Master 2 Internship Offer, 2025-2026

Laboratory: Department *"Physics and Engineering for Living Systems"*
Centre Interdisciplinaire de Nanoscience de Marseille (CINaM), Campus de Luminy
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Physical mechanisms of red blood cell genesis

Context. Erythropoiesis is the process of generating red blood cells (RBCs). In mammals, RBCs do not contain nuclei and the enucleation process of the RBC precurors is still unclear. Moreover, once enucleated, the cells still need to mature to become real RBCs. This maturation can start in the bone marrow and end in the microcirculation, but it has been poorly studied from a physics point of view and the mechanical changes during maturation are not elucidated yet. The main reasons are that (i) it is difficult to fabricate an in vitro device that mimics the bone marrow aperture geometry, and (ii) the force quantification is challenging due to the strong interactions between the cell and the surrounding fluid in the narrow slits.

Project Description. The master project focuses on investigating the role of forces in the maturation process, when the cells exit the bone marrow through its highly constraining narrow slits. We will use an in vitro microfluidic approach based on a microfluidic device mimicking the bone marrow slits. Our technology reproducing µm-wide slits is unique worldwide (Figure 1) and will allow us to apply controlled stress on the cells by tuning flow and slit geometry.
Here, we will consider the population of cells which have spontaneously enucleated before exiting the bone marrow. We will study how these cells transit through slits as they mature and mechanically change (shape, rigidity…). Is the role of the slit to prevent them from exiting till a certain degree of maturation/deformability? If so, we will establish the mechanical properties that are selected by the slit 'fitness test'.
The student will:

- extract RBC precursors (from mouse bone marrow) and quantify their maturation dynamics using fluorescence microscopy.
- fabricate microfluidic devices from a pre-existing mold,
- perform microfluidic experiments to observe and quantify retention/passage using high-speed videomicroscopy of enucleated cells at different stages of maturation.

Experimental results will be confronted to predictions from a numerical model in which the mechanical and molecular parameters of cells and nuclei are tuned (Z. Peng, Uinv. Illinois at Chicago, USA).

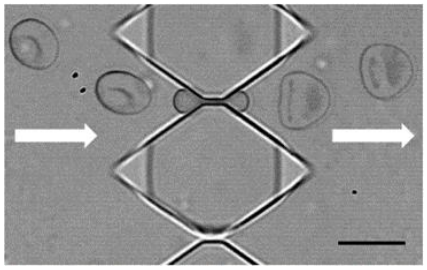

Figure 1. Previous work showing an RBC passing through a biomimetic splenic slit (0.95 x 3 x 4.7 μm^3) under a controlled flow (white arrows) (from [1]. Scale bar: 10 µm.

Expected profile. We are looking for a motivated candidate, with a strong taste for experimentation and learning new techniques. The student will have preferentially a background in mechanics/physics/biophysics, with a strong interest in biological questions and interdisciplinary research. Experience in microscopy and/or biology is a plus.

References.

P. Gambhire et al., High aspect ratio sub-micrometer channels using wet etching: Application to the dynamics of red blood cell transiting through biomimetic splenic slits, Small 13, 1700967 (2017). https://doi.org/10.1002/smll.201700967.
A. Moreau et al., Physical mechanims of red blood cell splenic filtration. Proc. Natl Acad. Sci. USA 120, e2300095120 (2023). https://doi.org/10.1073/pnas.2300095120.