Ínnía

Offer #2025-08871

PhD Position F/M Computational analysis of mRNA degradation

Contract type : Fixed-term contract

Level of qualifications required : Graduate degree or equivalent

Fonction : PhD Position

Level of experience : Recently graduated

About the research centre or Inria department

The Centre Inria de l'Université de Grenoble groups together almost 600 people in 24 research teams and 9 research support departments.

Staff is present on three campuses in Grenoble, in close collaboration with other research and higher education institutions (Université Grenoble Alpes, CNRS, CEA, INRAE, ...), but also with key economic players in the area.

The Centre Inria de l'Université Grenoble Alpes is active in the fields of highperformance computing, verification and embedded systems, modeling of the environment at multiple levels, and data science and artificial intelligence. The center is a top-level scientific institute with an extensive network of international collaborations in Europe and the rest of the world.

Context

The Ph.D. project will be carried out in the project-team <u>MICROCOSME</u> at Inria – Univ Grenoble Alpes under the supervision of Delphine Ropers within the framework of the RECOM ANR project. MICROCOSME is an interdisciplinary team that includes applied mathematicians, engineers, computer scientists, computational biologists as well as experimentalists from the

Assignment

Mechanistic models are essential to unravel the molecular mechanisms driving cellular responses. However, the integration of high-throughput data with mechanistic knowledge is limited by the availability of scalable computational approaches able to disentangle biological and technical sources of variation.

The objective of the PhD thesis is to combine mechanistic modelling and statistical inference approaches to analyse dynamical transcriptomics data in the context of mRNA degradation in the model bacterium *Escherichia coli*. The candidate will be able to build on the team's previous work showing how the combination of mechanistic and statistical modelling approaches can be used to infer kinetic parameters from dynamic transcriptomic data and identify novel regulatory mechanisms such as competitive effects in mRNA decay [1,2]. The thesis is part of the ANR project RECOM, which aims to assess the role and importance of this regulatory mechanism through mathematical modelling and experiments. In close collaboration with our biologist partner from the Toulouse Biotechnology Institute, the aim of the PhD thesis is to a) adapt or extend the mechanistic modelling and statistical framework to analyse new types of data and experiments performed within and outside the project [3,4] and, in close collaboration with the biologists, b) interpret the results biologically and c) propose experiments to validate the model predictions.

[1] T.A. Etienne, M. Cocaign-Bousquet & D. Ropers (2020). Competitive effects in bacterial mRNA decay. *Journal of Theoretical Biology*, 504, 110333.

[2] T.A. Etienne, C. Roux, E. Cinquemani, L. Girbal, M. Cocaign-Bousquet & D. Ropers (2022). A nonlinear mixed-effects approach for the mechanistic interpretation of time-series transcriptomics data. Preprint. https://inria.hal.science/hal-03652397/.

[3] T. Esquerre, S. Laguerre, C. Turlan, A.J. Carpousis, L. Girbal & M. Cocaign-Bousquet (2014). Dual role of transcription and transcript stability in the regulation of gene expression in *Escherichia coli* cells cultured on glucose at different growth rates. *Nucleic Acids Research*, 42(4), 2460-2472.

[4] L. Hamouche, L. Poljak & A.J. Carpousis (2021). Polyribosome-dependent clustering of membrane-anchored RNA degradosomes to form sites of mRNA degradation in *Escherichia coli*. *Mbio*, *12*(5), 10-1128.

Main activities

The PhD candidate will:

- Develop estimation strategies (simplification and/or reduction of mechanistic models of mRNA degradation, development of nonlinear mixed effects - NLME - models) to estimate degradation parameters from RNA-Seq datasets.

- Assess the utility of the NLME framework for medium- to low-throughput data sets (microfluidic RT-qPCR) and possibly propose alternative statistical inference approaches.

- Apply the different estimation strategies to various datasets obtained in the bacterium *E. coli* subjected to various perturbations, assess the quality of model estimation, and interpret the estimation results.

Skills

Interested candidates are expected to have a good background in statistical inference and mathematical modelling, and to be strongly interested in biological applications. Good relational skills and English skills are also important for the project

Benefits package

- Subsidized meals
- Partial reimbursement of public transport costs
- Leave: 7 weeks of annual leave + 10 extra days off due to RTT (statutory reduction in working hours) + possibility of exceptional leave (sick children, moving home, etc.)
- Possibility of teleworking (after 6 months of employment) and flexible organization of working hours
- Professional equipment available (videoconferencing, loan of computer equipment, etc.)
- Social, cultural and sports events and activities
- Access to vocational training
- Social security coverage

Remuneration

2200 euros gross salary /month

General Information

- Theme/Domain : Modeling and Control for Life Sciences Biologie et santé, Sciences de la vie et de la terre (BAP A)
- Town/city : Montbonnot
- Inria Center : <u>Centre Inria de l'Université Grenoble Alpes</u>
- Starting date : 2025-10-01
- **Duration of contract :** 3 years
- Deadline to apply : 2025-06-30

Contacts

- Inria Team : MICROCOSME
- PhD Supervisor : Ropers Delphine / <u>delphine.ropers@inria.fr</u>

About Inria

Inria is the French national research institute dedicated to digital science and technology. It employs 2,600 people. Its 200 agile project teams, generally run jointly with academic partners, include more than 3,500 scientists and engineers working to meet the challenges of digital technology, often at the interface with other disciplines. The Institute also employs numerous talents in over forty different professions. 900 research support staff contribute to the preparation and development of scientific and entrepreneurial projects that have a worldwide impact.

The keys to success

The candidate is expected to be proactive and open to collaboration in an interdisciplinary environment.

Warning : you must enter your e-mail address in order to save your application to Inria. Applications must be submitted online on the Inria website. Processing of applications sent from other channels is not guaranteed.

Instruction to apply

Applications must include a CV, covering letter, copy of diploma and valid proof of disabled worker status.

Applications must be submitted online via the Inria website. Processing of applications submitted via other channels is not guaranteed.

Defence Security :

This position is likely to be situated in a restricted area (ZRR), as defined in Decree No. 2011-1425 relating to the protection of national scientific and technical potential (PPST). Authorisation to enter an area is granted by the director of the unit, following a favourable Ministerial decision, as defined in the decree of 3 July 2012 relating to the PPST. An unfavourable Ministerial decision in respect of a position situated in a ZRR would result in the cancellation of the appointment.

Recruitment Policy : As part of its diversity policy, all Inria positions are accessible to people with disabilities.