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THE RECENT EVOLUTION OF THE QUADRUPOLE ION TRAP MASS SPECTROMETER—AN OVERVIEW

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INTRODUCTION

For those of us who have been engaged in ion trap research for the past two or more decades the current dramatic explosion in instrumental development and applications provides not only a sense of fulfilment, but also amazement at the speed with which this small and formerly rather esoteric device has burgeoned so as now to be seen as a standard instrument for mass spectrometry. Because of the rapid advances in this field it was felt to be opportune to bring together in one volume of this journal a collection of research papers which represent the numerous efforts which are presently being made to enhance the versatility of the ion trap, to extend its performance and to provide further insight into the theory and practice of its operation. As part of this compilation it was thought desirable, therefore, to include an overview which would provide a newcomer to the field with sufficient background to appreciate the significance of the contributions which follow. This survey does not, therefore, purport to be a comprehensive review of the history and development of the trap, nor does it provide a full treatment of the theory underlying its operation. The aim is rather to offer the reader an introductory account of how the trap operates in its current mode of use, and to indicate the key stages of development which have been reported over the past ten years.

The history of the ion trap dates back to the pioneering work of Paul and Steinwedel [1], which was recognized by the shared award of the 1989 Nobel Prize to Wolfgang Paul [2]. Detailed accounts of the early development of the quadrupole-type devices as mass spectrometers were published by Dawson and Whetten [3] and Dawson [4]. A full treatment of the theory of the trap is

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to be found in the now-standard text *Quadrupole Storage Mass Spectrometry* by March and Hughes [5]: this includes a historical account by the present author which has recently been expanded into a full-scale review [6]. Other reviews on specific topics have been contributed by Cooks and co-workers [7,8].

THEORY AND OPERATING PRINCIPLES OF THE ION TRAP MASS SPECTROMETER

As implied by its name, this instrument operates on the basis of first storing ions and then facilitating their detection according to their mass/charge ratio. In all there have been three essentially different means by which this has been achieved, and these have been explained in detail elsewhere [5,6]. Initially mass-selective detection was employed, in which the motion of the ions was sensed by means of tuned circuits [9] such that a response was obtained for each m/z value in turn; this approach had certain similarities with ion cyclotron resonance, with the merit that the ions were detected non-destructively. This method, which was at the time not generally appreciated by mass spectroscopists, then gave way to mass-selective storage in which the ions were trapped according to their mass/charge ratios and then detected by pulse-ejecting them from the trap into an external detector [10,11]. Whilst this arrangement gave satisfactory mass spectra, albeit over a limited mass range, the instrumentation was somewhat complex, and did not appear to offer particular advantages over, for example, the quadrupole mass spectrometer. One development which did, however, prove to be of some interest was the combination of the ion trap, termed by us the QUISTOR (for quadrupole ion store), with the quadrupole mass analyser [12,13]. In this system ions could be trapped either in a broad-band or in a mass-selective mode [14] for a pre-determined period of time before ejection and external mass analysis. In this way various physical and chemical studies could be performed on the trapped ions, and this technique has been employed extremely effectively by Lifshitz and co-workers in their studies on time-resolved photoionization mass spectrometry (TPIMS), as evidenced by the paper contributed to this volume [15].

Current analytical use of the trap, however, relies upon the more recently developed technique of the mass-selective ejection of ions [16,17], first pioneered commercially by Finnigan MAT [18] and marketed under the name "Ion Trap Detector" (ITD$^{\text{TM}}$). The operation of this instrument is best considered in terms of the schematic diagram shown in Fig. 1 and the description which follows. The ion trap consists of three cylindrically symmetric electrodes: two endcaps and a ring. Each of these has accurately machined hyperbolic internal surfaces, and in the normal mode of use the endcaps are

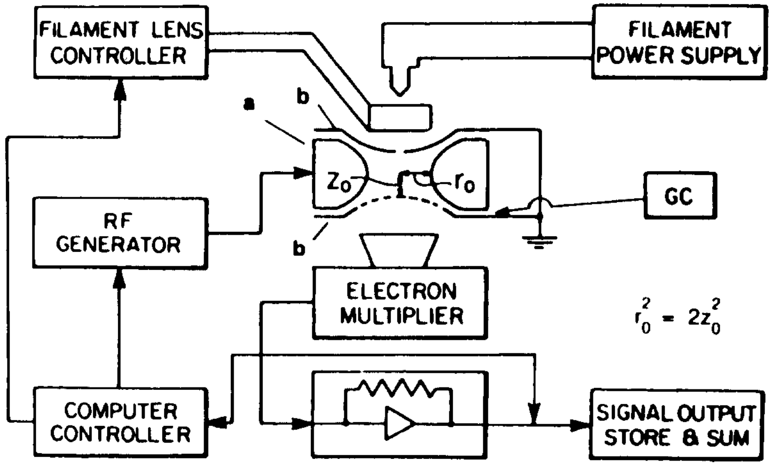

Fig. 1. Schematic diagram of the Ion Trap Detector (ITD™). The ring electrode and the endcap electrodes are labelled "a" and "b" respectively.

connected to earth potential whilst a r.f. oscillating "drive" potential, typically 1.1 MHz, is applied to the ring electrode. Ions are created within the trap by injection of electrons, or may be injected from an external source, and a range of m/z values may be held in bound, or "stable", orbits by virtue of the r.f. potential; alternatively a single m/z value or a range of m/z values may be stored by the superimposition of an appropriate d.c. potential on top of the r.f. drive potential (see below for further details). As the amplitude of the r.f. potential is then increased the motion of the ions becomes progressively more energetic such that eventually they develop unbound ("unstable") trajectories along the axis of symmetry (the z axis) and, in order of increasing m/z value, exit the device through holes in one of the endcaps and impinge on a detector. In this way a mass spectrum is generated, and generally a successive series of such spectra, termed "micro-scans" is summed prior to display and recording. The sequence of operation may be seen from the timing diagram or "scan function" shown in Fig. 2.

The theory behind the operation of the ion trap is best considered by examining the equations for the electric field within the trap and for the resulting motion of the ions. The shape of the potential developed within the trap when the electrodes are coupled to the r.f. and d.c. potentials as indicated above is described by

$$\phi = \frac{1}{2}(U + V\cos\Omega t)\left(\frac{x^2 + y^2 - 2z^2}{r_0^2}\right) + \frac{U + V\cos\Omega t}{2} \tag{1}$$

where U represents the maximum d.c. potential and V the maximum r.f. potential applied between the ring and the endcap electrodes, Ω is the angular

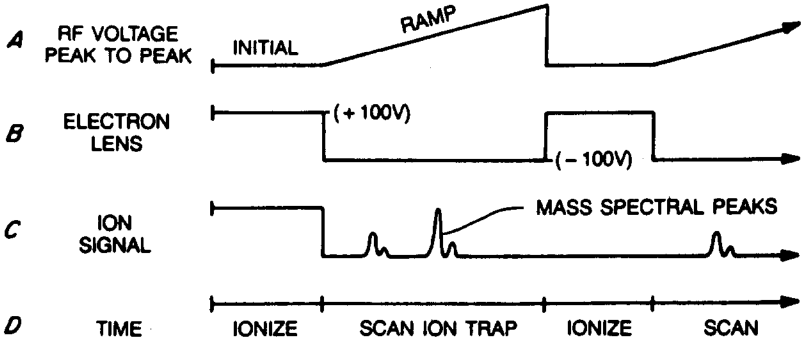

Fig. 2. Timing sequence ("scan function") for the operation of the ion trap in the mass-selective ejection mode.

frequency of the r.f. drive potential and r_0 the internal radius of the ring electrode; this particular geometry corresponds to the case in which $r_0^2 = 2z_0^2$, where $2z_0$ is the closest distance between the two endcaps. The oscillation of the r.f. potential causes the field to periodically reverse in direction so that the ions are alternately focussed and de-focussed along the z axis, and vice versa in the radial plane.

The force acting upon an ion of mass m and charge ze is given by

$$F = -ze \cdot \nabla\phi = m\vec{A} \tag{2}$$

from which the forces acting upon the ion in each of the perpendicular directions are given by

$$\left(\frac{m}{e}\right)\ddot{x} + (U + V\cos\Omega t)\frac{x}{r_0^2} = 0 \tag{3}$$

$$\left(\frac{m}{e}\right)\ddot{y} + (U + V\cos\Omega t)\frac{y}{r_0^2} = 0 \tag{4}$$

$$\left(\frac{m}{e}\right)\ddot{z} - 2(U + V\cos\Omega t)\frac{z}{r_0^2} = 0 \tag{5}$$

It will be noted that none of these expressions contains cross-terms between x, y and z with the result that the motion may be resolved into each of the respective perpendicular coordinates. The x and y components are identical and may be treated independently provided that we ignore any angular momentum which the ions may have around the z axis. Because of the cylindrical symmetry the x and y components are often combined to give a single radial r component using $x^2 + y^2 = r^2$.

The z component of motion is out of phase by half a cycle with respect to the x and y motions (hence the minus sign) and the factor of two arises because of the asymmetry of the device brought about by the need to observe the Laplace condition $\nabla^2\phi = 0$ when applied to eqn. 1. These equations are all examples of the Mathieu equation, which has the generalized form

$$\frac{d^2u}{d\xi^2} + (a_u + 2q_u \cos 2\xi)u = 0 \tag{6}$$

where

$$u = x, y \text{ or } z \tag{7}$$

$$\xi = \Omega t/2 \tag{8}$$

$$a_z = -2a_x = -2a_y = -\frac{8eU}{mr_0^2\Omega^2} \tag{9}$$

and

$$q_z = -2q_x = -2q_y = -\frac{4eV}{mr_0^2\Omega^2} \tag{10}$$

Thus the transformations 7–10 relate the Mathieu parameters a_z and q_z to the experimental variables and also to the "time" variables Ω and t. The a and q parameters are quite fundamental to the operation of the trap since they determine whether the ion motion is stable (i.e. the ions remain trapped) or unstable. The diagram shown in Fig. 3 (which is actually only a small portion of a much larger family of curves) defines the areas within which the axial (z) and radial (r) components of motion are stable, the region of overlap indicating the a_z, q_z coordinates corresponding to those ions which are held in the trap.

The scan function (Fig. 2) for the operation of the ion trap may therefore be seen as comprising a time period during which (Fig. 3) the a_z, q_z coordinates for the ions remain constant, at points lying on the q_z axis close to the origin, followed by movement of the coordinates along the axis until they reach the right-hand boundary whence the ions develop unstable trajectories along the z axis of the trap.

The lines drawn across the stability region in Fig. 3 are so-called iso-β lines, and describe the detailed trajectories of the ions at that point; the boundaries of the diagram correspond to β_r, $\beta_z = 0$ and β_r, $\beta_z = 1$, with the boundary $\beta_z = 1$ being that at which mass-selective instability is normally achieved during a mass spectral scan. Specifically the parameter β occurs in the general solution of the Mathieu equation given below:

$$u(\xi) = A \sum_{n=-\infty}^{\infty} C_{2n} \cos(2n + \beta)\xi + B \sum_{n=-\infty}^{\infty} C_{2n} \sin(2n + \beta)\xi \tag{11}$$

This equation is an expression for the frequency spectrum of stable trajec-

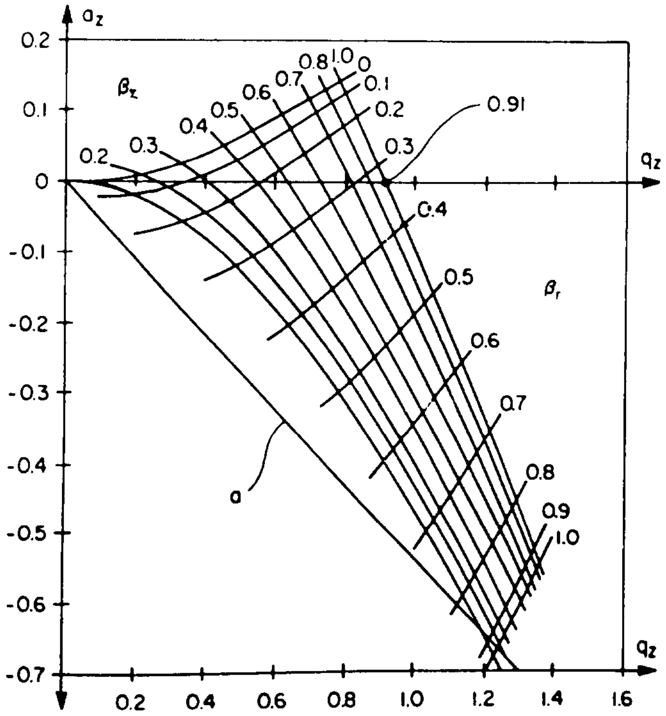

Fig. 3. Stability diagram for the ion trap. The "scan line" "a" is the locus of possible a_z, q_z coordinates for mass-selective storage. The value of $q_z = 0.91$ corresponds to q_{ej} in the mass-selective ejection mode and the lines labelled β_r and β_z describe the oscillatory characteristics of the ion motion (see text).

tories of the ions in which the C_{2n} coefficients represent the amplitudes of oscillation and the $(2n + \beta)\xi$ terms the respective frequencies of the infinite number of components. The quantities β and C_{2n} may be calculated from a and q using a series of recurrence relations in the form of continued fractions [5,19]. When ω_n is defined as the angular frequency in rad s^{-1} of the nth order term, where n is an integer, then

$$\omega_{u,n} t = (2n + \beta_u)\xi \qquad (12)$$

whence from eqn. 8 with $n = -\infty, \ldots, -1, 0, 1, \ldots, \infty$, we have:

$$\omega_{u,n} = (n + \beta_u/2)\Omega \qquad (13)$$

The strongest component occurs when $n = 0$, so that the fundamental frequency corresponds to $\omega_{u,0} = \beta_u/2$. In practice, of course, the ion possesses both radial and axial components of motion so that the respective fundamental frequencies will be β_r and β_z. The resulting ion trajectories have the general appearance of Lissajous' figures, in which a high frequency ripple ("micromotion") is superimposed upon a lower frequency "secular" motion. If the values of β_r and β_z are increased, for example by increasing the amplitude of the r.f. drive potential, then the nature of the motion becomes much more violent: this characteristic motion of the trapped ions plays an important part in the operation of the ion trap, especially in experiments where it is desired to pump kinetic energy into the ions by resonant excitation through application of auxiliary oscillating fields applied between the endcap electrodes (see later).

STAGES OF DEVELOPMENT

Improvements in performance

We have seen in the previous section how the ion trap may be operated in the mass-selective ejection mode. The chief advantage over the two previous methods of generating mass spectra is that the equipment is considerably simpler. Thus detection relies on the use of relatively cheap channeltron electron multipliers rather than complex circuitry, and the ejection of ions from the trap occurs "naturally", through the effects of "unstable" trajectories as opposed to the application of d.c. pulses to the endcaps required by the mass-selective storage mode. The instrument is also readily amenable to computer control using a personal computer. However, in its simplest implementation mass-selective ejection does not yield particularly high quality spectra, and much early effort was devoted to improving the performance of the trap such that it was at least as good as other more conventional instruments aimed at the same market, e.g. "benchtop" GC–MS. This section describes three especially important improvements.

The effect of a light buffer gas

Very early on in the development of the trap, before it was publicly announced, it was discovered that the presence of a significant background pressure of a light buffer gas, e.g. 10^{-3} Torr of helium, produces a dramatic improvement both in resolution and in sensitivity [16]. This apparent contradiction of effects may be explained in terms of the moderating effect resulting from collisions between the ions and the helium atoms, resulting in a "cooling" of the kinetic energy of the former and the migration of the ions towards the centre of the trap, in both the axial and radial directions. Thus simple modelling calculations [20] have shown that on reaching the threshold for trajectory instability the ions tend to start from essentially the same position in the trap so that not only are they all well bunched as they leave, but they are also focussed tightly along the z axis so that they are transmitted to the detector efficiently.

"Automatic gain control" (AGC)

Despite the improvements brought about by the use of the buffer gas, the early mass spectra reported with the ion trap showed significant distortions as the sample concentration was changed. This was clearly unsatisfactory for analytical applications such as GC–MS, where quantitative integrity of the output as the analyte peaks are being eluted is essential. In particular there could be a significant mismatch between the electron ionization (EI) mass spectra recorded with the ion trap compared with those obtained with "standard" instruments and held in mass spectral library collections.

The problems are essentially two-fold. On the one hand high sample concentrations combined with significant trapping times, e.g. several milliseconds, lead to the occurrence of ion/molecule reactions [12], thus changing the identities of the ions being analysed and also causing a loss of quantitative response. Secondly, the build-up of ion density within the trap can lead to space-charge effects, substantially modifying the electric fields to which the ions are being subjected (thereby causing, for example, shifts in the positions of the boundaries of the stability diagram [21]), resulting in changes in the mass/charge ratio assignments of the ions. To overcome these problems the method of "automatic gain control" (AGC) was introduced [22]. Here the idea is to incorporate two ionization stages into the scan function. The first ionization time is of fixed duration (e.g. 0.2 ms), after which ions formed from the background gases (typically up to *m/z* 44) are removed and the remaining analyte ions detected without further mass analysis. This "total ion" signal is then used to calculate the optimum ionization time for the second stage in order to avoid the effects noted above. This occurs each time the scan function is repeated, and the resulting ionization times are recorded along with the spectral intensities in order to normalize the data before retrieval. This extremely elegant method, in which a degree of "machine intelligence" is employed, has established ion trap mass spectrometry as a standard quantitative analytical method, as indicated by the work of Yost et al. [23].

Axial modulation

A further substantial improvement in performance has been obtained through the technique of "axial modulation". One of the inherent features of the ion trap in this mode of operation is that while the ions of lower mass/charge ratio are being "scanned" out of the trap into the detector, the higher *m/z* ions are still in the trap, and the space-charge potential which they contribute causes a broadening of the peaks arising from the ions being ejected. This can be demonstrated by observing the improvement in spectral quality when the immediately higher mass ions are first removed from the trap, e.g. by employing a superimposed d.c. field (see later) before the lower mass ions are analysed [24]. This deleterious effect on peak shape can be dramatically reduced by applying a supplementary oscillating field (≈ 6 V (p–p) at a frequency of about half that of the r.f. drive potential) between the endcap electrodes during the analytical portion of the scan function [25]. At this point, just as the ions are being ejected, their secular motion enters into resonance with the supplementary field so that the ions are energized as they suddenly "come into step" and are therefore much more tightly bunched as they are ejected. This technique of axial modulation has been employed with spectacular success as a means of extending the mass/charge range of the trap, and application of a supplementary oscillating field is also the basis of studying the collision-induced dissociation of ions in the trap (see later).

The use of alternative scan functions

With the exception of the scan function for automatic gain control, the techniques described so far have relied on a time variation of the r.f. potential substantially the same as that shown in Fig. 2. However, one of the merits of having a system which works under computer control is that it is relatively easy to reprogram the time profile of the r.f. potential and to regulate the application of d.c. potentials superimposed upon the r.f. potential in order to provide alternative modes of operation.

Chemical ionization

It has long been realized [26] that because of the long storage times within the trap, ion/molecule reactions of the type employed in chemical ionization may be facilitated, but at much lower reagent gas pressures (typically 10^{-5} Torr) than those used in conventional high pressure sources on magnetic sector and quadrupole instruments. The idea is to incorporate an ionization period into the scan function at constant low amplitude r.f. potential during which the reagent ion concentration is established, and to follow this by a second "reaction period" of a few milliseconds duration, at a slightly higher r.f. potential, where the analyte ions can then be formed and stored; the r.f. drive potential is then ramped in order to mass-selectively eject the ions, as for the EI scan function described earlier. Several papers describing detailed ion trap chemical ionization (CI) studies have appeared, including a very thorough account by Brodbelt et al. [27] and a comparison between CI with the QUISTOR/quadrupole system, the ITD$^{\text{TM}}$ and a high pressure source by Boswell et al. [28]. Dorey [29] has commented on the increased fragmentation observed in ion trap CI with methane compared with that in a conventional source, and has attributed this to the increased kinetic energies of the reagent ions in the former.

The merits of performing CI with the ion trap are that there are no additional pumping requirements, in contrast to conventional CI, and that under computer control it is relatively easy to program alternative EI–CI spectral scans. In addition, ionization conditions can be optimized using "automatic reaction control" (ARC), analogously to AGC, and furthermore, using the ion isolation technique described below it is possible to mass-select the reagent ion and so make chemical ionization much more specific [30].

Ion isolation

It is evident from the above description of the operation of the ion trap in the mass-selective storage mode that it is possible to apply d.c. and r.f. potentials such that a single value, or narrow range of values, of m/z may be stored. The application of this to the study of ion chemistry in the QUISTOR was first proposed by Bonner [31], and applied by Fulford and March [32] under the title of the "selective ion reactor". More recently, this approach has been incorporated into the scan functions employed for the mass-selective ejection mode as a means of isolating a single ion prior to performing a subsequent experiment [33]. A common means of isolating a specified value of m/z is for the amplitude of the r.f. drive potential to be adjusted so that the value of q_z for the ion is 0.78, that is the "working" a_z, q_z coordinate lies on the q_z axis, below the upper apex of the stability diagram in Fig. 3. A negative d.c. potential is then applied to the ring electrode such that the working point moves to a value of a_z just below the apex: in this way, ions of lower m/z are lost through instability at the $\beta_z = 1$ boundary (that is in the axial direction), whilst ions of higher m/z are unstable in the radial direction, at the $\beta_r = 0$ boundary. After about 2 ms the d.c. potential is then returned to zero and the r.f. potential reduced to a lower value for the next stage of the experiment. Alternative means of ion isolation include the use of a more complex scan function to render low m/z ions unstable at $\beta_z = 1$ and high m/z ions unstable at $\beta_z = 0$ [34], and McLuckey et al. [35] have described a combination of d.c. and r.f. potential scans designed to isolate a specified range of m/z values.

With this simple means of ion isolation it is easy to increase the versatility of the ion trap, and it is indeed essential for the tandem (MS–MS) studies described later. Analytical applications include the selection of specific reagent ions for chemical ionization, a technique which has been exploited by Strife and Keller [36] and Berberich et al. [37], and elsewhere in this issue Creaser et al. [38] have shown how multiple ionization–isolation steps and simultaneous ionization and isolation may be used to enhance the population of selected ions.

Alternative scanning modes for the ion trap

With mass-selective ejection we have seen that mass analysis is achieved by rendering the trajectories of ions with successively greater m/z values unstable at the $\beta_z = 1$ boundary. Experiments utilizing the $\beta_z = 0$ boundary as a means of extending the mass/charge range are described below. However, two alternative means of generating mass spectra with the ion trap have been reported recently. One [39,40] involves the application of a swept supplementary frequency to the endcap electrodes, followed by Fourier transformation of the image currents of the motion of the kinetically excited ions induced in the electrodes. This approach, which is analogous to the FT-ICR experiment, gave recognizable mass spectra, although the quality of the data recorded in these early experiments did not suggest that there was much to be gained from this mode of operation at this stage.

A second method of scanning has been described by Griffiths and Heesterman [41]. This may be imagined as combining the mass-selective storage and mass-selective ejection methods. Ions are created by a gated electron beam whilst the r.f. and d.c. potentials are stepped in the form of a staircase. The amplitudes of the potentials are maintained at a constant ratio and adjusted so that the a_z, q_z coordinates of each m/z value in turn are held just under the top apex of the stability diagram (see Fig. 3) in a manner analogous to that employed in the ion isolation technique described above. As the potentials are then incremented to the next step any trapped ions are expelled towards an external detector since the coordinates now lie outside the $\beta_z = 0$ stability boundary. This mode of operation possesses some limitations when compared to analysis by mass-selective detection, although the system does have the merit of simplicity and ease of operation. The authors suggest that the device should be well-suited to use as a low cost gas analyser.

Tandem mass spectrometry

One of the most exciting developments in the field of ion trap mass spectrometry has been the adaptation of the device for MS–MS, especially in conjunction with collision-induced dissociation (CID) [42]. Here the idea is first to create or inject the ions, isolate the parent ion which is to be dissociated (see above), and then resonantly excite the axial component of the ion motion by applying a supplementary sinusoidal "tickle" potential, which is tuned to the fundamental secular frequency of the ion, between the endcaps. This is analogous to the axial modulation experiment described above, but here the amplitude of the tickle potential is carefully adjusted so as not to cause the ions to be ejected. Under these conditions the ions are effectively pulled away from the centre of the trap so that they acquire energy from the r.f. drive potential and undergo energetic collisions with the helium buffer gas. The fragment ions resulting from the dissociation are then analysed by increasing the amplitude of the r.f. drive potential in the normal manner. This is a "tandem-in-time" experiment, again similar to MS–MS using FT-ICR, and is clearly less expensive to implement than "tandem-in-space" analysis with a quadrupole or magnetic sector instrument. Indeed, because the system operates under software control, once the initial hardware modifications have been made it is extremely easy to modify the scan function in order to implement higher order MS–MS experiments, especially as the fragmentation efficiencies are so high with the ion trap [43]. One possible limitation is the extent of energy deposition which may be achieved during resonant excitation with the ion trap compared with the triple quadrupole instrument. Thus in an elegant series of experiments Brodbelt et al. [44] have shown that the upper limit of internal excitation is ≈ 5.8 eV.

Another area of difficulty is that efficient excitation of the selected ion is only possible if the frequency of the tickle potential is accurately tuned. As a result, MS–MS analysis with the trap can involve a fairly lengthy tuning procedure in order to optimize the performance for each m/z value being studied. Software modifications described by Pannell et al. [45] and by Todd et al. [46] have shown ways in which this problem may be overcome. The latter account describes the technique of "dynamically programmed scans" which enables the ion trap to be used for the tandem mass analysis of "unknown" samples, where one is not aware of which species to select as parent ions until the first conventional mass spectrum has been run; parent ions are then selected according to pre-set threshold criteria and their collisionally-induced MS–MS spectra recorded in turn. Another advantage of this approach is that the data can be presented in a form which readily allows parent ion (fixed product) and neutral loss spectra to be deduced. An alternative technique, developed by Johnson et al. for performing MS–MS parent ion scans with the ion trap by the simultaneous resonant excitation of multiple ions is described elsewhere in this volume [47]. The laser photodissociation of trapped mass-selected ions has been reported [48], an evident advantage over collisional-dissociation by resonant excitation being that, provided the ions absorb at the photon frequency employed, there is no requirement to fine-tune the conditions in order for the ions to be energized, a potentially advantageous situation for analysis by GC–MS–MS with the ion trap [49]. Penman et al. [50] have also shown how the frequency tuning problem may be overcome using dynamically programmed scans to generate conditions under which a ramped d.c. potential is applied to the ring electrode during the application of the tickle potential across the endcaps.

The modelling of the application of supplementary electric fields has been examined by March and co-workers [51,52] and three distinct modes of resonant excitation have been defined. In the conventional mode, equal but out-of-phase r.f. potentials are applied to each endcap to give what has been termed dipolar excitation. Alternatively, the endcaps can be connected in phase so as to produce a quadrupolar excitation field superimposed upon the quadrupolar field of the r.f. drive potential. Finally there is monopolar excitation in which the supplementary potential is connected to one endcap whilst the other is grounded; this method was employed in the initial QUISTOR resonant ejection (QRE) experiments, described by Fulford et al. [53], in which ions could be selectively removed from the trap in a manner akin to axial modulation. One outcome of these simulation studies was the realization that other series of resonant frequencies exist, especially in the quadrupolar mode (including some which lead to radial excitation of the ions), and these effects have been observed experimentally [54,55].

Extension of the mass/charge range

As marketed commercially by Finnigan MAT [18] the ITD™ has an upper mass/charge limit ($(m/z)_{\max}$) of 650 Da e^{-1}, which is determined by rearrangement of eqn. 10 to give

$$(m/z)_{\max} = \frac{4eV_{\max}}{q_{\mathrm{ej}} r_0^2 \Omega^2} \tag{14}$$

where q_{ej} ($= 0.908$) is taken as being the value of q_z at which ion ejection occurs and $V_{\max}$ is the maximum value (zero–peak) of the r.f. drive potential ($\approx 16\,\mathrm{kV}$). Thus in order to increase the value of $V_{\max}$ for a given maximum r.f. amplitude one may reduce the values of r_0 and/or Ω, or reduce the value of q_{ej}. In the initial attempts to increase the mass/charge range, Todd et al. [56] decided to try and avoid changing the basic physical and electronic configuration of the trap, and developed the technique of "reverse scans" in which a positive d.c. potential is superimposed upon the r.f. drive potential fed to the ring electrode. Reducing these potentials together, keeping the ratio between them constant, makes the a_z, q_z coordinates move along a scan line which cuts the $\beta_z = 0$ boundary, thus causing mass-selective instability to occur in the reverse order (i.e. high m/z before low m/z value) compared with the conventional mode of scanning. Values of m/z up to about 2000 were analysed by this method, and this work, together with accounts of alternative scan functions which also make use of the $\beta_z = 0$ boundary, is presented elsewhere in this volume [57].

In their attack on the problem of extending the mass/charge range, Kaiser et al. [58] showed how lowering the values of both r_0 and Ω could be employed to yield quite acceptable mass spectra up to m/z 2600 (i.e. from eqn. 14, reducing the value of r_0 by two increases $(m/z)_{\max}$ by four). However, the major breakthrough has been [59] through their use of axial modulation (see above) but applying supplementary frequencies corresponding to ion ejection at very low values of β_z, e.g. 0.01, rather than $\beta_z = 1$. This has the effect of increasing

$(m/z)_{max}$ by a factor of 100, and the method has been verified by recording mass spectra of clusters of caesium iodide, generated using an external Cs^+ ion bombardment source, up to m/z 45000 Da e^{-1}. Further details of these methods and a comparison between the three are included in the paper by Kaiser et al. published in this volume [60].

The use of external ion sources

With the exception of the reference to caesium iodide cluster ions mentioned in the last section, all the work described so far has involved the use of ions created within the trap, either by electron or chemical ionization; two reports upon the use of laser desorption have also appeared in the literature [61,62]. However, there are clear advantages to be gained from creating ions externally, for example with a fast atom bombardment ionization source, and injecting them into the trap for subsequent analysis. The difficulty of trapping ions formed in this way is that, unless the ions enter the trap at the correct phase angle of the r.f. drive potential, they will not have the correct combination of velocity and displacement to remain in stable orbits, as has been noted in several theoretical discussions on the subject [63–65] and experimentally by Ho et al. [66]. This problem is, however, overcome when helium buffer gas is present, and Louris et al. [67] have described a successful system in which an external EI source (mounted in place of the conventional filament assembly of the ITD^{TM}) was combined with an einzel lens to gate the ion beam. The efficiency of trapping was clearly mass-dependent, and the authors rationalized their results in terms of the model of "pseudopotential wells" [68], which approximates the trajectories of the ions to that of simple harmonic motion about the centre of the trap. Pedder et al. [69] have described a system in which ions from an off-axis CI source were employed to create and inject negative ions into the trap. The in-trap chemical ionization of nitroaromatics using OH^- was first demonstrated by McLuckey et al. [70]: the use of ion/molecule reactions for the production of negative ions overcomes the difficulty that because thermal electrons and heavy negative ions cannot be held in the trap simultaneously, on account of their difference in mass, electron attachment processes are generally not observed. Suter et al. [71] recently described a hybrid mass spectrometer system consisting of magnetic and electric sectors, followed by a retardation system in which the 3 kV ions are decelerated down to 5 eV before injection into a QUISTOR (supplied with helium buffer gas); after trapping, during which ion chemistry can be allowed to occur, the ions are pulse-extracted for analysis with a quadrupole mass spectrometer in a manner analogous to the original QUISTOR/quadrupole experiments [12]. A sector (BE)/ion trap mass spectrometer has also been reported by Schwartz et al. [72].

Another system which involves the trapping of injected ions makes use of an atmospheric sampling glow discharge ionization (ASGDI) source, and has been described by McLuckey et al. [73]. Using a differentially pumped arrangement, atmospheric gases enter through an orifice into a region held at a pressure of 0.2–0.8 Torr, where a d.c. discharge is maintained between a pair of electrodes. The ions are then drawn through a second orifice and a pulsing lens to the ion trap where they enter through a hole in an endcap. This source has been shown to be capable of detecting organic explosives at the parts per 10^{12} level, and therefore the combination of this mode of ionization with the capabilities of the ion trap has great potential in the field of trace contaminant monitoring. Again the trapping efficiency has been characterized in terms of the operating conditions of the trap, as well as the pressure and nature of the buffer gas. One important result is that in arresting the motion of the injected ions, collision-induced dissociation may occur, possibly on the electrode surfaces themselves, and whilst the ions may still be mass-selected for subsequent MS–MS analysis, the intensities of the higher mass species are inevitably decreased. An alternative approach, which is especially useful in the production of negative ions in the trap, is to inject externally created reagent anions and then form the analyte ions via chemical ionization [74], and a recent study has demonstrated that NO_3^- ions formed in the glow discharge have at least two different stable forms [75].

In a further development from the Oak Ridge National Laboratory, electrospray ionization [76] has now been combined with ion trap mass spectrometry, using the above source but without the discharge operating [77]. Thus, multiply protonated biomolecules may be examined at low *m/z* values, as with triple quadrupole instruments [78], but with the added feature that through the addition of a reagent species, such as dimethylamine, the relative rates of proton transfer between the charge states of the analyte ions and the reagent may be determined [79]. Thus, the possibility of using chemical means for additional characterization of, for example, peptide ions and their fragments is opened up.

New designs of trap

All the work described so far has involved the use of ion traps having ideal geometry so that the ions are subjected to pure quadrupolar electric fields. Because of field imperfections, e.g. non-ideal spacing of the electrodes or contamination of the electrode surfaces, it is sometimes possible to obtain non-ideal effects, such as the unexpected ejection of ions through the influence of non-linear resonances observed during the reverse scanning experiments [57]. An interesting recent development is the deliberate incorporation of higher order hexapole and octopole field contributions [80] into the field geometry of the QUISTOR as a means of enhancing its performance. An account of the simulation of the operation of the trap under these conditions is included elsewhere in this volume [81].

Ion energetics and ion chemistry

It has already been noted above that chemical ionization may easily be performed with the ion trap by simply modifying the scan function. Indeed, unintentional "self-chemical ionization" may occur [82,83] if care is not taken to control the sample pressure. Rate constant data for ion/molecule reactions may be acquired by varying the storage time during which the reactions are occurring and from this an idea of the energy distribution of the ions (i.e. the "temperature") can be obtained [84,85]. A detailed review of ion chemistry by Nourse and Cooks has already been cited [7] and the same authors have contributed a paper on proton affinity determinations with the ion trap to this volume [86]. The use of a pulsed-valve gas inlet system for the study of ion/molecule reactions in the trap has been described by Emary et al. [87].

Chromatography combined with the ion trap

The original purpose of developing the ITD™ was for use as a "benchtop" mass spectrometer in combination with capillary gas chromatography, and indeed the bulk of the sales of the instrument have been for this application. However, preliminary experiments have been reported with other types of system, using both "internal" and "external" ionization. Thus Todd and co-workers were able to successfully combine an ion trap with a super-critical fluid chromatography column (SFC) operating with carbon dioxide as the mobile phase [88,89] and obtained EI mass spectra of polycyclic aromatic compounds which matched the NBS library spectra. The limiting factor on performance appeared to be the pressure of carbon dioxide in the ion trap, which increased as the pressure-programmed elution of the sample took place. Reference experiments in which the mass spectral intensities were monitored as a function of CO_2 pressure indicated an improvement in signal level at increased pressure, presumably because of charge-transfer effects.

A thermospray LC–ion trap system has also been described [90] in which very fast pumping was employed to keep the operating pressure at 2×10^{-4} Torr at an effluent rate of 0.51 s^{-1}. Phenylalanine and adenosine, both dissolved in 80:20 methanol:water, gave recognizable spectra, but the performance was evidently degraded by space-charge due to ions arising from the high background pressure of solvent; it was suggested that the application of a supplementary oscillating field between the endcap electrodes to resonantly eject these ions should lead to an improvement in spectral quality.

CONCLUSIONS

In writing this overview we have been conscious not only of what we have included, but what has been omitted. Thus, very little has been said about sensitivity and detection levels, or about the vast range of analytical applications to which the ion trap is now being applied, and for this we apologize. Without the support of those analysts who have invested their employers' resources in this instrumentation, there would be no means of furthering the development of the device, and indeed no excuse for continued efforts to push the performance of the instrument to greater and greater limits.

In the immediate future one would expect these advances to include improved resolution, combination of the trap with other separation methods, the automation of the acquisition of MS–MS data, and the exploration of alternative designs of trap and of non-destructive means of ion detection. As a longer term goal, the ion trap offers the very real prospect of playing a central role in creating "expert" analytical systems, capable of characterizing complex chemical samples without operator intervention. We are sure that most ion trap users would approve of these aims.

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