Additional Separation for Ambient Ionisation Mass Spectrometry: The Development of a DESI-FAIMS-MS Interface

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1. Introduction

Ambient ionization mass spectrometry has been increasingly used to investigate the distribution of molecules in samples or objects, in situ, without the need for sample preparation.

Disadvantages include:

- Complex biological samples have inherent matrix effects.
- No pre-separation means analysis cannot be selective.
- Highly abundant analytes may suppress the detection of lower abundance species.
- In tandem mass spectrometry, isobaric interferences can result in overlapping fragments which present a significant challenge for spectral interpretation.

In-source separation techniques such as field asymmetric ion mobility spectrometry (FAIMS) can be used when chromatographic separation techniques cannot be deployed.

- FAIMS separates ions according to field-induced changes in their collision cross section (Figure 1).

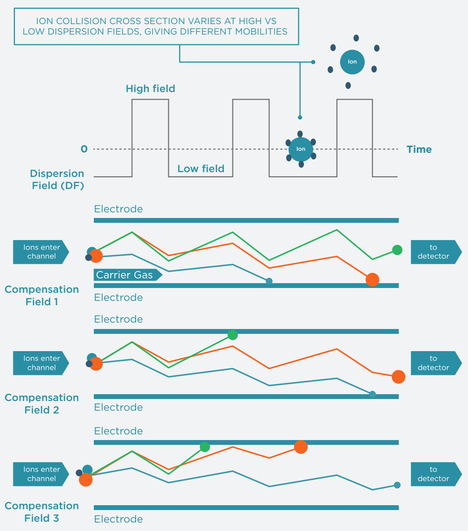


Figure 1. FAIMS separates ions according to field-induced changes in their collision cross section

- As the field reverses polarity and changes magnitude, the ion changes direction and speed.
- Each ion has specific net sideways drift velocity.
- By applying a DC compensation field (CF), this drift can be corrected, focussing ions through the device.
- Analogous to atmospheric pressure quadrupole.
- Highly orthogonal to *m/z* separation offering a means to increase peak capacity for the analysis of complex samples by ambient ionization mass spectrometry.
- Can selectively transmit ion of interest prior to mass spectral detection.

A recent study[1] demonstrated the use of FAIMS in combination with desorption electrospray ionization (DESI) (Figure 2).

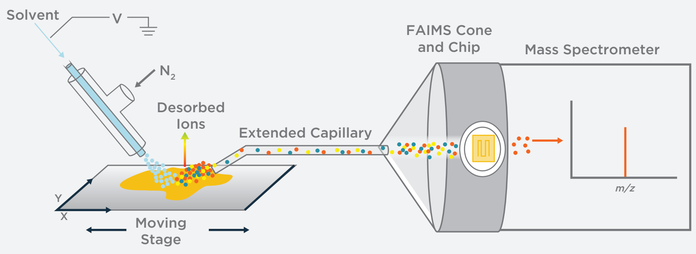


Figure 2. Schematic representation of selective FAIMS transmission of ion of interest using DESI-FAIMS-MS

- DESI-FAIMS-MS resulted in enhanced mass spectral detection compared with DESI-MS alone.
- Increased s/n due to suppressed background.
- Increased absolute signal as trap was preferentially filled with FAIMS-transmitted low abundance ions, rather than naturally high abundance species.

Here we describe optimisation of the mechanical integration of a desorption electrospray ionization (DESI) system, with FAIMS.

2. Methods

Experiments were carried out using an ultraFAIMS-T1 system (Owlstone Medical Ltd., Cambridge, UK) installed on Q-Exactive and Thermo Elite mass spectrometers (Thermo Scientific, San Jose, CA) with a 2D Omni Spray (Prosolia Inc., Indianapolis, IN) (Figure 3).

ultraFAIMS is a miniaturised FAIMS device in which the electrodes are formed from a micro-manufactured chip.

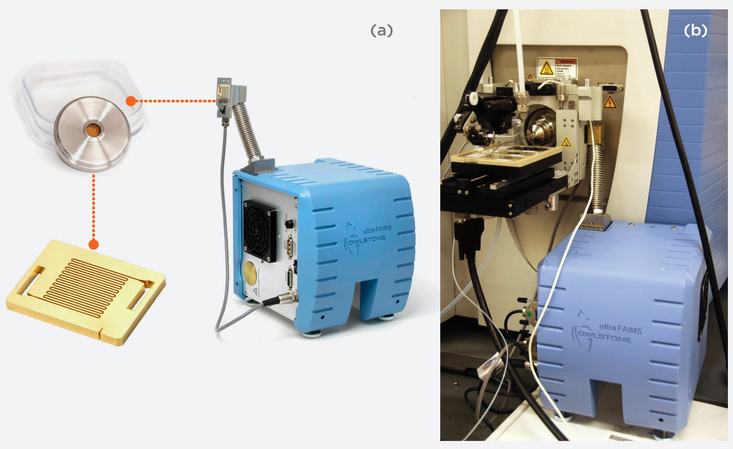


Figure 3. (a) ultraFAIMS T1 device and (b) installed on Q-Exactive with 2D Omni Spray

3. DESI-FAIMS interface designs

To integrate the ultraFAIMS device and Omni Spray source an extension to the transfer capillary is required (Figure 4).

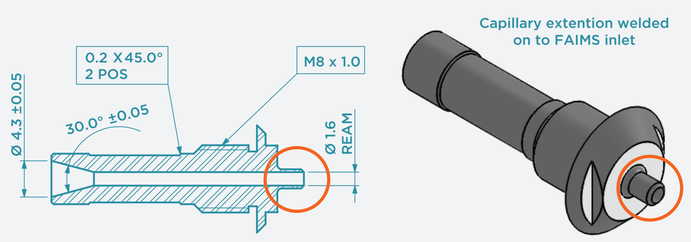


Figure 4. Standard FAIMS inlet design indicating part needing extension

Key goals of the design were to:

- Deliver a carrier gas velocity profile through the FAIMS chip optimized for high separation performance.
- Minimize transmission losses.

In the first design iteration (DI1), an unheated extended transfer tube of 5” was welded on to the FAIMS inlet (Figure 5).

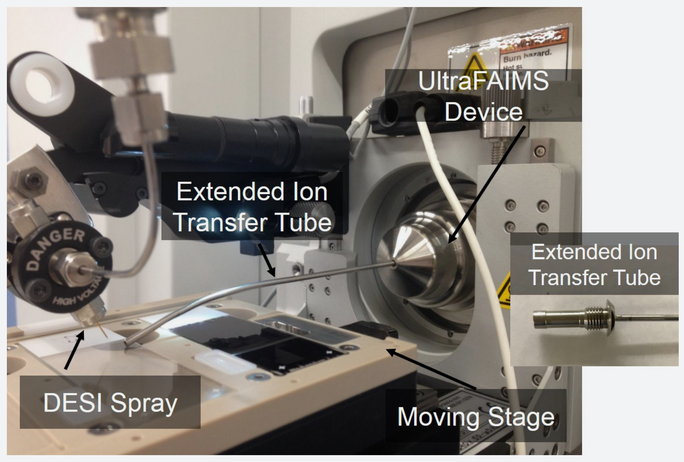


Figure 5. (a) ultraFAIMS T1 device and (b) installed on Q-Exactive with 2D Omni Spray

- Inner diameter (ID) of 0.067” was used to best replicate the standard FAIMS inlet ID.
- Previously optimised for flow rate through the FAIMS chip for optimal full width at half maximum (FWHM)[2].
- Different thickness walls were tested (Figure 6).

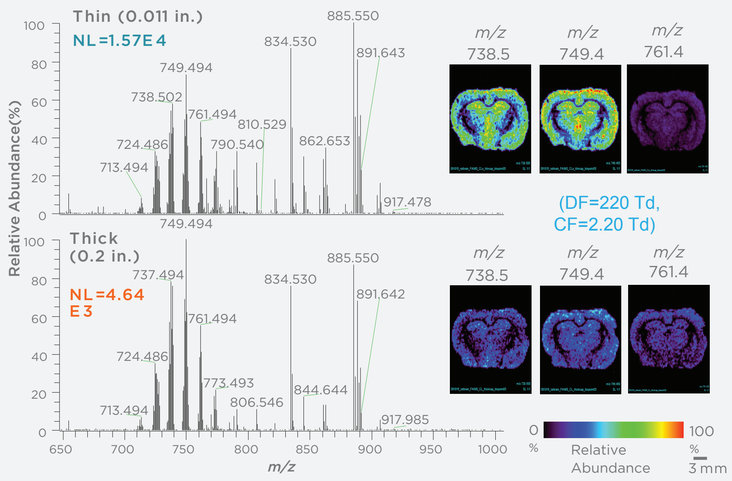
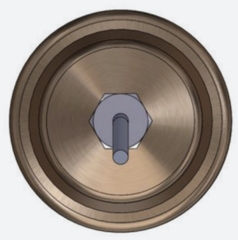


Figure 6. Comparison of thickest and thinnest walled capillaries with FAIMS voltages set to transmit cardiolipins

- Thinnest walls gave best sensitivity
- Direction is fixed as a result of being welded
- Small changes in capillary direction could account for differences in signal intensity.

Options:

1. Fix the capillary in the optimal location.
2. Make the direction of the bend adjustable (Figure 7).



- Having the capillary attached to a Swagelok nut allows it to be rotated upon its axis.
- Allows adjusting of capillary angle towards stage.
- When nut is tightened it will lock its orientation.

Figure 7. Rotation of capillary towards stage via Swagelok nut

A modified FAIMS inlet (DI2) was designed to take a 1/16” Swagelok nut (Figure 8).

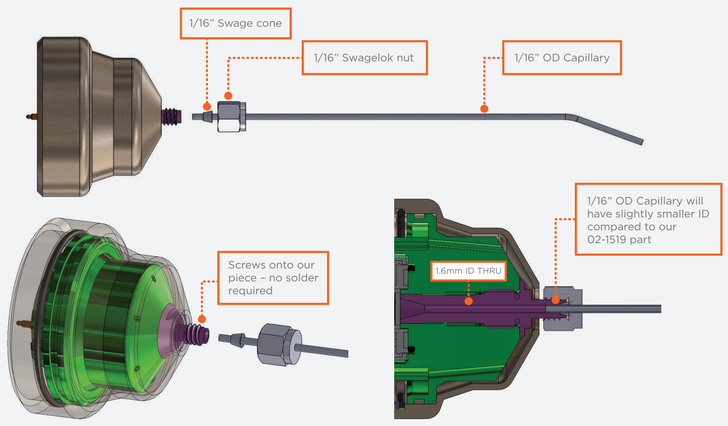


Figure 8. 1/16” Swagelok nut DESI-FAIMS interface design (DI2)

It was expected that the two different DESI-FAIMS interfaces may exhibit differences in flow through the FAIMS chip.

- 1/16” OD capillary will have slightly smaller ID compared to front insert (Figure 9).

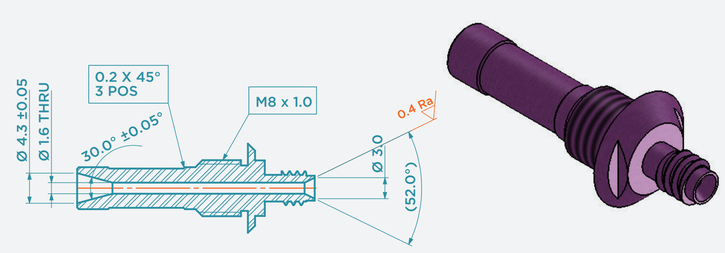


Figure 9. Customised 1/16” Swagelok nut DESI-FAIMS inlet design

- The narrower ID may produce higher transmission and wider FAIMS peak FWHM, due to an increase in flow rate through FAIMS device.

4. DESI-FAIMS data

CF sweeps were acquired by rastering across a mouse kidney section, selected due to its high homogeneity, with both the DI1 and DI2 capillaries.

Increased resolution between the doubly and singly charged cardiolipin peaks was achieved using the DI2 capillary due to narrower, more Gaussian FAIMS peaks (Figure 10).

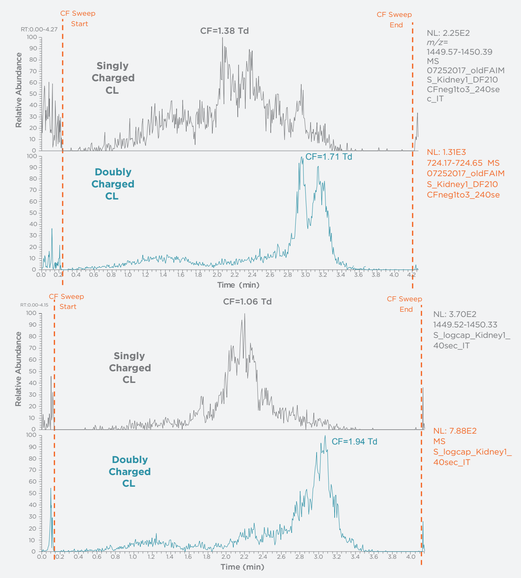


Figure 10. DESI-FAIMS spectra of doubly and singly charged cardiolipin peaks from DI1 (left) and DI2 (right).

Hypothesized that this is due to the ability to change capillary wall thickness.

- Tubing wall thickness of 0.013″ was used; thinner than the original design.
- Counteracts potential increased flow from narrower ID.

DI2 also allowed the capillary length to be varied with ease.

- The MRFA signal intensity between DESI, DI1 and two DI2 capillaries (5” and 2”) was compared (Figure 11).

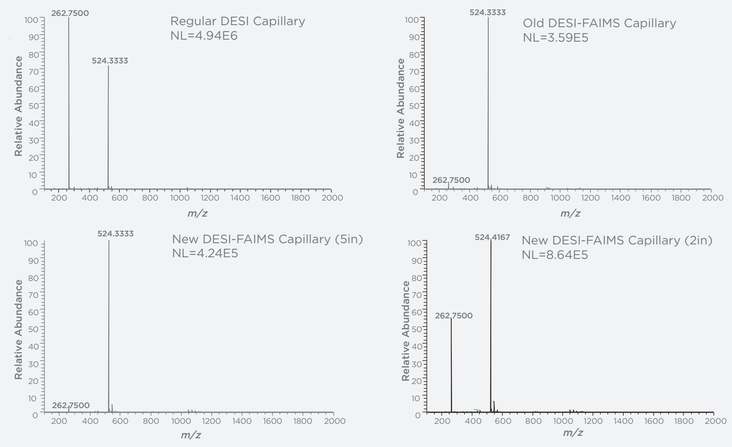


Figure 11. MRFA signal intensity between DESI, DI1 and 5” and 2” capillary DI2 inlets

The longer DESI-FAIMS capillaries showed little transmission of the doubly charged *m/z* 262 ion, but the signal was more abundant with the shorter capillary.

- Possibly due to greater path travelled by the ions resulting in charge reduction.
- Suggests capillary could be tailored to the application.

5. Conclusions

ultraFAIMS provides a practical means of adding additional in-source separation for ambient ionisation mass spectrometry.

The optimised DI2 inlet resulted in increased resolution and allowed sensitivity to be optimised via use of different length capillaries and wall thicknesses.

Future experiments will look at increasing performance further by investigating different dimension inlets and capillaries, and different capillary lengths and materials.

References

1. Feider, C.L.; Elizondo, N.; Eberlin, L.S.; *Anal*. Chem. **2016** *88* (23)
2. Brown *et al*.; Optimization and performance characterization of a microscale FAIMS chip coupled to an Orbitrap mass spectrometer. Poster presented at 62nd ASMS Conference on Mass Spectrometry and Allied Topics, 2014, June 15 - 19, Baltimore, MD

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