Dynamics of cell-matrix interactions studied in a fully controllable 3D fiber system

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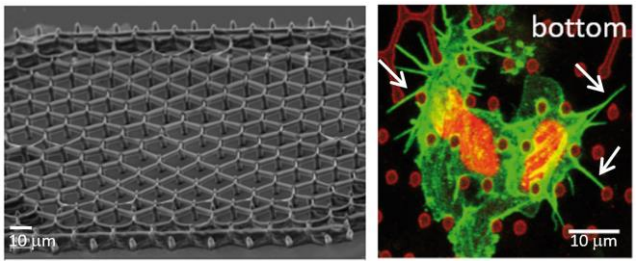
Cells evolve in a 3D fiber network, the extracellular matrix, whose local topography, mechanics and chemistry guide their movements and fate. While numerous biomaterials have been engineered to obtain the desired properties at the mesoscale (size of several cells), controlling the 3D architecture and the chemistry of fibers at a subcellular scale necessitates specific techniques like two-photon polymerization. Our team has developed over the years a full toolbox to produce at will complex 3D geometries and fiber networks, in hybrid polymers, hydrogels or protein materials, which also allows the measurement of traction forces exerted by cells.

We use this toolbox to address with a new perspective the interactions between cells and extracellular matrix in a variety of biological processes, with focus on vascular physiopathology and migration of tumor cells. The internship will be aimed at understanding these fundamental mechanisms, which meets considerable medical needs in the fields of bioimplants and cancer. We previously focused on early steps of the formation of new blood vessels (angiogenesis), where leader tip cells invade extracellular matrix emitting exploratory filopodia important for angiogenesis, and observed that these filopodia could be induced by microtopography alone (Ucla et al, 2022). We are now building more complex 3D structures in order to study the mechanisms on migration in response to physical cues of the environment, including gradients of stiffness (durotaxis), of fiber density (topotaxis), or chirality of the architecture. In parallel, we are developing an original method to measure the associated traction forces. Our system provides now an ideal tool to understand finely the dynamic adaptation of cell collective migration to the microenvironment.

This internship aims to optimize the creation of new 3D microstructures promoting multicellular engagement and collective migration guided by patterns with varied properties like stiffness, local fiber density, spatial organization including network chirality, or protein coating. The cell migration properties, as well as the formation of membrane protrusions in response to the local geometrical and mechanical constraints, will be characterized from a biology perspective (stainings, pharmacology) and from a physics one (migration speed, dynamics of protrusion formation, exerted forces).

The intern will primarily be trained to microfabrication by two-photon polymerization, cell culture and microscopy - spinning disk, Light Sheet microscopy. Depending on the intern's profile and interests, the internship may also include chemical developments for the biomaterials used (surface functionalization, protein polymerization), image analysis by Artificial Intelligence (Convolution Neural Networks) or participation in the modeling of the forces exerted by cells based on local deformations.



Arrays of hexagons on pillars built by two-photon microscopy (left), leading to the generation of endothelial filopodia in the bottom plane (arrows) (HUVECs cells, actin/nuclei labeling, right).

Ucla P, Ju X, Demircioglu M, Baiz S, Muller L, Germain S, Monnot C, Semetey V, Coscoy S. (2022) Dynamics of endothelial engagement and filopodia formation in complex 3D microscaffolds. ***Int. J. Mol. Sci.***, *23*(5), 2415.