Post-doc position in Computational biology

A large scale regulatory network logical model and a regulated genome scale metabolic model to assess the regulatory role of sRNAs in *E. coli* adaptation to environmental changes

Location: Institute of Mathematics of Marseille (I2M)

Duration: 18 months

Starting date: As soon as possible...

Scientific context: This position is in the context of the collaboratif ANR project *KineBioTics*, with the LCB (https://lcb.cnrs.fr/team/py/). The applicant will be part of the MABioS team (http://mabios.math.cnrs.fr/index.html) at I2M.

In *Escherichia coli* and other bacteria, small regulatory RNAs (sRNAs) were shown to play crucial roles in a wide variety of pathways. It remains to understand the dynamical properties and advantages of RNA regulation as compared to classically studied protein regulators. The goal of the proposed project is to develop a series of models disclosing the role of (some) sRNA in *E. coli* adaptation to environmental changes, with a particular focus on the Fe-S cluster biogenesis. The hired postdoc will develop a workflow to (semi)-automatically

- extract the complete regulatory network as currently available from the *E. coli* reference database regulonDB [1],
- define an annotated Boolean model for this regulatory network through an extension of the tool GINsim, which is devoted to logical modelling [2]
- perform a thorough analysis of this genome scale regulatory network confronted to existing data related to e.g. *E. coli* stress adaptation and antibiotics resistance.
- reduce the complete regulatory network to transcription factors regulating metabolic genes (and possibly relevant sRNAs), and use it as regulatory constraints for a GSMM (to be retrieved from the BiGG database [3]).
- use Flux balance analysis (FBA) and its variants to predict effects of genetic changes (including sRNA perturbations) on growth, metabolite yields, and reaction fluxes,
- expand the logical model of Fe-S cluster biogenesis regulatory network by extracting from the complete regulatory model the regulation of Fe-S cluster biogenesis, involved in membrane permeability and resistance to specific antibiotics, [4].

This workplan can be modulated depending on the candidate preferences.

Competence: A good understanding of biological networks is expected, with a proficiency in computational programming. Experience in modelling will be a plus.

Contact: Élisabeth Remy (elisabeth.remy@univ-amu.fr) and Claudine Chaouiya (claudine.chaouiya@univ-amu.fr).

References

[1] Santos-Zavaleta A *et al.* (2019) RegulonDB v 10.5: tackling challenges to unify classic and high throughput knowledge of gene regulation in E. coli K-12. *Nucleic Acids Res.*, 47(D1):D212-D220. doi: 10.1093/nar/gky1077

[2] A. Naldi *et al.*(2018) Logical modelling and analysis of cellular regulatory networks with GINsim 3.0. *Frontiers in Physiology, Systems Biology*, 9:646. doi:10.3389/10.3389/fphys.2018.00646

[3] Norsigian CJ *et al.* (2020). BiGG Models 2020: multi-strain genome-scale models and expansion across the phylogenetic tree. *Nucleic Acids Res* 48:D402–D406.

[4] Hammami F *et al.*(2023) Analysis of a logical regulatory network reveals how Fe-S cluster biogenesis is controlled in the face of stress. *Microlife* 4:uqad003. doi: 10.1093/femsml/uqad003.