a dimer in a GC rich sequence forming a curved complex which matches to the shape of minor groove. This is an example of how a linear compound with chemical functionalities in an optimum position can form intra as well as intermolecular interactions with DNA. Our finding that TTA sequences are difficult to target, can be selectively recognized by stacked minor groove dimers opens a new way to interact with that sequence. These investigations indicate that compound design tools can be used to obtain new types of specific binding to DNA.

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1285-Pos Board B195
Solution Structure of a Novel Heterocyclic Dication Stacked as a Dimer with a Unique Mixed GC/AT Containing Motif
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The search for small-molecules that can target regulatory nucleic acid elements is an ever-growing field driven by the passion that such molecules can potentially alter gene expression and thus influence diverse cellular functions. In recent years, small-molecules preferentially binding to GC sequences have attracted the scientific community to further understand and establish DNA base-pair recognition rules. Biophysical studies from our group have shown that DB293, a phenyl-furan-benzimidazole aromatic dication, and DB1878, an indole analog, target GC containing sequences in a highly cooperative manner. Current high resolution NMR studies of the two compounds with 5'-CTATGACTCTCGTCATAG-3' hairpin sequence (binding site highlighted) have confirmed a strong cooperative dimerization of the compound at the 5'-ATGA-3' site. Strong NOE interactions between DB1878 and specific DNA protons along the minor groove indicate an anti-parallel orientation of the two molecules in the minor-groove. Very interestingly, the two DB1878 molecules recognize the ATGA sequence in what we termed as an "in-out" model, where the furan rings of the two molecules are opposite to each other. This unique stacking mode enables the furan ring of one of the molecules to recognize the guanine amino group. Mutation studies show that replacing the central GC base-pair with any other base completely altered the binding affinity, thereby suggesting the importance of that base-pair for compound recognition. Further analyses of the complex have shown that the two DB1878 molecules stack with optimal cation-pi type interactions and with favorable van der Waals interactions along the minor groove. The structure reported here is completely different from known DNA recognition, and represents an entirely new DNA recognition paradigm.

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1286-Pos Board B196
Effect of a Thymine Cyclobutane Dimer Lesion on the Stability of a DNA Oligonucleotide Duplex
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Ultraviolet irradiation from sun exposure can lead to permanent, covalent damage to DNA. In particular, adjacent pyrimidines can become fused via a [2+2] cycloaddition to form a cyclobutane pyrimidine dimer. The cis-syn thymine cyclobutane dimer lesion, hereafter called the thymine dimer, has traditionally been considered to be one of the more ‘bulky and destabilizing’ lesions. Published structures of the thymine dimer lesion reveal that the backbone around the lesion is pinched, the DNA is kinked, and the canonical Watson-Crick base pairing with the opposite adenines is disrupted through the loss of one hydrogen bond, weakening the interactions with the complementary strand. Nonetheless, other recent studies hint that the effect of the thymine dimer lesion on the double-stranded duplex may be surprisingly subtle. Using a variety of methods including UV melting, calorimetry, small reactive chemical probes, and NMR spectroscopy, we study the stability of the thymine dimer lesion in DNA oligonucleotides of varying length and sequence context. We consider the contributions of the lesion to kinetic and thermodynamic destabilization, and well as to both local and long-range effects on duplex stability.

1287-Pos Board B197
Investigation of Trinucleotide Repeat Structure in Nucleosome Core Particles
Catherine B. Volle, Sarah Delaney.
Genomic instability at trinucleotide repeat regions can lead to several well known neurological diseases. In particular, Huntington’s disease (HD) is caused by an expansion of CAG/CTG repeats in exon 1 of the huntingtin gene. It is well known that oligonucleotides composed of CAG or CTG repeats adopt hairpin structures and that CAG or CTG repeats contained in plasmids also form hairpins. It has been proposed that this type of non-canonical DNA structure formation is involved in the expansion of the HD gene. Additionally, the repair of the 8-oxo-7,8-dihydroguanine lesion seems to play a role in secondary structure formation and expansion at this locus. However, genomic DNA is packaged into chromatin and the effect of this packaging on the structure of CAG/CTG repeats, or on their potential to form non-canonical structures, remains unknown. In this work we will examine the structure of CAG/CTG repeats and the effect oxidative damage has on the repeat structure in nucleosome core particles, the most basic unit of chromatin packing.

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1288-Pos Board B198
Simulations of Viral DNA Packaging and Ejection: Geometrical Order and Topological Disorder
Davide Marenduzzo, Enzo Orlandini, Andrzej Stasiak, De Witt Summers, Luca Tibbona, Cristian Micheletti.
The packing of DNA inside bacteriophages arguably yields the simplest example of genome organisation in living organisms. Cryo-em studies showed that DNA in bacteriophages epsilon-15 and phi-29 is neatly ordered in concentric shells close to the capsid wall, while an increasing level of disorder was measured when moving away from the capsid internal surface. On the other hand the detected spectrum of knots formed by DNA that is circularised inside the P4 viral capsid showed that DNA tends to be knotted with high probability, with a knot spectrum characterized by complex knots and biased towards torsus knots and against achiral ones. Existing coarse-grained DNA models, while being capable of reproducing the salient physical aspects of free, unconstrained DNA, are not able to reproduce the experimentally observed features of packaged viral DNA.
Here we show, using stochastic simulation techniques, that both the shell ordering and the knot spectrum can be reproduced quantitatively if one accounts for the preference of contacting DNA strands to juxtapose at a small twist angle, as in cholesteric liquid crystals. The DNA knots we observe are strongly debranched and, intriguingly, this is shown not to interfere with genome ejection out of the phage.

1289-Pos Board B199
Prohead RNA Sequence Variation
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Prohead RNA (pRNA) is an essential component of the self-assembling phi29 bacteriophage DNA packaging motor. Although different species of bacteriophage share only 12% similarity in pRNA sequences, the secondary structure for prohead RNA is conserved. The NMR structure of the most conserved loop sequence, the E loop hairpin, reveals a UU pair, a U-turn, and a syn guanosine. Comparison of the pRNA E loop hairpin to ribosonal RNA hairpins and predictions from MC-SYM provides benchmarks for improving RNA structure prediction. All the different pRNA sequences self-assemble in dimers, trimers, and higher order multimers. The energetics for dimerization in different pRNA sequences are similar despite very different sequences in the loop-loop interactions. The architecture surrounding the interlocking loops contributes to the stability of the pRNA quaternary interactions, and sequence variation outside the interlocking loops may counterbalance the changes in the loop sequences. Thus, the evolutionary divergence of pRNA sequences maintains not only function and secondary structure, but also the stabilities of quaternary interactions. The self-assembly of the different pRNA sequences can be fine-tuned with variations in salt, temperature, and concentration. The ability to control pRNA self-assembly holds promise for the development of nanoparticle therapeutic applications and further biophysical studies of the structure and function of pRNA in the packaging motor.

1290-Pos Board B200
Is the Hepatitis C Virus Life Cycle Progression Mediated by Swapping Kissing RNA Partners?
Sumangala S. Shetty, Shetty, Dr. Mihaela-Rita Mihai.escu.
Hepatitis C Virus (HCV) infection is a major health problem, with an estimate of 200 million people infected worldwide. With no protective vaccine or therapy available, the need to find a conserved and functionally essential therapeutic target within the HCV genome is imperative. Genomic HCV RNA contains several highly conserved stem loop structures, serving as cis-acting regulatory elements (CREs). We recently showed that a 100% conserved and functionally vital, 55 nucleotide sequence (X55) within the 3' untranslated region of the HCV genome is involved in genomic homodimerization via kissing interactions. Interestingly the same X55 region has also been shown to be involved in essential interactions for the HCV replication, with a conserved stem loop (SBSL3.2) sequence located within the coding region of the HCV genome.