Bidirectional flow filter: high-purity filtration of biomolecules in low-sample volumes using electrically driven microfluidics

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The analysis of small samples volumes is boosting the field of life and medical science, from basic research on single-cell systems, through point-of-care diagnostics, to forensic analysis. Despite great advances made on analytical techniques such as digital immunoassay, nanopore detection and next-generation sequencing, little progress has been made on low-volume sample preparation technologies, which are key for the success of such analytical techniques.

Recently we developed a low-volume separation method, termed bidirectional flow filter (BFF), which utilizes microscale bidirectional flow, i.e. adjacent streams with velocities in opposite directions, to separate species based on their diffusivities. High diffusivity species introduced into the inlet of a bidirectional flow device experience a net zero velocity and therefore penetrate into the channel only by molecular diffusion, while low diffusivity species are advected downstream by the outgoing flow (Fig. 1a). The BFF can be used as sample-preparation step to selectively separate a mixture of species based on their diffusivity. As proof of concept, we used the BFF to purify genomic DNA from short DNA strands (Fig. 1b-c) and we analyzed the retrieved solution using loop-mediated isothermal amplification (LAMP), to show the presence of the long DNA and the absence of the short DNA.

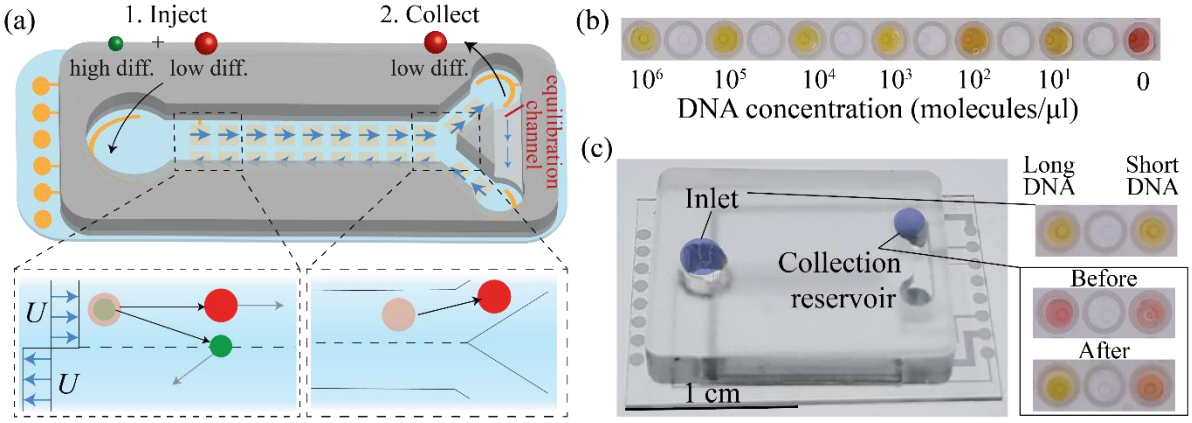

Fig. 1. (a) Working principle of the bidirectional flow filter (BFF). The sample containing low- and high-diffusivity species is injected in a microfluid chip with established bidirectional flow generated by an array of gate electrodes. High-diffusivity species (green) rapidly sample different streamlines thus experiencing a net-zero velocity, while low-diffusivity species (red) maintain their advection trajectory toward the collection reservoir (top right outlet) where they can be extracted. (b-c) Demonstration of DNA separation and extraction using the BFF. (b) Calibration of the colorimetric LAMP reaction: yellow for DNA concentration above 10 molecules/µ, and pink/red for absence of DNA. (c) LAMP showing DNA purification. Inlet: the presence of long and short DNA fragments is confirmed by a positive LAMP (yellow); Collection reservoir: initially the reservoir shows no DNA presence (pink for both DNA lengths) whereas after the LAMP shows the presence of only the long DNA.