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LAB-ON-CHIP FOR DNA ANALYSIS WITH LOW RESOLUTION LENGTH AND CONCENTRATION

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The performances of microfluidic systems based on viscoelastic fluids for particle or molecule separation are increasing rapidly, thus raising interest for biological and chemical analysis [1]. We recently reported that the operations of DNA separation and concentration could be performed on-line using electro-hydrodynamic bidirectional actuation in microfluidic channels containing viscoelastic fluids [2] such as polyvinyl pyrrolidone (PVP) or polyethylene glycol (PEG). So far, we proved the relevance of this technology for the processing of DNA molecules larger than ~100-200 bp, and we report here the optimization of the geometry of the channels as well as the constitution of the viscoelastic matrix to achieve fast sample analysis (up to 1 μ L/min) and low Resolution Length (RSL) for high performance separation [3].

For this study, we designed microfluidic chips in silicon with one constriction and two channel profiles, a reference linear shape compared to e.g. a polynomial profile (Fig. 1A). A viscoelastic fluid containing the fluorophore-labeled DNA or RNA at a typical concentration of 50 nM is introduced into the chip. The flow can be oriented in either direction of the funnel-shaped region with an opposing electric field that stops the molecules at a position that depends on their molecular weights [2]. Fluorescence videos/images are collected during typical acquisition times of 30 s (Fig. 1B-C), and then analyzed to extract the resolution and RSL to define the optimal set of experimental conditions (Fig. 1D-E).

After careful improvement of the viscoelastic solution, we confirmed our previous results that the linear profile does not allow the separation of DNA fragments smaller than 200 bp (Fig. 1D). The RSL for fragments of 500-600 bp and 800-1000 bp is to be 20 and 25 bp, respectively. The constriction with a power-law geometry yielded better resolution, especially for low molecular weight samples with a clear separation of fragments down to 50 bp (Fig. 1E). After careful improvement of the viscoelastic solution, which shows that low molecular weight polymers enable better separations, we confirmed our previous results that the linear profile does not allow the separation of DNA fragments smaller than 200 bp (Fig. 1D). The RSL for fragments of 500-600 bp and 600-800 bp is 50 and 33 bp, respectively. The constriction with a power-law geometry yielded better resolution, especially for low molecular weight samples with a clear separation, especially for low molecular weight samples better resolution, especially for low molecular weight a power-law geometry yielded better resolution, especially for low molecular weight samples with a clear separation of 10 reaching 6 bp.

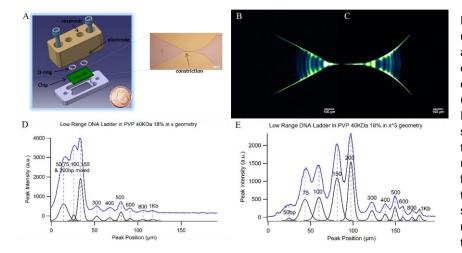


Fig. 1 : DNA separation and enrichment using electro-hydrodynamic actuation in a viscoelastic fluid. (A) Drawing of the device containing a glass bonded silicon chip comprising two different geometries (bright field image). (B) and (C) Low Range DNA ladder enrichment and separation in PVP 40 KDa 18% (wt%) in the linear and power-law geometries respectively. (D) and (E) Graphs showing fluorescence intensity distribution along the symmetry axis of the constriction shown in (B) and (C) respectively. The numbers above the peaks correspond to the sizes of the different ladder bands.

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