Projet PGMO 2014 présenté par
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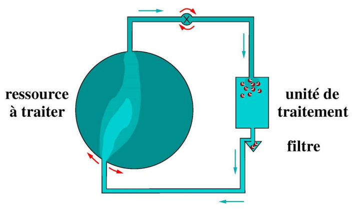
OPTIBIO : New Challenges in the Optimal Control of Bioprocesses

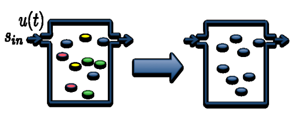
1 Introduction and objectives of the project

The chemostat apparatus has been invented simultaneously by Novick & Szilard and Monod in the fifties, for the so-called "continuous culture" of micro-organisms [1,2]. Since then the so-called "chemostat model" has served for many real world applications that describe microbial growth, such as waste-water treatment [3] or in pharmaceutical industries. It can be used to describe the competition of n species growing on a single limiting resource as proposed in [2] :

$$\begin{cases} \dot{x}_i = (\mu_i(s) - u)x_i, \\ \dot{s} = -\sum_j \mu_j(s)x_j + u(s_{in} - s), \end{cases} \quad (1)$$

Heren x_i and s stand respectively for the i-th species and nutrient concentrations. The functions $\mu_i(\cdot)$ are the specific growth rate of the micro-organisms. The operating parameters are the the input nutrient concentration s_{in} and the dilution rate u chosen as a **control variable** in this setting. Such a model is used as a good representation of the functioning of bioreactors in the biotechnology, or for ecological investigations [4,5] or still of the growth of micro-organisms in natural environments, such as mountain lakes.



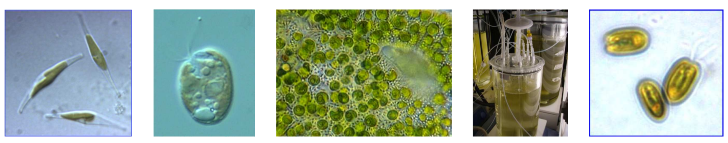


In view of its many applications, it is therefore of great importance to improve the control strategies driving such systems. The recent expectations of sustainable development raise new optimization problems that take into account auxiliary outputs, such as biogas production, that have not been mathematically formulated and yet tackled. Mathematical problems that come from the modeling of these processes are often difficult to solve, and one objective of the proposal is to **develop new mathematical methods in order to address these issues**.
From a mathematical point of view, this model has conducted to the study of many problems from dynamical systems to optimal control theory. Several important mathematical results have been discovered in the last decades for deterministic and stochastic optimal control problems based on this system over a finite horizon (see e.g. [6,7,8]). There remain several important questions which can have a great impact on the biotechnology industry:

- Optimization of bioprocess over an infinite horizon.
- Development of accurate methods in order to deal with uncertainties that affects the chemostat model (uncertainties come from unknown parameters or noise from the measurements).
- Stabilization of the chemostat model including delay in the system.

2 Optimal control problem related to bioprocesses

In this section, we describe a typical problem arising in the context of micro-algae [6,7]. We consider system (1) describing a perfectly mixed chemostat with n species and one limiting resource. Our aim is to provide an optimal feedback control to optimize the selection of the species of interest.



The set of admissible controls is given by $\mathcal{U} := \{u : [0, +\infty] \to [0, u_{max}] \; ; \; meas.\}$, where u_{max} denotes the maximum dilution rate, and the target set $\mathcal{T}$ is given by

$$\mathcal{T} := \left\{ x \in E \; ; \; x_1 \geq (1 - \varepsilon) \sum_{1 \leq i \leq n} x_i \right\},$$

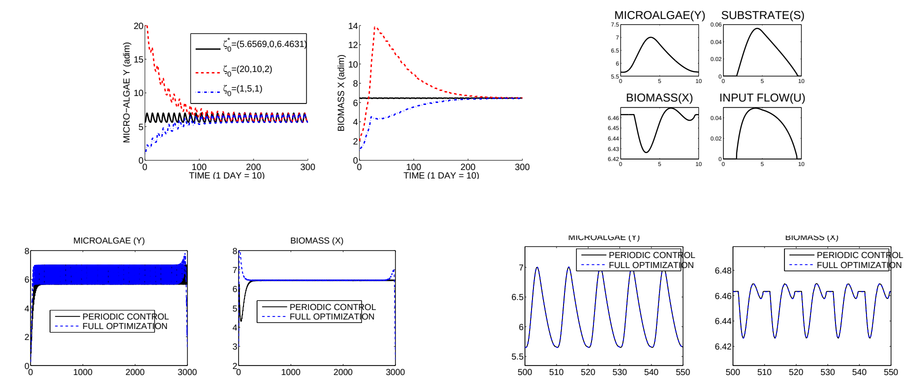
corresponding to the selection of the first species. The optimal control problem reads as follows. Given an initial condition, our aim is to find a *feedback control* u steering the solution $x(\cdot)$ of (1) from x^0 to the target $\mathcal{T}$ in minimal time:

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

where $t(u)$ is the first entry time in the target $\mathcal{T}$.

4 Numerical Simulations : direct and indirect methods

Another aspect of the project is to develop an open-source toolbox for solving optimal control problems, with collaborations with industrial and academic partners. Optimal control (optimization of dynamical systems governed by differential equations) has numerous applications in transportation, energy, process optimization, and biology. The software `bocop` [9] is developed since 2010 in the framework of the Inria-Saclay initiative for an **open source optimal control toolbox**, and is supported by INRIA team **Commands**.



The current version of the toolbox [9] implements a so-called direct transcription method, with an ongoing expansion to global optimization through *dynamic programming* (HJB) techniques. We plan to use this approach for further numerical investigations.

5 Conclusion and Perspectives

The optimal syntheses of infinite horizon problems (or non fixed terminal time such as minimal time) are time independent, which is of great interest for practionners. In the spirit of [7], one would like to maximize a cost :

$$\max_{u(\cdot) \in \mathcal{U}} \int_0^{\infty} e^{-\delta t} x_j(t) u_j(t) \, dt, \quad (2)$$

that corresponds to the production of a species j in (1) over an infinite horizon. However, it requires the use and development of new methods that could be based on model predictive control **MPC**, see e.g. [10]. In particular, it could be interesting to study optimality conditions when state constraints are considered over an infinite horizon, and the discretization of such problems. This methodology could be also used for maximizing the bio-gas production (2) over a long period in a series of interconnected chemostats. Keeping in mind these ideas one other objective is to study these optimal control problems under *uncertainties over an infinite horizon*. Hence, the objective of the present project is to contribute to the development of new control strategies that could be transfered to specialists in industrial biotechnologies. The outputs of the project, in terms of new control laws, would also directly serves the community of researchers in bioprocesses.

6 References

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