3D nematic-like tissues : Topological dynamics and interplay with muscle cell differentiation.

Keywords :
Mechanobiology, 3D tissues, nematic

Supervisor : Myriam Reffay (myriam.reffay@u-paris.fr)
Laboratory : Matière et Systèmes Complexes 10 rue Alice Domon et Léonie Duquet 75013 PARIS
Website : https://mreffay-research.fr
Lab website : https://msc.u-paris.fr/

Scientific context

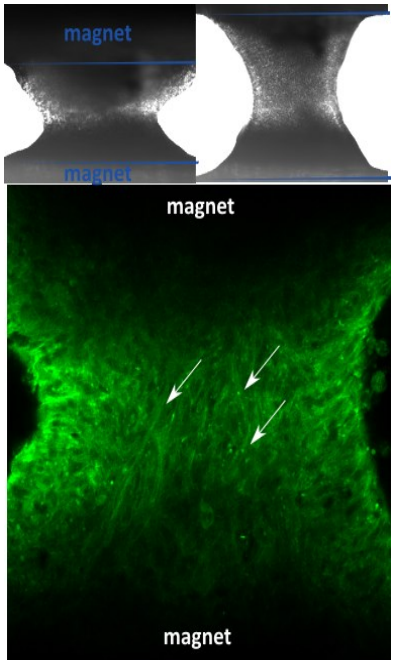

Figure 1 : Myoblasts cells trapped between two micro-magnets and stretched. Fused cells are visible (white arrows).

Cell-generated forces in tissues allow biological tissues to contract, stretch, align and organize themselves, especially during muscle formation. Indeed, muscles have a fascinating multi-scale architecture that supports both their active and passive functions. This complex architecture hinders the creation of artificial muscles. The impact of physical constraints on muscle cell differentiation is therefore fundamental to understanding muscle pathologies. In addition, muscle cells reveal as model nematic cells [1,2], they are elongated and alignment is promoted. This property reveals as fundamental in the major step of muscle differentiation which is fusion.
In recent years, we have developed an original approach based on the use of magnetic nanoparticles [3,4,5,6] to create 3D functional muscular tissues. Magnetic nanoparticles penetrate into cells to endow them with magnetic properties, so that they can be remotely stimulated by a magnet to form multicellular aggregates of controlled size, shape and content, and deformed to access their mechanical properties [7] or to control cell fate [4,8].

By trapping cells between two facing micromagnets, we are able to apply our approach to muscle progenitor cells, to align and fuse them. Lateral surfaces and inner core of the aggregate show topological defects that we would like to correlate with differntiation pattern.

Internship project

The aim of this internship is first to observe the dynamic of creation and annihilation of topological defects when mechanical constraints are applied on a 3D-tissues. Moreover as topological defects arise as hotspots for differentiation in in vitro pattern of myoblasts [2] or in the formation of model organisms such as hydra, differentiation patterns will be compared. To do so, we will monitor the dynamic of actin filaments using 2-photon microscopy and analysing 3D orientation. Single molecule fluorescent in situ hybridization will be performed on the 3D-micro-tissues to determine differentiation pattern.

This is a synergistic project that will be carried out in close collaboration with Cochin Institute and Institut Curie. It will use a variety of techniques including confocal and two-photon microscopy, mechanical manipulation, magnetic forces, cell biology.

The Complex Systems Laboratory (MSC-UMR7057) in Paris is a renowned interdisciplinary research centre with expertise in life sciences, physics, chemistry and engineering.

[1] G. Duclos et al. Nat. Physics (2017)
[2] P. Guillamat et al. Nat. Materials (2022)
[3] F. Mazuel et al. Phys. Rev. Lett (2015)
[4] V. Du et al. Nat. Comm. (2017)
[5] G. Mary et al. Cancer (2022)
[6] I. Nagle et al. Front. Cell Dev. Biol. (2022)
[7] I. Nagle et al. Elife (2022)
[8] I. Nagle et al. preprint (2024)