Miniature mass analyzers

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Increased efforts are being made to develop miniature mass spectrometers, including those which are hand-portable, and to retain the performance characteristics of traditional laboratory instruments as much as possible in the miniature instruments. This review of miniature mass analyzers emphasizes analytical performance and compares the relative merits of each type of miniature mass analyzer. Miniature instruments discussed include sector, Wien filter, time-of-flight, linear quadrupole, quadrupole ion trap and Fourier transform ion cyclotron resonance mass spectrometers, as well as combinations of and variations on these major types. Special considerations that apply to small mass analyzers are noted and suggestions are made regarding the possible future development of this field.

KEYWORDS: miniature instrumentation; mass spectrometer; mass analyzers; in situ analysis; ion traps; sectors

INTRODUCTION

An area of increasing interest in mass spectrometry is that of miniature instrumentation and field portability. Miniature and field portable instruments are ideal for a variety of in situ analysis applications that include environmental analysis and remediation, process monitoring, emissions monitoring and control, emergency response applications and chemical and biological weapons detection. Recent, although uneven, progress has been made on the miniaturization of each component system (sample introduction, ion source, mass analyzer, ion detection, data acquisition and vacuum systems) of a variety of mass spectrometer types. Mass spectrometers that are portable and even hand-held have been developed, although those that are portable do not always utilize miniature mass analyzers. This review will focus on miniaturized mass analyzers; portable or transportable instruments that do not incorporate miniaturized mass analyzers are excluded. A review of all field-portable mass spectrometry instrumentation is beyond the scope of this paper and the reader is directed elsewhere. Each of the types of mass analyzers that are being used in miniaturized form will be examined and a brief discussion of the analytical qualities of specific miniature instruments of each type will be presented. Because there is no standard set of analytical qualities used in all of the papers reviewed, not all characteristics (e.g. mass range, resolution, sensitivity, overall size, operating voltage, power consumption, etc.) are available for each instrument. Also, it should be noted that there is no exact definition of 'miniature' when dealing with mass analyzers and the term is used here to describe analyzers that are significantly smaller than those used in the corresponding standard laboratory mass spectrometers.

One important aspect of all miniature analyzers is the effect of operating pressure on performance. Pressure determines the mean free path of ions, so affecting performance of the mass analyzer. As a result of miniaturization, the mean free path of ions is reduced because of the reduced distance of travel and hence the fewer number of collisions the ion makes with background gases, compared with a larger instrument operated at an identical pressure. As a result, miniaturization benefits all mass analyzers, although not equally. Even so, resolution is still greatly affected by pressure, even in miniature instruments, and it is the main feature degraded under higher operating pressures for all type of analyzers.

Analyzers such as time-of-flight and ion cyclotron resonance have a relatively strong pressure dependence on performance (resolution and sensitivity) and even miniaturized versions of these analyzers require relatively low-pressure operation. The time-of-flight analyzer depends on few collisions so that ions may travel through the flight tube and be discriminated from their flight times for high-resolution performance. Under higher pressure conditions, collisions with background gas decrease mass resolution. The same is true to an even greater extent for ion cyclotron resonance mass analyzers: high-resolution performance requires unimpeded motion of the ions to insure long transient lifetimes for maximum resolution and to prevent ion coupling and peak merging effects.

Linear quadrupoles are able to operate under somewhat higher pressures than time-of-flight and ICR instruments, while even a full-scale laboratory quadrupole ion trap is relatively pressure tolerant. In fact, higher pressure operation (millitorr for a full-scale analyzer (1 Torr = 133.3 Pa)) is necessary to obtain the best resolution and sensitivity, because of the need for a buffer gas, typically helium, to improve ion cooling.
The effects of pressure on performance, then, highlight the importance of miniaturized pumps for use with miniature analyzers. As will be seen, miniature analyzers of various types have been successfully operated for a variety of applications, but it is the associated pumping components that are not yet available. Use of these analyzers in a truly miniature mass spectrometer system requires advances in vacuum technology. Currently the limiting factor for cost, power, size, and mass of the miniature mass spectrometer is the availability of appropriate pumping systems.

**SECTOR ANALYZERS (ELECTRIC, MAGNETIC AND CROSSED FIELD)**

Sector mass spectrometers are known for their high resolution and high mass accuracy and for the ability to perform ion energy analysis. However, they are typically larger than most other laboratory mass spectrometers and employ heavy magnetic (B) and, often, electric (E) sectors. The ability to perform a variety of tandem mass spectrometric (MS/MS) scans in multi-sector instruments adds to their value for chemical analysis, although the use of multiple analyzers makes the instrument much larger than the alternative tandem-in-space instrument, the triple quadrupole or a tandem-in-time instrument such as the Paul ion trap. Offsetting some of these disadvantages for miniaturization is the fact that, unlike linear quadrupoles and ion traps, sector instruments do not require an r.f. field. R.F. fields typically require more power than the variable-amplitude static fields necessary for the operation of most sector instruments; moreover, static fields can be generated with less complicated electronics, which aids in the miniaturization of the electronics package and therefore the entire instrument. Of even greater advantage is the possibility of using small permanent magnets that require no power at all (see below) instead of the relatively high power needed for traditional electromagnets used in laboratory instruments. Because of the long history and wide use of sectors in analytical mass spectrometry, miniaturized sector mass analyzers were some of the first to be reported.

Operation of both electric and magnetic sector instruments is based on the balance between centrifugal force and the force exerted on the ions by the electric or magnetic field. The equation for magnetic sectors is given in Eqn (1):

$$\frac{mv}{z} = Br_B$$  \hspace{1cm} (1)

where $mlz$ is the mass-to-charge ratio of the ion, $v$ is the axial velocity of the ion, $B$ is the magnetic field strength and $r_B$ is the radius of the ion’s path through the magnet. The equation shows that a magnetic sector is actually a momentum-to-charge analyzer and it is only when all ions are accelerated through a common potential, $V$, that the magnetic sector can function as a mass analyzer. The mass analysis equation for this condition is given in Eqn (2):

$$\frac{m}{z} = \frac{B^2 r_B^2}{2V}$$  \hspace{1cm} (2)

In this case, mass analysis occurs by scanning the magnetic field of the sector, or, more rarely, the accelerating voltage. Alternatively, mass analysis can be performed using a non-scanning (static) magnetic field if used in conjunction with an electric sector in a image plane instrument such as the Mattauch–Herzog geometry double-focusing instrument.

Equation (3) gives the force balance equation for an electric sector:

$$\frac{mv^2}{z} = Er_E$$  \hspace{1cm} (3)

where $E$ is the electric field strength, $r_E$ is the radius of ion motion through the sector and $v$ is the ion velocity. From this equation it can be seen that an electric sector is a kinetic energy-to-charge analyzer and not a mass analyzer unless the ions of interest have a fixed velocity.

High performance with sectors is achieved using double-focusing mass spectrometers in which an electric (E) and magnetic (B) sector are arranged in series, and placed so that the velocity dispersion in the electric sector cancels out the velocity dependence of the magnetic sector. A common way to achieve mass analysis simultaneously with velocity focusing is with a magnetic (B) and, often, electric (E) sectors. Historically, the two most common geometries were the Nier–Johnson and Mattauch–Herzog, both of which, in their standard forms, use an electric sector followed by a magnetic sector. The Nier–Johnson instrument provides focusing to a point at the exit of the magnetic sector and an intermediate focal point between the sectors. The Mattauch–Herzog geometry focuses different ions onto different positions on a focal plane upon exiting the magnetic sector and has the advantage of being a non-scanning instrument.

A small non-scanning Mattauch–Herzog geometry sector mass spectrometer has been designed to allow for fast analysis of the effluent from a microbore gas chromatograph used in environmental monitoring. The non-scanning nature of this instrument, and also the ability to record an entire spectrum simultaneously, allows rapid data acquisition (useful for measuring effluent from a fast chromatographic separation) and increased sensitivity over scanning sector instruments which only allow ions of a single $mlz$ ratio to be recorded at one time. Using new materials to construct a lighter magnet, two instruments with focal planes of 12.7 and 5.1 cm and $mlz$ ranges 25–500 and 40–240 Th (1 Th = 1 Da/charge), respectively, have been constructed.6 The larger instrument has unit mass resolution at 500 Th and can detect the order of 100 ppb of benzene while also displaying a dynamic range of ~1000. Using a discrete focal plane array detector capable of measuring single ions, this instrument showed resolution of all krypton isotopes and a mass measurement accuracy of better than 0.1 Th.7

Another Mattauch–Herzog geometry double-focusing plasma-source instrument has been described for elemental analysis. The instrument has an electric sector $r_E = 16.03$ cm and a magnetic sector with high mass radius of travel ($r_B$) of 9.29 cm and a low mass radius of travel ($r_L$) of 3.90 cm and a 7.6 cm long focal plane. The instrument was designed for mass windows of 7–38 and 42–238 Th so that Ar ions would not impinge upon the detector. Initial results were taken using a 2.54 cm diameter micro-channel plate (MCP) array detector with a phosphor screen for electron to photon conversion which resulted in $r_H = 10$ cm and $r_L = 9$ cm. Preliminary results for mass accuracy show the average difference between measured and theoretical isotope ratios for Cu and Zn to be 11.0%.
whereas for Mg the value was 3.7%. Although taken under less than ideal conditions, the calculated detection limit (signal-to-noise ratio 3) from spectra for Ni was 8 ppm, whereas for Pb it was 1 ppm. Detection limits are projected to increase by 2–3 orders of magnitude as the instrumental parameters are optimized. Resolution was noted to be poor, and changes to improve ions focusing and slit widths were proposed. Peak shapes were found to be non-Gaussian, but were a result not of the mass analyzer, but the array detector.

Another double-focusing miniature mass analyzer, again with the EB configuration and again using static fields, has also been described. However, in this case the Nier–Johnson geometry was used so that ions of a single mass-to-charge ratio were transmitted to a fixed-point detector; mass spectra are obtained by scanning the accelerating voltage used to extract ions from the source. This procedure has been used previously for laboratory scale instruments. The use of the Nier–Johnson geometry with a miniaturized analyzer provides a simple method of mass analysis without the complication of scanning a magnetic field. The miniature instrument uses two electron multiplier detectors placed at different positions on exiting the magnetic sector in order to provide two different radii ($r_E$), in the magnetic sector mass analysis equation [Eqn (2)]. The appropriate choice of detector position maximizes performance over a desired mass range, allowing the instrument to be operated in two modes corresponding to ‘high’ and ‘medium’ mass ranges. The ‘medium’ range covers 7–44 Th with an $r_E$ of 3.6 cm and the ‘high’ mass range covers 39–255 Th and uses an $r_E$ of 9.0 cm. The electric sector angle is 40° with an $r_B$ of ~13 cm. The relative size of the analyzer can be appreciated by considering the total size of the entire instrument: 17 × 37 × 57 cm with a mass of 20 kg without a computer. Resolution in the high-mass range was reported as 131 ($m/Δm$, using the unusual definition of 4% valley) for the molecular ion of benzene, whereas that achieved in the medium mass range was 56 (with an unusual 1.6% valley definition) for N$_2^+$ (air). The limit of detection for toluene in air using electron ionization (EI) was 1 ppm. An example of the performance for a model compound, chlorobenzene, is shown in Fig. 1 (displayed using the uncorrected non-linear $m/z$ axis characteristic of a sector mass spectrometer). A similar double-focusing instrument was designed using the magnetic sector characteristics of the high-mass range in which the exit angle of the magnet pole was optimized and a single magnet radius $r_B$ and hence mass range was used. Preliminary results of analysis of compounds dissolved in water were reported.

A double-focusing analyzer using superimposed fields from an electric sector and a magnetic sector has also been developed. An academic version of this type of instrument [Fig. 2(a)] uses a 90° electric sector with $r_B$ 20 mm and has an EI source with ion optics that are scanned in concert with the electric sector voltage to perform mass analysis. The analyzer, with magnet, ion source and detector, weighs 0.7 kg and measures 3.5 × 6 × 7.5 cm. Figure 2(b) shows a residual gas spectrum of the vacuum system at a pressure of 3 × 10⁻⁶ Torr, with a resolution of 92 (50% valley) for the N$_2^+$ ion. The achievable mass range is 100 Th with a sensitivity of ~10 ppm and a maximum resolution of 106 at $m/z$ 28 (N$_2^+$). Without batteries, the entire mass spectrometer system including pumps and electronics weighs ~18 kg. Among other applications, it has been used for in situ monitoring of volcanic gases.

A miniature sector mass spectrometer for in situ analysis of ions in plasma processes has also been described. The analyzer uses a varying ion accelerating/extracting potential and a static 0.28 T magnet and measures 58 × 38 × 47 mm. The device can be operated using voltages less than 100 V and in scan times of the order of 15 s. The resolution is low (~7, 50% valley), but this was demonstrated to be adequate for various plasma analysis applications.

Figure 2. (a) Schematic of a double-focusing crossed electric and magnetic field analyzer with \( r_L = 20 \) mm and a total size of \( \sim 2.5 \) cm square, showing the ion source, mass analyzer and detector.\(^\text{14}\) (b) Residual gas analysis spectrum from the double-focusing crossed electric and magnetic field analyzer.\(^\text{13, 14}\) Reprinted with permission from Dr Jorge A. Diaz, University of Minnesota.
Another type of analyzer that has seen something of a rebirth in the miniaturization effort is the linear crossed electric and magnetic field analyzer (the Wien filter). A miniature Wien mass filter has been built using micromachining technology with a 1.0 cm long analyzer and a 1.0 T permanent magnet. Initial results show a peak with full width at half-maximum (FWHM) of 2 Th at m/z 129 (Xe+).

Various other types of small mass analyzers using electric and magnetic fields have been proposed and studied, although in most cases the instruments have seen only limited use and only preliminary results have been published. An unusual instrument is a miniature mass analyzer that uses a field emission array electron source.17 The mass analyzer consists of two nested cylinders with field emitters mounted on the outer surface of the inner cylinder and ion detector(s) located on the inner surface of the outer cylinder with the radius of the analyzer being a few centimeters. Ionized molecules are subjected to crossed electric and magnetic fields that cause ions of differing masses to have different deflection angles and therefore impinge upon the outer cylinder detectors at differing positions. In a somewhat related development, a group at the Jet Propulsion Laboratory has designed an array of four miniature Bessel boxes as electrostatic energy analyzers. Each kinetic energy analyzer has a length of 2.6 mm and a width of 0.8 mm and is etched on a silicon wafer.

Linear quadrupoles

By far the most common miniature mass analyzers are linear quadrupoles, which are used as both single analyzers16,19–23 and arrays of quadrupoles.24,25 Besides miniaturization per se, one of the driving forces behind development of miniature quadrupoles is the desire to have an instrument that can operate effectively at relatively high (millitorr range) pressures. Conventional quadrupole mass analyzers are pressure tolerant compared with most other types of analyzers and even higher pressure operation is allowed as a result of the reduction in ion pathlength through the analyzer and the consequent reduction in the number of collisions with background gas. As noted in the Introduction, this advantage of operation at higher operating pressure compared with full-size analyzers is shared by all miniature instruments.

Linear quadrupoles operate using both r.f. and d.c. voltages applied to the four rods of the analyzer. Using the appropriate amplitude and sign of the applied voltages, the trajectories of ions of a range of mass-to-charge ratios can be made to be stable in both the x- and y-directions as they travel through the rod assembly. The quadrupole operates as a mass analyzer when conditions are selected such that only ions of a single mass-to-charge ratio have stable trajectories, all others being unstable in the x- and/or y-directions and hence being lost from the two-dimensional trapping field. By scanning the applied d.c. (U) and r.f. (V) voltages applied to the rods at a fixed U/V ratio (typically 0.17), a full mass spectrum can be obtained as the trajectories of ions corresponding to a single mass-to-charge ratio (or a small range of values) in turn become stable under the operating conditions and pass along the axis of the rods to the detector. The mass analysis equation:

\[ \frac{m}{z} = \frac{2V}{q_1\omega^2 r_0^2} \]

shows how m/z is related to the applied r.f. voltage (V), the Mathieu stability parameter \( q_1 = q_z \), the angular frequency of the applied r.f. (\( \omega \)) and the inscribed radius of the rod assembly (r0). A scan of V (with U also scanned such that V/U is constant) therefore yields a mass-selective stability mass spectrum.

The first fully micromachined quadrupoles, constructed of metallized glass electrodes mounted in silicon,21 having rods 0.5 mm in diameter and 20–30 mm in length, were fabricated by a collaborative group from Imperial College and Liverpool University in the UK.16,19–21,23 At a frequency of 6 MHz, calculations show that the 30 mm long analyzer requires less than 50 V r.f. to analyze for ions up to m/z 100, reducing the power consumption of the device greatly compared with a full-scale quadrupole with the same mass-to-charge range.23 Peak widths of 2.7 Th (10% valley) were recorded at 40 Th. The device was reliably operated up to pressures of 10^-4–10^-3 mbar (~7.5 × 10^-5–7.5 × 10^-4 Torr), although the upper limit was attributed to limitations in the ion source and not the quadrupole itself. The resolution of the device is lower than that of similar miniature quadrupole arrays (described below) and the pressure tolerance is slightly poorer; upper mass limit and sensitivity data were not given. Nevertheless, this work represents an important advance in miniaturized mass spectrometry.

Another miniature quadrupole analyzer, with 0.5 in (1.27 cm) long rods and r0 = 0.013 in (0.330 mm), machined using electrical discharge machining and operated at an r.f. frequency of 13 MHz, has been designed for use as a residual gas analyzer (RGA).22 El spectra of N2+ (from air) show peak widths of ~0.9 Th (10% valley). A spectrum of the isotopes of krypton in a gas mixture (Fig. 3) illustrates the resolution of the device. The resolution was shown to be relatively constant, even up to pressures of 10 mTorr; response is linear for Ar+ partial pressure from 10^-5 Torr to nearly 1 mTorr, although a loss of 50% in sensitivity was found at pressures above 2–3 mTorr (~50 times higher pressure than typically used for full-scale quadrupole mass analyzers). The calculated minimum detectable partial pressure is ~10^-11 Torr at a base pressure of 2 × 10^-8 Torr, corresponding to <10 ppm of CO2 in 1 mTorr of argon. Although the sensitivity and resolution of both miniature quadrupole systems described here are lower than those of full-scale laboratory quadrupoles, these instruments do allow for use at higher pressures without undue sacrifice of overall performance and as such are useful for a number of applications. Single-stage linear quadrupoles lack the capability to perform multiple stages of mass analysis like trapping instruments unless built in tandem (e.g. the triple quadrupole instrument),27 currently there are no examples of miniature tandem quadrupoles in the literature, although one expects this to be the next step in the evolution of miniature quadrupoles.

A miniature quadrupole mass analyzer described previously22 has been used for in situ chemical analysis in an underwater mass spectrometer system.28 The mass spectrometer was developed for use on an autonomous
underwater vehicle (AUV) for measurement of dissolved gases and organic species in sea water. The system uses a membrane introduction interface and an EI source, coupled to a quadrupole mass filter with a mass range of 1–100 Th. A small turbomolecular drag pump and two diaphragm pumps in series provide the vacuum of $10^{-6}$ Torr (when not sampling sea water). The entire mass spectrometer system is constrained to fit in an area in the AUV with a maximum diameter of 0.46 m and a length of 1.96 m and to use only 48 V d.c. and 400 W h of energy during a typical run time of 4 h. In laboratory tests, the mass spectrometer system showed detection limits below 1 ppb for the 91 Th ion of toluene.

Two groups have developed arrays of quadrupole analyzers in order to utilize the benefits of high pressure and lower r.f. amplitudes of the mini-quadrupole analyzers. The use of an array allows recovery of the loss in sensitivity associated with miniaturization of the individual analyzers. The voltage and power requirements can be reduced substantially, higher operating pressures can be used (as is the case for single miniature quadrupoles) and, more importantly, because of the array geometry, the acceptance area of the device can equal that of a full-scale quadrupole, thus greatly increasing sensitivity over a single miniaturized quadrupole mass analyzer. Ferran and Boumselleck have built a $4 \times 4$ array of rods, forming nine quadrupole analyzers (weighing $\sim 25$ g) and operated the device using an EI source. The rods are 0.5 mm in radius, 10 mm long and mounted in a glass base. The array gives a linear response to argon over six decades of pressure (up to 10 mTorr) and can analyze ions up to 100 Th with 50 V d.c. and 300 V r.f. at 11 MHz. Reduced sensitivity was seen above 10 mTorr. A mass range of $\sim 300$ Th was demonstrated with $n$-docosane ($\text{CH}_3(\text{CH}_2)_{20}\text{CH}_3$); air monitoring at 3 mTorr showed peak widths (FWHM) of 0.5 Th and the ability to detect Ne at concentrations down to 9 ppm.

A similar device has been built at the Jet Propulsion Laboratory, also consisting of a $4 \times 4$ array of 1 mm radius, 25 mm long rods forming nine mass analyzers [Fig. 4(a)]. Power consumption for all components (including EI ion source, r.f./d.c. potentials and detector) is 7.5 W at 300 Th. The r.f. drive frequency can be operated at 5.3, 7.1 or 12.9 MHz; this allows higher resolution for lower mass ions by selecting the higher drive frequencies. Resolved isotopic patterns for Kr [Fig. 4(b)] and Xe, as well as a full-scale mass spectrum of C$_8$F$_{12}$, were recorded over the instrument’s mass range of 1–300 Th with peak widths of 0.1–0.5 Th (FWHM). The sensitivity was found to be $(0.2–2.7) \times 10^{12}$ counts Torr$^{-1}$ s$^{-1}$ for a variety of atomic gases. The improved performance achieved relative to the earlier instrument was attributed to more precise positioning and machining of the rods to tolerances of 0.1 and 0.05%, respectively, thereby minimizing undesirable higher order (non-quadrupolar) field effects on resolution.

Time-of-flight

Time-of-flight (TOF) mass spectrometers have also become part of the miniaturization revolution. Because of their relatively low cost, simple design and high mass-to-charge range, full-sized TOF mass spectrometers are often the analyzers of choice for high sensitivity, high $m/z$ range work in the laboratory, especially for species of biological interest. These properties would also seem to make them easily amenable to miniaturization for use for similar purposes. One problem with TOF analyzers is that, unlike linear quadrupoles and quadrupole ion traps, there is the need for relatively low operating pressures. This requires more powerful pumps that are, at this time, the main factor limiting the degree of miniaturization possible.
Figure 4. (a) Instrumental design of a miniature linear quadrupole array, showing a miniature ionization source, the quadrupole rod array and ceramic jigs for positioning, and an electron multiplier detector. Each quadrupole rod is 25 mm long and has a radius of 1 mm.25 (b) Krypton isotope mass spectrum from the linear quadrupole array showing experimental data points, overlaid with Gaussian fits to the data.25 Reprinted with permission from Rev. Sci. Instrum. 68(3), 1393 (1997). Copyright 1997 American Institute of Physics. American Institute of Physics 1997.
Mass analysis in a TOF mass spectrometer, as the name suggests, is based on the measurement of the flight time (t) of ions accelerated by a voltage (V), and passing through a distance (d). The mass-to-charge analysis equation is

\[ m/z = \frac{2Vt^2}{d^2}. \]  

(5)

TOF is highly dependent upon the initial kinetic energy, position and time spread of the ions, all of which must be minimized or compensated for by more or less complex focusing schemes for maximum performance.

A noteworthy effort in miniaturization of a TOF-MS instrument is that undertaken at Johns Hopkins University (Applied Physics Laboratory), with the design of the “tiny-TOF.” The device was designed for rapid detection of chemical and biological warfare agents, environmental monitoring and law enforcement applications in the field. The first published design was for a 20 cm long, 500 g reflectron TOF, later improved as described below. A ~10 cm coaxial reflectron TOF using matrix-assisted laser desorption/ionization (MALDI) has shown mass ranges >10,000 m/z, sensitivity in the picomole range and a resolution of 300–1000 (FWHM). The Johns Hopkins group has also developed a miniature 2.0 in (~5 cm) endcap reflectron mass spectrometer for use in a miniature device and has shown results from initial tests of the improved resolution which results from higher order kinetic energy focusing and a mass range of ~3000 Th. Development is under way to couple an air sampling interface to the portable TOF analyzer in a prototype instrument [Fig. 5(a)] which deposits aerosol particles on a video cassette tape for transport past a nozzle that applies the MALDI matrix and then to the ion source, where samples are ionized using a laser pulse. New mass analyzer developments include use of a ‘pseudo-tandem’ TOF arrangement that uses an electronic gate to select a parent ion and relies on detecting all post-source decay (PSD) or metastable ions from the selected parent as a method of recording tandem mass spectra (instead of a true tandem TOF instrument in which two time-of-flight tubes are arranged in series and fragment ions from the first are mass analyzed in the second). Spectra resulting from parent selection using the gate were shown for a peptide mixture [Fig. 5(b)], as well as for biogent simulants.

A miniature converging annular TOF analyzer with an EI source has been designed for environmental monitoring of volatile organic compounds. The mass resolution (50% valley) of the instrument is 270 at m/z 91 (toluene) and the dynamic range is a 20 cm long, 4 g reflectron TOF; later improved as described below. A ≈20 cm coaxial reflectron TOF analyzes surface material ablated from a 30–50 µm spot by a pulsed Nd: YAG laser. A steel NIST standard demonstrated the performance of the device for elemental analysis over a range of ion kinetic energies; single-shot detection limits were 18 ppm (34S) with a resolution of ~200 (50% valley).

An instrument that uses a quadrupole ion trap coupled to a miniature TOF mass analyzer (QitTOF) has been developed for monitoring in the field (J. A. Syage, Syagen Technology, personal communication 2000). The ion trap is simply used to accumulate and store ions before they are analyzed in the TOF. Miniature linear and coaxial reflectron TOF analyzers were developed with resolutions of 150 and 300, respectively. When the atmospheric sampling threshold ionization source, ion trap and dual-microchannel plate detector are included, the linear TOF measures 30 cm and weighs ~0.7 kg. Two field-portable TOF systems have been developed with total weight and power specifications of 13.6 kg, 120 W and 22.7 kg, 250 W. Figure 6(a) shows a spectrum of disopropyl methanephosphonate (DIMP), which is relevant for chemical warfare agent detection, taken with the 22.7 kg linear TOF instrument. Figure 6(b) shows reproducibility and response times for the molecular ion (m/z 124) of dimethyl methylphosphonate (DMMP) at 9 ppm and the molecular ion (m/z 180) and fragment ion (m/z 97) of DIMP at 5 ppm. The mass range of the instrument is 20–400 Th; detection limits are 20–50 ppb for air sampling of DIMP and DMMP and <1 ng g⁻¹ soil for DIMP and DMMP in solid samples.

A collaborative group of Japanese and German scientists is building a novel miniature multi-pass TOF analyzer with four cylindrical electric sectors and eight quadrupole lenses in which higher resolution is achieved as a result of multiple passes of the ion beam through the analyzers. The device, although currently not miniature, is intended for a small package to be launched for comet analysis. Another instrument uses a 10 cm TOF analyzer in a compact high-speed GC-TOF instrument developed for natural gas and refinery gas analysis. Run times are <60 s and the resolution is ~110 (50% valley); only a limited mass range, up to 58 Th, is needed for the gas analysis application. Scientists at Argonne National Laboratory are also designing a miniaturized TOF with laser desorption ionization, built to fit into a briefcase-sized package.

A miniature mass analyzer has been constructed with a plasma electron source and an unusual TOF analyzer in which ions are separated by velocity in a 12.5 MHz travelling dipole field applied to a set of electrodes. A time-varying acceleration field applied as the ions leave the source sets the instantaneous injection velocity. The mass analyzer is composed of two sets of 100 µm wide electrodes, spaced by 100 µm, on either side of the channel, a few millimeters long, into which the ions are injected. Simulations of performance have been performed, but no data have been presented on the mass analysis capabilities of the device.
Quadrupole ion traps

Paul ion traps, although more limited in resolution and mass accuracy than FT-ICR and TOF instruments, offer some advantages as miniature mass analyzers. One is the high sensitivity of ion traps, which is especially useful for applications such as environmental and process trace monitoring. Quadrupole ion traps can operate at higher pressures than any other type of analyzer, even linear quadrupoles, and performance is actually enhanced when a few millitorr of helium are deliberately added to the trapping volume. Another major advantage of quadrupole ion traps, like FT-ICR, is the ability to perform multiple stages of MS with no modification, except the application of the appropriate voltages. Quadrupole ion traps, as typically operated, share the disadvantages...
of linear quadrupoles in that they require r.f. fields, and thus more power, and need higher r.f. drive frequencies to maintain resolution as the size of the electrodes is decreased.

Quadrupole ion traps, like linear quadrupoles, can be used as mass analyzers because of the control available over the stability of ion motion in an electric field. In the case of the ion trap, voltages applied to a hyperboloid ring and two hyperboloid endcap electrodes are chosen to allow ions of a wide mass range to have stable trajectories. Then, as trapping conditions are altered, the ions’ motion becomes unstable in order of their mass-to-charge ratios. As a result they are ejected from the trap and impinge upon an external detector after passing through an aperture in one of the endcap electrodes. The mass analysis equation for mass selective instability scan of the

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quadrupole ion trap is

\[ m/z = \frac{8V}{q_2 \Omega^2 (r_0^2 + 2z_0^2)} \]  

(6)

where \( V \) is the voltage of the applied r.f. trapping signal, \( q_2 \) is the dimensionless Mathieu parameter related to the ion’s stability in the \( z \)-direction, \( \Omega \) is the angular r.f. drive frequency and \( r_0 \) and \( z_0 \) are the inner radius and center to endcap electrode distances, respectively. Mass analysis is typically performed by ramping the applied r.f. voltage to cause ions of increasing \( m/z \) to become unstable in the \( z \)-direction and hence to be ejected into the detector. This experiment is performed at a selected value of \( q_2 \) (often 0.908 or a value lower than this if ions are scanned into a resonance created by the application of a supplementary a.c. signal on the endcap electrodes).

The first miniature quadrupole ion trap was built in a collaborative study between this lab at Purdue and Los Alamos National Laboratory. Half- and quarter-sized (0.5 and 0.25 cm inner radius) ion traps were constructed to extend the mass-to-charge range and ions up to 70,000 Da were observed, although with poor mass resolution.

Current work in the area of miniature ion traps has been focused on cylindrical quadrupole ion traps (CITs) rather than ion traps with hyperboloid trapping electrodes. Because of the simplified electrode design, often consisting merely of flat endcaps and a barrel-shaped ring electrode, CITs are much simpler to machine than hyperbolic ion traps, and can therefore be miniaturized more easily. A miniature CIT with an \( r_0 \) of 2.5 mm that showed resolution of \( \sim 100 \) (50% valley definition) for \( m/z \) 146 of dichlorobenzene (Fig. 7) and detection limits of 500 ppb for toluene in water using a membrane inlet system, has been described. Spectra show a mass-to-charge range of 219 Th using perfluorotributylamine (PFTBA). Simulations and field calculations aided in optimization of the trap geometry.

Even smaller CITs with ring electrode radii of 0.5, 1.0 and 2.0 mm have been developed and used with laser ionization of volatile organic compounds. Peak widths of \( \sim 0.25 \text{ Th} \) using axial modulation were obtained for the 0.5 mm radius trap. A mass-to-charge range of 30–400 Th was possible with mass accuracy of 1 Th. Mass accuracy was limited to 1 Th as a result of jitter between scans. The total number of ions trapped was calculated to be \( \sim 1000 \), although no experiments on the limits of detection have been reported. Recently these authors have used an electron gun for ionization and shown spectra for Xe with peak widths of \( \sim 0.2 \text{ Th} \) for the calibration compound, PFTBA.

Miniature CITs lend themselves to the design of ion trap mass analyzer arrays as a result of the simple construction of each mass analyzer. An array in which the inner radius of the cylinder determines the mass-to-charge ratio of trapped ions has been reported. By varying the radii of the individual CITs in an array, low-resolution spectra can be obtained with an imaging detector without the need to scan the r.f. voltage; this new design greatly reduces the power requirements and electronic complexity of the overall instrument. By performing an r.f./d.c. (apex) isolation or selected waveform isolation experiment, ions falling into a designated \( m/z \) range can be trapped in each CIT element as determined by the trap radius and the isolating voltages used. A variety of experiments then can be performed, from full low-resolution spectra to selected ion monitoring for compounds of interest. In the full spectrum case, data processing algorithms will be necessary to obtain chemical identification from the low-resolution output data from the array.

A second type of CIT array functions similarly to the previously described linear quadrupole arrays.

Figure 7. Mass spectrum of o-dichlorobenzene recorded using a cylindrical ion trap with 2.5 mm inner radius. Reprinted with permission from Analytical Chemistry 70, 4896 (1998). Copyright 1998 American Chemical Society. American Chemical Society 1998.
CIT arrays consist of multiple traps of the same dimensions arranged in parallel and operated using the same applied voltages. Scanning results in the simultaneous ejection of ions from all traps in the standard mass analysis mode. As with the quadrupole array instrument, the parallel CIT array was designed to regain dynamic range and sensitivity lost as a result of miniaturization. Spectra from parallel arrays with CITs of \( r_0 = 2.5 \) mm show the improved sensitivity achieved with four CITs compared with two CITs (obtained when two channels of the four CIT array were blocked). A resolution of 180 (50% valley) was achieved for the molecular ion peak of dichlorobenzene using an r.f. drive frequency of 2.0 MHz. Detection of a 100 ppm Kr in Ar mixture at a total pressure of \( 5 \times 10^{-5} \) Torr (uncorrected) with a manifold pressure of \( 2 \times 10^{-7} \) Torr shows the sensitivity of the array.

**Ion cyclotron resonance**

Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometers are the instruments of choice for high resolution and high mass accuracy, but are often cost and size prohibitive. They are capable of analyzing species over a wide \( m/z \) range and are commonly used for the study of ion chemistry owing to the ability, like the quadrupole ion trap, to perform MS\(^n\) in a single analyzer cell.\(^{59}\) One advantage that FT-ICR has is the ability to detect ions non-destructively and, therefore, to perform ion remeasurement on the same ion population. The performance of FT-ICR is increased with the use of higher field magnets, and this is in turn one of the problems associated with designing a miniature FT-ICR instrument since field strength tends to scale with size and weight. Another problem with the miniaturization of FT-ICR is that the performance of the instrument depends heavily on the quality of the vacuum, and the pumping requirements are greater than for instruments such as the linear quadrupole or quadrupole ion trap.

As in the case for magnetic sectors, FT-ICR operates on the balance of the force exerted by the static magnetic field and the centrifugal force of the ions, resulting in the ions undergoing cyclotron motion in the direction perpendicular to the magnetic field. Balancing the two forces yields the equation

\[
m/z = \frac{B}{\omega_c}
\]

the mass analysis equation for FT-ICR, where \( B \) is the magnetic field strength and \( \omega_c \) is the angular ion-cyclotron frequency. The typical FT-ICR mass analyzer consists of a cubic cell of three sets of parallel plates. The magnetic field traps ions in the direction perpendicular to the field, while to one set of plates is applied a voltage to trap them in the direction parallel to the magnetic field. The other two pairs of plates are used for excitation and detection, respectively. Because the cyclotron frequency is dependent on the mass-to-charge ratio of the ion, mass analysis can be achieved through measurement of the cyclotron frequencies of the ions. Detection of the frequencies is through measurement of the induced image current on the detection plates after the ions have been excited into coherent motion. Ion excitation is achieved via a voltage pulse that has frequency components resonant with the ion cyclotron frequencies. The excitation pulse causes the ions to absorb energy and increase their radius of travel in a coherent fashion, allowing them to be detected. The time-dependent image current signal of the ions is then recorded and can be Fourier transformed and converted into a mass spectrum.

Preliminary results from two portable FT-ICR mass spectrometers have been shown\(^{60, 61}\) one uses a 0.5 T permanent magnet and has a mass range of 15–300 Th.\(^{61}\) The other fits into an \( 18 \times 12 \times 3.5 \) in (\( \sim 46 \times 30 \times 9 \) cm) briefcase, uses a permanent 0.44 T magnet and runs on four 12 V laptop PC batteries, with no upper mass range specified.\(^{60}\) With a miniature piezoelectric inlet valve and a miniature ion pump (base pressure \( 5 \times 10^{-4} \) Torr), a resolution of 500–1000 for a sample pressure of \( 10^{-7} \) Torr was achieved. The limited data available from the two instruments mean that it is too early to compare the relative merits of each system.

**CONCLUSIONS**

Interest in miniature mass analyzers for a wide variety of applications is increasing rapidly. It is expected that as vacuum technology is improved and pumps become smaller, developments in this field will become even more rapid. This is because in many cases, it is not the mass analyzer itself, but the associated vacuum and electronic components that limit development of an entirely miniaturized instrument. Applications for miniature instruments are as varied as the applications for full-sized analyzers, although complete instruments that are hand-held will allow \textit{in situ} analysis in otherwise inaccessible environments. It is not too much of an extrapolation to be able to look forward to a time when mass spectrometers will be ubiquitous sensors, and perhaps even consumer devices.

**Acknowledgements**

This work was supported by the US Office of Naval Research. E.R.B. acknowledges an ACS Analytical Division Fellowship sponsored by The DuPont Company. The authors thank the numerous scientists who contributed to the preparation of this paper, through suggestions and comments and by providing information about instruments for inclusion in this review. They include Phil Berger, David Bomse, Said Boumsellek, Ara Chutjian, Jorge A. Diaz, Robert E. Ellefson, David P. Fries, Barrie W. Griffiths, Stephen A. Lammert, Henk Meuzelaar, Sabatino Nacson, David B. Salzman, R. Tim Short, Jack A. Syage and Bill Whitten.

**REFERENCES**