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Multivariate Signal Processing for Quantitative and Qualitative Analysis of Ion Mobility Spectrometry data, applied to Biomedical Applications and Food Related Applications

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by

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CHAPTER ONE
Ion Mobility Spectrometry as potential technology in biological scenarios

1.1. Introduction

Ion Mobility Spectrometry (IMS) is a fast, unexpansive and portable spectrometer which has been used for binary detection of explosives, warfare agents, and illicit drugs. Moreover, in the last years other fields have been attracted by this technology for in-situ applications, among of them medicine, food control and quality control, pharmaceutics. This implies the need for the use of advanced data processing and spectral analysis techniques instead of the use of simply processing for binary detection.

This chapter introduces the IMS technology and some specific features of these instruments, such as non-linear behavior and competitive effect of the ions. These characteristics have to be taking into account in the signal processing analysis of the spectra. Moreover, a summary about state of the art of IMS in bio-related applications is detailed in this chapter.

1.2. Ion Mobility Spectrometry

Ion Mobility Spectrometry, firstly known as plasma chromatography in 1970, is a portable, handheld device that characterizes trace levels of chemicals on the basis of velocity of gas-phase ions in an electric field at ambient pressure (Eiceman and Karpas, 2005). Moreover, the use of IMS is comparatively simple, fast and economic providing significant value in chemical analysis.

The IMS consist of two sequential processes, the formation of ions which are representative of a sample, and the determination of these ions according to their mobilities in an electric field. There are four main parts on the IMS, as it is show in Figure 1.1: *(i)* ionization source region, *(ii)* drift tube, *(iii)* shutter grid and *(iv)* a detector - typically a faraday plate. In principle, the sample, which is vapor or gas chemicals, is transported by a carrier gas either air or nitrogen and then ionized in the ionization source region *(i).* That gives rise to different chemical reaction between neutral ions and the molecules of the sample. The ionized molecules are injected into the drift tube *(ii)* through an electrostatic shutter grid *(iii)* acting as ion gate. As soon as the gate grid opens, a weak electric field (about 100-300 V cm^{-1}) accelerates the set of ions into the drift tube *(ii)* until they reach a constant velocity. In addition, a drift gas, which is placed inside the drift tube, goes on opposite direction to keep neutral species out of the tube. At the end of the drift tube, there is a collector *(iv)* where the charge of the ions is converted in a current output. The final spectrum contains different peaks depending on the mobility of the gas-phase ions; thereby peaks at lower drift time are related with small molecules. Consequently, the moderate selectivity of the instrument is given by the differences in the drift time (Borsdorf et al., 2011, Eiceman and Karpas, 2005).

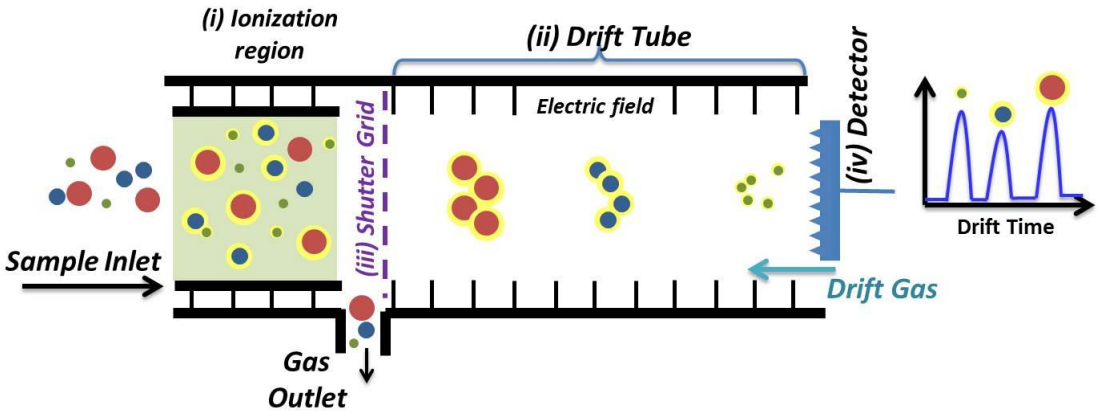

Figure 1.1 Schematic representation of Ion Mobility Spectrometer (IMS). (i) Ionization source region in which the sample is ionized, (ii) Drift tube where the ionized molecules are accelerated by an electric field, (iii) shutter grid allows the ionized molecules go into drift tube and (iv) detector where the charge of molecules are converted into a current output.

Either positive-ion or negative-ion formation can be produced depending on the ionization source, i.e. radioactive sources. Actually, the gas phase ion-molecules reactions either in air or nitrogen are described by principles of thermodynamics, kinetics and molecular structure as well as experimental conditions such as temperature, pressure, moisture and concentration.

Actually, the drift velocity of ions through the drift tube can be replaced by a mobility coefficient K ($cm^2V^{-1}s^{-1}$) Eq. 1.1. Initially, this coefficient depends on the length of the drift tube (L), the electric field (E) and the drift time of the ions to arrive at the collector (t_d) (Eiceman et al., 2003, Eiceman and Stone, 2004, Borsdorf and Eiceman, 2006, Creaser et al., 2004). Nonetheless and in order to be able to compare different commercial devices operating at different ambient conditions, it is recommendable to normalize the mobility coefficient. Thus, the normalized mobility coefficient (K_0), or normalized reduced mobility, can be corrected to standard conditions of temperature (T in Kelvin) and pressure (P in Torr) of the gas atmosphere (Eiceman and Karpas, 2005) using Eq. 1.2.

$$K = \frac{L}{Et_d} \qquad \text{Eq. 1.1}$$

$$K_0 = K\frac{273}{T}\frac{P}{760} \qquad \text{Eq. 1.2}$$

Some uncertainties such as changes in temperature, pressure, gas composition, collision cross sections may lead changes in the K_0 values. Nevertheless, K_0 can provide a measure of mass and shape of ions, therefore K_0 can be understood as a method to compare analytes from both different samples and commercial instruments.

Additional changes can be done in the reduced mobility coefficient in order to relate the reduced mobility to the chemical identity of the ions. The new mobility coefficient is

given by Eq. 1.3, though it cannot be applicable when large organic ions are measured (Eiceman et al., 2014).

$$K = \frac{3e(2\pi)^{1/2}(1+\alpha)}{16N\left(\mu k T_{eff}\right)^{1/2}\Omega_D\left(T_{eff}\right)} \qquad \text{Eq. 1.3}$$

where *e* is the electron charge; *N* is the number of neutral gas molecules at the measurement; *α* is a correction factor; *μ* is the reduced mass of ion and gas of the supporting atmosphere, T_{eff} is the effective temperature of the ion determined by thermal energy and the energy acquired in the electric field; and Ω_D is the effective collision cross section of the ion at the temperature of the supporting atmosphere.

In addition, the mobility coefficient of unknown analyte $K_{(unknown)}$ can be obtained based on a standard coefficient $K_{(standard)}$ by Eq. 1.4. This equation takes into account the reduced mobility $K_{(standard)}$ and drift time $t_{d(standard)}$ of a reference compound, and knowing the drift time of the unknown compound $t_{d(unknown)}$, the reduced mobility of the unknown compound $K_{(unknown)}$ can be determined.

$$\frac{K_{(unknown)}}{K_{(standard)}} = \frac{t_{d(standard)}}{t_{d(unknown)}} \qquad \text{Eq. 1.4}$$

Despite of the fact that reduced mobility K0 can be used for compound identification, formation of cluster ions, which according to IUPAC(McNaught and Wilkinson, 2006) is an ion formed by the convination of two or more atoms or molecules of one or more chemical species with an ion, can lead a miss interpretation of K_0. Thus, there is an extra complexity in the interpretation of the resulting spectra which must be solved with signal processing strategies.

1.2.1. Ionization source

The most common ionization source is based on radioactive source. The reactant ions, which are also known as the term “water-based ionization”, are produced by emitting -β particles of an average of 17 keV that collide with the molecules from the supporting atmosphere, either pure air or nitrogen. Thus lead a set of ions with the following identity $H_3O^+(H_2O)_m(N_2)_n$ where values of m and n are governed by temperature and moist (Kim et al., 1978, Eiceman, 2002). This set of positive ions are known as reactant positive ions. Additionally, reactant negative ions are also produced by collision with the emitted beta-particles. The identity of the reactant ion in negative polarity with clean air is $O_2^-(H_2O)$ (Eiceman and Karpas, 2005)

The ionization source region (Figure 1.1 *(ii)*) works as a reservoir of these reactant ions both positive and negative. In the case of the positive iones, the incoming molecules (*M*) undergo collisions with reactant ions generating the product ions. The leading

process of product ion formation is known as proton transfer Eq. 1.5 which happen when *M* have a greater proton affinity than the reactant ions. This process is also known as “soft ionization” because no fragmentation occurs in the ionization process.

$$\underbrace{M}_{Analyte} + H_3O^+(H_2O)_m(N_2)_n \Leftrightarrow \underbrace{MH^+(H_2O)_{m-1}(N_2)_n}_{Protonated\ Monomer} + \underbrace{H_2O}_{Water\ neutral} \qquad \text{Eq. 1.5}$$

$$\underbrace{M}_{Analyte} + \underbrace{MH^+(H_2O)_{m-1}(N_2)_t}_{Protonated\ Monomer} \Leftrightarrow \underbrace{M_2H^+(H_2O)_{m-1}(N_2)_n}_{Proton-bound\ dimer} + \underbrace{H_2O}_{Water\ neutral} \qquad \text{Eq. 1.6}$$

When, the concentration of *M* increases, the production of product ions raises. Thus, the protonated monomer may be clustered with an additional analyte molecule (*M*) forming a proton-bound dimer Eq. 1.6. There can be formation of proton bound trimers, tetramers, and so forth with further increases of *M* (Eiceman, 2002).

In the negative polarity the product ion is formed by the association of a molecule (M) and oxygen anion, and the stabilization of the cluster ion is produced by displacemet of a water molecule Eq. 1.7. (Eiceman and Karpas, 2005).

$$\underbrace{M}_{Sample} + \underbrace{O_2^-(H_2O)_n}_{\substack{Negative\\ reactant\ ion}} \leftrightarrow \underbrace{MO_2^-(H_2O)_n^x}_{Cluster\ ion} \leftrightarrow \underbrace{MO_2^-(H_2O)_{n-x} + xH_2O}_{Product\ ion+water} \qquad \text{Eq. 1.7}$$

There is a wide variety of ion sources for IMS besides radioactive sources, among them, photo-discharge lamps, lasers, electrospray ion sources, flames, corona discharges, and surface ionization source. The interest of using non-radioactive sources has risen since some technical and experimental limitation has found for using beta emitters such as permissions, licensing procedures and lack of freedom to relocate such spectrometers(Borsdorf et al., 2011). Nonetheless, radioactive sources are favored over the other alternatives owing to low maintenance, reliability and stable operation for producing reactant ions, light weight and simplicity of the use. As it was mentioned before, the most used radioactive source is 10mCi ^{63}Ni which maximum energy for emitting electrons is 67keV with an average energy of 17keV. The typical application of radioactive source is explosive and chemical agent detection (Buxton and Harrington, 2001, Ewing et al., 2001)

The point-to-plane corona discharge (CD) ion source has been deeply explained elsewhere (Tabrizchi et al., 2000, Shumate and Hill, 1989, Wittmer et al., 1994). The ionization occurs by electrical discharge that is produced by a needle and an opposite conductor. Reactant ions are formed similar to radioactive source and these ions are subsequently used for ion-molecule reaction with the sample (Eiceman and Karpas, 2005, Tabrizchi et al., 2000). The main drawbacks of this kind of sources are the high

maintenance needed and the requirement of using power supply. Applications such as characterize biogenic amines (Karpas et al., 1994, Karpas et al., 2002b, Chaim et al., 2003) or monitoring compounds in water (Borsdorf et al., 2001) or air (Khayamian et al., 2003, Khayamian et al., 2001) are the most typical in this kind of ionization source.

The mechanism of photoionization is either photo-discharge lamps or lasers. The sample is irradiated with a lamp, i.e. ultraviolet (10 eV), in which photons from the lamp are emitted and excite the surrounding gas. In contrast of the other ionization sources, this spectrometer do not produce a reactant ion peak. If the ionization potential of the analyte is less than or equal to the proton energy of the lamp, the formation of positive ions occur through the Eq. 1.8. The main advantage of this kind of source is to permit the detection of compounds that are not detectable by the radioactive sources due to low proton affinity. Nonetheless, a requirement of power supply and maintenance is needed as well as poor long-term stability. Sometimes, the use of a dopant is required for enhancing the sensibility of the spectrometer or yield a reactant ion for undergoing to a charge transfer in a way analogous to beta sources (Eiceman and Karpas, 2005). There are different applications in the field of food industry where UV-IMS has been used (Menendez et al., 2008, Garrido-Delgado et al., 2011b), and biomedical applications (Vautz et al., 2004b, Vautz et al., 2004a, Baumbach et al., 2005). Nonetheless, it is important to remark that most of them are not directly used in the industry, they are currently in development.

$$M + h\vartheta \rightarrow M^+ + e^- \qquad \text{Eq. 1.8}$$

Note that many times the ionization source is directly related to the application needs, as it can be seen in Table 1.1. For instance, lasers have been used to get pesticides on fruit surfaces (Borsdorf et al., 2009), matrix-assisted laser desorption ionization(MALDI) provide gas-phase ion from laser ablation of metals (Eiceman et al., 2007). In the case of measuring liquids, electrospray ionization (ESI) is the best way to get a reliable response which is totally suitable in environmental analysis (Shumate and Hill, 1989, Wittmer et al., 1994, Dion et al., 2002, Steiner et al., 2002). In the perfume industry glow discharge ion source is used for characterize perfume odors (Zhao et al., 2009).

Ion Source	Type of Chemicals	Maintenance	Cost	Comments
Radioactive	Universal	Low	Medium/low	Licesing required
Corona Discharge	Universal	High	Medium	Electrode replacement required
Photoionization UV,laser	Selective	Medium	Medium	Low efficiency
Surface ionization	Selective (N, P, As,S)	High	Medium	Complex
Electrospray	Liquid samples	Medium	Medium	Long clearance time
Desorption Electrospray Ionization (DESI), Direct analysis in real time for solid surfaces (DART)	Solid Samples	Medium	Medium	Long clearance time
Secondary electrospray ionization (SESI)	Solid, liquid, and vapor	Medium	Medium	Research stage
MALDI	Macromolecules	High	High	Biological mainly
Flame	Selective	Medium	Low	Structural information lost
Plasma	Universal	Medium	Medium	Research stage
Glow Discharge	Universal	Medium	Medium	Research stage
Alkalication	Selective	Medium	Medium	Research stage

Table 1.1 Summary of Ionization Techniques used in Ion Mobility Spectrometry (IMS) taken from the book of Ion Mobility Spectrometry (Eiceman et al., 2014)

1.2.2. Non-linear behavior of IMS

From a quantitative and signal processing point of view, the nonlinearities present in the dynamics of the IMS are challenging and bring new opportunities to develop strategies for the spectra analysis. Under the nonlinear behavior of the IMS, a compound is not likely to be linked with a unique peak in the resultant spectrum, but there may be more peaks associated to it. This behavior can be attributed to different causes as the presence of impurities, charge competition and charge transfer reactions between the ionized compounds, concentration dependence, and fragmentation of the target product ion.

Formation of protonated monomer Eq. 1.5 and proton-bound dimer Eq. 1.6 can be easily observed, especially when the target ion is present at high concentrations. Figure 1.2 shows a synthetic example of the behavior of the compound *(M)* when the concentration increases with time. As the concentration of the compound increases, the reactant ion drops while the intensity of the protonated monomer increases (see at the top of Figure 1.2). As the increasing of the concentration continues, the proton-bound dimer appears and the intensity of its peak grows, and at the same time, the protonated monomer starts to decrease slowly and the reactant ion peak drops further.

A spectrum at different time period of the measurement is shown at the bottom of the Figure 1.2. In the *A* spectrum just the reactant ion peak (RIP) is shown. Then in a second stage (spectrum *B*) a peak of the protonated monomer emerges together with a decrease of the RIP. The last spectrum *C* shows a peak from the proton-bound dimer and a small peak of RIP together with a decrease in the intensity of the protonated monomer peak.

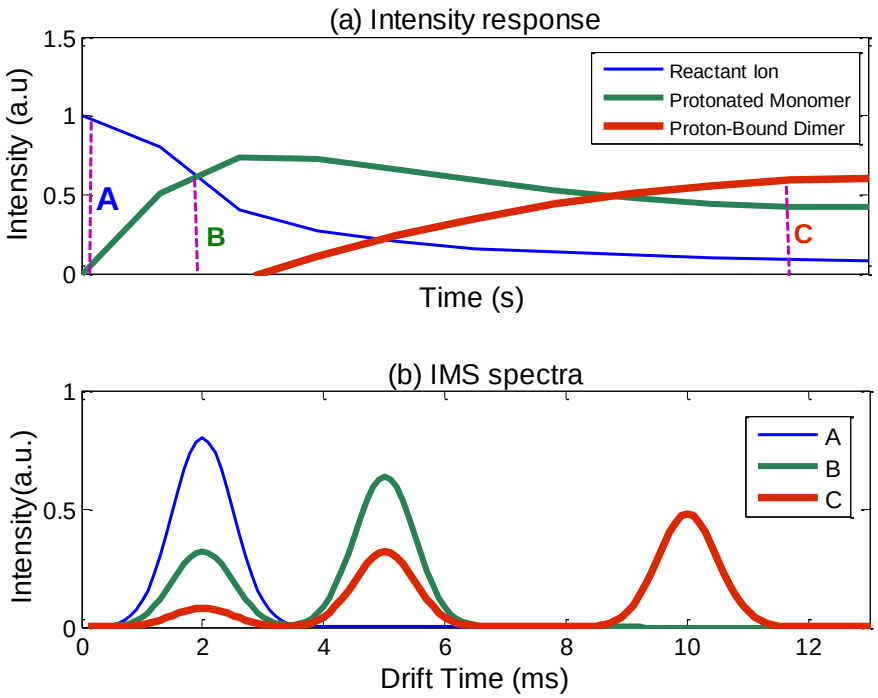

Figure 1.2 Synthetic representation of the behavior in the formation of protonated monomer and proton-bound dimer. (a) The intensity response of reactant ion peak, protonated monomer peak and proton-bound dimer. (b) Spectra at different instants (A) just reactant ion peak, (B) protonated monomer and reactant ion peaks, and (C) proton-bound dimer, protonated monomer and reactant ion peak.

Despite of the fact that this phenomenon is well known and commonly noticeable in different scenarios, the nonlinear effect in a complex matrix has received scarce attention from a signal processing perspective. For instance, one of the two peaks is usually discarded when quantification is performed, but it may lead uncertainties in final results. Moreover, the fact of choosing one peak or the other is far to be easy. On the other hand, in real samples where many unknown peaks can appear in spectra, it can happen that a single analyte may lead more than one peak. Thus, discarding peaks will

introduce errors in the spectra analysis. However, the use of multivariate techniques might bring reasonable solution to this problem.

1.2.3. Proton affinity and Dopant Effect

Proton affinity information has been used as a tool for enhancing the selectivity of the IMS and diminishing the complexity in the spectra analysis. Figure 1.3 shows an example about how proton affinity works in the IMS. In this case, a dopant is added to the drift gas leading a degree of selectivity to IMS. The figure depicts what happen when the dopant is set up at different levels. For instance, when the IMS have a radioactive ionization source, which typical configuration is “water chemistry”, IMS is not able to detect compounds with lowest proton affinity than water (alkanes). In a real application, this can also be challenging because there will be a competitive effect between all the compounds present in the sample and also, the background can mask the informative compounds. Of course, the masking effect of the background can be reduced using a dopant compound with a higher proton affinity than water, generating, consequently, an increase of the IMS selectivity to the substance of interest.

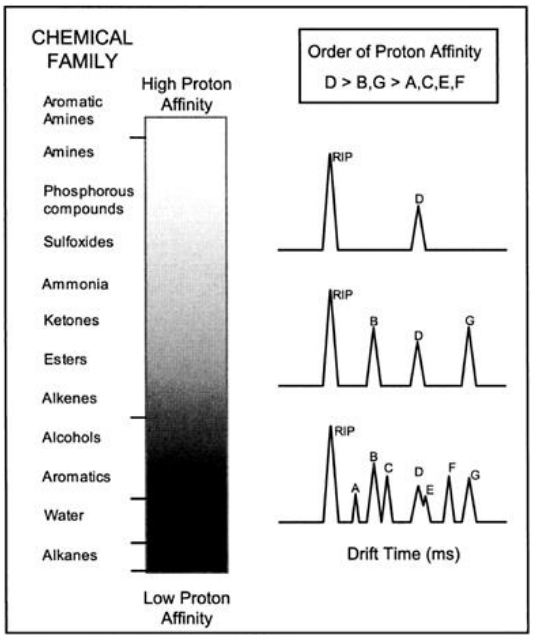

Figure 1.3 Hypothetical example about the selectivity of IMS under different threshold of proton affinities (Eiceman and Karpas, 2005)

Moreover, the use of a dopant with a specific proton affinity may not lead the creation of product ions with a lower proton affinity than the dopant, even for high concentrations. For instance, to reject alcohols, the dopant should have at least a proton affinity similar to esters. However, this advantage sometimes turns into a drawback when all the compounds in the sample are equaled important. Thus, the competitive ionization may mask the presence of some compound and affect the quantitative determination of them. This is a main issue in non-target studies, when the compounds present in the sample are unknown as well as their proton affinities. In this context, there are just a few publications about the quantitative response of the compounds in mixture, among them (Eiceman et al., 1990, Puton et al., 2008, Puton et al., 2012, Marquez-Sillero et al., 2011). Puton (Puton et al., 2012) studied the relationship between the output of the IMS and the concentrations of two compounds in

a mixture introduced in the ionization source. They tested three different combinations of compounds, one as a dopant and the other as the substance of interest. In addition, the concentration range was enough high to favor the proton-bound dimer formation. He explained about the non-linear behavior present between the signal and concentration, and demonstrated that the presence of an admixture can differently affect the detection of an analyte. In addition, when two compounds have similar proton affinities, the proton-bound dimer formation will depend on the admixture concentration.

Apart from the competitive ionization issue, the selectivity of the IMS is also limited by the peak-to-peak resolution (R_{pp}) formalisms as Spangler (Spangler, 2002) determined.

This parameter can be calculated using information from the drift time (t_d) and the full-width-at-half-height (FWHH) (w_h) for the mobility peak by Eq. 1.9. When two peaks are closer, the R_{pp} can be determined by Eq. 1.10 where sub-indices refer to two neighboring peaks. This factor is really important to choose a commercial device for a particular application or as a feature to be considered in signal processing strategies for resolving problems such as deconvoltue overlapping peaks.

$$R_{pp} = \frac{t_d}{w_h} \qquad \text{Eq. 1.9}$$

$$R_{pp} = \frac{2(t_{d2} - t_{d1})}{1.7(w_{h2} + w_{h1})} \qquad \text{Eq. 1.10}$$

1.3. Sampling introduction techniques to IMS

Besides the fact of choosing the proper ionization source, the efficient way to transfer the sample into the ionization region is also challenging. Since the IMS needs gas-phase ions, all samples must be transformed from their original state to a gas phase state. Therefore, the introduction methods are totally linked with the application.

The easy way is through direct injection which means introducing the sample into the IMS by flowing a carrier gas directly to the ionization region (Eiceman et al., 2014, Eiceman and Karpas, 2005). Depending on the application, the need of using a membrane between the sampling section and ionization region to eliminate humidity or any kind of impurities is absolutely necessary (Creaser and Stygall, 1995, Johnson et al., 1997). Membrane can be also used for pre-concentrate the sample, thus a small air-sampling pump is enough for diffusing the sample into the ionization region (Kanu et al., 2005, Kanu and Thomas, 2006).

Actually, the need of a sample pre-concentration process it is not uncommon; especially when semi-volatile compounds are the main focus. Thus the use of sorbing traps such as Carbosieve or Tenax is frequently used. Thermal desorption and solid phase microextraction (SPME) are also used to increase the sensitivity of the spectrometer (Creaser et al., 2000, Perr et al., 2005).

Liquid samples or solid samples require a different sampling methodology in order to vaporize the sample and get gas state for IMS analysis. There are several methodologies, among of them syringe injection (Metro and Keller, 1973), exponential dilution flask (Spangler and Lawless, 1978), permeation tubes (Okeeffe and Ortman, 1966), diffusion tubes(Rawa-Adkonis et al., 2003) and thermal desorption ovens(Nanji et al., 1987). The typical methodology is to place the sample into a permeation tube, syringe injection or diffusion vessel, and then heated it (Borsdorf and Eiceman, 2006). The main advantage of this technology is the simplicity and get a sort of concentration control. One option is the use of permeation tubes together with a mass flow controller to control both temperature and gas inlet flow and therefore accurately concentration estimation of the sample. One commercial device is Owlstone Gas Generator (Owlstone, 2014), that allows to calculate the concentration of a sample that is placed in a permeation tube. There are more sophisticated techniques such as electrospray(Bohrer et al., 2008, Dion et al., 2002) due to it allows direct injection of liquid samples without any additional source (Harper, 2000). The analysis of solid is typically solved by thermal desorption where samples are vaporized in an inlet oven. The carrier gas of IMS flows through the inlet oven and sweep the volatile constituent into the analyzer (Stlouis and Hill, 1990, Borsdorf et al., 2005). In recent years, another version of this method has been used such as thermal pyrolysis where the temperature is high enough for causing chemical decomposition (Tripathi et al., 2001). In a similar vein, the use of laser of ablation of surfaces promote chemical decomposition and its use has become more popular for study solid samples such as soil or bacteria (Eiceman et al., 2007).

1.3.1. Main biological and biomedical applications with Stand Alone IMS

At the outset of IMS use, the leading applications were fully related to detection of explosives, illegal drugs and chemical warfare agents (Hannum et al., 2000, Buxton and Harrington, 2001, Ewing et al., 2001, Kanu et al., 2005, Bunte et al., 2006, Tabrizchi and Ilbeigi, 2010, Nousiainen et al., 2011, Grate et al., 2012, Synder et al., 1995, Jafari et al., 2007, Armenta and Blanco, 2012, Moran et al., 2012, Nakagawa et al., 2012, Steiner et al., 2002). Certainly, the success in this field opened the possibility of using this technology over other new areas. Portability and fast response are interesting characteristics that makes the IMS technology suitable for fast and may be on-line measurements. Nowadays, the new applications cover fields such as environmental monitoring, food industry, pharmaceutical quality control, clinical and biological applications. The widespread use of IMS has been reported in recent interesting reviews (Armenta et al., 2011, Marquez-Sillero et al., 2011, Borsdorf et al., 2011, Karpas, 2013). Just a brief summary of the reported use of IMS as standalone device in the context of biological and biomedical fields is presented below.

In the field of foodomics (Karpas, 2013), the main applications have been focused in quality test for either food spoilage or freshness, or detect adulteration in beverage or food. For instance, biogenic amines were studied as indicator of bad odor of spoilage of fish or meat. Karpas (Karpas et al., 2002b) found a correlation between trimethylamine (TMA), cadaverine, and putrescine and laboratory cultures of micro-organisms from spoilage food. In addition, a calibration model was built for quantify the freshness in chicken meat using patterns of TMA (Bota and Harrington, 2006). Another study was carried out using a UV-IMS for measurement solid samples which were placed in a membrane inlet (Menendez et al., 2008) and the relation of biogenic amines were also found. In beverages, applications for discriminate wine origin (Garrido-Delgado et al., 2011a), virgin olive oil grades (Garrido-Delgado et al., 2011b) using classification models have been also studied. The determination of TCA in both corks and wine has been carried out with and without pre-concentration techniques (Karpas et al., 2012, Marquez-Sillero et al., 2012). There are also studies for determining the feeding adulteration of Iberian pigs which has an economical effect in this industry (Alonso et al., 2008). Other studies related to seek toxic or harmful chemicals ion food are in the spotlight in this field (Jafari, 2006, Jafari et al., 2007, Jafari and Khayamian, 2008, Jafari and Khayamian, 2009, Jafari et al., 2011a, Jafari et al., 2012).

Because of its portability, its fast response and easy to handle measurements, the use of IMS as clinical diagnostic tool hasalso been explored in recent years. In this sense, the spectra of applicability ranges from drugs determination to medical diagnoses from different human biological samples. Different compounds have been investigated in urine, saliva, plasma and blood using IMS with different ionization sources in which electro spray is the most common one (Lu et al., 2009, Alizadeh et al., 2008, Shahdousti and Alizadeh, 2011, Jafari et al., 2011b). The exhaled breath has been studied as potential tool for detect some diseases in both human (Perl et al., 2009) and animal models(Guaman et al., 2012, Vautz et al., 2010) .Biogenic amines have been also studied as biomarkers for diagnosing bacterial vaginosis diseases (Karpas et al., 2002a, Chaim et al., 2003, Marcus et al., 2012, Sobel et al., 2012, Karpas et al., 2013). In fact, there is already a commercial corona discharge-IMS developed by 3QBD – Israel (3QBD) which provides a diagnostic in less than 60 seconds.

1.3.2. Other IMS configurations and applications

Other configurations can be feasible following the same formalism of IMS. As it is known, the drift velocity is directly proportional to field strength (*E*). As long as, the electric field changes during a measurement, the ions can be characterized by their acceleration into the drift tube which was produced by the electric field variations. These instruments are called either differential mobility spectrometers (DMS) or high-field asymmetric waveform ion mobility spectrometry (FAIMS). In this case an asymmetric field is applied perpendicular to the gas flow which cause the ion swarm oscillates (Eiceman and Karpas, 2005, Li et al., 2011, Kolakowski and Mester, 2007, Aksenov et al., 2012). A difference in mobility is determined instead of a reduced mobility as IMS. Some applications can be found, among of them, in fields of environmental analysis (Ungenthum et al., 2009), pharmaceutical bionalysis (Hatsis et al., 2009, Guddat et al., 2009), and determination of spoilage in meat(Awan et al., 2008b, Awan et al., 2008a).

In order to face the complexity in biological samples, some complementary techniques can be used jointly with the IMS devices for improving its performance, also known as hyphenated techniques. For example, coupling pre-separation devices arise as alternative for enhancing selectivity and interpretability. Gas chromatography coupled to IMS has been deeply used due to allow to enhance selectivity by changing temperature through a ramp temperature configuration. Multicappillary columns (MCC) is a GC simplification working in isothermal mode reducing the analysis time significantly. In the context of clinical diagnosis, the main application is related to exhaled breath analysis (Baumbach et al., 2005, Ruzsanyi et al., 2005, Westhoff et al., 2007, Bunkowski et al., 2009a, Bunkowski et al., 2009b, Maddula et al., 2009, Junger et al., 2010). There are other studies in wine (Camara et al., 2013, Marquez-Sillero et al., 2012) and olive oil characterization (Garrido-Delgado et al., 2011b).

Another hyphenated technique consist on coupling IMS and mass spectrometry (IMMS). While the connection GC-IMS is relatively easy due to ambient operational conditions, the IMMS requires considering that MS works in vacuum conditions. Nevertheless, nowadays there are available several configurations of IMMS (Borsdorf et al., 2011, Kanu et al., 2008). The coupling allows the identification of the ionized molecules of the IMS. There is a widespread application in the scope of this technique, among of them, proteomics (Zolla et al., 2007, Wang et al., 2010), metabolomics (biomarkers) (Pluskal et al., 2010, Fenn and McLean, 2008)and final product quality control(Strege et al., 2008, Zhang and Li, 2010).

1.4. Summary

Because of its portability, its fast response and easy handling, IMS devices are a promise alternative/complement to consolidate techniques. IMS instruments can be adapted to operate in real-time, on-line and/or point of care conditions. The applications of IMS comprise different fields among of them explosive and illicit drug detection, clinical, food industry, pharmaceutical.

This chapter has summarized the IMS dynamics in order to understand how the IMS spectra are produced. The IMS spectra datasets include different non desirable issues as non-linear behaviors, lack of sensitivity, ion charge competition and limit of detection in mixtures, etc. In order to face the complexity of data sets, intelligent signal processing is needed for overcoming the above described issues.

This thesis is mainly focused in the spectra from standalone spectrometer, thereby there is not going to be present any hyphenated techniques. It is remarkable to also face up real-time and on-line IMS capabilities due to it is expected to lose some information that is necessary to be enhanced through signal processing techniques.

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