BP 19: Membranes and Vesicles II

Time: Wednesday 9:30–13:00 Location: H46

BP 19.1 Wed 9:30 H46

Atomistic Insights into pH-Dependent Structural Transitions in Lipid Mesophases: A Combined MD/SAXS Approach — •Akhil Sudarsan[1], Julian Philipp[2], Joachim Rädler[2], and Nadine Schwierz[1] — [1]University of Augsburg, Augsburg, Germany — [2]Ludwig Maximilians-University, Munich, Germany

Lipid nanoparticles (LNPs) are crucial delivery vehicles for mRNA-based therapeutics, enabling the encapsulation and release of negatively charged nucleic acids through ionizable lipids that exhibit pH-dependent fusogenic activity. This study investigates ionizable DLin-MC3-DMA (MC3) lipid/cholesterol mesophases that mimic the core structure of LNPs, focusing on the inverse hexagonal (H_{II}) and inverse micellar (L_{II}) phases, both featuring an internal water domain surrounded by ionizable lipids. By combining experimental SAXS data and molecular dynamics (MD) simulations, we show that the L_{II} phase, which is stable at higher pH, transitions to H_{II} at lower pH. We also calculate the water content of the simulated core phases through comparison with scattering data and elucidate the distribution of lipids in these mesophases. We further developed an approach to compute scattering profiles directly from MD simulations, which corrects for artifacts arising from periodic boundary conditions, enabling direct, model-free comparisons between experimental and simulated data enhancing the reliability of the structural interpretations. In summary, integrating SAXS experiments and MD simulations offer molecular insights into the dynamic behaviour and pH-dependent structural transitions of ionizable lipid mesophases.

BP 19.2 Wed 9:45 H46

The effect of long-chain sphingolipids on lipid bilayers — •Clara Rickhoff, Annemarie Quas, and Andreas Heuer — Institut für Physikalische Chemie, Universität Münster, Münster, Germany

Lipid bilayers are found to form microdomains, so called rafts, that support a sorting of compounds in the bilayer, and that way are thought to be essential for cellular processes, such as vesicular traffic. One type of raft that is found in lipid bilayers of e.g. yeast cells in experiments are sphingolipid-enriched and sterol-depleted domains, that seem to form gel-like domains. In our work, we conduct MD simulations of lipid bilayers containing different concentrations of long-chain sphingolipids in order to investigate their effect on the membrane at the atomistic level. The remaining part of the lipid bilayer is chosen close to experimental results (Wedlich-Söldner group, University of Münster). From these simulations we gain insight into structural properties such as of e.g. the order parameter, the RDF or the interdigitation. This allows a deeper understanding of the order of the long-chain spingolipids, their effect on the overall membrane structure and the coupling between the leaflets.

BP 19.3 Wed 10:00 H46

Engineering asymmetric lipid vesicles for protein delivery — •Kevin Jahnke, Chenjing Yang, and David Weitz — Harvard University, Cambridge, USA

The delivery of therapeutics to cells is crucial for the treatment and prevention of diseases. To enhance targeting and protect therapeutics from degradation, they are often encapsulated into drug delivery vehicles like lipid nanoparticles, liposomes and viral vectors. However, there is no universal vehicle for all cargo types including small molecules, nucleic acids and proteins. Here, we present a method for engineering lipid vesicles with asymmetric leaflets and demonstrate their ability to deliver mRNA and proteins to cells (Yang,.., Weitz, Jahnke; biorxiv 2024). We show that leaflet asymmetry modulates the biophysical properties of lipid vesicles, leading to an enhanced vesicle uptake by cells, and an up to 5-fold increased transfection efficiency with mRNA. Additionally, we show that asymmetric vesicles can deliver a variety of proteins, including the gene-editing protein Cas9 and Cas9/sgRNA complexes. By modifying lipid vesicles with polysaccharides (Jahnke et al.; PNAS 2024) or the engineering of lipid-polymer hybrid vesicles, we further achieve the targeted delivery to specific cell types. Our method and findings expand the parameter space for engineering drug delivery vehicles and demonstrate the pivotal role of leaflet asymmetry in determining the biophysical properties of lipid vesicles. Consequently, our work leads to many applications, including the formation of more efficient, universal drug carriers that enable the delivery of proteins to cells.

BP 19.4 Wed 10:15 H46

Vesicle to bicelle decomposition can be correlated with the lipid's main phase transition: a direct evidence using chain-deuterated lipid — •Carina Dargel[1,2], Lara H. Moleiro[2], Aurel Radulescu[3], Tim J. Stank[2], and Thomas Hellweg[2] — [1]University of Münster, Institute of Physical Chemistry, Münster, Germany — [2]University of Bielefeld, Physical and Biophysical Chemistry, Bielefeld, Germany — [3]FZ Jülich, Jülich Centre for Neutron Science (JCNS) at Heinz Maier-Leibnitz Zentrum (MLZ), Garching, Germany

Mixtures of the phospholipid 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) and the saponin β-aescin form bicelles above a critical saponin concentration. Modification of the membrane's phase state by temperature increase induces a structural growth of the bicelles resulting in membrane-like DMPC-aescin aggregates or mixed small unilamellar vesicles.

The temperature-induced transition is fully reversible, independent of the aescin content. Furthermore, the decomposition of the mixed vesicles back to bicelles shows a prominent hysteresis effect, which is correlated with the main phase transition temperature T_m of the lipid. This correlation was demonstrated for the first time by taking advantage of the shift of the membrane's T_m due to chain-deuteration and thus the use of d54-DMPC by both turbidimetry and small angle neutron scattering (SANS)[1].

[1] Dargel *et al.* (2025), Journal of Colloid and Interface Science, 679, 209-220.

BP 19.5 Wed 10:30 H46

Exploring DNA Linkers for Biomimetic Cell Adhesion of Red Blood Cells — •Sebastian W. Krauss[1], Roger Rubio-Sánchez[1], Bortolo M. Mognetti[2], Lorenzo Di Michele[1], and Pietro Cicuta[3] — [1]CEB, University of Cambridge, UK — [2]ULB, Brussels, Belgium — [3]Department of Physics, University of Cambridge, UK

Ligand-receptor interactions are fundamental to cellular membrane dynamics, influencing a range of processes like cell-cell signaling and viral infections. These interactions govern how adjacent membranes recognize, bind, and respond to one another. To better understand these mechanisms, we developed a biomimetic approach that grants precise control over the strength of interactions between opposing membranes. Our strategy employs short membrane-anchored amphiphilic DNA nanostructures featuring single-stranded 'sticky-ends', which are designed to bind through complementary sequences, providing an adaptive platform for membrane-membrane interactions [Chem. Comm. 57, 12725 (2021)]. We implemented our platform to functionalize red blood cells (RBCs), creating cellular aggregates with programmable morphologies, ranging from doublets to star-like geometries. Additionally, we used DNA-functionalized particles to selectively bind RBCs. By tuning the sequence, we precisely controlled interaction strength, enabling RBCs to progressively envelop beads. Furthermore, we employed optical tweezers to observe the rapid formation of strong bonds in situ [manuscripts in preparation]. This system offers insights into the forces and dynamics of RBC aggregation and their interactions with pathogens, such as Plasmodium species responsible for malaria.

BP 19.6 Wed 10:45 H46

Investigating Endosomal Escape Mechanisms of PEI-DNA Polyplexes with Computer Simulations — •Jonas Lehnen[1], Friederike Schmid[1], and Giovanni Settanni[2] — [1]Physik, Johannes Gutenberg Universität, Mainz — [2]Physik, Ruhr-Universität Bochum

Nucleic-acid-based therapeutics have recently demonstrated their potential thanks to the successful COVID-19 vaccination campaign. They have been already approved or in the latest stages of clinical trials as remedies for a broad range of pathologies, including cancer and genetic diseases. These approaches make use of complex delivery vehicles to take the nucleic acids to the target tissues. The presently used lipid-based nanoparticles still face a relatively low delivery rate and side effects. Polyplexes, formed by the aggregation of cationic polymers with the anionic nucleic acids, may provide a valid alternative. The transfection mechanism for these polyplexes is an ongoing topic of research. We use coarse grained molecular dynamics simulations to investigate contributing factors to the endosomal escape process which

is a crucial limiting step in the transfection process. Our simulations model an endosome containing a polyplex, evaluating key factors such as the surface tension of the endosome caused by osmotic swelling and the interactions between the polyplex and the endosomal membrane, which are key factors in the predominant theories.

BP 19.7 Wed 11:00 H46

Modeling endosomal membrane budding patterns — •Felix Frey and Andela Saric — Institute of Science and Technology Austria, Klosterneuburg, Austria

Lipid membranes define cells and structure their interior. Endosomes, which are organelles that host molecular cargo sorting processes, are enclosed by flexible membranes from which small vesicles continuously pinch off. The reshaping of the endosomal membrane is mediated by filamentous proteins of the ESCRT-III family. Strikingly, in endosomes of flowering plant cells, arrays of concatenated membrane vesicles can form, which are connected either in parallel or in series with the membrane base. Here we combine coarse-grained molecular dynamics simulations and continuum theory with electron tomography to study the budding patterns at plant endosomal membranes [1]. We find that changes in ESCRT-III filament properties, such as curvature and membrane binding energy, determine the formation pathways and shapes of the emerging vesicle networks.

[1] E. Weiner*, E. Berryman*, F. Frey*, A. González Solís* et al., Proc. Natl. Acad. Sci. U.S.A. 121.44 (2024): e2409407121. *Equal contributions.

15 min. break

Invited Talk BP 19.8 Wed 11:30 H46

Rolling vesicles: From confined rotational flows to surface-enabled motion — •Laura R. Arriaga[1], Paula Magrinya[1], Pablo Palacios[1], Pablo Llombart[1], Rafael Delgado-Buscalioni[1], Alfredo Alexander-Katz[2], and Juan L. Aragones[1] — [1]Department of Theoretical Condensed Matter Physics, Condensed Matter Physics Center (IFIMAC) and Instituto Nicolás Cabrera, Universidad Autonoma de Madrid, 28049, Madrid, Spain — [2]Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

Friction forces are essential for cell movement, yet they also trigger numerous active cellular responses, complicating their measurement in vivo. In this talk, we will introduce a synthetic model designed to measure friction forces between biomimetic membranes and substrates. The model consists of a vesicle with precisely controlled properties, fabricated via microfluidics, encapsulating a single ferromagnetic particle that is magnetically driven to rotate. The rotation of the particle generates a confined rotational flow, setting the vesicle membrane into motion. By adjusting the magnetic field frequency and vesicle size, the rotation frequency of the vesicle can be finely controlled, resulting in a rolling vesicle that functions as an effective tribological tool. At low frequencies, molecular contact between the membrane and substrate dominates frictional interactions, providing a measurement of the contact friction coefficient. Adjusting membrane fluidity within this model will enable the study of frictional processes in more complex biomimetic systems.

BP 19.9 Wed 12:00 H46

Dynamics of a microswimmer near a deformable boundary — •Sagnik Garai, Ursy Makanga, Akhil Varma, and Christina Kurzthaler — Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Straße 38, 01187 Dresden, Germany

We study the hydrodynamic interactions of swimming microorganisms with nearby deformable boundaries omnipresent in their natural habitats. The boundary, characterized by its surface tension and bending rigidity, is deformed by the disturbance flow produced by the microswimmer and thereby modifies its swimming velocities. Describing the far-field flow of the agent as a combination of a force and torque dipole, we compute small deformations of the boundary. We further use the Lorentz reciprocal theorem to obtain leading-order corrections of its swimming velocities and compute a phase diagram based on the swimmer's initial orientation and the material properties of the deformable boundary. Our results reveal that pushers can both re-orient away from the boundary, leading to overall hydroelastic repulsion, or hover near the boundary, while pullers exhibit enhanced attraction. These findings demonstrate that the complex elasto-hydrodynamic interactions can generate behaviors that are fundamentally different to swimming near planar walls.

BP 19.10 Wed 12:15 H46

Uptake of microgels by membrane wrapping — •Tanwi Debnath[1], Jiarul Midya[1,2], Thorsten Auth[1], and Gerhard Gompper[1] — [1]Theoretical Physics of Living Matter, Institute for Advanced Simulation, Forschungszentrum Jülich, 52425 Jülich, Germany — [2]School of Basic Sciences, IIT Bhubaneswar, 752050, India

The interaction of nano- and microcarriers with lipid-bilayer membranes plays a key role for cellular engulfment and drug delivery [1]. The physico-chemical parameters of the particles that control engulfment are their size, shape, and deformability [2]. Microgels are particularly versatile because their elasticity can be tuned in a wide range by changing the density of crosslinkers. Using a mass-spring model for the microgel and a continuum model for the membrane, we study microgel wrapping at lipid-bilayers. We use the Hertz theory to characterize the microgel's Young's modulus and Poisson's ratio. With the help of triangulated membranes and energy minimization, we determine the interplay of microgel and membrane deformation. We predict wrapping diagrams for microgels with various Young's moduli at membranes with various tensions. A higher microgel deformability increases the stability of partial-wrapped states; there is a transition from oblate at low wrapping fractions to cup-like shape at high wrapping fractions. Our results on this tunable and responsive system will allow the design of the microgels with optimal elastic properties for biomedical applications. [1] S. Dasgupta et al., J. Phys. Condens. Matter **29**, 373003 (2017). [2] J. Midya et al., ACS Nano **17**, 1935 (2023).

BP 19.11 Wed 12:30 H46

Shaping Cellular Interfaces — •Susanne Liese[1], Xueping Zhao[2], Tiemei Lu[3], Marcel Mokbel[4], Sebastian Aland[4], Evan Spruijt[3], Frank Jülicher[5], and Christoph Weber[1] — [1]Universität Augsburg — [2]University of Nottingham Ningbo China — [3]Radboud University, Nijmegen — [4]TU Freiberg — [5]Max Planck Institute for the Physics of Complex Systems

The interaction between liquid droplet-like coacervates and biological membranes is central to cellular organization and drives essential processes including endocytosis, intracellular transport, and signaling. In our research, we uncover the complex dynamics underlying these interactions, demonstrating how non-equilibrium processes, chemical activity, and mechanical deformations dictate the behavior of droplet-membrane systems. We demonstrate that non-equilibrium binding of biomolecular condensates to membranes gives rise to rich physical phenomena, and we also reveal how membrane reshaping contributes to behaviors such as anomalous wetting and deformation-driven uptake. By integrating experiments, theoretical models, and computational simulations, our work provides new insights into the mesoscale physics of cellular systems and reveals the intricate interplay of chemical and mechanical forces at the droplet-membrane interface. This understanding advances both fundamental biology and potential applications in synthetic biology and intracellular delivery.

BP 19.12 Wed 12:45 H46

Biomolecular condensates wetting membranes - dynamical insights from numerical simulations — •Sebastian Aland — HTW Dresden — TU Freiberg

Biological cells use membranes and condensates (liquid-like droplets) to compartmentalize their interior. As every structure within a cell is either enclosed by a membrane or by a liquid interface it is fundamental to understand what happens if these two come into contact. Recent studies suggest that membrane-droplet interactions are involved in various key biological processes. As experimental image resolution is limited at the corresponding length and time scales, numerical methods are essential to shed light on the dynamics of the process. Using a combination of sharp and diffuse interface models, we derive a mathematical model to describe the interplay of a thin elastic membrane with a two-phase fluid. We demonstrate that the wetting interaction by capillary forces leads to a range of fascinating phenomena like droplet wrapping, endocytosis and an inverted cheerios effect.