Posters

– 23. Biomimetic structures and systems –

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Superstructure-dependent non-intercalative drug binding to DNA origami nanostructures

F. Kollmann[1], S. Ramakrishnan[1], M. A. Kostiainen[2], G. Grundmeier[1], V. Linko[2], A. Keller[1]

[1]Technical and Macromolecular Chemistry, Paderborn University, Paderborn, Germany; [2]Biohybrid Materials, Department of Bioproducts and Biosystems, Aalto University, Aalto, Finland

DNA origami nanostructures are widely investigated with regard to their applicability in fields as diverse as nanoelectronics, molecular sensing, and drug delivery. For the latter application, drug loading of the DNA origami delivery systems is typically achieved via intercalation between the base pairs of the DNA double helices. By employing DNA origami nanostructures with deliberately underwound double helices, intercalator loading can be tuned.

Here, we investigate the binding of the drug methylene blue (MB) to different 2D and 3D DNA origami nanostructures. MB has been used extensively as a therapeutic agent to treat numerous diseases, including malaria and methemoglobinemia, and is currently investigated as a potential photosensitizer for photodynamic therapy. Furthermore, MB may interact with DNA via intercalation, groove binding, and electrostatic interactions. Using UV-Vis spectroscopy, we observe non-intercalative binding of MB to the DNA origami, with the measured dissociation constants depending on DNA origami superstructure. Our results may contribute to the design of DNA origami-based drug carriers with tailored loading and release properties.

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The interaction between amyloid-β peptides and model membranes containing cholesterol and melatonin

T. Kondela[1], B. Demé[2], N. Kučerka[1,3]

[1]Faculty of Pharmacy, Comenius University in Bratislava, Slovakia; [2]Institut Laue-Langevine, Grenoble, France; [3]Frank Laboratory of Neutron Physics, Joint Institute for Nuclear Research in Dubna, Russian Federation

Alzheimer's disease (AD) is a devastating neurodegenerative disease caused by the formation of senile plaques, primarily consisting of amyloid-beta (Ab) peptides. The crucial role in this process is imparted by peptide-membrane interactions, changing the structural properties of membrane. These changes are known to be modulated also by membrane composition. In particular, cholesterol increases the order of lipid hydrocarbon chains and increases the stiffness of membrane. On the other hand, melatonin increases the fluidity of membrane. Our previous experiments [Drolle et al., BBA 2013] revealed the counteracting effect of melatonin to that of cholesterol in neat lipid membranes. We have extended our investigations recently by including transmembrane Ab peptide in these model membranes. Small angle neutron diffraction measured at four different contrast conditions was utilized for an unambiguous determination of structure in transversal direction. The obtained bilayer structure reflected the elevated amounts of cholesterol by its thickening, while the fluidizing effect of melatonin evoked the membrane thinning. Results of our experiments possibly confirm the melatonin's potential role in preventing the development of AD.

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Biophysical characterization of lipopeptides involved in membrane fusion

A. Koukalová[1], Š. Pokorná[1], N. L. Mora[2], A. L. Boyle[2], R. Šachl[1], M. Hof[1], A. Kros[2]

[1]J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech Republic, Czech Republic; [2]Leiden Institute of Chemistry, Leiden University, Netherlands

Membrane fusion is a key process naturally occurring in cells as it facilitates e.g. delivery of chemicals across biological barriers to specific cellular locations. Intracellular fusion in vivo is triggered by a specific interaction of SNARE protein complex forming coiled-coil bundles. Designing of an efficient and specific system that might be useful for in vivo applications, e.g. direct drug delivery into cytosol, requires a good understanding of molecular mechanism behind the fusion event. The present study aims to contribute to the current knowledge by advanced fluorescent microscopic techniques. We use a reduced system in which fusion-related proteins are replaced by two complementary synthetic lipopeptides consisting of peptides K4[(KIAALKE)4] or E4[(EIAALEK)4], a PEG linker and a cholesterol anchor. Model lipid membranes are used as biophysical models of the plasma membrane. Our interest is to study the interaction of K/E peptide with lipid membranes and examine their aggregation behavior. The data show that peptide K tends to aggregate and interact with the membrane more strongly than peptide E, which might decrease the efficiency of membrane fusion. Their behavior, however, heavily depends on the membrane lipid composition.

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A comparative study on the fusion kinetics of different SNARE families

S. Krüger[1], P. Halder[2], R. Jahn[2], C. Steinem[1]

[1]Georg-August-University, Germany; [2]Max-Panck-Institute for biophysical Chemistry, Germany

Membrane fusion is a fundamental process in every living cell. For the sorting of different cargoes in the organism a highly regulated sequence of vesicle docking and merging of two bilayers is required. Therefore, different model systems have been developed to study SNARE (**s**oluable **N**SF-**a**ttachment **re**ceptor proteins)-mediated fusion focusing on the neuronal SNARE-system (Syntaxin-1a, SNAP25, VAMP-2). In recent years further SNARE families have been characterized, among them the late-endosomal SNAREs (Syntaxin-7 and 8, vti1B and VAMP-8).

To ensure fusogenity of the neuronal system, a stabilized complex (ΔN49) with a soluable fragment of the vesicle-SNARE Synaptobrevin-2 was developed. Anisotropic measurements showed that this fragment might hinder the kinetics of fusion drasticly, since the removal and the final zippering of the tetrameric complex takes around 5 sec. In contrast endosomal SNARE-proteins form a tetrameric *coiled-coil*-complex with each protein donating one SNARE-motif and one transmembrane domain to the complex.

Using bulk and single vesicle fusion assays like pore spanning membranes, we study the differences in membrane fusion within both SNARE-families. In theory, the new SNARE-family allows for different topologies as well as faster fusion kinetics.