LadHyX Seminar – November 23, 10:45

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Using physics to understand cell behavior on microgrooved substrates

Adherent cells in vivo reside on extracellular matrices (ECMs) that possess a topographical organization at different scales. Various types of engineered microstructured substrates have been developed to study the impact of basal topographical cues on cell behavior in vitro. Amongst them, microgrooves mimicking the anisotropic organization of the ECM have been shown to align and elongate different cell types. However, how cells detect and respond to microgrooves remains unclear. We are investigating these questions using vascular endothelial cells (ECs), which in vivo form a monolayer lining the inner surfaces of blood vessels. In particular, we wish to understand how ECs respond to microgrooves at different scales, from single cells to collective behavior in monolayers.

In this seminar, I will present various experimental observations on EC interactions with microgrooved substrates and will discuss some ideas on the use of physical concepts and models to help understand these interactions. At the single cell scale, ECs cultured on parallel arrays of microgrooves (width = 5 µm, depth = 1 to 5 µm) are elongated, and they align and migrate in the groove direction. The extent of elongation and alignment increases with groove depth. Interestingly, these changes in cell shape on microgrooves are also associated with significant vertical (Z) deformations of the cells and their nuclei which can be completely confined within a groove. To understand these cellular deformations from a physical and mechanical point of view, we are exploring both analytical and numerical approaches. An example is exploring if a simple model whereby the cell is considered as a fluid inside an elastic membrane that interacts with the microgrooves is sufficient for predicting the cell morphologies observed experimentally.

At the monolayer scale, we have described the emergence of a specific pattern of collective movement in the form of periodic antiparallel cell streams with a characteristic width of 100-150 µm, significantly larger than either the grooves (5 µm) or individual cells (50 µm). Modeling the EC sheet as an active fluid with the microgrooves acting as constraints on cell orientation accurately predicts the occurrence of the periodic anti-parallel cell streams. In aligned monolayers, I have also observed different morphologies of cell-cell junctions parallel and perpendicular to the grooves, suggesting an anisotropic distribution of forces. To test this notion, we wish to explore the use of vertex models to analyze the dynamics of cell shapes and forces within aligned EC monolayers.