A BRIEF RETROSPECTIVE OF ESI-CE/MS, CURRENT STATUS AND NEW APPLICATIONS

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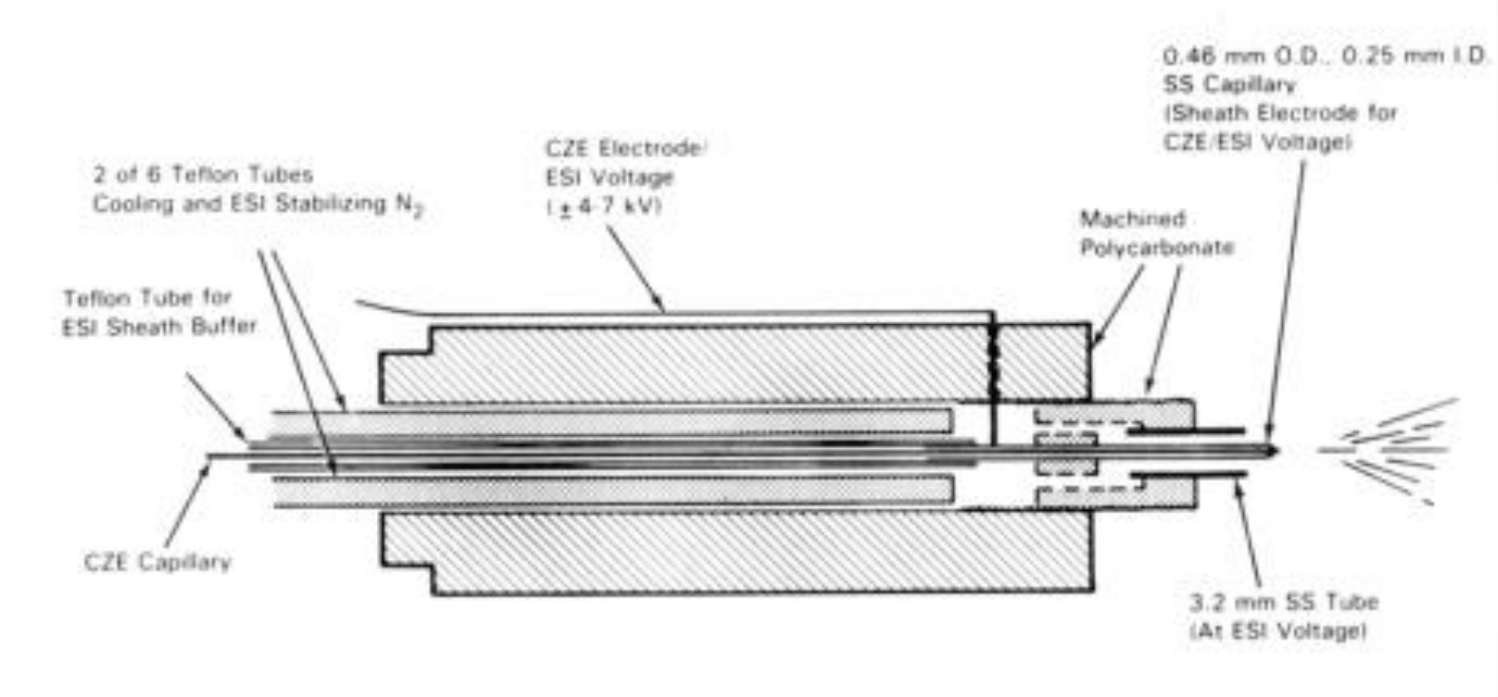
Review Main Challenges for CE-ESI/MS:

- No outlet vial/end electrode available when spraying into an MS
- How to apply the field between CE capillary exit and MS inlet or vice-versa to obtain an electrospray and at the same time maintain a field to drive the CE
- In CE, currents are typically 100-1000x larger than electrospray current; a safe electrical circuit and secure ground for handling the currents and fields
- In contrast with HPLC-ESI/MS, the solvent flow in CE, i.e. the EOF is a dependable parameter.
- BGE's with non-volatile constituents is incompatible with vacuum detection in MS. A BGE must be used which may be suboptimal for the CE separation

CE-ESI/MS Coupling Retrospective

- 1988; Initial work with coaxial sheath solvent, R.D. Smith et al.*



Sheath solvent delivered at 5-10 µL/min
Electrode in liquid electrical contact applying ES-voltage
Inert sheath gas to protect the spray
Stable electrospray

R. D. Smith et al, Anal. Chem. 60, 436, (1988)
R.D. Smith, C.J. Barinaga, H.R. Udseth, Anal. Chem., 60, 1948 (1988)
R.D. Smith, H.R. Udseth, Nature, 331, 639 (1988).

CE-ESI/MS Coupling Retrospective

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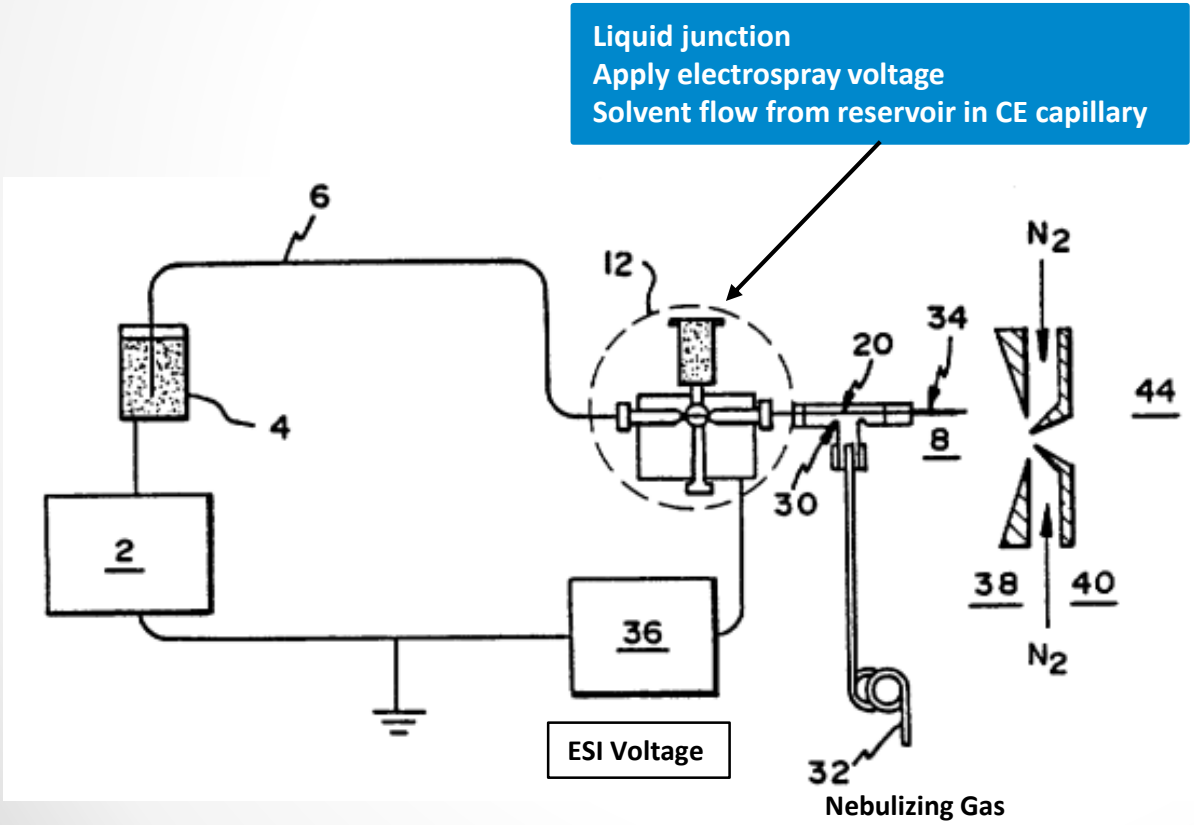
- 1988; Ion spray approach with liquid junction, J.D. Henion et al.*



J.D. Henion et al., J. Chrom. A, **458**, 313 (1988)
J.D. Henion et al. US4994165 Patent, 1991

Sensitivity ~2 µM

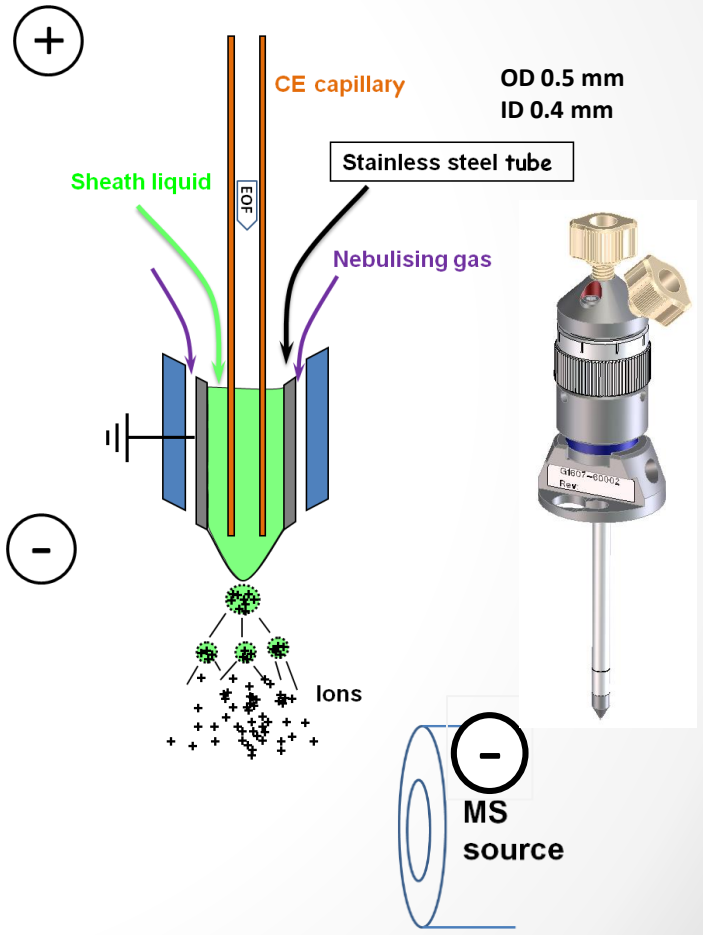
CE-ESI/MS Coupling Retrospective

- Since then in practice, skilled users had to resort to in-house adaption of commercial (nano)LC-MS sprayers to do CE-ESI/MS
- In 1995, Hewlett-Packard (Agilent Technologies) introduced Triple Tube Sprayer and an integrated CE-MS system

Characteristics of "Triple Tube" Sprayer Interface

- **Sheath solvent** is added to the CE effluent at a rate of typically 1 - 10 µL/min. Spray becomes independent of BGE composition and of the EOF
- **Spray needle** (gray) is grounded. Common return path for CE and ESI current. Bubbles are transported out. ESI voltage provided by MS
- **Nebulizing gas** to assist spray formation
- **Sheath solvent composition** dominates electrospray ionization chemistry
- **Compliant with different ionization modes**: ESI, APCI, APPI
- **Orthogonal configuration** (LC-MS) lets neutrals & big droplets pass

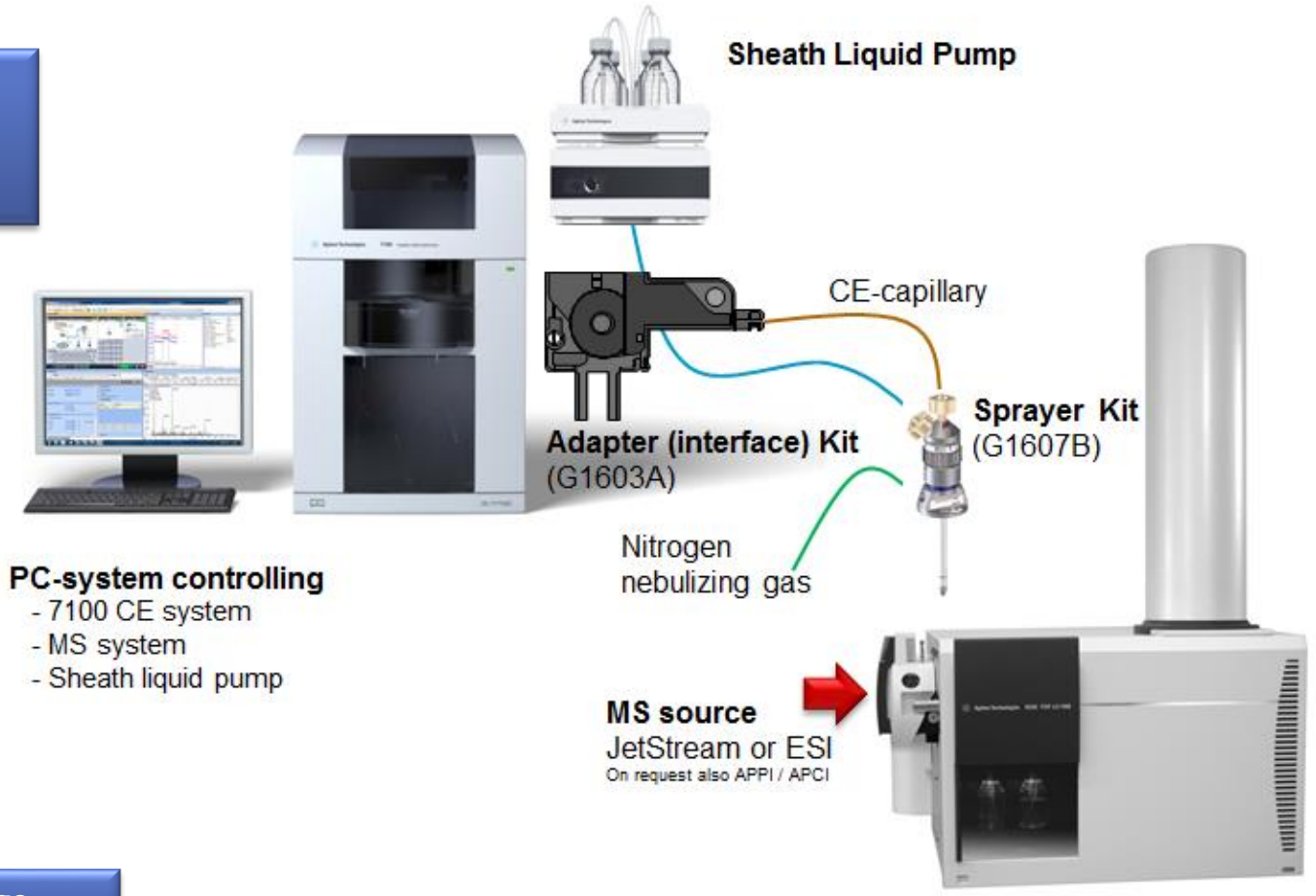
Agilent Triple Tube Sprayer IF



CE-ESI/MS - Current Status

Agilent MassHunter SW Control

Single point SW control
- 7100 CE instrument
- TOF,QTOF,QQQ
- LC make-up flow



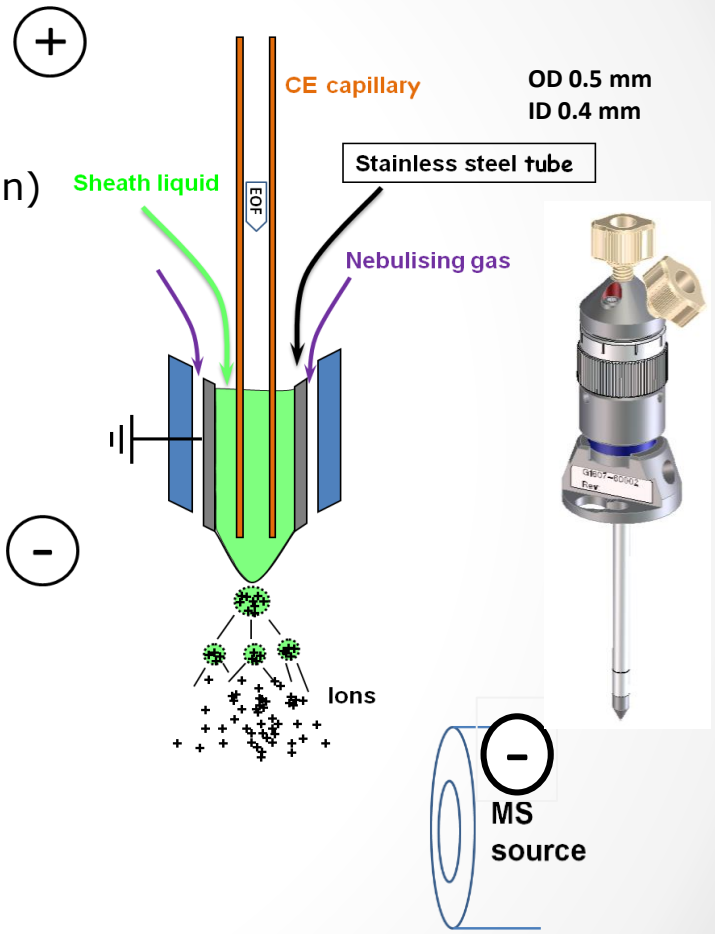
The Agilent CE/MS Advantage

Single vendor solution:	➡	direct and competent support
Sheath Liquid Interface:	➡	allows multiple ionization modes, ESI, APCI and APPI
Fast Switch LCMS ►CEMS:	➡	multiple sources; fits all Agilent 6000 series MS

CE-ESI/MS - Current Status

Agilent Triple Tube Sprayer IF

- ☺ Since 1995 a complete commercial system for CE-ESI/MS
- ☺ Proven robustness and reliability
- ☺ Decoupled CE separation and ionization chemistry
- ☺ Typical sensitivity 0.5 - 10 µM (in sample concentration)



Be aware……

Sensitivity may become compromised

- ☹ Solute concentration is reduced 5 - 50x by the sheath solvent depending on the actual EOF
- ☹ Because of the higher flow rate no benefit of nano-electrospray (<100 nL/min)

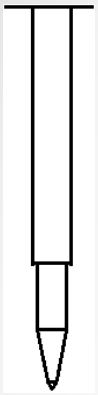
Pneumatic assistance required to establish the spray may cause an undesirable hydraulic flow, which need counter measures

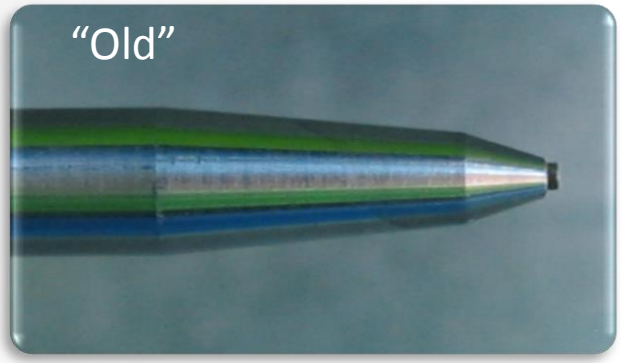
Galvanic reactions on the sprayer needle

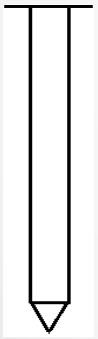
Agilent Approaches to Improve Sensitivity of CE/MS

- Improve interfacing
  - Design of spray needle
  - Conventional ESI vs. Jetstream IF
- Improve ion transfer

New, Compatible Sprayer Needle Assembly







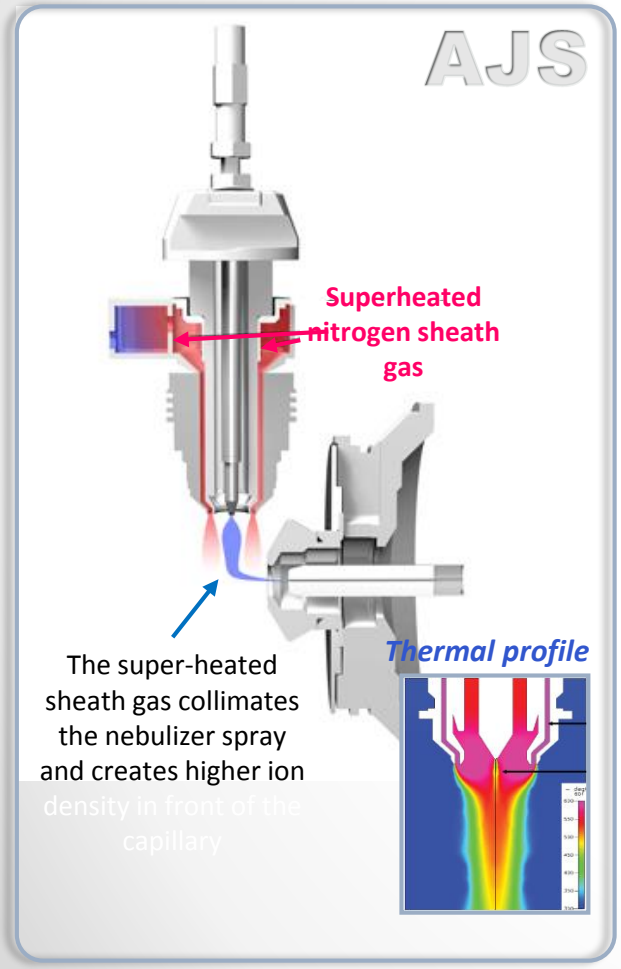
Changes:

- Needle Tip Geometry
- Co-alignment of spray needle with outer tube
- Length (1 mm shorter!)

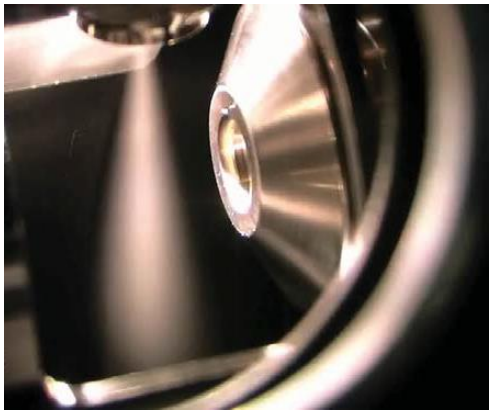
The new sprayer assembly fits all Agilent MS sources

Agilent Jet Stream Technology

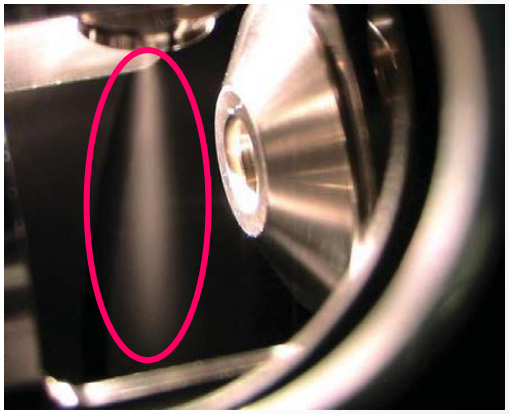
Available on Agilent 6000 Series MS Systems



25 °C



350 °C



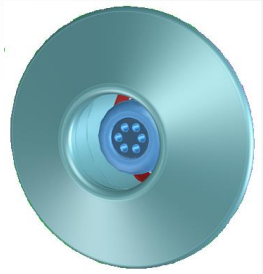
Agilent Jet Stream Thermal Gradient Focusing Technology, Technical Note 5990-3494EN (2009)

LC-MS ✓

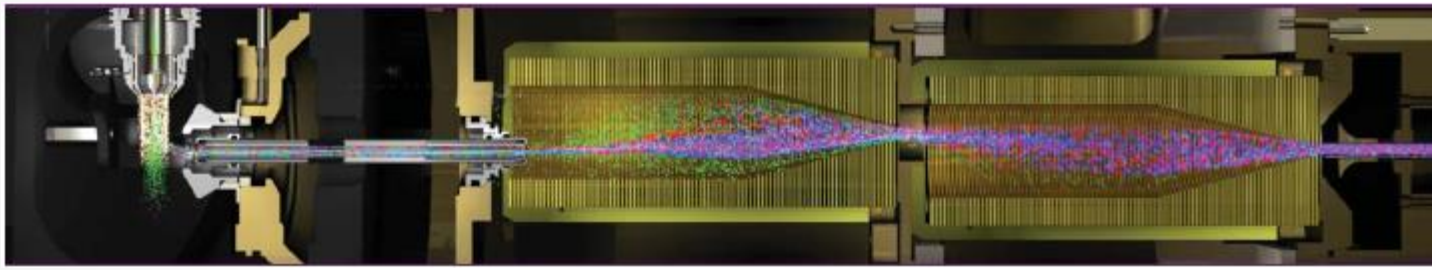
CE-MS ?

Improve Ion Transfer Technology

- Hexabore inlet capillary
  - Permeability equal, 6x higher flow



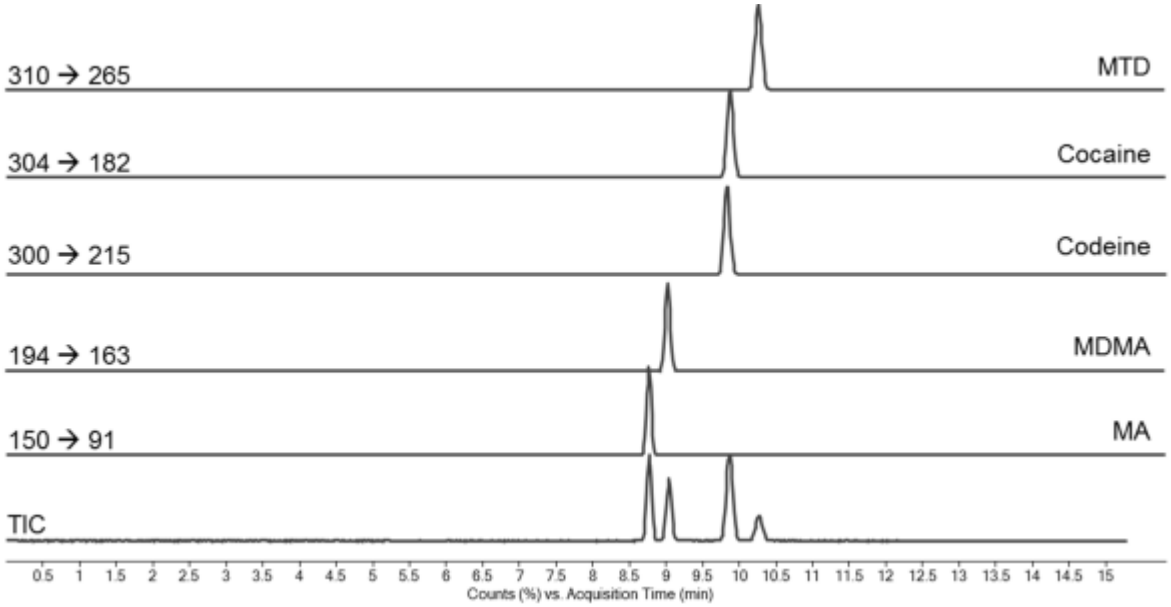
- Dual ion funnel (DIF) technology



Available on Agilent QQQ and QToF series.

Current Status of CE-ESI/MS Coupling Agilent Triple Tube Sprayer IF

Aqueous Standard Drugs of Abuse*



Concentr.	MA	MDMA	Codeine	COC	MTD
LOD [ng/mL]	0.5	0.5	5	2	50

Sensitivity: ~ 2 - 200 nM concentration in standard

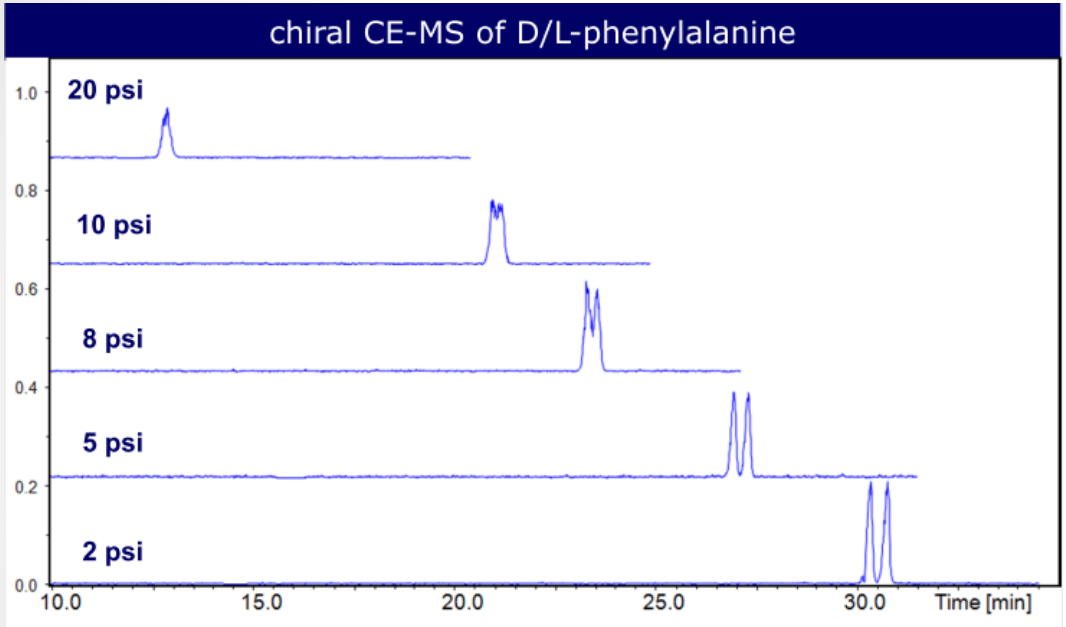
*I. Kohler et al., Analytica Chimica Acta, 780 (2013) 101

Sample Preconcentration Methods for CE-MS

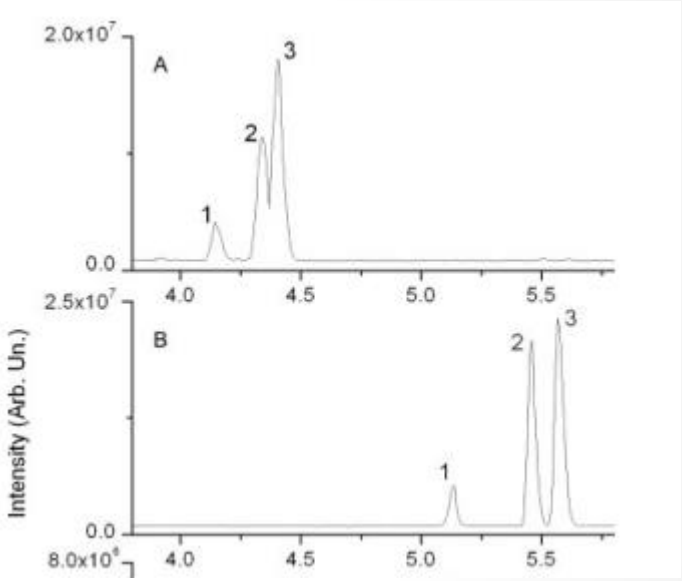
Field-amplified sample stacking (FASS)
Dynamic pH-junction method
pH-mediated FASS
Transient isotachophoresis (tITP)
In-capillary solid-phase extraction (SPE)
Liquid phase micro-extraction (LPME)

Hydraulic Flow in CE/MS Capillary

Influence of nebulizing gas pressure on flow and dispersion*



Under pressure inlet vial**

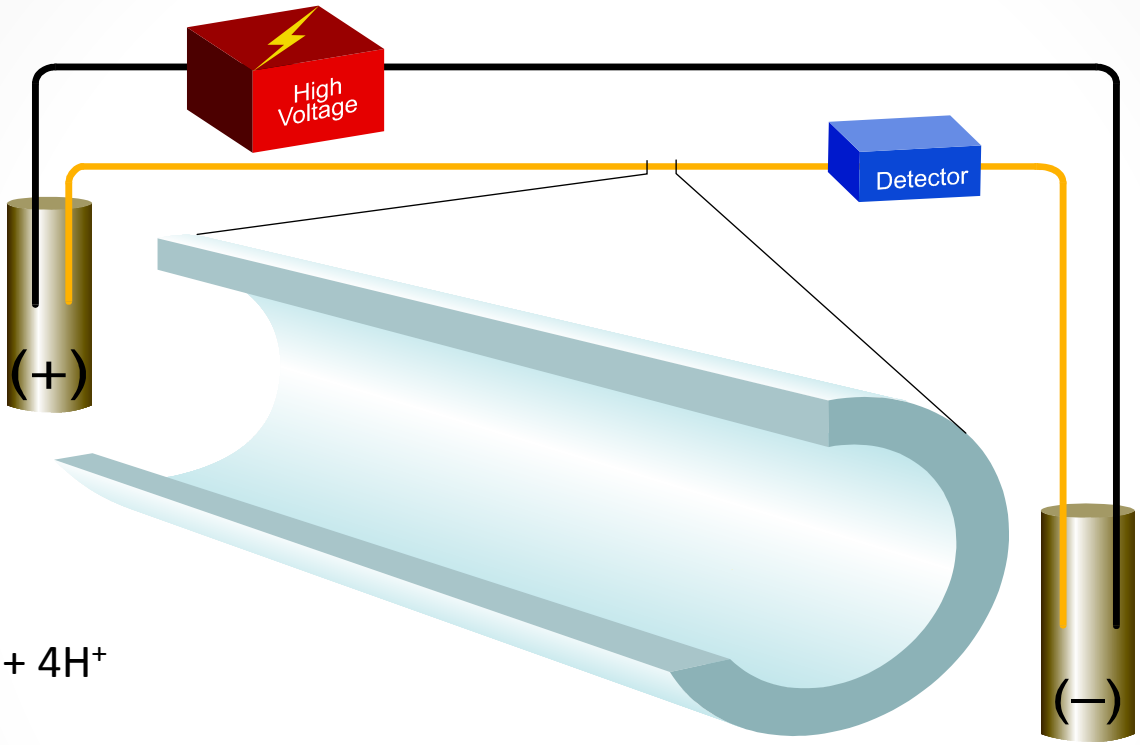


A. 0 mbar inlet vial
B. -50 mbar inlet vial

*Example courtesy of Prof. Govert Somsen, VU Amsterdam
G.W. Somsen et al., Electrophoresis 2006, **27, 2091–2099

Electrochemical Reactions in CE @ Platinum Electrodes*

Inlet Anode - normal polarity



Outlet - Cathode

Oxidation

$2H_2O - 4e^- = O_2 + 4H^+$

Reduction

$2H_2O + 2e^- = H_2 + 2OH^-$

$4H_2O + 4e^- = 2H_2O_2 + 2H_2$

* Courtesy David Chen, University of British Columbia

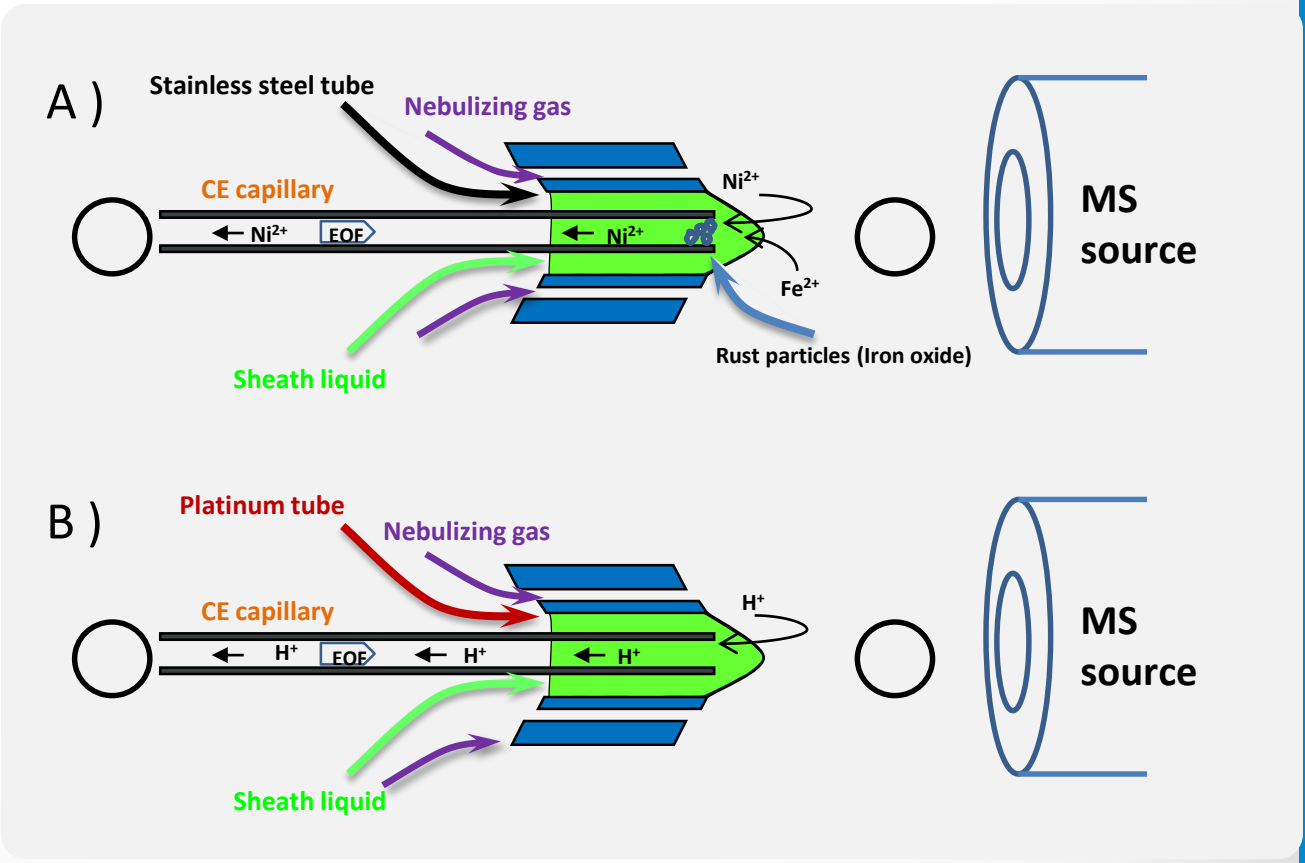
Electrochemical Reactions in CE-MS @ SST Electrode*

CE-MS of anions

Capillary coated with a cationic layer

Reverse polarity ➔EOF and mobility towards the outlet

Spray needle becomes the anode



Platinum Electrospray needle assembly for CE-MS, G7100-60041

* Soga et al., *Anal. Chem.* ***2009, 81, 6165–6174***

Conclusions

Agilent CE/MS System

- Only fully integrated CE/MS system on the market
  - Since 1995 only complete commercial system for CE-ESI/MS
  - Proven robustness and reliability
  - Decoupled CE separation and ionization chemistry
  - Typical sensitivity 0.5 - 10 µM (in sample concentration)
- Multiple ionization modes, ESI, APPI, APCI
- Compliant with standard ESI and JetStream sources and therefore with full MS portfolio
- Backed with application support
- Integrated SW control
  - 61xx series with OpenLab
  - 63xx, 64xx and 65xx series with MassHunter