BP 2: Membranes and Vesicles I

Time: Monday 9:30–13:00 Location: H 2032

BP 2.1 Mon 9:30 H 2032

Membrane fusion as a pathway to fission — •Russell Spencer and Marcus Müller — Georg-August Universität Göttingen, Institute for Theoretical Physics, 37077 Göttingen, Germany

Remodeling of biological membranes, such as fusion and fission, is involved in a variety of basic, cellular processes. This work investigates the mechanisms and pathways for the fission of phospholipid membranes, in particular double-membrane fission as it occurs in mitochondrial division. We employ self-consistent field theory and utilize the string method to find the Minimum Free Energy Path (MFEP) in order to determine the most likely pathway for the transition. The complex landscape of possible rearrangements gives rise to multiple possible mechanisms for double membrane fission. The simplest pathway involves the local constriction, hemifusion and fission of the inner membrane, without contact with the outer membrane. Intriguingly, we also uncover a new mechanism whereby local fusion contact between the inner and outer membrane can catalyze the fission of the inner membrane. Not only does the new mechanism have a lower total free energy barrier, but also an intermediate metastable state, allowing the system to ratchet its way up the rate-limiting step.

BP 2.2 Mon 9:45 H 2032

Adhesion energy controls lipid binding-mediated endocytosis — R Groza[1], K Schmidt[1,2], P Müller[1], P Ronchi[3], C Schlack[1], U Neu[1], D Puchkov[4], R Dimova[2], C Matthaeus[5], J Taraska[5], T Weikl[2], and •H Ewers[1] — [1]Freie Universität Berlin — [2]MPI Colloids and Interfaces — [3]EMBL — [4]FMP — [5]National Institutes of Health

Many bacterial toxins and viruses deform membranes through multivalent binding to lipids for clathrin-independent endocytosis. How membrane deformation and endocytic internalization are mechanistically linked is unclear. Here we show that many lipid-binding virions induce membrane deformation for clathrin-independent endocytosis, suggesting a common mechanism based on multivalent lipid binding by globular particles. We create a synthetic cellular system consisting of a lipid-anchored receptor in form of GPI-anchored anti-GFP nanobodies and a multivalent globular binder with 180 regularly-spaced GFPs on its surface. We show that these 40 nm diameter particles bind to cells expressing the receptor, deform the plasma membrane upon adhesion and become endocytosed in a clathrin-independent manner. We explore the role of the membrane adhesion energy in endocytosis by using receptors with affinities varying over 7 orders of magnitude. Our system shows that once a threshold in adhesion energy is overcome, membrane deformation and endocytosis occurs reliably. Membrane deformation by globular binders is thus sufficient for internalization to occur and is a common, purely biophysical mechanism for lipid-binding mediated endocytosis of particles.

BP 2.3 Mon 10:00 H 2032

Effect of the receptor nanoclustering on the activation of natural killer cells through biomechanical feedback — •Piotr Nowakowski[1], Ashish Pandey[2], Carlos Ureña Martin[2], Muhammad Abu Ahmad[3], Avishay Edri[3], Esti Toledo[2], Sivan Tzadka[2], Jonas Walther[4], Guillaume Le Saux[2], Angel Porgador[3], Mark Schvartzman[2], and Ana-Sunčana Smith[4,1] — [1]Division of Physical Chemistry, Institut Ruđer Bošković, Zagreb, Croatia — [2]Department of Materials Engineering, Ilse Katz Institute for Nanoscale Science and Technology, Ben-Gurion University of the Negev, Beer-Sheva, Israel — [3]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel — [4]Institut für Theoretische Physik, IZNF, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

Natural killer (NK) cells are part of the immune system responsible for rapid recognition and elimination of virus-infected or tumor cells. The exact mechanism of this recognition is not yet known but it is expected to be related to the observed formation of nanoclusters of receptors on the membrane of NK cell. We propose a phenomenological model of activity of NK cell based on biomechanical feedback between number of connected receptors, activity of NK cell, and fluctuations of the membrane. We test the model in experiment: using nanolithography we create patterns of ligands of various shapes and measure the activity of cells after binding to them. Our theoretical model qualitatively explanes the dependence of activity on the structure of nanoclusters and overall density of ligands that is observed in the experiment.

BP 2.4 Mon 10:15 H 2032

Polysaccharide functionalization reduces lipid vesicle stiffness — •Kevin Jahnke and David A. Weitz — Harvard University, Cambridge, USA

The biophysical properties of lipid vesicles are important for their stability and integrity, key parameters that control the performance when these vesicles are used for drug delivery. The vesicle properties are determined by the composition of lipids used to form the vesicle. However, for a given lipid composition, they can also be tailored by tethering polymers to the membrane. Typically, synthetic polymers like polyethyleneglycol are used to increase vesicle stability but the use of polysaccharides in this context is much less explored. Here, we report a general method for functionalizing lipid vesicles with polysaccharides by binding them to cholesterol. We incorporate the polysaccharides on the outer membrane leaflet of giant unilamellar vesicles (GUVs) and investigate their effect on membrane mechanics using micropipette aspiration. We find that the presence of the glycolipid functionalization produces an unexpected softening of GUVs with fluid-like membranes. By contrast, the functionalization of GUVs with polyethylene glycol does not reduce their stretching modulus. Furthermore, we explore the effect of polysaccharide functionalization of lipid vesicles for drug delivery. We find that it increases the uptake of small unilamellar vesicles (SUVs) by cells and leads to an improved transfection. This work provides the potential means to study membrane-bound meshworks of polysaccharides similar to the cellular glycocalyx; moreover, it can be used for tuning the mechanical properties of drug delivery vehicles.

BP 2.5 Mon 10:30 H 2032

Mechanical properties of pure protein membranes made from fungal hydrophobins — •Kirstin Kochems[1], Friederike Nolle[1], Hendrik Hähl[1], Michael Lienemann[2], and Karin Jacobs[1] — [1]Department of Experimental Physics & Center for Biophysics, Saarland University, Saarbrücken, Germany — [2]VTT Technical Research Centre of Finland Ltd., Espoo, Finland

As strongly amphiphilic proteins, fungal hydrophobins are known to self-assemble at water-interfaces into stable monolayer films. Contacting of two formed monolayers results in stable bilayers, that can be studied in a microfluidic surrounding or via atomic force microscopy (AFM)[1].

By transferring monolayer films from the water-air interface to perforated substrates, we can use force spectroscopy indentation measurements to examine the mechanical properties of pore-spanning hydrophobin mono- and bilayers. We find that the hydrophobin layers show a high stability and a higher Young's modulus in comparison with phospholipid membranes.

[1] Hähl, H. et al., Adv. Mater 29, 1602888 (2017).

BP 2.6 Mon 10:45 H 2032

Mechanical regulation of endocytosis by protein condensate capillary forces — •Max Ferrin[1,2,3], Tyler Harmon[2], David Drubin[3], and Frank Jülicher[1] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Institute Theory of Polymers, Leibniz Institute of Polymer Research, Dresden, Germany — [3]Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA

Clathrin-mediated endocytosis (CME) is the primary pathway for internalization of extracellular and membrane cargo in eukaryotic cells. It is characterized by a patch of the plasma membrane invaginating and pinching off to generate a cytoplasmic vesicle. Recently, experimental evidence has begun to accumulate in support of proteins assembling into liquid-like condensates at nascent CME sites, but potential functional consequences are lacking in the literature. Given that condensate capillary forces influence membrane bending in other biological systems, we constructed a mathematical model to probe the mechanical influence of a protein droplet on endocytosis. Preliminary analysis of the model shows that a droplet can regulate the progression of endocytosis by stalling invagination until a threshold distance or droplet volume, and driving toward completion after passing the threshold. Further model analysis will characterize the critical parameters that

set this regulatory behavior, as well as make predictions of CME dynamics that can be tested experimentally.

15 min. break

Invited Talk BP 2.7 Mon 11:15 H 2032

The fascinating membrane morphology of the endoplasmic reticulum — •Reinhard Lipowsky — Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany

Our body contains an enormous number of biomembranes that enclose our cells and most intracellular organelles. A particularly intriguing example is provided by the membrane of the endoplasmic reticulum (ER), which extends throughout the whole cell as a bicontinuous network of membrane nanotubes connected by three-way junctions, thereby generating a surface with a very high topological genus. [1]

A long-standing puzzle of the ER morphology is the straight appearance of the nanotubes in the light microscope, which form contact angles close to 120 degrees. Another puzzling aspect are the nanoscopic shapes of the tubules and junctions. Furthermore, both the formation and the maintenance of the nanotubular networks require GTP and GTP-hydrolyzing membrane proteins. In fact, the nanotubes are destroyed when the supply of GTP is interrupted.

It has been recently argued [1] that all of these puzzling observations are intimately related to each other and to the dimerization of two membrane proteins anchored in the same membrane. The dimerization process can generate an effective membrane tension that stabilizes the ER geometry and prevents the tube destruction, thereby maintaining the integrity of the ER.

[1] R. Lipowsky, S. Pramanik, A. S. Benk, M. Tarnawski, J. P. Spatz, R. Dimova. Elucidating the Morphology of the Endoplasmic reticulum. ACS Nano 17:11957-11968 (2023) DOI: 10.1021/acsnano.3c01338

BP 2.8 Mon 11:45 H 2032

Biomolecular condensates on geometrically structured lipid membranes — •Katja Zieske — Biophysics, Max Planck Institute for the Science of Light, Erlangen, Germany

Biomolecular condensates are supramolecular assemblies of proteins and RNA molecules and have been studied extensively, due to their ability to spatially structure cells and to spatially confine biological reactions. However, little is known about the interactions of liquid-liquid condensates with geometrically structured lipid membranes and the consequences of these interactions on cellular length scales. Here, we used a cell-free bottom-up approach to reconstitute liquid-liquid condensates at geometrically structured lipid membranes. Our results demonstrate how lipid membranes and liquid-liquid condensates interact under various experimental conditions and point towards an important role of membrane geometry-controlled wetting-effects in intracellular organization.

BP 2.9 Mon 12:00 H 2032

Membranes interacting with biomolecular condensates: wetting, remodeling, and damage stabilization — •Agustin Mangiarotti[1], Macarena Siri[1], Claudio Bussi[2], Nicky Tam[1], Leonel Malacrida[3,4], Maximiliano Gutierrez[2], Reinhard Lipowsky[1], and Rumiana Dimova[1] — [1]Max Planck Institute of Colloids and Interfaces, Potsdam, Germany — [2]The Francis Crick Institute, London, UK — [3]Departamento de Fisiopatología, Hospital de Clínicas, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay — [4]Advanced Bioimaging Unit, Institut Pasteur of Montevideo and Universidad de la República, Montevideo, Uruguay

Membrane wetting by biomolecular condensates recently emerged as an important phenomenon in cell biology, playing a key role in diverse processes across different organisms. By performing a systematic analysis of the interaction of protein and polymer condensates with giant unilamellar vesicles as model membranes, we have demonstrated that these interactions can lead to remodeling processes, which are governed by the interplay of adhesion, membrane elasticity, and interfacial tension. Moreover, we showed that condensate wetting can promote the stabilization of damaged membranes, uncovering a new mechanism for biomolecular condensates in cell physiology. Finally, we explored the interaction mechanism between condensates and membranes at a molecular scale, using nano-environmental sensors and state-of-the-art microscopy techniques combined with phasor analysis. With this approach, we found that biomolecular condensates can modulate membrane lipid packing and hydration by wetting.

BP 2.10 Mon 12:15 H 2032

Modeling the reshaping of membranes across the tree of life — •Felix Frey, Miguel Amaral, and Andela Saric — Institute of Science and Technology Austria, Klosterneuburg, Austria

All biological cells are defined by flexible lipid membranes that are constantly reshaped as cells divide or relay materials across them. Interestingly, various membrane designs have evolved across the tree of life. In archaea, one of the two prokaryotic domains that often live at extreme conditions, membranes are typically organized into monolayers. Therefore, archaeal membranes are supposed to react differently when subjected to curvature compared to bilayer membranes in eukaryotes. However, the physical behavior of archaeal monolayer membranes during bending deformations has never been characterized. Here, we develop the first particle-based model for archaeal monolayer membranes. Our computer simulations reveal how archaeal membrane monolayers self-assemble, how they withstand high temperatures and how they deform when they adsorb small particles. In addition, we explore how imposing external membrane curvature dictates the organization of membrane lipids and creates membrane plasticity. Our findings demonstrate that archaeal monolayer membranes behave significantly different from bilayer membranes, potentially explaining why various membrane designs have evolved across the tree of life.

BP 2.11 Mon 12:30 H 2032

Physicochemical properties of microplastic particles affect their cellular uptake and maturation — •Simon Wieland[1,2], Anja FRM Ramsperger[1,2], Wolfgang Gross[1], Matteo Kumar[1], Johanna Bodrogi[1], Christian Laforsch[2], and Holger Kress[1] — [1]Biological Physics, University of Bayreuth, Germany — [2]Animal Ecology I, University of Bayreuth, Germany

Microplastics are an abundant contaminant in the environment, raising concerns about harmful effects on organisms. Therefore, many studies investigating effects of microplastics on cells, tissues, and organisms were published. These studies often rely on commercial model microplastics, usually polystyrene microspheres. While nominally very similar, their physicochemical properties can differ, making it difficult to compare the results of different studies. We now show that nominally identical polystyrene microspheres from eight different manufacturers differ in their ζ-potential, which determines their cellular interactions and internalization by macrophages. We monitored the actin cytoskeleton during particle uptake and found that phagocytosis or macropinocytosis drive the internalization. The uptake time differed between particle types and was correlated with the particles ζ-potential. Furthermore, we examined the subsequent maturation and acidification of internalized microplastics. We found that the maturation kinetics strongly differed between particle types. Unraveling the kinetics and mechanisms of microplastic internalization and maturation in cells is essential to understand their potentially harmful effects.

BP 2.12 Mon 12:45 H 2032

Understanding the Interface of Plastic Nanoparticles and Biomimetic Cell Membranes — •Una Janke, Emma Weilbeer, Wanda Levin, Norman Geist, and Mihaela Delcea — Institut für Biochemie, Felix-Hausdorff-Str. 4, 17489 Greifswald

Plastics and the release of polymeric particles into the environment is a burning issue, not least because plastic nanoparticles (NPs) are potentially harmful to both the surrounding and human health. As soon as they enter the body, NPs have contact to various biological fluids (e.g. blood) and with cell membranes containing different types of lipids and numerous membrane proteins. To understand the complex interaction of NPs with the cellular interface, we have chosen a representative model system comprising of the commonly used plastic polystyrene and an artificial biomimetic membrane containing the platelet receptor integrin αIIbβ3 which undergoes conformational dynamics, e.g. in the presence of manganese ions. The combination of biophysical methods, such as dynamic-light-scattering, enabled the characterisation of the protein corona around the polystyrene nanoparticles (PS-NPs) with different surface charges and its stability over time. Moreover, the interaction of the PS-NPs with the engineered biomimetic membranes was analysed by quartz-crystal-microbalance and the results were confirmed by cell interaction analyses and molecular dynamic simulations studies. Our results reveal that protein corona formation prevents unspecific binding of PS-NPs to membranes, whereas the absence of corona induces surface charge-dependent aggregation of PS-NPs, as well as strong binding to model cell membranes.