Master 2 project 2023-2024

Laboratory : Dpt « Physics and Engineering for Living Systems »
Centre Interdisciplinaire de Nanoscience de Marseille (CINaM), Campus de Luminy, Marseille
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Microfluidic experiments to decipher confined cell migration

Keywords: cell mechanics, microfluidics, videomicroscopy, image analysis

Context. Cell migration under confinement is a crucial mechanobiological process which can be observed during development and embryogenesis, immune response or cancer metastasis. During these processes, cells may need to migrate through pores of sub-cellular (10–30 µm width) or sub-nuclear (2–10 µm width) dimensions. The nucleus is the largest and stiffest organelle, composed of the nucleoplasm, a viscous fluid, and the nuclear envelope (NE), a very thin membrane whose stiffness may be around 10 kPa. Some studies have attempted to investigate the effect of NE defects on nuclear mechanics and confined migration, but little has been done so far on the role of nuclear content organisation (*i.e.*, heterochromatin density) and nucleo-cytoskeletal link. **We aim to assess the role of mechanical properties of these components during confined migration**.

M2 project. Our group in CINaM recently developed a microfluidic device in which cells pass through microchannels under controlled pressure drop (Figure). From the dynamics of cell deformation mechanical parameters can be derived. This approach allowed us to discriminate cells with a higher viscosity linked to alterations of lamin A/C, a component of the NE [Ref]. Here, we will use the same device with cells actively migrating through constrictions without pressure drop, to assay the mechanical properties involved in confined migration. Specific cell responses to targeted modulations known to occur in diseases like cancer (chromatin, cytoskeleton, nucleo-cytoskeleton links) will give insight into the molecular mechanisms at play. During the internship, the student will carry out all experimental steps: fabricating microfluidic chips, culturing cells, performing microfluidic experiments, and analyzing the videomicroscopy data. She/he will perform trial experiments to select the treatment that induce the strongest differences then perform a thorough study. The experiment-derived mechanical parameters will be injected in a computational model developed by a collaborator (R. Allena, Université de Nice) to simulate the cell phenotypes inside the channels.
There will be a possibility of continuing with the project as a PhD student.

Expected profile: Preferentially a physicist with interest towards experiments and biological questions, or a biologist with interest towards biophysical approaches. The subject is however flexible and can be adapted to fit specific interest and skills of the candidate.

Reference:
Enhanced cell viscosity: a new phenotype of lamin A/C alterations. C Jebane, AA Varlet, M Karnat, LM Hernandez-Cedillo, A Lecchi, F Bedu, C Desgrouas, C Vigouroux, MC Vantyghem, A Viallat, JF Rupprecht, E Helfer#, C Badens#. iScience **26**, 107714 (2023). https://doi.org/10.1016/j.isci.2023.107714

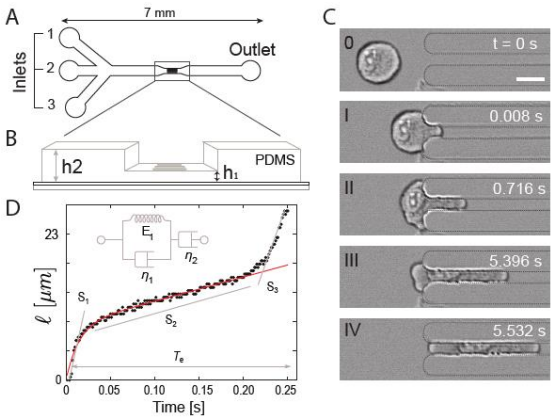

Figure. *A-B) Schematics of the microfluidic device (A, top view) and of the channel region (B, zoomed 3D-view) made of polydimethylsiloxane (PDMS). C) Timelapse of a 24-µm cell entering a 6-µm wide constriction. Scale bar: 15 µm. D) Typical time evolution of the cell tongue length l(t) in the constriction, with linear approximation of the 3 displayed regimes (slopes S_1-S_3) and analytical fit (in red) of the 2 first regimes using a rheological model.*