BP 16: Membranes and Vesicles II

Time: Wednesday 9:30–12:30 Location: H 0112

BP 16.1 Wed 9:30 H 0112

Structural changes in lipid monolayers induced by synapsin and vesicles investigated by X-ray reflectivity and GID — Hendrik Bruns[1], •Titus Czajka[1], Charlotte Neuhaus[1], Christian Hoffmann[2], Dragomir Milovanovic[2], and Tim Salditt[1] — [1]Institut für Röntgenphysik, Georg-August-Universität Göttingen, Germany — [2]Laboratory of Molecular Neuroscience, DZNE, Berlin, Germany

Neurotransmitter release happens upon fusion of synaptic vesicles (SVs) carrying the neurotransmitter with the presynaptic membrane. SVs act as the trafficking organelles and are clustered in pools to facilitate the rapid release of neurotransmitters into the synaptic cleft. While the process of SV fusion mediated by SNARE complexes is well understood, the influence of the vesicle pool and its mediating protein, synapsin, on the membrane-vesicle interaction is less clear. To this end, we have carried out X-ray reflectivity (XRR) and grazing incidence diffraction (GID) experiments on lipid monolayers at controlled surface pressures in a Langmuir trough at ID10 (ESRF). Interaction between monolayer and SVs is measured in the monolayer plane by GID measurements, allowing the measurement of lipid molecule tilt angles. Density profiles modelled to fit the XRR data additionally reveal changes in the structure along the third dimension. We hypothesise that synapsin protein has a stiffening influence on the monolayer and also strengthens the interaction between monolayer and SVs, thus highlighting the importance of the protein not only to the clustering of SVs but potentially to the docking process as well.

BP 16.2 Wed 9:45 H 0112

Physics and slowerance of the erythrocyte sedimentation rate — •Alexis Darras, Thomas John, Lars Kaestner, and Christian Wagner — Saarland University, Saarbruecken, Germany

Red blood cells (or erythrocytes) sedimentation rate (ESR) is a physical parameter of blood which is often checked in medical diagnosis. It is indeed well known that in case of inflammation, the increase in fibrinogen and other proteins induces a higher ESR. A higher ESR is clinically established as a disease marker. Recently, we demonstrated that Red Blood Cells (RBCs), when left at rest and suspended at physiological volume fractions, form percolating aggregates as wide as the container. It follows that they sediment following a so-called " gel collapse", governed by the geometry of the percolating aggregate acting as a porous material. In this talk, by comparing physical models to experimental sedimentation curves, we show how this knowledge can help to quantify physically meaningful parameters that characterize the details of the collapse dynamics. Amongst others, we provide a dependency of the maximal sedimentation velocity as a function of the initial RBC volume fraction (i.e. the hematocrit), which was a long-sought correction for ESR measurements from anemic patients. We also review how those parameters make it possible to experimentally distinguish between healthy samples and some conditions where the ESR is slowed down. In particular, this opens new perspective to use the ESR as an objective marker to detect diseases where the RBCs are deformed and/or rigidified.

BP 16.3 Wed 10:00 H 0112

Origin of red blood cell slippers in confined geometries — •Berin Becic and Stephan Gekle — Biofluid Simulation and Modeling, Department of Physics, University of Bayreuth, Bayreuth, Germany.

Red blood cells flowing in confined geometries such as blood vessels or microchannels exhibit fascinatingly rich dynamics. The two main types of motion are a stationary parachute-like state and the so-called slipper state. The main characteristic of the latter is the steady rotation of its membrane. As a result the current understanding of this state relates it closely to the similarly rotating tank-treading state in pure shear flows.

Based on a numerical approach we here show that this analogy is inaccurate and that instead the slipper mode is more closely related to the tumbling mode in shear flows. In channel flow, tumbling becomes partly suppressed due to flow curvature thus creating the slipper mode. We obtain this insight by using a boundary-integral simulation technique which allows us to systematically dissect the contribution of different flow components (linear and/or parabolic in different directions) as well as the influence of the confining walls.

BP 16.4 Wed 10:15 H 0112

Molecular Origin of Plasma Membrane Heterogeneity and its Function — •Madhusmita Tripathy[1,2] and Anand Srivastava[1] — [1]Molecular Biophysics Unit, IISc Bangalore, India — [2]Department of Chemistry, TU Darmstadt, Germany

Plasma membrane(PM) heterogeneity has long been implicated in various cellular functions such as cell signaling and vesicle trafficking. However, their molecular origin and mechanistic principles governing their function are not well understood, as their nanoscopic and highly dynamic nature limit both direct experimental measurements and their interpretation. Toward this, we employ computer simulation to study model membranes with coexisting liquid ordered (Lo) and liquid disordered (Ld) phases. We characterize membrane heterogeneity using a non-affine deformation framework [1] and probe the three-dimensional lipid packing defects [2], both of which can be considered as conjugates. In doing so, we formalize the seemingly trivial connection between membrane packing and local membrane order. We use this connection to explore the mechanistic principles behind preferential localization of proteins in mixed phase membranes and membrane permeability of small molecules. Our observations suggest that heterogeneity in liquid membranes follow some generic features, where functions may arise based on packing-related basic design principles [3].

[1] S. Iyer, M. Tripathy and A. Srivastava *Biophys. J.***(2018)** 115, 117
[2] M. Tripathy, S. Thangamani and A. Srivastava *J. Chem. Theory Comput.***(2020)** 16, 12, 7800
[3] M. Tripathy and A. Srivastava *Biophys. J.***(2023)** 122, 13, 2727

BP 16.5 Wed 10:30 H 0112

Mesoscopic modeling for protein-membrane interplay with realistic kinetics — •Mohsen Sadeghi — Freie Universität Berlin

Biomembranes achieve their multitude of functions in an organized and collaborative interplay with membrane-associated proteins. Quantitative analysis of the dynamics of membranes interacting with a population of proteins in a consistent model that incorporates kinetics as well as protein structural information and flexibility is essential in fully describing these processes. Achieving this paves the way for understanding and potentially manipulating complex vital pathways. Here, we present our dynamic framework for modeling membranes and proteins [1, 2], which includes our novel approach to hydrodynamic coupling [3]. We present results on the dynamics of membrane-bound toxins [4,5,6], and the first computational model of the whole human cytomegalovirus particle, highlighting the organization of proteins in the viral tegument [7]. We make the case for how large-scale mesoscopic simulations offer unprecedented insight into the complex cellular dynamics, and provide access to spatiotemporal scales relevant to cell biology.

[1]. Sadeghi & Noé, Nat. Commun. (2020) 11:2951. [2]. Sadeghi, Weikl & Noé, J. Chem. Phys. (2018) 148:044901. [3]. Sadeghi & Noé, J. Chem. Phys. (2021) 155:114108. [4]. Sadeghi & Noé, J. Phys. Chem. Lett. (2021) 12:10497-10504. [5]. Sadeghi, Soft Matter (2022) 18:3917-3927. [6]. Sadeghi, bioRxiv (2023) 2022.11.09.515891. [7]. Bogdanow, et al. Nat. Microbiol. (2023) 8:1732.

15 min. break

BP 16.6 Wed 11:00 H 0112

Dense membrane packings: Predicting optimal configurations — •Stefanie Heyden[1] and Michael Ortiz[2] — [1]ETH Zurich, 8093 Zurich, Switzerland — [2]Caltech, Pasadena CA 91125, USA

In which way does a membrane fold to minimize its elastic energy? This question is directly tied to a better understanding of membrane packings encountered in nature, as well as facilitating the design of soft structures.

Here, we present a simple mathematical framework to predict optimal packing configurations of densely packed membranes. Membranes are represented by means of a director field and the corresponding boundary value problem is derived. Numerical solutions show foliations comprising many closed surfaces, based on which a distribution of cuts is introduced to minimize the total crease energy.

BP 16.7 Wed 11:15 H 0112

Coarse-grained Simulations of Fibril Formation on Local Structures of Two-Component Membranes — •Paul Louis Sonek and Friederike Schmid — Johannes Gutenberg University, Mainz, Germany

The cell membrane is one of the most essential parts of the cell. It consists of different components, such as phospholipids and cholesterol, forming local membrane domain structures. It has been hypothesized that many neurodegenerative diseases like Alzheimer's, Huntington's, and Parkinson's might be associated with a disturbance of the cell membrane induced by fibril formation of peptides.

In our research, we use generic coarse-grained lipid and peptide models to inspect the fibril formation near the local domain structures of our model membrane. The fibrils form primarily on top of the membrane for configurations with low amounts of our model cholesterol. However, we can observe that fibrils partly nucleate into the membrane for configurations with large amounts of cholesterol, seemingly forming an aggregate that disrupts the membrane structure. This observation correlates with the fact that membranes in the brain have larger amounts of cholesterol.

Our results may shed light on possible mechanisms responsible for the toxic effects of amyloids.

BP 16.8 Wed 11:30 H 0112

Quantification of mRNA and siRNA content of Lipid Nanoparticles — •Bernhard Kirchmair[1], Judith Müller[1], Thomas Kellerer[2], and Joachim Rädler[1] — [1]Ludwig-Maximilians-Universität München — [2]Hochschule München

Lipid Nanoparticles (LNPs) have been proven to be promising vectors to deliver mRNA to mammalian cells. Advanced strategies using multi-component nucleic acid motifs require a reliable quantification of the stoichiometric ratios. This project seeks to quantify the mRNA-content when varying the LNP size and surface composition. Employing Fluorescence Correlation Spectroscopy (FCS) measurements, assisted by Dynamic Light Scattering (DLS), both size and concentration of LNPs in solution can be estimated, allowing to obtain the average number of mRNA strands per particle. Based on this, using Fluorescence Cross Correlation, the stoichiometric ratio of short interfering RNA (siRNA) and mRNA, both fluorescently labeled, will be determined. Controlled co-formulation of siRNA and mRNA is expected to allow for regulated mRNA expression.

BP 16.9 Wed 11:45 H 0112

Interplay of phospholipids and saponins - why the application of complementary techniques is important — •Carina Dargel[1,2], Friederike Gräbitz-Bräuer[2], Lionel Porcar[3], 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]Institut Laue-Langevin (ILL), Grenoble, France

Scattering methods are a common tool to analyze structural changes in systems comprising, e.g., phospholipids mixed with natural surfactants such as saponins. Small-angle X-ray and neutron scattering (SAXS and SANS) have been extensively used to study the interaction of the saponins glycyrrhizin and aescin with the phospholipid 1,2-dioleoyl-*sn*-glycero-3-phosphoglycerol (DOPG), which carries a negatively charged head group. While for a small unilamellar vesicle (SUV) system prepared from the zwitterionic lipid 1,2-dimyristoyl-*sn*-glycero-3-phosphocholine (DMPC), membrane solubilization and thus bicelle formation was observed upon saponin addition[1], hardly any interaction could be detected for the DOPG-saponin mixtures[2,3]. Instead, DOPG SUVs coexist with saponin micelles/monomers. The investigated system clearly demonstrates the importance of using complementary techniques such as SAXS and SANS to avoid misleading conclusions from only a single method.

[1] Geisler *et al.* (2019), *Molecules*, 25(1), 117.; [2] Dargel *et al.* (2021), *Molecules*, 26(16), 4959; [3] Gräbitz-Bräuer & Dargel *et al.* (2023), *Colloid and Polymer Science*, 1-14

BP 16.10 Wed 12:00 H 0112

Application of Homogenization Techniques to Gas-Phase Deposited DPPC Films on Silicon Substrates: Unveiling Phase Transitions in Dry Environments of DPPC Bilayers — •Nicolás Moraga[1], Daniel Saavedra[1], Nancy Gomez-Vierling[1], Marcelo A. Cisternas[2], María José José Retamal[3], and Ulrich G. Volkmann[1] — [1]Instituto de Física, Pontificia Universidad Católica de Chile, Santiago, Chile — [2]Escuela de Ingeniería Industrial, Universidad de Valparaíso, Chile — [3]Facultad de Ingeniería, Universidad Finis Terrae, Santiago, Chile

The study investigates homogenization techniques for dipalmitoylphosphatidylcholine (DPPC) phospholipid bilayers deposited on single crystal silicon substrates through vapor phase deposition. Initial deposition employed physical vapor deposition (PVD) with controlled thickness and rate. Subsequent annealing, conducted in varied environments (in air and dry N2 at STP, vacuum), and temperature ramps in a dry N2 atmosphere (different pressures up to 1000 Torr) were explored as homogenization methods. The research emphasizes the critical role of precise and reproducible deposition rates during annealing in achieving homogeneity in DPPC bilayers. Different annealing conditions led to diverse effects on homogeneity, indicating distinct outcomes in air, nitrogen environments at different pressures, and high vacuum. The study revealed not only topographical changes but also documented phase transitions, suggesting the formation of lipid bilayers even in dry environments without the need for hydration. Acknowledgements: ANID Fellowships (NM, DS, NGV).

BP 16.11 Wed 12:15 H 0112

RNA adsorption dynamics onto membrane models for lipid nanoparticles — •Horacio V. Guzman — Departamento de Física Teórica de la Materia Condensada, Universidad Autónoma de Madrid, E-28049 Madrid, Spain

RNA is a functionally rich molecule with multilevel, hierarchical structures and complex dynamics in the presence of different substrates. Much remains to be elucidated in terms of the RNA conformations and specific molecular interactions that modulate its adsorption to lipid membranes. Lipid nanoparticles (LNPs) are particularly promising as mRNA delivery medium due to their remarkable ability to transport genetic material to targeted cells. Yet, the design of LNPs remains challenging, owing to poorly understood mechanisms and factors that modulate RNA and LNP adsorption to membranous substrates. In our study, we perform an exhaustive modeling exploration of the influence of membrane composition on the adsorption behavior and conformation of an RNA fragment. Our approach is based on all-atom molecular simulations, including five distinct membrane models with lipid composition selected from commercially available LNPs. The membrane models account for crucial variables, such as surface charge, topological features, unsaturation degree of the fatty acid tails, and cholesterol content. Our results elucidate RNA adsorption modes and associated membrane response. We characterize adsorption dynamics in light of structural analysis for RNA, reorganization of membrane surface charge, as well as changes in the hydrophilic/hydrophobic interactions, which bear profound implications for enhancing their stability.