2991-Pos Board B146
Optical Tweezers Controlled Nanopore Detection of Nucleosomes along a DNA
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Nucleosomes, the fundamental packaging unit of DNA inside eukaryotic cells, have both structural as well as functional roles in gene regulation. Genome-wide maps of nucleosome positions have significantly contributed towards our general understanding of regulation at transcription start sites, promoter regions and promoter boundary demarcations, but very little is known about the nucleosome positioning at local, single gene level. This calls for sensitive single-molecule tools to probe nucleosome positioning along a chromatin fiber. Nanopores have been used as a structural biosensor for DNA, DNA-bound proteins and very recently for nucleosomes [1]. Translocation of a biomolecule through the nanopore results in characteristic changes in the nanopore current which provides a direct readout of the molecular volume of the translocating complex. Resolving specifically positioned nucleosomes on DNA is however challenging due to lack of control on the speed of translocation. Here we use an optical tweezers assay to control the translocation of nucleosome arrays through a nanopore. An array of nucleosomes along a single DNA molecule is tethered to an optically trapped bead and the molecule is inserted into a nanopore at a controlled speed. Simultaneous measurements of force and nanopore current signals provide data on the position of nucleosomes on DNA. These experiments extend the reach of the nanopore platform into the study of chromatin biology.
[1] Soni and Dekker, Nano Lett. (2012).

2992-Pos Board B147
The Architects of the Archaeal Chromatin
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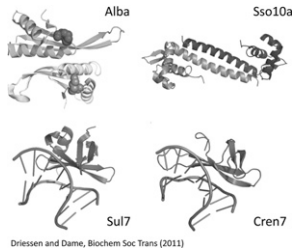
Architectural proteins play an important role in organizing and compacting the genome in all three kingdoms of life. Archaeal chromatin proteins show similarities with both bacterial and eukaryotic chromatin proteins.The thermophilic model organism Sulfolobus expresses four different chromatin proteins: Cren7, Sul7, Alba and Sso10a. To characterize the architectural properties of these proteins we use a single-molecule approach. We have observed that these proteins are all able to compact DNA, exhibiting different sets of binding modes. In addition to DNA compaction and organization, these proteins are believed to play an important role in maintaining genome integrity at high environmental temperatures. High temperature single-molecule measurements showed how DNA structure is affected by temperature and how chromatin proteins affect DNA stability at these temperatures.



2993-Pos Board B148
Modeling Long Chromatin Fibers based on In-Vivo Nucleosome Positioning Maps
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In the nucleus of eukaryotes DNA is wrapped around histone proteins forming so-called nucleosomes, the basic unit of chromatin. This packaging controls DNA accessibility, thus influences directly gene expression, DNA repair and recombination. The precise structure of chromatin *in-vivo* is still under debate, because experimental probing of chromatin in the nucleus remains difficult and evidence for proposed models is rare. The majority of theoretical models imply a uniform nucleosome repeat length. However, *in-vivo* nucleosomes exhibit more irregular patterns. It has been shown that the internucleosomal distance has a great impact on the local and global structure of the chromatin arrangement.
Here we investigate the influence of nucleosome positioning on the three-dimensional chromatin structure by modeling chromatin fibers comprising more than 1000 nucleosomes. The spacing of nucleosomes was based on *in-vivo* nucleosome positioning maps from mouse embryonic stem cells and differentiated cells derived from these. We determined non-overlapping nucleosome configurations from MNase assisted high throughput sequencing assays by a simulation procedure. In the next step, we derived a three-dimensional coarse-grained chromatin model from nucleosome positioning data, including fundamental physical properties like elasticity, electrostatics and nucleosome interactions. To improve the understanding of how structural differences and function are linked, we simulate models of gene-clusters at different stages of cell differentiation.

2994-Pos Board B149
Bayesian Reconstruction of Chromatin Conformation from FISH and Hi-C Data
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Global and local chromatin conformations play important roles in gene regulation, chromosomal translocations, and copy number variations in interphase and dividing cells. Chromatin conformation is highly dynamic, varying with cell state and cell cycle, as well as heterogeneous across cell populations. Thus, unbiased, objective computational procedures are needed to infer local and global chromatin conformation from noisy structural datasets including fluorescence *in situ* hybridization (FISH) and Chromosome Conformation Capture. Here, we present such objective, Bayesian procedure that infers the least-biased distribution of chromatin conformational states from FISH and Hi-C datasets accounting both for heterogeneity in the underlying cell population as well as error in the observed data. We demonstrate that the procedure generates unbiased structural ensembles that simultaneously reproduce both contact probabilities measured from Hi-C data and distributions of pair-wise distances measured from FISH. The procedure accounts for minimal physical constraints including nuclear volume and DNA topology without over-parameterizing structural models as commonly is performed using molecular or Brownian dynamics approaches that employ *ad hoc* harmonic restraints and objective function minimization algorithms.

2995-Pos Board B150
Population Properties of Self-Avoiding Polymer Chain Models of Chromosomes in a Confined Space of Nucleus
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Global architecture of cell nucleus and the spatial organization of chromatin play important roles in gene expression and nuclear function. Single-cell imaging and chromosome conformation capture-based techniques provide information on chromosome conformations and their spatial organizations. Here we propose a polymer model to study the higher order chromatin organization in the nucleus. This model is based on generating self-avoiding chains with appropriate diameters of chromatin fiber in a confined space where the excluded volume effect is taken into consideration. using a sequential importance sampling technique, we are able to generate 10,000 independent conformations explicitly and study their statistical properties, such as spatial distance vs. genomic length relationship and loop forming probability. This model can capture many scaling properties of chromatin folding reported experimentally and can also explain many biological properties of chromatin fibers.

2996-Pos Board B151
Polymer Models of Yeast S. Cerevisiae Genome Organization
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Three-dimensional (3D) chromosomal organization impacts critical cellular processes including transcription, replication, and genomic stability. Despite the ubiquity of these challenges, a growing body of evidence suggests that major features of interphase chromosomal organization significantly vary across eukaryotes.
A series of recent studies using optical and 3C-based experimental approaches has shown that on a global level the yeast genome is organized in a confined polymeric brush with the chromosomal centromeres tethered to the spindle pole body and telomeres tethered to the nuclear periphery. This happens to be in a striking difference with the human genomic organization, which chromosomes are shown to assume the fractal globule conformation with domains of active and inactive chromatin.
In this work we investigated the implications of a Rabl-like chromosome organization using stochastic simulations of polymer dynamics and an exactly solvable polymer model. We showed that depending on the position along the genome, genomic loci are exposed to different mechanical stresses that may affect their biological function. This nonuniformity of the environment is