Master 2 project 2023-2024

Laboratory : **Department « Physics and Engineering for Living Systems »**
Centre Interdisciplinaire de Nanoscience de Marseille (CINaM), Campus de Luminy, Marseille
Lab website : http://www.cinam.univ-mrs.fr/cinam/team/physique-et-nano-micro-ingenierie-pour-le-vivant/
Supervisors : **Emmanuèle HELFER** E-mail: emmanuelle.helfer@univ-amu.fr
Simon REGAL E-mail: simon.regal@cnrs.fr

Experimental study of red blood cell enucleation

The internship is part of the RedEnuc project, which aims to describe the physical mechanisms at play in enucleation during mammalian erythropoiesis. Erythropoiesis is the process of generating red blood cells (RBCs). RBCs, which circulate in the bloodstream to transport oxygen and pass through extremely thin capillaries, do not have nuclei. In vivo, erythroblasts (RBC precursors with nuclei) exit the bone marrow to reach the bloodstream through very narrow inter-endothelial gaps, thus undergoing strong external squeezing forces. So far, the mechanisms at play in enucleation are poorly understood. Such understanding is crucial for improving in vitro production of RBCs as enucleation efficiency is currently rather low (30%).

Here, we focus on the role of the mechanical constraints on the extrusion and detachment of the nucleus from the erythroblast when exiting the bone marrow. We aim to mimic the bone marrow environment in a microfluidic device with narrow slits reproducing the inter-endothelial gaps, and to quantify the relationship between the forces exerted by the slits and the cell deformation during passage through the slits. In a previous work, we developed a technique to fabricate a unique microfluidic device with slits thinner than 1 µm (Figure 1, [1]), which then allowed to study the mechanism of RBC passage through the narrow splenic slits [2]. The device is currently upgraded for this project.
The student will perform microfluidic experiments on erythroblasts to determine the experimental parameters for efficient enucleation. She/he will acquire videomicroscopy data and learn image analysis to extract the cell deformation and nucleus extrusion rate. Based on her/his experimental results, she/he will also participate in designing new geometry of the microfluidic device if needed.

There will be a possibility of continuing as a PhD student.

Expected profile:
M2 student in physics/biophysics/biology, with strong interest in interdisciplinary experimental work.

Competences:

- Rigorous
- Meticulousness
- Motivation
- Inventiveness

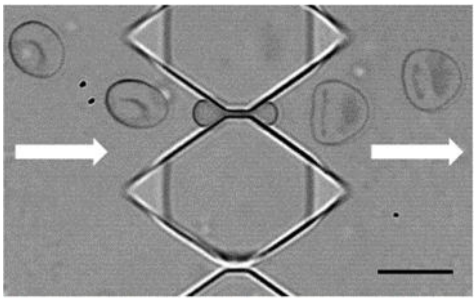

Figure 1: The image shows a deformable RBC passing through a biomimetic splenic slit (0.95 x 3 x 4.7 µm^3) under a controlled flow indicated by the white arrows. Scale bar: 10 µm.

[1] 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). doi: 10.1002/smll.201700967.
[2] A. Moreau *et al.*, « Physical mechanisms of red blood cell splenic filtration », PNAS, in press. doi: 10.1101/2023.01.10.523245.