Offer #2025-08964

PhD Position F/M Development and validation of small-scale models of metabolite production in bacteria

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : PhD Position

Level of experience : Recently graduated

About the research centre or Inria department

The Centre Inria de l'Université de Grenoble groups together almost 600 people in 22 research teams and 7 research support departments.

Staff is present on three campuses in Grenoble, in close collaboration with other research and higher education institutions (Université Grenoble Alpes, CNRS, CEA, INRAE, …), but also with key economic players in the area.

The Centre Inria de l'Université Grenoble Alpe is active in the fields of high-performance computing, verification and embedded systems, modeling of the environment at multiple levels, and data science and artificial intelligence. The center is a top-level scientific institute with an extensive network of international collaborations in Europe and the rest of the world.

Context

The PhD project will be carried out in the project-team MICROCOSME at the Centre Inria de l'Université de Grenoble Alpes and the Laboratoire Interdisciplinaire de Physique (LIPhy, CNRS/UGA) under the joint supervision of Hidde de Jong (

https://team.inria.fr/microcosme/hidde-de-jong/) and Noël Scaramozzino (https://liphy.univ-grenoble-alpes.fr/fr/recherche/equipes/biop-fluctuations-regulations-et-evolution-systemes-vivants) within the framework of the project MuSiHC supported by the PEPR B-BEST (https://anr.fr/en/france-2030/call-for-proposals-details/call/pepr-b-best-biomasses-biotechnologies-et-technologies-durables-pour-la-chimie-et-les-carburants-1/). MICROCOSME and LIPhy provide an interdisciplinary research environment fostering close collaborative interactions between applied mathematicians, microbiologists, computer scientists, control engineers, and biophysicists.

Assignment

The project MUlti-SIze Hybrid Cell Models (MuSiHC) aims at developing novel hybrid approaches to the modeling of cells and bioreactors for the production of added-value compounds. In particular, the project will develop a toolkit of hybrid models of different sizes, combining a mechanistic description with AI/ML components [1], to obtain more reliable cell and bioreactor simulations. As a proof of concept, the project will focus on *Escherichia coli* as a platform for the bioproduction of 1,3-propanediol (1,3-PDO), a high-value compound with vast applications in the chemical industry.

The proposed PhD project is concerned with the development of a small-scale, dynamic models [2,3] for optimizing the production of 1,3-PDO by *E. coli*, involving such tasks as model formulation and reduction, running mini-bioreactor experiments for model calibration, using the models to identify conditions for optimal metabolite production, and the experimental test of these conditions. The PhD project involves active collaboration with other MuSiHC partners at INRAE (Jean-Loup Faulon, Wolfram Liebermeister) and Toulouse Biotechnology Institute (César Arturo Aceves Lara). Beyond the specific application of MuSiHC, the project aims at identifying general principles for the development and validation of small-scale models of biotechnological production systems.

[1] Faure, L., Mollet, B., Liebermeister, W., & Faulon, J. L. (2023). A neural-mechanistic hybrid approach improving the predictive power of genome-scale metabolic models. *Nature Communications*, 14(1):4669. https://doi.org/10.1038/s41467-023-40380-0

[2] Baldazzi, V., Ropers, D., Gouzé, J. L., Gedeon, T., & de Jong, H. (2023). Resource allocation accounts for the large variability of rate-yield phenotypes across bacterial strains. *eLife*, 12:e79815. https://doi.org/10.7554/eLife.79815

[3] Wortel, M. T., Noor, E., Ferris, M., Bruggeman, F. J., & Liebermeister, W. (2018). Metabolic enzyme cost explains variable trade-offs between microbial growth rate and yield. *PLoS Computational Biology*, 14(2):e1006010. https://doi.org/10.1371/journal.pcbi.1006010

Main activities

The PhD project is an interdisciplinary project involving both the development of mathematical models describing the biological system and experimental work to calibrate and validate the models:

- Reduction of a medium-scale, kinetic model to a small-scale, whole-cell model of the production of 1,3-propanediol (1,3-PDO) by *Escherichia coli*, using previously developed reduction methods and taking inspiration from existing small-scale resource allocation models.
- Performance of experiments with selected *E. coli* strains on an in-house mini-bioreactor platform to obtain data (growth, gene expression, metabolite concentrations) for the calibration of the model.
- Use a combination of optimization and simulation approaches to identify conditions maximizing 1,3-PDO production.
- Validation of the predicted optimal operating conditions by performing the corresponding mini-bioreactor experiments, including the quantification of 1,3-PDO production.

Skills

Interested candidates are ideally expected to have some experience with the mathematical modelling of biological systems and/or laboratory work in microbiology, but we are open to consider students from a range of fields (microbiology, mathematical biology, ecology, biophysics, …) with good scholarly results and motivated by interdisciplinary research.

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 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

Remuneration

2200 gross salary/month

General Information

- **Theme/Domain :** Modeling and Control for Life Sciences
  Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city :** Montbonnot
- **Inria Center :** Centre Inria de l'Université Grenoble Alpes
- **Starting date :** 2025-10-01
- **Duration of contract :** 3 years
- **Deadline to apply :** 2025-09-30

Contacts

- **Inria Team :** MICROCOSME
- **PhD Supervisor :**
  De Jong Hidde / hidde.de-jong@inria.fr

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

The candidate is expected to be motivated by problems in the life sciences that cut across different scientific fields and to have the communicative skills to work in an international environment with colleagues from different educational backgrounds.

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.

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.