sites. We performed a 50 ns MD simulation of 1id3 yeast nucleosome and analyzed DNA motions in terms of calculated relaxation times and slopes of power law distributions for all 145 inter base pair steps. Relaxation times were found by fitting the autocorrelation functions of DNA helix parameters. Those for base pairs interacting with histone core could not be obtained due to the power law nature of dynamics at detected sites. Our results suggest that relaxation of DNA structure in the nucleosome is governed by two processess: 1) fast exponential decay (25 - 250 ps) followed by power law relaxation for base pairs that are more than 3.4 A away from the protein, and, 2) slow power law relaxation extending to 50 ns observed for base pairs interacting with histone subunit (less than 3.4 A away from protein). Proximity analysis confirms the presence of 14 histone-DNA interaction sites while autocorrelation and Fourier analysis proves to be useful for the studies of relaxation dynamics in nucleosomes.

2972-Pos Board B19

Side-by-side And End-to-end Attraction Of Double-stranded DNA

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Genomic DNA is densely packed inside the cell nucleus and viral capsids. Such close packing suggests that electrostatic repulsion between negatively charged DNA in the condensed state is balanced by counterion-induced attraction. Indeed, effective attraction between DNA in high-valence electrolytes has been experimentally demonstrated. Several theoretical models have been proposed to explain DNA attraction, however, specific microscopic mechanisms could not be unequivocally determined. Here, we report sub-microsecond all-atom molecular dynamics (MD) simulations of the effective force between double-stranded DNA in the side-by-side and end-to-end orientations. In a typical simulation, two DNA molecules were placed in an electrolyte solution a certain distance away from one another. An external harmonic potential was applied to keep the distance between the molecules constant, which allowed the effective mean force to be computed directly by averaging over 160 ns-long trajectories. We found that, in a side-by-side conformation, two DNA molecules can form a bond state in the presence of magnesium ions. In the bond state, DNA molecules contact each other via negatively charged phosphate groups, bridged by magnesium ions. For DNA in a monovalent electrolyte, the effective attractive force is too weak to induce DNA condensation in the presence of thermal fluctuations. In the end-to-end orientation, the attraction was found to take place regardless of the electrolyte concentration. The presence of a phosphate group at the 5′-ends of the fragments was found to direct DNA end-to-end self-assembly and produce bound states resembling a continuosus DNA molecule. Our simulations suggest that the end-to-end attraction, rather than being mediated by counterions, is likely caused by hydrophobic and the van der Waals interactions between terminal nucleobases of the fragments.

2973-Pos Board B20

Comparing Short dsRNA and dsDNA: Charge Screening Efficiency and Counterion Distribution

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Action of short double-stranded RNA (dsRNA) helices is a key component in the RNA interference mechanism. Since past theoretical and experimental work on nucleic acid electrostatics mainly focused on DNA, we conducted a comparative investigation of electrostatic effects in RNA and DNA. Using resonant (anomalous) and non-resonant small-angle x-ray scattering, we characterized the charge screening efficiency and counterion distribution around short (25bp) double-stranded DNA and RNA molecules of comparable sequence. Compared to dsDNA, we find that dsRNA molecules appear charge neutral on shorter length scales under conditions of lower bulk salt concentrations. The experimental results agree well with ion-size-corrected nonlinear Poisson-Boltzmann calculations. We propose that differences in electrostatic properties aid in selective recognition of different types of short nucleic acid helices by target binding partners.

2974-Pos Board B21

Structural Energetics of Two RNA-DNA Hybrids

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Intrinsic transcription terminators in bacteria are specific signals encoded in the base sequence of the DNA template. A canonical intrinsic terminator consists of a GC-rich dyadic sequence, followed by a track of five or more adenines in the template strand. The formation of a hairpin structure by the GC-rich dyadic sequence in the RNA transcript, and the low stability of dA-rU base pairs in the transcription RNA-DNA hybrid are believed to be the major contributors to the termination of transcription at these sites. In the present work, we have investigated two RNA-DNA hybrids corresponding to the GC-rich dyadic sequence in the tR2 terminator of phage λ. The stability of individual base pairs in these RNA-DNA hybrids was characterized and compared from measurements of the exchange rates of imino protons using nuclear magnetic resonance spectroscopy. The measurements also allowed determination of opening and closing rates for selected base pairs. The results indicate that a dA-rU base pair is destabilized relative to a dT-rA base pair in the same base sequence context. This destabilization is enhanced when two dA-rU base pairs are next to each other. The results also reveal that dG-rC base pairs have different stabilities from dC-rG base pairs. The magnitude of these differences depends on the base sequence context of the dG-rC/dC-rG base pairs, and on their proximity to dA-rU base pairs. (Supported by a grant from the NIH).

2975-Pos Board B22

Is the Formation of the Correct Nucleating Loop the Rate-Limiting Step in Hairpin Formation in ss-Polynucleotides?

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Numerous kinetics measurements on the formation of single-stranded (ss) DNA and RNA hairpin structures with ~4-20 nucleotides (nt) in the loop and ~5-8 base-pairs in the stem, indicate that the time required to form hairpins is ~10-500 microseconds. If ss-polynucleotide chain is treated as an ideal semiflexible polymer with a statistical segment length of ~4 nt, the theoretical estimate for the end-to-end contact time for an ~10-nt long chain is expected to be tens-of-nanoseconds. To explain this discrepancy in timescale, we proposed that the formation of the nucleating loop, prior to the zipping step, is slowed down as a result of transient trapping in misfolded conformations, with mis-paired base-pairs, non-native hydrogen bonding, or intrastrand stacking interactions in the unfolded state. Experimental measurements of end-to-end contact formation indicate that loop closure times for 4-nt poly(dT) loops are ~400 ns, and for 4-nt poly(dA) loops are ~8 microseconds, thus confirming that intrachain interactions slow down the configurational diffusion of the chain (Wang and Nau, J. Am. Chem. Soc. 2004, 126, 808). Interestingly, despite this evidence for intrachain interactions slowing down diffusion, the hairpin closing times for both ssDNA and RNA hairpins are found to scale with the length of the loop as $L^{2.2\text{-}2.6}$, in reasonable agreement with the scaling behavior expected for loop-closure of a semiflexible polymer.
Here, we present a kinetic zipper model that explicitly includes all misfolded microstates with non-native contacts, to describe the hairpin relaxation rates. The temperature and loop-size dependence for the relaxation rates is described in terms of two free parameters, the configurational diffusion coefficient that is relevant for the single-strand chain dynamics, and one parameter that characterizes the strength of non-native interactions prior to the formation of the nucleating loop.

2976-Pos Board B23

RNA Bending and Stabilization by Carbocyclic Sugars Constrained to North and South Conformations

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Carbocyclic sugars in modified nucleotides constrained to north/south conformations have A/B form (C3'/C2' endo) that can change the bending of RNA duplexes and rigidify nucleotides due to their locked sugar puckers. The dynamic behavior of an RNA dodecamer and an HIV kissing loop complex which contain several modified nucleotides with north/south carbocyclic sugars are being studied by explicit solvent molecular dynamics (MD) simulations. In the RNA dodecamer, two pairs of north carbocyclic sugars are substituted into the center region of dodecamer inducing an increased bending of the dodecamer axis. Similar bending behavior is also observed in an HIV kissing loop complex. Two pairs of north carbocyclic sugars are substituted into each stem of the HIV kissing loop complex and the angle between the kissing loop and both stems tips is reduced due to the north carbocyclic sugars. In order to rigidify the kissing loop complex, 12 north carbocyclic sugars are uniformly substituted into both stems and the average RMSD of the structure is found to be smaller than the unmodified kissing loop complex. In addition, it is observed that when a single strand of the RNA dodecamer contains north carbocyclic sugars, it can cause bending in the other unmodified strand. Stabilization of the kissing loop complex can also be obtained by substituting south carbocyclic sugar conformations into the flanking bulged-out base regions where it was found that the x-ray kissing loop complex had C2' endo south sugar conformations. These results suggest that proper use of north and south carbocyclic sugars can bend and stabilize RNA complexes without applying any external constraints.