The role of membranes in cellular mechanics

Epithelial cells frequently form a dense continuous cobblestone-like sheet that is frequently exposed to a variety of mechanical challenges encompassing osmotic stress and external forces. The response to external forces was investigated and the question of how individual polar epithelial cells organized in confluent monolayers respond to pharmaceutical stimuli targeting the key players of cellular mechanics was answered. In particular, we ask how epithelial cells respond to changes in cortical and membrane tension by surface area regulation if challenged by diverse chemical and mechanical cues. Here, a tension-based model is used that allows capturing the relevant modes of cell deformation. Together with independent measurements of membrane tension, cortical tension and excess surface area of confluent MDCK II cells it is possible to draw a mechanistic picture of how confluent cells respond to mechanical stimuli in general. Changes in tension are provoked by external stimuli directed towards the contractile actomyosin cortex (cytochalasin D, blebbistatin), and changes in the excess surface area are produced by cholesterol extraction (methyl-β-cyclodextrin), ezrin knock-down, PIP2 injection or inhibition of dynamin (dynasore). A combination of AFM-indentation experiments with membrane–tether pulling at the same position allowed us to simultaneously monitor changes in membrane tension, cortical tension and excess surface area. Generally, we observed that removing or producing excess surface area of the plasma membrane readily adjusts membrane tension that is pivotal for the mechanical response of confluent cells. We found that isolated apical membranes from confluent MDCK II monolayers display similar mechanical properties as the apical side of living MDCK II cells in a confluent monolayer confirming that membrane mechanics in conjunction with cytoskeletal adhesion dominates the elastic response of confluent epithelial cells at large strain.