Nano-Electrospray Ionization Sources Operating at Atmospheric and Sub-Atmospheric Pressure

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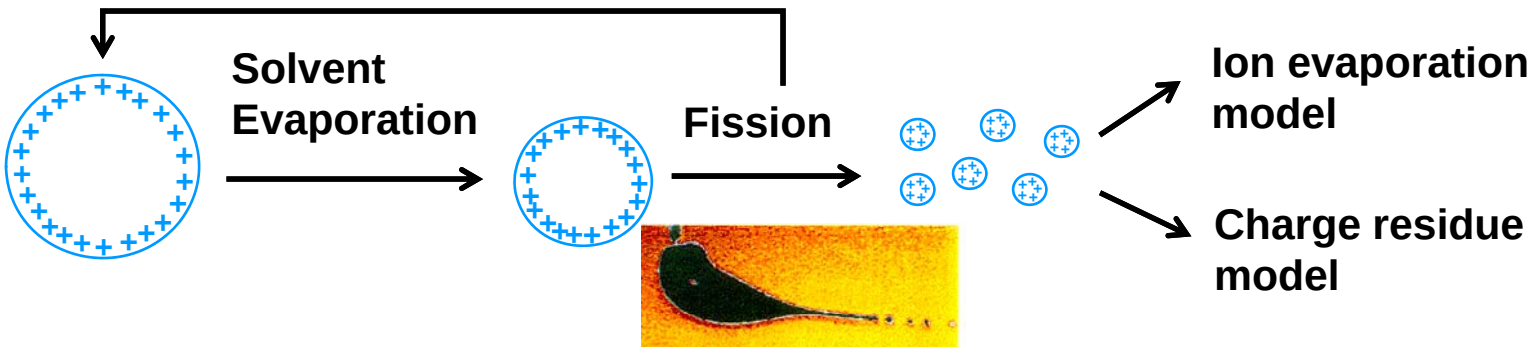
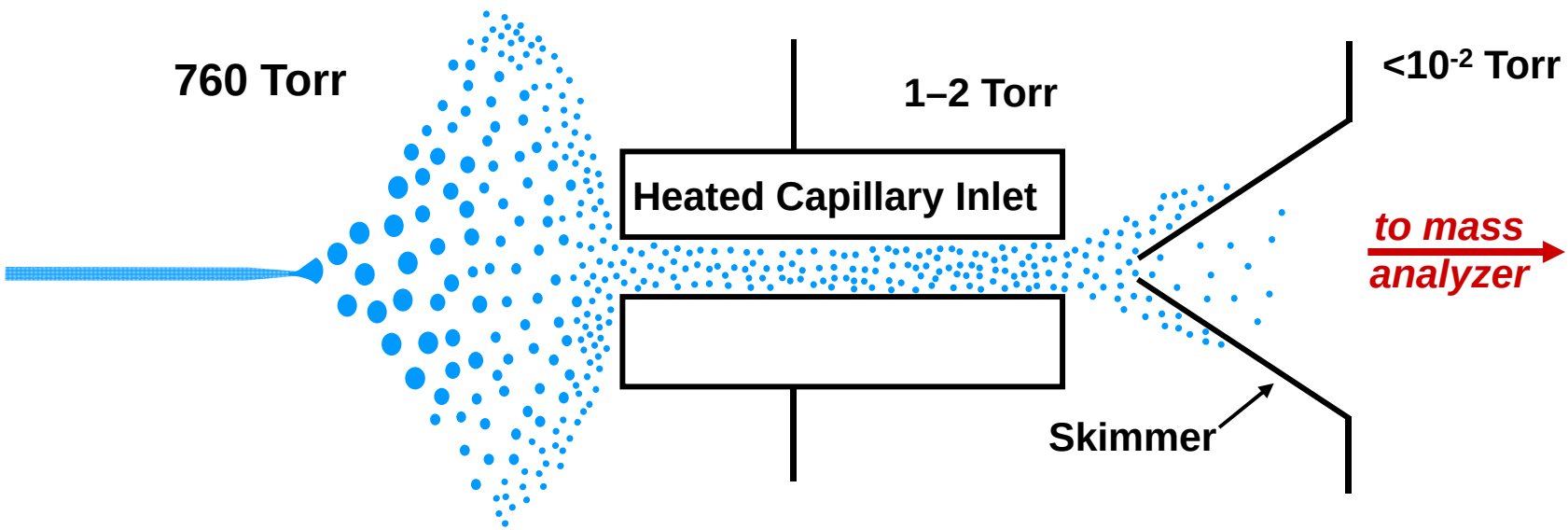
Current challenges in ESI-MS

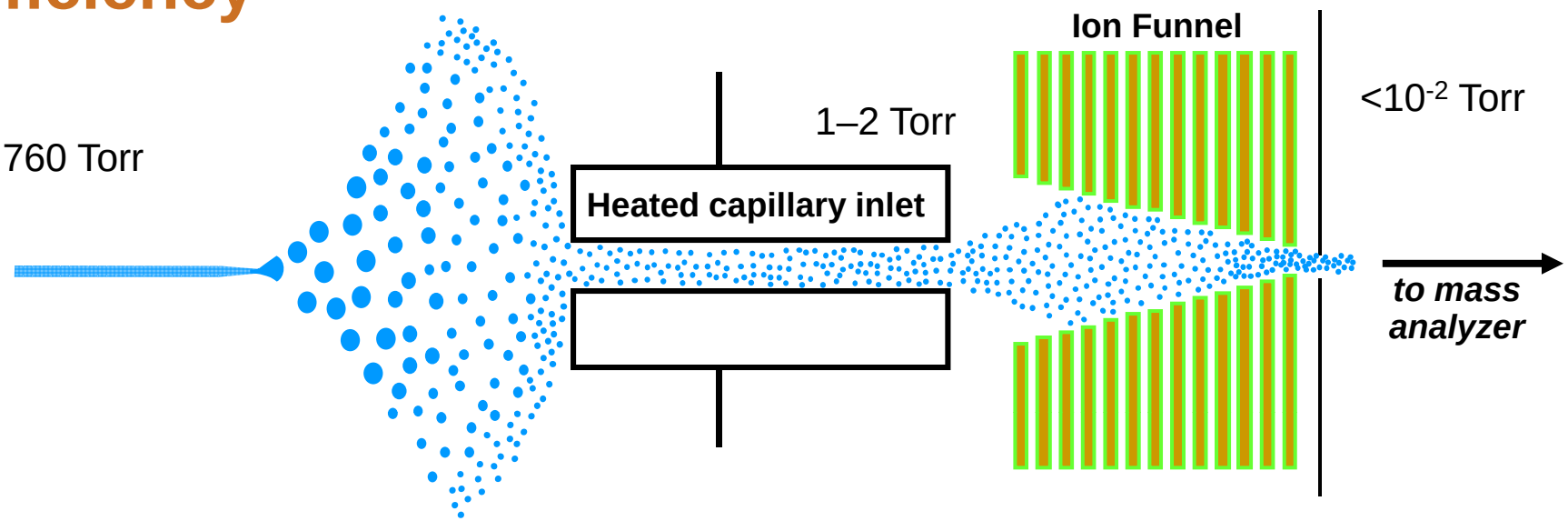
Electrospray ionization efficiency

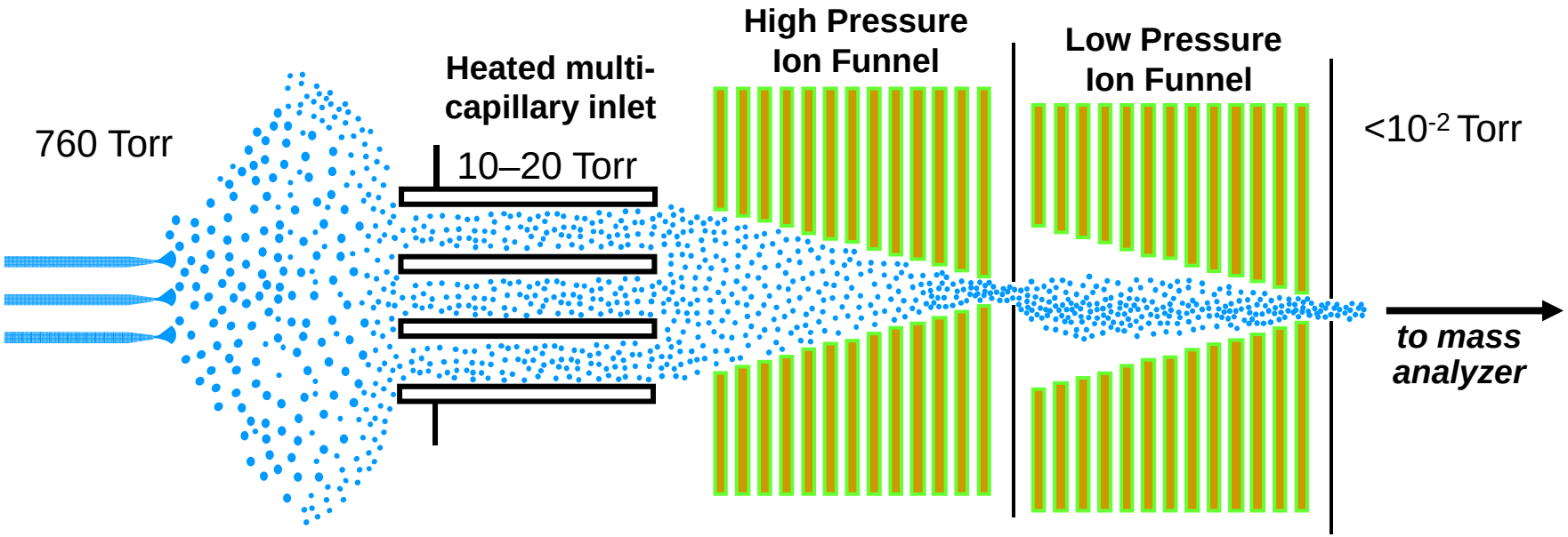


Ion transmission efficiency



Technologies for improving ion transmission efficiency





Rapid Commun. Mass Spectrom. **1997**, *11*, 1813–1817.

Multi-emitter electrospray for high ionization efficiency

- **9 emitters, 2-3 fold increase in signal intensity**

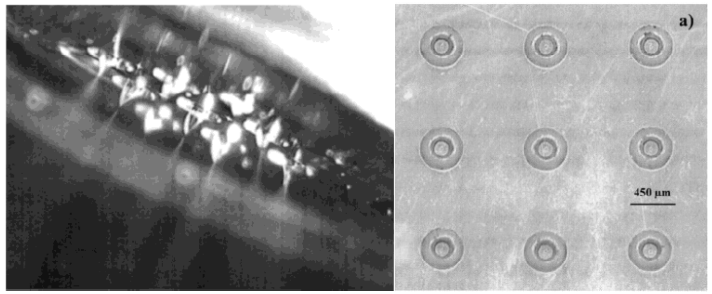
  Generation of Multiple Electrosprays using Microfabricated Emitter Arrays for Improved Mass Spectrometric Sensitivity
  K. Tang, Y. Lin, D. W. Matson, T. Kim, R. D. Smith

- **19 emitters, 11-fold increase in signal intensity**

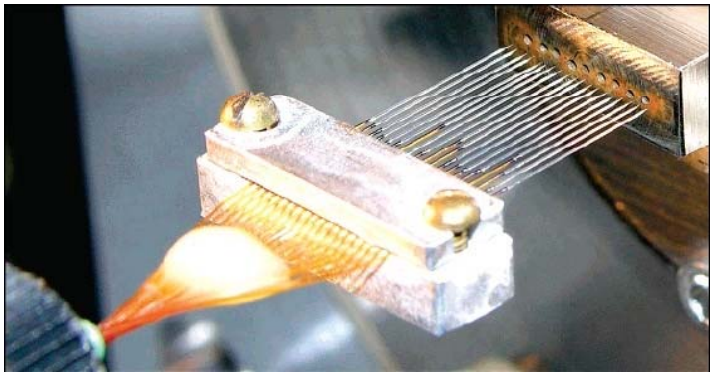
  Capillary-Based Multi Nanoelectrospray Emitters: Improvements in Ion Transmission Efficiency and Implementation with Capillary Reversed-Phase LC-ESI-MS
  R. T. Kelly, J. S. Page, R. Zhao, W.-J. Qian, H. M. Mottaz, K. Tang, R. D. Smith

- **Radial array, increased stability and signal intensity**

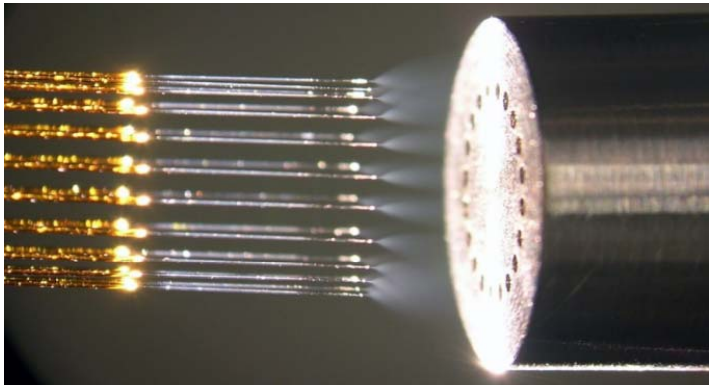
  Nanoelectrospray Emitter Arrays Providing Interemitter Electric Field Uniformity
  R.T. Kelly, J. S. Page, I. Marginean, K. Tang, R. D. Smith



Anal. Chem. **2001**, 73, 1658-1663.

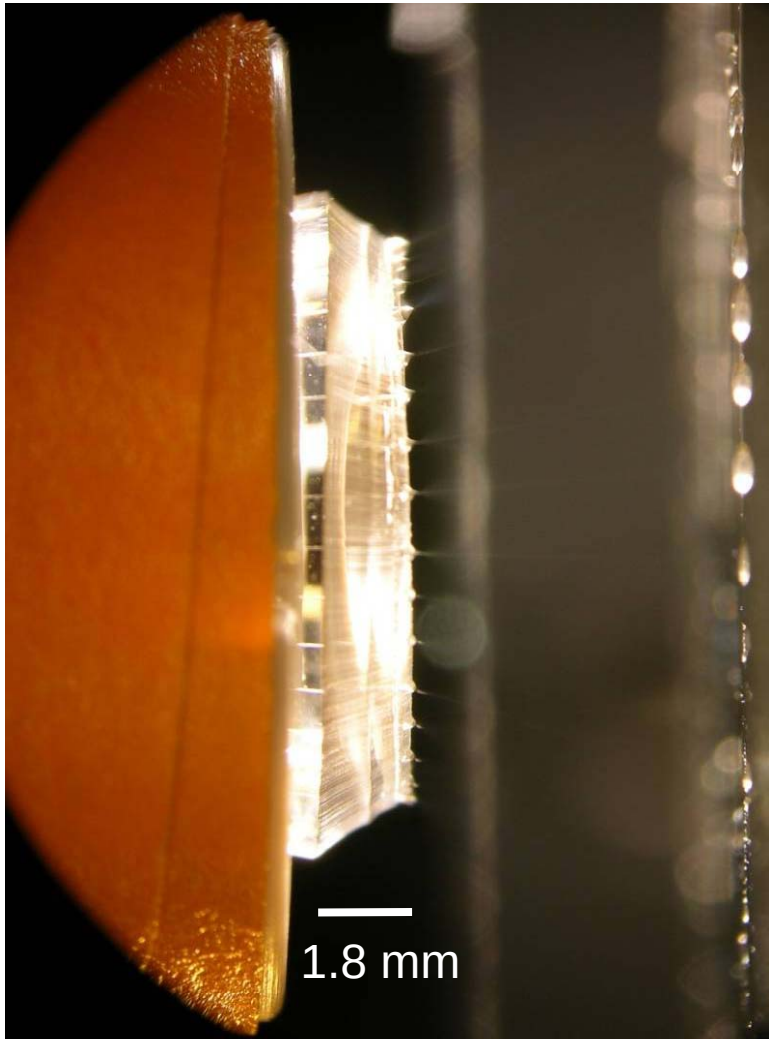


Anal. Chem. **2008**, 80, 143-149.



Anal. Chem. **2008**, 80, 5660-5665.

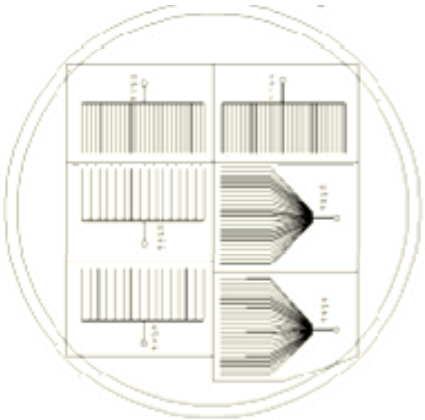
Alternative microfluidics multi-emitter designs



- **Polydimethylsiloxane (PDMS) substrates**
- **Various emitter patterns**
- **Rapid conversion of idea to device (~few days)**
- **Batch fabricate**

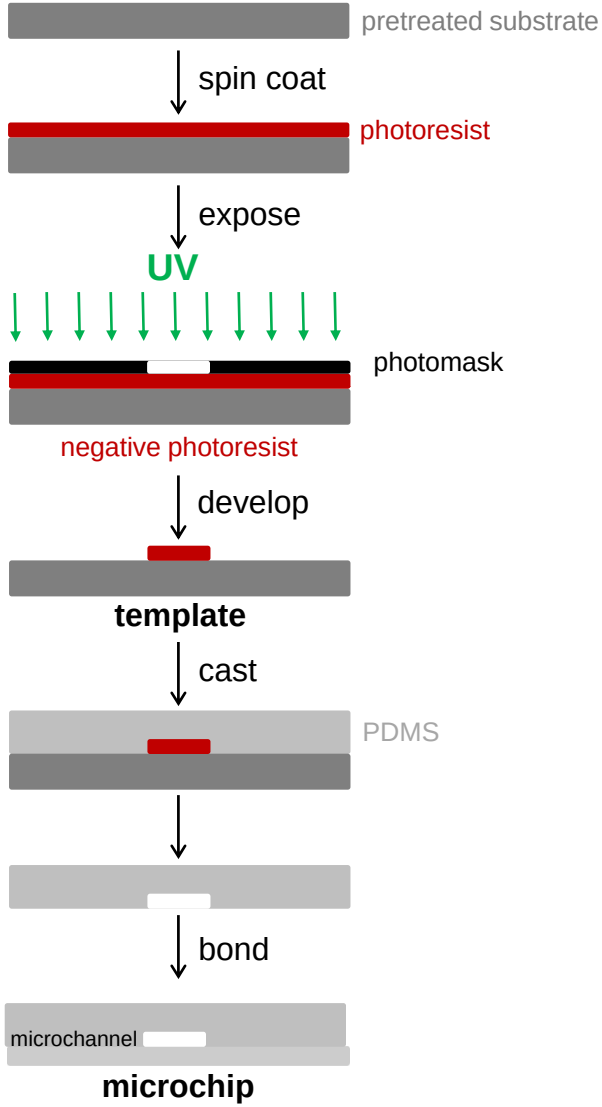
Soft lithography fabrication of microfluidic multi-emitters

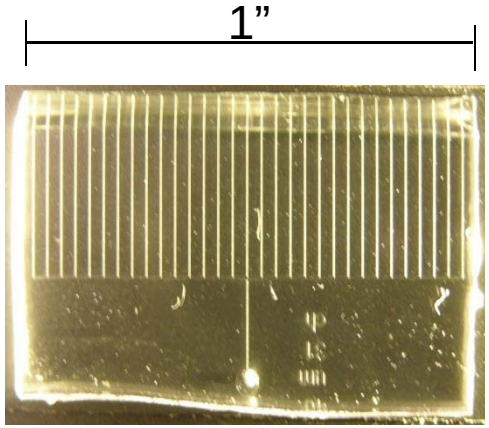
- **Mask design**
  - AutoCAD

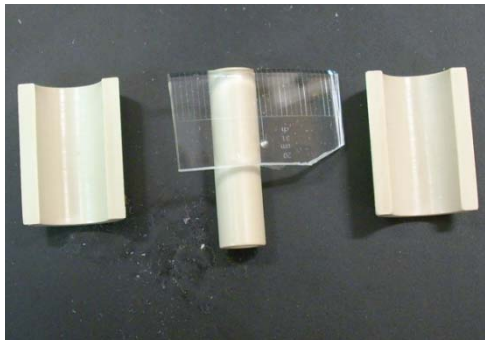


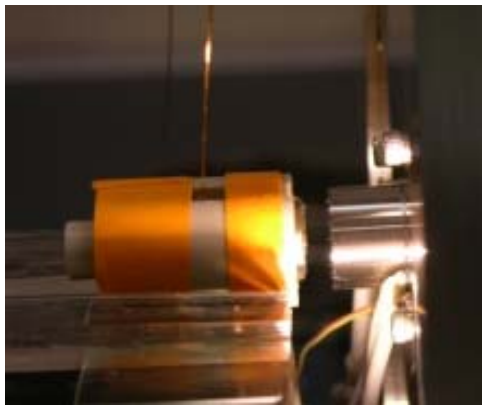
- **Template fabrication**
  - Photolithography

- **Microdevice fabrication**
  - Elastomeric PDMS
  - Casting

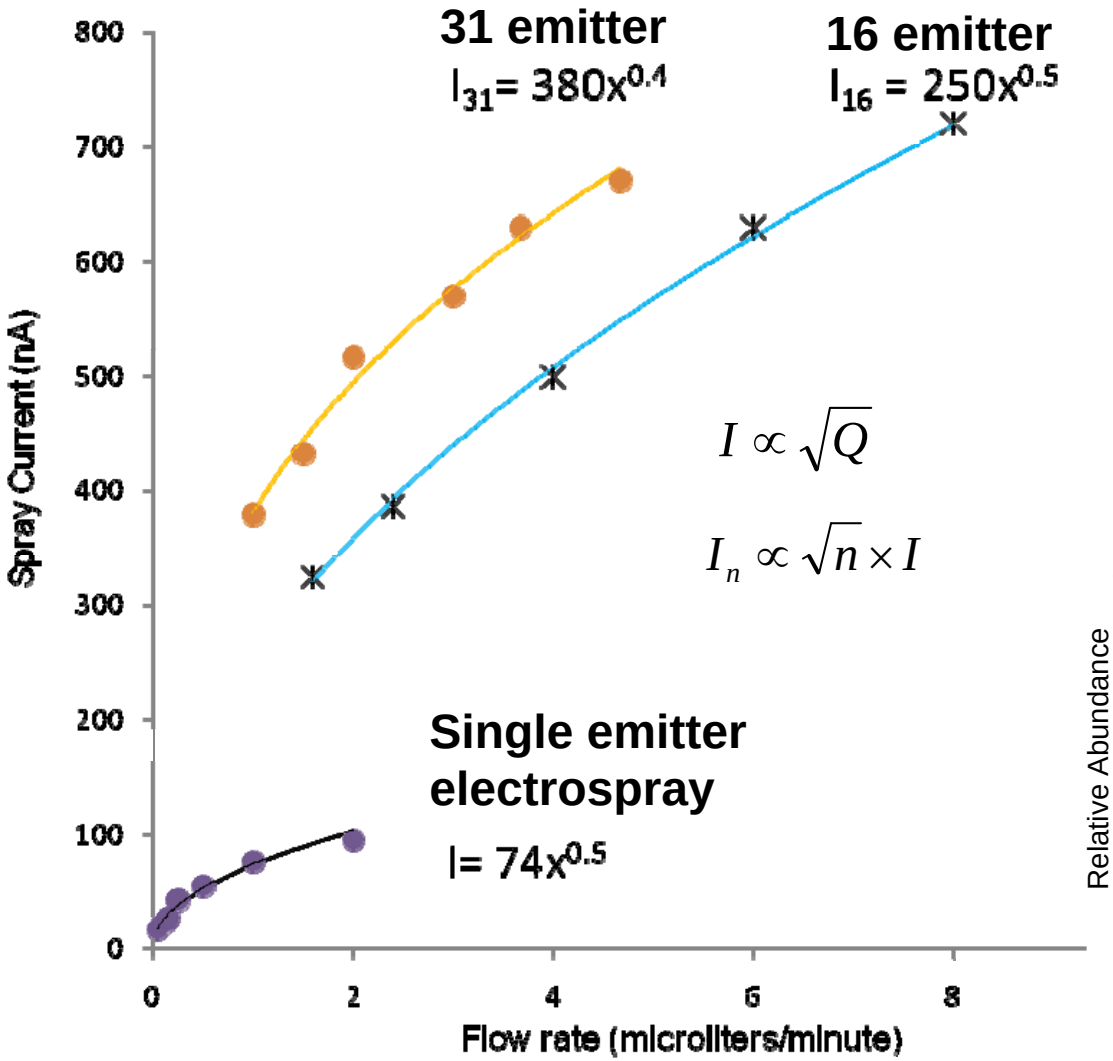




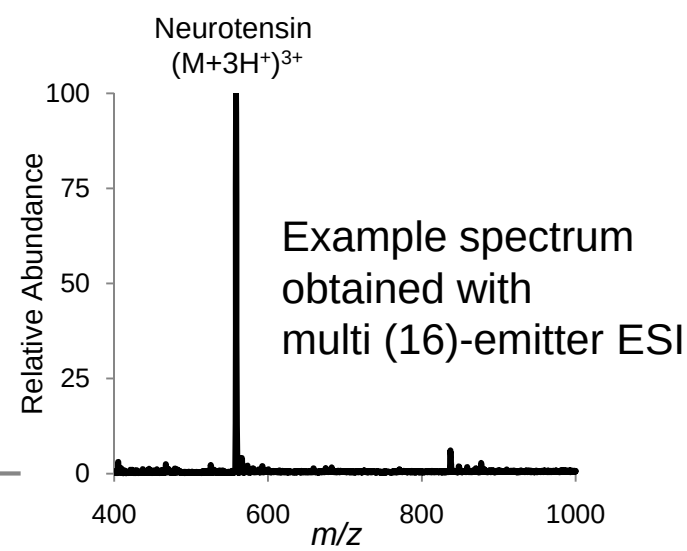




Microfluidic multi-emitters *vs.* single emitter electrospray

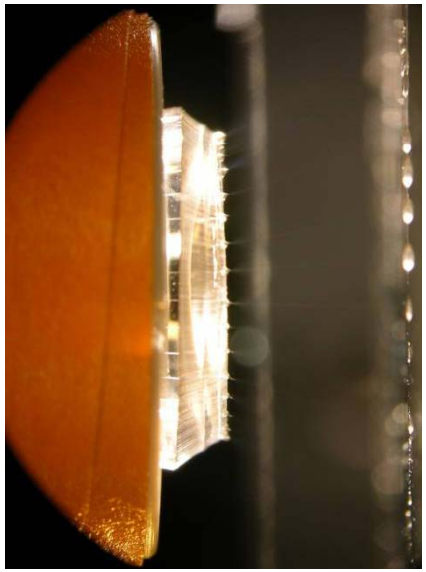


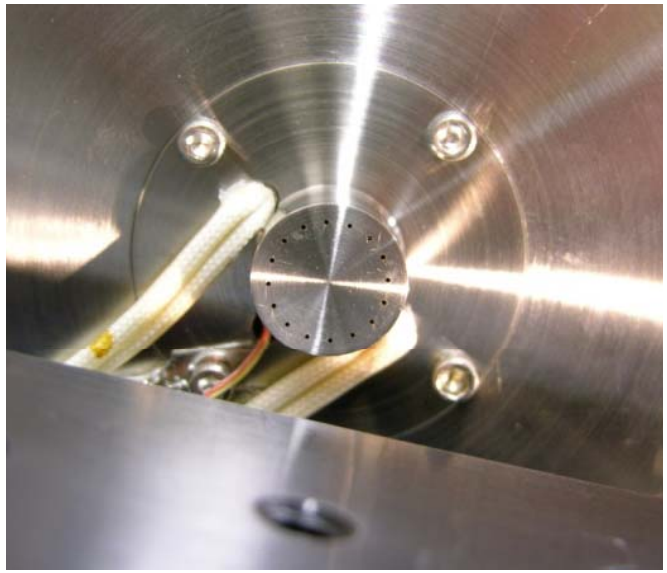
- Increase in spray current (5X) is proportional to the square root of both the flow rate and number of emitters
- Data fits to cone jet model

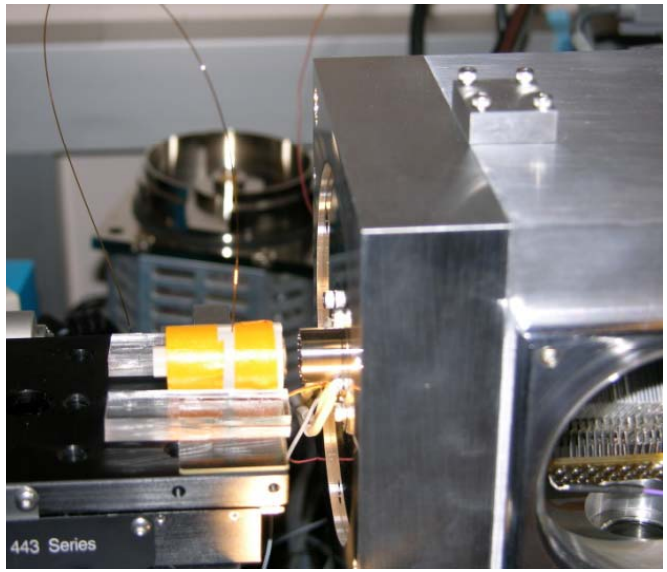


J. Fluid Mech. **1994**, *260,* 155-184.
Anal. Chem. **2001**, *73*, 1658-1663.

Future multi-emitter evaluation and refinement

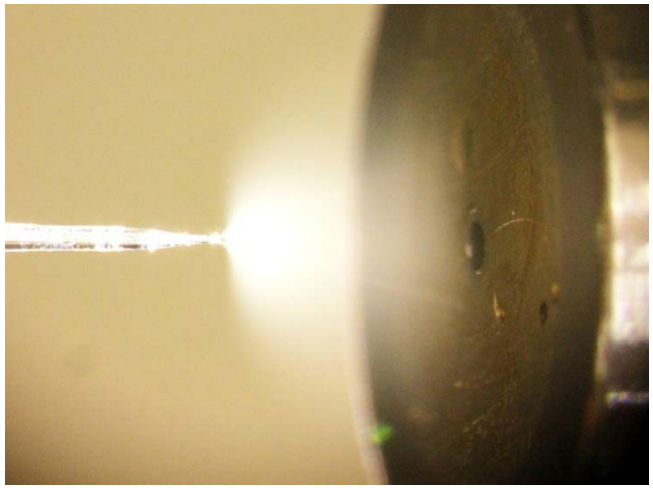


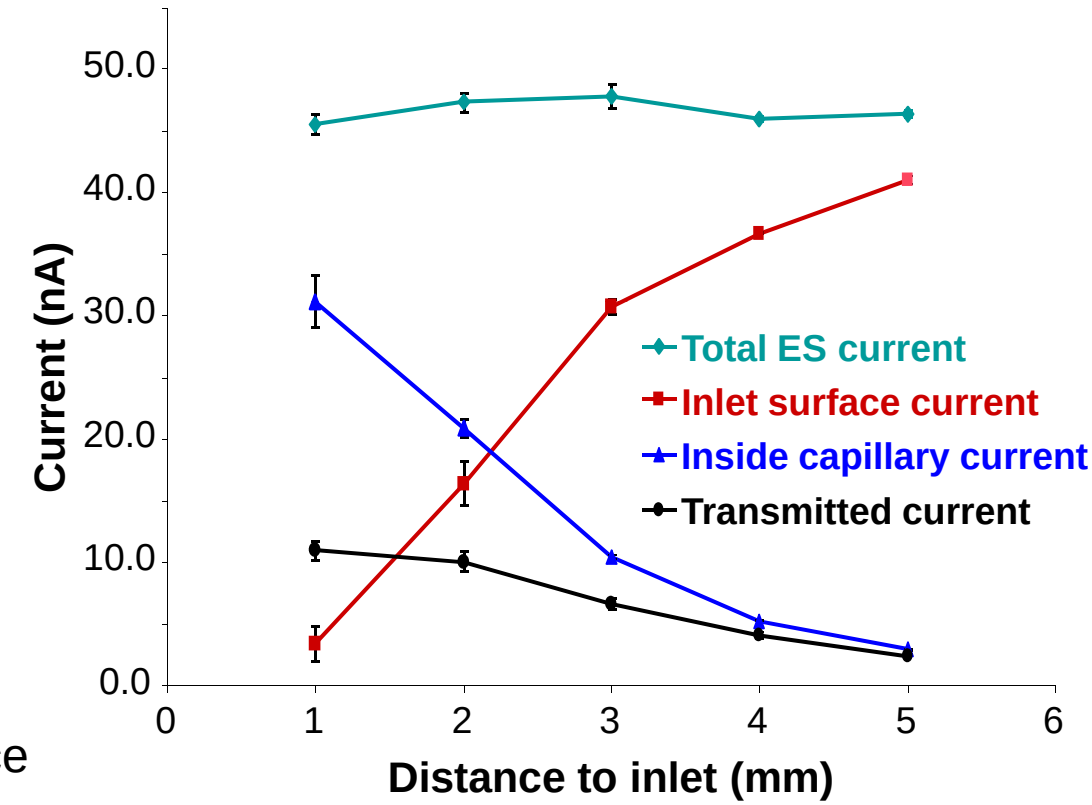




- **Couple multi-emitter with LC-MS**
- **Integrate lab-on-a-chip techniques**
- **Implement with subambient pressure ionization with nanoelectrosray (SPIN) source**

Increasing ion abundance by reducing losses associated with atmospheric pressure interface



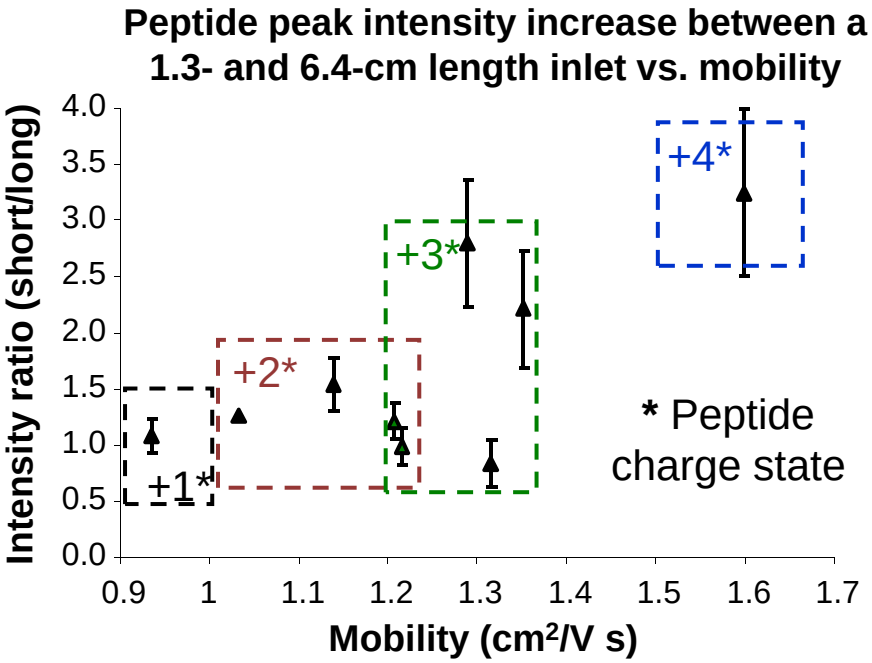


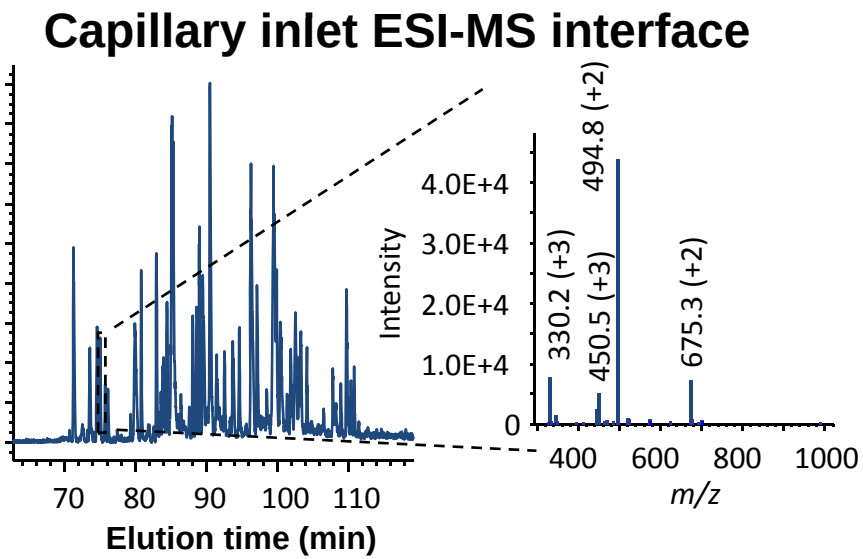
- Large losses associated with the typical heated capillary atmospheric pressure interface
- 80 - 90 % of total electrospray current (sample) is lost to the front and inside surfaces of the inlet capillary

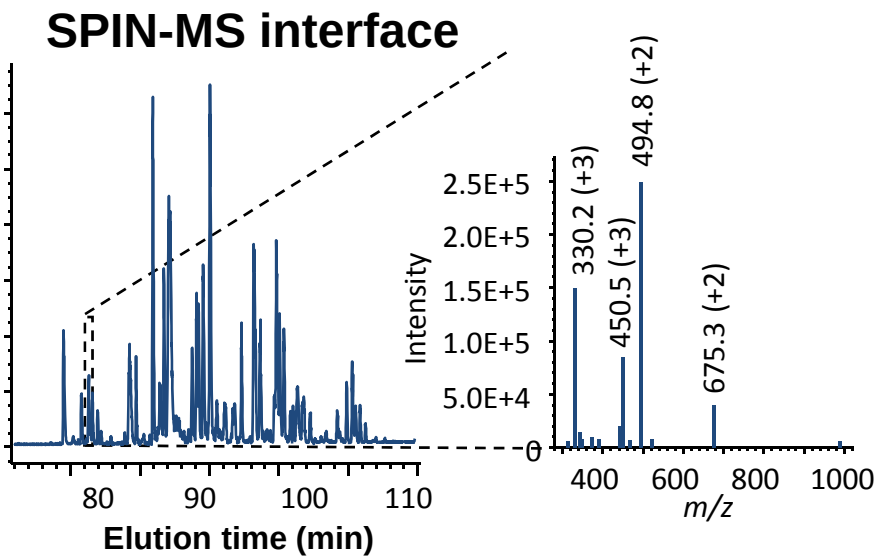
Anal. Chem. **2008**, 80, 6573.
J. Am. Soc. Mass Spectrom. **2007**, *18*, 1582.
J. Am. Soc. Mass Spectrom. **2005**, *16*, 1702.

Eliminating inlet transmission biases

- Higher mobility species are lost at a greater rate in capillary inlets leading to intensity biases
- Use of SPIN source reduces these biases leading to higher intensities for higher charge state peptides
- Better quantitative data

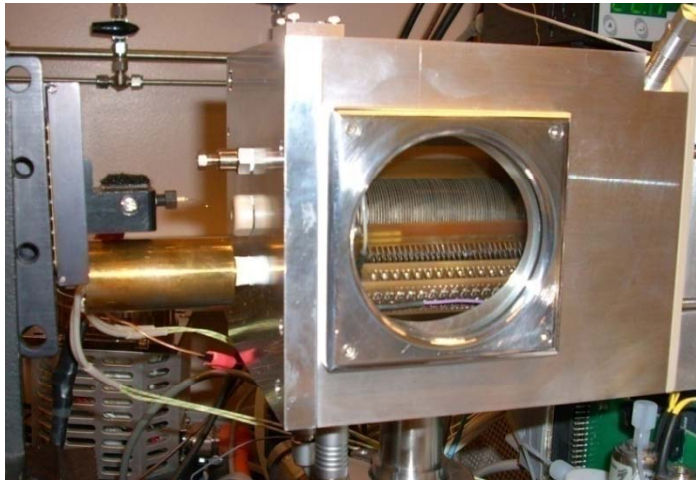




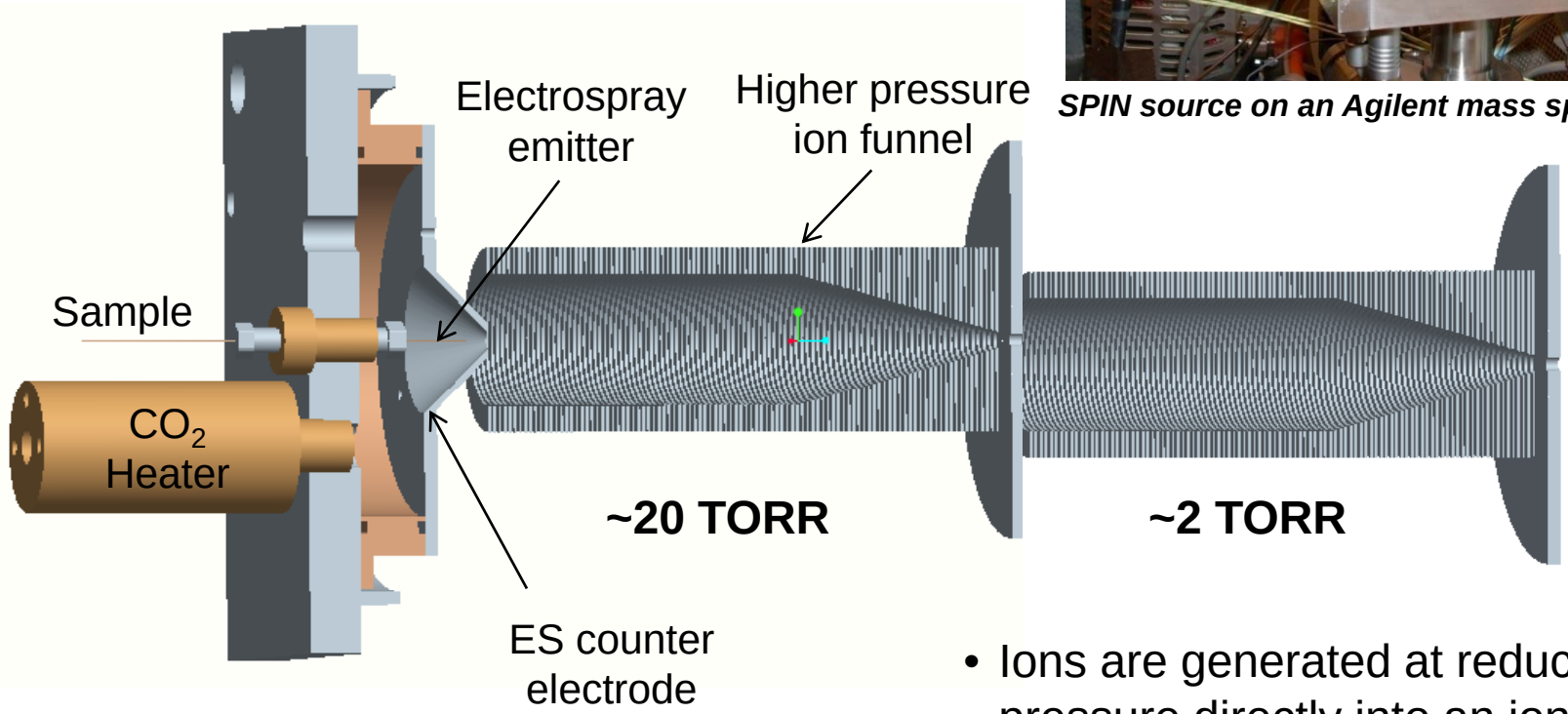


J. Am. Soc. Mass Spectrom. **2009**, 20, *12*, 2265-2272.

SPIN: high efficiency ionization source for improved ion abundance



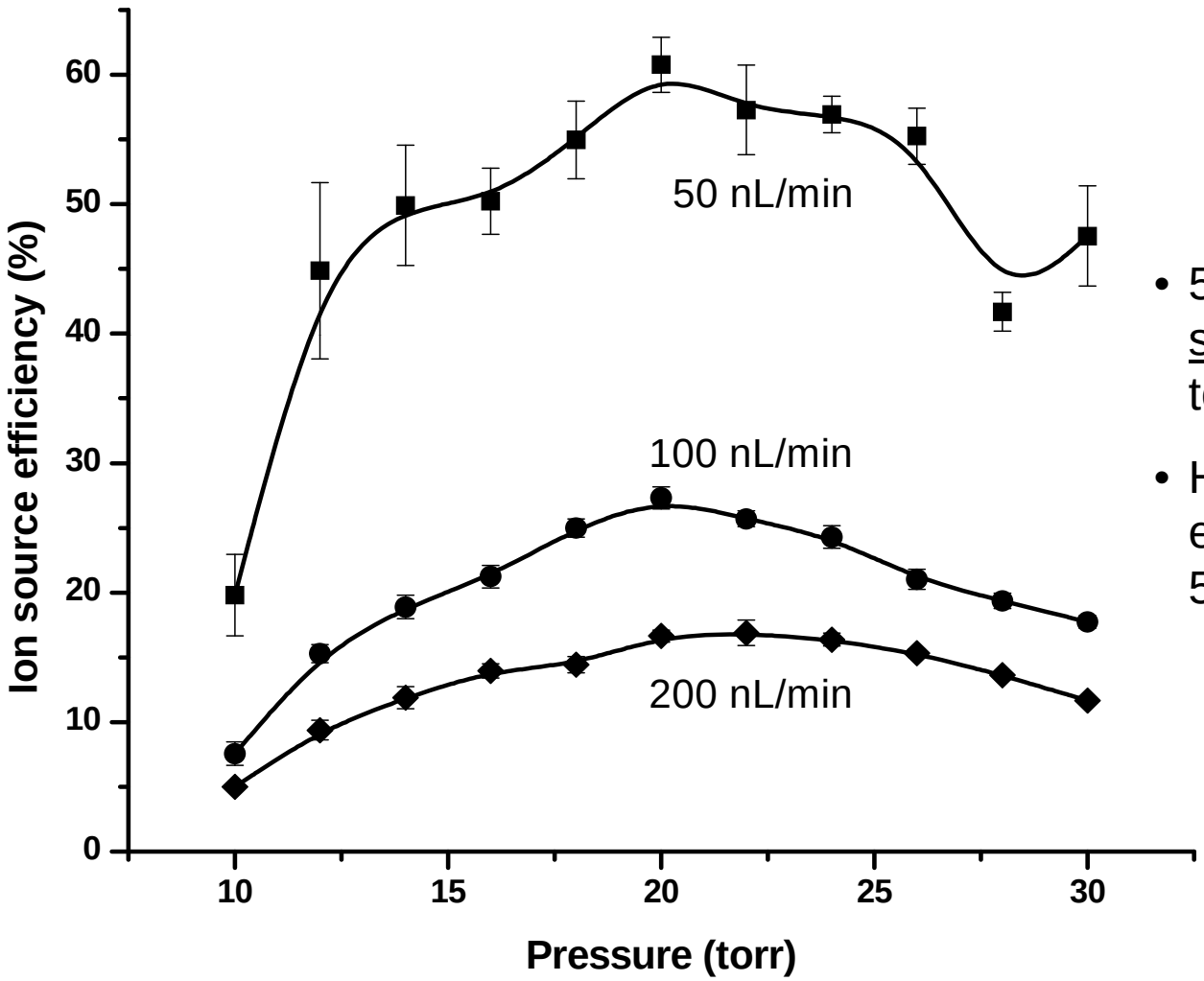
SPIN source on an Agilent mass spectrometer



- Ions are generated at reduced pressure directly into an ion funnel
- Solvent desolvation is aided by use of a heated sheath gas
- HPLC compatible

Anal. Chem. **2008**, *80*, 1800-1805.
Appl. Phys. Lett. **2009**, *95*, 184103.

SPIN source efficiency

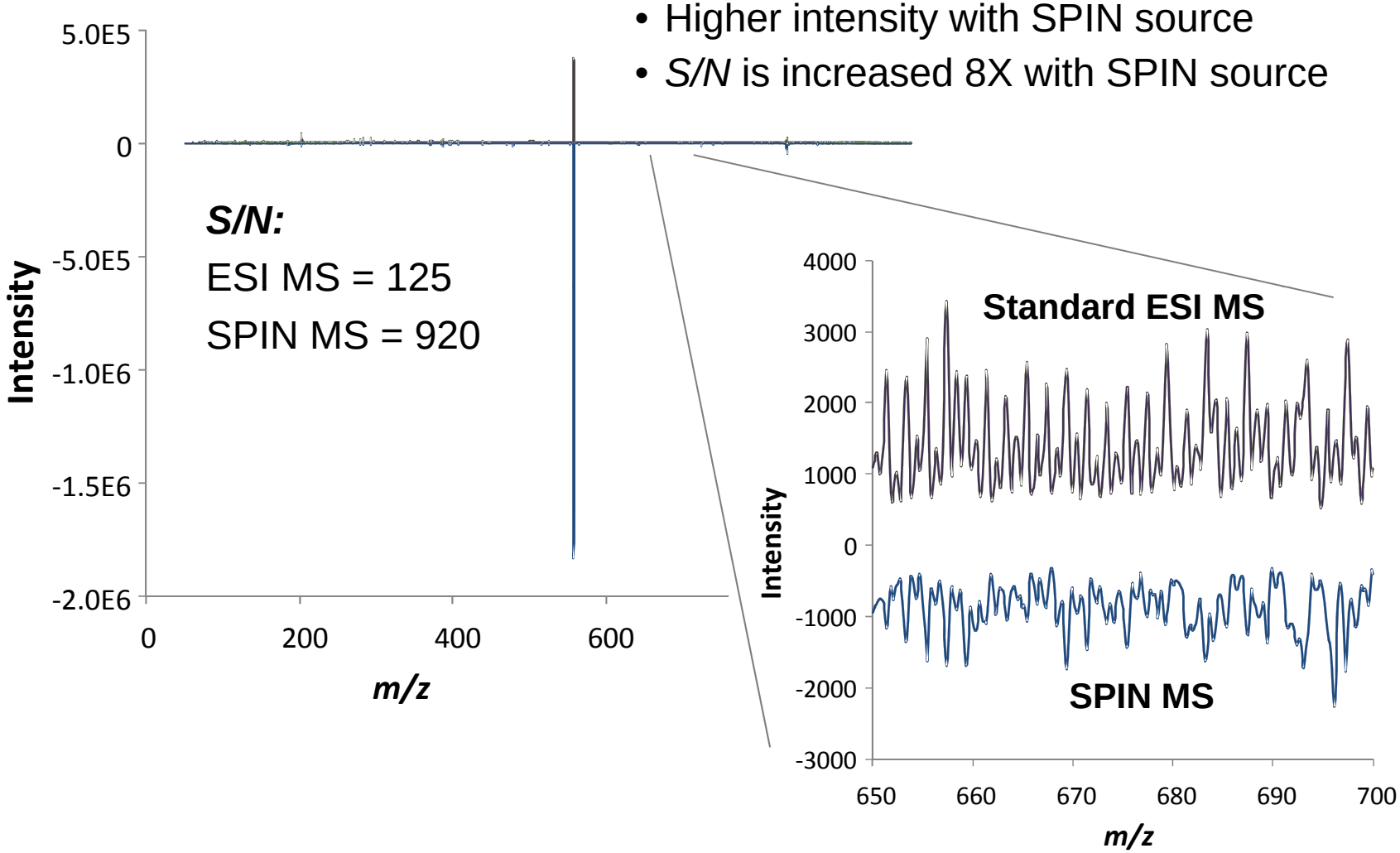


- 50% of analyte from <u>solution</u> is transmitted to high vacuum
- Highest source efficiency achieved at 50 nL/min

MP 614 *Marginean et al.*

SPIN MS *vs.* ESI MS

- Higher intensity with SPIN source
- *S/N* is increased 8X with SPIN source



Conclusions

- **Multiemitter ESI arrays provide a 5-fold increase in spray current**
- **Improvements in the design and implementation of the SPIN source have resulted in:**
  - **~50% ion source efficiency**
  - **Higher intensity and *S/N* ratio compared to ESI MS**

Acknowledgements

- PNNL Biological Separations and Mass Spectrometry Group
- EMSL Microfabrication Center
- Agilent Technologies
- NIH National Center for Research Resources