Fully Streched Single DNA Molecules in a Nanofluidic Chip Show Large-Scale Structural Variation

When stretching and imaging DNA molecules in nanofluidic devices, it is important to know the relation between the physical length as measured in the lab and the distance along the contour of the DNA. Here a single DNA molecule longer than 1 Mbp is loaded into a nanofluidic device consisting of two crossing nanoslits (85nm x 50 microns) connected to microchannels. An applied pressure creates a stagnation point at the crossing of the nanoslits. The drag force from the fluid stretches the DNA. We determine the degree of stretching of the molecule (i) without the use of markers, (ii) without knowing the contour length of the DNA, and (iii) without having the full DNA molecule inside the field-of-view. The analysis is based on the transverse motion of the DNA due its Brownian motion, i.e. the DNA's response to the thermal fluctuations of the liquid surrounding it. The parameter values obtained by fitting agree well with values we obtain from simplified modeling of the DNA as a cylinder in a parallel flow. Secondly, DNA molecules stained with the intercalating dye YOYO-1 are de- and renatured locally following a modified version of the protocol used in Ref. 1. The result is a melting pattern which reflects the local AT/GC-content. Single molecules are loaded into the chip and imaged. Due to the almost complete stretching of the DNA, structural variations in the size range from kbp to Mbp can be detected and quantified from the melting pattern alone.
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