

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

Niveau de diplôme exigé : Bac + 5 ou équivalent  
Fonction : Doctorant

### A propos du centre ou de la direction fonctionnelle

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.

### Contexte et atouts du poste

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/bis/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.

### Mission confiée

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.

[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

### Informations générales

- **Thème/Domaine** : Optimisation et contrôle de systèmes dynamiques  
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Ville** : Montbonnot
- **Centre Inria** : CRI Grenoble - Rhône-Alpes
- **Date de prise de fonction souhaitée** : 2021-10-01
- **Durée de contrat** : 3 ans
- **Date limite pour postuler** : 2022-03-31

### Contacts

- **Equipe Inria** : IBIS
- **Directeur de thèse** :  
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### A propos d'Inria

Inria est l'institut national de recherche dédié aux sciences et technologies du numérique. Il emploie 2600 personnes. Ses 200 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3500 scientifiques pour relever les défis du numérique, souvent à l'interface d'autres disciplines. L'institut fait appel à de nombreux talents dans plus d'une quarantaine de métiers différents. 900 personnels d'appui à la recherche et à l'innovation contribuent à faire émerger et grandir des projets scientifiques ou entrepreneuriaux qui impactent le monde. Inria travaille avec de nombreuses entreprises et a accompagné la création de plus de 180 start-up. L'institut s'efforce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

### L'essentiel pour réussir

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

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

### Consignes pour postuler

#### Sécurité défense :

Ce poste est susceptible d'être affecté dans une zone à régime restrictif (ZRR), telle que définie dans le décret n°2011-1425 relatif à la protection du potentiel scientifique et technique de la nation (PPST). L'autorisation d'accès à une zone est délivrée par le chef d'établissement, après avis ministériel favorable, tel que défini dans l'arrêté du 03 juillet 2012, relatif à la PPST. Un avis ministériel défavorable pour un poste affecté dans une ZRR aurait pour conséquence l'annulation du recrutement.

#### Politique de recrutement :

Dans le cadre de sa politique diversité, tous les postes Inria sont accessibles aux personnes en situation de handicap.

**Attention**: Les candidatures doivent être déposées en ligne sur le site Inria. Le traitement des candidatures adressées par d'autres canaux n'est pas garanti.

[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.

## Principales activités

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.

## Compétences

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.

## Avantages

- 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