BP 4: Membranes and vesicles II (joint session BP/CPP)

Time: Monday 15:00–16:15 Location: H10

BP 4.1 Mon 15:00 H10

Screening of small molecules with bilayer-modifying properties using coarse-grained simulations — •Alessia Centi, Kurt Kremer, and Tristan Bereau — Max Planck Institute for Polymer Research, Mainz, Germany

Small molecules, including alcohols and anesthetics, can alter the lateral organization of plasma membranes by preferentially partitioning between domains, thereby affecting lipid bilayer properties and stability. Although lipid segregation is key to many biological processes, precise understanding of the physical and chemical properties governing membrane phase behaviour is still lacking. Gaining more fundamental insight into the underlying mechanism is pivotal for developing enhanced drugs that can act through targeted domain phase separation.

In this work, we employ coarse-grained simulations based on the MARTINI force field [1] as a screening tool to identify compounds which can affect phase separation in model membranes. Hence, our approach based on a combination of molecular dynamics simulations and potential of mean force calculations, provides a rapid and affordable platform for gaining a better understanding of the driving forces of lipid domain stabilisation/destabilisation.

[1] S. J. Marrink, et al. Journal of Physical Chemistry vol. 111 p. 7812-7824, 2007.

BP 4.2 Mon 15:15 H10

Drug-membrane permeability across chemical space — •Roberto Menichetti, Kiran H. Kanekal, and Tristan Bereau — Max Planck Institute for Polymer Research, Mainz, Germany

Unraveling the link between the chemical structure of a small drug-like molecule and its rate of passive permeation across a lipid membrane is of fundamental importance for pharmaceutical application. However, the elucidation of a structure-permeability relationship in terms of few molecular descriptors has been so far hampered by the overwhelming number of possible compounds. In this work, we reduce a priori the size of chemical space by relying on physics-based coarse-grained models, and perform high-throughput coarse-grained simulations (HTCG) to cover a subset of chemical space both efficiently and broadly. This comprehensive exploration allows us to derive a smooth surface relating the permeability of a compound to two simple molecular properties—the bulk partitioning free energy and acid dissociation constant. By projecting HTCG predictions back to atomistic resolution, we provide an estimate of the permeability coefficient for more than 500,000 small molecules in the range $30-160$ Da. Our large scale analysis establishes a clear connection between specific functional groups and the resulting permeability, enabling for the first time inverse molecular design. This study further highlights that favoring the incorporation of certain groups will reduce the range of accessible permeabilities, thus affecting bioavailability.

[1] R. Menichetti, K. H. Kanekal, and T. Bereau, arXiv preprint arXiv:1805.10158 (2018).

BP 4.3 Mon 15:30 H10

X-Ray Reflectivity Investigation of Structure and Kinetics of Photoswitchable Lipid Monolayers — •Jonas Erik Warias[1], Svenja Carolin Hövelmann[1], Franziska Reise[2], Andrea Sartori[1], Rajendra Prasad Giri[1], Chen Shen[3], Thisbe Lindhorst[2], Olaf Magnus Magnussen[1], and Bridget Mary Murphy[1,4] — [1]Institut für Experimentelle und Angewandte Physik, University of Kiel, Germany — [2]Otto Diels-Institut für Organische Chemie, University of Kiel, Germany — [3]Deutsches Elektronen Synchrotron, Hamburg, Germany — [4]Ruprecht Heansel Laboratory, University of Kiel, Germany

The mechanical and dynamic properties of phospholipid membranes are of importance for biological functions, such as switching of embedded proteins and cell transportation. In order to investigate these properties we study model systems in which amphiphilic photoswitchable molecules are integrated into Langmuir films of phospholipids. We have modified glycolipids to contain an azobenzene photoswitch between the chain and the head group and successfully embedded those in a monolayer of dipalmitoylphosphatidylcholine (DPPC). This allows us to reversibly change the azobenzene-glycolipid orientation between trans- and cis-conformation by illumination with UV and blue light. We have followed the structural changes in this model membrane and the switching kinetics of the system with Langmuir isotherms and in situ X-ray reflectivity at the LISA diffractometer P08, PETRA III. Strong changes in membrane conformation upon switching have been observed and an additional phase transition has been discovered.

BP 4.4 Mon 15:45 H10

On the propagation of acoustic waves along the membrane based on the thermodynamic state of the interface — •Kevin Kang and Matthias Schneider — Technische Universität Dortmund

Biological membranes form hydrated, quasi-2D elastic interfaces, and it has been proposed that acoustic waves propagating along the membrane play a fundamental role in biological communication. Here we investigate whether thermodynamic principles can be applied on interfaces to study mechanical signaling along membranes. Using fluorescent probes embedded on an lipid monolayer assembled at the air-water interface, we excite the monolayer and measure the acoustic waves propagating along the membrane using FRET. We find that stimulation near the phase transition region of the state diagram (liquid-expanded/liquid condensed) can generate all-or-none type pulse, and the threshold behavior and the pulse shape show similarity with the nervous impulse. Altering the environment (pH, Ca2+, temperature, etc.) changes the material properties of the membrane (e.g. lateral compressibility), and the observed pulse characteristics (velocity, amplitude, period, etc.) generally agree with those expected from the compressibility profile. Furthermore, these characteristics also appear consistent with pulses seen in various excitable systems (squid axons, algae, etc.) under varying environmental conditions (e.g. increase in conduction velocity with increase in temperature). These results altogether show that the signaling properties along the interface can be derived from its state diagram and the thermodynamic properties, and they support a physical basis of communication in living systems.

BP 4.5 Mon 16:00 H10

Stochastic dynamics of nanoparticle and virus uptake — •Felix Frey, Falko Ziebert und Ulrich Schwarz — Institute for Theoretical Physics and BioQuant-Center, Heidelberg University, Germany

Biological cells constantly transport material and information across their plasma membrane. In particular cells routinely take up particles of diverse shapes and sizes between 10-300 nm, especially viruses, which often come in either spherical or cylindrical shapes. In general, particle uptake requires that the gain in adhesion energy overcomes the cost of plasma membrane bending. We first show by using a simple deterministic model that cylindrical particles are taken up faster than spherical particles for the same radius and volume. We then investigate stochastic effects, which might be relevant because of the small system size. We find that now spherical particles can be taken up faster because the mean first passage time is affected by multiplicative noise for the sphere rather than additive noise as in the case of the cylinder. Our findings suggest that stochasticity is equally important as geometry during particle uptake.