

2025 Activity Report

RESEARCH CENTRE: Inria Centre at Université Côte d'Azur

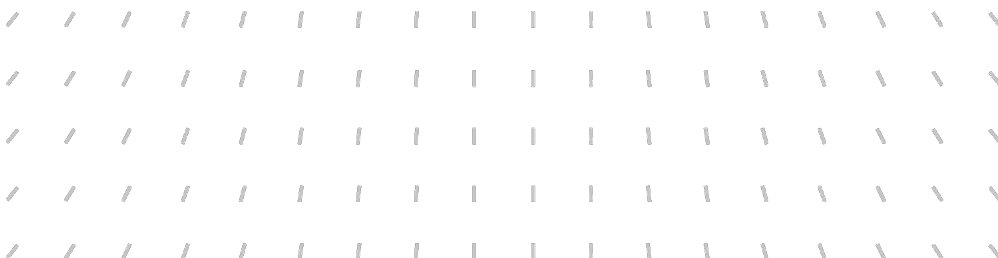
IN PARTNERSHIP WITH: INRAE, CNRS, Université Côte d'Azur

Project-Team

MACBES

Modelling And Control of Biological and Ecological
Systems

In collaboration with Institut Sophia Agrobiotech, Institut de pharmacologie moléculaire
et cellulaire



Project-Team MACBES

Creation of the Project-Team: 2023 July 01

Each year, Inria research teams publish an Activity Report presenting their work and results over the reporting period. These reports follow a common structure, with some optional sections depending on the specific team. They typically begin by outlining the overall objectives and research programme, including the main research themes, goals, and methodological approaches. They also describe the application domains targeted by the team, highlighting the scientific or societal contexts in which their work is situated. The reports then present the highlights of the year, covering major scientific achievements, software developments, or teaching contributions. When relevant, they include sections on software, platforms, and open data, detailing the tools developed and how they are shared. A substantial part is dedicated to new results, where scientific contributions are described in detail, often with subsections specifying participants and associated keywords. Finally, the Activity Report addresses funding, contracts, partnerships, and collaborations at various levels, from industrial agreements to international cooperations. It also covers dissemination and teaching activities, such as participation in scientific events, outreach, and supervision. The document concludes with a presentation of scientific production, including major publications and those produced during the year.

Keywords

Computer sciences and digital sciences

- A6. – Modeling, simulation and control
- A6.1.1. – Continuous Modeling (PDE, ODE)
- A6.1.4. – Multiscale modeling
- A6.2.6. – Optimization
- A6.3.4. – Model reduction
- A6.4.1. – Deterministic control
- A6.4.4. – Stability and Stabilization
- A6.4.6. – Optimal control
- A8.7. – Graph theory
- A8.11. – Game Theory

Other research topics and application domains

- B1.1.2. – Molecular and cellular biology
- B1.1.7. – Bioinformatics
- B1.1.8. – Mathematical biology
- B1.1.10. – Systems and synthetic biology
- B2.4.1. – Pharmacokinetics and dynamics
- B3.1. – Sustainable development
- B3.5. – Agronomy
- B3.6. – Ecology

Contents

Project-Team MACBES	1
1 Team members, visitors, external collaborators	5
2 Overall objectives	6
3 Research program	6
3.1 Network interactions for cell function and growth	7
3.2 Dynamics and control for synthetic biology	7
3.3 Modeling agro-ecological interactions	7
3.4 Design and control of managed ecosystems	7
4 Application domains	8
5 Social and environmental responsibility	8
5.1 Impact of research results	8
6 Highlights of the year	8
6.1 Awards	8
7 New results	9
7.1 Network interactions for cell function and growth	9
7.1.1 Cellular response and cell-to-cell variability	9
7.1.2 Intercellular communication in peripheral clocks	10
7.1.3 Cell economy and control of cell growth	11
7.1.4 Modeling microbial communities	11
7.2 Dynamics and control for synthetic biology	11
7.2.1 Dynamics in networks of cellular oscillators	11
7.2.2 Optimization and optimal control in the cell	12
7.3 Modeling agro-ecological interactions	12
7.3.1 Ecophysiological modeling of plant-microbiota interactions	12
7.3.2 Epidemiological modeling of plant-enemy interactions	13
7.4 Design and control of managed ecosystems	14
7.4.1 Design and control of synthetic microbial ecosystems	14
7.4.2 Design of biological control strategies	14
7.4.3 Sustainable management of plant resistance	14
7.4.4 Behavioral Epidemiology and Evolution of Plant Pathogens	15
8 Partnerships and cooperations	15
8.1 International initiatives	15
8.1.1 Associate Teams in the framework of an Inria International Lab or in the framework of an Inria International Program	15
8.2 National initiatives	15
8.3 Regional initiatives	17
9 Dissemination	17
9.1 Promoting scientific activities	17
9.1.1 Scientific events: organization	17
9.1.2 Scientific events: selection	17
9.1.3 Journal	18
9.1.4 Invited talks	18
9.1.5 Contributed talks	18
9.1.6 Scientific expertise	18
9.1.7 Research administration	19

9.2	Teaching - Supervision - Juries - Educational and pedagogical outreach	19
9.2.1	Teaching	19
9.2.2	Supervision	20
9.2.3	Master theses and Internships	21
9.2.4	Juries	21
9.3	Popularization	21
9.3.1	Specific official responsibilities in science outreach structures	21
9.3.2	Productions (articles, videos, podcasts, serious games, ...)	22
9.3.3	Others science outreach relevant activities	22
10	Scientific production	22
10.1	Major publications	22
10.2	Publications of the year	23
10.3	Cited publications	26

1 Team members, visitors, external collaborators

Research Scientists

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- Valentina Baldazzi [INRAE, Researcher, HDR]
- Madalena Chaves [INRIA, Senior Researcher, HDR]
- Jean-Luc Gouze [INRIA, Senior Researcher, HDR]
- Ludovic Mailleret [INRAE, Senior Researcher, HDR]
- Jérémie Roux [CNRS, Researcher, HDR]
- Suzanne Touzeau [INRAE, Researcher]

Post-Doctoral Fellow

- Marielle Pere [CNRS, Post-Doctoral Fellow, until Oct 2025]

PhD Students

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- Benjamin Böbel [INRIA]
- Marine Courtois [INRAE until Sep 2025 and then UNIV COTE D'AZUR, ATER]
- Timothé Fagart [UNIV COTE D'AZUR, from Nov 2025]
- Javier Innerarity Imizcoz [UNIV COTE D'AZUR]
- Aurelien Kambeu Youmbi [UNIV DSCHANG CAMEROON]
- Frank Kemayou Mangwa [UNIV DOUALA, CAMEROON]
- Armando Borel Kenne Meli [École Nationale Supérieure Polytechnique, YAOUNDÉ, CAMEROON]
- Pauline Mazel [UNIV COTE D'AZUR]
- Joseph Junior Penlap Tamagoua [INRIA until Aug 2025 and then UNIV COTE D'AZUR, ATER]

Technical Staff

- Kelian Bonhomme [INRIA, Engineer, from Feb 2025 until Aug 2025]

Interns and Apprentices

- Timothé Fagart [UNIV COTE D'AZUR, Intern, from Apr 2025 until Sep 2025]
- Ainatiana Loyens [INRIA, Intern, until Jun 2025]

Administrative Assistant

- Maeva Jeannot [INRIA]

Visiting Scientist

- Pierre Bernhard [INRIA]

External Collaborators

- Odile Burckard [INRAE, until Nov 2025]
- Vincent Calcagno [INRAE, HDR]
- Frédéric Hamelin [INSTITUT AGRO RENNES-ANGERS]
- Louise Van Oudenhove De Saint Gery [INRAE]

2 Overall objectives

Understanding and controlling dynamics are at the core of major challenges in biology and ecology central to human and environmental health. With the increasing availability of experimental data time-series in these fields and better comprehension of the fundamental biological mechanisms, building models is required to fully grasp these dynamics. The objective of MACBES is to apply and develop methodologies of control theory and computational biology to specific applications in biology and ecology: the ecologically friendly protection and management of ecosystems, such as agroecosystems, and the characterization and deciphering of mammalian cell responses to their environment, in particular the effect of network interactions and developments in synthetic biology. MACBES has privileged access to biological data generated by the partners within the Common Project Team which allows for the development of the most relevant models related to its applications.

Control theory provides answers to questions related to identify parameters, reconstruct non-measured quantities of interest, regulate and control the system towards a desired state and optimize the yield of a given product. In computational biology, the tools of theoretical ecology and evolutionary biology provide answers on what a system will become.

The development of dynamical models representing mechanisms and interactions within our systems of interest is a first step in our approach. We develop models built in continuous ordinary differential equations, impulsive models, discrete models, or hybrid models, to better represent the variety of biological processes. In their diversity, these models are often built on representations of simplified biological processes, which yield systems that have particular structures that can be exploited: their variables are positive, some interactions can be modeled as mass transfers, they can be monotonic, . . . Such models allow for analytical and numerical developments that help explaining the dynamics and the functioning of biological processes. These models are the cornerstones on which we can apply the comprehensive toolbox of control theory.

The link of our models to data depends on the context. On the one hand, we are at a turning point where the availability of “omics” and cell level data exceeds our capacity of interpretation, while on the other hand it may still be difficult to obtain reliable and useful data time-series to understand ecosystem dynamics, though that could soon change too with the development, reliability and increasing affordability of remote sensing data through drones. Therefore, apprehending the complexity of these processes and interactions through this abundance of data or despite data scarcity, requires the construction of specific mathematical models with specific calibration approaches, that face the large uncertainties and variability that are intrinsic to biological systems. In addition, to limit the impact of uncertainties and calibration errors on our results, we also develop models and control theoretic approaches relying on qualitatively described functions, through which generic answers can be sought that are valid over a wide range of situations and parameter values.

MACBES is a common project-team between Inria, INRAE, CNRS and Université Côte d’Azur, associating researchers of Inria d’Université Côte d’Azur, Institut Sophia Agrobiotech (ISA - UMR INRAE CNRS and Université Côte d’Azur, Models and Methods for Plant Protection team), and Institut de Pharmacologie Moléculaire et Cellulaire (IPMC - UMR CNRS and Université Côte d’Azur). MACBES was created on July 1st, 2023 and is one of the two project-teams following the Biocore project-team.

3 Research program

The research program is organized around four axes involving common tools from control theory and computational biology, with models built using continuous ordinary differential equations, impulsive models, discrete models, or hybrid models. Control theory provides answers to questions related to the need to

identify parameters, reconstruct non-measured quantities of interest, regulate and control the system towards a desired state and optimize the yield of a given product. In computational biology, we use the tools of theoretical ecology and evolutionary biology to provide answers on what a system will become. The four main research axes of MACBES are detailed in the following.

3.1 Network interactions for cell function and growth

Cells have evolved highly sophisticated intracellular communication pathways to enable their development and growth, under multiple environmental stresses and stimuli (growth factors, hormones, different types of drugs, temperature or light changes, etc.). In a modular view of a biological organism, each task is executed by a specific network, or module. These modules often interact with each other, one task triggering the next in a chain of events or cyclic phenomena: cascades of signaling networks, genetic-metabolic interactions, oscillatory behavior. One of the greatest challenges at the interface between biology and mathematics is to decipher and reproduce the complex behavior arising from the interconnection of two or more modules. The ability to reproduce the complexity of cellular responses will lead to a better capacity for regulation and balancing of factors towards healthy behaviors.

3.2 Dynamics and control for synthetic biology

Synthetic biology aims at joining elements from both biology and engineering to construct cellular circuits that perform a desired function or induce a particular type of response. It is also a complementary approach to (traditional) molecular biology: newly creating and assembling synthetic cellular circuits from basic biological components (such as DNA, proteins, or metabolites) to form a “whole organism”, serves as a proof of principle towards understanding the mechanisms of biological networks. One of the main bottlenecks in synthetic biology is how to integrate the new circuit into the cell’s machinery, without upsetting the cellular resource allocation balance. To tackle this problem, understanding resource allocation in the cell and the interconnection of cellular oscillators is a crucial challenge.

3.3 Modeling agro-ecological interactions

Plants are involved in a wide range of biotic interactions. Some are beneficial to plant health, as for pollinators or symbiotic organisms, whereas others are detrimental, as in the case of pathogens or herbivores. The dynamics and outcome of these interactions depend on the ecological conditions, including the phenotypes of the interacting species, their physiology and the abiotic environment in which the interactions take place. Our aim is to develop models relevant to several biotic interactions involving plants and other organisms, from the ecophysiological scale and the intimate interaction between plants and their partners, to the ecological interactions between populations and communities inhabiting crop fields.

3.4 Design and control of managed ecosystems

In several contexts, such as bioreactors in industry or cropping systems in agriculture, it might be desirable to create an ecosystem that does not exist as is in nature. Putting together species that have mutualistic behaviors, whose synergy allows for the production of some desired output, or that protect one another, can enhance the functioning of the resulting ecosystem. Without fully designing an ecosystem from scratch, it might also be necessary to take control actions to improve the functioning of an existing ecosystem or to restore a degraded ecosystem to a previous, desirable, state. The exploitation of natural or synthetic microbial communities for the accomplishment of processes of interest is being pursued in a vast range of scenarios, from established applications in the biotechnology and pharmaceutical industries, to innovative applications in medicine and environmental sciences. Larger scale managed ecosystems can simply be natural ecosystems into which one wants to re-introduce or maintain endangered species, but they can also be exploited ecosystems such as forests, agricultural fields, fish farms. . . A special focus is put in MACBES on the development of pest/pathogen control methods in agroecosystems.

4 Application domains

As highlighted in the research program, in MACBES, we tackle real-life problems and contemporary challenges with respect to safe food, food security, human and environmental health. We develop mathematical techniques to characterize and decipher cell responses to their environment in research axes 3.1 and 3.2, and we deal with ecologically friendly methods for the protection and management of ecosystems, in particular of agroecosystems, in research axes 3.3 and 3.4.

5 Social and environmental responsibility

5.1 Impact of research results

The application of MACBES research for the development of ecologically friendly methods for crop protection aim at sustainable agroecosystems. Central to our work is the reduction of chemical pesticide usage, whose deleterious impact on health and the environment is well-documented. The applications concerning cell dynamics may impact the development of new anti-cancer drugs and in general aim at a better understanding of mechanisms affecting human health.

6 Highlights of the year

The role of sequestration mechanisms in circadian clocks. A sequestration mechanism can be described as a mutual repression or inactivation between two molecular species: the two molecules bind each other and the activity of both is repressed. This mechanism forms the basis of a negative feedback loop at the core of peripheral circadian clocks. We have studied a clock model and shown that the sequestration mechanism is responsible for a strong robustness of the oscillatory dynamics by: (i) maintaining the oscillations at a similar period for a large region of parameters and (ii) generating a phase response curve with only a short time window where interactions with another signal are possible, thus restricting the response to undesired signals. This work appeared in a special issue at *Interface Focus* [2].

Transition between cell states of drug-sensitivity. Through a set of experiments, Roux's lab explored the response of cells to a sequence of treatments with different death drugs. These experiments showed that cells which are tolerant relative to an apoptosis drug have increased vulnerability to necroptosis, another form of cell death. To complement experimental work, we developed a compartmental model explaining the emergence of drug-tolerant cell populations, and the fluxes between drug-sensitivity states. We found that drug-sensitivity states coexist in a clonal population of cancer cells with continuous transitions between them, which are sufficient to explain both the sustained resistance to repeated treatments and how alternating drug treatments ameliorates the overall treatment efficacy. This work appeared in the journal *Molecular Systems Biology* [10].

Control instead of eradication through the sterile insect technique. The sterile insect technique traditionally aims at eradicating crop pest populations through massive sterile pest male releases that disrupt the pest reproduction. In reality, a small fraction of released males escape sterilization and remain fertile. In this work, we showed that when residual fertility is below a threshold value, wild populations can be driven to extinction by flooding the landscape with sterile males. Nevertheless, we also showed that, to the contrary to what is usually advocated, all is not lost when residual fertility exceeds this threshold: pests are not eradicated but can be brought to a sufficiently low level where crop damage are curtailed [15].

6.1 Awards

Odile Burckard won the PhD Thesis Prize for the speciality Automatique, Traitement du Signal et des Images (ATSI) from the Doctoral School on Sciences and Technology for Communication and Information (EDSTIC, Univ. Côte d'Azur), for her work on "Mathematical analysis of cycle dynamics and synchronization of mammalian peripheral circadian clocks", defended in November 2024.

Aurelien Kambeu Youmbi won the best poster award at the Conference on Models in Population Dynamics, Ecology, and Evolution (MPDEE) in Bilbao for his work on bioeconomic modeling and control of the diamondback moth in cabbage crops [41].

7 New results

7.1 Network interactions for cell function and growth

Participants: Odile Burckard, Benjamin Böbel, Madalena Chaves, Giada Fiandaca, Marielle Péré, Kelian Bonhomme, Jérémie Roux, Jean-Luc Gouzé, Valentina Baldazzi, Pauline Mazel, Frédéric Grognard.

7.1.1 Cellular response and cell-to-cell variability

Transition between cell states of drug-sensitivity. Persister cells can be described as cells which are tolerant to a pro-apoptotic treatment with a given death drug. Through a set of experiments with different death drugs, Roux's lab explored the response of persister cells to subsequent treatments with a different drug from the one they originate from. These experiments showed that persister cells relative to apoptosis have increased vulnerability to necroptosis, another form of cell death. To better understand these transitions between states of vulnerability to cell death, we developed a compartmental model explaining the emergence of drug-tolerant cell populations, and the fluxes between drug-sensitivity states. We found that drug-sensitivity states coexist in a clonal population of cancer cells with continuous transitions between them, which are sufficient to explain both the sustained resistance to repeated treatments and how alternating drug treatments ameliorates the overall treatment efficacy. This work was part of Marielle Péré post-doc and appeared in the journal *Molecular Systems Biology* [20].

Cell response through the apoptotic pathway. To analyze the considerable amount of data from fate-seq [57], we proposed an ODE model of the molecular pathways involved in cell death triggered by Tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL). This model reproduces the trajectories along time of the apoptosis signaling dynamics, in particular the amount of active caspase-8 protein. To calibrate the model, we use single-cell time-trajectories from clonal HeLa cells [58], where the concentration of active caspase-8 is monitored by a Förster resonance energy transfer (FRET) reporter.

Based on this model and using the method previously developed in [3], we successively identified several new elements that play a role in caspase-8 apoptosis signaling. First, two mathematical factors to better reproduce the signaling kinetics include the saturated form of caspase degradation (as opposed to linear degradation) and the interaction between TRAIL and its receptors, where the latter appear according to a cooperative (sigmoidal) form. Second, a new component (protein Flip) should be included in the model, by its capacity to modulate the model's signaling response. Flip has both an anti-apoptotic role by competing with pre-caspase-8 at death-inducing signaling complex (DISC) level, and also a pro-apoptotic role since the complex composed of TRAIL, its receptor, Flip and two pre-caspase-8 molecules contribute to caspase-8 activation. These results were presented by Giada Fiandaca at the conference on "Model design, optimization & control" at Université Côte d'Azur, October 13-17.

An hyperplane partitions the state space into apoptotic and tolerant regions. Following the work described in the previous paragraph, in a third step, we identified three major parameters which define a dose-dependent hyperplane that partitions the state space into apoptotic and tolerant regions. Increasing drug dose translates this separating surface, thus increasing the apoptotic region and altering the outcome only for cells positioned near the boundary, from tolerant to apoptotic. This geometric perspective explains fractional killing in clonal populations and shows how drug-tolerant persister cells can arise from reversible variation in cell state. It further suggests that shifting state-space distributions relative to the decision surface may offer new strategies to limit persistence. These results were presented by Giada Fiandaca at the conference on "Model design, optimization & control" at Université Côte d'Azur, October 13-17, and have been submitted to a journal.

Analysis of RNAseq data to recover cell signatures. Through the fate-seq methodology developed in [57] by Jérémie Roux lab, larges sets of RNAseq data are available, on different cell lines (HeLa, PANC, and others), in response to treatment with anti-cancer drugs. These data were analyzed to recover cell signatures consisting of the groups of genes that are differentially expressed after treatment, relative to non treated cells. This analysis identified some pathways that become systematically active in response to the drugs, in particular the NF κ B pathway in PANC cells. This pathway is also implicated in the regulation of the protein Flip, one of the major components in the apoptosis model described above, and suggests new directions for model development. This work was performed by Kelian Bonhomme in the context of project Cellema and is a starting point for his PhD thesis.

Optimization and optimal control of cancer treatment. This research line addresses the optimal control of acute myeloid leukemia, with the objective of limiting cancer progression while reducing the side effects of chemotherapy. A new collaboration has been initiated on this topic with the Stiehl group at RWTH Aachen (Germany). The approach relies on a dynamical system describing the evolution of healthy and leukemic cell populations, structured into stem and post-mitotic compartments, building on earlier work by T. Stiehl. A dynamical systems analysis reveals a regime in which constant treatments generate a continuum of equilibria, around which optimal control solutions exhibit a turnpike structure corresponding to efficient long-term regulation of leukemic cells. A global sensitivity analysis with respect to the optimization criterion identifies the main biological mechanisms influencing therapy outcomes. This work constitutes the core of the PhD thesis of Pauline Mazel, co-supervised by Walid Djema (GREENOWL), and is currently under review in Bulletin of Mathematical Biology [56].

7.1.2 Intercellular communication in peripheral clocks

Coupling of peripheral clocks. The intercellular interactions between peripheral circadian clocks, located in tissues and organs other than the suprachiasmatic nuclei of the hypothalamus, are still very poorly understood. To investigate this question, we performed a theoretical and computational study of the coupling between two or more clocks, using a reduced model of the mammalian circadian clock previously developed in [50]. Based on a piecewise linearization of the dynamics of the mutual CLOCK:BMAL1 / PER:CRY inactivation term, we proposed a segmentation of the circadian cycle into six stages, to help analyze different types of synchronization between two clocks, including single stage duration, total period, and maximal amplitudes. Our model reproduces some recent experimental results on the effects of different regimes of fasting/feeding alternance in liver circadian clocks of mice [52]. Through the analytical study of the above piecewise linear model of the clock, we proposed an algorithm to generate biologically-consistent circadian oscillators. Our study provides a characterization of the cycle dynamics in terms of four fundamental threshold parameters and one scaling parameter, as it recapitulates the main observations from the literature. Moreover, our analysis shows robustness of the circadian system and its period, and identifies critical points for correct cycle progression [12]. This work is in collaboration with F. Delaunay (ANR InSync), and was part of Odile Burckard's' PhD thesis (defended in November 2024, EDSTIC prize, see Section 6.1).

Characterization of circadian cycles. A large variety of mathematical models have been developed to study the dynamics and quantitative properties of the circadian oscillator and better understand circadian clock mechanisms. To better analyze and compare quantitatively all these circadian cycles, we developed a method based on a previously proposed circadian cycle segmentation into stages [52]. We notably identified a sequence of eight stages that characterize the progress of the circadian cycle. To distinguish these stages in a given cycle, our method requires only a set of three time series for three main clock proteins (CLOCK:BMAL1, PER:CRY, REV-ERB), either from an experimental dataset or obtained numerically from a mathematical model. Our method permits to assess the agreement of mathematical model cycles with biological properties or to detect possible inconsistencies. The strength of our method is to provide a benchmark for characterization, comparison and improvement of new mathematical models of circadian oscillators in a wide variety of model systems [13]. This work is in collaboration with F. Delaunay (ANR InSync), and was part of Odile Burckard's' PhD thesis.

Trends in the shared period of two coupled oscillators. The coupling of two similar biological oscillators has been often studied to answer questions regarding their modes of interaction and synchronization. However,

one question which is still rarely approached concerns the relationship between the free-running periods of each system and the final period of the whole coupled system. Fixing a context for the coupling, we performed a systematic numerical and analytical study and characterized the final period in terms of the free-running periods, for different classes of oscillators (Kuramoto, relaxation oscillators, and peripheral circadian clocks). The case of synchronization of Kuramoto oscillators through a mean-triggered global event will be presented at the conference on Dynamical Systems Applied to Biology and Natural Sciences (DSABNS 2026, Granada, Spain). This is part of Benjamin Böbel PhD thesis.

7.1.3 Cell economy and control of cell growth

Two macroscopic criteria for characterizing microbial growth are growth rate and growth yield. The former refers to the rate of conversion of a substrate into biomass, and the latter to the efficiency of the process, that is, the fraction of substrate taken up by the cells that is converted into biomass. In a previous work, we developed a coarse-grained model of microbial growth and used it to explore the variability of rate-yield phenotypes obtained by change in proteome allocation strategy [51]. Numerical analysis showed that the mapping from allocation parameters to rate and yield phenotype is generally not biunivocal. Outside the Pareto frontier, connecting the maximum yield and the maximum growth rate points, the same rate-yield phenotype can be attained for very different underlying allocations, corresponding to a distinct functioning of the cell. In collaboration with H. de Jong (MICROSCOSME team) and T. Gedeon (University of Montana), we mathematically explained this observation under very general assumptions and collected experimental data on growth rate, growth yield, and glycogen storage in *E. coli* to support our conclusions. An article is currently in preparation on this topic.

7.1.4 Modeling microbial communities

Microbial communities are ubiquitous in life. Advances in sequencing and measuring technologies have enabled the collection of multi-omics data, including metagenomics, metabolomics and metatranscriptomic data. In collaboration with the Inria team PLEIADE (Bordeaux), the PhD thesis of Sthyve Tatho aims to develop a mathematical model of microbial community capable of integrating these time series of multi-omics data at a community scale. Called cMFA, the method aims to (i) quantify the individual contribution of each member of the community to overall system dynamics, based on external measurements of metabolite dynamics, and (ii) infer its intracellular distribution of metabolic fluxes. The approach was first evaluated using a set of synthetic benchmarks, proving able to cope with increasing data noise level, incomplete metatranscriptomic data and large community sizes. cMFA was then applied to experimental data of real microbial communities involved in cheese fermentation [54] and soil denitrification [53]. The results showed excellent reconstruction of exchange fluxes and good agreement with metatranscriptomic data. This work has been presented at several national and international conferences [28, 48, 43, 44, 45, 47]. An article is currently under preparation.

7.2 Dynamics and control for synthetic biology

Participants: Benjamin Böbel, Timothé Fagart, Madalena Chaves, Javier Innerarity Imizcoz, Jean-Luc Gouzé.

7.2.1 Dynamics in networks of cellular oscillators

Phase response curves to characterize oscillator coupling. One of the features of the mammalian circadian clock (also present in the model of [50]) is a “sequestration mechanism” which consists of the mutual inhibition of two protein complexes, by their binding to each other. While bound, the activities of both complexes are repressed. We show that this sequestration repression mechanism plays a fundamental role in the dynamics of the circadian clock. By analyzing a reduced piecewise affine model derived from [50] and a simplification associated to the sequestration mechanism, we first prove the existence of a periodic trajectory and then construct the phase response curve (PRC) for this reduced system. The PRC exhibits a short time window where interactions with another signal are possible. The form of the PRC can thus be used to

understand the effective interaction between several coupled oscillators and the robustness of synchronization in a coupled network of oscillators. This work is part of Benjamin Böbel PhD thesis, appeared in a special issue at *Interface Focus* [11] and was presented at CMSB25 [40].

Modeling 12 hour biological oscillators. Biological rhythms with a period of 12 hours have very recently been identified in the liver of mice. Very little is known about these 12 hour rhythmic processes, but a negative feedback loop circuit involving protein XBP1 appears to be at the core of the oscillator. We have constructed a first mathematical model of the XBP1 circuit, based on a combination of the Goodwin oscillator with a positive feedback loop due to the splicing (a shortening of the messenger RNA) of protein XBP1. The model was analyzed in a piecewise affine framework using the theory of Glass and Pasternak to conclude on the existence of periodic solutions. This theory can be extended to the case of distinct degradation rates for each variable as well as distinct rates within each domain of the state space. This work is in collaboration with F. Delaunay (through the Idex-Académie 4 OSCILLA12 project), it was the internship topic of Timothé Fagart and the starting point of his PhD thesis research.

7.2.2 Optimization and optimal control in the cell

Optimal allocation of resources in bacteria. Using optimal control techniques, we study the optimal allocation between metabolism and gene expression during bacteria growth, in collaboration with Inria Microcosme and MCTAO project-teams. We developed different versions of the problem, and considered problems where the aim is to optimize the production of a product in a batch or fedbatch bioreactor; the input of substrate may also be fluctuating (e.g. periodic) or controlled [24]. This work is part of the ongoing PhD work of Javier Innerarity Imizcoz, in collaboration with W. Djema (GREENOWL) and F. Mairet (IFREMER Nantes). Moreover, in collaboration with A. Yabo (INRAE Montpellier), we studied with optimal control techniques the new resource repartition of a cell reacting to a thermal stress by producing chaperones, for refolding damaged proteins [39, 34].

7.3 Modeling agro-ecological interactions

Participants: Valentina Baldazzi, Frédéric Grognard, Suzanne Touzeau, Ludovic Mailleret, Aurelien Kambou Youmbi, Frank Kemayou Mangwa, Joseph Junior Penlap Tamagoua, Armando Borel Kenne Meli, Ainatiana Loyens, Jean-Luc Gouzé.

7.3.1 Ecophysiological modeling of plant-microbiota interactions

Plant-RKN interactions. Root-knot nematodes (RKN) are microscopic root parasites that cause considerable yield losses in numerous crops worldwide. We are particularly interested in understanding the mechanisms that underlie plant tolerance, that is the ability of certain plants to sustain RKN infestation with limited damages. To address this, we built an ecophysiological model of plant growth coupled with a model of nematode population dynamics. The model was calibrated for two plant species with contrasted RKN susceptibility, using experimental data produced at INRAE [35].

Our results showed that tolerance does not depend on a single factor but can arise through multiple physiological pathways. Among the traits contributing to tolerance, fruit dynamics emerge as a particularly influential factor, suggesting that plants with early reproductive traits could be advantageous in managing RKN parasitism.

In order to get a better grip on the system dynamics, a reduced version of the plant-nematode model was developed, which admits three equilibria: a trivial extinction equilibrium, a pest-free equilibrium, and a coexistence equilibrium which corresponds to a tolerant plant.

A stability analysis was performed. Moreover, numerical explorations highlighted the major and dual role of resource production on tolerance: high production rates not only boost plant growth but also enhance

nematode proliferation. By highlighting the balance between plant growth resource allocation and parasitic pressure, this work sheds light on the mechanisms underlying plant tolerance [37].

This work is part of the PhD thesis of Joseph Junior Penlap Tamagoua.

Plant-microbial community interactions. In natural soils, plants interact with a remarkable diversity of micro-organisms. The excretion of inorganic and organic molecules from living roots is thought to influence the structure of microbial communities, providing substrates and signals for specific classes of bacteria. However, how the plant selects and control its investment into exudation has not been elucidated so far.

In order to answer this question, we developed a minimal model of the interaction between a plant and two bacterial guilds, with each guild providing an essential resource to the plant. In turn, the plant can influence microbial growth by allocating some of its resources to guild-specific root exudates. Preliminary numerical analysis showed that an effective plant exudation strategy depends on both microbial traits and environmental conditions (e.g. external fertilization). Next steps include the analytical study of the system and application of classical control and optimal control methodologies to investigate exudation strategies that optimize plant growth under contrasting environmental conditions.

7.3.2 Epidemiological modeling of plant-enemy interactions

Semi-discrete models. Semi-discrete models have shown their relevance in modeling biological phenomena whose nature presents abrupt changes over time [55]. In plant epidemiology, they can represent seasonality or external perturbations of natural systems, such as harvest. We developed and analyzed such models in the context of biological control applied to cabbage diamondback moth [41] or banana burrowing nematodes [25], and of the sterile insect technique in Marine Courtois's PhD thesis. They are exploited in Arindam Mandal's post-doc at ISA for the development of models representing yearly choices by the growers between clean seeds and farmer seeds in a seasonal environment. They also were at the core of Ainatiana Loyens's internship in which he evaluated the interference between different crop protection methods, including one with instantaneous mortality events that were modeled through semi-discrete systems.

Epidemiological models in tropical agriculture. We developed and analyzed dynamical systems describing plant-parasite interactions, in order to better understand, predict and control the evolution of damage in crops, with applications in tropical agriculture, in the framework of the EPITAG associate team with Cameroon (section 8.1.1).

- Cabbage is a very important food crop for small farmers in Cameroon. We developed a model of self-financing of the crop, which includes the interaction between cabbage and the diamondback moth, one of its major pest. The main point of this model is the inclusion of the financial balance of the farm, used for buying young plants and biopesticide spraying. We extended this model to represent biological control deployment by considering a parasitoid presenting mutual interference. We studied and compared different release strategies: initial, continuous or discrete releases [41]. This work is part of Aurelien Kambeu Youmbi's ongoing PhD thesis.
- Bananas are major staple foods in many tropical countries. These plants are affected by burrowing nematodes (*Radopholus similis*) that create root lesions and induce great damages. We developed a model of plant-pest interactions with the original feature that infestation intensity may vary within the root. We did a bifurcation analysis and solved an optimal control against the pest, consisting in maximizing profit thanks to the application of biostimulants. The optimal control obtained is pseudo-periodic, suggesting that overyielding occurs [36]. We extended the model to a multiseasonal context, combining continuous dynamics, which describe the growth and interactions between host and pest during a cropping season, with periodic discrete jumps, corresponding to harvest and replanting. We analyzed the model and determined the stability of the pest-free periodic solution. We then studied optimal control strategies [25]. This work is part of Frank Kemayou Mangwa's ongoing PhD thesis.
- Cassava is another major staple food in many African countries. It is affected by African cassava mosaic disease, which is a viral disease whose vector is the white fly. We are developing and analyzing an epidemiological model representing these dynamics [42]. This work is part of Armando Borel Kenne Meli's ongoing PhD thesis.

Impact of predation risk on optimal foraging. In this work, we built on our re-analysis of the Marginal Value Theorem (MVT) to study the effect of predation risk on the optimal foraging strategy, thereby building a risk-MVT. This risk-MVT is at the intersection between Charnov’s MVT and Brown’s giving-up density (GUD) theory. It can incorporate most types of predation risks, from mere disturbance situations to death of the forager. It gives contrasting answers depending on the type of risk, but always tends to predict that individuals should be bolder in riskier environments [14].

7.4 Design and control of managed ecosystems

Participants: Jean-Luc Gouzé, Frédéric Grogard, Suzanne Touzeau, Ludovic Mailleret, Marine Courtois, Aurelien Kambeu Youmbi, Frank Kemayou Mangwa, Armando Borel Kenne Meli, Joseph Junior Penlap Tamagoua.

7.4.1 Design and control of synthetic microbial ecosystems

In the framework of ANR project Ctrl-AB, we considered a synthetic algal-bacterial consortium. The co-culture of *E. coli* with *Chlorella* could lead to higher biomass and lipid productivity. We studied the effects of control on the system in the framework of optimization or optimal control [23] (PhD thesis of Rand Asswad, Grenoble, in collaboration with E. Cinquemani (MICROCOSME) as well as O. Bernard and W. Djema (GREENOWL)).

In collaboration with W. Djema (GREENOWL) and T. Bayen (Univ. Avignon), we also worked on species selection in competition for two substitutable substrates. Using control and optimal control techniques, we studied the maximization of cell growth rate for a generic model [16].

7.4.2 Design of biological control strategies

Sterile insect technique. The sterile insect technique (SIT) consists in releasing irradiated sterile individuals, usually males, that can mate but produce no offspring. SIT is used to reduce pest populations in an agricultural context. However, a small fraction of irradiated insects may escape sterilization and remain fertile. We showed that when residual fertility is below a threshold value, wild populations can be driven to extinction by flooding the landscape with sterile males. Nevertheless, even if the residual fertility exceeds the aforementioned threshold value, substantial decreases in outbreak levels can be achieved [15]. We extended these results to take remating into account through both a continuous dynamics formalism and an agent based model, showing the importance of reproductive mechanisms in shaping the efficiency of SIT control strategies [49, 21, 33]. Finally, the impact and optimization of discrete-time impulsive sterile male releases was considered in Marine Courtois’s PhD manuscript. This work pertains to Marine Courtois’s defended PhD thesis.

Optimal control for tropical agriculture. Controlling tropical pests is particularly challenging, as their dynamics are often explosive in tropical environments. Optimal control is relevant to counter this spread; hence we made use of this tool burrowing nematodes, as described in section 7.3.2.

7.4.3 Sustainable management of plant resistance

We studied other plant protection methods dedicated to fight plant pathogens. One such method is the introduction of plant cultivars that are resistant to one pathogen. This often leads to the appearance of virulent pathogen strains that are capable of infecting the resistant plants.

We built a generic spatio-temporal epidemiological model representing (fungal) disease spread on annual field crops in a multi-pathogen context. This work benefits from data collected at INRAE and is being pursued in the ENDURANCE and PAPEETE projects (see section 8.2).

Also, applying such an approach to efficiently protect cassava against African cassava mosaic disease is part of Armando Borel Kenne Meli’s PhD thesis.

7.4.4 Behavioral Epidemiology and Evolution of Plant Pathogens

In this work, we aimed at better understanding the interaction between human behavior and plant epidemiology. Our work on this topic started with the consideration of clean seed systems, and the evolution of their use at landscape scale in a seasonal context. We considered that growers could choose between clean seeds and farmer seeds at the beginning of each cropping season, with clean seeds devoid of disease and farmer seeds carrying some disease depending on the epidemiological status of the crop the year before. We supposed that this choice was made following imitation dynamics, the proportion of growers adopting clean seeds depending on this proportion and on the disease prevalence the year before. We found the counterintuitive situation where the usage of more resistant strains resulted in a reduced usage of clean seeds and so in a more important disease impact. We then considered that commercial clean seeds could contain a small percentage of infected seeds and evaluated what impact this could have on the resulting behavioral strategies. This work is performed in Arindam Mandal's post-doctoral stay at ISA within the BEEP project.

8 Partnerships and cooperations

8.1 International initiatives

8.1.1 Associate Teams in the framework of an Inria International Lab or in the framework of an Inria International Program

Participants: Suzanne Touzeau, Frédéric Grogard, Ludovic Mailleret, Jean-Luc Gouzé, Aurelien Kambeu Youmbi, Frank Kemayou Mangwa, Armando Borel Kenne Meli.

EPITAG2

Title: Epidemiological Modeling and Control for Tropical Agriculture

Duration: 2025-2027

Coordinator: Samuel Bowong (sbowong@gmail.com)

Partners:

- University of Douala (Cameroon)

Inria contact: Suzanne Touzeau

Summary: Crop pests and pathogens are responsible for considerable yield losses and represent a threat to food security. Their control is hence a major issue, especially in Cameroon, where agriculture is an important sector in terms of revenues and employment. Furthermore, to limit the harmful effects of chemical pesticides on the environment and health, friendlier alternatives should be preferred. The main objective of EPITAG is to study the epidemiology and sustainable management of tropical crop diseases and pests, mathematically and numerically, with a focus on major food and cash crops in Cameroon. Using tools from dynamical systems and control theory, its approach consists in developing and analyzing models describing plant-parasite interactions, in order to better understand, predict and control the damages in crops. To tackle these issues, master and PhD students are jointly supervised.

8.2 National initiatives

- **ANR Ctrl-AB:** The objectives of the Ctrl-AB project (2021-2025) are (i) to develop new control methods for the optimization of the productivity of a microbial community, and (ii) to demonstrate the effectiveness of these methods on a synthetic algal-bacterial consortium. This project is now coordinated by Eugenio Cinquemani, Microcosme Grenoble.

- **ANR - InSync:** “Circadian clock synchronization in hepatocytes” (2022-2027). This project aims to decipher intercellular synchronization mechanisms responsible for robust rhythms in peripheral clocks. Focusing on hepatocytes, and using both 2D cultures and 3D spheroids, we study cell communication patterns and cell clock synchronization. Project coordinated by Madalena Chaves.
- **ANR - SuzuKIISS:ME** “Gérer *Drosophila* SuzuKII grâce aux Insectes Super Stériles : Maturation et Efficacité” (2022-2025). This project covers the ground from the development of the operational capacity and release strategies to deploy Sterile Insect Techniques (SIT), to the socio-economic impact of SIT on the control of the fruit fly *Drosophila Suzukii*.
- **ANR - BEEP:** “Behavioural Epidemiology and Evolution of Plant Pathogens” (2024-2028). This project is the first to couple behavioral dynamics and pathogen evolution in plant health, aiming at identifying where the interplay between growers’ behavior and pathogen epidemiological and evolutionary dynamics leads. This project is coordinated by Frédéric Hamelin.
- **ANR - ENDURANCE:** “ENhanced DURability AgaiNst Crop Enemies” (2024-2028). This projects aims at giving elements of answers on how to use and deploy pathogen resistances in crops in order to prevent rapid pathogen adaptation. It will study the genetic determinism(s) of resistance breakdown (the so-called virulence in the phytopathology literature), the evolution over time of the virulence allele(s) in pathogen populations and integrate this information into relevant epidemiological models.
- **EcoPhyto - PAPEETE:** “Promouvoir l’Agroécologie par la prédiction intégrative du risque sanitaire à partir de données Participatives d’Épidémiosurveillance à l’Échelle du Territoire” (2024-2027). This project aims at using epidemiosurveillance data to reduce the intensive use of agrochemicals. It will assess health, production and economic risks to help farmers in their decision-making. By focusing on wheat diseases in an intensive agricultural zone and by involving players from the farming world, the tool developed in the project will constitute a proof of concept that can be generalized to other crops and regions.
- **EcoPhyto - CACOLAC:** “Conceptual framework for analyzing combinations of agroecological levers” (2024-2027). The models developed in this project will provide a better understanding of the impact of management measures on the local and landscape dynamics of pests and diseases. These results will complement previous scientific work by better representing the effects of levers, taking into account the landscape dimension of practices and/or the multitude of direct and indirect interactions in communities.
- **PEPR Agroécologie et Numérique - MISTIC** “Microbiomes de plantes cultivées et TIC” (2023-2028). The objective of MACBES within this flagship project of the PEPR is to model and analyze plant microbial communities and their functioning, as well as to design minimal microbial communities guaranteeing maintained functions.
- **ITMO Cancer Aviesan - Cellema:** The objective of this project (2022-2025) is to determine the molecular factors that regulate tumor cell response dynamics to immune cell cytotoxicity and contribute to the development of diagnosis tools for the rational design of cancer combination therapies. We use single-cell response data to develop mathematical models and combine them with machine learning algorithms to enhance prediction of same-cell responses. Project coordinated by Madalena Chaves, in collaboration with Jérémie Roux and D. Oyarzun (Univ. Edinburgh).
- **SIGNALIFE:** Our team was part of this Labex (scientific cluster of excellence, 2nd period 2020-2024) whose objective was to build a network for innovation on Signal Transduction Pathways in life Sciences, and is hosted by Université Côte d’Azur. The Labex SIGNALIFE is funding the Innovation Program Young Entrepreneur Program (YEP) coordinated by Jérémie Roux, entitled “Combination Target Discovery in Oncology Drug Development: Accelerating Precision Treatment for immunotherapies, using Predictive Single-cell Pharmacodynamics” (2022-2025).
- **PSI DYNABIO** Our team is part of this Initiative of Excellence Structural Program on “Dynamics in networks of biomolecules” (2025-). This program is a follow-up to Labex Signalife (see above) and joins most of the science laboratories at Université Côte d’Azur with the objective of giving rise

to new emerging projects on the regulation and interaction mechanisms of biological molecules, by developing new approaches at the interface of biology, computer science, mathematics, chemistry, and physics. DYNABIO funds medium-term positions and PhD fellowships on these topics.

- **IHU RespirERA** This project for a new Institut Hospitalo-Universitaire (running over 10 years, 2023-2033), is dedicated to Respiratory Health, Environment and Aging, to improve treatment and reduce incidence of pulmonary diseases linked to pollution and aging. Partners include University Côte d'Azur, the Centre Hospitalier Universitaire de Nice, and Inserm for a 20 million Euros funding. MACBES will participate on modeling signaling pathways related to tumor cell death and identification of drug targets, with the expected supervision of a PhD student and a Post-doctoral fellow. Project coordinated by Paul Hofman, Charles-Hugo Marquette and Marius Ilie.

8.3 Regional initiatives

- **IDEX-Académie 4 OSCILLA12** A one-year project (2024-2025) aimed at the experimental analysis and mathematical modeling of biological rhythms of 12h hours. A collaboration between Franck Delaunay (IBV) and Madalena Chaves, this is an interdisciplinary internships by pairs ("stages environnés en binômes interdisciplinaires") project funded by Académie 4 "Complexité et Diversité du Vivant" (IDEX Univ. Côte d'Azur).

9 Dissemination

9.1 Promoting scientific activities

9.1.1 Scientific events: organization

- We organize a regular scientific seminar together with the GREENOWL project-team in which external guests and collaborators are regularly invited.
- We organized a Workshop on Biosystems Modeling with the GREENOWL project-team on November 26th at the Laboratoire d'Océanographie de Villefranche-sur-Mer, where all PhD students and postdocs of both teams presented their work of the year.

Member of the organizing committees

- Ludovic Mailleret was an organizer of the "Populate" summer school "Population Balance: From Fundamental to Applied Science" that took place in Grasse from June 16 to June 25.
- Benjamin Böbel was an organizer of the Inria PhD seminar and of the "Monde des Mathématiques Industrielle" (MOMI 2025) conference in May.

9.1.2 Scientific events: selection

Member of the conference program committees

- Suzanne Touzeau was a member of the scientific board of the "12ème Colloque de la Société Française de Phytopathologie", Bordeaux, May 2025.

Reviewer

- All MACBES members have been reviewers for the major control conferences: IEEE CDC, European Control Conference, MTNS,...

9.1.3 Journal

Member of the editorial boards

- Suzanne Touzeau is an Academic Editor of the PLOS One journal.
- Madalena Chaves is an Associated Editor of SIAM Journal on Applied Dynamical Systems (SIADS), since January 2015. She is an Associated Editor of the Conference Editorial Board (CEB) of the IEEE Control Systems Society, since August 2020. She is also an Associated Editor for the new IEEE Open Access Journal on Control Systems since 2021.
- Madalena Chaves was the Guest Editor of a special issue of the Interface Focus journal [29] on “Combinatorial models for evolving representation of dynamical behaviors in biological networks”, following a workshop on the same topic organized at the Lorentz Center (Leiden) in 2023.

Reviewer - reviewing activities

- All MACBES members have been reviewers for the major journals in their field: Automatica, IEEE Transactions on Automatic Control, Journal of Mathematical Biology, Mathematical Biosciences, New Phytologist...

9.1.4 Invited talks

- Madalena Chaves was a keynote speaker at the conference on “Model design, optimization & control” at Université Côte d’Azur, October 13-17.
- Suzanne Touzeau gave a talk at the monthly seminar of the International Centre for Applied Mathematical Modelling and Data Analytics, Federal University Oye-Ekiti, Nigeria, October 2025 (online).

9.1.5 Contributed talks

- Pauline Mazelel gave a talk on "Stratégies optimales de traitement du cancer dans un modèle de population cellulaire avec compétition entre cellules saines et cancéreuses" at the "Journée contrôle optimal et applications" in Avignon on June 13.
- Joseph Junior Penlap Tamagoua gave a talk on "Plant tolerance to nematodes" in March at the conference “From Data to Models” at Inria d’Université Côte d’Azur in March.
- Benjamin Böbel, Pauline Mazel and Javier Innerarity Imizcoz gave talks at the Complex Days of Academy 2 of Université Côte d’Azur in February.

9.1.6 Scientific expertise

- Madalena Chaves was a member of the jury for the selection of (6) PhD fellowships of the PEPR “Santé des Femmes, Santé des Couples”.
- Madalena Chaves was a member of the selection committee for a “Maitre de Conférences” at Aix-Marseille Université.
- Madalena Chaves was a member of the HCERES (Evaluation, Research, and Higher Education) expert committee for the evaluation of the unit: MISTEA - Mathématiques, informatique et statistique pour l’environnement et l’agronomie, at INRAE, Montpellier.
- Frédéric Grogard was a member of the HCERES expert committee for the evaluation of the unit: UMR MIA Paris-Saclay - Applied Mathematics and Computer Science.
- Jean-Luc Gouzé is a member of the steering committee of DYNABIO (see 8.2), Université Côte d’Azur. He is a member of the board of the SFBT (French Speaking Society for Theoretical Biology) and of the COSP of EUR DS4H.

- Madalena Chaves is a member of the scientific committee of DYNABIO.
- Suzanne Touzeau is a scientific officer at the Centre International de Mathématiques Pures et Appliquées (CIMPA) and hence a member of the steering council and executive team (since 2024). In 2025, she acted as CIMPA representative for three research schools in Cuba (June), Kenya (July), and Cameroon (September).

9.1.7 Research administration

- Madalena Chaves and Ludovic Mailleret are members of the INRAE Commission Scientifique Spécialisée (CSS) for Mathématique, Informatique, Sciences et Technologies du numérique, Intelligence artificielle et Robotique (MISTI).
- Madalena Chaves is the president of the local Inria committee NICE for welcoming external researchers (post-docs, “délégations”). She was also a member of the local Inria committee for doctoral studies (CSD). She is a representative of Inria at the Canceropole PACA and belongs to the local Inria group for organization of the Morgenstern Colloquium (4/5 speakers each year).
- Madalena Chaves is the coordinator of the UE Biologie Systémique 1 of the new Master option on Bioinformatics and Computational Biology of the EUR Sciences du Vivant et de la Santé.
- Suzanne Touzeau is a member of the steering committee of the INRAE Metaprogramme SuMCrop “Sustainable Management of Crop Health” (since 2016).
- Valentina Baldazzi and Suzanne Touzeau are elected members of the Institut Sophia Agrobiotech council.
- Within Univ. Côte d’Azur, Frédéric Grogard is a member of the scientific council of the Center of Modeling, Simulation and Interactions (MSI). He was a member of the steering committee of Academy 3, Space, Environment, Risk and Resilience of Univ. Côte d’Azur until September. He is since a member of the steering committee of Academy 4 “Complexity & Diversity of the Living Systems”. He is co-head of the MSc Risk [17].
- Ludovic Mailleret is the head of the M2P2 team (Models and Methods for Plant Protection) of ISA. He is in the Unit and scientific council of Institut Sophia Agrobiotech, and in the council of the INRAE PACA centre.

9.2 Teaching - Supervision - Juries - Educational and pedagogical outreach

9.2.1 Teaching

- Licence: Joseph Junior Penlap Tamagoua (77h TD), "Analyse 1", Prépa intégrée - L1 level, Polytech Nice Sophia - Université Côte d’Azur, France
- Licence: Joseph Junior Penlap Tamagoua (36h TD), "Analyse 2", Prépa intégrée - L2 level, Polytech Nice Sophia - Université Côte d’Azur, France
- Licence: Pauline Mazel (24h TD), “Analyse et modélisation”, L1, Portail Sciences de la Vie, Université Côte d’Azur, France
- Licence: Pauline Mazel (40h TD), “Statistiques”, L1, Portail Sciences de la Vie, Université Côte d’Azur, France
- Licence: Frédéric Grogard (42h ETD) and Ludovic Mailleret (24h ETD), “Equations différentielles ordinaires et systèmes dynamiques”, L3, 1st year Engineering in Modeling and Applied Mathematics, Polytech Nice Sophia, Université Côte d’Azur, France
- Master: Frédéric Grogard (14h ETD) and Ludovic Mailleret (17.5h ETD), “Bio-Mathématiques”, M1, 2nd year Engineering in Modeling and Applied Mathematics, Polytech Nice Sophia, Université Côte d’Azur, France.

- Master: Frédéric Grogard (30h ETD) "Elements of mathematical modeling", M1, MSc in Environmental Hazards and Risks Management, Université Côte d'Azur, France
- Master: Jean-Luc Gouzé (20.25h ETD), Madalena Chaves (13.5h ETD), "Modeling biological networks by ordinary differential equations", M1, 2nd year Engineering in Génie biologique, Polytech Nice Sophia, Université Côte d'Azur.
- Master: Joseph Junior Penlap Tamagoua (31.5h ETD), "Valorisation de données", M1, 2nd year Engineering in Modeling and Applied Mathematics, Polytech Nice Sophia, Université Côte d'Azur, France. [December 2025 - March 2026]
- Master: Joseph Junior Penlap Tamagoua (27h Suivi), "Projet d'études et de recherche", M2, 3rd year Engineering in Modeling and Applied Mathematics, Polytech Nice Sophia, Université Côte d'Azur, France. [November 2025 - February 2026]

9.2.2 Supervision

- PhD defended: Marine Courtois [30]. "Modélisation de la technique de l'insecte stérile dans un contexte agricole : comment intégrer les réalités biologiques et techniques pour optimiser son déploiement ?", Université Côte d'Azur, November 27, 2025. Supervisors: Ludovic Mailleret, Suzanne Touzeau, Louise Van Oudenhove De Saint Gery and Frédéric Grogard.
- PhD in progress: Aurélien Kambeu Youmbi. "Self-Financing Model for Cabbage Crops with Pest Management", University of Dschang, Cameroon, since 2020. Supervisors: Berge Tsanou (University of Dschang), Suzanne Touzeau and Frédéric Grogard.
- PhD in progress: Rand Asswad. "Développement de stratégies de contrôle pour les consortiums microbiens synthétiques", since 2022, Université Grenoble-Alpes. Supervisors: Jean-Luc Gouzé and Eugenio Cinquemani (MICROCOSME, Inria Grenoble).
- PhD in progress: Joseph Junior Penlap Tamagoua. "Ecophysiological modeling of plant-nematode interactions: Understanding the origins and consequences of differential plant susceptibility", Université Côte d'Azur, since 2022. Supervisors: Valentina Baldazzi, Frédéric Grogard and Suzanne Touzeau.
- PhD in progress: Frank Kemayou Mangwa. "Mathematical modeling and analysis of the impact of Radopholus similis on the banana-plantain production", University of Douala, Cameroon, since 2022. Supervisors: Samuel Bowong (University of Douala), Suzanne Touzeau and Frédéric Grogard.
- PhD in progress: Benjamin Böbel. "Mathematical models for robustness and control of intercellular coupling and synchronization between peripheral circadian clocks", since April 2023. Supervisors: Madalena Chaves and Jean-Luc Gouzé.
- PhD in progress: Javier Innerarity Imizcoz "Allocation optimale de ressources pour des modèles mathématiques de micro-organismes dans des conditions environnementales dynamiques", since October 2023, Université Côte d'Azur, Supervisors: Jean-Luc Gouzé, Walid Djema (GREENOWL) and Francis Mairet (Ifremer Nantes).
- PhD in progress: Pauline Mazel "Modeling, analysis and control of cancer cell population dynamics", Université Côte d'Azur, since 2023. Supervisors: Walid Djema and Frédéric Grogard.
- PhD in progress: Sthyyve Tatho. "Intégration de données multi-omiques pour l'analyse de la dynamique de communautés microbiennes en santé des plantes", Université Bordeaux, since January 2024. Supervisors: Simon Labarthe (INRAE Bordeaux) and Valentina Baldazzi.
- PhD in progress: Armando Borel Kenne Meli. "Modélisation et analyse de la dynamique de la mouche blanche, vecteur de la mosaïque africaine du manioc", University of Yaoundé I, since September 2024. Supervisors: Jean-Jules Tewa (University of Yaoundé I), Suzanne Touzeau and Frédéric Grogard.

- PhD in progress: Scott Heslop. "A demo-genetic approach to inferring the demographic impact of crop resistance bypasses: application to *Leptosphaeria maculans*, the causal agent of blackleg disease in rapeseed", Université de Lorraine, since February 2025. Supervisors: Pascal Frey (INRAE Nancy), Fabien Halkett (INRAE Nancy), Isabelle Fudal (INRAE Île-de-France - Versailles-Saclay), Suzanne Touzeau.
- PhD in progress: Kelian Bonhomme. "Mathematical modeling of cell death signaling pathways to understand the variability of tumor cell responses to anticancer treatments", since October 2025. Supervisors: Jérémie Roux and Madalena Chaves.
- PhD in progress: Timothé Fagart. "Mathematical analysis and control of biological oscillators, under local and global environmental inputs", since November 2025. Supervisors: Madalena Chaves and Jean-Luc Gouzé.

9.2.3 Master theses and Internships

- M2. Farah Kafnemer. Towards supervision strategies for anaerobic digestion bioreactors: observers and control design. ESSA Tlemcen, 5 months. Supervision: W. Djema (GREENOWL) and co-supervised by A. Ghouali (ESSA Tlemcen) and Jean-Luc Gouzé.
- M2; Ainatiana Loyenstiana Loyens. Interaction between exogenous mortality and biological control. Aix Marseille Université. Supervision: Frédéric Grogard, Ludovic Mailleret, Louise Van Oudenhove de Saint-Géry.
- M2. Timothé Fagart. Mathematical modeling and experimental analysis of biological oscillations of 12 hours. École Centrale Lyon. Supervision: Madalena Chaves, Franck Delaunay (Institut de Biologie de Valrose).
- L2. Athénaïs Vermande. State of the art on the Warburg effect. Université Côte d'Azur. Supervision: Pauline Mazel and Walid Djema (GREENOWL).

9.2.4 Juries

- Madalena Chaves was member of the jury for the PhD thesis of Nadine Ben Boina (Aix-Marseille University, May 7), as reviewer and of Ali Elouze (Université Paris Cité, December 10), as examiner.
- Madalena Chaves was member of the jury for the HDR of Valentina Lanza (Université Le Havre Normandie, March 6), as reviewer.
- Madalena Chaves is in the Comité de Suivi Doctoral of: Adel Anabi (Univ. Côte d'Azur), Joseph Penlap (Univ. Côte d'Azur), Clémence Métayer (Institut Curie), Pauline Delpierre (Université de Lille), and Julien Blohm (Université de Montpellier).
- Jean-Luc Gouzé was president of the jury for the PhD thesis of Gildas Dadjo (Université de Montpellier, September 25).
- Suzanne Touzeau was a member of the jury for the PhD theses of Ségolène Lireux (Université Marie & Louis Pasteur, Besançon, April 10) and Gildas Dadjo (Université de Montpellier, September 25).
- Suzanne Touzeau is in the Comité de Suivi Doctoral of Adèle Sahut (Avignon Université).

9.3 Popularization

9.3.1 Specific official responsibilities in science outreach structures

- Suzanne Touzeau is a member of the editorial board of Interstices, an online scientific outreach journal, published by Inria, to explore digital sciences.

9.3.2 Productions (articles, videos, podcasts, serious games, ...)

- Madalena Chaves gave an all-audience talk on “Circadian clocks: mathematical models of biological oscillators” at a four day MathC2+ workshop at Inria (June 17-20). This workshop welcomed 40 highschool students (“seconde”), motivated by mathematics and science.

9.3.3 Others science outreach relevant activities

- As part of Inria suggestions, Madalena Chaves contributed a text on “The mathematical study of biological oscillators” as a possible topic for a TIPE (Travaux d’Initiative Personnelle Encadrés). TIPE are a requirement in the program of French scientific preparatory schools (“prépas scientifiques”). Each year, a theme is decided at national level, specifically for 2025-2026: “Cycles, Boucles”.

10 Scientific production

10.1 Major publications

- [1] V. Baldazzi, D. Ropers, J.-L. Gouzé, T. Gedeon and H. de Jong. ‘Resource allocation accounts for the large variability of rate-yield phenotypes across bacterial strains’. In: *eLife* 12 (31st May 2023), pp. 1–29. DOI: [10.7554/eLife.79815](https://doi.org/10.7554/eLife.79815). URL: <https://hal.inrae.fr/hal-04145943>.
- [2] B. Böbel, M. Chaves and J.-L. Gouzé. ‘Circadian Clock Model with Sequestration Repression Motif: Existence of Periodic Orbits and Entrainment Properties’. In: *Interface Focus* 15.3 (22nd Aug. 2025). DOI: [10.1098/rsfs.2025.0008](https://doi.org/10.1098/rsfs.2025.0008). URL: <https://hal.science/hal-05060049> (cit. on p. 8).
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