Regulation of actin filaments dynamics by proteins and mechanical stress

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Abstract:
Many essential cellular processes such as cell division, migration and morphogenesis are carried out largely thanks to the actin cytoskeleton organised into various architectures. To decipher the activities of actin regulatory proteins in charge of the dynamics of those networks, we combine microfluidics and fluorescence microscopy approaches. Formins are one of the central players to assemble actin networks in cells. They are processive filament elongators and accelerate the polymerization rate of filament. We show that formins processivity depends of the speed of assembly and are surprisingly sensitive to mechanical pulling forces (Cao et al, eLife 2018). Using polarization microscopy, we are able to investigate the importance that formins can freely rotate at the filament barbed ends when filaments are crosslinked with each others in actin networks. ADF/cofilin are the most essential proteins to regulate the disassembly of filaments. We characterize their ability to sever filaments and promote their disassembly from both ends. Strikingly, we show that the barbed ends of ADF/cofilin-decorated filaments can hardly stop depolymerizing, even when actin monomers and capping proteins are available (Wioland et al. Current Biology 2017). In addition, we quantify the impact of mechanical tension, curvature and torque on the binding and severing activity of ADF/cofilin. We find that the mechanical context can dramatically increase the rate of filament severing by ADF/cofilin.

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