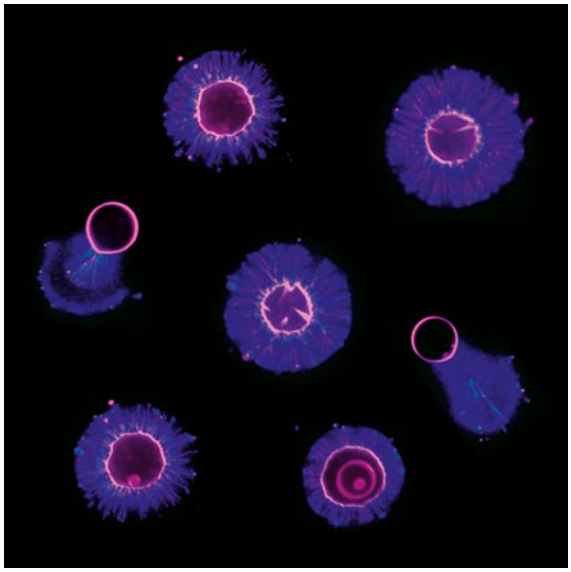
by Cécile Sykes
CNRS research director, Institut Curie, France – DOI: https://doi.org/10.1051/epn/2020501

Living Soft Matter Physics : active protein networks govern cell shape changes

A living cell contains flexible, semi-flexible and stiff filaments, forming the cell skeleton, called the cytoskeleton, the detail of which is described in Timon Idema's article. How does this filamentous network rearrange to drive cell shape changes to achieve cell functions such as division and motility?

With the metaphor of a spaghetti bowl, the force you need to apply when tossing with your spoon depends on spaghetti (or filament) density, how much they are cooked (their flexibility), and how they stick together. In particular, cells or cell assemblies are *elastic*, especially at short time scales: when deformed, they recover their initial shape. Pinch your cheek for a few seconds, it will go back. However, at longer time scales, over minutes, days, years, cells can flow: they are *viscous*. Look at your elbow skin and compare it with a baby one : it has flown.



▲ Liposomes (membrane marked in pink) on the surface of which the polymerisation of actin is activated and generates the growth of a branched network of actin (purple marks filament ends). Membrane tubes mimic the initiation of endocytosis in cells, and cone shapes mimic dendritic filopodia of neuronal cells. We can also observe actin "comets" propel liposomes and mimic actin-based propulsion of bacteria such as *Listeria monocytogenes*. Liposomes are between 10 and 20 microns in diameter.

Unlike macromolecular polymer networks (or a spaghetti bowl), living matter is *alive*, consumes chemical energy through hydrolysis of adenosine triphosphate. Proteins in the cytoskeletal network assemble, slide, or change conformation, therefore complexifying the simple picture of passive elasticity and viscosity. These cytoskeletal networks are able to actively deform a membrane, and drive cell shape changes.

The cell membrane separates the cell content from the outside and has a bending energy that amounts to a few dozen times the thermal energy, it is soft and deformable therefore fluctuate at room (or body) temperature. Underneath the cell membrane lies a network of branched and entangled protein filaments (Blanchoin *et al.*, 2014). Actin filaments have the peculiar property that their growth is activated at the membrane through the formation of new branches in the network.

"Simplicity is complexity resolved" is a quote from the famous sculptor Constantin Brancusi. Likewise, physicists try to make things simple, as a cell is a complex system. Stripped-down experimental systems were developed that reconstitute cell functions with purified components. Whereas one single filament would simply push by growing against the membrane, strikingly, the complex growth of a branched network generates both inward and outward membrane deformations, which is an extraordinary property of these networks. This push or pull depend on the detailed organisation of the network, the growth velocity of their filaments, and membrane tension, as supported by models based either on reaction kinetics or cooperative properties of actin networks (Dürre *et al.*, 2018; Simon *et al.*, 2019). Further modeling, inspired by these controlled experiments, will help to decipher how cells control their membrane deformations for various functions, from virus uptake to cell motility which dysfunction leads to various diseases. ■

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