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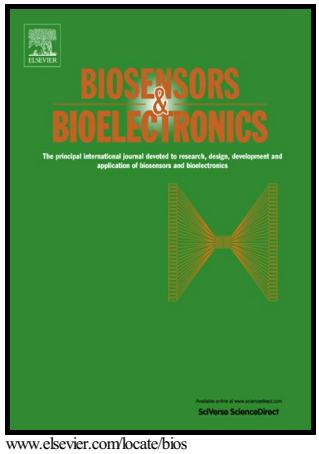

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Microfluidic magnetic fluidized bed for DNA analysis in continuous flow mode

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Abstract:

Magnetic solid phase substrates for biomolecule manipulation have become a valuable tool for simplification and automation of molecular biology protocols. However, the handling of magnetic particles inside microfluidic chips for miniaturized assays is often challenging due to inefficient mixing, aggregation, and the advanced instrumentation required for effective actuation. Here, we describe the use of a microfluidic magnetic fluidized bed approach that enables dynamic, highly efficient and simplified magnetic bead actuation for DNA analysis in a continuous flow platform with minimal technical requirements. We evaluate the performance of this approach by testing the efficiency of individual steps of a DNA assay based on padlock probes and rolling circle amplification. This assay comprises common nucleic acid analysis principles, such as hybridization, ligation, amplification and restriction digestion. We obtained efficiencies of up to 90% for these reactions with high throughput processing up to 120 μL of DNA dilution at flow rates ranging from 1-5 μL/min without compromising performance. The fluidized bed was 20-50% more efficient than a commercially available solution for microfluidic manipulation of magnetic beads. Moreover, to demonstrate the potential of this approach for integration into micro-total analysis systems, we optimized the production of a low-cost polymer based microarray and tested its analytical performance for integrated single-molecule digital read-out. Finally, we provide the proof-of-concept for a single-chamber microfluidic chip that combines the fluidized bed with the polymer microarray for a highly simplified and integrated magnetic bead-based DNA analyzer, with potential applications in diagnostics.

Key words:

[1] *Authors contributed equally to this work*