



Microchip Electrospray Emitters for Stable Cone-Jet Mode Operation in the Nano-Flow Regime

Ryan T. Kelly¹, Keqi Tang¹, Daniel Irimia², Mehmet Toner² and Richard D. Smith¹

¹Biological Sciences Division, Pacific Northwest National Laboratory, Richland, WA

²Center for Engineering in Medicine and Surgical Services, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Simple elastomeric ESI interface for coupling microfluidics with mass spectrometry

Overview

- ❖ Microfluidics technology enables the processing of trace samples to be integrated with fast, efficient separations on a single device
- ❖ Coupling of microfluidics with electrospray ionization (ESI)-MS promises to provide a powerful platform for proteomics analyses
- ❖ Operation of the ESI source in the cone-jet mode at nL/min flow rates provides uniformly small, highly charged droplets that enable efficient ionization for high-sensitivity MS analysis
- ❖ We have developed a simple, robust microchip ESI interface.¹ The stable cone-jet mode operation, novel auxiliary channel used to supply the electrospray voltage, and the sub-nL post-column dead volume offer promise for coupling with high-resolution microchip separations

Introduction

Despite widespread interest in combining lab-on-a-chip technologies with MS-based analyses, the coupling of microfluidics to ESI-MS remains challenging. We report a robust, integrated poly(dimethylsiloxane) (PDMS) microchip interface for ESI-MS using simple and widely accessible microfabrication procedures. The interface uses an auxiliary channel to provide electrical contact for the stable cone-jet electrospray without sample loss or dilution. The electric field at the channel terminus is enhanced by two vertical cuts that cause the interface to taper to a line rather than to a point, and the formation of a small Taylor cone at the channel exit ensures sub-nL post-column dead volumes.

Cone-jet mode electrospray was demonstrated for up to 90% aqueous solutions and for extended durations. Comparable ESI-MS sensitivities were achieved using both microchip and conventional fused silica capillary emitters, but stable cone-jet mode electrosprays could be established over a far broader range of flow rates (from 50–1000 nL/min) and applied potentials using the microchip emitters. This attribute of the microchip emitter should simplify electrospray optimization and make the stable electrospray more resistant to external perturbations.

Methods

Device Fabrication

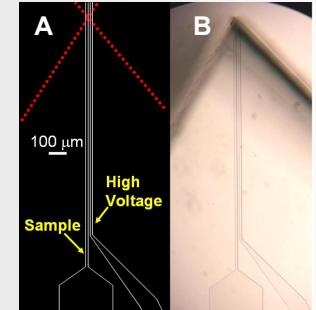


Figure 1. Top view of the microchip ESI device. (A) Drawing of the microchannels used for photomask creation. Dashed lines indicate where cuts are made to create the emitter structure. (B) Top view of a completed device.

- 8 μm deep features are patterned in PDMS from an SU8-on-silicon template.
- The patterned substrate is irreversibly bonded to a blank PDMS substrate using a corona surface treater.²
- Vertical cuts produce an electric field enhancing taper at the apex.
- Analyte is infused through 'sample' channel via a syringe pump.
- Electrical contact for electrospray is provided in the Taylor cone via the electrolyte-filled 'high voltage' channel.

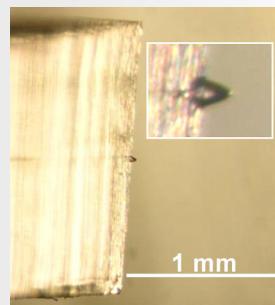


Figure 2. Side view of a microchip during ESI operation with a close-up view of the Taylor cone in the inset.

Emitter Characterization

Data in Figs. 9 and 10 were acquired using an LCQ ion trap mass spectrometer (Thermo Fisher, Waltham, MA). Fused silica capillary emitters were chemically etched as described previously. Electrospray current measurements were obtained using a stainless steel charge collector connected to a picoammeter.³

Results

Cone-Jet Mode Operation

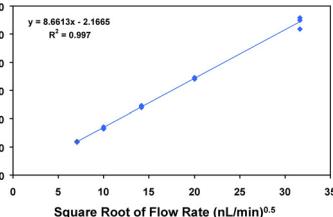


Figure 3. Emitted current vs. the square root of flow rate. Replicates were obtained using three different microchips. The electrosprayed solution was 5 mM ammonium acetate in 1:1 H₂O/MeOH at 200 nL/min.

- Cone-jet mode operation is verified by the linear relationship⁴
- Linear relationship also indicates that contribution to flow via the high-voltage channel is negligible (verified by spiking standards into the high voltage channel¹)
- High-voltage channel thus serves as a "liquid electrode", providing electrical contact without diluting the sample

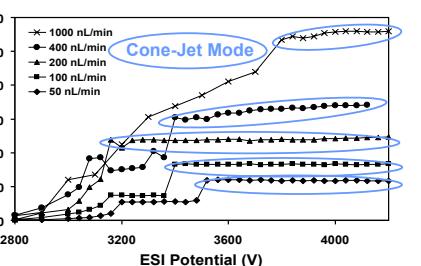
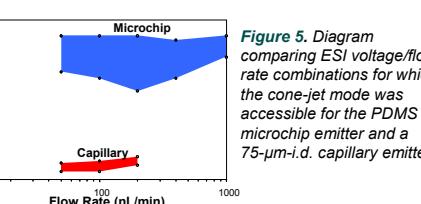


Figure 4. Electrospray current vs. voltage curves for a microchip emitter. Same conditions as for Figure 3.



- Emitters taper to a line rather than to a point
- Native hydrophobicity of PDMS enables sub-nL Taylor cones
- Minimal dead volume ensures compatibility with on-chip separations

- Cone-jet mode operation is stable over a far broader range of flows and voltages for the microchip than for the conventional emitter
- Broad cone-jet stability ensures robust operation with minimal fine-tuning

Electrospray Images

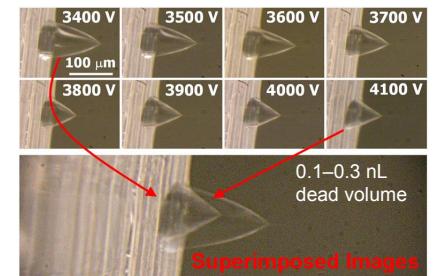


Figure 6. Taylor cone images from a microchip emitter spraying 5 mM ammonium acetate in 1:1 H₂O/MeOH at 200 nL/min.

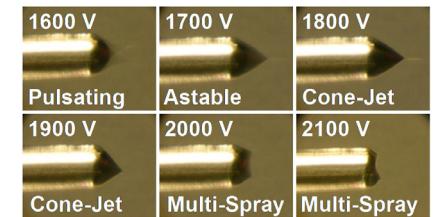


Figure 7. Electrospray images from a 75- μm -i.d. chemically etched fused silica capillary. The solution and flow rate were the same as for Fig. 6.

- The Taylor cone of the microchip emitter decreases in length and diameter at the base in response to an increasing electric field (Figure 6)
- This flexibility enables the Taylor cone angle to be largely preserved
- With the base diameter of the capillary emitter fixed, the electrospray is destabilized at higher voltages (Figure 7)

Extended Operation

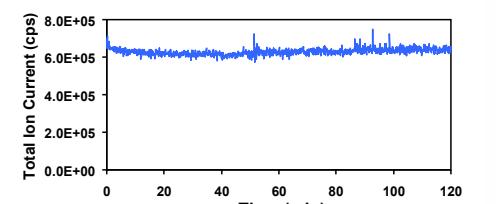


Figure 8. Evaluation of long-term electrospray stability. Total ion current from the infusion of a 10 μM solution of angiotensinogen 1-14 at 200 nL/min. Electrolyte was periodically added to the open high-voltage reservoir to counteract evaporative losses

Comparison of Mass Spectra

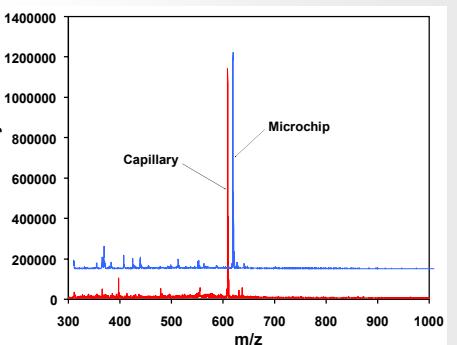


Figure 9. Infusion of 1 μM reserpine at 50 nL/min. The mass spectra from the microchip emitter are offset horizontally by 10 $m\text{/z}$ units as well as vertically for clarity.

- Peak intensity is nearly identical for the microchip and conventional emitters
- The few background peaks unique to the microchip emitter are low in intensity, indicating that the PDMS is compatible with common solvents used for MS (i.e., minimal contamination from the substrate)

Stability Comparison

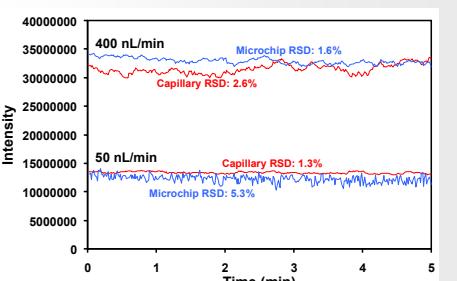


Figure 10. Stability comparison between microchip and capillary-based emitters. Base peak signal for 1 μM reserpine

- Similar stability for conventional and microchip emitters at 400 nL/min
- At 50 nL/min, the microchip emitter is less stable than the conventional emitter, but still provides reasonable stability

Conclusions

- The notable features of the microchip ESI interface presented here include:
 - Straightforward device creation, using a single photomask and common microfabrication procedures
 - An electrolyte-filled auxiliary channel provides electrical contact for ESI without introducing dead volume or diluting the sample
 - Decoupling the ESI circuit from the sample channel should enable ready implementation with electrically driven microfluidics separations
 - Robust performance at flow rates as low as 50 nL/min
 - Similar sensitivity and signal stability compared with conventional fused silica capillary emitters
 - Stable operation in the cone-jet mode over a broad range of flow rates and applied potentials
- Future work will focus on coupling the interface with integrated microdevices for proteomics analyses, combining sample preparation and separation with ESI-MS.

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Contact Information

Ryan T. Kelly, PhD
Biological Sciences Division, K8-98
Pacific Northwest National Laboratory
P.O. Box 999, Richland, WA 99352
e-mail: ryan.kelly@pnnl.gov