Master 2 internship in computational biology with funded PhD position

Global regulation of bacterial transcription by chromosome topology

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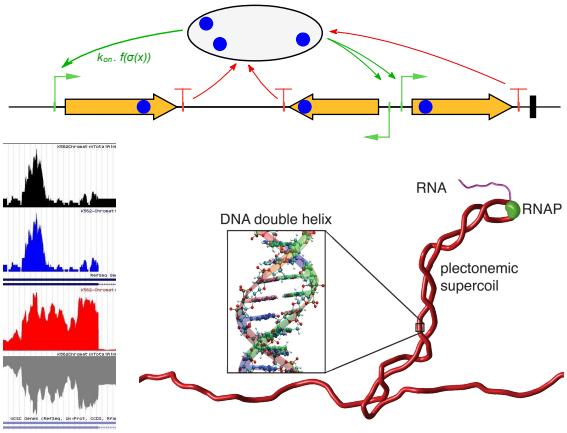

DNA topology (or supercoiling) is a fundamental mechanism of compaction of the bacterial chromosome. The student will analyze and model the mechanisms by which it plays a role as a global and multi-scale transcriptional regulator. In contrast to usual regulation mechanisms based on transcription factors which target specific genes, DNA topology influences gene expression in a global, non-specific manner in a wide range of species. In bacteria, modifying the topology thus allows for a rapid re-programming of the expression program along the whole chromosome, for instance in response to an external stress [1]. Accordingly, accumulating data show that gene expression is organized spatially on the chromosome following topological and architectural domains [1,2], and depends for instance on the presence and orientation of neighbor genes [3]. These features are evolutionarily conserved and cannot be explained by current regulation models.

This computational biology study will be based on an analysis of recent high-throughput sequencing data obtained in the team on the pathogenic bacterium *Dickeya dadantii* as well as published data on other organisms. **Depending on the student's background, skills and preferences, it may either be centered (1) on the analysis of new high-throughput expression and DNA topology mapping data ; or (2) on the development of mathematical/biophysical models of the underlying molecular mechanisms.** Since the explored regulation mechanism is based on the fundamental physical properties of the DNA double helix, it probably constitutes an important ancestral and widespread mode of regulation currently underestimated [3] ; the study may thus have an important fundamental impact by relating the chromosome's physical features to its biological function.

We are looking for a highly motivated Master 2 student with a background in bioinformatics (preferred), biology, biophysics or biochemistry. The project requires general experience in programming (Python preferred); experience in the handling of biological data is preferred. Students with experimental skills are also encouraged, as experimental approaches could optionally be included as a complement in the project. **A fully funded PhD position is available for September 2020 (ANR contract), as a natural follow-up of the internship.**

1. X. Jiang et al., Chromosomal "Stress-Response" Domains Govern the Spatiotemporal Expression of the Bacterial Virulence Program, *mBio* 2015
2. J. Cevost et al., ThreaDNA : predicting DNA mechanics' contribution to sequence selectivity of proteins along whole genomes, *Bioinformatics* 2018
3. B. El Houdaigui et al., Bacterial genome architecture shapes global transcriptional regulation by DNA supercoiling, *Nucleic Acids Research* 2019 https://doi.org/10.1093/nar/gkz300