particularly for off-target DNAs. This result unravels dynamical and structural aspects of the NTS regulation for the target-specific cleavage and thereby provides molecular insights into rational design of engineered Cas9 with improved specificity.

2507-Pos
Alpha-Synuclein Binds to DNA and Modulates its Physical Properties
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Parkinson's disease (PD) is a neurodegenerative disease that is estimated to affect 2 % of the population older than 60 years. α-synuclein (aS) is a 140-residue protein, and its assembly process into amyloid fibers is directly related to PD. Research on Parkinson's disease (PD) mostly focuses on the ability of aS to form oligomers and amyloids, and how such species promote brain cell death. However, there are indications that aS also plays a gene-regulatory role in the cell nucleus.
In this study, we investigate the interaction between monomeric aS and DNA in vitro with single molecule techniques. Using a nanofluidic channel system, we discovered that aS binds to DNA, and by studying the DNA-protein complexes in nano-channels of different size, we found that the binding of aS increased the stiffness of DNA, where the persistence length is increased by ∼30% at high coverage. In addition, using atomic force microscopy, we observed that the aS binding occurs as small protein clusters scattered along the DNA at low protein-to-DNA ratio, and the DNA is fully covered by aS at high protein-to-DNA ratio.
Recent studies have shown that DNA interactions may be a common property of proteins associated with neurodegenerative disorders such that, in addition toxic amyloid formation, these proteins may also alter expression profiles of disease-modifying genes. Single DNA molecule techniques, such as the approach in our study here, may be useful to characterize putative DNA binding of many other proteins involved in neurodegeneration.

2508-Pos
Simulation of H2A.B Containing Histone Variant Nucleosome
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The H2A.B histone is a highly evolving vertebrate specific variant of the H2A histone family. It has been implicated in increased gene expression, and experiments have shown that incorporation of H2A.B into nucleosomes results in more extended structures with fewer wrapped DNA basepairs. To study the molecular mechanisms of H2A.B, we have performed a series of conventional and enhanced sampling molecular dynamics simulation of H2A.B and canonical H2A containing nucleosomes. Results of adaptively biased molecular simulations show that, substitution of canonical H2A with H2A.B results in geometrical changes such as unwrapping of 10 to 15 basepairs of DNA on each side of the nucleosome and an increase in the diameter and radius of gyration, which is in agreement with previous AFM, FRET and SAXS experiments. In addition, ensemble fitting to experimental SAXS data, demonstrates that the histone octamer is largely intact for both H2A.B and canonical containing nucleosomes. Finally, the H3 and H2B histone tails are specifically important in robustness of the nucleosome core structure and maintaining its connection to DNA.

2509-Pos
Quantifying Anticancer Drug Doxorubicin Binding to DNA using Optical Tweezers
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Doxorubicin is a successful anticancer drug approved for use in the 1970s and is considered to be one of the most effective cancer treatment methods today. Although Doxorubicin has positive survival statistics it has very negative side effects in many cases. Bleeding from the soles of the palms and feet, along with excruciating pain is often exhibited through the administration of this drug. Based on the preliminary findings utilizing optical tweezers we anticipate that this study will provide critical information about the drug binding mechanism. Single molecule biophysics techniques have provided useful insight into the DNA-binding mechanisms of small molecules. For this reason, in this study we quantify the binding kinetics and affinity of Doxorubicin to DNA using optical tweezers. The optical tweezers allow us to trap a single DNA molecule and manipulate it in the presence of various concentrations of Doxorubicin. Preliminary results suggest that DNA melting facilitates the intercalation process in the nanomolar range, implying a higher binding strength than the previously reported micromolar range.

Posters: Membrane Physical Chemistry II

2510-Pos
Intrinsic Curvatures from Global X-Ray Scattering Data Analysis of Inverted Hexagonal Phases
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The intrinsic lipid curvature C_0 is an important parameter for the stored elastic energy strain in membranes and plays a substantial role in lipid/protein interactions. We explored a model-based approach for C_0 determination applying a full q-range small-angle X-ray scattering data analysis of inverted hexagonal phases. The technique was tested on different phosphatidylethanolamines and mixtures of dioleoyl phosphatidylethanolamine with diverse lamellar phase forming lipids, including phosphatdiylcholines of various hydrocarbon chain composition, as well as sphingomyelin. For these mixtures, we included a non-linearity term for lipid mixtures based on the effective lipid headgroup size. We discuss advantages and challenges of our approach and present results for intrinsic curvatures of lipids previously not accessible from experiment.

2511-Pos
Statistical Analysis of Acyl Chain Confinement in Lipid Membranes
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One measure of acyl chain confinement in lipid membranes is provided by order parameters that are obtained from ^{2}H NMR spectroscopy. A statistical model that uses a mean-filed approach can be used to relate the measured parameters to a torque field experienced by the various carbon segments as a function of position along the membrane normal [1]. We use Molecular Dynamics (MD) simulations to determine to what extent acyl chain conformations can be captured by mean-field approximations especially for carbon segments closer to the bilayer center where chain disorder is high. We show that the mean-field approximation holds surprisingly well and it can therefore be used to characterize the confinement (stress) field across the entire bilayer. [1] Petrache et al., Biophys. J. 2000.

2512-Pos
Parameterization of the Charmm Force Field for Ether Lipids and Model Linear Ethers
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Linear ethers such as polyethylene glycol (PEG) have extensive industrial and medical applications. Additionally, phospholipids containing an ether linkage between the glycerol backbone and hydrophobic tails are prevalent in human red blood cells and nerve tissue. This study uses *ab initio* results to revise the CHARMM additive (C36) partial-charge and dihedral parameters for linear ethers and develop parameters for the ether-linked phospholipid 1,2-di-O-hexadecyl-*sn*-glycero-3-phosphocholine (DHPC). The new force field, called C36e, more accurately represents the dihedral potential energy landscape and improves the densities and free energies of hydration of linear ethers. C36e allows more water to penetrate into a DHPC bilayer, increasing the surface area per lipid compared to simulations carried out with the original C36 parameters, and improving agreement with X-ray and neutron scattering data. Preliminary results for the densities and free energies of hydration of linear ethers in the polarizable Drude FF are presented. New Drude linear ether models are developed based on C36e and compared with the current Drude models.

2513-Pos
Protonation States and Conformations of Inositol and Phosphoinositol Phosphates from Molecular Simulations
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