MECHANICS OF ACTIN NETWORKS IN CELL PROTRUSIONS

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Cells must generate mechanical forces in order to perform a wide range of important cell movements. One example of this is the directed translation of cells known as crawling motility [1], a behavior exhibited by human neutrophils and other cells of the immune system that is essential for the body's defense against pathogens. Crawling motility is characterized by a sequence of steps that begins with protrusion of the cell membrane in the direction of movement. The force necessary for protrusion is generated by a network of filaments formed from the cytoskeletal protein actin. Monomeric actin polymerizes into non-covalent polymer filaments that are organized by actin-binding proteins into branched and cross-linked actin filament networks. These networks provide eukaryotic cells with mechanical stability and generate forces for shape change and movement by growing in a directional manner. Sometimes called a polymerization motor, actin polymerization indirectly links ATP hydrolysis with steady-state assembly and disassembly of the filament, a process known as "treadmilling" [2], forming a cycle that can do work.

In this talk, I will present recent work investigating the mechanics of growing actin networks *in vitro*. My students and I have developed a force microscopy technique based on the atomic force microscope (AFM) for quantifying actin network properties, and we have used the technique to characterize actin network growth and mechanical properties under controlled loads. The force microscopy technique uses a dual-cantilever configuration to minimize the influence of sample drift so that network displacements can be measured continuously over long times [3]. Our results with re-constituted actin networks grown in cytoplasmic extract show three distinct behaviors: First, the velocity of growing actin networks is insensitive to increases in load over a range of forces prior to stall. Second, the velocity of actin network growth is dependent on loading history rather than instantaneous load as previously thought, implying that a single force-velocity relationship does not capture network behavior. Third, mechanical property measurements reveal that growing actin networks exhibit non-linear elasticity with increasing load. Our results are only partially explained by existing models of actin-based motility and pose new challenges for theoretical prediction of actin network mechanics and dynamics.

References

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