

Regulation and integrated functions of the actin cytoskeleton

Guillaume Charras^{a,b} and William M. Brieher^{c,*}

^aLondon Centre for Nanotechnology, London WC1H 0AH, United Kingdom; ^bDepartment of Cell and Developmental Biology and Institute for the Physics of Living Systems, University College London, London WC1E 6BT, United Kingdom; ^cDepartment of Cell and Developmental Biology, University of Illinois, Urbana-Champaign, IL 61801

The actomyosin cytoskeleton is at the heart of many of the most dramatic cell and tissue shape changes, but linking molecular-scale organization and activity to cellular shape changes remains a substantial challenge. The dazzling array of force-generating structures assembled through the interplay of actin-binding proteins was on show in the Minisymposium on actin dynamics and structure in studies examining actin network functions in tissues, isolated cells, and in vitro.

Myosin contractility is the best-studied mechanism for force production in isolated cells. However, until recently, it was widely believed that myosins only generate steady contraction. New evidence presented by **Michelle Baird** (Waterman lab) suggests that myosin IIA can also generate pulsatile contractions. Downstream of contractility, the resulting traction forces exerted on the cell matrix or an adjacent cell depend on the extent of coupling between adhesion molecules and the actin cytoskeleton. **Kenneth Buck** (Forscher lab) presented evidence that localized Arp2/3-dependent actin assembly can shield adhesion molecules from the forces generated by actin retrograde flow and provide a pushing force in the anterograde direction.

The role of actin polymerization in generating protrusive forces is well established in the lamellipodium, a protruding sheet of membrane at the leading edge of migrating cells. Lamellipodia have been most studied in cells crawling on planar substrates, but cells in

vivo can also migrate along fibrils of matrix. **Charlotte Guetta-Terrier** (Gauthier and Ladoux labs) analyzed cell motility on fabricated nanofibers coated with extracellular matrix to mimic this type of cell movement. Under these conditions, cells assemble an Arp2/3-dependent, fin-like structure that emanates from the cell body and travels along the fiber at a constant rate for up to several hundred micrometers.

By studying how cells from the inner progenitor layer of the frog epidermis can move to the outer, mature epithelium, **Jakub Sedzinski** (Wallingford lab) revealed that actin polymerization also plays a role in apical surface expansion. The force necessary for this “apical emergence” is generated primarily by the emerging cell rather than by the neighboring cells. Formin-mediated actin assembly in the apical cortex of the emerging cell provides a pushing force sufficient to expand the apical membrane. Cortical actin was also the topic of a presentation by **Guillaume Charras**, who presented his group’s work on how this actin network is generated. Cortical actin lies just beneath the plasma membrane, where it plays important roles in cell mechanics and morphogenesis. Charras and colleagues showed that blebs shorn from cells can reform the cortical actin network. This enabled determination of cortical composition and identified Arp2/3 and mDia1 as the only two actin nucleation factors present in the cortex. **Matt Smith** (Paluch lab) presented new computational approaches devised to understand how tension is controlled by the properties and organization of actin filaments in the cortex. He showed that actin filament length and arrangement can modulate cortical tension, providing a new level of regulation for cell surface tension in addition to myosin contractility. **Josh Winkelman** (Kovar lab) presented work showing that differences in filament spacing arising from distinct cross-linkers may represent a sorting mechanism for localization of subsets of actin-binding proteins to different structures, such as myosin motors for the generation of contractility.

Although it is widely recognized that actin polymerization can generate mechanical forces, a potential role for depolymerization has been invoked in theoretical work but is poorly documented experimentally. **Philippe Bun** (Lénart lab) described an actin network that forms in the nuclear region encompassing chromosomes during the first meiotic division in starfish oocytes. This network collects chromosomes under the plasma membrane to ensure a successful division of these very large cells. Experiments and modeling suggested that chromosome movement is driven by asymmetric assembly and disassembly of the actin network to create a pressure gradient that pushes the chromosomes toward the plasma membrane. Part of the reason that forces generated by depolymerization have rarely been documented is that the molecular mechanisms of depolymerization remain poorly understood. **Vivian Tang** (Tang and Brieher labs) presented recent progress on understanding the mechanism of action of cofilin, coronin, and Aip1 in depolymerizing actin filaments. This revealed a new mode of catastrophic depolymerization of filaments mediated by Aip1 where long stretches of F-actin rapidly dissociated into monomers.

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*Address correspondence to: William M. Brieher (wbrieher@illinois.edu).

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