BP 16: Biological Membranes I

Time: Tuesday 10:15–13:00 Location: ZEU 260

Invited Talk BP 16.1 Tue 10:15 ZEU 260

The dynamic organization in the membrane of a G-protein-coupled receptor is related to its functional state — •Laurence Salomé — IPBS, Toulouse, France

The analysis of membrane diffusion is the most promising approach to investigate the compartmentalization of G-protein-coupled receptors, particularly as relevant to receptor signalling processes. We developed two complementary techniques: the fluorescence recovery after photobleaching (FRAP) performed at variable spot radius and the single particle tracking (SPT). We report the results of our study of a G-protein-coupled receptor involved in pain treatment, the human muopioid receptor (hMOR), using these techniques. We will survey the effects of the presence of distinct agonist ligands, antagonist ligand or the activation of other receptors on the diffusional behaviour of the receptor. Our observations suggest that the functional state of a receptor is correlated to its dynamic organisation in the plasma membrane.

BP 16.2 Tue 10:45 ZEU 260

Dynamic structure formation of membrane proteins — •Gernot Guigas[1], Diana Morozova[2], and Matthias Weiss[1] — [1]Experimental Physics I, University of Bayreuth — [2]Cellular Biophysics Group, German Cancer Research Center, Heidelberg

Cellular membranes are not mere passive envelopes but act as a reaction space for a multitude of vital cellular processes. While it is generally anticipated that biomembranes are highly dynamic and self-organizing entities, molecular mechanisms that underlie structure formation on lipid bilayers are still far from being fully understood. Here, we show by means of coarse-grained membrane simulations that proteins can form higher-order structures due to membrane-mediated interactions. Structure formation originates from characteristic protein-induced bilayer perturbations that particularly affect the coupling between membrane leaflets. Examining transmembrane proteins as well as peripheral membrane proteins, we observe the formation of protein oligomers and templates, even between proteins residing in different membrane leaflets. Also raft-like cross-leaflet associations of proteins and lipid patches are observed. Key parameter of this structure formation is the protein geometry. Apart from their potential influence on the organization of biomembranes, these effects may also support the formation of templates for signaling processes, the assembly of transport intermediates, or protein sorting events.

BP 16.3 Tue 11:00 ZEU 260

Spatio-temporal modeling of MARCKS protein binding at biological membranes — •Sergio Alonso and Markus Bär — Physikalisch-Technische Bundesanstalt

Proteins inside the cell strongly interact with biological membranes. Depending on the lipid composition of the membrane and the interaction with other proteins, they can spontaneously bind by an electrostatic interaction with acidic phospholipids. We consider a simple model of membrane organization into domains based on a cyclic binding and unbinding of the unfolded MARCKS protein at membranes composed by acidic lipids known as myristo-electrostatic (ME) switch. The function of such proteins is the protection of the phospholipids from hydrolysis by enzymes. Membrane-bound MARCKS may be phosphorylated by Protein kinase C (PKC), which produces the unbinding of the protein. This process is activated by Calcium. Finally, phosphatases dephosphorylate the MARCKS proteins in the cytoplasm, which may bind again at the membrane.

The model describes the formation of membrane domains under nonequilibrium conditions, because the ME switch consumes ATP and leads to non-vanishing currents of proteins. Two main mechanisms of domain formation are obtained: a long-wave instability and a mechanisms based on the bistability of two spatially homogeneous steady-states.

Finally, we compare the predictions of our model with experiments in living cells obtained from the literature and with experimental measurements obtained in vitro.

BP 16.4 Tue 11:15 ZEU 260

Bending and breaking the influenza lipid envelope — •Sai Li[1], Frederic Eghiaian[1], Christian Sieben[2], Andreas Herrmann[2], and Iwan Schaap[1] — [1]Drittes Physikalishes Institut, Georg-August-Universität Göttingen, Germany — [2]Division of Molecular Biophysics, Humboldt-Universität zu Berlin, Germany

Lysosomes, enveloped viruses, synaptic and secretory vesicles are all examples of natural nano-containers (diameter ~100 nm) which specifically rely on their lipid bilayer to protect and exchange their contents with the cell. We have used Atomic Force Microscopy (AFM) and Finite Element Modeling to investigate the mechanical properties of the influenza virus lipid envelope. The mechanical properties of small, spherical vesicles made out of PR8 influenza lipids were probed by an AFM tip applying forces up to 0.2 nN, which led to an elastic deformation up to 20% on average. We found that influenza liposomes were much softer than what would be expected for a gel phase bilayer and highly deformable. We observed that the stiffness of the influenza envelope increased weakly (within one order of magnitude) with temperature, which is consistent with previous suggestion that influenza lipids do not undergo a major phase transition. Influenza liposomes were in most cases able to withstand wall-to-wall deformation, and forces over 1 nN were generally required to rupture the influenza envelope. In contrast to other viruses that pack their contents in stiff protein shells, the influenza virus seems to rely mainly on its highly flexible lipid envelope to protect its genome.

15 min. break

BP 16.5 Tue 11:45 ZEU 260

Structure Formation in Membranes with Quenched Protein Obstacles — •Timo Fischer and Richard Vink — Institut für Theoretische Physik, Georg-August-Universität Göttingen, Friedrich-Hund-Platz 1, 37077 Göttingen

There is growing consensus that membrane lateral structure is heterogeneous, and characterized by micro-domains of different size and compositions. From equilibrium thermodynamics, the formation of micro-domains could be explained by critical fluctuations near a critical point of a demixing transition. Away from the critical point, one would either have a homogeneous mixture or a macroscopic demixing of the membrane components. Such a phase transition is indeed seen in model membranes, and was shown to belong to the Ising universality class. In the membranes of living cells, however, no macroscopic demixing is seen.

Using Monte-Carlo simulations of a simple model of a two-component membrane we investigate how randomly-distributed static obstacles, such as trans-membrane proteins coupling to the inner structure of the cell, influence the fate of the demixing transition. Our findings are compatible with a change in universality from Ising to random-field Ising (RFIM) [1]. This change in universality class elegantly accounts for the non-observation of macroscopic demixing in living cells, since the RFIM does not phase separate in two dimensions. Instead, we find equilibrium micro-structures, which suit well to the expected heterogeneous structure of the membrane.

[1] T. Fischer, RLC Vink, arXiv:1011.0538v1

BP 16.6 Tue 12:00 ZEU 260

Atomistic Simulations of Hydration Forces between Biological Surfaces — •Emanuel Schneck, Felix Sedlmeier, and Roland Netz — Technical University of Munich

Biological surfaces interact via a complex interplay of various forces, some of which still elude a quantitative theoretical description. For instance, the experimentally observed repulsion between hydrophilic surfaces at short distances, known as hydration repulsion, is not yet fully understood, despite its crucial role in controlling the equilibrium distance between biomembranes. In this study we use atomistic molecular dynamics simulations to quantify the water-mediated repulsion between extended hydrophilic surfaces as a function of their distance. By using a novel method, based on the determination of the pressure-dependent chemical potential of water between the surfaces, we obtain pressure-distance relationships with very high accuracy. For rigid surfaces we find oscillations in the repulsion strength, originating from the discrete nature of water molecules. For soft surfaces we find a monotonic increase in the repulsion strength with decreasing water layer thickness. The latter case resembles the interaction of soft, hydrophilic biomembrane surfaces. Here, our results show quantitative agreement with experiments over the whole data range.

BP 16.7 Tue 12:15 ZEU 260

Molecular Dynamics simulations of phase separation of ternary lipid-cholesterol structure — •Davit Hakobyan and Andreas Heuer — WWU Münster, Institut für Physikalische Chemie, Corrensstraße 30, 48149 Münster, Germany

This project is supported by SFB 858

The separation of liquid-ordered and liquid-disordered phases of lipids in membranes is a subject of continued experimental and theoretical investigations. Yet, the driving force of phase separation is still to be understood. Comparison of energetic and entropic components between cholesterol-saturated lipid and cholesterol-unsaturated lipid complexes [1] indicates that phase separation is the consequence of a cooperative effect of lipids and cholesterols interactions. Here we present the results of coarse-grained (CG) simulations using MARTINI potential [2] for binary dipalmitoyl phosphatidylcholine (DPPC) /dilinoleyl phosphatidylcholine (DUPC) and ternary DPPC/DUPC/CHOL systems. Investigation of temporal evolution of order parameters as a function of nearest-neighbors shows rather clear distinction between systems with and without CHOL. For the former case the order parameter for the saturated DPPC is differentiated among nearest neighbors while for the latter case it is not, which might be thought of as a distinctive property of phase separated and mixed systems. The numerical analysis is complemented by studying a more detailed united atom model of the same system.

[1] Z. Zhang, et al., J. Phys. Chem. B, 111, 12888-12897, 2007.
[2] S.J. Marrink, et al., J. Phys. Chem. B, 111, 7812-7824, 2007.

BP 16.8 Tue 12:30 ZEU 260

Calculating Partition Coefficients From Atomistic Computer Simulations — •Axel Arnold[1], Thorsten Köddermann[2], and Dirk Reith[2] — [1]ICP, Universität Stuttgart, Germany — [2]Fraunhofer SCAI, St. Augustin, Germany

The partition coefficient (log POW) of a substance measures its solubility in octanol compared to water. This can be seen as a simple model for its solubility in biological membranes, which is a rough estimate for toxicity. If a substance is hardly soluble in octanol, it is practically impossible for it to enter (human) cells, and therefore it is less likely to be toxic. On the other hand, for novel drugs it might be important to penetrate the cell through the membrane, or even integrate into it.

Being able to determine the log POW *a priori* from computer simulations would therefore be an important step towards virtual drug design. Up to now, heuristic approaches based on functional groups are mostly used to estimate the log POW, and only there were only a few computer simulations studies trying to calculate the partition coefficient *ab initio*.

We present a method to reliably calculate log POW values from atomistic computer simulations. It is based on the calculation of solvation free energies using thermodynamic integration. First results demonstrate that this generic approach is able to predict log POW values for alcohols better than the classical heuristic methods.

BP 16.9 Tue 12:45 ZEU 260

The pico- to nanoscond dynamics in phospholipid bi- and monolayers — •Sebastian Busch[1] and Tobias Unruh[2] — [1]Technische Universität München, Forschungs-Neutronenquelle Heinz Maier-Leibnitz (FRM II) and Physik Department E13, 85748 Garching bei München, Germany — [2]Friedrich-Alexander-Universität Erlangen-Nürnberg, Lehrstuhl für Kristallographie und Strukturphysik, 91058 Erlangen, Germany

The dynamics of phospholipid molecules on the pico- to nanosecond time scale was studied with incoherent quasielastic neutron scattering.

Looking at stacks of bilayers [1], it was found that the observed motions of the molecules agree very nicely with preceding MD simulations [2]. The effect of several additives (except cholesterol) was negligible on this time scale [3].

In this contribution, we will concentrate on the evolution of the dynamics of the phospholipid molecules when going from stacks of bilayers to single bilayers (vesicles) and monolayers (as a stabilizing layer on oil-in-water dispersions).

[1] S. Busch et al., JACS 132(10):3232, 2010
[2] E. Falck et al., JACS 130(1):44, 2008
[3] S. Busch et al., BBA Biomembranes, in print, doi:10.1016/j.bbamem.2010.10.012