Actin: A molecular wire, an electrical cable?

Filamentous (F)-actin is an example of a biological macromolecule that is a polyelectrolyte which, under physiological pH ranges, accumulates solvated counter ions in its vicinity to balance locally exposed surface charges. F-actin is a major component of the cytoskeleton in cells and is made up of actin monomers bound by specific self-assembling sites to form double-helical filaments (Goldmann et al., 2005). Each subunit of the actin filament contains high-affinity divalent cation binding sites that are usually occupied in the cytosolic milieu by Mg$^{2+}$ and Ca$^{2+}$ ions. Saturation of these binding sites is, however, insufficient to promote actin polymerization which is driven by millimolar concentration of monovalent ions. It has been reported that from conformations of the sequence of muscle actin, each monomer subunit exposes roughly 11 excess negative charges with an average charge spacing of 2 Å in its polymerized tertiary structure (Tang and Janmey, 1996). This value is less than the charge spacing of 1.7 Å for DNA, suggesting that although F-actin is not as highly charged as DNA, the phenomenon of counter ion condensation is still possible. Evidence of polyelectrolyte behavior has been shown in the formation of para-crystalline bundles of F-actin by divalent and polyvalent cations, and it has been reported (Lin and Cantiello, 1993; Xian et al., 1999) that the general features are analogous to the condensation of DNA (Bloomfield, 1991). Over the years, several theories have been developed based on the cylindrical-rod cell model in its primitive form. The assumption is that the charges are distributed uniformly along the length of the polyelectrolyte. The counter ion condensation theory of Manning (Manning, 1978) has provided a very useful quantitative description of the key features of polyelectrolyte counter ion interactions.

Since actin filaments are closely associated with a variety of ion channels (cf. Janmey, 1998) that can be viewed in this context as cellular electric current generators, it has been assumed that ion channel—actin interfaces may be part of a novel electrodynamic signaling mechanism based on the ability of actin filaments to conduct electrical signals (Chasan et al., 2002; Cantiello et al., 2005). This electrical interface may influence the ionic composition and generate electrical signals to couple the associated actin networks. It has, therefore, been suggested that electrical signals generated at membrane interfaces, for example by ion channel activity, may be transduced by intracellular structures, such as F-actin or indeed microtubule networks, acting as novel intracellular conductors (Janmey, 1998; Tuszyński et al., 2004). It is exciting to imagine these conductors as having a potential signal transduction role. For this to occur, a tight interaction between ion transport proteins and actin filaments would have to exist in the cytoskeleton of most cells. Some studies have already demonstrated that, for instance, the spectrin cytoskeleton containing ankyrin and actin is structurally linked to ion transport proteins including the band 3 anion exchanger (Drenckhahn et al., 1985) and the Na$^+$, K$^+$-ATPase (Nelson and Veshnock, 1987). Studies by Dr. Cantiello’s group have indicated that actin filaments might also control ion channel activity (Cantiello et al., 1991, 2005; Raychowdhury et al., 2004).

Thus, a functional interface between the ion transport molecules and the underlying cytoskeleton may be indicative of a dynamic mechanism whereby cell membrane generated signals could be conducted directly to intracellular compartments. It is known that intracellular electrical currents play a relevant role in cell and organizational development (Manning, 1978; Jaffe, 1981). However, the nature and specific location of intracellular, electrically preferred, conductive pathways in the intracellular milieu are still unknown. It is conceivable that conduction by electrically stimulated actin filaments may serve as a novel signaling mechanism to convey intracellular information regarding the ionic extracellular environment. Experiments have indicated that actin filament organization can be modified by electric fields (Luther et al., 1983) and that cells respond to electric fields (Onuma and Hui, 1988). This idea is based on the assumption that actin filaments may behave as biological cables and that actin filaments are closely associated with a variety of ion channels. To further understand this mechanism, ion channel activity can be envisioned as that of ‘electric current generators’ capable of generating discrete ion currents that couple to the associated actin filaments.

To directly evaluate the biological relevance of information processing along microtubules in solution, Cantiello et al. have recently modified their dual ‘patch-clamp’ device to measure locally, longitudinally generated electrical signals (Priel et al., 2006). The conductance determined from these measurements was of the order of up to 9 nS. In first experiments, we used atomic force microscopy (AFM, with an adapted multimode head) on polymerized actin deposited on graphite at...
ambient temperature. After fluid evaporation, the conductance measured vertically through the actin filaments in point contact mode with a standard silicon cantilever covered with platinum was about 6 pS. The topology of actin filaments was captured by tapping mode using a standard silicon cantilever and a tip consisting of WC06. [About 15 μM G-actin was polymerized in 5 mM Tris–HCl (pH 7.5), 2 mM MgCl2, 100 mM KCl, 1 mM DTT and 1 mM ATP for 30 min at ambient temperature and 30 μM phallolidin was added to stabilize F-actin. A droplet of 10 μF-actin was then deposited on the graphite surface and AFM measurements were conducted after complete fluid evaporation in tapping and point contact mode. A current of up to 1.5 V was applied to the platinum tip which was grounded via an amperc meter.]

Although the AFM values are much smaller compared to those generated for microtubules by the patch clamp method (which might be due to the nature of the molecules, presence of electrolytes, charge changes during polymerization, etc.), they are still intriguing in that microtubules as well as F-actin may act as a molecular wire, i.e. electrical cable. Further research efforts from biologists and physicists alike are needed to quantify electrically induced ionic currents by microtubules as well as F-actin and to initiate investigations of the functional relevance of such signals in a biological context in different environments. The ability of microtubules, F-actin and possibly DNA to support ionic waves may prove a novel intracellular signaling mechanism.

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References


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