BP 2: DNA and Chromatin

Time: Monday 10:30–13:15 Location: PC 203

BP 2.1 Mon 10:30 PC 203

Structure and dynamics of interphase chromosomes — Angelo Rosa[1] and •Ralf Everaers[2] — [1]Institute for Biocomputation and Physics of Complex Systems, Corona de Aragón 42, 50009 Zaragoza (Spain) — [2]Université de Lyon, Laboratoire de Physique, École Normale Supérieure de Lyon, CNRS UMR 5672, 46 allée d'Italie, 69364 Lyon Cedex 07, France

During interphase chromosomes decondense, but FISH experiments reveal the existence of distinct territories occupied by individual chromosomes inside the nuclei of most eukaryotic cells. We use computer simulations to show that the existence and stability of territories is a kinetic effect which can be explained without invoking an underlying nuclear scaffold or protein-mediated interactions between DNA sequences. In particular, we show that the experimentally observed territory shapes and spatial distances between marked chromosome sites for human, *Drosophila* and budding yeast chromosomes can be reproduced by a parameter-*free* minimal model of decondensing chromosomes. Our results suggest that the observed interphase structure and dynamics are due to generic polymer effects: confined Brownian motion conserving the local topological state of long chain molecules and segregation of mutually unentangled chains due to topological constraints.

BP 2.2 Mon 10:45 PC 203

Higher-order folding of chromatin and the Random Loop Model — •Manfred Bohn[1], Dieter W. Heermann[1], and Roel van Driel[2] — [1]Institut für Theoretische Physik, Universität Heidelberg, Philosophenweg 19, 69120 Heidelberg — [2]Swammerdam Institute for Life Sciences, University of Amsterdam, Kruislaan 318, 1098 SM Amsterdam

Remarkably little is known about the higher-order folding motifs of the chromatin fiber inside the cell nucleus. Folding depends among others on local gene density and transcriptional activity and plays an important role in gene regulation. Strikingly, at fiber lengths above 5 to 10 Mb (mega base pairs) the measured mean square distance $< R^2 >$ between any two points on the chromatin fiber is independent of genomic distance. The formation of loops on different length scales seems to play an important role in transcriptional regulation. We analyze the data with respect to different polymer models on short fiber lengths. For long fiber lengths above 10 Mb, where simple models fail in explaining experimental results, we propose a polymer model that explains the leveling off by means of random looping. An analytical expression is calculated for the mean square displacement over the thermal ensemble. The quenched average over the disorder of loops is performed numerically. A detailed investigation of this model shows that only a small number of loops on all scales are necessary to fit experimental data.

BP 2.3 Mon 11:00 PC 203

Genome size variation in eukaryotes: its causes and consequences — •A. G. Cherstvy — FZ Juelich, IFF, 52425 Juelich

The genome size - C value - of animals reveals about 10000 fold variation. The DNA length in fishes varies about 350, while in mammals/birds only 2-4 times. Complexity of organisms and number of genes are not related to DNA content (C value paradox). The genomes of salamanders and lungfishes are 20-40 times longer than of humans, while the gene numbers are quite close. Even some invertebrates have much longer DNA (grasshoppers and amphipods). In higher eukaryotes, only a couple of percent of DNA are actually coding for proteins. The rest, "useless", DNA is probably needed to organize DNA in chromatin/chromosome. It also determines the cell/nucleus size and speed of cellular processes. A naive expectation that evolution should remove this parasitic DNA does not work. On the contrary, the genome of lungfishes, remained unchanged over last 200-300 million years, is known to grow in some eras. But, the genome of Latimeria chalumnae - another living fossil - remained constant at about the human size. C-value can vary strongly between closely related species (some fishes, crustaceans amphipods, etc). E.g., amphipods of cold waters live longer, mature/grow slower, and produce less broods than their hot water colleagues. We will compare and contrast some extreme examples of the genome sizes known, discuss physical/biological mechanisms affecting C-value, outline the role of genome duplication and repetitive DNA sequences, study longevity vs genome size correlations for some species, and speculate about developmental consequences.

BP 2.4 Mon 11:15 PC 203

Phase diagram of chromatin within the two angle model for spherical and cylindrical shape of the nucleosomes — •Dieter Heermann and Philipp Diesinger — University of Heidelberg, Institute of Theoretical Physics, Philosophenweg 19, D-69120 Heidelberg

We have studied the phase diagram for chromatin within the framework of the two-angle model. We reveal the fine-structure of the excluded-volume borderline for spherical type nucleosomes and for cylindrical shape nucleosomes. Thus we where able to give a Ramachandran like diagram for the chromatin fiber. Furthermore, we examined how fluctuations in the distribution of the H1 histones or changes of the vertical distance between the in and outgoing DNA strand affect the chromatin fiber and its biophysical properties.

BP 2.5 Mon 11:30 PC 203

Time resolved access to linker histone/DNA structure formation — •Rolf Dootz, Heather Evans, and Thomas Pfohl — Max-Planck-Institut für Dynamik und Selbstorganisation, Göttingen, Germany

Linker histones H1 are of central importance in genome organization and regulation. Combining small angle X-ray microdiffraction and microfluidics allowed for time resolved access to H1/DNA interaction dynamics and structure formation on relevant molecular length scales. The observed X-ray patterns indicate that the interaction of H1 with DNA is a two step process: an initial unspecific binding of H1 proteins to DNA is followed by a rearrangement of molecules in the formed assemblies. Our results suggest that the conformational transition of H1 tails from their rather extended conformation in aqueous solution to their fully folded state upon interaction with DNA may be responsible for the conformational phase transition of H1/DNA assemblies. We believe those findings have a direct bearing on the understanding of chromatin fiber folding into higher order structures.

15 min. break

BP 2.6 Mon 12:00 PC 203

Gold Nano-Stoves for Microsecond DNA Melting Analysis — •Calin Hrelescu[1], Joachim Stehr[1], Ralph A. Sperling[2], Gunnar Raschke[1], Michael Wunderlich[3], Alfons Nichtl[3], Dieter Heindl[3], Konrad Kürzinger[3], Wolfgang J. Parak[2], Thomas A. Klar[1], and Jochen Feldmann[1] — [1]Photonics and Optoelectronics Group, Physics Department and CeNS, Ludwig-Maximilians-Universität München, Amalienstr. 54, 80799 Munich, Germany — [2]CeNS, Ludwig-Maximilians-Universität München, Amalienstr. 54, 80799 Munich, Germany and Fachbereich Physik, Philipps Universität Marburg, Renthof 7, 35037 Marburg, Germany — [3]Roche Diagnostics GmbH, Nonnenwald 2, 82372 Penzberg, Germany.

In diagnostics, medicine and biophysics, the melting analysis of DNA is a very important tool. In current temperature ramp techniques the typical time scales for a DNA melting analysis range from several minutes up to one hour. Especially for high throughput DNA analysis a faster detection of the DNA melting point is highly desirable, as well as the successful identification of mutants of the target DNA. We exploit the characteristic plasmonic properties of DNA bound gold nanoparticle aggregates to optically induce and detect the melting of double stranded DNA. The aggregates are used as very efficient light absorbers to locally convert optical energy from laser pulses into thermal energy. Pulsed optical experiments show that heating on a microsecond timescale is sufficient to melt DNA molecules. Only one single laser pulse is needed to distinguish between a perfectly matching target and a target with a point mutation.

BP 2.7 Mon 12:15 PC 203

Conformational DNA separation by dielectrophoresis — •Jan Regtmeier[1], Ralf Eichhorn[2], Alexandra Ros[1], and Dario Anselmetti[1] — [1]Experimental Biophysics & Applied Nanoscience, Bielefeld University, Universitaetsstr. 25, 33615 Bielefeld, Germany — [2]Condensed Matter Theory, Bielefeld University, Universitaetsstr. 25, 33615 Bielefeld, Germany

In modern biotechnology and pharmaceutics applications, topologically closed circular DNA plays an important role. For instance, plasmids are used as genetic vectors in DNA recombinants, and for in vivo gene therapy. The latter makes high purification and exact characterization of plasmid DNA indispensable.

We extend our previous studies [1] and present the separation of DNA fragments with equal number of base pairs according to their conformation (supercoiled from linear DNA fragments). The separation is performed in a microfluidic poly(dimethylsiloxane) (PDMS) chip within 210 s. The device consists of a cross injector and a microstructured separation channel with a periodic array of nonconducting posts. The application of an AC voltage induces dipoles in the DNA molecules, which couple to the inhomogeneous electric field in the post array (dielectrophoretic trapping). Superimposed application of a DC voltage induces DNA migration and separation, based on differences in DNA polarizabilities. A detailed analysis of the trapping times allows quantification of the DNA polarizabilities.

[1] Dielectrophoretic Manipulation of DNA: Separation and Polarizability, J. Regtmeier et al., Anal. Chem. 79, 3925-3932 (2007)

BP 2.8 Mon 12:30 PC 203

Thermodynamic Analysis of Interacting Nucleic Acids with Application to Biosensing Devices — •Justin Bois[1] and Niles Pierce[2] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]California Institute of Technology, Pasadena, CA, USA

DNA and RNA are versatile construction materials. By appropriately designing base sequences, synthetic nucleic acid systems can be programmed to self-assemble into complex structures. An understanding of the underlying free energy landscapes of these systems is crucial for their design, characterization, and control. This talk will focus on theoretical and computational tools to characterize the equilibrium properties of an entire test tube of interacting nucleic acid strands. The utility of the approach will be demonstrated by elucidating the empirical behavior of a new class of DNA-based instrument-free biosensors currently under development.

BP 2.9 Mon 12:45 PC 203

DNA Melting: a combination of Poland-Sheraga and lattice models — •Ralf Everaers — Université de Lyon, Laboratoire de Physique, École Normale Supérieure de Lyon, CNRS UMR 5672, 46 allée d'Italie, 69364 Lyon Cedex 07, France

Key biological and nano-technological processes require the (partial) association and dissociation of complementary DNA strands. We present a variant of the Poland-Scheraga model which reproduces experimental data for melting temperatures for arbitrary strand length over the full experimental range of strand concentration and ionic strength of the solution. Furthermore, we show results for a corresponding lattice model of associating heteropolymers with identical melting behavior. The lattice model treats long-ranged excluded volume interactions between all parts of the molecule explicitly, provides access to an ensemble of three dimensional structures (and hence the response to external mechanical forces) and can be used for studying the kinetics of the melting transition.

R. Everaers, S. Kumar and Ch. Simm, **Phys. Rev. E** *75*, 041918 (2007).

D. Jost and R. Everaers, *submitted*.

BP 2.10 Mon 13:00 PC 203

Protein-DNA interactions: reaching and recognizing the targets — •A. G. Cherstvy[1], A. B. Kolomeisky[2], and A. A. Kornyshev[3] — [1]Theorie-II, IFF, FZ Juelich, D-52425 Juelich, Germany — [2]Department of Chemistry, Rice University, Houston, Texas 77005, USA — [3]Department of Chemistry, Imperial College London, SW7 2AY, London, UK

Searching and recognizing the targets by DNA binding proteins is one of the fundamental biological processes. Some proteins (e.g. the lac repressor) can find their targets 10-100 times faster than predicted by the 3D diffusion rate. However, recent single-molecule experiments showed that the 1D diffusion constants of protein motion along DNA are very small. This controversy pushed us to revisit the problem of target search. We present a theoretical approach which describes some physical-chemical aspects of the target search and DNA-protein recognition. We consider the search process as a sequence of cycles, with each cycle consisting of 3D and 1D track. It is argued that the search time contains three terms: for the motion on 3D, and 1D segments, as well as the correlation term. We show that the acceleration in search time can be reached by a parallel scanning for target by many proteins. Also, we show how the complementarity of charge patterns on a target DNA sequence and on the protein may result in electrostatic recognition of a specific track on DNA by the protein and lead to its subsequent pinning. We estimate the depth and width of the potential well near the recognition region and typical times proteins can spend in the well.