CompBio@TrEE

COLLÈGE DE FRANCE 1530

Master internship in biophysical modeling

Quantitative modeling of transcription dynamics in the context of DNA topology regulation

Subject: The understanding of natural genetic networks and the development of synthetic circuits rely on rationalizing the fundamental processes involved in gene expression. At the most basic level, this requires the development of quantitative models of the transcription process [1], which describes how a molecular machine, RNA polymerase, "reads" the DNA sequence to produce messenger RNA (which is then translated into protein).

During transcription, RNA polymerase moves along the DNA molecule, unwinding the double helix and generating torsional stress on either side of the molecular machine. In cells, this stress is relieved by specialized enzymes known as topoisomerases, which can modify the topological properties of DNA. Topoisomerases are ubiquitous enzymes across all living organisms [2], playing a crucial role in molecular processes that involve DNA unwinding and/or overwinding, such as gene transcription and DNA replication.

The internship will focus on advancing the quantitative modeling of the coordinated activities of RNA polymerases and topoisomerases. Specifically, we aim to extend a model we recently developed [3] to rationalize the behavior of a minimal in vivo system. One key objective will be to show how extending the model can account for various experimental observations reported in the literature that remain unexplained. Additionally, we will work on designing minimal experiments to validate or refute the molecular scenarios underpinning the model.

Location: The internship will take place at the CIRB, Collège de France, in Olivier Espeli's lab. The modeling will be supervised by Ivan Junier, a biophysicist from TIMC in Grenoble, who will be visiting Olivier Espeli's lab in 2025.

Profile: Candidates should have a background in mathematical modeling, statistical physics, or biophysics. They should be interested in interdisciplinary research, particularly in questions addressing the functioning of living organisms.

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References:

[1] Junier, Ghobadpour, Espeli & Everaers, 2023. DNA supercoiling in bacteria: state of play and challenges from a viewpoint of physics based modeling. Front. Microbiol. 14, 1192831.

[2] Borde, Bruno & Espéli, 2024. Untangling bacterial DNA topoisomerases functions. Biochemical Society Transactions BST20240089.

[3] Boulas, Bruno, Rimsky, Espeli, Junier & Rivoire, 2023. Assessing in vivo the impact of gene context on transcription through DNA supercoiling. Nucleic Acids Research gkad688.