Owlstone Nanotech Inc.

UltraFAIMS for LC-MS

A New Dimension in Mass Spectrometry

Owlstone Whitepaper

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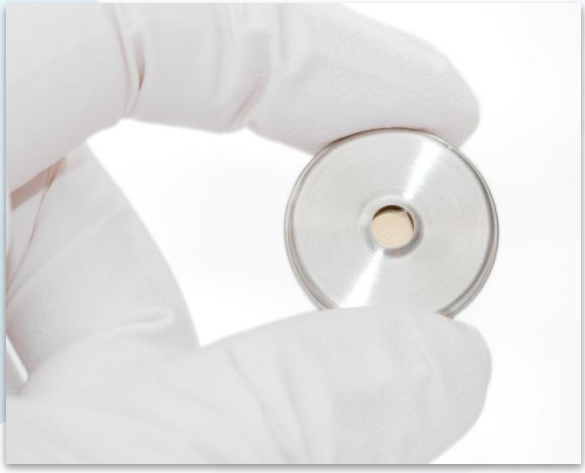
OW-000962-MC (2nd Edition)



Introduction

In the never-ending quest to analyze complex mixtures – pharmaceutical formulations, biological samples, food ingredients, environmental samples, and so on – the most powerful weapon available is the mass spectrometer. Since JJ Thomson first used his “mass spectrograph” in 1912 to distinguish the two isotopes of neon, scientists and inventors have striven to build more and more powerful instruments capable of penetrating the composition and structure of smaller amounts of more complicated analytes.

Key to being able to analyze a particular compound or molecule is whether or not it can be separated from other species that are also present in the sample. There are two ways of achieving more separation. Either you improve the resolution of the mass spectrometer, so that even smaller differences in the mass-to-charge ratio of the ions can be resolved, or you apply another separation technique upstream of the mass spectrometer to spread out the ions so they aren’t all arriving at the same time in the mass spectrometer, and then analyze them sequentially.

Both approaches have been important – mass spectrometers with the ability to resolve peaks separated by tiny fractions of a mass unit are now available, and upstream separation using gas- and liquid-chromatography is routine – and the combination of these approaches is extremely powerful. But despite this, the interest in alternative separation techniques continues, as chemists look for ways of tackling separation problems that existing techniques cannot solve. One of the alternative approaches that has elicited much interest in recent years is field-asymmetric waveform ion mobility spectrometry, or FAIMS.

FAIMS – THE BASICS

Ion mobility spectrometry (IMS) is a technique for distinguishing ions according to differences in the speed that they migrate through a buffer gas under the influence of an electric field.

If an electric field is applied to an ion surrounded by a buffer gas, the ion will drift in the direction of the field. Different ions reach different drift velocities and the ratio between the velocity, *v*, and the electric field, *E*, is known as the mobility, *K*.

$$K = \frac{v}{E}$$

Low-fields

At low electric fields (less than around 10kV/cm), the mobility is independent of electric field. Linear drift tube IMS (DTIMS) exploits this to separate ions on the basis of the time taken to travel a fixed distance in a known field – ions with a higher mobility will travel faster than lower mobility ions and reach the detector sooner.

Travelling wave IMS (TWIMS) also operates in the low electric field regime – when the ratio of electric field strength to buffer gas density is small – but rather than applying a constant drift field, it works by applying travelling voltage waves to a stacked-ring ion guide. Ions with a lower mobility slip behind the waves and reach the detector later than ions with a higher mobility. The travelling wave technique has a high transmission efficiency compared with conventional drift tube IMS.

The downside of low-field mobility techniques is that that in the low-field, the mobility of an ion is closely correlated to its mass, which means that ions that are not well-separated by m/z are also less likely to be separated by DTIMS or TWIMS.

High-fields

At high electric fields, the mobility of an ion is no longer constant but becomes a function of the electric field strength. Applying an alternating asymmetric high/low electric field to an ion creates a net drift in the direction of the field but, unlike in low-field IMS, the net drift velocity is now a function of the difference in high- and low-field mobility of the ion. This effect is the basis of field-asymmetric ion mobility spectrometry (FAIMS).

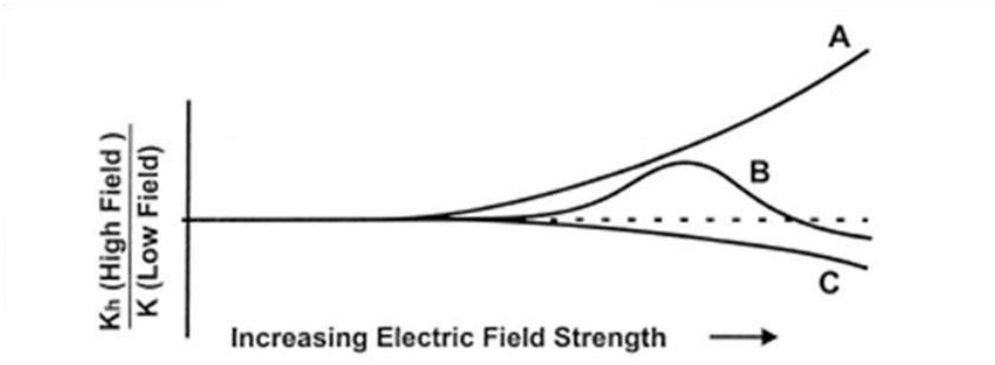


Figure 1: Variation of ion mobility K in increasing electric fields – at low fields, the mobility is essentially constant, but as the field continues to increase, the mobility starts to vary. A number of different types of behavior (A, B and C) have been observed [1]

In FAIMS spectrometers, ions are carried by a buffer gas flow through a gap between two closely-spaced electrodes. The separation field (also known as the dispersion field, or DF) is applied across the gap in a direction perpendicular to the gas flow. The field causes the ions to drift sideways, towards one or other electrode. To counteract this sideways drift, and allow the ions to pass through the electrode region, a DC field is applied in the opposite direction. This is called the compensation field (CF). Any given magnitude of CF will compensate only a specific drift velocity, and hence only ions that have this net drift velocity as a result of the applied DF will be transmitted. If the CF magnitude is varied, different sets of ions will be transmitted. In FAIMS devices, the CF is typically swept through a range of values to produce a spectrum of transmitted ions. This can be repeated for different DF magnitudes to produce a two-dimensional spectrum.

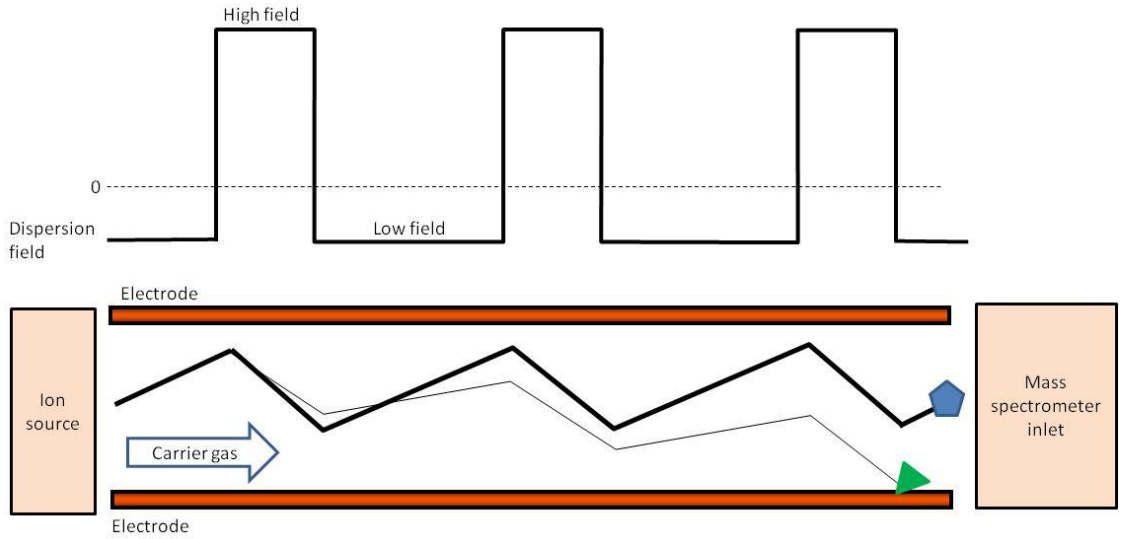


Figure 2: Schematic representation of how a FAIMS device works. Ions are carried through the device by the gas flow. Applying the high-frequency alternating dispersion field causes a net lateral drift of ions towards one or other electrode, depending on their mobility-field dependence. Most ions would thus be annihilated at the electrodes (e.g. the green ion). By applying a specific compensation field in the direction opposing the lateral drift, some ions (e.g. the blue ion) are enabled to pass through the FAIMS device. By sweeping the compensation field through its full range, all ions species are eventually transmitted.

An additional dimension of separation

Separation by FAIMS is highly orthogonal to separation by LC, IMS and MS, which maximizes the benefit of the additional separation stage

Stand-alone versus hybrid FAIMS

In stand-alone FAIMS devices, such as Owlstone's Lonestar™ product, ions passing through the electrodes reach a detector that measures the amount of charge accumulated over the time period corresponding to each CF step, producing a FAIMS spectrum that can be analyzed to detect and quantify specific analytes.

In hybrid FAIMS devices - for example FAIMS-Mass Spectrometer (FAIMS-MS) systems, the ions transmitted by the FAIMS device enter the downstream instrument for subsequent analysis. Used in this way, the FAIMS device pre-

separates or filters the ions based on their differential mobility to enhance the subsequent analysis. Since the differential mobility of an ion tends not to be closely correlated to its mass (unlike the low-field mobility), a combined FAIMS-MS system has a significantly increased ability to separate different ion species compared with the equivalent MS alone.

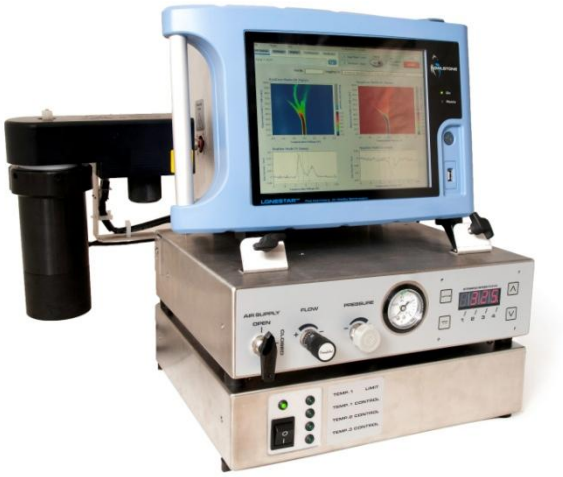


Figure 3: Owlstone Lonestar™ stand-alone gas analyzer

Ultra-fast analysis

Ion residence time in the ultraFAIMS chips is less than 250μs, enabling extremely fast differential mobility separation on timescales compatible with UHPLC and MRM analysis

WHAT IS DIFFERENT ABOUT OWLSTONE ULTRAFAIMS?

Owlstone's ultraFAIMS spectrometer is a miniaturized FAIMS device. Using innovative manufacturing methods, the gap between the electrodes has been reduced to between 35 and 100μm – the smallest gap dimensions of any FAIMS spectrometer yet developed.

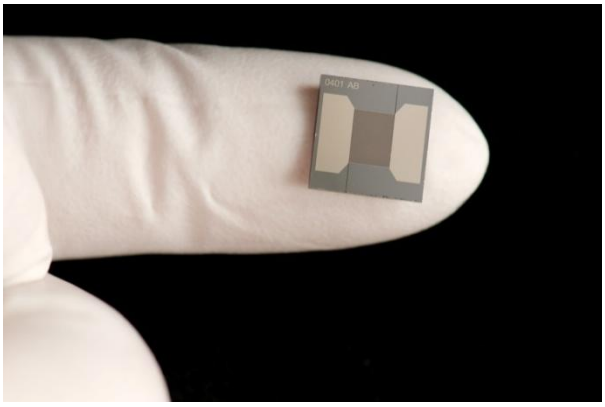


Figure 4: Owlstone FAIMS chip (35μm design) showing size of the device

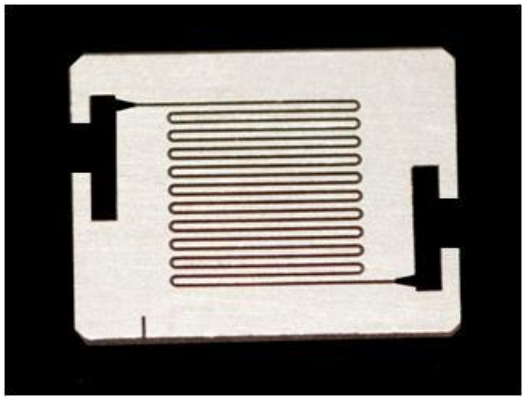


Figure 5: Owlstone ultraFAIMS chip (100μm design), showing the interdigitated electrode structure

So, why is a small gap good?

Fundamentally, a small gap enables the device to separate a wider range of analytes more quickly.

Reducing the width of the gap means that higher dispersion fields can be used in the device. Ultimately, the maximum dispersion field that can be applied across an air gap is limited by the point at which the applied voltage causes the air to break down, leading to arcing between the electrodes. The physics of the breakdown process means that as the gap width narrows, the breakdown field limit increases – so for example, whereas with a 1mm gap the limit is ~30kV/cm[1], with a 100μm gap, the limit rises to ~100kV/cm. It is also much more practical to generate these higher fields in the ultraFAIMS device, since the small size means that the voltages needed to produce the higher fields are actually much lower than in macro-scale FAIMS instruments.

Ultra-high dispersion fields

Dispersion fields in the ultraFAIMS system reach twice the field strength of previous devices, maintaining peak capacity despite short separation timescales and opening up a new regime for exploring ion behaviour

Reaching these extreme dispersion fields increases the range of analytes that can be separated. This is because the access to higher fields leads to greater scope for changes in mobility between the high- and low-field portions of the cycle (e.g. due to changes in shape, clustering, dipole formation etc), thus a greater possibility of moving the ion away

[1] All figures are for DC fields (Paschen curve). Literature suggests that the limits are lower for high-frequency AC fields.

from the zero compensation field point on the spectrum. This increases the likelihood of the ion of interest being separable from other background ions.

Another important benefit of reaching these extreme dispersion fields is that it dramatically speeds up the separation stage [2] since the residence time that is required to achieve a given resolution is proportional to the fourth to sixth power of the dispersion field – so, for example, a doubling of the dispersion field increases the speed of separation by a factor of ~15-60. This makes the ultraFAIMS device fast enough that the FAIMS stage is no longer the limiting factor in an LC-FAIMS-MS analysis and you can combine it with LC separation in real-time without the need for multiple infusion experiments to establish the CF settings needed.

To compensate for the narrowness of the channel (which would otherwise limit the number of ions that could be transmitted), the device uses an interdigitated electrode structure to create multiple parallel gaps with identical fields applied. Figure 5 shows the design of the interdigitated electrodes. The use of multiple channels means space-charge effects are also reduced – it is more effective to transmit ions through several channels than through a single channel of equivalent cross-section – and ensures that the device does not reduce the conductance of the mass spectrometer inlet.

Robust and easy to use

UltraFAIMS fields can be disabled to transmit all species simultaneously so the device doesn't need to be constantly taken on and off the Mass Spectrometer. Chips are easy to clean or replace periodically.

WHY USE ULTRAFAIMS WITH LC-MS?

Combining separation techniques is most beneficial when the separations from each stage are based on unrelated properties of the analytes, for example affinity to a stationary phase (in LC) and mass-to-charge ratio (in MS) – the separations are described as being orthogonal. The major benefit of combining FAIMS separation with LC-MS is that the differential mobility property is not highly correlated to m/z and therefore it has a good potential to separate peaks that would otherwise not be resolved. This contrasts with low-field IMS techniques, which are not very orthogonal to mass spectrometry.

But to be able to benefit from this orthogonality, you need to be able to do the FAIMS separation quickly enough so that it fits into the LC-MS timescale. This is why ultraFAIMS is so powerful in this context – the ion separation time is so short (fractions of milliseconds) that the full compensation field can be swept within the duration of a single LC peak, so you get the benefit of the full peak capacity of the FAIMS device rather than being limited to selecting only a few compensation field settings. The ultraFAIMS system can cycle through up to 500 independent CF values per second (for MRM analysis), or in continuous scanning mode, can produce up to 4 full spectra per second.

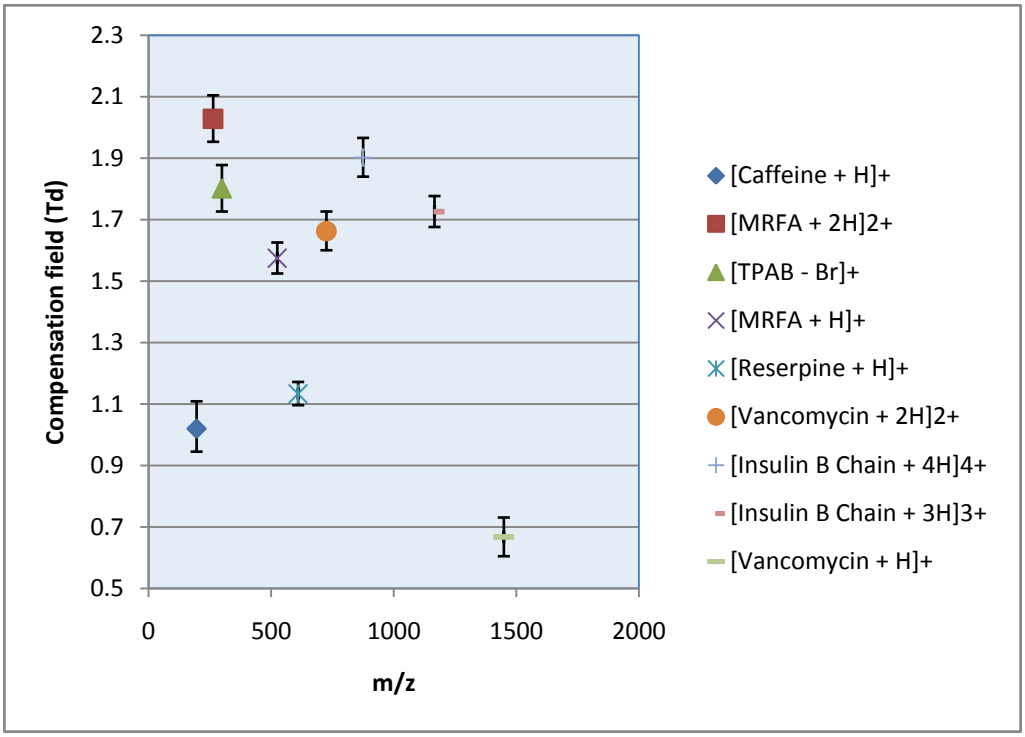


Figure 6: Experimentally determined ultraFAIMS CF values for a range of ions, showing high orthogonality (low correlation) between CF and m/z (Data provided by Colin Creaser and Rob Smith, University of Loughborough)

So what can ultraFAIMS-MS do?

UltraFAIMS separation is a novel technique, and applications are being explored. The following sections illustrate some example applications. For the latest application information, check our website (www.ultrafaims.com).

Improve Level of Quantitation

UltraFAIMS can be used in a targeted mode to filter out chemical noise in order to improve detection of low abundance ions. In this mode, a compensation field value (or series of values) is applied that transmits the ion(s) of interest. Ions that require different compensation field values cannot pass through the device, and so the mass spectra acquired are much cleaner.

In this example, the ultraFAIMS system was used for the determination of an ibuprofen metabolite, (R/S) ibuprofen 1-β-O-acyl glucuronide (IAG), in a background of urine. UltraFAIMS separation reduced matrix chemical noise, improved the limit of quantitation approximately two-fold, increased the linear dynamic range and improved reproducibility for determination of the drug metabolite at biologically relevant concentrations in urine (see Table 1) [3].

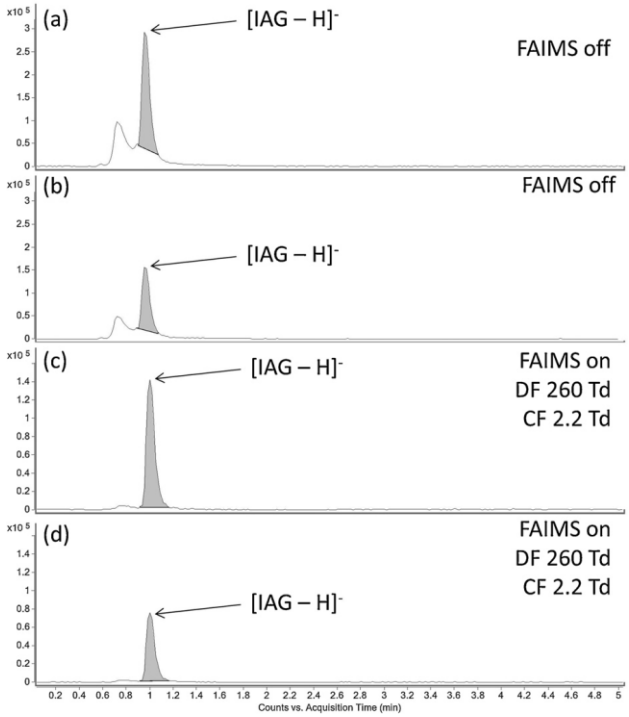


Figure 7: Selected ion chromatograms (m/z 381) for IAG (highlighted) spiked into urine (0.55 μg/ml) analyzed by UHPLC–MS (FAIMS off) using a mass window of (a) m/z 381 ± 0.02 and (b) m/z 381 ± 0.008; and by UHPLC–FAIMS–MS (FAIMS on) with selective transmission of IAG (DF 260 Td, CF 2.2 Td) using a mass window of (c) m/z 381 ± 0.02 and (d) m/z 381 ± 0.008.

Table 1: A comparison of LOQ, LDR (R^2) and intra-day reproducibility for the determination of IAG spiked into urine (15.5 μg/ml, n=5)

	FAIMS off	FAIMS on
LOQ (μg/ml)	0.018	0.010
LDR (μg/ml)	0.018-11	0.010-11
R^2	0.9991	0.9987
Intra-day (% RSD)	5.0	2.7

Reduce Chemical Background Noise

UltraFAIMS can be used during untargeted screening as a way of reducing chemical noise in order to increase the number of low abundance ions detected. In this mode, rather than sitting on a fixed compensation field value (or series of values), the CF is repeatedly swept very quickly over the full range to provide an additional nested level of separation during LC-MS. Multiple full sweeps can be carried out per second, so even short LC peaks can be explored in this way.

The following example shows the separation of two of the charge states of [Val4]-Angiotensin from a PEG 415 background.

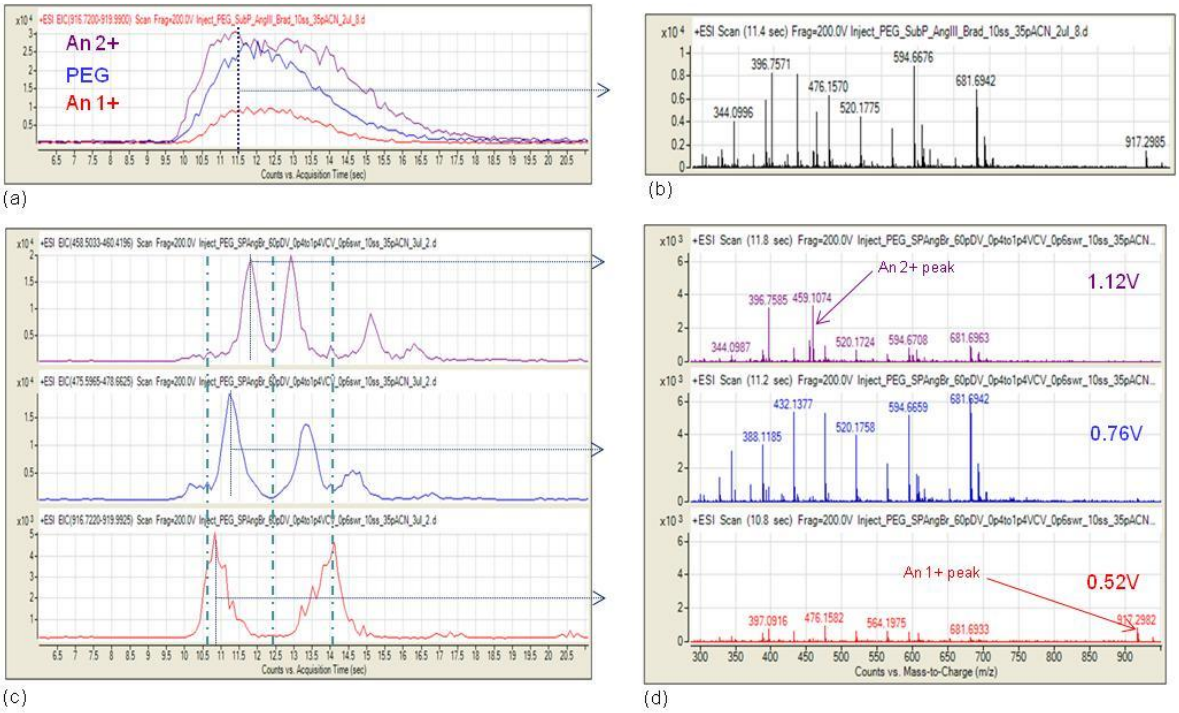


Figure 8: LC injection of [Val4]-Angiotensin and PEG 415 (Column: 75mm x 5mm Poroshell 300SB-C8; mobile phase: gradient water:acetonitrile mixture with 1% formic acid) (a) extracted chromatograms for the two angiotensin charge states and PEG 415 ion (as labelled) without FAIMS separation showing co-elution, (b) mass spectrum at the time marked in (a), (c) extracted ion chromatograms of the same 3 ions during an ultraFAIMS compensation field sweep with dispersion field set at 156Td, showing the different ions appearing at different compensation field values (time axis is equivalent to CF axis), (d) mass spectra at the times marked in (c), showing the angiotensin ions (top and bottom plots) separated from the PEG background (middle plot).

[Data provided by Michael Ugarov, Agilent Technologies – from poster presentation IMSC 2009]

The next example shows another example of the ultraFAIMS device being used to reduce chemical noise and improve detection of low abundance ions. In this case, a fixed compensation voltage was applied to transmit the ion of interest, the Leucine H^+ ion [4].

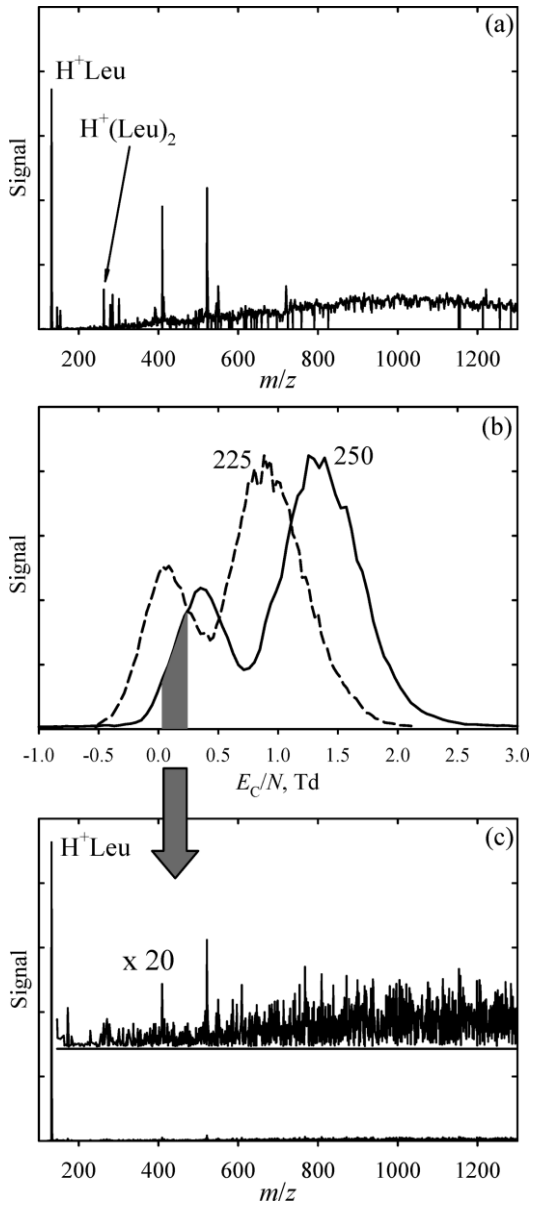


Figure 9: Data for leucine solution in a complex matrix: (a) total MS spectrum; (b) FAIMS spectra for two dispersion field values, 225 and 250Td (c) MS spectrum integrated over the compensation field (CF) range of 0.03-0.24 Td marked in (b) with an inset showing the baseline magnified by x20 – this figure shows that by selecting a small part of the CF range, much of the background is filtered out, enhancing the signal to noise ratio of the Leucine H+ ion by a factor of 20.

Assist metabolite characterization or drug impurity identification

In this example, the ultraFAIMS device was used to reduce the intensity of the excipient ions present in the sample in order to improve the signal-to-noise ratio of the parent drug ion and metabolites.

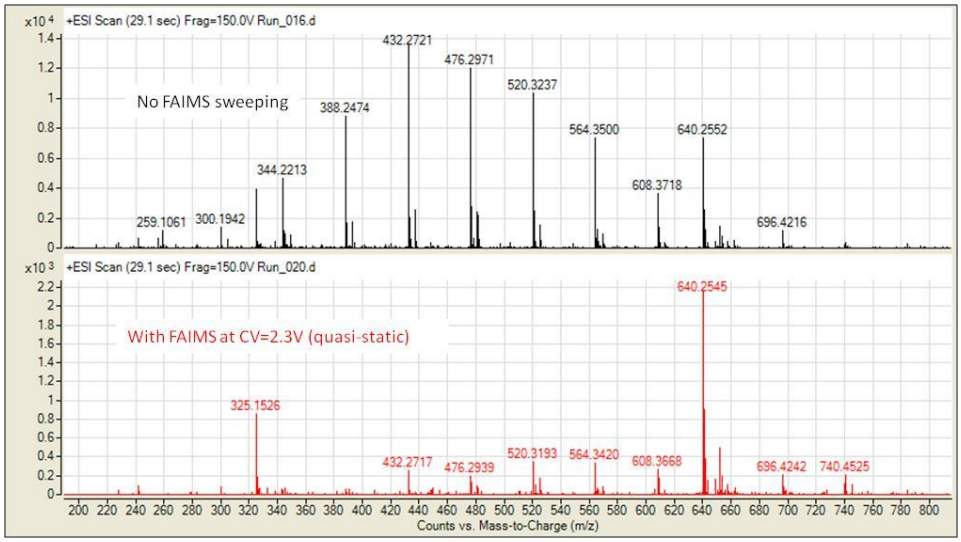


Figure 10: 10µl injection of sample containing parent drug (m/z 640) and metabolite ions (m/z 242 and 325) plus PEG 400 (top) with no FAIMS sweeping, and (bottom) with FAIMS compensation field of 2.9Td and a dispersion field of 260Td. In the bottom plot, the intensity of the PEG ions is significantly reduced, improving detection of the parent and metabolite ions.

[Data supplied by Dan Weston, Astra Zeneca, UK – oral presentation at BMSS 2010]

Similarly, the following example shows the enhancement of the loperamide peak (*m/z 477)* and several other unknown ions (*m/z* 365, 381, 585) from a urine matrix background by stepping the compensation voltage between selected points in the range.

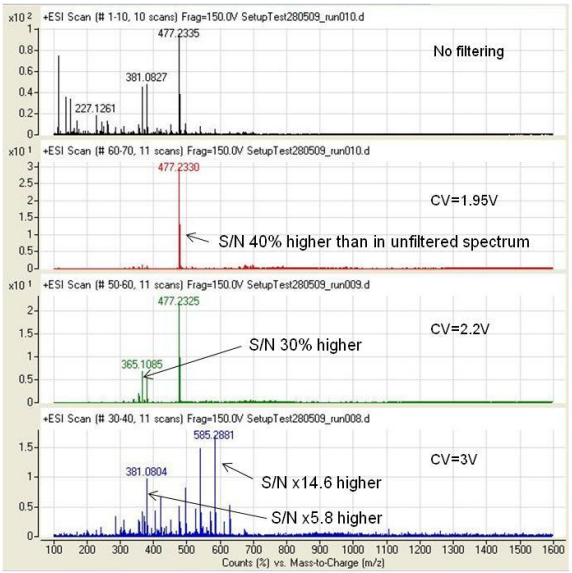


Figure 11: Mass spectra of loperamide spiked into urine matrix, (black) with no FAIMS separation, and (red/green/blue) during a FAIMS sweep with spectra pulled out at various points in the CV range covered (CV values and signal-to-noise improvements are indicated on the plots)

[Unpublished data, from Owlstone Ltd]

Improve mass measurement

Since there is low correlation between the compensation field that allows an ion to pass through the FAIMS device and its mass-to-charge ratio, it is often possible to use FAIMS to separate isobaric ions, enabling the accuracy of mass measurement to be improved.

In this example, ions derived from pharmaceutical excipients 2-hydroxy-4-octyloxybenzophenone (HOBP, m/z 327.1955) and PEG 400 excipients were chosen as test analytes because the protonated HOBP and PEG n=7 oligomer (m/z 327.2013) are sufficiently close in mass (17.7 ppm mass difference) that these ions could not be resolved by the reflectron TOF mass analyzer (required resolution ~ 130K). Robust accurate mass measurement of these ions is therefore not possible without separation prior to mass analysis. The two components were analysed as a mixture containing a 20 fold molar excess of the PEG. CV sweeps (-1 to +4 V) with the DF set to 48 kV/cm were used to determine the optimum CV required for selected transmission. The selected ion response for m/z 327.2 (Figure 12) shows that the protonated PEG n=7 and HOBP ions are resolved by FAIMS, and the mass error of the HOBP ion thus selected is reduced from 12ppm (without FAIMS) to 3ppm [5].

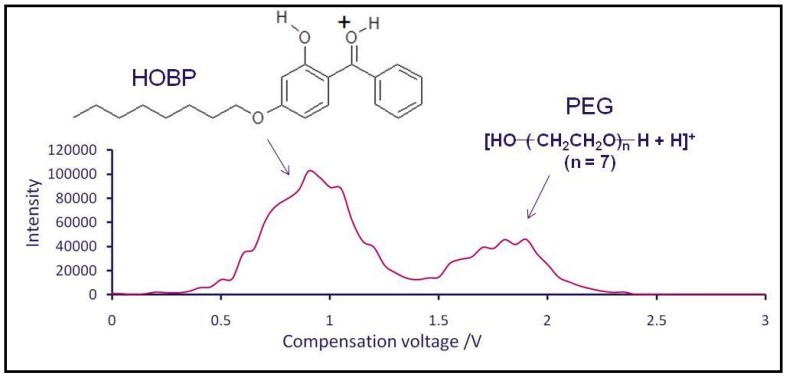


Figure 12: CV scan of m/z 327.2 with resolved protonated PEG 400 (n=7, m/z 327.2013) and protonated HOBP (m/z 327.1955) ions

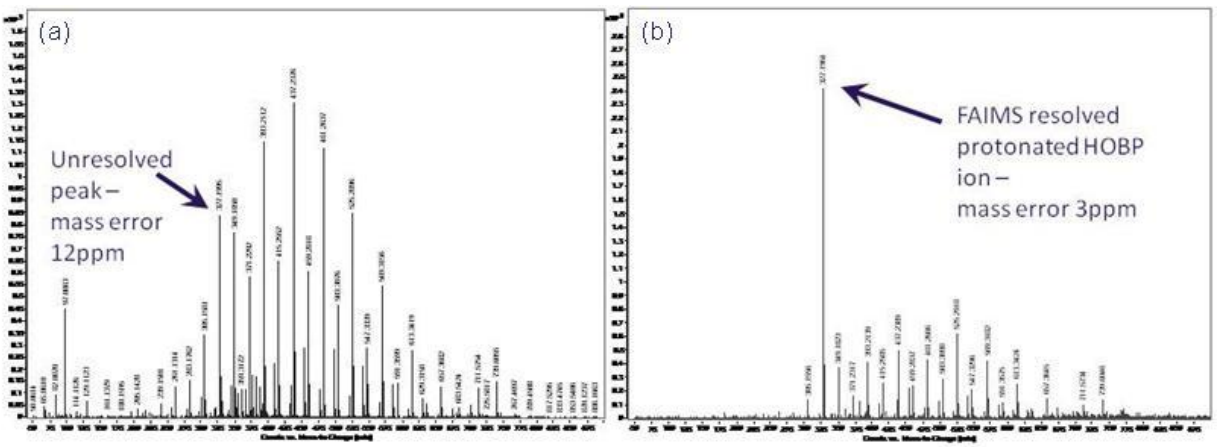


Figure 13: Mass spectra of the mixture of PEG400 and HOBP (a) without FAIMS sweeping, and (b) with FAIMS compensation field of 0.75-0.88Td and dispersion field of 260Td, showing improved mass accuracy for the HOBP ion.

Enhance protein and peptide analysis

UltraFAIMS has been shown to readily separate protein and peptide charge states. Singly charged peptides appear to cluster at similar compensation fields, which means they can be selected as a group. In contrast, multiply charged ions tend to be more spread out across the CF range and can often be selected individually. This is illustrated in Figure 14.

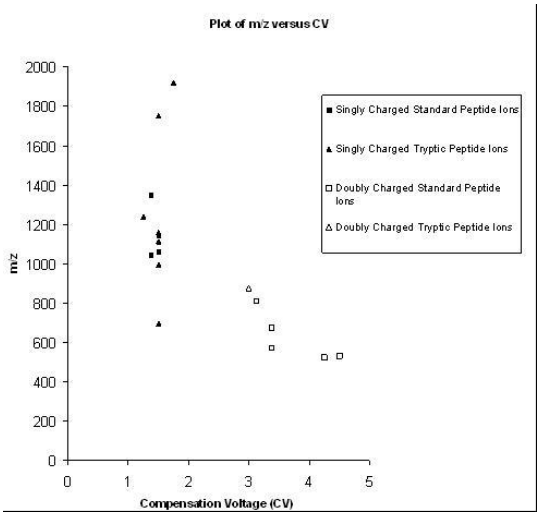


Figure 14: Compensation voltage vs m/z plot of singly and doubly charged peptide ions

The example below makes use of the preferential selection of singly charged ions from a tryptic digest of the protein AAG. The FAIMS pre-selection enhanced the singly charged peptide ion responses, including enabling detection of ions previously masked by high intensity multiply charged species or lost in the baseline noise. The resulting spectrum (Figure 15b) demonstrates the use of the ultraFAIMS device to generate $[M + H]^+$ data equivalent to a peptide mass fingerprint (PMF) obtained by MALDI ionization and commonly used to identify proteins from PMF databases. The peak list obtained in this case was searched against the SwissProt protein PMF database using the MASCOT search engine. AAG was identified as the top hit with a significant confidence score of 61 (where 56 or above is deemed statistically significant at a 95% confidence interval) [6].

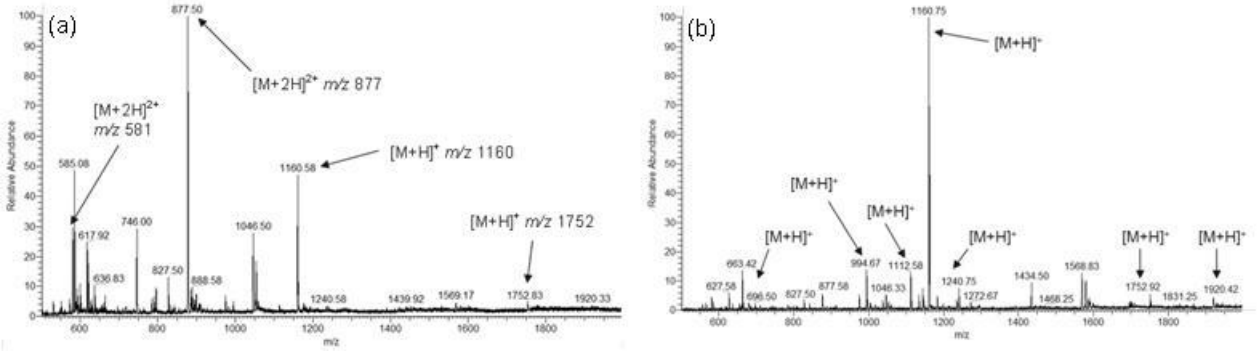


Figure 15: (a) Mass spectrum of the AAG tryptic digest with no FAIMS separation. (b) The mass spectra obtained with the CV window set to +1.5 to +1.7V to isolate the singly charged ions.

In the next example, the ultraFAIMS chip was used to separate a large protein (BSA) from a complex matrix of smaller proteins (e.g. ubiquitin) and small molecules (lab waste water), due to the different differential mobility behaviour of the larger ions. This capability may be useful to track protein digestion and verify its completion or to prevent lower-mass ions in top-down analyses of proteins and their complexes from entering an MS system (where they take up the limited charge capacity of ion traps or guides and create MS interferences) [7].

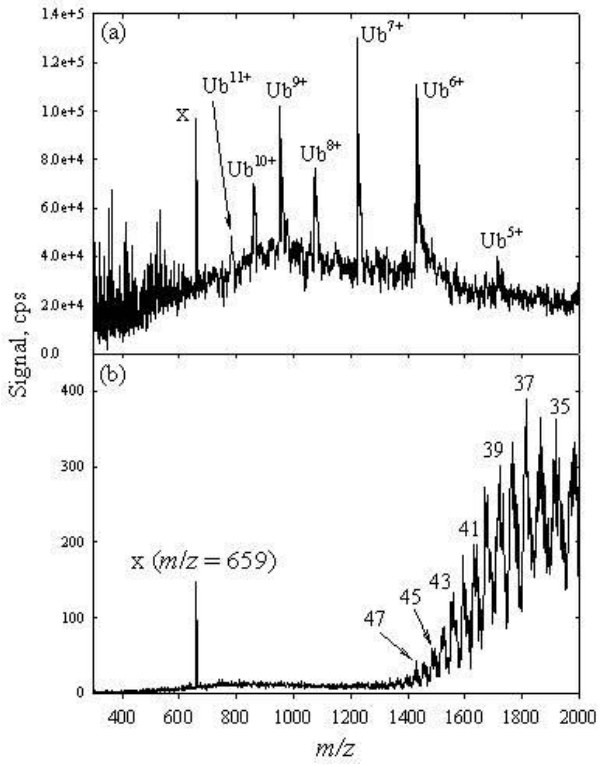
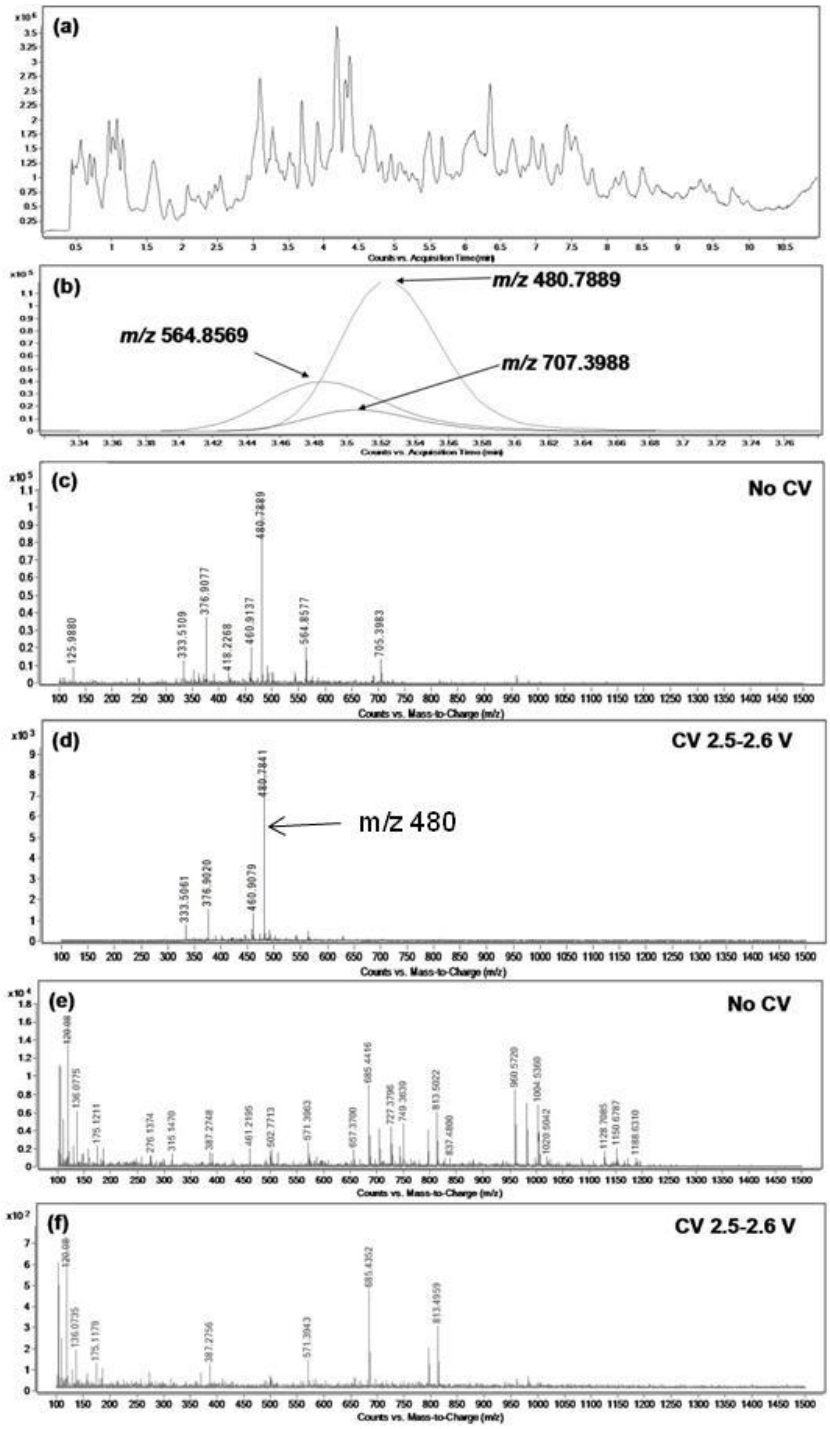


Figure 16: Mass spectra for the solution of ubiquitin and trace of BSA in a complex matrix measured (a) without FAIMS (resolved Ub ions are labeled) and (b) with FAIMS at CF= 0Td (charge states of BSA are labeled for odd z).

Pre-select ions prior to in-source CID

FAIMS followed by in-source CID may be used as a means of isolating and fragmenting ions in the absence of MS/MS capability.



This example shows the use of ultraFAIMS to isolate a single multiply-charged peptide ion from several co-eluting peptides during UHPLC analysis of a tryptic digest, followed by in-source fragmentation using the TOF fragmentor voltage. With FAIMS pre-selection of the parent ion, the product ion spectrum was far simpler than that obtained without FAIMS separation. The peak list obtained from the product ion spectrum was searched against the SwissProt protein database. With no FAIMS separation, the LC-CID-MS method yielded no significant hits on the database, and therefore, no protein was identified. However, with the CV set to 2.5−2.6V, human serum albumin (HSA) was identified as the top hit, the only significant match, with a confidence score of 34 (where 27 or above was deemed statistically significant at a 95% confidence interval), based on the fragmentation of the doubly charged FQNALLVR tryptic fragment (m/z 480.7854) [6].

Figure 17: LC-MS and LC-FISCID-MS analysis of human plasma tryptic digest: (a) TIC, (b) selected ion chromatograms at 3.4−3.6min, (c) LC-MS spectrum of peaks at 3.52min without FAIMS separation, (d) LC-FAIMS-MS spectrum with FAIMS selection of the m/z 480 ion (CV of 2.5−2.6V), (e) LC-in-source CID-MS spectrum without FAIMS selection, and (f) LC-FISCID-MS spectrum with FAIMS selection of the m/z 480 ion and in-source CID (CV 2.5−2.6V, fragmentor voltage 340V).

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Acknowledgements

Our thanks to the following groups and individuals for the work they have carried out with Owlstone ultraFAIMS systems and for allowing us to include data here:

- Professor Colin Creaser, Lauren Brown and Rob Smith of the Centre for Analytical Science, Department of Chemistry, University of Loughborough, UK
- Dr Alex Shvartsburg & co-workers, Environmental Molecular Sciences Laboratory, Pacific Northwest National Laboratory, Washington, USA
- Dan Weston, Andy Ray and Anthony Bristow, Astra Zeneca R&D, UK
- Michael Ugarov, Agilent Technologies, Santa Clara, USA

UltraFAIMS Frequently Asked Questions

What is ultraFAIMS?

UltraFAIMS is a microscale chip-based field asymmetric ion mobility spectrometer designed for interfacing with mass spectrometers to provide extra separation of ions based on their differential mobility.

Can it be interfaced with any mass spectrometer?

The ultraFAIMS chip has a very small footprint (approx 2mm thick and 17mm in diameter) and can be floated to 6kV, which means it can be interfaced with most mass spectrometers. Our objective is to develop interfaces compatible with a wide range of mass spectrometers (see our website for up to date information on available interfaces), and we also provide a development kit for users who would like to develop a bespoke interface.

Does it work with ionization sources other than electrospray?

Yes, any ionization source can be interfaced with the device provided it produces desolvated gas phase ions. Our stand-alone products use radiation sources, corona ionization and UV ionization, and ultraFAIMS has been interfaced with standard ESI, nanospray, DESI and extractive electrospray sources.

Do I have to remove the ultraFAIMS device when I don't need extra separation?

Not necessarily. When the ultraFAIMS separation fields are disabled, the device transmits all ion species simultaneously and this makes it extremely quick to switch between FAIMS and non-FAIMS mode. Inevitably there will be some ion losses while the device is in place, so when sensitivity is critical you may wish to remove the device. This can be done in a few minutes without venting the mass spectrometer.

How does it work?

In a FAIMS device, ions pass between a pair of electrodes across which an alternating high/low electric field is applied. This electric field, known as the dispersion field (DF), makes the ions drift towards one or other electrode, with the drift velocity being a function of the field strength, the charge on the ion and the way the mobility of the ion changes between the high and low field portions of the cycle. The change in mobility is due to changes in the collision cross section of the ion resulting from structural rearrangements or clustering/declustering with neutral ions under the influence of the field. The net sideways drift means that most ions collide with the electrodes and are annihilated. However, ions can be selectively transmitted by superimposing a DC field, the compensation field (CF), in the opposite direction across the electrodes to cancel out the sideways drift – at different CF values, different species are transmitted. FAIMS devices can generally all operate in filtering mode, where the CF is held at a fixed value to transmit a subset of ions, or gradually stepped through a discrete range of values. Certain FAIMS devices, including ultraFAIMS, are also able to operate in scanning mode, where the CF is repeatedly swept through a range of values, producing a spectrum of ions separated by differential mobility.

How do I decide what settings to use?

In many cases you can use whatever LC, source and MS settings you normally use for the method you are running. To find the FAIMS parameters, the easiest way is to run a two-dimensional sweep – in which the CF is repeatedly swept over the full range, with the DF gradually being increased in steps. You can then review the data produced to determine what CF and DF values appear to give the best separation of the analytes you are interested in. You might then choose to cycle through a sequence of static CF/DF points, e.g. for targeted analysis, or to fix the DF and continue sweeping the CF through all or part of the full range for a more untargeted analysis.

Do I need additional gases or consumables?

The system does not require any additional gas flow to operate and the only consumables is the ultraFAIMS chip itself. Solvent modifiers or alternative gases can optionally be added to the carrier gas flow to enhance separation in some cases, but these are not essential.

Can modifiers be used to enhance separation with ultraFAIMS?

Yes, as mentioned above, the addition of solvent vapours to the carrier gas at the low percent concentration level does change the differential mobility behaviour of ions in the ultraFAIMS device, and this can provide a way of significantly enhancing separation – this is thought to be due to clustering/declustering of the analyte ions with the solvent molecules causing a change in differential mobility. Effective modifiers include methanol, butanol, acetone, acetonitrile, and isopropanol, although currently the behaviour of different modifiers is hard to predict *a priori*, so selection of a modifier tends to be an empirical process. Gases such as carbon dioxide, argon, helium or hydrogen can also be used as modifiers (typically at much higher concentrations than solvent vapours).

What peak capacity does it provide and how much does it affect transmission?

Without modifiers, the basic peak capacity of the device is around 10-15, and transmission compared to the non-FAIMS mode typically ranges from approximately 5-100%, though this is analyte specific. In many cases, the absolute transmission is not the key metric, but rather the increase in signal-to-background provided by the device – this is very application dependent but results so far have shown that increases of up to several orders of magnitude are possible.

How do you clean the chip and how long does it last?

The chip module can be removed from the interface for cleaning in a couple of minutes. It can then be submerged in suitable cleaning solvents and sonicated for a few minutes. The choice of solvent will depend on what analytes and solvents you have been running through the device. Once the chip has dried thoroughly, it can be replaced onto the interface. Chip lifetime is very dependent on usage and frequency of cleaning, but they typically last a few months before any performance degradation is seen. The chip module is a consumable part and replacements can be ordered from Owlstone.