

PhD studentship: Cross-species Design of Resource-Aware Genetic Circuits

We are looking for a PhD candidate to develop resource-aware genetic circuits with broad host-range compatibility.

Background. Bioengineering of genetic circuits and metabolic pathways has a wide range of applications. However, cellular resource burden of heterologous circuits and pathways often results in their loss due to mutations and negative selection. Therefore, recent years have seen the emergence of several theoretical and experimental approaches for building more resource-aware designs. Yet, much like bioengineering broadly, most efforts towards resource-aware design are currently limited to a small subset of laboratory model organisms, many of which are incompatible for industry applications. In this doctoral project, we will develop tools for dynamic feedback control of burdensome circuits and pathways to make them cross-species compatible. We expect the results of this work to facilitate rapid implementation of genetic circuits and metabolic pathways in non-model organisms, with reduced burden. The toolbox will not only help reduce cellular burden, thus improving overall productivity, but also expedite the use of the most compatible chassis organism for the target biotechnology application.

Position. The 3-year doctoral position will be hosted in the Cellular Computing Group at the Micalis Institute (INRAE Jouy-en-Josas, University of Paris-Saclay). The expected start date is October 2024.

Funding. The PhD position is funded by the [Tbox4BioProd](#) project, as part of the French government's Priority Research Programmes and Equipment (PEPR) action [B-BEST](#). The project is a collaboration between several leading French research labs: Micalis Institute, CBS Montpellier, and Genoscope.

Applicant profile. We are looking for a highly motivated candidate with experience in experimental synthetic biology, including microbiology and molecular biology techniques. Although not essential, some background in programming, bioinformatics, or computational modelling would be an added advantage. They should have strong communication skills and the willingness to work collaboratively with other members of the team and project collaborators, including biologists, mathematicians, and computer scientists. A Master's degree or equivalent is required for PhD registration at the *Structure et dynamique des systèmes vivants* (SDSV) doctoral school of the University of Paris-Saclay.

Application process. For questions regarding the position and/ or the application process, please contact manish.kushwaha@inrae.fr and ioana.popescu@universite-paris-saclay.fr. To apply, please send a cover letter and a CV (with contact details of at least two referees).

Application deadline. 15 June 2024. Applications will be considered as they are received.

Selected References:

1. Kushwaha, M. & Salis, H. M. A portable expression resource for engineering cross-species genetic circuits and pathways. *Nat. Commun.* **6**, 7832 (2015).
2. Adams, B. L. The Next Generation of Synthetic Biology Chassis: Moving Synthetic Biology from the Laboratory to the Field. *ACS Synth. Biol.* **5**, 1328–1330 (2016).
3. Huang, H.-H., Qian, Y. & Del Vecchio, D. A quasi-integral controller for adaptation of genetic modules to variable ribosome demand. *Nat. Commun.* **9**, 5415 (2018).
4. Darlington, A. P. S., Kim, J., Jiménez, J. I. & Bates, D. G. Dynamic allocation of orthogonal ribosomes facilitates uncoupling of co-expressed genes. *Nat. Commun.* **9**, 695 (2018).
5. Patel, J. R., Oh, J., Wang, S., Crawford, J. M. & Isaacs, F. J. Cross-kingdom expression of synthetic genetic elements promotes discovery of metabolites in the human microbiome. *Cell* **185**, 1487–1505.e14 (2022).