

Exploration of the contribution of cytoplasm biophysical properties to cell migration.

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Team: Cytoskeleton dynamics and motility

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Context:

The cytoplasm is the largest cellular compartment, and it contains most of the cell's proteins and encompasses most of the metabolic reactions that support cell function and life. In this complex environment molecules constantly jiggle around under the influence of thermal fluctuations and find each other through diffusion. Yet, organized and reproducible processes emerge from this chaotic and stochastic environment. Indeed, cell survival depends on molecules and proteins finding each other, at the right time, in the right location, and at the right rate. This project aims to understand how the cytoplasm's physical properties affect cellular function using cytoskeleton dynamics and the context of cell migration.

Cell migration is a multifaceted process that requires the reorganization of the entire cell and the establishment of a new organelle, the lamellipodium. Within the lamellipodium, the actin cytoskeleton is dynamic and polarized. Its constant polymerization pushes the membrane forward and generates a constant retrograde flow. This retrograde flow is the engine driving cell motility forward through anchoring to the cell substrate. This project aims to explore how the well-oiled and reproducible process of cell migration is influenced by the physical nature of the cytoplasm.

We aim to use a diverse array of microscopy methods (particle tracking, lifetime, FRET, FRAP) to estimate cytoplasm physical properties (viscosity and crowding) in migrating cells to decipher how these properties participate in the process of migration. We will first generate cell lines, expressing the different sensors. Then, we will develop the microscopy and image analysis workflows to measure cytoplasmic viscosity and crowding. The goal is to further our understanding of the process of cell migration from a biophysical standpoint focusing on the cytoplasm. Are cytoplasmic properties the same in a migrating and non-migrating cell? Are they the same in the front and the back of the cell? Can they be manipulated to influence cell migration? This is the kind of question we will try to answer.

This internship will allow the student to work at the interface of biology, physics, and microscopy. The student will leave the laboratory with experience in microscopy and image analysis as well as a better understanding of the cytoplasm and its physical properties. The student will gain valuable experience in basic molecular biology and cell culture techniques.

Recommended literature:

- Molines et al., *Dev. Cell.*, 2022.

Physical properties of the cytoplasm modulate the rates of microtubule polymerization and depolymerization.

- Garner, Molines et al., *Biophysical J.*, 2023.

Vast heterogeneity in cytoplasmic diffusion rates revealed by nanorheology and Doppelgänger simulations.

- Delarue et al., *Cell*, 2018.

mTORC1 Controls Phase Separation and the Biophysical Properties of the Cytoplasm by Tuning Crowding.

- Neurohr and Amon, *Trends in Cell Biology*, 2020.

Relevance and Regulation of Cell Density.

- Seetharaman and Etienne-Manneville, *Trends in Cell Biology*, 2020.

Cytoskeletal Crosstalk in Cell Migration