Feeling the force: Understanding mechanosensation through local stress calculations and steered simulations

Since the initial discovery of pressure-sensitive (membrane-stretch activated) channels in bacteria, numerous other mechanosensitive (MS) channels have come to light including the Piezo family, two-pore domain potassium channels (K2P), transient receptor potential (TRP) channels, and angiotensin II type 1 (AT1) receptors. It is expected that an increasing number of MS proteins, such as the newly uncovered G-protein coupled receptor GPR68, will be revealed in coming years thanks to novel high throughput techniques. Bacterial MS channels such as MscL (MS channel of large conductance) act as emergency release valves during hypo-osmotic shock, and are ideal model systems for biophysical characterization. I will present our ongoing efforts in understanding the role of lipid chemical structure in the elastic properties of model biomembranes and the force transduction mechanisms in the activation of the bacterial channel MscL through novel 3D local stress calculations and tension-mimicking accelerated methods.