

Ion trap mass spectrometry *

Raymond E. March

Department of Chemistry, Trent University, Peterborough, Ont., K9J 7B8 (Canada)

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ABSTRACT

Enhanced trajectory control in the quadrupole ion trap, in the presence of helium buffer gas, has brought about enormous improvements in mass range (mass limits in excess of 70 000 Da have been achieved), mass resolution (full width at half-maximum, 1 130 000 at m/z 3510), and multistage tandem mass spectrometry (MS)^{*n*} where $n \leq 13$. The compatibility of the ion trap with external ion sources, such as electrospray and atmospheric pressure discharges, has greatly extended the range of application of the ion trap. Brief descriptions of the diagrammatic representation of ion trajectory stability and ion trapping theory precede a review of axial modulation, mass-selective axial ion ejection, ion isolation, collision-induced dissociation, tandem mass spectrometry and dynamically programmed scans. The progress made during the past 3 years in all aspects of ion trap mass spectrometry is reviewed.

INTRODUCTION

In the fall of 1989, the Royal Swedish Academy of Sciences awarded half of the Nobel Prize in physics [1] jointly to Wolfgang Paul [2] of the University of Bonn and to Hans Dehmelt [3] of the University of Washington. The awards were made “for the development of the ion trap technique . . . which has made it possible to study a single electron or single ion with extreme precision”. A popular account of their contributions is given elsewhere [4].

The award has brought recognition to the ion trapping field in which activity has been intense since the advent of the commercial version of the ion trap as a mass spectrometer [5] in 1983. In that year, the field of ion trapping entered a new phase with the discovery, by George Stafford and Paul Kelley of Finnigan Co., of mass-selective axial ion instability [5] with enhanced mass resolution.

Accounts of the early development of the quadrupole ion trap have been presented by Dawson and Whetten [6] and by Dawson [7]. A detailed account of the theory and practice of ion storage in the ion trap by March and Hughes, together with an historical account by Todd, has been published recently [8].

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In addition, full-scale reviews have been presented by Todd [9], and by Cooks et al. [10]; Todd and Penman have given an overview [11], and other reviews of specific aspects have been contributed by Griffiths [12], by Cooks and co-workers [13,14], by Yost and co-workers [15] and by March [16].

The progress made in the field of quadrupole ion trap mass spectrometry in recent years has been quite extraordinary: the mass range of the ion trap with respect to mass-selective ejection (as opposed to ion containment) has been shown to exceed 70 000 Da [17]; a mass resolution of 1 130 000 has been achieved [18]; detection limits are in the attomole (10^{-18} mol) region in favourable cases. Other notable advances are the following: a dynamic range approaching 10^6 [19]; a variable scanning rate from 5550 to 17 Da s $^{-1}$ [18,20]; routine ion isolation [21]; tandem mass spectrometry to the eighth, or higher, degree, (MS) n , $n \geq 8$ [22–25]; three forms of resonance excitation (axial modulation [26], ejection [27], and collision- (and surface-)induced dissociation [28]); ion frequency absorption spectra [29,30]; compatibility with external ion sources, particularly electrospray [31], atmospheric sampling glow discharge ionization (ASGDI) [32], and liquid chromatography [33]; alternative scan functions [34,35]; modified ion trap geometry [36–38]; trajectory simulations [39–41]; and the demonstration of phase transitions [42]. The most prolonged storage with detection of ions appears to be 2.748×10^5 s [30].

Throughout this review, scan functions, which depict the temporal variation of the potentials, have been emphasized as it is from the potentials that the fields are created within the ion trap, which permit us to achieve such an extraordinary measure of ion trajectory control.

THEORY

The ion trap is composed of a central electrode having the form of a hyperboloid of one sheet (or ring electrode) located between two hyperboloids of two sheets (or end-cap electrodes). The geometry of the device is described by the relationship

$$r_0^2 = 2z_0^2 \quad (1)$$

where r_0 is defined as the radius of the ring electrode and $2z_0$ is the separation between the end-cap electrodes. Only the value of r_0 needs to be chosen in order to specify a trap; in practice, r_0 has been varied from 1–25 mm. A cross-section of the ion trap is shown in Fig. 1. The device is commonly referred to by physicists as the “Paul trap”, while chemists have followed Dawson [7] by describing it as the “quadrupole ion trap” (this description is confusing to some students who expect to find a fourth electrode!), or the school of Todd which coined the name “QUISTOR” [43] (from QUadrupole Ion STORe). Today, the device is known simply as “the ion trap”. An

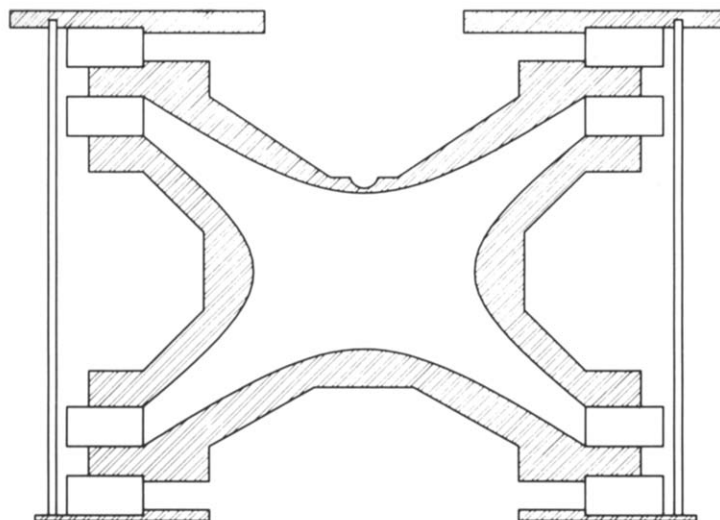


Fig. 1. The three-dimensional quadrupole ion trap with rotational symmetry about the z axis.

overview [8] of this quadrupole storage device appeared in 1989 and, as a crude measure of activity in this field, has been followed by some 300 publications.

An attractive feature of ion trap studies is that the mathematics of ion trajectory stability within the trap follow the Mathieu second-order differential equation [44] which was developed more than 120 years ago to account for the vibratory behaviour of stretched skins:

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

where u represents the radial and axial coordinate axes, r and z respectively, and ξ is a dimensionless quantity equal to $\Omega t/2$, Ω being the radial frequency of the alternating component of the potential ϕ_0 . When the trap is operated in mode II [45], that is, with the end-caps earthed and ϕ_0 applied to the ring electrode, the dimensionless quantities, a_u and q_u , are given by

$$a_z = -2a_r = \frac{-8eU}{mr_0^2\Omega^2} \quad (3)$$

and

$$q_z = -2q_r = \frac{-4eV}{mr_0^2\Omega^2} \quad (4)$$

where V is the zero-to-peak amplitude of the potential ϕ_0 , and U is the d.c. component of the potential ϕ_0 . For an ion to be trapped, its trajectory must

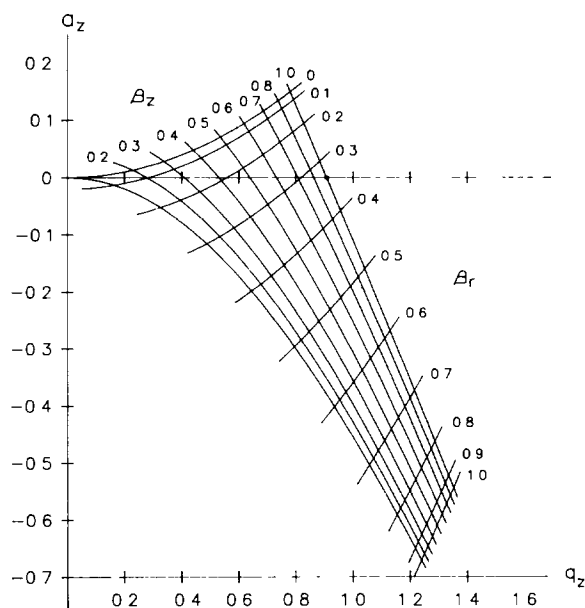


Fig. 2 Stability region near the origin for the three-dimensional ion trap showing the iso- β lines.

be stable both radially and axially. A stable trajectory can take the form of a Lissajous figure which is defined by the radial and axial frequencies of ion motion. Upon this figure is superimposed a ripple at the frequency of the drive radiofrequency (r.f.) potential applied to the ring electrode. The stability, or instability, of a trajectory can be portrayed by a stability diagram in which the regions of radial stability are overlapped by those of axial stability. In a stability diagram, shown in Fig. 2, the ordinate and abscissa are expressed in terms of the dimensionless quantities a_z and q_z respectively. It is perhaps worth emphasizing here that an appreciation of the stability diagram is vital to an understanding of ion behaviour within the trap. The stability diagram applies to devices of all sizes, that is, for all values of r_0 , and to the total range of mass-to-charge values. An ion for which the working point, that is, the coordinates a_z and q_z , falls within the stability diagram exists in a pseudopotential well and, provided the kinetic energy of the ion does not exceed the trapping potential, the ion is trapped. The diagram resembles a fishing net with an odd-shaped rim and where the depth of the net varies from about 1 eV close to the origin to more than 10 eV near the $\beta_z = 1$ stability boundary. The working point may be moved by variation of the d.c. and/or r.f. potentials.

Representative iso- β_r and iso- β_z lines are shown in Fig. 2. The values of β_r and β_z at any point in the stability diagram determine the frequency spectrum of stable ion trajectories; β_u is a function of the stability parameters a_u and q_u .

The frequency spectrum of stable ion trajectories is given by

$$\omega_{u,n} = (n + \beta_u/2)\Omega \quad n = -\infty, \dots, -1, 0, 1, \dots, \infty \quad (5)$$

where ω_n is defined as the frequency of the n th order, $u = x, y$ or z , n is an integer, and β_u is a function of the now well-known stability parameters a_u and q_u . When $n = 0$, the fundamental frequency ω_0 in either the r or z direction is given by

$$\omega_{u,0} = \beta_u \Omega/2 \quad (6)$$

The form of an ion trajectory in the r, z plane has the general appearance of a Lissajous curve composed of two frequency components $\omega_{r,0}$ and $\omega_{z,0}$ of the secular motion, with a superimposed micromotion of frequency $\Omega/2\pi$ (Hz), where

$$\omega_{r,0} = \beta_r \Omega/2 \quad \omega_{z,0} = \beta_z \Omega/2 \quad (7)$$

The essential features of the theory of ion confinement in quadrupole ion traps have been presented for the case of a single ion in the trap. While a single-ion system is of great interest to physicists (*vide infra*) it has little appeal to analytical chemists who must deal with ensembles of ions and must consider, therefore, space charge effects arising from the proximity of charged particles within the trap.

ION TRAP DETECTOR (ITDTM) AND ION TRAP MASS SPECTROMETER (ITMSTM)

The geometry and sizes of the electrode structure in the ITD and ITMS are virtually identical, as are the drive electronics except for the drive frequencies which are 1 MHz in the ITD and 1.1 MHz in the ITMS. The ion trap of the ITD is compactly housed as it is employed generally as the mass-selective detector for a gas chromatograph, while the ion trap of the ITMS is located in a spacious vacuum chamber to permit ready modification to this research instrument. The major difference between the two models, and the source of much of the fourfold difference in prices, lies in the accompanying software. The ITD software permits automatic gain control (AGC), chemical ionization (CI), automatic reaction control for CI (ARC-CI) [46] and generation of mass spectra by mass-selective axial instability. The ITMS software permits AGC, CI, ARC-CI, generation of mass spectra, ion isolation, resonance excitation with a supplementary r.f. potential, tandem mass spectrometry, axial modulation and alternative scan functions. Many of the exciting developments with respect to enhancement of ion trap capabilities reviewed here have been made with the ITMS, while most of the recent applications have been carried out with the ITD.

Briefly, mass-selective axial instability entails the controlled and directional destabilization of the trajectories of gaseous ions, stored in the ion trap in

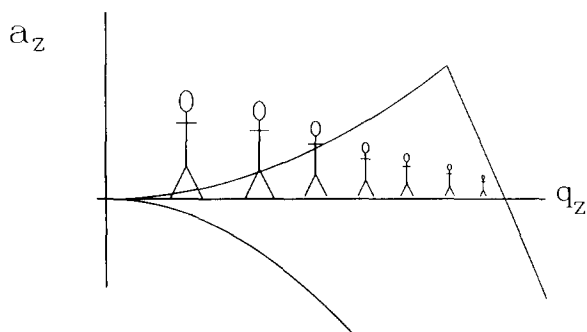


Fig. 3. Schematic representation of working points in the stability diagram for several species of ions stored concurrently. The arrangement of working points with respect to mass-to-charge ratio is depicted by figures which differ in size

order of their mass-to-charge ratios, by scanning the amplitude of the r.f. potential applied to the ring electrode. A schematic representation of the location of working points on the q_z axis for singly charged ions as a function of mass is shown in Fig. 3. This destabilization is related to changes in the trajectory-controlling parameters which can be depicted as movement on a stability diagram (vide infra). When an ion trajectory is destabilized axially, axial excursions of the ion from the centre of the trap increase until they exceed the dimension z_0 and strike an end-cap electrode. For ions to be ejected through a small perforation in this electrode, and to impinge upon the electron multiplier beyond, radial excursions of the ion must be comparable to the size of this perforation. An essential feature of operation of this novel method was the use of helium at a "background" pressure of 10^{-3} Torr! Collisions with helium are accompanied by momentum losses which cause progressive diminution of the average displacements of the ions from the centre of the trap. Physically, the ions are clustered thus at the centre of the trap and reside in the minimum of the pseudopotential well where they may be stored for long periods.

Let us consider an ion oscillating close to the centre of the trap as a result of these momentum-dissipating collisions with helium; its working point is fixed within the stability diagram. Changes in U and/or V can move the working point such that it passes through any one of the four boundaries of the stability diagram, $\beta_r = 0, 1$ and $\beta_z = 0, 1$ shown in Fig. 2. When the working point passes through the $\beta_r = 0, 1$ boundaries the ion leaves the trap radially; similarly, when the working point passes through the $\beta_z = 0, 1$ boundaries, the ion leaves axially. Secondly, a cloud of ions focused at the centre can be excited resonantly upon irradiation by either of the fundamental secular frequencies given in eqn. (7). Radial excitation will cause the ions'

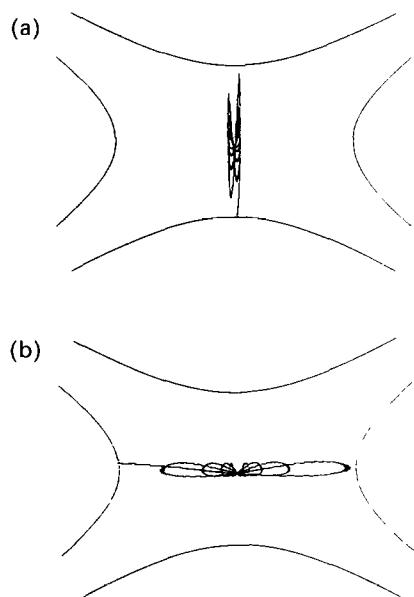


Fig. 4 (a) The trajectory of an ion, focused initially near the centre of the trap, and excited axially. (b) The trajectory of an ion, focused initially near the centre of the trap, and excited radially

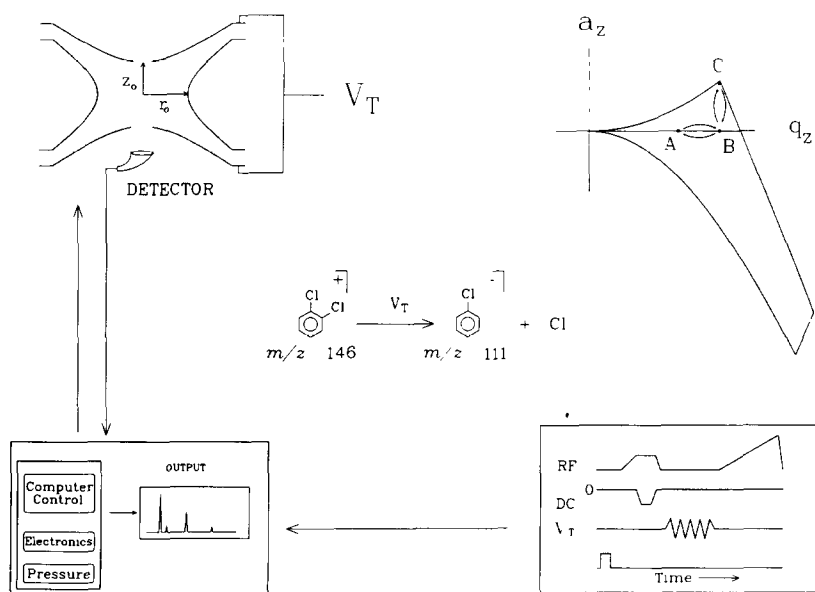


Fig. 5 Schematic representation of the five aspects of quadrupole ion trap mass spectrometry to be considered.

trajectories to form a flat disc, while with axial excitation the trajectories will form a cigar, as shown in Fig. 4.

We are now poised to review the progress made in the past 3 years but, in order to appreciate more fully the finer points of quadrupole ion storage mass spectrometry, one must bear in mind the following five basic elements for which the mnemonic is the acronym “TRAPS”: T, the electrode assembly of the ion Trap, including electron gun and detector; R the Reaction or process under study; A, the Apparatus including all of the experimental parameters, e.g. pressure, ion signal intensities etc.; P, the Profile of potentials or scan function, that is, the temporal variation of the fields within the ion trap; and S, the Stability diagram. The five elements are shown pictorially in Fig. 5.

ENHANCEMENT OF ION TRAP PERFORMANCE

Mass range

In 1988, the upper limit of the mass range of the ITD and ITMS in normal operation was 650 Da per charge, although the highest mass analysis (m/z 1466) had been achieved by Todd et al. using the reversed-scanning technique in which ions are ejected at the $\beta_z = 0$ boundary with $q_z = 0.27$ [47]. At the International Mass Spectrometry Conference in Bordeaux, Cooks et al. undertook the objective of extending the mass/charge range of the ion trap to 10 000 within a year [48].

From eqn. (4), the mass range can be extended in four ways: by ejection at a value of q_z less than 0.908 which is the value of q_z for normal mass-selective axial instability [5]; by increasing the maximum r.f. voltage; decreasing the value of r_0 ; and decreasing the r.f. frequency. A new trap with $r_0 = z_0 = 7$ mm (i.e. a smaller ring but the same end-cap electrodes and end-cap spacing) yielded about 900 Da [49]. The same new trap but with slightly reduced frequency yielded 1166 Da. When r_0 was reduced to 5 mm and the normal geometry retained, ions from UltramarkTM-1621, a fluorinated phosphazine, up to m/z 1921 were observed in good agreement with electron ionization (EI) mass spectra as shown in Fig. 6 [50,51]. When UltramarkTM-3200 was used, ions up to m/z 2509 were observed as shown in Fig. 7. What appears to be noise between the major peaks in Fig. 7 is actually low abundance signals from fragment ions less than 0.05% of the base peak. The resolution here ($m/\Delta m$, where Δm is the full width at half-maximum (FWHM)) is 450 at m/z 1821, i.e. the peaks are ± 2 Da wide at half-height. However, the effective scan rate for this trap was four times the normal, i.e. $4 \times 5555 \text{ us}^{-1}$ or $22\,220 \text{ Da s}^{-1}$! Decreasing the scan rate did achieve some improvement in resolution, but more of this later.

In an ion trap used as a mass spectrometer there is a limit to which r_0 can



Fig. 6. Comparison of the ion trap spectrum of Ultramark™-1621 with a standard EI mass spectrum [50].

be usefully reduced in order to increase the mass range. We now undergo a change of tack. It is possible to eject ions at a value of q_z less than 0.908 using quadrupole resonance ejection (QRE) [52,53] or modified axial modulation [54], as shown schematically in Fig. 8. The ladder in Fig. 8 represents the enhancement of kinetic and, eventually, internal energy as the ion is resonantly excited. A supplementary r.f. voltage of amplitude $(6-10)V_{(0-p)}$ and of fixed frequency was applied to the end-cap electrodes [27]. When the r.f. drive potential is ramped the fundamental axial secular frequencies come into resonance with the supplementary r.f. voltage; the ions are excited rapidly and are ejected from the trap when their kinetic energies exceed the trapping

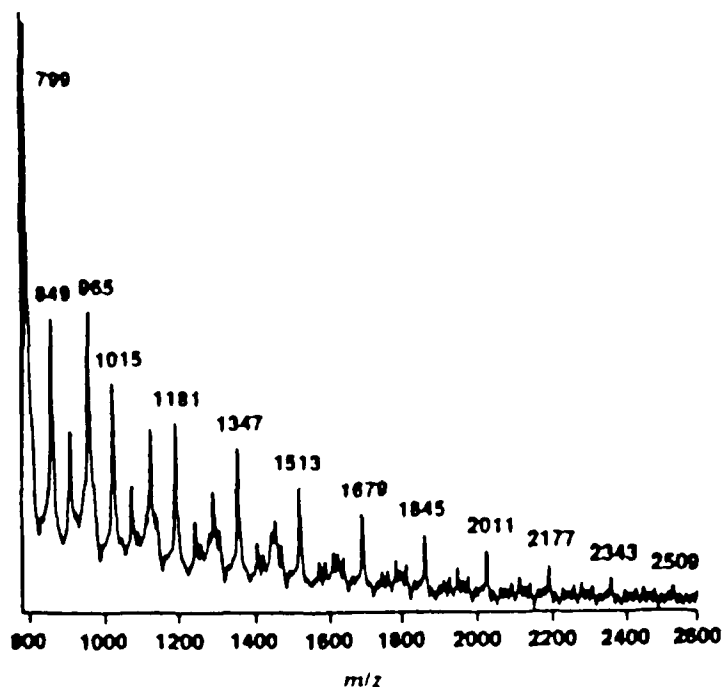


Fig. 7. Mass spectrum of Ultramark™-3200 in a region near the upper-mass limit of the half-size ion-trap [50].

potential well-depth. Secondary-ion mass spectrometry, using 5–7 keV Cs^+ ion bombardment of solid tetraalkylammonium salts, peptide samples and CsI was implemented [27]. The $\text{Cs}_{n+1}\text{I}_n^+$ cluster ions formed from CsI were resonantly ejected at $q_z = 0.027$, which corresponds to $\beta_z = 0.020$, using a supplementary frequency of 11 kHz. The upper limit of the resulting mass spectrum as shown in Fig. 9 corresponds to $n = 80$, that is, 20 918 Da per charge. Two points should be noted; firstly, there is a crowding of the masses with the result that the number of data points per mass unit was decreased, and secondly, these data matched the highest masses recorded with a Fourier-transform ion cyclotron-resonance instrument [55].

When resonance ejection was combined with an axial modulation frequency of 4.600 kHz ($\beta_z = 0.01$) and a reduction in the drive frequency from 1.1 to 0.92 MHz, where the change in frequency corresponds to a 1.7-fold increase in mass range, the expected mass limit of 70 000 Da per charge became accessible, i.e. there was a 111-fold increase in mass range [17]. In Fig. 10 is illustrated a region of the CsI mass spectrum from 22 to 46 kDa; the base peak $(\text{CsI})_{122}\text{Cs}^+$, m/z 31 830, corresponds to the stable $5 \times 7 \times 7$ cluster ion while m/z 44 560 corresponds to the $(\text{CsI})_{171}\text{Cs}^+$ cluster and to a $3 \times 3 \times 19$

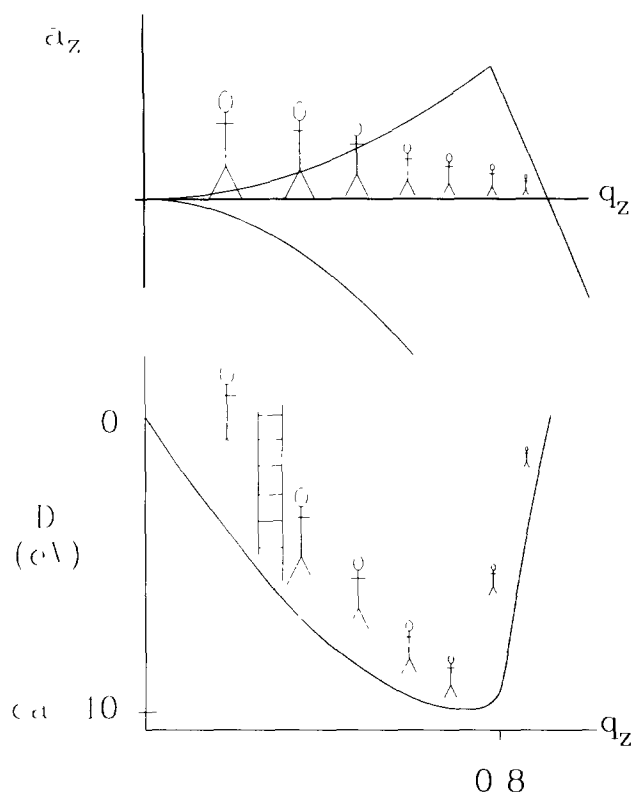


Fig. 8 Diagrammatic representation of ions stored concurrently in the ion trap showing the position in the stability diagram and the potential well depth. The ladder represents ejection by resonance excitation

array. The mass resolution ($m/\Delta m$) was about 3000. Also shown in Fig. 10 is the associated scan function. The extension of the mass range is a tremendous achievement in mass spectrometry.

Mass resolution

The normal mass resolution as defined above of the ITD and ITMS is about $3 \times m$, e.g. the mass resolution at m/z 502 is 1700. The first improvement in mass resolution was due to "axial modulation", as described in a patent by Syka and co-workers [56]. Here, a low amplitude r.f. voltage of frequency slightly less than half the r.f. drive frequency was applied to the end-cap electrodes [54]. Axial modulation appears to bring about an enlargement of the ion cloud with concomitant reduction in space charge perturbation and the dispersion of the working point, so that the range of effective

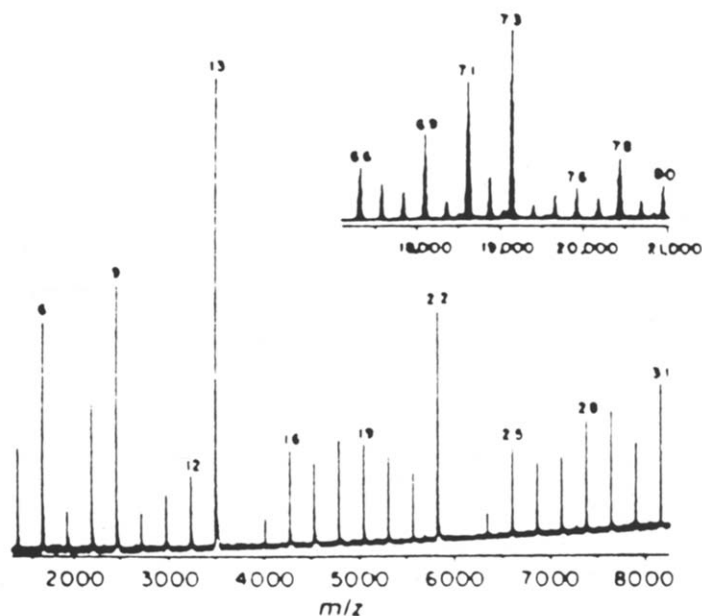


Fig. 9. Mass spectrum of CsI using an axial modulation frequency of 28 kHz ($q_z = 0.071$, $\beta_z = 0.050$). The insert shows data recorded at 11 kHz ($q_z = 0.071$, $\beta_z = 0.020$). Cluster sizes of Cs^+ (CsI) $_n$ are indicated by values of n [27].

working points of an ion ensemble being ejected from the ion trap is reduced. Thus the width of the associated peak in the mass spectrum is reduced. This process of ion cloud enlargement requires time. A combination of modest ion trap size and frequency reduction with axial modulation realized a mass resolution of 3000 [17].

Within the past few months the achievable mass resolution of the ion trap has been increased in two enormous bounds. Firstly, Schwartz et al. [20] succeeded in reducing the r.f. voltage scan rate, normally fixed at 5555 Da s^{-1} , by a factor of 20 so that the time interval required to scan one mass unit was increased from $190 \mu\text{s Da}^{-1}$ to about 3.8 ms Da^{-1} . With axial modulation and the reduced scan rate, the mass resolution was increased by the same factor, as shown in Fig. 11, to 33 000. The separation between successive masses should be noted. Secondly, Cooks and co-workers have achieved a mass resolution of 1 130 000 for the CsI cluster ion at m/z 3510 [18]. This extraordinary result, shown in Fig. 12, was achieved when the scan rate was slowed by a factor of 333; this factor was realized by a combination of $2000 \times$ attenuation divided by $6 \times$ mass range extension by resonance ejection with $q_z \approx 0.15$. The FWHM of m/z 3510 peak in Fig. 12 is $3.5 \times 10^{-3} \text{ Da}$. The achievements of Professor Cooks' group and the Finnigan MAT group, both separately and in collaboration, merit our enthusiastic appreciation.

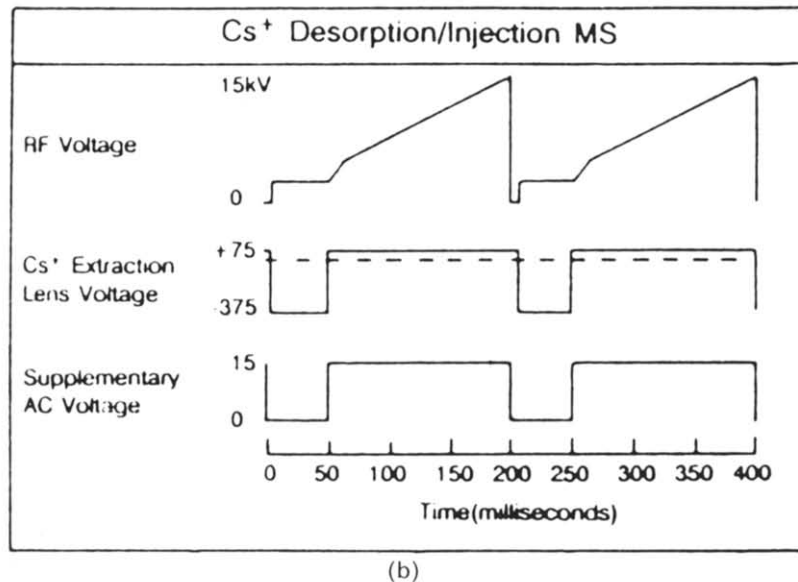
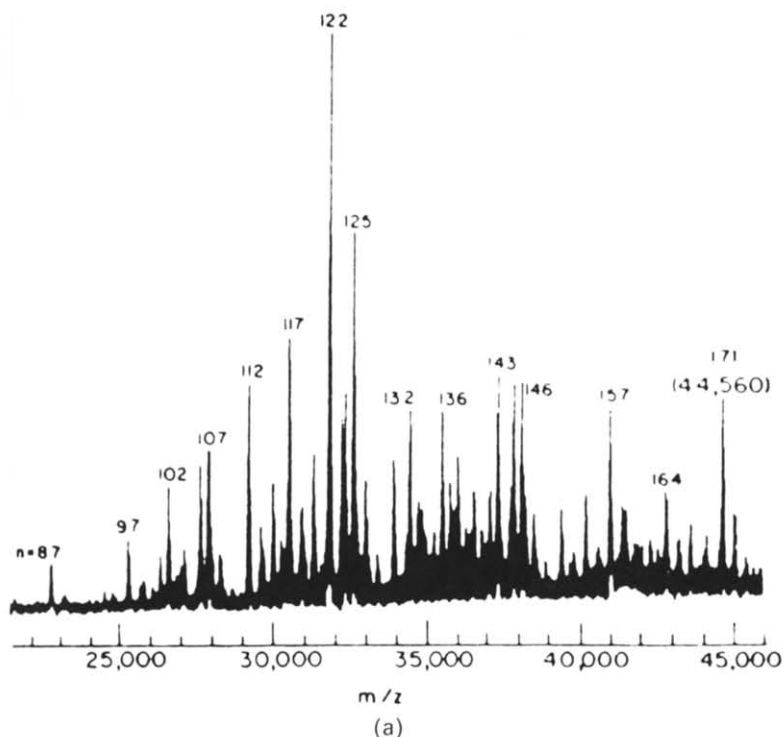


Fig 10 (a) Mass spectrum of CsI acquired using an axial modulation frequency of 4600 Hz ($q_{\text{eject}} = 0.02$, $\beta_z = 0.014$). The drive frequency was reduced from 1.1 to 0.092 MHz to achieve an additional 1.43-fold increase in mass. (b) Ion trap scan function used to record the mass spectra generated by Cs⁺ secondary ion mass spectrometry [17].

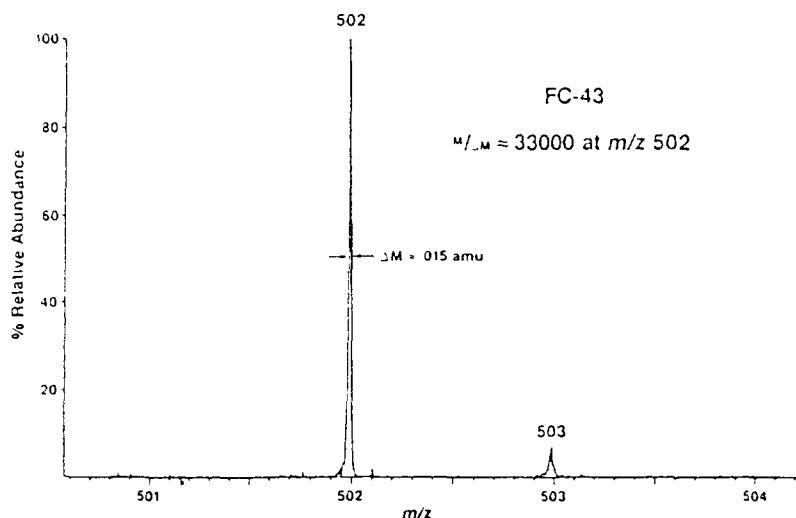


Fig. 11. The mass-to-charge ratio 502 region of FC-43 obtained with a scan rate of 27.8 Da s^{-1} [20].

ION ISOLATION

The process of ion isolation, which is performed so facily in the ion trap, and is essential to the operation of the ion trap as a tandem mass spectrometer, is equivalent to the operation of a sector or mass filter in the older

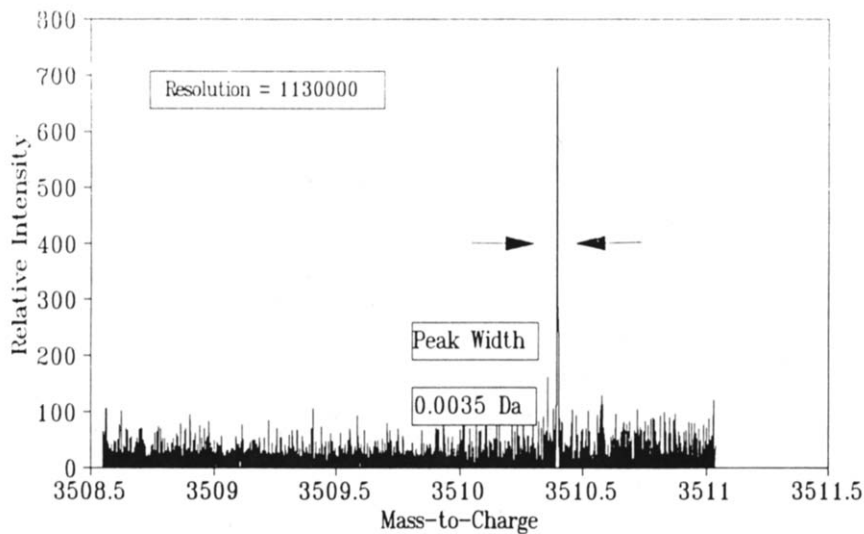


Fig. 12 The CsI cluster ion at m/z 3510 showing mass resolution in excess of 10^6 [18]

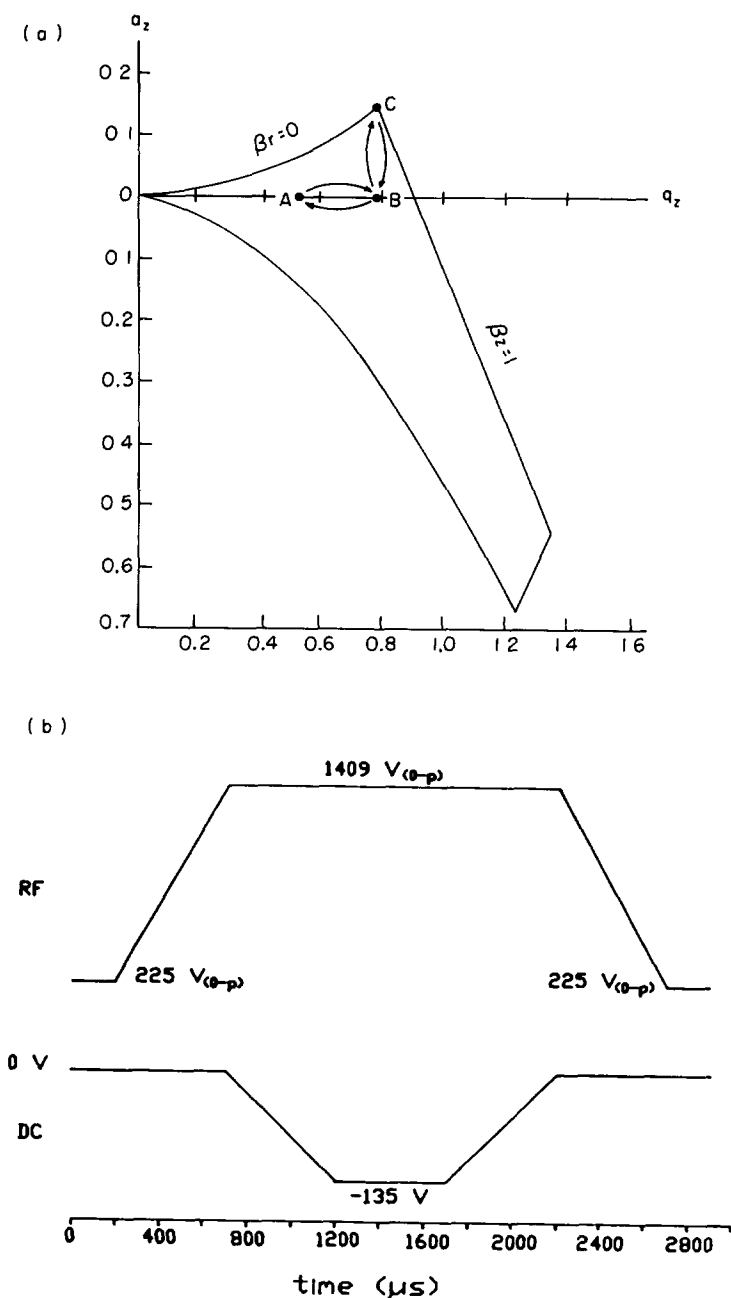


Fig. 13 (a) Stability diagram for the quadrupole ion trap showing the changes in location of the working points for an ion undergoing isolation (b) A scan function for ion isolation using rf and dc voltages. The ordinate shows the relative voltage amplitudes (not to scale), and the abscissa shows the time scale of the ion isolation process [58]

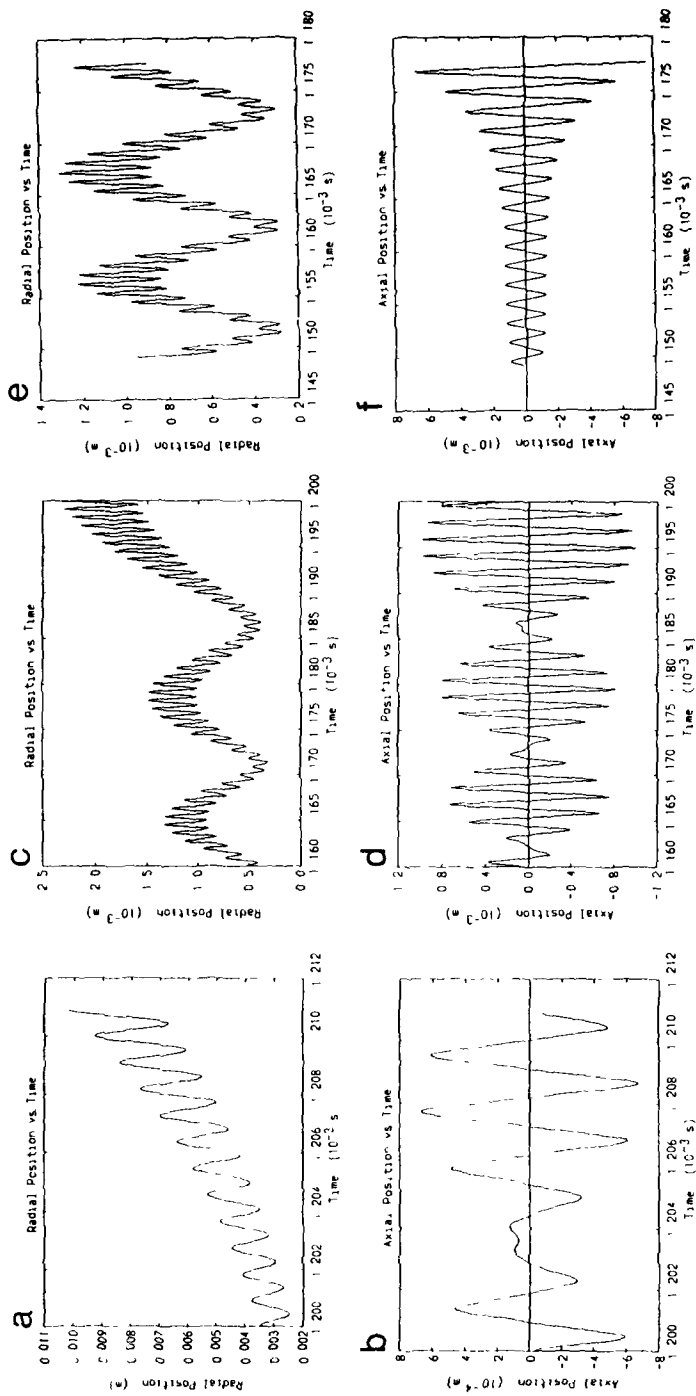


Fig. 14 Trajectory simulation of m/z 144, 146 and 148 with q_z equal to about 0.77 during application of a d.c. ramp such that the final value of a_z is about 0.15: (a) m/z 148, radial excursions over the time period 1200–1210.9 μ s, (b) axial excursions over the same time period; (c) m/z 146, radial excursions over the time period 1160–1200 μ s, (d) axial excursions over the same time period, (e) m/z 144, radial excursions over the time period 1147–1177 μ s; (f) axial excursions over the same time period [58].

forms of mass spectrometers. Strife and co-workers [21,57] have described, for the first time with the ITMS, the process of ion isolation with reference to the tandem mass spectrometry of prostaglandins.

Let us consider three ion species of similar m/z ratio, for example, m/z 144, 146 and 148. Initially, the working points of all three ion species lie close to point A on the q_z axis in Fig. 13(a). The working points can be moved along the q_z axis by increasing V until that for m/z 146 lies directly below the upper apex of the stability diagram as shown by point B in Fig. 13(b). Upon the application of an appropriate value of $-U$, the working point for this ion is located just inside the upper apex, at C, while the working points of m/z 144 and 148 pass through the $\beta_z = 1$ and $\beta_r = 0$ boundaries respectively, and these ion species are lost axially and radially respectively. Stable trajectories are maintained only for those ion species whose working points lie within this apex; all other ion species are ejected. The r.f. and d.c. voltages are then reversed, and the working point of the isolated ion species is restored to a low value of q_z on the q_z axis. The trajectories of these ionic species during the ion isolation process have been simulated recently in a collision-free system [58]; the temporal variation of the radial and axial positions are shown in Fig. 14. It should be noted that the final radial excursion for m/z 148 equals 1 cm, i.e. r_0 , and the axial excursion for m/z 144 equals 0.707 cm, i.e. z_0 .

Two alternative methods for isolating a range of masses have been demonstrated wherein the d.c. voltage is replaced by a fixed frequency during the r.f. scan or vice versa [59]. An operational scenario is shown in Fig. 15 in which

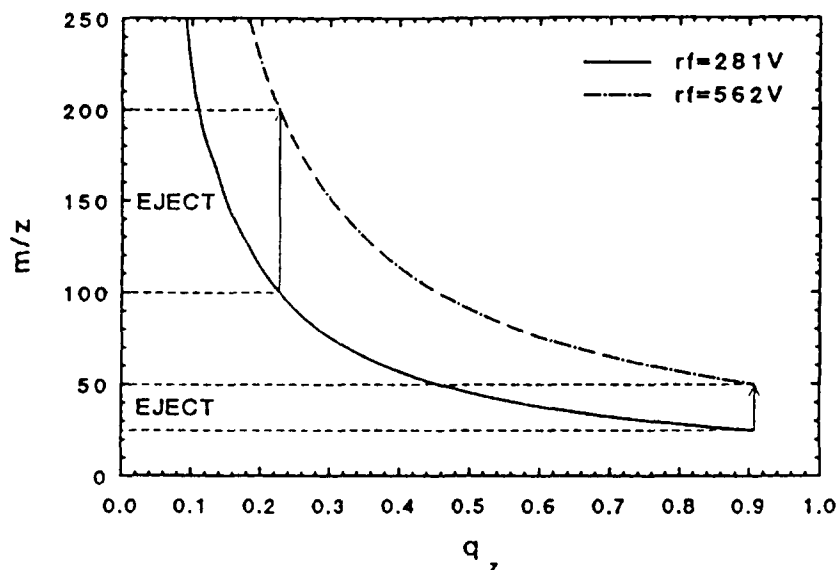


Fig. 15 Diagram for selective ejection of ions at m/z 100–200 via the simultaneous r.f.-ramp/fixed-frequency resonance ejection technique [59].

the m/z ranges 25–50 and 100–200, indicated by broken lines, are simultaneously ejected, by axial instability and resonance ejection respectively, while the m/z range 50–100 and m/z above 200 are retained in the trap. The r.f. potential is ramped from a high-mass cut-off of 25 Da per charge to 50 Da per charge; the resonance frequency corresponds to $a_z = 0$, $q_z = 0.227$ [59]. A comparative study has been made of selective mass storage and two-step isolation [60].

COLLISION-INDUCED DISSOCIATION

There are many examples reviewed here where collision-induced dissociation (CID) has been used to produce fragment ions for subsequent examination or mass analysis. While CID is wrought facily by resonance excitation, both the frequency dependence of energy absorption and the kinetics of the process are complex. A major effort has been made by trajectory simulation and experiment to characterize the processes involved. For further information on these studies and others where CID has been employed, the reader is referred to those sections dealing with tandem mass spectrometry, trajectory simulation, dynamically programmed scans and temperature.

EXTERNALLY GENERATED IONS

The injection of externally generated ions into the ion trap has long been considered [61], treated theoretically [62–64] and realized experimentally [65–67]. The presence of helium bath gas in the ITD and ITMS provides the opportunity for many momentum-moderating collisions, which results in a high trapping probability [68–70]. Louris et al. [71,72] first described the use of an external EI source and einzel lens assembly with a modified ITD [73]. Trapping efficiency was mass dependent and the results were interpreted in terms of the pseudo potential well model. Single-pulse laser photodissociation of trapped molecular ions was reported. The confinement in the ion trap of externally generated ions had been clearly demonstrated, and laser desorption [74] for the analysis of non-volatile biomolecules appeared feasible. Resonance effects due to the application of a supplementary r.f. voltage to the end-cap electrodes during injection of ions have been described [75,76].

The EI source has been replaced with a Cs^+ gun [27] for the study of high mass species such as gramicidin S [77] under particle bombardment. Yost and co-workers have reported the off-axis injection of ions from an external CI source [78]. The detection efficiency for ion injection of Ar^+ as a function of kinetic energy is shown in Fig. 16. An ASGDI source coupled with an ion trap has been described by McLuckey et al. [32] and is shown in Fig. 17. In this

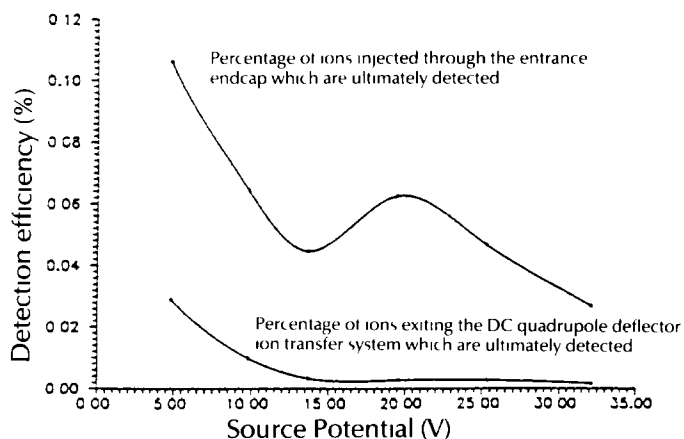


Fig. 16. Detection efficiencies of ion injection system [78].

differentially pumped apparatus, atmospheric gases pass through an orifice into a region maintained at about 0.5 Torr; ions formed in a d.c. discharge are drawn through a second orifice, a lens system, and enter the trap through a hole in an end-cap electrode. When negative ions are used for analysis of explosives, detection limits in the parts-per-trillion range are obtained using tandem mass spectrometry [10,79]. In an elegant study of NO_3^- ions formed in the glow discharge, it was shown that the anion existed in two forms [80].

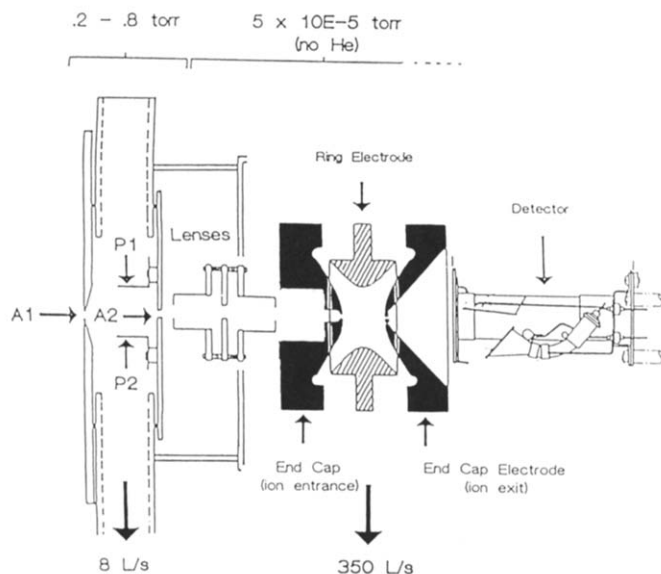


Fig. 17. A schematic diagram of the ASGDI source/ITMS combination [32].

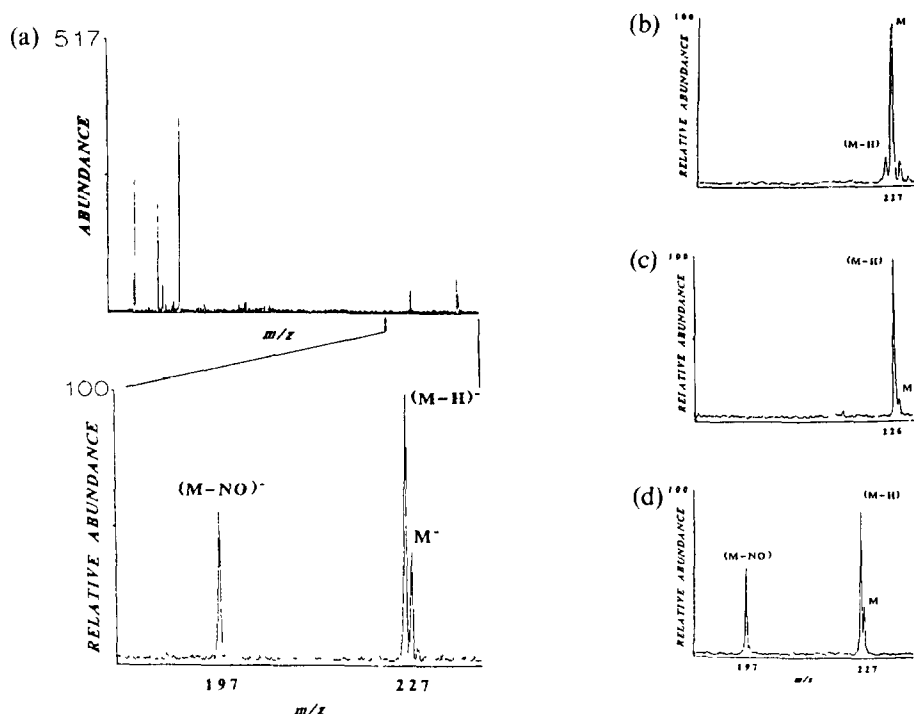


Fig. 18 (a) Mass spectrum obtained by injection of a mixture of reactant anions (OH^- , NO^- , O_2^- and NO_2^-) into the ion trap containing TNT vapour, after a reaction time of 300 ms. (b)–(d) Mass spectra of TNT in the molecular ion region obtained by selected reagent anion chemical ionization using O_2^- , NO_2^- and OH^- respectively [81]

Negative ion chemical ionization in an ITMS has been demonstrated using reagent anions formed externally and injected into the ion trap [81]. The mass spectrum shown in Fig. 18(a) was obtained with all reagent anions, i.e. OH^- , NO^- , O_2^- and NO_2^- , whereas those shown in Fig. 18(b)–18(d) were obtained with O_2^- , NO_2^- and OH^- respectively as reagent anions. Reagent anion selection gave greater control over the ionization mechanism(s) than is afforded in conventional high pressure CI [82].

An exciting recent development in mass spectrometry has been the use of electrospray ionization for the analysis of involatile and labile biomolecules [83]. Through the production of multiply protonated ($10\text{--}50 \text{ H}^+$) species [84], the m/z values of high mass ions are proportionately lower than ion masses and are brought within range of most mass spectrometers [85]. Electrospray ionization has been combined with the ion trap with spectacular results [31]. A positive-ion electrospray mass spectrum of bovine serum albumin is shown in Fig. 19; the base peak corresponds to 41-fold protonation and peaks are

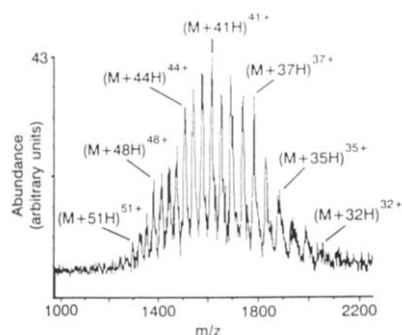


Fig. 19. Positive ion electrospray mass spectrum of bovine serum albumin. During the data acquisition period, about 124 fmol of analyte flowed through the capillary needle [31].

identified to 51-fold protonation. The improvement in mass resolution with a reduced mass scanning rate is seen readily in Fig. 20 for an electrospray mass spectrum of horse heart myoglobin (molecular weight 16 900) [20]. The addition of a reagent species such as dimethylamine permits determination of the relative rates of proton transfer between individual multiply charged states

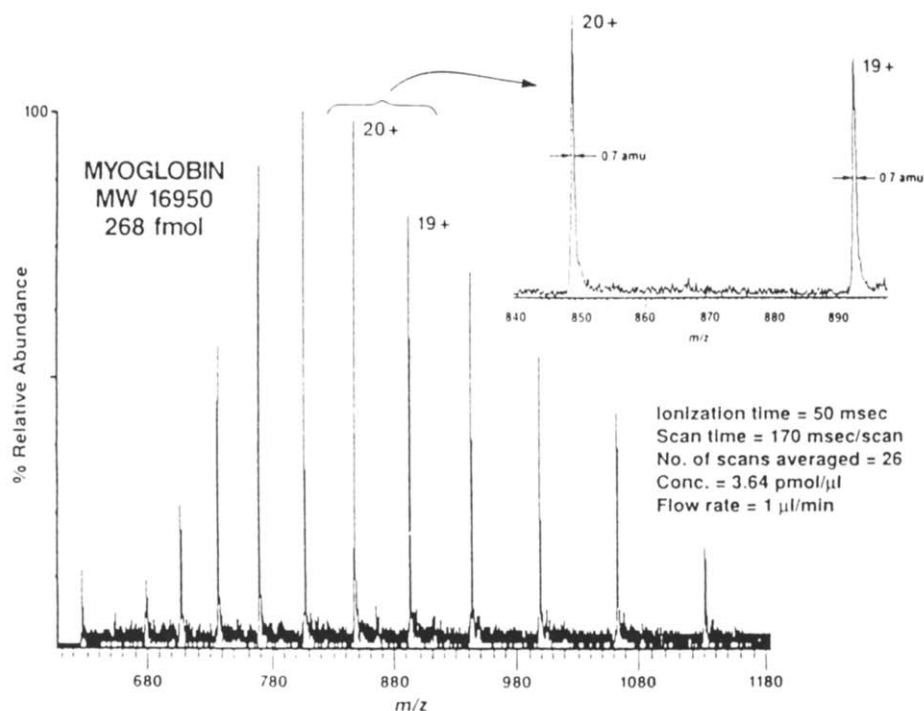


Fig. 20. Electrospray ion trap mass spectrum of horse heart myoglobin (molecular weight 16 900) at a scan speed of 5550 Da s^{-1} [20].

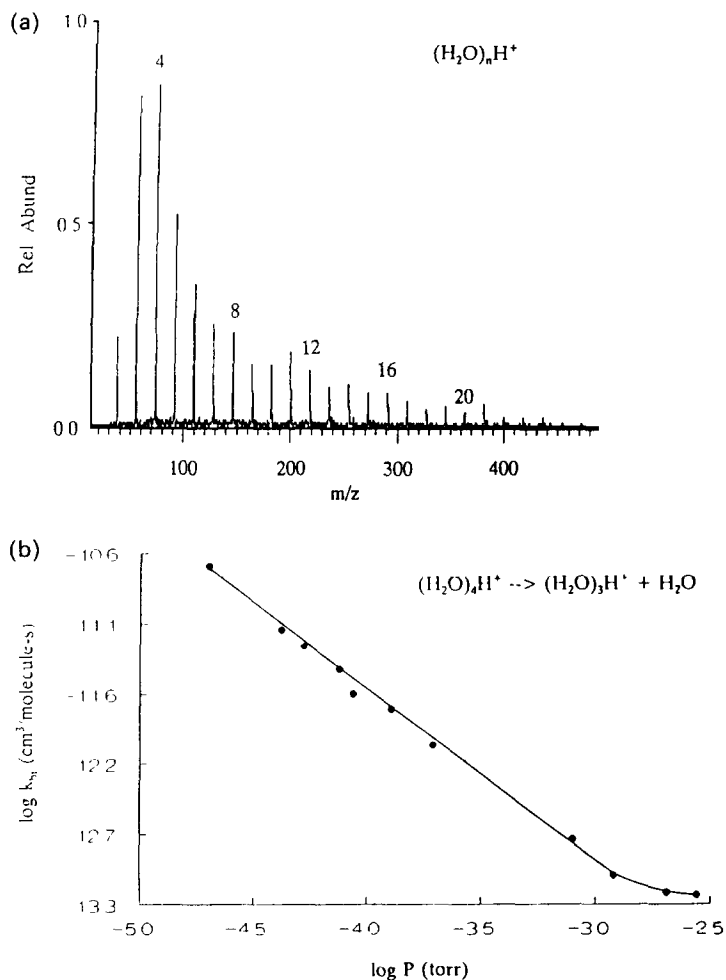


Fig. 21 (a) Electrospray mass spectra of water acquired with a quadrupole ion trap. (b) A plot of the logarithm of the decomposition rate constant k_d for the protonated water tetramer vs. the logarithm of the bath gas pressure [91]

and the reagent [86]. The possibility now exists of using chemical means for additional characterization of peptide ions [87-89], such as g-bungarotoxin tryptic peptides [90]. Somewhat more prosaic studies may also be undertaken: for example, in Fig. 21(a) is shown the electrospray mass spectrum of water [91] where the base peak is $(H_2O)_4H^+$; isolation of this ion species permits evaluation of the decomposition rate constant for the protonated water tetramer, as shown in Fig. 21(b). The utility of electrospray ionization in combination with the ion trap has been examined for a variety of systems [92,93], including free base and metalloporphyrins [94].

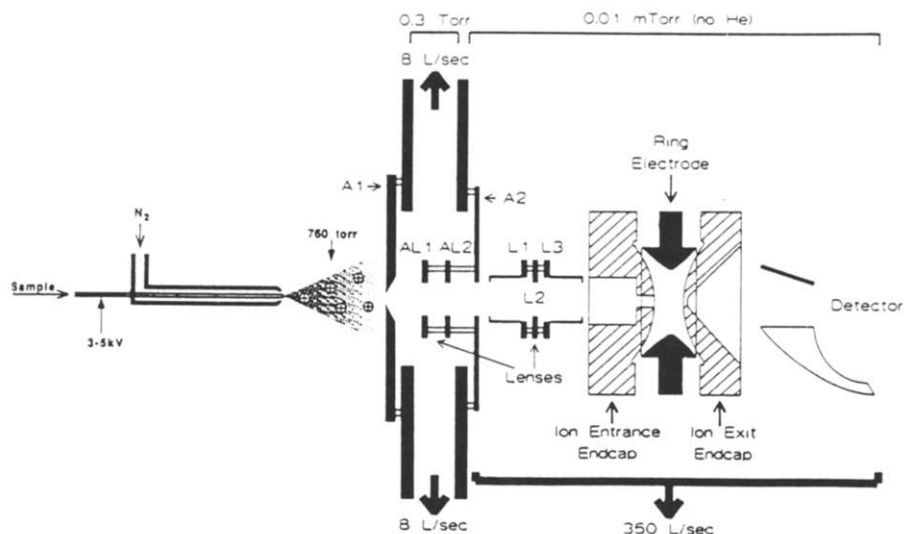


Fig. 22. Cross-sectional view of the ion spray liquid chromatograph interface coupled with an ion trap mass spectrometer. Drawing is not to scale [33]

The first on-line coupling of microbore high performance liquid chromatography (HPLC) with an ITMS has been reported by McLuckey et al. [33]; a cross-sectional view of the coupled LC–ITMS combination is shown in Fig. 22. Three representative LC–MS mass spectra are shown in Fig. 23. The authors demonstrated the use of LC–(MS)³ on an in-line analysis of a tryptic digest. Data can be obtained at subpicomole levels for proteins as heavy as 10–20 kDa. Thermospray LC–ITMS results have been reported recently [95,96].

The storage of externally generated ions is discussed also in the section on hybrid instruments.

TANDEM MASS SPECTROMETRY

The combination of two mass spectrometers coupled together is greater than the sum of the parts. The veracity of this statement was demonstrated clearly by J.J. Thomson [97] when he built a special instrument in which a beam of positive ions passed successively between the poles of two perpendicular magnets. A field-free region between the two magnets presented a novel opportunity for a mass-selected ion to suffer a collision with background gas, with subsequent mass analysis by the second magnet of the charged product. Yet some 60 years were to pass before tandem mass spectrometry was applied to the analysis of mixtures (ref. 8, p. 340). The first comprehensive review of the state of the art of tandem mass spectrometry [98]

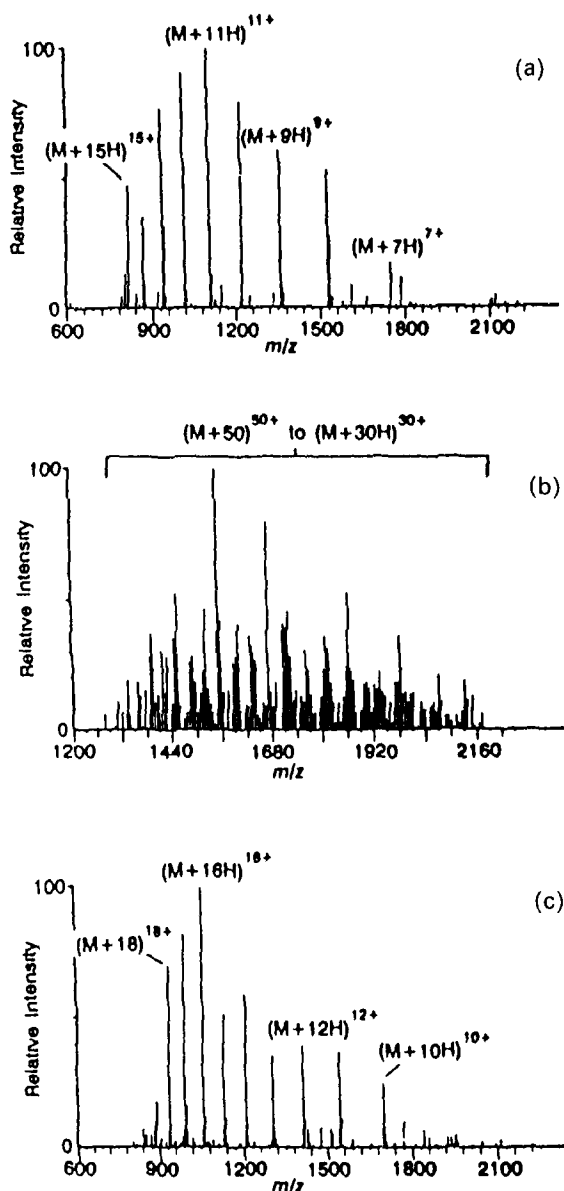


Fig. 23 LC-MS spectra of (a) cytochrome c, (b) HSA, and (c) myoglobin, obtained by averaging several scans over the corresponding peaks in the TIC [33].

appeared concurrently with the announcement of the Finnigan MAT ITD [5] in 1983. A further review of MS-MS, the acronym for tandem mass spectrometry, appeared recently [99]. The largest tandem mass spectrometers are composed of four sectors, that is, “tandem in space” while one penta-

quadrupole [100] has been constructed. However, because the ion trap operates in a pulsed mode by employing a series of discrete steps, the instrument generates MS–MS data from activities which are “tandem in time”. The limiting value of n in $(MS)^n$ depends principally upon residual ion intensity; the prerequisites for $(MS)^n$, including both instrumental and chemical factors, have been discussed in detail by Glish and co-workers [24]. The propensity of the ion trap to perform consecutive mass-selective scans with intervening opportunities for ion isolation, CID, photodissociation, ion/molecule reactions etc. has made available a radically different type of mass spectrometer. Some alternative scanning methods for the ITMS have been proposed [101].

Excellent examples of the application of tandem mass spectrometry, involving the associated stages of ion isolation and CID, have been afforded by a number of structure investigations on a variety of substances; unfortunately, the wealth of chemical knowledge gleaned thus far exceeds the space available here. The investigations include the following: the $[M-H]^+$ ions of chalcone (2-propen-1-ona-1,3-diphenyl) [102]; pyranocoumarins [103]; differentiation of the isomeric dimethoxyindoles [104,105] and the methyl and dimethyl derivatives of 8-desmethylneserine which are potential anti-proliferative agents [106]; substituted aryl ketones as models for the collisional activation process [107]; eicosanoids [108]; fragmentations in methyl ketones [109]; direct ion monitoring [110]; protonated lactones [111]; selective ion/molecule reactions [112]; direct sampling of physiological media [113]; esterification [114]; biomolecules [115]; applications of r.f./d.c. scan functions [116]; quantitative assays [117] and analysis of crude extracts [118]; combined capillary GC–ITDMS [119]; and distonic radical cations $\cdot CH_2(CH_2)_nOH_2^+$ ($n = 0-2$) and their conventional counterparts $CH_3(CH_2)_nOH^+$ ($n = 0-2$). This last example is of particular interest in that it illustrated the difficulty in accessing fragmentation pathways in excess of about 30 kcal mol^{-1} and in competition with low energy rearrangement processes [120]. Environmental applications include rapid analysis of volatile organic compounds [121] and of fossil-derived fuels [122] in water and soils, detection of trace organic compounds in air using thermal desorption [123], and in situ pyrolysis and thermal desorption [124].

An interesting example of the use of the ITMS in three cases where conventional tandem mass spectrometry is precluded by isobaric interferences is reported [125]; a comparison of ^{12}C parent ion and ^{13}C parent ion $(MS)^n$ mass spectra, where $n > 2$, permitted the unambiguous determination of daughter ion formulae. A discussion of sensitivities in the ITMS for EI and CI has been presented by Glish and co-workers [126]; with respect to benzophenone, the data indicated a lower limit of detection with EI. The ITMS has been used for ambient air analysis [127], and the detection of volatile organic compounds in air [128–131]; detection limits in the latter study were

in the mid to low parts per billion regime. The implementation of parent and neutral loss scanning in the ITMS has been reported [132].

An ITMS was used for the low energy aspect of a study of high and low energy collisional activation of 2,2,6-trimethylcyclohexanone [133]; consecutive activation sequences in the ITMS are described. The process of examining by ion isolation and CID each ion in a complete mass spectrum can be tedious, even for a system of very modest complexity such as sulphur [134,135], and so the process has been automated [136]. The proton affinity of sulphur (S_8) was estimated as $180 \text{ kcal mol}^{-1}$ [135].

Energy-resolved mass spectrometry

Energy-resolved mass spectrometry (ERMS) involves the entire problem of quantification of ion excitation induced by resonance irradiation; nevertheless, when constant experimental conditions are maintained in a given trap, it is possible to utilize three variants of the excitation process. Of the three variants applied to the differentiation of the 3-, 4- and 5-hydroxyindoles [137], that is, variation, in turn, of the amplitude of the supplementary r.f. tickle voltage, the duration of application of the tickle, and of the working point parameter β_z , the first variant proved to be the most effective in this case. The ERMS may also be effected by control of the kinetic energy of externally generated ions entering the ion trap [138].

Strife et al. compared the performances of the ion trap with a reverse geometry instrument [21]. The enhanced daughter ion collection efficiency in the ITMS is clearly an advantage but comparison of CID mass spectra remains subject to the quite considerable difference in collision energies in the two instruments [133]. A performance comparison of the ITMS with the triple quadrupole instrument (TQMS) with respect to tandem MS–MS daughter ion spectra, CID efficiencies, limits of detection, and dynamic range was carried out [139,140] using two alkyl phosphonates. While both instruments yielded daughter ion spectra with comparable relative abundances, the ITMS had greater efficiencies of fragmentation, collection, and mass selection and transmission of daughter ions to the detector. Full daughter ion spectra were obtained with the ITMS using 15 pg of diisopropyl-methylphosphonate (DIMP), 100 times less than that required by the TQMS. The GC–CI–CID mass spectrum of protonated DIMP, m/z 181, and the associated scan function are shown in Fig. 24. The ITMS may well be the most sensitive MS–MS instrument ever. It was reported that ions in the ITMS gained more internal energy upon resonance excitation than did ions upon collision in the triple quadrupole mass spectrometer [140], but the contrary state was found elsewhere [141]. A comparison is made of energy-resolved data on hydroxyindole

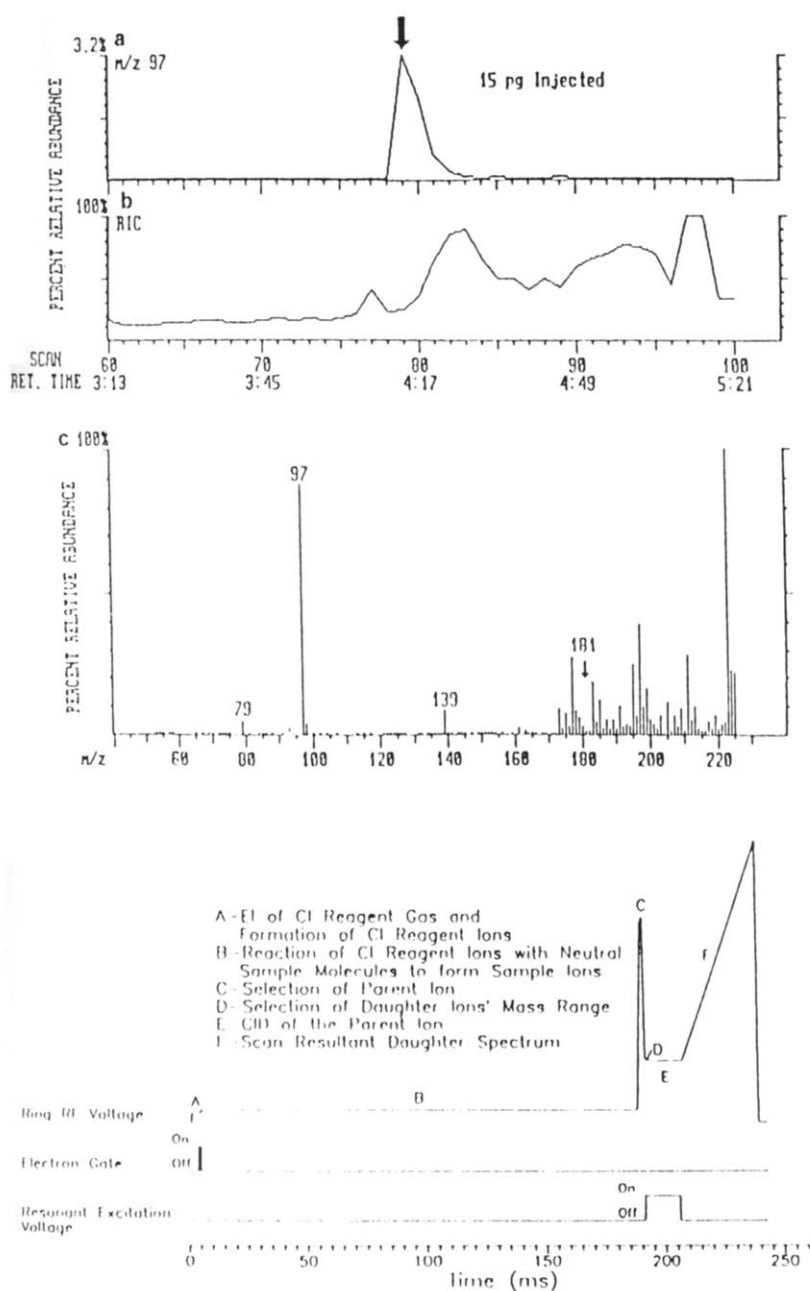
GC/PCI-CAD of DIMP m/z 181

Fig. 24. GC/PCI-CID with full daughter scan determination of 15 μ g of DIMP on the ITMS. a, trace of m/z 97; b, trace of RIC; and c, daughter ion mass spectrum. It should be noted that the ions above m/z 173 were not ejected prior to performing CID. The arrow indicates the retention time of DIMP. The associated scan function of the ITMS is also shown [140].

isomers obtained with an ITMS and a triple quadrupole [142], and charge exchange [143].

Internal energy deposition

Species-specific resonance irradiation can lead to the kinetic excitation of a single ion species in the ion trap. In subsequent collisions with helium buffer gas, fractions of ion kinetic energy are converted to internal energy and, in the limit, the ion dissociates. Daughter ions produced by dissociation can be trapped with high efficiency and are mass analysed subsequently. As the ion trap is eminently well suited for CID, much effort has been directed to understanding the processes involved. The secular frequencies of ion motion may be readily excited by the imposition of a supplementary r.f. potential to the end-cap electrodes. There are three possible modes of connection [39,144,145] to give three variants of excitation, or “tickling”: monopolar, first used in quadrupole resonance ejection (QRE) and where the tickle voltage is applied to one electrode while the other is earthed; dipolar, where the potentials on the two end-cap electrodes are out-of-phase; and quadrupolar, where they are in phase. Dipolar excitation is employed with the ITMS, while the ITD can be readily modified for monopolar excitation [146]. In a study of the relevant parameters in collisional activation in the ITMS [147], it was reported that the maximum internal energy of resonantly excited ions is limited by the presence, in substituted aryl ketones, of low energy reaction channels [107]. Both argon and helium were used as collision gases in this study by the group of Traldi.

Once the tandem mass spectrometric cycle of ion isolation, CID and daughter ion analysis has been completed, the cycle may be repeated with isolation of a daughter ion, CID and granddaughter ion analysis [148]. While the appearance energy of the product ion in each cycle may be of the order of 5 eV, the appearance energy of the granddaughter ion from the parent molecule has required 10 eV. In a sequence of ten steps from pyrene, it has been shown that some 29 eV of internal energy can be deposited in stages by the resonance excitation process [23,149,150]. The absorption of this large amount of energy is analogous to the step-wise increase in potential energy of a fish as it ascends a fish ladder, as shown in Fig. 25. A good example of repetitive resonance excitation is afforded by a study of the saturated sterane, cholestane [22]; mass spectra obtained using successive stages of CID on a series of ions derived from the molecular ion of cholestane are shown in Fig. 26, together with the associated (MS)⁷ scan function. The ion of m/z 217 is characteristic of steranes and is referred to below in the analysis of crude oils. An alternative method for the deposition of relatively large amounts of internal energy, sufficient to cause high energy fragmentation of somewhat

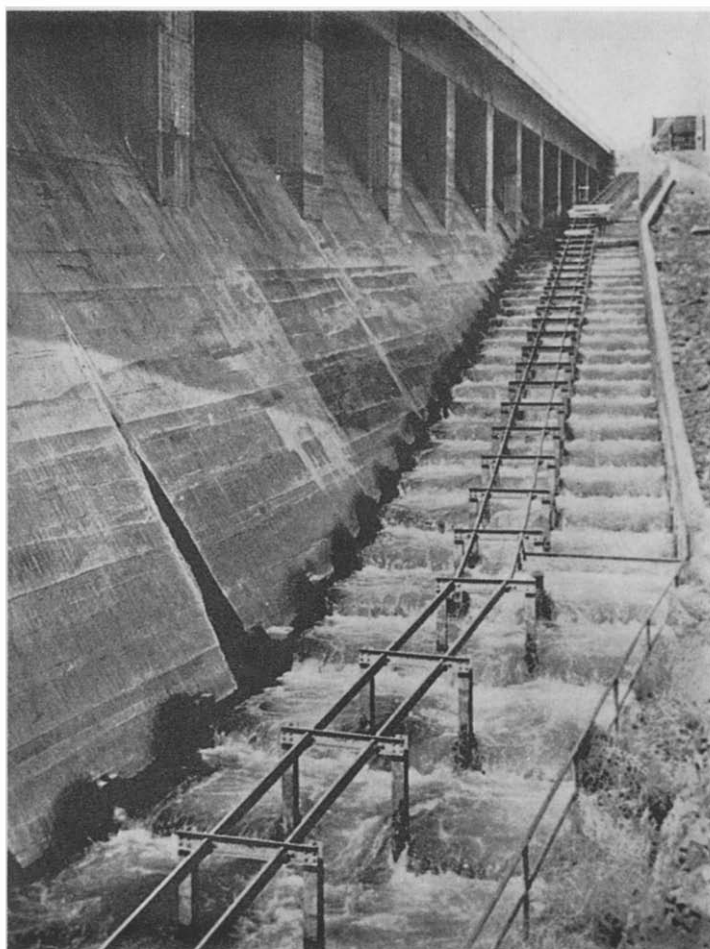


Fig. 25. Fish ladder. Collier's Encyclopaedia, Crowell-Collier, Vol. 10, 1963, p. 10.

intractable molecular ions such as pyrene and benzene, has been demonstrated by the application of short-duration, fast-rising, high voltage d.c. pulses to end-cap electrodes [28]. Ions are destabilized rapidly in the radial direction, and they strike the ring electrode whereupon fragmentation occurs; daughter ions rebound from the electrode and are stored.

GC-ITMS

While the ITD functions quite capably as a mass spectrometric detector to a gas chromatograph to yield both EI and CI mass spectra, the next level of sophistication is to incorporate rapid interrogation procedures similar to

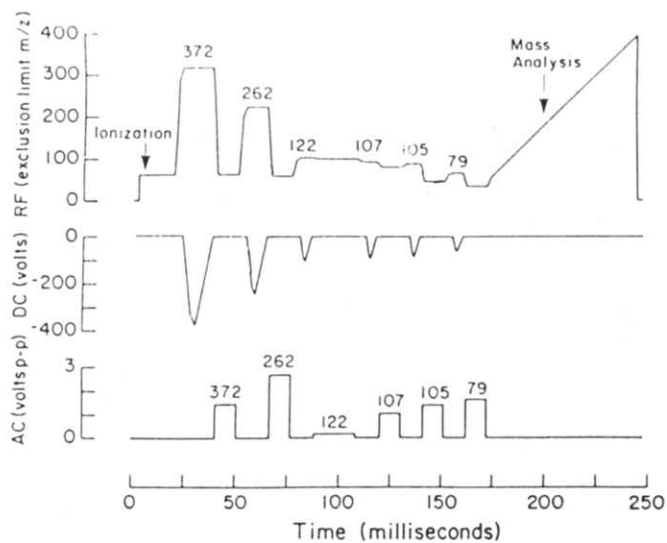
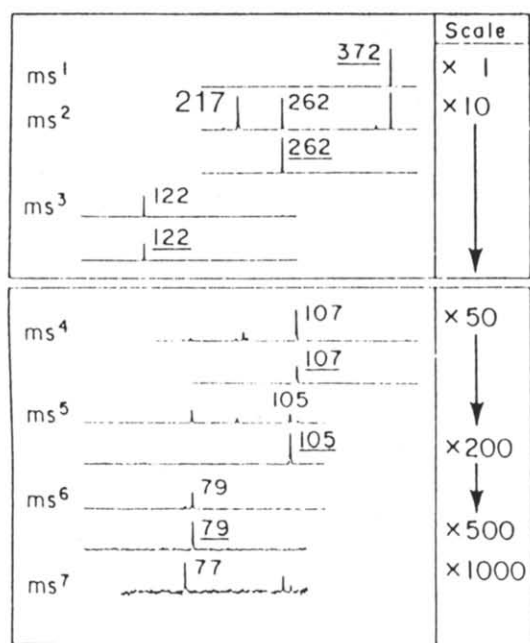


Fig. 26. Mass spectra obtained using successive stages of CID on a series of ions derived from the molecular ion of cholestane. The (MS)⁷ mass spectrum was obtained with the scan function shown and corresponds to the series of dissociations. m/z 372 $\rightarrow$ m/z 262 $\rightarrow$ m/z 122 $\rightarrow$ m/z 107 $\rightarrow$ m/z 105 $\rightarrow$ m/z 79 $\rightarrow$ m/z 77 [22].

those of automatic gain control (AGC) [151] and automatic reaction control for CI (ARC-CI) [152]. The GC-ITMS combination is not without complication when one attempts to utilize the high sensitivity of the ion trap and its capabilities as a tandem mass spectrometer on the GC time scale. A major problem is the rapid assignment of an effective resonance frequency. Yost and co-workers have focused upon the interrogation of components eluting from the GC column by employing strategies of combinations of r.f., d.c. and tickle waveforms in order to improve the selective ionization of trace components and the selective storage of trace analyte ions [153]. The problems associated with the recognition and enhanced efficiency of resonance excitation of specific analyte ions on the GC time scale are under investigation in several laboratories [154–156]. An automated resonance excitation technique using frequency-assignment pre-scans and broadband excitation has been explored [156]. Modified forms of resonance excitation using broadband excitation signals [154,157] can be combined with frequency pre-scans as a strategy to utilize the full potential of GC-ITMS [157].

ION TRAPPING STUDIES

Ion trap detector

The ITD and ITMS have been used in a miscellany of interesting applications which, unfortunately, are reviewed all too briefly here. Some perspectives on the future of analytical chemistry involving the ion trap have been given by Yost and co-workers [15]. The ITD combined with GC has been used for the determination of volatile organic compounds in drinking water with USEPA Method 524.2 [158], and of trace levels of herbicides and their degradation products in surface and ground waters [159]. The detection limit in this latter study was 60 pg with a signal-to-noise ratio greater than 10. The authors report [159] that the low cost of instrumentation, ease of automation, enhanced sensitivity and specificity make this technique an ideal screening method for use in national assessments of chemical quality of surface and ground waters. A transportable purge-and-trap GC-ITD has been developed for the in situ characterization of chemical waste sites [160]. The instrument has been tested under field conditions, and showed a detection limit for trichlorethylene in water in the low parts per trillion range. Other systems studied with the ITD include the fragmentation of amines in NH_3CI [161].

3,4-(Methylenedioxy)methamphetamine is a ring-substituted amphetamine (MDMA) or “designer drug”. In view of the controversy surrounding MDMA and its listing as a Schedule 1 drug by the U.S. Drug Enforcement

Agency, research is underway using the ITD to clarify the pharmacology and toxicology of the drug. Identification of the *in vivo* (in rats [162,163] and in humans [164]) and *in vitro* metabolites of MDMA [162,165] has been carried out.

A simple inexpensive membrane probe combined with an ITD has been applied to the detection of low levels of environmentally significant organic compounds directly from water [166]. The system responded rapidly and accurately to concentration changes of benzene, chloroform and 1,2-dichloroethane in a mixture. This method clearly has potential for monitoring industrial waste streams. Direct sampling of environmental target compounds is rapid [167]. A mobile ITD for environmental monitoring has been developed [168], and real-time, *in situ* point monitoring has been carried out [169]. Detection at the parts per billion level of ten organic compounds of environmental interest using capillary membrane tubing and an ITD has been reported [170]; CI mass spectra were readily obtained. This ITD–capillary membrane system shows considerable potential for well-water analysis with no sample pre-concentration. As part of an extensive research program on the utilization as animal feed of lignocellulosics, a pyrolysis GC–ion trap study (Py–GC–ITD) has been carried out; ITD mass spectra are reported [171] for lignins produced by various acids and bases. Current lignocellulosic surpluses exceed 4.4 billion tonnes yearly worldwide.

Crude oil analysis

China is the oldest producer of oil in the world. It is recorded that in 211 B.C. bamboo drillstrings were used to drill oil wells at Chi-liu-ching in Sichuan Province [172]. Both the method of drilling and analysis (if any existed at that time) have changed considerably; the known locations of oil are shown in Fig. 27. The six recently published GC–ITD papers concerned with the analysis of crude oil are divided equally between those concerned with crude oil samples from China [172–174] and those concerned with samples from Oklahoma [175–177]. The ITD combined with GC offers a relatively inexpensive system for routine analysis of crude oils for biomarkers, with particular attention placed on the determination of sterane and terpane distributions. A total ion chromatogram of a test mixture is shown in Fig. 28. Steranes and terpanes are most widely used in geochemical applications, giving characteristic fragments at m/z 217 (see Fig. 26) and m/z 191 respectively. Single-ion chromatograms of m/z 217 (Fig. 29) show the presence of a number of stereoisomers and homologues; these spectra show that this oil is derived from Viola Limestone. One may use also the distribution of terpanes as shown in the single-ion chromatograms of m/z 191 (Fig. 30) so as to confirm the derivation of an oil from suspected source rocks. “The ITD is

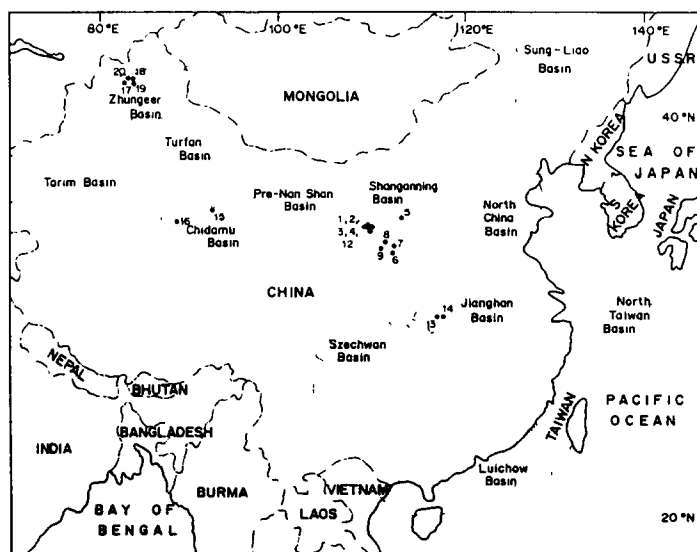


Fig. 27. A map of China indicating the location of oil fields [172]

economic for the analysis of biomarkers, it brings the method within reach for a far greater number of analytical chemists than was previously possible; sensitivity and chromatographic resolution of the ITD are comparable to those of more sophisticated quadrupole or magnetic sector instruments” [173].

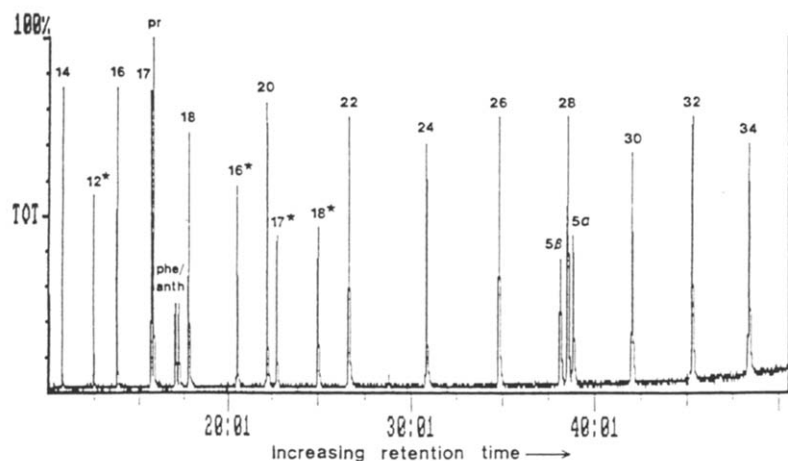


Fig. 28. Total ion current chromatogram of test mixture used to verify chromatographic and mass spectrometric conditions. Key. numbers refer to chain length of *n*-alkanes, starred numbers refer to carboxylic acid methyl esters; pr, pristane (2,6,10,14-tetramethylpentadecane); phe, phenanthrene; anth, anthracene; 5 α and 5 β , 5 α - and 5 β -cholestane respectively [173].

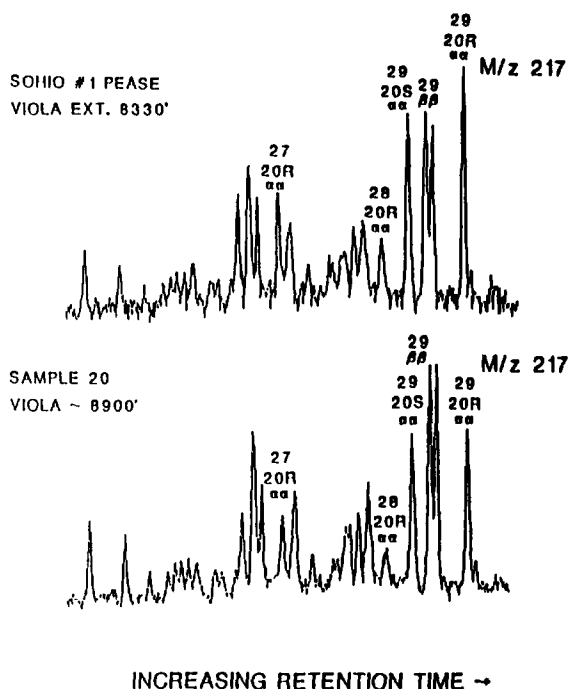


Fig. 29 Partial m/z 217 chromatograms of saturated fractions isolated from a sample of Viola Limestone and an oil reservoir in the Viola Limestone. Key: numbers refer to the carbon number of the steranes [173].

Chemical ionization

Chemical ionization mass spectra for a variety of compounds have been compared using a conventional high pressure source, a QUISTOR-MS902 combination and an ITD operating in the CI mode [178]. The ITD had a larger mass range than the QUISTOR, although the latter has the advantage that it may be readily retrofitted to sector instruments as a low pressure source. The extent of fragmentation was greater in the ITD than in the high pressure source which tended to produce adduct ions, in agreement with earlier results [179]. The dynamic range of the ITD in the CI mode has been shown to be increased some 50-fold when the ion trap operation includes the ARC function [180]. Dimethyl ether has been evaluated as a selective CI reagent in the ion trap for mono- and bi-substituted oxyaromatic compounds and was found to demonstrate, by adduct ion formation, both functional group and position selectivity; this selectivity was not observed using a conventional CI source [181]. Chemical ionization using mass selection of reactant ions yielded mass spectra which were easily interpreted on the basis of the energetics of ionization of the sample by the selected reagent ion [182].

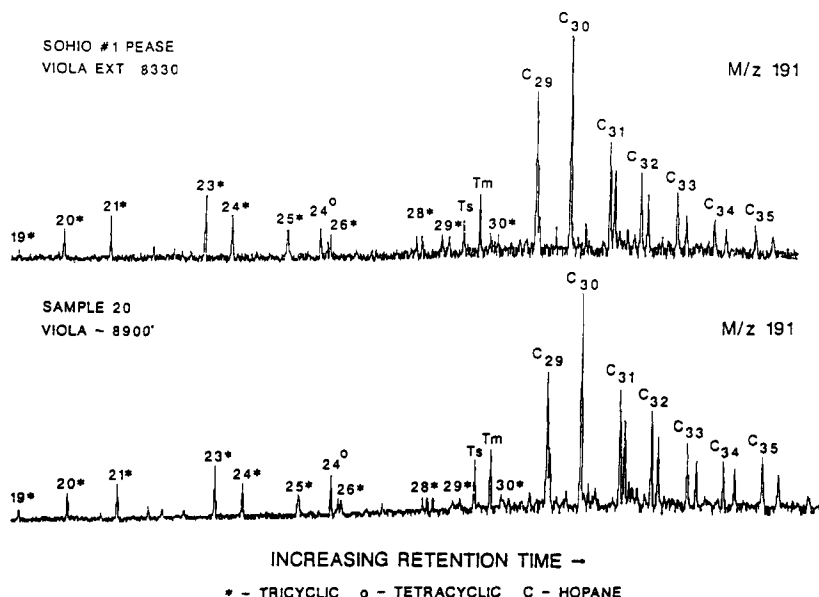


Fig. 30. Partial m/z 191 chromatograms of the samples shown in Fig. 29. Key: numbers refer to the carbon number of the tricyclic sterpanes (*), a tetracyclic terpane (O, C₂₄) and the 17 α -; 21 β -hopanes (C); T_s, 18 α -22,29,30-trisnorneohopane (C₂₇); T_m, 17 α -22,29,30-trisnorhopane (C₂₇) [173]

Pseudomolecular ions, $(M + 1)^+$, arising from self-CI [183], are observed with increasing intensity as storage time is prolonged and as the concentration of parent molecule is increased; such behaviour could interfere with library-based identification (a common criticism of ion trap detection). Horman and Traitler showed that full-scan mass spectra of methyl stearate, using from 2 pg to 225 ng of analyte, combined with GC retention data were readily recognized by library algorithms [184]. Pseudomolecular ions in the ITD were found to be no detriment to the analyst [185,186].

The ITD has been used in the CI mode for a number of investigations. These studies include routine plasma profiling of neuroactive molecules such as the cholinergic drug arecoline in plasma from treated Alzheimer patients [187], and analysis of fragrance compounds in a mixture containing 25 perfume components [188], where only linalool failed to give molecular weight information.

Ion/molecule reactions

The ion trap continues to serve as a reaction vessel for the study of ion/molecule reactions, that is, where a selected ion reacts with a neutral

which may or may not be the parent molecule. Let us examine two cases. Almost all isomers of C_5H_8 (except *cis*- and *trans*-1,3-pentadiene) were distinguished by monitoring the products of each neutral isomer with mass-selected ions from the same isomer [189]. The second case involves the gas-phase halomethylation of several organic compounds, which has been investigated using CH_2Cl^+ as the reagent ion [190], and the methylation of the isomeric dihydroxybenzenes using the dimethylfluoronium ion [191]. The enhanced capability of the ion trap for tandem mass spectrometry was utilized in each case to probe the structures of product ions using CID. The ion/molecule reactions of protonated cyclohexene oxide and the isomeric protonated cyclohexanone with ethyl vinyl ether have been investigated using an ITD, a triple quadrupole and a BQu hybrid mass spectrometer [192].

Relative gas-phase basicities may be determined in the ion trap using both the proton-transfer equilibrium technique and the kinetic method [193]. Both methods serve to illustrate the capabilities of the ion trap. The former method requires measurement of the rate constants of the forward and reverse proton-transfer reactions with a compound of known basicity, while in the latter method the proton-bound dimer formed from two bases is collisionally activated to cause dissociation into the individual protonated bases. The relative abundances of the protonated bases formed from the competitive dissociation reactions of the dimer relate to their relative basicities. The basicity of 1-adamantanamine was found thus to be $903.9 \pm 0.8 \text{ kJ mol}^{-1}$ [193]. Using the kinetic method, Nourse and Cooks [194] determined the proton affinities (PAs) for *o*-, *m*- and *p*-methylbenzoic acid to within $\pm 0.2 \text{ kcal mol}^{-1}$, with the major contribution to the estimated uncertainties arising from those in literature PA values for the reference compounds. As a probable consequence of the low internal energy of the proton-bound dimers, they were able to measure PA differences of $0.1 \text{ kcal mol}^{-1}$ or less, and estimated that differences as small as $0.04 \pm 0.02 \text{ kcal mol}^{-1}$ were detectable. The same authors examined the effect on PA of deuterium labelling [194]. The thermodynamic vs. kinetic control of ion/molecule reactions has been examined [195]. The rate coefficients for electron transfer from H_2 and from Be to Be^{2+} ions have been reported [196]; an excellent example of the asymmetry of the frequency absorption spectrum is shown in Fig. 2 of ref. 196. The ITD has been employed [197] as a detector for supercritical fluid chromatography (SFC).

Pulsed gas introduction

While ion isolation in the ion trap facilitates the choice of the charged reactant in an ion/molecule encounter, choosing a neutral reactant other than the parent molecule is not readily possible. However, pulsed solenoid valves can be used for gas introduction to enhance control of collision gas [66] or

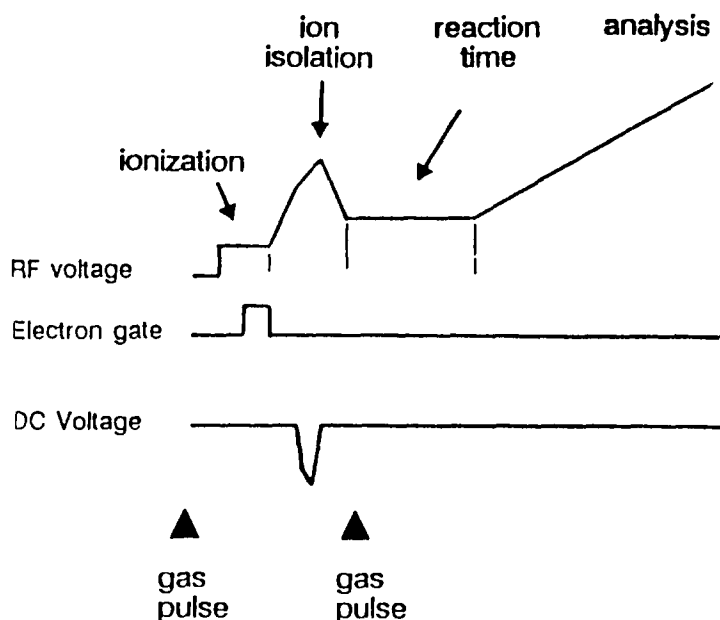


Fig. 31. The sequence of r.f. and d.c. voltages used in the ion trap to generate ions (ionization), mass select the ion of interest (ion isolation), store the ionic products formed during ion/molecule reactions (reaction time), and analyse the ionic products (analysis). A typical EI time was 0.5 ms and the ion isolation time was 4–7 ms, the reaction time was varied from 0 to 1600 ms. The arrows indicate the times when the pulsed valve was opened in different experiments [198].

neutral reagents to bring about specific ion/molecule reactions [198]. The ability to change rapidly the type of neutral molecules in the trap for CI (first arrow in Fig. 31) and for CID or ion/molecule reaction (second arrow in Fig. 31) has been demonstrated [198]. An excellent example of the efficiency of pulsed gas introduction is afforded by carbon addition reactions in the investigation of the location of C=C bonds in C_6 – C_{23} linear alkenes [199].

Temperature

It is important to consider separately the “temperatures” of the neutral species and of the ions. The temperature of the neutrals is usually determined by that of the manifold but, in precise quantification, correction should be made for diminution of carrier gas pressure wrought by temperature programming of GC columns [200]. Quantitative discrimination of up to 10% can occur as a function of column temperature. In the two accounts of the effects of increase in manifold temperature, increased fragmentation in methane CI mass spectra of *n*-alkanes was observed [201] in an ITD, while enhanced CID was reported [202] in an ITMS.

Johnson and Yost reported that underivatized morphine failed to undergo CID in an ITMS [139], while Lim et al. [202] found that an abnormally high tickle fluence was required to obtain daughter ions from the protonated trifluoroacetyl derivative of 2,4,5-trihydroxymethamphetamine. However, upon raising the manifold temperature to some 180°C, daughter ion intensities were increased dramatically [202]. Effective ion temperatures have been probed using ion/molecule reactions with well-characterized cross-section energy dependences, namely, the Ar^+/N_2 charge exchange reaction [203,204] and the reaction of O_2^+ with CH_4 [205,206]. Effective ion energies for the former reaction ranged from 0.1 to 0.3 eV over the N_2 pressure range studied, and were comparable to that of 0.08 eV for the latter reaction. An effective temperature of 335 K was calculated from the collisional activation of proton-bound dimers of substituted pyridines [193].

In a detailed account [207] of the various means of measuring the “ion temperature”, the author differentiates clearly between collisionally cooled and uncooled systems. For uncooled systems, ion temperatures depend upon the pseudopotential well depth and are generally quoted in electronvolts per electronvolt potential well depth [208]. Direct evidence for an instantaneous mean ion kinetic energy of 1.3 eV (uncooled system) has been obtained by a time-of-flight method [209], and is consistent with microwave resonance frequency shifts [208].

Novel aspects of ion trap behaviour

While the normal form of the r.f. drive potential V is $V_0 \cos \Omega t$, confinement in an ion trap has been demonstrated using a periodic impulse potential of the form $V_0 \cos \Omega t / (1 - k \cos 2\Omega t)$ with $0 \leq k < 1$ [210]. This potential is of interest as it presents large zero potential temporal zones during which ions may be injected without modification of their initial energies. A new scanning method has been developed which incorporates both mass-selective storage and mass-selective ejection [211,212]. The method uses a stepped r.f. scan function, and ion instability is induced in the region of the upper apex of the stability diagram. The r.f. and d.c. drive voltages are increased incrementally as shown in Fig. 32. During each interval between steps, pulsed ionization produces a variety of ions of which only a very narrow m/z range will have stable trajectories. The next drive voltage step is imposed upon the ion trap following a time delay which allows ions with unstable trajectories to leave the ion trap. The same principle of ion isolation and ion ejection, though directed to broad mass ranges, is discussed in detail by McLuckey et al. [59]. Novel scans for the ITMS have been developed for selected ion monitoring [35], and sequential multiple scan monitoring [213] has been applied to a mixture of sulphamethazine and tetrachlorodibenzo-*p*-dioxin.

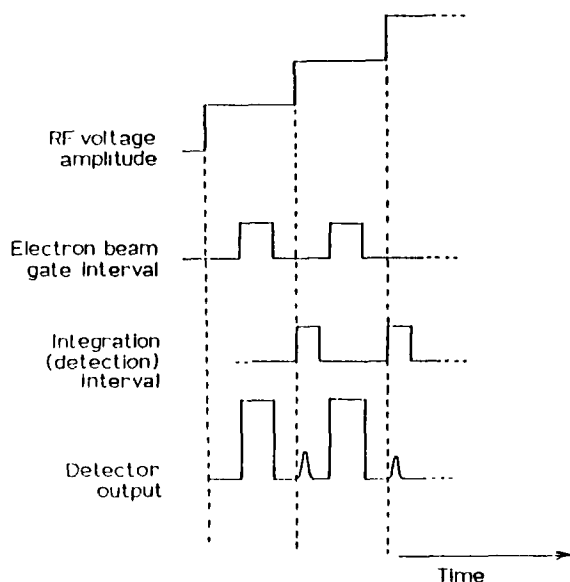


Fig. 32. Scanning and timing waveforms for the QUISTOR mass spectrometer [211].

Ion ejection

An interesting aspect of mass-selective axial instability is that ions ejected thus through an end-cap electrode do not require post-ejection acceleration. In part, the ejected ions are influenced by the field due to the negative potential on the electron multiplier and, in part, the ions exit the ion trap with some hundreds of electronvolts of kinetic energy [214]. In a recent study, the kinetic energies of ions ejected from both an ITD and an ITMS, at $q_z = 0.908$, $\beta_z = 1$, were measured by a retarding potential method [41]. Average kinetic energies increase with mass, a typical value being 2900 eV with a distribution of 900 eV (FWHM) for m/z 502. Resonant ejection of the same ion species at $\beta_z = 0.48$ showed a maximum kinetic energy of only 644 eV. Simulations of ion motion yielded maximum kinetic energies in good agreement with the experimental data.

SPECTROSCOPY

The sensitivity of ion traps for spectroscopic applications, where only small quantities of atoms are available, was investigated [215] using ^{137}Ba . A trapping efficiency of 2% was obtained for $^{137}\text{Ba}^+$ ions created by surface ionization near an end-cap electrode using helium at a pressure of 10^{-6} mbar. Some 10^7 atoms are necessary for a resonance fluorescence experiment. Confine-

ment of about 10^5 ions for many hours permitted precise determination of the hyperfine structures of $^{135}\text{Ba}^+$ and $^{137}\text{Ba}^+$ [216]. The high sensitivity of the stored-ion technique is used in the investigation of ground state hyperfine splitting of radioactive isotopes; for example, radioactive $^{131}\text{Ba}^+$ and $^{133}\text{Ba}^+$, produced by nuclear reactions and collected at the ISOLDE facility at CERN, showed splittings of $\Delta\nu(131) = 9\,107\,913\,698.97(50)\text{ Hz}$ and $\Delta\nu(133) = 9\,925\,453\,554.59(10)\text{ Hz}$ using quantities of about 10^{12} atoms [217]. This experiment is the first step of a systematic study of hyperfine anomalies of isotopic chains of elements. The ground state hyperfine splitting [218] and the relativistic Doppler effect of $^{199}\text{Hg}^+$ have been investigated [219]. Collisional de-excitation of the metastable D states of Ba^+ by He, Ne, N_2 and H_2 were determined in an ion trap experiment [220]. A method for trapping a single Ba^+ ion has been described [221]. High resolution microwave spectroscopy on trapped $^{171}\text{Yb}^+$ ions [222] and $^{173}\text{Yb}^+$ ions [208] has been carried out, in addition to a determination of the lifetime ($\tau = 52 \pm 1\text{ ms}$) and collisional depopulation rates of the metastable $5\text{D}_{3/2}$ state of Yb^+ [223]. The lifetime of the metastable $6\text{P}_{3/2}$ level of Pb^+ is reported as $41.2 \pm 0.7\text{ ms}$ [224]. Collisions between $\text{Xe}(nf)$ Rydberg atoms with SF_6 molecules in a quadrupole ion trap produce unstable excited SF_6^-* molecular ions [225]. Two-photon transitions involving trapped Hg^+ ions have been reported [226]. Ion traps afford the opportunity to study ion collisions at much lower energies than is possible in conventional ion beams. Experimental studies in ion storage have been directed toward the production of ions with higher charge and lower energy, and measurement of small cross-sections [227]. The feasibility of using an ion trap for a precision measurement of the ground state hyperfine structure of hydrogen-like Na^{10+} has been examined [228]. The capabilities and current limitations of multicharged ion research using ion traps have been reviewed and compared with storage rings [229]. Thompson has written an excellent review of the precision aspects of ion traps [230].

Laser-ion trap combination

In addition to the rapid instrumental development of the ion trap as a mass spectrometer, increasing attention is being paid to combinations of the ion trap with other instruments such as lasers, gas chromatographs, electrospray, and dynamic and static mass spectrometers as discussed above. Mass spectrometry and its use in tandem with laser spectroscopy have been reviewed recently [231]. The potential benefits of resonance-enhanced laser multiphoton ionization of NO in an ITD have been investigated [232]. The $2 + 2$ photoionization scheme proved to be more than 10 times more efficient than EI; the limit of detection corresponded to the concentration of the $^{14}\text{N}^{18}\text{O}$ isotope at $13 \pm 3\text{ ppb}$. Laser desorption (LD) from probes within the storage

volume itself of ion traps has been reported where the laser beam is directed radially through the ring electrode. In addition to LD of molecular and fragment ions, combined LD–EI produced further fragment ions [233,234]. Laser ablation sampling inside the cavity of an ion trap has been used to obtain direct atomic mass spectrometric analysis of solid metal samples [235]. A pulsed Nd:YAG laser beam was used to ablate sample pins inserted radially through the ring electrode; a mass spectrum of silver solder was obtained (Fig. 33). Tandem mass spectrometry on ions produced by LD has been demonstrated [236]. Fixed-wavelength laser ionization tandem mass spectrometry has now been applied to mixture analysis [237].

An early rationale for the study of ion traps was the determination of appearance potential curves of products of slow unimolecular dissociations [238]; such curves were obtained some years later [239] by time-resolved photoionization mass spectrometry (TPIMS). The application of TPIMS to the slow dissociations of the thiophenol molecular ions yielded photoionization appearance energies [72,240] in good agreement with EI data. The photon energy scale of TPIMS has been extended to about 21 eV using the Hopfield continuum in helium in conjunction with ion trapping; new experimental results for $C_7H_7^+$ formation from toluene have been presented [241].

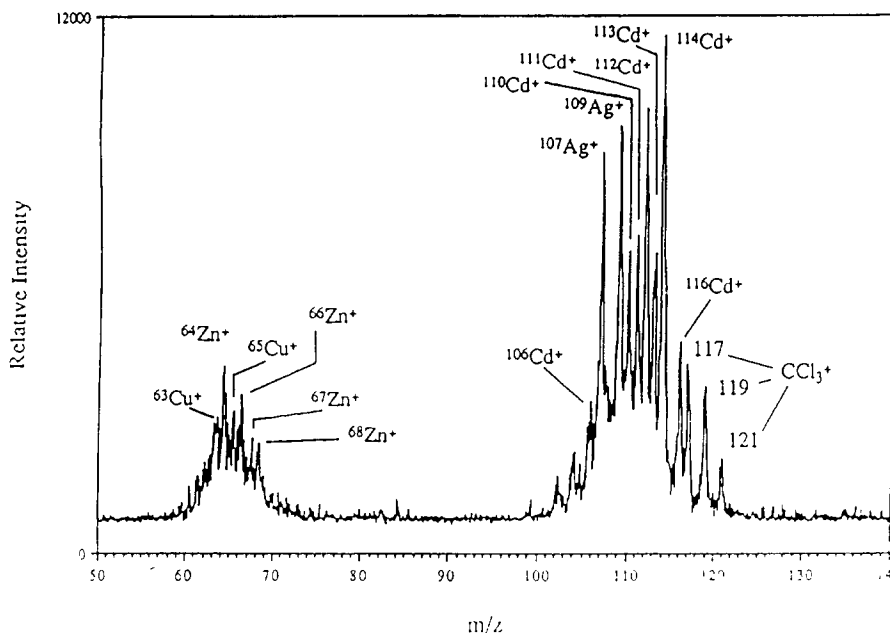


Fig. 33. LAITMS spectra of silver solder [235].

HYBRID AND NOVEL MASS SPECTROMETERS

A hybrid mass spectrometer of BEQiQu geometry (B, magnetic sector; E, electric sector; Qi, ion trap; Qu, quadrupole mass filter) has been developed [242–244] using a deceleration lens system to couple the ion trap to the high resolution stage (BE) [245]. The transmission efficiency is about 80% as ions are decelerated from 3 keV to 30 eV; below 1000 Da, no mass discrimination was observed. Ions were stored for up to 8 s [243]. In this instrument, the QiQu component is floated at the high-voltage ion source potential which is disadvantageous. Mass-selective axial ejection can obviate the need for the Qu stage as has been shown with a BEQi instrument [138]. An ion trap with $r_0 = 0.5$ cm replaced the Qu element of a commercial BEQuQu instrument (Finnigan HSQ-30); ion trap operation was supported by a commercial system for an ITD. In Fig. 34 is shown the daughter ion mass spectrum from m/z 1320 ions, mass-selected by the BE components. This figure illustrates the enhanced range of the “small” ion trap and the fragmentation of m/z 1320 ions, with an injection energy of some tens of electronvolts, by collision with helium.

Although a QuQuQi is not strictly a hybrid instrument, which is defined as having both static and dynamic sectors, the performance characteristics of a QuQuQi instrument [246–248] are reviewed here where the Qi component was an ITMS. Injection of ions selected by the quadrupole removes matrix and extraneous analyte ions, thus improving ion trap performance by

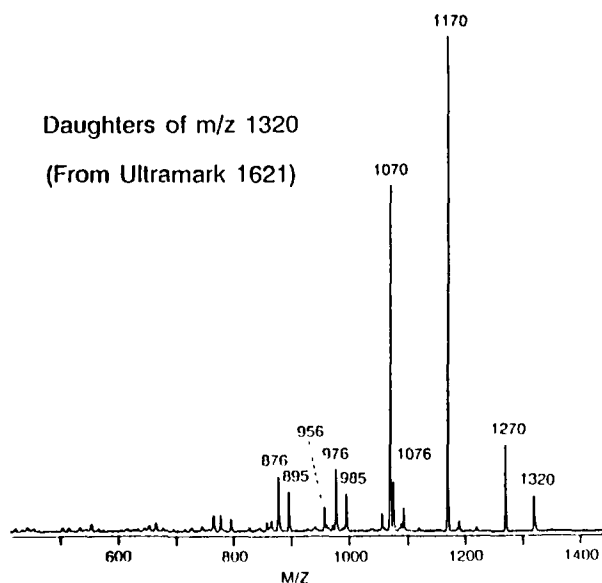


Fig. 34. Daughter spectrum of m/z 1320 generated by electron impact of Ultramark-1621, and recorded by a mass-selective instability scan of the ion traps [138].

reducing space charge. A QuQiQu instrument [68,244,249] obviates the high voltage problems encountered with true hybrid instruments and is to be used primarily for the study of organic negative ion/molecule reactions [244].

RESONANCE EXCITATION

One of the merits of the ITMS is the relative ease with which the instrument may be operated in the tandem mode in order to study the sequential mass spectrometry of collisionally excited ions. In these experiments the ion of interest is first selected according to its m/z ratio, and then its translational motion is excited through the application of a supplementary oscillating “tickle” field applied between the end-cap electrodes. While care must be taken to ensure that the frequency of the tickle field is in resonance with the frequency of the secular macromotion of the ion being studied, very little was known of the individual steps in the overall process.

As the total efficiency of the CID process is vital to the tandem mass spectrometric performance of the ion trap, groups at Kent, Trent and Provence Universities decided some 3 years ago to embark upon a collaborative program of experimentation and trajectory simulation of resonance excitation. The program consisted of the development of microcomputer programs for calculating trajectories of ions, both unperturbed by resonance radiation and subjected to resonance radiation applied in three modes, spectral analysis of ion trajectories in both collision-free and collisional systems, experimental investigation of atomic and small molecular ion absorption in the r.f. range, and experimental investigation of resonance excitation of an organic compound, 1,2-dichlorobenzene.

Recent activity in the field of ion trajectory simulation and the application of such simulations to resonance excitation are reviewed.

Ion trajectory simulation

Relatively few simulation studies of ion trajectories have been carried out and reported during the past 4 years. Representative trajectories for trapped ions of three different masses, with working points on the q_z axis and in a collision-free and resonance-free system, have been calculated by integration of the Mathieu equation [73]. Moore and co-workers [250] have applied finite element analysis to the calculation of fields within the ion trap from which trajectories were calculated. Some previously unpublished trajectory plots by Bexon and Todd and by Fies, Jr., for ions stored within the ion trap and subjected to collisions with helium buffer gas, appeared in a recent publication by Todd [9]. Bexon and Todd calculated one-dimensional (axial) trajectories of m/z 25 ions showing the effect of regular collisions with helium atoms; the

motion of m/z 69 ions in the r - z space plane both with and without helium buffer gas was calculated by Fies, Jr.

The HYPERION program developed by Pedder and Yost [251] for the calculation of ion trajectories uses a modified form of the Mathieu equation together with a fourth-order Runge–Kutta algorithm. A parallel capacitor model was used for dipolar excitation; the simulated final kinetic energy as a function of tickle frequency at constant fluence compared well with experimental loss in parent ion intensity as a function of tickle frequency. In the absence of a tickle voltage, HYPERION reduces to the unperturbed Mathieu equation for trajectory simulation and calculation of ion kinetic energy.

An ion trap simulation program (ITSIM) has been used with great success by Cooks and co-workers [252]. The features of the program permit simulation of external ion injection, bath gas dampening and resonance excitation. The equations used to calculate the development of an ion's trajectory have a modified form of the "conventional equations of ion motion" for an ion trap. Plots of unperturbed ion motion and ion axial ejection by resonance excitation have appeared recently [10]. Two further simulations have been carried out with ITSIM: firstly, rapid radial excitation to instability upon the application of a short duration high voltage d.c. pulse to the end-cap electrodes [28] is compatible with the observed fragmentation pattern induced by collisions with a surface (ring electrode); and secondly, calculated ion kinetic energies upon ejection agree well with experimental values [41].

March et al. have developed a series of programs for ion trajectory calculation: integration of the Mathieu equation (MA) for the calculation of unperturbed trajectories and to provide a standard to which their other programs reduce when specialty features are eliminated; a specific program for quadrupole resonance (SPQR) [39,40]; a field interpolation method (FIM) for examination of resonance excitation (a tickle voltage) applied in monopolar and dipolar modes [253]; and a field interpolation with continuously ramped d.c. and r.f. potentials method (FIRM) [58].

The trajectory of m/z 134 in an unperturbed collision-free system was calculated using FIM for a period of 5 ms in time steps of 1 ns. The trajectory was calculated also using the Mathieu analytic solution. An exacting comparison of the calculated trajectories is made by comparing the temporal variation of ion kinetic energy, and the radial and axial positions during the final 10 μ s as shown in Figs. 35(a)–35(c). Excellent agreement is evident. In quadrupolar irradiation, a supplementary r.f. voltage of low amplitude V_t is applied in-phase to each end-cap electrode; in dipolar mode, the tickle voltage is applied out of phase, and the monopolar mode is self-evident. The major observation was that quadrupolar irradiation at an axial frequency component permits selection of energy channelling into either radial or axial motion, and absorptions were observed at $\beta_u\Omega$ and $(1 \pm \beta_u)\Omega$ owing to

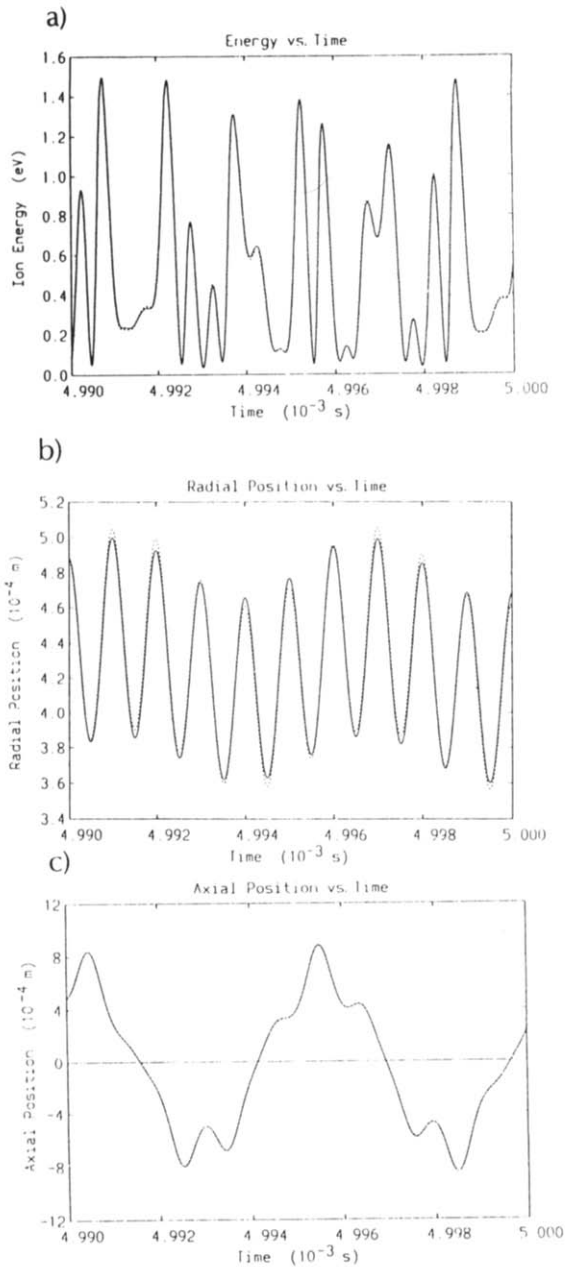


Fig. 35. The trajectory of m/z 134 calculated for the non-resonant case using FIM (---), for a period of 5 ms using time steps of 1 ns. The working point was ($a_z = 0$, $q_z = 0.4997$), $r_0 = 1$ cm, and the drive frequency was 1 MHz. The trajectory was calculated also using the Mathieu (—) analytic solution. Temporal variations of (a) kinetic energy, (b) radial position, and (c) axial position during the final $10 \mu\text{s}$ of the calculated trajectories [58].

parametric resonance. Relative absorption coefficients were calculated as the reciprocal of the irradiation fluence required for ion ejection, $V_t t_t$, where t_t is the duration of application of the tickle voltage.

A Taylor–McLaurin expansion in the solution of the trajectory equations, used in the phase space formalism, has been proposed for the calculation of ion trajectories in the ion trap [254]; however, no example of this method has been developed thus far.

Direct comparison among these trajectory simulation programs when applied to resonance excitation is obviated by the lack of information on simulation parameters, such as ion initial position and velocity, initial phase and time step. Collaborative work is underway to remedy this situation.

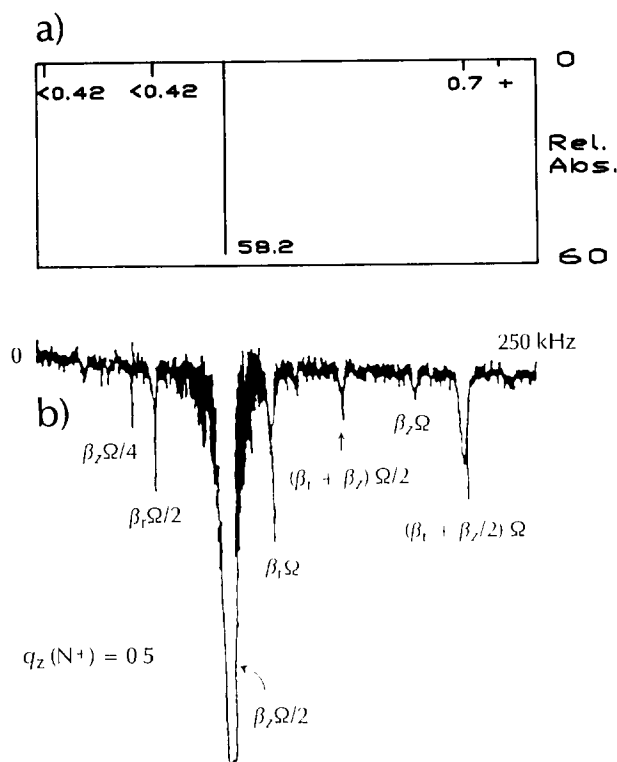


Fig 36 Dipolar excitation. (a) Relative absorption coefficients obtained from trajectory simulation using FIM, m/z 134, auxiliary potential amplitude $10V_{(o-p)}$, $q_z = 0.4997$; the small coefficients at $(\beta_1 - \beta_2/2)\Omega$, $\beta_1\Omega/2$ and $\beta_2\Omega$ should be noted (b) Ion ejection signals of N^+ due to the interruption of the confining, or drive, voltage over the tickle frequency range, 0–250 KHz, $q_z = 0.50$; drive frequency is 0.5 MHz. The “absorption” peaks denote frequencies at which prior resonant ejection, both axial and radial, occurred [253].

Resonance absorption experiments

The trajectory simulation data have been compared with two sets of experimental results. Firstly, frequency-dependent absorption signals obtained in dipolar mode together with relative absorption coefficients obtained by trajectory simulation are shown in Fig. 36; corresponding data for quadrupole excitation are shown in Fig. 37 [29,207,253,255]. Despite the disparity in experimental conditions, there is a remarkable degree of consistency among the data. Secondly, power absorption in CID experiments [256,257] wrought by dipolar and quadrupolar irradiation modes, using a modified ITD, has been compared with simulation data [253]. The molecular isomer of lowest mass of 1,2-dichlorobenzene, m/z 144, was isolated and, upon irradiation in dipolar and quadrupolar modes, formed a daughter ion of m/z 111 by loss of ^{35}Cl . Dynamically programmed scans [256,258] permitted incremental changes (0.1 ms) in the irradiation period over the range 0–10 ms. It was

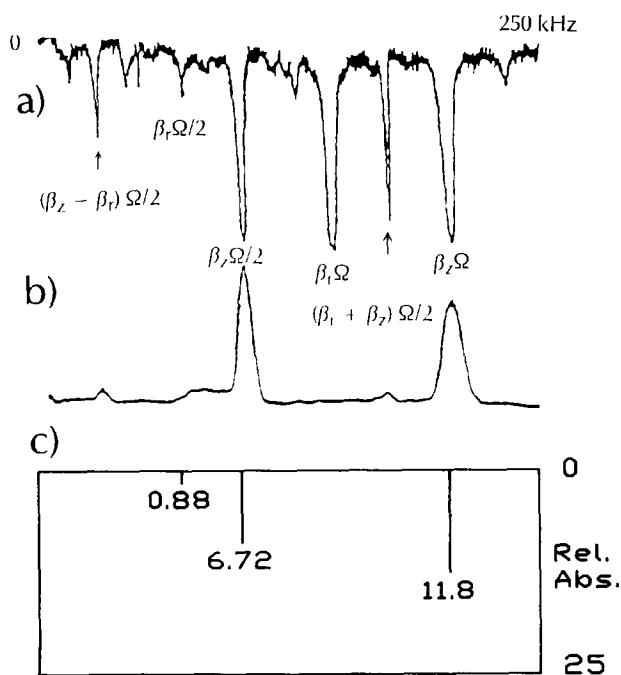


Fig. 37 Quadrupolar excitation. (a) Ion ejection signals of N^+ due to interruption of the confinement voltage, where “absorption” signals denote those frequencies at which prior resonant ejection, both axial and radial, occurred (b) Ion ejection signals of N^+ due to resonances with the z component of ion motion over the tickle frequency range 0–250 kHz. (c) Relative absorption coefficients obtained from trajectory simulation using FIM. m/z 134, auxiliary potential amplitude $10V_{(0-p)}$, $q_z = 0.4997$ [253]

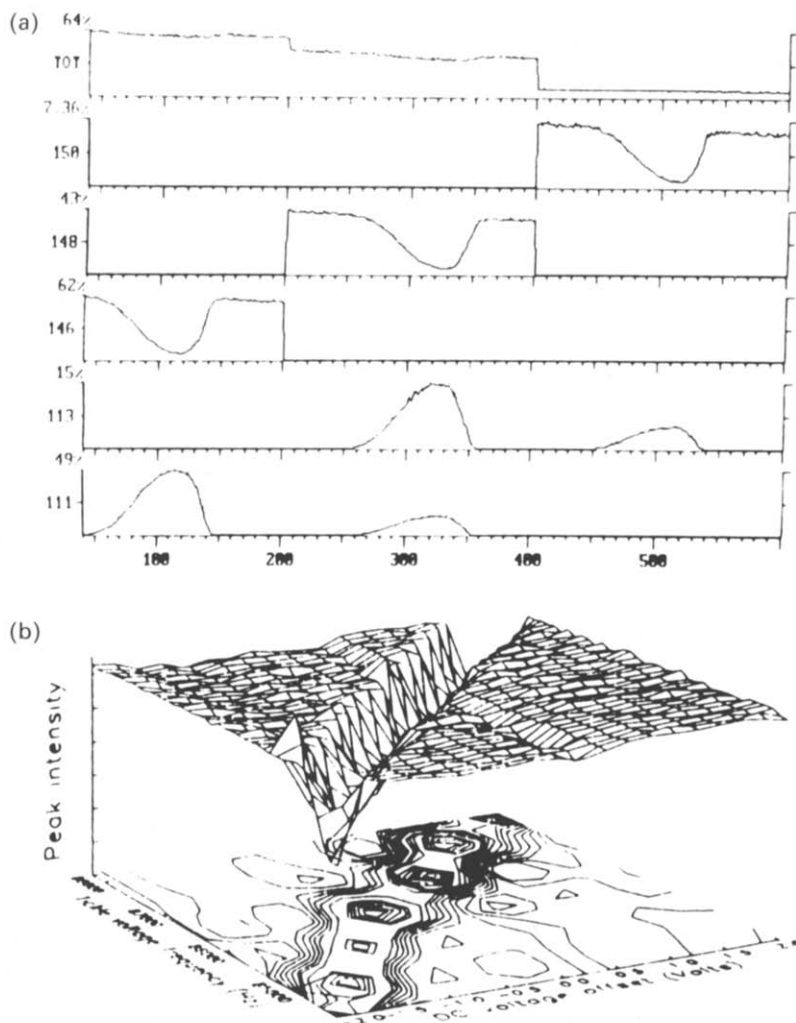


Fig. 38 (a) Ion fragmentogram of the parent ions and principal daughter ions from 1,2-dichlorobenzene recorded for $q_z = 0.30$. The horizontal axis represents three frequency sweeps where scans 0–200, 201–400 and 401–600 cover the range 116.39–118.39 kHz for the 146^+ , 148^+ and 150^+ ions respectively. (b) Three-dimensional and contour plots showing the variation with frequency and d.c. offset of the peak intensity for resonant excitation of m/z 264 from perfluorotributylamine ($q_z = 0.22$, $\beta_z = 0.157$, tickle amplitude, 400 mV for 5 ms) [34].

assumed that the reciprocal of the fluence required for 50% dissociation of parent ions would be a measure of power absorption. The experimental ratio of dipolar-to-quadrupolar power absorptions was 10.6 compared with the ratio of 5.03 obtained by simulation. The agreement was judged to be satisfactory for these initial experiments.

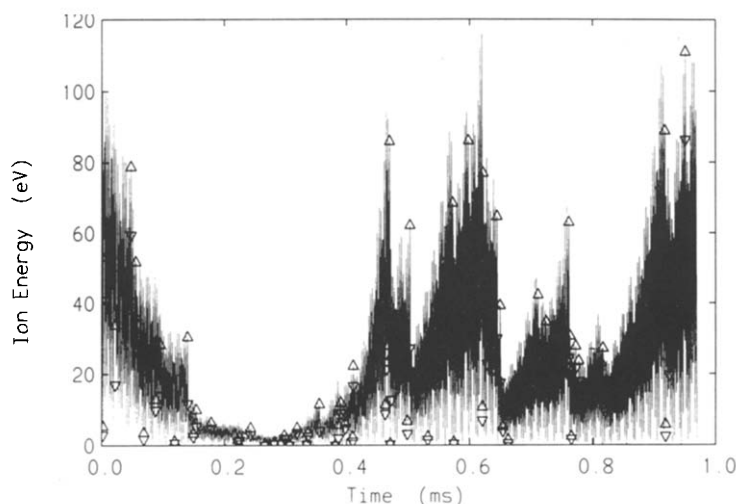


Fig. 39 Calculated temporal variation of ion kinetic energy (averaged over one r.f. cycle) in the presence of helium as collision gas. A delayed auxiliary potential, imposed after 0.3 ms of storage time, was reduced in amplitude after 0.45 ms of storage time to 80% of the initial value and held constant at that value throughout the remainder of the simulation. Upright and inverted triangles represent, respectively, the instantaneous ion kinetic energies before and after each collision [260]

Dynamically programmed scans are enormously powerful in that they yield ion fragmentograms (Fig. 38(a)) and a three-dimensional data presentation, or an ion intensity map, wherein ion current is plotted against two parameters, such as d.c. voltage and exclusion limit m/z [22], or a d.c. voltage and tickle voltage frequency [11,34,256,259] as shown in Fig. 38(b). The method of dynamically programmed scans has been combined with trajectory simulation in the following way. The kinetic energy was calculated for an ion created within the ion trap; as shown in Fig. 39, ion kinetic energy was lost as the ion became focused at the centre of the trap under the influence of collisions with helium. After 0.3 ms, the ion was tickled at a relatively high (boil) tickle voltage whereupon it became excited and would have been ejected had not the tickle voltage been reduced at 0.45 ms to half of the original value. Excitation could be prolonged at this level with the result that ion kinetic energy was high but the ion was not adjusted; this mode of operation was termed “simmering” [260]. The $(MS)^3$ spectrum of 1,2-dichlorobenzene was examined in detail using a dynamically programmed scan in which the total fluence of irradiation was maintained constant but the boil and simmer fluences were varied. In Fig. 40 is shown a plot of daughter ion (m/z 111) signal intensity vs. that of a granddaughter ion (m/z 75 by loss of HCl from m/z 111); the abscissa represents also increasing boil fluence [261]. The ratio of granddaughter-to-daughter ion intensities increased at higher boil fluences, indicating that a

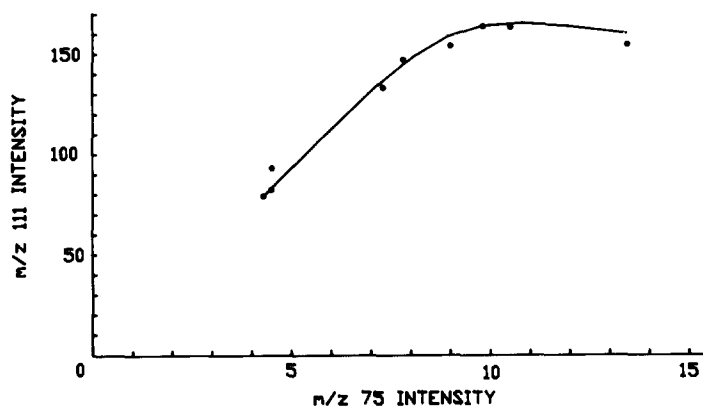


Fig. 40 A plot of signal intensities of the daughter ion m/z 111 from 1,2-dichlorobenzene, and the granddaughter ion m/z 75 (by loss of HCl from m/z 111). The “boil” and “simmer” fluences were varied while the total resonance fluence was maintained constant, the “boil” fluence was increased along the abscissa [261]

measure of control over the relative weights of reaction channels can be achieved.

OTHER TYPES OF ION TRAP

Beatty

An alternative geometry for small quadrupole ion traps was proposed by Beatty [262] in which the electrodes could be machined by simple lathe cuts; the end-cap electrodes have cylindrical symmetry with conical boundaries. A Beatty trap has been constructed [263] for an experimental study of laser evaporative cooling of trapped negative ions; two theoretical studies of this problem were published recently [263,264].

Cylindrical

Cylindrical ion traps have attracted modest attention yet continue to be used particularly by the group in Orsay. This group has recently compared the effective potential and storage capacity of a hyperbolic trap with those of a cylindrical trap [265], and found that greater densities and total numbers of ions can be achieved in a cylindrical trap compared to one with hyperbolic geometry, in agreement with earlier observations [266]. In an unpublished report [267], a cylindrical trap with a mesh barrel electrode surrounded by a tritiated foil was found to store ions. Ionization is probably caused by spala-

tion of electrons upon impact of β particles with the stainless steel trap electrodes. The TPIMS studies discussed above use a cylindrical ion trap.

Multipole

A new development in ion traps has been the introduction of small percentages of “even” multipoles (hexapole and octopole) to the quadrupole field [36–38]. Such multipole fields add higher order terms to the field strength, which are manifested by two strong effects on ion movement within the ion trap. Firstly, resonance phenomena no longer cause an indefinite growth of the secular amplitude, as there is a frequency shift with increasing amplitude which causes a phase shift between the initial resonance frequency and the secular frequency; the increasing maximum excursion of the ion from the centre of the trap is arrested as resonance absorption no longer occurs. Secondly, multipole fields cause non-linear resonances when working points correspond to certain simple values of β_r and β_z . The electrodes can be easily shaped to form exact superpositions of the quadrupole field with known octopole and hexapole components. In all cases, the centre of the field has an exact quadrupole form; deviations due to multipole contributions are visible only away from the centre as is seen in Fig. 41.

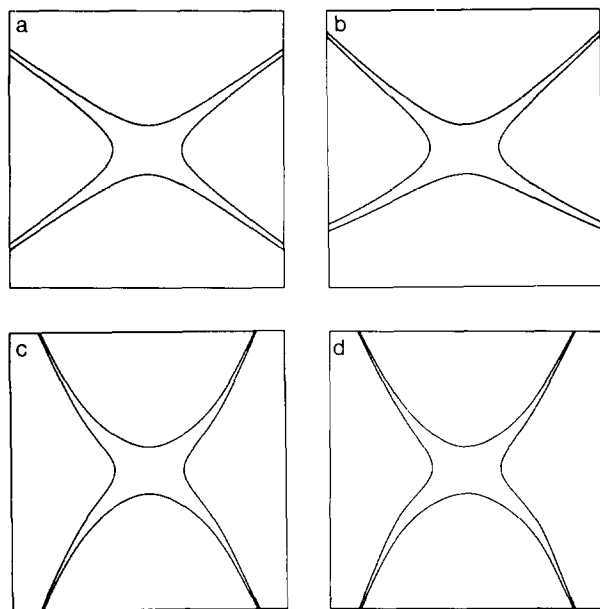


Fig. 41. Cross-sections of multipole traps. (a) quadrupole ion trap (0% hex, 0% octo); (b) 10% hex, 0% octo, (c) 0% hex, 10% octo, (d) 10% hex, 10% octo [260].

Penning

While the Penning trap is beyond the purview of this review, references to accounts of recent work are given here [268–283].

ORDER vs. CHAOS, CRYSTAL vs. CLOUD

Statistical methods have been used to compute the spatial and energetic properties of an ion cloud confined in an ion trap; the influence of space charge and the shape of the velocity distribution of the cooling buffer gas were investigated [284]. The fundamental secular frequency $\omega_{0,z}$ has been determined experimentally using time-of-flight detection of ions ejected from the ion trap [285]. Ion–ion collisional relaxation, or collisional cooling, continues to be actively studied owing to advances in laser cooling of small numbers of stored ions, and the “crystallization” of cold, stored ion clouds [42,286,287]. The rate of energy transfer between the radial and axial degrees of freedom of protons in the ion trap has been quantified [288]. A beautiful experiment of some 30 years ago showed charged particles of aluminium dust cooled by the viscous drag of the background gas and arranged in a crystal-like structure. The result of a more recent experiment [289] is given in Fig. 42 which shows charged fragments of acrylic plastic trapped in a mesh cylindrical ion trap at atmospheric pressure. In a video recording of the same experiment, charged fragments execute rotational movement about the axis of symmetry, and in both directions. Strong coupling of the charged cloud is seen owing to the high ratio of the nearest-neighbour potential to particle kinetic energy [290]. With sufficient laser cooling of individual atomic ions at low pressure, it is possible to observe a phase change; this change is manifested by significant jumps in the fluorescent intensity of the ions as a function of the detuning Δ between the laser frequency and the atomic transition frequency [42,286]. In Fig. 43 are shown two, three, five and seven ions confined by the pseudopotential in an ion trap, crystallized into ordered structures in a plane perpendicular to the symmetry axis of the trap [286], and showing very elegantly the balance of Coulomb repulsion with pseudopotential well confinement. Blümel has shown theoretically that stable Coulomb clusters of both positive ions and negative ions may co-exist in the ion trap [291].

CONCLUSIONS

The principal advances made in the ion trapping field during the past 3–4 years have been quite spectacular; the increased mass range, increased mass resolution, tandem mass spectrometric operation to the n th degree, and coupling with external sources, particularly electrospray, have contributed

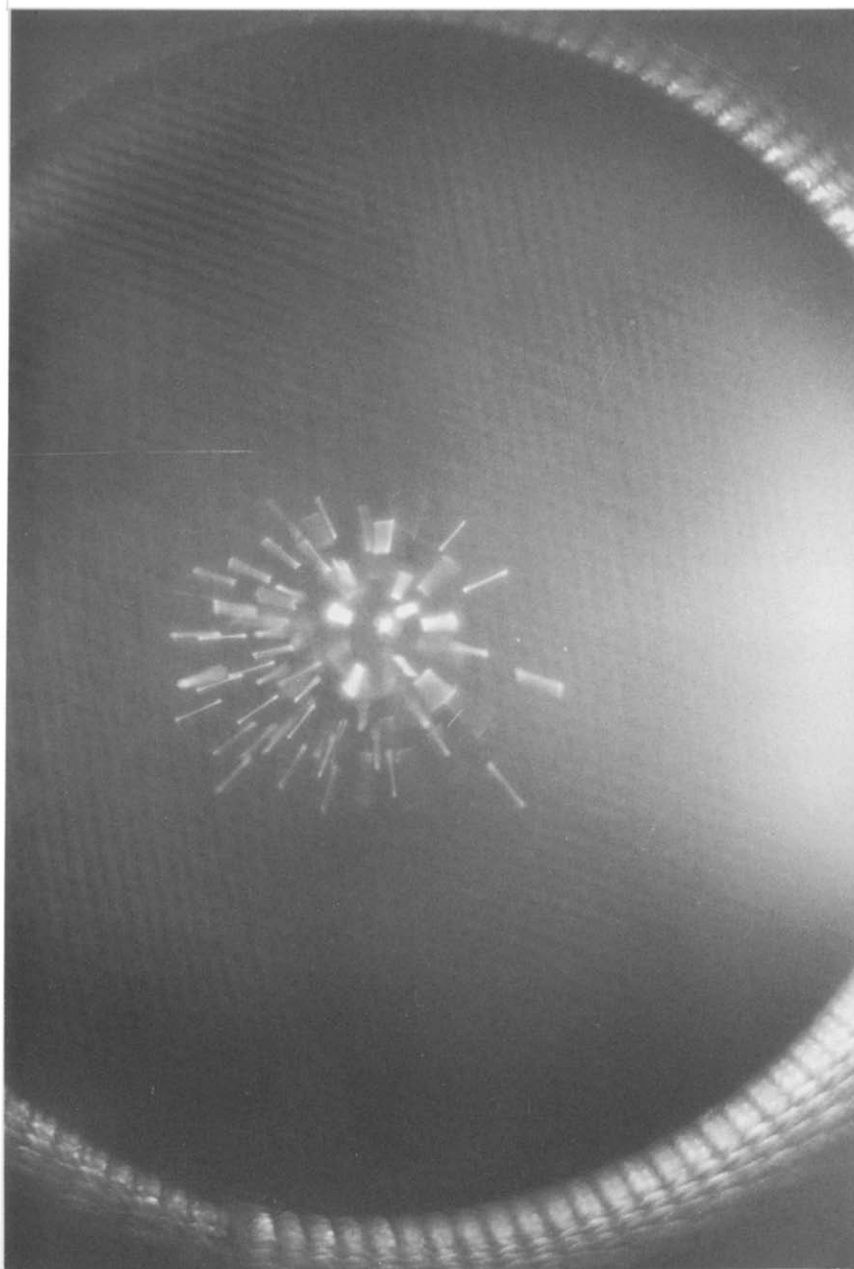


Fig. 42. Photograph of charged acrylic particles confined in a meshed cylindrical trap at atmosphere pressure and arranged in a quasi-crystalline structure (F Vedel and M Vedel).

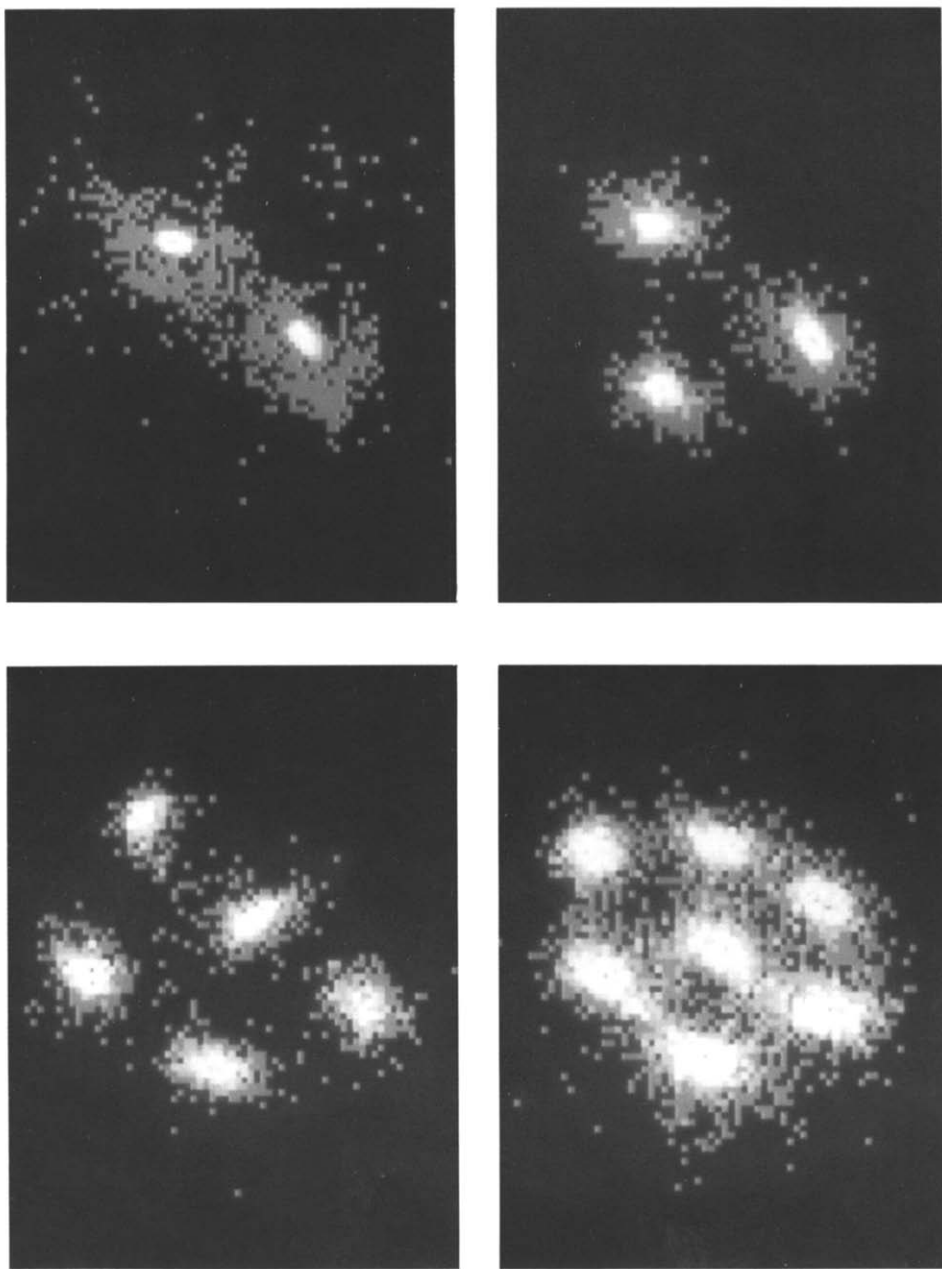


Fig. 43. Two, three, five and seven ions confined by the dynamical potential of a Paul trap and crystallized into an ordered structure in a plane perpendicular to the symmetry axis of the trap. The average separation of the ions is $20\text{ }\mu\text{m}$ (H. Walther).

to the realization of an entirely new type of mass spectrometer. As these advances have been made almost concurrently, there has not been sufficient time for the new knowledge to be applied throughout the field. Thus, the ion trap will become a powerful analyser for electrospray ions derived from on-line separation of biomolecules. At the next International Mass Spectrometry Conference, the incorporation of these advances in a variety of applications will be manifest. For example, the shortcomings of the HPLC–ITMS system [33] for on-line HPLC–MS analyses, that is, mass accuracy, mass range, mass resolution, automation of tandem mass spectrometry are in principle correctable on the basis of the advances reviewed here. We may expect to see the following developments: an improvement in peak position stability which is impaired at present when scan rates are attenuated; further development of GC strategies for peak recognition; pulsed modification of helium pressures for optimization of resonance excitation, ion isolation, and mass selection, in turn; use of temperature as a parameter for both neutral and ion; and perhaps the achievement of a mass range of 500 000 [27].

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