Detection of Dimethyl Sulfate Using a LONESTAR™ Portable Analyzer

Detecting DMSO4 at concentrations as low as 0.35 ppb

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Contents

Summary

This report details the excellent performance of the LONESTAR™ portable analyzer as a continuously sampling ambient air monitor for dimethyl sulfate (DMSO4) detection. LONESTAR™ is able to detect DMSO4 at concentrations as low as 0.35 ppb. Such high sensitivity requires that Lonestar only has to use a small sampling volume which can be diluted using a clean makeup air flow. This aids DMSO4 detection under variable environmental conditions.

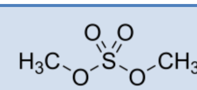
Introduction

Dimethyl sulfate (DMSO4, Table 1) has been used since the beginning of the 20th century as a methylating agent in industrial chemical synthesis. Its use continues to be widespread despite it being highly toxic and a probable carcinogen. The toxicity, volatility and availability of DMSO4 have also led to it being identified as a potential chemical warfare agent[1]

DMSO4 is readily absorbed through the skin and mucous membranes as well as the gastrointestinal tract. One of the most dangerous aspects of DMSO4 use is that the effects of exposure are often delayed by a period of up to 10 hours, which can allow potentially fatal exposures before realisation that there is a problem. Due to its significant vapor pressure at 20°C (0.5 mmHg) a common mode of contact with DMSO4 is via inhalation. DMSO4 hydrolyses into the neurotoxin methanol and sulfuric acid on contact with mucous membranes. This results in damage to the eyes and respiratory tract and potentially fatal pulmonary edema. DMSO4 is also likely to damage DNA and other cellular macromolecules via methylation.

The National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) to DMSO4 is 0.1 ppm (0.5 mg m-3) (NIOSH Potential Occupational Carcinogens). Accurate monitoring of DMSO4 concentration in the ambient air of an industrial or research setting is vital to protect workers from exposure to DMSO4.

Table 1 Properties of dimethyl sulphate

Chemical	Dimethyl Sulphate
CAS	77-78-1
Molecular weight	126.13g/mol
Structure	
Boiling Point	188C

[1] Rippey, J. C. R. and Stallwood, M. I., Nine cases of accidental exposure to dimethyl sulphate—a potential chemical weapon, *Emerg Med J*,2005, 22:878-879 doi:10.1136/emj.2004.015800

The LONESTAR™ Ambient Air Monitor

The LONESTAR is an analytically powerful, portable chemical analyzer that can be operated by non-specialists. Incorporating Owlstone's proprietary FAIMS technology (see Appendix A), the instrument combines high sensitivity and selectivity. Lonestar can be used to continuously monitor the atmosphere of an industrial environment and raise the alarm in response to changes in the background chemical signature of the air. New methods can be developed using Owlstone's EasySpec software, making the LONESTAR suitable for a broad range of applications in industry.

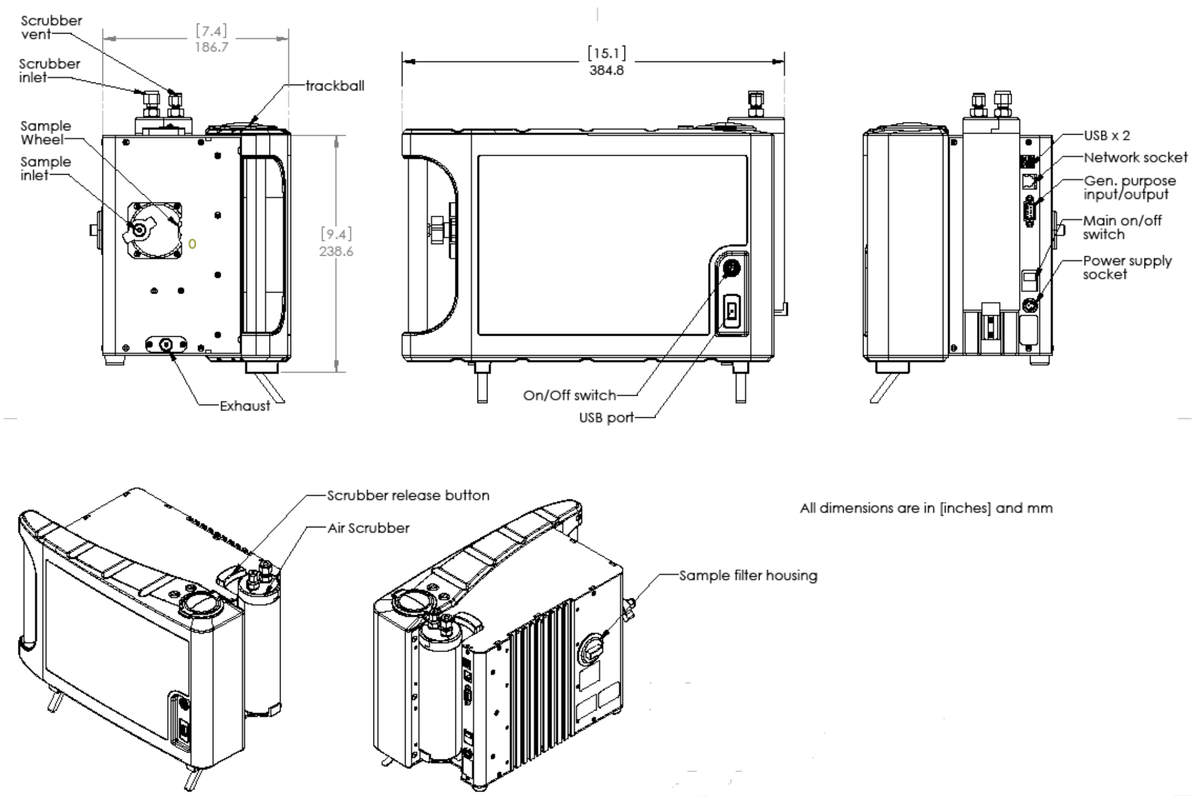


Figure 1 LONESTAR connection figures

Instrumentation and Methodology

The Lonestar instrument was calibrated using a DMSO4 permeation source as a gaseous chemical standard. The aim was to assess the linearity and repeatability of Lonestar's response to DMSO4. To achieve this, known gaseous concentrations of DMSO4 were generated using a calibrated permeation source in conjunction with an Owlstone Vapor Generator (OVG-4, see Appendix B).

Permeation source calibration

DMSO4 was purchased from Sigma Aldrich and a permeation source was constructed and calibrated gravimetrically. The calibration is shown in Figure 2, which shows the loss of mass from the source by permeation of DMSO4 over a period of time. The slope of the plotted linear fit to the data gives a DMSO4 permeation rate of 81 ng min^{-1}.

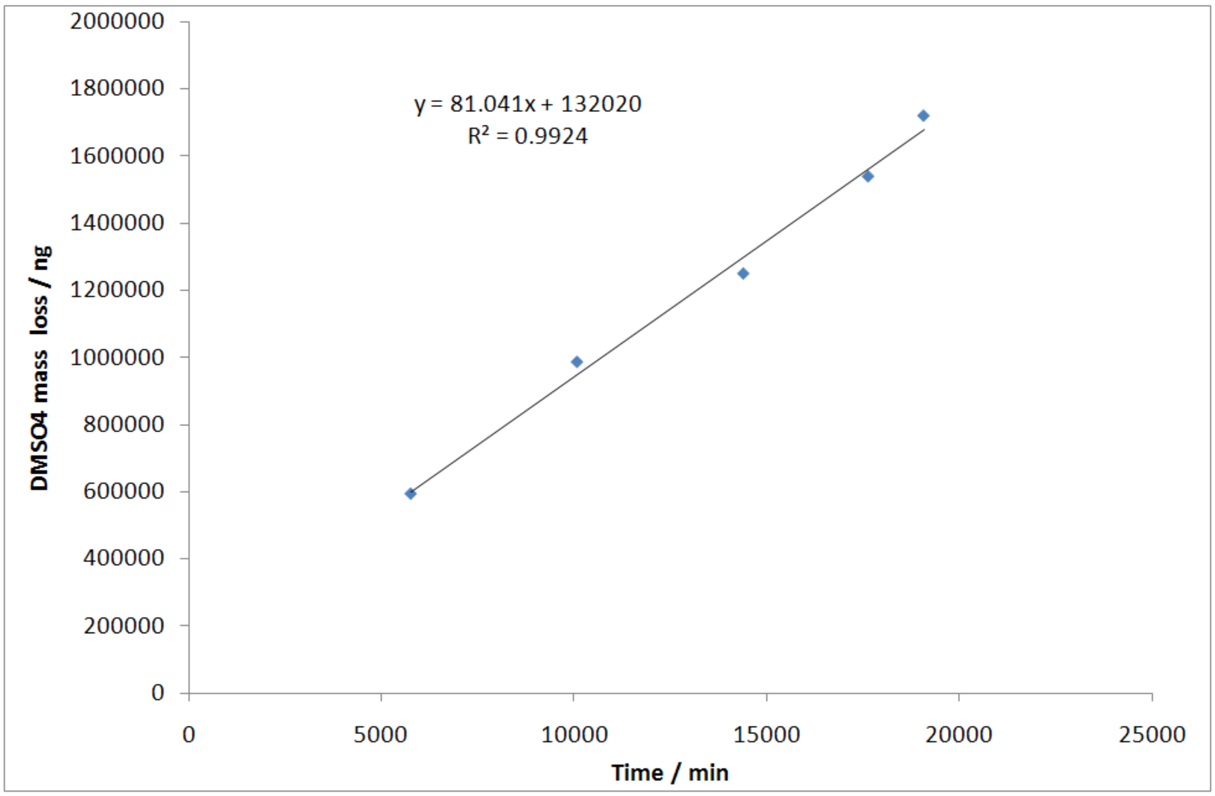


Figure 2 DMSO4 permeation source calibration, where the slope of the regression line gives a permeation rate of 81 ng min^{-1}

Experimental set up

The calibrated permeation source was placed into an Owlstone vapour generator (OVG-4, see Appendix B) set to 50°C. The DMSO4 containing air flow from the OVG-4 was connected to a Lonestar analyzer for analysis (Figure 3). Differing split flow regimes were employed to produce varying DMSO4 gaseous concentrations (detailed in Table 2). Ten repeat FAIMS spectra were collected using the Lonestar instrument at each concentration.

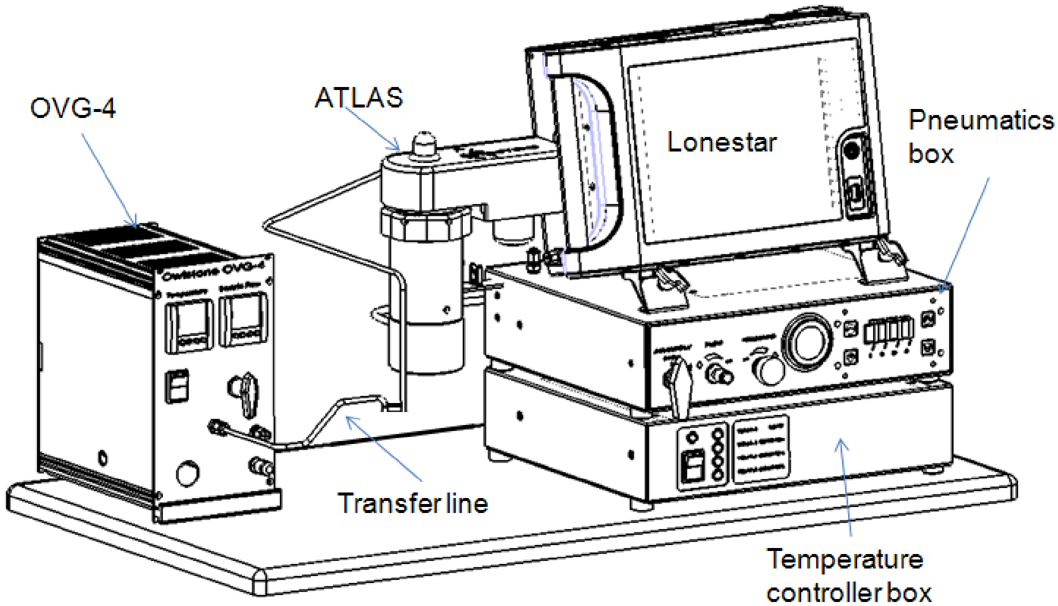


Figure 3 Experimental set-up, including the Owlstone vapor generator which housed the DMSO4 permeation source at 50°C. The OVG-4 was connected to the Lonestar via the at line sampling module (ATLAS)

Table 2 List of DMSO4 concentrations generated for Lonestar analysis

Sample number	Concentration $ppb_{v/v}$	Number of reps.
1	4.92	10
2	3.93	10
3	2.62	10
4	2.50	10
5	1.49	10
6	0.67	10
7	0.35	10

Results and Discussion

The first step of the experiment was to identify the DMSO4 response in the FAIMS spectra. For comparison, a blank response (DMSO4 permeation source not present) was compared to the responses where the DMSO4 permeation source was present (Figure 3). In the blank response the positive (hydronium ions) and negative (hydrated oxygen) reactive ion peaks (RIP) can be seen. The DMSO4 response is clearly visible as two peaks (monomer and dimer) in the positive spectrum and also as a strong response in the negative mode.

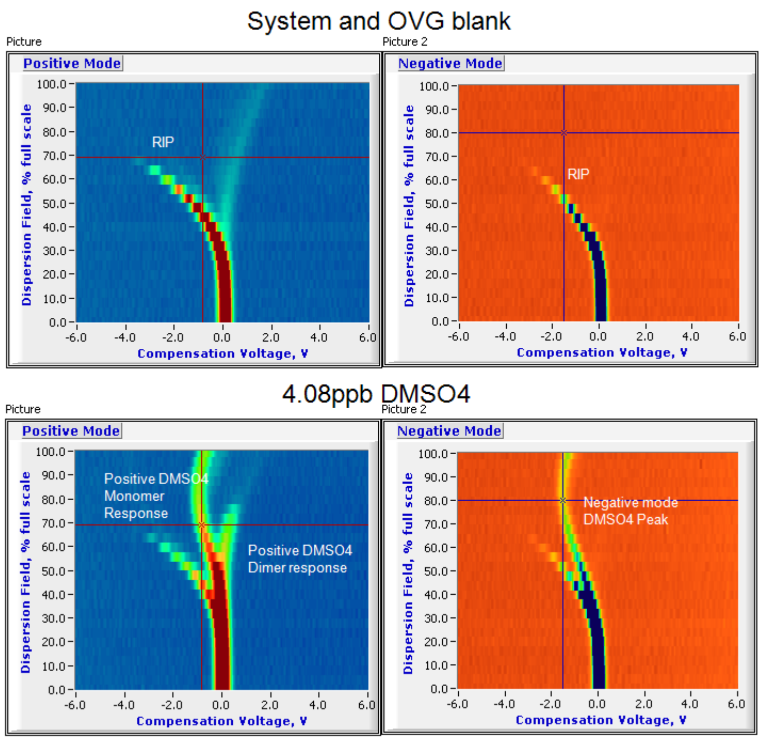


Figure 4 Comparison of Lonestar blank matrices (top) against a 4.08ppb DMSO4 response (bottom). The blank spectra show the positive (blue) mode RIP made up of hydronium ions and the negative mode (red) RIP response from hydrated oxygen molecules. Peaks caused by DMSO4 are clearly visible in both the positive and negative modes of the Lonestar spectra.

The repeatability of the detection technique for DMSO4 is illustrated in Figure 4 (in which 10 repeat sample spectrums are overlaid), resulting in a relative standard deviation (RSD) of < 10%, as shown in Table 3.

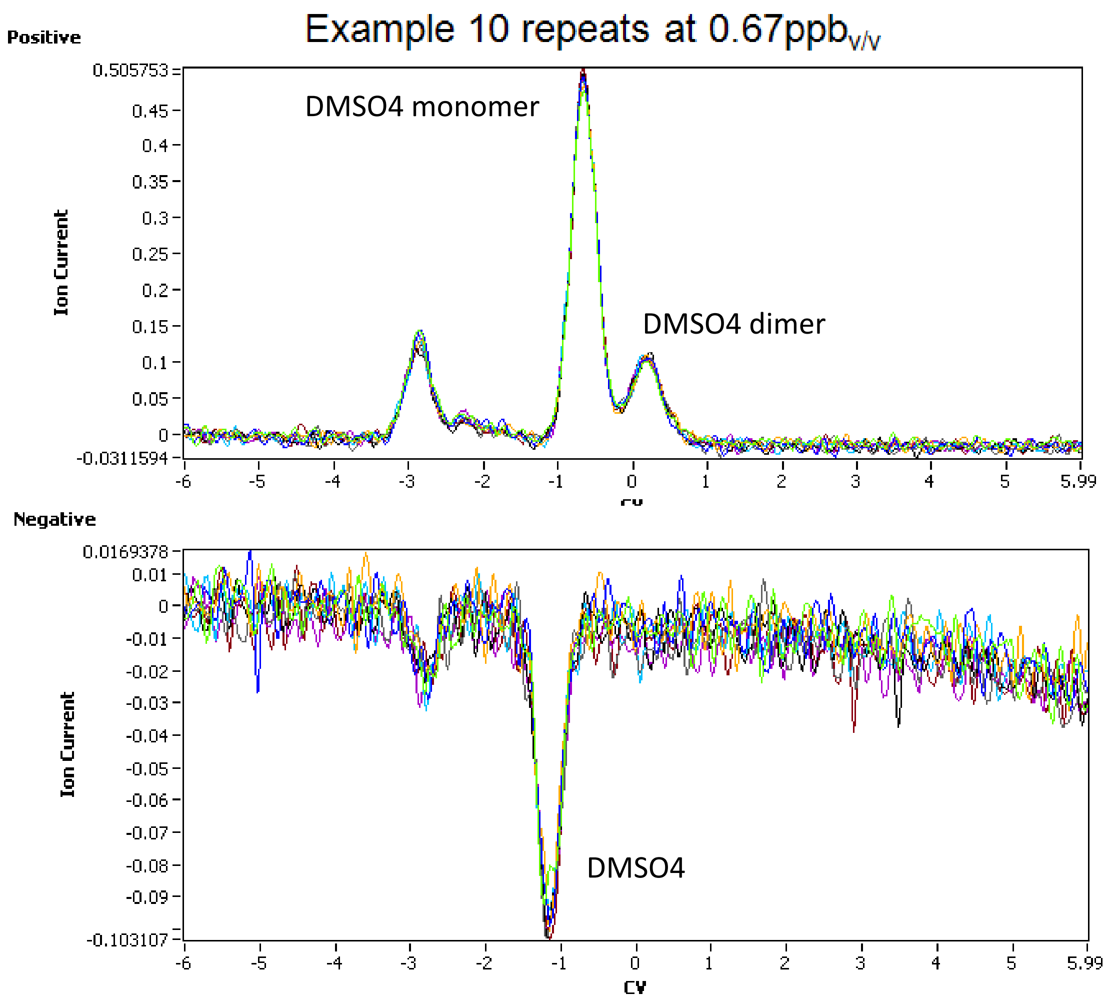


Figure 5 Example overlaid CV spectra from 10 repeated DMSO4 measurements at 0.67ppb.

Figure 6 shows CV spectra taken at a series of different DMOS4 concentrations. The monomer peak reaches saturation at the higher concentration levels as the formation of the dimer ion becomes more favourable.

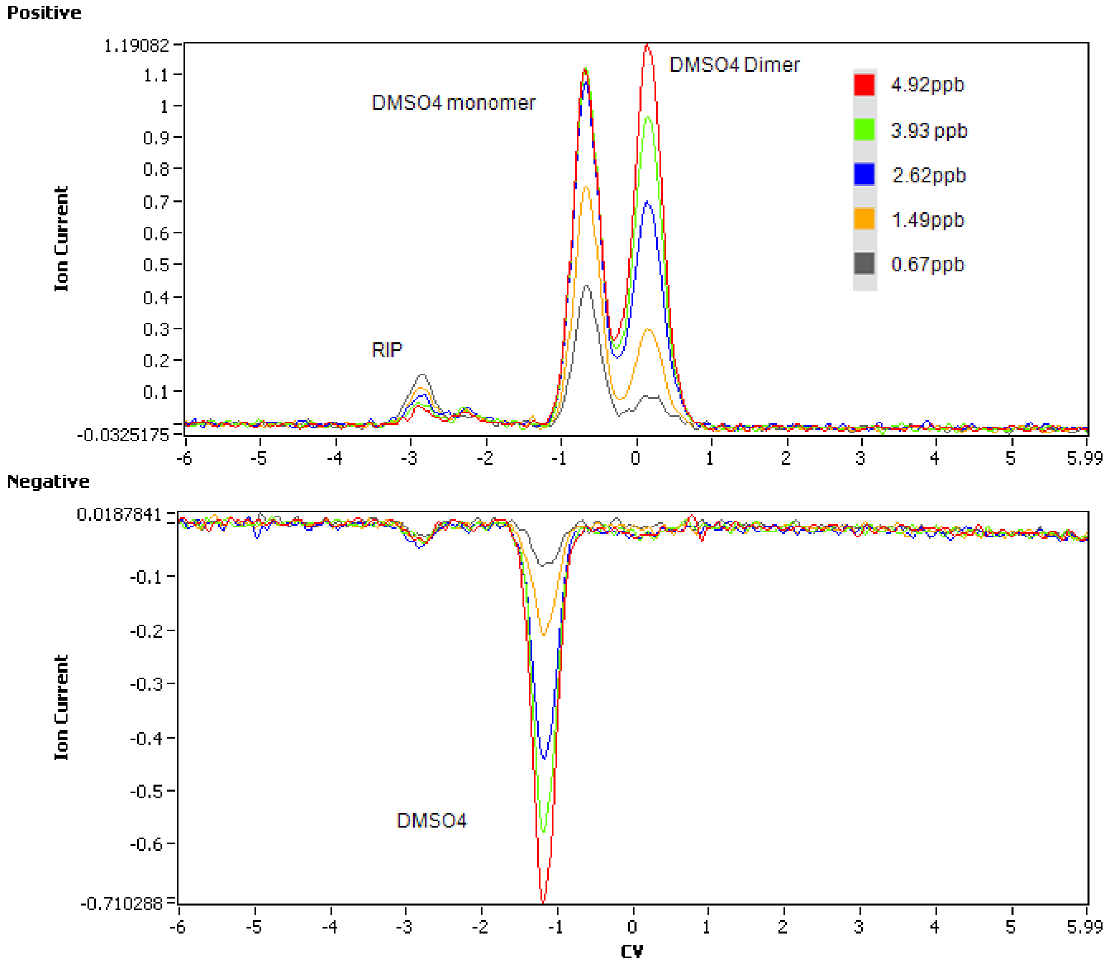
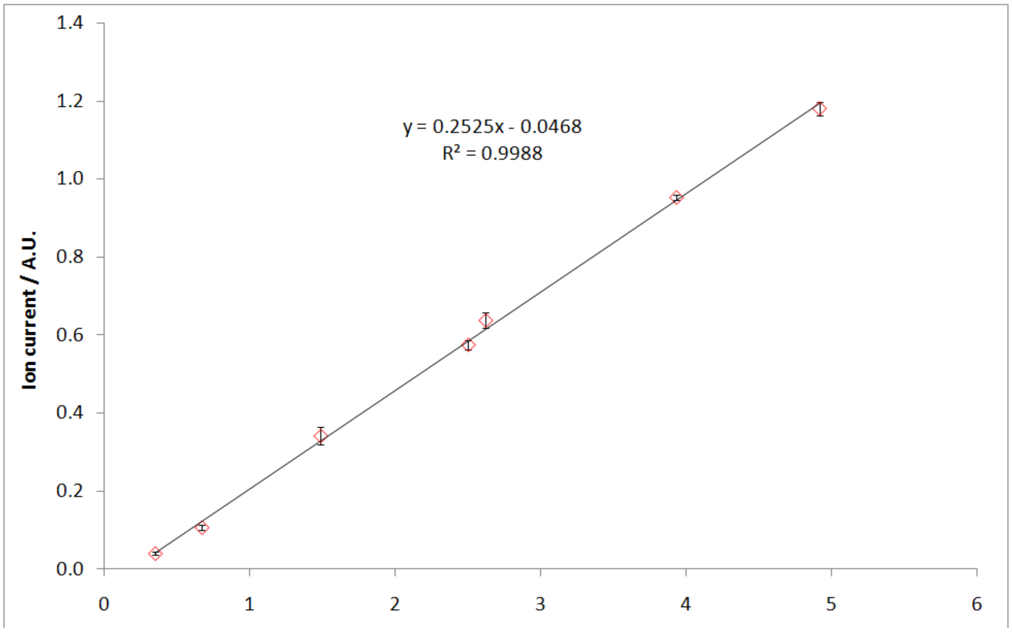


Figure 6 Example overlaid CV spectra of DMSO4 at various concentration levels (see legend)

As both the intensities of the dimer ion peak in the positive mode and the negative mode peak were exhibiting linear trends with concentration it was decided to use these responses to create the DMSO4 calibration curve. Figure 7 shows the resulting linear calibrations lines. The extracted data from these two peaks and associated standard deviations and relative standard deviations from the 10 replicates are presented in Table 3.



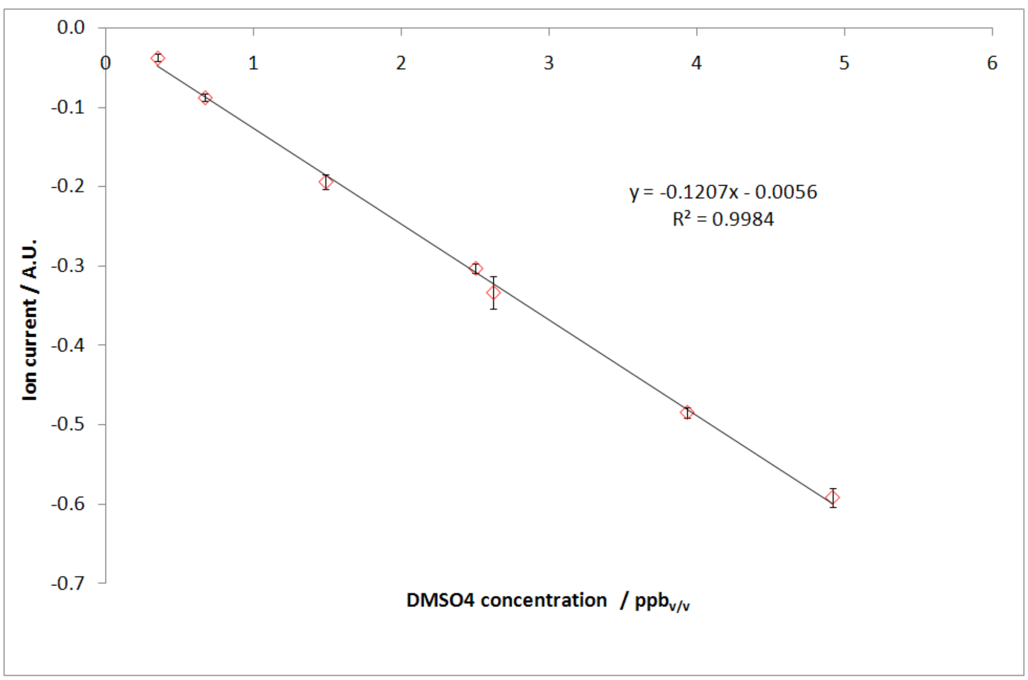


Figure 7 DMSO4 calibration using the positive mode dimer ion (top) and Negative mode response (bottom). Standard error bars are where n=10

Table 3 Extracted calibration data (see plots below) for DMSO4 using the negative mode peak height and the Dimer positive mode peak height, presented with the standard deviation (STDEV) and relative standard deviation (RSD) where n=10.

Conc. / $ppb_{v/v}$	Neg PH / A.U.	Neg PH STDEV	Neg PH / RSD	Positive Dimer PH / A.U	pos STDEV	Dimer RSD
4.92	-0.59	0.012	2.06	1.18	0.02	1.44
3.93	-0.48	0.007	1.38	0.95	0.01	0.79
2.62	-0.33	0.021	6.28	0.64	0.02	2.99
2.50	-0.30	0.006	1.94	0.58	0.01	2.04
1.49	-0.19	0.009	4.79	0.34	0.02	6.57
0.67	-0.09	0.005	5.40	0.11	0.01	6.69
0.35	-0.04	0.005	11.99	0.04	0.00	9.67

Conclusions

The results presented in this report demonstrates the Lonestar Poratable Analyzer's ability to detect sub-PPB concentrations of dimethyl sulfate (DMSO4). The lonestar instrument's response to DMSO4 had linear range of 0.5 -5 ppb with an RSD < 10% (where n=10). Such high sensitivity requires that Lonestar only has to use a small sampling volume, which can be diluted using a clean makeup air flow. This aids DMSO4 detection under variable environmental conditions.

Appendix A: FAIMS Technology at a Glance

Field asymmetric ion mobility spectrometry (FAIMS), also known as differential mobility spectrometry (DMS), is a gas detection technology that separates and identifies chemical ions based on their mobility under a varying electric field at atmospheric pressure. Figure 8 is a schematic illustrating the operating principles of FAIMS.

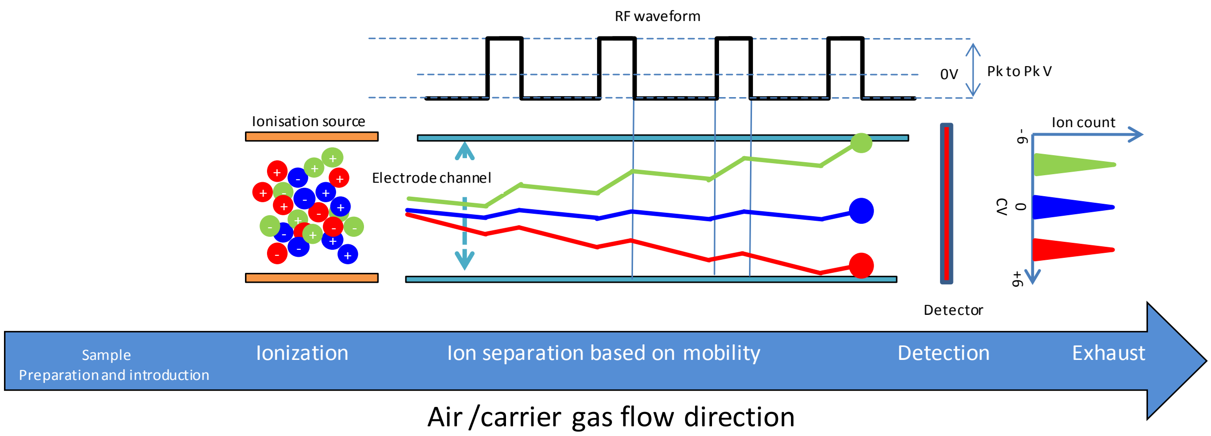


Figure 8 FAIMS schematic. The sample in the vapour phase is introduced via a carrier gas to the ionisation region, where the components are ionised via a charge transfer process or by direct ionisation, dependent on the ionisation source used. It is important to note that both positive and negative ions are formed. The ion cloud enters the electrode channel, where an RF waveform is applied to create a varying electric field under which the ions follow different trajectories dependent on the ions' intrinsic mobility parameter. A DC voltage (compensation voltage, CV) is swept across the electrode channel shifting the trajectories so different ions reach the detector, which simultaneously detects both positive and negative ions. The number of ions detected is proportional to the concentration of the chemical in the sample

Sample preparation and introduction

FAIMS can be used to detect volatiles in aqueous, solid and gaseous matrices and can consequently be used for a wide variety of applications. The user requirements and sample matrix for each application define the sample preparation and introduction steps required. There are a wide variety of sample preparation, extraction and processing techniques each with their own advantages and disadvantages. It is not the scope of this overview to list them all, only to highlight that the success of the chosen application will depend heavily on this critical step, which can only be defined by the user requirements.

There are two mechanisms of introducing the sample into the FAIMS unit: discrete sampling and continuous sampling. With discrete sampling, a defined volume of the sample is collected by weighing, by volumetric measurement via a syringe, or by passing vapor through an adsorbent for pre-concentration, before it is introduced into the FAIMS unit. An example of this would be attaching a container to the instrument containing a fixed volume of the sample. A carrier gas (usually clean dry air) is used to transfer the sample to the ionization region. Continuous sampling is where the resultant gaseous sample is continuously purged into the

FAIMS unit and either is diluted by the carrier gas or acts as the carrier gas itself. For example, continuously drawing air from the top of a process vat.

The one key requirement for all the sample preparation and introduction techniques is the ability to reproducibly generate and introduce a headspace (vapour) concentration of the target analytes that exceeds the lower limits of detection of the FAIMS device.

Carrier Gas

The requirement for a flow of air through the system is twofold: Firstly to drive the ions through the electrode channel to the detector plate and secondly, to initiate the ionization process necessary for detection.

As exhibited in Figure 9, the transmission factor (proportion of ions that make it to the detector) increases with increasing flow. The higher the transmission factor, the higher the sensitivity. Higher flow gives a larger full width half maximum (FWHM) of the peaks but also decreases the resolution of the FAIMS unit (see Figure 10).

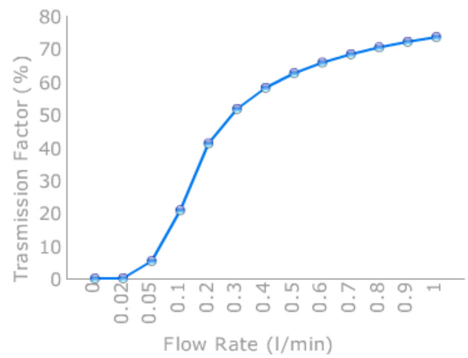


Figure 9 Flow rate vs. ion transmission factor

The air/carrier gas determines the baseline reading of the instrument. Therefore, for optimal operation it is desirable for the carrier to be free of all impurities (< 0.1 ppm methane) and the humidity to be kept constant. It can be supplied either from a pump or compressor, allowing for negative and positive pressure operating modes.

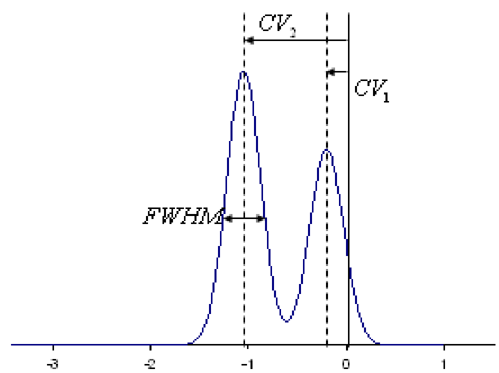


Figure 10 FWHM of ion species at set CV

Ionisation Source

There are three main vapor phase ion sources in use for atmospheric pressure ionization; radioactive nickel-63 (Ni-63), corona discharge (CD) and ultra-violet radiation (UV). A comparison of ionization sources is presented in Table 4.

Ionisation Source	Mechanism	Chemical Selectivity
Ni^{63} (beta emitter) creates a positive / negative RIP	Charge transfer	Proton / electron affinity
UV (Photons)	Direct ionisation	First ionisation potential
Corona discharge (plasma) creates a positive / negative RIP	Charge transfer	Proton / electron affinity

Table 4 FAIMS ionization source comparison

Ni-63 undergoes beta decay, generating energetic electrons, whereas CD ionization strips electrons from the surface of a metallic structure under the influence of a strong electric field. The generated electrons from the metallic surface or Ni-63 interact with the carrier gas (air) to form stable +ve and -ve intermediate ions which give rise to reactive ion peaks (RIP) in the positive and negative FAIMS spectra (Figure 11). These RIP ions then transfer their charge to neutral molecules through collisions. For this reason, both Ni-63 and CD are referred to as indirect ionization methods.

For the positive ion formation:

$N_2 + e- \rightarrow \mathbf{N_2^+} + e-$ (primary) + e- (secondary)
$\mathbf{N_2^+} + 2N_2 \rightarrow \mathbf{N_4^+} + N_2$
$N_4+ + H_2O \rightarrow 2N_2 + \mathbf{H_2O^+}$
$H_2O+ + H_2O \rightarrow \mathbf{H_3O^+} + OH$
$H_3O+ + H_2O + N_2 \leftrightarrow \boldsymbol{H^+(H_2O)_2} + N_2$
$H^+(H_2O)_2 + H_2O + N_2 \leftrightarrow \boldsymbol{H^+(H_2O)_3} + N_2$

For the negative ion formation:

$O_2 + e- \rightarrow \mathbf{O_2^-}$
$B + H_2O + \mathbf{O_2^-} \leftrightarrow \boldsymbol{O_2^-(H_2O)} + B$
$B + H_2O + O_2^-(H_2O) \leftrightarrow \boldsymbol{O_2^-(H_2O)_2} + B$

The water based clusters (hydronium ions) in the positive mode (blue) and hydrated oxygen ions in the negative mode (red), are stable ions which form the RIPs. When an analyte (M) enters the RIP ion cloud, it can replace one or dependent on the analyte, two water molecules to form a monomer ion or dimer ion respectively, reducing the number of ions present in the RIP.

$$H^+(H_2O)_3 + M + N_2 \leftrightarrow \underbrace{M\boldsymbol{H^+(H_2O)_2}}_{\text{Monomer}} + N_2 + H_2O \leftrightarrow \underbrace{M_2\boldsymbol{H^+(H_2O)_1}}_{\text{Dimer}} + N_2 + H_2O$$

Dimer ion formation is dependent on the analyte's affinity to charge and its concentration. This is illustrated in Figure 11A using dimethyl methylphsphonate (DMMP). Plot A shows that the RIP decreases with an increase in DMMP concentration as more of the charge is transferred over to the DMMP. In addition the monomer ion decreases as dimer formation becomes more favourable at the higher concentrations. This is shown more clearly in Figure 11B, which plots the peak ion current of both the monomer and dimer at different concentration levels.

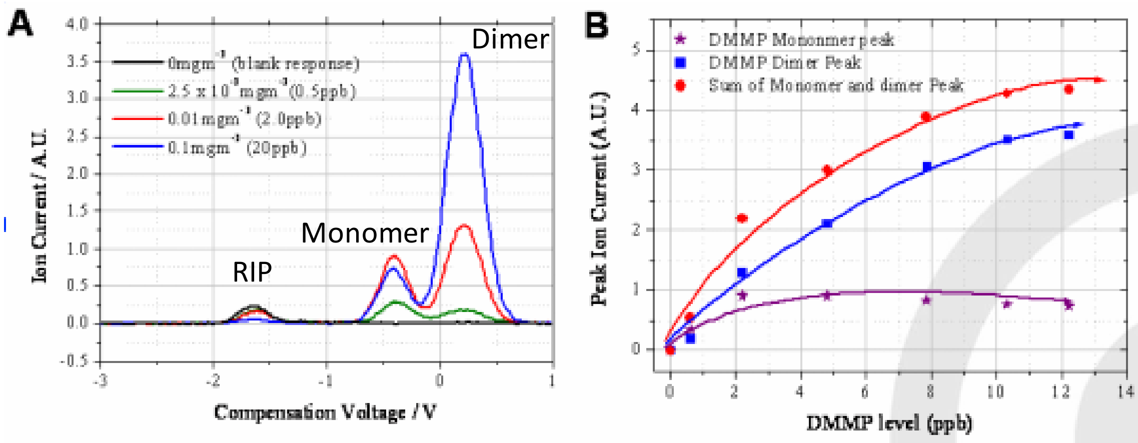


Figure 11 DMMP Monomer and dimer formation at different concentrations

The likelihood of ionization is governed by the analyte's affinity towards protons and electrons (Table 5 and Table 6 respectively).

In complex mixtures where more than one chemical is present, competition for the available charge occurs, resulting in preferential ionisation of the compounds within the sample. Thus the chemicals with high proton or electron affinities will ionize more readily than those with a low proton or electron affinity. Therefore the concentration of water within the ionization region will have a direct effect on certain analytes whose proton / electron affinities are lower.

Chemical Family	Example	Proton affinity
Aromatic amines	Pyridine	930 kJ/mole
Amines	Methyl amine	899 kJ/mole
Phosphorous Compounds	TEP	891 kJ/mole
Sulfoxides	DMS	884 kJ/mole
Ketones	2- pentanone	832 kJ/mole
Esters	Methly Acetate	822 kJ/mole
Alkenes	1-Hexene	805 kJ/mole
Alcohols	Butanol	789 kJ/mole
Aromatics	Benzene	750 kJ/mole
Water		691 kJ/mole
Alkanes	Methane	544 kJ/mole

Table 5 Overview of the proton affinity of different chemical families

Chemical Family	Electron affinity
Nitrogen Dioxide	3.91eV
Chlorine	3.61eV
Organomercurials	
Pesticides	
Nitro compounds	
Halogenated compounds	
Oxygen	0.45eV
Aliphatic alcohols	
Ketones	

Table 6 Relative electron affinities of several families of compounds

The UV ionization source is a direct ionization method whereby photons are emitted at energies of 9.6, 10.2, 10.6, 11.2, and 11.8 eV and can only ionize chemical species with a first ionization potential of less than the emitted energy. Important points to note are that there is no positive mode RIP present when using a UV ionization source and also that UV ionization is very selective towards certain compounds.

Mobility

Ions in air under an electric field will move at a constant velocity proportional to the electric field. The proportionality constant is referred to as mobility. As shown in Figure 12, when the ions enter the electrode channel, the applied RF voltages create oscillating regions of high ($+V_{HF}$) and low ($-V_{HF}$) electric fields as the ions move through the channel. The difference in the ion's mobility at the high and low electric field regimes dictates the ion's trajectory through the channel. This phenomenon is known as differential mobility.

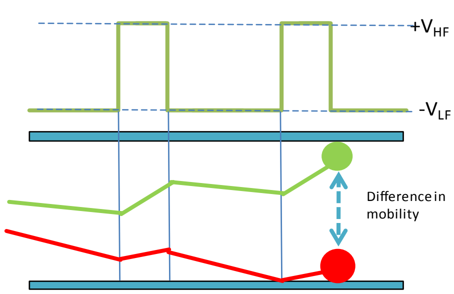


Figure 12 Schematic of a FAIMS channel showing the difference in ion trajectories caused by the different mobilities they experience at high and low electric fields

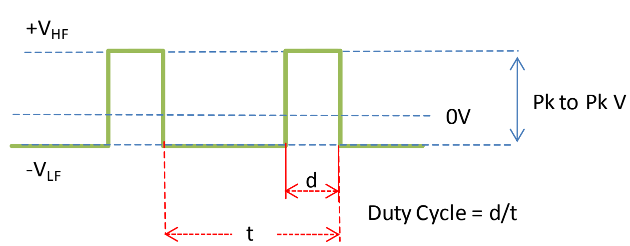


Figure 13 Schematic of the ideal RF waveform, showing the duty cycle and peak to peak voltage (Pk to Pk V)

The physical parameters of a chemical ion that affect its differential mobility are its collisional cross section and its ability to form clusters within the high/low regions. The environmental factors within the electrode channel affecting the ion's differential mobility are electric field, humidity, temperature and gas density (i.e. pressure).

The electric field in the high/low regions is supplied by the applied RF voltage waveform (Figure 13). The duty cycle is the proportion of time spent within each region per cycle. Increasing the peak-to-peak voltage increases/decreases the electric field experienced in the high/low field regions and therefore influences the velocity of the ion accordingly. It is this parameter that has the greatest influence on the differential mobility exhibited by the ion.

It has been shown that humidity has a direct effect on the differential mobility of certain chemicals, by increasing/decreasing the collision cross section of the ion within the respective low/high field regions. The addition and subtraction of water molecules to analyte ions is referred to as clustering and de-clustering. Increased humidity also increases the number of water molecules involved in a cluster ($MH^+(H_2O)_2$) formed in the ionisation region. When this cluster experiences the high field in between the electrodes the water molecules are forced away from the cluster reducing the size (MH^+) (de-clustering). As the low field regime returns so do the water molecules to the cluster, thus increasing the ion's size (clustering) and giving the ion a larger differential mobility. Gas density and temperature can also affect the ion's mobility by changing the number of ion-molecule collisions and changing the stability of the clusters, influencing the amount of clustering and de-clustering.

Changes in the electrode channel's environmental parameters will change the mobility exhibited by the ions. Therefore it is advantageous to keep the gas density, temperature and humidity constant when building detection algorithms based on an ion's mobility as these factors would need to be corrected for. However, it should be kept in mind that these parameters can also be optimized to gain greater resolution of the target analyte from the background matrix, during the method development process.

Detection and Identification

As ions with different mobilities travel down the electrode channel, some will have trajectories that will result in ion annihilation against the electrodes, whereas others will pass through to hit the detector. To filter the ions of different mobilities onto the detector plate a compensation voltage (CV) is scanned between the top and bottom electrode (see Figure 14). This process realigns the trajectories of the ions to hit the detector and enables a CV spectrum to be produced.

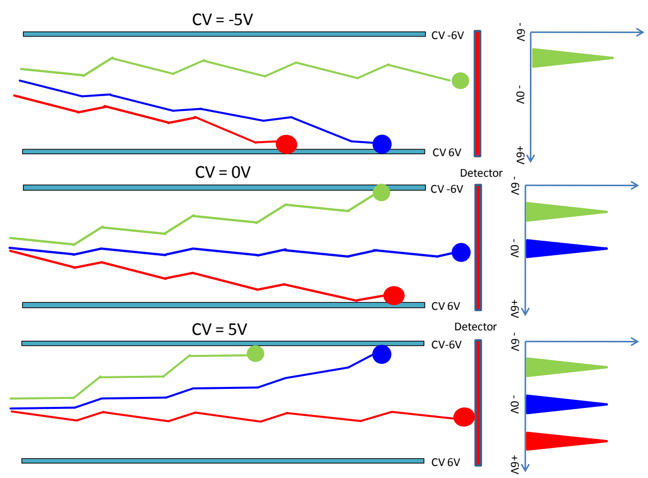


Figure 14 Schematic of the ion trajectories at different compensation voltages and the resultant FAIMS spectrum

The ion's mobility is thus expressed as a compensation voltage at a set electric field. Figure 15 shows an example CV spectrum of a complex sample where a de-convolution technique has been employed to characterize each of the compounds.

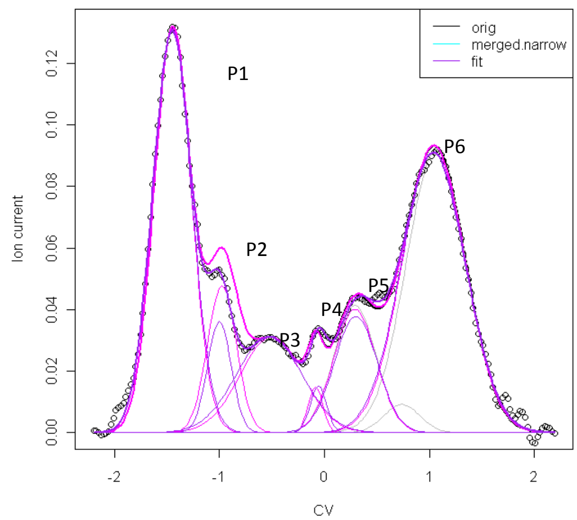
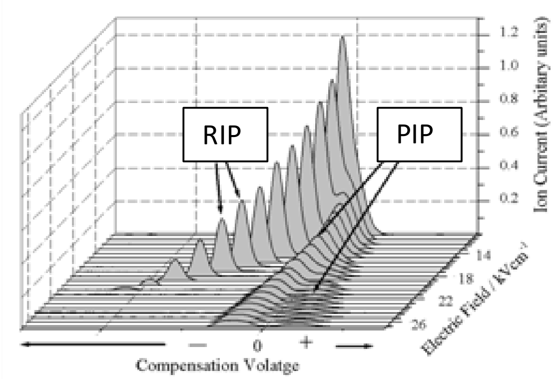


Figure 15 Example CV spectra. Six different chemical species with different mobilities are filtered through the electrode channel by scanning the CV value

Changing the applied RF peak-to-peak voltage (electric field) has a proportional effect on the ion's mobility. If this is increased after each CV spectrum, a dispersion field matrix is constructed. Figure 16 shows two examples of how this is represented; both are negative mode dispersion field (DF) sweeps of the same chemical. The term DF is sometimes used instead of electric field. It is expressed as a percentage of the maximum peak-to-peak voltage used on the RF waveform. The plot on the left is a waterfall image where each individual CV scan is represented by compensation voltage (x-axis), ion current (y-axis) and electric field (z-axis). The plot on the right is the one that is more frequently used and is referred to as a 2D color plot. The compensation voltage and electric field are on the x, and y axes and the ion current is represented by the color contours.



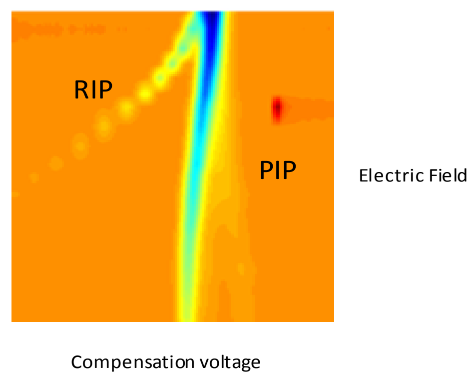


Figure 16 Two different examples of FAIMS dispersion field matrices with the same reactive ion peaks (RIP) and product ion peaks (PIP). In the waterfall plot on the left, the z axis is the ion current; this is replaced in the right, more frequently used, colorplot by color contours

With these data rich DF matrices a chemical fingerprint is formed, in which identification parameters for different chemical species can be extracted, processed and stored. Figure 17 shows one example: here the CV value at the peak maximum at each of the different electric field settings has been extracted and plotted, to be later used as a reference to identify the same chemicals. In Figure 18 a new sample spectrum has been compared to the reference spectrum and clear differences in both spectra can be seen.

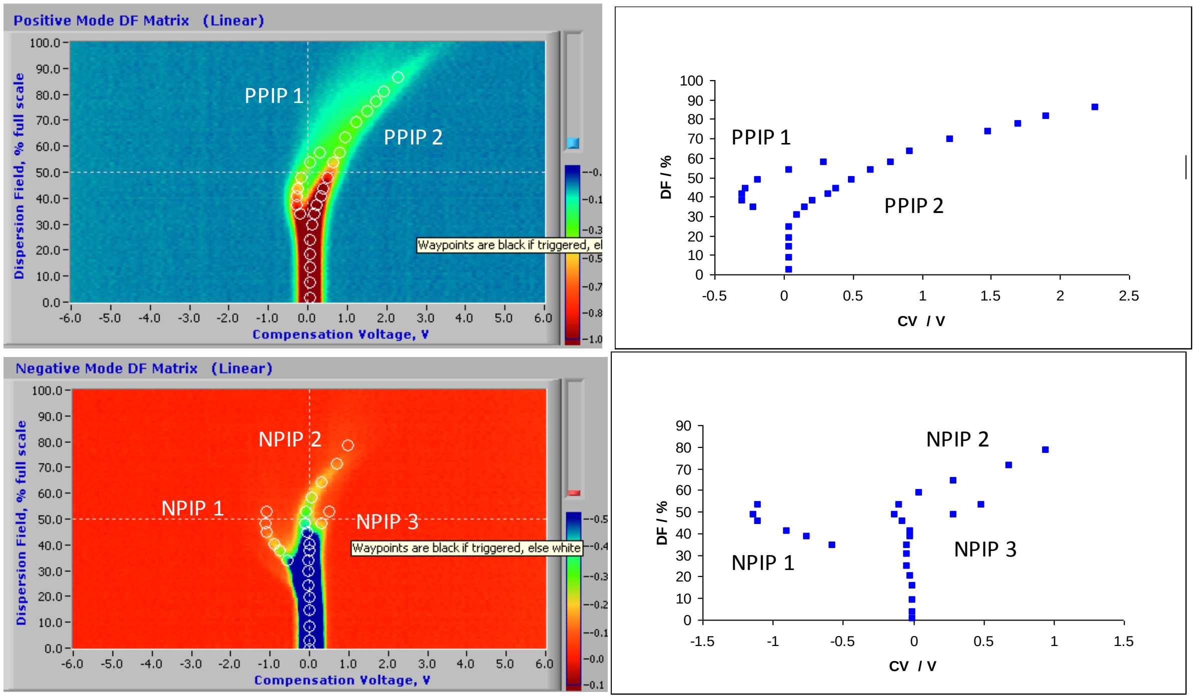


Figure 17 On the left are examples of positive (blue) and negative (red) mode DF matrices recorded at the same time while a sample was introduced into the FAIMS detector. The sample contained 5 chemical species, which showed as two positive product ion peaks (PPIP) and three negative product ion peaks (NPIP). On the right, the CV at the PIP's peak maximum is plotted against % dispersion field to be stored as a spectral reference for subsequent samples.

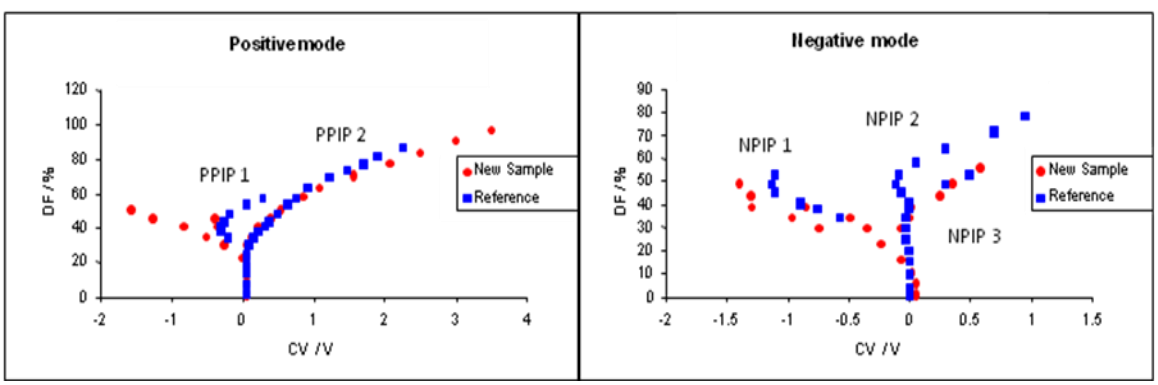


Figure 18 Comparison of two new DF plots with the reference from Figure 10. It can be seen that in both positive and negative modes there are differences between the reference product ion peaks and the new samples

Appendix B: Generating Calibration Standards with the OVG-4

Calibration standards can be generated using permeation tubes and Owlstone's OVG-4 Calibration Gas Generator. The permeation tubes are gravimetrically calibrated to NIST traceable standards. For this study an acetaldehyde permeation source was used as a confidence check to ensure that the Lonestar was operating within defined parameters.

BENEFITS

- High number of available analyte compounds, including solids and liquids as well as gases
- Easy generation of multi-component mixtures using combinations of tubes
- Cost savings by elimination of multiple expensive gas cylinders
- Reduced risk of exposure to dangerous chemicals due to small quantities used
- Fast and easy sample replacement
- Elimination of hazards associated with high pressure cylinders
- Quick and easy to set up and generate blended gas mixtures
- Adjustable concentration levels from ppm to ppb
- High accuracy and precision, even at the lowest concentrations
- Superior long term stability and repeatability*
- Portable, with compact footprint
- Easily integrated with the Owlstone Humidity Generator (OHG) for realistic environmental testing

**Owlstone offers an optional service for regular validation and instrument calibration*

The Owlstone OVG-4 is a system for generating NIST traceable chemical and calibration gas standards. It is easy to use, cost-effective and compact and produces a very pure, accurate and repeatable output.

The very precise control of concentration levels is achieved using permeation tube technology, eliminating the need for multiple gas cylinders and thus reducing costs, saving space and removing a safety hazard. Complex gas mixtures can be accurately generated through the use of multiple tubes.

By swapping out permeation tubes the OVG-4 can be used to generate over 500 calibration standards to test and calibrate almost any gas sensor, instrument or analyzer, including FTIR, NDIR, Raman, IMS, GC, GC/MS.

Current customers include – SELEX GALILEO, US Army, US Air Force, US Defence Threat Reduction Agency, Home Office Scientific Development Branch, DSTL, Commissariat à l'Énergie Atomique, EADS, United Technologies, Alphasense, Xtralis, LGC, Genzyme, IEE, Institut de la Corrosion, Rutherford Appleton Laboratory, University of Cambridge, Cranfield University among others.