Unravelling single long double-stranded DNA molecules in microflows for optical interrogation

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The application of microflows to deliver controllable forces at the micrometre scale on long polymeric molecules identifies microfluidic devices as an attractive tool for non-contact manipulation and delivery to confined channels for optical interrogation [1]. As demonstrated, long genomic DNA molecules stretched by shear and 'elongational' microflows are suitable for genome mapping analysis [2]. Nanosized channels provide an attractive approach for confining single long genomic fragments for optical interrogation [3]. Unfortunately, the delivery of DNA molecules into a nano-sized entry/pore is not efficient.

We investigate the potential for unravelling and stretching of DNA based upon the shear forces present under the pressure-driven laminar flow conditions inside a microchannel of dimensions comparable to the length of the DNA. We fabricated a series of shaped and straight channels [4] and evaluated the extension length of λ-DNA molecules at the exit of the flow. It was shown that the coiling up of the DNA strands is mitigated in the curved microfluidic channels.

To understand the mechanism behind this improvement we performed numerical simulations combining a computational fluid dynamics (CFD) model of the microchannel with Brownian dynamics of a coarse-grain model of λ-DNA molecules. A comparison of the simulation results for a serpentine channel with those of a straight channel supports the experimentally found improvement of DNA stretching in the former (Figure 1).

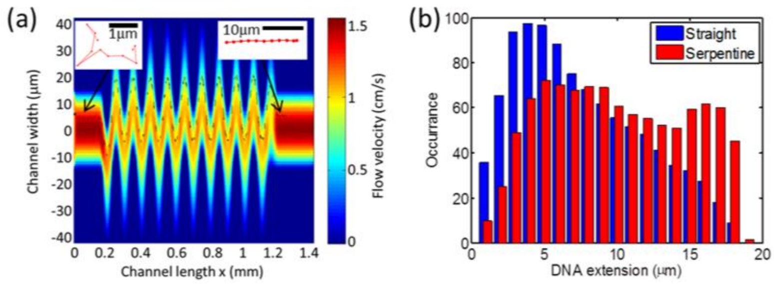

Fig1. (a) Flow velocity profile on a serpentine channel with a simulation of DNA dynamics. Insets show the shape of DNA before and after the channel. (b) Extension distribution of single λ-DNA molecules after 1.4 mm straight and serpentine channels (1000 simulations each).

A detailed analysis of the DNA dynamics suggested that the elastic molecular forces opposing the stretching of the molecule are pulling the DNA out of the central flow line towards the inside of a microchannel bend and thus into regions of larger shear forces. To confirm our simulation results, practical studies have been recently performed; a bespoke microscope system was built for efficient detection of DNA molecules labelled with fluorescent intercalators travelling within different regions of microfabricated microfluidic devices and will be discussed.

References

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