In vivo study of the dynamics and mechanics of actin cortex in different cellular contexts

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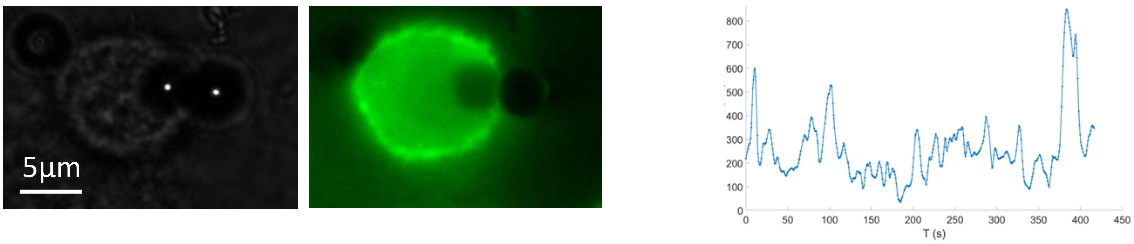
The cell cortex is a thin meshwork of actin filaments found below the plasma membrane of eukaryotic cells. This structure participates to many cellular processes such as migration, division, endo/exocytosis. A large number of its basic characteristics remain however elusive, such as its thickness, dynamics or mechanical properties, but also simply its composition. As an example, the pathways of actin nucleation in the cortex have only recently been identified. Within the cortex, the molecular motor myosin is identified as the main responsible of cortical tension and contractile properties. The interplay between this motor and the network architecture can lead to interesting variations in the resulting tension. The mechanics of the cortex can be probed by twisting a magnetic bead attached to the cellular membrane but this measure is strongly model-dependent. Knowing the visco-elastic properties of the cortex is necessary to assess the importance of the cortex in the overall stiffness of a cell. Lastly, the first values for the thickness of the cortex have only been recently reported, using fluorescent images and comparing the position of labeled membrane and labeled cortex.

Recently, we developed a new technique that gives access to dynamic measurements of the cell cortex in live single cells. In addition, this method potentially provides the most direct and unambiguous measure of the mechanical properties of the cortex. We showed that the cortex of dendritic cells, known to have a fast migratory behavior, has a thickness in the range 100-200 nm with large temporal variations up to 1000 nm due to the actin cortex. We tested the impact of several sources of activity (actin polymerization and contractility) and discover that even if they all collaborate to the measured temporal variations, the myosin motors is the most important player. We currently attribute these temporal variations to instabilities of the cortex layer induced by its contractile properties.



Left: bright field and fluorescence images of a Lifeact dendritic cell whose actin cortex is pinched between two beads. Right: temporal evolution of the cortex thickness (vertical axis: nm) for the cell shown on the images (horizontal axis: sec).

The first part (Master 2 internship) of this project will be devoted to connect the temporal variations of the cortex thickness to tension by changing the latter either using microfluidics pipette or laser ablation. The focus of the main part (PhD) will be to understand the interplay between biophysical properties of actin cortex – activity, mechanics, contractility – and the cell shape changes.
Our long-term goal is to use the cell pincher to unravel the role of the actin cortex when cells change their shape like migration, spreading or division of particular interest to embryonic development and to a large range of pathologies from cancer to atherosclerosis.

The project will be conducted at PMMH, situated on the site of Jussieu, in close collaboration with the lab of Matthieu Piel of Institut Curie, situated at Institut Pierre Gilles de Gennes. This collaboration has been already installed and strengthened during a previous PhD (2016-2019).

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