Ion mobility spectrometry detection for gas chromatography

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Abstract

The hyphenated analytical method in which ion mobility spectrometry (IMS) is coupled to gas chromatography (GC) provides a versatile alternative for the sensitive and selective detection of compounds after chromatographic separation. Providing compound selectivity by measuring unique gas phase mobilities of characteristic analyte ions, the separation and detection process of gas chromatography–ion mobility spectrometry (GC–IMS) can be divided into five individual steps: sample introduction, compound separation, ion generation, ion separation and ion detection. The significant advantage of a GC–IMS detection is that the resulting interface can be tuned to monitor drift times/ion mobilities (as a mass spectrometer (MS) can be tuned to monitor ion masses) of interest, thereby tailoring response characteristics to fit the need of a given separation problem. Because IMS separates ions based on mobilities rather than mass, selective detection among compounds of the same mass but different structures are possible. The most successful application of GC–IMS to date has been in the international space station. With the introduction of two-dimensional gas chromatography (2D-GC), and a second type of mobility detector, namely differential mobility spectrometry (DMS), GC prior to mobility measurements can now produce four-dimensional analytical information. Complex mixtures in difficult matrices can now be analyzed. This review article is intended to provide an overview of the GC–IMS/DMS technique, recent developments, significant applications, and future directions of the technique.

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Keywords: Ion mobility spectrometry; Differential mobility spectrometry; Gas chromatography; Detectors; Separation and detection techniques; Sampling techniques

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1. Introduction

1.1. Fundamental principles of GC–IMS

There are basically two types of ion mobility spectrometers which have been interfaced to gas chromatography for detecting analytes. The first type of mobility detector is IMS, and several excellent reviews have discussed the fundamental principles behind ion mobility measurements [1–6]. After separation by gas chromatography, individual components are introduced into the ionization region of an ion mobility spectrometer where they are converted to gas phase ions. These ions are then exposed to a weak homogenous electric field, and travel down a drift tube according to their mobility through a counter flowing drift gas. If mixtures of compounds are introduced into the IMS, then a mixture of gas phase ions is created. These ions can be separated according to their differences in mobilities through the counter flowing drift gas. This separation forms the basis of the analytical method known as ion mobility spectrometry. IMS is a highly efficient separation technique in that the ion separation is carried out within a milliseconds time scale with separation efficiencies as high as 100,000 theoretical plates.

In ion mobility measurements, the time required for an ion to transverse a region filled with inert drift gas and under the influence of a weak homogenous electric field is related to the mobility (\(K\)) of the ion [7]. In the presence of low-field conditions, the mobility of an ion through the drift gas is given by the following equation:

\[
K = v_d E^{-1} \tag{1}
\]

where \(v_d\) is the velocity of the drifting ion and \(E\) is the electric field.

In order to permit comparison of measurements obtained from different environments, ion mobilities are reported as reduced mobility (\(K_0\)) values and can be calculated from the following equation:

\[
K_0 = \left( \frac{L^2}{V t_d} \right) \left( \frac{273.15}{T} \right) \left( \frac{P}{760} \right) ^{0.5} \tag{2}
\]

where \(L\) is the length of the drift region, \(V\) is the voltage applied across the drift region, \(t_d\) is the drift time of the ion, \(T\) is the absolute temperature in K and \(P\) is the pressure in Torr. Ion mobility measurements are highly reproducible and any two measurements from different environments should typically agree to within 2%.

Ion mobility theory reviewed by Revercomb and Mason [2] gave the fundamental relationship between ion mobility and collision cross section at the molecular level as the equation:

\[
\Omega = \left( \frac{3q}{16N} \right) \left( \frac{2\pi}{\mu KT} \right)^{0.5} \left( \frac{1}{K_0} \right) \tag{3}
\]

where \(q\) is the charge on the ion, \(N\) is the number density of the drift gas, \(\mu = \text{reduced mass} = \frac{mM}{m+M}\), \(m\) is the mass of the ion, \(M\) is the mass of the drift gas, and \(\Omega\) is the collision cross-section of the ion in the drift gas, and \(K_0\) is the reduced mobility.

Fig. 1 illustrates the principal components and operation of an IMS detector interfaced to a one-dimensional capillary gas chromatograph. The principal steps of operation in Fig. 1 are as follows. A complex mixture is vaporized by a GC injector and separated into individual components by a capillary column. Individual neutral components of the mixture are then transported into the reaction region of the IMS where they are ionized. The ionization process can lead to protonated monomer and sometimes dimer ions. Ions formed in the reaction region are injected into the drift region. Individual ions then move at a constant velocity towards the IMS detector. The significant advantage of the interface between a GC and an IMS is that when adequate chromatography is obtained only single compounds

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Fig. 1. Schematic cross-section of a capillary GC–IMS. P: pressure regulators; I: injectors; D: detectors; O: oven; G: glass column connector between deactivated capillary column and GC capillary column; DC: deactivated capillary column.
Fig. 2. Schematic diagram showing the effect on ion trajectories through a differential mobility spectrometer produced by rf-induced motion of the ions between two parallel plates during the application of an asymmetric waveform $V(t)$. $\alpha$ represent a coefficient of expansion of the ions generated. The spectrum attached to the schematic was reprinted from R. Guevremont, High-field asymmetric waveform ion mobility spectrometry: a new tool for mass spectrometry, J. Chromatogr. A 1058 (2004) 3–19. Copyright (2004) with permission from Elsevier.

enter the reaction region of the IMS at a time, such that charge competition problems with IMS may be eliminated.

When the instrument operating conditions are held constant, ion mobility depends only on the charge, reduced mass, and collision cross-section ($\Omega$). Mobility and therefore separation is controlled by the reduced mass ($\mu$) for small atomic ions in a neutral drift gas. For ions much more massive than the drift gas molecules, the reduced mass is nearly equal to the drift gas mass $M$, and $K$ varies only with $q$ and $\Omega$. Ion size, shape, and polarizability determine collision cross-section. For those ions, which fall between these two extremes, e.g. polyatomic ions, separation is a function of both mass and shape [8]. Thus:

$$K_0 \alpha \left( \frac{1}{\mu^{0.5}} \right) \text{ or } \left( \frac{q}{\Omega} \right) \text{ or } \left( \frac{1}{\mu^{0.5} \Omega} \right)$$  (4)

A second type of ion mobility detector used after gas chromatography is known as a differential mobility spectrometer (DMS) [9]. In DMS, identity of ion species are based on the difference in the mobility coefficient of a compound in both high and low strength electric fields. This approach offers a greatly simplified drift tube design over conventional mobility spectrometers. The DMS drift tube does not require ion-shutters, voltage dividers, and aperture grid typical of conventional IMS. Fig. 2 is an illustration of the principle of operation in a planar DMS system. In this schematic, the lower plate is maintained at ground potential while the upper plate has an asymmetric waveform, described by $V(t)$, applied to it. A stream of carrier gas transports these ions longitudinally down the drift tube between a gap (0.5 mm). The asymmetric rf electric field that is applied to the electrodes allowed the ions to oscillate in a perpendicular direction to the carrier gas flow while moving down the drift tube with the carrier gas. Ions with different mobility differentials will be displaced to unique positions in the $y$-direction for a given residence time. All the other parameters including the value of the maximum electric field, the volume of the ion filter region, the duty cycle and the flow rate to a first order approximation, are essentially the same for all ion species.

To avoid displaced ions hitting the lower or upper plate and becoming neutralized it is necessary to apply a low direct current (dc) voltage that will compensate for the rf-induced motions of the ions. When the low dc field ($|E_c| < |E_{\min}| \ll |E_{\max}|$) is applied in addition to the rf-field, in a direction opposite to the average rf-induced ($y$-direction) motion of the ion, the trajectory of a particular ion species can be “straightened”. This allows the ions of a particular species to pass unhindered between the ion filter electrodes. The dc voltage that “tunes” the filter and produces a field, which compensates for the rf-induced motion is characteristic of the ion species and is called the compensation voltage. A complete spectrum for the ions in the gas sample can be obtained by ramping or sweeping the dc compensation voltage applied to the filter. The ion current vs. the value of the sweeping voltage forms the DMS spectra.

1.2. The ionization processes

Although many different methods have been proposed to ionize sample molecules prior to IMS detection, $^{63}$Ni and photo-ionization with a UV-lamp have been the most successful for GC–IMS. Original ion mobility spectrometers used $^{63}$Ni foil to ionized organic sample vapors by ion–molecule reactions in ion plasma generated by the beta emissions from $^{63}$Ni [10–12]. In most cases, $^{63}$Ni, with a total activity of 10–15 MBq beta radiation has been used to produce background ions from nitrogen gas:

$$N_2 + \beta^- \rightarrow N_2^+ + \beta'^- + e^- \quad (60 \text{ keV})$$  (4)

Here, $\beta^-$ is the beta particle emitted from the $^{63}$Ni source and $\beta'^-$ is the beta particle after some of its energy has been used in
ionization of nitrogen molecules. N$_2^+$ ions, although short-lived and therefore do not appear in the mobility spectrum, initiate a series of ion-molecule reactions with trace amounts of H$_2$O, NO, and NH$_3$. The resulting stable secondary ions have previously been identified as (H$_2$O)$_n$H$^+$, (H$_2$O)$_n$NO$^+$, and (H$_2$O)$_n$NH$_3^+$ [10–12] for $n = 1–3$. These background ions are called reactant ions and can undergo further ion–molecule reactions to produce product ions. When O$_2$ is present in the drift gas, negative reactant ions, (H$_2$O)$_n$O$_2^-$ or (H$_2$O)$_m$(CO$_2$)$_n$O$_2^-$ ($n = 1–3$ and $m = 1–2$) are also formed [11]. Negative reactant ions are capable of producing negative product ions by ion-molecule reactions.

An alternate means to achieve atmospheric pressure ionization for GC–IMS has been the use of photo-ionization [13,14]. In this process an ultraviolet light is used as a means of ionizing an analyte exiting a GC column. Compounds like aromatic hydrocarbons or heteroatom containing compounds whose species have ionization potentials within the reach of commercially available UV lamps could be successfully ionized. For example, compounds like benzene which have a low ionization efficiency with $^{63}$Ni radioactive sources were successfully ionized with photo-ionization and analyzed by IMS [14].

2. The GC–IMS concept

IMS as a new dimension for GC was originally known as plasma chromatography (PC), and was first reported in 1970 [12]. It was noted that a GC can be used to introduce individual components of a mixture into an IMS for detection and peak characterization. In addition, it was realized that an IMS could serve as an ion interface between a GC and a mass spectrometer (MS), providing a three-dimensional analytical information. Fig. 3(a) is a photograph of a Model Alpha/II IMS–MS that lead Cohen et al. to propose a schematic block diagram of the first GC–IMS–MS interface (Fig. 3(b)).

3. Transfer lines

An important aspect of the interface created for GC–IMS/DMS is the transfer line. A number of important factors need to be considered when developing a transfer line for an interface between a GC and an IMS/DMS. The most important factors are maintaining the integrity of the resolution, achieving quantitative transfers, and matching flows.

4. Effect of temperature and pressure on IMS/DMS responses

Temperature and pressure plays an important role in ion mobility measurements. Past investigations have shown that the relationship for drift time vs. temperature is non-linear, whereas those for drift time vs. pressure are linear [15,16]. These results were in agreement with the mobility theory. Lower IMS operating temperatures will result in increase moisture in the IMS reaction region. Investigations by Karasek et al. [17] and Tabrizchi et al. [15,16] have shown that the reason for the non-linear behavior of drift time vs. temperature was the result of clustering of neutral molecules to the ions. For higher IMS operating temperatures, however, resulting in less moisture in the reaction region, neutral vapors will detach themselves from the primary ion. The effect of hydration and clustering of ions at low temperatures have also been shown to decrease resolving power of an IMS drift tube [18]. Since temperature of an IMS have been proven to be an important aspect in ion mobility measurements, it is important that methods for accurate temperature recordings are developed. Thus, Thomas et al. in 2002 [19] reported a method that used reduced mobility standards and developed a cell constant to accurately measure the temperature of the drift gas of an IMS cell. It was demonstrated in this work that the temperature normally recorded on the outside of the drift tube wall may not be an accurate reflection of the actual temperature of the drift gas.

With elevated and low temperatures, Eicenam et al. have reported that chemical class information is encoded in mobility spectra as fragments that are unique to functional groups and consistent within a chemical class [20]. This development opens the door for discussions for fragmentation chemistry with IMS. It is worth noting, however, that responses obtained from IMS even when GC is utilized as a separation step are non-linear at high concentrations. The reason for this non-linearity even when...
optimized temperatures are used is attributed to the $^{63}$Ni radioactive ionization mechanism used with IMS systems. Thus, linear dynamic range reported for IMS so far have hardly exceeded the low parts per million ranges.

5. First GC–IMS spectra

The first IMS spectrum after GC separation was obtained in 1972 [21]. The experiment was designed to enable comparison of both a flame ionization detector (FID) and an IMS detector. A Varian Aerograph Model 1400 GC equipped with an FID detector operating with nitrogen carrier gas at 30 ml min$^{-1}$ was employed in the design. The stainless steel column was 6 ft long with an o.d. of 1/8 in., containing 6% load of SE-30 on 80/100 mesh Anachrom ABS. The injection port was operated at 190°C, the oven at 155°C and the FID detector at 205°C. Effluent from the GC column was split so that the amount entering the FID was twice of that entering the IMS region. The IMS was a Beta VII model (Franklin GNO Corporation, West Palm Beach, Florida, 33402) permitting recording of single 20 ms scans. Its reaction chamber and drift tube were operated in the negative ion mode at 3000 V. The inlet temperature was 193°C while the drift gas temperature was 199°C, and carrier and drift gases were both air.

With this configuration an FID response and IMS spectra were recorded and compared from a gas chromatogram of musk ambrette. Fig. 4(a) is an FID response of musk ambrette dissolved in benzene. Fig. 4(b) shows the negative IMS spectra of musk ambrette from the GC effluent. For a 10 ng sample of musk ambrette, a splitter was used to allow 2/3 of 10 ng into the FID (6.7 ng) region and only 1/3 of the 10 ng (3.3 ng) into the IMS. The authors calculated responses for detection limits in Fig. 4(a) and (b) and concluded in their report that IMS should have a lower detection limit when compared to an FID. They further speculated without proof that based on their results, IMS may have a better signal-to-noise ratio than an FID.

6. GC–IMS detection modes

Ion mobility spectrometer is a versatile GC detector with six types of detection modes possible: positive and negative IMS spectra, continuous positive and negative product ion monitoring, continuous electron current monitoring, and continuous positive reactant ion monitoring [22,23]. When operated in the positive ion mode to monitor for positive background reactant ions, IMS can provide GC responses similar to (but in most cases more sensitive) those obtained with an FID [24]. When operated in the negative ion mode using nitrogen as the drift gas, IMS can provide electron current GC responses comparable to those obtained with an electron capture detector (ECD) [24]. In addition, when the mobility of product ions are monitored in both positive and negative ion modes, IMS provides molecular selective detection [25], which is not possible with either an FID or an ECD. With its six modes of operation, IMS can supply a wealth of information about trace components eluted from a GC. Because of its multimode aspect, IMS showed in the early 1970s the potential for development into a consolidated GC detector for the rapid analysis and identification of compounds. Furthermore, IMS detectors can be tuned such that only signals at specific drift times can be monitored, thereby allowing only analyte of interest in the spectrum. This approach opens up the possibility of tunable selective or non-selective responses.

In 1973, Cram et al. coupled a GC to an IMS and successfully analyzed Freon samples in the negative ion mode [26]. A comparison was made between IMS and FID Freon responses. It was reported in this work, that IMS operating with only 0.1% duty cycle showed comparable signal-to-noise ratios to an FID. For a 100% duty cycle of an FID and only 0.1% duty cycle for the IMS, the authors calculate detection limits and concluded that IMS should have a lower detection limit than an FID [21]. Reproduced from the Journal of Chromatographic Science by permission of Preston Publications, A Division of Preston Industries, Inc.
Positive and negative mobility spectra of aromatic mono- and di-carboxylic acids and some of their esters were obtained by Karasek and Kim [27]. GC–IMS was further used in 1976 [28] for the determination of part-per-million levels of sec-butyl chlorodiphenyl oxides in biological tissues. In this investigation, the GC was used to provide separation of matrix components from components of interest thereby reducing the effect of ion–molecule interactions. Comparison of responses obtained from GC–FID, GC–MS and GC–IMS responses showed that the results were in excellent agreement, demonstrating the reliability of GC–IMS for the analysis of sec-butyl chlorodiphenyl oxides.

7. The early problems of GC–IMS

Although a series of articles throughout the 1970s has been published demonstrating the potential of IMS as a GC detector, technical difficulties prevented the routine application of this technology. Firstly, the extreme sensitivity of the method led to complication or elimination of responses, largely due to chromatographic factors such as column bleeding, residual solvents and un-separated components. Contamination from the carrier gas was also a major factor. Secondly, cell volumes of commercial instruments used in the initial investigations were so large that adsorption and diffusion effects caused serious loss of quantitative reproducibility and chromatographic resolution. The development of column technologies reduced interferences from column bleeding but yet still the shortcomings in IMS detector designs rendered IMS impractical for use with high resolution separation techniques. It was apparent that if IMS was to be successfully employed as a reliable detector for GC, it needed to be designed differently to account for the problems encountered with the early GC–IMS systems.

8. Capillary GC–IMS

The modern age for mobility measurement after capillary gas chromatography can be tracked back to the work of Baim and Hill [25]. The ion mobility spectrometer in this work was constructed specifically for interfacing with a capillary gas chromatography (GC) and addressed some of the problems in the earlier GC–IMS systems. Specific modifications were made to the standard design for IMS with the aim of reducing the loss of chromatographic resolution in the detector by reducing the loss of neutral sample species in the ionization region. These modifications included: (a) a unidirectional gas flow, (b) an enclosed drift tube, (c) a reduced ionization cell volume, and (d) an introduction of sample between the ionization region and the first ion gate. The IMS constructed for this project is shown in Fig. 5. In this design, the ionization and drift regions were 4.8 and 7.5 cm, respectively, and an electric field of about 200 V cm$^{-1}$ was maintained down the tube. The entire tube (ionization and drift regions) was operated at 140 °C. Injections of gasoline samples were separated on the capillary column of the GC. Separation from the GC was followed by investigations with non-selective negative peak detection mode, non-selective positive peak detection mode, and several selective mobility monitoring modes in the IMS part. IMS as a tunable selective detector was demonstrated by monitoring responses of xylenes in one mode and substituted naphthalenes in another mode.

IMS was further demonstrated as a selective and non-selective detector for GC in another report by Baim et al. when terpenes from orange extracts were monitored for all product ions having drift times between specific intervals [29]. Fig. 6(a) and (b) are example spectra illustrating the selective nature of IMS to product ions from orange extracts. In Fig. 6(a), the methanol solvent peak from which the orange extracts were prepared was “tuned out” and this exposed several additional small peaks in the chromatogram. In Fig. 6(b) however the instrument was tuned to monitor only product ions with drift times between 9 and 10 ms. Thus, the complex chromatogram in Fig. 6(a) was reduced to one with only a few dominant peaks. This selectivity allowed detection of two terpenes without interference by neighboring peaks.

The IMS constructed for interfacing to a GC was also investigated in the negative ion mode [30]. The detector was tuned to monitor chlorine ion, and five pesticides at 100 pg cm$^{-3}$ were investigated. Example of the selective negative product ion monitoring mode is shown in Fig. 7. Other studies that were carried out with the constructed instrument included the positive ion mode quantification of 2,4-dichlorophenoxyacetic acid (2,4-D) residues in soil extracts [31] (soil samples were collected from Walla Walla in Washington, Tennessee, and Chehalis in Washington), minimum detectable limit investigations [32,33], qualitative and quantitative capabilities of a GC–IMS using direct axial sample introduction [32], and investigating the ability to selectively monitor compounds which respond universally to standard photo-ionization detector by equipping the IMS with a UV photo-ionization ion source [34]. Fig. 8(a) compared responses from FID, ECD and IMS to typical soil samples from a garden in a residential area of Walla Walla in Washington.
Fig. 6. (a) Non-selective product ion mode chromatogram of orange extract in methanol obtained by monitoring all product ions having a drift time between 5.5 and 12.5 ms. Reprinted with permission from Baim et al. [29]. Copyright (1982) ISC Inc. (b) Selective product ion mode chromatogram of orange extracts in methanol obtained by monitoring ions having a drift time between 9 and 10 ms. Peaks 1 and 2 were found to correlate to α-pinene and limonene, respectively. Reprinted with permission from Baim et al. [29]. Copyright (1982) ISC Inc.

Fig. 7. Chloride ion monitoring at $K_0 = 2.92 \text{cm}^2/(\text{V} \cdot \text{s})$. (1) Lindane; (2) heptachlor; (3) aldrin; (4) dieldrin; (5) p,p′-DDT. Sample contained 100 pg cm$^{-3}$ of each pesticide in hexane [30]. Copyright (1983) Wiley–VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

D was derivatized before the analysis and the arrow represents the responses of 2,4-D methyl ester. This data demonstrated that by tuning the IMS detector to selectively monitor 2,4-D methyl ester drift time, other interfering peaks seen in the FID and ECD responses were eliminated. Fig. 8(b) shows a non-selective reactant ion mode and selective product ion mode chromatogram obtained from Tennessee soil samples. Quite recently a technique that utilized a multi-capillary column in combination with IMS equipped with a radioactive and UV ionization sources was developed for the determination of MTBE and BTX in gaseous and aqueous matrices [14], rapid on-site detection of ground and surface water contaminants [35], detection of health relevant analytes from surfaces [36], and detection of volatile organic metabolites in human breath [37]. Fig. 9(a) and (b) shows the IMS topographic plots for a healthy patient and a patient suffering from lung infection. In Fig. 10, the patterns of peaks found exclusively from a patient suffering from pulmonary disease are shown. In most IMS investigations, ions with similar mobilities cannot be separated from each other. This phenomenon was described as cross-sensitivity [38]. Capillary GC has also been investigated to eliminate cross-sensitivity effects in IMS [22,38].

Among signal processing methods developed for IMS spectra acquisition was the Fourier transform (FT) mode in which the ion shutter of a traditional drift tube is operated in an unconventional manner, and the importance of avoiding overload in the detector was realized [39]. Improvements in the sensitivity of IMS systems were achieved with the development of FTIMS. FTIMS uses up to 25% of the ion current instead of just 2% used by traditional pulse-mode ion gate method of IMS [39]. FTIMS have been reported to also eliminate the need for the aperture grid (located in front of the collecting electrode) in IMS, and
Fig. 8. (a) Comparison of FID, ECD and IMS responses to typical soil samples collected at Walla Walla, Washington. Arrow denoted the retention time of 2,4-D methyl ester. The concentration in the original soil of 2,4-D was 235 ppb. Reprinted from Baim and Hill [31]. Copyright (1983) with permission from Elsevier.

(b) Non-selective reactant ion mode and selective product ion mode chromatograms to typical soil samples collected from Tennessee. The peak interfering with quantification of 2,4-D in the non-selective mode is eliminated by selectively monitoring 2,4-D product. Concentration of 2,4-D in the original soil was 469 ppb. Reprinted from Baim and Hill [31]. Copyright (1983) with permission from Elsevier.
serve as a transducer for eliminating mechanical vibrations and electronic noise. In developing a hand-held field GC–IMS system, the presence of an aperture grid may ultimately raise the detection limit due to increase in vibration noise. The IMS constructed specifically for operation with a GC was operated in an FT mode and used for obtaining qualitative and quantitative data of 5,5′-disubstituted barbiturates [40]. In a study in which the effect of electronegative and electropositive contaminants on an ion mobility detector after GC was investigated [41], comparison was made to the conventional electron capture detector (ECD) and flame ionization detector (FID). This study concluded the following: (1) contaminated responses did affect the IMS but no more severely than in the conventional ECD and FID; (2) the IMS exceeded both the ECD and FID in terms of detection limit level and baseline stability; (3) in positive ion mode operation, the IMS detected lower quantities of naphthalene than the FID. Furthermore, when subjected to carbon tetrachloride doping, the IMS detected hexane while an FID could not.

In an attempt to reduce the frequency of false positive responses on commercial IMS instruments commonly used for explosives and drugs detection in the field, a rapid pre-separation technique by making use of GC packing materials was recently developed [42]. The work demonstrated that with a little modification to the thermal desorber and adjustment of software capabilities on currently available commercial IMS instruments, the frequency of false positives responses commonly associated with drugs and explosives detected in the field may be reduced. Added to this, the retention time at which the most intense response occurred could be utilized to separate false positive responses from drugs or explosives with the same drift times and vice versa. Implementation of a rapid GC type separation prior to detection may allow a greater degree of confidence in the rapid detection (<10 s) of drugs, explosives and chemical warfare agents in the field.

9. Portable/commercial instruments

The use of a portable/commercial GC–IMS was demonstrated and shown to successfully separate headspace vapors from complex liquid mixtures of analytes in 1992–1994 [43–45]. Despite the stringent small physical dimensions of this unit with respect to laboratory GC–IMS, these portable devices demonstrated potential for separating mixtures of analytes in a two-dimensional space. The unit successfully demonstrated the possibility of monitoring indoor and outdoor air for classes of compounds using a GC–IMS. A schematic cross-section and photograph of the first portable GC–IMS introduced in 1993 and 1994 are shown in Fig. 11(a) and (b). The sample introduction system for the commercial GC–IMS in Fig. 11(b) was done by pyrolysis. One important aspect of the unit in Fig. 11(b) was that the IMS was pumped down, and a short column was used to perform transfer line GC. The driving force for the carrier gas was created by making use of the pressure drop between the almost ambient pressure inlet and the vacuum of the IMS cell [45]. These developments have been successfully implemented in the international space station, and to date, is the most successful application of GC–IMS in the field [46,47].

Despite some success of GC–IMS as a portable unit, several problems were not addressed. Firstly, the sampling system used in the instrument required that the IMS operate at subambient pressures. At sub-ambient pressure operation, small
fluctuations in pressure may have a significant effect on the reproducibility of the IMS. Secondly, temperatures as high as 300 °C may be required for the GC separation, but the IMS system was not heated. GC devices required that the GC detector be operated at temperatures higher than the separation temperature to prevent band broadening and contamination from overlapping peaks in the detector. Thirdly, the GC–IMS interface used a bi-directional flow pattern, sweeping neutral analytes into the drift region of the IMS where they could undergo ion-molecule reactions that would complicate the spectrum. Finally, the IMS was operated in the pulsed mode and contained an aperture grid.

To address some of the problems listed above, a GC–IMS system was evaluated in the laboratory for its potential use as a hand-held field portable monitoring device [48]. This device was free of vibration noise, provided good chromatographic separation, achieved low detection limits (in the picogram range on-column), had an elevated IMS temperature, operated at ambient pressure, provided good reproducibility of ion mobility data under varying operating conditions, had FT electronics, and utilized a uni-directional flow pattern. Fig. 12 is a schematic cross-section of the potential hand-held field portable GC–IMS system. In Fig. 13 the sensitivity and selectivity of the hand-held portable GC–IMS was demonstrated. The figure shows chromatography and ion mobility detection of 38 ml of a 1-ppmV TO-14 mixture. This study concluded that for field portable GC–IMS instruments, the IMS portion should be heated to increase response of compounds that undergo dissociative electron capture to decrease interferences from humidity and to keep the instrument clean. Furthermore, the IMS portion of a field portable GC–IMS should be as large as possible to increase IMS resolving power and to reduce the loss of ions to the walls.
of the detector during ion transit down the tube. However, these improvements are yet to be utilized in field settings.

10. Pyrolysis (py) GC–IMS

Pyrolysis (py)-GC–IMS analysis of bacterial materials, including Bacillus spores and nucleic acids was reported by Meuzelaar et al. in 1991 [49]. This study followed systematic detections using py–GC–IMS of biopolymers relevant to bio-agent detection as well as potential interferences [50]. The sequences of events in a py–GC–IMS detection process are as follows:

(a) Pyrolysis (py) converts a solid sample to vapor by rapid heating;
(b) GC separates the vapor mixture into individual components;
(c) IMS separates the individual components according to their charge/size ratios.

Thus, using pyrolysis to convert large solid biological substances such as proteins and bacteria into low mass energy species, followed by separation, IMS has shown to detect these compounds [51–54].

In 1997, biological compound information was generated by a quartz tube py–GC–IMS bread board system under controlled sample introduction of bacterial suspension [55]. In addition, a commercially air-to-air aerosol concentrator was further interfaced to the quartz tube pyrolysis port of the py–GC–IMS [52]. This instrument was used for bacteria vapors detection. GC–IMS was also shown to be promising for the inspection of cargo containers [56]. Ambient pressure IMS have been shown to be well suited for outdoor, field applications [49–53]. Outdoor bio-aerosols consisting of gram-positive bacillus atrophaeus spores,
gram-negative pantoea agglomeran cells, ovalbumin protein and MS-2 coliphage virus were released during formal trials at western deserts and prairie test sites in the USA and Canada. With the use of a py–GC–IMS data space, differentiation of the four bioaerosols was possible by visual determinations of the dispersion of the pyrolysate peaks [53–55]. These series of tests documented the first detection and differentiation of outdoor released bio-aerosols with atmospheric pressure and temperature IMS after py–GC analysis.

Quite recently, a fielded py–GC was interfaced in parallel to an IMS and a time-of-flight mass spectrometry (TOFMS) [57]. This configuration was constructed in a similar fashion to the py–GC–IMS–MS laboratory system used for the detection and identification of picolinic acid markers [52].

Fig. 14 is a schematic cross-section of the py–GC–IMS and py–GC–TOFMS system. In this investigation, evidence was presented that the outdoor fielded py–GC atmospheric pressure and temperature IMS bio-aerosol detector can produce biochemical information that can be correlated with gram-stain reactions used for gram-positive and gram-negative microorganism taxonomy.

Snyder et al. in 2005 demonstrated thermogravimetry analysis mass spectrometry (TGA-MS) and an outdoor fielded bioaerosol py–GC–IMS instrumentations for the analysis of biological samples [58]. The TGA-MS generated laboratory thermo-analytical rate of kinetic reaction results. This data was...
related to the data from the py–GC–IMS detector that processes biological species by pyrolysis heating [58]. The work demonstrated qualitative biochemical product evolution over time from bacillus spores. It was reported that the TGA-MS instrument provided characterization and interpretation of the heating parameters and their inter-relationships with the outdoor fielded py–GC–IMS bioaerosol detector for microorganisms. This work also claimed the TGA-MS was used to modify, optimize, and refine the heating parameter settings on the pyrolysis side of the py–GC–IMS for bacterial analysis. It was claimed that the outdoor bioaerosol py–GC–IMS produced similar thermal product evolution information when compared to the more sophisticated TGA system [58].

In 2006, an open tube py–GC–IMS and a close tube solid phase micro-extraction (SPME)–GC–IMS were compared for the analysis of water samples contaminated with chemical warfare agents [59]. It was reported that by incorporation of the close injector and using of SPME as a sample preconcentrator, detection limits for the detection of tributylphosphate was lowered by two orders of magnitude. Thus, the open tube py–GC–IMS was shown to be useful for aerosol particulates, and not optimal for liquid chemical analysis.

Bioaerosol monitoring and characterization are serious challenges in the 21st century. py–GC–IMS systems have demonstrated that individual bioaerosol responses can be reliable under certain conditions. However, the confidence and reliability of data analysis and conclusions of a bioaerosol event can be greatly improved when multiple system responses on the same analyte are considered. Snyder et al. demonstrated these sequence of events by spatially situating a mass base py–GC–IMS and particle-based UV–vis fluorescence technologies for spore and protein bioaerosol detection in the southeastern prairie region in Alberta, Canada [60]. Detection and qualitative characterization followed by verification with reference samplers of outdoor ambient air bioaerosols were reported. Fig. 15 shows a py–GC–IMS data space response sets for three disseminated bioaerosols in the outdoor prairie environment at the defense research and development Canada in Suffield, Alberta, Canada [60]. Fig. 16 shows a response set of three bioaerosol detectors accompanied with their individual agar plate ground truth for trial 17 in the investigation [60].

11. GC–DMS

Field asymmetric waveform IMS (FAIMS) was introduced as an analytical method for measuring mobility of ions in air in 1987 [61] when the first scientific publication was published in Russia. However, it was not until 1993 [62] that the method was described quantitatively. The technology was successfully transferred to a micro-machined differential mobility spectrometry (MicroDMx) sensor and the name changed occurred from FAIMS to DMS in 2001. Since DMS was introduced, it has shown real promise for near real-time on-site detection of explosives [63,64], chemical warfare agents [65], toxic industrial chemicals and materials [66], and environmental contaminants [67–70]. Of interest to this review was the use of solid phase micro-extraction (SPME) combined with GC–DMS for analysis of 1,2,4-trichlorobenzenes in surface waters collected around the UK [65] and SPME with the use of a modified GC detector directly coupled to a DMS for the analysis of hydrocarbons in water [70].

Recently, a micro-fabricated drift tube for differential mobility spectrometry (DMS) was utilized with py–GC to chemically characterize bacteria through three-dimensional plots of ion intensity, compensation voltages from DMS and chromatographic retention times [71]. Fig. 17 is an example spectra of a graph with the vertical dotted lines indicating the beginning and end of the formal biomonitoring aerosol particle analyzer (FLAPS) and py–GC–IMS (biological agent warning analyzer total ion count plot) detectors along with their respective response agar plate ground truth for window 8 period bioaerosol testing. With the exception of the bottom plot, the instrument responses were the upper trace and the ground trace was the lower trace. The right ordinate represents the agent containing particle per liter of air (ACPLA) for the lower trace in the first three panels, and the left ordinate represents the upper trace in the first three panels. In the lower plot of the py–GC–IMS section, a GC–IMS cycle time average is shown as a solid line connecting the open circles, and the real-time ground truth is shown as sharp peaks. The series of graphs in the bottom panel partitions the total ion count (TIC) plot responses into three separate curves. Each bacterial symbol represents the summation of the respective peak areas marked as arrows in Fig. 15. The vertical dotted lines indicate the beginning and end of the formal bioaerosol for trial 17 (T17) [60]. Copyright (2004) Wiley–VCH Verlag GmbH & Co. KGaA. Reproduced with permission.
Fig. 17. Compensation voltage vs. retention time for the 50 peaks of highest intensity in py-GC/DMS analyses of E. coli (grey signals) and M. luteus (black signals) for positive polarity ions. (1) Pyridine; (2) 2-furancarboxaldehyde; (3) 5-methyl-2-furancarboxaldehyde; (4) crotonic acid; (5) benzeneacetaldehyde; (6) phenol; (7) p-cresol; (8) phenylacetone; (9) pyridine-2-carboxylic acid (picolinic acid); (10) benzenepropenone; (11) indole; (12) 3-hydroxybutyric acid; (13) 1-tridecene; (14) 2-pyridinecarboxamide; (15) dodecanal; (16) 2-tridecanone; (17) 1,7-dihydro-6(H)-purin-6-one (hypoxanthine); (18) n-dodecanoic acid; (19) n-tetradecanoic acid. Reprinted with permission from Schmidt et al. [71]. Copyright (2004) American Chemical Society.

SPME coupled with a one-dimensional gas chromatography differential mobility spectrometry (GC–DMS) was investigated to evaluate the benefits for classifying fuels [73]. In this work, a fuzzy rule-building expert system (FuRES) was used as a multivariate classifier for data obtained from the SPME–GC–IMS system and compared to optimized partial least square (PLS) classifiers. This development made use of a three-dimensional (3-was cube) analytical information (edge was sample, retention time, and compensation voltage), and it is now possible to produce characteristic profiles of fuels and a classification rate of 95 ± 0.3% was reported. The same approach, FuRES combined with a two way GC–DMS, was recently applied to arson investigations [74].

12. Summary and conclusion

Over the past 35 years, gas chromatography coupled with ion mobility spectrometers has been demonstrated to be a powerful analytical method for the determination of compounds in complex samples. There are a number of advantages to adding an IMS as an ambient pressure detector for GC:

1. The first unique advantage of GC–IMS systems is that it combines data into a 2D-matrix. The result of this data format is the ability to derive a contour plot revealing both retention time and drift time information. With the introduction of DMS, the analytical information of compensation voltage was added.

2. Because gas chromatography separates in the minute to second time scale and ion mobility spectrometry separates in the millisecond time scale, multiple IMS spectra can be obtained for each gas chromatographic peak.

3. IMS coupled with high resolution capillary gas chromatography is a versatile detector which can function as an FID, ECD, ion spectrometer and molecular selective detector. When coupled with portable GC instruments, it provides an added dimension of separation that increases the peak capacity of rapid analytical methods for field analyses.

4. In a GC–IMS configuration, a complex mixture of ions can be separated by the GC before entering the IMS ion source. Each compound in the mixture arrives individually at the IMS ion source. Thus, the GC part of the interface brings an advantage to IMS by eliminating cross-sensitivity/charge competition effects. The GC interface offers an additional advantage of separation before ionization.

5. In IMS analysis, humidity effects have been documented to be problematic for gas analysis at the parts per billion ranges. Adding a GC as the sample introduction step to an IMS can help reduce humidity effects.

6. One problem with GC is the non-reproducibility of retention time. As the stationary phase aged, retention times vary, and they also vary from one column to the next making chromatographic retention difficult to reproduce. Reduced mobility measurements (despite variations in temperatures and pressures) are absolute, related directly to the structure of the compound. Thus, IMS as a detector for GC offers some advantage of reproducibility.
7. Most applications have been developed with the combination of the two-dimensional approach of GC–MS. However, the difficulty with adding a mass spectrometer to a GC is expense and instrument complexity. Mass spectrometry requires a vacuum, which is difficult to maintain on a routine basis in day to day field operations. Thus, IMS brings significant advantage to a GC with its portability, less complex instrumentation, high throughput, ease of operation, and low cost.

Recent advances in IMS with respect to liquid chromatography and mass spectrometry may rekindle interest in this potentially powerful analytical method for the rapid determination of volatile compounds in complex matrices.

The use of IMS as a gas chromatography detector for quantitative analysis is somehow limiting especially with IMS instruments of low resolving powers as those used in the field. Despite IMS high selectivity and sensitivity, small size, speed of analysis, and low power consumption as demonstrated by a series of publications for over three decades, quantifying responses remains a problem. This is mainly because the response from IMS is non-linear. Thus, linear dynamic range and limit of quantification still limits the use of IMS as a superior detector for gas chromatography.

The future direction of this technique lies with interfaces of 2D-GC. A 2D–GC–IMS/2D–GC–DMS provide a four-dimensional analytical information of retention time 1, retention time 2, ion intensity, and drift time/compensation voltage. A Hadamard matrix may be expected to increase responses remains a problem. This is mainly because the response from IMS is non-linear. Thus, linear dynamic range and limit of quantification still limits the use of IMS as a superior detector for gas chromatography.

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