crystalline domains is compromised, the interconnectivity is greatly improved as a result of the rigid and sufficiently long chains that link the domains, like bridges that link islands (Fig. 1c).

The model suggested by Noriega *et al.* may help to rationalize the unexpectedly high $\mu$ in these emerging polymers, and triggers further discussion on many aspects that remain puzzling. The long chains that link semicrystalline domains must be sparsely packed compared with the packing in organic single crystals, which usually exhibit a remarkable degree of long-range crystallinity. Moreover, these chains must inevitably carry defects in their backbones that would break the conjugation and create bottlenecks for intrachain conduction, thus destroying the links between the domains and reducing the mobility. Furthermore, high values of mobility in conjugated polymers are typically extracted from steep slopes of device characteristics recorded in a non-equilibrium transport regime when very high source–drain voltages (up to 100 V) are applied across very short channels (5–100 μm), thus generating extremely high in-plane electric fields in the range $10^3$ to $10^5$ V cm$^{-1}$. It is thus likely that these devices are driven out of electric and thermal equilibrium, and effects akin to polaron detrapping or an elevated local temperature might play a role. This contrasts sharply with the situation in small-molecule single-crystal transistors, where an extremely ordered molecular lattice allows charge transport over macroscopic distances in the centimetre range, with equilibrium charge-carrier mobilities of 1–20 cm$^2$ V$^{-1}$ s$^{-1}$ (depending on the crystal type, orientation and other intrinsic factors), measured under very small in-plane electric fields of 10–100 V cm$^{-1}$ (ref. 7). It is clear that mobilities in these systems are obtained in drastically different transport regimes, and perhaps relate to different physical processes. Further systematic studies of charge transport in a broader range of electric fields, length scales and temperatures will be therefore required to fully understand the interesting and sometimes surprising behaviour of the novel conjugated polymers. Nevertheless, the works by Zhang *et al.*[5] and Noriega *et al.*[6] have convincingly demonstrated that charge transport in high-molecular-weight conjugated polymers can be highly tolerant to disorder thanks to the long and rigid polymeric chains that improve film interconnectivity. ❐

*Vitaly Podzorov is at the Physics Department of Rutgers University, 136 Frelinghuysen Road, Piscataway, New Jersey 08854, USA.*
*e-mail: podzorov@physics.rutgers.edu*

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CELLULAR MECHANOSENSING

# Sharing the force

Cells can sense their environment by applying and responding to mechanical forces, yet how these forces are transmitted through the cell's cytoskeleton is largely unknown. Now, a combination of experiments and computer simulations shows how forces applied to the cell cortex are synergistically shared by motor proteins and crosslinkers.

Andreas R. Bausch and Ulrich S. Schwarz

When it comes to the response of cells to dynamic changes in mechanical loading, the actin cytoskeleton is the main player[1]. It is able to adapt its structure to mechanical perturbations, and this adaptation has also been seen in reconstituted systems that mimic it[2,3]. Yet the underlying molecular mechanisms are far from being understood. It has become increasingly clear that what makes the actin cytoskeleton mechanosensitive is not a single mechanotransduction process, but that there exists a complicated network of mechanosensitive processes that integrates many different signals into a complex response. This is especially true for the interaction of cells with substrates[4,5]. Now, Douglas Robinson and colleagues report in *Nature Materials* a systematic experimental and modelling investigation of the role of a large range of proteins in mechanosensing[6]. Their findings demonstrate that different types of mechanical load lead to different rates of accumulation of cytoskeletal motor and crosslinker proteins, and that these proteins synergistically share the transmitted forces.

Engineering materials that have the adaptive properties of biomaterials — such as bone or muscle, which dynamically adjust their structural properties and repair themselves (within certain limits) in the event of failure — has been a long-standing dream of materials scientists. The adaptive and regenerative properties of such tissues are strongly connected to the genetic programs of the cell types involved, and therefore progress in the design of cell-based biomimetic active materials relies on a better understanding of gene expression and differentiation in response to mechanical signals[7]. However, in contrast to the higher level of organization of tissues involving different cell types, at the level of single cells sensing and actuating components are tightly integrated with each other, and adaptive responses occur faster (on the timescale of seconds or minutes) as a result of local activation and reorganization of such components. In fact, the cell's cytoskeleton is an active material with an integration density that is unsurpassed by man-made materials[8–10]. Therefore, instead of tapping into the complexity of genetic programming, materials scientists increasingly turn towards active filament networks such as the cytoskeleton in their search for adaptive design principles.

Robinson and co-workers used micropipette aspiration — a standard procedure for measuring the mechanical properties of cells[11] — to study the social amoeba *Dictyostelium discoideum*, which is known for its dynamic actin cortex and a relatively weak adhesion to substrates[12]. Sucking a cell into a glass capillary is a powerful technique for investigating

whether a particular cell type reacts like a solid or a fluid, and to extract the corresponding material properties (such as Young's modulus or the viscosity) on the basis of a detailed understanding of the underlying mechanical processes[13,14]. In fact, Robinson and collaborators set up a multiscale computer simulation for the mechanical network of the cortex, which clarified which kind of mechanical deformation occurs in which part of the cell. They found that the base of the aspirated part of the cell mainly experiences shear, while the cell's tip is mostly under tension. This defines two well-separated regions of the cortex with different mechanical conditions.

Using standard tools from molecular and cell biology, the researchers carried out a tour de force study of 37 putatively mechanosensing proteins by tagging them with a fluorescent marker and following their relocalization under mechanical loading. The experiments revealed that the dominant motor protein myosin II and the rod-shaped actin crosslinker α-actinin accumulated at the dilated region at the tip, and that the equally important but V-shaped crosslinker filamin localized to the sheared region at the base (Fig. 1). This suggests that the response of the different actin-binding proteins is sensitive to different types of mechanical deformation. Robinson and co-workers then proceeded to show that the computer model incorporating the known molecular properties of these proteins reproduces the experimentally found relocalization response on the cellular length scale.

The researchers also showed how different proteins synergistically work together in the cortex. By using various types of mechanical perturbation, they demonstrated how the force applied by a biaxial stretch to the membrane trickles down to the cortex through molecular bridges and then distributes over myosin II and crosslinking proteins. They also changed the molecular properties of a given protein, and monitored how the contribution of the other proteins changed as a result of the different loading conditions in the different parts of the cortex. Such 'load sharing' is a general principle that occurs in many biological phenomena, most prominently in cell adhesion[15]. By investigating the force-sharing mechanism for the actin cortex of simple cells, Robinson and colleagues' findings add to the growing effort of dissecting how the information on mechanical loading is processed in a distributed network of mechanosensitive processes.

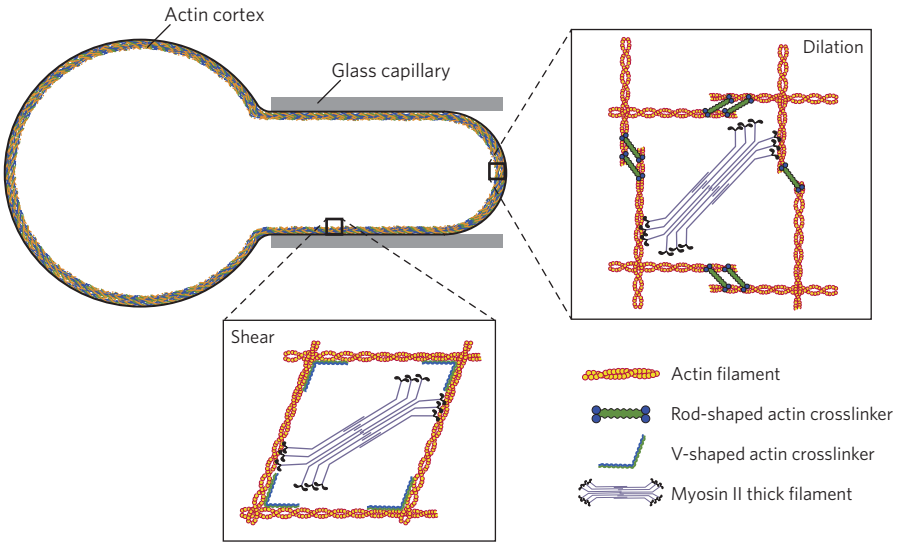


**Figure 1 |** Schematic of the micropipette-aspiration experiment[6]. The cylindrical extension of the cell sucked into the micropipette has a well-defined mechanical load, with dilation at the tip and shear at the base (see insets). This leads to different responses of the cytoskeletal proteins localized in the actin cortex of the cell. Force is transmitted from the membrane to the cortex by bridging molecules. In the cortex, the load is shared mainly by the myosin II motors (assembled into bipolar thick filaments) and a variety of actin crosslinkers (including the rod-shaped α-actinin and the V-shaped filamin, which re-localize to regions of dilation and shear, respectively).

Because of the large range of relevant processes involved, both the experiments and the simulations in Robinson and co-authors' study are relatively complex. For the design of well-controlled active materials, theoretical models based on simple physical principles with few parameters as well as experimental biomimetic systems with few components built from the bottom-up would be needed. This effort should be extended to less complex systems and be made more quantitative, for example by using fluorescent markers that report the mechanical loading of single molecules[16].

Interestingly, the response of myosin II proteins to mechanical loading is an excellent example of the sought-after adaptive behaviour of active biomaterials: by being localized to regions of large stress, myosin II reinforces and contracts the regions that are in danger of being torn apart. The fact that a contractile response, mediated by an increase of the local network activity, is found as a counteracting response and not only as a fortification of the networks through an increase of the crosslinking proteins shows that the highly active nature of the cytoskeleton is key to its adaptive function. Certainly, when it comes to designing synthetic adaptive materials, the actin cytoskeleton constitutes a continuous source of inspiration. ❐

*Andreas Bausch is at the Lehrstuhl für Zellbiophysik E27, Technische Universität München, 85748 Garching, Germany. Ulrich Schwarz is at the Institute for Theoretical Physics, University of Heidelberg, Philosophenweg 19, 69120 Heidelberg, Germany.*
*e-mail: abausch@mytum.de; Ulrich.Schwarz@bioquant.uni-heidelberg.de*

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