MS Atmospheric Pressure Ionisation Sources: Their Use and Applicability

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It can be argued that a mass spectrometer, of any geometry, is nothing without its ion source– since, without the generation of ions there is nothing for the mass spectrometer to separate and detect. Historically, ion sources were maintained under vacuum to facilitate ionisation of the sample and to enable easy transfer of the ions into the high vacuum region of the mass spectrometer. Ions were predominantly formed by Electron Ionisation (EI) or Chemical Ionisation (CI), with the analytes entering the ion source in the gas phase, or being formed as gaseous species within the ion source, for example by thermal desorption. This low pressure/high vacuum requirement made coupling LC to MS particularly challenging.

In 1982, Patrick J. Arpino characterised LC-MS as 'A difficult courtship' (modelling it as the attraction between a fish and a bird – a species of the water and a species of the air) [1]. The primary difficulty is that of accommodating a large volume of solvent into a region of very low pressure and the concomitant demands placed on the instrument's pumping system.

Since the early days of API, the development of ion sources has continued unabated, with in excess of 20 ambient (or near ambient) ionisation techniques [2,3] available to the intrepid analyst. Whilst the ion source itself is of vital importance, almost equally important is the correct selection of the most appropriate ionisation source for the types of molecules being analysed, along with relevant optimisation, and knowledge about the expected behaviour of the ionisation source.

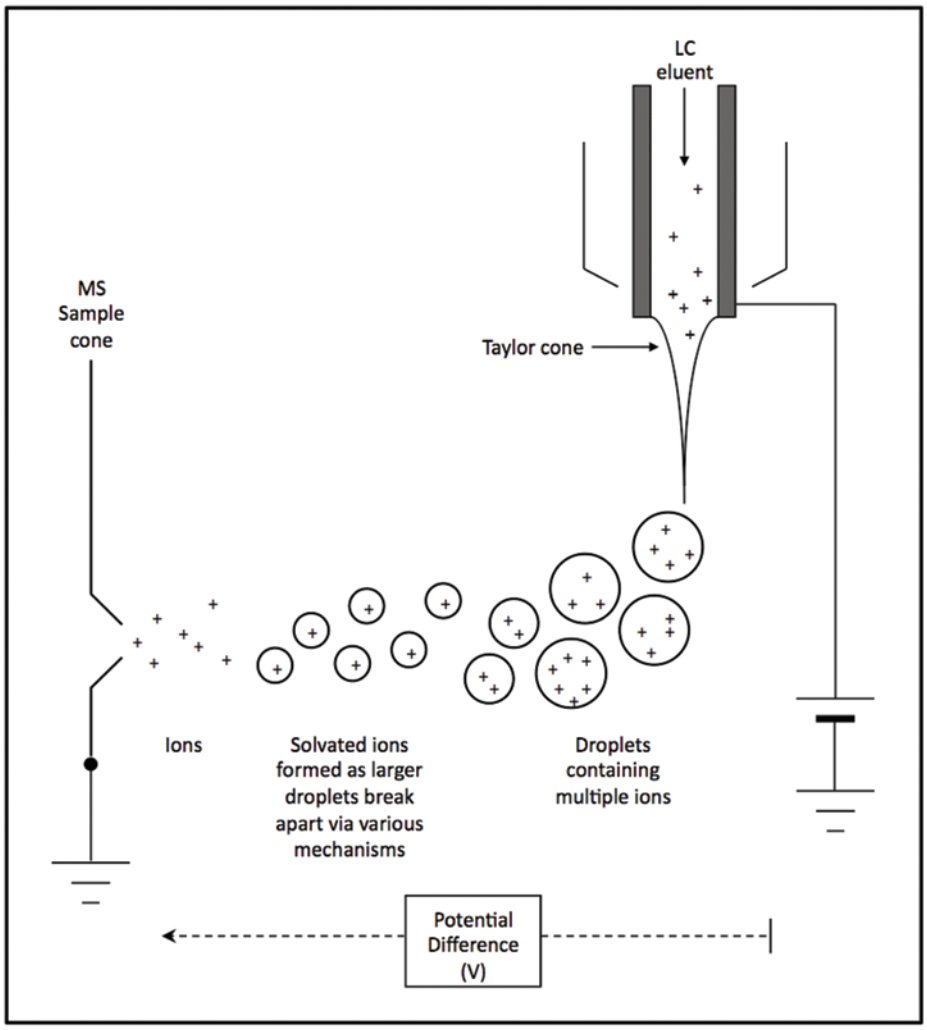


Figure 1: Schematic showing the ionisation process in electrospray ionisation (ESI).

In this work [4], we provide an overview of different atmospheric pressure ionisation techniques, including: electrospray ionisation (ESI), Atmospheric Pressure Chemical Ionisation (APCI), Atmospheric Pressure Photoionisation (APPI), Atmospheric Solids Analysis Probe (ASAP), and Waters' novel UniSpray ion source. Included is information about their ionisation mechanisms, optimisation, and types of small molecules for which they are most applicable. Ions produced by UniSpray ionisation are compared with ions produced by ESI, APCI, APPI, and ASAP ionisation sources for a range of small molecules, including PAHs, pesticides, and polymer additives. However, owing to time and availability constraints, many other ionisation options have not been investigated. One, or more, of the ion sources not covered here might be equally appropriate for ionisation of compounds mentioned in this work.

Electrospray Ionisation (ESI)

Figure 1 shows a simple schematic of the ionisation process in electrospray ionisation (ESI). Some debate still remains regarding the precise mechanism of ion formation in ESI. Typically, analyte and solvent molecules are believed to undergo electrochemical

reactions either through redox reactions at the liquid/metal interface of the capillary tip or through acid/base reactions in solution [5]. These processes form ions in solution; the figure shows positive ions but negative ions could be generated in a similar manner.

To transfer the ions into the gas phase, two main general mechanisms are proposed [6]: the 'ion evaporation mechanism' (IEM) where the electric field at the surface of highly charged, small droplets becomes sufficient to field desorb ions directly from the surface, or the 'Charge Residue Model' where ions eventually become desolvated as solvent molecules leave the droplet surface. Evidence suggests that smaller ions are more likely to enter the gas phase via the IEM, whereas larger, multi-charged species are more likely to follow the CRM [6,7]. Modifications or related processes to these two mechanisms have also been proposed [8].

ESI can be a highly efficient ionisation process at low flow rates (<1 µL/min) and produces 'soft ionisation' owing to the small differences in proton affinities between the analyte and reagent ions. However, since there is a practical limit to the amount of charge that can be transferred to the liquid droplets, ESI is known to suffer from 'ion suppression' effects where analytes compete for available charge with coeluting components and solvent contaminants. This latter effect is exacerbated at higher flow rates [9]. Extensions of basic ESI theory, such as reducing the liquid to extremely low flow rates - for example to 30 nL/min in the case of nanoelectrospray - have proved effective, especially in sample-limited studies of proteins and amino acids [10].

Atmospheric Pressure Chemical Ionisation (APCI)

Horning first introduced APCI in 1973 to analyse volatile compounds using various introduction techniques, one of which was HPLC [11]. Figure 2 shows a simple schematic of the ionisation process in atmospheric pressure chemical ionisation (APCI). In contrast to ESI, APCI does not have a voltage applied to the capillary tip through which the analyte solution passes, instead it uses a corona discharge to initiate ionisation in the gas phase. High energy electrons from the corona discharge cause a cascade of ion/molecule reactions that can ultimately generate positive ions related to the analyte [12]. Figure 3 illustrates the series of reactions that can take place involving atmospheric species [13]. Electrons initially ionise atmospheric species –

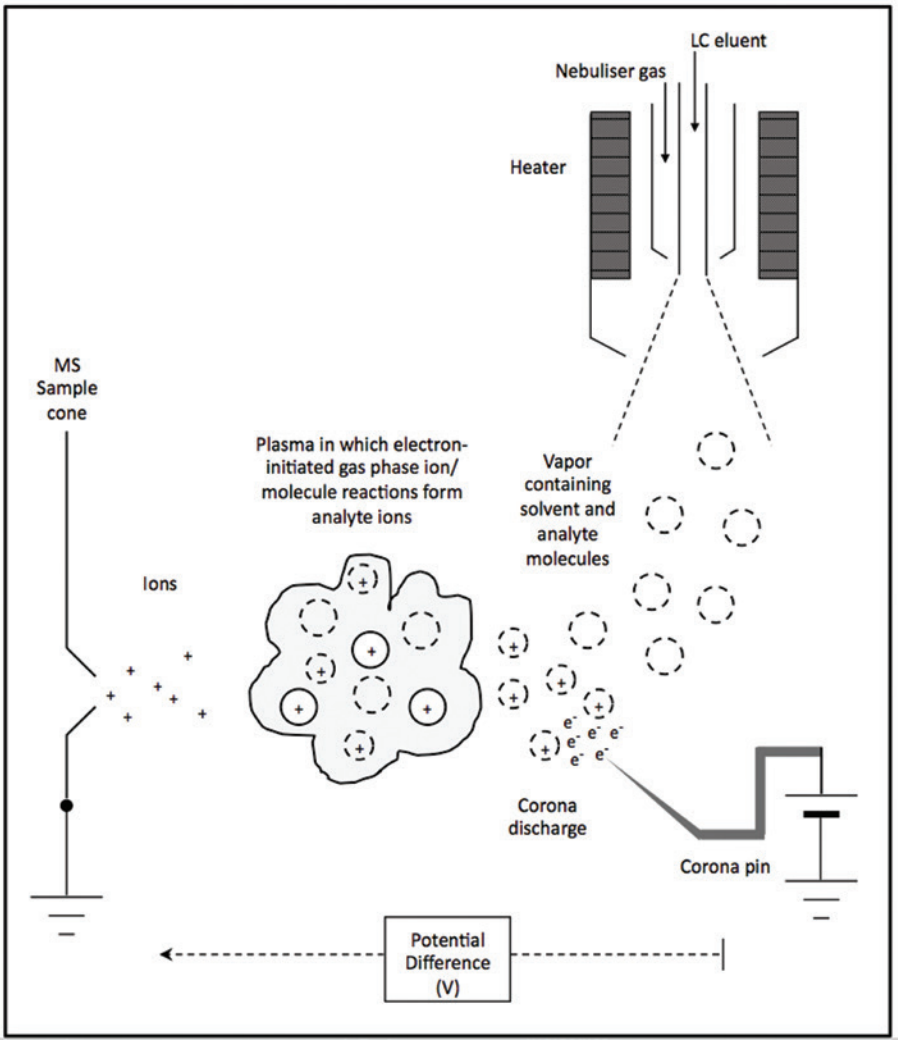


Figure 2: Schematic showing the ionisation process in atmospheric pressure chemical ionisation (APCI).

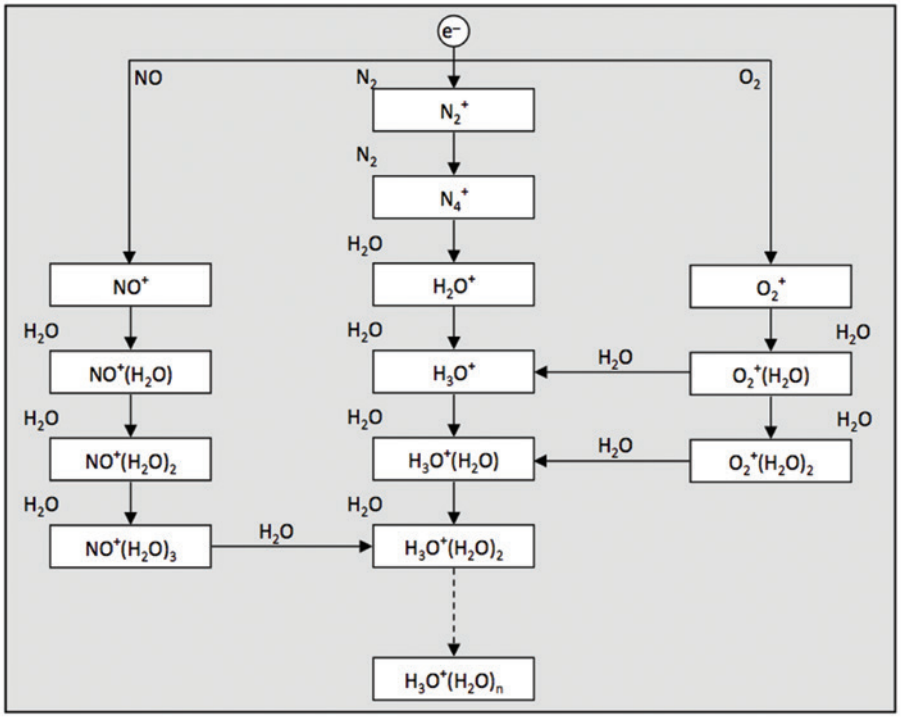


Figure 3: Schematic of reactions involving atmospheric species that can form positive ions in APCI [13].

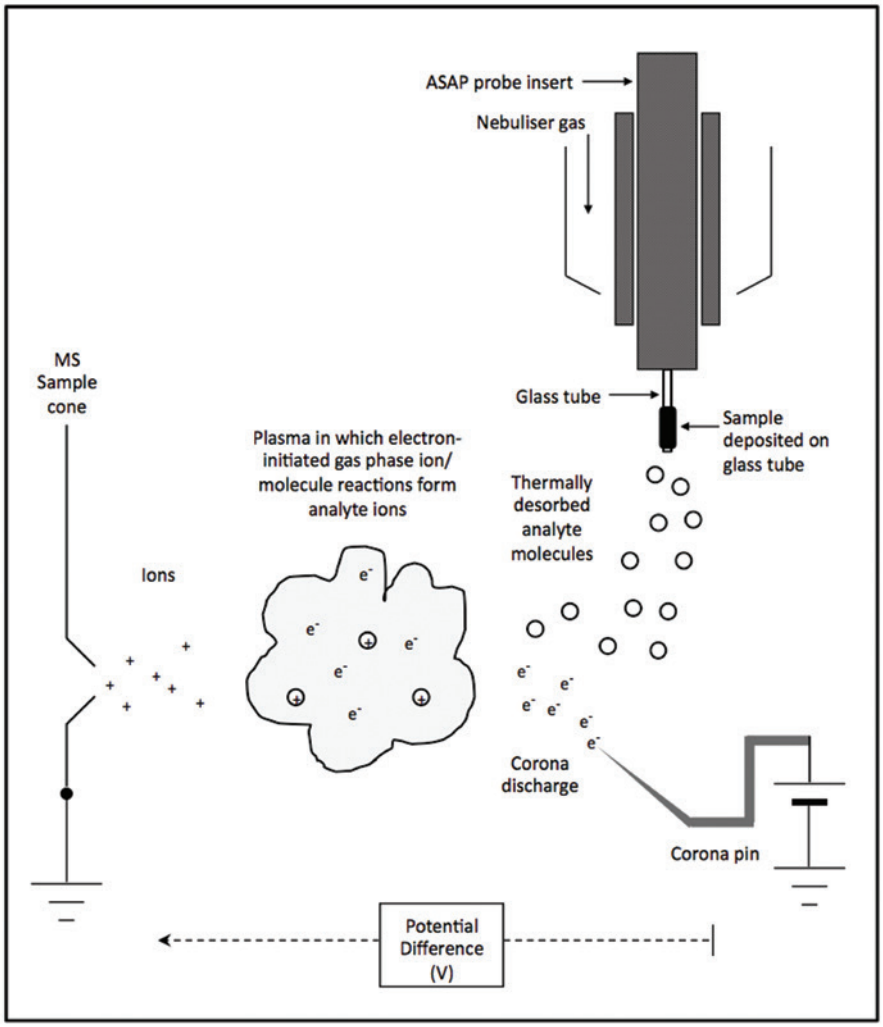


Figure 4: Schematic showing the ionisation process for the atmospheric solids analysis probe (ASAP).

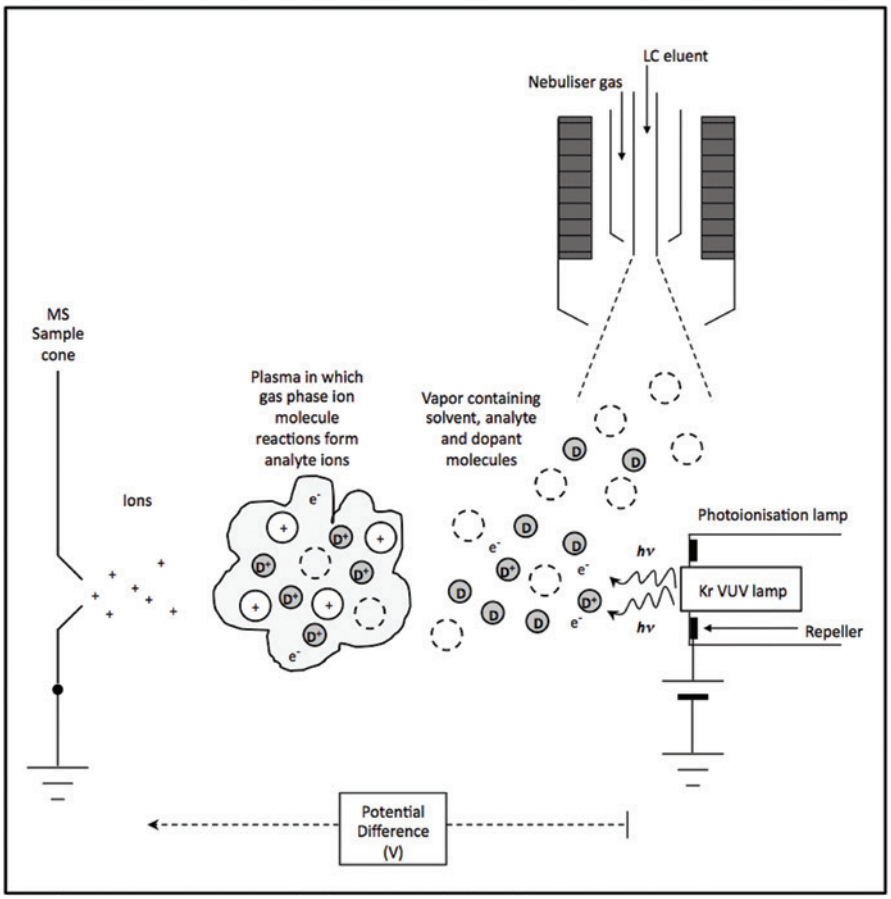


Figure 5. Schematic showing the ionisation process in atmospheric pressure photoionisation (APPI).

primarily nitrogen molecules – by electron bombardment. A sequence of clustering and/or charge transfer reactions take place; finally, the protonated water clusters formed from these reactions can go on to produce positive analyte ions via charge exchange or proton exchange mechanisms. Alternatively, electrons can interact with gas phase molecules that can then go on to react with the analytes, typically via proton abstraction, resulting in the formation of negative ion species of interest.

The strong desolvation capabilities of the heated nebuliser probe allow APCI sources to be utilised at very high flow rates (>2 mL/min). In contrast with ESI, corona discharge ionisation facilitates ionisation of non-polar analytes and is compatible with normal phase mobile phases [9].

Atmospheric Solids Analysis Probe (ASAP)

The Atmospheric Solids Analysis Probe (ASAP) [14] is an ionisation technique that utilises APCI ionisation mechanisms for samples that are introduced into the ion source as solid deposits, solutions, or suspensions on the tip of a small glass tube held by the probe. Heated nebuliser gas desorbs molecules from the tip of the glass tube, as shown in Figure 4.

There is no chromatographic eluent so this approach is, essentially, dry compared with classical APCI. For ASAP, ionisation mechanism theories similar to those for APCI (Figure 3) can be applied, however ASAP does seem to offer a pathway (or pathways) to ionising some species that are not so readily ionised by APCI, for example polyolefins [15]. This is possibly due to the absence of excess solvent in the source atmosphere, resulting in fewer solvent-related cluster species, which is likely to enhance charge exchange mechanisms [16]. ASAP also offers the ability to undertake some degree of thermal degradation or pyrolysis-like experiments because the nebuliser gas can be heated to in excess of 400°C, which could be of interest in particular application areas such as polymer analysis. In addition, the ability to ramp the temperature applied in ASAP analysis enables the acquisition of boiling point profiles and simplification of highly complex samples [17], despite no chromatographic separation, by volatilising components according to their individual boiling points.

Atmospheric Pressure Photoionisation (APPI)

Similar to APCI, APPI is a gas phase ionisation technique in which a series of gas phase ion/molecule reactions initiate ion formation. Unlike APCI, APPI does not use a corona discharge – instead, photons are emitted by a vacuum ultraviolet (VUV) lamp and photoionise gaseous species forming radical cations and electrons. The radical cations and/or the electrons can further react with other gas phase species, such as solvent molecules, to produce analyte ions [18,19]. Figure 5 shows a simple schematic of the ionisation process in atmospheric pressure photoionisation (APPI).

The most commonly used VUV lamp is a krypton lamp, which emits photons with approximately 10 eV energy. Any species within the atmosphere of the source can absorb the photons. If the species has an ionisation energy (IE) (sometimes called ionisation potential (IP)) below 10 eV it can be ionised and form radical cations and electrons. It is possible for analytes of interest to absorb photons and be photonionised directly, provided their IE is below 10 eV; however, with many samples this is statistically unlikely as the analytes are at very low concentration compared with matrix and other background species. To overcome the potential limitations of relying on direct photoionisation, it is typical to add an additional solvent, known as a dopant, that has an IE below 10 eV. Examples of solvents that can be used as dopants, along with their IE and Proton Affinity (PA) values, are shown in Table 1. The dopant is easily photoionised and the resulting dopant radical cations initiate gas phase ion/molecule reactions that subsequently form analyte positive ions.

The dopant undergoes direct photoionisation, as described in the following scheme:

$$D + h\nu \rightarrow D^* \rightarrow D^{+\cdot} + e^-$$

(where D = dopant molecule and hν is the energy of the photon).

Table 2 shows key reactions that are believed to be involved in positive ion formation in APPI. Both the IE and the PA of all species present in the ion source atmosphere can influence the ionisation mechanisms. In positive ion mode, APPI can form a variety of different ions, including $[M - H]^+$ and $[M - H_2]^+$ [21], and $[M + H]^+$ and $M^{+\cdot}$ via reactions shown in Table 2, depending on the relative gas phase acidity or basicity of species present in the ionisation source.

Table 1: Gas phase ion energetics data for some typical dopant molecules.

Dopant	IE (eV) [20]	PA* (kJ.mol^{-1}) [20]
Acetone	9.70	812
Tetrahydrofuran (THF)	9.40	822
Benzene	9.24	750
Chlorobenzene	9.07	753
Bromobenzene	9.00	754
Toluene	8.83	784
Anisole	8.20	840

**PA: Proton Affinity*

UniSpray (US)

A novel UniSpray® (US) ionisation source has been developed that uses a unique approach to generating ions for mass spectral analysis (Figure 6) [22,23]. This atmospheric pressure ionisation source comprises a grounded capillary from which analyte solution elutes that is nebulised by high velocity nitrogen gas. The eluent spray impacts on a cylindrical, stainless steel target rod held at high voltage, typically ~0.5 - 4.0 kV, offering the potential to ionise analytes with greater efficiency. The impact point is optimised to be offset from the centre of the rod and upstream of the mass spectrometer inlet, which causes the flow of the eluent spray to bend around the profile of the rod due to the Coandă effect. The aerodynamic flow associated with the UniSpray cross-flow geometry produces a number of other important effects such as droplet impacts, surface microvortices, and shedding vortices that are believed to influence source performance [22].

The spectra generated when using UniSpray closely resemble those from ESI analyses so, although there is no voltage applied to the capillary tip, it is likely that the eluent contains ions formed from solution phase redox reactions and other physical processes. It is also possible that surface-based effects on the impactor pin, and additional gas phase phenomena, could further contribute to ion formation. An increase in response has been observed for UniSpray compared with other atmospheric pressure ionisation techniques [23]. It is well established that droplet size plays an important role in ion production yield

Table 2: Key reactions for positive ion formation in APPI.

Reaction Equations†	Requirements	Type of Reaction
$D^{+\cdot} + M \rightarrow D + M^{+\cdot}$	if IE (M) < IE (D)	Charge exchange
$D^{+\cdot} + S \rightarrow [D - H]^{\cdot} + [S + H]^+$	if PA (S) > PA ([D – H]·)	Proton exchange
$[S + H]^+ + M \rightarrow S + [M + H]^+$	if PA (M) > PA (S)	Proton exchange
$D^{+\cdot} + M \rightarrow [D - H]^{\cdot} + [M + H]^+$	if PA (M) > PA ([D – H]·)	Proton exchange
$M + h\nu \rightarrow M^* \rightarrow M^{+\cdot} + e^-$	if IE (M) < ~10 eV	Direct photoionisation

† D = dopant molecules, M = analyte molecules, S = solvent molecules or solvent clusters.

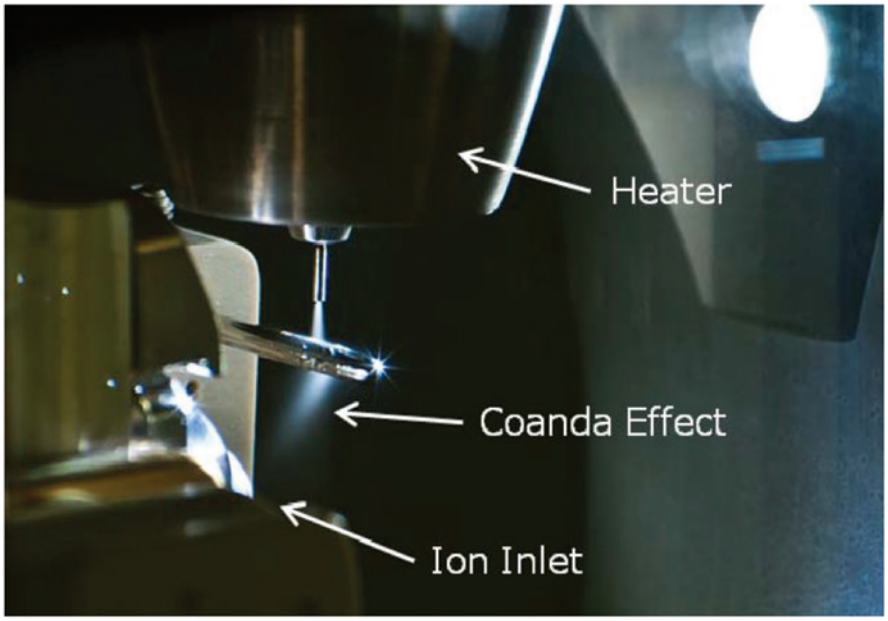


Figure 6: Internal view of the UniSpray ionisation source.

[24,25]. Therefore, it seems that a significant portion of this observed increase can be attributed to the formation of much smaller droplets when the eluent spray interacts with the impactor pin, followed by rapid ion desolvation from these smaller droplets.

Methods and Example Data [4]

The performance of each source was investigated using a simple technique that did not involve any chromatography. For ESI, APCI, APPI, and UniSpray, solutions of standards, which covered a broad range of small molecules, were combined with suitable representative LC mobile phase via the on-board instrument fluidics. In the case of ASAP, the glass capillary tube was dipped directly into the solutions. Examples of representative compounds from each standard mix can be seen in Table 4.

Methods

- Solvent standard solutions were prepared at suitable analytical concentrations using appropriate solvents: ~0.1 - 1.0 µg/mL for the small molecules mixes, ~0.1% for the engine oils, and ~1 mg/mL crude oil samples.
- UniSpray responses were evaluated at three different impactor pin voltages: 0.5 kV, 1.0 kV, and 3.0 kV.
- APCI responses were evaluated at four different corona currents: 1 µA, 5 µA, 10 µA, and 12 µA.
- ASAP responses were evaluated at two different corona currents: 1 µA, and 12 µA.
- High resolution mass spectral data, with ion mobility, were acquired using a SYNAPT G2-S*i* HDMS instrument and reviewed in MassLynx v.4.1 MS software.

HDMS conditions:

- Cone voltage: 50 V
- Source temp: 120°C
- IMS Wave velocity: 1000 m/s (fixed)
- IMS Wave height: 40 V
- IMS cell pressure: 3.3 mbar
- All data were acquired by combining sample solutions with representative mobile phases-either 1:1 MeOH:H_2O, 100% MeOH, or 1:1 MeOH:Toluene—depending on the ionisation technique under consideration or the classes of compounds being analysed.
- A separate evaluation was also undertaken specifically looking at the response of oilfield additives analysed by ESI and UniSpray.
- A C12 quaternary ammonium salt and a 12OH amine compound were separated using an ultra-high performance supercritical fluid chromatography (UHPSFC) system coupled to a tandem quadrupole MS.

UHPSFC conditions [26]:

- Solvent A: supercritical CO_2
- Solvent B: MeOH + 2% H_2O + 50 mM ammonium acetate
- Column: ACQUITY HSS C18 SB, 1.8 µm, 3.0 x 100 mm
- Temperature: 40°C
- Pressure: 150 bar
- Injection volume: 2 µL
- Gradient table (Table 3):

Table 3: UHPSFC gradient table.

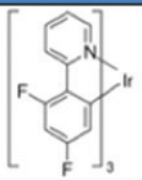
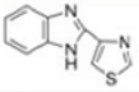
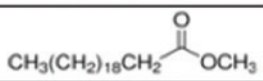
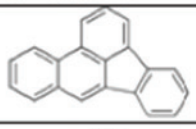
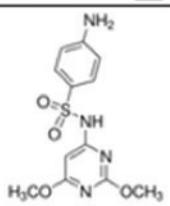
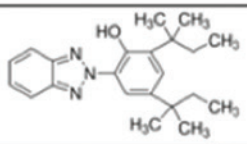
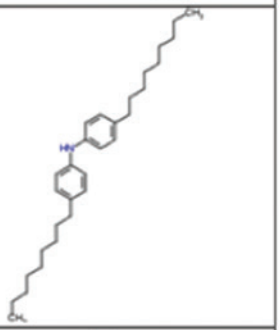
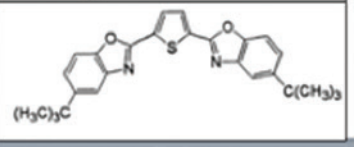
Time (min)	Flow rate (mL/min)	%A	%B
0	1.50	100	0
2.0	1.50	60	40
2.3	1.50	60	40
4.0	1.50	100	0

Results and Discussion [4,26]

Table 5 shows a summary of the responses from each ion source for the representative compounds shown in Table 4. The yellow highlighted values indicate the largest response for each compound and hence the best ion source for those types of compounds. An X indicates that there was no reliable detected response for the given compound with that ionisation technique. All representative compounds formed protonated species, but the PAH compounds also formed radical cations ($M^{+\cdot}$) and the sulfadimethoxine that was chosen as representative of the cosmetics and allergens mix 1 also formed a sodiated molecule.

Table 6 shows data focussing on the small compound mix of polymer additives. Responses for all components of this mix are shown for the four liquid flow ion sources under investigation. In each case, the most intense ion observed is given, with the colour of the text indicating the type of ion: black = protonated molecule, blue = sodiated

Table 4: Example representative compounds for each small molecule mix. Also analysed was a Safaniya vacuum residue petroleum sample (not illustrated in table).

Type of Samples	Example Compound	Molecular Formula	Relative Monoisotopic Mass	Structure
OLEDs	Ir(Fppy)3	$C_{33}H_{18}F_6IrN_3$	761.1011	
Pesticides	Thiabendazole	$C_{10}H_7N_3S$	201.0361	
FAMEs	Methyl heneicosanoate	$C_{22}H_{44}O_2$	340.3341	
PAHs	Benzo[*b*]fluoranthene	$C_{20}H_{12}$	252.0939	
Cosmetics & Allergens (mix 1)	Sulfadimethoxine	$C_{12}H_{14}N_4O_4S$	310.0736	
Cosmetics & Allergens (mix 2)	UV 328 (Tinuvin 328)	$C_{22}H_{29}N_3O$	351.2311	
Engine Oil	Oil additive (4-Nonyl-N-(4-nonylphenyl)aniline)	$C_{30}H_{47}N$	421.3709	
Polymer Additives	Uvitex OB	$C_{26}H_{26}N_2O_2S$	430.1715	

molecule, red = hydride ion abstraction, and brown = radical cation. The highlighted yellow values indicate the largest response for each compound and hence the best ion source for that particular compound.

It was also noted that the optimal impactor pin voltage depended upon the type of adduct being formed. Protonated species gave a better response with a higher applied voltage (e.g. 3.0 kV), whereas sodiated species gave a better response with a lower applied voltage (e.g. 0.5 kV). This phenomenon is illustrated further in Figure 7. Axes linked spectra for two of the polymer additives, Uvitex OB and Irganox 245, are shown. Uvitex OB favours ion formation via protonation and Irganox 245 favours ion formation via sodiation. The differing responses for different applied impactor pin voltages can clearly be seen.

To illustrate the performances of the different ionisation sources with different classes of compounds, axes linked spectra were generated. Figure 8 shows a zoomed region of the mass spectra acquired from analysis of an organic light emitting diode (OLED) mix of compounds. The illustrative compound of interest forms an isotopic cluster of ions around *m/z* 762. UniSpray showed the most intense absolute response with APCI and ASAP producing almost similarly intense responses.

Figure 9 shows a similar zoomed region of the mass spectra acquired from analysis of a polycyclic aromatic hydrocarbon (PAH) mix of compounds. The illustrative compound of interest forms an isotopic cluster of ions around *m/z* 252 since these compounds typically form radical cations. Interestingly, ESI is able to ionise the compound whereas UniSpray shows little to no response. APPI produced the most intense response with APCI showing a similar ion pattern but less intense and ASAP showing little to no response.

Table 5: Summary of responses for representative compounds from each standard mix, the yellow highlighted values indicate the best responses and hence the best ionisation technique for each compound.

	ESI+		APCI+		APPI+		US+		ASAP+	
Samples	Max. response (Peak height)	Max. response (Peak area)	Max. response (Peak height)	Max. response (Peak area)	Max. response (Peak height)	Max. response (Peak area)	Max. response (Peak height)	Max. response (Peak area)	Max. response (Peak height)	Max. response (Peak area)
OLEDs *m/z* 764 $[M+H]^+$	2.87e5	23441	4.45e5	41548	2.07e5	16969	7.35e5	63698	2.94e5	40198
Pesticides *m/z* 202 $[M+H]^+$	3.78e6	375125	3.55e5	37737	2.62e5	26865	1.52e7	1552255	5.45e6	578515
FAMEs *m/z* 341 $[M+H]^+$	7.16e4	5134	1.59e5	16185	X	X	X	X	2.89e5	28585
PAHs *m/z* 253 $[M+H]^+$ (*m/z* 252) $(M^{+\cdot})$	X (1.48e6)	X (147131)	1.78e6 (7.95e5)	188870 (72772)	3.02e6 (2.34e6)	254391 (206398)	X *(8.06e3)*	X *(670)*	1.20e5 (8.25e4)	11946 (6864)
Aller. mix 1 *m/z* 311 $[M+H]^+$ (*m/z* 333) $([M+Na]^+)$	1.36e7 (4.66e6)	1433816 (491988)	2.04e6 (2.72e4)	199304 (1879)	Error during acquisition	Error during acquisition	1.41e7 (4.75e6)	1497566 (497550)	7.65e3	670
Aller. mix 2 *m/z* 352 $[M+H]^+$	4.10e6	799211	3.46e6	604629	2.13e6	207647	4.48e6	835396	1.33e6	127819
Eng. Oil *m/z* 422 $[M+H]^+$	7.83e6	812933	1.98e7	2025327	2.40e7	2547684	6.32e7	6706421	Not acquired	Not acquired
Pol. adds. *m/z* 430 $[M+H]^+$	1.58e6	156425	1.46e5	15318	2.10e5	21215	2.54e6	262162	Not acquired	Not acquired

Table 6: Summary of responses for the polymer additives mix comparing the responses of the four liquid flow ion sources. The yellow highlighted values indicate the best responses and hence the best ionisation technique for each compound.

			APCI+		APPI+		ESI+		US+	
Name	Formula	Relative Monoisotopic Mass (neutral)	Ion Observed	Ion Intensity (µA on pin)	Ion Observed	Ion Intensity	Ion Observed	Ion Intensity	Ion Observed	Ion Intensity (kV on pin)
Diethyl phthalate	$C_{12}H_{14}O_4$	222.0892	X	X	X	X	$[M+Na]^+$	2.91e5	$[M+Na]^+$	1.49e6 (0.5 kV)
Tinuvin P	$C_{13}H_{11}N_3O$	225.0902	$[M+H]^+$	1.92e6 (1 µA)	$[M+H]^+$	1.35e6	$[M+H]^+$	1.41e6	$[M+H]^+$	2.01e6 (3.0 kV)
Dibutyl sebacate	$C_{18}H_{34}O_4$	314.2457	X	X	X	X	$[M+Na]^+$	1.10e6	$[M+Na]^+$	5.72e6 (0.5 kV)
Diphenyl phthalate	$C_{20}H_{14}O_4$	318.0892	X	X	X	X	$[M+Na]^+$	4.24e5	$[M+Na]^+$	3.17e6 (0.5kV)
2-hydroxy-4-octyloxy benzophenone	$C_{21}H_{26}O_3$	326.1882	$[M+H]^+$	1.47e5 (1 µA)	$[M+H]^+$	2.06e5	$[M+H]^+$	3.45e5	$[M+H]^+$	4.47e5 (3.0kV)
Tinuvin 327	$C_{20}H_{24}ClN_3O$	357.1608	$[M+H]^+$	1.07e6 (1 µA)	$[M+H]^+$	1.25e6	$[M+H]^+$	1.03e6	$[M+H]^+$	8.62e5 (3.0 kV)
TCP	$C_{21}H_{21}O_4P$	368.1177	$[M+H]^+$	2.04e5 (1 µA)	$[M+H]^+$	2.80e5	$[M+H]^+$	1.29e6	$[M+Na]^+$	6.23e6 (0.5 kV)
Uvitex OB	$C_{26}H_{26}N_2O_2S$	430.1715	$[M+H]^+$	1.46e5 (1 µA)	$[M+H]^+$	2.10e5	$[M+H]^+$	1.58e6	$[M+H]^+$	2.54e6 (3.0 kV)
Cyasorb 2908	$C_{31}H_{54}O_3$	474.4073	$[M+H]^+$	4.79e4 (1 µA)	$[M+H]^+$	4.74e4	$[M+H]^+$	1.15e5	$[M+Na]^+$	1.45e5 (0.5 kV)
Irganox 1076	$C_{35}H_{62}O_3$	530.4699	$[M-H]^+$	5.80e3 (1 µA)	$M^{+\cdot}$	6.32e4	$[M+Na]^+$	5.86e5	$[M+Na]^+$	1.94e6 (0.5 kV)
Irganox 245	$C_{34}H_{50}O_8$	586.3506	$[M+Na]^+$	1.21e4 (1 µA)	$[M+H]^+$	1.43e4	$[M+Na]^+$	1.46e6	$[M+Na]^+$	9.98e6 (0.5 kV)
Irganox 1098	$C_{40}H_{64}N_2O_4$	636.4866	$[M+H]^+$	3.24e4 (1 µA)	$[M+H]^+$	5.18e4	$[M+Na]^+$	5.93e5	$[M+Na]^+$	4.36e6 (0.5 kV)
Tinuvin 360	$C_{41}H_{50}N_6O_2$	658.3995	$[M+H]^+$	2.02e5 (1 µA)	$[M+H]^+$	2.13e5	$[M+H]^+$	4.91e5	$[M+H]^+$	3.50e5 (3.0 kV)
Ethanox 330 (Irganox 1330)	$C_{54}H_{78}O_3$	774.5951	$[M-H]^+$	9.04e3 (1 µA)	$M^{+\cdot}$	1.97e4	$[M+Na]^+$	4.47e4	$[M+Na]^+$	8.23e4 (0.5kV)
Uvinul 3030	$C_{69}H_{48}N_4O_8$	1060.3472	X	X	X	X	$[M+Na]^+$	6.72e3	$[M+Na]^+$	1.01e4 (0.5 kV)
Irganox 1010	$C_{73}H_{108}O_{12}$	1176.7841	X	X	X	X	$[M+Na]^+$	8.81e3	X	X

The Safaniya vacuum residue petroleum sample was analysed using direct infusion. Figure 10 illustrates the full spectra acquired with each ionisation source. Here we can see the value of having different ionisation techniques available to ensure comprehensive coverage of such a complex sample.

The focused comparison of UniSpray with ESI for the analysis of oilfield additive chemicals revealed a very large improvement in response when using UniSpray compared with ESI. Figure 11 shows the calibration curves for a 12OH amine additive and Figure 12 shows the calibration curve for a C12 quaternary ammonium salt.

Both compounds were analysed over the concentration range 10 ppt to 2 ppm. In the case of the 12OH amine, UniSpray offered up to a 17-fold increase in response and for the C12 quaternary ammonium salt up to a six-fold increase in response was observed.

Key structural features of any analyte can indicate which ionisation technique might be suitable for that analyte. Some of these structural features are summarised in Table 7.

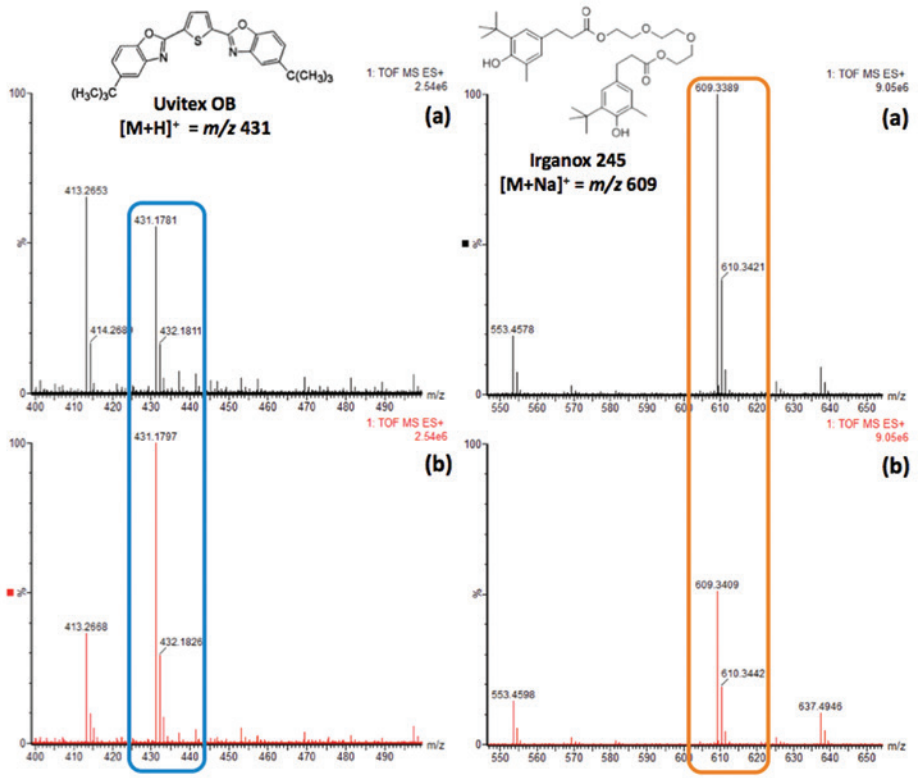


Figure 7: Positive ion UniSpray ionisation mass spectra for protonated Uvitex OB and sodiated Irganox 245. Upper spectra labelled (a) have 0.5 kV applied to the impactor pin lower spectra labelled (b) have 3.0 kV applied to the impactor pin.

Source Optimisation and Use Guidance [4]

- **ASAP**
  - o Acquire using corona current rather than corona voltage.
  - o Evaluate several different corona currents including higher values, for example 10 µA.
  - o For a rapid, triage-like sample analysis, a 30-second ballistic temperature ramp can be used to volatilise the sample and evaluate what ions can be seen.
  - o For separation according to the boiling point profile of the sample, a slower temperature ramp can be used.
- **APPI**
  - o In most cases a dopant will enhance the ionisation process.
  - o Start by trying toluene as a dopant, this will typically work well. If required, try other dopants according to their IE and the IE of your analyte or analytes.
  - o For exact mass data acquisitions, the dopant can be prepared 1:1 dopant:MeOH with leucine enkephalin dissolved in the MeOH so that a lock mass ion will be acquired in Function 1. The leucine enkephalin ion can be used for internal mass correction.
  - o Use a low to medium repeller voltage, e.g. 0.5 kV.
  - o Ensure that the lamp is pushed all the way into the source housing (position 2 on the source housing).
  - o APPI shows a better response with lower flow rates.
  - o The dopant flow rate should, ideally, be in the range 10 to 50% of the eluent flow rate.

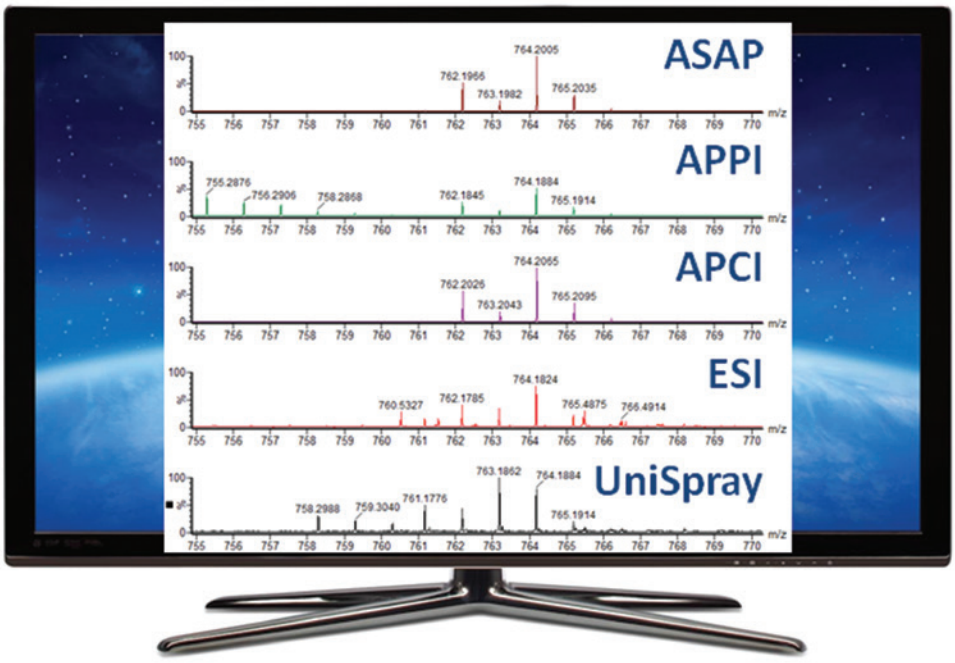


Figure 8: Zoomed regions of spectra acquired for the OLED compound mix using each different ionisation source.

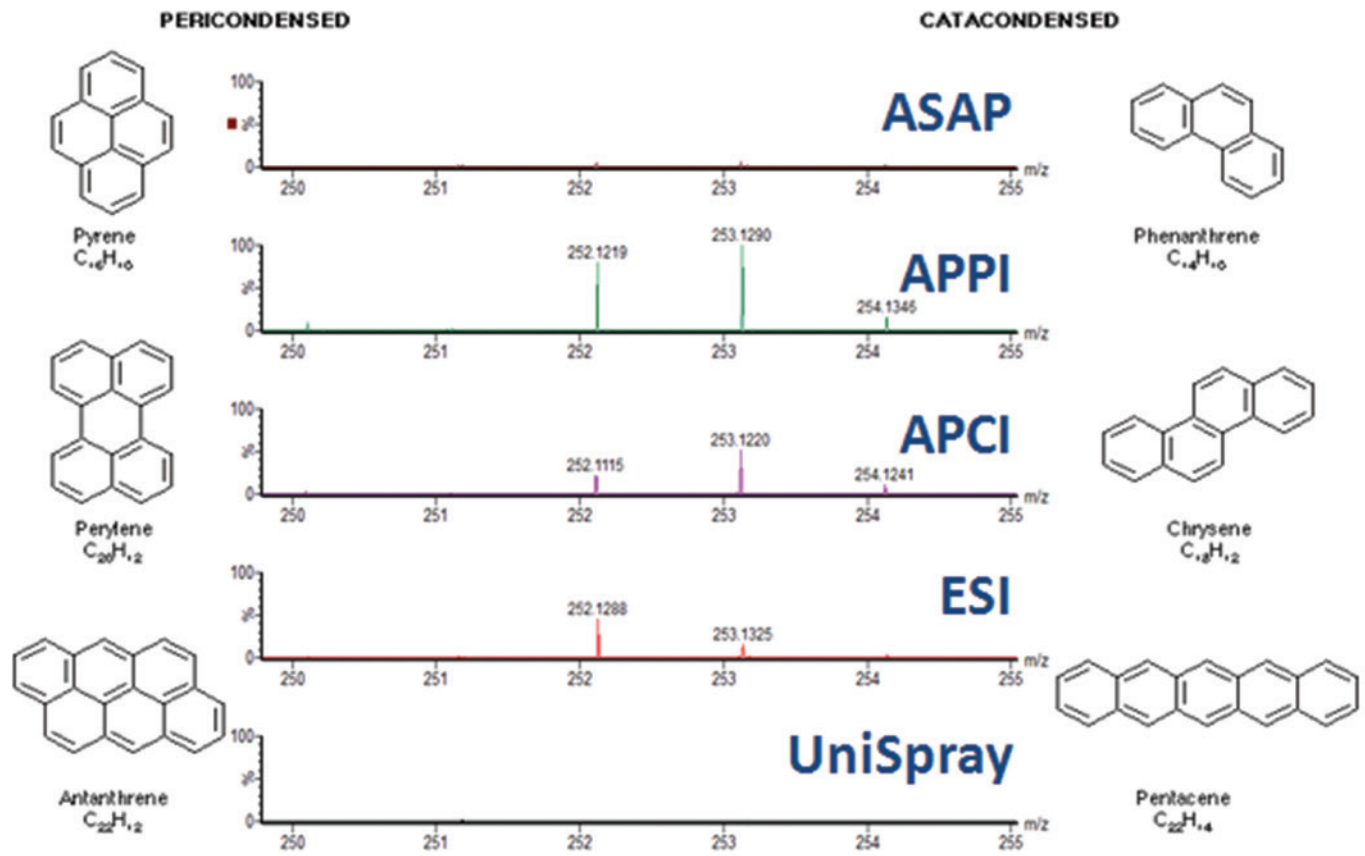


Figure 9: Zoomed regions of positive ion API mass spectra acquired for the PAH compound mix using each different ionisation source.

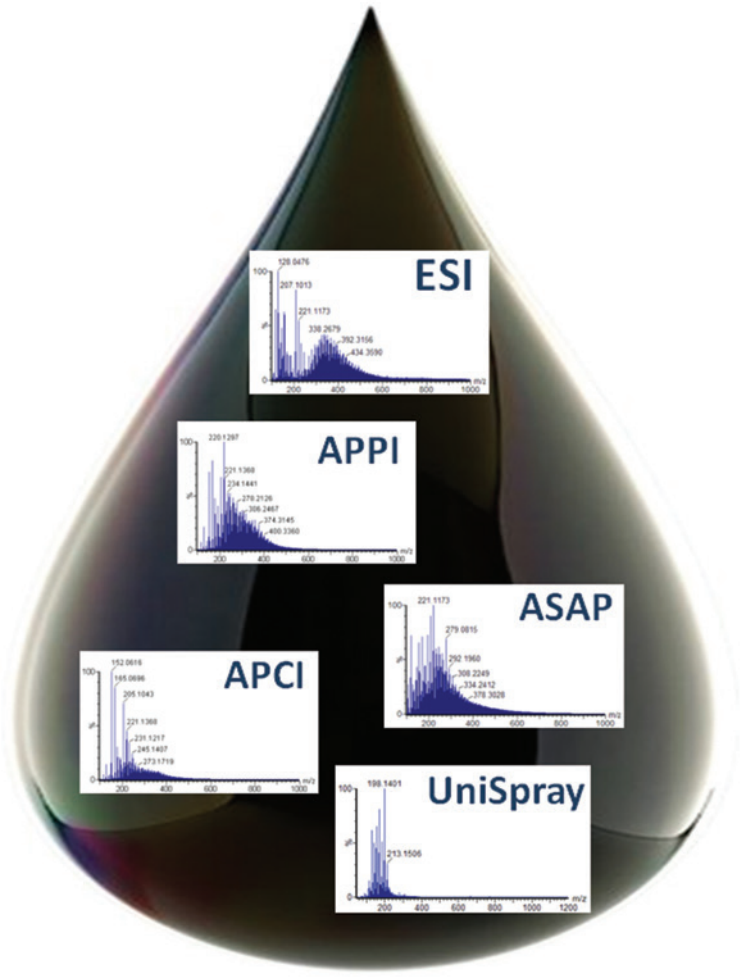


Figure 10: Full spectra acquired for the Safaniya vacuum residue sample using each different ionisation source.

- **APCI**
  - o Acquire using corona current rather than corona voltage.
  - o Evaluate several different corona currents including higher values, for example 10 µA.
  - o In general, for less complex samples, values up to 5 µA should be sufficient.
  - o The amount of water in the source may affect the ionisation efficiency since water clusters play a role in the ionisation mechanism for APCI.

- **UniSpray**
  - o Try several different impactor pin voltages to optimise for the compounds of interest.
  - o Always check for sodium adducts since these are formed very readily for many of the compounds investigated in this work.
  - o Optimising the position of the spray onto the surface of the impactor pin is very important. Ensure it is slightly off centre from the MS inlet to utilise the Coandă effect.

Conclusions

ESI is likely to be the first choice for most day-to-day analyses and, where it is

available, UniSpray should also be evaluated as an early option. If chromatographic separation is not required then ASAP would be the recommended technique of choice since it offers very broad coverage of compound classes and can be evaluated in a matter of minutes to ascertain its applicability for the analysis. Overall, for a problem-solving laboratory, having a wide range of ion sources available would be beneficial to enable the ionisation of the broadest range of different molecules. Once an appropriate ion source for a particular analysis has been identified the selected technique can be routinely implemented; however, if new ionisation techniques are developed, such as UniSpray, these might offered improved responses for established analyses.

- UniSpray has been demonstrated to have broad applicability across several classes of compounds but it is not necessarily the best ionisation source for all molecules.
- UniSpray is a valuable additional component in the 'tool box' available to mass spectrometrists to address sample diversity.
- Other complementary ionisation techniques, such as APCI and APPI, are also required to ensure the maximum coverage of the most challenging samples.
- UniSpray was observed to have differing impactor pin optimised voltages depending on the adduct formed by the analyte of interest (sodiation versus protonation).
- UniSpray showed a significant improvement in response compared with ESI for the analysis of selected oilfield chemicals.
- Structural and functional characteristics of a molecule can influence the choice of the most suitable ionisation technique.

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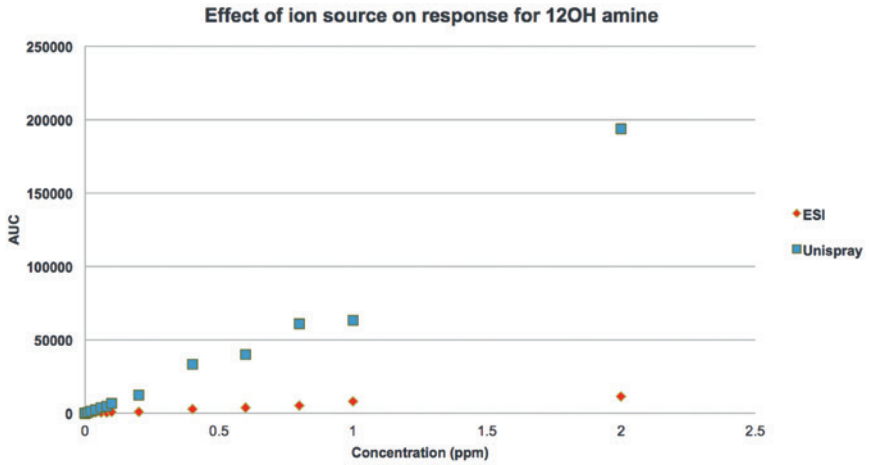

Figure 11: Calibration curves for a 12OH amine compound analysed by ESI (red diamonds) and UniSpray (blue squares).

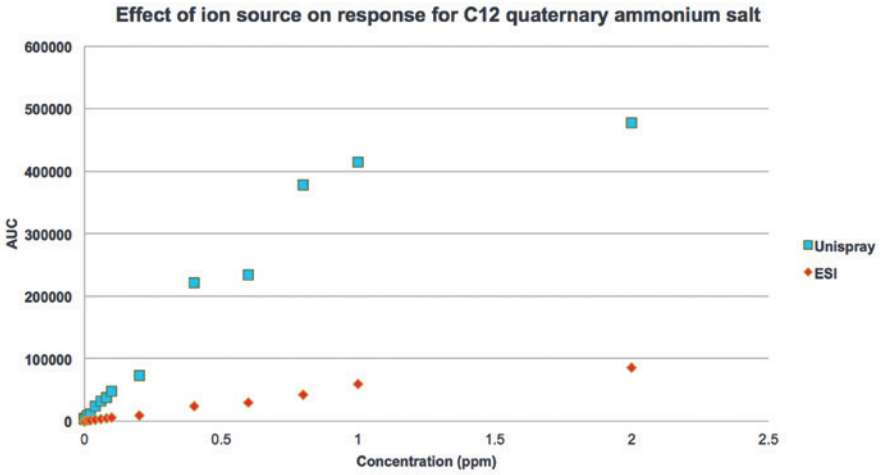

Figure 12: Calibration curves for a C12 quaternary ammonium salt compound analysed by ESI (red diamonds) and UniSpray (blue squares).

Table 7: Summary of some key structural features that make a molecule amenable to ionisation by a particular ionisation source.

Ion Source	Appropriate Structural Characteristics	Example Compounds/Classes
UniSpray or ESI	Polar molecules, *e.g.* containing oxygen or nitrogen atoms, hydroxyl groups, amine groups, carboxyl groups, *etc.* that can form ions in solution	Pesticides, *e.g.* tebuconazole, thiabendazole Veterinary drugs, *e.g.* flubendazole, oxolinic acid
APCI or ASAP	Non-polar species particularly with non-aromatic ring structures	Steroids, *e.g.* 17α-hydroxyprogesterone Biocide compounds, *e.g.* tributyltin chloride Phytosterols, *e.g.* campesterol
APPI or ASAP	Non-polar aromatic species or species with regions of delocalised electron density. Species with chromophores	PAHs, *e.g.* pyrene, anthracene Vitamin B12 UV stabilizers, *e.g.* Tinuvin compounds
ASAP	Some saturated species	Low molecular weight poly(ethylene) FAMEs, *e.g.* methyl heneicosanoate

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