

## 2021-03628 - Post-Doctoral Research Visit F/M Statistical Learning of the Intestinal Microbiota Metabolism in Space and Time: Metabolic model modelling and reduction

**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 **systems biology profile**.

The main objective of the SLIMMEST project is to resolve a numerical bottleneck in **spatio-temporal modeling of microbiota: the coupling between microbe-scale metabolic models with community-scale dynamics described with PDE models**. The recruited person will provide expertise in **system biology, microbial metabolism, and community-wide metabolic network modeling**. Missions will include modelling and simplification of metabolic models in order to identify metabolic drivers of ecosystems. Such drivers will in turn be used by the second postdoc scientist of the project to develop machine learning techniques and build a partial differential equations (PDE) model of the gut microbiota.

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 recruited person will be taken to carry the **metabolic-modelling related part of the SLIMMEST project**.

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 metamodelling of metabolism in a scalable framework applied to communities of the gut microbiota.

The mission of this postdoc position is to **develop methods suitable to the reduction of metabolic models for a community**. The purpose is to simplify the metabolism of an ecosystem by **targeting crucial functions that are main drivers of the ecosystem**. The results will be used in mathematical models by the second postdoc scientist of the project.

For that purpose, we must **model the metabolism of bacteria** from their genome, and connect metabolic networks to the available literature resources on pathways of interest such as short-chain fatty acid production. The **simplification of the community metabolism** will be performed by **modelling constraints and solving combinatorial optimisation problems**. In addition, the successful candidate will contextualise the results of community metamodelling back to metabolic networks. The first application of the project will be a model of the murine gut microbiota, with expectations to successfully scale up the size of the community during the project.

#### For a better knowledge of the proposed research subject:

- J. D. Orth, I. Thiele, and B. Ø. Palsson, « What is flux balance analysis? ». In : Nat Biotechnol, vol. 28, no. 3, pp. 245–248, 2010, doi:10.1038/nbt.1614.
- 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 Ebenhöf, 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.

### General Information

- **Theme/Domain :** Computational Biology  
Biologie et santé, Sciences de la vie et de la terre (BAP A)
- **Town/city :** Talence
- **Inria Center :** CRI Bordeaux - Sud-Ouest
- **Starting date :** 2021-10-01
- **Duration of contract :** 2 years
- **Deadline to apply :** 2021-12-31

### Contacts

- **Inria Team :** PLEIADE
- **Recruiter :**  
Frioux Clemence / [clemence.frioux@inria.fr](mailto:clemence.frioux@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 some basic knowledge in biology or previous application of her/his methods in life sciences.

The candidate would ideally have a computer science PhD in a field related to bioinformatics or systems biology.

Background or previous experience in metabolic modelling is a real asset.

### 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.

**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.

- Clémence 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 Lagkourvardos 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.
- Arun S Moorthy et al. « A spatially continuous model of carbohydrate digestion and transport processes in the colon ». In : PloS one 10.12 (2015), e0145309.
- 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.
- Clémence 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 high quality metabolic models of a simplified model of murine gut microbiota using state-of-the-art methods. Model them using qualitative and quantitative (Flux Balance Analysis) techniques.
- Develop methods to simplify a community of metabolic models using logic constraints and combinatorial optimisation.
- 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 community-scale metabolic modeling. This expertise will be crucial to build the community scale problem and to analyse the results to identify the metabolic significance of the results.
- Participate in supervising students in the team.

## Skills

### Technical skills and level required:

- Systems biology skills: metabolic network modelling or skills in a close area.
- Python programming
- Data analysis: Python or R
- 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 appreciated: logic programming (e.g. Answer Set Programming) is a plus but is not mandatory.

## Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

## Remuneration

2653€ / month (before taxes)