Internship for M2 and 5th year Engineering Schools in Biophysics/Mathematics/Computer Science
Duration: 4-6 months from February 2026
Location: Computational Systems Biology, LPHI, University of Montpellier, CNRS, INSERM, and Transcription & Development, IGMM, CNRS, University of Montpellier.

Supervision: Prof. Ovidiu Radulescu (LPHI) and Dr. Mounia Lagha (IGMM).

From Specific Mechanisms to Universal Laws of Stochastic Transcription: the Case of *Drosophila* Development

We often picture gene transcription as a simple switch: when 'on,' genes make RNA; when 'off,' they remain silent. In reality, the process is far more complex. Even in the active state, RNA production is intermittent, and gene activity is better described as a temporal sequence alternating between ON (active) and one or multiple OFF (inactive) states. This sequence does not follow a fixed, deterministic logic but is instead governed by stochastic laws. Increasing the probability of entering the ON state can elevate gene expression. However, the random succession of ON and OFF states generates intrinsic variability in expression, known as intrinsic noise, which imposes fundamental limits on how precisely cells can adopt specific cell fates.

Our research has revealed that transcription is not restricted to a single inactive OFF state. Rather, specific genes in particular regulatory contexts can transition through multiple OFF states, each with distinct durations, representing distinct regulatory checkpoints. Understanding the number and timing of these states is therefore essential to quantitatively predict how gene expression noise influences biological processes.

To investigate stochastic gene expression, we have developed tools to directly observe RNA production with single-molecule precision in single cells in vivo, using genetic manipulations and quantitative imaging. We have used Markov chains to effectively describe the regulatory checkpoints and the transitions between them. Over the past decade, we have accumulated a large dataset probing stochastic gene expression during the first hours of *Drosophila* development. While subsets of these data have been analyzed for specific projects, a unified analysis to uncover general principles is still lacking.

During this internship, we will revisit these datasets with a unifying perspective, searching for universal laws that govern gene expression and its regulation. For example, gene expression adapts to changing conditions by modulating transcriptional parameters, represented in our models as transition rates between states. Since multiple parameter combinations can produce similar outcomes, we aim to test whether certain solutions are preferred or whether all possible solutions are realized. Additional investigations will address scaling laws of expression variability: while Poisson processes predict that the standard deviation scales with the square root of the mean, gene expression often follows alternative scaling laws. Because embryonic gene expression is spatially extended, we will also examine how local transcriptional stochasticity contributes to, and interacts with, the variability of large-scale spatial expression patterns. Finally, we will explore fundamental constraints, such as the information-theoretical and statistical-physics bounds that noise imposes on developmental precision.

References.

Dufourt et al., Nat Comm 2018. DOI: 10.1038/s41467-018-07613-z.
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Bellec et al., Nat Comm 2022. DOI: 10.1038/s41467-022-28855-y.
Pimmett al., Nat Comm 2021. DOI: 10.1038/s41467-021-24461-6 .
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Pimmett, McGehee et al., Development 2025. DOI: 10.1242/dev.204706.

Douaihy et al., NAR 2023. DOI: 10.1093/nar/gkad629.
Radulescu et al, Bull Math Bio 2025. DOI: 10.1007/s11538-024-01385-y.

For more information, see www.laghalab.com and https://systems-biology-lphi.cnrs.fr.

Expertise required: notions of probabilistic modeling, Python or Matlab coding.

Application: Send a CV + cover letter + transcripts + names of references to ovidiu.radulescu@umontpellier.fr.