

Membrane curvature and proteins involved in cellular membrane trafficking

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Subjects / Tools-Methodologies:

- 1 : Membrane curvature / optical tweezers
- 2 : protein-induced deformation / lipid nanotube
- 3 : cellular trafficking / micromanipulation

Summary of lab's interests

Our group develops a multidisciplinary approach to understand the role of the membranes in important cell functions such as intracellular trafficking, information transport; we also study the relation between cell membrane organization and their mechanical properties. In this perspective, we design simple model systems most often based on Giant Unilamellar Vesicles (GUV) to mimic these functions. GUVs are convenient model membrane systems because they are composed of a limited and controlled number of components, which can be varied. In addition, the effect of proteins can be monitored either by incubation with cytosolic proteins or by reconstitution of membrane proteins. Using model systems, the role of physical membrane parameters can be investigated. In the last years, we have developed a large expertise in the physics of membrane nanotubes pulled out from GUVs or from cells. We now routinely use these tubes either as membrane templates with a controlled curvature or, by measuring the force exerted on the tube and thus the membrane tension, we probe the organization of cell. As much as possible, we perform comparative between model systems and living cells. Our experimental techniques range from quantitative optical microscopy (DIC, phase contrast, Reflection Interference Contrast Microscopy (RICM), confocal, TIRF) to mechanical measurements and micromanipulation (micropipette aspiration, optical tweezers), and combinations of them. Our projects are directly inspired by biological questions and most of the time developed in collaboration with biologists from Curie or outside and with theoreticians (mostly from our lab or around).

Summary of project

Intracellular trafficking, pathogen internalization by cells induce many membrane deformation events, such as vesicle or tubule formation. A large number of the proteins involved in these membrane deformations have been identified. They have often been divided in 2 classes by biologists: proteins inducing curvature, such as the super-family of BAR-domain proteins (amphiphysin, endophilin for instance) and the proteins sensing curvature (for instance, the ALPS domain of Arf-GAP). These aspects are currently highly debated in the biology community. It has been shown with the first type of proteins that they are able to form tubules when in the presence of liposomes. A classical approach in biology is to directly relate the diameter of the tubules with the intrinsic curvature of the shape of the single protein, independently of the properties of their membrane substrate and of the mechanical properties of the protein assembly. For the second type, experiments by B. Antony (Nice) on liposomes with different diameters have shown that there is a critical diameter

o the order of 50 nm below which ALPS binding is strongly amplified. However, the deforming capacity of these curvature-sensing proteins is still not clear. These 2 aspects, curvature-sensor or -inductor, are probably coupled and dependent on protein concentration. We propose to use a quantitative physical approach to address this question. With our set-up combining optical tweezers, confocal microscopy and pipette micromanipulation, we will measure the effects of proteins of these different families binding on membrane nanotubes with controlled curvature as a function of protein bulk concentration. We will find the binding conditions in terms of curvature and protein concentration. We will also measure the effect of protein binding on the force on the tube, and provide a mechanical description of the protein mesoscopic assemblies. This project will be developed in collaboration with the theory group of our lab (J. Prost et J.F. Joanny) and the cell biology group of B. Goud in our Institute. Eventually, we aim to propose a general modeling of membrane deformations induced by these proteins.