

M2 internship: February – July 2026

Tumor cell migration upon interstitial flow in a fully controllable 3D fibers-on-chip system

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Project description :

Context. Tumors alter their microenvironment chemically and physically. The presence of **tumor cells** can cause changes in the density of collagen fibers in the **extracellular matrix** (ECM), and in their rigidity, degradation and alignment (1). It has been observed that ECM fibers form specific and recognizable architectures around solid tumors, named **Tumor-Associated Collagen Signatures (TACS)** (2). These matrix architectures influence the migration of cells of the tumor microenvironment, with expected consequences in the ability of cancer cells to invade and metastasize, and of immune cells to reach the tumor (3). In tumors, these mechanical cues associated to ECM architecture are strongly coupled to global mechanical cues, in particular arising from interstitial flow. Interstitial fluid is normally present in tissues at near-zero pressure to supply nutrients to cells. In the presence of a solid tumor, interstitial pressure and flow strongly increase (4), influencing the behavior and morphology of tumor cells. The aim of our project is to evaluate the influence of the coupling between the physical properties of the ECM and the interstitial fluid flow on cancer cell migration.

In order to mimic these coupled mechanical constraints, we are currently developing a microfluidic system with three-dimensional fiber matrices, using two-photon polymerization technique. Two-photon technique allows a total control of the fiber matrix, and we have previously developed an original system to reproduce types of fibers architectures that can be found around tumors and study inside subcellular-scale mechanical properties including 3D forces (5). We are now coupling this system to microfluidic chips to study interstitial fluid flow in a controlled fiber environment. Using this system, we will be able to study the combined effects of fiber matrix architecture and interstitial fluid flow on tumor cell's migration. This microfluidic system, currently in development, still needs to be optimized to be used as a model for different tumor micro-environments.

Aims of the internship. This internship aims to optimize the creation of microfluidic chips with fully controlled 3D fiber networks mimicking the organization of extracellular matrix at sequential steps of tumor development. The intern will optimize the production protocol for the microchips, the flow control and the cell seeding, and will be able to design new fibers, matrix architectures and microchips. In the lab, the student will design and produce PDMS microfluidic chips, print 3D fibers (using TPP) and test out the microfluidic system with tumor cells. The end goal is to characterize the cell migration properties in response to the architecture of the microenvironment and the global flow, from a biology

perspective (stainings, pharmacology) and from a physics one (migration speed, dynamics of protrusion formation, exerted forces).

Training and lab environment. We are looking for a student with an interest in microfluidics, design and biological applications. A wide variety of profiles can be accepted for this internship, which will be adapted according to the initial student's training in biology, chemistry or physics.

The intern will primarily be trained to microfabrication by two-photon polymerization, and in microfluidics. It will also be possible to be trained in cell culture and microscopy (spinning disk). Depending on the intern's profile and interests, the internship may also include COMSOL simulations, or chemical developments for the biomaterials used.

The student will work at Institut Pierre-Gilles de Gennes to produce the chips and at Institut Curie to use the two-photon polymerization set-ups dedicated to this project and perform cell culture and imaging experiments. They will work closely with the PhD student who developed this microfluidic system for her PhD. The project will benefit from the rich infrastructure of Institut Curie, Institut Pierre-Gilles de Gennes and Chimie Paris (microfluidics and microfabrication, state-of-the-art imaging platform, cell culture, modeling of biophysical phenomena, and wide expertise in chemistry).

References.

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2. Xi G, Guo W, Kang D, Ma J, Fu F, Qiu L, et al. Large-scale tumor-associated collagen signatures identify high-risk breast cancer patients. *Theranostics.* 2021;11(7):3229–43.
3. Szulcowski JM, Inman DR, Proestaki M, Notbohm J, Burkel BM, Ponik SM. Directional cues in the tumor microenvironment due to cell contraction against aligned collagen fibers. *Acta Biomater.* 2021 July;129:96–109.
4. Salavati H, Debbaut C, Pullens P, Ceelen W. Interstitial fluid pressure as an emerging biomarker in solid tumors. *Biochim Biophys Acta BBA - Rev Cancer.* 2022 Sept;1877(5):188792.
5. P Ucla et al., Quantifying cell traction forces at the single-fiber scale in 3D: An approach based on deformable photopolymerized fiber arrays (2025) *Proc. Natl. Sci. USA*, in press, <https://doi.org/10.1073/pnas.2507677122> (preprint in : <https://www.biorxiv.org/content/10.1101/2024.11.14.623421v1>)

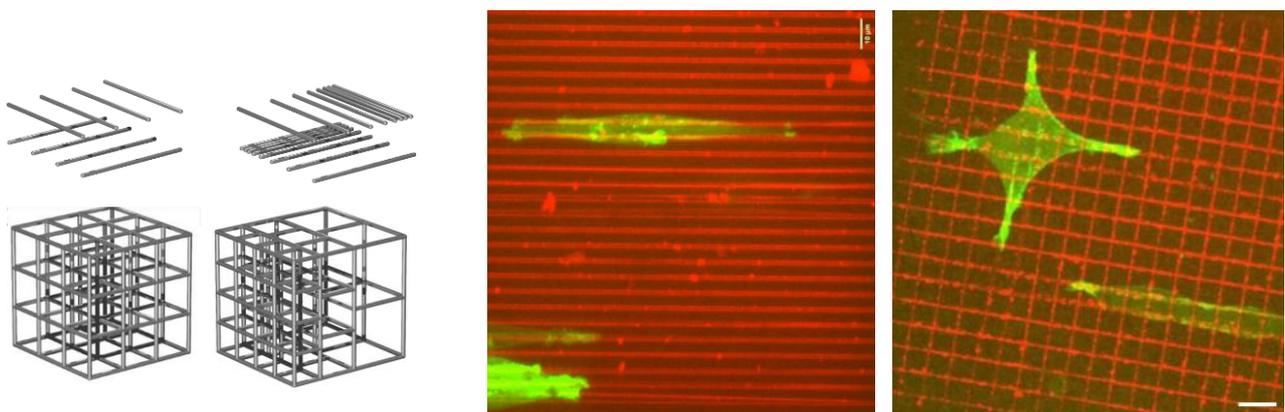


Figure: Left, examples of fiber matrix architectures that can be printed within our two-photon polymerization system. Right, breast tumor cells (MDA-MB-231 and MCF10DCIS.com, LifeAct-GFP in green) on different matrix architectures, scale bar : 10 μm.