of telomeric sequences in real-time. In the presence of its antisense sequence, the folded G-quadruplex structures (in 150 mM Na+) can be disrupted and converted to the unfolded conformation, and the conversion frequency depends strongly on the antisense concentrations. In the great excess of antisense sequence, the conversion efficiency is about 10 % in our single-molecule essay (N >100). However, in the presence of Li+ ions, the efficiency of antisense interaction increases significantly to 50 %. Since Li+ ions have been proposed to destabilize the G-quadruplex structure, our results suggest the antisence sequence interacts with the unfolded or, at least, partially unfolded state of telomeric sequences. Experiments of structure conversion between 150 mM Na+ and 100 mM K+ ions, and effects of structure conversion in the presence of a G-quadruplex stabilizer (BMVC) will also be discussed.

1762-Pos Board B606

Conformational Stabilization Of G-quadruplex DNA By Metalloporphyrins

Xiuyi Liu[1,2], Yasemin Kopkalli[2], Lesley Davenport[1,2].
[1]Ph.D. Program in Biochemistry, Graduate Center of CUNY, New York, NY, USA, [2]Department of Chemistry, Brooklyn College of CUNY, Brooklyn, NY, USA.

Formation and stabilization of the human telomeric G-quadruplexed DNA *in vitro* has been found to inhibit the enzyme telomerase, which is overactivated in tumor cells. Quadruplex interacting agents (QIAs), ligands that bind and stabilize the human telomeric G-quadruplex DNA, have been recognized as potential chemotherapeutic agents. Porphyrins are promising QIAs with the additional versatility of central metal-ion chelation. In the present study we have investigated the effects of various metal ions (Co (III), Cr (III), and Mn (II)) bound to the base porphyrin mesoporphyrin IX (MPIX) on the overall binding selectivity and specificity with the G-quadruplex conformation, using fluorescence, absorbance and circular dichoism spectroscopies. Our data suggests that all three metal-porphyrin derivatives exhibit high binding selectivity for G-quadruplex over double-stranded DNA, and appear to promote a conformational switch from antiparallel to parallel quadruplex conformation. Changes in the metalloporphyrin absorption spectra on binding with the G-quadruplex DNA suggests intercalating, groove binding or external stacking interactions. In addition, melting curve data reveal that all three metalloporphyin derivatives can stabilize the G-quadruplexed DNA over N-methyl mesoporphyrin IX (NMM), with a central methyl group instead of a metal ion, in the order: NMM < Co(III) MPIX < Mn(II) MPIX < Cr(III) MPIX. Consequences of our studies for design of potential new QIAs will be discussed.

1763-Pos Board B607

Simulated Single-Molecule FRET Trajectories: A Comparative Analysis Between Three Telomeric G-quadruplexes

Gavin D. Bascom[1], Tia Guinn[2], Ioan Andricioaei[1].
[1]University Of California: Irvine, Irvine, CA, USA, [2]University Of Michigan, Ann Arbor, MI, USA.

The human telomeric DNA sequence d[AGGG(TTAGGG)3] is known to have multiple conformations in vitro. The primary objective of this study is to understand folding and unfolding mechanisms of three human telomeric quadruplexes. Relative stabilities of two quadruplex structures, an anti-parallel and parallel form, were studied using molecular simulations and molecular modeling techniques. A third mixed form which contains the sequence d[TTGGG(TTAGGG)3A], along with the parallel and anti-parallel form was pushed away from its original conformation via a bias command on the sugar-phosphate backbone. It was found that the anti-parallel conformation was the most stable, in that it remained closest to its original conformation. Common characteristics are seen throughout the simulations, particularly stacking near the 3′ end that outlasts the rest of the structure. In an effort to understand the unfolding mechanism or transition state between observed structures, theoretical FRET signals were calculated by analyzing the movement of backbones during simulation. The movement of the backbone in simulations supports published results, namely that similar structures are seen in other studies, and the theoretical FRET signals show similarities to single molecule studies. Clustering by rmsd values shows 7 distinct possible unfolding mechanisms with similarities to published results. A more complete understanding of the stabilizing and destabilizing factors involved in quadruplexes will allow further research into the possible manipulation of the cell cycle and has been cited as an important and promising aspect in the field of cancer research.

1764-Pos Board B608

Holliday Junction Mechanics Studied Using an Angular Optical Trap

Scott Forth[1], Christopher Deufel[1,2], Michelle D. Wang[1,3].
[1]Cornell University, Ithaca, NY, USA, [2]Mayo Clinic, Rochester, MN, USA, [3]Howard Hughes Medical Institute, Ithaca, NY, USA.

The Holliday junction is a four-way DNA structure which plays a crucial role during homologous recombination and double-stranded DNA break repair. In vivo, the branch point can migrate spontaneously or with the assistance of helicase-like motor proteins. In this work, we mechanically migrate a Holliday junction using an angular optical trap. While applying a constant tension to the DNA molecule, we simultaneously measure the extension change and torque as the junction is torsionally driven to a new position. We determine that there exists a simple thermodynamic relationship between the torque required to stabilize the junction and the force working to destabilize it. We propose that this assay can have important uses in single molecule studies of motor proteins, particularly as a calibrated nano-torque wrench.

1765-Pos Board B609

Fullerenes May Induce Physical Changes of DNA - an Optical Tweezers Study

Fabian Czerwinski[1], Michael A. Sørensen[2], Lene B. Oddershede[1].
[1]Niels Bohr Institute, University of Copenhagen, Copenhagen, Denmark, [2]Department of Molecular Biology, University of Copenhagen, Copenhagen, Denmark.

Fullerenes are fascinating symmetric carbon nanostructures. Nowadays, they are widely used because of their characteristic physical and chemical properties. Until now research has mainly focused on commercial applications of fullerenes. Only a few investigations have addressed the potential biological hazards, one of which is that fullerenes are believed to alter the elastic properties of DNA upon (irreversible) binding.

In our experiments we use optical tweezers with sub-piconewton and nanometer resolution to probe the structural changes and the potential damages that fullerenes may induce on single DNA molecules. Force-extension relations of these molecules are obtained under physiological conditions while varying the concentration of different types of fullerenes, through well-defined microfluidics, in order to assess hypothesized damages. Custom-made Labview software allows for precise equipment control, various feedback options, and very fast on-the-fly data streaming.

It has been theoretically predicted [1] that certain fullerenes can function as a minor-groove binder to double-stranded DNA, thus altering its elastic properties significantly. This may be why fullerenes are capable of causing severe damage inside living organisms. They form DNA regions that are inaccessible which prevents proper enzymatic catalysis. A further goal of the study is to establish fullerenes as a tool for a more detailed investigation of DNA-minor-groove binding as well as DNA-protein interactions, such as the traffic of polymerases or the packing by prokaryotic proteins. [1] Zhao, Striolo, and Cummings: BiophysJ (89):3856-62, 2005.

1766-Pos Board B610

Kinetics of DNA force-induced melting

Micah J. McCauley[1], Leila Shokri[1], Ioulia Rouzina[2], Mark C. Williams[1].
[1]Northeastern University, Boston, MA, USA, [2]University of Minnesota, Minneapolis, MN, USA.

Force spectroscopy studies probe nucleic acid structures by exerting tension along the molecule. As it is stretched, double-stranded DNA reveals a sudden increase in length at a constant force, a transition referred to as overstretching. Thermodynamic and chemical evidence have demonstrated that overstretching is actually force induced melting, a transition to single-stranded DNA as base pairing and base stacking are disrupted. We present a predictive model of force induced melting in which thermal fluctuations induce local melting and re-annealing of DNA. These fluctuations are stabilized by the application of tension during the overstretching transition, favoring the conversion to single stranded DNA as the applied force is increased, analogous to the thermal melting of DNA. This model quantitatively predicts small changes in the melting force as the pulling rate is varied. We then test our model for force-induced melting by systematically measuring the midpoint of the transition as a function of pulling rate. Our results suggest that DNA force-induced melting occurs cooperatively with a domain size of 100-200 base pairs.

1767-Pos Board B611

Spectroscopic Studies of Position-specific DNA 'Breathing' Fluctuations at Replication Forks and Primer-Template Junctions

Davis Jose[1], Kausiki Datta[1], Neil P. Johnson[2], Peter H. von Hippel[1].
[1]Institute of Molecular Biology, University of Oregon, Eugene, OR, USA, [2]Institut de Pharmacologie et de Biologie Structurale, CNRS UMR 5089 205 route de Narbonne 31077 Toulouse, France.

The properties of single- (ss) and double-stranded (ds) DNA sequences at replication forks and primer-template DNA junctions are central to the function of the protein complexes that drive DNA replication, transcription, recombination and repair. Significant base-pair 'breathing' (or 'fraying')