Intermittent depolymerization of actin filaments caused by the photo-induced dimerization of protomers

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Abstract

The cytoskeleton of eukaryotic cells is continuously remodeled by polymerization and depolymerization of actin. Recently, abrupt changes in the depolymerization rate of individual actin filaments have been reported [1]. These intriguing dynamic changes have been proposed to reflect the structural plasticity of filaments, which would become more stable as they evolve from a loose to a tight helical conformation [2]. The idea that filaments stabilize with age is at odds with the well-accepted view that ATP hydrolysis weakens interactions between protomers in the filament.

Here, using a new microfluidics setup for the accurate observation of individual actin filaments [3], complemented by a theoretical analysis, we confirm the existence of abrupt dynamical changes, which correspond to transient interruptions of the depolymerization process. These interruptions, or "pauses", appear randomly over time and are independent of the smooth acceleration of depolymerization caused by ATP hydrolysis. We show that these pauses do not result from a global stabilization of actin filaments but from local events, as a consequence of fluorophore labeling and exposure to light. Our setup allows the collection of information on the dynamics of unlabeled filaments, and we show that such filaments depolymerize without exhibiting pauses. Finally, we show that the exposure of fluorescent actin filaments to light results in the formation of covalent dimers, and that these dimers dissociate more than a thousand-fold slower than monomers from the barbed end of depolymerizing actin filaments, giving rise to interruptions of depolymerization.

[1] Kueh, Brieher and Mitchison, "Dynamic stabilization of actin filaments" *PNAS* 105, 16531–16536 (2008).

[2] Kueh and Mitchison, "Structural Plasticity in Actin and Tubulin Polymer Dynamics" *Science* 325, 960 – 963 (2009).

[3] Jégou et al. "Individual actin filaments in a microfluidic flow reveal the mechanism of ATP hydrolysis and give insight into the properties of profilin" *PLoS Biology*, in press (2011).