Activity Report 2016

ExemplE

Exemple of RAweb

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME

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ExemplE

Keywords:

1. Members

Research Scientists

Jean-Luc Gouze [Team leader, Inria, Research Scientist, HdR]
Valentina Baldazzi [INRA, Research Scientist]
Olivier Bernard [Inria, Research Scientist, HdR]
Pierre Bernhard [Univ. Nice, Research Scientist]
Madalena Chaves [Inria, Research Scientist, HdR]
Frederic Grognard [Inria, Research Scientist]
Ludovic Mailleret [INRA, Research Scientist]
Antoine Sciandra [CNRS, Research Scientist, HdR]
Jean-Philippe Steyer [INRA, Research Scientist, HdR]
Suzanne Touzeau [INRA, Research Scientist]

Engineers

Martin Laviale [Inria, Engineers, until Aug 2016]
Christophe Vasseur [Inria, Engineers, until May 2016]

PhD Students

Sofia Almeida [Univ. Nice, PhD Student]
Nicolas Bajeux [Univ. Nice, PhD Student]
Margaux Caia [INRA, PhD Student]
Stefano Casagranda [Inria, PhD Student, granted by Conseil Régional PACA]
Lucie Chambon [Inria, PhD Student, from Oct 2016]
Charlotte Combe [___EMPLOYEUR???___, PhD Student, until Jun 2016]
David Demory [Inria, PhD Student]
Luis Gomes Pereira [Inria, PhD Student, from Oct 2016]
Ghjuvan Grimaud [___EMPLOYEUR???___, PhD Student, until Jun 2016]
Claudia Lopez Zazueta [___EMPLOYEUR???___, PhD Student]
Carlos Martinez Von Dossow [___EMPLOYEUR???___, PhD Student]
Elsa Rousseau [___EMPLOYEUR???___, PhD Student]

Post-Doctoral Fellows

Ivan Egorov [Inria, Post-Doctoral Fellow, from Jul 2016]
Natacha Go [INRA, Post-Doctoral Fellow, from May 2016]
Pierre-Olivier Lamare [Inria, Post-Doctoral Fellow]
Marjorie Alejandra Morales Arancibia [Inria, Post-Doctoral Fellow, from Sep 2016]
Camille Poignard [Inria, Post-Doctoral Fellow, until May 2016]

Administrative Assistant

Marie-Line Meirinho [Inria, Assistant]

Others

Anais Bacquet [Inria, ___PROFESSION???___, from Feb 2016 until Jul 2016]
Caroline Baroukh [INRA, ___PROFESSION???___]
Quentin Bechet [___EMPLOYEUR???___, ___PROFESSION???___]
Eric Benoit [Univ. la Rochelle, ___PROFESSION???___, HdR]
Hubert Bonnefond [___EMPLOYEUR???___, ___PROFESSION???___]
Steven Glenn Daniel [Inria, ___PROFESSION???___, from Feb 2016 until Jul 2016]
Frederic Fabre [INRA, ___PROFESSION???___]

Jerome Grenier [Inria, ___PROFESSION???___, from Apr 2016 until Oct 2016]
Christina Kozia [Inria, ___PROFESSION???___, from Apr 2016 until Sep 2016]
Francis Mairet [___EMPLOYEUR???___, ___PROFESSION???___]
Francesco Novellis [___EMPLOYEUR???___, ___PROFESSION???___]
Eric Pruvost [Univ. Paris VI, ___PROFESSION???___]
Sophie Rabouille [CNRS, ___PROFESSION???___]
Jeremie Roux [CNRS, ___PROFESSION???___]
Ambre Vaisseix [Inria, ___PROFESSION???___, from Apr 2016 until Aug 2016]

2. Overall Objectives

2.1. Introduction

BIOCORE is a joint research team between Inria (Centre of Sophia-Antipolis Méditerranée), INRA (ISA - Institut Sophia Agrobiotech and LBE - Laboratory of Environmental Biotechnology in Narbonne) and UPMC-CNRS (Oceanographic Laboratory of Villefranche-sur-mer - LOV, UMR 7093/ Université P.M. Curie, 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 cells or individuals and performing some tasks 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 laws to maintain a variable at a given level, 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).
- CO2 fixation by micro-algae, with the aim of capturing industrial CO2 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 for biological modeling and supervision of biological processes.

National, international and industrial relations

- Collaboration with IFREMER (Nantes), INRA (MISTEA Montpellier, BIOGER Grignon. IAM Nancy, Agrocampus Ouest, MaIAGE Jouy-en-en-Josas, BioEpAR Nantes), CIRAD Montpellier, Centre d'Océanologie de Marseille, LOCEAN (Paris), GIPSA Grenoble, IBIS, BANG, ANGE and MODEMIC Inria teams.
- Participation in the French groups ModStatSAP (Modélisation et Statistique en SantÃ© des Animaux et des Plantes), GDR Invasions Biologiques and PROBBE (Processus biologiques et bioinspirés pour l'Ã©nergie).
- Université Catholique de Louvain (Belgium), UniversitÃ© de Mons (Belgium), University of Stuttgart (Germany), Rutgers University (USA), MacMaster University (Canada), University Ben Gurion (Israel), Imperial College (United-Kingdom), Massey University (New Zealand), Universidad Tecnica Federico Santa Maria and Universidad de Chile (Chile), Roslin Institute / University of Edinburgh (UK).
- Participation to national programmes: ANR *Blanc* projects Gemco and FunFit, ANR *BioME* projects Facteur 4 and Purple Sun, ANR projects Funfit and Phycover, *Projet d'Investissement d'Avenir* RESET, UMT Fiorimed, and Labex SIGNALIFE.

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 human. 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, 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 (eg. 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 (eg. 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 . 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 (eg., 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.

3.3. LaTeX Test Page

Exemples d'équations :

- Equation en mode "mathématique" :

$y = x^2$

- Equation en environnement "equation" :

$$P\begin{pmatrix}\theta_1\\ \vdots\\ \theta_r\end{pmatrix} = Q + R, \tag{1}$$

- Equation en environnement "displaymath" :

$$\sum_0^\infty y = x^4$$

- Autre exemple :

$$\forall f \in C^\infty\left(\left[-\frac{T}{2};\frac{T}{2}\right]\right), \forall t \in \left[-\frac{T}{2};\frac{T}{2}\right], f(\tau) = \sum_{k=-\infty}^{+\infty} e^{2i\pi\frac{k}{T}t} \times \underbrace{\frac{1}{T}\int_{-\frac{T}{2}}^{\frac{T}{2}} f(t)e^{-2i\pi\frac{k}{T}t}dt}_{a_k=\widetilde{f}\left(\nu=\frac{k}{T}\right)}$$

Exemple de caractères spéciaux :
math pi : π
lettres : æ Æ à À â Â ä Ä ç Ç é É è È ê Ê ë Ë î Î ï Ï ô Ô ö Ö ù Ù û Û ü Ü ÿ þ Þ

Exemples d'images :

- Image en jpeg : voir image 1

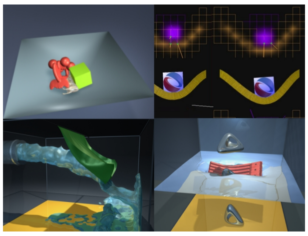

Figure 1. An example of a jpeg image

- Image en eps : voir figure 2
- Image en pdf : voir image 3

4. Application Domains

4.1. Domain 1

5. Highlights of the Year

5.1. Highlights of the Year

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Figure 2. An example of an eps file

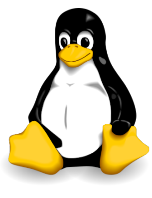

Figure 3. An example of a pdf file

5.1.1. Awards

6. New Software and Platforms

6.1. HeliosAlgae

- Contact: Bernard Olivier
- URL: ___ URL ??? : à indiquer dans BIL https://bil.inria.fr ___

6.2. In@lgae

KEYWORDS: Simulation - Microalgae system - Productivity
FUNCTIONAL DESCRIPTION

In@lgae is a simulation platform. Its objective is to simulate the productivity of a microalgae production system, taking into account both the process type and its location and time of the year.

- Participants: Etienne Delclaux, Francis Mairet, Quentin Bechet and Olivier Bernard
- Contact: Olivier Bernard
- URL: ___ URL ??? : à indiquer dans BIL https://bil.inria.fr ___

6.3. Odin

KEYWORDS: Bioinformatics - Biotechnology
SCIENTIFIC DESCRIPTION

This C++ application enables researchers and industrials to easily develop and deploy advanced control algorithms through the use of a Scilab interpreter. It also contains a Scilab-based process simulator which can be harnessed for experimentation and training purposes. ODIN is primarily developed in the C++ programming language and uses CORBA to define component interfaces and provide component isolation. ODIN is a distributed platform, enabling remote monitoring of the controlled processes as well as remote data acquisition.It is very 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 through explicit management of confidence indexes.
FUNCTIONAL DESCRIPTION

ODIN is a software framework for bioprocess control and supervision. It also contains a Scilab-based process simulator which can be harnessed for experimentation and training purposes. ODIN is a distributed platform, enabling remote monitoring of the controlled processes as well as remote data acquisition.It is very 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 through explicit management of confidence indexes.

- Participants: Melaine Gautier, Florian Guenn, Fabien Dilet, Olivier Calabro, Romain Primet, Serigne Sow, Olivier Bernard, Mathieu Lacage and Francesco Novellis
- Contact: Olivier Bernard
- URL: https://team.inria.fr/biocore/software/odin/

6.4. SimFast

- Contact: Olivier Bernard
- URL: ___ URL ??? : à indiquer dans BIL https://bil.inria.fr ___

6.5. Platforms

6.5.1. Platform A

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6.5.2. Platform B

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7. New Results

7.1. New result 1

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

8.2. Bilateral Grants with Industry

9. Partnerships and Cooperations

9.1. Regional Initiatives

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9.2. National Initiatives

9.2.1. National programmes

- **ANR-Purple Sun:** The objective of this project (ANR-13-BIME-004) is to study and optimize a new concept consisting in coupling the production of microalgae with photovoltaic panels. The main idea is to derive the excess of light energy to PV electricity production, in order to reduce the phenomena of photoinhibition and overwarming both reducing microalgal productivity.
- **ANR-Facteur 4:** The objective of this project to produce non OGM strain of microalgae with enhanced performance. BIOCORE is involved in the directed selection of microalgae with interesting properties from an industrial point of view. The theory of competition is used to give a competitive advantage to some species. This competitive advantage can be provided by an online closed loop controller.
- **ANR-Phycover:** The overall objective of the PHYCOVER project is to identify a modular wastewater treatment process for the production of biogas. The method combines three modules. First, a high-rate algal pond is dedicated to the treatment of municipal wastewater. Then, an anaerobic digester capable of co- digesting biomass products (and others organic matter resources) to significantly reduce biological and chemical contaminants while producing a sustainable energy as biogas is analysed. A final module transforms the residual carbon, nitrogen and phosphorus into high-value microalgae dedicated to aquaculture and green chemistry.
- **ANR-FunFit:** The objective of this project (2013-2017) is to develop a trait-based approach linking individual fitness of fungal plant pathogens to ecological strategies. The idea is to derive eco-epidemiological strategies from fitness optimization in colonized environments and during colonization, as well as understanding the coexistence of sibling species. This project is co-coordinated by F. Grognard.
- **ANR-TripTic:** The objective of this project (2014-2018) is to document the biological diversity in the genus of the minute wasps *Trichogramma*, and to study the behavioral and populational traits relevant to their use in biological control programs.

- **ANR-GESTER:** “Management of crop resistances to diseases in agricultural landscapes as a response to new constraints on pesticide use”, ANR Agrobiosphère, 2011–2016. This project aims at producing allocation scenarios of resistant varieties at the scale of cultivated landscapes, that will allow to limit disease development while ensuring sustainable efficiency of genetic resistances. BIOCORE participates in this project via MaIAGE, INRA Jouy-en-Josas.
- **ANR-MIHMES:** “Multi-scale modelling, from animal Intra-Host to Metapopulation, of mechanisms of pathogen spread to Evaluate control Strategies”, ANR – Investissement d’avenir, action Bioinformatique (ANR-10-BINF-07) & Fond Européen de Développement Régional des Pays-de-la-Loire (FEDER), 2012–2017. This project aims at producing scientific knowledge and methods for the management of endemic infectious animal diseases and veterinary public health risks. BIOCORE participates in this project via MaIAGE, INRA Jouy-en-Josas.
- **RESET:** The objective of this project is to control the growth of *E. coli* cells in a precise way, by arresting and restarting the gene expression machinery of the bacteria in an efficient manner directed at improving product yield and productivity. RESET is an “Investissements d’Avenir” project in Bioinformatics (managed by ANR) and it is coordinated by H. de Jong (Ibis, Inria)
- **SIGNALIFE:** Biocore is part of this Labex (scientific cluster of excellence) whose objective is to build a network for innovation on Signal Transduction Pathways in life Sciences, and is hosted by the Université Nice Sophia Antipolis.
- **OPTIBIO:** This project is devoted to the analysis of optimal control problems related to bioprocesses. The project is funded by Programme Gaspard Monge pour L’Optimisation et la Recherche Opérationnelle and coordinated by T. Bayen (U. Montpellier 2).
- **UMT FIORIMED:** FioriMed is a Mixed Technology Unit created in January 2015 to strengthen the production and dissemination of innovation to the benefit of ornamental horticulture. Horticultural greenhouses are seen as a "laboratory" for the actual implementation of agroecology concepts with the possibility of generic outcomes being transfered to other production systems. The main partners of UMT FioriMed are ASTREDHOR (National Institute of Horticulture) and the ISA Joint Research Unit of INRA-CNRS-Univ. Nice.

9.2.2. Inria funding

- **Inria Project Lab-Algae** *in silico***:** The Algae in silico Inria Project Lab, funded by Inria and coordinated by O. Bernard, focuses on the expertise and knowledge of biologists, applied mathematician and computer scientists to propose an innovative numerical model of microalgal culturing devices. The latest developments in metabolic modelling, hydrodynamic modelling and process control are joined to propose a new generation of advanced simulators in a realistic outdoor environment. The project gathers 5 Inria project teams and 3 external teams.

9.2.3. INRA funding

- **Take Control:** This project, “Deployment strategies of plant quantitative resistance to take control of plant pathogen evolution,” is funded by the PRESUME call of the SMAcH INRA metaprogram (Sustainable Management of Crop Health). BIOCORE is a partner together with INRA PACA (Sophia Antipolis and Avignon) and INRA Toulouse (2013-2016). This project provides the major part of the funding for the experiments held for Elsa Rousseau’s thesis.
- **K-Masstec:** “Knowledge-driven design of management strategies for stem canker specific resistance genes”, INRA Metaprogramme SMaCH, PRESUME action, 2013–2016. The project aims at developing efficient strategies for the deployment of genetic resistance in the field, based on knowledge issued from the understanding of the molecular interaction between distinct avirulence genes, and mainly the discovery of non-conventional gene-for-gene interactions.

9.2.4. Networks

- **GDR Invasions Biologiques:** The objectives of this GDR are to encourage multidisciplinary research approaches on invasion biology. It has five different thematic axes: 1) invasion biology scenarios, 2) biological invasions and ecosystem functioning, 3) environmental impact of invasive species, 4) modeling biological invasions, 5) socio-economics of invasion biology. L. Mailleret is a member of the scientific comittee of the GDR .
- **ModStatSAP:** The objective of this INRA network is to federate researchers in applied mathematics and statistics and to promote mathematical and statistical modelling studies in crop and animal health. S. Touzeau is a member of the scientific committee.
- **Seminar:** BIOCORE organizes a regular seminar “Modeling and control of ecosystems” at the station zoologique of Villefranche-sur-Mer, at INRA-ISA or at Inria.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.2. Collaborations in European Programs, Except FP7 & H2020

9.3.3. Collaborations with Major European Organizations

9.4. International Initiatives

9.4.1. Inria International Labs

GREENCORE

Associate Team involved in the International Lab:

9.4.1.1. GREENCORE

Title: Modelling and control for energy producing bioprocesses

International Partner (Institution - Laboratory - Researcher):

(Chile) - DEPARTMENT??? - PERSON???

Start year: 2014

See also: https://team.inria.fr/eagreencore/

The worldwide increasing energy needs together with the ongoing demand for CO2 neutral fuels represent a renewed strong driving force for the production of energy derived from biological resources. In this scenario, the culture of oleaginous microalgae for biofuel and the anaerobic digestion to turn wastes into methane may offer an appealing solution. The main objective of our proposal is to join our expertise and tools, regarding these bioprocesses, in order to implement models and control strategies aiming to manage and finally optimize these key bioprocesses of industrial importance. By joining our expertises and experimental set-up, we want to demonstrate that closed loop control laws can significantly increase the productivity, ensure the bioprocess stability and decrease the environmental footprint of these systems. This project gathers experts in control theory and optimization (BIOCORE, UTFSM) together with experts in bioprocesses (PUCV and UFRO) and software development (CIRIC).

9.4.1.2. Other IIL projects

9.4.2. Inria Associate Teams Not Involved in an Inria International Labs

9.4.3. Inria International Partners

9.4.3.1. Declared Inria International Partners

9.4.3.2. Informal International Partners

9.4.4. Participation in Other International Programs

9.5. International Research Visitors

9.5.1. Visits of International Scientists

9.5.1.1. Internships

9.5.2. Visits to International Teams

9.5.2.1. Sabbatical programme

9.5.2.2. Explorer programme

9.5.2.3. Research Stays Abroad

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

10.1.1.2. Member of the Organizing Committees

10.1.2. Scientific Events Selection

10.1.2.1. Chair of Conference Program Committees

10.1.2.2. Member of the Conference Program Committees

10.1.2.3. Reviewer

10.1.3. Journal

10.1.3.1. Member of the Editorial Boards

10.1.3.2. Reviewer - Reviewing Activities

10.1.4. Invited Talks

10.1.5. Leadership within the Scientific Community

10.1.6. Scientific Expertise

10.1.7. Research Administration

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

10.2.2. Supervision

10.2.3. Juries

10.3. Popularization

11. Bibliography

Publications of the year

Scientific Books (or Scientific Book chapters)

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