Postdoctoral Position

Biomechanics of Topography-Induced Nuclear Deformations

Vascular Biomechanics and Bioengineering Group – LadHyX, Ecole Polytechnique (Palaiseau, France)

Supervisors: Claire Leclech (CNRS Research Scientist) & Abdul Barakat (CNRS Director of Research, PI)

Context | The cell nucleus is not only the site of gene expression but also the largest and stiffest organelle. Nuclear deformability strongly influences the ability of cells to migrate and adapt in complex environments. Alterations in nuclear mechanics are associated with several pathologies, including laminopathies (a group of rare diseases such as muscular dystrophies and cardiomyopathies) and cancer.

Our team investigates how cells respond to the topography of their environment using microstructured culture substrates. In particular, we employ microgrooved substrates that mimic the organization of biological surfaces *in vivo.* **We recently demonstrated that microgrooves can induce striking, dynamic 3D nuclear deformations**, and we have begun to uncover the underlying biological mechanisms. Importantly, in patient-derived laminopathy cells, we observed severe nuclear shape defects. These findings provide proof-of-concept that microgrooves can serve as a diagnostic tool for pathological alterations in nuclear mechanics (patent filed).

Project Aims | Building on these results, the postdoctoral fellow will explore both the **mechanical basis and the functional consequences of topography-induced nuclear deformations**, while also contributing to the development of a diagnostic platform for nuclear pathologies.

- Aim 1 – Nuclear mechanics: Dissect the reciprocal interplay between nuclear deformation dynamics and nuclear mechanics. This will involve experimental modulation of nuclear properties (e.g., drugs, genetic perturbations), complemented by computational modeling (in collaboration with Rui Travasso, University of Coimbra, Portugal).

- Aim 2 – Functional consequences: Investigate whether topography-induced nuclear deformations impact chromatin compaction and chromosome territory organization (super-resolution microscopy, collaboration with the LOB imaging platform at Ecole Polytechnique). Assess potential transcriptional changes using RNA-seq.

- Aim 3 – Diagnostic applications: Develop the microgroove system as a novel diagnostic tool for nuclear pathologies. Following our proof-of-concept with muscular dystrophy mutations, we are extending this approach to additional laminopathy syndromes and working towards a prototype device for clinical use (collaborations with Institut de Myologie, St Antoine & Cochin Hospitals in Paris, Timone Hospital in Marseille). Longer-term applications include cancer, where the system may help predict the invasive potential of tumor or circulating cells.

Host Laboratory | The project will be supervised by Claire Leclech, a young CNRS researcher and expert in cell–topography interactions who initiated the nuclear deformation project, and Abdul Barakat, CNRS Director of Research, Professor at Ecole Polytechnique, and head of the vascular biomechanics and bioengineering group at LadHyX.

The group has longstanding expertise in cellular and vascular biomechanics, mechanobiology of vascular cells (experimental and computational), and medical device design. Being part of LadHyX (Hydrodynamics Laboratory) offers a highly interdisciplinary environment with physicists and engineers. The lab is located on the green and dynamic Ecole Polytechnique campus in Palaiseau, just outside Paris.

Candidate Profile | We seek a motivated, independent, and collaborative researcher with the following qualifications:

- PhD in cell biology, biophysics, biomechanics, or a related field
- Prior experience in nuclear biology and/or mechanobiology desirable
- Strong interest in interdisciplinary projects at the interface of biology, physics, and medicine
- Ability to work autonomously on this project while contributing to team efforts and mentoring junior researchers

The position is funded for one year with possibility for extension, starting in 2025/beginning of 2026.

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Relevant references:

- **Leclech, C. et al. Micro-Scale Topography Triggers Dynamic 3D Nuclear Deformations. Adv. Sci. (2025) doi:10.1002/advs.202410052.**
- Roellinger, B., Thenier, F., Leclech, C. et al. Clustering cell nuclei on microgrooves for disease diagnosis using deep learning. Sci Rep 15, 22476 (2025). https://doi.org/10.1038/s41598-025-05788-2
- Leclech, C., et al. Distinct Contact Guidance Mechanisms in Single Endothelial Cells and in Monolayers. Adv. Mater. Interfaces 10, (2023).
- Leclech, C. et al. Topography-induced large-scale antiparallel collective migration in vascular endothelium. Nat. Commun. 13, 2797 (2022).