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# Optimal configuration of capillary electrophoresis microchip with expansion chamber in separation channel

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**Abstract**

This study develops a novel capillary electrophoresis (CE) microfluidic device featuring a conventional cross-form injection system and an expansion chamber located at the inlet of the separation channel. The combined injection system/expansion chamber arrangement is designed to deliver a high-quality sample band into the separation channel such that the detection performance of the device is enhanced. Numerical simulations are performed to investigate the electrokinetic transport processes in the microfluidic device and to establish the optimal configuration of the expansion chamber. The results indicate that an expansion chamber with an expansion ratio of 2.5 and an expansion length of 500 μm delivers a sample plug with the correct shape and orientation. With this particular configuration, the peak intensities of the sample are sharp and clearly distinguishable in the detection region of the separation channel. Therefore, this configuration is well suited for capillary electrophoresis applications which require a highly sensitive resolution of the sample plug. The novel CE microfluidic device developed in this study has an exciting potential for use in high-performance, high-throughput chemical analysis applications and in many other applications throughout the field of micro-total-analysis-systems.


*Keywords:* Injection system; Expansion chamber; Capillary electrophoresis; Micro-total-analysis-systems

## 1. Introduction

The emergence of microfluidic chip-based capillary electrophoresis (CE) devices has revolutionized the manner in which chemical and biological assays are performed [1–5]. The advantages of these devices include a smaller sample size, an improved analytical performance, a more rapid response time, the ability to integrate multiple processes on a single device, a higher throughput, the possibility to perform parallel analyses, and reduced cost. Current micromachining technology now enables a series of micro-total-analysis-system devices to be fabricated on a single substrate of glass, quartz or plastic poly(dimethylsiloxane) (PDMS), polycarbonate (PC), poly(methylmethacrylate) (PMMA)). Typically, these devices feature a number of different functional units, including sample handlers, separators, mixers, chemical reaction chambers, pretreatment chambers, collectors, filters, sorters, preconcentrators, cytometers, and on-line detection arrangements, etc. [6–9]. In a concept commonly referred to as "lab-on-a-chip", combinations of these functional components are integrated serially on a single microchip in order to carry out the complete assay of a material [10–12].

Developing a thorough understanding of the mechanisms governing electrokinetic manipulations, particularly those associated with discrete injections and separations, is essential when seeking to optimize the design of compact microchips. Many experimental and theoretical studies have been performed to investigate the sample transport phenomena in microfluidic chips. Seiler et al. [13] integrated sample injection and separation systems in a CE microchip fabricated on a planar glass chip. The authors demonstrated the feasibility of using electrokinetic pumping to drive the sample through the microchip and confirmed the ability of the glass-based CE microchip to carry out the successful electrophoretic separation of the sample. Effenhauser et al. [14] employed double-T injectors to perform the high-speed separation of antisense oligonucleotides in a

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microfluidic CE device on a glass substrate using electroosmotic forces to inject the sample.

The injector designs in traditional microfluidic devices were based on the floating sample introduction method, in which voltages were applied only to the sample/sample waste channels during injection, leaving the buffer/separation channels to float, and only to the buffer/separation channels during separation, leaving the sample/sample waste channels to float [15–19]. Crabtree et al. [20] found that slight pressure gradients at the reservoirs caused sample distortion and led to sample leakage from the upper and lower microchannels after several runs. The authors reported that this phenomenon reduced the detection performance of the device. Fu and co-workers [21–24] identified severe sample leakage in the floating sample injection method when high voltage gradients were established. It was found that the sample leakage effect increased the signal baseline as the number of injection runs increased and reduced the separation efficiency as a result. Consequently, the authors developed a low-leakage injection technique designed specifically to improve the detection performance of microfluidic devices. Various pinched and gated [25–32] sample introduction protocols have been proposed to limit the leakage effect induced in the floating sample injection method. Slentz et al. [25] investigated the sampling bias caused by differences in analyte turning in gated injections. Sinton and co-workers [26,27] proposed a three-step technique for discrete sample injections in straight-cross microfluidic chips. Ermakov et al. [28,29] performed computer simulations to investigate the effects of electrokinetic focusing at the intersection of the sample/buffer inlet channels and the separation channel and established the optimal voltage parameters for pinched and grated injections. Other studies focused on the sample bias caused by the pinched and gated injection methods. For example, Jacobson and co-workers [30–32] addressed pinched injections. This technique is a variation on the conventional pinched valve injection with the addition of an intermediate dynamic injection step, in which the sample is pumped directly into the intersection and three connecting channels.

Hydrodynamic pumping injection has been considered as a means of reducing electrokinetic bias. Bai et al. [33] investigated pressure-driven pinched injections using syringe pumps for microfluidic devices and successfully applied the method to sample injections in capillary zone electrophoresis chips. This injection method is particularly suitable for the injection of complex biological samples in microchip-based analyses. Solignac and Gijs [34] used a flexible membrane to apply a pressure pulse to the sample inlet while performing electrokinetic injections in a cross-form intersection device in an attempt to reduce the electrokinetic bias. Baldock et al. [35] presented a variable volume injector for sample delivery in a miniaturized isotachophoretic device based on hydrodynamic pumping in the injector and electrokinetic pumping in the separator. Implementing a U-shaped injection channel angled at 45° in a syringe pump-based sample handling system was found to improve the resolution of the injected zones.

The separation microchannel of a microfabricated electrophoresis microchip is generally designed within a compact area. Recent studies have proposed the use of serpentine microchannels as a means of increasing the separation efficiency, reducing the manufacturing cost, and supporting product miniaturization. Jacobson and Hergenroden [36] performed experimental and theoretical investigations into band traverses in a U-shaped channel. A theoretical resolution analysis of chip-based separations was presented and the band broadening effect observed in the turns was linked directly to the angle of the turn and the width of the separation channel. Culbertson and Jacobson [37] demonstrated that constant radius corners increase the sample dispersion flow in electrokinetic microchannels and therefore offset the benefit provided by the additional separation length. The stretching of an analytical band as it traverses a turn is commonly referred to as the racetrack effect. Fu and co-workers [38,40], Paegel et al. [39] performed theoretical and experimental investigations into band traverses in a folded square U-shaped channel. The authors concluded that band tilting in the detection area was corrected, and the racetrack effect reduced, when the bend ratio (defined as the ratio of the microchannel width in the separation portion to the width in the turn portion) was 4:1. Griffiths and Nilson [41–43] used numerical methods to optimize the geometry of two-dimensional microchannel turns and designed the multi-folded channels such that the turn-induced spreading of the solute band was minimized. Molho et al. [44] used a simulation approach to design and evaluate a novel compensating corner geometry designed to reduce the racetrack effect in the serpentine electrophoretic separation channels of a microchip. Ramsey et al. [45] used Geiffiths's result to carry out a high-efficiency, two-dimensional separation of protein digests on a lab-on-a-chip microfluidic device.

Achieving high-resolution detection results in a chip-based microfluidic device requires that the sample bands injected into the separation channel be of the correct shape and orientation. Therefore, this study develops an integrated microfluidic device which combines a cross-form injection system with an expansion chamber at the inlet of the separation channel to deliver high-quality sample bands into the separation channel. Fig. 1 presents a schematic illustration of the proposed CE microchip. This paper provides a detailed description of the proposed high-resolution separation technique and adopts a numerical approach to evaluate the performance of the microfluidic device with different expansion chamber configurations. It will be shown that the high-quality sample bands delivered into the separation channel through the expansion chamber with the optimal configuration significantly improve the detection resolution of

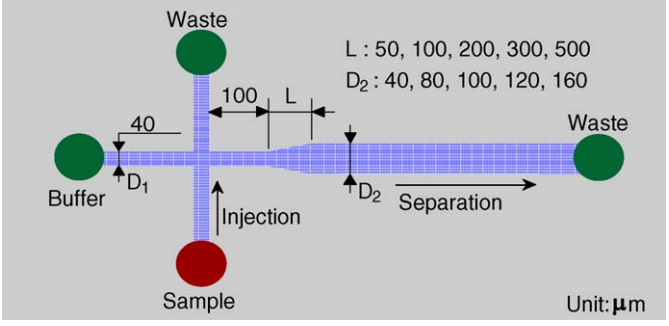


Fig. 1. Schematic illustration of proposed capillary electrophoresis microchip.