies $r \in \{0,1\}$.

3.2 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

$$\begin{aligned} H := & r\left[(\lambda_x - \lambda_s)\mu(s)x - kx\lambda_x + \lambda_0\right] \\ & + u\left[\lambda_v + \frac{\lambda_s(s_{in} - s) - \lambda_x x}{v}\right]. \end{aligned} \tag{16}$$

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 $(\lambda_0, \lambda(\cdot)) \neq 0$, λ 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:

$$\begin{cases} \dot{\lambda}_x = -r(\lambda_x - \lambda_s)\mu(s) + rk\lambda_x + \frac{u}{v}\lambda_x, \\ \dot{\lambda}_s = -r(\lambda_x - \lambda_s)x\mu'(s) + \frac{u}{v}\lambda_s, \\ \dot{\lambda}_v = \frac{(s_{in} - s)\lambda_s - x\lambda_x}{v^2}u, \end{cases} \tag{17}$$

and such that we have the maximization condition:

$$\mathbf{u}(t) \in \text{argmax}_{\mathbf{v} \in \mathbf{\Omega}'} H(\xi(t), \lambda(t), \lambda_0, \mathbf{v}), \tag{18}$$

for a.e. $t \in [0, t_f]$. The transversality condition reads as:

$$\lambda(t_f) \in -N_\mathcal{T}(\xi(t_f)),$$

where $N_\mathcal{T}(\xi)$ denotes the normal cone to $\mathcal{T}$ at the point $\xi(t_f)$ (see e.g. Vinter [2000]). In particular, as $x(t_f)$ is free, we obtain $\lambda_x(t_f) = 0$. 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 λ_0 is non-zero can be proved as in Bayen et al. [2012]). An extremal trajectory is a quadruplet $(\xi(\cdot), \lambda(\cdot), \mathbf{u}(\cdot), \mathbf{t_f})$ satisfying (12)-(17)-(18). As we deal with a minimal time problem, the Hamiltonian is zero along an extremal trajectory. Let ϕ_1 (resp. ϕ_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 ϕ_1 and ϕ_2. For a.e. $t \in [0, t_f]$, we have by (18):

$$\begin{cases} \phi_1 \leq 0 \text{ and } \phi_2 = 0 \Longrightarrow \; r = 0, \\ \phi_2 \leq 0 \text{ and } \phi_1 = 0 \Longrightarrow \; u = 0, \end{cases} \tag{19}$$

and we have also:

$$r(t)\phi_1(t) + u(t)\phi_2(t) = 0, \tag{20}$$

for a.e. $t \in [0, t_f]$, hence ϕ_1 and ϕ_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 Bayen et al. [2012]). When $\phi_1 = \phi_2 = 0$ on some time interval, then, we say that the trajectory has a *singular arc*. By differentiating, we obtain:

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

where

$$\psi := \frac{x(s_{in} - s)}{v}(\lambda_s - \lambda_x)\mu'(s). \tag{21}$$

When the derivative of the growth function μ admits a zero (typically in the case where μ 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 $k = 0$.

Lemma 3. Let $I = [t_1, t_2]$ a singular arc. Then, we have $s(t) = \overline{s}$ for $t \in [t_1, t_2]$ where $\overline{s}$ is such that $\mu'(\overline{s}) = 0$.

Proof. We have $\phi_1(t) = \phi_2(t) = 0$ for all $t \in I$. By differentiating, 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 gives $-kx\lambda_x + 1 = 0$ contradicting the fact that λ_x is vanishing on J. Consequently, we have $\mu'(s(t)) = 0$ for all $t \in I$, which proves the Lemma. □

To study properties of singular arcs (in the Haldane case), we define:

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

By using the fact that $\dot{s} = 0$ along a singular arc, we obtain the next proposition.

Proposition 4. 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, if $v_1 := v(t_1)$, the concentration of biomass and the singular control u_s to steer the system from a volume v_0 to a volume $v \in [v_0, v_1]$ are given by:

$$x(v) = \frac{v_0}{v} x_0 + \left[1 - \frac{v_0}{v}\right]\overline{x},\ u_s(v) = \alpha x v. \quad (22)$$

Moreoever, the corresponding time $t_1 = t_1(v_1, x_0, v_0)$ is given by:

$$t_1(v_1, x_0, v_0) = t_0 + \frac{1}{\beta}\ln\left(\frac{x_0 v_0 + \overline{x}[v_1 - v_0]}{x_0 v_0}\right). \quad (23)$$

Next, we assume the following condition that will ensure the controllability of the singular arc with a control $r = 1$ for (12) (see also Dochain and Rapaport [2011], Bayen et al. [2012]):

Hypothesis 3.1. Initial conditions in E are such that:

$$\mu(\overline{s})\left[\frac{M_0}{s_{in} - \overline{s}} + v_m\right] \leq 1, \quad (24)$$

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

Notice that along a trajectory, we have $M = v(x + s - s_{in})$, where M is strictly decreasing by (11). Together with (22), 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 3.1. It follows that this hypothesis guarantees that the singular control satisfies the bound $u_s \leq 1$.

3.3 Optimality result for Haldane growth function

We assume in this subsection that μ is of Haldane type, and that $\overline{s} > s_{ref}$. We will prove that the singular arc strategy (see Definition 3.1) is optimal for any value of k using Pontryagin maximum principle. The proof relies on the exclusion of extremal trajectories.

The next lemma gives properties of the trajectory during an impulse of volume and is fundamental in the following.

Lemma 5. 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:

$$[\lambda_x^0 - \lambda_s^0][\mu(s(t_1)) - \mu(s_0)] \geq 0, \quad (25)$$

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

$$\phi_1 = (\lambda_x^0 - \lambda_s^0)x_0\mu(s) - 1 - kx_0\lambda_x^0. \quad (26)$$

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 (26). □

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 6. 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 λ_x is decreasing, and using $\lambda_x(t_f) = 0$, 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 (25), 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 25 that along the impulse, we have $\lambda_x - \lambda_s = \frac{v}{v_0}[\lambda_x^0 - \lambda_s^0]$. Thus, at time t_1, we get $\lambda_x(t_1) - \lambda_s(t_1) = \frac{v_m}{v_0}[\lambda_x^0 - \lambda_s^0] < 0$, which is a contradiction. □

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 7. 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 (21) 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 5, 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 8. 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 ϕ_2 satisfies $\dot{\phi}_2 = \psi$, therefore we get $\lambda_s(t_0) - \lambda_x(t_0) \geq 0$. From Lemma 5, we obtain that $\lambda_x(t_0) - \lambda_s(t_0) > 0$ (because μ 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 the substrate concentration cannot decrease until $s = \overline{s}$ with a control $u = 0$ at a volume value $v_0 < v_m$. 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 $r = 0$ (Impulse), and an arc $u = 0$ (No Feeding) on some time interval $[t_1, t_2]$.

Proposition 9. 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 8, 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 neighborhood of t_1. If we have $r = 0$ until the maximal volume, we know from Lemma 6 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 7 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 6).

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 10. 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 10. From Lemma 5, 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:

$$\dot{\varphi} = x\mu'(s)\varphi - \frac{1}{x}. \tag{27}$$

Assume that there exists $\tau \leq t_3$ such that φ is vanishing. We can assume that $\varphi < 0$ on $[t_2, \tau)$ so that $\dot{\varphi}(\tau) \geq 0$. On the other hand, (27) implies that $\dot{\varphi}(\tau) = -\frac{1}{x(\tau)} < 0$, and we have a contradiction, which proves the claim.

Claim 11. If a sequence $S_{[t_3,t_4]}$ satisfies $\varphi(t_3) < 0$, then we have $\varphi(t_4) < 0$.

Let us prove Claim 11. On the interval $[t_3, t_4]$, we have $\phi_1 = \phi_2 = 0$ and $\mu'(\overline{s}) = 0$ which gives:

$$\dot{\varphi} = \frac{u_s}{v}\varphi - \frac{1}{x}, \tag{28}$$

where u_s is the singular control (recall (22)). From (28) 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 5, Claims 10 and 11, 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 10 (recall that Claim 10 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 $(\overline{s}, v_m)$ in the plane (s, v), 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 3.1. Let $(x_0, s_0, v_0) \in E$.
(i) If $v_0 \geq \gamma_1(s_0)$, the singular arc strategy consists of an impulse to $v = v_m$, followed by an arc $u = 0$ until s_{ref}.
(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 12. 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 8 implies that $r = 0$ until v_m. If $v_0 < \gamma_1(s_0)$, Lemma 8 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 necessarily contains a switching point to $r = 0$ at some time $t_1 > t_0$, and we can apply Lemma 8 to exclude this possibility. Now, Proposition 9 implies that the trajectory is singular until $v = v_m$.

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Assume now that $s_0 > \overline{s}$. From Lemma 7, we have $u = 0$ until the singular arc. From Proposition 9, the trajectory remains singular until v_m, which ends the proof. □

Theorem 12 implies the following result.

Theorem 13. In the Haldane case, the feedback control law $\mathbf{u}_{SA}$ given by

$$\mathbf{u}_{SA}(s_0, x_0, v_0) := \begin{cases} (0, u), & \text{if } s_0 < \overline{s},\ v_0 < v_m, \\ (1, u_s(v)), & \text{if } s = \overline{s},\ v_0 < v_m, \\ (1, 0), & \text{if } v_0 = v_m \text{ or } s_0 > \overline{s}, \end{cases} \tag{29}$$

is optimal.

Proof. The result is a rephrasing in term of feedback control of Theorem 12. Note that in (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 Definition 13). □

3.4 Optimality result for Monod growth function

We now consider the case where the growth function is of type Monod. Using similar arguments as in the Haldane case, we can prove that the strategy "fill and wait" (see Definition 3.2) is optimal for any value of $k > 0$.

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 (see Eq.(14)).

Definition 3.2. 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 $s_0' > s_{ref}$.

Theorem 14. In the Monod case, the feedback control law $\mathbf{u}_{FW}$ given by

$$\mathbf{u}_{FW}(s_0, x_0, v_0) := \begin{cases} (0, u), & \text{if } v_0 < v_m, \\ (1, 0), & \text{if } v_0 = v_m \text{ and } s_0 > s_{ref}, \end{cases} \tag{30}$$

is optimal.

The proof of this result relies on similar arguments as in the Haldane case, and we have not detailed the proof for brevity.

3.5 Fed-batch bioreactor with mortality and recycle

In this section, we investigate the case where both coefficients k and k' are non-zero. In the impulsive framework, (1) becomes:

$$\begin{cases} \dot{x} = \left(r[\mu(s) - k] - \dfrac{u}{v} \right) x, \\ \dot{s} = r[-\mu(s) + k']x + \dfrac{u}{v}(s_{in} - s), \\ \dot{v} = u. \end{cases} \tag{31}$$

Now, by setting $\nu(s) := \mu(s) - k'$, (31) becomes:

$$\begin{cases} \dot{x} = \left(r[\nu(s) - k''] - \dfrac{u}{v} \right) x, \\ \dot{s} = -r\nu(s)x + \dfrac{u}{v}(s_{in} - s), \\ \dot{v} = u, \end{cases} \tag{32}$$

where $k'' = k - k' > 0$. In view of Proposition 1, we can apply the result of Theorem 14 and 13 to the system (32) 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_α remain invariant for (32). Moreover, if μ is of type Monod, then ν is increasing on $[\tilde{s}_1, +\infty]$, and if μ is of type Haldane, ν 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 ν in place of μ. We thus obtain the following theorem.

Theorem 15. (i) When μ is of type Monod, the strategy fill and wait is optimal in the domain E_m.
(ii) When μ is of type Haldane, the singular arc strategy is optimal in the domain E_α.

4. CONCLUSIONS

In this work, we have extended the result of Moreno [1999] in presence of mortality and nutrient recycling. Thanks to Pontryagin maximum principle, we could characterize similarly the optimal feedback control in this framework. 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 Moreno [1999] still holds. We hope that this kind of analysis could be extended to more general situations, in particular when the recycling effect includes a delay.

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