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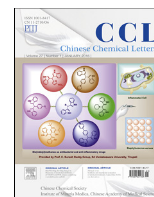

Original article

Open channel-based microchip electrophoresis interfaced with mass spectrometry *via* electrostatic spray ionization

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ABSTRACT

The coupling between open channel-based microchip electrophoresis and mass spectrometry *via* electrostatic spray ionization is proposed for *in situ* detection of fractionated analytes. Electrophoretic separation is performed in an open channel fabricated in a plastic substrate. The solvent of background electrolyte is evaporated from the open channel because of Joule heating during electrophoresis, leaving the dried electrophoretic bands to be directly analyzed by mass spectrometry *via* scanning electrostatic spray ionization. Proof-of-concept results are obtained with fluorescent dyes and antibiotics as the test samples, demonstrating an efficient on-chip detection platform based on the electrophoresis and electrostatic spray ionization mass spectrometry.

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1. Introduction

Microfludic system has been recently reported as an interface between liquid chromatography and mass spectrometry (MS) hyphenation for online protein digestion [1] and enrichment [2]. It also provides an attractive concept for the online coupling of electrophoresis and MS by incorporating the miniaturized microchips into commercial electrospray ionization (ESI)-MS instruments [3]. Alternatively, the microchip electrophoresis can be hyphenated offline with matrix-assisted laser desorption/ionization (MALDI)-MS by collecting the fractionated samples in a rotating ball inlet [4] of MALDI source, or introducing the separated samples to MALDI chamber through on-chip "monitoring windows" [5]. Furthermore, electrophoresis has been reported to be performed in completely open channels [6], closed-open-closed channels [7], or pseudo-closed channels with removable covers [8] for subsequent offline MALDI-MS detection.

Recently, a new ambient ionization strategy, namely electrostatic spray ionization (ESTASI), has been presented for the *in situ* generation of molecular ions from samples deposited on an insulating surface [9]. It features the screening of dried samples under ambient conditions, showing great flexibility for MS-based

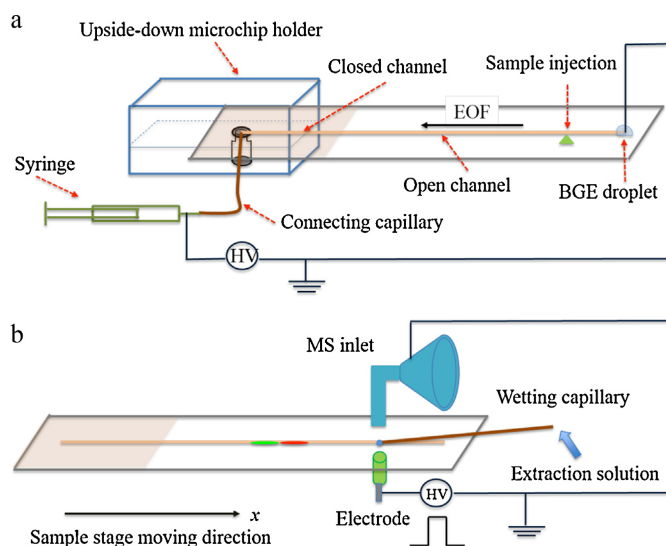

Fig. 1. Schematic representation of (a) open channel-based microchip electrophoresis and (b) ESTASI-MS scanning of the open channel. EOF: electroosmotic flow; HV: high voltage.

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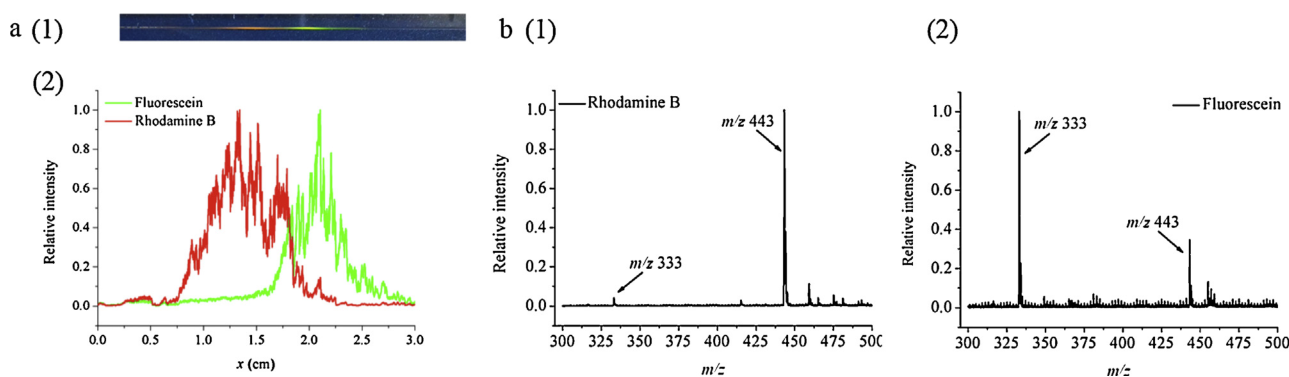

Fig. 2. (a) Bands of fluorescent dyes (0.5 mg/mL fluorescein, and 0.1 mg/mL RhB) by open channel-based microchip electrophoretic separation with digital camera imaging under UV excitation at 254 nm (1) and electropherogram from *in situ* scanning ESTASI-MS (2). (b) Mass spectra of RhB obtained at $x = 1.32$ cm (1) and fluorescein at $x = 2.09$ cm (2).

chemical and biochemical analysis. As an attractive alternative to MALDI for the offline coupling of MS with electrophoresis, ESTASI has been reported for the ionization of isoelectric focusing electrophoretic bands in polyacrylamide gels [10]. Herein, ESTASI is further proposed for *in situ* ionization and detection of dried electrophoretic bands obtained in open channel.

2. Experimental

Information about the chemicals and materials, as well as the microchip fabrication procedure, is included in Supporting information. Open channel based microchip electrophoresis was performed for two fluorescent dyes as illustrated in Fig. 1a to optimize experimental conditions. After the electrophoretic separation and solvent evaporation, dried fractions formed in the open channel were *in situ* ionized by ESTASI, as schematically shown in Fig. 1b. Electrophoretic separation and MS detection of antibiotics was afterwards carried out with the same protocol for further proof-of-concept. More details about the experimental procedure can be found in Supporting information.

3. Results and discussion

The optimization of conditions for the microchip electrophoresis and ESTASI-MS detection is in the Supporting information. Glycerol was employed to reduce the longitudinal diffusion of electrophoretic bands during solvent evaporation in the open channel. The electrophoretic bands of fluorescent dyes obtained under optimized separation conditions were imaged by a digital camera (Fig. 2a (1)), and analyzed by *in situ* ESTASI-MS to generate the electropherogram (Fig. 2a (2)). The MS peak intensities for rhodamine B (RhB) and fluorescein were normalized, respectively, and plotted as a function of position in the microchannel. The wide electrophoretic bands in both detection modes were attributed to the sample overloading in order to make the dyes easily visible under UV excitation. Compared with those in Fig. 2a (1), the peak widths in the extracted ion electropherogram were slightly broadened, possibly resulted from the increased mobility of glycerol under the high temperature of the ionization source. A less important factor was contributed to the delayed detection in offline hyphenation. However, its influence on the band broadening is almost negligible because of the very high viscosity of glycerol under room temperature. The channel with fractionated sample in glycerol can be stored under 4 °C for long term.

Fig. 2b presents the mass spectra extracted from the electropherogram. At $x = 1.32$ cm, the migration distance of RhB, the mass spectrum demonstrates a very strong peak of RhB with a tiny peak of fluorescein. In contrast, at $x = 2.09$ cm, the peak of fluorescein is predominant, while RhB still produces a peak with noticeable signal-to-noise ratio (S/N) due to its higher ionization efficiency. All in all, open channel microchip electrophoresis and ESTASI-MS experiments performed for fluorescent dyes demonstrate the *in situ* detection of electrophoretic bands by MS, which was further proven by the proof-of-concept results obtained with antibiotic mixture as the test sample (Fig. S2 in Supporting information).

4. Conclusion

A novel interface between open channel-based microchip electrophoresis and MS is developed *via* ESTASI. In contrast with the prevalent offline coupling of CE to MALDI-MS based on CE effluent collection, the main characteristic of the proposed interface is the *in situ* ionization and detection of electrophoretic bands. Remaining challenges lie in the loss of the separation resolution and detection sensitivity, which could be further improved by applying narrow channel or highly efficient electrophoretic mode. Nevertheless, the proposed new interface can be potentially applied for two-dimension scanning of microarray-based high throughput electrophoresis.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.cclet.2015.09.017.

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