

# A MEMS Electropray Nozzle for Mass Spectroscopy

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## SUMMARY

In this paper, we present our development of a micron-sized MEMS electropray nozzle and demonstrate its application for electropray mass spectroscopy (MS). The fabricated and tested micromachined electropray nozzles are typically 40 $\mu$ m long and with 1-3  $\mu$ m orifice diameters. They also have built-in particle filters. This micromachined nozzle has been successfully interfaced with a mass spectrometer (Finnigan Mat LCQ Ion Trap) to perform standard characterization using a solution of gramicidin S at a flow rate of 50 nL/min and a voltage potential of 4 kV. This MEMS nozzle has demonstrated valid MS analyses with lower flow rates, and it has many advantages over the traditional complex preparation of a glass-capillary.

**Keywords:** micro-channels, mass spectroscopy, chemical analysis

## INTRODUCTION

Miniaturization of chemical analysis systems has been gaining popularity as MEMS technology has become more robust, feasible, and widely accepted as the technology for tomorrow's chip based chemical analysis systems. Over the past decade, several key steps have been taken in fabricating compact liquid chromatographs and capillary electrophoresis chips [1]. There has been significant advancement in MEMS based chemical separation systems, but on-chip detection can only be performed mainly by methods such as UV absorbance and electro-chemi-luminescence. These optical methods are not viable for most biomolecule (protein and peptide) detection; they are no match for the femtomole sensitivity and versatility (minimal liquid sample preparation) provided by a mass spectrometer (MS). Furthermore, because of this tremendous advantage in sensitivity, mass spectrometry is ideally suited for detection from small sample volumes. This femtomoles sensitivity, then can be crucial for MEMS chemical systems where only small sample volumes are available. Nevertheless, current mass spectrometers are still big compared to MEMS systems. How to couple MEMS systems to a MS becomes an issue.

One method by which MEMS chemical systems can generate ions for MS analysis is with electropray ionization (ESI). ESI has distinct advantages over other ionization strategies. Firstly, it can detect large molecules (theoretical limit ~200,000 Da, practical limit, 70,000 Da) *directly* from the liquid sample. This capability is imperative for MEMS protein and peptide analysis where techniques like PCR amplification are futile. Other advantages include: the softest ionization (compared to other methods), ease of use, and complete compatibility with

liquid chromatography. Therefore, we have chosen to use ESI in this work.

Conventional ESI is done using glass capillaries. Consequently, if MEMS devices are interfaced using the conventional technique the liquid sample must be piped out with conventional capillary tubing to the MS intake where the sample molecules are ionized and then, detected. This increase in overall system dead volume, and in effect, can compromise all advantages gained in MEMS miniaturization of the liquid separation stage. What is needed then is an on-chip interface that has the advantage of directly connecting the two systems together. Until recently, this bridge between the chip based chemical analysis devices and the MS has remained uncrossed.

The purpose of this work, then, is to build this bridge between MEMS and MS using ESI. Recently, Xue [2] and Ramsey [3] have both attacked this same problem by interfacing flat-edged glass microchannels with cross-sections of 10 $\mu$ m deep by 60 $\mu$ m wide to a MS and demonstrating electropray (ES). Our device structure is very different from Xue's and Ramsey's. Instead of employing a "blunt" orifice, we have fabricated an overhanging silicon nitride micro-channel 1 $\mu$ m high by 2 $\mu$ m wide which dramatically reduces wetted surface area at the ES tip. Reduction of this orifice diameter and tip surface area will reduce the size of the fluid cone during electropray, thus reducing dead volume. The reasoning behind this assumption is provided in the next section. In addition to reducing dead volume, our nozzle design also includes an important feature of integrated particle filter structures which minimize this MEMS ESI tip from clogging. Lastly, interface with a mass spectrometer has proven the feasibility of this building this bridge between MEMS nozzle technology and MS.

## MICRO-ELECTROSPRAY

The method of ESI works perfectly but only with liquid samples. Electropray ionization (ESI) is an important technique of generating ions for mass spectroscopic analysis of chemical and biological liquid samples. [4,5] With its growing popularity, a lot of experimental data and understanding has been acquired by various groups such as Fenn (1985) and Wilm (1994), so today ESI is an accepted technique for MS. ESI occurs when fluid in a capillary tip is subjected to a potential drop (1-4 kV). Because of the high electric field, charge is induced on the surface of the fluid at the tip. Spraying occurs when coulombic forces are large enough to overcome the surface tension forces. Figure 1 shows a typical ESI source, a glass capillary packed with a filter and the MS inlet. Note that it is very important to have particle filters in the system to prevent clogging of the tip.

The physics of ESI show that scaling down the ESI tip from typically 100 $\mu$ m to 1 $\mu$ m ID would result in a significant improvements due to a smaller dead volume (minimum sample

required for operation), a more stable electrospray, lower sample flow rates and lower voltages required for ionization [6].

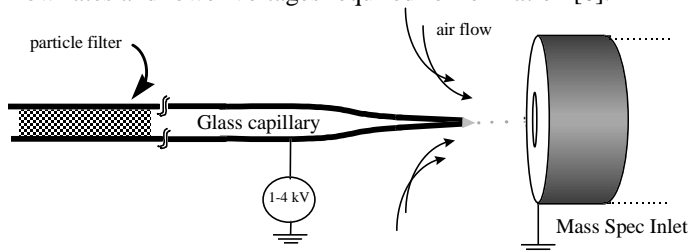


Figure 1: Typical electrospray configuration

A close-up photograph (Fig. 2) of electrospray from a 370µm OD (160µm ID) capillary illustrates the possible savings in dead volume with a smaller ES tip. The almost “solid” looking cone of fluid is called the Taylor cone. The flow rate, here, is ~1µL/min with a potential of 1250V between the fluid and the MS inlet.

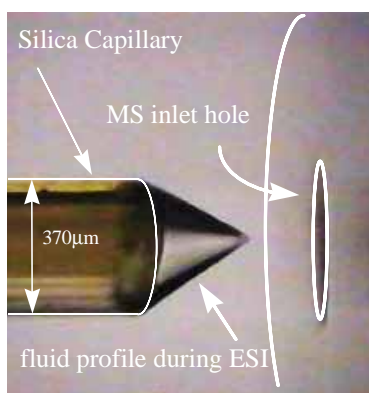


Figure 2: Electrospray from a capillary

Wilm and Mann [6] have developed the following mathematical model of this phenomenon

$$r_e = \left( \frac{\rho}{4\pi^2\gamma \left[ \left( \frac{U_a}{U_t} \right)^2 - 1 \right] \tan\left(\frac{\pi}{2} - \nu\right)} \right)^{1/3} \cdot (dV/dt)^{2/3} \quad (1)$$

where  $r_e$  represents the radius of the emission region at the tip of the Taylor cone,  $\gamma$  the surface tension of the liquid,  $\rho$  the density of the liquid,  $U_a$  the applied voltage,  $U_t$  the voltage at which the cone is formed,  $\nu$  the cone angle, and  $dV/dt$  the flow rate. This equation predicts that  $r_e$ , the emission radius can be reduced with a reduction in flow rate. To see if MEMS type nozzles are compatible with this theoretical model, let us calculate the emission radius size for a practical case - the case for which our MEMS nozzle has been tested (1:1 water : methanol solution). Using the following:  $\gamma = 0.03531 \text{ Nm}^{-1}$ ,  $\rho = 896 \text{ kg m}^{-3}$ ,  $U_a=4000\text{V}$ ,  $U_t = 1000\text{V}$ ,  $r_e$  is calculated as 33 nm. It is shown that  $r_e$  is much smaller than 1µm, so MEMS nozzles do make sense. If  $r_e$  were larger than the normal MEMS sizes, then scaling down the nozzle might not have any merit.

With this trend toward smaller ESI tips, the conventional way of fabricating these 1-3µm diameter tips becomes difficult even with a micro-capillary puller. In addition to being time consuming, the major problem of this technique is to yield

reproducible tip geometries. Finally, particle filters have to be inserted manually to prevent the tiny capillaries from clogging with debris. Many of these problems now are taken care of simultaneously with our micromachined electrospray nozzles. The capability to fabricate micron-sized tips with micromachining is advantageous in many ways: 1) the shape and finish of the tip can be reproducible from chip to chip, 2) complex MEMS filter structures can be constructed inside the micromachined liquid channel in order to filter out debris, and 3) mass production is available due to batch processing.

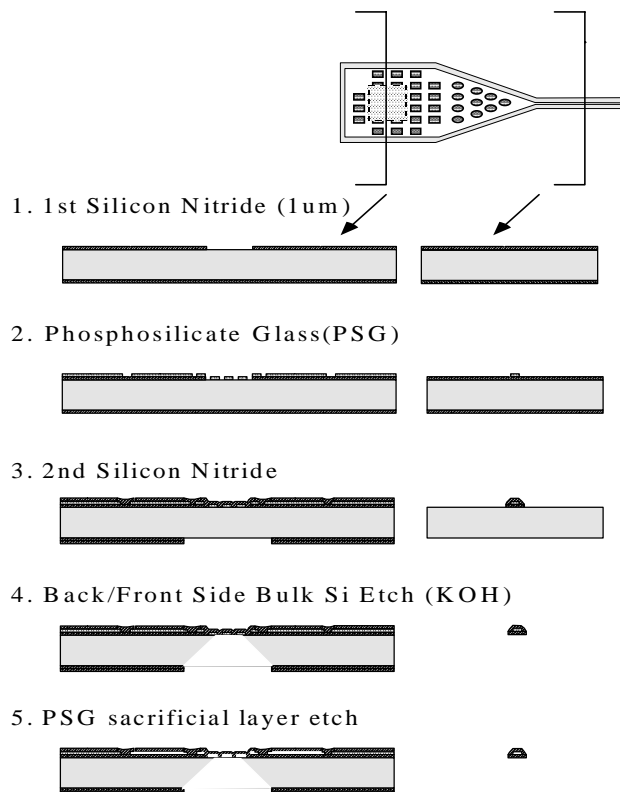


Figure 3: Major fabrication steps

## DESIGN and FABRICATION

The silicon micromachined nozzle consists of a “sandwich” of 1µm phosphosilicate glass (PSG) enclosed by two silicon nitride layers each 1µm thick on a 500µm silicon substrate. The silicon nitride layers form the overhanging channel after the wafer is back etched with KOH. Figure 4 shows a 3-D view of the device with a capillary tubing attached to the inlet hole (dashed lines) from the backside of the silicon substrate.

The fabrication sequence begins with a 1µm deposition of LPCVD silicon nitride. Next, the silicon nitride is patterned with  $\text{SF}_6/\text{O}_2$  plasma. This step opens up inlet holes so that access to the channel is permitted after the backside KOH etch. After patterning the silicon nitride, a 1µm layer of PSG is deposited and patterned with buffered HF. The PSG acts as the sacrificial layer for the micro-channel. In addition to forming the channel, the patterning of the rectangles

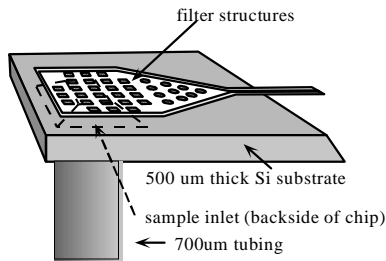


Figure 4: 3-d view of ES Nozzle

into the PSG serves to strengthen the inlet roof as well as create particle filter structures inside the channel. (Fig. 5)

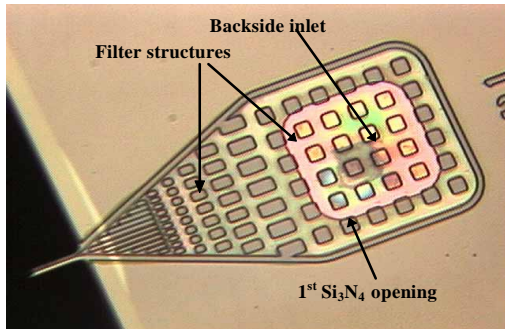


Figure 5: Top view showing particle filters

To complete the “sandwich,” one more layer of 1 $\mu$ m silicon nitride is deposited and patterned. When this nitride layer is deposited on PSG, it becomes the roof of the channel, and in the areas where the PSG has been etched, this second nitride contacts the first nitride, the channel floor. Next, square backside windows are patterned into the wafer for the subsequent KOH bulk etching step. The bulk etching takes place from the front and back side simultaneously. From the front side, the KOH etch removes the silicon under the channel, thus defining the nozzle tip, and on the back side the wafer is etched until the nitride inlet holes have been reached. After rinsing the KOH off, the dies are etched for approximately 40 minutes in 49% HF to remove the sacrificial PSG inside the channel. The chips are subsequently rinsed in DI water overnight and baked dry. For testing, the connection is made by gluing a 700 $\mu$ m OD fused silica capillary to the backside inlet. (Fig.7) Figure 6 below shows relevant dimensions of one nozzle design. The major fabrication process steps are shown in two cross-sectional views in Figure 3.

There are several limitations of the PSG sacrificial layer type process. Firstly, the channel length is limited because of the diffusion limited HF etching which has only two available entrances to attack the PSG. The additional time required for a longer channel would also etch and consequently, weaken the silicon nitride wall. Since the overall length of the channel is limited to 300 $\mu$ m, one of the walls of the backside inlet window is not as structurally strong.

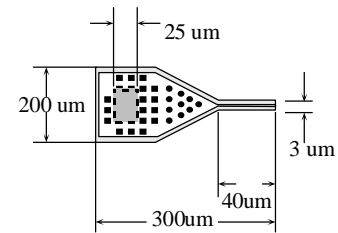


Figure 6: Typical nozzle dimensions

Figure 7 shows the additional narrowing of this wall due to the undercut during KOH etching. We are currently implementing a modified process, which eliminates all of these drawbacks.

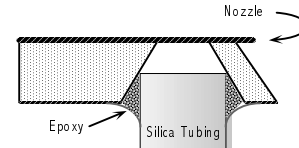


Figure 7: Nozzle cross-sectional view

## EXPERIMENTS AND RESULTS

Fabricated nozzles were first extensively tested for structural rigidity and channel blockage by injection of DI water into the inlet. Many of the 1 $\mu$ m nozzles were prone to clogging at the very tip. Contamination from the sacrificial etch and crystallization of particles in the drying process is believed to be the cause of this clogging. This clogging problem was greatly reduced by a 24+ hr rinse in DI water, and a tip burn-in with an alcohol lamp. The liquid meniscus was monitored visually through a microscope as it traveled out to the tip. From video footage of this moving meniscus in the 2  $\mu$ m channel, we estimated a flow rate of 3.6 nL/min. Although the pressure drop of the fluid as it traveled through the nozzle channel was not measured, the reduction of the overall channel from ~200  $\mu$ m to a micron size posed no significant back pressure when the channels were not clogged. A close-up of the nozzle orifice is shown in Figure 8. The 1  $\mu$ m channel height and particle filters ensured that no particulate matter was deposited at the nozzle tips from the sample fluid.

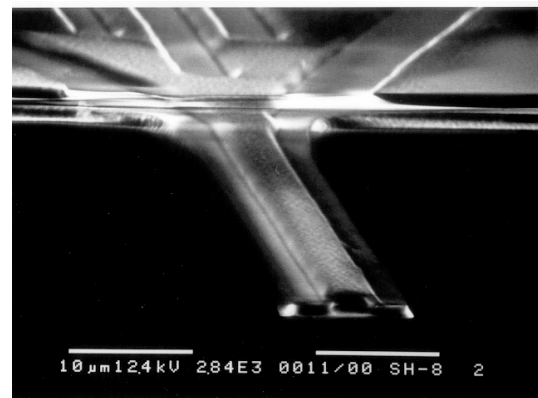


Figure 8: SEM photograph

The pyramidal liquid port on the back of the micromachined chip was converted to a tubular configuration by the addition of a short section of 740  $\mu\text{m}$  OD x 530  $\mu\text{m}$  ID Fused Silica Capillary (FSC)(Polymicro Technologies, Phoenix, AZ). The FSC extension was positioned within the liquid port using a crude micro-manipulator with visual confirmation of joint alignment from a Leica X 1000 stereo microscope. The extension was secured using a standard two-part epoxy resin. Once cured, the extension was cut to a final length of one cm. Liquid connection to the chip interface was achieved using a multi-laminate fused silica transfer line constructed as follows. The running length of transfer line (10-15 cm) was constructed from 150  $\mu\text{m}$  OD x 25  $\mu\text{m}$  ID FSC. Each end of the transfer line was inserted into a 2-3 cm section of 350  $\mu\text{m}$  OD x 155  $\mu\text{m}$  ID FSC until flush and then sealed with epoxy resin. Upon drying, one end of the butted transferline was inserted into the 530  $\mu\text{m}$  ID FSC extension and sealed in the same manner.

Chip performance was analyzed using a standardized solution of Gramicidin S. The test sample was dissolved in 50:50 MeOH:Water, 1% HOAc (by volume) at a final concentration of 4 pmole/ $\mu\text{l}$ . A Harvard Apparatus model 44 syringe pump fitted with a 50  $\mu\text{l}$  gastight syringe (Hamilton, Reno, NV) was used to deliver the test compound to the M-M interface via a separate 75 cm length of 350  $\mu\text{m}$  OD x 75  $\mu\text{m}$  ID FSC transfer line. A 2.5 cm section of 22 gauge Platinum tubing (Hamilton) was fitted to the end of the transfer line to provide the necessary liquid-metal contact for sample ionization. Final connection to the M-M transfer line was through a Supelco Capillary Butt connector using a 0.4 mm to 0.8 mm ID dual sided Vespel ferrule (Supelco Inc., Bellefonte, PA).

The standard ESI interface to the Finnigan Mat LCQ Ion Trap mass spectrometer was replaced with a custom Polyacrylic platform upon which a XYZ micropositioning translational stage (model 460A XYZ, Newport Corp., Newport Beach, CA) had been mounted. The nozzle chip was secured to the XYZ stage using a modified micro clamp (clothes pin) and precisely positioned under a high-power stereomicroscope (Zeiss, STEMI SV8, 200 mm lens, 25x ocular). A fiber optic cold light source (Schott, model KL1500) was used for illumination. The high voltage lead from the mass spectrometer was modified to terminate in a small alligator clamp to facilitate the connection to the Platinum electrode. The nozzle was centered in front of the heated capillary inlet of the mass spectrometer at a distance of 0.25 mm to 0.4 mm.

The Finnigan Mat LCQ Ion Trap mass spectrometer was operated under manual control through the "Tune Plus" view over a scan range from 500 to 1200 AMU. The maximum injection time was 500 ms with an AQC setting of  $1.0 \times 10^8$  for full mass range analysis. A 4 kV potential was applied to the Platinum electrode for sample ionization. Figure 9 shows a mass spectrum analysis of gramicidin S. The group of doubly charged ions ( $m/z$  ratios 571.3-572.3) characteristic of gramicidin S have been clearly detected above the background ions. The additional peaks in the spectrum seem to have come from epoxy residue. Although epoxy contamination remains an important issue when the nozzle is used by itself, on-chip integration with other separation devices should eliminate this problem. The sensitivity of this MS analysis is comparable to that of conventional ESI sources.

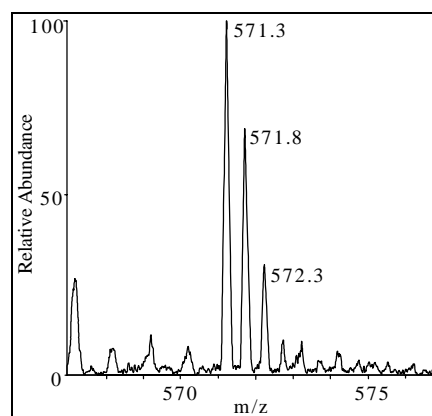


Figure 9: MS scan of gramicidin S using MEMS nozzle

## CONCLUSION

We have demonstrated the feasibility of this nozzle design for nano-flow electrospray. The use of micromachining also adds a level of repeatability in the nozzle tip that is unavailable with conventional tips. This robustness in fabrication now may be employed to study electrospray physics at even smaller dimensions. Furthermore, the integration of micro-particle filters has made the nozzle a much more convenient tool for MS. This MEMS device now has the possibility to be integrated with other chip-based chemical analysis systems, thus, increasing the potential of high sensitivity chemical detection with MEMS systems.

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