# Master 2 - Systèmes Biologiques et Concepts Physiques

## Research projects 2021-2022

## Mucociliary clearance-on-a-chip

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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 (Mustafa ElGharib), two PhD students (Stefan Rouach, Jana Szabová), two 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. The three research topics of the group deals with cell mechanics, development of theranostic agents for nanomedicine and biophysics of lung functions (more information here).

### Project description

Fine airborne particulate matter is released from production facilities, construction sites and wildfire, among other sources, and their inhalation is shown to be a major source of premature mortality in Europe and in the world. Among them, ultra-fine particulate matter and nanoengineered materials (size < 100 nm), namely nanoparticles, cause the most adverse effects due to their accessibility to the distal ends of the lungs [1-3]. Luckily, the body has barriers and defense mechanisms along the airways which traps and disposes of inhaled nanoparticles (Fig. 1A). ***Mucociliary Clearance*** consists of a mucus layer covering the airway epithelium and a continuous clearance of mucus from the airways via ciliary waves (Fig. 1B) [4,5]. Nevertheless, trapped nanoparticles may cross this barrier through the mucus pores (Fig. 1C) and reach the underlying epithelial cells [6]. A mimic of mucociliary clearance built on a microfluidic chip is aimed to be developed to serve as a non-biological model for particle removal examinations (Fig. 1C, 1E and 1F).

The microfluidic platform consists of an array of micropillars made out of PDMS. To make the pillars, a mixture of dimethylsiloxane and iron particles will be cast on a mold and cured. Following published protocols, micropillars of length 10 to 50 µm and diameter 2 to 10 µm will be achieved [7,8]. For cilia beating, the microfluidic chip has incorporated a micromanipulator terminated by a magnet able to deflect the micropillars (Fig. 1E). By imposing an asymmetric displacement of the micromanipulator,

we can simulate mechanical conditions equivalent to metachronal waves. Preliminary results were obtained in preparation of the project, showing that the mechanics of the MCC device is operative and functional (Fig. 1F).

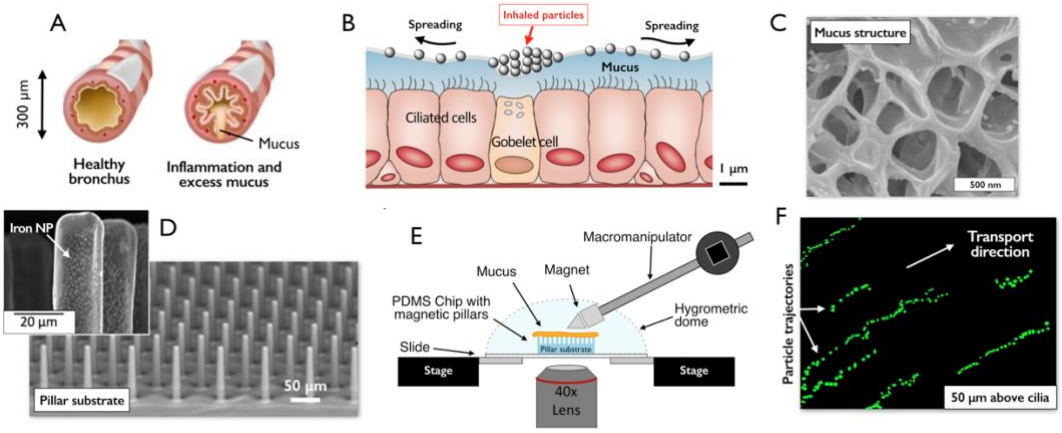


**Figure 1**: ***A)*** *Schematic representation of healthy and diseased bronchus.* ***B)*** *Representation of the mucociliary clearance mechanism in the bronchial region of the lungs.* ***C)*** *CryoSEM of mucus [6].* ***D)*** *Pillars loaded with magnetic particles and pillar substrate.* ***E)*** *Schematic representation of the device mimicking the mucociliary clearance.* ***F)*** *Traces of 1 µm particles followed by optical microscopy above beating cilia (0.2 Hz).*

The objectives of the project are outlined as follows:
**Aim 1**: To develop a mimic of mucociliary clearance using magnetic micropillars and a chip that integrates electromagnets and measure the velocity field of tracer particles above the beating pillars.
**Aim 2**: On a longer term, to study the clearance of nanoparticles in mucociliary clearance mimic apparatus and to explore its potentials for future applications.

This project will contribute to the existing knowledge, while the developed mimic apparatus will serve as an alternative model for future particles inhalation toxicology and pharmacology, as well as pulmonary disease diagnosis investigations.

## References


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