The Mechanosensitivity of Actin Bundles

Cells' ability to sense their environment is essential for many cellular processes including cell division, migration and morphogenesis. The actin cytoskeleton, which has been shown to be mechanosensitive, is organized into different architectures that carry out various functions within the cell. Filopodia, which are finger-like structures consisting of actin filaments bundled in parallel, emerge at the cell front and orient the cell in response to its mechanical environment. These actin filaments are elongated at their barbed ends by formins and Ena/VASP and cross-linked by the bundling protein fascin. These two machineries are thought to collaborate to design a unique type of actin network that governs filopodium dynamics, yet the exact mechanism by which these two key proteins synergize, and how mechanosensing is achieved in filopodia, are not well understood. Core questions such as: how actin filaments self-assemble in a bundle; how forces are transmitted along filopodia; how fascin and formin synergize to control the growth of actin filaments in filopodia remain to be addressed.

To tackle these questions, we use a microfluidics-based approach to reconstitute, *in vitro*, a minimal system to recapitulate the mechanosensitivy of actin bundles. We have probed the activity of the actin binding proteins formins and fascins in a large range of biochemical conditions : first on single filaments, then scaling up to bundles of several filaments. We have incorporated fluorescence polarization into the microfluidics setup to characterize the rotational behavior of actin filaments elongated by formin and bundled by fascin. This bottom-up approach allows us to understand actin bundle mechanosensitivity and brings us closer to obtaining a comprehensive description of force generation and transmission in formin and fascin generated bundles.