Research projects 2020-2021

Master M1&M2 – PhD – Post-Doc

Biomechanics of living 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 one postdoc (to be hired), one PhD students (Stefan Rouach), three 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. Our objectives also deal with applications in medicine, biology and in the environment. It includes the development of tools for imaging and therapy in vivo, microfluidics and microrheology as well as the study of living system-machine interfaces (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. During cancerization, the cytoskeleton and lamins, that are giving its rigidity to the nucleus, are directly modified. Recent studies suggest that cancer cells acquire specific mechanical properties allowing them to deform more strongly than healthy cells [2,3].

Rheology is the study of flow and deformation of fluids when they are submitted to mechanical stresses. Conventional rheometers determine the relationship between strain and stress on samples of a few milliliters. Microrheology in contrast 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 [4]. 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 [5,6]. The technique will be applied to healthy and cancerous cells of different metastatic grades [7]. More specifically, the work will deal with i) the synthesis of magnetic/fluorescent 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).

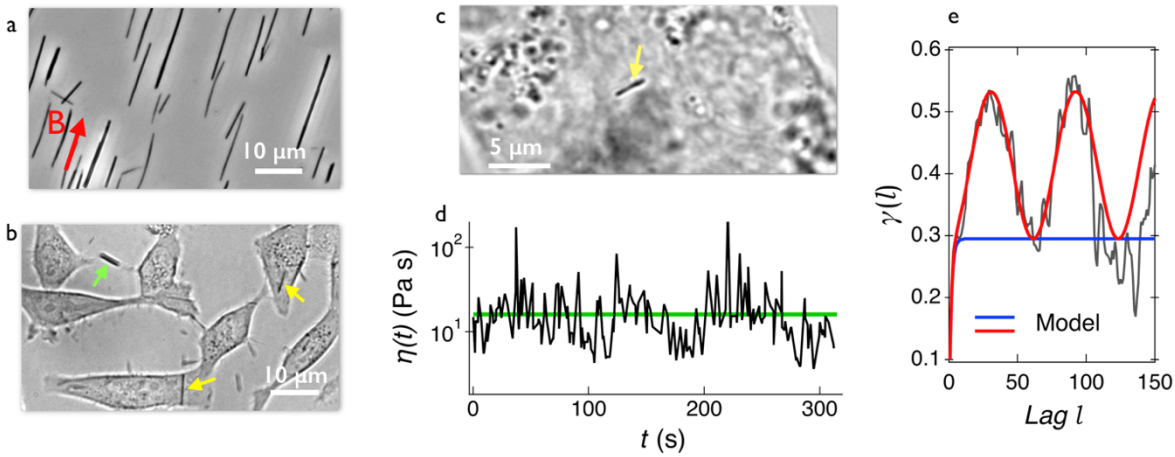

***Figure 1** : a) Phase contrast optical microscopy image of magnetic wires under a static magnetic field. b) Optical microscopy images of NIH/3T3 fibroblasts after their incubation with magnetic wires; c) Single magnetic wire in a living cell; d) Time dependence of the intracellular viscosity [7,8]; e) Variogram obtained from intracellular viscosity time series together with model fitting [8].*

More recently, for healthy cells, we have found anomalous transient responses characterized by intermittent phases of slow and fast rotation, revealing significant fluctuations (Figure 1). The time dependent viscosity was analyzed from a time series perspective by computing the autocorrelation functions and the variograms, two functions used to describe stochastic processes in mathematical finance. The resulting analysis gives evidence of specific cellular times in the ranges 1 - 10 s and 100 - 200 s, not previously disclosed. This approach will be made in collaboration with Claude Bostoen from the Dutch Polymer Institute [8].

During this internship, the student will 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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[3] J. Guck, S. Schinkinger, B. Lincoln, F. Wottawah, S. Ebert, M. Romeyke, D. Lenz, H.M. Erickson, R. Ananthakrishnan, D. Mitchell, J. Kas, S. Ulvick, C. Bilby, Optical deformability as an inherent cell marker for testing malignant transformation and metastatic competence, *Biophys. J.*, 88 (**2005**) 3689-3698.
[4] J. Fresnais, J.-F. Berret, B. Frka-Petesic, O. Sandre, R. Perzynski, Electrostatic Co-Assembly of Iron Oxide Nanoparticles and Polymers: Towards the Generation of Highly Persistent Superparamagnetic Nanorods, *Adv. Mater.*, 20 (**2008**) 3877-3881.
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[8] C.L. Bostoen, J.-F. Berret, A Mathematical Finance Approach to the Stochastic and Intermittent Viscosity Fluctuations in Living Cells, *Soft Matter*, 16 (**2020**) 5959-5969.