

## Microfluidic Capillary Electrophoresis for In-line Dual-stage Enrichment and Unattended Sampling: From Instrumental Conception to Bioanalytical Applications

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### Summary

In bioanalysis with capillary electrophoresis (CE), we often encounter the challenges of insufficient detection sensitivity (e.g. for detection of biomarkers in biological matrices) and real-time monitoring of target molecules in biological fluids. To address these challenges, we report herein the development of new microfluidic CE setups for i) in-line dual enrichment stages to boost the detection performance in CE and ii) automatic sampling and monitoring of the analyte concentrations from a continuous micro-flow. With the dual-enrichment stages, two completely different preconcentration approaches can be realized in the same capillary, without any loss of pretreated samples. In the first stage, a dynamic magneto-extraction of target analytes on circulating magnetic beads is implemented within the capillary. Then, electrokinetic preconcentration of eluted analytes via large volume sample stacking is carried out to focus them into a nano band, prior to CE separation of enriched analytes. For this purpose, the movement of magnetic beads and analyte's flow inside the capillary was precisely controlled with different push-pull pressure / vacuum controllers and valves that are conventionally employed for microfluidics. Magnetic fields were generated via different magnetic tweezers set along the capillary to allow capture and release of magnetic beads containing enriched analytes. The developed enrichment principle and its associated instrument were demonstrated for CE separation of target double-stranded DNA, with enrichment factors of up to 125. Different ways to integrate the microfluidic CE system with a novel lab-on-valve setup to allow automatic sampling from a continuous flow and analyte separation without any manual intervention are under investigation.