



Femto-Electrospray Ionization: Current Dynamics and Signal-to-Noise Enhancement

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Highlights:

- FemtoESI pulsation and continuous ESI modes with fA to nA currents.
- FemtoESI regime produces higher surface-to-noise compared to nanoESI
- Characterization of low flow regime.

Introduction:

- Current measurements reveal the characteristics of two distinct electrospray regimes.
- The identification of electrospray onset based on spray current and total ion count analysis.
- The current dynamics reflect the performance of electrospray ionization and can be revealed by analyte's signal-to-noise ratio enhancements.

Methods:

- The Borosilicate emitter tips having 2-3 μm outer diameter were used.
- The low flow electrospray current characterization using Keithley electrometer with 10 fA (DC) resolution.
- Direct infusion in femtoESI and nanoESI regime for samples with micro to nano molar concentration on LTQ velos mass analyzer.
- Noise is the standard deviation of a region with no significant signal where background signal are with-in 20 folds variation, calculated using MATLAB.

Hypothesized difference in low flow ESI VS. nanoESI

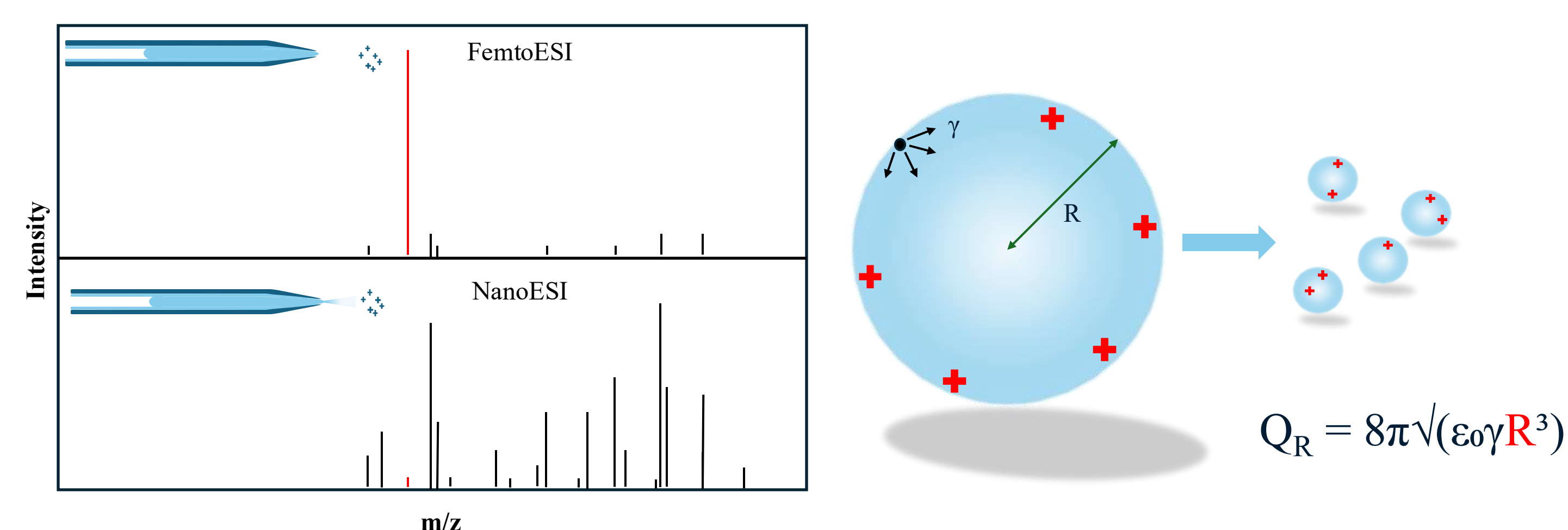


Figure 1. Low flow electrospray is known to generate smaller sized parent droplets, resulting in higher surface charge density on droplets and ultimately enhances ionization efficiency.

On-Demand alternation of electrospray

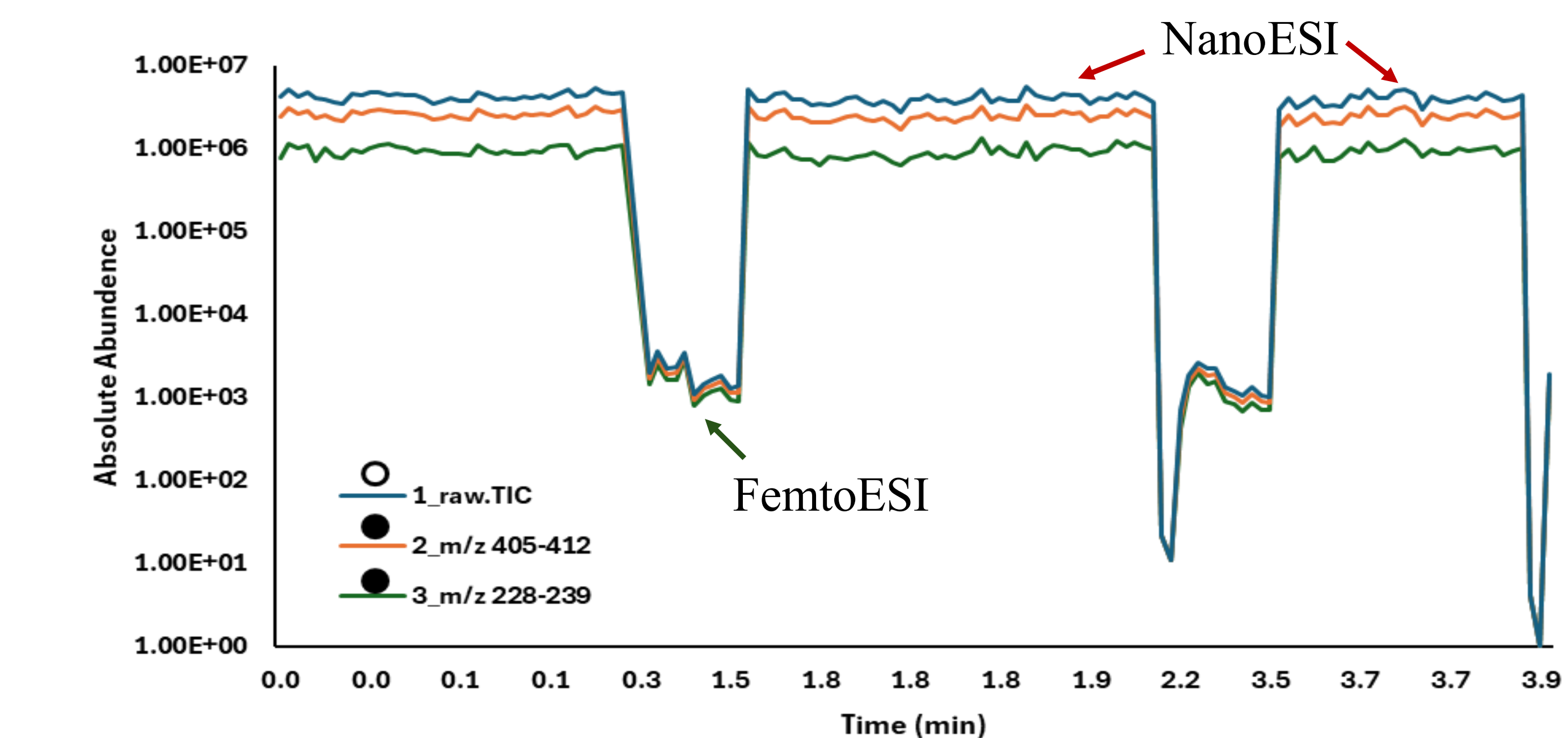


Figure 2. Extracted ion chromatogram and total ion chromatogram gives visual comparison of signal intensity of two regimes, nanoESI (10^7) and FemtoESI (10^3). 1. TIC 2. EIC for m/z 405-412 and 3. m/z 228-239.

Femto-ESI optimization using current and TIC measurements

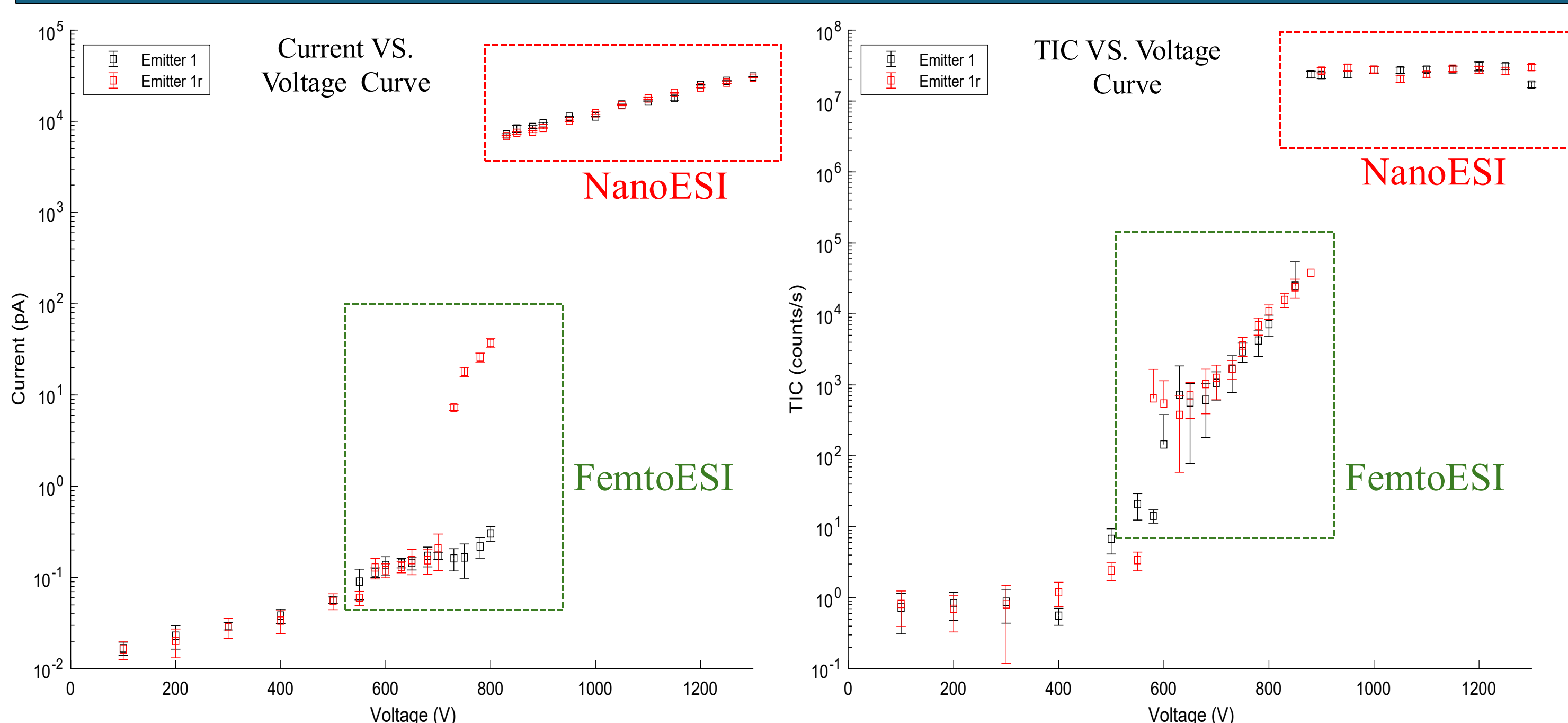


Figure 3. Two distinguished current regimes for aq. 1 μM N-(n-dodecyl)-N, N, N-trimethylammonium bromide solution (DTAB) using was repeated using same emitter shown as **1** (Black) and **1r** (Red). The I-V with (~ 100 fA) and TIC-V curve, both indicate the onset around 580-600 V.

Exemplary Signal-to-Noise ratio (S/N) Calculation

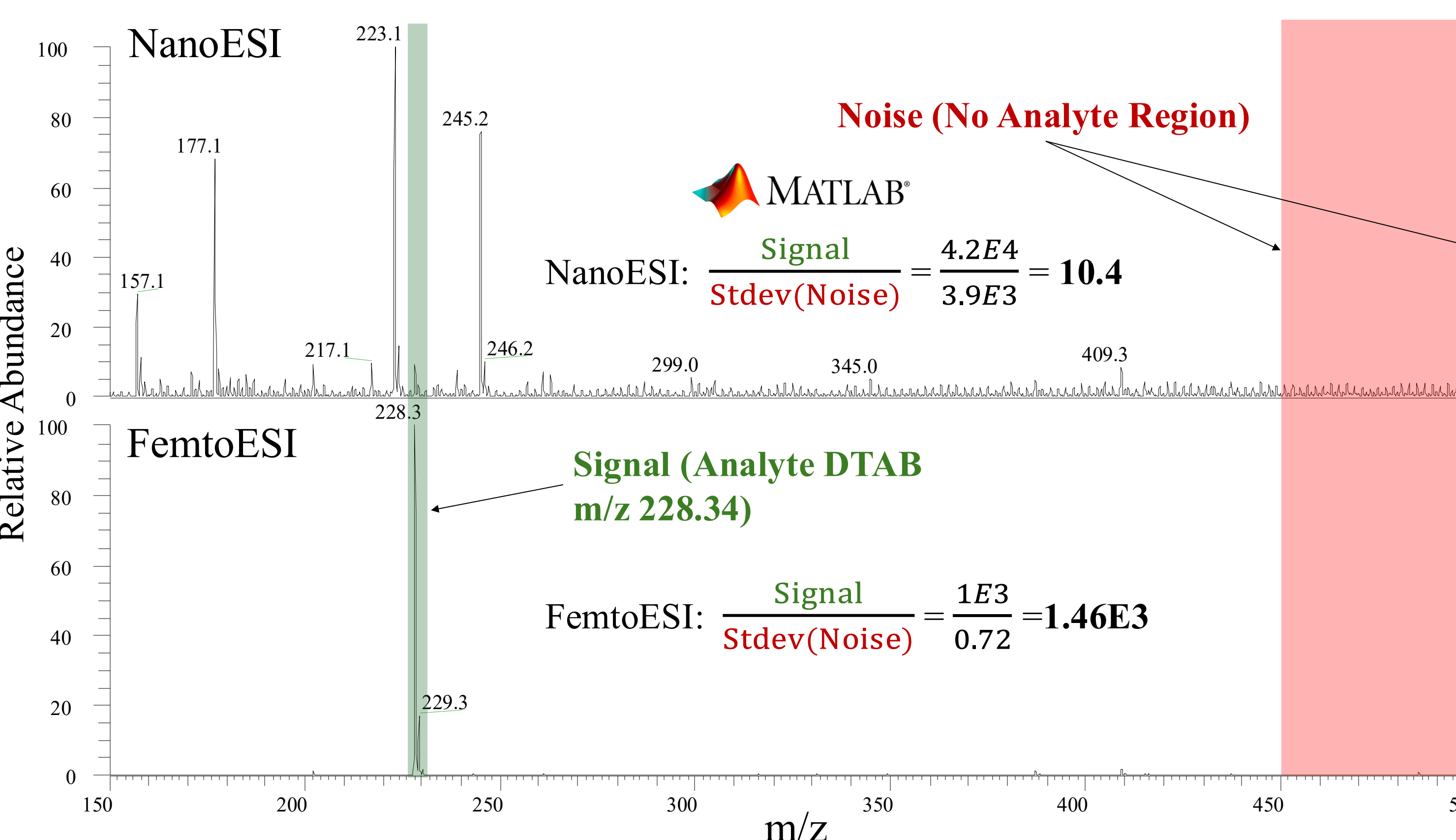


Figure 4. Standard deviation of m/z values in **no analyte region** is treated as noise and analyte intensity is directly isolated using same MATLAB script. The ratio of these two quantities has been reported as signal-to-noise ratio.

Signal-to-noise ratio visualization for pre-charged analytes

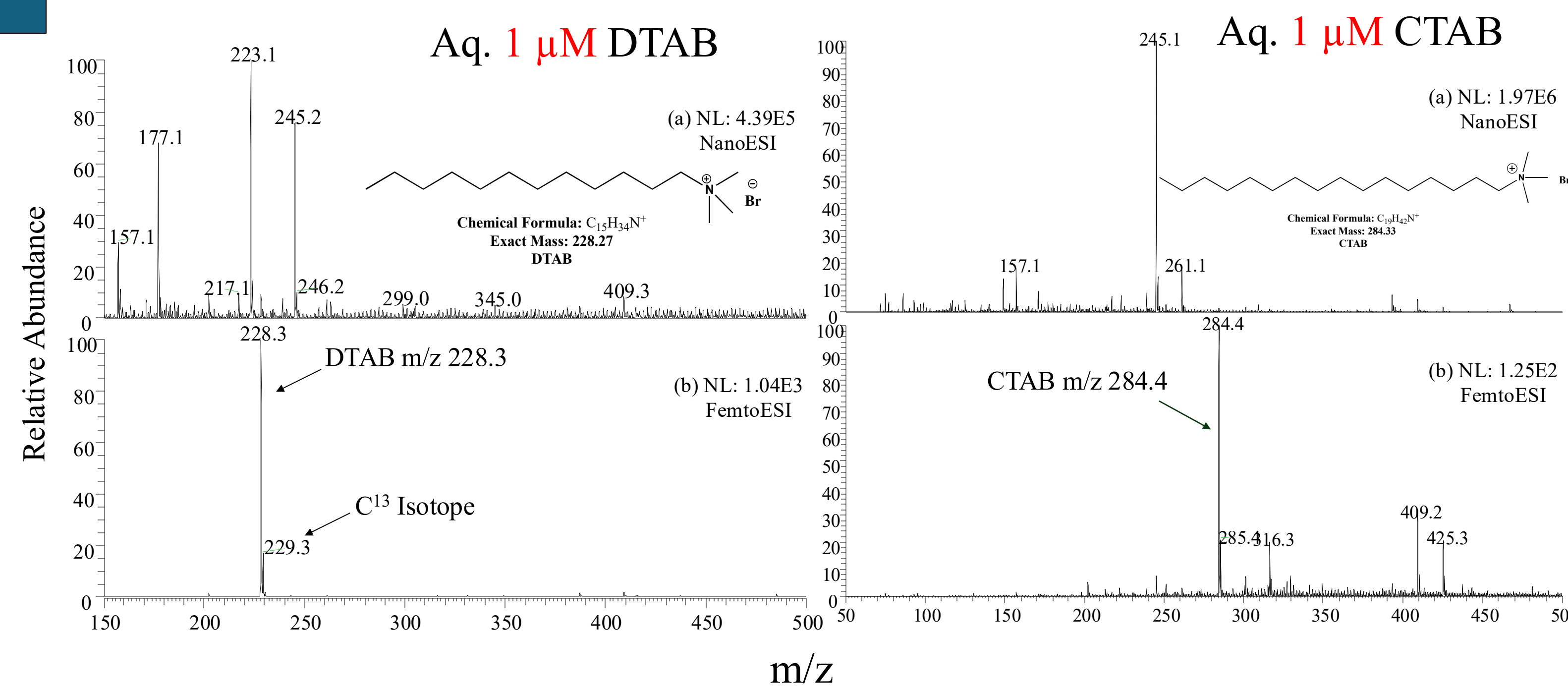


Figure 5. Mass spectrum of Aq. 1 μM of DTAB (left) and N-(n-hexadecyl)-N, N, N-trimethylammonium bromide (CTAB, right) in nanoESI (Top) and FemtoESI (bottom) gives visual compares of signal-to-noise ratio of analyte at 228.34 m/z.

Effect of reduced concentration on signal-to-noise ratio

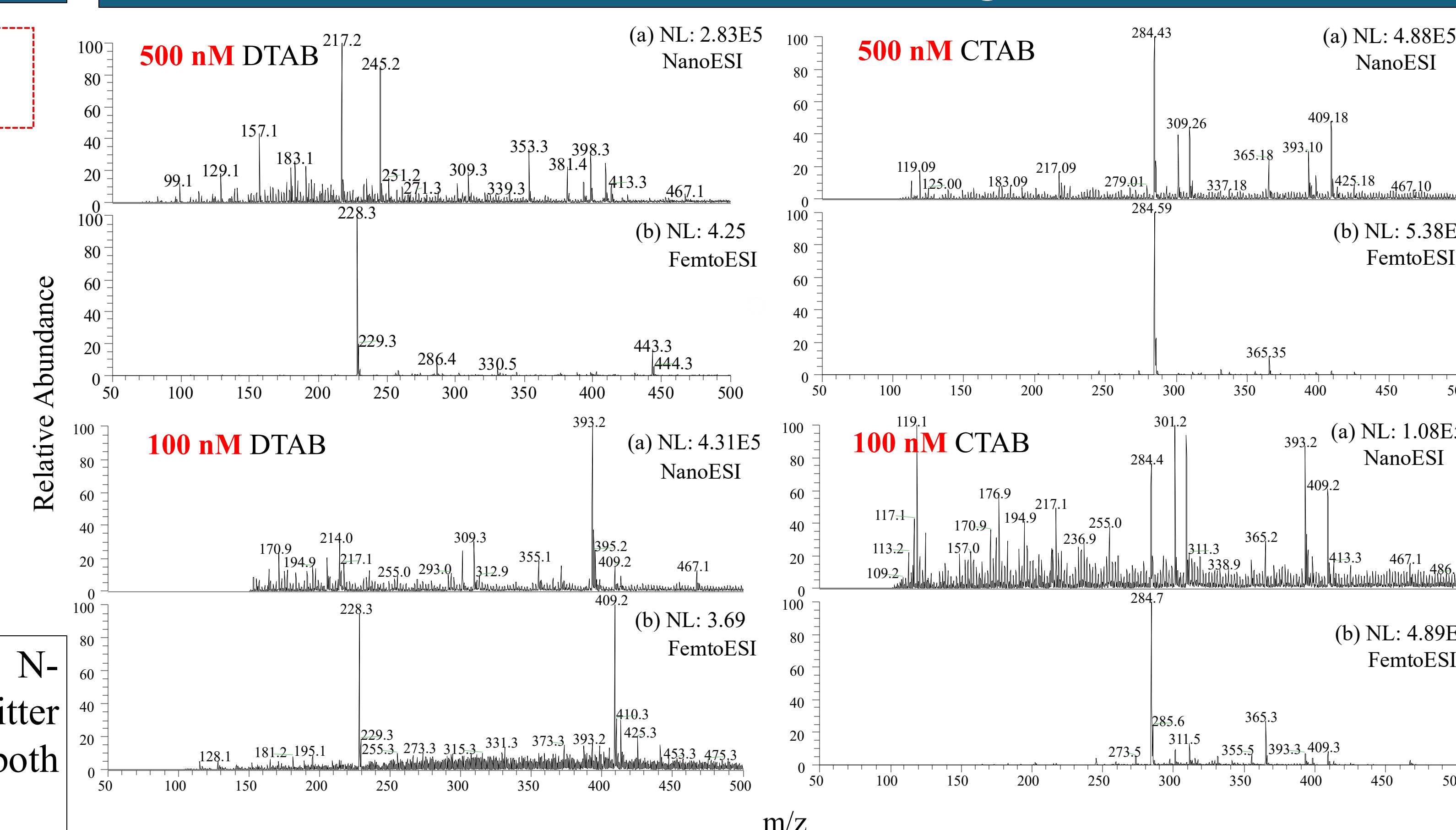


Figure 6. Mass spectrum of DTAB (left) and CTAB (right) 500 nM and 100 nM in nanoESI (Top) and FemtoESI (bottom) gives visual comparison. The signal-to-noise ratio of both analytes are summarized in table below.

Signal-to-noise ratio results

DTAB Concentration	FemtoESI SNR	nanoESI SNR	(FemtoESI/nanoESI) SNR
1 μM	1.46E3	1.04E1	139
500 nM	1.78E2	5.9E0	29
100 nM	6.39E1	1.23E0	52

CTAB Concentration	FemtoESI SNR	nanoESI SNR	(FemtoESI/nanoESI) SNR
1 μM	2.4E2	7.2E0	33
500 nM	4.2E3	9.7E1	43
100 nM	3.9E2	3.1E1	12

Conclusions:

- Based on IV measurements low flow electrospray exhibit highly diverse ionization patterns, including nA to pA currents.
- These patterns are reproducible within an experiment, but are highly sensitive to alignment, voltage, and emitter tips geometrical variations.
- FemtoESI signal-to-noise is >10 times that of nanoESI across 10-fold dilution. Note: Although signal-to-noise ratio show no apparent trend.
- In this work, the femtoESI regime was achieved 2 to 3-folds lower than typical 10^5 - 10^6 nanoESI normalized level (NL). The TIC of nano and femtoESI mode are approximately 10^7 and 10^3 respectively.

Acknowledgements:

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References:

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