RESEARCH CENTRE

Inria Centre at Université Côte d'Azur

IN PARTNERSHIP WITH:

CNRS, INRAE, Sorbonne Université

2024

ACTIVITY REPORT

Team

BIOCORE

Biological control of artificial ecosystems

Inria teams are typically groups of researchers working on the definition of a common project, and objectives, with the goal to arrive at the creation of a project-team. Such project-teams may include other partners (universities or research institutions)

IN COLLABORATION WITH: Laboratoire d'océanographie de Villefranche (LOV)

DOMAIN

Digital Health, Biology and Earth

THEME

Modeling and Control for Life Sciences

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Team BIOCORE

Creation of the Team: 2024 January 01

Keywords

Computer sciences and digital sciences

A1.5.1. – Systems of systems

A6. – Modeling, simulation and control

A6.1.1. – Continuous Modeling (PDE, ODE)

A6.1.3. – Discrete Modeling (multi-agent, people centered)

A6.1.4. – Multiscale modeling

A6.1.5. – Multiphysics modeling

A6.2.1. – Numerical analysis of PDE and ODE

A6.2.6. – Optimization

A6.4. – Automatic control

A6.4.1. – Deterministic control

A6.4.3. – Observability and Controlability

A6.4.4. – Stability and Stabilization

A6.4.6. – Optimal control

A8.1. – Discrete mathematics, combinatorics

A8.2. – Optimization

A8.7. – Graph theory

A8.11. – Game Theory

A9.2. – Machine learning

Other research topics and application domains

B1.1.7. – Bioinformatics

B1.1.8. – Mathematical biology

B1.1.10. – Systems and synthetic biology

B2.4.1. – Pharmaco kinetics and dynamics

B3.1. – Sustainable development

B3.1.1. – Resource management

B3.4. – Risks

B3.4.1. – Natural risks

B3.4.2. – Industrial risks and waste

B3.4.3. – Pollution

B3.5. – Agronomy

B3.6. – Ecology

B3.6.1. – Biodiversity

B4.3. – Renewable energy production

B4.3.1. – Biofuels

1 Team members, visitors, external collaborators

Research Scientists

- Olivier Bernard [Team leader, INRIA, Senior Researcher, HDR]
- Francesca Casagli [INRIA, Researcher]
- Walid Djema [INRIA, ISFP]
- Antoine Sciandra [CNRS, Senior Researcher, until Nov 2024]

Faculty Member

- Bastien Polizzi [UNIV FRANCHE-COMTE, Associate Professor Delegation, from Sep 2024]

Post-Doctoral Fellows

- Joel Ignacio Fierro Ulloa [INRIA, from Oct 2024 until Nov 2024]
- Solene Jahan [INRIA, Post-Doctoral Fellow, from Dec 2024]
- Emna Krichen [Inria, Post-Doctoral Fellow, until Mar 2024]

PhD Students

- Joel Ignacio Fierro Ulloa [INRIA, until Sep 2024]
- Ali Gharib [Inria, until Nov 2024]
- Javier Innerarity Imizcoz [UNIV COTE D'AZUR]
- Pauline Mazel [UNIV COTE D'AZUR]
- Diego Penaranda Sandoval [INRIA, until Mar 2024]
- Manon Pugnet [UNIV COTE D'AZUR, from Nov 2024 until Nov 2024]
- Romain Ranini [INRIA]
- Tehreem Syed [TU Dresden.]

Technical Staff

- Hubert Bonnefond [INRIA, Engineer, until May 2024]
- Amélie Talec [CNRS, Engineer]

Interns and Apprentices

- Baptiste Boerkmann [UNIV COTE D'AZUR, Intern, from Jul 2024 until Aug 2024]
- Mahe Faron [INRIA, Intern, from Jun 2024 until Aug 2024]
- Pablo Rademacher Barcelo [INRIA, Intern, from Mar 2024 until Jun 2024]
- Annalisa Reali [INRIA, Intern, until Mar 2024]
- Théo Seminara [UNIV COTE D'AZUR, Intern, from Jul 2024 until Aug 2024]
- Dominique Yessouroun Lagos [INRIA, Intern, until Apr 2024]

Administrative Assistant

- Maeva Jeannot [INRIA]

External Collaborators

- Térence Bayen [Univ. Avignon]
- Hubert Bonnefond [Darewin Evolution, from Jun 2024]
- Charlotte Gaviard [CNRS, from May 2024 until Nov 2024]
- Francis Mairet [IFREMER]
- Diego Penaranda Sandoval [Luxembourg Institute of Science and Technology, from Mar 2024]

2 Overall objectives

BIOCORE is a joint research team between Inria (Inria centre at Université Côte d'Azur), INRAE (ISA - Institut Sophia Agrobiotech and LBE - Laboratory of Environmental Biotechnology in Narbonne) and Sorbonne Université-CNRS (Oceanographic Laboratory of Villefranche-sur-mer - LOV, UMR 7093/ Sorbonne Université, Villefranche sur Mer, Team: Processes in Pelagic Ecosystems - PEPS).

Sustainable growth of living organisms is one of the major challenges of our time. In order to tackle it, the development of new technologies is necessary, and many of these new technologies will need to use modeling and computer tools. BIOCORE contributes to this theme, in the general field of design and control of artificial ecosystems (or biosystems). Its general goal is to design devices, systems and processes containing living organisms to decrease pollution, use of chemicals, or to produce bioenergy in a sustainable way. We build biological/ecological models in close collaborations with biologists and bioprocess engineers, and validate them with experimental platforms. Our activities are structured in three levels: mathematical and computational methods, a methodological approach to biology, and applications.

Research themes:

Mathematical and computational methods:

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

A methodological approach to biology: system study at different scales

- At the intra-individual level: theoretical and experimental study of simple metabolic-genetic networks, coarse grained models of the internal state.
- At the level of interactions between individuals in the population: individual behavior, resource allocation.
- At the scale of interaction between populations: interaction between prey and predator populations in a trophic network or competition between species in a chemostat.
- At the scale of interaction between ecosystems: coupling of two artificial ecosystems as a unique bioprocess or interactions between an artificial ecosystem and the surrounding natural ecosystem.

Fields of application:

- Bioenergy, in particular the production of lipids (which can be used as biofuel), methane and hydrogen by microorganisms (with LOV and LBE).
- CO_2 fixation by micro-algae, with the aim of capturing industrial CO_2 fluxes (with LOV). This theme can also include artificial ecosystems developed to improve the prediction of carbon fluxes between the ocean and the atmosphere.
- Design and optimization of ecologically friendly protection methods for plants and micro-plants artificial production systems (with ISA and LOV). This theme focuses in particular on biological control programs to control pathogens and pest invasions in crops and bioreactors.
- Biological waste treatment with microorganisms in bioreactors to reduce pollution emission levels (in collaboration with LBE).

Software development:

- Software tools for biological modeling and supervision of biological processes.

National, international and industrial relations

- National collaborations: IFREMER (Nantes), INRAE (MISTEA Montpellier, MaIAGE Jouy-en-en-Josas, BioEpAR Nantes), CIRAD Montpellier, Institut Méditerranéen d'Océanologie, LOCEAN (Paris), GIPSA Grenoble, MICROCOSME, ANGE, MCTAO, MACBES and VALSE Inria teams.
- Participation to national programmes: ANR projects PhotoBioFilmExplorer, Ctrl-AB, Barrier, UMT Fiorimed, and Labex SIGNALIFE.
- International collaborations: Université de Mons (Belgium), Politecnico de Milano (Italy), Imperial College (United Kingdom), Norwegian University of Science and Technology (Norway), Pontificia Universidad Católica de Valparaíso and Universidad de Chile (Chile), University of Edinburgh (UK), National University of Mexico (Mexico), International University of Rabat (Morocco) RWTH Aachen UniklinikK (Germany), ETH Zürich (Switzerland).

3 Research program

3.1 Mathematical and computational methods

BIOCORE's action is centered on the mathematical modeling of biological systems, more particularly of artificial ecosystems, that have been built or strongly shaped by man. Indeed, the complexity of such systems where life plays a central role often makes them impossible to understand, control, or optimize without such a formalization. Our theoretical framework of choice for that purpose 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). In modeling the ecosystems that we consider, mainly through ordinary differential equations (ODEs), the state variables are often population, substrate and/or food densities, whose evolution is influenced by the voluntary or involuntary actions of man (inputs and disturbances). 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.). Developing a model in biology is however not straightforward: the absence of rigorous laws as in physics, the presence of numerous populations and inputs in the ecosystems, most of them being irrelevant to the problem at hand, the uncertainties and noise in experiments or even in the biological interactions require the development of dedicated techniques to identify and validate the structure of models from data obtained by or with experimentalists.

Building a model is rarely an objective in itself. Once we have checked that it satisfies some biological constraints (*e.g.*, densities stay positive) and fitted its parameters to data (requiring tailor-made methods), we perform a mathematical analysis to check that its behavior is consistent with observations. Again, specific methods for this analysis need to be developed that take advantage of the structure of the model (*e.g.*, the interactions are monotone) and that take into account the strong uncertainty that is linked to life, so that qualitative, rather than quantitative, analysis is often the way to go.

In order to act on the system, which often is the purpose of our modeling approach, we then make use of two strong points of Control Theory: 1) the development of observers, that estimate the full internal state of the system from the measurements that we have, and 2) the design of a control law, that imposes to the system the behavior that we want to achieve, such as the regulation at a set point or optimization of its functioning. However, due to the peculiar structure and large uncertainties of our models, we need to develop specific methods. Since actual sensors can be quite costly or simply do not exist, a large part of the internal state often needs to be re-constructed from the measurements and one of the methods we developed consists in integrating the large uncertainties by assuming that some parameters or inputs belong to given intervals. We then developed robust observers that asymptotically estimate intervals for the state variables [41]. Using the directly measured variables and those that have been obtained through such, or other, observers, we then develop control methods that take advantage of the system structure (linked to competition or predation relationships between species in bioreactors or in the trophic networks created or modified by biological control).

3.2 A methodological approach to biology: from genes to ecosystems

One of the objectives of BIOCORE is to develop a methodology that leads to the integration of the different biological levels in our modeling approach: from the biochemical reactions to ecosystems. The regulatory pathways at the cellular level are at the basis of the behavior of the individual organism but, conversely, the external stresses perceived by the individual or population will also influence the intracellular pathways. In a modern "systems biology" view, the dynamics of the whole biosystem/ecosystem emerge from the interconnections among its components, cellular pathways/individual organisms/population. The different scales of size and time that exist at each level will also play an important role in the behavior of the biosystem/ecosystem. We intend to develop methods to understand the mechanisms at play at each level, from cellular pathways to individual organisms and populations; we assess and model the interconnections and influence between two scale levels (*e.g.*, metabolic and genetic; individual organism and population); we explore the possible regulatory and control pathways between two levels; we aim at reducing the size of these large models, in order to isolate subsystems of the main players involved in specific dynamical behaviors.

We develop a theoretical approach of biology by simultaneously considering different levels of description and by linking them, either bottom up (scale transfer) or top down (model reduction). These approaches are used on modeling and analysis of the dynamics of populations of organisms; modeling and analysis of small artificial biological systems using methods of systems biology; control and design of artificial and synthetic biological systems, especially through the coupling of systems.

The goal of this multi-level approach is to be able to design or control the cell or individuals in order to optimize some production or behavior at higher level: for example, control the growth of microalgae via their genetic or metabolic networks, in order to optimize the production of lipids for bioenergy at the photobioreactor level.

4 Application domains

4.1 Bioenergy

Finding sources of renewable energy is a key challenge for our society. We contribute to this topic through two main domains for which a strong and acknowledged expertise has been acquired over the years. First, we consider anaerobic digesters, the field of expertise of the members of the team at the Laboratory of Environmental Biotechnology (LBE), for the production of methane and/or biohydrogen from organic wastes. The main difficulty is to make these processes more reliable and exploit more efficiently the produced biogas by regulating both its quality and quantity despite high variability in the influent wastes. One of the specific applications that needs to be tackled is the production of biogas in a plant when the incoming organic waste results from the mixing of a finite number of substrates. The development of control laws that optimize the input mix of the substrates as a function of the actual state of the system is a key challenge for the viability of this industry.

The second topic consists in growing microalgae, the field of expertise of the members of the team at the Oceanographic Laboratory of Villefranche-sur-Mer (LOV), to produce biofuel. 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 modeling and control strategies. Predicting and optimizing the productivity reached by these promising systems in conditions where light received by each cell is strongly related to hydrodynamics, is a crucial challenge.

Finally, for the energy balance of the process, it is important to couple microalgae and anaerobic digestion to optimize the solar energy that can be recovered from microalgae, as was explored within the ANR Symbiose project (2009-2012) [2].

4.2 CO2 fixation and fluxes

Phytoplanktonic species, which assimilate CO_2 during photosynthesis, have received a lot of attention in the last years. Microalgal based processes have been developed in order to mitigate industrial CO_2. As for biofuel productions, many problems arise when dealing with microalgae which are more complex than bacteria or yeasts. Several models have been developed within our team to predict the CO_2 uptake in conditions of variable light and nitrogen availability. The first modeling challenge in that context consists in taking temperature effects and light gradient into account.

The second challenge consists in exploiting the microalgal bioreactors which have been developed in the framework of the quantification of carbon fluxes between ocean and atmospheres. The SEMPO platform (simulator of variable environment computer controlled), developed within the LOV team, has been designed to reproduce natural conditions that can take place in the sea and to accurately measure the cells behavior. This platform, for which our team has developed models and control methods over the years, is an original and unique tool to develop relevant models which stay valid in dynamic conditions. It is worth noting that a better knowledge of the photosynthetic mechanisms and improved photosynthesis models benefits both thematics: CO_2 mitigation and carbon fluxes predictions in the sea.

4.3 Biological depollution

These works are carried out with the LBE, mainly on anaerobic treatment plants. This process, despite its strong advantages (methane production and reduced sludge production) can have several locally stable equilibria. In this sense, proposing reliable strategies to stabilize and optimize this process is a key issue. Because of the recent (re)development of anaerobic digestion, it is crucial to propose validated supervision algorithms for this technology. A problem of growing importance is to take benefit of various waste sources in order to adapt the substrate quality to the bacterial biomass activity and finally optimize the process. This generates new research topics for designing strategies to manage the fluxes of the various substrate sources meeting at the same time the depollution norms and providing a biogas of constant quality. In the past years, we have developed models of increasing complexity. However there is a key step that must be considered in the future: how to integrate the knowledge of the metabolisms in such models which represent the evolution of several hundreds bacterial species? How to improve the models integrating this two dimensional levels of complexity? With this perspective, we wish to better represent the competition between the bacterial species, and drive this competition in order to maintain, in the process, the species with the highest capability to consume the organic pollutant.

5 Social and environmental responsibility

Since its creation, team BIOCORE has been actively engaged in contributing to sustainable growth of living organisms and the production of bioenergy in a sustainable way. Through our expertise in the development of new technologies, mathematical models, and computer tools, BIOCORE contributes to the general field of design and control of artificial ecosystems (or biosystems). The general goal of BIOCORE is to design systems and processes containing living organisms for treating pollution, reducing the use of chemicals, or to produce bioenergy in a sustainable way. We build biological/ecological models in close collaborations with biologists and bioprocess engineers, and validate them with experimental platforms. Our main applications are:

- Bioenergy, in particular the production of lipids (which can be used as biofuel), methane and hydrogen by microorganisms (with LOV and LBE).
- CO_2 fixation by micro-algae, with the aim of capturing industrial CO_2 fluxes (with LOV).
- Design and optimization of ecologically friendly protection methods for plants and micro-plants artificial production systems (with ISA and LOV).
- Biological waste treatment with microorganisms in bioreactors to reduce pollution emission levels (in collaboration with LBE).

Some members of our team (O. Bernard and W. Djema) are also participants in the local committee for sustainable development (CLDD) of Inria Centre at Université Côte d'Azur. This committee is active in various ways, and organizes events to introduce, inform, and familiarize the community to sustainable development questions and actions.

Some Biocore members did presentations and participated in outreach events on sustainable development (see Section 11.3)

6 Highlights of the year

- The Biocore project team led to the MACBES project team (created in July 2023) and to GreenOwl project team in november 2024. The Biocore project team thus finished in December 2024.
- During the PhD of Ali Gharib, we proposed a new model associated to an automatic calibration strategy to represent the thermal dynamics in solar photobioreactors. Before, for complex geometries of photobioreactors, temperature evolution within the reactor could only be predicted for a few days. With the developped approaches, it becomes possible to predict temperature for months [11, 12].
- A benchmarking study was conducted to develop the ABACO2 algal-bacterial models for wastewater treatment [16] and compare with the ALBA model, providing guidelines on their application, trade-offs between complexity and accuracy, and calibration strategies. This work was developed in collaboration with the Department of Chemical Engineering, Universidad de Almería, Spain, within the framework of the H2020 Digitalgaesation International Training Network.

7 New software, platforms, open data

7.1 New software

7.1.1 Odin

Name: Platform for advanced monitoring, control and optimisation of bioprocesses

Keywords: Bioinformatics, Biotechnology, Monitoring, Automatic control

Scientific Description: ODIN is a distributed application, whose graphical interface can be launched remotely through the Internet. The application, developed in Erlang, is architected around an MQTT broker. It is robust and tolerant to hardware failures in order to avoid that a wrong manipulation can have harmful consequences on the biotechnological process.

Thus, the implementation of a new algorithm is done by a plugin written in Python language. Modifying one of these algorithms does not require recompiling the code.

Functional Description: This application proposes a framework for on-line supervision of bioreactors. It gathers the data sampled from different on-line and off-line sensors. ODIN is a distributed platform, enabling remote monitoring as well as remote data acquisition. In a more original way, it enables researchers and industrials to easily develop and deploy advanced control algorithms, optimisation strategies, together with estimates of state variables or process state. It also contains a process simulator which can be harnessed for experimentation and training purposes. It is modular in order to adapt to any plant and to run most of the algorithms, and it can handle the high level of uncertainties that characterises the biological processes. The architecture is based on Erlang, and communication between modules through a MQTT Broker with Python for running the algorithms. ODIN is developed in collaboration with the INRIA Ibis research team.

News of the Year: A diagnosis module was implemented to detect issues in the hardware or in the connection between the various modules. The calibration module was updated also allowing actuator calibration. Finally, the python module for managing the priorities accesses to the different elements of the platform was updated.

URL: https://team.inria.fr/biocore/software/odin/

Contact: Olivier Bernard

Participants: Olivier Bernard, Nicolas Niclausse, Eugenio Cinquemani, Tamas Muszbek, Thibaud Kloczko, Nicolas Chleq, Jean-Luc Szpyrka, Pierre Fernique, Julia Elizabeth Luna, Come Le Breton, Jonathan Levy, Amine Lahouel, Tristan Cabel, François Caddet, Erwan Demairy, Riham Nehmeh, Marc Vesin, Carlos Zubiaga Pena

7.2 New platforms

Participants: Amélie Talec, Antoine Sciandra, Olivier Bernard, Francesca Casagli, Solène Jahan.

The experimental Phytopulse platform, located at the LOV and jointly developed, is made of continuous photobioreactors driven by a set of automaton controlled by the ODIN+ software, a powerful and unique tool which gave rise to a quantity of very original experiments. Such platform improved knowledge of several biological processes such as lipid accumulation or pigment dynamics under light fluctuation, nitrogen or temperature stress [27]. Amélie Talec is responsible for the Phytopulse Platform.

8 New results

The Biocore contributions are in different scientific fields. We develop theoretical methodologies which can apply to many types of biological systems, and invest more specifically in some systems for which we develop tailored approaches. The description of our new results follows this dichotomy.

Mathematical methods and methodological approach to biology

8.1 Mathematical analysis of biogical models

Participants: Walid Djema , Olivier Bernard, Pablo Rademacher.

Competition for resources in nature has been studied in the lab, in simplified environments such as the chemostat to observe the fate of the competitions of N species growing on a limiting essential substrate [6]. Periodic environments are already a first approximation of more realistic conditions. We studied the competition between two species assuming that they are affected by a periodically varying factor such as temperature. During the master internship of Pablo Rademacher, we showed that robust coexistence (for a set of parameters of non-zero measure) can happen thanks to temperature fluctuations, and we quantify numerically the domain of coexistence.

8.2 Interval observer design for biogical models

Participants: Walid Djema , Olivier Bernard.

Dynamical systems involving cooperative dynamics are convenient for designing interval observers [41]. The necessary and sufficient condition ensuring that a real matrix of dimension 3 is similar to a Metzler matrix was proposed [7] leading to interval observer design for a family of continuous-time systems. We extended this work assuming a delay in the available measurement. An updated design was proposed, and was adapted to interval observer design for a standard model representing the love between Laura and Petrarch, which produces chaos and limit cycles. This work is carried out in collaboration with F. Mazenc (DISCO).

Fields of application

8.3 Experimental developments

Participants: Olivier Bernard, Antoine Sciandra, Francesca Casagli, Annalisa Reali, Emna Krichen, Amélie Talec.

Various experiments were carried out in the phytopulse platform for determining the ability of biofilms to grow with different sources of nitrogen. This experimental platform was used to control the long term stress applied to a population of microalgae using optimal control strategies [36]. This Darwinian selection procedure generated several new strains with higher lipids or pigments of interest after several months in the so called selectiostats [31]. These experimental works were carried out in the frameworks of the ISS incubated Darewin project, and in the pre-maturation Phycoplus project funded by CNRS.

Experimental works were carried out in the framework of the ANR Photobiofilm explorer project with microalgal biofilm that were grown from lab scale to pilot scale, with the objective of tracking antimicrobial activities [43]. The architecture of the biofilms was also observed for different species with confocal microscopic techniques [15]. Other experiments were carried out at CentraleSupelec within the PhD of David Morgado Pereira in order to observe the development of biofilm from *Haematococcus pluvialis* and their astaxanthin production during a nitrogen starvation stage [14].

These works have been carried out in collaboration with A. Talec (CNRS/Sorbonne Université - Oceanographic Laboratory of Villefranche-sur-Mer LOV).

8.4 Estimation of carbon fluxes in the ocean

Participants: Olivier Bernard, Lionel Guidi, Antoine Sciandra, Romain Ranini, Amélie Talec.

Participation in experimental campaigns. R. Ranini took part to the Tara Europa campaign (30 days in Italian coastal waters aboard Tara), where he was in charge of the plankton net processing lab. The data recorded along the campaign will be used for the setup of his modeling on the particle size distribution in marine water determined by the local biotic and abiotic environment.

Modeling thermal adaptation in microalgae. We studied a broad range of species and their response to temperature. Algorithms were developed to automatically calibrate the parameters of the CTMI (Cardinal Temperature Model with Inflexion) and the Hinshelwood models [42]. It turns out that the optimal temperature, the minimal and the maximal temperature for growth are strongly correlated. Relationships between these cardinal temperatures and key parameters from the environment (sea surface temperature, solar flux, ...) were explored. Some of the relationships stay valid also for a broad range of microorganisms such as yeast and bacteria.

Use of AI for improving the oceanic carbon flux estimates. The objective of this work is to provide a model describing the particle size distribution (PSD) as a function of the environmental conditions using Artificial Intelligence approaches, so as to better represent the amount of organic carbon which will be exported in the deep layers of the ocean. We introduced a more accurate model than Junge's law, aiming to reduce biases in vertical carbon flux assessments. It highlights limitations in state of the art modeling used to predict PSD distribution, particularly for slopes and convexity. The approach uses XGBoost (eXtreme Gradient Boosting) with 0D environmental snapshots for efficiency but sacrifices detailed temporal and spatial information. This work is carried out within the OceanIA Inria challenge, and is the core of the PhD thesis of Romain Ranini.

8.5 Metabolic modeling

Participants: Olivier Bernard, Antoine Sciandra, Walid Djema, Francesca Casagli, Bruno Assis Pessi.

A metabolic model has been set up and validated for the microalgae *Chlorella vulgaris*, on the basis of the DRUM framework [1] , in order to simulate autotrophic, heterotrophic and mixotrophic growth, and to determine how to reduce substrate inhibition. The model was extended to other substrates such as glucose or glycerol [1]. After a calibration phase, the model was successfully challenged with data from 122 experiments collected from scientific literature in autotrophic, heterotrophic and mixotrophic conditions [48].

As part of B.A. Pessi PhD thesis, this metabolic modeling framework is extended to describe a co-culture of bacteria and microalgae. First, by modeling a thiamine auxotroph *E. coli* to maximize the production of lactate [47]. Then, we extend the previous developed metabolic model to describe a co-culture of *Chlorella* with the bacteria *E. coli* overproducing the vitamin biotin. We represent the influence of biotin concentration in the accumulation of lipids. The model results show that a biotin overproducer *E. coli* could support the needs of vitamin by *Chlorella* and favor lipid accumulation [17].

8.6 Modeling biofilms

Participants: Olivier Bernard, Antoine Sciandra, Francesca Casagli, Ali Gharib, Emna Krichen, Amélie Talec, Eric Pruvost.

Several models have been developed to represent the growth of microalgae within a biofilm. A first structured physiological model [49] uses mixture theory to represent the microalgae growth, based on the consideration of intracellular reserves triggering the processes of growth, respiration and excretion. We consider separately the intracellular storage carbon (lipids and carbohydrates) and the functional part of microalgae [19]. The model corroborated observations realized at the LGPM (CentraleSupelec) [10, 15]. Another approach accounts for the dynamics of the light harvesting systems when cells are submitted to rapid successions of light and dark phases [28]. A simpler model was developed [40]. An optimization work determined the maximal productivity of a photosynthetic biofilm growing on a conveyor belt [39]. The model was used to identify the worldwide potential of microalgal biofilms under different climates [46]. This study was extended considering the environmental impact if the culture has to be heated in winter.

8.7 Modeling photobioreactors

Participants: Olivier Bernard, Antoine Sciandra, Walid Djema, Francesca Casagli, Ali Gharib, Ignacio Fierro Ulloa, Annalisa Reali, Emna Krichen.

Modeling the coupling between photosynthesis and hydrodynamics. We consider a coupled physico-biological model describing growth of microalgae in a raceway pond cultivation process, accounting for hydrodynamics. Our approach combines a biological model (based on the Han model) and shallow water dynamics equations that model the fluid dynamics into the raceway pond [28]. We developed an optimization procedure dealing with the topography to maximize the biomass production over one lap or multiple laps with a paddle wheel. The results show that a flat topography is optimal in a periodic regime. We then studied the influence of mixing, assuming that a mixing device can redistribute the algae so that they can have access to light [30]. A strategy to optimally mix the algae was derived especially by alternating high and low light [28].

Modeling temperature dynamics in bioreactors. Temperature plays a key role in the microalgae dynamics. We developed a heat transfer model to simulate the temperature evolution in the process medium, depending on the meteorology, and its impact on algal productivity. We proposed a general framework to simulate these multiphysics systems, keeping a balanced degree of complexity between the biological and the physical models [34].

Based on this heat-transfer model, we proposed an auto-adaptive heat-transfer model together with an autotuning procedure [12] that can predict the temperature evolution inside different type of raceway ponds or more complex cultivation systems (photobioreactors with complex geometries) using weather forecasts. We also considered the influence of a greenhouse on the medium temperature and the model training automatically adapted to accurately predict temperature [11]. The model was tested under five different climatic conditions (Narbonne, Milan, Bonaire, Wageningen, Nice), and was even able to reproduce the dynamics of biofilm growth under a greenhouse, in collaboration with the Inalve start-up [23].

Modeling chemical speciation and pH in bioreactors A robust chemical model that accurately describes ionic speciation is essential for understanding and optimizing the growth of microorganisms such as microalgae and bacteria. We developed a chemical model to simulate ionic equilibria in highly saline environments, considering activities rather than concentrations of ions, together with ionic strength, a key factor in ion pairing phenomena. The originality of the approach we developed consists in transforming the initial problem (algebraic equation system) in the solution of a differential equation system, reducing the unknows from 40 to 5. Using experimental data from Total energy pilot-scale applications and PHREEQC software, the most significant ion pairing products were identified and incorporated into the new chemical model in Matlab. On top of this, dedicated experiments and pH measurements were carried out at the Laboratory of Oceanography of Villefranche sur Mer. The experimental data and PHREEQC simulation results were used for validating the outcomes of the new chemical model. The model demonstrated good accuracy in predicting pH, ionic strength, ion pairing products, and ionic composition of saline solutions. This study was the main subject of Annalisa Reali's master thesis at Politecnico di Milano under the supervision of F. Casagli and O. Bernard, within the framework of the ANR BARRIER project.

8.8 Bioenergy and wastewater treatment

Participants: Olivier Bernard, Antoine Sciandra, Walid Djema, Francesca Casagli, Ali Gharib, Annalisa Reali, Emna Krichen.

A comprehensive hybrid modeling approach for predicting biological dynamics: application to algae-bacteria systems Algae-bacteria systems are promising for wastewater remediation, but challenges exist in improving efficiency and reducing costs at an industrial scale. Mathematical models, particularly mechanistic models (MM), are useful for simulating biological processes, but they are complex and not suited for efficient process control. Artificial Neural Networks (ANN) have potential but may not preserve essential properties like mass conservation. Hybrid models combine MM and ANN, maintaining physical laws while adapting to data. This study presents a hybrid approach applied to the ALBA model, simulating algae-bacteria dynamics [20]. The model was calibrated and validated on pilot-scale applications. The hybrid approach predicts key variables accurately, with performance dependent on the data used for training. A trade-off exists between generalization and accuracy, requiring consideration for each specific case. The hybrid model was developed in a Python package that is based on JAX.

Extending Algae-Bacteria Model for Predicting Microbial Communities in Wastewater Treatment Bacteria and microalgae coexist and interact in wastewater treatment, exchanging oxygen, CO2, vitamins, and protection through allelopathy or toxin degradation . These interactions promote microbial symbiosis, diversity, and variability. Modeling these dynamics is challenging but aided by data from an experimental campaign carried out at the University of São Paulo State University (Brasil) who, on top of routine measurements, did omics analyses to estimate diversity. Including microbial structure improves predictability but increases model complexity, requiring a balance between detail and operability. This work [26] extends the ALBA model to include a refined desciption of the present microorganisms, improving microbial community predictability during wastewater treatment.

In addition, microalgae-bacteria systems for wastewater remediation, commonly applied in high-rate algal-bacteria ponds (HRABP), are limited by effluent clarification and load capacity, due to sub-optimal operational conditions. We studied the introduction of membrane filtration to address these issues by decoupling solid retention time (SRT) from hydraulic retention time (HRT). The M-ALBA model, an extension of the ALBA model with a membrane separation compartment, was developed to predict membrane-assisted HRABP performance (model developed in Matlab). Simulations showed that decoupling SRT and HRT improves nitrogen removal, reduces ammonia volatilization, and achieves better performances compared to the case where membrane were not applied. This work enhances understanding of microalgae-bacteria interactions in membrane systems. This work was done in collaboration with the Escuela de Ingeniería Bioquímica, Pontificia Universidad Católica de Valparaíso (Chile).

8.8.1 Control and Optimization of microalgae production

Participants: Olivier Bernard, Francesca Casagli, Ignacio Fierro, Ali Gharib, Walid Djema.

Optimal control of microalgae The Simplified Auto Tuning Heat Exchange (SATHE) model ([12], [11]) has been integrated into optimal control strategies and Model Predictive Control (MPC), showcasing its versatility and relevance. The objective was to develop strategies maximizing productivity by maintaining the algae in a trade-off for light and temperature.

One of the primary goals of controlling artificial cultures (bioreactors) is to promote the most suitable microbial species for biotechnological applications. Key objectives include enhancing microalgae photosynthesis in dense cultures and maximizing lipid production for biofuel applications. Over the past year, various formulations of optimal control problems were explored and applied, continuing the research efforts aligned with the interests of collaborators, particularly the DareWin startup (created by the GreenOwl team). For instance, this year, studies focused on the competition between microbial species and the time-optimal selection of the most advantageous species in the presence of substitutable substrates within the culture medium (a paper is under review in Journal of Optimization Theory and Applications).

Optimization of the microalgae production through light pattern Dynamic light regimes strongly impact microalgal photosynthesis efficiency. Finding the optimal way to supply light is then a tricky problem, especially when the growth rate is inhibited by overexposition to light and, at the same time, there is a lack of light in the deepest part of the culture. We used the Han model to study the theoretical microalgal growth rate by applying periodically two different light intensities [28]. For a large light period, we demonstrate that the average photosynthetic rate can be enhanced.

Microalgal growth is affected by the dynamics of photon harvesting processes, such as photoinhibition and photoacclimation. Taking into account these phenomena, we propose and solve an optimal control problem to maximize the production of biomass [22]. Theoretical and numerical properties of the problem were described, where Turnpike-like properties were observed using Pontryagin's maximum principle and the BOCOP software for numerical simulations.

This was the subject of the PhD thesis of Ignacio Fierro in the framework of the ITN Digitalgaesation.

Optimization of the microalgae production through temperature control A model predictive control algorithm was elaborated based on simple microalgae models coupled with physical models where culture depth influences thermal inertia. Optimal operation in continuous mode for outdoor cultivation was determined when allowing variable culture depth. Assuming known weather forecasts considerably improved the control efficiency. This was the subject of the PhD thesis of Ali Gharib in the framework of the ITN Digitalgaesation.

8.9 Biological depollution

Participants: Olivier Bernard, Antoine Sciandra, Jean-Philippe Steyer, Francesca Casagli, Annalisa Reali.

We consider artificial ecosystems including microalgae, cyanobacteria and bacteria in interaction. The objective is to more efficiently remove inorganic nitrogen and phosphorus from wastewater, while producing a microalgal biomass which can be used for biofuel or bioplastic production [44, 50]. We designed and calibrated a model, that was validated with more than one year of data [5]. The model analysis revealed that despite pH regulation, a strong limitation for inorganic carbon was found to hinder the process efficiency and to generate conditions that are favorable for N_2O emission. A control strategy regulating alkalinity turns out to be necessary to enhance the performance and avoid harmful emissions [4]. We developed a general framework for simulating biotechnological processes affected by meteorology, integrating, on top of the core biological model, a heat transfer model and a chemical sub-model for computing the speciation of all the dissociated chemical molecules [34]. The developed framework is a powerful tool for advanced control and optimization of environmental processes, which can guide the scaling-up and management of the most innovative bioprocesses. In this framework was implemented the ABACO-2 model, in order to couple the biological model with the chemical model [16]. We explored and quantified, through a modeling study, the advantage of adding a solid/liquid separation system to uncouple Hydraulic Retention Time (HRT) and Solid Retention Time (SRT), in order to maximize the algal productivity and the nitrogen recycling [3].

A work was started to simplify these models and enhance their calibration by considering artificial neural networks, which are integrated in a way that the full model respects some key constraints (positivity, boundness, ...). A dedicated strategy was developed [35, 33] and successfully applied to experimental data from two pilot plants. This approach allows a fast calibration strategy for new processes by combining the hypothesis on mass balance and stoichiometry and the artificial neural networks. Another approach with neural ODE was also developed for representing microalgae growth in photobioreactors [37, 38].

The coupling between a microalgal-bacteria high rate pond and an anaerobic digester is a promising alternative for sustainable energy production and wastewater treatment by transforming carbon dioxide into methane using light energy [44]. The challenge when dealing with anaerobic digestion effluent for feeding the algae-bacteria process is the potential low alkalinity which can induce a competition between nitrifying bacteria and algae [32]. We showed that this competition for inorganic carbon can create conditions favorable for N_2O emission. We studied the metabolism of *Chlorella vulgaris* growing on fermentation products and developed a metabolic model [48] that was validated with a large number of experiments covering various working modes (autotrophic, heterotrophic, mixotrophic).

8.10 Optimizing waste-to-energy systems for profitable energy production.

Participants: Walid Djema.

In collaboration with Othman Cherkaoui from the University of Rabat, a model for optimal waste valorization and investment strategies was developed to enhance biogas production and reduce pollution [9]. This work involved the analysis of a bioeconomic model designed to optimize both waste storage management and financial investments in the sector. The model is dynamic and incorporates two control variables, where turnpike phenomena and singular arcs prominently emerge in the control strategy. A detailed analysis was conducted under conditions of periodic waste input, complemented by a sensitivity analysis of the control problem with respect to the system's key parameters. J.-L. Gouzé (Inria MACBES) is also involved in this work.

8.11 Life Cycle Assessment

Participants: Olivier Bernard, Jean-Philippe Steyer, Diego Penaranda, Francesca Casagli, Arnaud Hélias.

Environmental impact assessment. We have studied the environmental impact of protein production from microalgae in an algal biofilm process, using a Life Cycle Assesment (LCA) approach and compared it to other sources (fisheries, soy,...). We have analyzed the updated version of the production system and proposed several optimizations to reduce the environmental impact. This study confirms the interest of microalgae for reducing the environmental impact [45] compared with other sources of proteins like fishmeal or soy. More generally, this work proposes a new approach to assess and reduce the environmental footprint of processes which use non mature technologies (PhD thesis of D. Penaranda in collaboration with M. Morales from the Norwegian University of Science and Technology).

A study was carried out to assess the environmental benefit of using microalgae-bacteria to process wastewater, and in particular digestates from anaerobic digestion [44][8]. Various scenarios were simulated using the ALBA model [32] assuming an industrial plant located in Rennes (Brittany, France) dealing with an actual climatology and for various conditions of Hydraulic and Solid retention times, alkalinity addition and biomass valorization for generating energy. In total, 72 different scenarios were explored, for which LCA was carried out. The results were compared to scenarios where the digestates are classically treated in a wastewater treatment plant. It results that the microalgae approach makes sense from an environmental point of view [45].

This work is the result of a collaboration with Arnaud Helias of INRAE-LBE (ITAP, Technologies et méthodes pour les agricultures de demain, Montpellier).

8.12 Development and application of optimal control strategies for biological systems

8.12.1 Optimal therapeutic control in cancer

Participants: Walid Djema, Pauline Mazel.

Generalized versions of Lotka-Volterra models were analyzed to represent interactions between cancerous and healthy cells, facilitating the design of strategies for chemotherapy and targeted therapies. By employing Pontryagin's Maximum Principle (PMP), the proportion of healthy cells was maximized under specific constraints [25]. This project, which involves ongoing advancements in modeling, analysis, and control, is being conducted in collaboration with RWTH Aachen University Uniklinik in Germany. This is the main subject of the PhD thesis of Pauline Mazel. In a different context, another type of competition between cell populations was investigated, focusing on the issue of resistance developed by certain cells to treatments. The study aimed to explore strategies to overcome this resistance through optimized drug administration protocols that activate distinct cell death pathways. In this regard, in collaboration with J. Roux and M. Péré from the MACBES team at Inria, a novel model was developed and calibrated: this model provides promising applications and future perspectives in the domain of therapeutic control.

8.12.2 Optimal resource allocation for metabolite production.

Participants: Walid Djema, Javier Innerarity Imizcoz.

Strategies for resource allocation in bacteria under periodic and time-varying environmental conditions were investigated using a dynamic ODE model and PMP. The results revealed that optimal control can yield complex structures with higher-order singular arcs (Chattering phenomena). These findings demonstrate that maximum growth can be achieved under periodic conditions, emphasizing the crucial role of a key molecule (named ppGpp) in regulating protein precursors in *E. coli* ([13], [24]). This is the main subject of the PhD thesis of Javier Innerarity Imizcoz. J.-L. Gouzé (Inria MACBES) and F. Mairet (IFREMER) are also involved in this work.

8.12.3 Optimal control of algae-bacteria consortia.

Participants: Walid Djema, Olivier Bernard.

An algae-bacteria consortium was optimized to maximize biomass production in a bioreactor in collaboration with MICROCOSME and within the framework of the ANR project (Ctrl_AB) [18]. In a new project supported by Idex-UniCA (OPTI-ABh), in collaboration with Ifremer Nantes (F. Mairet), we explore pollutant removal approaches that favor algae growth while activating bacterial mechanisms to neutralize more resistant pollutants. Numerical tools were utilized to determine microbial strategies for bioprocess control. This is the main subject of the PhD thesis of Rand Aswad, Grenoble, in collaboration with E. Cinquemani (Microcosme). J.-L. Gouzé (Inria MACBES) is also involved in this work.

8.12.4 Agroecosystem optimization.

Participants: Suzanne Touzeau, Frédéric Grognard, Frank Kemayou Mangwa, Walid Djema.

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. As part of a collaboration with the MACBES Team (F. Grognard, S. Touzeau and F. Kemayou Mangwa) with their EPITAG associate team with Cameroon, 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 an overyielding phenomenon. This work, carried out in collaboration with F. Mairet (IFREMER), is part of Frank Kemayou's ongoing PhD thesis.

9 Bilateral contracts and grants with industry

Participants: Olivier Bernard, Diego Penaranda.

9.1 Bilateral contracts with industry

- **Inalve:** with the Inalve start-up, we develop a breakthrough process that we patented, in which microalgae grow within a moving biofilm. The objective of the collaboration is to optimize the process by enhancing productivity, while assessing and reducing the environmental footprint.

9.2 Bilateral grants with industry

- **Inalve:** Inalve is funding half of the PhD thesis of Diego Penaranda-Sandoval on the life cycle analysis of processes with low technological maturity. The other half is coming from a PACA region grant.

10 Partnerships and cooperations

10.1 International initiatives

- We collaborate with M. Morales (NTNU, Norway) for Life Cycle Assesment studies.
- In the framework of the OceanIA project, we work with L. Marti and N. Pi Sanchez from Inria Chile (Santiago, Chile) on hybrid modeling.
- We have long term collaboration with D. Jeison and C. Martinez from PUCV (Valparaíso, Chile) on modeling and control of algae-bacteria processes.
- We collaborate with E. Ficara, Professor at Politecnico di Milano, Department of Civil and Environmental Engineering, DICA (Milan, Italy), on wastewater recovery with algae-bacteria systems.
- We collaborate with Gustavo Henrique Ribeiro da Silva, Professor at São Paulo State University (Unesp), Departamento de Engenharia Civil e Ambiental (São Paulo, Brazil) on wastewater treatment modeling.
- A collaboration with RWTH Aachen Uniklinik was initiated in 2024 with Thomas Stiehl, Head of the Institute of Computational Biomedicine Disease Modeling at RWTH Aachen Uniklinik (Aachen, Germany). The work focused on the modeling and analysis of the hematopoietic niche, as well as the development of control approaches aimed at proposing novel therapeutic strategies.
- A collaboration is ongoing with Nadia Raïssi from Mohammed V University (Rabat, Morocco). The project focuses on optimizing waste treatment processes with a specific emphasis on sustainable development in Morocco.
- We collaborate with Mustafa Khammash, Head of the Control Theory and Systems Biology Laboratory at ETH Zurich (Switzerland), to develop new theoretical control tools for supporting experimental designs conducted at ETH for algae-bacteria consortium cultures.

10.2 International research visitors

10.2.1 Visits of international scientists

- In the framework of the ITN DigitAlgaesation, we had the visit of Lars Stegemüller from DTU (April 20^{th} to 20^{th}, 2024), and Giovanni Consoli (Univ. Padova) (September 2^{nd} to 6^{th}, 2024)
- Mustafa Hani Khammash visited us in March 2024.
- Rolf Findeisen gave a seminar in November 29^{th}, 2024.

10.2.2 Visits to international teams

- Walid Djema was a recipient of the 2024 Franco-German Program by DAAD for research visits in Germany. The project, titled *Integrative Mathematical Modeling for Understanding and Controlling Hematopoietic Stem Cell Dynamics and Acute Leukemia*, was carried out from November 30^{th}, 2024, to January 1^{st}, 2025, at the Institute for Computational Biomedicine - Disease Modeling, RWTH Aachen University. A collaboration was established with Dr. Thomas Stiehl's team, focusing on the modeling, analysis, and control of acute myeloid leukemia.

10.3 European initiatives

10.3.1 H2020 projects

DigitAlgaesation DigitAlgaesation project on cordis.europa.eu

Title: A knowledge-based training network for digitalisation of photosynthetic bioprocesses

Duration: From March 1^{st}, 2021 to February 28^{th}, 2025

Partners:

- INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET AUTOMATIQUE (INRIA), France
- IMPERIAL COLLEGE OF SCIENCE TECHNOLOGY AND MEDICINE, United Kingdom
- MINT ENGINEERING GMBH, Germany
- UNIVERSITA DEGLI STUDI DI PADOVA (UNIPD), Italy
- SIEMENS PROCESS SYSTEMS ENGINEERING LIMITED (SPSE Ltd), United Kingdom
- PROVIRON HOLDING NV (PROVIRON), Belgium
- TMCI PADOVAN SPA, Italy
- DANMARKS TEKNISKE UNIVERSITET (TECHNICAL UNIVERSITY OF DENMARK DTU), Denmark
- UNIVERSIDAD DE ALMERIA (UNIVERSIDAD DE ALMERIA), Spain
- WAGENINGEN UNIVERSITY (WU), Netherlands
- CENTRALESUPELEC, France
- TECHNISCHE UNIVERSITAET DRESDEN (TUD), Germany
- GOTTFRIED WILHELM LEIBNIZ UNIVERSITAET HANNOVER (LUH), Germany

Inria contact: Olivier Bernard

Coordinator: Fabrizio Bezzo (Univ. Padova)

Summary: Microalgae and other photosynthetic microorganisms represent a highly promising source for food, feed, chemicals, and fuels. Europe has been leading world research and industrial deployment of microalgae based technologies. However, despite the enormous potential and the impressive R&D effort, industrial use of microalgae is still at its first developmental stage. A major step forward can derive by the development and implementation of digital technologies, capable of automatizing and optimizing culture conditions at industrial scale. Europe has a tradition of leading researches in the field of automatic control for biotechnological processes. As envisaged by DigitAlgaesation, the widespread definition and adoption of effective tools for better design and operation urgently requires skilled multidisciplinary scientists and engineers, who can develop and implement the next generation of sustainable production process with enhanced productivity, reduced environmental impact and costs, despite climate fluctuations that may strongly affect microalgae productivity. All this demands a European commitment to concerted, inter- and transdisciplinary research and innovation.

DigitAlgaesation will train 15 early-stage researchers (ESRs) in all aspects of microalgae technological innovation to pave the way towards a knowledge-based breakthrough in monitoring methods and instrumentation, biological modeling and simulation, and automatic control. By training in scientific, technical and soft skills, they will become highly sought-after scientists and engineers for the rapidly emerging microalgae-based industry and broader bioprocessing industries of Europe.

10.4 National initiatives

10.4.1 National programmes

- **ANR PhotoBioFilm Explorer:** The first objective of the PhotoBioFilm project (2021-2024) is to explore the activity of the molecules produced within a microalgae biofilm, and explaining its resistance to contamination. The second objective is to identify, characterize and produce novel biocompounds with benefits for human or animal health. The target is antibiotics, but other activities will be tested, especially antiviral activities. Biocore will be in charge of the biofilm modeling and the optimization of the production of the molecules of interests. Project coordinated by O. Bernard.

- **ANR Ctrl-AB:** The objectives of the Ctrl-AB project (2021-2024) 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. Interestingly, coculturing of *E. coli* with *Chlorella* leads to higher biomass and lipid productivity. Improved growth of *Chlorella* occurs despite competition of *E. coli* for the same substrates. On top of its ability to produce molecules like vitamins, which are necessary for algal growth, bacteria also produce carbon dioxide (CO_2), which is the substrate of the photosynthesis of the algae. The algae can produce oxygen (O_2) fueling bacterial growth, thus giving rise to a mutualistic pattern of interactions giving rise to several challenges for modeling and controlling this artificial ecosystem. Project coordinated by J.-L. Gouzé.

- **ANR Barrier:** This proof of concept project (2023-2027) with multidisciplinary expertise is willing to demonstrate, from the laboratory to a pilot process, that selected bacteria can protect microalgae when growing in contaminated wastewaters, providing higher algal resilience, productivity and bioremediation efficiency in wastewater treatments. It is coordinated by O. Pringault (IRD, Mediterranean Institute of Oceanography).

- **SIGNALIFE:** Biocore was part of this Labex (scientific cluster of excellence, 2^{nd} period 2020-2024) whose objective is to build a network for innovation on Signal Transduction Pathways in Life Sciences, and is hosted by the University Côte d'Azur.

10.4.2 Inria funding

- **Inria Startup Studio, DareWin:** (2022-2024). The DareWin project is consolidating the bases of a startup which will develop Darwinian selection approaches in highly controlled bioreactors to naturally select and improve microalgal strains of industrial interest.

10.5 Regional initiatives

- Walid Djema was awarded the **"Booster Junior 2024, IDEX"** by Academy 2, "Complex Systems," UniCA, for the project titled *OPTI-ABh: Optimization of algae-bacteria consortia via hybrid PMP: Towards new optimal conditions for depollution.*

11 Dissemination

11.1 Promoting scientific activities

11.1.1 Scientific events: organisation

- We organize a monthly scientific seminar together with the MACBES project-team in which external guests and collaborators are regularly invited.
- We also organize a yearly four day-retreat together with the MACBES project-team where we share our work of the year; this year, it took place mid-October in Peyresq.
- Francesca Casagli is co-chair in the Task Group of IWA (International Water Association) on modeling phototrophic systems.
- F.Casagli and O.Bernard took part to the organization of a workshop on modeling phototrophic systems during the The 1st International Conference on Novel Photorefineries for Resource Recovery in Valladolid, Spain [21] .
- F.Casagli and O. Bernard are involved in the coordination and writing of a position paper for the IWA Task Group.

11.1.2 Member of the organizing committees

O. Bernard was in the organizing committee of the AlgoReseau in Nice "Focus on micro- and macro-algae work in the Mediterranean " which took place in July 11^{th} and 12^{th}, 2024, in Nice and Villefranche-sur-mer.

11.1.3 Chair of conference program committees

O. Bernard was the head of the academic scientific committee of the AlgaEurope conference which took place in December 10^{th} to 13^{th}, 2024 in Athens.

11.1.4 Member of the conference program committees

O. Bernard was in the scientific committee of 1st International Conference on Novel Photorefineries for Resource Recovery (Valladolid, September 2024).

11.1.5 Reviewer

- All BIOCORE members have been reviewers for the major 2024 conferences in our field: Conference on Decision and Control, European Control Conference, International Federation of Automatic Control ...
- The team is reviewing articles for the main journals of Automatic Control (Automatica, IEEE Transactions on Automatic Control, Journal of Process Control), for mathematics applied to biology (Journal of Mathematical Biology, Mathematical Biosciences), and for biology or biotechnology journals (Algal Research, Plos computational Biology, Bioresource Technology, ...).

11.1.6 Invited talks

- W. Djema was invited as a speaker at the *Optimal Control Day* organized by the FRUMAM in Marseille, in June 2024.
- F. Casagli was invited to give a talk within the INRAE workshop "Journée scientifique SPE NUM: les Approches hybrides IA - Systèmes dynamiques", on December 3^{rd}, 2024 in Montpellier. Title of the talk "Hybrid modeling of biological processes: application to microalgae/bacteria systems".

11.1.7 Master theses and internships

- W. Djema supervised the master intership of Dominique Y. Lagos, through the Inria-Chile internship program (3 months visit). Dominique worked on species selection in competition for two substitutable substrates.
- W. Djema supervised Baptiste Boerkmann (Univ. Lyon) during a summer internship (M1 level) lasting 2 months, starting on July 1, 2024. Baptiste explored the application of the hybrid Pontryagin's Maximum Principle (PMP) to a biotechnological model.
- W. Djema supervised Théo Séminara (MIAGE Sophia Antipolis), an undergraduate student (L3 level), during a 2-month internship starting on July 1, 2024. Théo focused on creating scientific content and managing digital communication.
- O. Bernard and T. Sari supervised the master thesis of Pablo Rademacher and his 3 months stay "Global warming effect on competition: Modeling the effects of global warming on competition of species on a chemostat", University of Chile.
- O. Bernard co-supervised the master thesis of Miguel Antonio González Serrano (Unam, Mexico)
- F. Casagli and O. Bernard supervised the master thesis of Analisa Reali (Politecnico de Milano, Italy) on modeling chemical speciation in saline reactors.
- In the framework of thr ITN Digitalgaesation, O. Bernard supervised the secondments stays of Lars Sebastian Stegemüller (DTU, Denmark) , Giovanni Consoli (Imperial College, London) and, together with F. Casagli, R. Nordio (Univ. of Almeria, Spain).

11.1.8 Scientific expertise

- W. Djema has been appointed as a member of the Scientific Council of Academy 4 "Complexity and Diversity of Life," Université Côte d'Azur (since 2023), representing Inria within the council.
- O. Bernard is in the Scientific Advisory Board of the "Ferment du futur" Grand challenge of France 2030. O. Bernard is a member of the scientific committe of IRD (Institute of Research for the Development) in the CSS5 section (models and data). He participated to the recruitement juries for researchers and research directors at IRD.
- O. Bernard was in the Scientific and Pedagogic committee of the UniCA- EUR LIFE and in the steering committee of Federal Recherche Institut (IFR) Marine Ressources (MARRES).
- O. Bernard is member of the scientific committees of Inalve and Darewin Evolution.

11.1.9 Research administration

- W. Djema has been appointed as a member of the Scientific Council of Academy 4 "Complexity and Diversity of Life," Université Côte d'Azur (since 2023), representing Inria within the council.
- W. Djema has been elected as a member of the Inria center's committee, Centre Inria d'Université Côte d'Azur (since January 2024).

11.2 Teaching - Supervision - Juries

11.2.1 Teaching

- Licence: W. Djema (40h ETD), P. Mazel (20h ETD); “Mathématiques pour Biologistes: Analyse et Modélisation", L1 Université Côte d'Azur UniCA, France.
- Licence: W. Djema (32h ETD); “Math0: Enjeux", L1 Université Côte d'Azur UniCA, France.
- Licence: W. Djema (12h ETD), P. Mazel (32h ETD); “Statistiques pour les Biologistes", L1 Université Côte d'Azur UniCA, France.

- Licence: O. Bernard (35h ETD), "Use and optimization of photobioreactors", Université de Pau et des pays de l'Adour, France.
- Licence: P. Mazel (16h TD), "Fondements mathématiques 1 - partie algèbre linéaire", L1, Portail Sciences et Technologies, Université Côte d'Azur, France
- Licence: W. Djema (12h ETD), J. Innerarity (30h EDT), "Mathematical Analysis": Ecole Centrale Méditerranée Nice.
- Master: O. Bernard (4.5h ETD), "Bioenergy from microalgae", M2, Master International Energy Management : alternatives pour l'énergie du futur, Ecole Nationale Supérieure des Mines de Paris, France.
- Master: O. Bernard (36h ETD), "Modeling biotechnological processes", M2, Ecole CentraleSupelec, Saclay, France.
- Master: O. Bernard (18h ETD), "Automatic Control applied to biotechnological processes", M2, Ecole CentraleSupelec, Saclay, France.
- Master: O. Bernard (6h ETD), "Cultivation and use of Microalgae", Master Mares, Université Côte d'Azur, France.
- Master: O. Bernard (24h ETD) and W. Djema (24h ETD), "Enseignement d'Intégration – "Automatic Control applied to biotechnological processes", CentraleSupélec, Paris-Saclay, France.
- Master: W. Djema (12h ETD) M. Chaves (8h ETD), "Biology of Systems" – Lectures, Master BIM, Valrose, Nice
- Master: W. Djema (15h ETD), F. Grognard (15h), "Elements of Mathematics" – Lectures on mathematics and programming Python, and modeling in ecology, Master RISK, IMREDD, UniCA, Nice

11.2.2 Supervision

- PhD: I. Fierro Ulloa. "Development and analysis of a digital twin for monitoring, control and optimization applications in microalgae: the Microalgae Model", since September 2021, UniCA. Defended on October 29th, 2024 Supervisor: O. Bernard.
- PhD: A. Gharib. "Robust control of microalgae processes accounting for future meteorology", since September 2021. (UniCA, ITN Digitalgaesation). Defended on November 29th, 2024. Supervisors: O. Bernard (director) and W. Djema (co-director).
- PhD: D. Penaranda Sandoval. "Environmental impact assesment of technologically immature processes", Université Côte d'Azur (UniCA), since September 2021. Defended on March 15th, 2024. Supervisor: O. Bernard. Supervisor: O. Bernard.
- PhD in progress: R. Ranini. "Deep learning approaches for enhancing models in oceanography", UniCA, since 2022. Supervisors: L. Guidi and O. Bernard.
- PhD in progress: Pauline Mazel. "Modeling and control of cancer cell population dynamics", since October 2023. Supervisors: F. Grognard (director, Macbes) and W. Djema (co-director, Biocore).
- PhD in progress: Javier Innerarity Imizcoz. "Optimal bacterial resource allocation for metabolite production", since November 2023. Supervisors: Jean-Luc Gouzé (director, Macbes), Francis Mairet (co-director, Ifremer Nantes) and W. Djema (co-supervisor, Biocore).
- PhD in progress: Manon Pugnet. "Optimal Control of the competition within microbial communities", Université Côte d'Azur, since 2024. Supervisor: O. Bernard and W. Djema.

11.2.3 Juries

- O. Bernard was member of the Individual monitoring Committee of Alexandre PETTI (Mines ParisTech).
- F. Casagli participated to the Individual monitoring Committee of the Ph.D. Irene MARTíNEZ MENÉNDEZ, from the Doctoral School EDSEVAB n°458. Title of the thesis: "Digital twins for the optimization of bioprocesses", Thesis director: César Arturo ACEVES-LARA, Thesis co-director: TONDA Alberto.
- O. Bernard was reviewer of the PhD thesis of Alberto Saccardo, University of Padova.
- O. Bernard was president of the PhD jury of MA Leca "Development of innovative strategies for the valorization of methanization digestates via Spirulina cultivation " at University of Pau, June 11^{th}, 2024.
- O. Bernard was reviewer of the PhD thesis of Andriamahefasoa RAJAONISON "Environmental Life Cycle Assessment of time dependent microalgal-based energy production systems", PSL University (prepared at Mines ParisTech), directed by T. Ranchin and P. Lopez-Pérez, September 3^{rd}, 2024.
- O. Bernard participated to the PhD jury of D. Penaranda as PhD Director ("Extrapolation of the environmental impact of low TRL environmental processes: Application to microalgae-based processes") on March 15^{th}, 2024 (University of Nice Côte d'Azur).
- O. Bernard participated to the PhD jury of I. Fierro Ulloa. "Development and analysis of a digital twin for monitoring, control and optimization applications in microalgae: the Microalgae Model", Defended on October 29^{th}, 2024. Supervisor: O. Bernard.
- O. Bernard and W. Djema participated to the PhD jury of A. Gharib. "Robust control of microalgae processes accounting for future meteorology", UniCA. Defended on November 29^{th}, 2024. Supervisors: O. Bernard (director) and W. Djema (co-director).
- O. Bernard was jury member of the PhD thesis of Julien Lopez, "Search for bioactive compounds and study of the effect of nitrogen substrate on the metabolism of Tetraselmis suecica in biofilms", Sorbonne University, December 5^{th}, 2024.

11.3 Popularization

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

- O. Bernard contributed to the Inria website Digital technology and the oceans: towards a better understanding of marine ecosystems;
- O. Bernard was interviewed by Mediapart for an article "Study phytoplankton to better understand oceans";
- The TedX Cannes conference given by F. Casagli in September 2023 When AI reveals Wastewater's hidden treasures was published on YouTube (5100 views in 2024).

11.3.2 Participation in Live events

- F. Casagli, W. Djema and O. Bernard participated to the cinéscience TEDx evening ("TEDxCannes fait son cinéma") (cinema CINEPLANET Antibes) for discussing and commenting the projection of the Tedex Video from F. Casagli;
- O. Bernard gave public conferences on "Introduction of LCA" in Science for All 06 outreach presentations in Cagnes-sur-mer (March 15^{th}, 2024) and Beaulieu-sur-mer (March 21^{st}, 2024);
- O. Bernard gave a public conference on the potential of microalgae at Saint Laurent University for All, February 22^{nd} 2024.

11.3.3 Others science outreach relevant activities

- W. Djema served as an Inria messenger for the Tournée du Climat et de la Biodiversité during its stop at Parc Phoenix in Nice from May 16^{th} to 18^{th}, 2024.

12 Scientific production

12.1 Major publications

[1] C. Baroukh, R. Muñoz-Tamayo, J.-P. Steyer and O. Bernard. 'DRUM: A New Framework for Metabolic Modeling under Non-Balanced Growth. Application to the Carbon Metabolism of Unicellular Microalgae'. In: *PLoS ONE* 9.8 (Aug. 2014). e104499. DOI: 10.1371/journal.pone.0104499. URL: https://hal.inria.fr/hal-01097327 (cit. on p. 11).

[2] O. Bernard. 'Hurdles and challenges for modelling and control of microalgae for CO2 mitigation and biofuel production'. In: *Journal of Process Control* 21.10 (2011), pp. 1378–1389. DOI: 10.1016/j.jprocont.2011.07.012. URL: http://hal.inria.fr/hal-00848385 (cit. on p. 7).

[3] F. Casagli, F. Béline, E. Ficara and O. Bernard. 'Optimizing resource recovery from wastewater with algae-bacteria membrane reactors'. In: *Chemical Engineering Journal* 451 (Jan. 2023), p. 138488. DOI: 10.1016/j.cej.2022.138488. URL: https://inria.hal.science/hal-03932262 (cit. on p. 14).

[4] F. Casagli, S. Rossi, J.-P. Steyer, O. Bernard and E. Ficara. 'Balancing Microalgae and Nitrifiers for Wastewater Treatment: Can Inorganic Carbon Limitation Cause an Environmental Threat?' In: *Environmental Science and Technology* 55.6 (16th Mar. 2021), pp. 3940–3955. DOI: 10.1021/acs.est.0c05264. URL: https://hal.inrae.fr/hal-03219531 (cit. on p. 14).

[5] F. Casagli, G. Zuccaro, O. Bernard, J.-P. Steyer and E. Ficara. 'ALBA: a comprehensive growth model to optimize algae-bacteria wastewater treatment in raceway ponds'. In: *Water Research* 190 (Feb. 2021), p. 116734. DOI: 10.1016/j.watres.2020.116734. URL: https://inria.hal.science/hal-03142211 (cit. on p. 14).

[6] F. Grognard, P. Masci, E. Benoît and O. Bernard. 'Competition between phytoplankton and bacteria: exclusion and coexistence'. In: *Journal of Mathematical Biology* 70.5 (2015), pp. 959–1006. DOI: 10.1007/s00285-014-0783-x. URL: https://inria.hal.science/hal-00968182 (cit. on p. 9).

[7] F. Mazenc and O. Bernard. 'When is a Matrix of Dimension 3 Similar to a Metzler Matrix ? Application to Interval Observer Design'. In: *IEEE Transactions on Automatic Control* (27th Oct. 2021), pp. 1–1. DOI: 10.1109/TAC.2021.3123245. URL: https://inria.hal.science/hal-03533716 (cit. on p. 10).

12.2 Publications of the year

International journals

[8] D. Carecci, A. Catenacci, S. Rossi, F. Casagli, G. Ferretti, A. Leva and E. Ficara. 'A plant-wide modelling framework to describe microalgae growth on liquid digestate in agro-zootechnical biomethane plants'. In: *Chemical Engineering Journal* 485 (Apr. 2024), p. 149981. DOI: 10.1016/j.cej.2024.149981. URL: https://inria.hal.science/hal-04908856 (cit. on p. 15).

[9] O. Cherkaoui-Dekkaki, W. Djema, N. Raissi, J.-L. Gouzé and N. El Khattabi. 'Optimal control of waste recovery process'. In: *International Journal of Dynamics and Control* (2024). DOI: 10.1007/s40435-024-01484-7. URL: https://inria.hal.science/hal-04711930 (cit. on p. 15).

[10] Y. Gao, O. Bernard, A. Fanesi, P. Perré and F. Lopes. 'The effect of light intensity on microalgae biofilm structures and physiology under continuous illumination'. In: *Scientific Reports* 14.1 (11th Jan. 2024). DOI: 10.1038/s41598-023-50432-6. URL: https://hal.science/hal-04686136 (cit. on p. 11).

[11] A. Gharib, W. Djema, F. Casagli and O. Bernard. 'Adaptive temperature model for microalgae cultivation systems'. In: *Journal of Process Control* 141 (Sept. 2024), p. 103280. DOI: 10.1016/j.jprocont.2024.103280. URL: https://inria.hal.science/hal-04868166 (cit. on pp. 8, 12, 13).

[12] A. Gharib, W. Djema, P. M. Fernández, R. Chin-On, M. Janssen and O. Bernard. 'Validation of an Adaptive Temperature Model for Closed Microalgae Cultivation Systems'. In: *Algal Research - Biomass, Biofuels and Bioproducts* (6th Jan. 2025), p. 103838. DOI: 10.1016/j.algal.2024.103838. URL: https://inria.hal.science/hal-04868308. In press (cit. on pp. 8, 12, 13).

[13] J. Innerarity Imizcoz, W. Djema, F. Mairet and J.-L. Gouzé. 'Optimal resource allocation in micro-organisms under periodic nutrient fluctuations'. In: *Journal of Theoretical Biology* (2024). DOI: 10.1016/j.jtbi.2024.111953. URL: https://inria.hal.science/hal-04726319. In press (cit. on p. 16).

[14] D. Morgado, A. Fanesi, T. Martin, S. Tebbani, O. Bernard and F. Lopes. 'Exploring the dynamics of astaxanthin production in Haematococcus pluvialis biofilms using a rotating biofilm-based system'. In: *Biotechnology and Bioengineering* (1st Mar. 2024). DOI: 10.1002/bit.28624. URL: https://hal.science/hal-04388661 (cit. on p. 10).

[15] D. Morgado, A. Fanesi, T. Martin, S. Tebbani, O. Bernard and F. Lopes. 'Non-destructive monitoring of microalgae biofilms'. In: *Bioresource Technology* 398 (Apr. 2024), p. 130520. DOI: 10.1016/j.biortech.2024.130520. URL: https://hal.science/hal-04823672 (cit. on pp. 10, 11).

[16] R. Nordio, E. Rodríguez-Miranda, F. Casagli, A. Sánchez-Zurano, J. L. Guzmán and G. Acién. 'ABACO-2: a comprehensive model for microalgae-bacteria consortia validated outdoor at pilot-scale'. In: *Water Research* 248 (Jan. 2024), p. 120837. DOI: 10.1016/j.watres.2023.120837. URL: https://inria.hal.science/hal-04397215 (cit. on pp. 8, 14).

[17] B. A. Pessi and O. Bernard. 'Dynamical Metabolic Model for Optimizing Biotin-Regulated Lipid Production in Microalgae-Bacteria Symbiosis'. In: *IFAC-PapersOnLine* 58.14 (2024), pp. 151–156. DOI: 10.1016/j.ifacol.2024.08.329. URL: https://inria.hal.science/hal-04871726 (cit. on p. 11).

International peer-reviewed conferences

[18] R. Asswad, W. Djema, O. Bernard, J.-L. Gouzé and E. Cinquemani. 'Optimization of microalgae biosynthesis via controlled algal-bacterial symbiosis'. In: CDC 2024 - 63rd IEEE Conference on Decision and Control. Milan, Italy: IEEE, 10th Oct. 2024, pp. 1–6. URL: https://inria.hal.science/hal-04727571 (cit. on p. 16).

[19] O. Bernard, M. Bestard, T. Goudon, L. Meyer, S. Minjeaud, F. Noisette and B. Polizzi. 'Numerical schemes for mixture theory models with filling constraint: application to biofilm ecosystems'. In: *ESAIM: PROCEEDINGS AND SURVEYS*. CEMRACS 2022 - Transport in physics, biology and urban traffic. Vol. 77. Marseille, France, France: EDP Sciences, SMAI, 2024, pp. 249–266. DOI: 10.1051/proc/202477249. URL: https://hal.science/hal-04907848 (cit. on p. 11).

[20] O. Bernard, F. Casagli, B. Chachuat and F. Bezzo. 'Will machine learning (finally) contribute to the microalgae sector?' In: Algaeurope 2024. Athens, Greece, 10th Dec. 2024. URL: https://inria.hal.science/hal-04883580 (cit. on p. 13).

[21] F. Casagli, O. Bernard and J.-P. Steyer. 'Why modelling phototrophic systems?' In: 1st International Conference on Novel PhotoRefineries for Resource Recovery PHOTOREFINERIES 2024. Valladolid (Spain), Spain, 9th Sept. 2024. URL: https://inria.hal.science/hal-04883871 (cit. on p. 20).

[22] I. Fierro, B. Chachuat and O. Bernard. 'Optimal control of photobioreactor accounting for photoinhibition and photoacclimation'. In: ADCHEM 2024 - 12th IFAC Symposium on Advanced Control of Chemical Processes. Toronto (CA), Canada, 14th July 2024. URL: https://hal.science/hal-04672599 (cit. on p. 14).

[23] A. Gharib, W. Djema, P. M. Fernández, R. Chin-On, M. Janssen, F. Casagli and O. Bernard. 'A breakthrough in the temperature prediction of microalgal processes'. In: AlgaEurope 2024. Athen, Greece, 10th Dec. 2024. URL: https://inria.hal.science/hal-04883505 (cit. on p. 12).

[24] J. Innerarity Imizcoz, W. Djema, F. Mairet and J.-L. Gouzé. 'Optimal cell growth under periodic environment'. In: MTNS 2024 - 26th International Symposium on Mathematical Theory of Networks and Systems. Cambridge (Angleterre), United Kingdom, 19th Aug. 2024. URL: https://inria.hal.science/hal-04724783 (cit. on p. 16).

[25] P. Mazel, W. Djema and F. Grognard. 'Optimal control for a combination of cancer therapies in a model of cell competition'. In: CDC 2024 - 63rd IEEE Conference on Decision and Control. Milan, Italy, 16th Dec. 2024. URL: https://hal.science/hal-04721156 (cit. on p. 15).

Conferences without proceedings

[26] B. A. Pessi, G. Ribeiro Silva, C. Pompei, O. Bernard and F. Casagli. 'Extending algae-bacteria model to dynamically predict microbialcommunity composition during sanitary wastewater treatment'. In: The 1st International Conference on Novel Photorefineries for Resource Recovery. Valladolid, France, 9th Sept. 2024. URL: https://inria.hal.science/hal-04879351 (cit. on p. 13).

Scientific book chapters

[27] H. Bonnefond, C. Combe, J.-P. Cadoret, A. Sciandra and O. Bernard. 'Potential of Microalgae'. In: *Green Chemistry and Agro-food Industry: Towards a Sustainable Bioeconomy*. Springer Nature Switzerland, 23rd Apr. 2024, pp. 133–153. DOI: 10.1007/978-3-031-54188-9_6. URL: https://inria.hal.science/hal-04868598 (cit. on p. 9).

Doctoral dissertations and habilitation theses

[28] J. I. Fierro Ulloa. 'Modelling and control of photobioreactors under dynamic light regimes'. Université Côte d'Azur, 29th Oct. 2024. URL: https://theses.hal.science/tel-04779495 (cit. on pp. 11, 12, 14).

Reports & preprints

[29] A. Abreu, D. Johns, H. Biswas, A. Knoll, H. Bonnefond, X. Lin Xin, C. Bowler, T. Makhalanyane, J.-P. Cadoret, A. McQuatters-Gollop, R. Casati, B. Meyers, G. Cawley, R. Milo, F. Cumming Jane, A. Mitra, M. Dai, H. Ogata, C. de Vargas, I. Probert, C. Duarte, E. Rocke, P. Falkowski, A. Sow Bamol, C. Fernandez, M. Stulgis, K. Flynn, H. Takeyama, L. Guidi, P. Tett, G. Hallegraeff, M. Thukral, K. Hamasaki, R. Tiffer-Sotomayor, P.-A. Hoffmann, F. Vincent, D. Iudicone and S. Wang. *PLANKTON-BASED SOLUTIONS TO SUPPORT LIFE ON OUR PLANET: 4 CO2 Sink carbon and mitigate climate change*. UN Compact, 2024. URL: https://hal.science/hal-04867698.

12.3 Cited publications

[30] O. Bernard, L.-d. Lu and J. Salomon. 'Optimal periodic resource allocation in reactive dynamical systems: Application to microalgal production'. In: *International Journal of Robust and Nonlinear Control* 33.9 (June 2023), pp. 4989–5010. DOI: 10.1002/rnc.6171. URL: https://hal.science/hal-03170481 (cit. on p. 12).

[31] H. Bonnefond, C. Gaviard, E. Pruvost, A. Talec, A. Sciandra and O. Bernard. 'Strain optimization by continuous selection pressure: a focus on phycocyanin production'. In: *AlgaEurope 2023*. Prague, Czech Republic, Dec. 2023. URL: https://hal.science/hal-04275349 (cit. on p. 10).

[32] F. Casagli, F. Béline, E. Ficara and O. Bernard. 'Optimizing resource recovery from wastewater with algae-bacteria membrane reactors'. In: *Chemical Engineering Journal* 451 (Jan. 2023), p. 138488. DOI: 10.1016/j.cej.2022.138488. URL: https://inria.hal.science/hal-03932262 (cit. on pp. 14, 15).

[33] F. Casagli and O. Bernard. 'Hybrid modelling of algae-bacteria processes for resource recovery'. In: *AlgaEurope 2023*. EABA (European Algae Biomass Association). Prague, Czech Republic, Dec. 2023. URL: https://inria.hal.science/hal-04397640 (cit. on p. 14).

[34] F. Casagli and O. Bernard. 'Simulating biotechnological processes affected by meteorology: Application to algae–bacteria systems'. In: *Journal of Cleaner Production* 377 (Dec. 2022), p. 134190. DOI: 10.1016/j.jclepro.2022.134190. URL: https://inria.hal.science/hal-03935662 (cit. on pp. 12, 14).

[35] F. Casagli, M. Scalabrino, I. Fierro and O. Bernard. 'Hybrid Machine LearningMechanistic Modeling Of AlgaeBacteria Processes Under Various Climatologies'. In: *WATERMATEX 2023 - 11th IWA symposium on modelling and integrated assessment*. Quebec city, Canada, Sept. 2023. URL: https://inria.hal.science/hal-04397307 (cit. on p. 14).

[36] I. Fierro, W. Djema and O. Bernard. 'Optimal control of microalgae culture accounting for photoinhibition and light attenuation'. In: *IFAC World Congress 2023*. Yokohama, Japan, July 2023. URL: https://inria.hal.science/hal-04251736 (cit. on p. 10).

[37] J. I. Fierro U and O. Bernard. 'Neural ODEs for phytoplankton modeling'. In: *Journées scientifiques INRIA Chile*. Valparaiso (Chile), Chile, 2023. URL: https://inria.hal.science/hal-04390836 (cit. on p. 14).

[38] J. I. Fierro U and O. Bernard. 'Physic-informed neural networks for microalgae modeling'. In: *ECCE 14 & ECAB 7 - 14th European Congress of Chemical Engineering and 7th European Congress of Applied Biotechnology*. Berlin, Germany, Sept. 2023. URL: https://inria.hal.science/hal-04390804 (cit. on p. 14).

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[40] Y. Gao, J. I. Fierro U, P. Perré, F. Lopes and O. Bernard. 'Microalgal biofilm behavior under light/dark cycles'. In: *IFAC-PapersOnLine* 56.2 (2023), pp. 9739–9744. DOI: 10.1016/j.ifacol.2023.10.288. URL: https://inria.hal.science/hal-04371850 (cit. on p. 11).

[41] J.-L. Gouzé, A. Rapaport and Z. Hadj-Sadok. 'Interval observers for uncertain biological systems'. In: *Ecological modelling* 133 (2000), pp. 45–56. URL: http://dx.doi.org/10.1016/S0304-3800(00)00279-9 (cit. on pp. 6, 10).

[42] G. M. Grimaud, F. Mairet, A. Sciandra and O. Bernard. 'Modeling the temperature effect on the specific growth rate of phytoplankton: a review'. In: *Reviews in Environmental Science and Bio/technology* (Aug. 2017). DOI: 10.1007/s11157-017-9443-0. URL: https://inria.hal.science/hal-01576871 (cit. on p. 11).

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[44] J. A. Oviedo, R. Muñoz, A. Donoso-Bravo, O. Bernard, F. Casagli and D. Jeison. 'A half-century of research on microalgae-bacteria for wastewater treatment'. In: *Algal Research - Biomass, Biofuels and Bioproducts* 67 (Sept. 2022), p. 102828. DOI: 10.1016/j.algal.2022.102828. URL: https://inria.hal.science/hal-03935846 (cit. on pp. 14, 15).

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