BP 10: DNA: supercoils, knots and melting

Time: Tuesday 14:00–15:45 Location: H43

Invited Talk BP 10.1 Tue 14:00 H43

Supercoils and their Removal — •Nynke Dekker — Molecular Biophysics Group, Kavli Institute of NanoScience Delft University of Technology, Lorentzweg 1, 2628 CJ Delft, The Netherlands

The intertwining of the DNA strands further ensures DNA integrity by physically linking the individual chains. However, this poses a number of topological problems during the cell cycle. For example, the progressive unwinding of the DNA template during DNA replication and the segregation of multiply intertwined daughter DNA molecules require changes in the linkage of DNA strands and helices. Similarly, RNA transcription can produce local unwinding of the DNA helix behind the transcription complex and local overwinding of the duplex ahead. Such excess local winding, termed supercoiling, influences a number of important cellular processes such as gene expression, initiation of DNA replication, binding kinetics of sequence-specific proteins to their targets, and site-specific recombination. The degree of supercoiling is consequently carefully controlled by the cell. We will examine the inherent dynamics of supercoil removal from a physical perspective using single-molecule techniques, and illustrate the importance of efficient removal by demonstrating how it is hampered under the influence of chemotherapeutic drugs.

BP 10.2 Tue 14:30 H43

Sequence-specific Topological Changes of Single DNA Molecules by Human Topoisomerase I in the Presence of Chemotherapeutic Drugs — •Fabian Czerwinski[1,2], Daniel Koster[1], Ludovic Halby[3], Ulrich Schwarz[2], Paola B. Arimondo[3], and Nynke H. Dekker[1] — [1]Kavli Institute of Nanoscience, Delft University of Technology, The Netherlands — [2]Center for Modelling and Simulation in Biosciences (BIOMS), Universität Heidelberg, Germany — [3]UMR5153 CNRS, Paris, France

Human topoisomerase I relaxes the superhelical tension associated with DNA replication, transcription and recombination by generating a transient nick in the DNA duplex. This allows the DNA to swivel about the intact strand before religating. Topoisomerase I is the sole target of the camptothecin family of anticancer compounds which stabilize the covalent enzyme-DNA complex and slow down the removal of DNA supercoils leading to lesions that can induce cell death.

Real-time activity of topoisomerase I can be monitored using magnetic tweezers. Combining these with camptothecin-associated triple-helix formation permits, for the first time, sequence-specific detection of the intercalation of single camptothecins to the enzyme-DNA complex. The imposed sequence-specificity allows repeated interrogation of a well-defined interaction, more clearly exposing the underlying biophysical processes. In the presence of a single camptothecin, the swivel rate is lower for the removal of positive supercoils than for negative ones, in agreement with in vivo experiments showing an accumulation of positive DNA supercoils in drug-treated cells.

BP 10.3 Tue 14:45 H43

Dynamics of Knotted Polymers in Nanochannels — •Wolfram Möbius[1], Erwin Frey[1], and Ulrich Gerland[2] — [1]Arnold-Sommerfeld-Zentrum für theoretische Physik, LMU München — [2]Institut für theoretische Physik, Universität zu Köln

We study the dynamics of knotted linear polymers in narrow channels with widths comparable to the polymer's persistence length. We use a combination of extensive Brownian dynamics simulations and simplified stochastic models to determine the modes of knot motion. In particular, we focus on the dynamics of knot motion along the polymer and the modes of changes in the knot's configuration. Both aspects of the dynamics can be understood within a coarse-grained stochastic model. The coarse-grained model describes our simulations quantitatively without any free parameters. Furthermore, we determine the modes of knot disassembly and the scaling behavior of the mean unknotting time as a function of the total polymer length for initially small knots.

BP 10.4 Tue 15:00 H43

Segregation of flexible polymers in confinement — •Axel Arnold — AMOLF, Amsterdam, Niederlande

During the cell replication cycle of a bacterium, it is necessary for it to replicate its DNA and separate the two resulting DNA strings such that exactly one string goes to each of the two daughter cells. It is commonly believed that a not yet detected active process has to be involved in this separation. However, scaling arguments show that the confinement of two polymers in a pore alone leads to an entropy-driven segregation which resembles an active process. Here, MD simulation results are presented which confirm the scaling predictions for the segregation time.

BP 10.5 Tue 15:15 H43

DNA melting curves in a snapshot — •Philipp Baaske and Dieter Braun — Ludwig Maximilians Universität München, Center for NanoScience, Amalienstr. 54, 80799 München

We developed a new method for measuring DNA melting curves. It combines fluorescence microscopy with laser based heating of aqueous solutions. The technique allows to measure the stability of DNA in only 150ms.

A IR-laser is focused to a microfluidic chamber (thickness 20 microns) and generates a spatial temperature distribution on the length-scale of several 100 microns. All temperatures between Tmax (e.g. 90°C) and Tmin (e.g. 20°C) are realized simultaneously. With a CCD camera two images of the fluorescence are taken: one without the laser and one with the laser switched on. From them a melting curve can be derived. The time of 150ms between the images is long enough for equilibration of the temperature and short enough to prevent thermophoresis from affecting the measurement. The state of doublestranded DNA is measured with the use of intercalating dyes and dye-quencher pairs.

In the case of doublestranded DNA the measurements are conducted in nonequlibrium because of the slow hybridization dynamics. For the fast intramolecular DNA hairpin kinetics the new technique compares well with state of the art measurements like uv absorption.

We show the possibility to discriminate single nucleotide polymorphisms (SNPs) in only 150ms, proving the use of an all optical technique for stability analysis of biomolecules.

BP 10.6 Tue 15:30 H43

Distribution of bubble lengths in DNA — •Saul Ares[1] and George Kalosakas[2] — [1]Max Planck Institute for the Physics of Complex Systems, Noethnitzer Str. 38, 01187 Dresden, Germany — [2]Department of Materials Science, University of Patras, 26504 Patras, Greece

The distribution of bubble lengths in double-stranded DNA is presented for segments of varying GC content, obtained using the Peyrard-Bishop-Dauxois model at 310 K. We provide an analytical description of the obtained distribution in the whole regime investigated, i.e. up to bubble widths of the order of tens of nanometers. The decay lengths and characteristic exponents of this distribution show two distinct regimes as a function of GC content. The observed distribution is attributed to the anharmonic interactions within base-pairs. Moreover, the same distribution is predicted by the completely independent Poland-Scheraga theory, and thus our results settles a bridge between these two different theoretical descriptions of DNA.