

Review Article

Review: Ion mobility spectroscopy a new method of analysis, its application and reproducibility problems

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Abstract

Ion Mobility Spectrometry (IMS) is a mass-selective technique in which the sample is vaporised, ionised, and with given initial velocity moved along a drift region towards a collector electrode. The drift times (milliseconds, ms) needed by the ions to reach the collector are proportional to their masses: the higher the mass, the longer the drift times. During our evaluation of ion mobility spectrometry in the screening it was found that reproducibility problem may occurred which is solve easily by using some methods, described in this review. Ion mobility spectroscopy is widely use for the drug analysis, hair analysis and other applications.

1. Introduction

The ion mobility spectrometer (IMS) was introduced as an analytical instrument in the late 1960s/early 1970s. The technique was then referred to as plasma chromatography. The principle of IMS is that a sample is being introduced in the instrument, brought into the vapour phase by flash heating, the vapour is ionised and the resulting ions are introduced into a drift tube. Ion mobilities are determined from ion velocities measured in the drift tube at ambient pressure and are characteristic for the analyte. Therefore, they can be used for the identification of substances. However, it is a potentially useful technique in some specific areas and developments went on mainly in military institutions. IMS can also be used as a detector for GC¹.

2. Principles and theory of Ion mobility Spectroscopy

The sample, collected on a filter substrate, is thermally vaporised in the desorber and carried in a stream of dried, filtered, ambient air through the heated transfer line into the ionisation reaction chamber. Ionisation is initiated by high energy electrons emitted from a Ni beta-ray 63 source. Every 20 ms, positive or negative ions are gated with a pulse width of 0.020 ms into the heated drift region. Here the ions move to the collector electrode under the influence of an electric field and against a counter flow of ambient air drift gas. In the positive mode used for drug detection, the drift gas contains trace amounts of nicotinamide (NTA), acting as both calibrant and reactant. The drift time required to reach the electrode is inversely proportional to the characteristic reduced mobilities (K) of the ions and is the means by which the ions are identified^{18, 19}.

In the drift region of the IMS slow ions move in a gas under the influence of an external electric field. Different forces act on the ion: Resistance encountered by gas molecules (both electrostatic and arising from geometry), the diffusive force and the electric field. The electric field drags the ions towards the detector and the average velocity of the ions is proportional to the magnitude of the electric field. The proportionality constant is called the ion mobility K (in cm² V⁻¹ s⁻¹). The movement of ions in IMS is complicated by the presence of the counter flowing gas. The ion is accelerated by the electric field until it collides with a gas molecule. By the collision it loses part or all of its momentum. Then it is accelerated again until the next collision. Therefore, increasing the electric field strength will increase the average velocity of the ion, but increasing the neutral gas density will diminish this effect by increasing the collision frequency and the kinetic energy loss during a collision. Additionally, electrostatic interactions between the ion and the neutral gas molecules are possible.

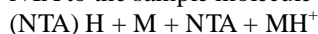
The mobility of ions in IMS was given by Revercomb and Mason^{1,4}:

$$K = (3e/16N) (2/\mu kT) [(1+eff/2)/_D T_{eff}]$$

where e is the ion charge, k is the Boltzmann constant, N is the density of neutral molecules, μ is the reduced mass of the ion-neutral collision pair defined as $\mu = mM/(m+M)$, m is the mass of the ion, M is the mass of the neutral molecule, T_{eff} is the effective temperature of the ions which is normally equal to the neutral gas temperature, $_$ is a correction factor which is generally less than 0.02 for $m < M$, and $_D(T)$ is the eff collision cross section which depends on the effective temperature. The reduced mobility can be used to identify an ion and is defined as $K = (d/Et) (P/760) (273/T)$ Where d is the distance (in cm) from the shutter grid to the electrometer, t is the time (in sec) it takes to travel this distance, E is the electric field strength (V/cm), P is the ambient pressure (Torr), and T is the drift tube temperature (K). In theory, reduced mobilities are independent of the conditions they are measured in, but in practice there are some restrictions to the variations in pressure, temperature and field strength. Also, the drift gas has an influence on the measured reduced mobility¹.

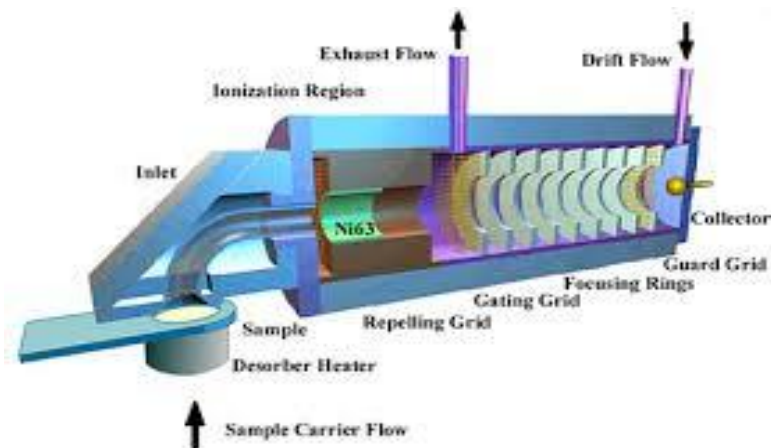
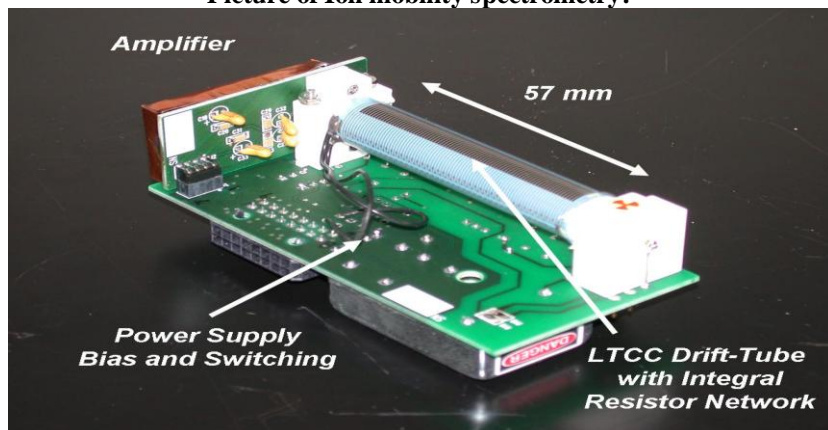
2.1. Ionisation process in Ion Mobility Spectroscopy (IMS)

Drift gas and NTA are constantly flowing in and are being ionised in the ionisation/ reaction chamber when the instrument is in the READY mode waiting for a sample to be introduced. The dominant ion in the READY mode is (NTA) H. In the ANALYZE mode when a sample is introduced, the dominant sample ionisation process is proton transfer from NTA to the sample molecule M:



The above reaction only proceeds if the proton affinity of M is greater than that of NTA. This is the case for most drug molecules which are therefore detectable as MH^+ under Ion scan IMS conditions. Any potential interference with proton affinities less than that of NTA are suppressed¹⁵.

Picture of Ion mobility spectrometry:



2.2. Interpretation in Ion Mobility Spectroscopy

Major advantages of IMS are its sensitivity in the sub-ppb or pg range, its continuous real time monitoring capability, its reasonable price due to instrumental simplicity and the easy automation. The excellent sensitivity of IMS is mainly due to the negligible loss of ions and neutrals to vacuum pumps, the walls of the cell or recombination processes^{1,5}. A major disadvantage of the IMS is its limited linear range. It is relatively easy to overload the IMS and, therefore, sample size must be controlled with care. Another weakness is the response variation that occurs with different background gas compositions and with different sample compositions. The reproducibility of IMS has not been studied extensively. Usually standard deviations of 5 to 25% are reported. Under similar conditions reduced motilities can be reproducible to within 1 to 2 %^{5,6}.

3. Reproducibility problem of ion mobility spectroscopy as encountered during analysis of some drug components

During our evaluation of ion mobility spectrometry in the screening for the abuse of the β -agonist clenbuterol in fattening of cattle it was found that the signals were not reproducible enough to allow quantitative or even semi-quantitative analysis. So that to improve the reproducibility of the signal use a hotplate for the evaporation of the solvent used to transfer the clenbuterol like drug to the TFE filter.

3.1 Methods use to solve reproducibility problems:

For e.g. for clenbuterol

First Study

Calibration curves for clenbuterol were determined twice daily (morning and afternoon) on four days. Amounts of about 5, 10, 20, 30, 50, 100, 200, 300 and 500 ng of clenbuterol were accurately pipetted on a TFE filter using the two standard solutions. The solvent was evaporated at room temperature and the filter was analysed with the Ion scan. For each amount, five replicates were analysed. Maximum amplitude, average amplitude over the total desorption time and average area over the total desorption time of the two clenbuterol peaks were determined. The within-assay was calculated by two-way ANOVA with replicates, between-assay and between-day precisions were calculated from the between-assay and between-day standard deviations. The assay averages for each amount (y ng) were normalised towards a 300 ng standard using the following equation:

$$\text{Normalised value} = (\text{assay average } y \text{ ng}) / (\text{assay average } 300 \text{ ng})$$

The same procedure was used for a normalisation towards a 100 ng standard. After normalisation, again between-assay and between-day precision were calculated¹⁶.

Second Study

Calibration curves for clenbuterol were determined on three different days. Amounts of about 5, 10, 20, 30, 50, 100, 200, 300 and 500 ng of clenbuterol were accurately pipetted on a TFE filter using the two standard solutions. The solvent was evaporated on a hotplate at a temperature of about 55°C before analysis with the Ion scan. For each amount, five replicates were analysed. Maximum amplitude, average amplitude and average area of the two clenbuterol peaks were determined. The within-assay and between-day precisions were calculated by one-way ANOVA. The assay averages for each amount (y ng) were normalised towards a 300 ng standard and a 100 ng standard as described for the first study. By using above two studies it is conclude that ion scan results for the quantitation of clenbuterol are in general not very reproducible. The use of a hotplate for the evaporation of the solvent may help to improve the within-assay variation¹⁶.

4. Common Applications of Ion mobility Spectroscopy

IMS is limited to analytes that can be vaporised under reasonable temperature conditions without undergoing too much decomposition. Major industrial and environmental applications of IMS are the monitoring of toxic chemicals, stack gases and chemicals that are considered hazardous to man or to the environment. For the detection of contra band explosives or drugs no quantitative measurements are required. IMS is particularly suited for these applications, because of the low detection limits and the fact that it operates at atmospheric pressure. Another advantage is that results can be obtained very quickly. IMS is also used for the detection of chemical warfare agents. In the positive mode, where organophosphorous compounds are detected, these instruments use alternate reagent ion chemistry with acetone as the dopant to eliminate interferences. In the negative mode, nerve and blister agents are detected¹. In other fields of applications are the semi-conductor industry (detection of surface contaminants), the identification of trees after stripping of the bark, the monitoring of microbotics in water, the monitoring of anaesthetics in operating rooms and the sensing of petrochemical fuels in soils (using headspace analysis). The coupling of GC and IMS has several advantages: GC can separate the analyte

from other substances in the mixture or from the matrix and brings it into the vapour phase. The IMS functions as a detector with very low detection limits and provides some degree of identification. The IMS has to be adapted and a special interface has to be designed to allow its use as a detector for the GC. Several environmental applications of GC-IMS have been published. IMS can be used for the differentiation between isomers of a compound, because their ions may have different collision cross sections and therefore different mobilities. The differences in collision cross section can arise from differences in geometrical structure, or in the internal charge distribution, or both¹.

4.1 Other Applications of Ion Mobility Spectroscopy in various regions such as drug analysis, hair analysis, etc.:

The primary advantages of IMS are the very short analysis time (~ 5-10 sec), detection limits in the ng to pg range, and the various options for sample introduction, such as: Applying a solution (e.g. an extract) on a filter substrate. Trapping particulate matter or vapours on a filter substrate. Bringing solid samples directly into the desorption chamber.

4.2 Hair Analysis:

Ion scan IMS can be a very rapid and simple tool for the detection of drugs in hair. Ion scan's ability to accept solid samples is of particular interest as a screening method for drugs in hair. Hair samples can be brought directly into the desorber, either as strands clamped into a holder, or as powdered material deposited on a filter substrate. However, two key factors are that:

- The drug of interest must accumulate in hair at sufficiently high levels.
- The intrinsic sensitivity of the instrument for the drug of interest must be sufficiently high. The latter may be negatively affected by the hair matrix itself and/or the presence of other drugs.

The Ion scan proved to be quite effective in detecting cocaine in human hairs at the ng/mg level¹⁵.

5.3 Drug Analysis

Ion mobility spectrometry conditions for the detection of the various drug samples, its components and other biologicals compounds:

Electric field		211 V/cm
Temperatures	Drift	235 °C
	Inlet	282 °C
	Desorber	293 °C
Flows	Drift Gas	300 ml/min
	Carrier Gas	200 ml/min
Materials	Drift Gas	Air (Dry, Purified)
	Carrier Gas	Air, (Dry, Purified)
	Calibrant	Nicotinamide

5. Conclusion

IMS can be a very rapid and simple tool for the detection of drugs in hair. However key factors are that: The drug of interest must accumulate in hair at sufficiently high levels. The intrinsic sensitivity of the instrument for the drug of interest must be sufficiently high. The latter may be negatively affected by the hair matrix itself and/or the presence of other drugs. As a result, the Ion scan proved to be quite effective in detecting cocaine in human hairs at the ng/mg level, but could not detect clenbuterol levels in calf hairs at the pg/mg level. Additional studies on a wider range of drugs and on various intrinsic properties of the Ion scan instrument (reproducibility, signal suppression, matrix interference) are needed to further assess the potentials of IMS in forensic applications.

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