of twist and bend in these experiments. To understand these experiments, we develop and solve a stochastic and elastic model for twist dynamics in a DNA molecule that is driven at one end and dissipates torsional energy through viscous drag at the other end. To ensure that torque fluctuations remain finite in our model, we include a term depending on the gradient-squared of twist strain. We find that the boundary conditions of our system quantize the spectrum of DNA twisting modes and modulate the dynamics in a striking way. To see this, we derive a nonequilibrium fluctuation relation for twist and construct the spatiotemporal correlation function. We find that a novel elastic correlation length controls spatial correlations between twist fluctuations. In the middle of a long DNA molecule, twist correlations initially decay as \( t^{-1/2} \) and crossover to \( t^{-1} \) decay at longer times. In contrast, in a shorter molecule, correlations decay exponentially with a decay time that depends on the magnitude of the viscous drag. For nearly straight DNA molecules, twist dynamics are affected by bending fluctuations at linear order, even though writhe dynamics are modulated by twist at this order. Our model for twist dynamics suggests several new single-molecule experiments, which could shed further light on DNA mechanics and dynamics.

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Strongly Bent DNA: Reconciling Theory and Experiment
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The majority of double stranded DNA (dsDNA) in living cells is strongly bent. There is little doubt that standard models that assume harmonic bending energy (Hooske’s law, worm-like chain) with effective persistence length of around 50 nm accurately describe the weak bending of DNA. However, it is not clear if these commonly used approximations are still adequate for the poorly understood strong bending regime, which is most relevant to biology. The available experimental evidence is controversial, with the most recent cyclization experiments of ~100 base-pair DNA fragments pointing to strongly bent dsDNA being considerably more flexible than expected. We present a general concept of polymer bending that naturally allows for a transition from the weak, harmonic deformation regime into the “soft” mode at large deformations. In this model, convexity properties of the bending energy potential of individual monomer sub-units of the polymer give rise to the transition between two bending modes. Namely, if the effective monomer deformation energy as a function of bending angle has a non-convex (concave up) region, then the deformation energy of the polymer is a linear function of the bending angle. The dsDNA effective bending potential determined from the angular distribution of base-pairs from PDB structures of DNA-protein complexes is in agreement with our model: it is harmonic in the weak bending regime and non-convex for strong bends. We propose a simple expression that replaces the harmonic approximation in the strong bending regime. The theory shows quantitative agreement with recent cyclization experiments of short dsDNA fragments. Atomistic molecular dynamics simulations point to short-range Lennard-Jones interactions as responsible for the onset of the linear bending regime of dsDNA.

1427-Pos Board B157

Electrophoretic Mobility of DNA is Controlled by the Surface Charge Density, not the Linear Charge Density as Expected from Counterion Condensation Theory
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The free solution mobilities of small single- and double-stranded DNA molecules with variable charge densities have been measured by capillary electrophoresis. The charge density was modified either by appending charged phosphate internucleoside linkers with neutral or positively charged groups to the thymine residues or by replacing some of the negatively charged phosphate internucleoside linkers with neutral or positively charged phosphorylamine linkers. Mobility ratios were calculated for each data set by dividing the mobility of the charge variant by the mobility of the unmodified parent DNA. Mobility ratios eliminate the effect of the background electrolyte on the observed mobility, making it possible to compare data obtained in different buffers. The mobility ratios observed for ss- and dsDNA charge variants increase logarithmically with increasing fractional charge density, as expected from Manning’s theory of DNA electrophoresis. Surprisingly, however, the mobility ratios are directly related to the surface charge densities of the ss- and ds-DNA molecules, not the linear charge density as expected from counterion condensation theory. The results therefore suggest that surface charge density may play a role in counterion condensation, as well as in electrostatic interactions between DNA and other charged molecules in the cell.

1428-Pos Board B158

Thermodynamics and Kinetics of Three Distinct Overstretched DNA Structures Produced by Large Tension
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Torsion unconstrained double stranded DNA undergoes an overstretching transition by tensile force at around 65 pN, which leads to DNA elongation of around 1.6-1.7-fold. Three possible elongated DNA structures have been proposed, namely: a single-stranded DNA under tension, DNA bubbles consisting two parallel, separated single-stranded DNA under tension, and a new form of base-paired double-stranded DNA. We have successfully identified all the three proposed structures and fully characterized their respective thermo-mechanical properties. In addition to completing the picture about the nature of DNA overstretching, these findings prove that a stable S-form DNA exists under certain solution conditions.

RNA Structure and Dynamics I

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Sugar Alcohol Osmolytes Demonstrate the Viscosity Dependent Folding Kinetics of RNA Tertiary Structural Motifs
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It is widely known that there exists a strong relationship between the solvent, including co-solutes (e.g., cations), and RNA that cooperatively defines the kinetics and thermodynamics of tertiary structure formation. In addition, small organic molecules, also known as osmolytes (Urea, TMAO, sugar alcohols, etc.), can have significant affects on RNA structure formation. Here, the kinetics of two tertiary structural motifs, a GAAA tetraloop-receptor and a kissing loop-loop interaction, are measured in the presence of various sugar alcohols (methanol, ethylene glycol, glycerol, etc.) at the single molecule level. As the size of the sugar alcohol is increased systematically from methanol to sorbitol the net thermodynamic effect changes from stabilizing (\( \Delta G < 0 \)) to destabilizing (\( \Delta G > 0 \)). This trend is reflected in the m-values, or per molal change in free energy, where Mmethanol = ~0.2 kcal/mole*m and Msorbitol = ~0.3 kcal/mole*m. In the case of glycerol, where Mglycerol = ~0, the RNA solvation is most similar to that of water, thus there is no preferential interaction with either the folded, unfolded or transition states. In the absence of strong chemical interaction, an explicit inverse viscosity dependence (1/\( \eta \)) is observed in both the folding and unfolding directions, as described by Kramers’ rate theory. These results indicate that the RNA free energy surface, including the transition state, is minimally perturbed by glycerol, and the major effect on folding is a reduction in kinetics due to increased friction felt by the RNA.

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De Novo Folding of RNA Hairpins by Temperature Replica Exchange
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Describing folding and thermodynamic behaviors of small RNA hairpins is a key step in elucidating the folding processes of larger RNA macromolecules. Experimental methods have been used to describe a wide range of dynamical behavior in RNA hairpins including the dynamics of loop residue interactions and folding rates of stems, but many questions surrounding the detailed mechanism of RNA hairpin formation remain unanswered. The order and directionality of stem nucleation and stem base-pair formation remains open for debate, as well as the effects of stem-length on the rate of hairpin formation and the frequency of base mismatches. All-atom molecular dynamics offers a methodology for analyzing heterogeneous, multiple-pathway folding processes and how they contribute to the overall thermodynamic behaviors of RNA hairpins. To that end, we analyzed the equilibrium folding of a hyperstable tetraloop with a four base-pair stem, r(ggcC GAaGgc), using recently published RNA parameters. Using microsecond-timescale temperature replica-exchange molecular dynamics simulations we are able to sample a large ensemble of conformational states adopted by RNA hairpins and describe the thermodynamic processes involved in hairpin formation. The results give us insights into the biophysical driving forces of RNA folding.