# Postdoctoral Research Position: Metabolic modelling of uncultured minimal bacteria

Location: Inria Talence & INRAE Villenave d'Ornon, Bordeaux, France

**Duration:** 2 years (renewable for an additional 2 years) **Funding:** INRAE EXPLOR'AE "Recherche à risque" Programme

# About the Project

The postodoctoral position is offered as part of a partnership between <a href="INRAE">INRAE</a> (the French National Research Institute for Agriculture, Food, and the Environment) and <a href="Inria">Inria</a> (the French National Institute for Research in Digital Science and Technology). It is funded by the TARGET project, promoted by <a href="INRAE's EXPLOR'AE">INRAE's EXPLOR'AE</a> "high-risk research" programme. The TARGET project is an <a href="Interdisciplinary">Interdisciplinary</a> initiative combining microbiology, culturomics, genetic engineering, systems biology, and modelling. It is a four-year research project. The postdoctoral position offered within this project is for an initial two-year period, with the possibility of renewal for an additional two years.

Context of the project. Since the late 19th century, microbiologists have been developing culture media and techniques to study microorganisms such as bacteria, archaea, yeasts, and filamentous fungi. However, only a small fraction of bacterial species are currently cultivable, severely limiting their study. While advances in metagenomics have highlighted this limitation, genome sequencing alone has not provided sufficient explanations for why many bacterial species remain unculturable. This lack of cultivability remains a scientific enigma and a major barrier to applications in fields such as disease control, antibiotic discovery, biomolecule production, microbiome management, and bioremediation. In bacteria that live in association with eukaryotic hosts, understanding metabolic interactions with their partners opens new possibilities for developing tailored culture media, thereby facilitating their study. Using grapevine Flavescence Dorée phytoplasma as a proof of concept, the TARGET project aims to demonstrate that integrating systems biology, genome engineering, and culturomics can help overcome the challenge of bacterial non-cultivability.

This postdoctoral position is part of the project's metabolic modelling work package, with objectives including the development of numerical models for the metabolism of minimal bacteria and Flavescence Dorée phytoplasma. These models will be used to predict suitable culture media. The project involves close collaboration between modellers and microbiologists to bridge computational and experimental approaches.

The recruited researcher will work in collaboration between <a href="Inria Pleiade">Inria Pleiade</a> team in Talence and <a href="Inria Pleiade">INRAE</a>
<a href="BFP">BFP</a> (Fruit biology and Pathology) unit at Villenave d'Ornon. At Inria, the work will be carried under the supervision of <a href="Clémence Frioux">Clémence Frioux</a>. Pleiade hosts researchers in mathematics, computer science and computational biology working on developing approaches for microbial community characterisation. Two teams are involved at INRAE: MOLLI (Pascal Sirand Pugnet) where most of the experimentations will be carried out, and META specialised in metabolic modelling. The co-supervisor of the position is <a href="Sylvain Prigent">Sylvain Prigent</a>, researcher in the META team.

## **Position Overview**

The work focuses on constructing metabolic models of Mollicutes and Flavescence Dorée phytoplasma (FDp) to better understand their metabolic functions and predict suitable growth media. Initially, the work will apply proven strategies to well-studied Mollicutes, refining models and predicting culture conditions, followed by validation experiments carried out by collaborators. A similar approach will then be used to develop and validate models for Spiroplasma citri and FDp. Comparative metabolic network analysis across Mollicutes will help generate functional insights, while further efforts will explore dynamic models of FDp metabolism within its hosts. Ultimately, the project aims to integrate symbiotic interactions into these models to enhance understanding of FDp physiology in insect vectors.

Strong collaborations are planned withing the TARGET consortium in order to provide hypotheses for new experimentations and to integrate into models experimental results.

See the following references for details on the team activities and approaches used in the project:

- Belcour, A., Got, J., Aite, M., Delage, L., Collén, J., Frioux, C., Leblanc, C., Dittami, S. M., Blanquart, S., Markov, G. V., and Siegel, A. (2023). Inferring and comparing metabolism across heterogeneous sets of annotated genomes using AuCoMe. Genome Research. <a href="https://doi.org/10.1101/gr.277056.122">https://doi.org/10.1101/gr.277056.122</a>
- Cerk, K., Ugalde-Salas, P., Nedjad, C. G., Lecomte, M., Muller, C., Sherman, D. J., Hildebrand, F., Labarthe, S., and Frioux, C. (2024). Community-scale models of microbiomes: Articulating metabolic modelling and metagenome sequencing. Microbial Biotechnology, 17(1), e14396. <a href="https://doi.org/10.1111/1751-7915.14396">https://doi.org/10.1111/1751-7915.14396</a>
- Ghassemi-Nedjad, C., Bolteau, M., Bourneuf, L., Paulevé, L., and Frioux, C. (2024). Seed2LP: seed inference in metabolic networks for reverse ecology applications. BioRxiv. <a href="https://doi.org/10.1101/2024.09.26.615309">https://doi.org/10.1101/2024.09.26.615309</a>

The successful candidate will contribute to the **metabolic modeling work package**, developing and refining computational models to explore microbial metabolism. The research will focus on Mollicutes and Flavescence Dorée phytoplasma (FDp), aiming to:

- Reconstruct, curate, and compare metabolic networks from genomic data.
- Use and develop various metabolic models: individual-scale models, dynamic models, and community models.
- Write scientific articles.
- Collaborate with microbiologists to refine models and guide experiments.

# **Expected Skills & Qualifications**

The profile we are looking for:

- **Experience in modelling / systems biology** Prior experience in computational modelling, particularly in the context of biological systems, is highly desirable.
- **Bioinformatics skills** Proficiency in handling genomic and metabolic data, with experience in relevant bioinformatics tools and pipelines.
- **Metabolic modelling** Ideally, familiarity with metabolic network reconstruction, constraint-based modelling, and dynamic models.
- Autonomy and strong analytical and writing skills Ability to work independently, synthesise complex information, and contribute to scientific publications.
- Interest in interdisciplinary research and collaborative work Willingness to engage with microbiologists and experimentalists to refine models and guide laboratory experiments.

## More precisely:

### **Technical Skills and Required Level:**

- · Experience in modelling and systems biology
- · Good programming skills, preferably in Python
- · Good practices in software development

#### Languages:

 Proficiency in English is expected for disseminating results through research papers and in conferences

#### **Interpersonal Skills:**

- · Ability to work collaboratively in an interdisciplinary environment
- · Strong analytical and problem-solving skills
- · Good communication and teamwork abilities

#### **Additional Desirable Skills:**

- Knowledge of metabolic modelling techniques
- · Experience in bioinformatics and data analysis
- · Familiarity with high-performance computing environments
- · Experience in collaborating with experimental biologists

## Job conditions

Gross monthly salary ranging from 2,788€ to 3,405€, depending on profile and previous experience.

#### Benefits:

- 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

# How to Apply

Interested candidates should submit:

- A CV detailing relevant experience.
- A **cover letter** outlining research interests and motivation.
- Contact details for two references.

Applications need to be deposited online on <a href="https://jobs.inria.fr/public/classic/fr/offres/2025-08783">https://jobs.inria.fr/public/classic/fr/offres/2025-08783</a>