



Offer #2021-03660

Post-Doctoral Research Visit F/M Statistical Learning of the Intestinal Microbiota Metabolism in Space and Time: Metamodeling for metabolic and PDE models coupling

Contract type : Fixed-term contract

Level of qualifications required : PhD or equivalent

Fonction : Post-Doctoral Research Visit

About the research centre or Inria department

The study of biology combines studies of forms (diversity) and modelling of processes (functional or evolutionary). Pleiade addresses the dual challenge of rapidly measuring relevant dissimilarities between biological objects and exploring the relationships between trait diversity and functional diversity at multiple scales. We develop algorithms, models, and software frameworks for applications in ecology, evolution and biotechnology.

Context

The position is funded by Inria and is part of the [Inria Exploratory Action](#) SLIMMEST: Statistical Learning of the Intestinal Microbiota Metabolism in Space and Time. This project consists in **two postdoc positions**: one scientist with a systems biology background, and a second with an applied mathematical background. Both scientists will work in close collaboration on an exciting project aiming at building a spatio-temporal numerical model of the gut microbiota. This particular offer concerns the **applied mathematician profile**.

The main objective of the SLIMMEST project is to resolve a numerical bottleneck in **spatio-temporal modeling of microbiotas**: the **coupling between microbe-scale metabolic models with community-scale dynamics described with PDE models**. The recruited person will develop **machine learning technics** to build approximations of complex metabolic models **to be used as a source function of a PDE model of the gut microbiota**. The candidate will work in close collaboration with the other postdoc providing expertise in system biology, microbial metabolism, and community-wide metabolic network modeling.

The two recruited candidates will be members of the Pleiade team, a joint research group between Inria and [INRAE](#), in the beautiful city of **Bordeaux**. [Pleiade](#) is an **interdisciplinary group** at the frontier of **computer science, mathematics, bioinformatics and biology**. One of our main research interests is to develop and validate new computational and numerical models for microbial ecology, that we dedicate to better understand the complex interactions occurring in complex communities of microorganisms known as microbiotas.

Assignment

Assignments:

The **dynamics of a microbial community** is driven by the metabolism of its microorganisms, the interactions between those microorganisms, and spatio-temporal interactions between them and the environment. Mathematical and computational models of such dynamics are crucial to **build mechanistic hypotheses of the biological observations, as well as predict the evolution of the ecosystems, and actions to lead ecosystems in a desired state**. SLIMMEST will combine logic programming and metamodeling of metabolism in a scalable framework applied to communities of the gut microbiota.

This position is dedicated to the application of a **machine learning method** (RKHS metamodeling) to approximate metabolic quantitative models of microbial metabolism, known as FBA models (Orth et al.). The main goal is to provide **very fast and accurate approximations of metabolic model outputs** to be used as a source function of a PDE model of the gut microbiota. The idea is to adapt existing RKHS metamodeling methods in the context of metabolic modeling. Several options will be studied to improve the speed and quality of metamodel computation, including dimension reduction, HPC methods and incorporation of biological knowledge, in close collaboration with the other postdoc of the SLIMMEST project. After learning of the metabolic models, a PDE model of a simplified murine gut microbiota (Lagkouvardos et al.) will be developed and analysed in collaboration with the second postdoc.

For a better knowledge of the proposed research subject:

- Arnaud Belcour et al. « Metage2Metabo, microbiota-scale metabolic complementarity for the identification of key species ». In : eLife 9 (2020), e61968. doi : 10.7554/elife.61968.
- Seth R Bordenstein et Kevin R Theis. « Host biology in light of the microbiome : ten principles of holobionts and hologenomes ». In : PLoS Biol 13.8 (2015), e1002226.
- Oliver Ebenhoeh, Thomas Handorf et Reinhart Heinrich. « Structural analysis of expanding metabolic networks. » In : Genome informatics. International Conference on Genome Informatics 15.1 (2004), p. 35-45. issn : 0919-9454.
- Cl  mence Frioux, Simon M Dittami et Anne Siegel. « Using automated reasoning to explore the metabolism of unconventional organisms : a first step to explore host-microbial interactions ». In : Biochemical Society Transactions 48.3 (2020), p. 901-913. issn : 0300-5127. doi : 10.1042/bst20190667.
- Simon Labarthe et al. « A mathematical model to investigate the key drivers of the biogeography of the colon microbiota ». In : Journal of theoretical biology 462 (2019), p. 552-581.
- Ilias Lagkovidatos et al. « The Mouse Intestinal Bacterial Collection (miBC) provides host-specific insight into cultured diversity and functional potential of the gut microbiota ». In : Nature microbiology 1.10 (2016), p. 1-15.
- Orth, J. D., Thiele, I., & Palsson, B. O. (2010). « What is flux balance analysis? ». Nature biotechnology, 28(3), 245-248.
- Alberto Noronha et al. « The Virtual Metabolic Human database : integrating human and gut microbiome metabolism with nutrition and disease ». In : Nucleic Acids Research 47.D1 (2018), p. D614- D624. issn : 0305-1048. doi : 10.1093/nar/gky992.
- Cl  mence Frioux et al. « Scalable and exhaustive screening of metabolic functions carried out by microbial consortia ». In : Bioinformatics 34.17 (2018), p. i934-i943. issn : 1367-4803. doi : 10.1093/bioinformatics/bty588.

Main activities

Main activities:

- Build fast and high-quality RKHS approximations of metabolic models of the murine gut microbiota.
- Develop dimension reduction methods to speed up RKHS computation.
- Build a PDE model of a simplified murine microbiota.
- Characterize the main functions and interactions that drive the community
- Analyse results of metamodelling by identifying and visualising metabolic functions provided by the simulations
- Share the results of the projects through scientific publications and code/documentation distribution

Additional activities:

- Collaborate with the second post-doc of the project by providing expertise on PDE and applied mathematics.
- Participate in supervising students in the team.

Skills

Technical skills and level required:

- Scientific computing for PDE solvers and applied mathematics.
- Python programming (or other scientific computing language)
- Real motivations for applications in biology
- Scientific writing

Languages:

- English for scientific communication
- English or French for day to day work

Relational skills:

- Ability to work in a collaborative environment
- Good communication skills (sharing results, supervising students)

Other valued skills: a background in statistics is not mandatory but would be a plus, and sufficient background in mathematics is required to learn new skills in statistical learning.

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- 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

Remuneration

2653€ / month (before taxes)

General Information

- **Theme/Domain** : Computational Biology
Scientific computing (BAP E)
- **Town/city** : Talence
- **Inria Center** : [Centre Inria de l'université de Bordeaux](#)
- **Starting date** : 2021-10-01
- **Duration of contract** : 2 years
- **Deadline to apply** : 2021-08-31

Contacts

- **Inria Team** : [PLEIADE](#)
- **Recruiter** :
Labarthe Simon / Simon.Labarthe@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 should have a taste for interdisciplinary projects. He/she would ideally have a previous experience of mathematical modeling applied to life sciences.

The candidate would ideally have a PhD in applied mathematics in a field related to PDE, numerical analysis or scientific computing. A previous experience in statistical learning methods, parameter inference or data processing would be positively valued.

Background or previous experience in PDE computation would be a real asset.

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

Thank you to send:

- CV
- Cover letter
- Support letters (mandatory)
- List of publication

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.