

2021-03625 - PhD Position F/M Development of control strategies for synthetic microbial consortia (funded PhD offer)

Level of qualifications required : Graduate degree or equivalent
Fonction : PhD Position

About the research centre or Inria department

Grenoble Rhône-Alpes Research Center groups together a few less than 650 people in 37 research teams and 8 research support departments.

Staff is localized on 5 campuses in Grenoble and Lyon, in close collaboration with labs, research and higher education institutions in Grenoble and Lyon, but also with the economic players in these areas.

Present in the fields of software, high-performance computing, Internet of things, image and data, but also simulation in oceanography and biology, it participates at the best level of international scientific achievements and collaborations in both Europe and the rest of the world.

Context

The project is in the context of the ANR project Ctrl-AB (<https://anr.fr/Projet-ANR-20-CE45-0014>). It is focused on theoretical and applied control in a highly interdisciplinary context. Based in Grenoble within the Inria project-team IBIS, it will be co-supervised by Eugenio Cinquemani (IBIS, <https://team.inria.fr/ibis/eugenio-cinquemani/>) and Jean-Luc Gouzé (BIOCORE, Inria Sophia-Antipolis, <http://www.sop.inria.fr/members/Jean-Luc.Gouze/JLGouze-fra.html>), both members of the ANR project CtrlAB. It will profit from the control-theoretic and systems-biology expertise of IBIS and BIOCORE, as well as from the interaction with other experimental partners of CtrlAB.

Assignment

In nature, microorganisms mostly occur in communities of different competing and/or cooperating species [We,Ko]. These interactions represent a challenge that goes beyond the characterization of single species, and a great opportunity for applications. Current experimental monitoring and bioengineering capabilities lay the ground not only for the quantitative understanding of natural communities, but also for the synthesis of artificial consortia and their control for e.g. waste treatment and biofuel production [Sh]. At present, full exploitation of microbial consortia presents great challenges ranging from appropriate modelling methods to design and deployment of real-time control systems [Zo].

This funded Ph.D. proposal concerns the analysis, development and application of feedback control approaches for microbial communities. The project is in the context of the ANR project Ctrl-AB, whose objective is the design, realization and automated control of an algal-bacterial consortium for the optimized synthesis of target proteins in lab-scale bioreactors [Ma,Bar]. With reference to mathematical (ODE-type, nonlinear) models describing the biosynthesis process resulting from this algal-bacterial consortium, the Ph.D. project will explore state-of-the-art feedback control approaches [Ram,Do,Bas,Fi] as well as novel directions in the control of microbial communities [Fo,Ca,Tr] by a combination of theoretical analysis and computer simulation.

In more detail, the Ph.D. project will be articulated along the following points:

1. Familiarization with existing literature on biochemical process control, and on the dynamical modelling of microbial communities
2. Controllability analysis of the algal-bacterial consortium models
3. Development, analysis and simulation of state-of-the-art feedback control methods for several algal-bacterial consortium control problems (regulation, real-time maximization of productivity, ...)
4. Exploration of data-driven control techniques and performance comparison with the approaches in 3.
5. Application to in-vivo experiments on automated platforms

[We] S.A. West, G.A. Cooper, "Division of labour in microorganisms: an evolutionary perspective". *Nature Rev Microbiol*, 14(11):716-723, 2016

[Sh] J Shong et al., "Towards synthetic microbial consortia for bioprocessing". *Curr Opin Biotechnol*, 23(5):798-802, 2012

[Ko] A Konopka et al., "Dynamics in microbial communities: unraveling mechanisms to identify principles". *ISME J*, 9(7):1488-1495, 2015.

[Zo] A.R. Zomorodi, D. Segrè, "Synthetic ecology of microbes: mathematical models and applications". *J Mol Biol*, 428(5):837-861, 2016

[Bar] C. Baroukh et al., "DRUM: A New Framework for Metabolic Modeling under Non-Balanced Growth. Application to the Carbon Metabolism of Unicellular Microalgae". *PLoS ONE*, 9(8):1-15, 2014.

[Ram] S. Ramaswamy et al., "Control of a continuous bioreactor using model predictive control". *Process Biochem*, 40(8):2763 - 2770, 2005.

General Information

- **Theme/Domain :** Optimization and control of dynamic systems
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city :** Montbonnot
- **Inria Center :** CRI Grenoble - Rhône-Alpes
- **Starting date :** 2021-10-01
- **Duration of contract :** 3 years
- **Deadline to apply :** 2022-03-31

Contacts

- **Inria Team :** IBIS
- **PhD Supervisor :**
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About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and entrepreneurial projects that have a worldwide impact.

The keys to success

Curiosity, motivation, initiative-taking, proactivity, propensity to team-work.

Strong interest in biological/biotechnological applications of systems and control theory.

Instruction to apply

Defence Security :

This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST). Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy :

As part of its diversity policy, all Inria positions are accessible to people with disabilities.

Warning : you must enter your e-mail address in order to save your application to Inria. Applications must be submitted online on the Inria website. Processing of applications sent from other channels is not guaranteed.

[Do] D. Dochain et al., "Extremum seeking control and its application to process and reaction systems: A survey". *Math Comput Simulat*, 82(3):369 – 380, 2011

[Bas] G. Bastin, D. Dochain. *On-line Estimation and Adaptive Control of Bioreactors*. Elsevier, 1990

[Fi] D. Fiore et al., "Feedback ratiometric control of two microbial populations in a single chemostat". *bioRxiv*, 2020. doi: <https://doi.org/10.1101/2021.03.05.434159>

[Tr] N.J. Treloar et al., "Deep reinforcement learning for the control of microbial co-cultures in bioreactors". *PLoS Comput Biol*, 16(4):e1007783, 2020

[Ca] L. Campestrini et al., "Data-driven model reference control design by prediction error identification". *J Franklin Inst*, 354(6):2628 – 2647, 2017

[Fo] S. Formentin et al., "Direct learning of LPV controllers from data". *Automatica*, 65:98 – 110, 2016.

Main activities

The main activities are those typical of interdisciplinary research. They include: literature reading, scientific development, programming and simulation, data processing, reporting and presentation, paper and thesis manuscript writing, collaboration with the team, the supervisors and other scientific partners, participation to conferences and workshops. Course-taking and teaching activities in accordance with doctoral school rules.

Skills

The interested candidate should have a solid preparation in mathematical analysis (dynamical systems) and control theory, as well as familiarity with or strong interest in biology/biotechnological applications. Some knowledge of machine learning is a plus. He/she will be working in a collaborative and international environment, and is thus expected to be open to scientific interaction, and to be proficient in English.

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage