The flatness of lamellipodia explained by the interaction between actin dynamics and membrane deformation

The crawling motility of many cell types relies on lamellipodia, flat protrusions spreading on flat substrates but (on cells in suspension) also growing into three-dimensional space. Lamellipodia consist of a plasma membrane wrapped around an oriented actin filament meshwork. It is well known that the actin density is controlled by coordinated polymerization, branching, and capping processes, but the mechanisms producing the small aspect ratios of lamellipodia (hundreds of nanometer thickness vs. several micrometer lateral extension) remain unclear.

The main hypothesis of this work is a strong influence of the local geometry of the plasma membrane on the actin dynamics. This is motivated by observations of co-localization of proteins with I-BAR domains (like IRSp53) with polymerization and branching agents along the membrane. The I-BAR domains are known to bind to the membrane and to prefer and promote membrane curvature. This hypothesis is translated into a stochastic mathematical model where branching rates and directions, capping rates, and polymerization speeds depend on the local membrane geometry through the principal curvatures and the corresponding directions. This requires the knowledge of the deformation of the membrane, being described in a quasi-stationary approximation by minimization of a modified Helfrich energy, subject to the actin filaments acting as obstacles. Simulations with this model predict pieces of flat lamellipodia without any prescribed geometric restrictions.