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

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Current challenges in ESI-MS

Electrospray ionization efficiency

- Solvent Evaporation
- Fission
- Ion evaporation model
- Charge residue model

Ion transmission efficiency

- 760 Torr
- 1–2 Torr
- <10\(^{-2}\) Torr
- Heated Capillary Inlet
- Skimmer
- to mass analyzer
Technologies for improving ion transmission efficiency

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. 2008, 80, 143-149.
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

\[ I \propto \sqrt{Q} \]
\[ I_n \propto \sqrt{n \times I} \]

**Single emitter electrospray**
\[ I = 74x^{0.5} \]

**31 emitter**
\[ I_{31} = 380x^{0.4} \]

**16 emitter**
\[ I_{16} = 250x^{0.5} \]

Example spectrum obtained with multi (16)-emitter ESI

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

**Graph:^

- Total ES current
- Inlet surface current
- Inside capillary current
- Transmitted current

**References:**

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

**Capillary inlet ESI-MS interface**

- Elution time (min)
- m/z
- Intensity

**SPIN-MS interface**

- Elution time (min)
- m/z
- Intensity

Peptide peak intensity increase between a 1.3- and 6.4-cm length inlet vs. mobility

- Use of SPIN source reduces these biases leading to higher intensities for higher charge state peptides
- Better quantitative data

* Peptide charge state

SPIN: high efficiency ionization source for improved ion abundance

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

SPIN source efficiency

- 50% of analyte from solution 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

**S/N:**

ESI MS = 125
SPIN MS = 920
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