Advances in Chip-based FAIMS/Triple Quadrupole MS: Instrumental Studies and Analytical Capabilities

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Overview

- The chip-based FAIMS/triple quad instrumental platform is described
- Chip-based FAIMS is compared to conventional planar FAIMS
- Capabilities for rapid CF/DF scans (10-100x faster than with conventional-sized FAIMS cells) are demonstrated
- The effects of modifier gases and solvent vapors on separation of isomeric ions are explored

Instrumentation

Chip high-field asymmetric waveform spectrometry (FAIMS) was done on a custom Owlstone FAIMS chip. The micro-fabricated planar FAIMS chip is composed of multiple micro-channels with a gap width of 100μm and a thickness of 700μm, as shown in **Figure 1** below. The chip is powered by a custom Owlstone FAIMS waveform generator that generated a dispersion field (DF) up to 350 Townsends (Td), corresponding to a dispersion voltage (DV) of ~600V_p, 60kV/cm, and a compensation field (CF) from -30 to 30 Td (compensation voltage (CV) of -50 to 50V). The chip was mounted to the capillary of an Agilent 6460 triple quadrupole mass spectrometer (TQMS).

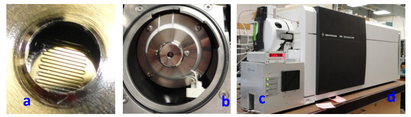


Figure 1. **a.** Owlstone FAIMS chip, **b.** Capillary mount, **c.** Owlstone FAIMS waveform generator, and **d.** Agilent 6460 TQMS.

Chip vs. Conventional Planar FAIMS

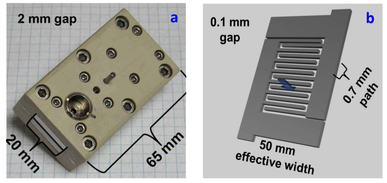


Figure 2. **a.** Conventional FAIMS planar cell (DV to 5000 V_p @ 2 MHz, 25 kV/cm, 150 Td) **b.** Owlstone FAIMS chip (20x narrower gap, 2.5x wider channel, 100x shorter path, DV to 600 Vp @ 27 MHz, 60 kV/cm, 350 Td)

Methods

Test compounds: 20 ppm solutions of *o*-, *m*-, and *p*-phthalic acid were prepared by dissolving pure standards in 90:10 methanol:water with 0.2 mM ammonium acetate.

Ionization and mass analysis: Samples were ionized by the Agilent Jetstream electrospray ionization (ESI) source, separated with the use of Owlstone FAIMS chip, and analyzed with an Agilent 6460 TQMS in either SIM or full-scan mode (or SRM or full-scan MS/MS mode).

Introduction of solvent vapors into the FAIMS cell: Modifier gases or solvent vapors were introduced into the heated counter current gas added around the interface capillary (and thereby into the FAIMS cell). Control of the flow rates of dry and solvated gases, as shown in **Figure 3,** permits varying the FAIMS carrier gas from 100% dried nitrogen to solvent-saturated nitrogen (up to 120,000 ppm methanol (12%), for instance).

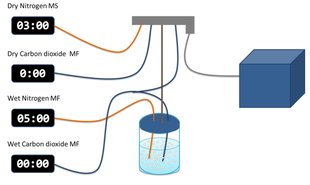


Figure 3. Schematic of the solvent vapor delivery system. MKS digital mass flow controllers regulate the flow of dry nitrogen and dry carbon dioxide to the cell, as well as providing nitrogen and carbon dioxide into an HPLC solvent degassing bottle containing methanol or other solvent.

Results and Discussion

CF/DF Scan Speed

The small size of the FAIMS chip and low operational voltages enable more rapid scanning of dispersion fields (DF) and compensation fields (CF) than with conventional FAIMS cells. Rapidly acquiring complete 3-dimensional CF/DF plots permits optimization of DF and CF for individual mixture components and can identify and differentiate co-eluting isobaric and isomeric compounds. As shown in **Figure 4** below, a comprehensive CF/DF scan can be obtained on the LC timescale.

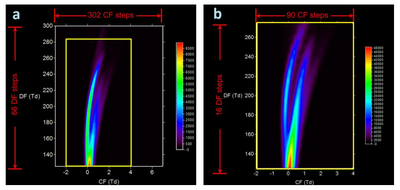


Figure 4. a. Comprehensive CF/DF scan of the *m*-phthalic acid [M-H]$^-$ ion taken in SIM mode with 20,000 steps in 11 minutes. For a more rapid CF/DF scan, you can limit the scan range and acquire fewer steps. **b.** Rapid CF/DF scan of the same ion taken in SIM mode with 1440 steps in 48 seconds. With reductions in scan overhead, we should be able to reduce this time to <10 seconds.

Solvent Effects on Conventional Planar FAIMS

Adding solvent vapor to the FAIMS cell can lead to clustering of the ions with solvent molecules. The extent of clustering varies between the high and low field periods of the asymmetric waveform. At lower field, the "cooler" ions cluster more, whereas at higher field, the "hotter" ions can decluster, as shown at right:

$$[Ion]^{\mp}_{High\ Field} \xleftrightarrow{K_f} [Ion]^{\mp} \bullet (Solvent)_n \quad Low\ Field$$

This change in effective ion size leads to significant changes in ion mobility and large compensation voltages. Adding solvent vapor to a planar FAIMS cell leads to dramatic CV shifts (**Figures 5 and 6**) with no increase in peak width (**Figure 7**), yielding impressive improvements in resolving power and peak capacity. Adding solvent vapor also results in significant increases in sensitivity in both APCI and ESI modes (up to 65x higher intensity with increasing field, **Figure 7**). These effects on CV shift and intensity both increase with increased solvent size. **Will we see the same effects in chip FAIMS (10x higher RF frequency, 100x shorter path)?**

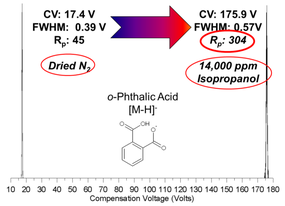


Figure 5. Effect of solvent on FAIMS.

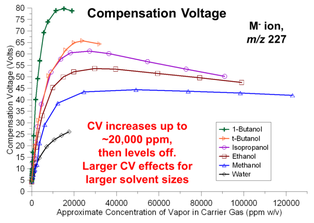


Figure 6. Solvent effects on CV vs. field.

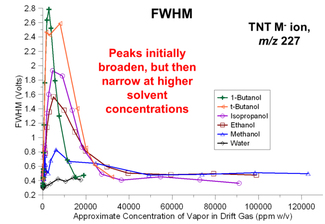


Figure 7. Solvent effects on peak width vs. field.

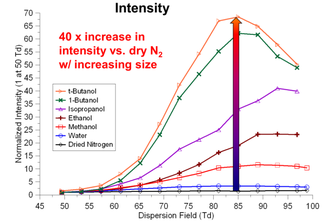


Figure 8. Solvent effects on intensity vs. field.

Solvent Effects on Chip-FAIMS

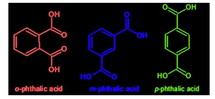
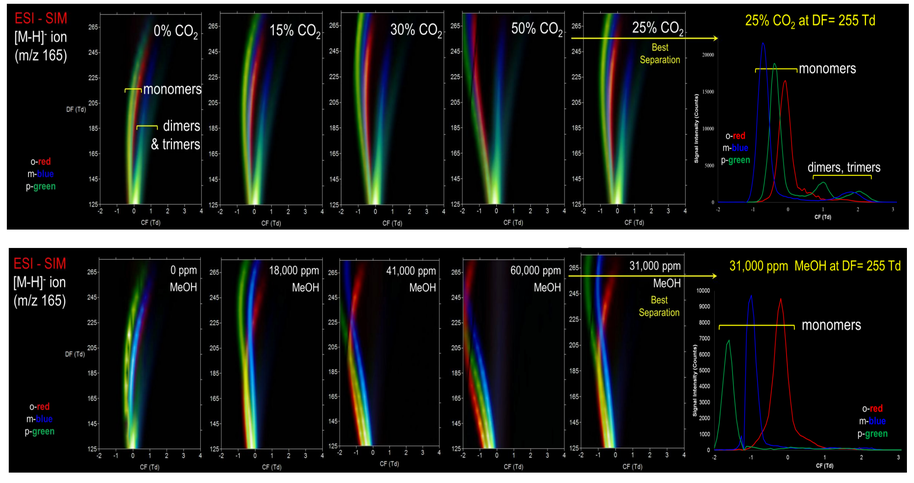
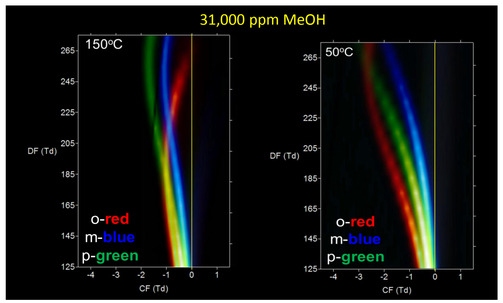


Figure 9. Effect of adding increasing concentration of carbon dioxide (top row) and methanol (bottom row) on separation of the [M-H]$^-$ ions of three positional isomers of phthalic acid. The figures on the right illustrate the best separation achieved.



Temperature Effects on FAIMS

Figure 10. Effect of temperature on solvent effects on Chip FAIMS. Decreasing the temperature increases the extent of clustering, but may also decrease ion intensity.

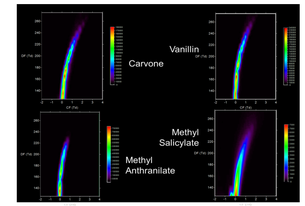


References

Barnett, D. A.; Ells, B.; Guevremont, R. *J. Am. Soc. Mass Spectrom.* 2000, 11, 1125.
Rorrer, L.C. III; Yost, R.A. *Int. J. Mass Spectrom*. 2011, 300, 173.

APCI and Other Compounds

Figure 11. Chip FAIMS has been applied to other compound classes, ionized by both ESI and APCI.



Conclusions

- Chip FAIMS is an ideal combination with a triple quad
- Chip FAIMS vs. FAIMS –
  - 20x narrower gap, 10x lower voltages
  - 100x shorter path, 20x higher frequency
- Chip FAIMS can provide complete CF/DF scans on the LC/MS time-scale (ultimately <10 sec), useful for optimization and compound differentiation
- Adding modifier gases or solvent vapors significantly improves ion separation
- The observation that peak width initially increases and then returns to narrow values at higher solvent concentrations suggests that the ions have a complete solvation sphere at low field

Future Work

- Ongoing studies are designed to more completely characterize the performance of Chip FAIMS on the triple quadrupole system, including transmission, resolution, and scan speed.
- With reductions in scan overhead, complete 3d CF/DF can plots should be acquired in less than 10 seconds.
- Extension of the solvent effect studies to other solvent vapors and other compounds classes.
- Application of the Chip-FAIMS-QQQ system to a variety of problems in trace analysis, quantitation, metabolomics and proteomics.

Acknowledgements

IMSC - 9/17/2012