



IMPRS UFAST Call for PhD applications 2022/2023



AP1- Project Title: Imaging the molecular dynamics of DNA single molecules confined in nanochannels

Title of PhD Project	Imaging the molecular dynamics of DNA single molecules confined in nanochannels
Type	Experimental
Supervisor(s)	Prof. Arwen Ruth Pearson Dr. Irene Fernandez-Cuesta
Affiliation(s):	UHH
Number of positions:	1
Abstract:	Next-generation DNA sequencing techniques will open the door for a revolution in medicine. Many of them (like nanopore or nanochannel-based sequencing) rely on single-molecule analysis. Here, the molecular conformation of the confined DNA plays a fundamental role, affecting the quality, speed, throughput and resolution of the technique. Still, there are no studies where the DNA molecules have been <i>directly imaged</i> in such confined spaces with enough resolution to observe the molecular conformation inside (stretched/Odjik regime, with isolated hairpins, partially coiled in blobs/de Gennes regime, etc). Here, we want push our expertise in flowing DNA in nanochannels to go further: we will flow DNA in suspended nanochannels and image the molecules with high resolution techniques. We will use cryo-EM to observe the molecular conformation in different nano-spaces with resolutions below 10nm. In addition, SAXS will be used as a complementary technique, to help in the reconstruction of the molecular structure. Furthermore, we will also study the dynamic behavior of the DNA: uncoiling mechanisms when transitioning from micro to nano spaces, recoiling from nano to micro, and how the topography and ionic strength play a role. For this we will use the nanochannel-devices as environmental liquid-cells for TEM, to observe the dynamics of the molecular flow with resolutions in the order of 50 to 100 nm. All these findings are essential not only to understand the fundamental mechanical-dynamic properties of DNA in confined spaces, but also to push DNA analysis technology forward.
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