Study of single λ-DNA molecule stretching based on microfluidic devices

Adnane Noual, Tim Humphreys, Peter Horak, and Tracy Melvin

Optoelectronics Research Centre, University of Southampton, Southampton SO17 1BJ, U.K.

Abstract:

Microfluidic devices are playing an increasingly important role in the manipulation of DNA-molecules for bio-medical analysis, and several micro-channels and designs have been proposed to achieve certain functionalities such as DNA-stretching and separation [1]-[2]. DNA-stretching is of paramount importance for genomic analysis as DNA mapping techniques require DNA molecules to be in a linearly stretched configuration, while in their relaxed state DNA strands tend to be in a coiled up state. Several methods to uncoil and stretch DNA based on fluid flow for use in single DNA-molecule mapping have been developed [3]-[4]. In this work, we report numerical simulations based upon computational fluid dynamics (CFD) and Brownian Dynamics (BD) [5]-[7] for the study of single λ-DNA molecule-stretching, undergoing pressure-driven flow. Our theoretical approach to describe the behaviour of the flowing DNA is based on the so-called 'coarse-grained' models [8]-[9]. The developed theory is to be eventually used to guide/optimise the design of microfluidic channel shapes for fabrication. However this theoretical approach is currently being applied to channel designs where experimental data already exists. First a straight micro-channel (30um wide) was evaluated theoretically; we demonstrated that the mean steady state stretch (ensemble average) is reached with a propagation time of ~0.5s, which corresponds to ~5mm channel length (for a maximal fluid velocity of 0.01m/s in the centre-line). We show, in particular, that once the equilibrium stretch (~45% of the ~21μm λ-DNA contour length) is achieved, the initial conditions such as the transverse input distribution or location as well as configuration of the input molecules have no further effect with respect to DNA stretching. Finally, we investigate the effect of several micro-channel shapes (incl. serpentines of 30 μm width) on DNA dynamics/stretching. Such serpentine microfluidic channels have already been demonstrated for focusing and ordering of polystyrene microspheres [10]. Indeed, experimental data obtained within my group already suggests that unravelling and stretching of long genomic DNA sequences is possible within microfluidic structures. It is envisaged that these types of microfluidic structures could become very important for emerging DNA sequence analysis applications.

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