Ion utilization efficiency: an effective way to compare different ESI-MS interfaces

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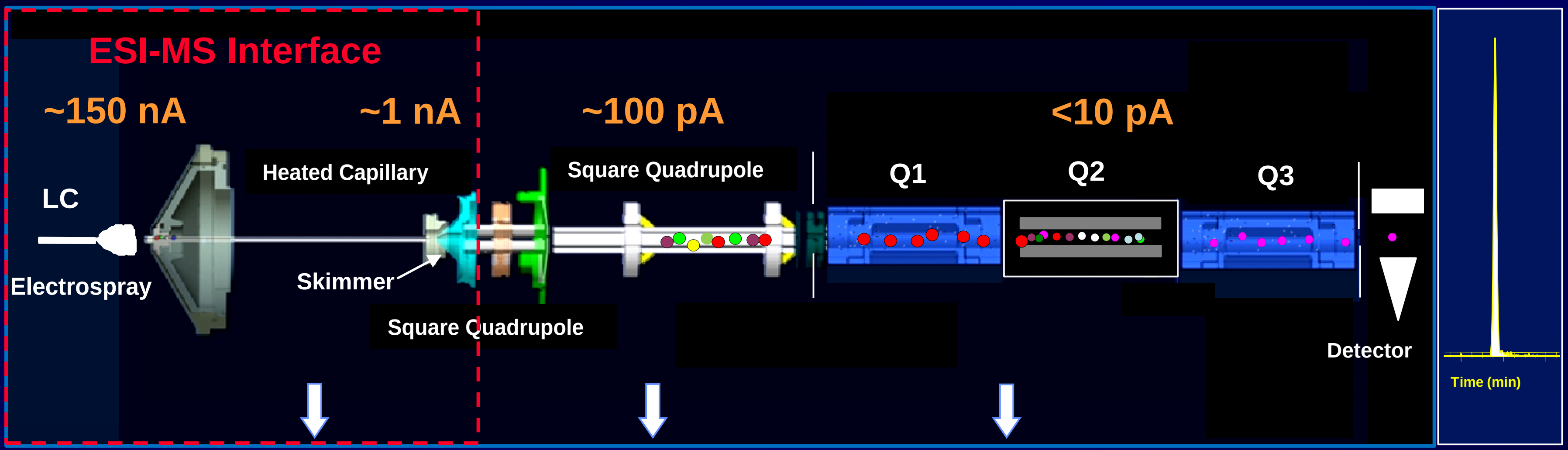
What Limits the ESI-MS Sensitivity?

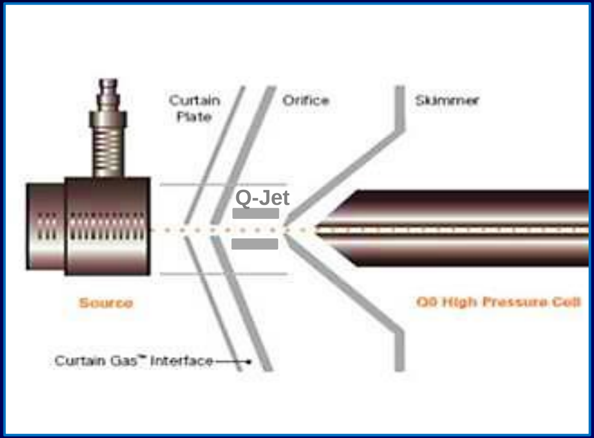


Triple Quad MS operating in SRM (MRM) mode

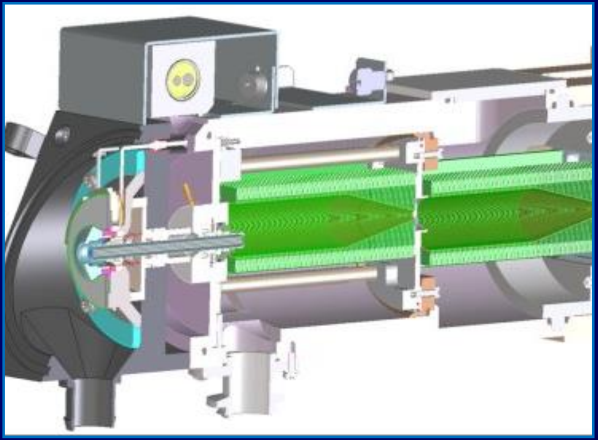
- Major ion loss (~99%) occurs in the ESI-MS interface region
- Developing a better ESI-MS interface to significantly improve ionization, ion sampling and ion transmission efficiencies has become a major R&D effort in MS instrumentation

Different ESI-MS interface designs on the commercial MS:

Sciex Interface:

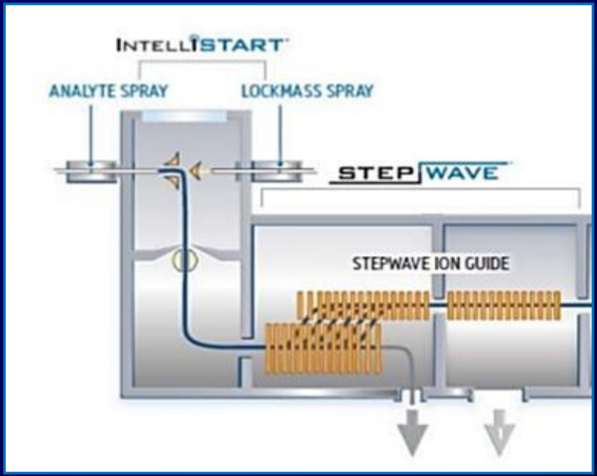


Agilent Interface:



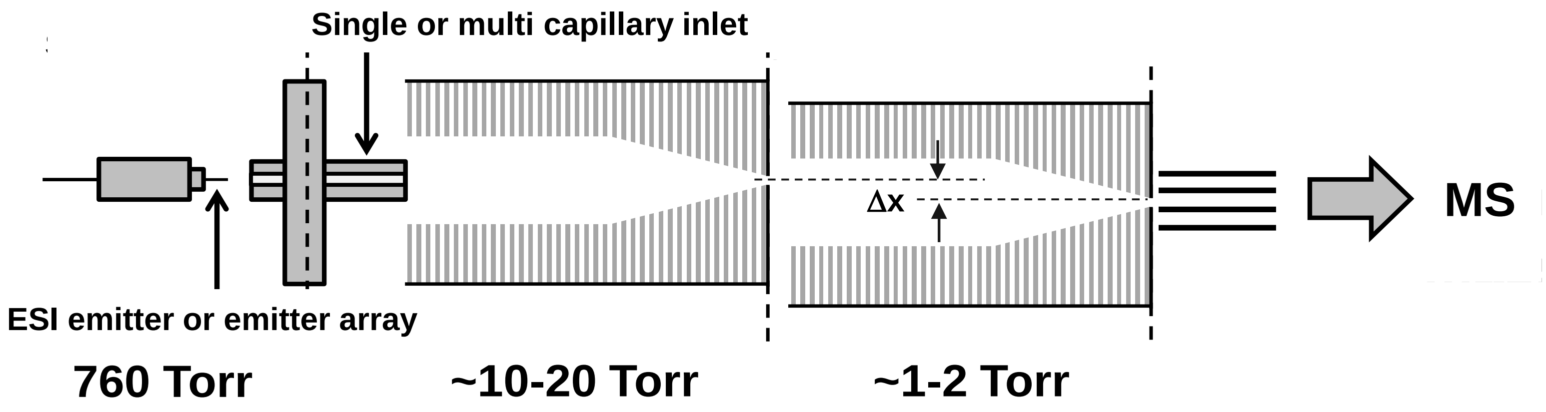
Thermo Interface:

Waters Interface:

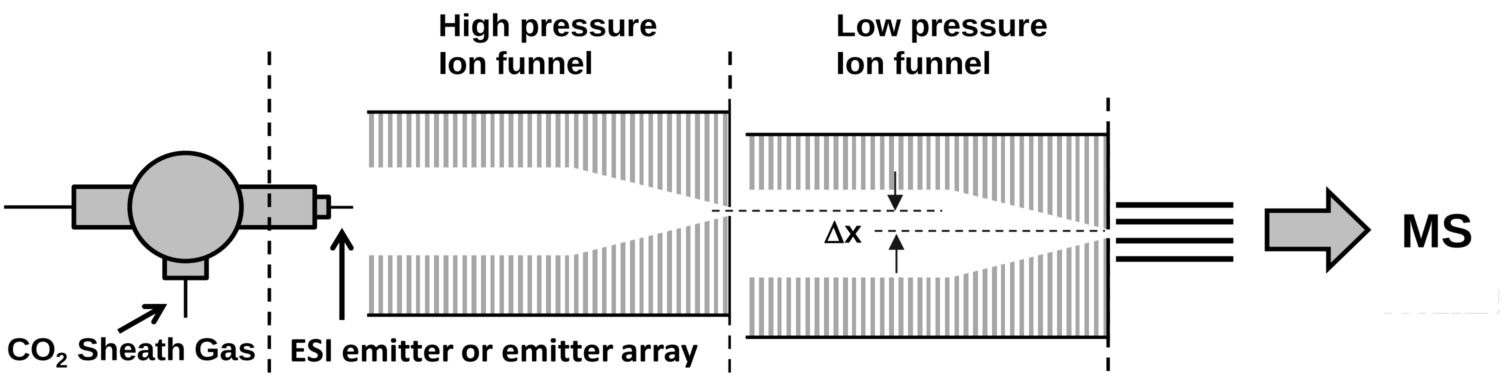


Two ESI-MS interfaces developed at PNNL:

a) Heated capillary/Tandem ion funnel interface

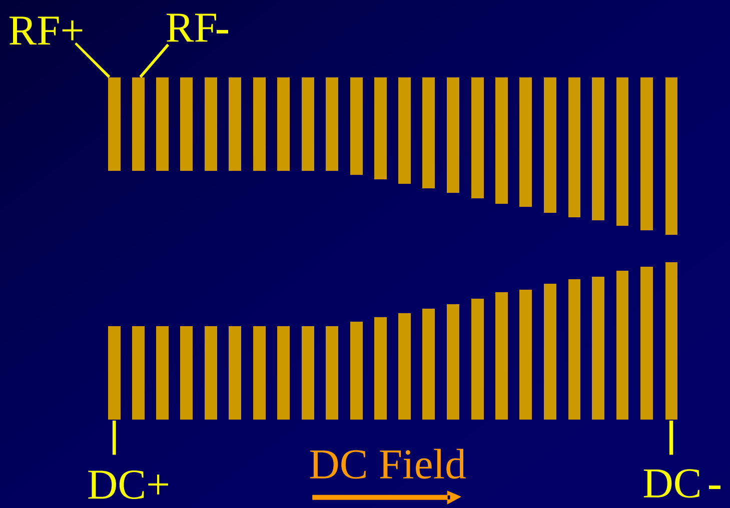


b) Subambient pressure ionization with nanoelectrospray (SPIN):



A key technology to our ESI-MS interface:

Electrodynamic ion funnel



$$RF^{+} = V{*}Cos(\omega t)$$

$$RF^{-} = V{*}Cos(\omega t + 180^{o})$$

a) Regular ion funnel:

RF: 500 – 1000 kHz, 50 – 120 $V_{p\text{-}p}$

Operating pressure: 1 – 5 Torr

b) High pressure ion funnel:

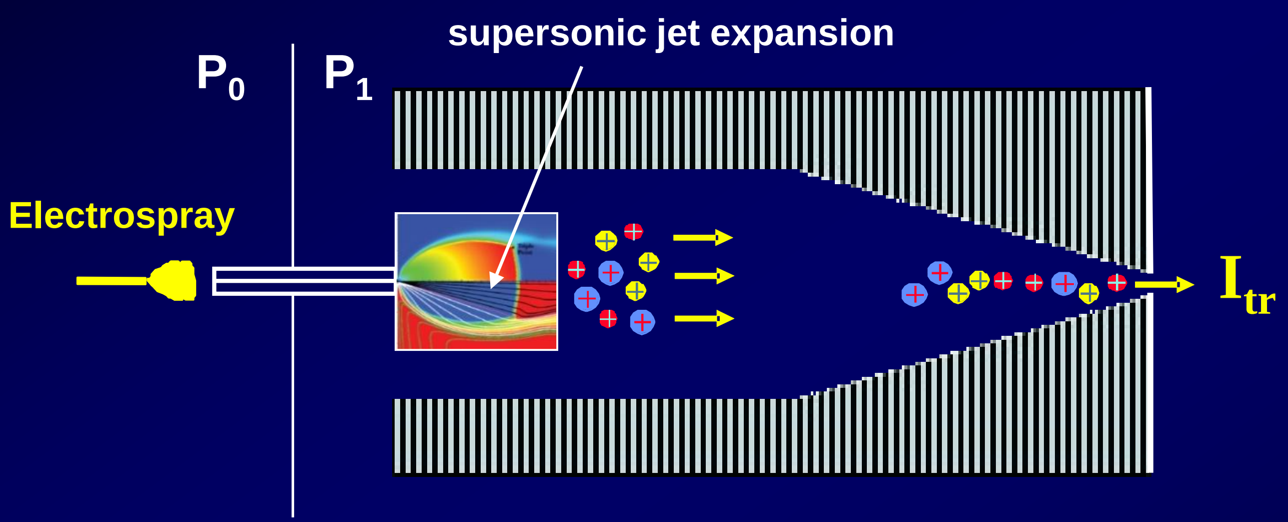
RF: 1200 – 2000 kHz, 200 – 400 $V_{p\text{-}p}$

Operating pressure: 5 – 25 Torr

Common methods to evaluate the performance of an ESI-MS interface:

- Direct measurement of electric current transmitted through the ESI-MS interface at a given ESI operating condition (<u>the measured current may not represent the useful ion current measured at the MS detector</u>)
- Based on the ion current at the MS detector at a given ESI-MS operating condition (mass spectrum total ion current) (<u>the measurement may not represent only the ESI-MS interface performance</u>)

Origin of the problem to the transmitted electric current I_{tr} measurement: supersonic expansion

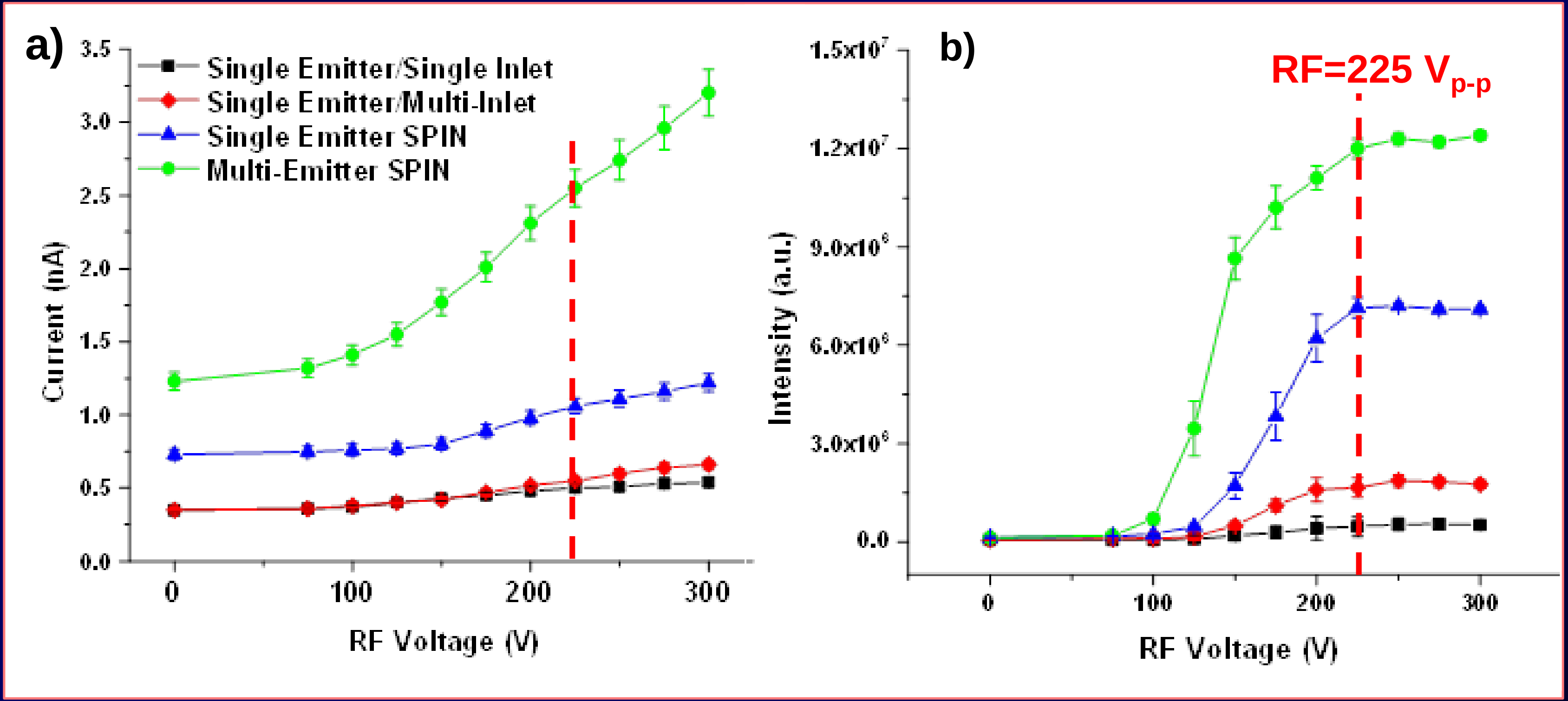


For adiabatic thermal expansion: $$\frac{P1}{P0} = \left(\frac{T1}{T0}\right)^{\kappa/(\kappa-1)}$$ (for air $\kappa=1.4$)

(For an incoming jet of 300 °C (573 K), the final jet temperature will be -86 °C (187 K) after the expansion with P_0 = 760 Torr and P_1 = 15 Torr.)

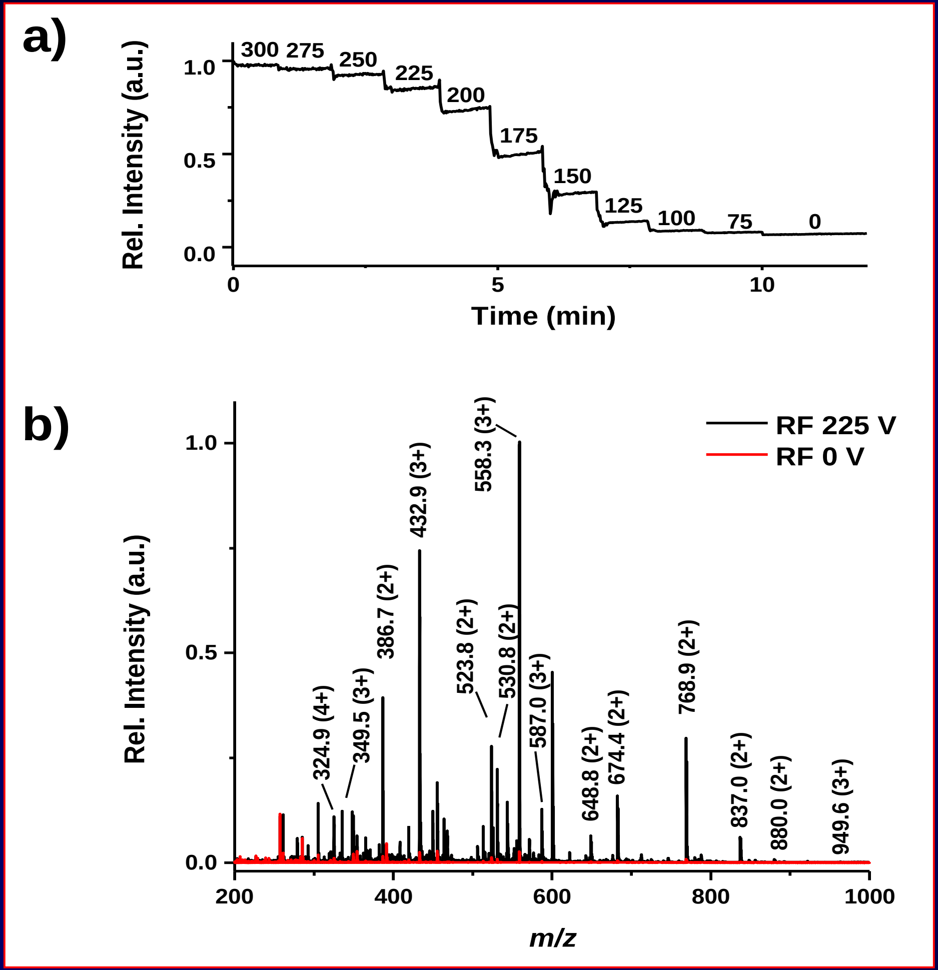
- **Formation of charged solvent/solvent-analyte clusters**

a) Transmitted electric current through the high pressure ion funnel and b) extracted ion current from the corresponding mass spectra for 3+ neurotensin (m/z = 558.3) at different high pressure ion funnel RF voltages and with different interface configurations.



High pressure funnel : 22 Torr ; Total ESI flow rate : 200 nL/min; Sample: a mixture of eight peptides (human angiotensin I, human angiotensin II, bradykinin, fibrinopeptide A, kemptide, neurotensin, porcine angiotensinogen, and Substance P) with 100 nM each in 90:10 Water : acetonitrile +0.1% Formic acid solvent.

a) MS total ion current at different high pressure ion funnel RF voltages and b) mass spectra at RF voltages of 225 V (black trace), and 0 V (red trace) using 100 nM peptide mixture for the single emitter/SPIN source configuration.



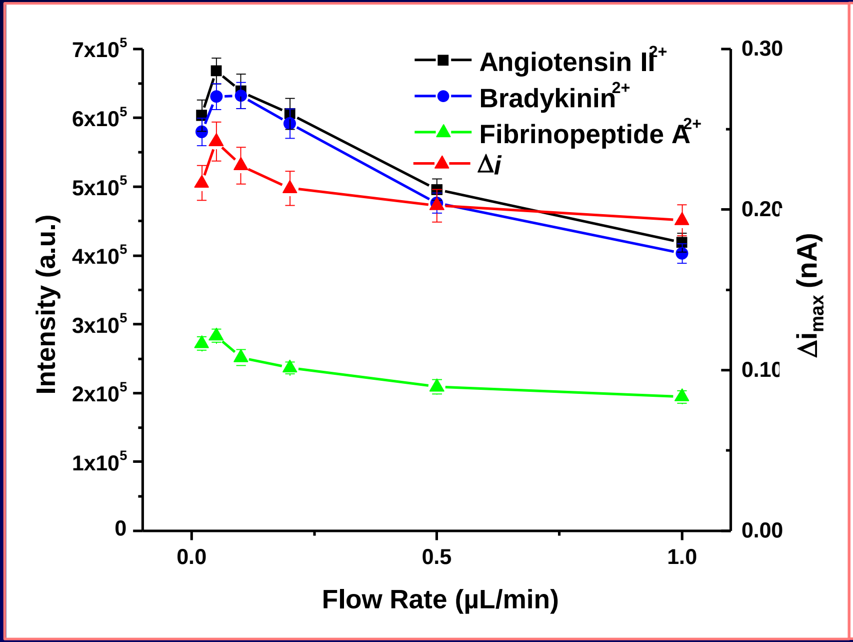
The fraction of the gas-phase ion current in the total transmitted electric current in any RF voltage can be approximated by,

$$\Delta i = i_{RF,on} - i_{RF,off}$$

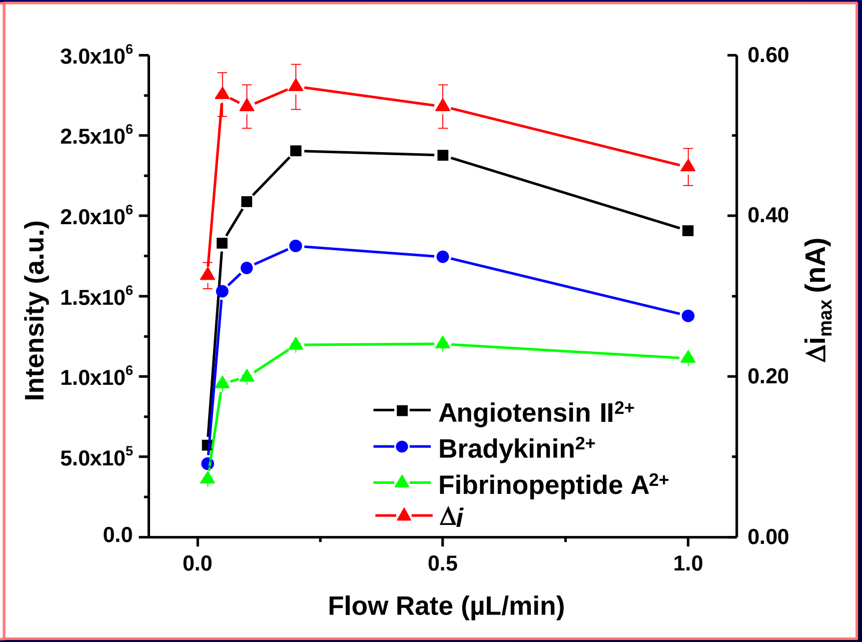
where 0 $V_{p\text{-}p}$ < RF < 225 $V_{p\text{-}p}$.

Δi_{max} (between RF= 0 V_{p-p} and 225 V_{p-p}) and analyte peak intensity at different ESI flow rates using two different interface configurations

a) single emitter/single capillary interface:



b) single emitter/SPIN interface



♦ Δi_{max} follows well with the analyte MS peak intensity in the entire ESI flow rate range from 20 nL/min to 1 mL/min for both interface configurations.

A effective parameter to compare the performance of different ESI-MS interfaces: Ion Utilization efficiency

Interface ion utilization efficiency: the percentage of analyte molecules in a sample solution being converted into gas phase ions and transmitted through the interface.

The maximum ion current, I_J, for analyte J if all the molecules in the solution were converted into gas phase ions:

$$I_J = QF \sum_{z=1}^{i(J)} z\delta_{z,J} C_J \qquad (1)$$

where Q is the liquid flow rate, F is the Faraday constant, $\delta_{z,J}$ is the fraction of J that carries z charges, C_J is the molar concentration, and $i(J)$ is the maximum charge state of J

The maximum total analyte ion current, I_A, for a mixture of N compounds under the complete ionization condition:

$$I_A = QF \sum_{J=1}^{N} \left(\sum_{z=1}^{i(J)} z\delta_{z,J} C_J \right) \qquad (2)$$

The ion utilization efficiency ε_J for analyte *J* in the sample mixture:

$$\varepsilon_J = \frac{\sum_{z=1}^{i(J)} \Delta i \, X_{z,J,TIC}}{I_J} \qquad (3)$$

where ***Δi*** is the fraction of gas phase ion current in the total transmitted electric current through a MS interface, $X_{z,J,TIC}$ is the ratio of extracted ion current (EIC) for z charge state of analyte J to the total ion current (TIC) from a corresponding mass spectrum

The ion utilization efficiency ε_A for all the analytes in the sample mixture:

$$\varepsilon_A = \frac{\Delta i X_A}{I_A} \qquad (4)$$

where X_A is the ratio of total analyte current (summing all the analyte EICs) to the TIC from the corresponding mass spectrum.

Comparison of ion utilization efficiencies under different MS interface configurations.

Peptide	Single Emitter/ Single Inlet ESI (100 nL/min)	Single Emitter/ Multi-Inlet ESI (100 nL/min)	Single Emitter/ SPIN (100 nL/min)	10 Emitter Array/ SPIN (200 nL/min)	Single Emitter/ SPIN (20 nL/min)
Fibrinopeptide A	4.8 ±0.1	3.3 ±0.6	9.6 ±0.3	9.3 ±0.7	17.2 ±0.4
Substance P	3.9 ±0.1	4.6 ±1.1	6.0 ±0.4	8.8 ±1.6	34.6 ±2.1
Angiotensinogen	4.9 ±0.1	2.1 ±0.6	5.6 ±0.3	10.2 ±2.0	11.0 ±1.2
Neurotensin	3.4 ±0.3	7.0 ±1.2	12.9 ±1.4	34.5 ±3.6	50.3 ±2.8
Bradykinin	3.9 ±0.2	7.5 ±1.1	2.8 ±0.2	7.0 ±1.6	30.0 ±1.6
Angiotensin II	4.9 ±0.2	5.1 ±0.8	3.9 ±0.7	9.6 ±1.3	34.7 ±1.8
Angiotensin I	5.1 ±0.4	5.8 ±1.2	7.0 ±0.5	16.4 ±2.1	48.7 ±4.4
Kemptide	3.2 ±0.1	5.0 ±0.9	1.9 ±0.4	6.0 ±0.5	20.7 ±1.1
Total analyte Ion utilization efficiency	4.0 ±0.3	4.2 ±0.8	6.5 ±0.3	13.0 ±2.3	26.7 ±1.8

Conclusions:

- The ion cloud transmitted through ESI-MS interface is in general a mixture of fully desolvated gas phase ions and ‘residue’ charged solvent and analyte/solvent clusters.
- The portion of fully desolvated gas phase ions correlates well with the final intensity of the ion current detected by MS.
- Ion utilization efficiency based approach provides an effective metric to evaluate the overall efficiency of an ESI-MS interface and allows performance comparison among different interface designs.
- Of all the interfaces evaluated in this study, an emitter array/SPIN-MS interface demonstrated the highest ion current/MS-signal intensity with the corresponding best ion utilization efficiency at a given total ESI flow rate.

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