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Project-Team COMORE

Modelling and Control of Renewable Resources

Sophia Antipolis - Méditerranée

THEME BIO

Activity Report

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Comore is a joint research team INRIA (Research Unit of Sophia-Antipolis, France) and CNRS (Laboratory of Biological Oceanography and Marine Plankton Ecology, UMR 7093/ Université P.M. Curie, Villefranche sur Mer, France).

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2. Overall Objectives

2.1. Overall objectives

Comore is a joint research team between INRIA (Research Unit of Sophia-Antipolis, France) and CNRS (Laboratory of Biological Oceanography and Marine Plankton Ecology, UMR 7093/ Université P.M. Curie, Villefranche sur Mer, France, Team: Analysis and Simulation of the Functioning of Ecosystems).

The endeavor of Comore is to develop and apply methods from control theory (feedback control, estimation, identification, optimal control) and from dynamical systems theory, to the mathematical modelling of living exploited resources (renewable resources) and their management. We apply and validate our results to various fields: phytoplankton growth, bioprocesses, pest control, fisheries, cell models...

Research themes:

Methodology:

- Mathematical properties of models in biology: mathematical studies of models and of their global behavior.
- Tools for modelling in biology: model design, validation, parameter identification.
- Software sensors for biological systems: using the model and on-line measurements, we estimate the variables that are not measured directly.
- Control and regulation for biological systems: we design laws to maintain a variable at a given level, or to optimize the yield of the system.

Fields of application:

- Modelling and control of the growth of marine phytoplankton: the phytoplankton is the basis of food chains in the oceans (fishes, etc), and plays a key role in the carbon cycle. In Villefranche-sur-Mer, we develop a fully automated chemostat (open bioreactor where cells grow) which is managed by computers for that objective.
- Modelling, estimation and control of bioreactors: the bioreactors have a growing importance in many domains related to the human environment: food (production), pharmaceuticals (production of medicines), environment (wastewater treatment), etc.
- Dynamics and control of ecosystems: we build models for ecosystems (insects, fishes) and try to achieve optimal regulation.
- Modelling of metabolic and genetic networks: we study the dynamical behavior of regulation networks in cells.

Software for biological modelling.

National, international and industrial relations

- Collaboration with IFREMER (Nantes), INRA (MIA Montpellier, LBE Narbonne, GMPA Grignon, URIH Sophia-Antipolis), Centre d'Océanologie de Marseille, LOCEAN (Paris), GIPSA Grenoble, IBIS and MERE INRIA teams.
- Participation in the French groups CoReV (Modèles et théories pour le Contrôle de Ressources Vivantes, Models and Control of Living Resources) and M3D (Mathématiques et décision pour le développement durable).
- Collaboration with Ecole Polytechnique de Montréal (Canada), Université Catholique de Louvain (Belgium), University of Marrakech (Marocco), Ecole Polytechnique de Mons (Belgium).
- European project Hygeia.
- ANR Biosys project Metagenoreg.
- ANR PNRB project Shamash

2.2. Highlights of the year

- Comore is taking part in the SYMBIOSE project in the Bioenergy section of the ANR. This project has been accepted this year. The objective of this project is both to improve the energetic balance of biofuel microalgal productions and to recycle nitrogen and phosphorus. The project proposes to study the coupling between a microalgal production system and an anaerobic digester.
- Comore developed a method to study the interplay between network structure and dynamics in a biological system (see research report [47]). The method analyses a Boolean model of the system and identifies a family of operational interactions, that is responsible for a given dynamical behaviour. For a model of apoptosis [33], two core families of interactions were identified that generate, respectively, oscillatory behaviour or bistability.
- Comore has proven that the competitive exclusion principle in a chemostat is valid for the Droop model with n species [74]; this result indicates that the “fittest” microorganism species outcompetes the others, so that it remains alone in the chemostat after some time. This generalizes the result that was known to be valid for bacteria-like microorganisms (Monod model) to micro-algae-like microorganisms whose growth depends on an internal nutrient quota (Droop model). This work has been presented at the workshop on "Differential Equations and Applications to Mathematical Biology" (Le Havre, June 23-27, 2008).

3. Scientific Foundations

3.1. Scientific Foundations

Keywords: *biological models*, *bioreactors*, *cell models*, *dynamical systems*, *ecosystems*, *environment*, *nonlinear control theory*, *optimization*.

Comore is interested in the mathematical modelling of biological systems, more particularly of ecosystems subject to a human action; the framework is thus that of renewable resources. It is now clear that it is important to understand how these complex dynamical systems work in order to regulate the exploitation of such resources by man. Our framework is Control Theory, whose central concept is “the system”, described by state variables, with inputs (action on the system), and outputs (the available measurements on the system). The systems that we consider are, mainly, ecosystems, that we generally model through a set of differential equations. The variables are, for example, the size or the density of populations. The inputs can be actions exerted on the ecosystem: e.g. action of man (fishing effort, introduction of food, etc), or action of an external factor (pollution, light, etc). The outputs will be some product that one can collect from this ecosystem (harvest, capture, production of a biochemical product, etc), or some measurements (number of individuals, concentrations, etc).

The Control Theory approach begins with the mathematical modelling of the system. This stage is fundamental and difficult, because one does not have rigorous laws as it is the case in physics. We develop techniques to identify and validate the structure of a model from a set of available noisy measurements: qualitative analysis of the data (extrema, relative position,...) is used to build a model which is able to reproduce the same qualitative pattern. We also work on methods that are dedicated to the identification of the mathematical functions that link the dynamics of a state variable to other variables. Finally, we verify that the model satisfies some biological constraints: for example the concentrations must remain positive or some mass balance relationship must be satisfied. A fundamental problem is the validation, or invalidation, of these models: how to accept, with a certain precision, a model by comparing it with noisy experimental data ? The traditional approach, which consists in identifying the parameters of the model by minimizing a criterion of variation between the outputs of the model and the data, is often inefficient. We are developing new methods that are more relevant for the experimentalists.

Having built a model that synthesizes the behavior of such a complex nonlinear biological system, we can now study its properties and understand the way it works. However, specific problems are posed by the biological origin of the models: functions or parameters are uncertain, or unknown. The quantitative conclusions that we can draw are therefore limited. One then seeks to study the qualitative behavior of the system, the existence of equilibria, their stability, the existence of periodic solutions... Answers to these qualitative questions are fundamental because they tell us whether or not the system is viable (does the model predict the extinction of any species, etc). Answers can often be found, in particular when the models have a strong structure belonging to a general class of systems, for which one develops adjusted techniques: for example the well-known Lotka-Volterra models in dimension n, describing the interactions between n species.

Once the dynamics of the considered living system have been understood we consider problems of regulation: how to maintain a variable at a given level. This is important, for example, in the framework of wastewater treatment where the tolerated pollution levels are determined by governmental laws. The main problem that we have to address is the control of a complex system when the model is uncertain. We mainly work on one class of biological systems, the bioreactors, that have a growing importance in many domains related to the human environment: food (production), pharmaceuticals (production of medicine), environment (wastewater treatment, plankton study), etc. The strong structure of these systems, for which the hydraulic flow plays an important role, is used in order to derive controllers.

Finally, we develop observers that use the model and on-line measurements to asymptotically estimate the variables that are not directly measured. These so called "software sensors" help monitoring some systems and replace some expensive measurements. For the design of such observers, we are faced with uncertainties that are specific to biological modelling: the model is uncertain (parameters, functions) while the inputs can also be affected by disturbances and the outputs highly variable. Therefore, we have to deal with these uncertainties in the design of observers. We have developed robust observers that assume that some parameter or input belongs to a given interval. The observer then asymptotically estimates intervals for the state variables. Other estimators are also considered.

The methods developed by our group are validated and tested on several applications.

4. Application Domains

4.1. Application Domains

Keywords: *biological models*, *biological networks*, *bioreactors*, *cell models*, *ecosystems*, *environment*, *plankton growth*, *wastewater treatment*.

In our work, applications are not clearly separated from methodology elements: often, “applications” raise methodological questions which can give rise to fundamental research problems for biology; as mentioned in the above section, we consider and analyze such questions, also in collaboration with biologists.

Modelling of Marine Plankton growth

This part of the work takes place at the Station Zoologique of the CNRS (Villefranche-sur-Mer, France), where we have developed a fully automated, computer driven, set of chemostats (continuous bioreactors where microalgae are growing). This system is particularly well suited to the application of methods resulting from control theory. Our current work consists in designing, studying and validating models of phytoplankton growth in a variable environment (light, nutrients, etc). Phytoplankton is the basis of the oceanic food web (zooplankton, fishes, etc). The existing traditional models (Monod, Droop) are often unsatisfactory and do not reproduce observed features well. We seek to obtain models which are valid during the transitory stages, far from the usually considered steady state conditions that are rarely reached in the sea. For the zooplancton, a size-structured model is considered, governed by predation. These two models are then incorporated in hydrodynamic models or models for the whole food web in order to predict the carbon fluxes within the ocean and at the interface between ocean and atmosphere.

Wastewater Treatment Processes

In collaboration with the Laboratory of Environmental Biotechnology of INRA (Narbonne, France), we work on anaerobic treatment plants. We build dynamical models that can reproduce the behavior of the system in standard operating mode and in degraded working modes (after a failure). Since only few on-line measurements are available, we design robust observers that take the large uncertainties encountered in this field into account and predict the internal state of the process. As an example, the concentration of influent organic matter to be treated, which is an important input, is rarely measured. The software sensors are used to monitor the processes and to help detecting failures.Control laws are build for the outputs of the wastewater to satisfy regulation policies and for the reactor to behave optimally.

Bioenergy

Finding sources of renewable energy is a key challenge for our society. We contribute to this topic in two main domains. First, we are working to improve the efficiency of anaerobic digesters that produce methane and/or biohydrogen from organic carbon. The main difficulty is to make these processes more reliable and valorise more efficiently their biogas. The second topic consists in growing microalgae to produce biodiesel. These microorganisms can synthesize lipids with a much higher productivity than terrestrial oleaginous species. The difficulty is to better understand the involved processes, which are mainly transient, to stimulate and optimize them on the basis of modelling and control strategies.

Ecosystems and Fisheries

The scale of the problems changes here; data are rare and noisy. We consider some important methodological problems in collaboration with IFREMER Nantes: how to model the stock-recruitment relationship of the fish (the relationship between the number of fertile adults and eggs they produce). How does one optimize the exploitation of fisheries with respect to some criteria?

We also consider (with URIH, INRA Sophia-Antipolis) problems of biological control in a greenhouse (e.g. the introduction of ladybirds to control pests). We first consider the problem of reactive biological control: upon detection of the presence of pests in the greenhouse, we determine the quantity and timing of the release of their natural enemies to control this pest population. In another framework, we study prophylactic biological control: we determine the periodicity and quantity of natural enemies releases in order to prevent a pest outbreak in high-valued crops (such as roses).

Metabolic and genetic networks

This application has many links with our previous work: in fact, we consider large networks made of small biological nonlinear elements (metabolic network, genes network, ...) and are interested in methods enabling us to describe the dynamical behavior of the system. The classical methods of analysis are difficult to apply here, because the dimension of the networks is too large. Therefore, we search for methods that use qualitative information on the network (the linear substructure, the graph of the network, the monotonicity of interactions and/or the order of magnitude of the concentrations and the interactions) or we describe the system by only using "idealized" nonlinearities, such as step functions (the resulting piecewise linear system being more amenable to a qualitative description).

In parallel with the analysis of systems of large dimension, we are also interested in identifying fundamental mechanisms underlying the complex networks of cellular interactions. These may comprise several levels of regulation, such as metabolic, signaling or genetic regulatory systems. In particular, we are interested in finding and studying basic groups of elements and interactions (i.e. reduced models), that are responsible for a given observed dynamical behavior. For this approach, we use the tools of model reduction theory. The interconnections among various cell regulatory systems are also studied, for instance, how can metabolism be regulated and/or controlled by genetic networks. For this analysis we will use more qualitative methods, such as piecewise linear ordinary differential equations, in conjunction with techniques from control theory (interconnected systems, feedback loops, stability notions).

5. Software

5.1. Software

We have developed a software focusing on *Data acquisition and Control*: a platform, named ODIN, has been developed with the objective of smart management of bioreactors (data acquisition, fault diagnosis, control algorithm,...). This software was developed in C++ and uses a Scilab engine to run the advanced algorithms developed within Comore. It has been been implemented and validated with 4 different applications.

6. New Results

6.1. Methodology

6.1.1. Mathematical study of models

Keywords: *biological models*, *dynamical systems*.

Participants: Jean-Luc Gouzé, Olivier Bernard, Frédéric Grognard, Madalena Chaves, Jonathan Hess, Pierre Masci, Laurent Tournier.

Study of structured models of cell growth

We have developed two structured mathematical models aiming at a macroscopic description of the whole cell population during its cycle, taking the total number or the total biomass of cells into account. These models are structured with respect to the cell position in its cycle. The first proposed model [25], [22] exhibits a limit cycle. The second model uses similar concepts, but uses a Droop model to describe the nitrogen storage in the cell.

Mathematical study of models of anaerobic plants.

We have studied an unstable biological model used for an anaerobic wastewater treatment plant [24] [68], [69]. This ecosystem can have two locally stable equilibria and an unstable one. The risk of destabilization associated to a control policy has first been evaluated on a static basis by estimating the size of the attraction basin associated to the working point. To study the dynamical behavior of the system we split the phase plane according to the sign of the derivatives of the state vector. A methodology has been proposed to monitor in real time the trajectory of the system across these zones; we show that a sequence of transitions from one zone to another allows for the determination of the position of the system in the phase plane. A dynamical risk has been defined based on the sequence of transitions and the zones are classified according to their dangerousness [23]. The proposed approach does not depend on the parameter values and is thus very robust.

Mathematical study of models of competing species

When several species are in competition for a single substrate in a chemostat, and when the growth rates of the different species only depend on the substrate, it is known that the generic equilibrium state for a given dilution rate consists in the survival of only one of the species. The species that requires the smallest substrate concentration in order to have a growth-rate equivalent to the dilution rate wins the competition; it is the survival of the most efficient species at this rate. This observation has been validated through laboratory experiments [67]. This competitive exclusion principle was already demonstrated in Monod model with n species and in Droop model with two species. By a qualitative study of the microorganisms internal quota, we demonstrated that it still holds in the Droop model with n species [74].

Towards a qualitative analysis of Lotka-Volterra systems

We study the dynamical behavior of an n-dimensional nonlinear differential equation of Lotka-Volterra in n-dimensional rectangles. More precisely, we give some necessary and sufficient conditions on the matrix of the system for the existence of rectangles (containing the unique positive equilibrium), the faces of which are *transverse* with respect to the flow (*i.e.* each face is crossed by the flow in a unique sense). These conditions are directly related to the type of stability of the equilibrium, and therefore to the *local* dynamics of the system around the equilibrium. Furthermore, we have been able, thanks to Lyapunov theory, to describe the *global* dynamics of the system within such transverse rectangles. Together with the analysis of the dynamics on rectangles that do not contain the positive equilibrium, these results provide a first step towards a qualitative analysis of the Lotka-Volterra nonlinear equation [40].

Bistability in biological systems

From a mathematical point of view, a system is bistable if it has two distinct, stable fixed points. In [15], the following generalization of the concept of bistability is proposed: a system is bistable if its state space contains two disconnected invariant sets. A general framework for analysis is proposed, where the interactions among variables are defined qualitatively as activation or inhibition functions, that is, differentiable, but defined within a (narrow) step-like tube. Bistability, with respect to two invariant sets, is characterized through a notion of input-to-state stability. In [18] this notion of bistability is used to analyze a small model of a caspase cascade at the core of apoptosis, or programed cell death. Conditions on the parameters are given that characterize different biological scenarios: healthy cells exhibiting bistability, or malfunctioning cells, where bistability disappears. In the latter scenario, the cell no longer has the capacity to choose between two stable modes. This is work in collaboration with T. Eissing and F. Allgöwer from the University of Stuttgart, Germany.

Towards reduction of models using orders of magnitude

We use the mathematical theory of singular perturbations to help reducing large systems through relevant approximations. In order to work with people coming from very different domains, it was useful to collect the different approaches of the slow-fast systems. [43]

Life history traits

In this work we study the evolution of a prey-predator system with seasonal character of the dynamics. We specify two main parts of the process. First, it is the evolution of the system during one season with a fixed length: the preys lay eggs continuously and the predators lay eggs or hunt the preys according to the solution of an optimal control problem. Secondly, we study the long-scale discrete dynamics over seasons. We investigate the qualitative behavior of the dynamics with respect to the parameters of the problem and show that, depending on the parameters of the model, extinction or co-existence of the predators and preys can be evidenced [50].

In a second work, we suppose that the evolution of the system during a season of fixed length is governed by optimal game dynamics with two players. On the one hand, the predator has the choice between foraging the food (eating preys) or reproducing for the next year (laying eggs at a rate proportional to its energy). On the other hand, the prey has a chance to hide from it but in this case it has a negative mortality rate and its population can decrease faster than if it would be foraged by the predator. The preys lay eggs at a constant rate whether they are hiding or eating. The aim of both is to maximize their population (the number of offsprings) for the next season. This non-zero sum dynamic game yields complex dynamics whose analysis gives rise to bang-bang control, bi-singular region,... [51].

6.1.2. Model design, identification and validation

Keywords: *biological modelling*, *bioreactors*, *qualitative analysis*.

Participants: Olivier Bernard, Jean-Luc Gouzé, Madalena Chaves.

Model design and identification

One of the main families of biological systems that we have studied involves mass transfer between compartments, whether these compartments are microorganisms or substrates in a bioreactor, or species populations in an ecosystem. We have developed methods to estimate the models of such systems [56]. These systems can be represented by models having the general structure popularized by [52], [61][42], and based on an underlying reaction network:

$$\frac{d\xi}{dt} = K\, r(\xi,\psi) + D(\xi_{in} - \xi) - Q(\xi)$$

We address two problems: the determination of the pseudo-stoichiometric matrix K and the modelling of the reaction rates $r(\xi,\psi)$.

In order to identify K, a two-step procedure is presented. The first step is the identification of the minimum number of reactions to be taken into account to explain a set of data. If additional information on the process structure is available, we showed how to apply the second step: the estimation of the pseudo-stoichiometric matrix associated with the reaction network [55]. These methods lead to identifiability conditions on the pseudo-stoichiometric coefficients and provide a framework for their estimation. They have been improved in order to better filter noise using modulating functions [58]. This approach has been applied to various bioproduction processes: activated sludge processes [11] and anaerobic digestion [30] [63] and, previously, vanillin production [56], lipase production [58], and cheese production [70].

The feasible parameter space for biochemical networks

Characterizing the space of parameters is of great importance for models of biological systems. For a given model, one may pose the problem of identifying all the sets of parameters which produce results compatible with the outcome of the biological system. The properties of the set of all feasible parameters (namely, volume, geometry and topology) provide a measure of the robustness of the system. Volume measures the size of the parameter space, but its geometry and topology indicate the distribution of the feasible parameters (eg., narrow/wide regions and connectedness). All properties play a role in determining how far the system may be disturbed while still retaining the same qualitative dynamical behaviour. A method is proposed in [16] for writing a full description of the feasible parameter set, as a hierarchy of intervals. Application of this method to the segment polarity genes network (of the fruit fly), shows that the space of parameters is composed of five disconnected regions of parameters, which are connected by faces of lower dimension. The effect of random perturbations in the parameters is studied in [17]. If perturbations are viewed as mutations, the existence of disconnected regions in the parameter space is related to the degree of robustness of the system's functions. This is work in collaboration with E. Sontag, A. Sengupta, and A. Dayarian from Rutgers University, USA.

Identifying operational interactions in genetic networks

For Boolean networks, we introduce the notion of *operational interactions*, corresponding to those interactions that are "active" in a certain region of the state space, and hence responsible for the dynamical behaviour in that region of the space. In [47], we develop a method to identify operational interactions, in two steps. The first step consists in the decomposition of the asynchronous transition graph of the Boolean network into its strongly connected components (SCCs). The second step consists in choosing a desired region of this transition graph (for instance, a SCC), computing its reachable set and using an identification algorithm to reconstruct the interactions which are responsible for the dynamics in this set of states. This method was applied to a Boolean model of an apoptosis network [33], and two distinct subsystems were found: one is responsible for generating oscillatory behaviour in the presence of an input, while the other subsystem is responsible for generating bistability in the absence of an input.

6.1.3. Nonlinear observers

Keywords: *bioreactors*, *hybrid observers*, *nonlinear observers*, *uncertain models*.

Participants: Jean-Luc Gouzé, Olivier Bernard.

Interval observers

We designed so-called bundles of observers [60][41] made of *a set of* interval observers. Each observer computes intervals in which the state lies, provided that the intervals inside which the parameters, the initial conditions and more generally all the uncertainties bounds are known. We then take the lower envelope of this set to improve the overall estimation.
We have extended the results of hybrid interval observers [66], introducing an optimality criterion to compute an optimal gain, leading to the best interval estimates [76],[28].

Recently, we have also introduced reverse time interval observers [78]. The objective is to improve the initial state estimate by running interval estimators in reverse time. The technique has been developed considering the optimal framework of [28], achieving remarkable improvements of the convergence rate. Application of this estimation scheme to an industrial wastewater treatment plant has demonstrated its efficiency on a real problem [77]. We also work on the estimation of the inputs of the biological process [37].

In order to demonstrate the efficiency of the interval observer design, even with chaotic systems, a special application of the interval observer has been developed for Chua's chaotic system. The interval estimation of the state variables are performed considering uncertainties on the parameters of the system and biased output [80]. These techniques have been improved by introducing a linear time varying change of coordinates. For some class of systems, it allows the design of interval observers when it was not possible in the original basis [75].

These interval observers have been extended to the case where only discrete time measurements are available [21] [86] [64], and applied to experimental data of phytoplankton growth.

6.1.4. Nonlinear control

Keywords: *Positive systems*, *adaptive regulation*, *bioreactors control*, *structural stabilization*, *uncertain systems*.

Participants: Jean-Luc Gouzé, Olivier Bernard, Frédéric Grognard, Pierre Masci, Sapna Nundloll, Andrei Akhmetzhanov.

Global stabilization of partially known positive systems

We deal with the problem of global output feedback stabilization of a class of n-dimensional nonlinear positive systems possessing a one-dimensional component whose mathematical form is unknown (but which is measured). We propose an output feedback control procedure, taking advantage of measurements of the uncertain part, which is able to globally stabilize the system towards an adjustable equilibrium point in the interior of the positive orthant. Though quite general, this result is based on hypotheses that might be difficult to check in practice. Then in a second step, through a theorem on a class of positive systems linking the existence of a strongly positive equilibrium to its global asymptotic stability, we propose other hypotheses for our main result. These new hypotheses are more restrictive but much simpler to check [26].

We have constructed strict Lyapunov functions for general nonlinear systems satisfying Matrosov type conditions [27], [36]. We illustrate the practical interest of our design using two globally asymptotically stable biological models.

Control of competition in the chemostat

We have designed a closed loop control procedure for microorganisms in the chemostat [35]. The objective is to select species with interesting characteristics in chosen environmental conditions. In particular, by controlling the dilution rate and the input substrate concentration, it is possible to select a species which maximises a criterion. In a first step we proposed controls for Monod's and Droop's models in order to achieve periodic substrate stresses, and to regulate the total biomass concentration. We showed that this regulation causes the selection of the fastest growing species if the system has a periodic behaviour, and derived new selection criteria. Finally, the method was simulated using Droop's model for selecting species which maximise these criteria.

This selection method was adapted to a model of anaerobic digestion during its start-up phase [73]. In such a model, we proposed controls which enable to select, among several hundred of species, the ones with maximum growth rate in the reactor steady state operating mode. A first experimental validation of this control strategy was done at the INRA-LBE Laboratory.

Mathematical study of impulsive biological control models

The global stability of the interconnection of a continuous prey-predator model in ODE and periodic impulses has been studied. This work has been done in the context of biological control of pests in a continuously grown greenhouse. The prey-predator dynamics is continuous and it is augmented by discrete components representing the periodic release of predators. Our analysis consists in establishing the existence and global stability of a pest-free periodic solution of the system driven by the repeated predator releases. The latter is achieved using Floquet Theory and is explicitly formulated as a minimal bound on the number of predators to release per unit of time (the minimal rate of predator release).

The influence of various parameters on the stability conditions has been investigated. We first considered the general predator-prey model with density dependent functional response and showed that the minimal rate is independent of the release period, but that this period should be as small as possible in order to be able to optimally counter unexpected pest invasions [44] [72].

We then investigated the effect of a periodic crop harvest (as happens in roses greenhouses) on this bound of the predators release rate and identified that this minimal rate is smallest if the release period is an integer multiple of the harvest period [29], [39].

Finally, the effects of two types of intrapredatory interferences have been analysed. We have compared the influence of the addition of a Beddington-DeAngelis term, representing interference for the access to the prey, to the trophic responses of a Rosenzweig-MacArthur with the effect of the addition of a quadratic term to the predators mortality (which is otherwise linear) of this same model, this term representing the squabbling between predators. In both cases, we show that the minimal rate that ensures stability is dependent on the period of release [82]. Both models point out that the rate required for pest eradication is lowered if releases are carried out more frequently rather than less so and that a given rate will work only for a range of release period values; the difference of the effects of these interferences is that, if the Beddington-DeAngelis interference is too strong, stability cannot be achieved for any rate, while a large enough rate can always be found in the other case. This result has been also shown for a generalised form of the Beddington-DeAngelis interference [81].

This work has been done in collaboration with L. Mailleret (URIH, INRA Sophia-Antipolis).

6.2. Fields of application

6.2.1. Growth of marine plankton

Keywords: *biological models*, *bioreactors*, *chemostat*, *plankton*, *population dynamics*.

Participants: Olivier Bernard, Jean-Luc Gouzé, Antoine Sciandra, Serena Esposito, Christophe Mocquet, Thomas Lacour, Eric Benoît, Jonathan Rault.

Growth of phytoplankton limited by light and nitrogen

Phytoplankton physiological adaptation to the environmental variables (e.g. light and nutrients) is a key process determining phytoplankton growth in the ocean. A model which describes growth of phytoplankton while light and nitrogen are both deficient was developed and studied in [84][6], and compared with Geider's classical model and with Pahlow's model. It was validated with data from *Rhodomonas salina* and *Isochrysis galbana*. The previous model was coupled to hydrodynamical equations to obtain a 1-D model (with the LOBSTER model issued from the LOCEAN, Laboratoire d'Océanographie et de Climatologie par l'Expérimentation et l'Analyse Numérique, in collaboration with Marina Levy).

Models of increasing complexity have been developed to include this process and improve phytoplankton carbon fixation predictions in various oceanic conditions. However comparisons between models results are rare. We attempt to investigate the variability of the carbon fixation estimates in relation to the model complexity. We calibrated six models of increasing complexity using the same data set of batch culture of *I. galbana*. Then we compared the carbon fixation and productivity predictions both at steady state and during transient states under pulsed nitrogen source. Surprisingly, carbon fixation estimates of the different models only slightly differ, both in stable environmental conditions and under frequently varying nutrients field. However inverse methods aiming at carbon fluxes estimation on the basis of the original models and on chlorophyll measurements increase these differences.

Experiments about the phytoplankton cellular cycle

We have run experiments to observe the response of a population of microalgal cells to various periodic light/dark or nitrate signals. The measurements performed with the diatom *Thalassiosira weissflogii* show the synchronicity of the cells for some conditions. These experiments support the hypothesis that uptake of nitrogen stops during cell division.

Size-structured growth model of zooplankton

The model built in [53] was adapted to zooplankton. Some parts of the model had to be modified, most notably the death by starvation and the maintenance energy. The simulations of the model were compared to the measures done using the Zooscan in the bay of Villefranche-sur-Mer. For this comparison, statistical tools were used on data from Villefranche and some parameters were found in the literature. The model and the data of Villefranche allow to identify other parameters [45]. This work was done to allow integration of the model in a bigger model which will explain a size-structured model of detritus (faeces of zooplankton for example) needed to explain the sedimentation and the carbon pump in the ocean.

Carbon fixation by coccolithophorids

A set of 18 models was developed and studied [13], [12] to describe the coupling between photosynthesis and calcification for algae that are responsible for large carbon fluxes in the ocean. The qualitative study of this set showed that the standard hypotheses usually made by physiologists disagree with observed behaviors, since experiments have shown that an increase in the CO_2 partial pressure paradoxically leads to a decrease in the calcification rate. An alternative where pH drives the carbon assimilation process has been proposed and validated.

Nonlinear control for phytoplankton's growth in the chemostat

Phytoplanktonic populations in the chemostat can be difficult to maintain in high nutrient concentrations corresponding to high dilution rates. We propose a control law which is able to reduce this structural sensitivity and is only based on qualitative structural properties of a class of models to which the classical Droop model belongs [71]. We assume that the CO_2 incorporation rate (or oxygen production rate) can be measured. The model is kept qualitative in the sense that the growth rate is not specified, and we only assume qualitative hypotheses (positivity, monotonicity)

A 2D model of spatial segregation of phytoplankton

We developed biological models to investigate the vertical distribution of the cyanobacteria Prochlorococcus and Synechococcus spp in the North Pacific (collaboration with Christopher A. Edwards, UCSC). We designed a 2D version that we are implementing at INRIA, in collaboration with G. Malandain (Asclepios). This model is designed to analyze the horizontal segregation of Prochlorococcus and Synechococcus spp along an onshore-offshore gradient in the California Coastal System

6.2.2. Modelling and optimization of lipid production

Keywords: *biological models*, *chemostat*, *optimization*, *plankton*, *population dynamics*.

Participants: Olivier Bernard, Antoine Sciandra, Frédéric Grognard, Pierre Masci, Thomas Lacour.

In the framework of the ANR project Shamash, various models have been developed to predict the lipid production in a culture of microalgae after a nitrogen starvation [32]. One of these models is an extension of the Biolov model [84], including a description of a lipid storage compartment. These models have been improved by adding a representation of light attenuation in the reactor. A procedure to calibrate the model has been developped in order to rapidly evaluate the main parameters for various oil producing species.

For providing oil productivity predictions and optimization strategies, simpler models were developed. We also designed optimal controllers for these models and deduced the obtained oil productivity.

6.2.3. Bioprocesses

Keywords: *biological depollution*, *bioreactors*, *wastewater treatment*.

Participants: Jean-Luc Gouzé, Olivier Bernard, Frédéric Grognard, Jonathan Hess.

Anaerobic digestion monitoring and control

Comore has developed models for anaerobic digestion processes and proposed dedicated methods to select the appropriate model [59] and calibrate them [69]. Finally, this work has mainly been focused on the design of control laws that stabilize Wastewater Treatment Plants (WWTPs), which tend to be unstable without feedback control [85].

The mechanistic model of the liquid-gas exchange coefficient $k_L a$ [69] has been simplified to be incorporated in a general model of anaerobic digestion. The simplified version still exhibits a linear trend between the $k_L a$ and the biogas flow-rate. It has been used to modify the model of [4]. This simplified model keeps a good accuracy and can be used to construct a control strategy.

The new model shows a linear relation between the dissolved CO_2 and the biogas quality (in terms of $\%CO_2$), which gives new prospects for the control of the biogas quality. A strategy based on the regulation of the alkalinity has been proposed, and two feedback control laws were tested; a simple PI based on the measurement of the partial pressure of CO_2, and a mixed law based on a linearising control of the alkalinity plus a PI term to account for potential modelling errors [34]. Experiments have been carried out at the LBE INRA Narbonne to validate these two controllers.

Various asymptotic, interval based software sensors have also been developed based on the possible sets of measurements [79], [77], [69], [80][28].

Experiments for the modelling of the quality of the biogas that is produced by anaerobic digestion

We have developed a model of the quality of the biogas, in order to design regulation strategies, so that the biogas quality remains constant and it can be used as an energy source [69][34]. This result has been patented [49].

Experiments have been carried out with the LBE INRA Narbonne, for testing the effect of the pH of the influent and of the reactor on the quality of the biogas.

6.2.4. Models of ecosystems

Keywords: *biological models*, *ecosystems*, *population dynamics*.

Participants: Jean-Luc Gouzé, Frédéric Grognard, Sapna Nundloll.

Biological control

With L. Mailleret (URIH, INRA Sophia-Antipolis), we have a collaboration about biological control. The studied problem consists in evaluating the effect of periodic release of predators and periodic harvest on the population of pests. We investigate the minimal predator-budget that should be invested in order to ensure pest eradication. The model proposed in [81] has been shown to be valid for a pest-natural enemy couple present in the greenhouses of INRA and the proposed strategy has been experimentally shown to be the most efficient. More details on the methodological aspect of this problem are given in Section 6.1.4, Nonlinear Control.

6.2.5. Metabolic and genomic models

Keywords: *biological networks*, *cell models*, *qualitative analysis*.

Participants: Olivier Bernard, Jean-Luc Gouzé, Frédéric Grognard, Laurent Tournier, Ibrahima Ndiaye, Madalena Chaves, Eric Benoît.

Dynamics of genetic regulatory networks

We are studying a class of piecewise-linear dynamical systems, $\dot{x} = f(x) - g(x)x$, where x is a n-vector of protein concentrations, the vector $f(x)$ and matrix $g(x)$ are piecewise constant and represent synthesis and degradation rates respectively. Piecewise-linear systems form the basis of an important class of models used for genetic regulatory networks, where the regulatory interactions between the genes are approximated as step functions. The use of step functions is motivated by the switch-like behavior seen experimentally in many of the interactions in gene expression and breakdown of proteins. The piecewise-linear models have the advantage that they are amenable to qualitative analysis and are well-suited to the qualitative character of the majority of experimental data from genetic regulatory networks. Current work in this project consists in continuing the work of Gouzé and Sari [65] and de Jong *et al* [87] by characterizing the equilibrium points and periodic orbits in this special class of systems. These methods and algorithms are used by the software GNA (Genetic Network Analyzer) developed by de Jong *et al* (HELIX, INRIA Rhône-Alpes).

As the dimension of the system increases, it becomes useful to reduce it, in some sense, in order to facilitate its analysis. Based on the discrete structure of piecewise affine systems, we developed a reduction method (see [31]) using the strongly connected components decomposition of the interaction graph. Thanks to this decomposition, we are able to express the initial dynamical system in a hierarchical form, allowing to decompose the dynamical analysis of the whole system (neglecting some transients) by subsequently analyzing asymptotic behaviors of the different subsystems. Such a method has been successfully applied to 6- and 9-dimensional piecewise affine models of the regulatory network underlying the response of bacterium *Escherichia coli* to a nutritional stress described by Ropers et al. [83].

Control of genetic regulatory networks

Since recent biological techniques allow for the synthesis of more and more elaborate gene regulatory networks, it seems appropriate to develop some control theoretic methodologies for these networks. We have thus introduced some new mathematical techniques whose purpose is the control of piecewise-linear equations towards a prescribed behavior. Namely, we suppose that the piecewise constant terms $f(x)$ and $g(x)$ depend on an input vector u. Then, our aim is to find piecewise constant feedback laws $u(x)$, such that the state transition graph mentioned above has a prescribed shape. We have characterized these feedback laws in terms of a system of affine inequalities for each vertex in the transition graph. If, moreover, each input variable affects one variable at the most, the solutions of these inequalities can in fact be obtained explicitly [19].

Periodic solutions of models of genetic regulatory networks

One important problem of piecewise-linear models of gene networks is their comparison with discrete analogues, which are all based on the state transition graph. Notably, loops in this graph may correspond to limit cycles of the piecewise-linear system, but also equilibria situated at the intersection of several thresholds. An important family of piecewise-linear systems is composed of those systems whose interaction structure is a negative loop involving all variables. These systems do all have a loop in their state transition graph. Using theorems about monotone operators acting on positive variables, we have shown that this loop always correspond to a unique, stable limit cycle [20].

Interaction between signaling and gene expression networks

A simple model, consisting of one protein (x) and one mRNA (y), was developed and fully analyzed [38]: the protein x activates transcription of the gene and also contributes to its own synthesis. The mRNA y (or its corresponding protein) contributes to the degradation of protein x. The idea that signaling or metabolic networks achieve an operational steady state much faster than the dynamics of gene expression was used to study the model in a “fast-slow” framework. It is shown how the signaling network can be regulated, by switching between two operational modes (or steady states), in response to gene expression patterns.

Conditions for the existence of an oscillatory cycle, as well as an estimate of its period, are provided. Some of the parameters are estimated from experimental data on the cell cycle of *Xenopus laevis* oocytes.

Qualitative models of apoptosis

An extended model of apoptosis, regulated via the NFκB pathway, is proposed in [33]. A Boolean model is constructed from the network of interactions, and analyzed using piecewise linear systems. This model captures various properties of apoptosis signaling, including bistability and the existence of oscillations in the presence of stimulus (in agreement with experimental results). Three variants of the model are considered, each with sligthly different wiring. By comparing the rates of apoptosis predicted by each variant with experimental data, one can infer which network wiring better reflects the biological system. This is work in collaboration with T. Eissing and F. Allgöwer from the University of Stuttgart, Germany.

Modeling segment polarity genes under cell division

The segment polarity genes play a major role in establishing the outline of *Drosophila*'s body segmentation during embryonic development. A Boolean model of the segment polarity network was analyzed in [62], where it was assumed that each segment in the embryo's body was four cells wide. In [14], this model is now extended to segments of any length n, to account for cell division. It is shown that the same gene expression patterns are obtained for n cells, and that the conditions for convergence to the wild type pattern are also generalized to segments of length n. Finally, this study indicates that cell division contributes to increase robustness of formation of the wild type pattern with respect to perturbations in biological processes. This is work in collaboration with R. Albert, from Pennsylvania State University, USA.

Algorithmic approaches to time and space scales in biochemical networks

We consider large metabolic and genetic networks with different scales with respect to time and space; moreover, the parameters have different order of magnitude. We designed the first steps of a method considering boxes (hyper rectangles) representing order of magnitude, and transition between boxes along a trajectory [46].

6.3. Software design

Keywords: *C++*, *Matlab*, *Scilab*, *monitoring platform*, *simulation platform*, *wastewater treatment*.

Participants: Olivier Bernard, Romain Primet.

Over the years, Comore has been developing a software framework for bioprocess control and supervision called ODIN [57]. This C++ application enables researchers and industrials to easily develop and deploy advanced control algorithms through the use of a Scilab interpreter. It also contains a Scilab-based process simulator which can be harnessed for experimentation and training purposes. ODIN is primarily developed in the C++ programming language and uses CORBA to define component interfaces and provide component isolation. ODIN is a distributed platform, enabling remote monitoring of the controlled processes as well as remote data acquisition. In 2008, software development effort has been directed to the graphical user interface, a synoptic view component, new drivers for the experimental hardware and integration of the PlantML data exchange format. PlantML is an XML format used to describe plant data wich helps quickly porting ODIN to new processes and brings easier integration with other software tools using this standard. ODIN has been tested with four different processes. ODIN is undergoing tests at the LBE-INRA in Narbonne".

7. Contracts and Grants with Industry

7.1. Microalgae for CO_2 trapping

- A contract between Comore, the Laboratory of Oceanography in Villefranche and Lafarge has been signed in order to assess and quantify the potential of microalgae for CO_2 trapping.

- Comore has had collaboration with EDF for the assessment of the potential of microalgae to mitigate CO_2 from powerplants.

8. Other Grants and Activities

8.1. National initiatives

- **Shamash:** Shamash is a project funded by the ANR in the national program for research in bioenergy. Its objective is to produce biodiesel from microalgae. Shamash is coordinated by O. Bernard, it includes 9 partners, for a total budget of 2.8 Millions Euros. The role of Comore is to design a model of the process in order to better understand the dynamical mechanisms that lead to the transient storage of lipids. The second step will then consist in defining optimal conditions to maximize the oil production. See http://www- sop.inria.fr/comore/shamash/
- **Symbiose:** Comore takes part to the Symbiose ANR project. The objective of this project is both to improve the energetic balance of biofuel microalgal productions and to recycle nitrogen and phosphorus. The project proposes to study the coupling between a microalgal production system and an anaerobic digester. The objectives of Comore are to propose a model of the coupled system, and to compute the optimal fluxes between the various compartments in order to optimize the energy recovery.
- **BFN - LEFE :** Comore takes part in the BFN project funded by INSU (Institut National des Sciences de l'Univers) within the LEFE program. The objective is to provide new data assimilation algorithms for improving state and parameter estimation in oceanography. http://www.mip.ups-tlse.fr/~auroux/LEFE/.
- **GDR BioH2:** The objective of this GDR is the development of new biotechnological processes based on microorganisms producing hydrogen. Comore is taking part mainly in the modelling and control aspects of the H_2 production processes involving anaerobic bacteria or microalgae.
- **MetaGenoReg:** The objective of this project, funded by ANR (Systems Biology), is to model and analyze the interaction between metabolic and genetic regulations, with the example of the carbon metabolism of E. coli. The project is directed by D. Kahn (Helix, INRIA).
- **StepContr:** The aim of this project is the advanced control of wastewater treatment bioprocesses when the input is known and periodic. This project, funded by "l'Agence Universitaire de la Francophonie", is steered by A. Karama (Univ. Marrakech), and also involves M. Perrier (Ecole Polytechnique de Montréal, Canada).
- **ARC CODA:** The objective of this INRIA funded project is to optimize the starting of anaerobic treatment plants. This is a joint project with the INRIA SEQUEL project, INRA LBE and the company Naskeo. The INRIA funding lasts until the end of 2008; the Coda project will keeop existing through INRA funding in 2009.
- **ECOGER:** We participate in one of the themes of this project, which is funded by INRA: "Ecology and adaptation of phytophagous insects and management of their populations". Comore's objective in this project is the mathematical modelling and optimization of biological control.
- **Color LutIns&co:** This INRIA funded project aims at modelling the influence of intra-guild predation on biological control; it merges techniques of game theory and control theory. This a joint project with INRA Sophia-Antipolis and I3S.
- **IA2L:** INRA-SPE is also funding a project on intra-guild predation in which we are taking part: "Interactions antagonistes entre auxiliaires : conséquences pour la lutte biologique".
- **Color ModZoo :** This INRIA funded project aims at modelling the size structured population of zooplancton, with a good adequation with the measures in the bay of Villefranche. This is a join project with LOV (Villefranche sur Mer) http://www.obs-vlfr.fr/LOV/ZooPart/ModZoo/.

- **ColAge:** This is a joint INRIA-INSERM consortium, and a proposal for an “Action d’Envergure”, which is partly funded by INRIA. The goal is to study bacterial growth and aging by using mathematical modelling and computational predictions to design a *de novo* biological system, and then implement this design *in vivo*. The project is directed by H. Berry (Alchemy, INRIA).
- **COREV:** Comore is an active participant in the research group COREV (Modèles et théories pour le contrôle de ressources vivantes et la gestion de systèmes écologiques).
- **RTP-M3D:** Comore is a participant in the RTP-M3D workgroup (Mathématiques et décision pour le développement durable) that is supported by the “Environment and sustainable growth” department of CNRS.
- **Seminar:** Comore organizes a regular seminar “Modelling and control of ecosystems” at the station zoologique of Villefranche-sur-Mer or at INRIA. In parallel with that seminar, we have had working group seminars with the MERE project-team of Montpellier, in order to maintain our collaborations.

8.2. European initiatives

- **European project HYGEIA:** HYGEIA (Hybrid Systems for Biochemical Network Modelling and Analysis) is a NEST ADVENTURE STREP European project. The objective of HYGEIA is to exploit recent developments in the area of hybrid systems to address open problems in modelling and analysis of biochemical networks, see http://www.hygeiaweb.gr/home.html. Hygeia officially ended in december 2008.
- **European Network of Excellence HYCON:** The objective of the NoE HYCON (Hybrid Control: Taming Heterogeneity and Complexity of Networked Embedded Systems) is establishing a long-lasting community of leading researchers and practitioners who develop and apply the hybrid systems approach to the design of networked embedded control systems as found, e.g., in industrial production, transportation systems, generation and distribution of energy, communication systems, genetic systems (see http://www.ist-hycon.org/).
- **BOOM:** The BOOM project - Biodiversity of Open Ocean Microcalcifiers - is aiming at elucidating the biodiversity of calcifying species. This encompasses the study of phylogeny from existing cultures and bulk DNA as well as culture isolation from in situ sample collection, genome size screening. Environmental and functional diversity are concerned with experimental laboratory physiological studies. Participants : http://www.obs-vlfr.fr/~gattuso/boom.php.

8.3. Visits

We only list the visitors that stayed more than 2 days or that presented a seminar in our project-team

- Hidde de Jong (INRIA Ibis, France), 1 week (cumulated visits);
- Ludovic Mailleret (INRA Sophia-Antipolis, France), 1 month (cumulated visits);
- Gregory Batt (Contraintes - INRIA Rocquencourt), 1 day;
- Claudine Chaouiya (TAGC Inserm U928, Université de la Méditerranée), 1 day;
- Thomas Sierocinski (IRMAR, Université de Rennes), 1 day;
- Rachid Bebbouchi (Université USTHB Alger), 5 days;
- Ouahiba Cherikh (Université USTHB Alger), 15 days;
- Louise van Oudenhove (Université Lyon I), 2 days;
- Delphine Ropers, Valentina Baldazzi and Sara Berthoumieux (INRIA Ibis), 2 days;
- Gael Bougaran (IFREMER Nantes), 3 days;
- Georges Bastin (Université Catholique de Louvain, Belgium), 4 days.

8.4. Project-team seminar

Comore organized a 3-day seminar in september at Saint-Etienne-de-Tinée. On this occasion, every member of the project-team presented its recent results and the permanent research scientists taught beginner's level classes about subjects related to their research.

9. Dissemination

9.1. Leadership with scientific community

J.-L. Gouzé is a member of scientific committees for the conferences POSTA 2009 Multidisciplinary International Symposium on Positive systems, theory and applications, Valencia, Spain) and for the conference "Stic et Environnement". He is a member of the board of the project-team committee at INRIA (Bureau du comité des projets), the co-head of an INRIA committee supervising the doctoral theses and is a member of the committee “Ecole Doctorale 85 Sciences de la Vie et de la Santé” of the University of Nice-Sophia-Antipolis. He is a member of the board of the SFBT (French Speaking Society for Theoretical Biology).

O. Bernard is the leader of the ANR project Shamash. He is in the technical committee of the Computer Applied to Biotechnology (CAB) conferences. He is in the scientific committee of the French conference "Stic et Environnement".

O. Bernard belongs to the Color committee of INRIA Sophia-Antipolis. He is in the specialists commission of University Aix-Marseille for the “Maître de conférences” jurys.

E. Benoît is vice-head (at the University of La Rochelle) of the ANR project ANAR (Analyse Non Linéaire et Application aux Rythmes Complexes du Vivant). He is the French representative of a CMEP collaboration (Comité Mixte d'Evaluation et de Prospective) between the universities of La Rochelle and of Alger. He is the scientific head of the SYD'02 workshop (Deuxième Colloque international en Systèmes Dynamiques, Alger)

9.2. Scientific popularisation - media

An article was written in a generalist scientific newspaper to explain our contribution in microalgae modelling [48].

A movie was made on the Shamash project, and it was included in an article in the Interstices web page: http://interstices.info/jcms/c_24036/projet-shamash-production-de-biocarburants-lipidiques-par-des-microalgues

A web page was also presenting the Shamash project on the science.gouv.fr site http://www.science.gouv.fr/fr/actualites/bdd/res/2938/biocarburants-et-microalgues-la-science-en-1ere-ligne/

The Shamash project has motivated many articles and broadcasts in the media: The most important newspapers are "Le Monde" (Des microalgues pour les biocarburants du futur, octobre 23d, 2008), "Figaro magazine" (Les algues, nouveau pétrole vert ? april 2008), "Enjeux - les Echos" (Les chercheurs carburent sur les microalgues, march 2008), "L'usine nouvelle" (La modélisation numérique sied aux algues, june 11, 2008).

Jean-Luc Gouzé and Frédéric Grognard did conferences entitled “Des coccinelles aux algues, modéliser l'environnement pour mieux le gérer”: Jean-Luc Gouzé at the Lycée de Vinci in Antibes in the framework of the “participative science” initiative of INRIA and Frédéric Grognard at the Centre International de Valbonne for the “Fête de la Science”. These high-school level talks were aimed at showing the importance of mathematics, and specifically mathematical modelling, for the solution of environmental challenges.

9.3. Teaching

J.-L. Gouzé, O. Bernard, F. Grognard and A. Sciandra gave two weeks of courses in november on mathematical models in biology at the Master on biological oceanography, Pierre et Marie Curie, Paris VI. J.-L. Gouzé taught courses on dynamical systems (6h) as well as F. Grognard (3h), O. Bernard on identification (3h) and classworks were taught by P. Masci (6h).

F. Grognard and E. Benoit taught classes in the MAM orientation (Mathématiques Appliquées et Modélisation) of EPU (Ecole Polytechnique Nice - Sophia Antipolis). F. Grognard gave a class on modeling and control of biological systems to 2nd year engineering students (MAM4 level). E. Benoît taught a class on modeling at the 3rd year level (MAM5) and on ordinary differential equations at the 1st year students (MAM3)

M. Chaves gave a course at EPU, to students at the Master level at the Dep. Genie Biologie, on modeling biological networks using ordinary differential equations (12h). I. Ndiaye gave lectures and project follow up (8h) for this course.

O. Bernard gave lectures at the Ecole Nationale Supérieure des Mines de Paris (3h) on bioenergy from microalgae. O. Bernard gave 12h lectures at the University of Santiago de Compostella (Spain) on advanced modelling, analysis and observation of bioprocesses.

E. Benoît taught courses for the CIMPA at Tlemcen (Algeria) about ordinary differential equations.

9.3.1. Theses

- Ongoing theses:
  1. S. Nundloll, “Modélisation et optimisation de la lutte biologique”, UNSA.
  2. I. Ndiaye, “Analyse mathématique et contrôle de modèles de réseaux de régulation génétique”, UNSA.
  3. C. Mocquet, “Interférence entre les processus de division cellulaire et de croissance somatique chez les autotrophes. Effets résultant sur la production primaire et modélisation des phénomènes en environnement variable” , Université P.M. Curie.
  4. T. Lacour, “Etude expérimentale des mécanismes de production de lipides par des microalgues”, Université P.M. Curie.
  5. P. Masci, “Etude et développement d’un système de sélection d’espèces dans un environnement dynamique multivariable”, UNSA.
  6. J. Rault, “Modélisation mathématique du plancton, structuré en taille. Conséquence sur la séquestration du carbone dans l’océan”, UNSA.
- Participation in PhD juries:
  O. Bernard was referee for the PhD Jury of F. Mairet . " Conduite de réacteurs biologiques multivariables à comportement complexe : application à un organisme végétal", Université Technologique de Compiègne on December, 2nd.
  O. Bernard was in the PhD Jury of Eva Van Derlinden. " Quantifying microbial dynamics as function of temperature: towards an optimal trade-off between biological and model complexity ", University of Leuven on December, 22nd.
  J.-L. Gouzé was referee for the HDR (tenure) of T. Bastogne, Univ. H. Poincaré, Nancy, "Modélisation expérimentale des systèmes dynamiques interconnectés -Applications en Biologie Systémique".
  J.-L. Gouzé was referee for the thesis of N. Meslem, Univ. Paris Est “Atteignabilité hybride des systèmes dynamiques continus par analyse par intervalle. Application à l’estimation ensembliste”, for the thesis of D. Ngom, Université G. Berger, Saint-Louis, Sénégal “Observation Et Régulation De Certains Modèles Discrets D’ Ecosystèmes”, for the thesis of W. Kepseu, Univ. Yaoundé 1, Cameroun, “Dynamique de deux réseaux d’oscillateurs biologiques non linéaires : Communication par Ca^{2+} et Quorum Sensing". He was in the jury of A. Crumière, Univ. de la méditerranée, Luminy, ”Circuits de rétroaction dans les réseaux génétiques de régulation intercellulaires”.
  E. Benoît was in the jury for the HdR of Emmanuelle Augeraud, University of La Rochelle, "Contribution à la modélisation de certaines structures démographiques dans des modèles économiques"

9.4. Conferences, invited conferences

Conferences with proceedings are not repeated here.

M. Chaves and J.-L. Gouzé were invited to give seminars at the symposium “The logic of gene regulatory networks”, organized by A. Goldbeter and M. Kaufmann in honor of Prof. René Thomas and his 80th birthday, at the Université Libre de Bruxelles, Belgium (May 2008).

M. Chaves and J.-L. Gouzé were also invited to participate and give seminars at the workshop “Discrete models of biological networks: from structure to dynamics”, organized by C. Chaouiya, E. Remy, and P. Ruet at the Centre International de Rencontres Mathématiques (CIRM, Marseille - Luminy), France (November 2008).

M. Chaves gave a seminar at the workshop “Mathematical Tools for Multi-Scale Biological Processes”, organized by P. De Leenheer, T. Gedeon, and X. Zhao at Montana State University, USA (June 2008).

J.-L. Gouzé was invited to give a talk at ECMTB08 European Conference on Mathematical and Theoretical Biology, Edinburgh (June 29-July 4, 2008).

J.-L. Gouzé was invited to give a talk at the MABEM workshop organized by E. Pecou in Nice (October 2008).

P. Masci did a talk on "Theoretical study of the competition for substrate between N microorganism species in the Droop model" at the workshop "Differential Equations and Applications to Mathematical Biology" (June 23-27, 2008) at the University of Le Havre, France. At this same workshop, F. Grognard did a talk on “Impulsive biological control with Beddington-DeAngelis interference: stability and convergence rate”. S. Nundloll also presented a poster on this topic at the “Workshop on Population Dynamics and Mathematical Biology” at the CIRM in Marseille France (June 16-20, 2008).

S. Nundloll did a talk on "The effects of intraspecific interference on an impulsive biological control model" at the Marrakesh International Conference and Workshop on Mathematical Biology in Marrakesh, Marocco (January 3-8, 2008). She presented a seminar on the same subject in the LAMETA group at INRA Montpellier, France (February 2008).

G. Bougaran and O. Bernard gave a talk to the conference “Applied Phycology” in Galway (June 22-27, 2008), on a “New model of colimitation between nitrogen and phosphorus”.

O. Bernard organized a conference for the French society of biology on the next generation of biofuels, where he gave an introductory talk.

O. Bernard was invited together with A.Sciandra to give a presentation at the Napoli zoological laboratory “Modelling and validation of phytoplankton in dynamical light and nutrient fields” (February 18-19, 2008).

O. Bernard was invited by C.Posten to give a presentation at the University of Karlsruhe (Institut für Mechanische Verfahrenstechnik und Mechanik) on “Modelling of growth and calcification of coccolithophorids” (May 9, 2008).

O. Bernard presented the Shamash project and its results at the PNRB forum the (February 26, 2008).

O. Bernard gave a talk at the “Ocean in a high CO_2 world” on “Predictions of carbon fixation during a bloom of *Emiliania huxleyi* is highly sensitive to assumed response to shift in pCO_2” (joined work with A.Sciandra and S.Rabouille) in Monac (October 6-9, 2008).

E. Benoît was invited to give a seminar at the mathematics department of the University of Mulhouse entitled “Notes sur les techniques d’étude des champs lents-rapides”. [43].

E. Benoît gave a seminar at the mathematics department of the University of Strasbourg entitled “Bifurcation delay - the case of the sequence: stable focus - unstable focus - unstable node” [54]

E. Benoît gave a talk at the international workshop SYD’02 (Bou Saada/Algérie): “Bifurcation delay - the case of the sequence: stable focus - unstable focus - unstable node”

E. Benoît and I. Ndiaye gave talks at the ANR ANAR meeting in La Rochelle on “Algorithmic approximations method taking of magnitudes into account and on the study” and “Parameter identification of a model coupling cell signaling and gene expression”, respectively (November 27-29, 2008).

Andrei Akhmetzhanov did a talk entitled “Inter- and intraseason dynamics of prey-predator optimal control models” at the International Conference “Differential Equations and Topology” dedicated to the Centennial Anniversary of L. S. Pontryagin, in Moscow (June 17-22, 2008) and a presentation on “Reproduction dynamics in a differential game between foraging predators and hiding preys” at the 13th International Symposium on Dynamic Games and Applications in Wroclaw, Poland (June 30-July 3rd, 2008).

10. Bibliography

Major publications by the team in recent years

[1] J. ARINO, J.-L. GOUZÉ, A. SCIANDRA. *A discrete, size-structured model of phytoplankton growth in the chemostat. Introduction of non constant cell division.*, in "J. Math. Biol.", vol. 45, 2002, p. 313-336.

[2] O. BERNARD, G. BASTIN. *On the estimation of the pseudo-stoichiometric matrix for mass balance modeling of biotechnological processes*, in "Math. Biosciences", vol. 193, 2005, p. 51-77.

[3] O. BERNARD, J.-L. GOUZÉ. *Closed loop observers bundle for uncertain biotechnological models*, in "J. Process. Contr.", vol. 14:7, 2004, p. 765-774.

[4] 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 "Biotech.Bioeng.", vol. 75, n^{o} 75, 2001, p. 424-438.

[5] M. CHAVES. *Input-to-state stability of rate-controlled biochemical networks*, in "SIAM Journal of Control and Optimization", vol. 44, 2005, p. 704-727.

[6] B. FAUGERAS, O. BERNARD, A. SCIANDRA, M. LEVY. *A modelling and data assimilation approach to estimate the carbon/chlorophyl and carbon/nitrogen ratios in a coupled hydrodynamical-biological model*, in "Nonlinear Processes in Geophysics", vol. 11, 2004, p. 515-533.

[7] J.-L. GOUZÉ. *Positive and negative circuits in dynamical systems*, in "Journal Biol. Syst.", vol. 6, n^{o} 1, 1998, p. 11-15.

[8] J.-L. GOUZÉ, A. RAPAPORT, Z. HADJ-SADOK. *Interval observers for uncertain biological systems*, in "Ecological modelling", vol. 133, 2000, p. 45-56.

[9] F. GROGNARD, F. MAZENC, A. RAPAPORT. *Polytopic Lyapunov functions for persistence analysis of competing species*, in "Discrete and Continuous Dynamical Systems-Series B", vol. 8, n^{o} 1, 2007, p. 73-93.

[10] L. MAILLERET, O. BERNARD, J.-P. STEYER. *Nonlinear adaptive control for bioreactors with unknown kinetics*, in "Automatica", vol. 40-8, 2004, p. 1379-1385.

Year Publications

Articles in International Peer-Reviewed Journal

[11] O. BARROU, A. KARAMA, E. LAKHAL, O. BERNARD, M.-N. PONS, J.-P. CORRIOU. *Estimation of a Reduced Model of the BSM1 Activated Sludge Wastewater Treatment Plant*, in "International Journal of Chemical Reactor Engineering", vol. 6, 2008, A63.

[12] O. BERNARD, A. SCIANDRA. *Generic analysis of the response of calcifying microalgae to an elevation of* pCO_2 *: qualitative vs quantitative analysis*, in "ARIMA", to appear, 2008.

[13] O. BERNARD, A. SCIANDRA, S. MADANI. *Multimodel analysis of the response of the coccolithophore Emiliania huxleyi to an elevation of* pCO_2 *under nitrate limitation*, in "Ecol. Model.", vol. 211, 2008, p. 324-338.

[14] M. CHAVES, R. ALBERT. *Studying the effect of cell division on expression patterns of the segment polarity genes*, in "J. Royal Society Interface", vol. 5, 2008, p. S71-S84.

[15] M. CHAVES, T. EISSING, F. ALLGÖWER. *Bistable biological systems: a characterization through local compact input-to-state stability*, in "IEEE Trans. Autom. Control", vol. 53(1), 2008, p. 87-100.

[16] M. CHAVES, A. SENGUPTA, E. D. SONTAG. *Geometry and topology of parameter space: investigating measures of robustness in regulatory networks*, in "J. Mathematical Biology", to appear, 2008.

[17] A. DAYARIAN, M. CHAVES, E. D. SONTAG, A. SENGUPTA. *Shape, size and robustness: feasible regions in the parameter spaceof biochemical networks*, in "PLoS Computational Biology", to appear, 2008.

[18] T. EISSING, M. CHAVES, F. ALLGÖWER. *Live and let die - a systems biology view on cell death*, in "Computers & Chemical Eng.", to appear, 2008.

[19] E. FARCOT, J.-L. GOUZÉ. *A mathematical framework for the control of piecewise affine models of gene networks*, in "Automatica", vol. 44, 2008, p. 2326-2332.

[20] E. FARCOT, J.-L. GOUZÉ. *Periodic solutions of piecewise affine gene network models: the case of a negative feedback loop*, in "Acta Biotheoretica", to appear, 2008.

[21] G. GOFFAUX, A. VANDE WOUWER, O. BERNARD. *Continuous - Discrete Interval Observers for Monitoring Microalgae Cultures*, in "Biotech. Progress", to appear, 2008.

[22] J.-L. GOUZÉ, V. LEMESLE. *Two simple growth models in the chemostat*, in "ARIMA", to appear, 2008.

[23] J. HESS, O. BERNARD. *Advanced dynamical risk analysis for monitoring anaerobic digestion process*, in "Biotechnology Progress", to appear, 2008.

[24] J. HESS, O. BERNARD. *Design and study of a risk management criterion for an unstable anaerobic wastewater treatment process*, in "J. Process. Contr.", vol. 18, 2008, p. 71-79.

[25] V. LEMESLE, J.-L. GOUZÉ. *A simple unforced oscillatory growth model in the chemostat*, in "Bulletin of Mathematical Biology", vol. 70, 2008, p. 344-357.

[26] L. MAILLERET, J.-L. GOUZÉ, O. BERNARD. *Global stabilization of a class of partially known positive systems*, in "Automatica", vol. 44, 2008, p. 2128-2134.

[27] F. MAZENC, M. MALISOFF, O. BERNARD. *A Simplified Design for Strict Lyapunov Functions under Matrosov Conditions*, in "IEEE Trans. Autom. Control", to appear, 2009.

[28] M. MOISAN, O. BERNARD, J.-L. GOUZÉ. *Near optimal interval observers bundle for uncertain bioreactors*, in "Automatica", to appear, 2008.

[29] S. NUNDLOLL, L. MAILLERET, F. GROGNARD. *The effect of partial crop harvest on biological pest control*, in "Rocky Mountain Journal of Mathematics", vol. 38, n^{o} 5, 2008, p. 1633-1661.

[30] J. RODRIGUEZ, E. ROCA, J. LEMA, O. BERNARD. *Determination of the adequate minimum model complexity required in anaerobic bioprocesses using experimental data*, in "J. Chem. Tech. Biotech.", vol. 83, 2008, p. 1694-1702.

[31] L. TOURNIER, J.-L. GOUZÉ. *Hierarchical analysis of piecewise affine models of gene regulatory networks*, in "Theory in Biosciences", vol. 127, 2008, p. 125-134.

Articles in Non Peer-Reviewed Journal

[32] J.-P. CADORET, O. BERNARD. *La production de biocarburants lipidiques avec des microalgues: promesses et défis*, in "Journal de la société de biologie", vol. 202, 2008, p. 201-211.

International Peer-Reviewed Conference/Proceedings

[33] M. CHAVES, T. EISSING, F. ALLGÖWER. *Regulation of apoptosis via the NFkB pathway: modeling and analysis*, in "Dynamics on and of complex networks: applications to biology, computer science and the social sciences", N. GANGULY, A. DEUTSCH, A. MUKHERJEE (editors), Modeling and Simulation in Science, Engineering and Technology, Birkhäuser, Boston, 2009.

[34] J. HESS, E. LATRILLE, O. BERNARD, J.-P. STEYER. *Control of the biogas quality produced during anaerobic digestion of wine distillery wastewater*, in "Proceedings of the 10th latin american workshop and symposium on anaerobic digestion", Easter Island, Chile, 2008.

[35] P. MASCI, O. BERNARD, F. GROGNARD. *Continuous Selection of the Fastest Growing Species in the Chemostat*, in "Proceedings of the IFAC conference", Seoul, Korea, 2008.

[36] F. MAZENC, M. MALISOFF, O. BERNARD. *Lyapunov Functions and Robustness Analysis under Matrosov Conditions with an Application to Biological Systems*, in "Proceedings of the ACC conference", Seattle, USA, 2008.

[37] M. MOISAN, O. BERNARD, J.-L. GOUZÉ. *High/low gain bundle of observers: application to the input estimation of a bioreactor model*, in "Proceedings of the IFAC conference", Seoul, Korea, 2008.

[38] I. NDIAYE, M. CHAVES, J.-L. GOUZÉ. *Study and parameter identification of a model coupling cell signaling and gene expression*, in "Proc. 16th Mediterranean Conf. Control and Automation (MED'08), Ajaccio, France", 2008.

[39] S. NUNDLOLL, L. MAILLERET, F. GROGNARD. *Global Stability in a General Impulsive Biological Control Model with Harvest*, in "Proceedings of the IFAC World Congress", Seoul, Korea, 2008.

[40] L. TOURNIER, J.-L. GOUZÉ. *Qualitative stability patterns for Lotka-Volterra systems on rectangles*, in "Hybrid Systems, Computation and Control HSCC 08", M. EGERSTEDT, B. MISHRA (editors), Lecture Notes in Computer Sciences (LNCS) 4981, Springer-Verlag, Saint-Louis, USA, 2008, p. 662-665.

Scientific Books (or Scientific Book chapters)

[41] O. BERNARD, J.-L. GOUZÉ. *State estimation for bioprocesses*, in "Bioprocess Control", D. DOCHAIN (editor), Wiley, Hoboken, 2008.

[42] O. BERNARD, I. QUEINNEC. *Dynamic models of biochemical processes: properties of models*, in "Bioprocess Control", D. DOCHAIN (editor), Wiley, Hoboken, 2008.

Research Reports

[43] E. BENOÎT. *Notes sur les techniques d'étude des champs lents-rapides*, Technical report, INRIA, 2008.

[44] L. MAILLERET, F. GROGNARD. *Global stability and optimisation of a general impulsive biological control model*, Research report, n^o 6637, INRIA, 2008, http://hal.inria.fr/inria-00320578/en/.

[45] J. RAULT. *Réalisation d'un modèle mathématique de dynamique des populations, structuré en taille, pour le zooplancton*, Rapport de stage de fin d'études, Ecole Polytechnique Universitaire de Nice - Sophia Antipolis, 2008.

[46] V. ROSANO. *Réalisation d'une maquette informatique pour la réduction de modèles biochimiques*, Rapport de stage de master MASS, Université de Nice Sophia-Antipolis, 2008.

[47] L. TOURNIER, M. CHAVES. *Uncovering operational interactions in genetic networks using asynchronous boolean dynamics*, Research report, n^o 6703, INRIA, 2008, http://hal.inria.fr/inria-00325914/en.

Scientific Popularization

[48] O. BERNARD, A. SCIANDRA. *Des micro-algues numériques*, in "La Recherche", vol. Juillet/Aout 2008 - 421, 2008.

Other Publications

[49] O. BERNARD, J. HESS, J.-P. STEYER, E. LATRILLE. *Bioréacteur et procédé pour la production de biogaz*, Brevet 07/08731, 2007.

References in notes

[50] A. AKHMETZHANOV, L. MAILLERET, F. GROGNARD. *Inter- and intraseason dynamics of prey-predator optimal control models*, in preparation.

[51] A. AKHMETZHANOV, L. MAILLERET, F. GROGNARD, P. BERNHARD. *Reproduction dynamics in a differential game between foraging predators and hiding preys*, in preparation.

[52] G. BASTIN, D. DOCHAIN. *On-line estimation and adaptative control of bioreactors*, Elsevier, 1990.

[53] E. BENOÎT, M.-J. ROCHET. *A continuous model of biomass size spectra governed by predation and the effects of fishing on them*, in "Journal of Theoretical Biology", vol. 226, n^{o} 1, 1 2004, p. 9-21.

[54] E. BENOÎT. *Bifurcation delay - the case of the sequence: stable focus - unstable focus - unstable node*, in "Discrete and Continuous Dynamical Systems", submitted, 2008.

[55] O. BERNARD, G. BASTIN. *Identification of reaction schemes for bioprocesses: determination of an incompletely known yield matrix*, in "Bioprocess and Biosystem Engineering", vol. 27, 2005, p. 293-302.

[56] O. BERNARD, G. BASTIN. *On the estimation of the pseudo-stoichiometric matrix for mass balance modeling of biotechnological processes*, in "Math. Biosciences", vol. 193, 2005, p. 51-77.

[57] O. BERNARD. *TELEMAC Deliverable 3.4: Final version of the Telemac advanced control module*, 2004.

[58] O. BERNARD. *Use of modulating functions for reaction network identification*, in "Proceedings of the 10th CAB conference", Cancun, Mexico, 2007.

[59] O. BERNARD, B. CHACHUAT, A. HÉLIAS, J. RODRÍGUEZ. *Can we assess the model complexity for a bioprocess ? Theory and example of the anaerobic digestion process*, in "Wat. Sci. Tech.", vol. 53, 2005, p. 85-92.

[60] O. BERNARD, J.-L. GOUZÉ. *Closed loop observers bundle for uncertain biotechnological models*, in "J. Process. Contr.", vol. 14:7, 2004, p. 765-774.

[61] O. BERNARD, I. QUEINNEC. *Dynamic models of biochemical processes: properties of the models*, in "Automatic Control of Bioprocesses", D. DOCHAIN (editor), chap. 2, ISTE, 2006, p. 23-52.

[62] M. CHAVES, E. D. SONTAG, R. ALBERT. *Methods of robustness analysis for Boolean models of gene control networks*, in "IEE Proc. Systems Biology", vol. 153(4), 2006, p. 154-167.

[63] C. G. DIÉGUEZ, E. ROCA, O. BERNARD. *Reduction of the Anaerobic Digestion Model N°1 for an industrial wastewater treatment plant by Principal Component Analysis*, in "Proceedings of the ECC conference", submitted, Budapest, Hungary.

[64] G. GOFFAUX, A. VANDE WOUWER, O. BERNARD. *Discrete-time interval observers applied to continuous cultures of phytoplankton*, in "Proceedings of the 7th NOLCOS conference", Pretoria, South Africa, 2007.

[65] J.-L. GOUZÉ, T. SARI. *A class of piecewise linear differential equations arising in biological models*, in "Dynamical systems", vol. 17, 2002, p. 299–316.

[66] J.-L. GOUZÉ, M. MOISAN, O. BERNARD. *A simple improvement of interval asymptotic observers for biotechnological processes*, in "Proceedings of the ROCOND 2006 conference", Toulouse, France, 2006.

[67] S. HANSEN, S. HUBBEL. *Single-nutrient microbial competition*, in "Science", vol. 207, n^{o} 28, 1980, p. 1491-1493.

[68] J. HESS, O. BERNARD. *Advanced dynamical risk analysis for monitoring anaerobic digestion process*, in "Proceedings of the 10th CAB conference", Cancun, Mexico, 2007.

[69] J. HESS. *Modélisation de la qualité du biogaz produit par un fermenteur méthanogène et stratégie de régulation en vue de sa valorisation*, Ph. D. Thesis, Université de Nice-Sophia Antipolis, 2007.

[70] A. HÉLIAS, O. BERNARD. *Assessing the main reactions in a bioprocess: application to cheese ripening*, in "Proceedings of the 10th CAB conference", Cancun, Mexico, 2007.

[71] L. MAILLERET, J.-L. GOUZÉ, O. BERNARD. *Nonlinear control for algae growth models in the chemostat*, in "Bioprocess and Biosystem Engineering", vol. 27, 2005, p. 319-328.

[72] L. MAILLERET, F. GROGNARD. *Global stability and optimisation of a general impulsive biological control model*, in "Mathematical Biosciences", submitted.

[73] P. MASCI, O. BERNARD, F. GROGNARD, E. LATRILLE, J.-B. SORBA, J.-P. STEYER. *Driving competition in a complex ecosystem: application to anaerobic digestion*, in "Proceedings of the ECC conference", submitted, Budapest, Hungary.

[74] P. MASCI, F. GROGNARD, O. BERNARD, E. BENOÎT. *Theoretical study of the competition for substrate between N microorganism species in the Droop model*, in preparation.

[75] F. MAZENC, O. BERNARD. *Interval observers for planar systems with complex poles*, in "Proceedings of the ECC conference", submitted, Budapest, Hungary.

[76] M. MOISAN, O. BERNARD, J.-L. GOUZÉ. *Near optimal interval observers bundle for uncertain bioreactors*, in "Proceedings of the 9th European Control Conference, Kos, Greece", 2007.

[77] M. MOISAN, O. BERNARD, J.-L. GOUZÉ. *Robust estimation using direct–reverse time interval observers: Application to an industrial bioreactor*, in "Proceedings of the STIC et Environnement 2007 Conference, Lyon, France", 2007.

[78] M. MOISAN, O. BERNARD. *A direct-reverse time interval observer. Application to biotechnological models*, in "Proceedings of the 7th IFAC Symposium on Nonlinear Control Systems, Pretoria, South Africa", 2007.

[79] M. MOISAN, O. BERNARD. *An interval observer for non-monotone systems: Application to an industrial anaerobic digestion process*, in "Proceedings of the 10th CAB Conference", Cancún, Mexico, 2007.

[80] M. MOISAN. *Synthèse d'observateurs par intervalles pour des systèmes biologiques mal connus*, Ph. D. Thesis, Université de Nice Sophia–Antipolis, 2007.

[81] S. NUNDLOLL, L. MAILLERET, F. GROGNARD. *Impulsive biological control with intra-specific predator competition: global stability and convergence*, in "Mathematical Biosciences and Engineering", in preparation.

[82] S. NUNDLOLL, L. MAILLERET, F. GROGNARD. *Two models of interfering predators in impulsive biological control*, in "Journal of Biological Dynamics", submitted.

[83] D. ROPERS, H. DE JONG, M. PAGE, D. SCHNEIDER, J. GEISELMANN. *Qualitative simulation of the carbon starvation response in Escherichia Coli*, in "Biosystems", vol. 84 (2), 2006.

[84] A. SCIANDRA, L. PAWLOWSKI, O. BERNARD. *A growth model for autotrophic phytoplankton and its validation using chemostat experiments co-limited by light and nitrogen*, in "Ecol. Model.", submitted.

[85] J.-P. STEYER, O. BERNARD, D. BATSTONE, I. ANGELIDAKI. *Lessons learnt from 15 years of ICA in anaerobic digestion processes*, in "Wat. Sci. Tech. ", vol. 53, 2006, p. 25-33.

[86] A. VANDE WOUWER, G. GOFFAUX, O. BERNARD. *Continuous - Discrete Interval Observers Applied to the Monitoring of Cultures of Microalgae*, in "J. Proc. Contr.", In revision, 2008.

[87] H. DE JONG, J.-L. GOUZÉ, C. HERNANDEZ, M. PAGE, T. SARI, J. GEISELMANN. *Qualitative simulation of genetic regulatory networks using piecewise-linear models*, in "Bulletin of Mathematical Biology", vol. 66, n^{o} 2, 2004, p. 301-340.