Incorporation of FAIMS into LC-MS ‘omics’ analysis

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‘Omics’ Analysis

- In non-targeted ‘omics’ experiments such as metabolomics and proteomics, typically liquid or gas chromatography (LC or GC) combined with mass spectrometry (MS) is used to separate and analyse complex biological matrices
- Molecular features can however be missed or remain hidden within the dataset using these techniques due to:
  - Trace level features unresolved from the noise
  - Unresolved isomeric or isobaric species
- We propose the use of field asymmetric waveform ion mobility spectrometry (FAIMS) in a scanning capacity (Figure 2) in conjunction with LC-MS to improve peak capacity and reduce chemical noise
- The data presented here used a miniaturised FAIMS chip (ultraFAIMS, Owlstone Ltd.) located in the modified ion source region of a time-of-flight-MS (Agilent 6230 TOF), in front of the MS inlet capillary (Figure 1)

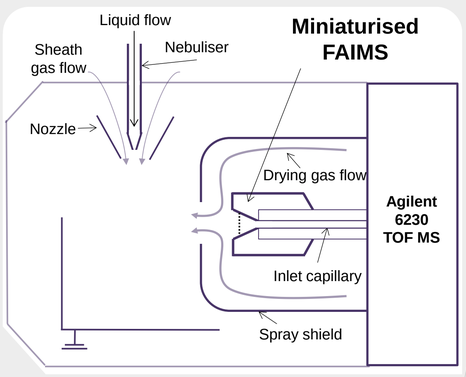

Figure 1: Schematic diagram of the modified Agilent JetStream electrospray source with miniaturised FAIMS device

What is FAIMS?

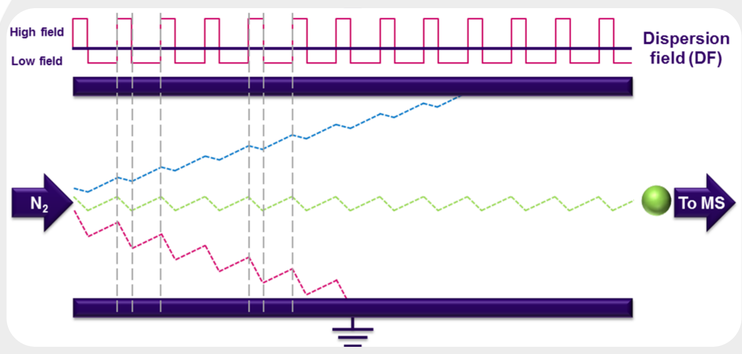

Figure 2: Representation of ion transmission through planar FAIMS electrodes

- FAIMS is a gas phase ion separation technique that utilises an oscillating high frequency (RF) waveform, known as the dispersion field (DF)
- Rapid separation of gas phase ions is a result of differences in an ion’s mobility in a buffer gas under alternating high and low electric fields (Figure 2)
- A small DC voltage known as the compensation field (CF) can be superimposed on the DF in order to selectively transmit ions, or scan through CF values to transmit ions
- Separation based on ion mobility makes FAIMS orthogonal to both LC and MS
- The main limitation to combining FAIMS with LC-MS for scanning experiments is scanning the FAIMS on a timescale compatible with a chromatographic peak
- The fast scanning capabilities of the miniaturised FAIMS chip (Figure 3) allows an entire FAIMS scan to be acquired per second, allowing enough data points per LC peak (Figure 4)

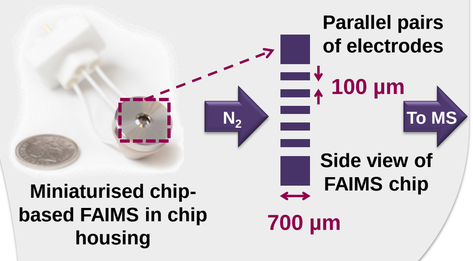

Figure 3: Miniaturised FAIMS device

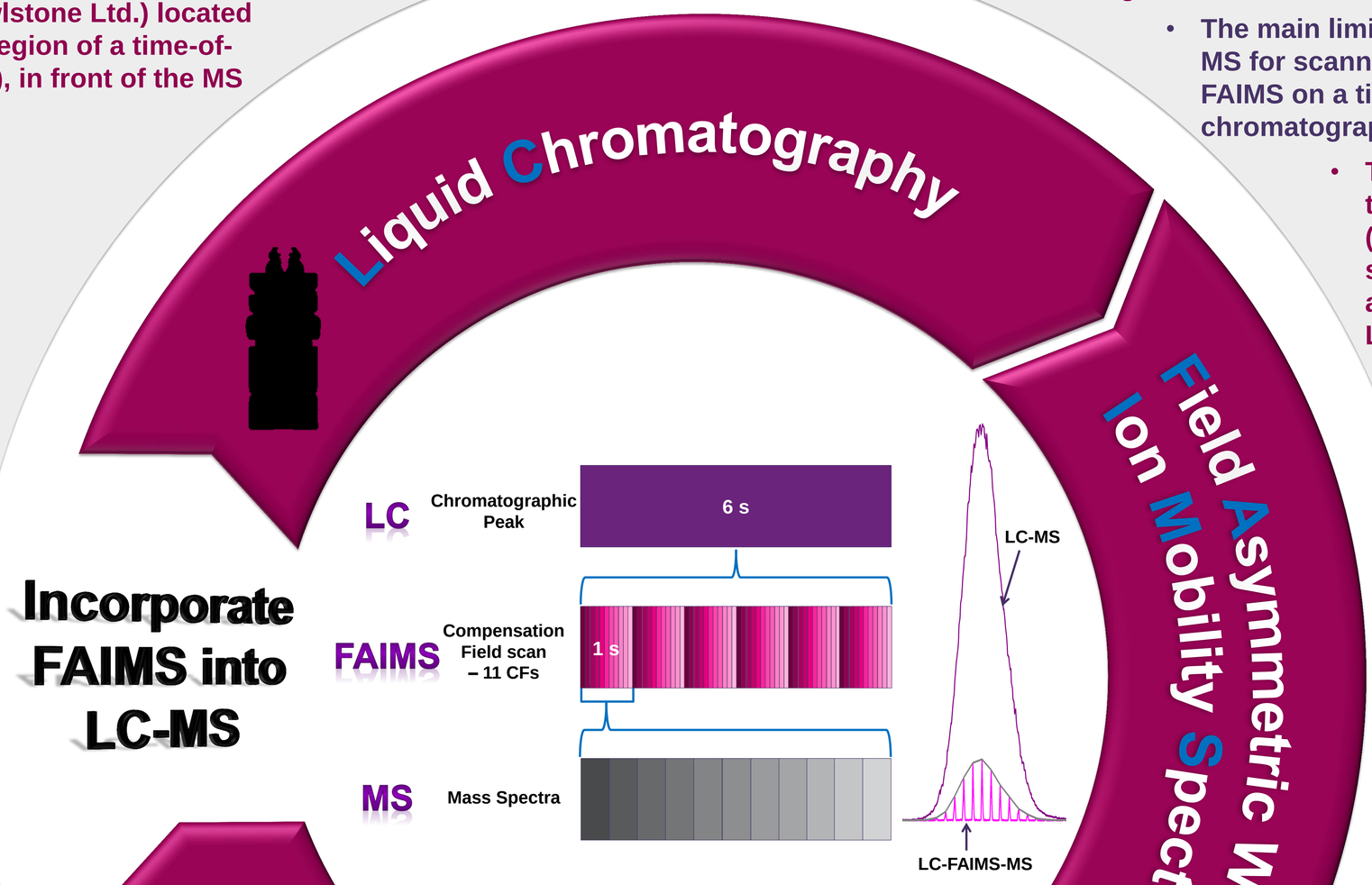

Figure 4: Representation of LC-FAIMS-MS peak and scan timescale and peak deconvolution for each CF

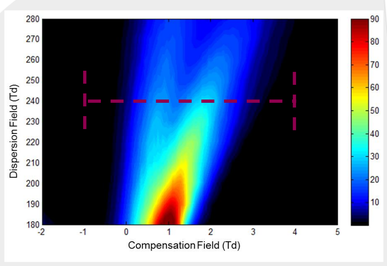

Figure 5: FAIMS-MS DF vs CF plot of human urine infusion

- FAIMS conditions for use in LC-FAIMS-MS analysis chosen from the direct infusion of human urine into FAIMS-MS (Figure 5)
- DF 240 Td, CF scanned between -0.9 – 4 Td at 0.49 Td step sizes

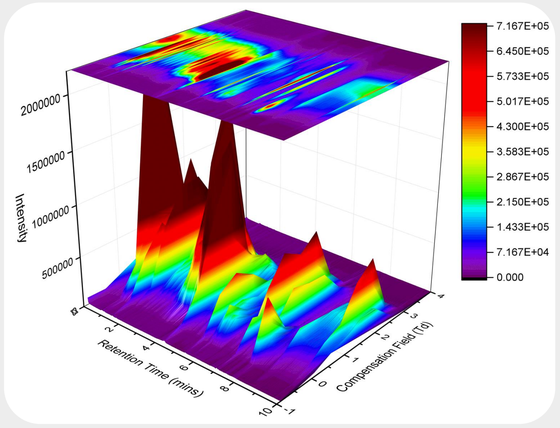

Figure 6: LC-FAIMS-MS heat map of total ion chromatograms at each CF

- From the deconvoluted total ion chromatograms (Figure 6) can already see multiple examples of peaks at the same retention time that appear in multiple FAIMS CFs, but we can look closer at individual *m/z* values (Figure 7)
- Ions at the same m/z and same retention time can be separated using FAIMS

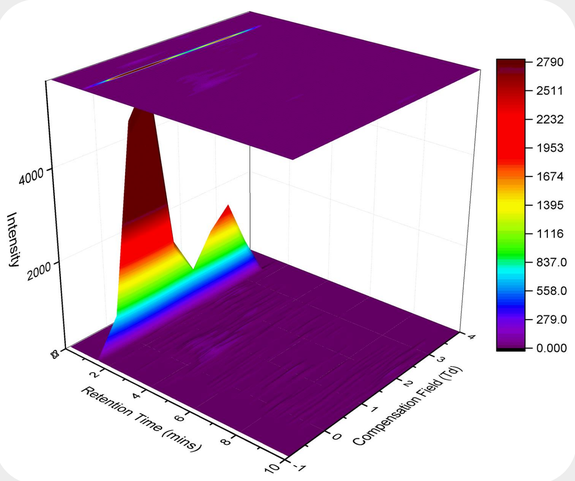

Figure 7: LC-FAIMS-MS heat map of *m/z* 359.316

LC-FAIMS-MS Peak deconvolution

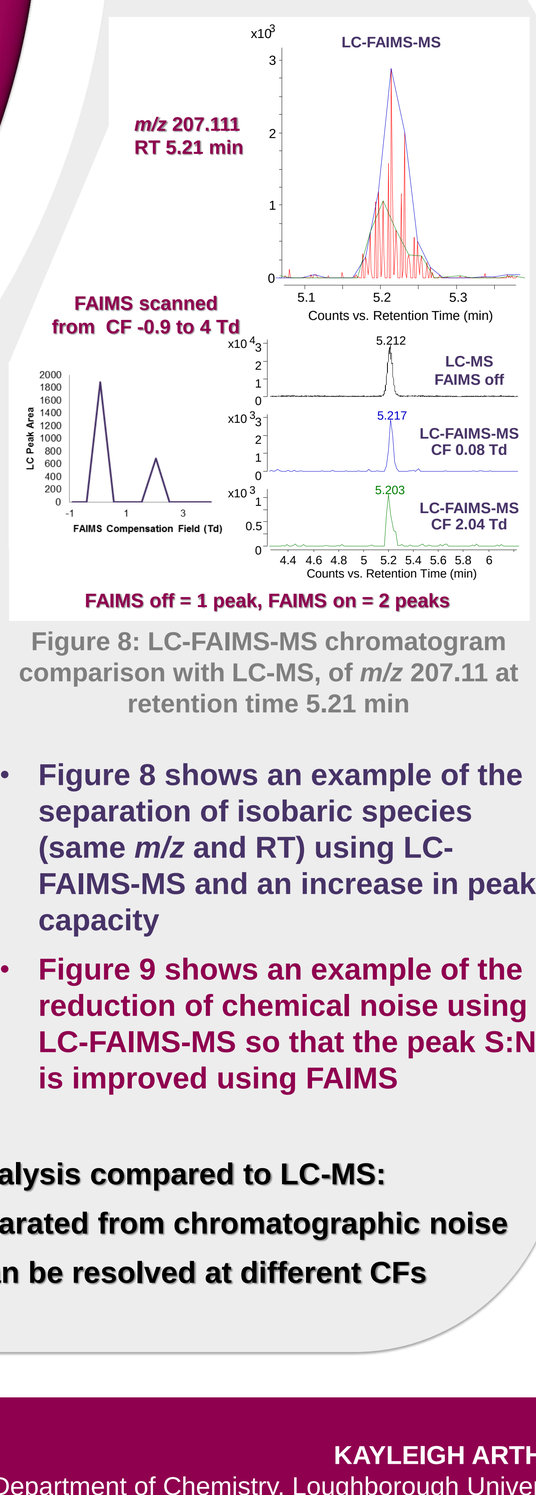

Figure 8: LC-FAIMS-MS chromatogram comparison with LC-MS, of *m/z* 207.11 at retention time 5.21 min

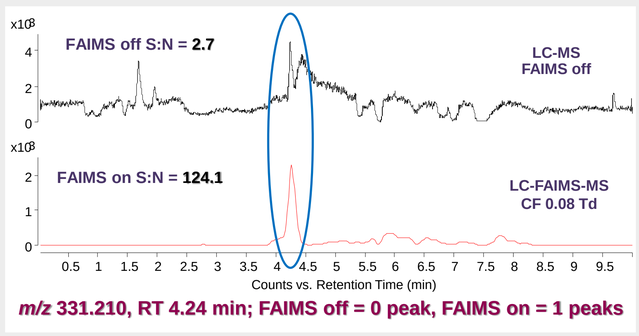

Figure 9: LC-FAIMS-MS chromatogram comparison with LC-MS, of *m/z* 331.21 at retention time 4.24 min

- Figure 8 shows an example of the separation of isobaric species (same *m/z* and RT) using LC-FAIMS-MS and an increase in peak capacity
- Figure 9 shows an example of the reduction of chemical noise using LC-FAIMS-MS so that the peak S:N is improved using FAIMS
- **Benefits from using LC-FAIMS-MS analysis compared to LC-MS:**
  - **Trace level features can be separated from chromatographic noise**
  - **Isomeric or isobaric species can be resolved at different CFs**
  - **Improved peak capacity**

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