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# Stochastic modeling and control of bioreactors $\star$

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**Abstract:** In this work we propose a stochastic model for a sequencing-batch reactor (SBR) and for a chemostat. Both models are described by systems of Stochastic Differential Equations (SDEs), which are obtained as limits of suitable Markov Processes characterizing the microscopic behavior. We study the existence of solutions of the obtained equations as well as some properties, among which the possible extinction of the biomass is the most remarkable feature. The implications of this behavior are illustrated in the problem consisting in maximizing the probability of reaching a desired depollution level prior to biomass extinction.

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## 1. INTRODUCTION

Since the works by Monod (1950) and Novick and Szilard (1950), bioreactors have been used to study microbial population dynamics, and the use of bioreactors for wastewater treatment and bioremediation has been widely studied for the last 40 years. Typically, there are three types of models for the analysis of a bioreactor-water resource system: the simplest from the mathematical point of view, that relies on the hypotheses of homogeneity of the concentrations in the resource and/or in the bioreactor as well as instant mixing (among others), is a system of nonlinear ordinary differential equations (ODE) (D'Ans et al. (1971, 1972); Smith and Waltman (1995)). Later, models with partial differential equations (PDE) that take into account fluid dynamics, mass conservation and pollutant diffusion have been introduced to address the inhomogeneity of the pollutant in the resource (Barbier et al. (2016)) or the bioreactor vessel (Diehl and Farås (2013b,a)); this effect naturally appears due to the speed of the reactions in the bioreactor and the slow diffusion speed as well as the slow mixing in large water resources; this is typically the situation of large scale reactors or large scale water resources. fluidized beds, settlers among others. The third kind of models are the stochastic models, that take into account

the uncertainty of different types of variables (Imhof and Walcher (2005); Campillo and Fritsch (2015); Collet et al. (2013)).

There are two main operation modes of the bioreactor for the water treatment. The sequencing-batch reactor (SBR) consists of a tank which is fed with a supply of nutritive elements at the beginning of and along the duration of the process. This type of system is widely used in the industrial and municipal wastewater treatment plants. With this operation mode, the objective of the controller is usually to attain a prescribed target in minimal time (Moreno (1999); Gajardo et al. (2008); Bayen et al. (2013)) or to maximize the production in a finite time interval (Hong (1986); Kurtanjek (1991); Tsoneva et al. (1998); Mazouni et al. (2010)). On the other hand, the chemostat mode of operation is the most widely used in bioremediation of water resources. The main characteristic is that the culture volume is constant, water with nutrient being added continuously to the system, and treated water being removed at the same rate. The reactor is operated in such a way to keep the system in a steady state by adding a constant nutrient concentration at a fixed rate, but the inflow rate can be *controlled* to change the desired steady state. The control objectives are usually to steer the system to a nominal point that maximizes a criterion (Zhang et al. (2003); Marcos et al. (2004); Bastin et al. (2009)) or to couple the reactor to a resource in order to treat it in minimal time (Gajardo et al. (2011, 2012); Ramírez et al. (2016)).

The deterministic model of bioreactor consists of the variables x, s, and v that denote the biomass and substrate concentration, and culture volume inside the bioreactor vessel. We assume that water with a concentration of

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nutrient  $s_{in}$  and without bacteria is poured into the bioreactor at an inflow rate  $u \in [0, u_{max}]$ . A standard assumption on the growth rate of microorganisms is that it is proportional to the mass of microorganisms and that it depends on the substrate concentration by means of the uptake function  $\mu(\cdot)$  (see Smith and Waltman (1995)). The yield coefficient of the reaction Y, which is the quantity of biomass produced when one unit of substrate is consumed by the reaction, is a positive constant. For the SBR the culture volume is bounded between a minimum volume  $v_{\min}$  assumed to be the lowest volume level of operation, and a maximum volume  $v_{\max}$  given by the maximum operative capacity of the tank. The usual deterministic model for the SBR is given by the equations

$$\begin{cases} \dot{x} = \mu(s)x - \frac{u}{v}x, \\ \dot{s} = -\frac{1}{Y}\mu(s)x + \frac{u}{v}(s_{\rm in} - s), \\ \dot{v} = u. \end{cases}$$
(1)

For the chemostat the input and output flow rates are equal, so the culture volume is assumed to be constant. The usual deterministic model of the chemostat is given by the equations

$$\begin{cases} \dot{x} = \left(\mu(s) - \frac{u}{v}\right)x, \\ \dot{s} = -\frac{1}{Y}\mu(s)x + \frac{u}{v}(s_{\rm in} - s). \end{cases}$$
(2)

In this work we extend these models to the stochastic case when there exists demographic stochasticity, that is, when the stochasticity comes from the randomness induced by the births and deaths in a large population. In the case of the stochastic SBR system, we show that the minimum expected time problem is meaningless, because with positive probability biomass extinction occurs. Thus, we are naturally led to consider the problem of maximizing the probability of reaching the target before extinction occurs. We sketch the proof of a Dynamic Programming Principle (DPP) for this problem. Analogous statements can be proved for the stochastic chemostat model but, for the sake of shortness, they will not be reproduced in this article.

We point out that the stochastic model we obtain, based on particle system approximations, allows us to justify the description of the dynamics of the macroscopic variables by means of a Stochastic Differential Equation (SDE). This is an important step, since then standard methods to dicretize SDEs can be implemented in order to approximate the stochastic dynamics. These discretizations can have a different scale than the original microscopic model, the latter being be difficult to handle numerically.

## 2. STOCHASTIC MODELS OF SBR AND CHEMOSTAT

In this section we want to establish continuous stochastic models for the SBR and the chemostat. We deduce the continuous model as a limit of individual-based birth and death processes including a *demographic stochasticity* parameter modelling fast birth and death rates of the microorganisms.

In what follows we denote by  $\hat{x}$  and  $\hat{s}$  the masses of microbial organism and substrate in the tank (in grams), and v the culture volume (in liters). Suppose that water with a concentration of substrate  $s_{in}$  is injected to (extracted from) the bioreactor's tank with an input flow rate (output flow rate)  $Q_{\rm in}$  ( $Q_{\rm out}$ ). The mixture in the bioreactor is continuously stirred by an agitator, so the distribution of cells and molecules in the tank can be assumed to be homogeneous. The changes of mass of each component are given by microscopical changes in the numbers of bacterial cells X and substrate molecules S, while the changes on the culture volume v are given by the continuous variation of the inflow and output flow rates. We suppose that the rate of change of the system (X, S) depends only of the current state of the system and of the volume at the current time t, and that two of the following events cannot occur at the same time: the division of a microbial cell, the death of a cell, the entry of a substrate molecule into the tank, and the consumption of a substrate molecule by a cell. For these reasons we model (X, S) as a time inhomogeneous birth and death process. Such process is determined by its jumps rate scheme, which is described as follows:

- the individual rate of the division of a cell depends of the concentration of available substrate at the time instant t by means of the growth function  $\mu(\hat{s}/v_t)$ ,
- the individual death rate of a cell is a constant β ≥ 0,
  the individual rate of exit of a cell (or a substrate molecule) is Q<sub>out</sub>/v<sub>t</sub>,
- the rate of entry of a substrate molecule is  $Q_{\rm in} s_{\rm in} K_s$ ,

where  $K_s$  is the amount of substrate molecules per gram, and the process of volume  $\hat{v}_t$  that starts with an initial volume  $v_0 \geq v_{\min} > 0$  is defined by

$$v_t = v_0 + \int_0^t (Q_{\rm in} - Q_{\rm out}) dr.$$

We will make the following assumption on the growth function  $\mu(\cdot)$ :

Assumption 1. The growth function  $\mu : [0, +\infty[ \mapsto [0, +\infty[$ is Lipschitz continuous, it satisfies that  $\mu(0) = 0$  and it is bounded by above by a constant  $\mu_{\max} > 0$ .

Since the number of particles of the system (X, S) is large, it is convenient to study the behavior of the system of mass  $(\hat{x}, \hat{s})$ . In order to do so, we introduce the scale parameter  $K := (K_x, K_s)$  whose components denote the numbers of cells and substrate molecules per gram respectively. Then, we can consider a discretization of the biomass and substrate mass given by  $\hat{x}^K := X/K_x$  and  $\hat{s}^K := S/K_s$ . The process  $(\hat{x}^K, \hat{s}^K)$  defined in that way has transitions in biomass (resp. substrate mass) of the size of  $1/K_x$  (resp.  $1/K_s$ ) and the jump rates on the biomass (resp. substrate mass) are of the order of  $K_x$  (resp.  $K_s$ ). This process takes values in the space  $D_K^2 := (\mathbb{Z}/K_x) \times (\mathbb{Z}/K_s)$ . When the components of K are large enough, the time evolution of the system of mass approaches to system that varies continuously in time. By means of this scaling we obtain a macroscopic limit model.

At the same time, due to the discrete nature of the individuals and the stochastic character of the process, we expect demographic randomness to occur at a macroscopic level. We introduce a parameter of demographic randomness  $\gamma \geq 0$  that models the variance of the birth and death rates of the bacterial population (Foley (1994)). For the SBR and the chemostat models, we introduce this demographic randomness as in Méléard and Villemonais (2012), where the analysis is carried out for a one dimensional state equation whose solution is conditioned to stay strictly positive.

## 2.1 SBR model

In this case the mode of operation is such that  $u := Q_{\text{in}} \in [0, u_{\text{max}}]$  and  $Q_{\text{out}} = 0$  (until  $v = v_{\text{max}}$ ), the rate scheme is given by the following expressions: denote by  $\hat{\xi} = (\hat{x}, \hat{s})$  a generic element in  $D_K^2$  at a time instant  $t \ge 0$ . The volume process is given by

$$v_t = v_0 + \int_0^t u_r dr. \tag{3}$$

The scheme of jumps of the process  $\eta^K$  can be summarized as follows:

• 
$$(\hat{x}, \hat{s}) \rightarrow \left(\hat{x} + \frac{1}{K_x}, \hat{s}\right)$$
 with rate  $K_x \hat{x} \left[\mu\left(\frac{\hat{s}}{v_t}\right) + \gamma K_x\right]$   
•  $(\hat{x}, \hat{s}) \rightarrow \left(\hat{x} - \frac{1}{K_x}, \hat{s}\right)$  with rate  $K_x \hat{x} \left[\beta + \gamma K_x\right]$ ,  
•  $(\hat{x}, \hat{s}) \rightarrow \left(\hat{x}, \hat{s} + \frac{1}{K_s}\right)$  with rate  $K_s s_{in} u$ ,  
•  $(\hat{x}, \hat{s}) \rightarrow \left(\hat{x}, \hat{s} - \frac{1}{K_s}\right)$  with rate  $K_x \hat{x} \mu \left(\frac{\hat{s}}{v_t}\right)$ .

This procedure generates a pure jump Markov process  $\eta_t^K := (\hat{x}_t^K, \hat{s}_t^K)$  that takes values in  $D_K^2$ . This process is characterized by its infinitesimal generator  $\mathscr{L}^K$ , which is the operator defined as follows: for  $\hat{\xi} = (\hat{x}, \hat{s}) \in D_K^2$ ,  $t \ge 0, \phi \in \mathscr{C}(\mathbb{R}^2)$ , and  $e_i$  the components of the canonical basis of  $\mathbb{R}^2$ ,

$$\mathscr{L}^{K}\phi(t,\hat{\xi}) = \lim_{h \searrow t} \frac{\mathbb{E}(\phi(\eta_{h}^{K}) \mid \eta_{t}^{K} = \hat{\xi}) - \phi(\hat{\xi})}{h - t}$$

that in this case has the explicit formula

$$\mathscr{L}^{K}\phi(t,\hat{\xi}) := K_{x}\hat{x}\left[\mu\left(\frac{\hat{s}}{v_{t}}\right) + \gamma K_{x}\right]\left[\phi\left(\hat{\xi} + \frac{e_{1}}{K_{x}}\right) - \phi(\hat{\xi})\right] \\ + K_{x}\hat{x}\left[\beta + \gamma K_{x}\right]\left[\phi\left(\hat{\xi} - \frac{e_{1}}{K_{x}}\right) - \phi(\hat{\xi})\right] \\ + K_{s}s_{\mathrm{in}}u\left[\phi\left(\hat{\xi} + \frac{e_{2}}{K_{s}}\right) - \phi(\hat{\xi})\right] \\ + K_{x}\hat{x}\mu\left(\frac{\hat{s}}{v_{t}}\right)\left[\phi\left(\hat{\xi} - \frac{e_{2}}{K_{s}}\right) - \phi(\hat{\xi})\right].$$

$$(4)$$

Notice that  $K_s/K_x = \frac{1/K_x}{1/K_s}$  denotes the amount of biomass generated by the consumption of one unit of substrate, which is by definition the yield coefficient Y. The scale parameters  $K_x, K_s$  can be expressed in terms of just one scale parameter  $K := K_x$  and Y as  $K_x = K$ ,  $K_s = YK$ .

An explicit pathwise representation of  $\eta^K$  as a semimartingale process can be obtained by applying Itô change of variable formula (see e.g. Ikeda and Watanabe (1981)):

$$\begin{cases} \hat{x}_{t}^{K} = \hat{x}_{0}^{K} + \int_{0}^{t} \left[ \hat{x}_{r}^{K} \mu \left( \frac{\hat{s}_{r}^{K}}{v_{r}} \right) - \hat{x}_{r}^{K} \beta \right] dr + M_{t}^{\gamma, K, (x)}, \\ \hat{s}_{t}^{K} = \hat{s}_{0}^{K} + \int_{0}^{t} \left[ us_{\text{in}} - \frac{1}{Y} \hat{x}_{r}^{K} \mu \left( \frac{\hat{s}_{r}^{K}}{v_{r}} \right) \right] dr + M_{t}^{\gamma, K, (s)}, \end{cases}$$
(5)

where  $M^{\gamma,K} = (M^{\gamma,K,(x)}, M^{\gamma,K,(s)})$  is a discontinuous local martingale associated to the process  $\eta^K$  whose quadratic variation terms can be explicitly computed:

$$\langle M^{\gamma,K,(x)} \rangle_t = \int_0^t 2\gamma \hat{x}_r^K dr + \frac{1}{K} \int_0^t \hat{x}_r^K \left[ \mu \left( \frac{\hat{s}_r^K}{v_r} \right) + \beta \right] dr,$$

$$\langle M^{\gamma,K,(s)} \rangle_t = \frac{1}{YK} \int_0^t \left[ s_{\rm in} u + \frac{1}{Y} \hat{x}_r^K \mu \left( \frac{\hat{s}_r^K}{v_r} \right) \right] dr,$$

$$\langle M^{\gamma,K,(x,s)} \rangle_t = 0.$$

$$(6)$$

It can be shown that  $\eta^K$  is non-explosive, i.e., almost surely,  $\eta_t^K$  is well-defined for all  $t \ge 0$ . The only term that is not divided by the scale parameter K is the first term of  $\langle M^{\gamma,K,(x)} \rangle$ , and as K tends to infinity, it is the only second order term that does not vanish. The limit process  $\eta^* := (\hat{x}_t, \hat{s}_t)_{t\ge 0}$  is shown to solve, in the weak sense, the Stochastic Differential Equation (SDE)

$$\begin{cases} d\hat{x}_t = \left(\mu\left(\frac{\hat{s}_t}{v_t}\right) - \beta\right)\hat{x}_t dt + \sqrt{2\gamma\hat{x}_t}dW_t, \\ d\hat{s}_t = \left(-\frac{1}{Y}\mu\left(\frac{\hat{s}_t}{v_t}\right)\hat{x}_t + us_{\rm in}\right)dt, \end{cases}$$
(7)

where v is given by (3) and  $(W_t)_{t\geq 0}$  is a standard onedimensional Brownian motion. This result is stated in the next proposition:

Proposition 2. Suppose Assumption 1 holds. The sequence of processes  $(\eta^K)_{K \in \mathbb{N}}$  with infinitesimal generator (4), and deterministic initial condition  $\eta_0^K = \hat{\xi}_0 = (\hat{y}, \hat{z})$ , is tight in  $\mathscr{P}(\mathbb{D}([0,\infty); \mathbb{R}^2))$  (the space of r.c.l.l. functions with values in  $\mathbb{R}^2$ ), and converges in distribution to a weak solution  $\eta^*$  of the stochastic differential equation (7) with the same initial condition  $\eta_0$ .

**Proof.** [Sketch of proof] We prove that the sequence of probability laws of the processes  $(\eta^K)_{K \in \mathbb{R}}$  is tight, and then there exists a law P on  $\mathbb{D}([0,\infty);\mathbb{R}^2)$  that is a weak limit of the sequence  $(\eta^K)_{K \in \mathbb{R}}$ . Using the pointwise convergence of the generators  $\mathscr{L}^K$  to the generator of (7), defined for  $\xi = (x, s)$  and  $\phi \in \mathscr{C}^2(\mathbb{R}^2)$  by the formula

$$\begin{split} \mathscr{L}\phi(t,\xi) = & \frac{\partial}{\partial x}\phi(\xi)\left(\mu\left(\frac{s}{v_t}\right) - \beta\right)x \\ & + \frac{\partial}{\partial s}\phi(\xi)\left(-\frac{1}{Y}\mu\left(\frac{s}{v_t}\right)x + us_{\mathrm{in}}\right) + \gamma x\frac{\partial^2}{\partial x^2}\phi(\xi), \end{split}$$

we prove that the limit law P is a solution of the martingale problem associated to (7), see e.g. (Karatzas and Shreve, 1991, Section 5.4), and thus, is a weak solution of (7).  $\Box$ 

Let us set  $\tilde{\gamma} := \sqrt{2\gamma}$  and define the limit process of concentrations  $(\eta_t)_{t\geq 0} = (x_t, s_t, v_t)_{t\geq 0}$ , where  $x_t := \hat{x}_t/v_t$ ,  $s_t := \hat{s}_t/v_t$ . Using Itô's formula (Ikeda and Watanabe, 1981, Theorem 1.5.5), we obtain that the dynamics of  $(\eta_t)_{t\geq 0}$  is characterized by the following SDE

$$\begin{cases} dx_t = \left[ \left( \mu(s_t) - \beta - \frac{u}{v_t} \right) x_t \right] dt + \tilde{\gamma} \sqrt{\frac{x_t}{v_t}} dW_t, \ t \ge 0, \\ ds_t = \left[ -\frac{1}{Y} \mu(s_t) x_t + \frac{u}{v_t} (s_{\rm in} - s_t) \right] dt, \\ dv_t = u dt. \end{cases}$$
(8)

Remark 3. If we suppose that  $\tilde{\gamma} = \gamma = 0$  (i.e. there is not demographic randomness), we recover the deterministic SBR model (1).

#### 2.2 Chemostat model

For the chemostat model we follow a similar approach than for the SBR case. In this case we have  $u := Q_{\text{in}} = Q_{\text{out}}$ , so the culture volume v is constant. Let us define as before  $\hat{x}_t^K$  the discretized biomass and  $\hat{s}_t^K$  the discretized substrate mass at a time instant t. The scheme of jumps and rates of the process  $\eta^K = (\hat{x}^K, \hat{s}^K)$  can be summarized as follows:

• 
$$(\hat{x}, \hat{s}) \rightarrow \left(\hat{x} + \frac{1}{K_x}, \hat{s}\right)$$
 with rate  $K_x \hat{x} \left[\mu\left(\frac{\hat{s}}{v}\right) + \gamma K_x\right]$ ,  
•  $(\hat{x}, \hat{s}) \rightarrow \left(\hat{x} - \frac{1}{K_x}, \hat{s}\right)$  with rate  $K_x \hat{x} \left[\beta + \gamma K_x + \frac{u}{v}\right]$ ,  
•  $(\hat{x}, \hat{s}) \rightarrow \left(\hat{x}, \hat{s} + \frac{1}{K_s}\right)$  with rate  $K_s s_{in} u$ ,

• 
$$(\hat{x}, \hat{s}) \rightarrow (\hat{x}, \hat{s} - \frac{1}{K_s})$$
 with rate  $K_x \hat{x} \mu \left(\frac{\hat{s}}{v}\right) + \frac{u}{v} \hat{s} K_s$ .

This process is characterized by its infinitesimal generator

$$\mathcal{L}^{K}\phi(\hat{\xi}) := \left[\phi\left(\hat{\xi} + \frac{e_{1}}{K_{x}}\right) - \phi(\hat{\xi})\right] K_{x}\hat{x} \left[\mu\left(\frac{\hat{s}}{v}\right) + \gamma K_{x}\right] \\ + \left[\phi\left(\hat{\xi} - \frac{e_{1}}{K_{x}}\right) - \phi(\hat{\xi})\right] K_{x}\hat{x} \left[\beta + \gamma K_{x} + \frac{u}{v}\right] \\ + \left[\phi\left(\hat{\xi} + \frac{e_{2}}{K_{s}}\right) - \phi(\hat{\xi})\right] us_{\text{in}}K_{s} \\ + \left[\phi\left(\hat{\xi} - \frac{e_{2}}{K_{s}}\right) - \phi(\hat{\xi})\right] \left[K_{x}\hat{x}\mu\left(\frac{\hat{s}}{v}\right) + \frac{u}{v}\hat{s}K_{s}\right].$$
(9)

As before, we have that  $\eta^K$  admits the following pathwise representation

$$\begin{cases} \hat{x}_t^K = \hat{x}_0^K + \int_0^t \hat{x}_r^K \left[ \mu\left(\frac{\hat{s}_r^K}{v}\right) - \beta - \frac{u}{v} \right] dr + M_t^{\gamma,K,(x)}, \\ \hat{s}_t^K = \hat{s}_0^K + \int_0^t \left[ -\frac{\hat{x}_r^K}{Y} \mu\left(\frac{\hat{s}_r^K}{v}\right) + u \left[ s_{\rm in} - \frac{\hat{s}_r^K}{v} \right] \right] dr \\ + M_t^{\gamma,K,(s)}, \end{cases}$$
(10)

where  $M^{\gamma,K} = (M^{\gamma,K,(x)}, M^{\gamma,K,(s)})$  is a discontinuous local martingale associated to the process  $\eta^K$  whose quadratic variation is

$$\langle M^{\gamma,K,(x)} \rangle_t = \int_0^t 2\gamma \hat{x}_r^K dr + \frac{1}{K_x} \int_0^t \hat{x}_r^K \left[ \mu \left( \frac{\hat{s}_r^K}{v} \right) + \beta + \frac{u}{v} \right] dr,$$
(11)  
 
$$\langle M^{\gamma,K,(s)} \rangle_t = \frac{1}{K_s} \int_0^t \left[ us_{\rm in} + u \frac{\hat{s}_r^K}{v} + \frac{1}{Y} \hat{x}_r^K \mu \left( \frac{\hat{s}_r^K}{v} \right) \right] dr,$$
(11)  
 
$$\langle M^{\gamma,K,(x,s)} \rangle_t = 0.$$

It can be proved that the birth and death process  $\eta^K$  is non explosive, and as K tends to infinity, the limit process  $\eta^* := (\hat{x}_t, \hat{s}_t)_{t\geq 0}$  is a weak solution to the SDE

$$\begin{cases} d\hat{x}_t = \left(\mu\left(\frac{\hat{s}_t}{v}\right) - \beta - \frac{u}{v}\right)\hat{x}_t dt + \sqrt{2\gamma\hat{x}_t}dW_t, \\ d\hat{s}_t = \left(-\frac{1}{Y}\mu\left(\frac{\hat{s}_t}{v}\right)\hat{x}_t + u\left(s_{\rm in} - \frac{\hat{s}_t}{v}\right)\right)dt, \end{cases}$$
(12)

where  $(W_t)_{t\geq 0}$  is a standard Brownian motion in  $\mathbb{R}$ . This result is stated in the next proposition:

Proposition 4. Suppose Assumption 1 holds. The sequence of processes  $(\eta^K)_{K \in \mathbb{N}}$  with infinitesimal generator (9), and deterministic initial condition  $\eta_0^K = \hat{\xi}_0 = (\hat{y}, \hat{z})$ , is tight in  $\mathscr{P}(\mathbb{D}([0,\infty);\mathbb{R}^2))$ , and converges in distribution to a weak solution  $\eta$  of (12) with the same initial condition  $\eta_0$ .

**Proof.** Analogous to the proof of Proposition 2.

Define  $\tilde{\gamma} = \sqrt{2\gamma}$ . The limit process of concentrations  $(\eta_t)_{t\geq 0} = (x_t, s_t)_{t\geq 0}$ , where  $x_t := \hat{x}_t/v$  and  $s_t := \hat{s}_t/v$  solve the SDE

$$\begin{cases} dx_t = \left[\mu(s_t) - \beta - \frac{u}{v}\right] x_t dt + \frac{\tilde{\gamma}}{\sqrt{v}} \sqrt{x_t} dW_t, \\ ds_t = \left[-\frac{1}{Y} \mu(s_t) x_t + \frac{u}{v} (s_{\rm in} - s_t)\right] dt. \end{cases}$$
(13)

- Remark 5. (i) If we suppose that  $\tilde{\gamma} = \gamma = 0$  (i.e. there is not demographic randomness), we recover the deterministic chemostat model (2).
- (ii) Note that in model (8) the form of the diffusion coefficient shows that the amplitude of the variations of the biomass decreases with the volume. This is an interesting behaviour that cannot be observed in the chemostat model (13), since there the culture volume is maintained constant.

## 2.3 Control problem.

From now on, we consider in both stochastic models (8) -(13) the variable u as a control process, instead of a constant parameter. We assume that the death rate  $\beta$  is null and, without loss of generality, the yield coefficient will be assumed Y = 1. In order to provide a rigorous framework, let  $(\Omega, \mathscr{F}, \mathbb{P})$  be a complete probability space that supports a one-dimensional Brownian motion  $W = (W_t)_{t \geq 0}$ . We say that the control process  $u : \Omega \times [0, +\infty[ \rightarrow \mathbb{R}]$  is admissible if  $u(\omega, t) \in U := [0, u_{\max}]$  for almost all (a.a.)  $(\omega, t)$  and uis adapted with respect to the natural filtration generated by the Brownian motion  $W(\cdot)$ , completed with the  $\mathbb{P}$ -null sets, that we denote by  $(\mathscr{F}_t)_{t \geq 0}$ . Let us discuss now the existence and uniqueness of solutions of the SDEs of the SBR

$$\begin{cases} dx_t = \left[\mu(s_t) - \frac{u_t}{v_t}\right] x_t dt + \tilde{\gamma} \sqrt{\frac{x_t}{v_t}} dW_t, \\ ds_t = \left[-\mu(s_t) x_t + \frac{u_t}{v_t} (s_{\rm in} - s_t)\right] dt, \\ dv_t = u_t dt, \end{cases}$$
(14)

and of the chemostat

$$\begin{cases} dx_t = \left[\mu(s_t) - \frac{u_t}{v}\right] x_t dt + \frac{\tilde{\gamma}}{\sqrt{v}} \sqrt{x_t} dW_t, \\ ds_t = \left[-\mu(s_t) x_t + \frac{u}{v} (s_{\rm in} - s_t)\right] dt. \end{cases}$$
(15)

for any admissible control u. The coefficients of these equations do not satisfy the standard Lipschitz condition w.r.t. the state variables (they are not even locally Lipschitz continuous) and, as a consequence, existence of solutions of (14) is not guaranteed by the usual results (see for instance, Ikeda and Watanabe (1981)). In order to study existence of solutions of (14) and (15) we consider a regularization and a truncation on the coefficients. By means of these approximations, we can prove the existence and uniqueness of solutions of the controlled SDEs (14) and (15) up to the extinction time, defined as the first time that the biomass  $x(\cdot)$  reaches 0, which, contrary to the deterministic case, is finite with positive probability. Indeed, the following result holds true:

Proposition 6. Let  $u = (u_t)_{t\geq 0}$  be an admissible control and  $\eta^u$  the solution of (14) (or (15)). Then, the probability that  $x^u = (x_t^u)_{t\geq 0}$  hits 0 at some time instant is positive.

**Proof.** [Sketch of proof] For the SBR model we use the controlled mass model

$$\begin{cases} d\hat{x}_t = \mu\left(\frac{\hat{s}_t}{v_t}\right)\hat{x}_t dt + \tilde{\gamma}\sqrt{\hat{x}_t} dW_t, \\ d\hat{s}_t = \left(-\mu\left(\frac{\hat{s}_t}{v_t}\right)\hat{x}_t + u_t s_{\rm in}\right) dt, \\ dv_t = u_t dt. \end{cases}$$

From comparison theorems such as (Ikeda and Watanabe, 1981, Theorem VI.1.1), we know that the biomass component  $\hat{x}$  can be bounded by above uniformly in the control by the process  $\bar{x}_t$  solution of the equation

$$d\bar{x}_t = \mu_{\max}\bar{x}_t dt + \tilde{\gamma}\sqrt{\bar{x}_t} dW_t,$$

which is a CIR process for which there exists strong solutions defined for all  $t \in [0, \infty)$  and pathwise uniqueness holds, see (Ikeda and Watanabe, 1981, Theorem IV.3.2). From (Lamberton and Lapeyre, 1996, Proposition 6.2.4) we see that its probability of extinction is strictly positive, which implies the same result for  $\hat{x}_t$ .

For the chemostat model, the same argument applies directly comparing the concentration process  $x_t$  with  $\bar{x}_t$  solution of the equation

$$d\bar{x}_t = \mu_{\max}\bar{x}_t dt + \frac{\tilde{\gamma}}{\sqrt{v}}\sqrt{\bar{x}_t}dW_t. \qquad \Box$$

2.4 Maximization of probability of attaining a target in the SBR

Typically, the problem of depollution of wastewater with the SBR consists of reaching a substrate concentration level  $s_{\text{out}} > 0$  with the tank at full capacity  $v_{\text{max}}$  in minimal time. A consequence of Proposition 6 is that the problem of minimization of expected treatment time is not well posed, since the expected treatment time will always be infinite, no matter what the control is. An interesting problem that arises is the maximization of the probability of reaching the target before extinction of the biomass. We consider the domain  $\mathcal{D} := [0, \infty) \times [0, s_{\text{in}}] \times [v_{\min}, v_{\max}]$ , the target set  $\mathcal{C} := (0, \infty) \times [0, s_{\text{out}}] \times \{v_{\max}\}$ , the full tank set  $\mathcal{V} := (0, \infty) \times [s_{\text{out}}, s_{\text{in}}] \times \{v_{\max}\}$ , the extinction set  $\mathcal{E} := \{0\} \times [0, s_{\text{in}}] \times [v_{\min}, v_{\max}]$ , and an initial condition  $\xi \in \mathcal{D}$ . For any Borel measurable set  $\mathcal{A} \subseteq \mathbb{R}^3$  and control  $u \in \mathscr{U}$ , we define the hitting times  $\tau_A^u := \inf\{t \ge 0 \mid \eta_t^u \in A\}$ . We define the cost function

$$J(\xi; u) = \mathbb{P}_{\xi} \left[ \tau_{\mathcal{C}}^{u} \le \tau_{\mathcal{E}}^{u} \right],$$

where  $\mathbb{P}_{\xi}(\cdot)$  denotes the probability law under  $\eta_0 = \xi$ . The problem is

$$(\mathcal{P}) \quad V(\xi) := \sup_{u \in \mathscr{U}} J(\xi; u). \tag{16}$$

This is the *reach-avoid* problem, in which we try to avoid the extinction of the biomass and reach the target set. This problem is adressed in a more general manner in Chatterjee et al. (2011) for the discrete time case and Esfahani et al. (2016) for the continuous time setting. Nevertheless, problem (16) does not satisfy the hypotheses of the dynamic programming principle stated in Esfahani et al. (2016), since the diffusion coefficient is degenerate, the target set and the extinction set do not satisfy the interior cone condition, and the payoff function is not lower semicontinuous in the whole domain. Moreover, this problem has a mixed control-state constraint; indeed, when the tank is full  $(v = v_{\text{max}})$  the control is forced to take the value u = 0. Nevertheless, on this set the cost does not depend of the controls, but of the initial condition  $\xi \in \mathcal{V}$ . We denote the cost function on  $\mathcal{V}$  by  $\tilde{v}(\cdot)$ .

Proposition 7. The function  $\tilde{v}(\cdot)$  is continuous on  $\mathcal{V}$ .

We restate problem  $(\mathcal{P})$  as a problem without the mixed control-state constraint. For this, we consider the cost function  $\tilde{v}(\cdot)$  previously defined, and we define the set  $\Gamma := \mathcal{C} \cup \mathcal{V} \cup \mathcal{E}$ . For every  $t \geq 0$ , define  $\mathbb{F}^t = (\mathscr{F}_r^t)_{r\geq 0}$ where  $\mathscr{F}_r^t$  is the  $\sigma$ -field  $\sigma(W_\theta - W_t : t \leq \theta \leq r \lor t)$ , completed with the  $\mathbb{P}$ -null sets. We define the set of admissible controls

$$\mathscr{U}_t = \left\{ u : \mathbb{R}_+ \times \Omega \to [0, u_{\max}] : u \text{ is } \mathbb{F}^t - \text{progressively measurable} \right\},\$$

where  $\mathbb{R}_+ := [0, \infty)$ , and denote  $\eta^{t,\xi,u}$  the solution of the controlled stochastic differential equation (14) with control  $u \in \mathscr{U}_t$  and initial condition  $\xi$  at initial time t. Define  $\tau^u := \tau^u_{\Gamma} = \tau^u_{\mathcal{C}} \wedge \tau^u_{\mathcal{V}} \wedge \tau^u_{\mathcal{E}}$ , the cost function

$$J(t,\xi;u) = \mathbb{E}_{t,\xi} \left[ \mathbb{1}_{\mathcal{C}}(X^u_{\tau^u}) + \tilde{v}(X^u_{\tau^u}) \mathbb{1}_{\mathcal{V}}(X^u_{\tau^u}) \right].$$
(17)

where  $\mathbb{E}_{t,\xi}(\cdot)$  is the expectation under the initial condition  $\eta_t = \xi$ , and the new value function

$$(\mathcal{P}_{t,\xi}) \quad V(t,\xi) = \sup_{u \in \mathscr{U}_t} J(t,\xi;u).$$
(18)

For  $t, t' \geq 0$ ,  $\xi = (y, z, w)$ ,  $\xi' = (y', z', w')$ , we say that  $(t', \xi') \twoheadrightarrow (t, \xi)$  if  $t' \nearrow t$  and  $w' \searrow w$ . We introduce, as in (Touzi, 2013, Section 3.2), the lower and upper semicontinuous envelopes of V,

$$V_{\star}(t,\xi) := \liminf_{\substack{(t',\xi') \to *(t,\xi)}} V(t',\xi'),$$
$$V^{\star}(t,\xi) := \limsup_{\substack{(t',\xi') \to *(t,\xi)}} V(t',\xi').$$

Proposition 8. (Dynamic Programming Principle). Let the initial condition  $(t,\xi) \in \mathcal{D}$  be fixed. For every  $\mathbb{F}^t$ -stopping time h, the value function  $V(\cdot)$  satisfies the dynamic programming inequalities:

$$V(t,\xi) \le \sup_{u \in \mathscr{U}_{t}} \mathbb{E}\left[V^{\star}(h \wedge \tau^{u}, \eta^{t,\xi,u}_{h \wedge \tau^{u}})\right],$$
(19)

$$V(t,\xi) \ge \sup_{u \in \mathscr{U}_t} \mathbb{E} \left[ V_{\star}(h \wedge \tau^u, \eta^{t,\xi,u}_{h \wedge \tau^u}) \right].$$
(20)

**Proof.** Similar to (Touzi, 2013, Theorem 3.3). A previous step is to prove, for each control  $u \in \mathcal{U}$ , the lower semicontinuity in probability of the function  $(t, \eta) \mapsto J(t, \xi; u)$  under the convergence  $\rightarrow$ .

As we stressed in the introduction a similar result holds true for the analogous problem involving the controlled chemostat model (15).

### 3. CONCLUSION

In this work, we have proposed a stochastic model for the SBR and for the chemostat. They are obtained from the natural demographic stochasticity that arises in a large bacterial population, leading to non-standard controlled stochastic systems. For small population sizes the extinction of the biomass can occur, which is a phenomenon that cannot be explained in the deterministic setting. This phenomenon implies, in particular, that the problem of minimal treatment time is not well defined. For this reason, caution is advised when considering an optimization criteria for the bioreactor in a stochastic framework. We propose a reach-avoid problem similar to Esfahani et al. (2016), consisting of the maximization of the probability of attaining the target while avoiding extinction; the proposed problem has several technical difficulties. We have proved that the controlled SDE is well-posed and also we have shown that the DPP (19)-(20) holds. From this result it is possible to show that V is a discontinuous viscosity solution of an associated Hamilton-Jacobi-Bellman (HJB). However, we are not aware of uniqueness principles for

this equation in the literature and so a characterization of the value function as the unique discontinuous viscosity solution of the associated HJB equation remains as a difficult and interesting subject of research.

The perspectives of future work are the proof of the existence of a (relaxed) optimal solution of problem ( $\mathcal{P}$ ) (see (16)), as well as the study of Markov chains approximations of the continuous problem, in the spirit of Kushner and Dupuis (2001).

## REFERENCES

- Barbier, S., Rapaport, A., and Rousseau, A. (2016). Modelling of biological decontamination of a water resource in natural environment and related feedback strategies. *Journal of Scientific Computing*, 1–14.
- Bastin, G., Nesic, D., Tan, Y., and Mareels, I. (2009). On extremum seeking in bioprocesses with multivalued cost functions. *Biotechnology Progress*, 25(3), 683–689.
- Bayen, T., Gajardo, P., and Mairet, F. (2013). Optimal synthesis for the minimum time control problems of fed-batch bioprocesses for growth functions with two maxima. J. Optim. Theory Appl., 158(2), 521–553.
- Campillo, F. and Fritsch, C. (2015). Weak convergence of a mass-structured individual-based model. Applied Mathematics & Optimization, 72(1), 37–73.
- Chatterjee, D., Cinquemani, E., and Lygeros, J. (2011). Maximizing the probability of attaining a target prior to extinction. *Nonlinear Anal. Hybrid Syst.*, 5(2), 367– 381.
- Collet, P., Martínez, S., Méléard, S., and San Martín, J. (2013). Stochastic models for a chemostat and long-time behavior. Adv. in Appl. Probab., 45(3), 822–837.
- D'Ans, G., Gottlieb, D., and Kokotovic, P. (1972). Optimal control of bacterial growth. Automatica, 8, 729–736.
- D'Ans, G., Kokotović, P., and Gottlieb, D. (1971). Timeoptimal control for a model of bacterial growth. J. Optim. Theory Appl., 7(1), 61–69.
- Diehl, S. and Farås, S. (2013a). Control of an ideal activated sludge process in wastewater treatment via an ode-pde model. *Journal of Process Control*, 23(3), 359 381.
- Diehl, S. and Farås, S. (2013b). A reduced-order ODE-PDE model for the activated sludge process in wastewater treatment: classification and stability of steady states. *Math. Models Methods Appl. Sci.*, 23(3), 369– 405.
- Esfahani, P.M., Chatterjee, D., and Lygeros, J. (2016). The stochastic reach-avoid problem and set characterization for diffusions. *Automatica J. IFAC*, 70, 43–56.
- Foley, P. (1994). Predicting extinction times from environmental stochasticity and carrying capacity. *Conser*vation Biology, 8(1), 124–137.
- Gajardo, P., Harmand, J., Ramírez C., H., and Rapaport, A. (2011). Minimal time bioremediation of natural water resources. Automatica J. IFAC, 47(8), 1764–1769.
- Gajardo, P., Ramírez, H., and Rapaport, A. (2008). Minimal time sequential batch reactors with bounded and impulse controls for one or more species. SIAM Journal on Control and Optimization, 47(6), 2827–2856.
- Gajardo, P., Ramírez, H., Riquelme, V., and Rapaport, A. (2012). Bioremediation of natural water resources via optimal control techniques. In *BIOMAT 2011*, 178–190. World Sci. Publ., Hackensack, NJ.

- Hong, J. (1986). Optimal substrate feeding policy for fed batch fermentation with substrate and product inhibition kinetics. *Biotechnol. Bioengng.*, 28, 1421– 1431.
- Ikeda, N. and Watanabe, S. (1981). Stochastic differential equations and diffusion processes, volume 24 of North-Holland Mathematical Library. North-Holland Publishing Co., Amsterdam.
- Imhof, L. and Walcher, S. (2005). Exclusion and persistence in deterministic and stochastic chemostat models. J. Differential Equations, 217(1), 26–53.
- Karatzas, I. and Shreve, S.E. (1991). Brownian motion and stochastic calculus, volume 113 of Graduate Texts in Mathematics. Springer-Verlag, New York, second edition.
- Kurtanjek, Z. (1991). Optimal nonsingular control of fedbatch fermentation. *Biotechnology and Bioengineering*, 37, 814–823.
- Kushner, H.J. and Dupuis, P. (2001). Numerical methods for stochastic control problems in continuous time, volume 24 of Applications of Mathematics (New York). Springer-Verlag, New York, second edition.
- Lamberton, D. and Lapeyre, B. (1996). Introduction to stochastic calculus applied to finance. Chapman & Hall, London.
- Marcos, N., Guay, M., Dochain, D., and Zhang, T. (2004). Adaptive extremum seeking control of a continuous stirred tank bioreactor with Haldane's kinetics. *Journal* of Process Control, 14, 317–328.
- Mazouni, D., Harmand, J., Rapaport, A., and Hammouri, H. (2010). Optimal time switching control for multireaction batch process. *Optimal Control Applications* and Methods, 31, 289–301.
- Méléard, S. and Villemonais, D. (2012). Quasi-stationary distributions and population processes. *Probab. Surveys*, 9, 340–410.
- Monod, J. (1950). La technique de la culture continue, théorie et applications. Annales de l'Institut Pasteur, 79(4), 390-410.
- Moreno, J. (1999). Optimal time control of bioreactors for the wastewater treatment. *Optimal Control Appl. Methods*, 20(3), 145–164.
- Novick, A. and Szilard, L. (1950). Experiments with the chemostat on spontaneous mutations of bacteria. *Proc* Natl Acad Sci U S A., 36(12), 708–719.
- Ramírez, H., Rapaport, A., and Riquelme, V. (2016). Optimal Feedback Synthesis and Minimal Time Function for the Bioremediation of Water Resources with Two Patches. SIAM J. Control Optim., 54(3), 1697–1718.
- Smith, H.L. and Waltman, P. (1995). The theory of the chemostat, volume 13 of Cambridge Studies in Mathematical Biology. Cambridge University Press, Cambridge. Dynamics of microbial competition.
- Touzi, N. (2013). Optimal stochastic control, stochastic target problems, and backward SDE, volume 29 of Fields Institute Monographs. Springer, New York.
- Tsoneva, R., Patarinska, T., and Popchev, I. (1998). Augmented lagrange decomposition method for optimal control calculation of batch fermentation processes. *Biopro*cess and Biosystems Engineering, 18(2), 143–153.
- Zhang, T., Guay, M., and Dochain, D. (2003). Adaptive extremum seeking control of continuous stirred-tank bioreactors. AIChE Journal, 49(1), 113–123.