# Design of actuable cellular scaffold for the study of lung fibrosis

## Master's degree internship offer

**Context:**

Cells evolve in protein matrices with varied physicochemical properties (2D or 3D, varying degrees of hardness, with various scales of roughness, hydrophilic or hydrophobic, etc.). These properties influence cellular fate, such as the differentiation capacity of stem cells or the invasive capabilities of cancer cells. Cells adapt to these various physicochemical properties by adjusting the signalling involved in their adhesion, with repercussions on all cellular responses. In this context, numerous studies are investigating the impact of these properties on cell fate. However, it is often difficult to isolate them from one another. At LTM, we use microfabrication tools to study the effects of the geometric organisation of the matrix and the rigidity of the architecture on cellular behaviour. To do this, we are developing 3D printing processes to design geometrically controlled cages at the micrometric scale based on 2-photon lithography (Fig. 1A).

Here we aim at studying idiopathic pulmonary fibrosis (IPF), a fatal progressive and unpredictable disease characterized by extracellular matrix deposition that leads to stiffening of the pulmonary parenchyma and destruction of functional lung tissue. This pathology involves 4 cell types (epithelial, endothelial, fibroblast and immune cells), whose individual contribution in the onset of the pathology has not been solved yet. Our intuition is that the fibroblasts, activated by immune cells secretions, trigger the onset of the disease by altering the mechanical properties of the tissue.

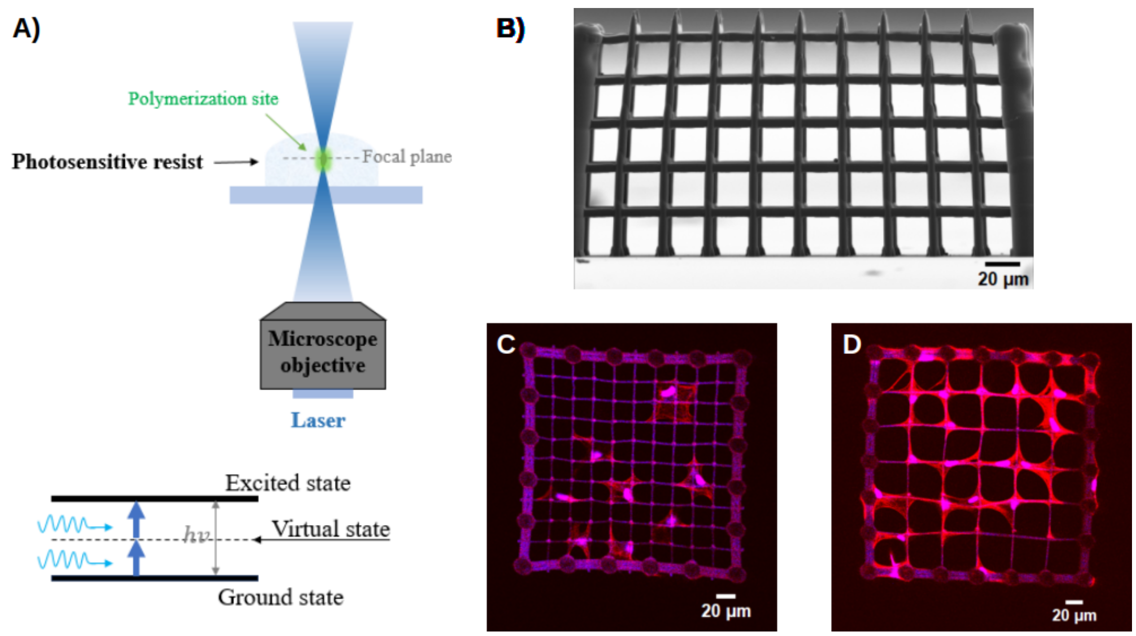


*Fig. 1: A) Principle of the two-photon lithography. B) 3D scaffold printed with Ormocomp resist, whose pore size is 20 µm and fibre size is 5,3 +/- 0,3 µm in any direction. C-D) NIH 3T3 fibroblasts grown in scaffolds whose fibre diameter is 3 µm and pore size is 20 µm (C) or 40 µm (D). the cells are labelled for actin cytoskeleton (red) and nuclei (blue). Cell morphology and area appear sensitive to pore size in this range of parameters.*

In previous studies, we have developed printing processes that allow us to design fibred scaffolds with controlled pores and fibres size (Fig. 1B). This has made it possible to study the role of geometric cues on fibroblasts behaviour (morphology, proliferation, migration, Fig. 1C,D). Nevertheless, in IPF, while lung fibroblasts are embedded into fibred matrices, they also experience mechanical stresses coming from breathing.

**Objective of the internship:**

Our objective here is thus to design 3D actuable scaffolds, able to exert physiological stresses on the cells. These scaffolds will be instrumental in subsequent studies to understand how mechanical cues influence the behaviour of activated fibroblasts in IPF, including their secretion of matrix proteins and soluble factors. This internship represents the initial phase of this project. Its key focus will be on developing a new photoresist compatible with 2-photon lithography that is loaded with magnetic nanoparticles whose exposure to magnetic field gradients makes it possible to actuate the printed scaffold. This formulation will thus have to consider the magnetic force needed to induce structural deformation of the scaffolds and the effect of magnetic charge on the photochemical reaction. Additionally, the intern will design and build a device capable of generating a magnetic field to apply low-frequency cyclic forces (in the Hz range) to the scaffolds. If time allows, preliminary cellular studies will be conducted to analyse the impact of the deformation of the scaffold on the behaviour of a model fibroblast cell line.

**Working environnent:**

This offer is a shared project between LTM and Spintec laboratories. LTM is a laboratory expert in the development of micro and nanotechnologies and their use for applications in the fields of microelectronics, biology, environment and energy. Spintec is a laboratory working in the field of spintronic, that has developed a strong expertise in the design of nanoparticles for biomedical applications. The intern will share his/her time between the two laboratories, being part of the Micro and Nanotechnologies for Health, Environment and Energy team at LTM (https://ltm.univ-grenoble-alpes.fr/research/minasee), and of the Health and Biology team in Spintec (https://www.spintec.fr/research/health-and-biology/).

This internship is a continuation of thesis work at LTM, which has led to established protocols for printing scaffolds for cell culture. The intern will work in contact with the PhD student, who will teach him/her the necessary skills for this technique.

The fabrication and characterization work will be conducted in clean room environments. Cellular assays will be conducted in a L2 laboratory. Imaging will be performed either on a videomicroscope that is settled in the L2 laboratory, or on a two photon microscope available as a facility of TIMC laboratory.

**Background and required skills:**

Training in physics or engineering, with a good understanding of the basics of mechanics, magnetism and optics. Some basic knowledge on polymerization processes and/or on cell biology will be appreciated.
The candidate must show rigour, curiosity, critical analysis, decision-making ability, and sociability. Ability to synthetize information and communicate it back in weekly meetings will be compulsory.

**Contact:**

Lab of Technologies of Microelectronics (LTM): https://ltm.univ-grenoble-alpes.fr

Alice NICOLAS
email: alice.nicolas@cea.fr

Jean-Hervé TORTAI
email: jean-herve.tortai@ltmlab.fr

SPINtronique et TEchnologie des Composants (SPINTEC): https://www.spintec.fr/

Hélène JOISTEN
email: helene.joisten@cea.fr