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Dopants and gas modifiers in ion mobility spectrometry

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Abstract

The ion mobility techniques, including the most commonly used drift-tube ion mobility spectrometry (IMS) and differential mobility spectrometry (DMS), are used successfully for the detection of a wide range of organic compounds in the gas phase. In order to improve detection quality, admixtures are added to gas streams flowing through the detector. Dopants mostly prevent the ionization of interfering chemicals however, better detection may be also achieved by shifting the peaks in the drift-time spectra, enabling ionization of analytes with low proton affinities and, thus, facilitating photoionization. Fundamental information about ion-molecule reactions including the role of dopants is presented. The term 'gas modifiers' refers to substances that influence the ion transport by changing the mobility of ions without changing the chemistry of the ionization. The mechanism of the gas modifier's interaction with an analyte in ion separation in drift tube IMS and DMS is explained in this paper.

Keywords: Ion-molecule reactions, ion mobility spectrometry, alternative reactant ions, detection of hazardous materials, dopants, gas modifiers

1. Introduction

Ion mobility spectrometry (IMS) is an analytical technique that is used for the fast analysis of gas mixtures containing organic compounds. The main advantages of this technique are the low limits of detection (limits of detection lower than 1 ppb), short response time, and the possibility of conducting selective measurements. Due to these qualities, IMS has been successfully applied for testing food products, analysis of exhaled air, and the detection of pollutants, industrial chemicals, explosives, chemical warfare agents, and drugs [1,2]. In IMS, the ions formed under atmospheric pressure in ion-molecule reactions are distinguished based on the study of their movement in an electric field. Traditionally, the separation is achieved using drift tube detectors (DT-IMS), but differential ion mobility spectrometry (DMS) also known as field asymmetric ion mobility spectrometry (FAIMS), aspiration ion mobility spectrometry (AIMS) and travelling wave ion mobility spectrometry (T-wave IMS) are also used [3,4]. DT-IMS and DMS are most often used IMS technologies. Our future considerations will be limited to these technologies.

More than four decades of IMS development has brought many different design solutions to ion mobility spectrometers, but nevertheless, the drift tube spectrometers are still the most often used. DT-IMS allows for the determination of ion mobility by measuring the time the ion needs to traverse the length of the drift tube in the electric field [5]. The principle of operation of DT-IMS is similar to the principle of the time-of-flight mass spectrometer (TOFMS). In time-of-flight mass spectrometers, ions with a certain kinetic energy are injected into the area without the electric field and they move at a constant speed that is proportional to the square root of their energy in a vacuum. The dependence of the ion current on the time (time-of-flight spectrum) is measured by the collector. In DT-IMS, the ions produced in the ionization source region are transferred to the drift tube, which is filled with a buffer gas at a

relatively high pressure. Velocities of the ions in the drift tube are proportional to the applied electric field. The scheme of the ion separation process in DT-IMS is shown in Figure 1a.

Fig. 1.

Recently, new apparatus, including those for DMS, have been developed and commercialized that have various applications for the detection and characterization of ions in the gas phase [6–9]. In DMS, the ions are distinguished based on differences in their mobilities in electric fields of high and low intensity. The dependence of ion mobility on the electric field is characteristic for the fields of high intensity, and the increase (or decrease) of ion mobility observed with the change of the field strength can be used to identify the analyte. The principle of ions separation in DMS is shown in Figure 1b.

The constructional benefits of DMS include significant simplification of the design of the analyzer, which is achieved by elimination of the shutter grid and the set of the electrodes forming the electric field. In addition, the currents generated by the positive and negative ions can be measured at the same time as ions are transported through the analyzer only in the gas stream in which ions of both polarities are present. DMS detectors can be miniaturized as a result of applying MEMS technology, which is impossible in conventional IMS due to the decrease in sensitivity and the resolving power with the reduction in size of the detector [10,11]. Information obtained from the DMS spectrum, *i.e.*, dependence of ion current on the compensation voltage, can be used for quantitative and qualitative analysis similarly to the drift-time spectra obtained from DT-IMS. Table 1 summarizes the information on the performance of DT-IMS and DMS/FAIMS analyzers.

Table 1

In many practical applications of IMS, appropriate admixtures are added to the gases passing through the detectors. In order to clarify the nomenclature and to facilitate understanding of the content of this article, these substances are divided into two groups – dopants and gas modifiers. The term dopants refers to the substances that are introduced into the stream of gas flowing through the detector, which change the course of the ion-molecule reactions, and in particular the substances forming the so-called alternative reactant ions. The substances affecting ion transport without changing the chemistry of the ionization are called modifiers. In most cases, dopants are introduced into the IMS instrument in order to suppress the ionization of interfering substances and to selectively ionize the analytes. Modifiers are introduced directly into the buffer gas in the drift region changing the mobility of the ions. The concentrations of the admixtures added to the gases flowing through the IMS detector are typically much higher than the concentration of the analyte. Dopants are introduced at concentrations at ppm levels, while the typical concentrations of the analytes are a thousand times smaller. The concentration of the modifiers may be greater than 1000 ppm. Introducing of dopants and gas modifiers into gas streams flowing through IMS detectors is a crucial technical problem. Concentrations of these substances may influence the peaks positions and affect quantitative characteristics of detection. Therefore, in many analytical applications, it is necessary to ensure the stability of the concentration of the admixture. Permeation standards constructed from vials covered by membranes are often used as sources of dopants [79,86]. Furthermore, a more sophisticated systems, e.g. based on injection of admixture with piezoelectric elements [46] are applied. Many studies and papers have been devoted to gas doping and modifier using in IMS. The most important mile stones of these studies are shown in the scheme in Figure 2.

Fig. 2.

The last review article on the use of dopants in IMS was published in 2008 [12]. Many new research results have been described in the following years, and we noted the need to update information on the use of the dopants and modifiers based on these new reports. We present the operation mechanisms of dopants and modifiers, and we review their applications in analytical practice.

2. Ionization of chemical compounds in IMS

An important stage in the measurements using IMS is the transformation of the analyte molecules into their ionic form. Sample ionization in the IMS detector goes through several stages, including primary ionization, which takes place under the influence of physical factors (*e.g.*, UV radiation β^-), and the ionization of the sample components through a series of ion-molecule reactions. The use of different ionization methods often leads to different final ion products [13–15], which implies that the effectiveness of the IMS analysis can be increased by selection of the appropriate ionization methods. The most commonly used ionization source in IMS is radioactive ^{63}Ni due to the stable production of reactant ions, high efficiency of ionization, simplicity of operation, and low noise [5]. However, due to restrictions relating to radiation safety and the problems with storage and transport, radioactive sources are increasingly being replaced by other elements that provoke the gas ionization. Alternative ionization techniques include UV ionization, corona discharge ionization, thermal ionization, matrix-assisted laser desorption/ionization (MALDI), and electrospray ionization (ESI), which is used for ion mobility spectrometry coupled to mass spectrometry [16,17]. The ESI method is particularly useful for the analysis of non-volatile organic compounds from samples in the liquid phase.

Usually the reactant ions are produced continuously in the ionization region, and then transferred by the electric field along the ionic reactor. When the molecules of the analyte or another component of the sample are not present in the carrier gas, reactant ions pass through the reaction region and do not participate in the ion-molecule reactions. The obtained drift-time spectra contain only the reactant ions peaks. The presence of sample components in the reaction region leads to collisions between their molecules and the reactant ions. As a result of these interactions, complex ions or transition states are created [5]. The stability of created ions can be very different. For many analytes that are effectively detected using IMS, the formation of stable ions occurs in practically every collision of the reactant ion with the analyte molecule. The ionization efficiency is determined by the so-called collision rate constant [18]. For the efficiency of chemical ionization, the important parameter is the proton affinity (PA). For compounds with a relatively high value of PA (higher than 840 $kJ \cdot mol^{-1}$ [19]) , *e.g.*, ammonia, amines, and organophosphates, the ionization efficiency is very high and does not depend on the PA value. In this case, the concentration of the produced ions depends on the process kinetics, and the reaction rate constant has a value close to the value of the collision rate constant. The ionization efficiency of the compounds with lower PA, *e.g.,* ketones and alcohols, is highly dependent on the proton affinity, and the process of creation of their ions is controlled thermodynamically [19].

The most important issues related to the chemistry of ion-molecule reactions are discussed below to facilitate the understanding of the mechanisms related to the application of dopants.

Ionization in the positive mode of detection

Hydronium ions $H_3O^+(H_2O)_n$ are the dominant reactant ions in pure carrier gas, *i.e.*, nitrogen and air in the positive mode of detection. The reactant ions collide with analyte molecules, which leads to the proton transfer reactions [5]:

$$H^+(H_2O)_n + M \leftrightarrow MH^+(H_2O)_n^* \quad (1)$$

$$MH^+(H_2O)_n^* + Z \leftrightarrow MH^+(H_2O)_{n-1} + H_2O + Z \quad (2)$$

where M is the analyte molecule and Z is a third body.

In the first step of this process, a transition state is created. Its excitation energy is transferred in a collision with a neutral molecule, Z, resulting in detachment of the water molecule. The result of the reactions (1) and (2) is the creation of the ion containing a molecule of the analyte, which is called the protonated analyte molecule or the monomer ion. When the concentration of the analyte increases, the dimer ions M_2H^+ are also created. It is also possible to create trimers and higher ions, but their decomposition is too fast to measure their mobility in the drift tube at ambient pressure. It should be noted that not only the analyte molecules can participate in ion-molecule reactions, but also interferents can take part in the proton transfer reaction, making detection of the analyte difficult. However, it is possible to control the composition of the reactant ions by adding a dopant to the carrier gas. This approach allows for ionization of only the selected components of the sample, and this simplifies the interpretation of the spectrum. When the dopant is present in the reaction region of the detector, the ionization course of the analyte is as follows:

$$H^+(H_2O)_n + D \leftrightarrow DH^+(H_2O)_{n-1} + H_2O \quad (3a)$$

$$DH^+(H_2O)_m + D \leftrightarrow D_2H^+(H_2O)_{m-1} + H_2O \quad (3b)$$

$$D_2H^+(H_2O)_k + M \leftrightarrow DMH^+(H_2O)_k + D \quad (4a)$$

$$DMH^+(H_2O)_k + M \leftrightarrow M_2H^+(H_2O)_k + D \quad (4b)$$

where M is the analyte molecule and D is the dopant.

Hydronium ions are converted to the alternative reactant ions in the reactions (3a) and (3b). Equations (4a) and (4b) show the processes of forming the analyte ions. The reaction (3a) corresponds to the proton transfer reaction, and may be further classified as substitution reaction. Product ions observed in the drift-time spectra in the case of the doped carrier gas may contain dopant dimer ions D_2H^+, dimer analyte ions M_2H^+, and asymmetric dopant dimers DMH^+. Under normal conditions, the concentration of the dopant is relatively high, which is why the hydronium reactant ions $H^+(H_2O)_n$ and the monomer dopant ions DH^+ are not observed. The degree of hydration of particular ions depends on the properties of the constituent molecules, as well as on the temperature and humidity of the gas in ionic reactor.

Ionization in the positive mode of operations in IMS is generally seen as the effect of interactions between hydronium ions and analyte molecules. Typically, this interaction involves the transfer of a proton from a hydronium ion to the molecule of the component of the sample. Other mechanisms of ionization are also possible. Particularly important are the processes of adduct formation or charge transfer observed, *e.g.*, for NO^+ ions [20,21]. These processes can be used to ionize compounds with low PA values.

Ionization in the negative mode of operation

Production of negative reactant ions is more complicated than the production of positive ions. In air, the dominant negative reactant ions are hydrated oxygen ions, $O_2^-(H_2O)_n$. Ions containing molecules of carbon dioxide, ozone, carbon oxides, and hydrated OH^- radicals are also observed. All these ions have similar mobilities and form one peak in the drift-time spectrum. When the analyte molecules are introduced into the reaction region, the ionization is achieved by the charge transfer reaction from oxygen ions (Equation 5), adduct formation (Equation 6), or the proton abstraction (Equation 7) [22,23].

$$O_2^-(H_2O)_n + M \leftrightarrow M^- + n(H_2O) + O_2 \qquad (5)$$

$O_2^-(H_2O)_n + M \leftrightarrow MO_2^- + n(H_2O)$ (6)

$O_2^-(H_2O)_n + M \leftrightarrow (M\text{-}H)^- + n(H_2O) + HO_2$ (7)

The formation of adducts is the dominant reaction when the concentration of the analyte is high. The course of the reaction is strongly dependent on the analyte concentration, temperature, and humidity in the reaction region of the IMS detector. The choice of reaction course is determined by the acidity of the proton in analyte molecule. At low acidity, the adduct is stable and the corresponding peak is visible in the spectrum. If the acidity of the proton increases, proton abstraction is observed [23].

When chlorine or chlorine derivatives are present in the drift-time spectra, Cl_2^- or Cl^- ions appear, while in the presence of nitric oxide and ammonia, NO_2^- ions are created [24]. In the presence of nitrogen oxides produced in the corona discharge (CD) area, other peaks of ions with a more complex structure are also observed [25]. Creation of NO_2^- ions, which are less reactive, can be minimized by increasing the distance between the electrodes in the CD ionization method.

When the carrier gas is pure nitrogen, electrons are the charge carriers, which can cause the ionization of chemical compounds with relatively high electron affinity (EA). Common processes are the dissociative and associative capture:

$e^- + M \rightarrow M_1 + M_2^-$ (8a)

$e^- + M \rightarrow M^-$ (8b)

3. Dopants and alternative reactant ions

In order to optimize conditions of detection of a given compound using IMS, it is necessary to select a suitable source of ionization, as well as the polarity and the operating temperature of the detector. The addition of an appropriate dopant to the carrier gas to control the ionization process is a very effective way of improving the selectivity of detection.

Furthermore, the dopants allow lower limits of detection to be reached. Dopants can cause a significant increase in the effectiveness of creation of the analyte ions and can help to reduce the complexity of the signal by suppressing the formation of impurities ions. Sometimes, dopants enable the ionization of the analytes with low proton affinity. Dopants can be classified according to different criteria that lead to the production of ions and the expected effect of doping, *e.g.*, the charge of detected ions and the ion-molecule reaction mechanism. In this article, dopants are divided into groups according to their potential use, *i.e.*, dopants suppressing the ionization of interferents, dopants shifting the peaks in the drift-time spectrum, and dopants enabling the ionization of analytes characterized by low PA values.

3.1. Dopants suppressing the ionization of interferents in the positive mode of operation in IMS

Due to the low detection limits in IMS and its sensitivity to the presence of many organic compounds, drift-time spectra have a complex structure that makes it difficult to obtain good analytical data. Therefore, it is necessary to find a solution to minimize the effects of the matrix [26]. The solution to this problem would be to add a small amount of admixture (dopant) into the reaction region at an appropriate concentration [27]. The importance of using dopants is that produced alternative reactant ions interact with the analyte and interferents in a different way to that of the regular reactant ions. When the dopant is not present in a carrier gas, the charge is shared between the analyte and the interfering substance. Their peaks appear in the drift-time spectrum, as shown in Figure 3a. When a properly selected dopant is present in the carrier gas, it reacts with the analyte, but does not react with the interferents (Figure 3b). As a result, the interferents do not form ions and their peaks are not present in the drift-time spectrum. Ammonium, acetone, and chloride ions are usually used as alternative reactant ions in order to improve the selectivity of the detection of certain

compounds in the positive and negative modes of operation. The reason is that the particles forming the alternative reactant ions have high electron or proton affinity. Only those compounds that are characterized by PA or EA values that are greater than those of the applied reactant ions may be ionized and detected. In the case of the positive mode of operation in IMS, it is important to select dopants with a PA value lower than that of the analyte and greater than that of the interferent.

Fig. 3

Ammonia

As already mentioned, the selectivity can be controlled by introducing a dopant in order to change the chemistry of ionization. Ammonia, when used as a dopant, produces clusters based on the NH_4^+ ion, which transfer the proton only to the compounds of greater PA. It can be used to eliminate interferences resulting from the presence of various organic compounds for the detection of, for example, chemical warfare agents (CWA), explosives, and drugs [28]. When the ammonia is introduced into the carrier gas, hydrated ammonium ions, which are alternative reactant ions, are formed [12]:

$$(H_2O)_nH^+ + NH_3 \rightarrow (H_2O)_{n-x}NH_4^+ + xH_2O \qquad (9)$$

When the ammonia concentration is relatively high, dimerization occurs and the monomer peak and the dimer peak appear in the drift-time spectrum. The dimerization reaction can be described by equation (10):

$$(H_2O)_nNH_4^+ + NH_3 \rightarrow [(H_2O)_{n-x}(NH_3)NH_4]^+ + xH_2O \qquad (10)$$

For the first time, in 1978, ammonia was added to the carrier gas in the IMS detector to selectively ionize amines [26]. The results of these studies show that ammonia effectively suppressed ionization of interferents from the solvent.

Ammonia has been successfully used as a dopant for optimizing detection conditions for CWA from a group of organophosphorus compounds. The use of ammonia as a dopant is of great importance in the elimination of false alarms [2]. The main product of the reaction occurring between the reactant ions and analyte is the dimer $(CWA)_2H^+$. Ionic products containing molecules of ammonia are also created, *e.g.*, $(CWA)H^+(NH_3)$ and $(CWA)_2H^+(NH_3)$. Vapors of various CWA, including nerve gas, blister agents, choking agents, and lachrymators, were detected with the IMS using corona discharge and ammonia as a dopant [29]. CWA analysis using proton-transfer-reaction mass spectrometry (PTR/MS) and ammonia as a dopant has also been conducted [30].

Another important group of compounds detected with IMS and ammonia as a dopant are drugs. IMS in positive mode is applied for the detection of alkaloids, like morphine and noscapine that are determined using a carrier gas doped with ammonia [31]. Ammonia was also used as a dopant in studies on using mixtures of different carrier gases (air, nitrogen, helium, neon, argon, carbon dioxide, nitrous oxide, and sulfur hexafluoride) doped with a small, constant amount of admixture of ammonia or methylene chloride for selective detection of drugs and explosives in the positive and negative modes of IMS [32].

As a general rule, compounds with high electronegativity, *e.g.*, explosives, are well detected in the negative mode of operation of IMS, while electropositive compounds, *e.g.*, drugs and amines, are detected based on the analysis of the drift-time spectra for positive ions. In some cases, the detection of explosives is also possible in the positive mode of IMS, and drugs in the negative mode [32,33]. Effects of temperature and the concentration of dopant on the drift-time spectra of triacetone triperoxide (TATP) and hexamethylene triperoxide diamine (HMTD) using a gas chromatograph in combination with ion mobility spectrometry and mass spectrometry (GC-IMS-MS) were tested [34]. Ammonia and dichloromethane were used as dopants in positive and negative modes, respectively. These studies demonstrate that

the detection of traces of TATP was possible only in the positive mode, and sensitive detection of HMTD was possible in both positive and negative modes. It was found using IMS-MS method and ammonia as dopant [35], that ionization products were a TATP-ammonia adduct of m/z 240 and a smaller ion of m/z 58. With increasing ammonia concentration, the content of the TATP-ammonia adduct decreased and the smaller ion dominated in the spectrum. Ammonia and dichloromethane have also been used as dopants in extensive studies of various explosives [36]. Created from the molecules of these compounds, alternative reactant ions interacted with the analyte vapors to form the positive and negative ions, respectively. The tested sample of explosives included trinitrotoluene (TNT), 1,3,5-trinitro-1,3,5-triazacyclohexane (RDX), ethylene glycol dinitrate (EGDN), nitroglycerin (NG), pentaerythritol tetranitrate (PETN), ammonium nitrate (NH_4NO_3), HMTD, and TATP.

Acetone and higher ketones

Acetone belongs to the group of compounds that have a moderate value of PA (lower than the PA value of ammonia); however, it can be successfully used to suppress the formation of impurities ions the ionization of many interferents. PA values for selected representatives of the given groups of compounds are listed in Table 2.

Table 2. [37–39]

Like ammonia, acetone is commonly used as a dopant for the detection of organophosphorus compounds (OPC) and the elimination of interferences in the spectrum caused by organic substances from the atmosphere, *e.g.*, hydrocarbons, alcohols, esters and others [12,40]. The two main groups of OPC are pesticides and CWA. For most of the organophosphorus compounds, the PA values are greater than 900 $kJ \cdot mol^{-1}$ [37].

With a relatively high concentration of acetone in the carrier gas, the dominant type of ions are acetone proton-bound dimers. In the drift-time spectra, hydronium ions or protonated molecules of acetone are not observed. Only the compounds with PA values higher than the acetone PA are ionized. When the acetone dimer interacts with the analyte molecule M of high PA, a substitution reaction occurs, as follows [5,41]:

$$(CH_3COCH_3)_2H^+(H_2O)_n + M \rightarrow (CH_3COCH_3)MH^+(H_2O)_{n-1} + CH_3COCH_3 + H_2O \quad (11)$$

Probably the oldest information about the application of acetone as a dopant to optimize the detection of CWA can be found in a USA patent from 1985 [42]. The effectiveness of the use of acetone as a dopant was examined by analyzing the OPC detection selectivity in the presence of a complex mixture of VOCs [27]. The results showed that the use of alternative reactant ions increases the selectivity of detection. Interesting results were presented by comparing the responses of analyzers for various dopants [43]. The IMS detector enabled the detection of alcohols, aldehydes, and other volatile organic compounds of low PA values when $H^+(H_2O)_n$ were the reactant ions. When dopants, including acetone, were used, the analyzers generated the signal only in the case of compounds of PA higher than the PA of the dopant [43].

Pesticides belonging to the group of organophosphorus compounds can be determined using the IMS detector with acetone as a dopant. It is also possible to mix the alternative reactant ions to improve selectivity. Better results are obtained than with the use of a single dopant. Dimethoate was determined with IMS using acetone as a dopant. Other dopants, were also used, *e.g.*, ammonia, ethanol, ether, and methanol. The best resolution and the highest peaks were observed after the addition of a mixture of ammonia and acetone for dimethoate [40].

Higher ketones are also used as dopants in IMS [44]. Acetone was, for example, replaced with 5-nonanone to separate ammonia, monomethylhydrazine (MMH), and

hydrazine (HZ) [45]. Acetone is not a suitable dopant for this purpose since it forms ionic complexes with HZ. In addition, ions formed by the potential interferents have mobility values that are similar to the acetone dimer ions. 4-Heptanone was also used as a dopant in the positive mode to detect vapors of alkanolamines, including monoethanolamine (MEA), 3-amino-1-propanol (PRA), 4-amino-1-butanol (BuA), and 5-amino-1-pentanol (PEA) [46]. The use of 4-heptanone effectively inhibited the ionization of the interfering substances from the diesel fumes, thus providing a good separation of alkanolamines.. Acetone and 4-heptanone were also used as dopants to detect alkanolamines in the presence of interfering substances, *e.g.*, ammonia, Freon 22, and diesel fuel. The separated peaks were visible in the spectrum when 4-heptanone was used as a dopant, which was not possible with the use of an acetone dopant [44].

Acetone was tested also as dopant in DMS [47]. The effect of suppressing of impurities ions formation was not studied but it was found that admixture of dopant has significant influence on separation of peaks in differential mobility spectrum.

Amides and amines

Nicotinamide is a dopant that is used in commercial drugs detectors based on IMS technology. Vapors of the sample components are introduced into the detector together with air doped with nicotinamide at a concentration of several ppm. The dopant plays a double role in the analyzer. First, it is a calibration standard for determining the mobility [48]. The reduced mobility coefficient for nicotinamide is 1.85 $cm^2V^{-1}s^{-1}$, and ions created by this compound almost cannot be hydrated, and thus, the water vapor concentration does not significantly affect the position of the corresponding peak in the drift-time spectrum. Identification of analytes is based on the value of the drift-time compared to the peak of nicotinamide. The second role of this dopant is to suppress the ionization of interferents. As in

previous cases, substances with a lower PA cannot be ionized during interactions with the alternative reactant ions. The illegal drugs are usually alkaloids with sufficiently high values of PA to take part in the proton transfer reactions, and consequently to form positive alkaloid ions. Nicotinamide is used as a dopant for the detection of cocaine, heroin, d-methamphetamine, and tetrahydrocannabinol. The presence of nicotinamide usually results in the stabilization of the large drug ions, while in the absence of nicotinamide, fragmentation of the ions formed from molecules of the drugs is enhanced [49]. IMS is increasingly being used to detect trace amounts of drugs in postal packages and imported products, and on suspects clothing and luggage, *etc*. Hair samples have also been analyzed using IMS and nicotinamide as a dopant. This method showed sufficient sensitivity only for externally contaminated hair samples (usually taken from drug traffickers). For pure samples of hair collected from, for example, drug addicts, satisfactory results were not obtained [50].

Nicotinamide is not only used to detect drugs. They are also used as dopants for the detection of explosives. Amides form reactant ions, and therefore, enable detection of explosive which are in the form of a peroxides [51].

Biogenic amines detection is of great importance in food quality control and medical tests. Particularly important are low molecular weight amines, such as trimethylamine (TMA) and triethylamine (TEA). Detection of these compounds with an IMS detector with air as the carrier gas is difficult because the drift time of ions formed from molecules of TMA and TEA are close to the drift time of hydronium reactant ions. In order to avoid the peaks overlapping, doping with higher amines is used, *e.g.,* n-nonylamine, which is used as the dopant in medical tests carried out with IMS [52]. Additionally, this method improves the selectivity of detection, since the high PA value of n-nonylamine reduces the generation of ionic products from interfering substances that are present in the samples [53–55]. IMS studies with and without the use of a dopant (n-nonylamine) for the detection of biogenic amines, including

spermidine, spermine, putrescine, and cadaverine, demonstrated that the determination of biogenic amines without the use of n-nonylamine is possible; however, the risk of spectral interferences occurs. In cases in which a high concentration of the dopant was used, the biogenic amines could not be identified, which was related to the competitiveness of the processes of direct ionization of n-nonylamine and the analyte [56]. Furthermore, a standard clinical diagnostic method for bacterial vaginosis (BV) was compared to the mucus tests carried out with IMS using n-nonylamine as a dopant. Compatibility between the results of the clinical method and the data obtained from the use of IMS was excellent [57].

Organophosphorus compounds

In some cases, n-nonylamine may be replaced with triethyl phosphate (TEP). This compound does not decompose in reaction with the water vapor contained in air, and therefore, it is easier to maintain its constant concentration in the carrier gas stream [58]. IMS with the carrier gas doped with TEP can be used to detect inflammation in animals [59]. The performances in measurements of biogenic amines by three ion mobility spectrometers operating under different conditions (ion sources, temperature, moisture content, type of reactant ions, and the structural characteristics of the drift tube) were also compared [60].

TEP is also used as a dopant for food quality control. Determination of biogenic amines in samples of bread with IMS using TEP as a dopant, which controls the ionization process, is fast, inexpensive, and objective. Different types of bread contain biogenic amines, especially volatile amines, including TMA, putrescine, and cadaverine, and their level increases with the progressive deterioration of bread [61].

Organophosphorus compounds are also used to detect and measure the concentration of ammonia. Due to the high PA value of ammonia its detection with IMS is characterized by very low limits of detection and a relatively wide dynamic range [33,62]. The particular

advantage of the IMS technique is that it allows ammonia to be measured *in situ*. Typically, measurements of ammonia in the atmosphere are based on a combination of different techniques, which extends the time of analysis. An IMS technique was used to measure the concentration of ammonia in a subtropical environment with high humidity [63]. The sample was introduced to the detector through the semipermeable membrane to remove moisture and large particles. Dimethyl methylphosphonate (DMMP) used as the dopant reacts with ammonia forming cluster ions [$(DMMP)_2(NH_4)^+$] of much lower mobility than the conventional reactant ions. The disadvantage of this method is that the signal intensity depends on the concentration of DMMP [63].

3.2. Dopants for negative mode of operation in IMS

The need to find a method for the detection of explosives has been one of the major causes of development of the IMS technique. Many explosive materials are characterized by a relatively high electronegativity, and therefore, they can be detected in the negative mode of operation in IMS. In order to improve the sensitivity and to avoid disturbances caused by interferents, dopants forming alternative reactant ions that provide a selective response are used. Dopants for the negative mode of IMS are volatile organic compounds that react in the ionization region producing alternative reactant ions, *e.g.*, Cl^-, Br^-, NO_3^-, NO_2^- [41,64–67].

When analyzing explosives with IMS, chlorinated hydrocarbons are introduced to produce chloride reactant ions in the ionization region. The most commonly used dopants are methylene chloride and dichloromethane. Bromide and iodide reactant ions can also be used to form adducts of the decomposition products of the explosives, but this method is not used regularly. Several halogenoalkanes were evaluated in a wide range of concentrations as dopants in the detection of TNT. The study [65] also determined the composition of reactant ions, as well as the TNT product ions, in the IMS detector. Dichloromethane has also been

successfully used as a dopant for the detection of explosives in the negative mode of IMS. $M \cdot Cl^-$ ions formed from molecules of explosive and chloride ions are more stable than the $M \cdot NO_3^-$ adducts observed when clean air is used as a carrier gas [35,36].

3.3. Dopants used for shifting peaks in the drift-time spectrum

Distinguishing ions based on the drift-time spectrum can be difficult due to the possibility of peaks overlapping. Adding a dopant to the carrier gas can be an effective way to increase the distance between the peaks in the spectrum and to ensure the correct identification of ions, even in the presence of interferents [64,68]. Shifting of peaks in the drift-time spectra is observed in the positive and negative modes of IMS. Most commonly used dopants for this purpose are water, ammonia, acetone, and halogenated chemical compounds. Dopants selected from the group of substituted phenols have proven to be effective in improving the selectivity in IMS for the detection of acidic gases in the air, *e.g.*, HF, HCI, Cl_2, NO_2, SO_2, and carbonyl sulfide. Acidic gases have a high EA and readily form negative ions, but their mobilities are similar to the mobility of standard reactant ions generated in the air. The two most widely used and most effective dopants are methyl salicylate (MS) and 2-hydroxyacetophenone (2-HAP). $(MS)O_2^-$ ions have lower mobility than the ions generated in the presence of acidic gases. Introduction of an acid gas to the reaction region in the IMS detector in the presence of the dopant causes the appearance of the peaks at lower drift times [12,68]. Interesting research that characterized the ions generated by dinitroalkanes in the positive mode of IMS in the presence of water, dichloromethane, and ammonia as dopants was described in [69]. It appears that dopants can be successfully used not only to achieve greater control of the ionization process and to obtain a more intensive response, but also to provide better separation of the peaks in the drift-time spectrum. Crown ether (18-Crown-6) was used as a dopant to shift the peaks in the drift-time spectrum in the

analysis of products of proteins digestion by trypsin using a multidimensional IMS-MS [70]. In this approach, non-covalent ion complexes of peptide-crown are formed by electrospraying the mixture in the gas phase. When analyzing the resolving power of DT-IMS, it should be noted that it is determined not only by the composition of gases but also by the operating temperature of the detector [71].

3.4. NO_x – dopants allowing for ionization of analytes with low PA values

Ionization of the analyte in the positive IMS mode may occur as an effect of the interaction with $NO^+(H_2O)_n$ ions. Such ions are formed when nitrogen monoxide (NO) is introduced into the ionization region. The course of the analyte ionization with the use of these ions is significantly different from the typical course for a proton transfer reaction with hydronium reactant ions. The reactions that occur most often are charge transfer reactions (12), adduct formation (13), and hydride abstraction (14) [72].

$$M + NO^+ \leftrightarrow M^+ + NO \quad (12)$$

$$M + NO^+ \leftrightarrow (M*NO)^+ \quad (13)$$

$$M + NO^+ \leftrightarrow (M\text{-}H)^+ + HNO \quad (14)$$

The choice of the reaction that occurs is related to the properties of the sample molecule M. Due to the possibility of ionizing analytes over different ionization mechanisms, nitric oxide is capable of ionization of most organic compounds, even of high IP and PA values. For example, substances with a high ionization energy do not take part in the charge transfer reaction, and for such substances, adduct formation or hydride abstraction are observed. Molecules with high electron density form adducts. Alkanes or molecules containing heteroatoms and aromatic compounds are ionized through hydride abstraction [72]. It should be noted that chemical ionization of hydrocarbons using nitric oxide may be obtained not only by hydride abstraction but also by different reaction pathways resulting in

the formation of different ion products [73,74]. The results of a detailed study of the composition of positive ions observed in air polluted by several straight and branched alkanes (C_5-C_6) and cyclohexane were described in [75]. The properties of the ion complexes were studied based on the observation of interactions with several reactant ions, including NO^+. The small PA values that characterize the alkanes are considered to be the cause of the poor response in IMS. It is related to the low efficiency of the proton transfer reactions from reactant ions, *i.e.*, $(H_2O)_nH^+$. In order to change the kind of reactant ions, the carrier gas introduced into the reaction region is doped with NO. This enables ionization of analytes with small PA values, such as alkanes and aromatic hydrocarbons. Research of the detection of compounds with a high PA has also been conducted. For example, the IMS-MS system with NO as the dopant was applied for determination of 2,4-lutidine, di-tert-butylpyridine (DTBP), and DMMP at various concentrations of NO, and the effect of temperature on the ionization efficiency was also studied [72].

The presence of NO^+ ions in the reaction region of IMS is inextricably linked with the use of corona discharge as the ionization source [76]. It has been shown that the use of such sources is effective to ionize volatile organic compounds with relatively low PA [21,77]. An interesting technical solution is to place a special chamber with corona discharge electrodes in the gas line before the inlet of the IMS detector [78]. The only purpose of this device is the production of nitrogen oxides used as dopants. A major advantage of this approach is the very short time of turning the presence of the dopant in the carrier gas on and off.

3.5. Dopants used in UV ionization detectors

In addition to the sources containing radioactive isotopes or sets of electrodes for a corona discharge, another ionization method commonly used in IMS is photoionization with ultraviolet (UV) radiation [79,80]. The earliest report on the use of photoionization ion

mobility spectrometry appeared in 1983 [81]. For ionization, a krypton lamp that emitted photons with an energy of 10.0 eV was used. The radiation from the lamp was perpendicular to the axis of the drift tube. Later, a photoionization ion mobility spectrometer using a discharge lamp filled with hydrogen (photons energy 10.2 eV) was constructed [82]. An ion mobility spectrometer with a radioactive ionization source and UV, as well as a multi-capillary column, was used for the determination of methyl tert-butyl ether (MTBE) and monoaromatic compounds (benzene, toluene, and m-xylene) in water [13]. The use of an ion mobility spectrometer equipped with two sources of ionization, *i.e.*, lamp for atmospheric pressure photoionization (APPI) and corona discharge system, allowed for a significant enrichment of the analytical information contained in the drift-time spectra [83]. In recent years, prototypes of DMS detectors equipped with an APPI ion source have been designed [80]. Regardless of the type of detector to facilitate the analytes photoionization, dopants are used in both positive and negative modes of detection, usually at low concentrations (~2 ppm).

As a general rule, photoionization in the positive mode of operation of IMS is used to detect chemical substances with an ionization potential (IP) that is lower than the photon energy. The addition of a suitable dopant enables ionization of a compound in which the IP is higher than the photon energy. One of possible mechanisms for photoionization in a positive mode using a dopant is the adduct formation, which then takes part in the interaction with another molecule of the analyte [84]:

$$D + h\nu \rightarrow D^+ + e^- \quad (15)$$

$$D^+ + M \rightarrow D^+M \quad (16)$$

$$D^+M + M \rightarrow [D^+M_2]^* \rightarrow (D\text{-}H) + M_2H^+ \quad (17)$$

where D is the dopant molecule and M is the analyte molecule.

In [80], a detailed description of the possible mechanisms of forming the protonated DMMP molecules as a result of photoionization using benzene as a dopant can be found. In addition, research on improving the quality of pesticides detection using APPI-DMS and benzene, chlorobenzene, and anisole as dopants has been described [84].

To use photoionization for the detection of chemical substances (*e.g.*, explosives) that have high values of IP and EA, the investigation can be carried out in the negative mode of operation of IMS. In this case, negative ions are produced by capturing the electrons produced during photoionization of molecules with a low IP.

The molecules characterized by low ionization energy and relatively high electron affinity can produce their own negative ions after prior photoionization. Particles with ionization energies greater than the maximum ionization energy of the photon need the proper dopant to provide electrons that form the negative reactant ions by interaction with the components of the carrier gas. The mechanism of the production of the reactant ions for this case can be described by the following series of reactions [79]:

$$\text{dopant} + h\nu \rightarrow e^- \quad (19)$$

$$O_2 + e^- \rightarrow O_2^- \quad (20)$$

$$O_3 + e^- \rightarrow O_3^- \quad (21)$$

$$O_2^- + nH_2O \rightarrow O_2^-(H_2O)_n \quad (22)$$

$$O_3^- + nH_2O \rightarrow O_3^-(H_2O)_n \quad (23)$$

$$O_2^-(H_2O)_n + O_3 \rightarrow O_3^-(H_2O)_m + O_2 + (n\text{-}m)H_2O \quad (24)$$

$$O_3^-(H_2O)_n + CO_2 \rightarrow CO_3^-(H_2O)_m + O_2 + (n\text{-}m)H_2O \quad (25)$$

Ionization of the analyte by ions generated in reactions (22–25) occurs through adduct formation, charge transfer, or proton abstraction. In studies carried out with a DMS detector with a photoionization source, it was possible to detect sulfur hexafluoride and nitrogen

oxides in the negative mode using acetone as a dopant [80]. Photoionization in the negative mode of IMS with use of dopants (dopant-assisted negative photoionization; DANP) is useful for the detection of ammonium nitrate fuel oil (ANFO), TNT, dinitroxydiethylnitramine (DINA), and PETN [79]. In this case acetone, benzene, toluene, n-hexane, and ethanol can be used as dopants. For each of the mentioned analytes, only one dominant ionic product is created. DINA and PETN can be directly ionized by attaching a CO_3^- ion forming ion adducts $DINA{\cdot}CO_3^-$ and $PETN{\cdot}CO_3^-$. $[TNT\text{-}NO]^-$, and $[TNT\text{-}CH_2]^-$ ions are generated at high concentrations of O_3. The DANP method using acetone as a dopant was applied for the detection of TNT, RDX, ANFO, and black powder [85]. The electrons from the ionization of acetone take part in the reactions (20) and (21). In next interactions $O_2^-(H_2O)_n$ and $CO_3^-(H_2O)_n$ ions are generated (reactions (22-25)). The relative contents of these ions depended on the direction of gas flow through the ionic reactor. The measurement system allowed rapid changes in the direction of flow, which enabled comparison of the drift-time spectrum for the two types of reactant ions, and as a result, additional analysis information was obtained.

3.6. Quantitative aspects of using dopants

Many reports determining the optimal concentration of dopant in either the positive or negative mode have appeared. In [34] and [35], which were mentioned in the previous section, the impact of the concentration of dopant (ammonia) on the detection of TATP was examined. It has been shown that the concentration of ammonia is essential for the process of chemical ionization. When ammonia is added to the ionization region in small quantities, $TATP{\cdot}NH_4^+$ adducts are formed; however, when the ammonia concentration increases, the content of these adducts decreases.

TNT ionization using CHCs (chloromethane, dichloromethane, trichloromethane, carbon tetrachloride, and chlorobenzene) as dopants in a wide range of concentrations was

also tested [65]. Ionization of the analyte with CHCs ions is characterized by interesting quantitative aspects. In the presence of CHCs in the ionization region, the efficiency of alternative ions formation depends on the reaction rate constant for the electron attachment of a given CHC. Creating clusters composed of neutral particles of the dopant and reactant ions adversely affects the ionization efficiency of TNT.

Analysis of the quantitative aspects of the application of dopants was presented in [86]. The use of acetone as a dopant can reduce the analytical signal when the analyte and the dopant PA are similar. This phenomenon was observed during detection of MTBE. For compounds with high values of PA (*e.g.*, DMMP), the efficiency of dimer ion formation does not depend on the concentration of the dopant. The same results were obtained when the higher ketones were used as dopants [87]. The explanation of the lack of dependence between dimer peak intensity and dopant concentration is not simple due to the fact that, in this case, not only ionization kinetics must be considered but also the ion transport phenomena affecting concentrations of reactant and product ions.

4. Gas modifiers for IMS

Modifiers are substances that are introduced directly into the IMS drift region in very large quantities (often more than 0.1% vol.) in order to selectively change the ion mobilities without changing the mechanism of their formation. In general, the separation is achieved by selective clusters formation of analyte ion and gas modifiers. The properties of these clusters have a significant impact on their mobility. The separation obtained with gas modifiers, enables the determination of complex mixtures of enantiomers, increases the range of observed changes in the drift-time spectrum, and improves the resolving power (peak capacity) [39,88-90].

4.1. Admixtures that change the drift conditions in DT-IMS

IMS is an analytical technique that allows separation of chiral compounds in the gas phase. This can be achieved based on the differences in the collision cross-sections during the movement of ions through the drift region filled with the chiral gas. The chiral modifier interacts differently with enantiomers resulting in changes of their mobilities, which enables their separation. Investigations were conducted for two chiral modifiers, S-(+)-2-butanol and R-(-)-2-butanol, which were added to the drift gas [90]. In both cases, shifting and separation of the methionine enantiomer peaks in the drift-time spectrum was achieved. Separation of the peaks for other components of racemic mixtures was also possible using the same chiral modifier. Separations of the enantiomer ions of atenolol, tryptophan, serine, threonine, glucose, and penicillamine in their racemic mixtures were also carried out effectively. Mobilities of α-amino acids, tetraalkylammonium ions, 2,4-lutidine, DTBP, and valinol were determined for 2-butanol used as a modifier gas [89]. In the same publication the processes of the analyte-modifier clusters formation were also described. In order to separate protonated caffeine (CH^+) and glucosamine (GH^+), an ethyl lactate (EL) admixture was used, which was effective due to the lower mobility of the $EL{\cdot}GH^+$ cluster than the $EL{\cdot}CH^+$ cluster. Theoretical calculations explain the results of the experiment, *i.e.*, there was a greater clustering tendency of GH^+ than that of CH^+ [91]. Ketone vapors were introduced into the drift gas to separate ammonia from hydrazine [38]. The best separation was obtained when 5-nonanone was used as a gas modifier. The interaction of the modifier with the analyte ion in this case results in the formation of ketone-hydrazine complexes. Based on the analysis of the drift time, as well as the results of mass spectrometry, the authors showed that the number of ketone molecules attached to the protonated molecule of the analyte is equal to the number of protons available for attachment. Ion mobilities of diamines (arginine, histidine, lysine, and atenolol) using different modifiers, *i.e.*, EL, nitrobenzene, 2-butanol, and tetrahydrofuran-2-

carbonitrile, have also been studied [92]. Introducing the modifier vapors to the buffer gas resulted in ion-modifier clusters formation. The efficiency of generating clusters is related to the size of the analyte molecule and the tendency to form intramolecular bridges. The introduction of modifiers causes only small changes in diamine ion mobilities due to the presence of intramolecular bridges that inhibit modifier molecule binding to the positively charged ion. The dependences of nitrobenzene [93] and ammonia [28] admixtures on the ion mobility of ions formed by amines have also been studied. When nitrobenzene was added to the buffer gas, the analyte ion mobility decreased as an effect of the formation of large analyte ion-nitrobenzene clusters. Minor changes in tetraalkylammonium and DTBP ion mobilities were explained by the presence of steric hindrance. In the case when ammonia was added to the buffer gas, the ion mobilities of amine derivatives and 2,4-lutidine decreased due to the formation of large analyte ion-ammonia-water clusters. Methanol was used as a gas modifier to separate tetratriethylammonium, asparagine, and valine, whose peaks overlapped in the IMS spectrum, which was effective due to the different inclinations of these compounds to form clusters with methanol [94]. Various gas modifiers (*e.g.*, 2-butanol, acetonitrile, 2-ethylhexyl salicylate, ethyl lactate, 4-methyl-2-pentanone, propionitrile, acrylonitryle, isovaleronitrile, triethylamine, aniline, and nitromethane) have been used in determining CWA and toxic chemicals in positive and negative modes of IMS, which helped to reduce the amount of false-positive errors [39]. It is also possible to use the drift gas modifier in the negative IMS mode. Chlorinated hydrocarbons were applied as admixtures to the drift gas for the detection of sulfur, the component of black powder [95]. The mobility of generated ions (S_3^-) is similar to the mobility of negative oxygen reactant ions. The use of chlorinated hydrocarbons as dopants to the carrier gas was not effective because of decreasing efficiency of sulfur ionization. For this reason admixtures were introduced into the drift gas.

Concentrations of modifiers influenced the drift time of chlorinated molecules while the position of S_3^- peak in spectrum was stable.

Besides creating the ion clusters, the presence of admixtures in the drift gas can create conditions for the ion-molecule reactions. As a result of these reactions, ionic products of different stabilities can be formed, which has a significant impact on the shape of the drift-time spectrum [96].

4.2. Modifiers used in DMS

It is assumed that the explanation of the dependence of mobility on the intensity of electric field can be based on three different models of interactions of ions with the neutral molecule [9]: rigid sphere scattering, long-range ion-dipole attraction, and clustering. Different effects are dominant for the different types of ions. However, the formation of ion-neutral molecule clusters is the most popular mechanism for explaining the relationship between the electric field intensity and the ion mobility in DMS [97]. It has been shown that the addition of a polar modifier to a DMS detector produces clusters whose composition depends on the ion energy, which is a function of electric field strength. For this reason, the ion mobilities at high and low electric fields intensities vary. Clusters containing analyte ions and neutral molecules of modifier are formed at low electric field intensity, while disintegration of the clusters occurs in a high electric field. The presence of the modifier increases the difference between the mobilities of ions in low and high electric fields, and consequently, increases the peak capacity and resolving power. The most popular polar modifiers used for improving peak capacity of DMS detectors are isopropanol, methanol, acetone, acetonitrile, and ethyl acetate [97–99]. The effect of the polar modifier (isopropanol) on the peak capacity was tested with DMS-MS [97]. The study included the detection of 70 compounds (different amines of m/z 112–735) in the positive mode and 24 acidic compounds of m/z 129–825 in the negative

mode of operation in DMS. However, it should be noticed that the effect of increasing peak capacity can be obtained not only by broadening the compensation voltage range resulting from using the modifiers. It is also possible to decrease peaks widths which depend on the ions' residence time in separation gap of DMS detector [98].

Detection of 140 substances with DMS was studied for few different modifiers [99]. Results of these research demonstrated very impressive increase of peak capacity for transport gas containing modifiers. Moreover, it was shown that data obtained from DMS with the modifier is orthogonal to retention times measured with liquid chromatography. Orthogonality of the data from DMS and mass spectrometer was also good, especially for low molecular weight ions. The position of the peak in the differential mobility spectrum depends on concentration of the gas modifier. The study performed for cylindrical FAIMS detector [100] indicates that most intensive changes of peak position as well as peak amplitude take place for modifier concentrations in the range of 0 to 0.1 % vol. For modifier concentrations higher than 1 % the saturation effect is observed, i.e., peak positions are relatively stable.

Detection of biomarkers of DNA damage was performed with DMS detector with isopropanol, 1-butanol and ethyl acetate gas modifiers [101]. It was shown that saturation effect is usually obtained at modifier concentration of about few % vol., but the dependence of peak position on modifier concentration varies for different pairs analyte-modifier. Theoretical analysis of obtained results was based on ion-modifier clustering kinetics. The DMS detector coupled with the mass spectrometer was used for liquid extraction surface analysis (LESA-DMS-MS) in which narcotic substances and their metabolites in *postmortem* samples were detected [102]. The application of an organic gas modifier (acetonitrile, acetone, and methanol) allowed the separation of 30 drugs and metabolites, including cocaine, morphine, and tramadol.

Water vapor is polar component of carrier gas that is always inherent in IMS. Its presence in DMS detectors influences the peaks positions in differential mobility spectra. Investigations carried out for OPCs [103] have shown that positions of peaks generated by protonated molecules of analytes change significantly when water concentration is higher than 50 ppm. It results in spacing of peaks. Such phenomenon is not observed in the case of dimer OPCs ions. Water is not used as the modifier which is intentionally added to the carrier gas. However, its presence in environmental samples influences the quality of DMS detection, especially possibility of proper analyte identification [104,105].

Non-polar aromatic compounds have also been used as modifiers [106]. Detection of toluene, ethylbenzene, p-xylene, trimethylbenzene, and naphthalene was performed with DMS using benzene as a gas modifier. These analytes can form a π - π bond with the modifier. The peak area of compounds with low values of PA (toluene and ethyl benzene) significantly decreased with increasing concentrations of benzene, and the peak area of compounds with high values of PA significantly increased when the modifier was introduced into the carrier gas. Increasing the peak area of the compounds with a high PA in DMS using ^{63}Ni as the ionization source is explained by the improvement in the efficiency of ion transport through the ion separator.

5. Summary

There are many different design solutions for IMS detectors; however, the drift tube spectrometers are still the most widely used. DMS detectors, which demonstrating numerous advantages, especially when combined with MS or GC columns, are increasingly being used. Due to the growing interest in ion mobility spectrometry as an analytical method, intensive research on the optimization of the conditions of measurement is being carried out. An

effective method of improving the detection with IMS is the use of admixtures in the gas flowing through the detectors.

The selectivity and sensitivity of measurements carried out with IMS depends mainly on the processes taking place in the reaction region of the detector. Adding an appropriate dopant to the carrier gas allows control of the reactant ions' composition, which is particularly important in the analysis of multicomponent mixtures containing both analytes and interfering substances. Properly selected dopants allow the creation of alternative reactant ions that ionize only selected components of the sample. Whether a given component of the sample is ionized is mostly determined by its proton (PA) or electron (EA) affinity. Some of the dopants can enable ionization by creating relatively strongly bonded ion adducts. This mechanism of ionization allows detection in both negative and positive modes of operation in IMS, which makes the detection of aromatic compounds with very low PA possible. Dopants are also used to facilitate the photoionization of analytes in both positive and negative modes. Chemical compounds with an ionization potential (IP) that is lower than the photons' energy are ionized and detected in the positive mode of operation of IMS. Substances with a high IP can be detected in the negative IMS mode, where ion products can be formed by electron capture or by charge transfer. Efficiency of both of these processes can be increased by the application of appropriate dopants.

In order to improve the quality of detection, gas modifiers that are usually placed directly into the drift region are also used. This approach allows the selective change of ion mobilities without changing the mechanism of their formation. In general, the separation is achieved by forming clusters of analyte ions with the gas modifiers. The introduction of modifiers to the drift region enables to distinguish enantiomers mixtures, and increases the peak capacity as well as the resolving power. Modifiers are used in both: traditional DT-IMS and DMS.

Information on dopants and modifiers applications in order to detect different analytes with DT-IMS and DMS are summarized in Table 3.

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Table 1. Comparison of DT-IMS and DMS methods.

PROPERTY	DT-IMS	DMS/FAIMS
principle of operation – identification of analyte ions	measurement of an ion's drift time through a defined distance	measurement of compensation voltage, which is determined by non-linear dependence between the ion velocity and the electric field
limit of detection	sub-ppb range	sub-ppb range
resolving power	higher than in DMS	lower than in DT-IMS
part of ions produced in reaction section used for generation of analytical signal	less than 1% in typical DT-IMS, 50% in Fourier Transform IMS	differential mobility spectrum is measured in scanning mode; for monitoring of the presence of one defined kind of ions, the effectiveness is determined by separation voltage
simultaneous detection of positive and negative ions	impossible using single detector	possible
complexity and cost of detector	high – especially for DT-IMS of high resolving power	much lower than in DT-IMS
complexity and cost of electronic circuits working with the detector	medium	higher than in DT-IMS
possibility of miniaturization	very limited	Micro Electro-Mechanical Systems (MEMS) detectors are in use
working with mass spectrometers	possible after complex adaptation of IMS detector and mass spectrometer	possible after simple modifications

Table 2. Values of proton affinities of selected chemicals.

Number	Chemical	Chemical family	Values of proton affinity [kJ· mol^{-1}]
1	pyridine	aromatic amines	930.0 [37]
2	nicotinamide	amide	918.3 [37]
3	*n*-nonylamine	amines	912.0 [37]
4	dimethylmethylphosphonate	organophosphorous compounds	898.0 [39]
5	5-nonanone	ketones	853.7 [38]
6	ammonia	-	853.6 [37]
7	hydrazine	-	853.2 [38]
8	4-heptanone	ketones	853.0 [37]
9	methyl acetate	esters	821.6 [5]
10	2-butanol	alcohols	815.0 [39]
11	acetone	ketones	812.0 [5]
12	1-hexene	alkenes	805.2 [37]
13	1-hexyne	alkines	799.8 [37]
14	benzene	aromatics	750.4 [5]
15	water	-	691.0 [37]
16	methane	alkanes	543.5 [37]

Table 3. Application of dopants and gas modifiers in detection of various analytes with DT-IMS and DMS techniques.

	IMS mode	mechanism of interaction	detected analytes	references
dopants for DT-IMS				
ammonia	positive	control of proton transfer, clusterization	amines, CWA, narcotics, explosives	[5,12,26,29–36,69]
acetone	positive	control of proton transfer	OPC, CWA, pesticides	[27,40,42–44,86]
higher ketones, *e.g.,* 5-nonanone, 4-heptanone	positive	clusterization, control of proton transfer	monomethyl hydrazine, hydrazine, alkanolamines	[12,44–46,87]
amides, *e.g.,* nicotinamide	positive	control of proton transfer	narcotics	[48–50]
	negative	production of stable adducts	CWA, peroxide explosives	[51]
amines, *e.g.*, *n*-nonylamine	positive	control of proton transfer, clusterization	biogenic amines	[53–57,86]
OPC, *e.g.,* TEP, DMMP	positive	control of proton transfer, clusterization	biogenic amines, ammonia	[51,58–63]
halogens	negative	production of stable adducts	explosives, propofol	[32,34,36,41,64–67]
methyl salicylate	negative	selective creation of clusters	acid gases	[5,68]
NO_x	positive	charge exchange, adduct formation, hydride abstraction	analytes with low PA, *e.g.*, alkanes and aromatic hydrocarbons	[21,72–78]
ɔants for DMS				
matics, *e.g.*, ɪzene, orobenzene, sole	positive	charge exchange, proton transfer (photoionization)	pesticides	[84]

acetone	negative	electron capture, charge exchange (photoionization)	sulfur hexafluoride, nitrogen oxides	[80]
acetone	positive	control of proton transfer	CWA	[47]
gas modifiers for DT-IMS				
chiral modifiers: S-(+)-2-butanol R-(-)-2-butanol	positive	changing of collision cross-section for ions moving in drift section, analyte-modifier cluster formation	stereoisomers	[90]
ketones, *e.g.,* 5-nonanone	positive	analyte-modifier cluster formation	separation of hydrazines and ammonia	[38]
ammonia	positive	analyte-modifier cluster formation	separation of amine derivatives, and 2,4-lutidine	[28]
nitrobenzene	positive	analyte-modifier cluster formation	separation of amine derivatives	[92,93]
ethyl lactate	positive	analyte-modifier cluster formation	separation of atenolol, arginine, histidine, lysine, caffeine, and glucosamine	[91,92]
methanol	positive	analyte-modifier cluster formation	separation of TTEA, asparagine, and valine	[94]
gas modifiers for DMS				
polar modiefiers, e.g., isopropanol, methanol, acetone	positive negative	clustering-declustering control	many different compounds, increasing peak capacity	[97–100]
isopropanol, utanol, ethyl tate	positive	clustering-declustering control	DNA damage markers	[101]
ohols, tone, tonitrile,	positive	clustering-declustering control	separation of drugs and metabolites	[102]
ızene (non-ar modifier)	positive	π-π modifier-to-analyte interaction	improvement in the sensitivity and selectivity of DMS for detection of aromatic compounds	[106]

Figure captions

Fig. 1 Scheme of separation of ions in DT-IMS (a) and DMS (b).

Fig. 2. Milestones in application of different types of dopants and gas modifiers in IMS techniques.

Fig. 3. Scheme of charge transfer during ionization without (a) and with dopant (b).