

Année de publication : 2021

Tsai Feng-Ching, Simunovic Mijo, Sorre Benoit , Bertin Aurélie, Manzi John, Callan-Jones Andrew, Bassereau Patricia (2021 Apr 6)

Comparing physical mechanisms for membrane curvature-driven sorting of BAR-domain proteins

Soft Matter : [DOI : 10.1039/D0SM01573C](https://doi.org/10.1039/D0SM01573C)

Résumé

Protein enrichment at specific membrane locations in cells is crucial for many cellular functions. It is well-recognized that the ability of some proteins to sense membrane curvature contributes partly to their enrichment in highly curved cellular membranes. In the past, different theoretical models have been developed to reveal the physical mechanisms underlying curvature-driven protein sorting. This review aims to provide a detailed discussion of the two continuous models that are based on the Helfrich elasticity energy, (1) the spontaneous curvature model and (2) the curvature mismatch model. These two models are commonly applied to describe experimental observations of protein sorting. We discuss how they can be used to explain the curvature-induced sorting data of two BAR proteins, amphiphysin and centaurin. We further discuss how membrane rigidity, and consequently the membrane curvature generated by BAR proteins, could influence protein organization on the curved membranes. Finally, we address future directions in extending these models to describe some cellular phenomena involving protein sorting.

Année de publication : 2020

Pernier Julien, Morchain Antoine, Caorsi Valentina, Bertin Aurélie, Bousquet Hugo, Bassereau Patricia, Coudrier Evelyne (2020 Sep 7)

Myosin 1b Flattens and Prunes Branched Actin Filaments.

Journal of Cell Science : [DOI : 10.1242/jcs.247403](https://doi.org/10.1242/jcs.247403)

Résumé

Abstract

Motile and morphological cellular processes require a spatially and temporally coordinated branched actin network that is controlled by the activity of various regulatory proteins including the Arp2/3 complex, profilin, cofilin and tropomyosin. We have previously reported that myosin 1b regulates the density of the actin network in the growth cone. Using in vitro F-actin gliding assays and total internal reflection fluorescence (TIRF) microscopy we show in this report that this molecular motor flattens the Arp2/3-dependent actin branches up to breaking them and reduces the probability to form new branches. This experiment reveals that myosin 1b can produce force sufficient enough to break up the Arp2/3-mediated actin junction. Together with the former in vivo studies, this work emphasizes the essential role played by myosins in the architecture and in the dynamics of actin networks in different cellular regions.

Aurélie Bertin , Nicola de Franceschi , Eugenio de la Mora , Sourav Maiti, Maryam Alqabandi, Nolwen Miguet, Aurélie di Cicco, Wouter H. Roos, Stéphanie Mangenot , Winfried Weissenhorn, Patricia Bassereau (2020 May 29)

Human ESCRT-III polymers assemble on positively curved membranes and induce helical membrane tube formation

Nature Communications : 11 : 2663 : [DOI : 10.1038/s41467-020-16368-5](https://doi.org/10.1038/s41467-020-16368-5)

Résumé

Endosomal sorting complexes for transport-III (ESCRT-III) assemble in vivo onto membranes with negative Gaussian curvature. How membrane shape influences ESCRT-III polymerization and how ESCRT-III shapes membranes is yet unclear. Human core ESCRT-III proteins, CHMP4B, CHMP2A, CHMP2B and CHMP3 are used to address this issue in vitro by combining membrane nanotube pulling experiments, cryo-electron tomography and AFM. We show that CHMP4B filaments preferentially bind to flat membranes or to tubes with positive mean curvature. Both CHMP2B and CHMP2A/CHMP3 assemble on positively curved membrane tubes. Combinations of CHMP4B/CHMP2B and CHMP4B/CHMP2A/CHMP3 are recruited to the neck of pulled membrane tubes and reshape vesicles into helical “corkscrewlike” membrane tubes. Sub-tomogram averaging reveals that the ESCRT-III filaments assemble parallel and locally perpendicular to the tube axis, highlighting the mechanical stresses imposed by ESCRT-III. Our results underline the versatile membrane remodeling activity of ESCRT-III that may be a general feature required for cellular membrane remodeling processes.

Année de publication : 2019

Julien Pernier, Remy Kusters, Hugo Bousquet, Thibaut Lagny, Antoine Morchain, Jean-François Joanny*, Patricia Bassereau*, Evelyne Coudrier* (2019 Nov 15)

Myosin 1b is an actin depolymerase.

Nature Communications : 10 : 5200 : [DOI : 10.1038/s41467-019-13160-y](https://doi.org/10.1038/s41467-019-13160-y)

Résumé

The regulation of actin dynamics is essential for various cellular processes. Former evidence suggests a correlation between the function of non-conventional myosin motors and actin dynamics. Here we investigate the contribution of myosin 1b to actin dynamics using sliding motility assays. We observe that sliding on myosin 1b immobilized or bound to a fluid bilayer enhances actin depolymerization at the barbed end, while sliding on myosin II, although 5 times faster, has no effect. This work reveals a non-conventional myosin motor as another type of depolymerase and points to its singular interactions with the actin barbed end.

Mijo Simunovic, Emma Evergren, Andrew Callan-Jones*, Patricia Bassereau* (2019 Oct 7)

Curving Cells Inside and Out: Roles of BAR Domain Proteins in Membrane

Shaping and Its Cellular Implications.

Annual Review of Cell and Developmental Biology : 35 : [DOI : 10.1146/annurev-cellbio-100617-060558](https://doi.org/10.1146/annurev-cellbio-100617-060558)

Résumé

Many cellular processes rely on precise and timely deformation of the cell membrane. While many proteins participate in membrane reshaping and scission, usually in highly specialized ways, Bin/amphiphysin/Rvs (BAR) domain proteins play a pervasive role, as they not only participate in many aspects of cell trafficking but also are highly versatile membrane remodelers. Subtle changes in the shape and size of the BAR domain can greatly impact the way in which BAR domain proteins interact with the membrane. Furthermore, the activity of BAR domain proteins can be tuned by external physical parameters, and so they behave differently depending on protein surface density, membrane tension, or membrane shape. These proteins can form 3D structures that mold the membrane and alter its liquid properties, even promoting scission under various circumstances. As such, BAR domain proteins have numerous roles within the cell. Endocytosis is among the most highly studied processes in which BAR domain proteins take on important roles. Over the years, a more complete picture has emerged in which BAR domain proteins are tied to almost all intracellular compartments; examples include endosomal sorting and tubular networks in the endoplasmic reticulum and T-tubules. These proteins also have a role in autophagy, and their activity has been linked with cancer. Here, we briefly review the history of BAR domain protein discovery, discuss the mechanisms by which BAR domain proteins induce curvature, and attempt to settle important controversies in the field. Finally, we review BAR domain proteins in the context of a cell, highlighting their emerging roles in cell signaling and organelle shaping.

Zack Jarin, Feng-Ching Tsai, Aram Davtyan, Alexander J.Pak, Patricia Bassereau, Gregory A.Voth (2019 Aug 6)

Unusual Organization of I-BAR Proteins on Tubular and Vesicular Membranes.

Biophysical Journal : 117 : 553-562 : [DOI : 10.1016/j.bpj.2019.06.025](https://doi.org/10.1016/j.bpj.2019.06.025)

Résumé

Protein-mediated membrane remodeling is a ubiquitous and critical process for proper cellular function. Inverse Bin/Amphiphysin/Rvs (I-BAR) domains drive local membrane deformation as a precursor to large-scale membrane remodeling. We employ a multiscale approach to provide the molecular mechanism of unusual I-BAR domain-driven membrane remodeling at a low protein surface concentration with near-atomistic detail. We generate a bottom-up coarse-grained model that demonstrates similar membrane-bound I-BAR domain aggregation behavior as our recent Mesoscopic Membrane with Explicit Proteins model. Together, these models bridge several length scales and reveal an aggregation behavior of I-BAR domains. We find that at low surface coverage (i.e., low bound protein density), I-BAR domains form transient, tip-to-tip strings on periodic flat membrane sheets. Inside of lipid bilayer tubules, we find linear aggregates parallel to the axis of the tubule. Finally, we find that I-BAR domains form tip-to-tip aggregates around the edges of membrane domes. These

results are supported by in vitro experiments showing low curvature bulges surrounded by I-BAR domains on giant unilamellar vesicles. Overall, our models reveal new I-BAR domain aggregation behavior in membrane tubules and on the surface of vesicles at low surface concentration that add insight into how I-BAR domain proteins may contribute to certain aspects of membrane remodeling in cells.

Nicola de Franceschi, Maryam Alqabandi, Winfried Weissenhorn, Patricia Bassereau (2019 Jul 5)

Dynamic and Sequential Protein Reconstitution on Negatively Curved Membranes by Giant Vesicles Fusion.

Bio-Protocol : 9 : e3294 : [DOI : 10.21769/BioProtoc.3294](https://doi.org/10.21769/BioProtoc.3294)

Résumé

In vitro investigation of the interaction between proteins and positively curved membranes can be performed using a classic nanotube pulling method. However, characterizing protein interaction with negatively curved membranes still represents a formidable challenge. Here, we describe our recently developed approach based on laser-triggered Giant Unilamellar Vesicles (GUVs) fusion. Our protocol allows sequential addition of proteins to a negatively curved membrane, while at the same time controlling the buffer composition, lipid composition and membrane tension. Moreover, this method does not require a step of protein detachment, greatly simplifying the process of protein encapsulation over existing methods.

Elena Beltrán-Heredia, Feng-Ching Tsai, Samuel Salinas-Almaguer, Francisco J. Cao*, Patricia Bassereau*, Francisco Monroy* (2019 Jun 20)

Membrane curvature induces cardiolipin sorting.

Communications Biology : 2 : 225 : [DOI : 10.1038/s42003-019-0471-x](https://doi.org/10.1038/s42003-019-0471-x)

Résumé

Cardiolipin is a cone-shaped lipid predominantly localized in curved membrane sites of bacteria and in the mitochondrial cristae. This specific localization has been argued to be geometry-driven, since the CL's conical shape relaxes curvature frustration. Although previous evidence suggests a coupling between CL concentration and membrane shape in vivo, no precise experimental data are available for curvature-based CL sorting in vitro. Here, we test this hypothesis in experiments that isolate the effects of membrane curvature in lipid-bilayer nanotubes. CL sorting is observed with increasing tube curvature, reaching a maximum at optimal CL concentrations, a fact compatible with self-associative clustering. Observations are compatible with a model of membrane elasticity including van der Waals entropy, from which a negative intrinsic curvature of -1.1 nm^{-1} is predicted for CL. The results contribute to understanding the physicochemical interplay between membrane curvature and composition, providing key insights into mitochondrial and bacterial membrane organization and dynamics.

Joanna Podkalicka, Patricia Bassereau (2019 Apr 1)

How membrane physics rules the HIV envelope.

Nature Cell Biology : 21 : 413-415 : [DOI : 10.1038/s41556-019-0312-7](https://doi.org/10.1038/s41556-019-0312-7)

Résumé

HIV particles incorporate host membrane proteins into their envelope to evade the immune system and infect other cells. A study now shows that Gag assembly on the host cell membrane produces a raft-like nanodomain favourable for protein partitioning due to a transbilayer coupling mechanism assisted by long saturated chain lipids and cholesterol.

Beber A, Taveneau C, Nania M, Tsai FC, Di Cicco A, Bassereau P, Lévy D, Cabral JT, Isambert H, Mangenot S*, Bertin A* (2019 Jan 24)

Membrane reshaping by micrometric curvature sensitive septin filaments

Nature communications : [DOI : 10.1038/s41467-019-08344-5](https://doi.org/10.1038/s41467-019-08344-5)

Résumé

Septins are cytoskeletal filaments that assemble at the inner face of the plasma membrane. They are localized at constriction sites and impact membrane remodeling. We report in vitro tools to examine how yeast septins behave on curved and deformable membranes. Septins reshape the membranes of Giant Unilamellar Vesicles with the formation of periodic spikes, while flattening smaller vesicles. We show that membrane deformations are associated to preferential arrangement of Septin filaments on specific curvatures. When binding to bilayers supported on custom-designed periodic wavy patterns displaying positive and negative micrometric radii of curvatures, septin filaments remain straight and perpendicular to the curvature of the convex parts, while bending negatively to follow concave geometries. Based on these results, we propose a theoretical model that describes the deformations and micrometric curvature sensitivity observed in vitro. The model captures the reorganizations of septin filaments throughout cytokinesis in vivo, providing mechanistic insights into cell division.

Année de publication : 2018

Feng-Ching Tsai*, Aurelie Bertin*, Hugo Bousquet, John Manzi, Yosuke Senju, Meng-Chen Tsai, Laura Picas, Stephanie Miserey-Lenkei, Pekka Lappalainen, Emmanuel Lemichez, Evelyne Coudrier*, Patricia Bassereau* (2018 Sep 30)

Ezrin enrichment on curved membranes requires a specific conformation or interaction with a curvature-sensitive partner.

elife : 7 : e37262 : [DOI : 10.7554/eLife.37262](https://doi.org/10.7554/eLife.37262)

Résumé

One challenge in cell biology is to decipher the biophysical mechanisms governing protein enrichment on curved membranes and the resulting membrane deformation. The ERM protein ezrin is abundant and associated with cellular membranes that are flat, positively or negatively curved. Using *in vitro* and cell biology approaches, we assess mechanisms of ezrin's enrichment on curved membranes. We evidence that wild-type ezrin (ezrinWT) and its phosphomimetic mutant T567D (ezrinTD) do not deform membranes but self-assemble anti-parallelly, zipping adjacent membranes. EzrinTD's specific conformation reduces intermolecular interactions, allows binding to actin filaments, which reduces membrane tethering, and promotes ezrin binding to positively-curved membranes. While neither ezrinTD nor ezrinWT senses negative curvature alone, we demonstrate that interacting with curvature-sensing I-BAR-domain proteins facilitates ezrin enrichment in negatively-curved membrane protrusions. Overall, our work demonstrates that ezrin can tether membranes, or be targeted to curved membranes, depending on conformations and interactions with actin and curvature-sensing binding partners.

Arthur Charles-Orszag, Feng-Ching Tsai, Daria Bonazzi, Valeria Manriquez, Martin Sachse, Adeline Mallet, Audrey Salles, Keira Melican, Ralitzia Staneva, Aurelie Bertin, Corinne Millien, Sylvie Goussard, Pierre Lafaye, Spencer Shorte, Matthieu Piel, Jacomine Krijnse-Locker, Françoise Brochard-Wyart, Patricia Bassereau, Guillaume Dumenil (2018 Aug 16)

Adhesion to nanofibers drives cell membrane remodeling through 1D wetting

Nature Communications : [DOI : org/10.1101/393744](https://doi.org/10.1101/393744)

Résumé

The shape of cellular membranes is highly regulated by a set of conserved mechanisms. These mechanisms can be manipulated by bacterial pathogens to infect cells. Human endothelial cell plasma membrane remodeling by the bacterium *Neisseria meningitidis* is thought to be essential during the blood phase of meningococcal infection, but the underlying mechanisms are unknown. Here we show that plasma membrane remodeling occurs independently of F-actin, along meningococcal type IV pili fibers, by a novel physical mechanism we term « one dimensional » membrane wetting. We provide a theoretical model that gives the physical basis of 1D wetting and show that this mechanism occurs in model membranes interacting with model nanofibers, and in human cells interacting with model extracellular matrices. It is thus a new general principle driving the interaction of cells with their environment at the nanoscale that is diverted by meningococcus during infection.

Nicola De Franceschi, Maryam Alqabandi, Nolwenn Miguet, Christophe Caillat, Stephanie Mangenot, Winfried Weissenhorn*, Patricia Bassereau* (2018 Aug 3)

The ESCRT protein CHMP2B acts as a diffusion barrier on reconstituted membrane necks.

Journal of Cell Science : 132 : jcs217968 : [DOI : 10.1242/jcs.217968](https://doi.org/10.1242/jcs.217968)

Résumé

Endosomal sorting complexes required for transport (ESCRT)-III family proteins catalyze membrane remodeling processes that stabilize and constrict membrane structures. It has been proposed that stable ESCRT-III complexes containing CHMP2B could establish diffusion barriers at the post-synaptic spine neck. In order to better understand this process, we developed a novel method based on fusion of giant unilamellar vesicles to reconstitute ESCRT-III proteins inside GUVs, from which membrane nanotubes are pulled. The new assay ensures that ESCRT-III proteins polymerize only when they become exposed to physiologically relevant membrane topology mimicking the complex geometry of post-synaptic spines. We establish that CHMP2B, both full-length and with a C-terminal deletion (ΔC), preferentially binds to membranes containing phosphatidylinositol 4,5-bisphosphate [PI(4,5)P₂]. Moreover, we show that CHMP2B preferentially accumulates at the neck of membrane nanotubes, and provide evidence that CHMP2B- ΔC prevents the diffusion of PI(4,5)P₂ lipids and membrane-bound proteins across the tube neck. This indicates that CHMP2B polymers formed at a membrane neck may function as a diffusion barrier, highlighting a potential important function of CHMP2B in maintaining synaptic spine structures.

Patricia Bassereau, Rui Jin, Tobias Baumgart, Markus Deserno, Rumiana Dimova, Vadim A. Frolov, Pavel V. Bashkirov, Helmut Grubmüller, Reinhard Jahn, H. Jelger Risselada, Ludger Johannes, Michael M. Kozlov, Reinhard Lipowsky, Thomas J. Pucadyil, Wade F. Zeno, Jeanne C. Stachowiak, Dimitrios Stamou, Artù Breuer, Line Lauritsen, Camille Simon, Cécile Sykes, Gregory A. Voth, Thomas R Weikl (2018 Jul 20)

The 2018 biomembrane curvature and remodeling roadmap.

Journal of Physics D: Applied Physics : 51 : 343001 : DOI : [10.1088/1361-6463/aacb98](https://doi.org/10.1088/1361-6463/aacb98)

Résumé

The importance of curvature as a structural feature of biological membranes has been recognized for many years and has fascinated scientists from a wide range of different backgrounds. On the one hand, changes in membrane morphology are involved in a plethora of phenomena involving the plasma membrane of eukaryotic cells, including endo- and exocytosis, phagocytosis and filopodia formation. On the other hand, a multitude of intracellular processes at the level of organelles rely on generation, modulation, and maintenance of membrane curvature to maintain the organelle shape and functionality. The contribution of biophysicists and biologists is essential for shedding light on the mechanistic understanding and quantification of these processes.

Given the vast complexity of phenomena and mechanisms involved in the coupling between membrane shape and function, it is not always clear in what direction to advance to eventually arrive at an exhaustive understanding of this important research area. The 2018 Biomembrane Curvature and Remodeling Roadmap of *Journal of Physics D: Applied Physics* addresses this need for clarity and is intended to provide guidance both for students who have just entered the field as well as established scientists who would like to improve their orientation within this fascinating area.

Alexandre Beber, Maryam Alqabandi, Coline Prevost, Fanny Viars, Daniel Levy, Patricia Bassereau, Aurélie Bertin*, Stéphanie Mangenot* (2018 Jul 16)

Septin-based readout of PI(4,5)P2 incorporation into membranes of giant unilamellar vesicles

Cytoskeleton : [DOI : 10.1002/cm.21480](https://doi.org/10.1002/cm.21480)

Résumé

Septins constitute a novel class of cytoskeletal proteins. Budding yeast septins self-assemble into non-polar filaments bound to the inner plasma membrane through specific interactions with L- α -phosphatidylinositol-4,5-bisphosphate (PI(4,5)P₂). Biomimetic in vitro assays using Giant Unilamellar Vesicles (GUVs) are relevant tools to dissect and reveal insights in proteins-lipids interactions, membrane mechanics and curvature sensitivity. GUVs doped with PI(4,5)P₂ are challenging to prepare. This report is dedicated to optimize the incorporation of PI(4,5)P₂ lipids into GUVs by probing the proteins-PI(4,5)P₂ GUVs interactions. We show that the interaction between budding yeast septins and PI(4,5)P₂ is more specific than using usual reporters (phospholipase Cd1). Septins have thus been chosen as reporters to probe the proper incorporation of PI(4,5)P₂ into giant vesicles. We have shown that electro-formation on platinum wires is the most appropriate method to achieve an optimal septin-lipid interaction resulting from an optimal PI(4,5)P₂ incorporation for which, we have optimized the growth conditions. Finally, we have shown that PI(4,5)P₂ GUVs have to be used within a few hours after their preparation. Indeed, over time, PI(4,5)P₂ is expelled from the GUV membrane and the PI(4,5)P₂ concentration in the bilayer decreases