DNA and chromatin dynamics studied by single molecule methods and computer modeling

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The organization of the genome in the cell nucleus is fundamental for cellular function: transcription and its regulation, genome duplication, epigenetic effects and chromosome folding are all intricately connected to genome architecture. On the lowest level of genome organization, DNA folding is determined by its bending and twisting properties; superhelical DNA is a well-known model system to study these properties. Recent experiments by fluorescence correlation spectroscopy (Shusterman et al., (1008) Phys Rev Lett. **100**:098102) suggest that the internal dynamics of DNA strongly depend on its superhelical state. Using a Brownian Dynamics model of DNA, we have attempted to identify the basis for these observations by modeling the Brownian motion of a fluorophore attached to the DNA in the focus of a confocal setup. The results suggest that translational diffusion by itself cannot explain the dependence of the dynamics on supercoiling. Possible explanations such as rotational dynamics of the fluorophore or changes in DNA twisting dynamics will be discussed.
The next level of genome organization is the association of DNA with histones to form nucleosomes and the chromatin chain. I will present recent simulations of nucleosome internal dynamics using a new coarse-grained model that allows computing trajectories of the nucleosome over tens of microseconds. These simulations show histone-tail-dependent opening dynamics of the linker DNA arms. Further insight into nucleosome opening is obtained from Brownian dynamics simulations of force-induced DNA unrolling, which describe quantitatively the force-extension curves from single-molecule pulling experiments and can be used to estimate the binding energy of DNA to the histone core.