Master 1/2 - Research projects 2022-2023

Biomechanics of cancer cells

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Describe the team that the student will join for the project.

The intern will join a group of researchers, composed of 2 postdocs, two PhD students, two M1/M2 interns, one biology engineer and one permanent position (J.-F. Berret, DR CNRS). Our research group develops novel functional structures, devices and systems with stimuli-responsive features at the nano and microscales. The three research themes of my group are cellular biomechanics, development of theranostic agents for nanomedicine and biophysics of lung function. Our objectives deal with applications in medicine, biology and in the environment (more information here).

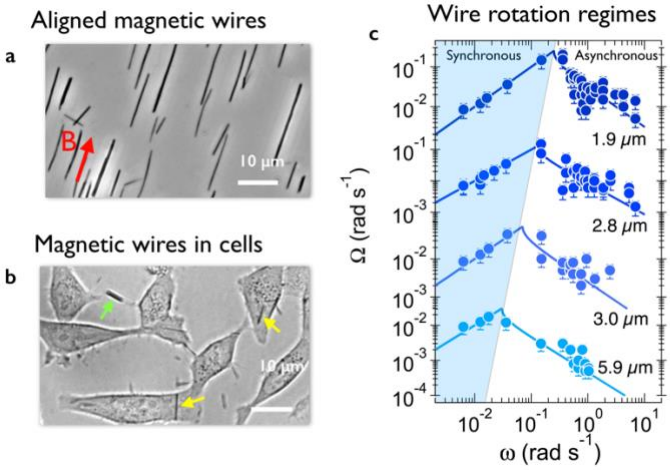
Project description

Mechanotransduction describes the molecular mechanisms by which cells respond to changes in their physical environment by translating mechanical stimuli into biochemical signals [1]. These mechanical changes or stimuli can be either forces exerted on the cell from the environment or intracellular forces arising from cell responses to stiffness or topography modifications. The mechanical properties of cells are mainly determined by the cytoskeleton and nucleus, and are essential in major cell functions such as homeostasis, growth, division and motility.

Beyond mechanotransduction, there are other reasons to study cellular biomechanics, and one of them is cancer. The course and prognosis of cancer depends on the characteristics of the tumor. Important properties are the tumor growth size and rate and the ability for the cells to invade distant tissues (metastatic process). Recent studies suggested that cancer cells acquire specific mechanical properties allowing them to be more deformable than healthy cells [1-4]. The proposed model is based on the assumption that, due to their lower viscosity and elasticity, metastatic cells can move inside a primary tumor by deformation, leading to their translocation to the blood compartment and invasion of distant organs [1,2].

Microrheology studies the motion of micron-size probe particles that are actuated by an external field. We have designed innovative micron-size probes in the form of elongated wires [5]. Magnetic wires of diameter 0.5 - 1 µm and length 1 - 10 µm will be produced following a novel bottom-up self-assembly method. Complete proof-of-concept studies confirm that this technology is capable of measuring the viscosity of fluids with accuracy [6,7]. The technique will be applied to healthy and cancerous cells of different metastatic grades [8]. Targeted cells will be the non-cancerous human epithelial breast cells

(MCF-10A) and human breast cancer cells with various metastatic potentials (MCF-7, MDA-MB-231) [9]. More specifically, the work will deal with i) the synthesis of magnetic nanowires, ii) the internalization and the tracking of wires by optical microscopy, iii) the identification of the cytoskeleton network associated with cell mechanics, using actin and microtubule depolymerizing drugs such as nocodazole, cytochalasin D, Latruculin A. Viscosity and elasticity coefficients from the cytoplasm will be obtained. Emphasis will be put on the relationship between metastatic cancer cells and biomechanics.



d Cell line viscosity

Eukaryotic cell lines	Viscosity (Pa s)
Mouse NIH/3T3 fibroblast	48 ± 8
Human cervical cancer cell (HeLa)	84 ± 29
Human epithelial breast cells MDA-MB-231	11 ± 5

***Figure 1**: **a)** Phase contrast optical microscopy image of magnetic wires under a static magnetic field. **b)** Optical microscopy images of NIH/3T3 fibroblasts after their incubation with magnetic wires. Yellow arrows show wires in the cytoplasm, green arrows outside cells; **c)** Diagram showing the transition between a synchronous and an asynchronous rotation behavior for wires internalized in NIH/3T3 cells upon increasing frequency. **d)** Viscosity of eukaryotic cell lines measured from magnetic wire actuation.*

Preliminary measurements on MDA-MB-231 show that these metastatic cells have a much lower viscosity than other cell lines (Fig. 1d). This internship will consist in completing the measurements on the additional cell lines to verify the hypothesis of a lower viscosity for the metastatic cells. The candidate will also have the opportunity to learn different techniques of physical-chemistry and biophysics, including the manipulation of nano/bio materials at the cellular level, optical microscopy, cell culture and magnetism.

References on this work

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