SUJET DE STAGE M2 (+ THESE)

Lengthscale discrimination in cellular rigidity sensing

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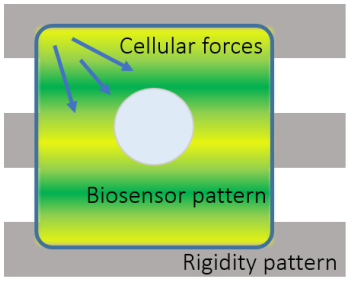
Context: In living tissues, eukaryotic cells evolve in a mechanically heterogeneous micro-environment. How cells perceive and react to the extra-cellular matrix stiffness local variations is crucial for migration or proliferation. Recent publications and some preliminary work point towards the existence of at least two distinct rigidity sensing mechanisms: on the micro-scale at focal adhesions, and on the cell scale through actin cytoskeleton tension. The existence of two parallel rigidity-sensing machineries raise the issue of the dialogue between local sensing and global sensing to provoke a consistent cell response.



Experimental scheme: Combining fluorescent biosensors, rigidity patterning and cellular forces microscopy, we aim at understanding the interplay between the local and global rigidity sensing mechanisms at the single-cell scale.

Objective: **Explore the local and global rigidity sensing mechanisms, and their interplay through biochemical signal processing.**

The recent development by the two supervisors of rigidity patterns and quantitative FRET imaging makes possible the experimental investigation of the cellular rigidity mechanotransduction. By combining these two novel techniques, the main goal of the internship will be to characterize the response function of specific FRET (Förster Resonance Energy Transfer) biosensors to a rigidity step. The identification of this critical lengthscale will be the basis for validating the choice of biosensors and for designing the PhD thesis experiments.

The ultimate goal of the PhD project is to propose a model describing how cells sense and react to heterogeneous rigidity environments as they encounter in real tissues. Playing with the rigidity patterns, spatial variations and stiffness values, the PhD candidate will characterize the cell response in terms of spatio-temporally resolved biochemical signals (biosensors) and intra and extra-cellular stresses. Having established the limits of micro-scale and cell-scale rigidity sensing mechanisms, the effect of rigidity gradients will be explored. If time allows, even more subtle patterns will be used to challenge the balance and dialogue between local and “global” rigidity sensing machineries. The physical modeling of the interplay between mechanical and biochemical signals will be done in collaboration with pr. Broedersz and pr. Frey from the LMU, Munich.