## Research projects 2018-2019

# Microfluidic realization of an Alveolus-on-a-Chip

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**Co-advisor:**
Dr. Yong Chen: ENS Paris

## Describe the team that the student will join for the project.

The intern will join a group of 5 researchers, composed of 3 postdocs (Evdokia Oikonomou, Victor Baldim, Milad Radiom), one intern (Larissa Ferreira) 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.

## Project description

Recent findings in cell biology have underlined the importance of the mechanical environment for cell growth and tissue differentiation. These studies emphasize the importance of designing cell culture systems that mimic the physical microenvironment of living organs as well as providing natural chemical cues. Indeed, for the cells to maintain their differentiated functions, we need to reconstitute the *in vivo* cellular microenvironment.

In response to that, and with the recent progress in micro-fabrication techniques, microfluidic devices have been designed to replicate specific microenvironments for 3D cell culture. The device consists in a PDMS chip, with micro-channels embedded by techniques such as photolithography. These channels supply a chamber where the cells are grown. Depending on the environment we want to mimic, mechanical or electrical stimulations can also be applied

to the chip. The PDMS material was chosen for its high gas permeability (ensuring oxygen supply to cells in micro-channels), its optical transparency (allowing to carry out real-time micro-fluorimetric measurements), and its high flexibility (allowing precise automated control of fluid flow). This kind of cell culture, differentiating a precise tissue and its specific microenvironment is generally referred to as “Organs-on-a-chip”.

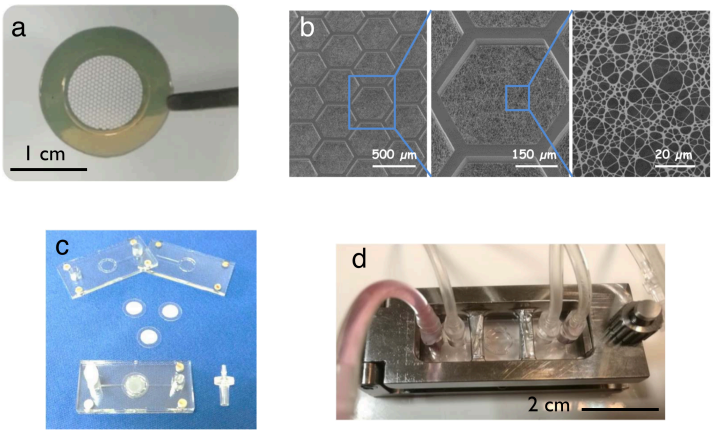


***Figure 1:*** *a&b) Polymer patch mimicking the alveolus. c&d) Microfluidic device able to apply pressure and deform the patch.*

In light of these recent innovations, we decided to focus on “Organs-on-a-chip” technology to better study the integration of living cells on a deformable environment able to simulate the mechanical constraints occurring in the alveoli. The first step of this project is to develop the “Alveolus-on-a-chip” device. The microfabrication will be performed at the Ecole Normale Supérieure of Paris, in collaboration with the group of Yong Chen and at the Université Paris-Diderot in collaboration with Pr. Armelle Baeza-Squiban.

The goal of the internship is to prepare polymer based patches (Fig. 1a and 1b) on which the cells will grow and form an epithelium identical to that of the lungs. In particular here, the mechanical properties of the layer will be studied applying varying pressures on one side of the chip (Fig. 1c and 1d) and measure the deformation of the patch, with and without cells. Observation will be made using optical microcopy and fluorescence. The objective is to reproduce the deformation of the alveoli during normal breathing with this device. This work will be carried out in the context of the ANR AlveolusMimics confronting physicists and biologists.

*Lung-on-a-chip*

**Huh, D., Matthews, B. D., Mammoto, A., Montoya-Zavala, M., Hsin, H. Y., & Ingber, D. E.** (2010). Reconstituting organ-level lung functions on a chip. *Science*, *328*(5986), 1662-1668.

**Bhatia, S. N., & Ingber, D. E.** (2014). Microfluidic organs-on-chips. *Nature biotechnology*.

*Nanoparticles and surfactant interactions*

**F. Mousseau, C. Puisney, S. Mornet, R. Le Borgne, A. Vacher, M. Airiau, A. Baeza-Squiban, J.F. Berret**, Supported pulmonary surfactant bilayers on silica nanoparticles: formulation, stability and impact on lung epithelial cells, *Nanoscale*, **9** (2017) 14967-14978.