Microchip ESI Source for Capillary Electrophoresis Time-of-Flight Mass Spectrometry

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We have developed a microchip device that integrates capillary electrophoresis (CE) and electrospray ionization (ESI). The device has been coupled to a time-of-flight mass spectrometer (TOFMS), and the system was evaluated for sensitive on-line detection of high speed peptide and protein separations. The structure consists of microfabricated channels, where samples are introduced and separations effected, and a fine fused silica capillary where the electrospray is established.

Two basic configurations were developed, both being able to promote stable electrospray operation using electrokinetic transport. Different alternatives for application of the electrospray voltage were examined, with preference given to an on-chip electrically permeable porous glass membrane configuration. The capillaries inserted at the exit end of the separation channel were either blunt-cut fine fused silica capillaries, or commercially available nanospray tips, the latter ones being capable of promoting a stable spray at flow rates as low as 20 to 30 nL/min. Operation for several hours was achieved, with relative standard deviations of 4-6 % of the monitored ion intensity. The effect of the capillary-chip junction on separation efficiency was also examined. Designs that provided the highest performance in terms of reliability and sensitivity, practicability for chip manufacture, and suitability for integration with microchip CE separations will be discussed.

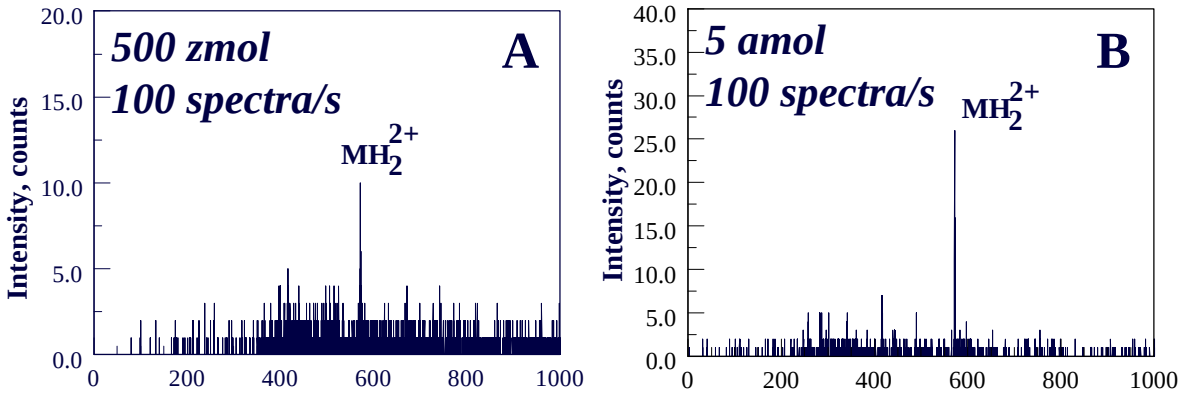

Figure 1. Microchip-nano-ESI-TOF mass spectra of gramicidin S. (A) 0.1 μM; (B) 1 μM solution. TOFMS acquisition: 5000 Hz, 50 summed spectra.

TOFMS detection with high speed data acquisition and storage rates of 50 to 100 spectra/s enabled sub-attomole quantities of compounds from low nanomolar concentration samples to be detected when using the microchip-nano-ESI configuration (Figure 1). Fast, on-chip protein digestion monitoring, with direct spraying from basic and acidic buffer systems, was possible using this device. Unlike conventional nanospray sources, however, the microchip coupled to the nanospray tip can be used to inject discrete samples and perform separations prior to detection (Figure 2). This is a desirable option not only when capillary electrophoresis (CE) injection/separations are considered, but also if the device is viewed as part of a fully integrated system used for high throughput analysis of multiple mixtures, which are amenable to analysis by infusion experiments, and do not necessitate a separation step prior to detection. The overall simplicity and ease-of-operation of the hybrid microchip nanospray source rank it favorable in comparison to previously reported microchip ESI devices.

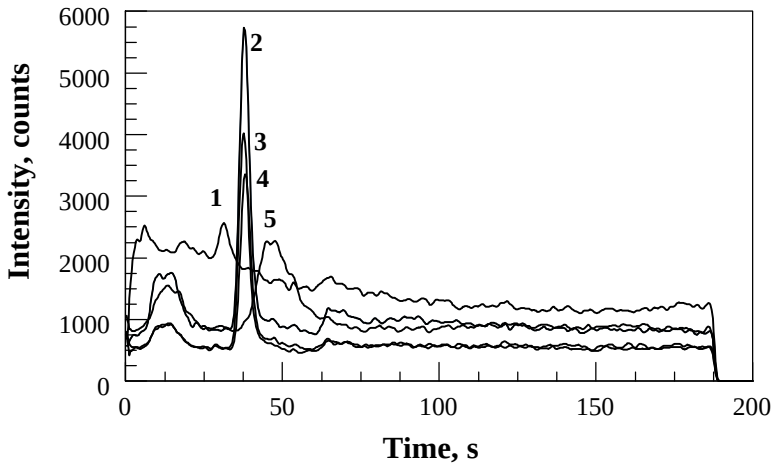

Figure 2. Microchip CE-TOFMS of a peptide mixture. Conditions: peptides (10 μM); $CH_3OH/H_2O/CH_3COOH$ (50:50:0.3 v/v) eluent; 0.2 s injection; 300 V cm^{-1} field strength in separation channel; TOFMS acquisition: 3.1 spectra/s; Peak identifications: (1) bradykinin, (2) rhodamine B, (3) leucine enkephalin, (4) methionine enkephalin, (5) gramicidin S.

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