Development of biomimetic emulsions for in vivo force measurements

Neuronal circuits assemble through a series of developmental steps including neuronal migration and axon growth, which are believed to be primarily guided by chemical cues. However, neurons are surrounded by a complex and dynamic environment exposing them to a variety of mechanical signals, including compression (pushing) or traction (pulling) forces exerted by neighboring cells or tissues. The role of mechanical forces in neuronal development remains largely unexplored *in vivo* [Gangatharan G et al., Biol. Cell, 2018]. In particular, it has been shown that purely extrinsic forces drive cell movements leading to the extension of neurons in the zebrafish olfactory placode [Breau et al., Nat. Comm., 2017]. The goal of this internship is to unravel the origin of these forces by developing new tools to measure their strength and orientation *in vivo*, through an interdisciplinary collaboration between Lea-Laetitia Pontani (Jean Perrin Laboratory, LJP) and Marie Breau (Developmental Biology Laboratory, LBD).

In particular, we use biomimetic oil droplets [Pontani et al., PNAS, 2012] as force probes inside the developing tissue of zebrafish embryos. While passive droplets have already been injected in the tissues, allowing us to map out compressive forces exerted in the placode, we now seek to obtain the full force map in the tissue, including pulling forces. To this end, we need to develop a new experimental system that could establish specific adhesion with the surrounding tissue. In previous studies, droplets have already been functionalized successfully with the extracellular domains of E-cadherin [Pontani et al., 2016, Biophys. J.]. However, dispersed emulsions cannot be injected directly in dense tissues such as the zebrafish embryo: the oil has to be microinjected in bulk and the surfactants are thus directly dissolved inside the oil.

The first goal of this internship will be to develop and characterize a new technique allowing for the microinjection of oil droplets that can establish specific adhesion in the Placode. The amount of functionalization will be characterized by labelling the proteins on the surface of the droplets and quantifying their fluorescence through confocal microscopy. The functionality of these proteins will also be verified through droplet aggregation assays. These experiments will be carried out at LJP. After this emulsion system is fully characterized *in vitro*, it will be injected in zebrafish embryos at LBD and imaged during their development through confocal microscopy. These experiments will allow us to decipher the origin of the extrinsic forces controlling morphogenesis in the zebrafish olfactory placode.

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