Deciphering various roles of actin interacting with cell membranes

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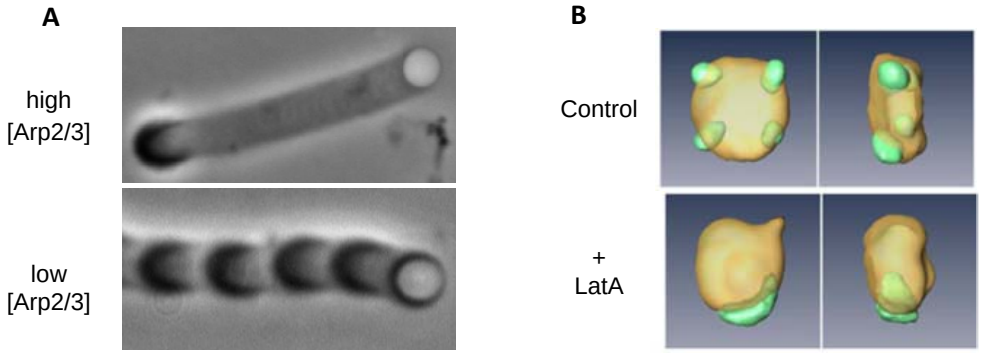
Actin is a major protein of the cytoskeleton which takes part into many cell processes like cell division, migration, morphogenesis… For example, in response to migration signaling, the cell induces the polymerization of an actin branched network towards the plasma membrane. This growing network exerts a pushing force against the membrane, leading to cell protrusion, the first step of cell migration. This process requires a tight regulation of the actin network in time and space. Such complexity has raised interest from both physics and biology communities, thus leading to studies combining interdisciplinary approaches.

Here, I will describe two studies showing the versatile function of a specific actin structure, the actin branched network generated by the Arp2/3 complex, depending where actin assembly is triggered.

In a first part, I will show an **in vitro approach** in which we reconstituted the branched actin array at the surface of giant unilamellar vesicles (GUVs) by anchoring an actin activator to the GUV surface. The growth of the actin network from the GUV surface induces GUV propulsion. Our macroscopic observations of actin-propelled GUVs shed light on molecular details of the mechanism of actin-based motility. We showed that efficient continuous propulsion is due to the right balance between the free diffusion of the actin activator at the GUV surface and its segregation while it is transiently interacting with the actin network, a balance which is controlled by the Arp2/3 complex [1].

In a second part, I will describe a **cell biology approach** in which analyzed the role of actin in intracellular transport. We studied the distribution of the actin activator on endosomal membranes, the WASH complex. Our observations suggest that actin contributes to the dynamic exchange of the activator between the cytosol and the endosomes. Moreover, we showed that actin polymerization regulates the organization of WASH into small and discrete domains at the surface of endosomes. Our data suggest a potential role of actin in proteo-lipidic domain compartmentalization of endosomes, a precursor step to endosomal sorting [2].



A) Actin-propelled GUVs in presence of optimized (top) or not (bottom) concentration of Arp2/3 complex. B) 3D-reconstruction of WASH domains (green) on enlarged endosomes (yellow). WASH domains are small and discrete in control cells whereas they coalesce upon actin depolymerization by Latrunculin A.

[1] Arp2/3 controls the motile behavior of N-WASP-functionalized GUVs and modulates N-WASP surface distribution by mediating transient links with actin filaments. V. Delatour*, E. Helfer*, D. Didry, K. H. D. Lê, J.-F. Gaucher, M.-F. Carlier, G. Romet-Lemonne. Biophys. J. 94, 4890-4905 (2008)

[2] Actin polymerization controls the organization of WASH domains at the surface of endosomes. E. Derivery*, E. Helfer*, V. Henriot, A. Gautreau. PLoS One 7, e39774 (2012)