INTERNSHIP PROPOSAL

Laboratory name: **Laboratoire Matière et Systèmes Complexes (MSC)**
CNRS identification code: **UMR 7057**
Internship director'surname: **Jean-François Berret**
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Internship location: **Université Paris Cité, Laboratoire MSC**

Thesis possibility after internship: YES
Funding: YES If YES, which type of funding: EDPIF

On-chip model of mucociliary clearance

Chronic respiratory diseases (CRDs) caused 4 million deaths worldwide in 2019.1 CRD treatments are often administered by inhalation in particulate formulations. However, mucociliary clearance (MCC) acts as an effective physical barrier that prevents drugs from reaching the target cells. This mechanism relies on the beating of cilia on the bronchi surface, which allows the displacement of the overlying mucus layer (see Figure 1A). Inhaled drugs are thus trapped by the mucus and quickly evacuated from the airways.
This project aims to model the mechanism of mucociliary clearance using a microfluidic chip, to assess drug penetration through the moving mucus and thus provide a screening platform for new drug formulations. We chose to design a non-cellular MCC model, which will provide an easy, quick, cheap, and reproducible alternative to cell-based MCC models.
The chip will be designed and fabricated by our collaborators at PHENIX (Sorbonne Université).2 It is composed of a circular channel with an open top to model the mucus/air interface (see Figure 1B). The channel will be covered with magnetic micropillars that can be remotely actuated via an underlying rotating magnet. Preliminary experiments showed that such an actuation of the pillars results in a beating similar to that of bronchial cilia. Different chip configurations will be fabricated.
The trainee will address the following scientific/technical questions:
- What is the velocity profile of mucus in the chip?
Particle tracking velocimetry will be used to determine the velocity profiles for different chip configurations and beating frequencies. Measurements will first be performed with Newtonian fluids of varying viscosities, before applying the optimized procedure to mucus.
- How to mimic particle deposition on the bronchi during inhalation, with the chip?
The trainee will design an exposure chamber connected to a nebulizer. The chip will be placed inside the chamber for deposition. The quantity and homogeneity of particle deposition will be measured via fluorescence spectroscopy and microscopy, using fluorescent particles.
- Does the chip reproduce the particle behaviour observed on cell-based MMC models?
Using the exposure chamber, fluorescent nanoparticles will be deposited on our chip as well as on commercially available MucilAirTM tissues (Epithelix). These are cultures of epithelial tissue from healthy and diseased donors, and they display mucus production and active cilia beating. We will use confocal fluorescence microscopy to monitor the 3D spatial distribution of nanoparticles within the mucus layer. The goal is to reproduce with our chip the particle behavior observed with MucilAirTM tissues.
The trainee will be co-supervised by Dr Marine Le Goas, who is working in Dr Berret's group as a postdoc.
More information on the internship can be found here: https://www.jean-francois-berret-website-pro.fr/p3-muccociliary-clearence/

Please, indicate which speciality(ies) seem(s) to be more adapted to the subject:

Condensed Matter Physics: YES Soft Matter and Biological Physics: YES
Quantum Physics: NO Theoretical Physics: NO