Project C1.2: Conformational transitions of polynucleic acids and peptides within ultraliquid films

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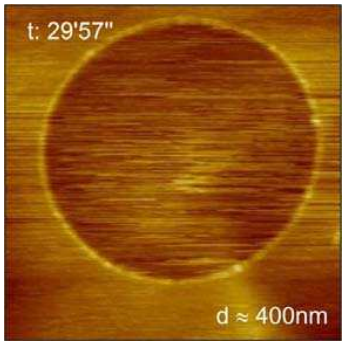
Outline. The interaction of macromolecules with interfaces often leads to conformational changes of these molecules. For example, flexible polyelectrolytes such as poly(styrene sulfonate) may be stretched out perfectly on a nanostructured molecular monolayer of amphiphiles (*Nano Lett.* **6** (2006) 1018), and the adsorption of amyloid *β*-peptides ((A*β*) peptides) to a water/vapor interface changes the secondary structure and aggregation behavior of the peptide. *Notabene*, soluble oligomers of Aß were shown to cause neuronal loss and to interfere with the normal function of synapses. They were described to be neurotoxic and to cause cognitive deficits long before amyloid plaques are detectable. Finally, plasmid DNA molecules embedded within ultrathin liquid films on the basal plane of graphite may be blown into perfect circles, overstretched to almost twice their B-form length (see Fig.), and finally broken (*Nano Lett.* **6** (2006) 2561). This constitutes a completely new approach to manipulate single macromolecules, since it allows to apply a static stress for a long time, and, moreover, to determine the moecular conformation in detail as a function of the applied stress.



SFM image of overstretched Plasmid-DNA ring within ultrathin liquid layer of alkylated amines

Research within the German group. Conformational transitions and early stages of aggregation of single amyloid *β* (A*β)* peptides shall be investigated on various amphiphilic monolayers self-assembled on the basal plane of highly oriented pyrolytic graphite, where the variation of the headgroup charge will be used to mimic cationic proteins in neuronal membranes. Plasmid DNA in its neat form, as well as specifically complexed with proteins shall be embedded within ultrathin liquid films on highly oriented pyrolytic graphite. Scanning force microscopy manipulation shall be employed to stretch, overstretch, and finally break the DNA, while the proteins are used as markers of certain DNA sequences. Of particular interest is the control over the unravelling of supercoiled DNA, since this requires a 3D-motion above a solid substrate.

Complementary work in US partner group. The mechanical properties of individual DNA molecules are of paramount importance for their behaviour in confined geometries, i.e. for their threading through small holes, which is a research subject in the Riehn-group. The Berkowitz group, on the other hand, is interested in the coil-helix transition of A*β* upon adsorption to cationic lipid monolayers. Their simulation work will complement the experimental work within this project and also the modelling within project C1.1 (Knecht).

Status of the project. This project pertains to project area C.1 in which biomolecules at interfaces will be studied. It will be carried out in close collaboration with project C1.1 (Knecht), which carries out MD simulations on the conformational transitions in A*β*, and project C2.3 (Hildebrandt), where protein interactions with nanostructures model membranes will be investigated.