

THE COMPLEX CHOREOGRAPHY OF GELSOLIN, A MASTER REGULATOR OF CYTOSKELETON

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The actin cytoskeleton is a major component of the cell and is involved in many crucial mechanisms. The regulation of the actin filaments network is thus key, one of the main regulator is the gelsolin (GSN) which is able to cleave actin filaments (severing), stay bound to the + end of the filament to stop polymerization (capping) and stay bound to the + end of actin monomers (sequestrating)¹.

The GSN is a 80kDa multidomain ubiquitous protein involved in important processes such as cell motility, ion-channel regulation, cell signaling, apoptosis, phagocytosis, secretion, platelet activation and modulation of phospholipase C activity².

Our research involves the characterization of the different physiological states of the gelsolin. It includes the modelisation of the gelsolin opening under the action of Ca²⁺ combining bioinformatics approaches in collaboration with Prof. Carlo Camilloni validated by measurements of inter domain distances with DEER-EPR method in collaboration with Dr. A. Bonucci. Aside, the different complexes of gelsolin and actin are being characterised starting with the capped complex using structural biology methods. A SAXS experiment at the ESRF has already been performed and suggests that we obtain a 1:1 actin gelsolin complex.

To go towards high resolution structure determination, SANS technique is envisaged to obtain low resolution structure of gelsolin alone in the capped conformation that could be used as a template for a cryo-EM experiment allowing a better resolution.

1. Feldt, J. *et al.* Structure, regulation and related diseases of the actin-binding protein gelsolin. *Expert Rev. Mol. Med.* **20**, e7 (2018).
2. Kwiatkowski, D. J. Functions of gelsolin: motility, signaling, apoptosis, cancer. *Curr. Opin. Cell Biol.* **11**, 103–108 (1999).

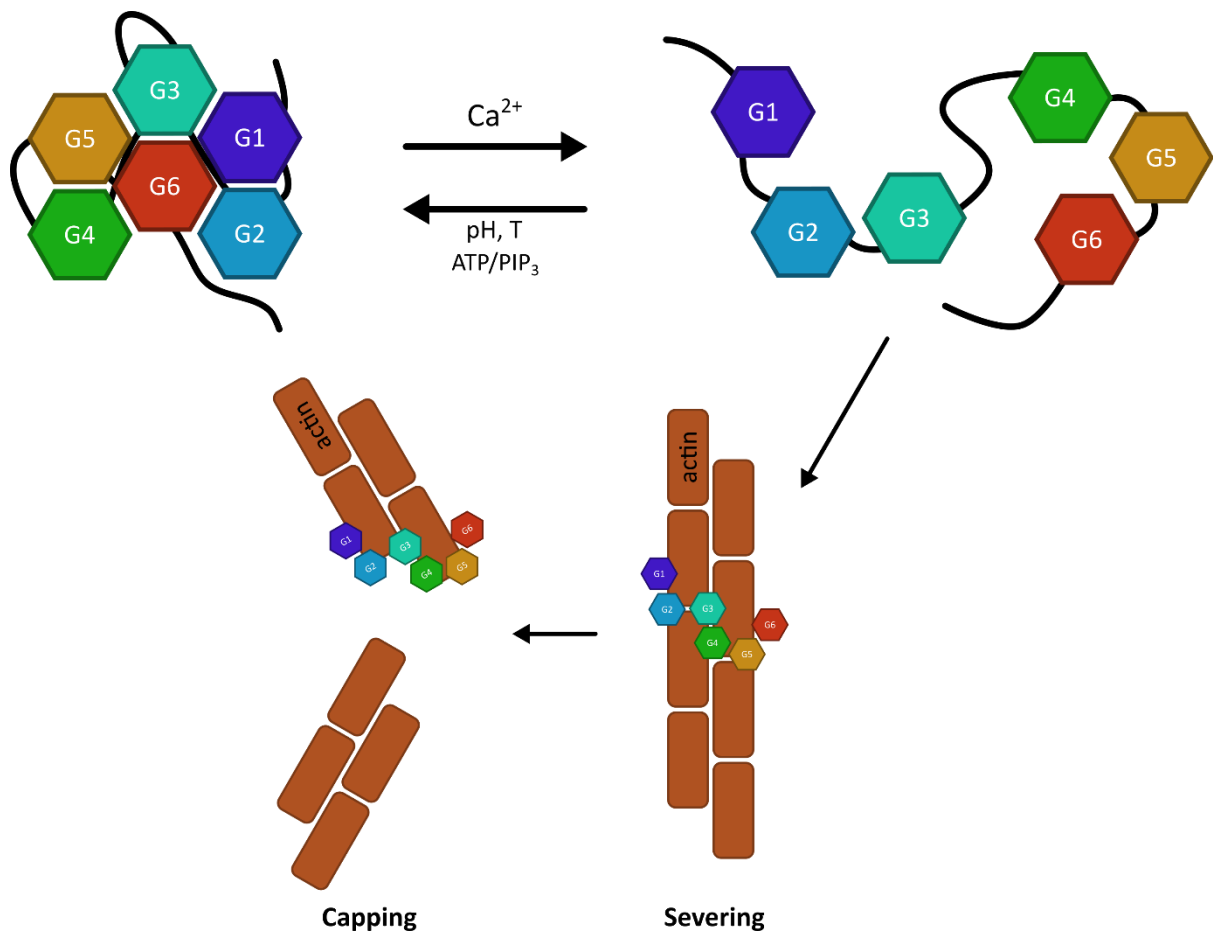


Figure: scheme presenting the actin transition from apoform to active conformation and the physiological mechanisms operated by gelsolin. The labels G1 to G6 represents the different domains of the protein.