



IN PARTNERSHIP WITH:
INRA

Activity Report 2012

Project-Team MODEMIC

Modelling and Optimisation of the Dynamics of Ecosystems with MICro-organismes

IN COLLABORATION WITH: Mathématiques, Informatique et STatistique pour l'Environnement et l'Agronomie

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
**Observation, Modeling, and Control
for Life Sciences**

Table of contents

| | |
|----------------------------------------------------------------------------------------------------------|-----------|
| 1. Members | 1 |
| 2. Overall Objectives | 2 |
| 2.1. Introduction | 2 |
| 2.2. Build, simulate and analyze new models of microbial ecosystems | 2 |
| 2.3. Validate hypotheses and identify models with experimental data | 3 |
| 2.4. Propose new strategies to pilot and optimize microbial ecosystems | 4 |
| 2.5. Develop a strategy of software production | 4 |
| 2.6. Highlights of the Year | 5 |
| 3. Scientific Foundations | 5 |
| 3.1. Modelling and simulating microbial ecosystems | 5 |
| 3.1.1. Macroscopic models | 5 |
| 3.1.2. Microscopic models | 6 |
| 3.1.3. Bridges between models | 7 |
| 3.2. Interpreting and analyzing experimental observations | 8 |
| 3.2.1. Assessment of community structures | 8 |
| 3.2.2. Characterization of the interactions | 9 |
| 3.2.3. Observation of spatial structures | 9 |
| 3.3. Identifying, controlling and optimizing bioprocesses | 10 |
| 3.3.1. Software sensors and identification | 10 |
| 3.3.2. Bioprocess stabilization | 10 |
| 3.3.3. Optimal control of bioreactors | 10 |
| 3.3.4. Plant design and optimization | 11 |
| 4. Application Domains | 11 |
| 4.1. Preservation of water resources | 11 |
| 4.2. Microbial ecology of soil | 11 |
| 4.3. Control of fermentation processes | 12 |
| 4.4. Animal digestive ecosystem | 12 |
| 5. Software | 12 |
| 5.1. VITELBIO | 12 |
| 5.2. SMC DEMOS | 12 |
| 6. New Results | 13 |
| 6.1. Theoretical results | 13 |
| 6.1.1. Models resource/consumer | 13 |
| 6.1.1.1. Theory of competition and coexistence | 13 |
| 6.1.1.2. Study of interconnected chemostats | 13 |
| 6.1.1.3. Aggregation models in the chemostat | 13 |
| 6.1.1.4. Overyielding in continuous bioprocesses | 13 |
| 6.1.2. Measuring taxonomic diversity of microbial communities | 14 |
| 6.1.3. A theory of genetic diversity within bacterial species | 14 |
| 6.1.4. Individual-based modelling for bacterial ecosystems | 14 |
| 6.1.5. Stochastic/discrete and stochastic/continuous modelling for biotechnology and population dynamics | 15 |
| 6.1.6. Optimal control of continuous bioprocesses | 15 |
| 6.1.7. Modelling the functioning of soil ecosystems | 16 |
| 6.1.8. Equivalence between models of fractured porous media | 17 |
| 6.1.9. Non-linear filtering for the chemostat | 17 |
| 6.1.10. Functional identification of growth functions in the chemostat | 17 |
| 6.1.11. Diffusive representation of integro-differential models | 17 |
| 6.2. Applications | 18 |

| | | |
|------------|----------------------------------------------------------------------------------|-----------|
| 6.2.1. | Modelling and control of Anaerobic Digestion processes | 18 |
| 6.2.2. | Hybrid modelling of biofilms in plug-flow reactors | 18 |
| 6.2.3. | Individual-based models for the bacterial degradation of the cellulose | 19 |
| 6.2.4. | Modelling and control of cascade biosystems to mimic batch wine making processes | 19 |
| 6.2.5. | Modelling and control of an ice cream crystallization process | 20 |
| 6.2.6. | Bioremediation of natural resources | 20 |
| 6.2.7. | Modelling and simulating terrestrial plant ecological dynamics | 20 |
| 6.2.8. | Modelling and inferring agricultural dynamics | 20 |
| 7. | Bilateral Contracts and Grants with Industry | 21 |
| 7.1. | CAFE | 21 |
| 7.2. | DIMIMOS | 21 |
| 7.3. | DISCO | 21 |
| 7.4. | MODECOL | 22 |
| 8. | Partnerships and Cooperations | 22 |
| 8.1. | International Initiatives | 22 |
| 8.1.1. | Inria Associate Teams | 22 |
| 8.1.2. | Participation In International Programs | 23 |
| 8.1.2.1. | CIRIC-Bionature | 23 |
| 8.1.2.2. | TREASURE | 23 |
| 8.1.2.3. | LIRIMA Stic-Mada | 24 |
| 8.2. | International Research Visitors | 24 |
| 8.2.1. | Visits of International Scientists | 24 |
| 8.2.2. | Visits to International Teams | 24 |
| 9. | Dissemination | 24 |
| 9.1. | Animation of the scientific community | 24 |
| 9.2. | Seminars and schools | 25 |
| 9.3. | Teaching | 25 |
| 9.4. | PhD's | 25 |
| 9.5. | Participation to thesis committees | 26 |
| 10. | Bibliography | 27 |

Project-Team MODEMIC

Keywords: Models, Microbial Ecology, Control Theory, Population Modeling, Multiscale Models, Individual-based Models

MODEMIC is a common INRA-Inria team that aims at sharing skills of researchers of both Institutes for developing, analysing and simulating new models of microbial ecosystems as efficient tools to understand, explore, pilot and manage industrial and natural bioprocesses. MODEMIC is located on the Montpellier SupAgro campus and it is housed by the UMR INRA-SupAgro MISTEA (Mathematics, Informatics and Statistics for Environment and Agronomy).

Creation of the Project-Team: January 01, 2011 , Updated into Project-Team: January 01, 2012 .

1. Members

Research Scientists

Fabien Campillo [Senior Researcher, Inria Sophia-Antipolis, HdR]
Céline Casenave [Junior Researcher, since September 2011, INRA]
Bart Haegeman [Junior Researcher, Inria Sophia-Antipolis, on secondment to CNRS, since September 2012]
Jérôme Harmand [Senior Researcher, INRA Narbonne, HdR]
Alain Rapaport [Team leader; Senior Researcher, INRA Montpellier, HdR]

Faculty Members

Térence Bayen [Associate Professor, Université de Montpellier II; “délégation” Inria since September]
Marc Joannides [Associate Professor, Université de Montpellier II]
Claude Lobry [Professor emeritus, Université de Nice, HdR]
Tewfik Sari [Professor, Université de Haute-Alsace; Senior Researcher Irstea Montpellier, HdR]

External Collaborators

Guillaume Deffuant [Senior Researcher, Irstea Clermont, HdR]
Annick Lesne [Senior Researcher, LPTMC Paris Jussieu, HdR]
Antoine Rousseau [Junior Researcher, MOISE Team-Project, Inria-Rhône-Alpes]

PhD Students

Walid Bouhafs [Université Tunis Carthage grant]
Boumediene Benyahia [COADVISE grant]
Amine Charfi [COADVISE grant]
Lamine Mamadou Diagne [AUF grant]
Coralie Fritsch [MESR and INRA grant]
Amel Ghouali [AVERROES grant]
Sonia Hassam [COADVISE grant]
Guilherme Pimentel [Univ. Mons (Belgique) and INRA grant]
Angelo Raheiririna [University of Fianarantsoa, Madagascar, LIRIMA grant]
Radhouene Fekih-Salem [AVERROES grant]

Post-Doctoral Fellows

Chloé Deygout [ANR DISCO grant, January and February]
Matthieu Sebbah [Inria-CIRIC grant, since October]

Visiting Scientists

Denis Dochain [CESAME, Univ. Louvain-la-Neuve (Belgium), 1 month]
Jaime Moreno [UNAM, Mexico City (Mexico), 1 week]
Hector Ramirez [Mathematical Engineering Department, Universidad de Chile, 2 weeks]

Administrative Assistant

Geneviève Carrière [AI, part time]

Others

Sébastien Barbier [MSc Student, Univ. Reims, 6 months]

Amine Boutoub [MSc Student, Univ. Tlemcen (Algeria), 2 months]

Alejandro Rojas-Palma [MSc Student, Univ. Chile, 3 months, Inria Internship]

2. Overall Objectives

2.1. Introduction

Natural or reconstituted microbial ecosystems are often very complex (high diversity, interactions within and between species, coupling with spatial processes: niches, aggregation, biofilm...) [83].

We bet that simple models (in the sense that they are manageable analytically and/or in a computer) of these ecosystems can explain their main functions, mainly concerning degradation and conversion. For this purpose, we investigate population models both deterministic (differential equations) and stochastic (stochastic differential equations, death-birth processes), as well as individual-based models.

Another challenge is to develop, from expert knowledge and experimental observations, models that are simple enough (i.e. without an exhaustive description of all microbial actors) to carry out model identification and selection as well as the determination of “control laws”, but realistic enough to be validated on real processes within a decision-making perspective (i.e. bioprocess control).

One of the main difficulties is to identify the limits of the validity of these models (especially in terms of population size, and of prediction of the coexistence of species). This requires a proper mathematical analysis as well as the development of adapted simulation tools.

2.2. Build, simulate and analyze new models of microbial ecosystems

We investigate different models of microbial ecosystems at different scales, that are related to various research questions for better understanding, predicting or piloting real plants.

Eight families of problems are covering our modelling activities:

1. study the mathematical properties (equilibriums, stability, limit cycles, bifurcation...) of macroscopic models that distinguish compartments of attached and free bacteria. We are looking for ecological conclusions in terms of coexistence of species.
2. study the mathematical properties of trajectories of a model that switches from a populational representation by differential equations to an individual-based model when the population falls below a given threshold. We expect from this study new insights on validity domains of macroscopic models and quantitative estimations of the variability around average trajectories.
3. build a framework for modelling the chemostat with stochastic processes at a macroscopic scale justified from hypotheses at the individual level. The classical “deterministic” chemostat is expected to be found as an average dynamics for large populations, but second order moments should provide relevant information about the variability about the deterministic approximation.
4. build and simulate IBMs, individual based models [79], of 1D biofilm and compare the spatial densities of biofilm and planktonic biomass with the numerical solutions of 1D PDE models.

The output of this study is to propose and justify attachment/detachment terms in the PDE, that are crucial in the determination of the thickness of the biofilm, and that are usually chosen in an heuristic way.

5. compare detailed ecological models of a multi-species community at a fine scale with low-complexity models at a coarser scale, in the spirit of the neutral model. Within a stochastically varying environment (that is assumed to have different impacts on each species), the coarse model could describe in an effective way the interaction between species and environment as a stochastic variability. The goal is to interpret the parameters of the global model in terms of properties of the fine-scale model.

6. study chemostat-like models with multi-resources and nutrient recycling, within the objective of representing microbial activity in soil ecosystems. The goal is to understand the influence of the choice of hypotheses about the growth terms (dependency in terms of product or minimum functions of each resource) and the recycling terms (from the dead biomass or during the division process) on the qualitative behavior of the system and its performances at steady state.
7. investigate the properties of a network of interconnected chemostats and understand the role of the size of the nodes and the connectivity.
8. couple numerical simulation of fluids dynamics in tanks with models of biotic/abiotic reactions. Then, we plan to compare the input/output behavior of these models with simple representations of networks of interconnected chemostats (see the previous point).

2.3. Validate hypotheses and identify models with experimental data

Among our current collaborations and projects (ANR DIMIMOS, ANR DISCO), we have identified five experimental devices that we consider relevant for back and forth exchanges between models and real-world observations for the coming years.

1. Molecular fingerprints. The LBE (Laboratory of Environmental Biotechnology) at Narbonne is a world leader for one of these techniques, the SSCP (Single Strand Conformation Polymorphism) that allows to estimate the biodiversity of a microbial ecosystem and serves as a comparison instrument over time or between ecosystems. A similar kind of signal from the proteins expressions is also obtained within the ANR DIMIMOS with the UMR MSE (Microbiologie du Sol et de l'Environnement) in Dijon.
2. Continuous cultures in chemostats. The chemostat device is the typical investigating device in microbiology. Spatial structures can be mimicked and controlled using interconnected chemostats. Because of contamination risks, experimentation in chemostat requires an adequate expertise which the LBE holds. We plan to launch new such experiments with microbial populations of interest for specialists of soil ecosystems, in collaboration with UMR Eco&Sols (Écologie fonctionnelle et biogéochimie des sols et agrosystèmes, Montpellier) and UMR BIOEMCO (Biogéochimie et écologie des milieux continentaux, Grignon).
3. Taylor-Couette reactors (with LBE Narbonne). These bioreactors are specifically designed for the culture of biofilms on *coupons*, that can be removed from the system for static analyses of biodiversity (SSCP) and microscopy. Experiments are already scheduled within a task of the ANR DISCO.
4. Flow-cell bioreactors (with Irstea Antony). It consists in small capillary tubular reactors continuously fed by a pump, under a microscope that has been designed for a continuous acquisition of images. We aim to compare biofilm models with the information provide by theses images.
5. Micro-plates cultures (with UMR MSE Dijon and LBE Narbonne). It contains a hundred of small wells in each of which a microbial community is grown in batch on the available substrate. Optical density measurements allow one to monitor simultaneously the biomass growth in the wells. These devices are convenient to study the effects of different initial compositions of the community under the same environmental conditions. We believe that it is also well suited to test neutral-like community models

Each measurement technique requires its own data analysis (filters, statistical analysis, image analysis...) to provide information that are relevant for the models. On the basis of these experimental observations, qualitative and quantitative validations of the models will be performed. Observers and image correlations are one of the techniques we are using.

2.4. Propose new strategies to pilot and optimize microbial ecosystems

We study optimal design and feedback control laws within the framework of ongoing projects, and distinguish two kinds of contributions:

1. based on already known models of chemostat or fed-batch reactors, but with explicit spatial considerations, for
 - the biological treatment of natural water resources, one of the main objective of the associated team DYMECOS with Chile, in collaboration with B. Ivorra from MOMAT (Modelos Matemáticos en Ciencia y Tecnología) group (Madrid) and A. Rousseau for the numerical computation of the pollutant spreading,
 - the design of interconnected networks of chemostats, in the following of the former ARC VITELBIO and also in collaboration with the MOMAT for the comparison and identification with hydrodynamics models.
2. based on new models developed in the scope of projects:
 - the Euro-Mediterranean project TREASURE coordinated by the team, where membranes are at the heart of a new generation of bioreactors of smaller size and well suited for Southern countries where the temperature is not too low.
 - the ANR DISCO 2010-2013, for which one of the output is expected in terms of control of biofilm reactors.

We plan to contribute to the development of new decision making tools to design, control, observe and optimize current and future bioprocesses, for the preservation of natural (aquatic or telluric) resources, where modelling and numerical simulations are clearly expected, and for the biotechnology industry whose objectives are to improve efficiency of bioprocesses under constraints of sustainable development (energetic consumption, biogas production...)

The tools based on geometric and optimal control of nonlinear systems and possibly on viability theory should be enhanced by software developments. We also expect to contribute to the numerical determination of optimal feedback laws for a class of problems relevant for the mentioned applications.

2.5. Develop a strategy of software production

Although the software production is not the main objective of the team, we aim to assemble models within *virtual ecosystems* (with the objective that it can replace or guide real experiments) in the four coming years. Co-developments of simulation software will be looked for within Inria or outside. Our working plan is in three steps:

1. In a first step, we shall develop prototypes or dedicated toolboxes in Scilab or Matlab within the team.
2. Simulations of IBM or PDE require significant efforts, in terms of computer implementation and numerical methods.

The main problem in the implementation of IBM's is the size of the population, particularly for applications in microbiology where the size of populations of bacteria can be very large. In agent-based models (ABM), population sizes are smaller and each individual features sophisticated behavior, while in IBM, population sizes are usually larger but with limited individual activities. The population size impacts both the execution time and the memory size, but the main bottleneck is the execution time because of the communication between the individuals. The idea will be to propose, through an object-oriented approach, data structures that will limit this communication. From the hardware point of view, grid computing could improve execution time but only on a limited range. These activities will have to be developed in association with specialists for our most ambitious developments: MOMAT already cited but also researchers from I3M (Institute of Mathematics and Mathematical Modelling of Montpellier) University of Montpellier 2/CNRS.

3. For the design and development of user-friendly and graphical interfaces that need to be easily accessible by biologists and bioprocess engineers, we shall look for the help of service companies specialized in agronomy and biotechnology applications (such as ITK Company, <http://itkweb.com>).

2.6. Highlights of the Year

- *The characterization of interconnections of chemostats that provide a global stability of bioprocesses with inhibition, mentioned in Section 6.1.1, has led to a patent application by INRA [59].*
- *Anaerobic membrane bioreactors (AnMBR) have a great potential for treating wastewater since they allow energy recovery (the biogas produced is mostly composed of methane) while guaranteeing a total separation of the treated water and of the microbial content of the process. However, their main drawback is the fouling of the membrane. In order to control the process while limiting the risk of clogging, we have developed a new model for AnMBR in coupling a two-step anaerobic model (called the “AM2” or the “AMOCO” model) with a model describing fouling dynamics [16].*
- *We have proposed hybrid models (deterministic/stochastic and continuous/discrete) of population dynamics as alternatives to conventional models based on ordinary differential equations. The later models are generally accepted as a good approximation of the former ones in large population asymptotic, but even in very large population size the two groups of models present drastically different behavior, notably in terms of persistence properties [15], see Section 6.1.5.*

3. Scientific Foundations

3.1. Modelling and simulating microbial ecosystems

Microbial ecosystems naturally put into play phenomena at different scales, from the individual level at a microscopic scale to the population level at a macroscopic scale, with sometimes intermediate levels. The size of substrate molecules is a thousand time smaller than the size of microorganisms and usually diffuse much faster. The substrate consumption of one microorganism is negligible at the population level but the sum of the consumption of its neighbors can modify the local concentration of substrate, which itself modifies microorganism growth, acting as a *feedback loop*. For other variables that change slowly (pH, temperature...) cumulative effects create intermediate time scales, coupling individual and environment dynamics. The very large populations justify macroscopic modelling but for some ecosystems, spatial structures seen at intermediate scale need to be tackled. This is typically the case of biofilm ecosystems, for which the biofilm structure is responsible of characteristics of the overall ecosystem. Models that are purely individual-based or purely populational are rarely truly satisfactory to incorporate current knowledge on microbial ecosystems at various scales and to push ahead mathematical analysis or to derive operational rules.

3.1.1. Macroscopic models

The starting point is the knowledge of biologists that report a large number of mechanisms discovered or shown on laboratory experiments at a population level, such as competition for a growth-limiting substrate, predation interactions, obligate mutualism or communication between bacteria. If each *elementary* mechanism is today well understood and modelled at a macroscopic level, the consideration of several mechanisms together in a single model is still raising several questions of understanding and prediction. This is typically the case when there is more than one growth-limiting substrate in the chemostat model or when one couples species competition with a spatial structure (flocculation, niches...).

1. Non-spatial models.

Ordinary differential equations (ODE) are the common way to describe the evolution of the size or concentration of species populations and their functional contribution in resource transformation (such as substrate degradation) in homogeneous or perfectly mixed compartments (or ecological niches). The well-known chemostat model [87] used in microbiology for single strain:

$$\begin{aligned}\dot{s} &= -\frac{1}{y}\mu(s)b + D(s_{in} - s) \\ \dot{b} &= \mu(s)b - Db\end{aligned}$$

(where s and b stand respectively for the substrate and biomass concentrations, $\mu(s)$ is specific growth function, D the dilution rate, s_{in} the input substrate concentration), has to be extended to cope with the specificity of microbial ecosystems in the following directions.

- very large number (hundreds or thousands) of species. This leads to the problem of characterization of their distribution during the transients, that is a way to study the *functional redundancy* of ecosystems.
- environmental fluctuations (input flow rate, input concentration, temperature, pH...). This impacts the efficiency of a microbial ecosystem, when biological and environmental time scales are different. *Singular perturbations* is the technique we use to separate *slow* variables from *fast* ones, leading to approximations of the dynamics on *slow manifolds* to be determined and analyzed.
- interactions due to several limited resources and trophic chains. Most of the literature on the chemostat considers models with single limited resource, while some work studied purely essential or substitutable resources.
- several populations of bacteria (for each species) to describe the effects of certain spatial structures that are artificially created in bioreactors or naturally found in soils, like flocks, colonies or biofilms: the planktonic (or free) cells and the biofilm (or fixed) biomass (for telluric ecosystems, such a distinction is also relevant to represent the sticking/non sticking characteristics of soil). Considering simple models of aggregates (that are not spatialized) can provide a simplified model of the dynamics of the overall biomass.
- *active* and *dormant* bacteria. This distinction is motivated by the observations made on ecosystems of sparse resources such as arid soils.

2. Spatial models.

In the spirit of lattice differential equations, representations in terms of networks of (abstract) interconnected bioreactors propose an intermediate level between models of average biomass (a single ODE) and a continuous representation of space (PDE). A model of interconnected bioreactors is a way to *implicitly* take into account spatial heterogeneity, without requiring a precise knowledge of it. It is similar to the island models used in ecology [85] but coupled with the dynamics of abiotic resources and hydrodynamics laws (transport, percolation, diffusion) governing the transfers between patches. This approach appears to be relevant for telluric ecosystems, for which pedologists report that microbial activities in soil are usually concentrated in *hot-spots* that could be seen as small bioreactors. Understanding the role of the topology of the interconnection network and how a spatial structure impacts the outputs is also relevant in biotechnology to improve the yield or stability of processes.

3.1.2. Microscopic models

In these models (birth and death processes, neutral models, individual-based models) the dynamic of the population is described in terms of discrete events: birth and death of individuals, or jumps in terms of biomass. These models can be gathered under the same framework that could be called *Markov stochastic processes with discrete events*. Most of the time they should be coupled with continuous components like the size of each individual or the dynamic of the resources (represented in terms of ODE or PDE).

The Markovian framework allows on the one hand sharp analyses and rescaling techniques [76]; on the other hand it induces a simplification in the memory structure of the process that is important in terms of simulation. Indeed, as the future state of the system depends from the past only through the present state, only the current state should be kept in memory for simulation.

We will consider three families of processes with discrete events, from simplest to most complex.

1. Birth and death processes.

These models [77] are of first importance in small population size. They indeed allow investigation of near-to-extinction situations in a more realistic ways than the classical ODE models: they permit the computation, analytically but most of the time numerically, the distribution of extinction time and the probability of extinction. Efforts should be made to developed efficient Monte Carlo simulation procedures and approximation techniques for extinction probability and time distribution evaluation. In larger population sizes, they are advantageously approximated by diffusion models (see next section).

2. *The neutral models.*

In *neutral* models [82] sizes of different species evolve as birth and death processes with immigration: all individuals have the same characteristics and are not spatialized. Such hypotheses could be considered unrealistic from a purely biological perspective, but these models focus on some precise properties to be simulated and predicted (for instance the biodiversity).

Comparing the prediction of species abundance of these models to real observations provides a way to justify or invalidate the neutral hypothesis. Extensions of the neutral model, that was originally introduced for forest ecology, have to be developed in order to better suit the framework of microbial ecology, such as the non constant size of the populations and spatialized variations.

3. *The individual based models.*

IBM's [68], [69] appear to be well suited to describe colonies or biofilms [88]: in addition to birth, death and movement events, one has to consider *aggregation* and *detachment* events. The mechanisms that lead to the emergence of spatial patterns of colonies, or the formation of biofilms, which adhere to surface via polymers generated by the bacteria under specific hydrodynamics conditions, are not well understood yet. Typically, one can consider that bacteria inside the aggregates are disadvantaged to access the nutrient.

IBM modelling is a convenient way to propose aggregation and detachment mechanisms at the individual level in terms of random events connected to the geometry of the neighborhood, and to compare generated images with microscopic observations (for instance the confocal microscopy).

One has to be aware that few methods are available to study systematically and rigorously the properties of IBM, contrary to models based on differential equations (ODE, PDE...).

3.1.3. *Bridges between models*

The “theory of a computational model”, that combine two kinds of models (typically ODE and IBM) that are different representations of the same objects, relies on two steps: the “program making” and the “theoretical study”, in the spirit of the *double modelling* approach (roughly speaking, it consists in grasping the complexity of a IBM by analyzing accurately the consequences of each hypothesis on the macroscopic behavior of the model, building an approximate model of its global dynamics). Two main tools can be considered.

1. *Change of scale.*

For IBM models (neutral or Markovian), we consider mean field and moments approximation techniques that provide information at the macroscopic (i.e. populational) level, to be compared with macroscopic models. From a birth-and-death process describing the individual level, a renormalisation can provide a stochastic differential equation at a meso-scale. The *diffusion approximation* technique can be understood as a numerical acceleration technique where the number of births and deaths follows a normal law. These stochastic models at meso-scale can provide additional information compared to deterministic models at a macro-scale, such as parameter identifiability or finite time extinction. The price to pay is to give much more conceptual and numerical efforts, that become less relevant for very large populations.

For PDE models on spatial domains described with regular patterns (such as models of biofilm), the homogenization technique allows to obtain simpler PDE with constant parameters.

2. *The multi-scale modelling.*

The spatial heterogeneity in microbial ecosystems requires to consider simultaneously several scales:

- a *physical* scale. In batch processes, nutrient diffusion can be modelled by adapting the heat equation with Dirichlet boundary conditions. In continuous reactors, a convection-diffusion equation with Neumann boundary conditions is considered instead, the speed vector field being provided by the equations of fluid mechanics. The spatial scale used for the discretization is given by diffusion and flow parameters.
- a *biological* scale, given by the size and mobility of bacteria. Usually, this scale is larger than the physical one (at least in the liquid phase).
- an *aggregation* scale of colonies or biofilms, even larger, that provides the spatial patterns.

It is always possible to describe all the processes at the smaller common scale and then use a global representation, but this leads to extremely long computation times. The challenge is to manage these overlapping scales together and guarantee the stability of the numerical schemes. This is the goal of the *multi-scale* approaches [84]. For microbial ecosystems, it consists in

1. proposing new representations of the various scales of aggregation of bacteria in a model, taking into account the attachment-detachment processes determined by the local hydrodynamics conditions. Here, discussions with specialists of fluid mechanics are required.
2. coupling diversity models (e.g. models based on the neutral assumption) with spatial models (that reproduce the patterns observed on images of microscopy) to better understand the link biodiversity/structure.
3. introducing new *control* variables, considered as independent variables, each of them describing a proper scale. For this purpose, we investigate different techniques available to determine such variables: *mean-field* approximation, *singular perturbations*, *unification by limiting layers* or
4. *renormalising*, that aims at detecting invariants among models of different scales.

3.2. Interpreting and analyzing experimental observations

The validation of microbial models on data is rarely a straightforward task, because observations are most of the time not directly related to the variables of the models. Techniques such as abundance spectrum provided by molecular biology or confocal imagery are relatively recent in the field of microbial ecosystems. The signals provided by these devices leave many research questions open in terms of data interpretation and experiments design. One can distinguish three kinds of key information that are needed at the basis of model assumptions:

- structure of the communities (i.e. who is present?),
- nature of interactions between species (competition, mutualism, syntrophism...),
- spatial structure of the ecosystems.

3.2.1. Assessment of community structures

Ecosystems biodiversity can be observed at different levels, depending on the kind of observations. One usually distinguishes:

1. *The taxonomic diversity*. Several techniques developed by molecular biologists can gather information on the genetic structure of communities:
 - *sequencing of a given gene in the community*. The RNA 16S gene is often chosen to identify bacteria or Archeae.
 - *molecular fingerprints*. Some regions in the sequence of the RNA 16S gene encode faithfully the taxa species and can be amplified by PCR techniques.
 - *the sequencing of the overall genetic material of a community* (meta-genomic)

All these techniques bring new problems of data interpretation to estimate in a robust manner the properties of communities. The signals are combinations of contributions of abundances from each taxon. For an ecosystem with a limited diversity, composed of known species, the signal allows to determine with no ambiguity the abundances. In natural ecosystems, the signal is more complex and it is hopeless to determine uniquely the taxa distribution.

2. *The functional diversity.* It is usually observed at a larger scale, measuring the performances of the overall ecosystem to convert organic matter. The taxonomic diversity does not usually provide such information (it is possible to study *functional genes* but this is much more difficult than studying the 16S one).

A convenient way to study the functional performance of microbial community dynamics is to grow the same microbial community on different substrate compositions, and monitor its performance on these different substrates. Neutral community models [82] provide a reference for what would happen if no functional differences are present in the community. The deviation of experimental observations from neutral model predictions can be considered as a measure of functional diversity.

Understanding the links between taxonomic and functional diversity is currently a tremendous research question in biology about genotype/phenotype links, that one can also find in the specific context of microbial ecosystems.

3.2.2. Characterization of the interactions

The role of biodiversity and its preservation in ecosystems are research questions currently largely open in ecology. The nature and number of interactions between bacterial populations are poorly known, and are most probably a key to understand biodiversity. In the classical chemostat model, inter-specific interactions are rarely considered. Also in theoretical ecology, interaction information is typically encoded in an *interaction matrix*, but the coupling with common abiotic resources and the stoichiometry is hardly addressed in the models.

The information provided by confocal microscopy is also a way to estimate the distance of interactions between microorganisms and substrates. This knowledge is not often documented although it is crucial for the construction of IBM.

3.2.3. Observation of spatial structures

Schematically, one can distinguish two origins of spatialization:

1. due the physics of the environment. In bioprocesses, this happens typically for large tank size (inducing *dead zones*) or sludge accumulation making the suspension closer from a porous medium than a liquid one. Numerical experimentation can be driven, coupling a solver of the equations of the fluid mechanics with microbiology equations. Then, the spatial distribution of the biomass can be observed and used to calibrate simpler models. Typically, a dead zone is modelled as a diffusive interconnection between two perfect (abstract) tanks.

But the biotechnology industry aims at considering more sophisticated devices than simple tanks. For instance, the fluidized bed technique consists in creating a counter-current with oxygen bubbles for preventing the biomass to leave the reactor. In more complex systems, such as soil ecosystems, it is difficult to obtain faithful simulations because the spatial structure is rarely known with accuracy. Nevertheless, local observations at the level of pores can be achieved, providing information for the construction of models.

2. due to the formation of aggregates (flocks, biofilms...) or biomass wall attachment. Patterns (from ten to a hundred micro-meters) can be observed with confocal microscopy.

Spatial distribution of bacteria, shape of patterns and composition of the aggregates help to express hypotheses on individual behaviors. But quantification and variability of images provided by confocal microscopy are difficult. An open question is to determine the relevant morphological indicators that characterize aggregation and the formation of biofilms.

3.3. Identifying, controlling and optimizing bioprocesses

The dynamics of the microbial models possess specificities that do not allow the application of the popular methods of the theory of automatic control [71], such as linear control, feedback linearization or canonical forms.

- positivity constraints. State variables, as well as control inputs, have to stay non-negative (input flow pump cannot be reversed because of contamination issues).
- non-linearity. Several models have non-controllable or non-observable linearizations when inhibition effects are present (i.e. change of monotonicity in the growth curves).
- model and measurement uncertainties. In biology, it is rarely relevant to consider model uncertainties as additive Gaussian or finite energy signals.

3.3.1. Software sensors and identification

Sensors in biology are often poor and do not provide the measurements of all the state variables of the models: substrate, strain and product concentrations. In addition, measurements are often spoilt by errors. For instance optical density measurements give an indirect measure of the biomass, influenced by abiotic factors that share the same medium.

Analytical techniques are well suited to ODE models of small dimension, such as:

- guaranteed set-membership observers, when the system is non observable or in presence of unknown inputs,
- (non-linear) changes of coordinates, when the system is observable but not in a canonical form for the construction of observers with exponential convergence.

Software sensors can be also derived with the help of simulation based approaches like particle filtering techniques [75], [74]. This method is suited to diffusion models that approximate birth and death processes. Such softwares will allow us to investigate the different sources of randomness: demography, environment, but mainly imprecision of the sensors.

Similarly, identification techniques for constant parameters are based on sensor models as well as demography and environmental randomness models. In this case, Bayesian and non-Bayesian statistical techniques can be used [73], [70].

3.3.2. Bioprocess stabilization

In bioprocesses, the most efficient bacterial species at steady state are often inhibited by too large concentrations of substrates (this corresponds to assuming that the growth function $s \mapsto \mu(s)$ in the classical chemostat model is non-monotonic). This implies that the washout equilibrium (i.e. disappearance of the biomass) can be attractive, making the bioprocess bi-stable.

A common way to globally stabilize the dynamics toward the efficient equilibrium is to manipulate the dilution rate D [71]. But a diminution of the input flow rate for the stabilization requires to have enough room for an upstream storage, which is an expensive solution especially for developing countries that need to be equipped with new installations.

Alternative ways are proposed to stabilize bioprocesses without restricting the input flow rate:

- either by *physical means*, in terms of recirculation and bypass loops, or membranes as a selective way to keep bacteria and their aggregates inside the tank and improve its efficiency.
- either by *biological means*. The *biological control* consists in adding a small quantity another species with particular growth characteristics, that will help the other species to win the competition in the end.

3.3.3. Optimal control of bioreactors

The filling stage of bioreactors, or “fed-batch”, is often time consuming because the quantity of initial biomass is small and consequently the population growth is slow. The minimal time is a typical criterion for designing a filling strategy, but the optimal feedback synthesis is non trivial and may present singular arcs when the growth function is non-monotonic [86].

Recent progress have been made in the consideration of

- multi-species in sequential reactors (having more than one strain makes significantly more difficult to analyze singular arcs because of the higher dimensions of the state space, and there is little literature on the subject),
- energy consumption of flow pumps and the value of byproducts of the biological reactions such as biogas in the criterion (instead of minimal time or as penalties). Recent concerns about sustainable development encourage engineers to look for compromises between those objectives under constraints on output concentrations.

3.3.4. Plant design and optimization

We distinguish two kind of setups:

1. *The industrial setup.* A research question, largely open today, is to identify networks of interconnections of bioreactors that are the most relevant for industrial applications in terms of the following objectives:
 - reasonably simple configurations (i.e. with a limited number of tanks and connections),
 - significant improvement of the residence time at steady state over single or simpler configurations, or shapes of the reservoirs such that the total volume required for a given desired conversion factor at steady state is reduced.
2. *The bioremediation setup.* Typically, the concentration of pollutant in a natural reservoir is solution of a transport-diffusion PDE, but the optimal control of the transport term is almost not studied in the literature.

4. Application Domains

4.1. Preservation of water resources

The biological decontamination of wastewater is our main application domain, in the continuation of the long collaboration with the INRA research laboratory LBE. We target applications from the decontamination industry, held by large groups as well as small companies specialized in specific pollutants (for instance in fish farming). We aim also to study connected application domains for

- the aquatic ecology where microorganisms play an important role in the quality of natural water resources,
- the re-use of water in arid climates for countries of North of Africa, within the euro-Mediterranean project TREASURE.

4.2. Microbial ecology of soil

This application domain is more recent for the team members. We target

- the research questions raised by agronomists, about the better understanding of the interactions and the biodiversity of microbial communities in soils, with the help of models and numerical simulations,
- the role of spatial structures on the functions or *ecological services* of microbial ecosystems, notably the soil fertility and the carbon sequestration.

4.3. Control of fermentation processes

Very closely to our studies about wastewater bioreactors and chemostat models, we target applications in fermentation processes:

- either for agro-food products. A typical application is the control of cascade fermenters in the study of wine fermentation with UMR SPO (Sciences Pour l'Œnologie, Montpellier), within the European project CAFE.
- either for the green chemistry. A typical application is the consideration of spatialization in enzymatic models of production of agro-polymers with UMR IATE (Ingénierie des Agro-polymères et Technologies Émergentes, Montpellier).

4.4. Animal digestive ecosystem

Ruminants absorb plant cells, mainly constituted by cellulose, from which the microbial population of their digestive system extracts carbon and energy to provide proteins and energetic molecules. This bio-conversion produces also important quantities of methane, a gas responsible of part of the greenhouse effect (the billion of cows on earth reject 20% of the methane linked to human activities). INRA researchers have shown that this methane production could be reduced by 30% by changing the proportion of fat acids in the their food, that also implies that the composition of their microbial ecosystem is modified.

This application domain of the microbial ecology is at an early stage. URH team (Unité de Recherche sur les Herbivores, Clermont) has developed an artificial rumen that is close to a chemostat, for testing different kind of nutrition diets. Preliminary contacts have been taken, and a modelling demand has been clearly formulated and will be taken up by MODEMIC. This theme falls into the research priorities for the environment preservation.

5. Software

5.1. VITELBIO

Participants: Jérôme Harmand, Alain Rapaport.

VITELBIO (Virtual TELluric BIOreactors) is a simulation tool for studying networks of interconnected chemostats with the objective of mimicking microbial activities in soil. The software, developed with the help of ITK Company, is accessible on a server from any web navigator and make use of Flex for the user interface and Octave for the numerical integration. An important effort has been made for obtaining a pleasant and easy interface that is appealing for microbiologists: the network can be drawn graphically on the screen and simulation results can be easily compared between (virtual) experiments, superposing trajectories curves.

This software is used by several researchers, from LBE (INRA Narbonne), UMR Eco & Sols (Montpellier), UREP (Unité de Recherche sur l'Ecosystème Prairial, INRA Theix), Biomeco (Paris-Grignon), UMR EGC (Environnement et grandes cultures, Paris-Grignon)... and also as a teaching support. Vitelbio is presented at <http://sites.google.com/site/vitelbio/> and it is accessible at <http://vitelbio.itkweb.fr>.

5.2. SMC DEMOS

Participant: Fabien Campillo.

SMC DEMOS (Sequential Monte Carlo demos) proposes a set of demonstration Matlab procedures for nonlinear filtering approximation via particle filtering (sequential Monte Carlo): bearing-only tracking with obstacles, tracking in digital terrain model, track-before-detect in a sequence of digital picture, mobile phone tracking based on the signal strength to nearby antenna. This software is deposited with the "Agence pour la Protection des Programmes" (APP, 7/7/2009), available at <http://www-sop.inria.fr/members/Fabien.Campillo/software/smc-demos/>.

6. New Results

6.1. Theoretical results

6.1.1. Models resource/consumer

The team maintains a significant activity about the theory of the chemostat model, proposing and studying extensions of the classical models.

6.1.1.1. Theory of competition and coexistence

Participants: Jérôme Harmand, Claude Lobry, Tewfik Sari.

In the papers [41], [50] we consider deterministic models of competition. We study the persistence of species. In [25] we study a syntrophic relation between microbial species. In [26], we give a global asymptotic stability result for a mathematical model of competition between several species in a chemostat, by using a new Lyapunov function. The model includes both monotone and non-monotone response functions, distinct removal rates for the species and variable yields, depending on the concentration of substrate.

6.1.1.2. Study of interconnected chemostats

Participants: Jérôme Harmand, Alain Rapaport.

We have shown how a particular spatial structure with a buffer globally stabilizes the chemostat dynamics with non-monotonic response function, while this is not possible with single, serial or parallel chemostats of the same total volume and input flow. We give a characterization of the set of such configurations that enjoy this property, as well as the configuration that ensures the best nutrient conversion. Furthermore, we characterize the minimal buffer volume to add to a single chemostat for obtaining the global stability. These results are illustrated with the Haldane function that models inhibition in micro-organisms growth [67].

In industrial applications, the attraction of the wash-out equilibrium is undesired because it presents a risk that may ruin the culture in case of disturbance, temporarily pump breakdown or presence of toxic material that could drive the state in the attracting basin of the wash-out equilibrium. This approach has led to a patent deposit by INRA [59] during the PhD of H. Haidar, a former PhD student of the team [80].

6.1.1.3. Aggregation models in the chemostat

Participants: Radhouene Fekih-Salem, Jérôme Harmand, Claude Lobry, Alain Rapaport, Tewfik Sari.

We have studied a model of the chemostat where the species are present in two forms, isolated and aggregated individuals, such as attached bacteria in biofilm or bacteria in flocks. We show that our general model contains a lot of models that were previously considered in the literature. Assuming that flocculation and deflocculation dynamics are fast compared to the growth of the species, we construct a reduced chemostat-like model in which both the growth functions and the apparent dilution rate depend on the density of the species. We also show that such a model involving monotonic growth rates may exhibit bi-stability, while it may occur in the classical chemostat model, but when the growth rate is non monotonic [21], [54]. This work is part of the PhD of R. Fekih-Salem co-supervised by A. Rapaport and T. Sari.

This research subject has been mainly motivated by the DISCO project (see Section 7.3).

6.1.1.4. Overyielding in continuous bioprocesses

Participants: Denis Dochain, Alain Rapaport.

We have shown that for certain configurations of two chemostats fed in parallel, the presence of two different species in each tank can improve the yield of the whole process, compared to the same configuration having the same species in each volume. This leads to a (so-called) “transgressive over-yielding” due to spatialization [35].

This work has been achieved during the stay of Prof. P. de Leenheer (Univ. Florida).

6.1.2. *Measuring taxonomic diversity of microbial communities*

Participant: Bart Haegeman.

Diversity is considered to be a main determinant of the behavior of microbial communities. However, measuring microbial diversity is challenging. Although metagenomic techniques allow us to sample microbial communities at unprecedented depths, the disparity between community (e.g., 10^{15} organisms) and sample (e.g., 10^5 organisms) remains large. We have studied what the diversity observed in a sample tells us about the real diversity of the community.

For a given empirical sample the aim is to construct the community from which this sample was taken. It turns out that a large set of community structures are consistent with the sample data. Some diversity metrics vary widely over this set of consistent communities, and are therefore difficult to infer from the sample data. Other diversity metrics are approximately constant over the set of consistent communities, and are therefore much easier to infer from the sample data.

The analysis of the set of consistent communities has yielded the following insights. First, it is impossible to robustly estimate the number of species from sample data. This is easy to understand. Microbial communities typically contain a large number of rare species, and these rare species are unlikely to be present in the sample. Hence, sample data are lacking crucial information to estimate species richness. Second, other diversity metrics, in particular Shannon and Simpson diversity, can be robustly estimated from sample data. We have constructed lower and upper estimates for a general class of diversity metrics, and we have shown that the difference between the extremal estimators, that is, the estimation uncertainty, is small for Shannon and Simpson diversity.

6.1.3. *A theory of genetic diversity within bacterial species*

Participant: Bart Haegeman.

With the wide availability of DNA sequencing, microbiologists are now able to rapidly sequence entire bacterial genomes. Comparison of these genomes has revealed a large genetic diversity within bacterial species. For example, one genome of the bacteria *E. coli* has about 4000 different genes, but a set of 10 genomes of *E. coli* has typically over 10000 different genes. Some of these genes are shared by all or almost all of the genomes, but many other genes are only present in one or a few of the genomes. This observation has important implications for the definition of bacterial species and for the description of the functional characteristics of bacteria.

In [23] we propose a theory for the frequency distribution of genes within a set of genomes. The model describes the genetic diversity as a balance between two forces. Demographic processes such as division and death tend to reduce the genetic diversity; horizontal gene transfer from other species can increase the genetic diversity. Our model predicts that the gene frequency distribution is U-shaped, meaning that there are a large number of genes present in only a few genomes, a small number of genes present in about half of the genomes, and a large number of genes present in almost all genomes. This prediction is consistent with the gene frequency distributions of six bacterial species we have analyzed (about 100 sequenced genomes in total). Importantly, the model does not assume any functional difference between the genes, that is, genes are considered to be selectively neutral. By showing that empirical gene frequency distributions can be reproduced by a neutral genome model, we contend that the frequency of a gene should not be interpreted as an indication of its essentiality or importance.

6.1.4. *Individual-based modelling for bacterial ecosystems*

Participants: Fabien Campillo, Chloé Deygout, Coralie Fritsch, Jérôme Harmand, Marc Joannides, Claude Lobry.

In terms of computational modelling of ecosystems, individual-based models (IBMs) are an interesting path to explore. We can outline two types of IBMs. On the one hand “detailed IBM” attempt to integrate in an ad-hoc way all the knowledge available about an ecosystem. On the other hand, “simplified IBM” are limited to one or several mechanisms to simplify the analysis. The former may be more realistic but are often difficult to analyze. Although the latter are too simplistic in realistic situations they lend themselves to the analysis and numerical analysis. We focus on the latter.

The IBMs offer an interdisciplinary language between biologists, biotechnologists, mathematicians, and computer scientists, to develop models in the form of relatively simple rules. In the case of simplified IBMs it is possible to translate these rules in the form of a branching Markov process with values in a space of measures. Using scaling methods, the IBMs can be approximated by integro-differential equations; using model simplification methods IBMs can be reduced to stochastic or ordinary differential equations. The mathematical interpretation of the IBMs and their analysis is relatively recent and still very few studies exist [78]. The numerical analysis of these models is yet to be built. Under certain conditions, IBMs themselves can be simulated through adapted Monte Carlo procedures.

The MODEMIC project-team develops many studies in the field of IBMs. The first is part of the ANR MODECOL on the modelling of clonal plant growth (see Section 7.4); the second is part of the ANR DISCO on modelling of biofilms (see Section 7.3); the third is also part of the ANR DISCO is dedicated to the modelling of biofilms in plug-flow reactors (see Section 6.2.2); the last one is the ongoing thesis of Coralie Fritsch at the École Doctorale I2E of the University of Montpellier 2, under the supervision of Fabien Campillo and Jérôme Harmand. The thesis aims at developing and analyzing “simple” individual-based microbial ecosystems models.

In all cases, we aim at developing the Monte Carlo simulation of the IBM as well as analyzing their links with integro-differential models. We also seek to make connections with non-IBM models proposed in Section 6.1.5.

6.1.5. Stochastic/discrete and stochastic/continuous modelling for biotechnology and population dynamics

Participants: Fabien Campillo, Marc Joannides, Claude Lobry.

In [14], we consider a stochastic model of the two-dimensional chemostat as a diffusion process for the concentration of substrate and the concentration of biomass. The model allows for the washout phenomenon: the disappearance of the biomass inside the chemostat. We establish the Fokker-Planck equation associated with this diffusion process, in particular we describe the boundary conditions that modelize the washout. We propose an adapted finite difference scheme for the approximation of the solution of the Fokker-Planck equation.

In [15], we consider a hybrid version of the classical predator-prey differential equation model. The proposed model is hybrid: continuous/discrete and deterministic/stochastic. It contains a parameter ω which represents the number of individuals for one unit of prey – if x denotes the quantity of prey in the differential equation model $x = 1$ means that there are ω individuals in the discrete model – is derived from the classical birth and death process. It is shown by the mean of simulations and explained by a mathematical analysis based on results in singular perturbation theory (the so called theory of Canards) that qualitative properties of the model like persistence or extinction are dramatically sensitive to ω . This means that we must be very cautious when we use continuous variables in place of jump processes in dynamic population.

6.1.6. Optimal control of continuous bioprocesses

Participants: Walid Bouhaf, Amel Ghouali, Jérôme Harmand, Alain Rapaport.

In continuous bioprocesses, a usual objective is to stabilize the output of the bioreactors about a desired steady state (in wastewater industry, this value is typically chosen under the norm of authorized discharge). It happens more and more frequently that transient trajectories are expected also to maximize a product of interest.

We have begun to study the maximization of the gaseous production of methane in anaerobic processes over a given period of time on specific problems. For the moment we have proven that the optimal trajectory consists in approaching a unique singular arc as fast as possible when only one limiting substrate has to be converted, but the problem is still open when involving several substrates [39]. Another problem arises for alternating aerobic-anoxic systems. Revisiting the results obtained several years ago within the framework of Djalel Mazouni's thesis, we aim at proposing optimal time control policies for sequencing batch reactors in which simultaneous nitrification and denitrification take place. The solution for the original problem is a difficult task but we have already proposed a solution for a slightly modified model [30]. These last results have been obtained within the framework of the PhD thesis of W. Bouhafs.

Reference points in batch processes can be mimicked by a series of continuously stirred bioreactors in series at steady state (see applications 6.2.4 and 7.1). We study the minimal time problem to drive the nutrients concentrations of a cascade of chemostats. The control variable is the dilution rates of each tank, under the constraint that each dilution rate is bounded by the one of the previous tank, that makes the system not locally controllable. For the particular case of two tanks with total mass at steady state, the planar feedback synthesis has been found but the problem is still under investigation for the general case.

One important issue in bioprocesses is to find optimal feedback control laws in order to steer a system describing a perfectly-mixed bioreactor to a given target value in a minimal amount of time. Finding adequate feeding strategies can significantly improve the performance of the system. A typical target (for fed-batch bioreactors) is to consider the substrate concentration to be lower than a given reference value at the end of the process. Other criterium can be studied such as the maximization of the production of biomass in a given time period. Singular strategies (in reference to the theory of singular arcs in optimal control theory) can be defined in this context and are natural due to the constraints on the system. One objective of our research is to characterize optimal feedback control laws using mathematical tools from optimal control laws, and also to develop numerical methods that can handle problems with a large number of parameters.

6.1.7. Modelling the functioning of soil ecosystems

Participants: Céline Casenave, Jérôme Harmand, Alain Rapaport.

In ecology, one of the important challenges is the understanding of the biodiversity observed in the natural ecosystems. Several models have been proposed to explain this biodiversity, and in particular the coexistence of different species. In these models, it is often assumed that, when they die, the micro-organisms are directly converted in an assimilable resource, that is a resource that alive organisms can consume. However, we know that it is not the case in reality. Indeed, the organic matter stemmed from the dead organisms has to be transformed in assimilable resource before it can be consumed. This transformation is performed by some micro-organisms which have this special ability.

We have proposed a new model of soil ecosystems, of chemostat type. This model is rather simple, but also original because it takes into account several mechanisms:

- the growth, the mortality and the respiration,
- the ability of some organisms to transform the non assimilable resources in assimilable ones,
- the advantage that an organism can gain from this ability of transformation.

For the moment, we have considered the case where only one or two types of organisms are present. The model is finally composed of 3 (or 4) nonlinear ordinary differential equations: one per type of organisms, one for the assimilable resource and one for the non assimilable one. The study of the equilibrium points has first shown the possibility of coexistence, at equilibrium, of the two organisms. Then, in numerical simulations, we have observed the possible existence of limit cycles, which can also explain the coexistence of organisms observed in the nature.

This problem is still under study; a working group (in particular with researchers of the UMR Eco & Sols, conducted by B. Jaillard) meet regularly to discuss about the problems of modelling in ecology.

We have also investigated the *sampling effect* that occurs when micro-biologists select randomly species in a natural ecosystem for studying reconstituted ecosystems in a controlled environment. We have proposed a very simple probabilistic model, that shows that observing average increases or decreases on the performances of these reconstituted ecosystems when modifying the size of the sampling, allows to infer kinds and proportions of the interactions among species present in the original ecosystem [65]. This research is conducted with the UMR Eco & Sols, Montpellier, (B. Jaillard) and the UMR BIOEMCO, Grignon (N. Nunan).

6.1.8. *Equivalence between models of fractured porous media*

Participants: Céline Casenave, Jérôme Harmand, Alain Rapaport, Alejandro Rojas-Palma.

In geosciences, models of fractured porous media are often described as a *mobile* zone driven by advection, and one or several *immobile zones* directly or indirectly connected to the mobile zone by diffusion terms. We believe that these models are also relevant to describe flows in soil or in porous media such as biofilms. They are very close from the spatial representations used in Section 6.2.6. We have shown, using a transfer function approach, that two schemes often used in the literature: the MINC (Multiple Interactive Continua) where diffusive compartments are connected in series, and the MRMT (Multiple Rate Mass Transfer) where diffusive compartments are connected in star around the mobile zone, are equivalent input-output representations [56], and providing formulas (up to three compartments) to pass from one representation to another. This result means that one can simply choose the most convenient approach when dealing with control or optimization without any loss of generality. We are currently working on the general case of n compartments with n larger than three, and looking for equivalent classes of configurations that could be half way between MINC and MRMT and fit better the spatial representations of real world.

This work is performed with the UMR GéoSciences Rennes (J.R. de Dreuzy), and has led to the internship of a Chilean MsC student (A. Rojas-Palma).

6.1.9. *Non-linear filtering for the chemostat*

Participants: Boumediene Benyahia, Amine Boutoub, Fabien Campillo, Jérôme Harmand.

Monte Carlo-based inference methods like particle filtering are bound to develop in the context of biotechnology. In contrast with the classical observer approach, inference through Monte Carlo methods can handle measurements in discrete time in low frequency and with low signal-to-noise ratio. Based on the stochastic modeling of the chemostat, these approaches may also be used for model selection and hypothesis testing.

In a preliminary work [28] we consider the bootstrap particle filter applied to a 2-dimensional chemostat model. The internship of Amine Boutoub dedicated to the study of particle filtering for more realistic chemostat models has recently started.

6.1.10. *Functional identification of growth functions in the chemostat*

Participant: Alain Rapaport.

We have proposed an adaptive control law that allows one to identify unstable steady states of the open-loop system in the single-species chemostat model without the knowledge of the growth function. We have then shown how to use a continuation technique to reconstruct the whole graph of the growth function, providing a new method for identifying non-monotonic growths [42], [27]. Two variants, in continuous and discrete time, have been studied. An analysis of the case of two species in competition has shown the ability of the method to detect a mixed culture for which dominance depends on the dilution rate, due to a property of stability loss in slow-fast dynamics. This method leaves open future extensions for extremum seeking problems.

This work has been conducted in cooperation with Universities of Exeter (J. Sieber) and Plymouth (S. Rodrigues), and the EPI SISYPHE (M. Desroches).

6.1.11. *Diffusive representation of integro-differential models*

Participant: Céline Casenave.

This work is done in collaboration with Emmanuel Montseny (LAAS/CNRS), Gérard Montseny (LAAS/CNRS), and Christophe Prieur (LIAFA/CNRS).

In lots of dynamic systems of Physics or others scientific fields such as Biology (Volterra models), dynamic integral operators, often of convolution type, are involved. Problems relating to integro-differential models are often difficult to solve, especially because these models are not time-local. In this context, the methodology called “diffusive representation” presents some interests: an integral operator is represented by its gamma-symbol, directly deduced from its transfer function. It can be formulated by means of a state realization whose dimension is numerically reasonable whatever the size of the system may be. In addition to this interesting practical side, the diffusive representation offers a unified mathematical framework, well adapted to analysis of integral convolution operators.

Several dynamic problems can be tackled in an original and quite simple way by using the diffusive representation. In fact, all the operatorial problems of modeling, simulation, control, model identification, model reduction, etc. can be formulated in such a way that the object of the problem is the gamma-symbol of the operator solution.

Several problems are under study:

- the identification of integro-differential models [66],
- the controllability of some SISO Volterra models [63],
- the simulation and the analysis of a model of porous media[64].

These works follow up on the ones developed during the PhD thesis of Céline Casenave, which deals with the problem of the operator inversion for the application to non local dynamic problems.

6.2. Applications

6.2.1. Modelling and control of Anaerobic Digestion processes

Participants: Boumediene Benyahia, Amine Charfi, Radhouene Fekih-Salem, Jérôme Harmand, Guilherme Pimentel, Tewfik Sari.

We consider the AM2 or AMOCO model developed in [72] and extend both the model in itself and its analysis to the following cases:

- Depending on the AM2 model parameters, the steady states were analytically characterized and their stability were analyzed [12]. Following this study, it was shown that the overloading tolerance, a parameter proposed in [81] to on-line monitoring anaerobic processes, may be not adapted under certain operating conditions and even lead to bad operating decisions.
- Within the framework of the PhD theses of Amine Charfi and Boumediene Benyahia, we have included the fouling dynamics of membranes into the AM2 and we have analyzed the resulting model (called the AM2b) [16], [29].
- We actually work towards two directions: (i) we are extending these results in including into the AM2 an additional process, *i. e.* the hydrolysis step in order to study bioprocesses treating solid waste (the resulting model being called the AM3) [36], [37]; (ii) we try to find links between complex models such as the ADM1 model and simple models such as the AM2b or the AM3 [40].

Apart from this work on the modelling of anaerobic digesters and membrane bioreactors, we have developed a number of specific simple models for control design accounting for the coupling of such processes with membrane modules in the chemostat (PhD thesis of G. Pimentel). This work aims at contributing to the efficient treatment of wastewaters produced in fish production farms. The work of G. Pimentel aims at studying the coupling of simple fouling models with the model of the chemostat in order to propose new simple models for control design.

6.2.2. Hybrid modelling of biofilms in plug-flow reactors

Participants: Fabien Campillo, Chloé Deygout, Annick Lesne, Alain Rapaport.

We have proposed a multi-scaled modelling that combines three scales: a microscopic one for the individual bacteria, a mesoscopic or “coarse-grained” one that homogenises at an intermediate scale the quantities relevant to the attachment/detachment process, and a macroscopic one in terms of substrate concentration.

Such a “hybrid” approach allows for modelling and understanding in plug-flow reactors the interplay between

- the formation of the biofilm at a microscopic scale, that starts from a small number of bacteria (thus a stochastic individual based description),
- the limitation of the biofilm, due the carrying capacity of the wall attachment, at a mesoscopic scale,
- the consumption of nutrient along the flow at a macroscopic level, as a solution of a coupled transport-reaction partial differential equation.

The numerical computation of such a model requires a software architecture that allows the simultaneous simulation of stochastic events at the bacteria scale and the continuous evolution (in space and time) of the substrate density.

This work has been conducted within the DISCO project (see Section 7.3) and the postdoctoral stay of C. Deygout hired by the project, in close collaboration with A. Lesne (LPTMC, Univ. Paris VI). A first paper on the simulation model has been published [17].

Within the DISCO project, experiments on real tubular plug-flow reactors have been simultaneously driven at IRSTEA Antony with the perspective of comparison with numerical simulations.

The multi-species case with different bacteria specialized in different environments (poor or rich in nutrient) is a work in progress.

6.2.3. Individual-based models for the bacterial degradation of the cellulose

Participants: Fabien Campillo, Chloé Deygout.

We propose an individual-based model for the degradation of one cellulose bead (dozens of micrometers in diameter) by cellulolytic bacteria. This model accounts for biofilm formation with minimal hypotheses: soluble substrate diffusion combined with bacterial chemotaxis-like movement in the liquid phase, lack of bacterial movement in the solid phase. The IBM results are qualitatively different from the main macroscopic degradation models previously used for cellulose degradation. It suggests that random and discrete processes could significantly impact the cellulose degradation dynamics by their effect on the spatial structuration of the colonized cellulose particles [44].

6.2.4. Modelling and control of cascade biosystems to mimic batch wine making processes

Participants: T rence Bayen, C line Casenave, J r me Harmand, Alain Rapaport, Matthieu Sebbah.

An experimental setup of four tanks connected in series has been designed by the research unit SPO (Montpellier) for studying four physiological stages of yeast as steady state. The manipulated variables are the flow rates Q_i of each tank with the constraint $Q_i \geq Q_{i-1} \geq 0$, and the objective is to reach simultaneously four set-points in the four tanks. We are studying two kinds of control strategies:

- a linearizing feedback law that drives exponentially the dynamics to the target. This is not the fastest strategy but it has good robustness properties. Nevertheless, the inputs constraint imposes to use saturation functions that provide satisfactory convergence in simulations but that is hard to prove mathematically.
- a minimal time feedback. Due to lack of local controllability imposed by the constraint on the inputs, the optimal synthesis is not smooth with the presence of “barriers”. The input constraint $Q_i \geq Q_{i-1} \geq 0$ is unusual in optimal control problems that are linear w.r.t. to the control. The optimality of candidate singular arcs is still open for this problem.

This summer, some experiments have been made to test the first feedback law on the experimental setup. The control law seems to perform work, but other experiments should be made next year with more reliable input flow pumps.

This work was conducted as a part of the European CAFE project (Computer-Aided Food processes for control Engineering) described in Section 7.1.

6.2.5. *Modelling and control of an ice cream crystallization process*

Participants: Céline Casenave, Denis Dochain.

In the ice cream industry, the type of final desired product (large cartons or ice creams on a stick) determine the viscosity at which the ice cream has to be produced. The control the viscosity of the ice cream at the outlet of a continuous crystallizer is therefore an important challenge. The problem has been studied in two steps. First, we have completed and validated on experimental data the reduced order model of the system. This model has been obtained by application of the method of moments on a population balance equation describing the evolution of the crystal size distribution. Then, we have proposed a nonlinear control strategy to control of the viscosity of the ice cream with the temperature of the refrigerant fluid of the crystallizer. This control strategy is based on a linearizing control law coupled with a Smith predictor to account for the measurement delay. The control has been validated on an experimental pilot plant located at IRSTEA (Antony, France).

This work was conducted as a part of the European CAFE project (Computer-Aided Food processes for control Engineering) described in Section 7.1.

6.2.6. *Bioremediation of natural resources*

Participants: Sébastien Barbier, Jérôme Harmand, Alain Rapaport, Antoine Rousseau.

The objective of this work is to provide efficient strategies for the bioremediation of natural water resources. The originality of the approach is to couple minimal time strategies that are determined on a simplified model with a faithful numerical model for the hydrodynamics. This work has been carried out in close cooperation with A. Rousseau. Based on a previous paper that deals with an implicit representation of the spatial inhomogeneity of the resource with a small number of homogeneous compartments (with a system of ODEs), we have implemented a coupled ODE-PDE system that accounts for the spatial non-homogeneity of pollution in natural resources. The main idea is to implement a Navier-Stokes model in the resource (such as a lake), with boundary conditions that correspond to the output feedback that has been determined to be optimal for the simple ODEs model of a (small) bioreactor. A first mathematical model has been introduced and numerical simulations have been performed in academic situations. During the internship of S. Barbier (co-advised by A. Rousseau and A. Rapaport) we built a reduced model that approximates the reference PDE model thanks to a set of ODEs with parameters. Numerical optimization is performed on these parameters in order to better fit the reference model. This will lead to a publication.

The study of the minimal time strategies on the system of ODEs has been mainly achieved in cooperation with Chilean researchers (P. Gajardo, Universidad Tecnica Federico Santa Maria, and H. Ramirez, Centro de Modelamiento Matemático) and a Chilean PhD student (V. Riquelme, Depto. Ingenieria Matematica, Universidad de Chile) within the associated team DYMECOS [57].

6.2.7. *Modelling and simulating terrestrial plant ecological dynamics*

Participant: Fabien Campillo.

This study is part of the ANR Syscomm MODECOL that is done in collaboration particularly with the University of Rennes I, the University of La Rochelle and Inria. The first semester of 2012 was the last part of the project. We propose a very original individual-based model for clonal plant dynamics in continuous time and space that focuses on the effects of the network structure of the plants on the reproductive strategy of ramets. The model is coupled with a PDE dynamics for resources. The basic structure of the IBM encompass a population of “ramets” (the individuals) connected by “stolons or rhizomes” (the network) [13], [22]. See <http://www-sop.inria.fr/members/Fabien.Campillo/software/ibm-clonal/> for more details.

6.2.8. *Modelling and inferring agricultural dynamics*

Participants: Fabien Campillo, Angelo Raheiririna.

The International Laboratory LIRMA supports this work that is done in collaboration with the University of Fianarantsoa in Madagascar and with Dominique Hervé (IRD, Fianarantsoa, Madagascar). The aim is to study the dynamics of agricultural plots on the edge of primary forest. In [32] a simple Markov model has been successfully confronted to a first data set with the help of maximum likelihood and Bayesian approaches. On a new data set developed by IRD, the Markov hypothesis has been rejected and we proposed to use semi-Markov models: for this new dataset the law of the sojourn time on certain states will depend on the next state visited, which is incompatible with the Markov hypothesis and which is consistent with the semi-Markov hypothesis.

7. Bilateral Contracts and Grants with Industry

7.1. CAFE

Participants: Céline Casenave, Jérôme Harmand, Alain Rapaport.

The objective of the CAFE European project is to provide new paradigms for the smart control of food processes, on the basis of four typical processes in the areas of bioconversion, separation, preservation and structuring, see details in <http://www.cafe-project.org>. The novelty of the project lies in the capacity of combining PAT (Process Analytical Technology) and sensing devices with models and simulation environment with the following objectives:

1. to extract as much as possible information from the process/plant in the form of precise estimations of unmeasured variables defining, in particular, product quality, and of physical parameters changing as the process dynamics does or difficult to know beforehand;
2. to save and encode the information in a reliable and usable way, basically via physical/deterministic models;
3. to develop control methods to keep uniform quality and production, despite the variability in the raw material and/or to respond to sudden changes in the demand.

MODEMIC is involved in the wine making supervision part (see Section 6.2.4) and in the ice cream crystallization control part (see Section 6.2.5).

7.2. DIMIMOS

Participants: Jérôme Harmand, Alain Rapaport.

DIMIMOS is an ANR SYSTERRA 2008 project of 4 years headed by the UMR Microbiologie du Sol et de l'Environnement (INRA Dijon).

This fundamental research project aims at better understanding the functional microbial soil ecosystems with respect to the turnover of soil organic matter (SOM). More specifically, we aim at evaluating the role of the microbial diversity in transforming SOM, in order to better manage the carbon in its biochemical global cycle within agro-ecosystems. This project must deliver new insights for managing agricultural productivity (allow better agricultural practices) while maintaining a high quality of soil over the long term.

For the final stage of the project, the theoretical results obtained in Section 6.1.7 need to be confronted with the data provided by the partners.

7.3. DISCO

Participants: Fabien Campillo, Chloé Deygout, Bart Haegeman, Jérôme Harmand, Annick Lesne, Claude Lobry, Alain Rapaport, Tewfik Sari.

DISCO (Multi-scale modelling bioDiversity Structure COupling in biofilms) is a three years project funded by the ANR SYSCOMM since the end of 2009, that aims at developing and studying computational and mathematical models of biofilm dynamics, taking into account the biodiversity (distribution of bacteria species) and spatial structure; see details in <https://sites.google.com/site/anrdisco/>.

Several “go back” between simulation models and experiments in plug-flow reactors performed at IRSTEA Antony have been conducted during the two postdoctoral years of C. Deygout hired by the project. A first paper on the simulation of a multi-scale model has been published [17] and a second one on the confrontation with experiments is in preparation (see Section 6.2.2).

At a macro-scale, the team has studied several extensions of the chemostat model dedicated to microbial ecosystems with biofilm (see Section 6.1.1 and the publication [21]).

A new collaboration has been launched with the HBAN team at IRSTEA Antony, within this project, about the modelling of cellulose degradation. Cellulose is typically available in small balls (but ten times larger than the average size of microorganisms) that are first converted by enzymatic activity into carbon substrate that can then be assimilated by the microorganisms. Some of the microorganisms are attached to these balls, creating a particular aggregates structure.

An IBM for the degradation of one cellulose bead (dozens of micrometers in diameter) by cellulolytic bacteria has been developed. Our aim is to determine the macroscopic degradation behavior. The initial stages of the degradation process may involve a very limited number of bacteria that cannot be properly modelled by classical models based on deterministic equations (see Section 6.2.3 and communications [44] and [43]).

The duration of the project has been extended by the ANR to May 2013, in order for the team to prepare a final restitution at Paris in spring 2013.

7.4. MODECOL

Participant: Fabien Campillo.

The ANR SYSCOMM Project MODECOL (January 2009/June 2012) involves three Inria project-teams (MODEMIC, MAESTRO and TOSCA) with the UMR Ecobio (Ecosystèmes, Biodiversité, Evolution, Rennes), the University of La Rochelle and the Universities of Houston and Berkeley. The aim of the Inria component is to propose individual-based models for terrestrial prairial plant communities’ dynamics in the context of water purifying from nitrate and pesticides. The results of the Inria component have been published [13] This year was also dedicated to the edition of a special issue of Ecological Modelling on “Modelling clonal plant growth” [22]. See <http://www-sop.inria.fr/members/Fabien.Campillo/software/ibm-clonal/> for more details.

8. Partnerships and Cooperations

8.1. International Initiatives

8.1.1. Inria Associate Teams

8.1.1.1. Associated team DYMECOS

Participants: Térence Bayen, Fabien Campillo, Jérôme Harmand, Claude Lobry, Alain Rapaport, Alejandro Rojas-Palma, Tewfik Sari, Matthieu Sebbah.

Program: **Associate Teams**

Title: DYnamical Microbial and Environmental eCOSystems

Inria principal investigator: Alain Rapaport

International Partners (Institution - Laboratory - Researcher):

Universidad de Chile / Departamento de Ingeniería Matemática - Universidad de Chile / CNRS (Chile) / Centro de Modelamiento Matemático (CMM) - Héctor Ramírez

Universidad Tecnica Federico Santa Maria (Chile) - Departamento de Matematica - Pedro Gajardo

Duration: 01/01/2010 - 31/12/2012

DYMECOS is an associated team with Chile, mainly with CMM (Centro de Modelamiento Matemático), Univ. de Chile, Santiago, DIM (Departamento de Ingeniería Matemática), Universidad de Chile, Santiago and Departamento de Matematica, Universidad Tecnica Federico Santa Maria (UTFSM).

Two kinds of investigations have been conducted:

- minimal time control problems of fedbatch processes with several species, and optimal strategies for the bioremediation of natural water resources,
- stochastic modelling of the chemostat.

The second Franco-Chilean Workshop on Bioprocess Modelling has been co-organized by the team and the Chilean partners in January at Pucón (see <https://sites.google.com/site/eadymecos/evenements>). The workshop gathers mathematicians, process engineers and micro-biologists.

C. Lobry, A. Rapaport and T. Sari have participated to the 3rd LAWOC (Latin American Workshop on Optimization and Control) held in Valparaiso, Chile [48], [52], [54].

This year, the team has received A. Rojas-Palma as a MSc Internship for 3 months, and M. Sebbah has been hired by Inria-CIRIC for a postdoctoral stay of 3 months in the team (Oct.-Nov. 2012) followed by 13 months in Chile (starting Jan. 2013).

8.1.2. Participation In International Programs

8.1.2.1. CIRIC-Bionature

The team has contributed to the writing proposal of the Bionature line of the CIRIC (Communication and Information Research and Innovation Center) in Chile.

The 16 months postdoctoral grant of M. Sebbah (3 months in France, 13 months in Chile) is supported by Inria-Chile within this research program (see Section 8.1.1.1).

8.1.2.2. TREASURE

Participants: Fabien Campillo, Jérôme Harmand, Claude Lobry, Tewfik Sari.

Program: **Euromediterranean 3+3**

Title: Treatment and Sustainable Reuse of Effluents in semiarid climates

Inria principal investigator: Jérôme HARMAND

International Partners (Institution - Laboratory - Researcher):

University of santiago de compostella (Spain) - Environmental engineering - Juan GAR-RIDO

National Research Center (Egypt) - Water Pollution Control - Helmy EL-ZANFALY

Université Française d’Egypte (Egypt) - mathématiques - Mohamed JAOUA

Institut National de la Recherche Agronomique (France) - dpts EA, MICA et MIA - Pascal NEVEU

University of Tlemcen (Algeria) - Automatic control - Brahim CHERKI

University of Patras (Greece) - Process Control Laboratory - Costas KRAVARIS

Centre de Biotechnology de Sfax (Tunisia) - Department of environmental engineering - Sami SAYADI

Université Cadi Ayyad de Marrakech -Faculté des Sciences de Semlalia - Dépt. de Mathématiques (Morocco) - Centre National de Recherche sur l’Eau et l’Energie - Laila MANDI

Ecole Nationale des Ingénieurs de Tunis (Tunisia) - Mathématiques - Nabil GMATI

The TREASURE network aims at integrating knowledge on the modelling, the control and the optimization of biological systems for the treatment and reuse of wastewaters in countries submitted to semi-arid climates under both socio-economical and agronomic constraints within the actual context of global changes. A special focus of the actual project concerns the integration of technical skills together with socio-economical and agronomic studies for the integrated solutions developed within the network to be evaluated and tested in practice in the partner’s countries and, as possible as it may be within the context of the actual research network, valorizing these proposed technologies with the help of industrial on site in partners from South.

8.1.2.3. LIRIMA Stic-Mada

Participants: Fabien Campillo, Angelo Raheiririna.

Program: **LIRIMA**

Title: Stic-Madagascar

Inria principal investigator: Fabien Campillo

International Partners (Institution - Laboratory - Researcher):

University of Antananarivo (Madagascar) - Lala Andriamampianina

University of Fianarantsoa (Madagascar) - Rivo Rakotozafy

The MODEMIC Project-Team is coordinator of the LIRIMA/Stic-Mada project for the theme: modelling and management of natural resources. In 2012, Angelo Raheiririna (co-advised with F. Campillo and R. Rakotozafy) made a 6 months stay in MODEMIC team-project, he will defend his thesis in January 2013 (see Section 6.2.8).

8.2. International Research Visitors

8.2.1. Visits of International Scientists

D. Dochain, from CESAME, Univ. Louvain-la-Neuve (Belgium), has spent one month in the team. D. Dochain is the coordinator of the CAFE project (see Section 7.1).

8.2.1.1. Internships

A. Rojas-Palma, MSc student at Univ. of Chile, has spent 3 months in the team, in the scope of the Inria Internships (see Section 8.1.1.1).

8.2.2. Visits to International Teams

B. Haegeman is on secondment to CNRS since September 2012. He is working at the Centre of Biodiversity Theory and Modelling which is part of the Station for Experimental Ecology in Moulis (Ariège).

9. Dissemination

9.1. Animation of the scientific community

- A. Rapaport is presently the head of the UMR INRA-SupAgro MISTEA (Mathematics, Informatics and Statistics for Environment and Agronomy) where the team is housed. A. Rapaport is: member of the piloting board of the “modelling” axis of the LabEx Numev (Digital and Hardware Solutions, Modelling for the Environment and Life Sciences) at Montpellier; member of the scientific board of the “Ecotechnologies” department of IRSTEA; member of the scientific board of the “BIOS” department of CIRAD. A. Rapaport has been the president of the AERES visiting committee of the Research team “MOTIVE” of IRSTEA.
- F. Campillo is member of the NICE (long term invited scientists selection); deputy elected member of the Inria Scientific Council; member of the internal communication working group of Inria Sophia Antipolis. F. Campillo was member of the INRA selection board for the selection of junior scientists (statistics and modelling).
- J. Harmand is the responsible for the treasure-2 network (a 3+3 Euromed project) that has been accepted for funding for the next 4 years); member of the scientific council of the Environment and agronomic INRA department; member of the advisory board of the INRA metaprogram MEM (Meta-omic and Microbial Ecosystems); member of the INRA evaluation commission STEA (“Sciences de la Terre, de l’eau et de l’atmosphère”). J. Harmand is member of the steering committee of the MEM INRA metaprogram. J. Harmand is member of the scientific committee of the INRA Environment and Agronomy department.

- J. Harmand and A. Rapaport are responsible of the INRA network MODYM (MODèles DYnamiques et Métabolites) sponsored by the Applied Mathematics and Informatics Departement (MIA) of INRA.
- B. Haegeman is Academic Editor for PLoS ONE.

9.2. Seminars and schools

The MODEMIC project-team animates several seminars:

- The MODEMIC seminar on mathematical modelling [<http://www-sop.inria.fr/modemic/seminaire/>].
- I3M and MODEMIC working group on stochastic models for ecology and biology [<http://www-sop.inria.fr/modemic/personnel/campillo/GT-modelisation.html>]; this working group is supported by the “laboratory of excellence” (LabEx) NUMEV (Digital and Hardware Solutions, Modelling for the Environment and Life Sciences).
- A new seminar SAMOCOD on Optimisation, Control and Dynamics bilocated at Montpellier and Avignon will be launched in January 2013 [<http://ens.math.univ-montp2.fr/SPIP/sem.php3?a=programme&sem=61>]. A. Rapaport is member of the organizing committee.

9.3. Teaching

- F. Campillo and M. Joannides have given a 20 hours lecture on “Stochastic modelling of ecosystems” at the Master 2 in Biostatistics in Université de Montpellier II.
- A. Rapaport has given a 25 hours lecture on differential equations with applications in the “Practical Mathematics” module for 1st year students in MSc in Mathematics at University Montpellier II.
- C. Casenave, F. Campillo, J. Harmand and A. Rapaport are in charge of two modules in the new MSc program “STIC - Environnement” at University Montpellier II:
 - Introduction to mathematical modelling, master I (50 hours)
 - Advanced mathematical modelling, master II (75 hours)
- C. Casenave, F. Campillo and A. Rapaport have delivered a 20 hours doctoral module at University Montpellier II, entitled “Modelling for biology and ecology – mathematical and computational methods”.
- A. Rapaport and T. Bayen have given six lectures on mathematical modelling for 1st year students of SupAgro Montpellier.
- A. Rapaport has given two lectures on Modelling and numerical simulations at the “EcoSystèmes” Master at University of Montpellier II.

9.4. PhD’s

Defended thesis:

- Boumediène Benyahia, “Modélisation et contrôle de bioréacteurs à membrane”; grant: Coadvise and Treasure; thesis in co-supervision Montpellier-Tlemcen (Algeria); started in October 2008; advisors: J. Harmand and B. Cherki (Tlemcen, Algeria).

Theses in progress:

- Mamadou Lamine Diagne, “Modélisation mathématique du Typha”; grant: AUF; thesis in co-supervision Mulhouse-Saint Louis (Senegal); started in October 2009; advisors: T. Sari and M.T Niane (Saint Louis, Senegal).
- Radhouene Fekih-Salem, “La compétition et la coexistence dans le Chemostat”; grant: Averroes; thesis in co-supervision Montpellier-Tunis; started in October 2010; advisors: A. Rapaport, T. Sari and N. Gmati (Tunis).
- Walid Bouhaf, “Commande optimale des réacteurs séquentiels discontinus”; grant: Université Tunis Carthage; thesis in co-supervision Montpellier-Tunis; started in October 2010; advisors: J. Harmand, F. Jean (ENSTA-ParisTech, Paris) and Nahla Abdellatif (Tunis, Tunisia).
- Amel Ghouali, “control en tamps minimal des réacteurs de digestion anaérobie”; grant: Averroes; thesis in co-supervision Montpellier-Tlemcen (Algeria); started in October 2011; advisors: J. Harmand and A. Moussaoui (Tlemcen, Algeria).
- Sonia Hassam, “Réduction de modèles de la digestion anaérobie”; grant: Univ. Tlemcen; started in October 2010; advisors: J. Harmand and B. Cherki (Tlemcen, Algeria).
- Angelo Raherinirina, “Modélisation markovienne de dynamique d’usage des sols”; grant: AUF, SCAC Madagascar, LIRIMA; started March 1st 2009; advisors: F. Campillo and R. Rakotozafy (Univ. Fianarantsoa Madagascar).
- Coralie Fritsch, “Simulation et analyse de modèles individu-centrés d’écosystèmes bactériens pour des procédés biotechnologiques”, école doctorale I2S; grant: INRA Metaprogram MEM and Univ. Montpellier II; started October 1st 2011; advisors: F. Campillo, J. Harmand.
- Guilherme Pimentel, “Modelling and control of bioreactors with membrane”; grant: Univ. Mons (Belgium) and INRA; thesis in co-supervision Montpellier-Mons; started October 2011; advisors: A. Rapaport, J. Harmand and A. VandeWouwer (Univ. Mons).
- Amine Charfi, “Modélisation du colmatage dans les réacteurs à membranes” grant: Coadvise and University of Tunis; started October 2009; advisors: J. Harmand and Nihel Benamar.

9.5. Participation to thesis committees

- F. Campillo (referee): M. Jean-Louis Marchand, “Conditionnement de processus markoviens”, Univ. de Rennes 1.
- F. Campillo (referee): M. Quentin Molto, “Estimation de biomasse en forêt tropicale humide Propagation des incertitudes dans la modélisation de la distribution spatiale de la biomasse en Guyane française”, Univ. des Antilles et de la Guyane.
- J. Harmand (referee): M. Thomas Guélon, “Déterminer l’influence de la distribution spatiale des bactéries sur les propriétés microscopiques de biofilms bactériens par des techniques d’homogénéisation”, Univ. Blaise Pascal, Clermont II.
- J. Harmand, T. Sari, C. Lobry (president of the committee): M. Boumediene, “Modélisation et observation des bioprocédés à membranes : application à la digestion anaérobie”, Univ. Montpellier 2 and Univ. Tlemcen, Algérie.
- A. Rapaport (president of the committee): M. Sebbah, “Stabilité d’inégalités variationnelles et prox-régularité, équations de Kolmogorov périodiques contrôlées”, Univ. Montpellier II.
- A. Rapaport (referee and president of the committee): Léontine Nkague Nkamba, “Robustesse des seuils en épidémiologie et stabilité asymptotique d’un modèle à infectivité et susceptibilité différentielle”, Univ. Metz and Univ. St-Louis du Sénégal.
- C. Lobry (president of the committee): Jonathan Rault “Modélisation structurée en taille du zooplancton” UNSA.

10. Bibliography

Major publications by the team in recent years

- [1] F. CAMPILLO, M. JOANNIDES, I. LARRAMENDY-VALVERDE. *Stochastic modeling of the chemostat*, in "Ecological Modelling", 2011, vol. 222, n^o 15, p. 2676-2689.
- [2] F. CAMPILLO, M. KLEPSTYNA, A. PIATNITSKI. *Homogenization of random parabolic operator with large potential*, in "Stochastic Processes and Their Applications", 2001, vol. 93, p. 57–85.
- [3] M. DUMONT, J. HARMAND, A. RAPAPORT, J.-J. GODON. *Toward functional molecular fingerprints*, in "Environmental Microbiology", 2009, vol. 11, n^o 7, p. 1717–1727.
- [4] P. GAJARDO, H. RAMIREZ, A. RAPAPORT. *Minimal time sequential batch reactors with bounded and impulse controls for one or more species*, in "SIAM Journal of Control and Optimization", 2008, vol. 47, n^o 6, p. 2827–2856.
- [5] B. HAEGEMAN, R. S. ETIENNE. *Entropy maximization and the spatial distribution of species*, in "The American Naturalist", 2009, vol. 175, p. E74–E90.
- [6] B. HAEGEMAN, D. VANPETEGHEM, J.-J. GODON, J. HAMELIN. *DNA reassociation kinetics and diversity indices: Richness is not rich enough*, in "Oikos", 2008, vol. 175, p. 177–181.
- [7] C. LOBRY, J. HARMAND. *A new hypothesis to explain the coexistence of n species in the presence of a single resource*, in "Comptes Rendus de l'Académie des Sciences, Série Biologies", 2006, vol. 329, p. 40-46.
- [8] N. MABROUK, G. DEFFUANT, T. TOELKER-NIELSEN, C. LOBRY. *Bacteria can form interconnected micro-colonies when a self-excreted product reduces their surface motility: evidence from individual-based model simulations*, in "Theory in Biosciences", 2010, vol. 129, n^o 1, p. 1–13, <http://www.springerlink.com/content/r276t7018n41pq23/>.
- [9] A. RAPAPORT, D. DOCHAIN, J. HARMAND. *Long run coexistence in the chemostat with multiple species*, in "Journal of Theoretical Biology", 2009, vol. 257, n^o 2, p. 252–259.
- [10] T. SARI. *A Lyapunov function for the chemostat with variable yields*, in "C. R. Acad. Sci. Paris, Ser. I", 2010, vol. 348, p. 747-751.

Publications of the year

Articles in International Peer-Reviewed Journals

- [11] T. BAYEN, P. GAJARDO, F. MAIRET. *Optimal Synthesis for the Minimum Time Control Problems of Fed-Batch Bioprocesses for Growth Functions with Two Maxima*, in "Journal of Optimization Theory and Applications", 2012, p. 1-33, <http://dx.doi.org/10.1007/s10957-012-0225-0>.
- [12] B. BENYAHIA, T. SARI, B. CHERKI, J. HARMAND. *Bifurcation and stability analysis of a two step model for monitoring anaerobic digestion processes*, in "Journal of Process Control", 2012, vol. 22, n^o 6, p. 1008-1019.

- [13] F. CAMPILLO, N. CHAMPAGNAT. *Simulation and analysis of an individual-based model for graph-structured plant dynamics*, in "Ecological Modelling", 2012, vol. 234, p. 93-105 [DOI : 10.1016/J.ECOLMODEL.2012.03.017], <http://hal.inria.fr/hal-00723209>.
- [14] F. CAMPILLO, M. JOANNIDES, I. LARRAMENDY-VALVERDE. *Approximation of the Fokker-Planck equation of the stochastic chemostat*, in "Mathematics and Computers in Simulation", 2012, to appear.
- [15] F. CAMPILLO, C. LOBRY. *Effect of population size in a predator-prey model*, in "Ecological Modelling", August 2012, vol. 246, p. 1-10 [DOI : 10.1016/J.ECOLMODEL.2012.07.015], <http://hal.inria.fr/hal-00723793>.
- [16] A. CHARFI, N. BENAMAR, J. HARMAND. *Analysis of fouling mechanisms in anaerobic membrane bioreactors*, in "Water Research", 2012, vol. 46, p. 2637-2650.
- [17] C. DEYGOUT, A. LESNE, F. CAMPILLO, A. RAPAPORT. *Homogenised model linking microscopic and macroscopic dynamics of a biofilm: Application to growth in a plug flow reactor*, in "Ecological Modelling", 2013, vol. 250, n^o 0, p. 15-24 [DOI : 10.1016/J.ECOLMODEL.2012.10.020], <http://www.sciencedirect.com/science/article/pii/S0304380012005224>.
- [18] M. L. DIAGNE, P. I. N'DIAYE, M. T. NIANE, T. SARI. *Comportement asymptotique d'un modèle à commutation de la prolifération du Typha*, in "ARIMA Revue africaine de la recherche en informatique et mathématiques appliquées", 2012, vol. 15, p. 101-122, <http://intranet.inria.fr/international/arima/015/015006.html>.
- [19] R. S. ETIENNE, B. HAEGEMAN. *A conceptual and statistical framework for adaptive radiations with a key role for diversity-dependence*, in "The American Naturalist", 2012, vol. 180, p. E75-E89.
- [20] R. S. ETIENNE, B. HAEGEMAN, T. STADLER, T. AZE, P. N. PEARSON, A. PURVIS, A. B. PHILLIMORE. *Diversity-dependence brings molecular phylogenies closer to agreement with the fossil record*, in "Proceedings of the Royal Society B: Biological Sciences", 2012, vol. 279, p. 1300-1309.
- [21] R. FEKIH-SALEM, J. HARMAND, C. LOBRY, A. RAPAPORT, T. SARI. *Extensions of the chemostat model with flocculation*, in "Journal of Mathematical Analysis and Applications", 2013, vol. 397, p. 292-306.
- [22] J. M. V. GROENENDAEL, C. MONY, M. GARBEY, F. CAMPILLO, A. E. HAMIDI. *Introduction to the special issue of Ecological Modelling: "Modelling clonal plant growth: From ecological concepts to mathematics"*, in "Ecological Modelling", 2012, vol. 234, p. 1-2, Introduction à un n^o spécial d'un journal [DOI : 10.1016/J.ECOLMODEL.2012.03.013], <http://hal.inria.fr/hal-00717348>.
- [23] B. HAEGEMAN, J. S. WEITZ. *A neutral theory of genome evolution and the frequency distribution of genes*, in "BMC Genomics", 2012, vol. 13, 196.
- [24] J. ROUYER, T. SARI. *As many antipodes as vertices on convex polyhedra*, in "Advances in Geometry", 2012, vol. 12, n^o 1, p. 43-61 [DOI : 10.1515/ADVGEOM.2011.030], <http://www.degruyter.com/view/j/advgeom.2012.12.issue-1/advgeom.2011.030/advgeom.2011.030.xml?format=INT>.
- [25] T. SARI, M. E. HAJJI, J. HARMAND. *The mathematical analysis of a syntrophic relationship between two microbial species in a chemostat*, in "Mathematical Biosciences and Engineering", 2012, vol. 3, n^o 9, p. 627-645.

- [26] T. SARI. *Competitive Exclusion for Chemostat Equations with Variable Yields*, in "Acta Applicandae Mathematicae", 2012, <http://link.springer.com/article/10.1007/s10440-012-9761-8>.
- [27] J. SIEBER, A. RAPAPORT, S. RODRIGUES, M. DESROCHES. *A new method for the reconstruction of unknown non-monotonic growth functions in the chemostat*, in "Bioprocess and Biosystems Engineering", 2012, to appear, <http://hal.inria.fr/hal-00604633>.

International Conferences with Proceedings

- [28] B. BENYAHIA, F. CAMPILLO, B. CHERKI, J. HARMAND. *Particle filtering for the chemostat*, in "20th Mediterranean Conference on Control and Automation (MED 2012), Barcelona", Barcelona, Spain, July 3-6 2012, p. 364-371.
- [29] B. BENYAHIA, B. CHERKI, T. SARI, J. HARMAND. *Quelques résultats sur l'observation du modèle AM2b*, in "Eleventh African Conference on Research in Computer Science and Applied Mathematics (CARI 2012)", Algiers (Algeria), 2012.
- [30] W. BOUHAFS, N. ABDELLATIF, F. JEAN, J. HARMAND. *Commande optimale en temps et en énergie d'un procédé biologique d'épuration d'eau*, in "Eleventh African Conference on Research in Computer Science and Applied Mathematics (CARI 2012)", Algiers (Algeria), 2012.
- [31] B. BRIGHI, A. FRUCHARD, T. SARI. *The Blasius equation*, in "Philosophie, méthodologie et applications de l'analyse non standard", Paris, A. FRUCHARD, V. GAUTHERON, T. SARI (editors), Publications de l'Université de Paris 13, 2012, p. 105-123, <http://www.math.univ-paris13.fr/laga/F/pdf/2012-01-12-Actes-Isambert/>.
- [32] F. CAMPILLO, D. HERVÉ, A. RAHERINIRINA, R. RAKOTOZAFY. *Markov analysis of land use dynamics: A Case Study in Madagascar*, in "Eleventh African Conference on Research in Computer Science and Applied Mathematics (CARI 2012)", Algiers (Algeria), 2012.
- [33] C. CASENAVE, D. DOCHAIN, G. ALVAREZ, H. BENKHELIFA, D. FLICK, D. LEDUCQ. *Steady-state and stability analysis of a population balance based nonlinear ice cream crystallization model*, in "ACC", Montreal, June 27-29 2012.
- [34] M. L. DIAGNE, T. SARI. *Moyennisation du modèle dynamique de la prolifération du Typha*, in "11ème Colloque Africain sur la Recherche en Informatique en Mathématiques Appliquées", 2012, http://www.cari-info.org/prog_cari12.php.
- [35] D. DOCHAIN, P. DE LEENHEER, A. RAPAPORT. *About Transgressive Over-Yielding in the Chemostat*, in "MATHMOD 2012 - 7th Vienna International Conference on Mathematical Modelling", Vienna, Austria, February 2012, <http://hal.inria.fr/hal-00726364>.
- [36] R. FEKIH-SALEM, N. ABDELLATIF, T. SARI, J. HARMAND. *Analyse mathématique d'un modèle de digestion anaérobie à trois étapes*, in "Eleventh African Conference on Research in Computer Science and Applied Mathematics (CARI 2012)", Algiers (Algeria), 2012.
- [37] R. FEKIH-SALEM, N. ABDELLATIF, T. SARI, J. HARMAND. *On a Three Step Model of Anaerobic Digestion Including the Hydrolysis of Particulate Matter*, in "MATHMOD", Vienna, Austria, February 2012.

- [38] B. FONTEZ, D. I. BATONON, F. CAMPILLO, P. LESCOAT. *Analyse bayésienne de courbes de croissance de poulets par un modèle hiérarchique défini à partir d'une équation différentielle stochastique à processus d'erreur autocorrélée*, in "44ième Journées de Statistique", Bruxelles, 21 au 25 mai 2012.
- [39] A. GHOUALI, T. SARI, C. LOBRY, A. MOUSSAOUI, J. HARMAND. *Analyse et contrôle optimal d'un bioréacteur de dépollution des eaux usées*, in "11ème Colloque Africain sur la Recherche en Informatique en Mathématiques Appliquées", 2012, http://www.cari-info.org/prog_cari12.php.
- [40] S. HASSAM, B. CHERKI, E. FICARA, J. HARMAND. *Model reduction and control of the ADM1 : a robust control approach*, in "20th Mediterranean Conference on Control and Automation (MED 2012)", Barcelona, Spain, July 3-6 2012.
- [41] C. LOBRY, T. SARI. *La modélisation de la persistance en écologie*, in "Philosophie, méthodologie et applications de l'analyse non standard", Paris, A. FRUCHARD, V. GAUTHERON, T. SARI (editors), Publications de l'Université de Paris 13, 2012, p. 163-184, <http://www.math.univ-paris13.fr/laga/F/pdf/2012-01-12-Actes-Isambert/>.
- [42] J. SIEBER, A. RAPAPORT, M. DESROCHES, S. RODRIGUES. *A new method for the reconstruction of unknown non-monotonic growth functions in the chemostat*, in "MED 2012 - 20th IEEE Mediterranean Conference on Control and Automation", Barcelona, Spain, July 2012, <http://hal.inria.fr/hal-00723246>.

Conferences without Proceedings

- [43] A. BIZE, F. CAMPILLO, C. DEYGOUT, M. JOANNIDES. *Un modèle individu-centré de dégradation bactérienne d'une bille de cellulose*, in "Les Biofilms au service des Biotechnologies — Journées thématiques du Réseau National Biofilm", Narbonne, 24–26 Janvier 2012.
- [44] A. BIZE, F. CAMPILLO, C. DEYGOUT, C. LOBRY, M. JOANNIDES. *An individual-based modeling approach for cellulose degradation by microbial biofilms*, in "Biofilm 5 International Conference, december 10-12", 2012.
- [45] F. CAMPILLO. *Stochastic modeling: a simulation (and analytical) approach*, in "2nd French-Chilean Workshop on Bioprocess Modeling Pucón", January 16-17 2012.
- [46] C. FRITSCH. *Moment closure methods for individual-based model*, in "Zif Research Group Stochastic Dynamics: Mathematical Theory And Applications – Workshop on Qualitative Behaviour Of Stochastic Systems And Applications", Bielefeld University, 2012.
- [47] J. HARMAND. *Modeling and control of the anaerobic digestion process : a review and some new results*, in "2nd French-Chilean Workshop on Bioprocess Modeling Pucón", Pucón, Chile, January 2012.
- [48] C. LOBRY. *Effect of population size in a Prey-Predator model*, in "LAWOC 2012 Latin American Workshop on Optimization and Control", Valparaiso, Chile, January 2012.
- [49] C. LOBRY. *L'ordinateur et la dynamique des populations, conférence Inaugurale*, in "Colloque de méthodes numériques et modélisation, MÉMO'2012 à l'occasion du 60ème anniversaire de Mohamed Jaoua", Tunis, Tunisia, 13 au 15 décembre 2012.

- [50] C. LOBRY. *La compétition dans le chémostat*, in "Des nombres et des Mondes", 2012, <http://hal.inria.fr/hal-00711218>.
- [51] C. LOBRY. *Les équations différentielles sont-elles un outil pertinent pour modéliser la dynamique des populations ?*, in "Colloque en l'honneur de Gauthier Sallet", Saint-Louis, Sénégal, 3 au 7 décembre 2012.
- [52] A. RAPAPORT, D. DOCHAIN. *Minimal time control of fed-batch processes for growth functions having several maxima*, in "LAWOC 2012 Latin American Workshop on Optimization and Control", Valparaiso, Chile, January 2012.
- [53] T. SARI. *Elastic strips*, in "Colloque de géométries", Mulhouse, 27-29 septembre 2012, <http://unica2.unica.it/~piu/Conf.html>.
- [54] T. SARI. *Extensions of the chemostat model with flocculation*, in "III Latin American Workshop on Optimization and Control LAWOC", Valparaiso (Chile), 2012, <http://www.am2v.cl/lawoc2012/>.

Research Reports

- [55] S. BARBIER. *Modélisation de stratégies de dépollution d'une ressource hydrique en milieu naturel*, Université de Reims Champagne-Ardenne, September 2012, MSc Engineering Mathematics report, U. Reims.
- [56] A. RAPAPORT, J.-R. DE DREUZY, J. HARMAND, A. ROJAS-PALMA. *Comparison of MINC and MRMT configurations: the n-dimensional case*, Catholic University of Valparaíso, Chile, November 2012.
- [57] V. RIQUELEME. *Bioremediation of natural water resources via optimal control techniques*, DIM, Univ. Chile, Santiago, 2012.
- [58] E. TAPIA. *A methodology for coupling DGGE and mathematical modelling. Application in bio-hydrogen productions*, Escuela de Ingeniería Bioquímica Pontificia Universidad Católica de Valparaíso Valparaíso, Chile, November 2012, submitted.

Patents and standards

- [59] A. RAPAPORT, J. HARMAND, I. HAIDAR. *Stabilisation de procédés biotechnologiques présentant une instabilité due à une inhibition par le substrat, par des configurations de type "poche"*, February 2012, n° BNT210061FR00, Brevet d'invention.

Other Publications

- [60] T. BAYEN, F. MAIRET. *Minimal time control of fed-batch bioreactor with product inhibition*, September 2012, Submitted, <http://hal.archives-ouvertes.fr/hal-00734225>.
- [61] T. BAYEN, F. MAIRET, P. MARTINON, M. SEBBAH. *Optimizing the anaerobic digestion of microalgae in a coupled process*, 2012, submitted.
- [62] T. BAYEN, F. MAIRET, M. MAZADE. *Optimal feeding strategy for the minimal time problem of a fed-batch bioreactor with mortality rate*, November 2012, submitted, <http://hal.archives-ouvertes.fr/hal-00759058>.

- [63] C. CASENAVE, G. MONTSÉNY. *System identification by operatorial cancellation of nonlinear terms - application to a class of Volterra models*, 2012, submitted.
- [64] C. CASENAVE, G. MONTSÉNY, C. PRIEUR. *Controllability of SISO Volterra Models via Diffusive Representation*, 2012, submitted.
- [65] B. JAILLARD, A. RAPAPORT, J. HARMAND, A. BRAUMAN, N. NUNAN. *Biodiversity and ecosystem functioning: the hidden weight of neutral elements in community assembly*, 2012, submitted.
- [66] E. MONTSÉNY, C. CASENAVE. *Analysis, simulation and impedance operator of a non local model of porous medium for acoustic control*, 2012, submitted.
- [67] A. RAPAPORT, I. HAIDAR, J. HARMAND. *The buffered chemostat with non-monotonic growth response functions*, 2012, to appear, <http://hal.inria.fr/hal-00766243>.

References in notes

- [68] D. L. DEANGELIS, L. J. GROSS (editors). *Individual-based models and approaches in ecology: populations, communities and ecosystems*, Chapman and Hall, 1992.
- [69] U. DIECKMANN, R. LAW, J. A. J. METZ (editors). *The Geometry of Ecological Interactions: Simplifying Spatial Complexity*, Cambridge University Press, 2000.
- [70] W. R. GILKS, S. RICHARDSON, D. J. SPIEGELHALTER (editors). *Markov Chain Monte Carlo in practice*, Chapman & Hall, London, 1996.
- [71] G. BASTIN, D. DOCHAIN. *On-line Estimation and Adaptive Control of Bioreactors*, Elsevier, 1990.
- [72] O. BERNARD, Z. HADJ-SADOK, D. DOCHAIN, A. GENOVESI, J.-P. STEYER. *Dynamical model development and parameter identification for an anaerobic wastewater treatment process*, in "Biotechnology and Bioengineering", 2001, vol. 75, p. 424-438.
- [73] F. CAMPILLO, V. ROSSI. *Convolution Particle Filter for Parameter Estimation in General State-Space Models*, in "IEEE Transactions on Aerospace and Electronic Systems", 2009, vol. 45, n^o 3, p. 1063-1071.
- [74] P. DEL MORAL. *Feynman-Kac formulae – Genealogical and interacting particle approximations*, Springer Verlag, New York, 2004.
- [75] A. DOUCET, N. DE FREITAS, N. J. GORDON. *Sequential Monte Carlo Methods in Practice*, Springer Verlag, New York, 2001.
- [76] S. N. ETHIER, T. G. KURTZ. *Markov Processes – Characterization and Convergence*, John Wiley & Sons, 1986.
- [77] W. FELLER. *An Introduction to Probability Theory and Its Applications, Volume 1*, Third, Wiley, 1968.
- [78] N. FOURNIER, S. MÉLÉARD. *A microscopic probabilistic description of a locally regulated population and macroscopic approximations*, in "Annals of Applied Probability", 2004, vol. 14, p. 1880-1919.

-
- [79] V. GRIMM, S. F. RAILSBACK. *Individual-based Modeling and Ecology*, Princeton University Press, 2005.
- [80] I. HAIDAR. *Dynamiques microbiennes et modélisation des cycles biogéochimiques terrestres*, Université Montpellier II, 2011.
- [81] J. HESS, O. BERNARD. *Design and Study of a risk management criterion for an unstable anaerobic wastewater treatment*, in "Journal of Process Control", 2007, vol. 18, p. 71-79.
- [82] S. P. HUBBELL. *The Unified Neutral Theory of Biodiversity and Biogeography*, Princeton University Press, 2001.
- [83] C. M. JESSUP, R. KASSEN, S. E. FORDE, B. KERR, A. BUCKLING, P. B. RAINEY, B. J. BOHANNAN. *Big questions, small world: microbial model systems in ecology*, in "Trends in Ecology and Evolution", 2004, vol. 19, n^o 4, p. 189–197.
- [84] A. LESNE. *Multi-scale approaches*, in "Encyclopedia of Mathematical Physics", J. FRANÇOISE, G. NABER, T. TSUN (editors), Elsevier, 2006, vol. 3, p. 465–482.
- [85] R. H. MACARTHUR, E. O. WILSON. *The Theory of Island Biogeography*, Princeton University Press, 1967.
- [86] J. A. MORENO. *Optimal control of bioreactors for the wastewater treatment*, in "Optimal Control Applications and Methods", 1999, vol. 20, p. 145-164.
- [87] H. SMITH, P. WALTMAN. *The Theory of the Chemostat: Dynamics of Microbial Competition*, Cambridge University Press, 1995.
- [88] O. WANNER, H. EBERL, E. MORGENROTH, D. NOGUERA, C. PICIOREANU, B. RITTMANN, M. VAN LOOSDRECHT. *Mathematical Modeling of Biofilms*, IWA Scientific and Technical Report No.18, IWA Publishing, 2006, IWA Task Group on Biofilm Modeling.