Offre n°2025-08964

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

Type de contrat : Fixed-term contract

Niveau de diplôme exigé : Graduate degree or equivalent

Fonction : PhD Position

Niveau d'expérience souhaité : Recently graduated

A propos du centre ou de la direction fonctionnelle

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.

Contexte et atouts du poste

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.

Mission confiée

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

Principales activités

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.

Compétences

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.

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 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

Rémunération

2200 gross salary/month

Informations générales

- **Thème/Domaine :** Modeling and Control for Life Sciences
  Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Ville :** Montbonnot
- **Centre Inria :** Centre Inria de l'Université Grenoble Alpes
- **Date de prise de fonction souhaitée :** 2025-10-01
- **Durée de contrat :** 3 years
- **Date limite pour postuler :** 2025-09-30

Contacts

- **Équipe Inria :** MICROCOSME
- **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 215 équipes-projets agiles, en général communes avec des partenaires académiques, impliquent plus de 3900 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 200 start-up. L'institut s'e?orce ainsi de répondre aux enjeux de la transformation numérique de la science, de la société et de l'économie.

L'essentiel pour réussir

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.

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.

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.