Theoretical modeling of cellular shapes and dynamics

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The outer membrane of a living cell is very different from an inert lipid bilayer or a vesicle. Most notably, there exists a strong coupling between the membrane and the underlying cytoskeletal network of the cell. The cytoskeleton is a dynamic formation of proteins that is continuously reshaping itself, and in the process applies forces to the membrane. The membrane of a living cell is therefore constantly deformed by the forces of the underlying cytoskeleton. It is this cytoskeleton that allows cells to have the large variety of shapes

The energy produced by the cell's metabolism, in the form of ATP, drives the motion of the cytoskeleton and membrane through the polymerization of cytoskeletal filaments (actin and microtubules), the action of cytoskeleton-bound molecular motors and membrane-bound ions pumps. The cytoskeleton modifies the physical properties, such as the tension, fluctuation amplitude and effective bending modulus of the lipid membrane.

In turn, the cytoskeletal organization can be influenced by the membrane shape (curvature) and tension. Our theoretical models allow us to achieve quantitative understanding of general mechanisms and make testable predictions.

For example, when the actin cytoskeleton is activated at the cell membrane, it applies a protrusive force pushing the membrane outwards. If furthermore, the activating proteins have a convex curvature, spontaneous shape instabilities follow, and the cell surface has growing finger-like protrusions (Fig.1). Such finger-like protrusions are a common feature in many cell types, from the dynamic filopodia of motile cells, to the stable stereocilia of hair-cells in the ear. Our model allows us to predict the typical separation between the protrusions, and the conditions for their initiation.

Alternatively, for proteins that induce contractility and have a concave (or arc-like) geometry, our model indicates an instability whereby the cytoskeleton and membrane develop a furrow, which is similar to that observed at the mid-plane of dividing cells (Fig.2).

When the contractile forces of the myosin motors are included in the model we also find that robust traveling waves result. The calculation of such waves is shown in Fig.3, and compared to some examples of such waves that are observed to propagate over the surface of living cells. Note that the cell membrane is a highly damped system, so the observation of traveling waves over large distances is entirely due to active (i.e. energy consuming) processes.

Finally, we present a model for the spontaneous formation of the distinct shape of the stereocilia of hair-cells in the ear. These structures are highly regulated and ordered, whereby an internal core of actin filaments is continuously polymerizing and de-polymerizing (treadmilling) (Fig.4). Additionally, there are a large number of myosin motors that move along the actin filaments, carrying cargo proteins towards the stereocilia tip and base. We show that the active localization of proteins that control the actin dynamics (Fig.4), can explain the observed stereocilia shape and internal actin dynamics.

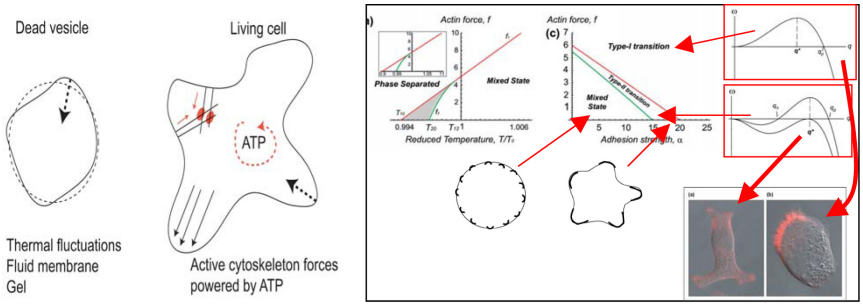

Fig. 1 *Left: Active forces of the cytoskeleton deform the cell membrane, while only random thermal fluctuations exist in a vesicle. Right: Our model calculations of the conditions where a shape transition of the cell is initiated by actin protrusive forces, compared to observed cellular shape transitions.*

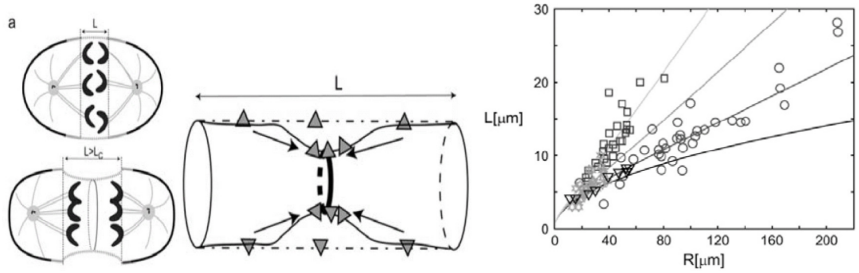

Fig. 2 *Left: As the chromosomes separate there is a contractile band that initiates a furrow when it reaches a critical length. Our model predicts this instability, and compares well to experimental measurements from various types of organisms (right).*

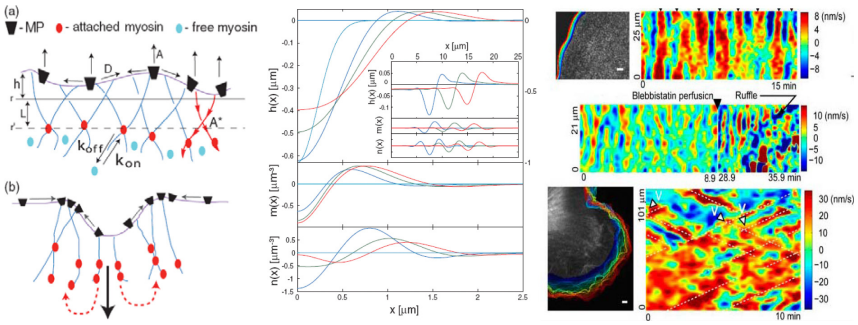

Fig. 3 *Left: Our model of coupled actin-myosin and membrane. The contractility is dominant and leads to a traveling wave. Middle: Calculated propagation of the waves. Actin and myosin oscillate and drive the membrane undulation. Right: Observed propagating waves on cells.*

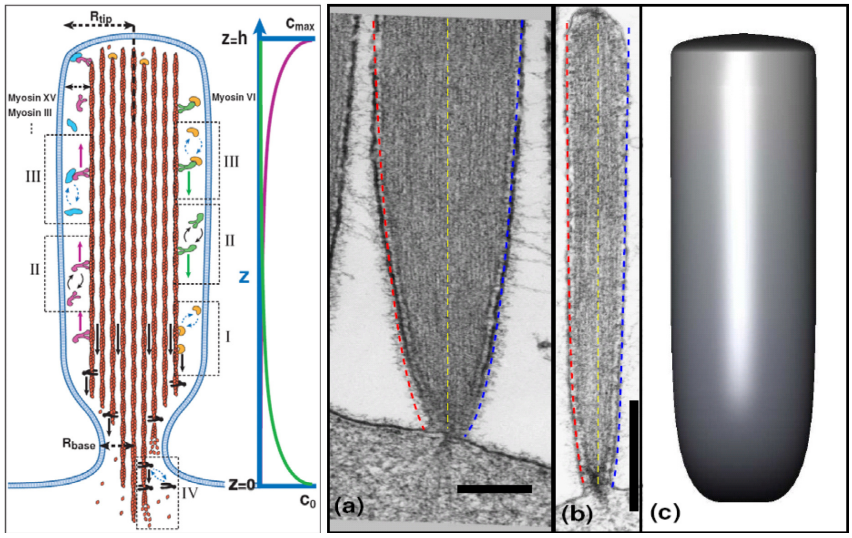

Fig. 4 *Left: Our model of the localization of actin-regulating proteins inside the stereocilia, due to the retrograde flow of actin and due to the motion of various myosin motors towards the stereocilia tip or base. The resulting exponential distributions are illustrated. Right: The calculated shape of the stereocilia using our model (dashed lines) compared to EM-sections (a,b). In (c) we plot the calculated shape, with the typical narrow base and the straight upper part.*

Selected publications

Gov, N.S. and Gopinathan, A. (2006) Dynamics of membranes driven by actin polymerization. Biophys. J., 90, 454.

Gov, N.S. (2006) Dynamics and Morphology of Microvilli Driven by Actin Polymerization. Phys. Rev. Lett. 97, 018101.

Shlomovitz, R. and Gov, N.S. (2007) Membrane Waves Driven by Actin and Myosin. Phys. Rev. Lett. 98, 168103.

Veksler, A. and Gov, N.S. (2007) Phase Transitions of the Coupled Membrane-Cytoskeleton Modify Cellular Shape. Biophys. J. 93, 3798-3810.

Shlomovitz, R. and Gov, N.S. (2008) Physical Model of Contractile Ring Initiation in Dividing Cells. Biophys. J. 94, 1155-1168.

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