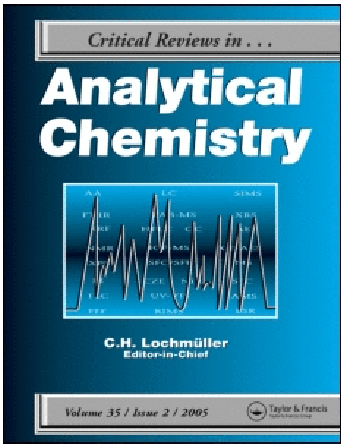

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Advances in Ion Mobility Spectrometry: 1980-1990

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Advances in Ion Mobility Spectrometry: 1980—1990

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I. INTRODUCTION

Ion mobility spectrometry (IMS) was first introduced in the late 1960s as an instrumental technique for detecting organic compounds at trace concentrations in air. Despite certain attractive features of IMS in environmental monitoring and laboratory studies, the growth of IMS from 1970 to 1980 exhibited some disappointing trends as suggested in Figure 1. Interest in IMS declined generally after 1976 by what may be ascribed to a broad disenchantment from unmet expectations and misunderstanding of response characteristics. A new cycle of interest in IMS began 1980 resulting in advances in all aspects of IMS. Additionally, small rugged IMS units suited for operation in hostile environments became available in fulfillment of the purposes originally suggested for IMS. This has occurred through unpublicized developmental programs within military establishments of the U.S. and the U.K.

New IMS instrumentation and refinements in the understanding of ion-molecule chemistry in air have provided IMS with a unique technological niche. A review of progress from 1980 to 1990 may be useful in assessing the current status of IMS and in provoking thoughts regarding future directions for IMS. Discussion of advances is presented in four sections: principles of IMS, instrumentation, ion-molecule chemistry at atmospheric pressure, and applications.

A. Principles of Ion Mobility Spectrometry

In IMS, vapors are drawn into a reaction region (or ion source region, see Figure 2) where ionization occurs conventionally through collisional charge transfer between a reservoir of charge, i.e., the reactant ions and neutral analytes, M. In air at atmospheric pressure, the most abundant reactant ions generated from a beta-emitting source are $(H_2O)_n{*}H^+$ and $(H_2O)_n{*}O_2^-$ which co-exist at near thermal energies in the reaction region. Product ions experience little or no fragmentation and exist commonly as M^+ and MH^+ or M^- and $M{*}O_2^-$ depending on the proton or electron affinities of the neutral vapor species. Ions formed in the reaction region are injected into the drift region by means of an ion shutter. In the drift region, ions move at particular drift times (t_d) through an electric field, E, or *circa* 200 V/cm. For a drift region with a given length, L (cm), the drift time is related to velocity (v_d, cm/s) and ion mobility (K, $cm^2/V{*}s$) through Equations 1 and 2:

$$v_d = L/t_d \tag{1}$$

$$K = v_d/E \tag{2}$$

Ions strike a flat plate detector and a mobility spectrum or plot of detector current (in pA or nA) vs. t_d (usually in ms) is produced. Conse-

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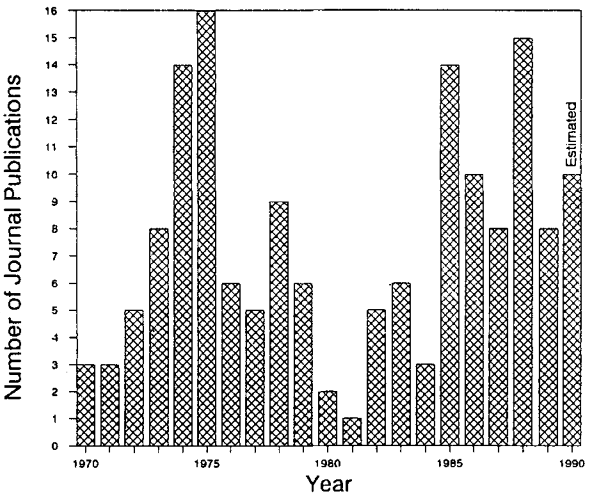


FIGURE 1. Trend in number of journal articles on IMS during the last 20 years. The listing came from computer searches of Chemical Abstracts and manual searches. Conference proceedings and abstracts from presentations were not included.

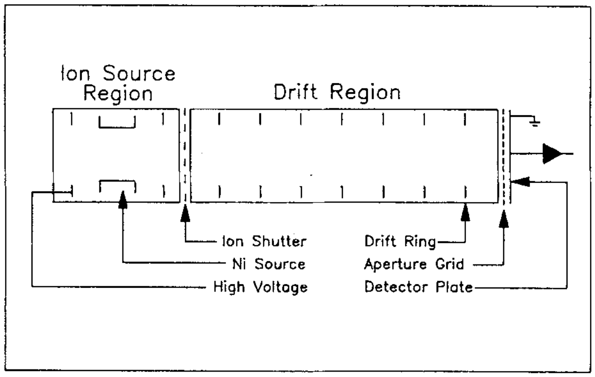


FIGURE 2. Functional components of ion mobility spectrometer drift tubes with a traditional radioactive beta emitting source. Details such as gas flows, inlets, voltage divider electronics, ring dimensions, and designs of shutters and grids were omitted to make the figure generally representative of IMS drift tubes. Some cell designs involve the use of a second ion shutter (not shown) for boxcar integration of spectra.

quently, the basis for selectivity in IMS is differences in drift times for ions as governed by ion mobilities. Drift times are dependent upon temperature and pressure and are normalized to reduced mobility constants, K_o, that are related to molecular properties through the Mason-Shamp equation.[1] In general, the equations for mobility constants are considered well established for small spherical ions but extrapolations to large organic molecules may be somewhat tenuous.[2] Practically speaking, *a priori* quantitative predictions of K_o values for organic molecules are presently impossible with high accuracy. Mobilities are inversely proportional to collisional cross-sections which means that IMS is an ion separator based on size/charge rather than mass/charge as found in mass spectrometers. The selectivity of an IMS system is also influenced by ion formation, but this is not well defined and is discussed below in the section on ion-molecule chemistry at atmospheric pressure.

B. Technology of Ion Mobility Spectrometry

The IMS drift tube or cell is the central element of an IMS instrument and establishes operating characteristics. The bulk of discussion in this review is concerned with advances in drift tubes and ion source chemistry. In addition, supporting electrical or mechanical components are necessary for a fully functional IMS instrument and these include: a high voltage power supply, a circuit for controlling the ion shutter, an amplifier for the detector, and a means to process the signal. In addition, a flow of gas is necessary not as an aid to ion separation but simply for sweeping impurities from the drift tube. A complete block diagram of an IMS including an oven is shown in Figure 3. Although a complete discussion of advances in these components is beyond the scope of this review their significance should not go unmentioned.

For example, the signal processing electronics for early IMS spectrometers were based upon boxcar integration, a rather slow and ineffective method. Availability, cost and performance of microcomputers and digital processing circuitry has made signal collection convenient and powerful. While not universally practiced for processing IMS signals, digital signal averaging (DSA) for signal to noise enhancement allows acquisition of mobility spectra in 0.5 to 5 seconds using 2 to 500+ scans. Consequently, reasonably fast ion-molecule events that occur in the ion source and drift regions can be measured and investigated.

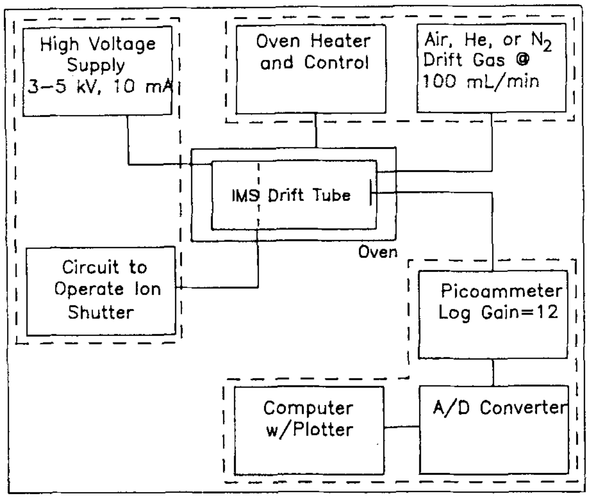


FIGURE 3. Block diagram of an ion mobility spectrometer including signal processing, electronics for operation, and mechanical sub-components.

II. INSTRUMENTATION

A major factor in the renewed interest in IMS has been the proliferation of various drift tube designs, alternate ionization sources, and improved concepts in IMS operation. This has occurred through the use of instruments assembled by individual investigators or by those willing to reconfigure commercial instrumentation. Additionally, parallel developments with commercial IMS systems were spawned by at least six IMS instrument companies. Developments in instrumentation will be described in three sections covering drift tubes, ion sources, and commercial units.

A. Drift Tubes in IMS

Instrumentation for IMS appeared early in commercial form[3] and showed a striking resemblance to designs common to the front end stage of drift tube mass spectrometers which were used to measure mobilities of small ions in vacuum.[4] Although these early designs exhibited adequate detection limits and were fully functional, deleterious memory effects plagued operations. Early drift tubes were too large for use in field studies and, encased in vacuum housings, were rendered somewhat unsuitable for studying new chemical, electronic, or physical configurations.

In 1982, Baim and Hill reported a drift tube design suited for use as a detector for gas chromatography with capillary columns.[5] Low residence times of column effluent in the IMS were achieved by operating the drift tube with unidirectional flow as shown in Figure 4 and memory effects were found to be minimal.[6] The tubes were geometrically similar to existing tube designs and were comprised of alternating layers of insulating rings and conducting rings (i.e., a segmented design). Clearance times were commonly less than 5 s which showed that unwanted memory effects were not intrinsic to IMS. These effects, when observed, were due to mechanical designs or pneumatics of the drift tubes. Evidently, the turbulence created by opposing flows where drift gas entered at the detector plate and carrier gas entered near the reaction region causing prolonged (mostly unacceptable) residence times.

An early concern with segmented drift tubes was the possible electric field perturbations from a step-wise rather than uniform change in potentials inherent with a traditional voltage divider. Guidelines for drift ring dimensions to yield uniform field gradients had been developed and experimentation suggested indirectly that such parameters did not seriously affect resolution.[7] Nonetheless, concerns persisted, and practical considerations with cell construction were aggravated by the large number of components necessary to assemble a segmented drift tube. This contributed to an increased cost in the manufacture and repair of IMS instruments. Carrico, et al. described[8] an IMS drift tube constructed from a ceramic cylinder coated with a semiconducting film on the inner surface as shown in Figure 5. This film, when cured at elevated temperatures, behaved much like a continuous voltage divider. Therefore, an analogous voltage gradient could be established throughout the tube length. This approach had been applied previously in other drift tubes in Japan.[9] Comparison of mobility spectra between the conventional segmented tube and this novel continuous tube design showed that effects over field imperfections in segmented drift tubes were not measurable. The simplicity of this design was potentially compromised by difficulties in ensuring reproducible, even fields through uniformly thick coatings. One commer-

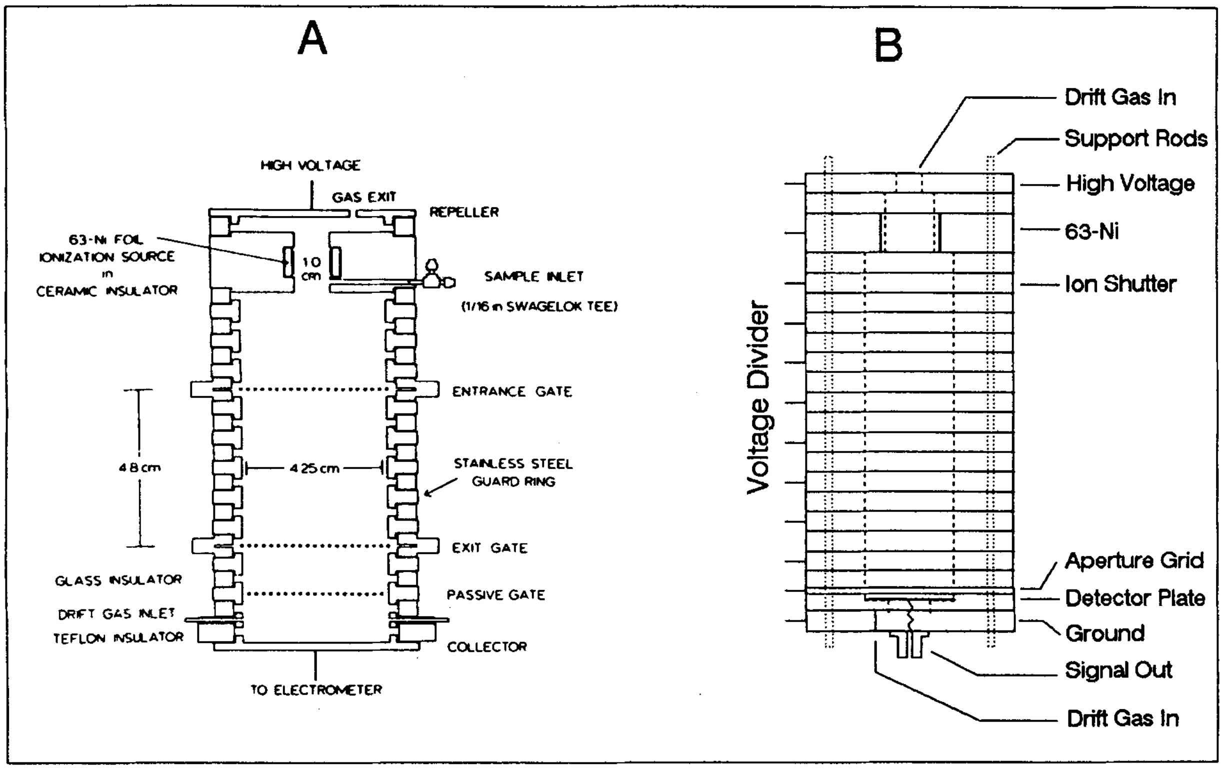


FIGURE 4. Drift tube designs from Washington State University (A) and New Mexico State University (B). Both tubes were operated with a unidirectional flow of drift gas to minimize residence times and memory effects. (From Baim, M. D. and Hill, Jr., H. H., *Anal. Chem.*, 54, 38, 1982; Leasure, C. S., Vandiver, V. J., Rico, G., and Eiceman, G. A., *Anal. Chim. Acta,* 175, 135, 1985. With permission.)

cial IMS (vide infra) is based on this design suggesting successful control over the manufacturing step. Nonetheless, the segmented tube remained the most common if not the most elegant design for IMS drift tubes.

An impediment to current and prospective IMS investigators had been an uncertainty regarding the effect of electric fields or voltages on specific components in the IMS drift tube. In recent studies, the influence on resolution and detector intensity from electric fields was systematically evaluated for each component in an IMS drift tube.[10] The drift region of an IMS cell was surprisingly tolerant of voltages, and effects on resolution were comparatively small, perhaps inconsequential so long as some voltage was imposed on the drift ring. In contrast, the electric field between the aperture grid and detector plate was preeminent in governing peak shape and resolution. Aperture grids made from conventional wire meshes attenuated ion current through ion collisions and contributed through microphonics to noise in signals. However, the aperture grid was essential in obtaining suitable peak shape in mobility spectra as shown in Figure 6. The other region of significance was that between adjacent wires in the ion shutter. Low fields did not block ion penetration and high fields caused ion collection (and annihilation) on the wires. These findings suggested that wide flexibility in fields and geometry in IMS cells may be possible.

A noteworthy occurrence during the 1980s was the development of IMS drift tubes of unconventional designs and of traditional designs in modified forms. In one concept, Blanchard[11] found that electric fields could be oscillated to selectively enrich and isolate ions of a certain mobility, which was reminiscent of ion trap concepts in mass spectrometry (Figure 7). Conceivably, a particular ion could be enriched to enhance detection limits or isolated ions could be fragmented and analyzed for improved capabilities in ion identification.

Two configurations of conventional drift tubes

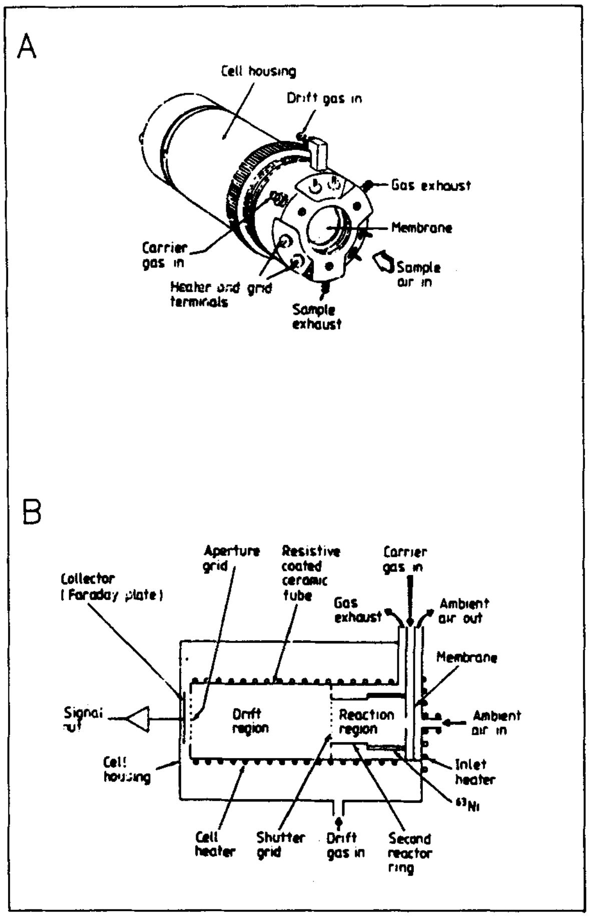


FIGURE 5. A continuous guard ring design for drift tubes in ion mobility spectrometry in which a ceramic tube coated with semiconducting film on the inner surfaces serves to apply a voltage gradient in the drift region. The assembled drift tube and a cross section are shown in Frames A and B respectively. (From Spangler, G. E., Vora, K. N., and Carrico, J. P., *J. Phys. E*, 19, 191, 1986. With permission.)

which received attention were twin drift tubes and multiple IMS systems. Twin drift tubes were contemplated (and patented[12]) early in IMS history and stem from interests to obtain mobility spectra for positive and negative ions simultaneously from the same ionization source. A practical obstacle to twin drift tubes included the operation of detector plates at elevated potentials. Only recently have twin drift tubes been successfully demonstrated[13] but virtually no literature reports exist. In contrast, multiple IMS systems in which several drift tubes are coupled in a linear ion path along with a decreasing voltage gradient have been demonstrated[14] in an at-

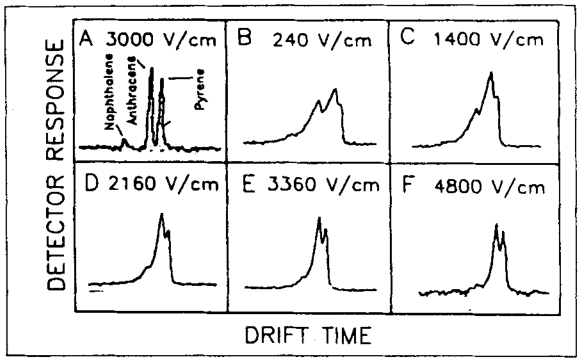


FIGURE 6. Mobility spectra for a polycyclic aromatic hydrocarbon mixture with (A) and without (B-F) an aperture grid. Electric fields were present between the aperture grid to detector (A) and between a regular drift ring and detector (B-F) in the absence of an aperture grid. From Eiceman, G. A., Vandiver, V. J., Chen, T., and Rico-Martinez, G., *Anal. Instrum.*, 18, 227, 1989. With permission.

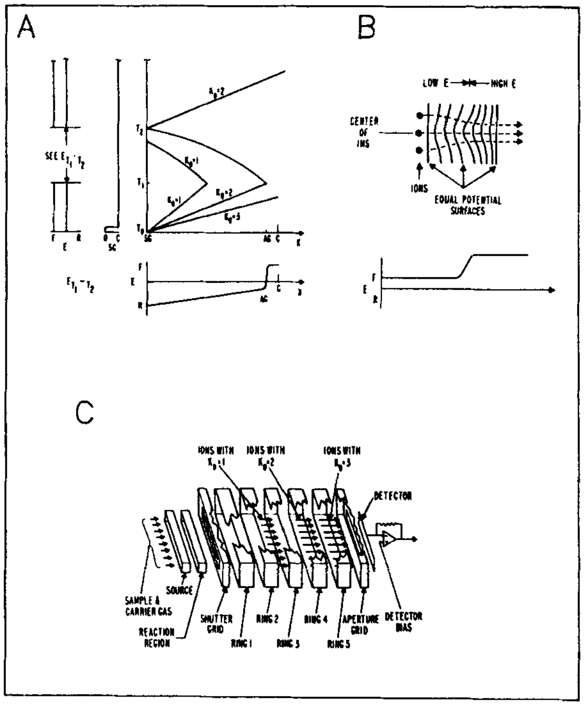


FIGURE 7. Schematic diagrams representing nonconventional control of fields proposed by Blanchard. In Frame A, ion with $K_o = 1$ is isolated while those with $K_o = 2$ and 3 are removed from the drift region by collisions with the wall, shutter, or aperture grid. In Frame B, the focus of ions to the center of the drift region through nonuniform fields is depicted. In Frame C, Blanchard's rectangular design for an IMS drift tube is shown. From Blanchard, W. C., *Int. J. Mass Spectrom. Ion Processes*, 95, 199, 1989. With permission.

tempt to improve specificity of detection. The concept of multiple IMS instrumentation is based upon isolation of a given reactant ion in a first drift region and introduction of that ion into a reaction region with selected vapor composition, where a second regime of ionization chemistry occurs. Ions from this second reaction region are analyzed in a second drift region in a manner which is functionally equivalent to triple quadruple mass spectrometers, except for operating pressures. A critical requirement of this design is the isolation of neutral vapors in individual regions of the IMS and this is not trivial with conventional drift tube designs at atmospheric pressure. One possible way of suppressing neutral vapor diffusion in multiple IMS is the use of separate laminar gas flows for each region. However, this concept has not been experimentally validated.

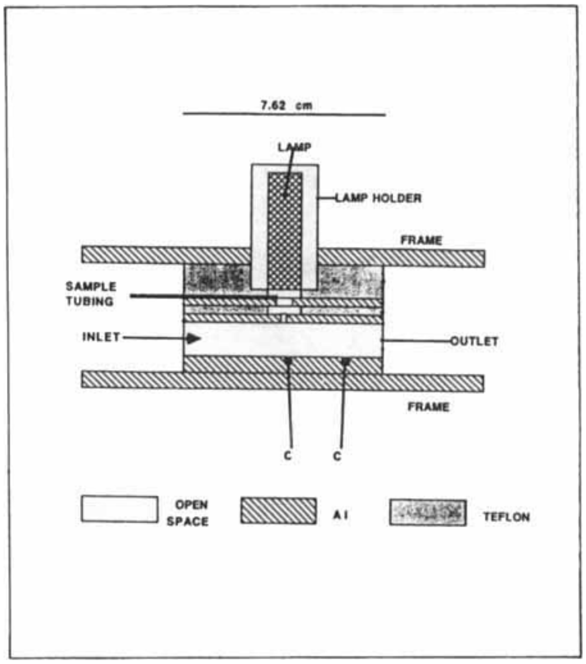


FIGURE 8. A cross section diagram of the ion mobility spectrometer (filter) for continuous monitoring of an ion of given mobility. IOns introduced at 90° angle into a flowing gas stream entering at the inlet strike the detector base and register a signal on wires (C) at given distances from the orifice. These distances correspond to certain ion mobilities. From Smith, J. P., unpublished manuscript. With permission.

Several groups have pursued the development and application of IMS for routine monitoring of specific substances through the development of specialized drift cell designs. Smith[15] demonstrated IMS cells based upon continuous monitoring with ion separations occurring laterally in space. In his design (Figure 8), ions are separated based on mobilities through a dependence on field and gas flow in a manner atypical of conventional mobility spectrometers. Moreover, control of field/flow variables permits continuous monitoring of a given mobility without advanced electronics. The advantages of this cell are clearly size, expense, and ease of assembly. Disadvantages including poor resolution appeared in the early prototype but a fair and exhaustive assessment of this cell has not occurred.

The concept of simple, disposable, IMS cells that would be useful for atmospheric monitoring came from European military development programs in the form of a cell called DICE, detection by ion combination effect[16] and a mini-ionization cell (MIC) developed for chemical agent detection.[17] In DICE and MIC, a continuous flow of gas is drawn through the cell and only ions of a certain mobility diffuse against the flow, and register a signal. The operation of these two units are analogous to an electronic cut-off filters and thus might be considered as a mobility filter rather than an ion separator. Nonetheless, these cells have rapid response, are inexpensive and represent novel configurations for IMS technology.

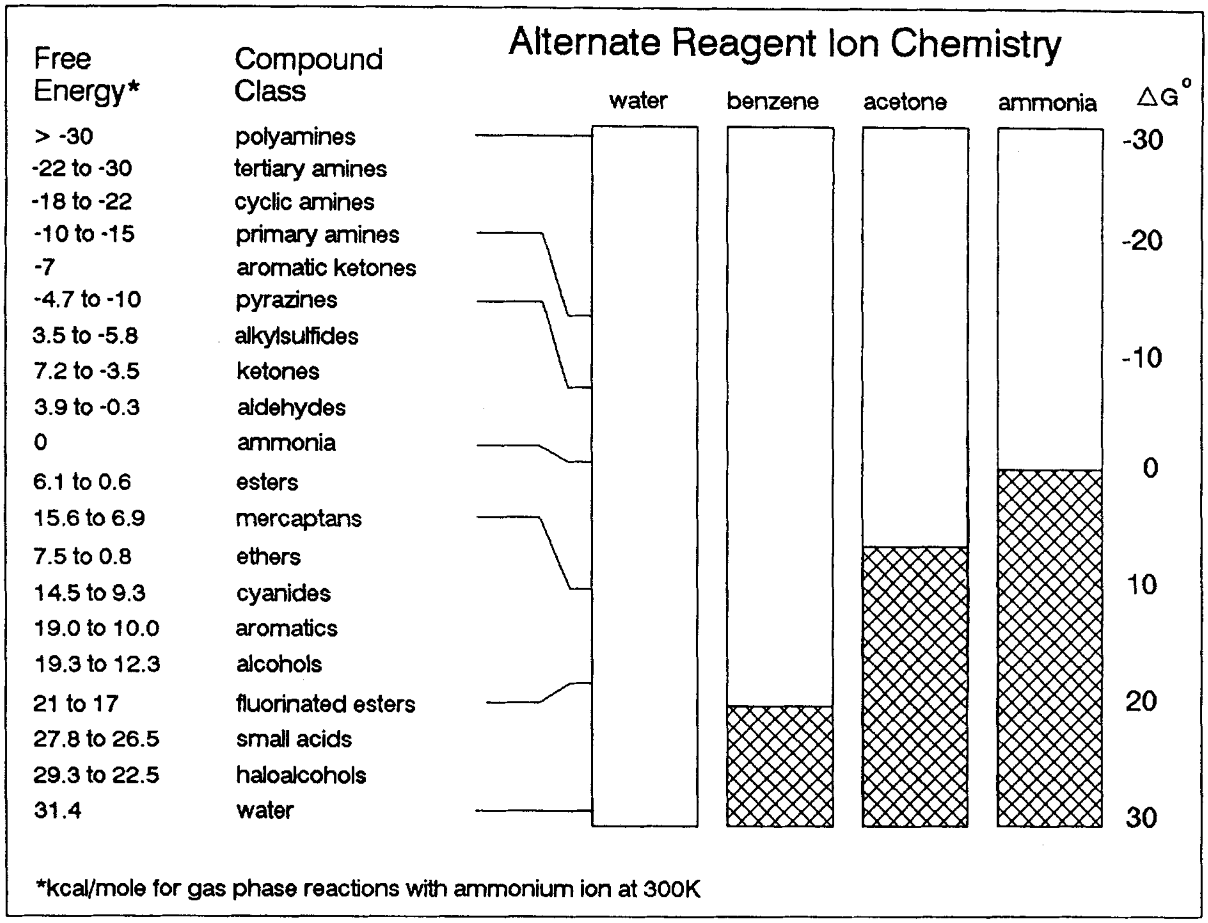
A final facet of IMS drift tubes that merits description is Fourier Transform(FT)-IMS[18] in which the ion shutter of a traditional drift tube is operated in an unconventional manner. In regular IMS, the shutter is opened, allowing ions to enter the drift region, for about 100 to 300 μsec every 15 to 30 msec which compromises significant ion yields through the IMS drift tube. In order to gain improved ion yields or detection limits, a reasonable solution is to improve the duty cycle of the shutter. In FT-IMS, the ions are introduced into the drift region before all ions from the previous shutter event have arrived at the detector. Fourier transform algorithms were expected to convert the frequency mobility spectrum to a time base spectrum with the consequence that the shutter would be opened substantially longer than in conventional methods. Unfortunately, ion-ion densities in IMS cannot exceed about 5 × 10^7 ions/cm^3 whereupon ion-ion repulsions in the drift region have been shown to cause band-broadening.[19] This occurred with the FT-IMS concept and only minor improvements in detection limits were achieved.

B. Ion Sources for IMS

Ionization of vapors represents the initial chemical event at the molecular level in an IMS measurement and serves to define the substances that will be observed in the subsequent mobility spectrum. In short, if an ion is not created in the ionization region, there will not be an ion peak in the mobility spectrum for the associated vapor. Most of the original IMS instruments contained abut 10 mCi of ^{63}Ni which was favored due to simplicity, stability, convenience, and high selectivity. This source, as traditionally employed, has serious deficiencies in limited linear range, inflexible selectivity, and regulatory requirements associated with radioactive material. To a first approximation, the properties of a ^{63}Ni source in IMS exhibits all the shortcomings of a direct current electron capture detector employed in gas chromatography. Other aspects of ^{63}Ni sources which affected early conclusions about the technology such as particulars of ion-molecule chemistry at atmospheric pressure are discussed below.

Lubman and Kronick[20-22] were the first to demonstrate that lasers were useful as ion sources in IMS, and supposed that multiphoton ionization could be used to selectively create ions in vapor mixtures. This was successfully shown for benzene in the presence of aniline. The basic premise is that the mobility spectrum would register only those compounds created by laser ionization in the reaction region. Eiceman et al.[23] examined the implications of beam characteristics as relevant to analytical chemistry and found difficulties in precision and stability with intensities in the beam cross sections. No solutions were proposed; however, immediate applications of lasers to IMS will be governed by the availability of stable and inexpensive lasers. Baim et al. proposed photodischarge lamps as inexpensive photoionization sources for GC-IMS[24] and later Leasure et al.[25] demonstrated that vacuum UV (i.e., hydrogen) discharge lamps were suited in a particular geometry for direct operation in air. In photoionization, proton affinities are not relevant; however, ionization potentials serve as a type of selectivity in terms of the wavelengths of the electronic transitions. The concept of laser based selective ionization was moderated by cross-ionization or charge exchange, and was observed with photoionization lamps in air at ambient pressure.[26] Consequently, charge will reside with the chemical species of lowest ionization potential, and the concept of selective ionization of a chemical mixture will be mitigated by the large number of collisions at atmospheric pressure and the charge exchange steps that occur during the collisions. These restrictions will not be altered unless reconfiguration of a source insures kinetic rather than existing thermodynamic control in the ionization region.

The use of conventional ^{63}Ni sources in IMS resulted in chemical sensors or analyzers that were susceptible to impurities in carrier gases or common atmospheric pollutants in airborne vapor monitoring. However, a major advantage of this source is the flexibility in adjusting ion-molecule chemistry. For example, the concept of adjusting proton affinities through the use of alternate reagent ions, ions created from a continuous leak of a selected compound into the ion source, was reported by Proctor and Todd in 1983.[27] In this concept, molecules with proton affinities below that of the reagent gas would not be detected and would be chemically transparent to the IMS, as shown in Figure 9. Alternate reagent ion chemistry has been employed in four practical instances.[28-31] Operation or monitoring of IMS in chemically complex environments can be compromised by the existence of small oxygenated chemicals that commonly are found in ambient air. The use of an acetone doped ion source serves as the basis for certain military IMS technologies and was shown to be highly effective in environmental monitoring and insensitive toward common interferences.[28] Spangler and Epstein have demonstrated that HF in air can be detected only when methylsalicylate is the reagent ion.[29] Hydrazines are especially sensitive and selective in IMS due to the proton affinities of these compounds.[30] However, effects of water and common polar solvents may be expected to result in complex spectra from the formation of ion-molecule



Free Energy*	Compound Class
> -30	polyamines
-22 to -30	tertiary amines
-18 to -22	cyclic amines
-10 to -15	primary amines
-7	aromatic ketones
-4.7 to -10	pyrazines
3.5 to -5.8	alkylsulfides
7.2 to -3.5	ketones
3.9 to -0.3	aldehydes
0	ammonia
6.1 to 0.6	esters
15.6 to 6.9	mercaptans
7.5 to 0.8	ethers
14.5 to 9.3	cyanides
19.0 to 10.0	aromatics
19.3 to 12.3	alcohols
21 to 17	fluorinated esters
27.8 to 26.5	small acids
29.3 to 22.5	haloalcohols
31.4	water

*kcal/mole for gas phase reactions with ammonium ion at 300K

FIGURE 9. Diagram of relationship between chemical classes and selectivity with alternate reagent ion chemistry. The chemical classes are organized according to proton affinity (high proton affinities at the top of the column). Proton affinities are given in terms of free energies (kcal/mole) from reactions with the ammonium ion. The shaded regions of scales for each alternate reagent ion correspond to those compound classes (see listing at left) with proton affinities below the reagent ions. Such compounds should be expected not to undergo ionization or to experience slight formation of product ions at elevated vapor concentrations. A caveat regarding this scheme is that response in mobility spectra from polar compounds with low proton affinities may occur through ion-molecule clustering rather than proton exchange.

clusters. A hand-held IMS equipped with an acetone doped ion source gave detection limits near 6 ppb and an interference free response toward acetone and Freon vapors.[31] However ammonia, a common interference, gave an ion cluster at the drift time for monomethylhydrazine (MMH). When 5-nonanone was used as the reactant ion, baseline resolution between ammonia and MMH occurred through ion-molecule mechanisms that are not yet thoroughly described.[31] Negative alternate reagent ion chemistry with Cl^- was demonstrated to improve detection limits for detection of explosive residues by IMS.[32] This presumably occurred through the formation of a single product ion rather than several product ions originating from multiple reactant ions common to IMS.

Several miscellaneous advances occurred with ion sources, representing significant but narrow advances that warrant brief mention. To illustrate, membrane inlets, similar to GC/MS interfaces, are not especially useful when IMS cells are operated at high temperatures where cluster ions do not present problems in shifting peak drift times. Moreover, detection limits are degraded with a membrane inlet because sampling losses occur from inefficient passage of some compounds through a membrane. However, membranes are essential for keeping water vapor level in drift tubes and peak drift times predictable at low or ambient temperatures.[33] Since ambient (20°C) temperatures in a hand-held IMS are favored to conserve power in battery operated instruments, membrane inlets represent the only practical inlet configuration for environmental monitoring with IMS.[28] Another advantage of a membrane-based inlet in IMS is the ease with which alternate reagent ion chemistry can be established with stable vapor levels of dopant chemicals. Direct laser desorption and ionization of organic films in air at atmospheric pressure with ion characterization by IMS suggests possible uses for IMS as a portable technology in screening surfaces for contamination.[34] Finally, a text was released on IMS encompassing ion chemistry, instrumentation and applications under the title *Plasma Chromatography,* edited by Timothy W. Carr.[35]

C. Commercial Instrumentation

Perhaps no single influence has been as revolutionary to the development of IMS as the availability in the late 1980s of small relatively inexpensive ion mobility spectrometers originating in military detection programs. Concerns about chemical warfare agents have brought remarkable research and development activity to IMS pertaining to practical instruments for detection of vapors in air. Only after nearly 20 years since inception have IMS units become available as practical devices for environmental, medical, and forensic technologies. This section is intended to portray the diversity and range of IMS products rather than list a complete offering or capability of individual vendors.

PhemtoChemProducts (PCP), Inc. is the successor company to the commercial entity in which IMS was originated, Franklin GNO. Nearly all of the original patents, dated from 1972 to 1974, were held on IMS technology by personnel from these companies. The rather large early designs[3] of the Beta VI and Beta VII have been reduced in size through the years and are now promoted as both field sensors and chromatographic detectors. A small bench scale unit is available and is shown in Figure 10.

Environmental Technology Group (ETG), Inc. is the former Bendix (Allied-Signal) company that obtained the US Defense Department project to fabricate a portable military IMS device, the automatic chemical agent detector and alarm (ACADA), which has been described in several articles.[36-38] A commercially available IMS, called the general purpose (GP)-IMS (Figure 11), has been promoted, and specialized versions of this unit have been pioneered for HF detection. The drift tube in the GP-IMS is based upon the continuous guard ring or minicell design cited earlier and shown in Figure 5.

Graseby Analytical, Ltd. and Graseby Ionics, Ltd. are separate but related metro-London based companies that began efforts in IMS when the U.K. Ministry of Defense placed contracts with Graseby Ionics, Ltd. to build and develop a military hand-held IMS detector for nerve and blister gas sensing on combat equipment.[39] The final product, called the chemical agent monitor (CAM), has been adopted NATO wide with expected deployment numbers in excess of 30,000. Graseby Analytical, Ltd. was founded to explore civilian markets for IMS, and offers the airborne vapor monitor (AVM) shown in Figure 12. The AVM is mechanically and electrically equivalent to the CAM and has been used for toluene di-isocyanate and hydrazine sensing.

Three of these companies (PCP, Inc., ETG, Inc., and Graseby Ionics, Ltd.) have historically been recipients of governmental defense funding which has figured prominently into the pioneering of IMS as a rugged small instrument (i.e., ACADA and CAM). Of these, ETG, Inc. and Graseby Ionics, Ltd. have assembly lines for mass production of IMS units. Several small companies comprised of a dozen employees or less have also become active in IMS ventures in recent years, and are indicative of a revitalized interest in IMS. These companies are noted below only briefly since their offerings consist largely of services or of unique instruments tailored to a user's requirements.

1. Scientech, Inc. (Pullman, WA) has developed and offers instruments with innovative corona spray ion sources.
2. CPAD, Ltd. An Ottawa-based company with interests in nonradioactive sources for contraband and explosives sensing.

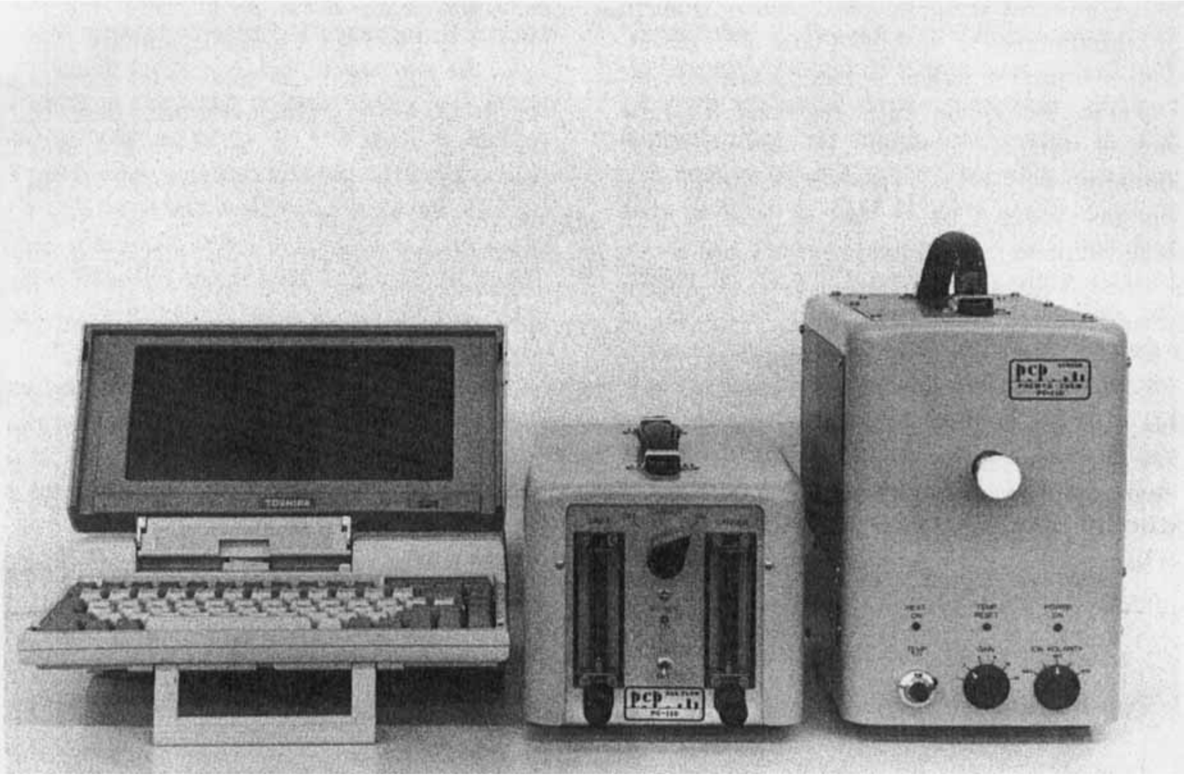


FIGURE 10. The ion mobility spectrometer manufactured by PCP, Inc. Used with permission.

3. Barringer, Inc. is a Toronto-based company with interests in airport security and for the use of IMS for compounds with low volatility.

III. ION MOLECULE CHEMISTRY AT ATMOSPHERIC PRESSURE IN IMS

In retrospect, disappointments regarding IMS in the early developmental period can be attributed to a misunderstanding of the chemistry of ionization in the IMS reaction region. Chemical aspects of ion formation at atmospheric pressure (and often in air) were not appreciated, and caused certain investigators to conclude that IMS was a curious but not practical or usable technology.[40] A reputation that IMS was not useful with chemical mixtures developed, and such attitudes have persisted. Fortunately, a model for ion behavior in air, more complete than that available in the 1970s, has emerged from investigations with IMS, IMS/MS, and atmospheric pressure chemical ionization (APCI)-MS. An essential element in these investigations has been the treatment of IMS as a quantitative detector, which was made possible by drift tubes with low memory effects. The five IMS chemistry categories described below encompass ion creation, ion behavior in the drift region, parametric effects, and IMS response with mixtures.

A. Proton and Electron Transfers

Prevalent ion-molecule reactions with ^{63}Ni sources are proton and electron transfers or formation of ion-clusters between a neutral gaseous vapor and a reservoir of reactant charge originating from beta emission under ambient conditions. In clean air, negative reactant ions exist as $CO_2{}^*O_2^-$ (m/z 76) and a large number of minor constituents[41,42] all of which can undergo collisional electron transfer or formation of adducts such as $M^*O_2^-$. If traces of chlorine or organochlorine impurities exist in the IMS cell, the major negative reactant ion is Cl^- and M^*Cl^- product ions can form. The intentional use of Cl^- as a reactant ion was recognized as a useful means of simplifying the ion molecule chemistry found with multiple reactant ions in clean air.[32] However, a concentration-dependent transition between O_2^- and Cl^- adducts was observed as an inadvertent consequence in the IMS/MS determination of volatile halogenated anesthetics.[43]

A preliminary theory for atmospheric pressure chemical ionization in IMS was proposed,[44] but never explored for more than a few compounds. Consequently, Vandiver sought to clarify these results as central elements in the model.[45] He found that presumptions in APCI rate theory were incomplete and did not adequately explain profiles from response curves. Certain vital predictive elements not obvious at a molecular level were missing from the theory, and the preponderance of evidence suggested that ^{63}Ni sources were under thermodynamic rather than kinetic control. Vandiver also concluded that determinations of absolute rate constants were limited by uncertainties regarding recombination coefficients and total reactant ion densities. At best, only relative rate constants could be obtained with existing IMS reactant region designs.

B. IMS Response with Mixtures

Traditionally, IMS has been effective as a chemical analyzer when the target analyte has ionization parameters vastly different from com-

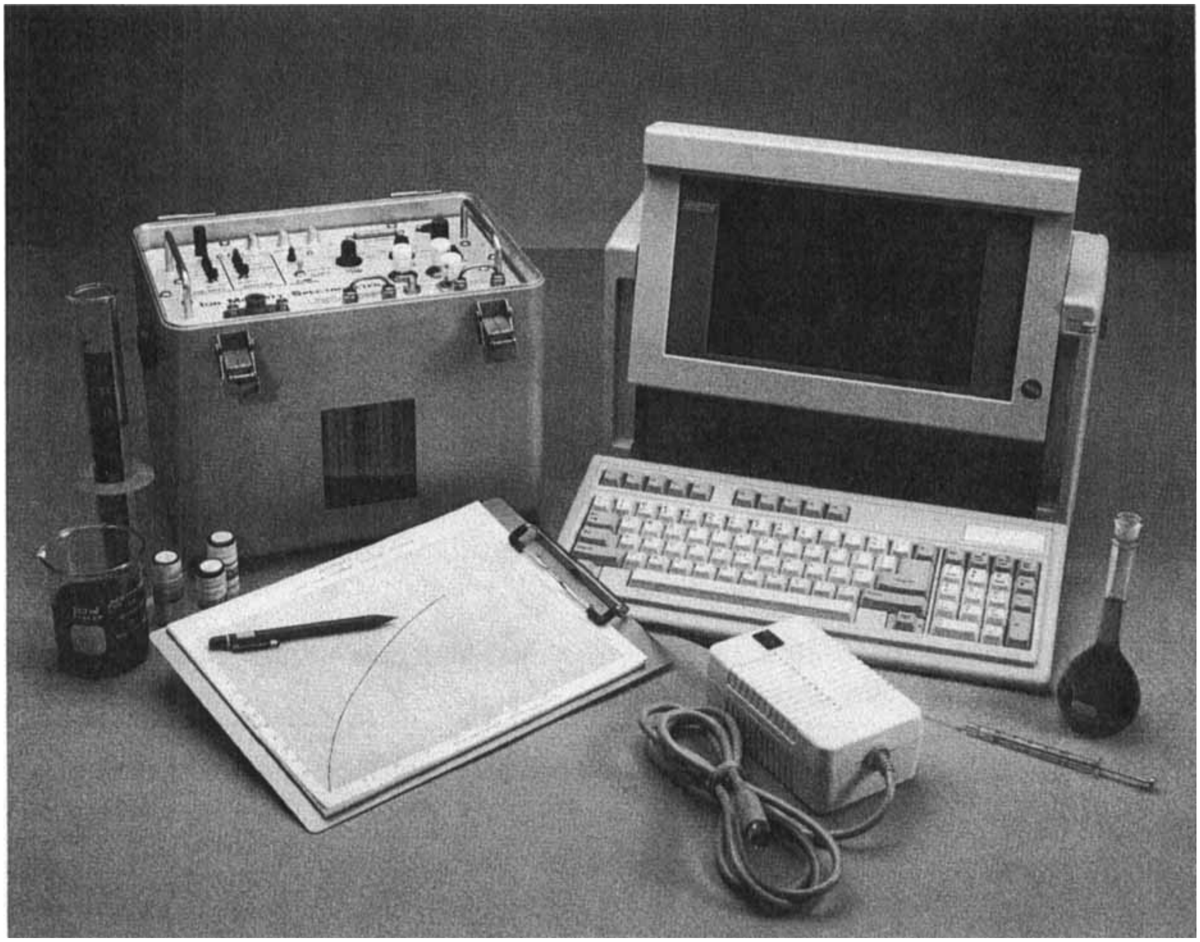


FIGURE 11. The ion mobility spectrometer manufactured by Environmental Technologies Group, Inc. Used with permission.

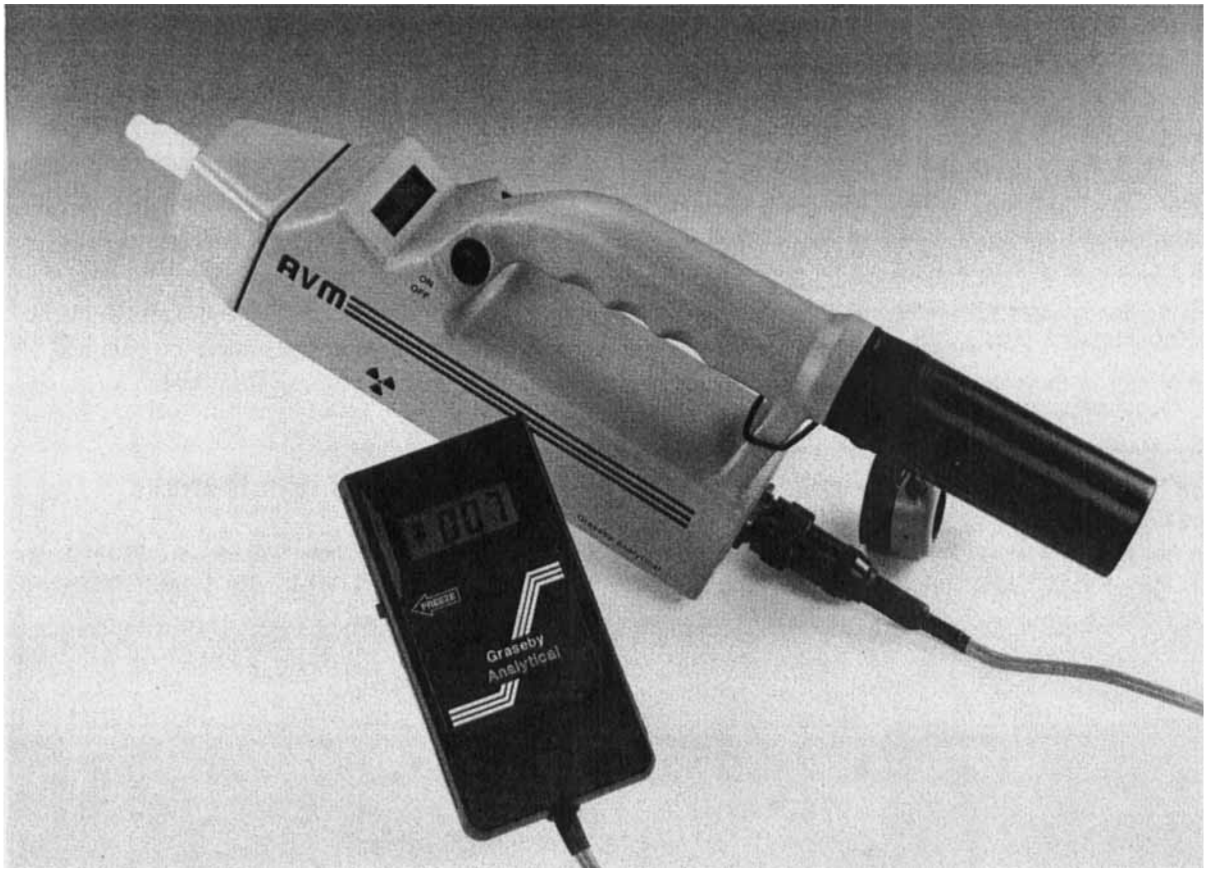


FIGURE 12. The ion mobility spectrometer with digital display unit manufactured by Graseby Analytical, Ltd. Used with permission.

ponents in the sample matrix. Presently, IMS has neither predictive nor interpretive properties when considering mixtures in which components have comparable ionization parameters. The dramatic effects from proton affinities on mobility spectra for binary and ternary mixtures was quantitatively demonstrated in 1985 with polycyclic aromatic hydrocarbons.[46] Differences of as little as 7.4 kcal/mole in proton affinities caused selectivity ratios of more than 10^2:1 to 10^3:1. In Figure 13, mobility spectra are shown for binary mixtures of polycyclic aromatic hydrocarbons in several gas phase concentrations. More complex spectra obtained with oxygenated compounds (analgesic pharmaceuticals) showed nearly composite (though not quantitatively proportional) mobility spectra with binary mixtures.[47] However, the use of a ternary mixture of the same compounds caused failure in simple visual recognition of component peaks, and these spectra seemed to be complicated by competitive ionization or possibly ion-molecule adducts between neutrals and ions of different analyte vapors. These findings strongly favor the use of a preseparation device to an IMS inlet in instances where molecules of similar ionization properties may exist in a sample.

C. Ion-Molecule Cluster Reactions

In IMS, the large number density of ions and molecules and the low near thermal energies of these ions is inviting for the formation of ion-molecule clusters. These clusters occur for reactant ions and product ions, and are dependent upon temperature and vapor concentrations of the neutrals. Karasek's work on reactant ions[48] is a comprehensive survey on water clusters that occur in the ion source, and comparable behavior

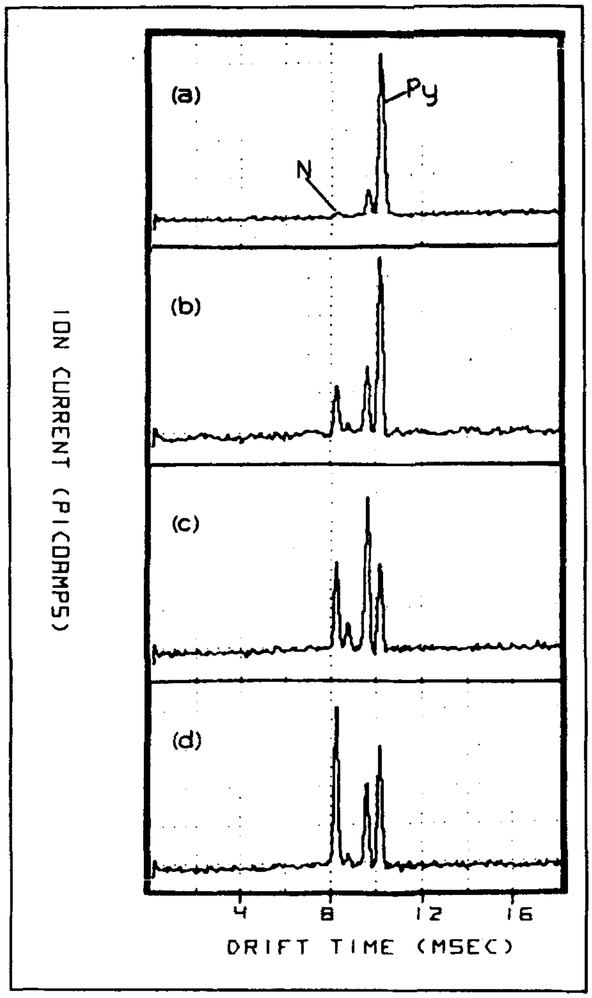


FIGURE 13. The effect of concentration on peak height with a binary mixture of polycyclic aromatic hydrocarbons. The proton affinities for naphthalene and pyrene are 196.3 and 208.5 kcal/mole, respectively, and are relative to proton affinity for that of ammonia (207 kcal/mole). Ratios of concentrations for naphthalene (N) to pyrene (Py): (a) 14,000:1, (b) 42,000:1, (c) 91,000:1, and (d) 720,000:1. From Vandiver, V. J., Leasure, C. S., and Eiceman, G. A., *Int. J. Mass Spectrom. Ion Processes,* 66, 223, 1985. With permission.

may be expected with alternate reagent ions. One would expect that such clusters form in the ion source. However, Preston[49] argued that ions and molecules could associate and dissociate in an equilibrium on a fast time scale in the drift region during ion transit between the ion shutter and detector plate. This was referred to as localized equilibrium (Equations 3 and 4), where M^+ is the product ion, S is a small polar molecule, $S{*}MH^+$ is a cluster ion, and M_2H^+ is a dimer ions.

$$MH^+ + S \rightleftharpoons S{*}MH^+ \qquad (3)$$

or

$$MH^+ + M \rightleftharpoons M_2H^+ \qquad (4)$$

This phenomenon was evident as a shift in drift time or K_o (Figure 14) without distortion in the peak shape. The thermodynamics of ion associations via IMS in air at atmospheric pressure were measured; hence, IMS should provide a unique tool for determining enthalpy and entropy of similar chemical systems.

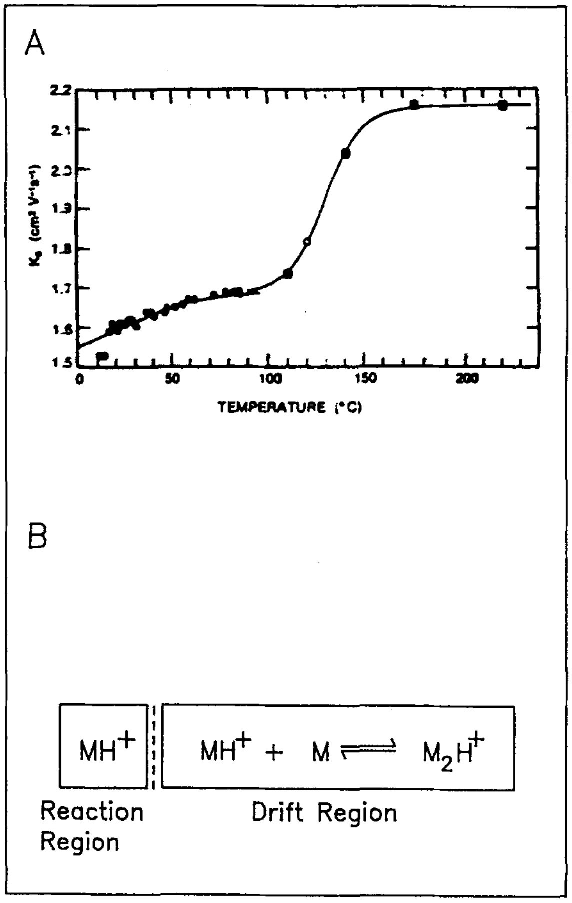


FIGURE 14. The effect of temperature on reduced mobility from ion-molecule cluster formation in the drift region of an IMS. The association of an ion and molecule results in a large cross section for collision and a low reduced mobility. In Frame A, K_o is plotted versus temperature for pyridine in air with 10 ppm of water. The formation of MH^+ eventually replaced by a dimer ion, M_2H^+ which was favored at low temperature. This process is depicted in Frame B.

D. Ion-Molecule Fragmentations

Mobility spectra published in the 1970s were rarely mass-identified; thus, interpretations of ion-molecule events were useful, but somewhat impaired. For example, distortions in baselines were discernible in published spectra but never rationalized. Recently, IMS-mass spectrometry was used to explore the origin of baseline perturbations with butylacetates.[50] Ions injected into the drift region intact were found to undergo fragmentation reactions while traversing the drift region on a time scale comparable to ion drift times. These reactions were irreversible (unlike the localized equilibrium phenomenon)[49] and were manifest as broad, unresolved, skewed peak shapes. Such fragmentations were reasoned to be intermolecular rearrangements and were highly sensitive to temperature. Although only one class of compounds, butylacetates, were examined in detail, comparable behavior of drift tube reactions may be anticipated with other acetates and possibly other polar or thermally unstable compounds.

E. Temperature, Pressure, and Concentration Effects

A serious limitation of the existing IMS data base,[51] which is otherwise useful to gain an appreciation of ranges of mobilities, is the dependence of mobility spectra upon temperature and concentration. The expected importance of this subject, although mentioned above, requires further consideration. Temperature effects in IMS were thought to be irrelevant since reduced mobility values were normalized for temperature. Lubman demonstrated in 1983 that mobility spectra for aromatic hydrocarbons were independent of temperature from 220 to 295°C.[52] Nonetheless, aromatic hydrocarbons are a rather stable class of compounds with an equilibrium between M^+ and MH^+, and an extrapolated conclusion that mobility spectra are independent of temperature should be rigorously avoided. Both ion cluster formation[49] and ion fragmentation in the drift region[50] (mentioned above) were found to be governed by temperature. Thus, comparison of mobility spectra of a given compound at different temperatures in IMS drift tubes can be compromised by the existence of wholly different mixtures of ions in the ion source. Mobility analysis will accurately reflect these differences; however, failure to appreciate that clustering and fragmentation occur in an IMS will certainly lead to flawed conclusions regarding the reproducibility of IMS. For example, the product ions formed for volatile halogenated anesthetics (vide supra) were influenced by temperature and shown to exhibit clear trends in ion population versus temperature.[43]

The effects of neutral vapor density (i.e., gas phase concentration of molecules) on mobility spectra were recognizable in many early reports on IMS response for various chemical classes. However, the interpretation was expressed in terms of time following vapor introduction. In retrospect, this time dependence was actually due to accumulation and decay of vapors in the ion source, which exhibited severe overload and memory effects. The effect of concentration was evident in the IMS characterization of halogenated anesthetics.[43] As the vapor levels were increased from about 10 ppb to 500 ppb, product ions went through a transition from X^-, to $M{*}Cl^-$ to $M{*}Br^-$ to M_2Cl^-. At high vapor concentrations, the drift times for the dimer ion changed to longer values, suggestive of shifts in cluster equilibria in the drift region.[49] A dramatic example of the dependence on concentration is the monomer-dimer equilibrium evident with phosphonate esters. This was illustrated in a concentration profile obtained for triethylphosphate (Figure 15).[28] Very little else may be said currently about this subject since so little has been published for quantitative IMS. However, any attempt to exploit IMS as a chemical detector for general purposes will require that these parameters are determined and reconciled to spectral matching algorithms. Effects from pressure have not been extensively investigated in IMS, and a single literature reference forms the basis for most conclusions.[53]

F. Ion Mobilities in IMS and Assorted Topics

Karpas has been a principle leader in research

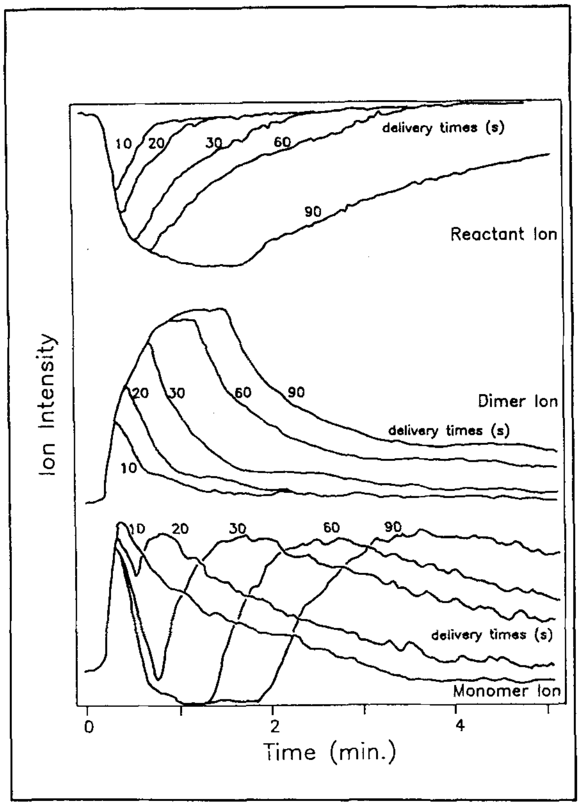


FIGURE 15. Ion intensities for the reactant ion (A), dimer ion (B) and monomer ion (C) for triethylphosphate from an IMS during the monitoring passage of a vapor cloud passing by the IMS. The passage of the vapor cloud also corresponded to a rise and decline in vapor concentrations. The vapor cloud was generated by delivering a set concentration of vapor into a flowing air stream for certain time periods identified in the figure. A rise in vapor concentration first caused formation of the monomer ion which was replaced with the dimer ion as vapor levels became elevated. When the vapor concentration returned to low levels, the dimer ion intensity decayed and the monomer ion was restored.

directed at describing ion mobilities in IMS. Recent studies[54] of the effect of drift gas have permitted discrimination between mass and polarizability effects on K_0. In addition, the established model for mobilities was modified through the introduction of an empirical mass dependent correction for the collision cross section.[55] The effect of structure and charge distribution on ion mobility suggested that the site of protonation, a subtle effect, caused unique dipoles which were effective in altering mobilities and permitting isomer separation.[56] A structural effect for ions of the same mass was examined by IMS/MS and demonstrated the usefulness of IMS as an investigative research tool.[57] Karpas also observed the effects of proton-induced cyclization on IMS mobilities and found that a diamine, when cyclized, exhibited faster drift times than the noncyclic amine.[58]

Peak shape factored prominently into several discussions of IMS. Glasser described the mathematics of ion peak shapes in IMS and proposed a dimensionless parameter to characterize IMS performance.[59] Practical aspects of resolution in IMS were addressed by Hill et al.[60] although no standard for resolution seems to have been adopted by IMS investigators worldwide. Recently, Karpas has suggested that amines be utilized as standards for calibration of mobilities in various IMS systems[61] and this approach appears to be a reasonable proposition. These advances suggest that a common basis for description and calibration of IMS instruments must soon be developed, particularly in view of the increased activity in IMS and number of new IMS units now available.

IV. APPLICATIONS OF ION MOBILITY SPECTROMETRY

While modern analytical IMS was first envisioned for military uses with chemical agents, early investigators saw broad opportunities from the very low detection limits and high selectivity offered by IMS. The early years of IMS development should be viewed as attempts by investigators to ascertain response characteristics in search of a unique application for IMS. During the last decade, several niches have been clarified and explored. The categories cited below have been areas where IMS has been shown to be exceptionally qualified for service and have received enough attention to merit discussion. It should be noted, however, that these applications are not fully developed (with the exception of chemical agent detection) and require further refinements. Further, these uses should not be considered to be a comprehensive list and new applications of IMS may be expected.

A. Mobility Detectors in Chromatography

An early utility of IMS, and one in which disabilities of APCI vagaries are eliminated or greatly reduced, is that of chromatographic detectors. Under such conditions, columns serve to deliver compounds individually to the ion source of the IMS, thereby avoiding (except for coelution of peaks) competitive charge exchange. Hill and co-workers have been especially effective in configuring IMS drift cells for capillary gas chromatography (GC),[62] supercritical fluid chromatography,[63] and recently, liquid chromatography.[64] As a chromatographic detector, IMS cannot provide structural information like electron impact-mass spectrometry (MS) but can give molecular ion information much like chemical ionization-MS. However, IMS in terms of size and power is similar to an electron capture detector (ECD) except the information from an IMS has much more content than an ECD trace. A review by Hill of IMS as a chromatographic detector has recently appeared in *Critical Reviews in Analytical Chemistry,* and should be considered an extensive and current discussion on the subject.[65]

B. Environmental Sensing

There was a tacit understanding from the start of modern analytical IMS that IMS could be a useful environmental sensor, and the military pursued this idea in a highly directed fashion. Surprisingly, IMS was not perceived and evaluated as an environmental monitor for industrial purposes until after 1980. Dam[66] was the first to demonstrate that IMS was suitable for monitoring certain toxic industrial chemical vapors. He recognized that ion chemistry in IMS was based on competitive charge exchange and that matrices may complicate detection limits and linear ranges. Consequently, a type of automated standard addition method for sampling gas streams was devised and used for continuous airborne vapor monitoring.

Eiceman and co-workers at Aberdeen Proving Ground, MD showed in field trials that the military configuration of IMS was useful as a point sensor for establishing the presence of contaminated patches of soils, and that plume boundaries and shapes could be determined with IMS.[28] They showed that IMS as a point sensor is vulnerable to wind direction, and that high resolution mapping of a plume needs to be accomplished with rastering or multiple sensors. The need for multiple sensors that encompass an industrial facility for perimeter monitoring is a reasonable extension of this conclusion.

C. Chemical Agents

The first example of the adoption of IMS technology in an expansive manner was the deployment by the US Army of hand-held Chemical Agent Monitors (CAM) produced by Graseby Ionics, Ltd. This adoption was aided by the rather strong proton affinities of nerve gases in the positive ion mode, which greatly diminished the possibility of false alarms from other proton accepting compounds present in atmospheric environments. The mobility spectra for phosphonate esters were reported[67] in the mid-1970s and the spectra were characterized by simple patterns as given in Table 1. The major effect of the military developmental program was IMS technology refined to military specifications to be produced as a simple to use and reliable field analyzer. Naturally, essential details on response characteristics of these instruments have not been disseminated; however, the extensive deployment of CAM suggests that this may be, to date, the most dramatic (though low profile) example of the translation of laboratory instrumentation to practical field worthy instrumentation.

D. Forensic Uses and Contraband Sensing

Perhaps no other single application of IMS has received as much attention and been extensively reported as that for the detection of narcotics and other illicit drugs. Remarkably, the bulk of recent work in roughly a dozen articles has come from a single investigator, Andre Lawrence at the National Research Council in Canada. His efforts have shown that IMS is suited for rapid screening of skin surfaces and blood samples for drug residues and has demonstrated the clinical advantages of IMS in speed and sensitivity. In each application, drug residues are

TABLE 1
Reduced Mobilities from IMS Characterization of Phosphonate Esters[a]

	K_o (cm^2/V*s)[b]		
Compound	**2.5—2**	**2—1.5**	**1.5—0.5**
Dimethylmethylphosphonate,	2.06		1.40
Sarin or GB		1.95, 1.84, 1.71	
Tabun or GA		1.82, 1.73, 1.63	
Soman or GD	2.06	1.92, 1.76, 1.65	
Diethyl-2-bromoethylphosphonate		1.69	1.15
Diethylcyanomethylphosphonate		1.82, 1.58	1.39, 1.13
Trimethylphosphonoacetate		1.92, 1.68, 1.54	1.26, 1.15
Dimethylmorpholinophosphoramidate		1.77, 1.57	1.14, 1.07
Triethylphosphonoacetate			1.45, 1.23 0.97
Parathion	1.78	1.27, 1.22	
Fenitrothion	1.80, 1.72	1.40, 1.31	
VX			1.26
Disyston	2.09		1.30
Dimethoate			1.34 1.47
Methyl parathion		1.80	1.36, 1.31
Thimet			1.37

Note: Assignment of ion identities were not confirmed by IMS/MS and were not included in this list. The listing was ordered in columns for ranges in mobility to accentuate differences in mobility spectra.

[a] Table adapted from Reference 67.

[b] Mobility spectra were obtained at 150°C and at low but undefined vapor concentrations. Ion source chemistry was based on water.

introduced into the IMS inlet and warmed. Application of IMS as a screening tool for cargo containers remains an elusive promise since response will occur only if drug vapors are delivered into the IMS ion source. The characterization of drugs by IMS has recently been reviewed.[68]

The possible utility of IMS in the detection of explosives has also been a technical lure for roughly a decade without any full commitment to a field IMS screening unit. A difficulty in obtaining details about IMS performance toward explosives is due to the dissemination of results principally at specialized conferences. Extensive work by Conrad et al. at Sandia National Laboratory (SNL) has established that detection limits and signatures are highly effective, so long as vapors are efficiently delivered to the ion source. The obvious disadvantage of IMS and related technologies is the low vapor pressure of contraband materials, particularly certain explosives and drugs, that will render IMS ineffective in some working environments. IMS is an attractive technology when samples can be collected and delivered easily to the ion source. This might be possible with laser desorption IMS if caveats regarding lasers are acceptable.[69] A useful review of IMS behavior with explosives was published in 1983.[70] More recent studies by a SNL group with a large reaction volume IMS showed detection limits of 1.8 × 10^9 molecules/s, or 0.3 ppt, for RDX vapors.[71] As with drug detection, delivering the vapors to the ion source constitutes the greatest obstacle to the use of IMS for in actual screening venues.

V. CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE DEVELOPMENT

The last decade in ion mobility spectrometry has been characterized by a diversity of research directions and by clarification of earlier misunderstood aspects of IMS. Whether these advances can effectively attract the necessary developmental support and acceptance in appropriate scientific and technical communities is uncertain but promising. Familiarity and acceptance of principles and performance of IMS may be motivated largely by the advent of small, low cost commercially offered IMS instruments suited for field uses. Despite the early perceived limitations of IMS, its compact size, low power requirements, and demonstrated capabilities have revitalized interest in IMS applications. For example, a consensus on technical niches for IMS, particularly in a GC-IMS configuration, may also be developing in environmental sensing.

Issues of ion-molecule chemistry at atmospheric pressure in air are not yet developed to a point where interpretive or predictive capabilities can exist without prior experimentation. This will continue into the immediate future, and a substantial effort at determining clear understandings of boundaries in performance relative to existing analytical tools will be necessary for general acceptance of IMS or possibly GC-IMS.

The extension of IMS to high molecular weight compounds[72] and inexpensive HPLC detectors may hold much promise although the identification limits of IMS will force the use of mass spectrometry.

Nascent aspects of ion mobility spectrometry which portend some remarkable advances include

1. **Signal processing.** In the last two years, several groups have started examining fully, the content of information stored in mobility spectra.[73,74] While this has been done previously for other instruments such as chromatographs, the use of improved signal processing may suggest an elevated level of interpretation of spectra.
2. **Biological IMS.** Efforts toward altering IMS inlets to accept biochemical reactions that signify the presence of microorganisms in a selective, speedy manner may offer a rapid sample screening method for organism detection for microbiologists, health officials, and the medical communities. Preliminary findings on this concept have proved promising[75,76] and efforts are on-going to refine bacteria detection by IMS.
3. **Radically new IMS cell designs.** The use of cell designs based on new configurations ranging from unconventional field control for ion trapping, refined multiple IMS systems and simple IMS drift tubes may provide the foundation for a new generation of ion mobility spectrometers markedly differing in shape and performance to existing units. Part of this could include the practical development of multi-IMS integrated networks in which the limitations of IMS point sensors are reduced through the deployment of many units across a large geographical area or an industrial facility. A final area of development in instrumentation will certainly have to include smaller and more affordable IMS/MS units that permit a large participation by IMS users in exploring the ion chemistry of particular applications.

VI. ACKNOWLEDGMENTS

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