Mirror doctoral project - Information Sheet

Project Title & Acronym	**Chronic Inflammation Shapes Non-Coding RNA-Mediated Transcriptional Condensates: Experimental and Modelling Approaches (INFLAM-nCOND-A)**
Scientific Co-Directors	Rosemary Kiernan and Andrea Parmeggiani
Doctoral Project 1	**Dynamic regulation of transcriptional condensates by enhancer and promoter-derived non-coding RNAs in inflammatory transcriptional states**
Phd Supervisor 1	Kiernan, Rosemary
Research Unit 1	UMR9002, IGH
Doctoral School 1	ED CBS2
Doctoral Project 2	**Statistical mechanics of nuclear transcriptional condensates: numerical and analytical models to study condensate assembly, dynamics and regulation via RNA fluxes**
Phd Supervisor 2	Andrea Parmeggiani and Jean-Charles Walter
Research Unit 2	L2C
Doctoral School 2	ED I2S

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What Is An IDIL Mirror Doctoral Project?

A mirror doctoral project bridges **two distinct disciplinary theses** within a **shared multidisciplinary research framework**.

The objective is to tackle a single research project through the lens of **two different disciplines to foster multidisciplinarity**. This requires utilizing the specific methods and references inherent to each of the fields involved.

For the Fall 2026 intake, the IDIL Graduate Program is funding **six mirror doctoral project**s, representing a total of **12 three-year doctoral contracts**.

Theses are funded from the outset for **3 years**, including the PhD student's salary and an environmental allowance.

Application procedure

To apply for an IDIL mirror doctoral contract, candidates must complete and **submit their application before the deadline using the form on our website**:
https://idil.edu.umontpellier.fr/candidatures-phd-contrats-doctoraux-en-miroir-idil-2026/

Since each IDIL mirror doctoral project integrates two different contracts in two distinct disciplines, candidates must **specify on the form which doctoral subject (A or B)** within the project they are applying for.

PhD Start Date: October 1st, 2026 **PhD End Date:** September 30th, 2029

Application Requirements

All documents must be submitted in **PDF format** for evaluation.

Mandatory Documents:

- **Cover letter**, signed and dated.
- **Curriculum Vitae (CV)**.
- **Academic transcripts** for L3, M1, and M2 (or all years of an equivalent degree, such as an Engineering degree) **including your ranking**. These transcripts must be combined into a **single PDF file**.

Optional Documents:

- Letter(s) of recommendation

PhD Subjects & Applicant Requirements

INFLAM-nCOND-A: Chronic Inflammation Shapes Non-Coding RNA-Mediated Transcriptional Condensates: Experimental and Modelling Approaches

PHD SUBJECT A – CHEMICAL AND BIOLOGICAL SCIENCES FOR HEALTH (CBS2)

Dynamic regulation of transcriptional condensates by enhancer and promoter-derived non-coding RNAs in inflammatory transcriptional states

Desired Candidate Profile:

We are seeking a highly motivated and curious candidate with a strong interest in **gene regulation, RNA biology, and nuclear organization**. Applicants should have a solid background in **molecular and cellular biology, biochemistry, or a related field**.
Prior experience in techniques such as **cell culture, RNA biology, genome-wide approaches, or fluorescence microscopy** will be considered an advantage, but is not essential. A strong willingness to learn new methods and engage with advanced experimental approaches is expected.
The project is carried out in a highly interdisciplinary environment in close interaction with a theoretical physics team. Candidates should therefore be enthusiastic about working at the **interface between biology and physics**, and open to engaging with conceptual and quantitative approaches.
Successful candidates should demonstrate:

- Strong analytical and problem-solving skills
- Ability to work both independently and collaboratively
- Curiosity, rigor, and motivation to engage in interdisciplinary research
- Good communication skills in English

PHD SUBJECT B – Information, Structures & Systems (I2S)

Statistical mechanics of nuclear transcriptional condensates: numerical and analytical models to study condensate assembly, dynamics and regulation via RNA fluxes

Desired Candidate Profile:

We are seeking a highly motivated and curious candidate with a strong interest in theoretical physics of biological and complex matter.
The successful candidate will hold a Master's degree in theoretical physics. A background in statistical physics and critical phenomena is highly desirable. While prior knowledge in biology is not mandatory, a strong motivation to engage with and learn biological concepts is essential to develop the interdisciplinary PhD subject.
During the PhD, the student will develop expertise in theoretical statistical physics, field theory, numerical simulation techniques, including Monte Carlo, molecular dynamics methods (e.g.

brownian dynamics) and numerical integration of systems of (nonlinear) partial differential equations, and will acquire strong skills in analytical calculations.
Successful candidates should demonstrate:

- Strong analytical and problem-solving skills in theoretical and computational physics
- Ability to work both independently and collaboratively
- Curiosity, rigor, and motivation to engage in interdisciplinary research, notably in living matter and complex systems physics.
- Good communication skills in English

Should you require any additional information, please contact the PhD supervisors or the IDIL team at the following email addresses:

- Rosemary Kiernan (PhD Supervisor – Subject A): rosemary.kiernan@umontpellier.fr
- Andrea Parmeggiani (PhD Supervisor – Subject B): andrea.parmeggiani@umontpellier.fr
- Jean-Charles Walter (PhD Supervisor – Subject B): jean-charles.walter@umontpellier.fr
- Administrative team: idil-team@umontpellier.fr

Version française

Résumé du projet

Titre : **L'inflammation chronique module les condensats transcriptionnels médiés par les ARN non codants : approches expérimentales et de modélisation**

Mots-clés : inflammation chronique ; ARN non-codants ; condensats transcriptionnesl ; modélisation biologique et physique; physique théorique de systèmes biologiques et complexes, dynamique des condensats, physique statistique et des polymères, matière active, transition de phase, physique non-linéaire

Résumés des projets de thèses (FR – max. 4000 caractères, espaces compris) :

Les maladies inflammatoires chroniques représentent un défi croissant pour la société et la santé publique à l'échelle mondiale. Leur incidence a fortement augmenté ces dernières décennies, en lien avec des facteurs environnementaux, alimentaires et liés au mode de vie. L'exposition prolongée à des polluants, des déséquilibres alimentaires et des stimulations inflammatoires faibles et répétées est désormais reconnue comme un facteur majeur d'activation immunitaire soutenue. Ces conditions sont associées à des altérations persistantes des programmes d'expression génique dans les cellules immunitaires innées, notamment les macrophages, qui maintiennent des états transcriptionnels inflammatoires longtemps après le stimulus initial.

Au niveau cellulaire, ces réponses inflammatoires durables ne peuvent pas être expliquées uniquement par des voies de signalisation transitoires, mais reposent sur des mécanismes régulateurs stables ou semi-stables opérant au niveau de la transcription et de l'organisation nucléaire. Des avancées récentes ont révélé que la transcription est spatialement organisée dans le noyau via des condensats biomoléculaires dynamiques, qui concentrent facteurs de transcription, coactivateurs et ARN polymérase II sur les régions régulatrices actives. Ces condensats sont de plus en plus considérés comme des régulateurs clés de la robustesse et de la réactivité transcriptionnelle, bien que les mécanismes contrôlant leur formation, stabilité et adaptabilité restent peu compris.

Une caractéristique majeure des régions régulatrices actives est la production locale d'ARN non

codants à courte durée de vie, tels que les enhancer RNAs-eRNAs et les PROMPTs. Ces ARN, produits à proximité spatiale et temporelle des condensats transcriptionnels, restent confinés au noyau et peuvent influencer activement le comportement des condensats via des effets dépendants de la concentration, des caractéristiques séquentielles et des interactions ARN-protéines, se positionnant comme des régulateurs dynamiques de l'organisation nucléaire plutôt que comme de simples sous-produits de transcription.

Ce projet doctoral en miroir constitue une nouvelle collaboration entre deux équipes, l'une en biologie expérimentale (IGH) et l'autre en physique théorique (L2C). Il vise à élucider comment les ARN non codants dérivés des amplificateurs et des promoteurs régulent dynamiquement les condensats transcriptionnels et contribuent à la persistance des états transcriptionnels inflammatoires. Le projet combine des perturbations expérimentales précises des niveaux d'ARN nucléaire, l'imagerie quantitative de la dynamique des condensats, et le séquençage ARN long read pour caractériser la longueur, la structure et les modifications des ARN. En parallèle, un projet miroir orienté physique-mathématique modélisera comment la concentration, les caractéristiques de séquence et la longueur des ARN influencent la formation et la stabilité des condensats, fournissant un cadre interconnecté reliant observations moléculaires et principes physiques.

En intégrant biologie expérimentale et physique théorique, ce projet cherche à établir un cadre mécanistique reliant la biologie des ARN, l'organisation nucléaire et l'inflammation persistante. Au-delà du contexte inflammatoire, il vise à révéler les principes généraux par lesquels des signaux environnementaux et métaboliques modulant la régulation génique à long terme agissent via l'organisation physique du noyau, apportant des perspectives sur l'interaction entre ARN, chromatine et condensats transcriptionnels.

CONTENU SCIENTIFIQUE

***Thématique** : ARN non-codants ; condensats transcriptionnels, régulation génique, principes physiques et modélisation des condensats nucléaires et transcriptionnels*

***Domaine** : biologie moléculaire, physique théorique de la matière vivante et des systèmes complexes*

Contexte scientifique : Les maladies inflammatoires chroniques constituent un défi majeur pour la société et la biomédecine, en raison de l'exposition prolongée à des facteurs environnementaux, alimentaires et liés au mode de vie, ainsi que d'expositions inflammatoires répétées. Ces pathologies se caractérisent par des programmes de transcription persistants, notamment dans les cellules immunitaires innées comme les macrophages. Les mécanismes qui stabilisent ces états transcriptionnels durables restent largement inconnus.

Des études récentes ont montré que la transcription est organisée spatialement dans le noyau via des condensats biomoléculaires, qui concentrent RNAPII, facteurs de transcription et coactivateurs aux régions régulatrices actives, y compris les enhancers et super-enhancers. Les propriétés physiques de ces condensats influencent l'efficacité, la réactivité et la stabilité transcriptionnelle. Les ARN non codants produits localement, tels que les eRNAs et PROMPTs, jouent un rôle clé en modulant la dynamique et l'organisation de ces condensats, faisant d'eux des régulateurs actifs plutôt que de simples sous-produits transcriptionnels.

Objectifs : Le projet doctoral miroir vise à élucider comment les ARN non codants dérivés d'amplificateurs (enhancers) et de promoteurs régulent l'organisation et la dynamique des condensats transcriptionnels, et comment cette régulation contribue à la persistance des états transcriptionnels associés à l'inflammation chronique. L'hypothèse centrale est que les ARN

nucléaires agissent comme des paramètres modulables contrôlant le comportement des condensats et permettant la mémoire transcriptionnelle à long terme. L'analyse théorique, fondée sur des approches de physique statistique et de systèmes non linéaires, permettra ainsi de mieux comprendre les mécanismes physiques qui gouvernent la formation et la régulation de ces condensats, ainsi que leurs régimes physiologiques et pathologiques, éclairant ainsi les principes de la théorie des condensats moléculaires et de la matière active biologique.

***Méthodes** : Le projet est structuré en deux volets complémentaires :*

Projet expérimental : Perturbation contrôlée de la production et de la dégradation des ARN nucléaires dans des modèles macrophagiques. Analyse de la transcription nascente et imagerie quantitative des condensats pour mesurer leur taille, nombre, distribution et dynamique. Techniques utilisées : TT-seq, imagerie confocale et de super-résolution, FRAP, et marquage de protéines clés.

Projet théorique : Modélisation physique des condensats par des approches de physique statistique, de physique non-linéaire et des simulations Monte Carlo. Étude de l'impact de la concentration, longueur et flux d'ARN, ainsi que de l'architecture nucléaire sur la dynamique et l'organisation des condensats. Interaction continue entre les données expérimentales et les modèles pour affiner les prédictions et guider la conception expérimentale.

Résultats attendus : Ce projet devrait établir un cadre mécanistique reliant la biologie des ARN, l'organisation nucléaire et les condensats transcriptionnels dans le contexte de l'inflammation chronique. Il permettra de comprendre les principes physiques de l'auto-organisation des condensats et leur rôle dans la régulation durable de la transcription. Les résultats devraient fournir des connaissances transférables à d'autres contextes cellulaires, enrichissant notre compréhension de la régulation génique et de l'architecture nucléaire.

Références bibliographiques (optionnel) :

Henninger, J.E. et al. RNA-Mediated Feedback Control of Transcriptional Condensates. Cell 184, 207 225 e24 (2021).

Hnisz, D., Shrinivas, K., Young, R.A., Chakraborty, A.K. & Sharp, P.A. A Phase Separation Model for Transcriptional Control. Cell 169, 13–23 (2017).

Hyman, A.A., Weber, C.A. & Julicher, F. Liquid-liquid phase separation in biology. Annu Rev Cell Dev Biol 30, 39–58 (2014). - Jülicher, F. & Weber, C.A. Droplet physics and intracellular phase separation. Annual Review of Condensed Matter Physics 15, 237–261 (2024).

Razin, S.V. & Gavrilov, A.A. Non-coding RNAs in chromatin folding and nuclear organization. Cell Mol Life Sci 78, 5489–5504 (2021).

Sharp, P.A., Chakraborty, A.K., Henninger, J.E. & Young, R.A. RNA in formation and regulation of transcriptional condensates. RNA 28, 52–57 (2022).

Shrinivas, K. et al. Enhancer Features that Drive Formation of Transcriptional Condensates. Mol Cell 75, 549–561 e7 (2019).

Wadsworth, G.M. et al. RNA-driven phase transitions in biomolecular condensates. Mol Cell 84, 3692 3705 (2024).

***Conditions matérielles de réalisation du projet (incluant, le cas échéant, les conditions de sécurité spécifiques)* : Le volet expérimental sera réalisé au sein du laboratoire de Régulation Génétique de l'IGH, équipé de plateformes avancées d'imagerie (confocale et super-résolution), de laboratoires de culture cellulaire conformes aux normes de biosécurité (niveau BSL-2 pour cellules humaines), et de dispositifs pour le séquençage à haut débit et le traitement des échantillons ARN. Toutes les manipulations de cellules humaines primaires et de lignées cellulaires, y compris l'utilisation de réactifs tels que LPS, cytokines et plasmides d'expression, seront effectuées conformément aux protocoles de sécurité et aux réglementations en vigueur. Les expériences optogénétiques et de perturbation des ARN seront réalisées dans des conditions contrôlées, avec formation préalable des étudiants aux risques chimiques et biologiques.**

Le projet théorique se développera dans l'Axe de Physique Théorique du Laboratoire Charles Coulomb.
Le jeune scientifique aura accès aux ressources documentaires (bibliothèques et références bibliographiques) et aux ressources informatiques (ordinateurs, logiciels de calcul) du Laboratoire Charles Coulomb et, si besoin, des ressources numériques de la plateforme de calcul MESO@LR et du CINES.

Les deux projets nécessiteront d'un travail interdisciplinaire interactif, comprenant un "bootcamp" conjoint et des réunions régulières bimensuelles afin de garantir que les données expérimentales alimentent les modèles et que les prédictions issues des modèles guident les expériences.

English version

Project's Abstract:

Title: **Chronic Inflammation Shapes Non-Coding RNA-Mediated Transcriptional Condensates: Experimental and Modelling Approaches**

Keywords*: : chronic inflammation; ncRNA; transcriptional condensates; biological and physical modelling; theoretical physics of biological and complex systems; condensate dynamics; statistical and polymer physics, active matter, phase transitions, nonlinear physics*

Abstracts of the PhD projects (EN – max. 4000 characters, including spaces):
Chronic inflammatory diseases represent a growing societal and public health challenge world-wide. Their incidence has increased markedly over recent decades, in parallel with environmental, dietary, and lifestyle changes. Long-term exposure to pollutants, dietary imbalances, and repeated low-grade inflammatory stimuli is now recognized as a major contributor to sustained immune activation. These conditions are associated with persistent alterations in gene expression programs in innate immune cells, particularly macrophages, which maintain inflammatory transcriptional states long after the initial trigger.

At the cellular level, long-lasting inflammatory responses cannot be fully explained by transient signalling pathways alone, pointing instead to stable or semi-stable regulatory mechanisms operating at the level of transcription and nuclear organization. Recent advances have revealed that transcription is spatially organized within the nucleus through the formation of dynamic bio-molecular condensates, which concentrate transcription factors, coactivators, and RNA polymerase II at active regulatory regions. These condensates are increasingly viewed as key regulators of transcriptional robustness and responsiveness, yet the mechanisms controlling their formation, stability, and adaptability remain poorly understood.

A defining feature of active regulatory regions is the local production of short-lived non-coding RNAs, including enhancer RNAs (eRNAs) and promoter upstream transcripts (PROMPTs). These RNAs are generated in close spatial and temporal proximity to transcriptional condensates and remain confined to the nucleus. Emerging evidence indicates that they can actively influence condensate behaviour through concentration-dependent effects, sequence-encoded features, and RNA-protein interactions, positioning them as dynamic regulators of nuclear organization rather than passive transcriptional byproducts.

This mirror doctoral project represents a new collaboration between two teams in experimental biology (IGH) and theoretical physics (L2C). It aims to elucidate how enhancer- and promoter-derived non-coding RNAs dynamically regulate transcriptional condensates, and how these mechanisms contribute to the

persistence of inflammatory transcriptional states. The project will combine precise experimental perturbations of nuclear RNA levels, quantitative imaging of condensate dynamics, and long-read RNA sequencing to characterize RNA length, structure, and modification patterns. In parallel, a mathematical-physics oriented mirror project will model how RNA concentration, sequence features, and length influence condensate formation and stability, providing an interdependent framework that links molecular observations to physical principles of condensate behaviour.

By integrating experimental biology and theoretical physics approaches, this work seeks to establish a mechanistic framework linking RNA biology, nuclear organization, and persistent inflammation. Beyond the context of inflammation, the project aims to uncover general principles by which environmental and metabolic cues modulate long-term gene regulation through the physical organization of the nucleus, providing insight into the interplay between RNA, chromatin, and transcriptional condensates.

SCIENTIFIC CONTENT

Research theme: ncRNA; transcriptional condensates; gene regulation; physical principles and modelling of nuclear and transcriptional condensates

Scientific field: Molecular biology; theoretical physics of living matter and complex systems

Scientific background: Chronic inflammatory diseases are associated with persistent transcriptional programs in innate immune cells, especially macrophages. These durable transcriptional states are not fully explained by transient signaling pathways, but rather involve stable nuclear mechanisms. Transcription is spatially organized in the nucleus through dynamic biomolecular condensates that concentrate RNA polymerase II, transcription factors, and coactivators at enhancers and super-enhancers. Nuclear non-coding RNAs, including enhancer RNAs (eRNAs) and promoter upstream transcripts (PROMPTs), are short-lived but locally enriched at active regulatory regions and have been shown to influence condensate dynamics. Understanding how ncRNAs regulate condensates is critical for deciphering transcriptional persistence in inflammation and more broadly for gene regulation.

Objectives: The objectives of this mirror PhD project are:
-Determine how enhancer- and promoter-derived ncRNAs regulate the formation, size, distribution, and dynamics of transcriptional condensates.
-Assess how RNA-dependent condensate regulation contributes to the persistence of inflammatory transcriptional states.
-Develop an integrated framework combining experimental and theoretical approaches to link RNA biology, nuclear organization, and transcriptional regulation. Theoretical analysis, based on approaches from statistical physics and nonlinear systems, will thus make it possible to better understand the physical mechanisms governing the formation and regulation of these condensates, as well as their physiological and pathological regimes, thereby shedding light on the principles of the theory of molecular condensates and biological active matter.

Methods:
Experimental project: Controlled perturbation of nuclear RNA levels using ASOs, RNA overexpression, and inducible degradation of RNA surveillance factors (e.g., MTR4). Quantitative fluorescence imaging (confocal and super-resolution) to measure condensate properties (size, number, distribution, dynamics). Nascent transcription profiling via TT-seq or 4sU-seq. Long-read RNA sequencing to characterize RNA length, structure, and modifications. Optogenetic induction of condensates for

dynamic studies.
Theoretical project: Statistical physics, field theory modeling and Monte Carlo simulations to describe condensate formation, dynamics, and stability under varying RNA concentrations, lengths, and nuclear organization constraints. Integration with experimental data to generate testable predictions.

Expected results: This project is expected to establish a mechanistic framework linking RNA biology, nuclear organization, and transcriptional condensates in the context of chronic inflammation. It will provide insight into the physical principles underlying condensate self-organization and their role in the durable regulation of transcription. The results should yield knowledge that is transferable to other cellular contexts, enhancing our understanding of gene regulation and nuclear architecture.

References (optional):

Material conditions for the project (including specific safety conditions, if applicable):
The experimental component will be carried out within the Gene Regulation laboratory at IGH, which is equipped with advanced imaging platforms (confocal and super-resolution), cell culture laboratories compliant with biosafety standards (BSL-2 for human cells), and facilities for high-throughput sequencing and RNA sample processing. All manipulations of primary human cells and cell lines, including the use of reagents such as LPS, cytokines, and expression plasmids, will be conducted in accordance with established safety protocols and current regulations. Optogenetic experiments and RNA perturbations will be performed under controlled conditions, with prior training provided to students on chemical and biological hazards.
The theoretical project will be carried out within the Theoretical Physics Division of the Charles Coulomb Laboratory. The young scientist will have access to the documentary resources (libraries and bibliographic references) and to the computing resources (computers, numerical modeling software) of the Charles Coulomb Laboratory and, if needed, to the digital resources of the MESO@LR computing platform and of the CINES.

Both projects will require interactive interdisciplinary work, including a joint "bootcamp" and bi-monthly meetings to ensure that experimental data inform the models and that model-derived predictions guide the experiments.

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KEY FIGURES

51857 students	**73** research facilities	**15** technology platforms
657 National and institutional diplomas	**17** faculties, schools and institutes	**9** doctoral schools
TOP 200 in the Shanghai ranking	**5132** employees including **2818** teachers, researchers and research assistants	**7800** scientific publications in 2022

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