Nature Reviews Molecular Cell Biology | AOP, published online 4 February 2009; doi:10.1038/nrm2635

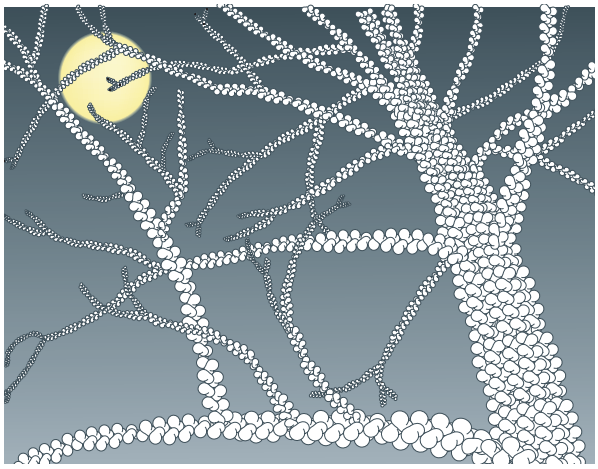
CYTOSKELETON

The making of a filament

> …high-resolution model for the structure of F-actin…

Actin exists in a dynamic equilibrium between monomeric globular (G)-actin and polymerized fibrous, or filamentous, (F)-actin. Polymerization is thought to activate the ATPase function of actin, which drives actin filament treadmilling (that is, the simultaneous polymerization at one end and depolymerization at the other). A new high-resolution model for the structure of F-actin provides the basis for understanding actin polymerization.

Actin has a nucleotide-binding cleft that is enclosed by the two major domains. In the G-actin conformation, the cleft is closed and the two domains form a propeller-like twist with each other. The new model, which is based on X-ray diffraction data at a resolution of 3.3 Å in the radial direction and 5.6 Å along the equator, shows a relative rotation of the two major domains by ~20°. This relative rotation gives the F-actin subunit a flat conformation, in which the cleft remains closed and the two domains are untwisted.



A second difference between G-actin and F-actin is the extended, open conformation of the DNase-I-binding loop (D-loop). The intra-strand interface between filament subunits is extensive and is similar to that in bacterial MreB, a structural and functional homologue of actin. Given its closed cleft and untwisted major domains, MreB resembles the flat conformation of F-actin.

Although the F-actin model is not of sufficiently high resolution to elucidate the ATPase mechanism, the domain rotation that is associated with the G- to F-actin transition moves the crucial Gln137 residue in the ATPase region and the γ-phosphate together. This might allow the bound ATP to be hydrolysed.

The flattening of the actin molecule generates changes in the intramolecular interactions between the two major domains that contribute to stabilizing the F-actin conformation. In addition, this flattening allows more extensive contacts between the subunits, which, together with the helical nature of the subunits, promote filament formation. However, the stabilizing effects of the contacts between subunits might be counteracted by the strain inside the subunit conformation — this dynamic balance could be responsible for multiple local conformations of F-actin.

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ORIGINAL RESEARCH PAPER Oda, T. *et al.* The nature of the globular- to fibrous-actin transition. *Nature* **457**, 441–445 (2009)