PhD studentship: Expression Costs of Synthetic Genetic Circuits

We are looking for a PhD candidate to develop experimental and computational methods for measuring and predicting the cost of synthetic genetic circuits in bacteria.

Background. Expression of heterologous genes is a crucial step for many biotechnological processes, including for information-processing sense-and-respond genetic circuits. As the size and complexity of synthetic genetic circuits increase, they progressively become too burdensome for a single cell. Consequently, many genetic circuits are lost to negative selection when the engineered organisms are grown for prolonged periods of time. In this work, we will develop experimental and theoretical methods to measure the cost of maintaining and executing synthetic genetic circuits inside cells. The quantitative models will be used to choose the most economical design architectures (with least resource competition and optimal circuit behaviour) for implementing a genetic circuit with a specific function. The circuit designs will be studied under different growth and stress conditions to assess the relationship between the calculated costs and the long-term evolutionary stability of the circuits. These analyses will help inform the decision of what is the upper size-limit of the circuits at which it would be more efficient to distribute the different functions across multiple cells in a community.

Position. The 3-year doctoral position will be hosted in the Systems and Synthetic Biology pole at the Micalis Institute (INRAe Jouy-en-Josas, University of Paris-Saclay), in partnership with LMF (ENS Paris-Saclay). The expected start date is October 2023.

Applicant profile. We are looking for highly motivated candidates with experience in experimental microbiology and molecular biology. They should have strong communication skills and the willingness to work collaboratively with other members of the team, including biologists, mathematicians, and computer scientists. Background in bioinformatics/ computational modelling is an advantage, but not essential.

Application process. For questions regarding the position and/ or the application process, please contact manish.kushwaha@inrae.fr or olivier.borkowski@inrae.fr. Formal deadline for the *Structure et dynamique des systèmes vivants* (SDSV) doctoral school is 31 March 2023.

Selected References:

(1) Li, G.-W., Burkhardt, D., Gross, C., and Weissman, J.S. (2014). Quantifying Absolute Protein Synthesis Rates Reveals Principles Underlying Allocation of Cellular Resources. Cell 157, 624–635.
(2) Zur, H., Cohen-Kupeic, Rachel, Vinokour, Sophie, and Tuller, Tamir (2020). Algorithms for ribosome traffic engineering and their potential in improving host cells' titer and growth rate. Scientific Reports 15.
(3) Ceroni, F., Algar, R., Stan, G.-B., and Ellis, T. (2015). Quantifying cellular capacity identifies gene expression designs with reduced burden. Nat Methods 12, 415–418.
(4) Ceroni, F., Boo, A., Furini, S., Gorochowski, T.E., Borkowski, O., Ladak, Y.N., Awan, A.R., Gilbert, C., Stan, G.-B., and Ellis, T. (2018). Burden-driven feedback control of gene expression. Nat Methods 15, 387–393.
(5) Balakrishnan, R., Mori, M., Segota, I., Zhang, Z., Aebersold, R., Ludwig, C., and Hwa, T. (2022). Principles of gene regulation quantitatively connect DNA to RNA and proteins in bacteria. Science 378, eabk2066.