M2 Project: Multi-scale mechanics of the cell cortex

In Eukaryotic organisms, the cell cortex is a thin shell of cross-linked cytoskeleton polymers underlying the plasma membrane. At the meso-scale, it is a visco-elastic active material that exhibits spatiotemporal fluctuations in thickness and stiffness[1]. This activity is key to support essential cell functions such as migration or division in response to environmental cues. However, little is known about cortex mechanics at the molecular scale. The overall aim of this project is to characterize the relationships between the mechanical properties and activity of the cortex to that of its molecular components.

To this end, we are implementing a strategy based on direct mechanical measurements at the molecular and meso- scales in live cultured cells combined with agent-based simulations. First, we have developed genetically encoded molecular tension sensors that enable quantification by fluorescence microscopy of the piconewton forces transmitted by specific crosslinkers of the cortex cytoskeleton and to transmembrane proteins[2]. Simultaneously, we use magnetic pinchers developed by collaborators Olivia du Roure and Julien Heuvingh to quantify the thickness and stiffness of the cell cortex[1]. The candidate will assess how these mechanical quantities across scales relate to each other upon stimulations and perturbations of epithelial cells, isolated or in the tissue. Second, we will develop an agent-based model within the Cytosim platform to determine the molecular composition of a cytoskeleton gel that recapitulates the mechanical relationships across scales observed in the cortex of live cells[3]. Specifically, the candidate will simulate various ratios of filaments:motors:crosslinkers and boundary conditions to retrieve the distribution of tensions across crosslinkers, the contractility, stiffness and thickness of the whole gel. Ultimately, we wish to identify the conditions that approach experimental results and predict the outcome of future experiments.

The student will benefit from a state-of-the-art laboratory with innovative techniques. In addition, the Jacques Monod Institute environment is an ideal setting for a student wishing to learn about cell biophysics and quantitative microscopy.

1. Laplaud, V. *et al.* Pinching the cortex of live cells reveals thickness instabilities caused by myosin {II} motors. *Sci. Adv.* **7**, eabe3640 (2021).
2. Gayrard, C. & Borghi, N. FRET-based Molecular Tension Microscopy. *Methods* **94**, 33–42 (2016).
3. Belmonte, J. M., Leptin, M. & Nédélec, F. A theory that predicts behaviors of disordered cytoskeletal networks. *Mol. Syst. Biol.* **13**, 941 (2017).

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