3419-Pos
Spectroscopic Studies of DNA-Drug Binding Affinities: Sequence Context and Methylation Effects
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Fluorescence spectroscopy studies of 7-Aminoacridinomycin D (7-AMD) binding to doxycyclines containing the Cre binding sequence demonstrate that binding affinity is directly related to both sequence context and cytosine methylation. Importantly, sequence-dependent changes in Tm as a function of methylation are observed. 

3420-Pos
Solution Structures and Ultraviolet Raman Spectra of Purines Reveal Systematic Shifts with Change in Protonation State
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We have investigated the effect of increasing protonation state on the spectroscopic signatures of purines and pyrimidines. We show that the increase in the UV absorbance of the base is accompanied by a decrease in the spectral width of the base. The effect of protonation on the vibrational modes of the purine and pyrimidine bases has been investigated using Raman spectroscopy.

3421-Pos
Preferential Site Binding of Monovalent Cations With the Random Coil Form of DNA
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We investigated the binding of monovalent cations to the random coil form of DNA using small-angle X-ray scattering (SAXS) and Fourier transform infrared spectroscopy (FTIR). The results showed that the monovalent cations preferentially bind to the random coil form of DNA, with a preference for the phosphate backbone over the sugar-phosphate backbone.

3422-Pos
Measuring DNA Condensation Driven by Cobalt Hexammine
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We investigate the mechanism of DNA condensation mediated by trivalent cobalt hexammine (cobhex) in solution, using 3 established experimental techniques. The amount of DNA precipitated out of the solution can be calculated by directly measuring the change of the UV absorption of the supernatant. In situ DNA attraction is monitored by changes in the low angle region of small angle X-ray scattering (SAXS) profiles. Wide angle X-ray scattering (WAXS) is also applied to explore shorter length scales. Comparison with simulations reveals details of cobhex association to DNA. Our results suggest that inter DNA attraction depends on the length of the helix and the association mode of the ions.

3423-Pos
A Reversible Switch on Two-Dimensional Small Interfering RNA Condensation
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Small interfering RNAs (siRNAs) are short (19-29bp) double stranded nucleic acids that efficiently mediate gene silencing in mammalian cells by directing the degradation of complementary target mRNA sequences. This has justified the recent development of technologies for siRNA transport into a host cell. Synthetic cationic lipid (CL) assemblies can efficiently be used to deliver siRNA, leading to highly specific gene silencing [1]. The ability of CL-siRNA constructs to efficiently knockdown genes is strongly correlated with the packing of the nucleic acid molecules within the lipid bilayer. We used Synchrotron X-ray diffraction to show that CL-siRNA self-assembly may lead to the formation of distinct 2D phases. This includes condensed 2D smectic and isotropic phases with reversible transitions between them mediated by a combination of electrostatic and thermal fluctuations effects.


3424-Pos
New Degradable Cationic Lipid-DNA Complexes for Gene Delivery
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Cationic lipids (CLs) continue to attract attention as synthetic nucleic acid (NA) vectors, and are broadly used for gene transfection and silencing including applications in clinical trials. However, these complexes exhibit suboptimal gene expression due to inefficiencies in overcoming the cellular barriers to transfection (Ahmad et al., J. Gene Med. 2005, 7, 739). After entry of the CL-DNA complex into the cell, two major barriers are efficient dissociation of DNA from the complex and the cytotoxicity of CLs. To address both these issues, we have synthesized a novel series of multi-valent lipids (CMVLs) with degradable disulfide bonds linking the positively charged headgroups of the CMVLs to their hydrophobic tails. The linker is designed to be cleaved in the reducing milieu of the cytoplasm open the way for the development of efficient non toxic CL-vectors of NAs. Funding provided by NIH GM-59288.

3425-Pos
Condensation of DNA: Effect of Cationic Charge and Lithium Ions
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DNA condensation is a fundamental property that affects DNA function in vivo. In solution, DNA condensation is mediated by electrostatic interactions between the positively charged cationic lipid headgroups and the negatively charged phosphate backbone of DNA. This interaction leads to the formation of a compacted structure that facilitates gene delivery and expression.

We investigated the effect of cationic charge on DNA condensation using small-angle X-ray scattering (SAXS) and Fourier transform infrared spectroscopy (FTIR). The results showed that the cationic charge affects the degree of DNA condensation, with higher charges leading to more compacted structures. Additionally, we examined the effect of lithium ions on DNA condensation, finding that lithium ions can increase the degree of condensation.

These findings are important for optimizing cationic lipid formulations for gene delivery applications. Understanding the role of cationic charge and lithium ions in DNA condensation can help in the development of more efficient and safer gene delivery systems.