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Mass Spectrometry and Its Use in Tandem with Laser Spectroscopy

E. R. GRANT AND R. G. COOKS

Mass spectrometry is undergoing rapid development, especially with the extension of its range into the hundreds of kilodaltons, the emergence of the quadrupole ion trap as a high-performance instrument, and the development of techniques for recording three-dimensional spectra. These advances are summarized in this review; in addition, the power of the combination of lasers and mass spectrometers is given particular emphasis. Their combination has contributed recently to chemical dynamics, to the study of cluster structure and reactivity, and to the elucidation of the properties of highly excited molecules and ions.

MASS SPECTROMETRY (MS) IS BOTH A SELF-CONTAINED discipline and an instrumental method used widely in the sciences. This article attempts to provide a snapshot of current activities of both types. In the first part, which covers recent advances in MS, we (i) discuss advances in ion production from biomolecules by laser desorption and by desolvation methods ("spray techniques"), especially those which yield intact multiply charged molecular ions and thereby extend the mass range of mass spectrometers into the tens and even hundreds of kilodaltons without requiring any changes in the instrument itself; (ii) summarize the state of the art in biomolecule structural analysis; (iii) present the rapid evolution of the simple quadrupole ion trap into a high-performance instrument capable of multiple stages of mass analysis (MS^n experiments), very high mass-to-charge (m/z) range, and exquisite sensitivity; (iv) emphasize the exciting multidimensional experiments made possible by multiple analyzer instruments; and (v) present MS evidence for the existence of elusive neutral molecules, including those important in astrochemistry. We further illustrate the applications of MS in the second part through a single representative topic—its use in physical chemistry research, especially in structural and dynamical studies on small molecules in combination with laser spectroscopy. Included is a discussion of laser multiphoton ionization (MPI) and dissociation and its applications to reaction dynamics, the dynamics of reactive scattering, and the properties of cluster species and other ions as elucidated by laser-based MS techniques.

Recent Advances in Mass Spectrometry

High molecular weight measurement. Traditionally a major application of MS has been the measurement of molecular weights of organic compounds in the mass range below 1000 daltons. The

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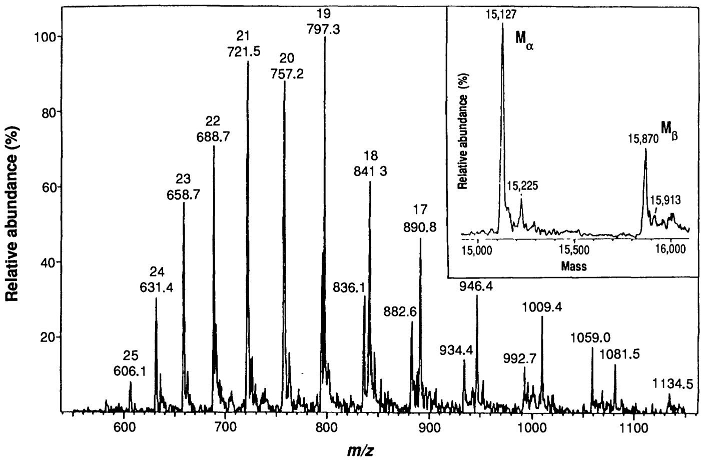


Fig. 1. Electrospray mass spectrum of a human blood sample (lysed and centrifuged) recorded with a triple quadrupole mass spectrometer and showing number of charges associated with the main peaks. The insert shows the mass spectrum after deconvolution for the charge state. [Courtesy of I. Jardine, Finnigan Corporation, reproduced with permission]

development of the desorption ionization (DI) methods [such as fast atom bombardment (FAB), secondary ion mass spectrometry (SIMS), and Cf-fission-fragment desorption] over the last decade has allowed nonvolatile, thermally fragile molecules to be ionized (*1*). Successes were obtained in measuring molecular weights of compounds up to 10,000 daltons and in a few cases, particularly through the ^{252}Cf desorption technique, (*2*) even higher.

This limitation has now been dramatically changed by the nearly simultaneous introduction of two methods. These methods, matrix-assisted laser desorption (*3*) and electrospray (ES) ionization (*4, 5*), provide similar results but differ sharply in their physical basis. Laser desorption is a DI method in which an energetic probe desorbs ions directly from the condensed (usually solid) phase. Singly charged ions are generated and time-of-flight (TOF) mass analysis is used to obtain the necessary high range in *m/z* (daltons per unit charge). The innovation in the experiment is the use of a matrix (such as derivatives of cinnamic or nicotinic acid) that strongly absorbs the photon energy [266-nm or 355-nm YAG (yttrium-aluminum-garnet) laser harmonics or 337-nm N_2 line] and hence liberates the analyte, which is present in low dilution and is not directly affected by the irradiation. The experiment builds upon previous work on matrix-assisted DI, but is remarkable in many ways, including (i) its very high sensitivity (sample sizes are often as little as 1 picomole), (ii) its immunity to suppression by salts, which can be deleterious to ^{252}Cf desorption, and (iii) its applicability to complex mixtures such as cell lysates and blood plasma (*6*). Mass measurement accuracy is in the range 0.1 to 0.01%, and the method has already been tested with large numbers of peptides, proteins, and glycoproteins (*6*). Recent work (*6a*) has shown that infrared lasers can also be used.

The ES method developed out of attempts to interface liquid chromatographs and mass spectrometers. Nebulization of liquid in a vacuum under the influence of an electric field liberates intact molecules that are multiply protonated (*4, 5*). High molecular weights, hundreds of kilodaltons for peptides and to tens of kilodaltons for oligonucleotides (7), are measured by increasing both *z* and *m* while keeping the quotient *m/z* within the range of normal mass analyzers (a few thousand). Remarkably, simple quadrupole mass spectrometers give an accuracy that approaches 0.01%. Because the number of charges is not fixed, numerous forms of molecular ion are generated and multiple *m/z* ratios are available so that *m* can be determined unambiguously and accurately. A quadrupole mass spectrometer was used to obtain the molecular weight of the hemoglobin of a patient with the hemoglobin defect, hemoglobin Volga. (Fig. 1) (*8*). A simple computer program converts the electrospray mass spectrum, recorded in the usual way as ion abundance against *m/z* ratio, to a plot of ion abundance against mass (Fig. 1, insert). These data reveal several minor components together with the major components of molecular weights 15,129 and 15,870 daltons, which are assigned as α-globin (calculated average molecular weight 15,126 daltons) and β-globin (15,867 daltons). The ions of mass 15,225 and 15,913 are tentatively assigned to the phosphate adduct of the α chain and the Volga form of the β chain (expected 15,911 daltons). Note that the major series of ions (*m/z* 606.1, 631.4, 658.7, 688.7, 721.5, 757.2, 797.3, . . .) corresponds to α-globin molecules carrying 25, 24, 23, . . . attached protons and hence this number of positive charges.

Remarkably, neither of these new techniques yields fragment ions [although fragmentation can be induced (*9*)] so that they promote the use of mass spectrometers simply for molecular weight determinations. This application of mass spectrometers contrasts with their use to elucidate molecular structure, as described below. Increasingly, the latter experiments use tandem mass spectrometers and they operate (at present) at far lower molecular weights than those discussed above. The techniques described above should see use in establishing purity of genetically engineered materials, for recognizing the presence of endogenous abnormal proteins, and for quantitating proteins and other biomolecules (*5*). We expect the direct analysis of spots on two-dimensional gels by MS to become useful (*10*). Capillary zone electrophoresis (CZE) combines well with MS (*11*) and should prove to be of value for high-quality separation and characterization of small amounts of sample.

Molecular structure determination. Peptide sequencing by MS (*12*) has progressed rapidly. Sample sizes are now becoming comparable to those required by Edman sequencing, but the MS method is faster and applies in cases (such as cyclic peptides or amino-blocked and other posttranslationally modified peptides) where the traditional methods do not.

The key to this work is the adoption of the MS/MS methodology (*13*), which was introduced some years ago for the analysis of complex mixtures. Ionization is often by FAB or SIMS and collision with a gas target fragments the mass-selected ion. The experiment has been performed on several different types of mass spectrometers, including triple-quadrupole, hybrid, Fourier transform–ion cyclotron resonance (FT-ICR), and four-sector instruments (*12*). Some of the most impressive work, including solutions to real problems, has come from the relatively simple triple-quadrupole instrument (*14*). However, the desire to operate at the maximum molecular weight possible has favored the use of four-sector instruments, which yield MS/MS data to ~3000 daltons on peptides. Recently, through the use of imaging detectors that simultaneously detect ions covering a range of masses, the sensitivity of these instruments has been improved by almost two orders of magnitude (*15*). Typical of the applications of four-sector mass spectrometers is the work of Rinehart and co-workers on blocked and cyclic neuropeptides of microbial and marine invertebrate origin (*16*). Recent studies by Morris *et al.* (*17*), which have emphasized posttranslational modifications of proteins, including both amino-and carboxyl-terminal substitution and truncation, as well as disulfide-bridge formation, are also noteworthy. These applications emphasize that MS methods are not limited to cross-checking results of standard SDS–polyacrylamide gel electrophoresis and DNA sequencing methods of peptide and protein structure determination. The MS/MS methodology is not limited to peptides, but also includes complex carbohydrates (*18*) and oligonucleotides (*19*).

The limitation of the MS/MS method to ~3000 daltons imposed by the collisional activation step has led to great interest in laser-

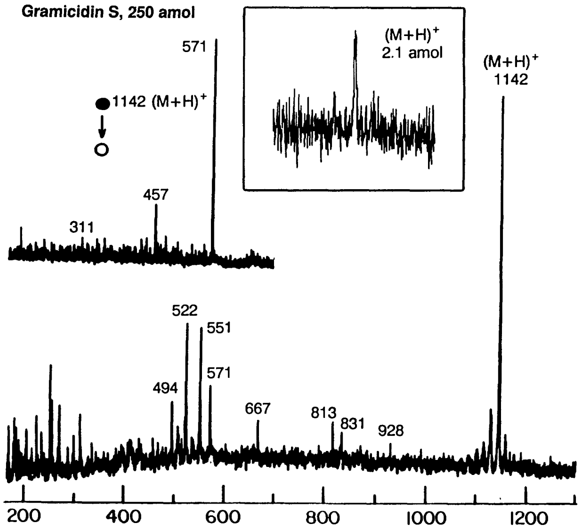


Fig. 2. Mass and MS/MS spectra of 250 amol of cyclic peptide gramicidin S. The base peak in the MS/MS spectrum, *m/z* 571, is due to the fragment proline-valine-ornithine. The insert shows a molecular weight determination on 1,300,000 molecules. [Adapted with permission © Wiley (*31*), with additional data taken by R. E. Kaiser, Jr., K. A. Cox, and R. G. Cooks]

based methods of activation, including multiphoton dissociation. This work has used ICR instruments, in which the trapped ions make an easy target (*20*), as well as sector and hybrid instruments (*21*). Also of potential value in chemical analysis are recent experiments that combine laser desorption of neutral molecules with MPI and dissociation in TOF instruments (*22*).

Quadrupole ion traps. In 1989 Paul shared in the Nobel Prize for Physics for his invention (*23*) of the quadrupole ion trap. In this device (*24*) radio-frequency (RF) potentials are applied to three electrodes of hyperbolic cross section in order to generate quadrupole electric fields in which the force on an ion is linearly proportional to its displacement from the origin. Ions of appropriate *m/z* ratios are trapped in this field where they undergo motion of characteristic frequency. Mass analysis is performed by increasing the amplitude of the applied RF voltage so that ions of increasing *m/z* undergo excursions of such a magnitude as to take them beyond the boundaries of the electric field for detection at an external electron multiplier.

Introduced commercially as a GC-MS instrument with a mass range of 650 daltons per charge in 1983, this mass spectrometer has undergone a rapid metamorphosis (*25*). Changes include (i) its use for tandem mass spectrometry (*26*), where ions of a particular *m/z* value are isolated, translationally excited by application of a signal of appropriate frequency, and collisionally dissociated; (ii) addition of capabilities for chemical ionization (*27*), electrospray ionization (*28*), and desorption ionization (*29*); and (iii) extension of the *m/z* range from 650 to values in excess of 50,000 (*30*). Because of the ion storage capability, ions are only lost during mass analysis, and this advantage, together with the use of electron multiplier detectors, results in excellent sensitivity. Several of the advantages of quadrupole ion traps are shown in Fig. 2. In this experiment liquid SIMS, in an external ion source, is used to ionize gramicidin S, an easily ionized cyclic peptide. Ions are injected into the trap, after which the collection of trapped ions is recorded as a mass spectrum. The protonated molecule, *m/z* 1142, is then isolated within the trap and irradiated at its secular frequency, which causes it to acquire translational energy and hence to dissociate upon collision to yield the fragments recorded in the MS/MS spectrum (*31*). The device is much more sensitive than other instruments and allows mass and MS/MS spectra to be recorded on 250 attomoles of sample and a measurable molecular ion to be recorded after loading just 2.1 amol (of the order of 10^6 molecules) onto the probe, although more typical sample sizes are in the femtomole range. These and other capabilities of the quadrupole ion trap, including its suitability for laser desorption (*32*), electrospray (*33*), and photodissociation (*34*), suggest that it could become one of the most important of all types of mass spectrometers.

Multidimensional MS. A new set of capabilities being developed is conveniently designated as multidimensional MS (*35*). In these experiments, which have grown out of tandem MS, more than two stages of mass analysis are performed, with separation between the mass analysis events occurring either in space (in multiquadrupole, multisector, or hybrid instruments) or in time (in quadrupole ion trap instruments and FT-ICR). Use of a sequence of mass analysis steps (MS^n) has proven its power in FT-ICR, for example, where ions are generated by laser desorption, mass-selected and reacted, and then a selected product is isolated and reacted, continuing through as many as six sequential steps. The rich gas-phase chemistry of transition metals, as well as other applications of ICR, owes much to this methodology (*36*).

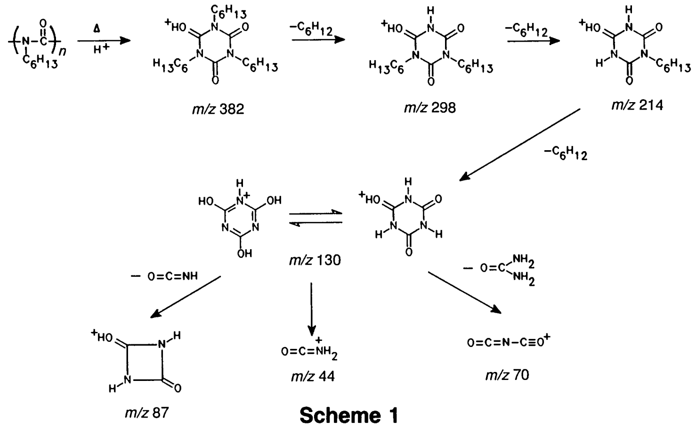
New experiments have now been introduced in which individual mass analyzers in an *n*-stage experiment are independently set—to select ions of particular *m/z* ratios—or scanned over a range of masses. The use of *n* stages of mass analysis allows a spectrum to be recorded that can have zero through *n* dimensions of *m/z*. These experiments provide chemical selectivity by recognizing functional groups through the characteristic mass changes associated with their ion-molecule or fragmentation reactions. A complete set of higher order experiments has been recognized that can facilitate highly selective searches of the MS^n data domain (*35*).

These experiments are best illustrated by examples. Two MS^3 experiments (there are a total of 15) are described; one is one dimensional in mass, the second is two dimensional. Both facilitate solutions to particular chemical questions by displaying chosen aspects of the four-dimensional data domain available by using three mass analyzers and an ion abundance detector.

A two-dimensional MS^3 experiment known as the familial scan (*35*) is shown in Fig. 3. The data display all parents and daughters (products) of a selected ion, in this case an unknown ion of *m/z* 130. The pyrolysis products of poly(*n*-hexylisocyanate) were ionized by desorption EI, and the familial spectrum was recorded on the resulting ionic mixture with a pentaquadrupole instrument (*37*). Since the same set of daughter ions is generated from *m/z* 130 itself as when *m/z* 214, 298, and 382 fragment through *m/z* 130 to lower mass ions, one concludes that each of these precursor ions generates an identical *m/z* 130 ion. Reading vertically down the right-hand diagonal axis, one notes equally spaced ions corresponding to the loss of 84 daltons (hexene units), suggestive of consecutive alkene eliminations. The reaction scheme shown in Scheme 1 was deduced from the data in Fig. 3.

A second type of MS^3 experiment, the reaction intermediate scan (*38*), gives a simple one-dimensional *m/z* output. In this experiment the first mass analyzer selects the compound of interest, the third establishes the *m/z* ratio of a characteristic fragment, and the second is scanned to reveal the intermediates that connect these two chosen ions. In the system just discussed, the only intermediates observed to connect the cyclic trimer *m/z* 382 and *m/z* 130 are *m/z* 214 and 298. This result is consistent with the conclusions drawn from the familial scan. Applications of these and related scans to biopolymers are beginning to be reported (*39*), and they facilitate structural identification through improved specificity in fragmentation patterns.

Elusive neutral molecules. The mass spectrometer serves as the arena



Scheme 1

in which most gas-phase ion chemistry is studied—a topic of continuing great interest as evidenced by recent work on distonic ions (*40*) (species in which the charge and radical sites are separated in the molecule), hydrazyl cations and dications (*41*), isolated dianions, such as the dicarboxylates $^{-}O_2C–(CH_2)_n–CO_2^{-}$ (n = 3 to 7) (*42*), and gaseous organoboranes (*43*)—and is increasingly the vehicle for the study of highly reactive neutral compounds. In neutralization reionization MS (*44*), mass- and structure-selected ions are used as precursors in the preparation of unusual neutral compounds. This method has been used to demonstrate the existence of a number of molecules not previously prepared in the laboratory, including C_6S_6 (benzene hexathione) (*45*), which was generated from the corresponding anion by charge stripping and then demonstrated to be stable by reionization: $C_6S_6^{\cdot -} \rightarrow C_6S_6 \rightarrow C_6S_6^{\cdot +}$. Other important molecules shown to be stable on at least the 10^{-5}-s time scale are the cumulenes C_nS_2 (n = 2 to 6), C_nOS (n = 2, 3, 4), and C_4O_2 (*46*). Several of these molecules are known to be present in interstellar space (*47*). Even so simple a molecule as the antiaromatic C_4H_4 compound cyclobutadiene has only recently been prepared, again by high-energy charge-changing collisions in the mass spectrometer (*48*). The addition of techniques to measure the kinetic energies of the fragments of dissociating neutral molecules (*49*) opens up to future study the reaction dynamics of polyatomic molecules by these sensitive beam-based methods.

Experiments Combining Laser Spectroscopy and Mass Spectrometry

Mass spectrometry impacts the practice of experimental physical chemistry in so many ways that it has become common to take its substantial powers of species identification and discrimination for granted. About 20 years ago, Busch and Wilson photolyzed NO_2 and collected NO products through a quadrupole to begin the modern age of photofragment spectroscopy (*50*). Now, few areas of gas-phase and interfacial physical chemistry can be found that exclude mass-resolved detection of charged particles.

Many of the most dramatic developments in physical chemistry continue to come from experiments that combine laser spectroscopy with MS. Biomolecules that are laser ablated into supersonic beams can be photoionized and dissociated by resonance MPI methods, allowing information to be obtained by spectroscopy or MS (*51*). That is, the molecule can be characterized by its optical absorption spectrum while monitoring the molecular or fragment ion, or by its mass spectrum while irradiating at a single photon energy. The following sections focus on applications that challenge the resolving power of both methods to extract new details on the structural and dynamical properties of isolated molecules, ions, and clusters. Recent results in MPI spectroscopy applied to isolated molecules and radicals are reviewed with emphasis on newer multiresonant methods that address unexplored aspects of electronic structure and radiationless dynamics. Also touched upon is the role of laser–mass-spectrometric methods in contemporary photofragmentation dynamics and cluster chemistry and photophysics.

Molecular spectroscopy and radiationless dynamics. In the mid-1970s, the discovery of resonant structure associated with MPI of simple gases by tunable lasers stimulated an explosion of activity in laser-source MS (*52*). The nature of this ion source and the needs of experiments dictated early directions in instrumentation. The spatial and temporal resolution of focused pulsed lasers naturally favor TOF mass analysis, by which one obtains the complete mass spectrum of ion products with a single laser shot, and a substantial fraction of initial work took this direction (*53*). Other early workers used quadrupole mass spectrometers to filter the products of MPI (*54*). By isolating single masses these instruments focused attention on the optical spectrum of intermediate resonant absorption. By rejection of dominant ion species, quadrupole approaches extend the dynamic range of MPI methods. Using either of these approaches, many laboratories now routinely exploit the sensitivity and generality of resonant laser ionization to obtain mass and electronic absorption spectra of a wide variety of molecules in free-jet expansions.

At present, physical chemists apply mass-resolved laser ionization most frequently as a general spectroscopic probe. Resonant patterns in mass-analyzed ionization-detected n-photon absorption provide a convenient means to scan the higher excited states of molecules, radicals, and complexes, as well as survey the composition of mixed beams. After early work, which emphasized diatomics and selected larger systems (*55*), substantial effort in simple one-color (one laser frequency) ionization-detected absorption spectroscopy has shifted to polyatomic molecules, where relatively simple experiments have brought into focus important questions concerning electronic structure and dynamics at high energy (*56*). In certain other cases, extensive jet-resolved vibronic structure in the ionization-detected two-photon absorption spectra of Rydberg states that are built on the electronically degenerate ion cores of symmetric hydrocarbons has provided an important new perspective on the irregular level structure of isolated molecules distorted by Jahn-Teller coupling (*57*).

Multiphoton ionization processes can be distinguished as nonresonant, resonant, and multiresonant. With double and multiple resonance come opportunities for photoselection, which can be used to eliminate rovibrational congestion in spectral regions of high transition density (*58*). It can also serve to open Franck-Condon envelopes, facilitating electronic transitions involving large geometry changes (*59, 60*). A wealth of important state-detailed information has been obtained by rotationally resolved double resonance to high Rydberg and autoionizing states in diatomic systems such as NO (*61*), H_2 (*62*), Li_2 (*63*), and Na_2 (*64*). These results have served as a major stimulus for theoretical progress on powerful scattering theory–based formalisms (*65*).

This particular approach to the rovibrational resolution of high Rydberg states has recently been extended for the first time to a polyatomic molecule, NO_2, where the presence of more than one normal coordinate introduces important topological questions of vibrational mode specificity in the coupling of electronic and excited internuclear degrees of freedom. With an extensive electronic absorption system in the visible and a sharp low-lying $3p\sigma$ Rydberg state a few electron volts higher, NO_2 is particularly well suited to multiresonant excitation (*66*). Recent work has confirmed mode selectivity in the dynamics of competitive channels of decay from its discrete states above 10 eV (*67*), consistent with the extension of a simple theory developed 20 years ago to explain the dynamics of vibrational autoionization in diatomics (*68*).

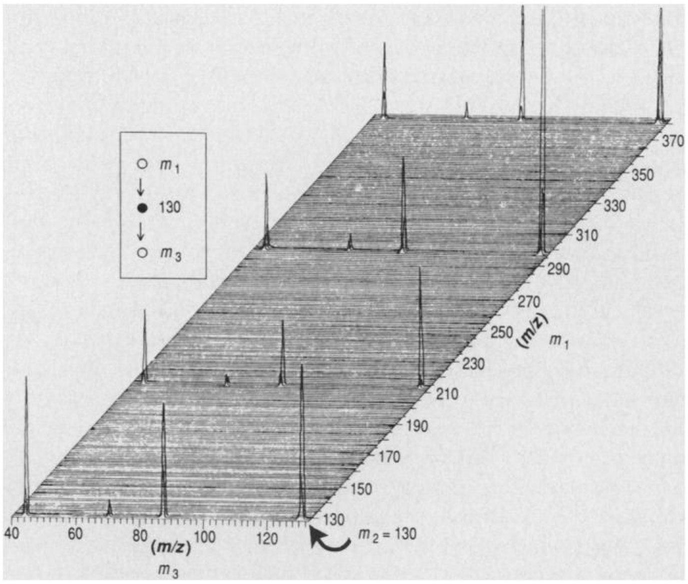


Fig. 3. Familial (MS^3) spectrum of m/z 130, sample poly(n-hexylisocyanate), generated using a pentaquadrupole mass spectrometer. The abscissa displays fragment ions generated, through m/z 130, from the initial ions displayed along the ordinate. [Data recorded by M. N. Eberlin and R. G. Cooks]

Double resonance also serves as a probe of intermediate states. Dynamics there can affect the character observed in the spectrum of subsequent transitions. Early work thoroughly established the time-dependent effect of intersystem crossing in the B_{2u} state of benzene on the cross section for subsequent near-threshold photoionization (*69*). More recently, picosecond time-resolved pump-probe photoelectron spectroscopy has charted the vibronic course of radiationless decay in this molecule (*70*). The first example showing the effect of intermediate relaxation in a dissociative continuum on the course of two-photon discrete-discrete absorption was established some time ago for NO_2 (*60, 71*). Similar behavior has been recently noted for Cl_2 (*72*) and methyl iodide (*73*). Ion dip methods, which monitor the laser-induced depletion of an ion signal, exploit the radiationless properties of intermediate states connected by stimulated emission to impress the shape of a resonance with a low ionization cross section on an ionization-detected absorption spectrum (*74, 75*).

A fast-growing area in which MS plays an essential role is that of free-radical structure and dynamics. Radicals are produced from molecular precursors, and ionization methods thus necessarily probe mixtures. Mass analysis readily isolates ionization-detected absorption spectra of minority species. Because many radicals are spin doublets with singlet Rydberg ion cores, their higher excited states tend to be sharp and their spectra are simpler than those of closed-shell neutrals. Progress has been greatest on small hydrides (*76*), on carbon-, silicon-, and germanium-centered radicals (*77*), formyl (*78*), and some larger organic molecules (*79*) and halogenated fragments (*80*). In addition, ultraviolet (UV) photoionization has provided the first experimental evidence for the existence of the carbon-centered COOH radical (*81*) as well as both single- and double-hydrogen bridged forms of B_2H_5 (*82*).

Reactive scattering dynamics. Mass spectrometric methods have historical and contemporary importance as universal detectors in crossed molecular beams research (*83*). Most recently, scattering instruments have been developed with rotatable sources for high-resolution laser-crossed molecular-beam photofragment spectroscopy (*84*), which represent, perhaps, the ultimate realization of the Wilson experiment. Among new results obtained with electron-impact source quadrupole mass spectrometers to record velocity spectra of fragments are product distributions and dynamical information on the UV photodissociation of benzene (*85*) and the concerted three-body fragmentation of s-tetrazine (*86*).

Laser ionization methods have also been profitably used in conjunction with translational spectroscopy to characterize photodissociation dynamics. Fragment internal-state distributions following photodissociation of water, ammonia, and hydrogen sulfide have been established by analyzing field-free flight times of protons after L_α laser ionization of photoejected hydrogen atoms (*74, 87*). This TOF method is now being extended to other ions (*88*) where it offers some evident advantages, including high-velocity resolution, together with potential generality and a natural facility for image detection of angular distributions. Scattering-angle distributions also provide dynamical and spectroscopic information on hypervalent neutral molecules in high-velocity beams formed by neutralization of mass-selected cations (*89*). Alternative pump-probe TOF methods also use a field-free period, in which the spatial distribution of ionized photoproducts is allowed to expand, followed by pulsed electrostatic extraction with imaging to acquire a record of the distribution of velocities (*90*).

Interestingly, sector mass spectrometers have long provided similar information on the dynamics of dissociation and the internal energies of the products through translational energy measurements on the products of high-energy (kiloelectron volt range) collisions, and more recently these methods have found application in studies of the structure and dynamics of dissociation of small multiply charged ions (*91*). A contrasting MS approach to the dynamics of reactive collisions uses mass-selected ion beams of relatively low translational energy and follows the translational-energy dependence of the cross section of endothermic reactions. The demonstration that Mn^+ reacts with ethane to form $MnCH_3{}^+$ only from an electronically excited state is representative of this type of experiment (*92*).

Conventional laser experiments characterize photodissociation dynamics by directly monitoring product internal states, and a number of workers have applied resonance-enhanced MPI in this way (*93*). In many cases mass separation has been key to the resolution of product populations. Ionization-detected absorption spectroscopy of photofragments provides one of the earliest examples of photoselected dynamics in resonant two-photon photodissociation (*94*). A related area of intense current theoretical interest is the coherent control of photostimulated processes (*95*). The first realization of such a process in actual practice has just been achieved by an experiment in which it is shown that the cross section for resonant ionization of mercury atoms can be modulated by altering the relative phase of laser fields competitively resonant in one- and three-photon absorption (*96*). The extension to molecules and the process of photodissociation is an active area of pursuit that promises rich theoretical dividends and that ultimately may have practical applications.

Properties of atomic and molecular clusters. The sensitivity and generality of laser MPI techniques make them ideal for the detection of dimer and cluster components of supersonic expansions. The natural combination with TOF-MS has significantly accelerated progress by aiding characterization; in many cases laser ionization can provide the complete mass spectrum of a cluster expansion in a single pulse. Research on the formation, properties, and reactions of dimers and clusters of atoms and molecules has expanded rapidly in the past 5 years with TOF, ICR, and sector MS featuring prominently (*97*). Here we highlight selected recent developments that reflect the scope of the field and the impact of laser MS methods.

Studies of the electronically excited states of van der Waals dimers and small clusters of stable molecules frequently focus on questions of structure together with photophysics and intramolecular energy

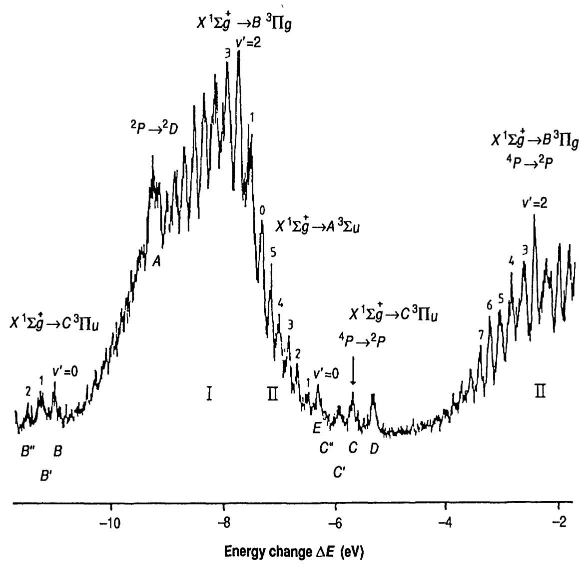


Fig. 4. Translational energy spectra for 3-keV C^+ scattered off N_2. [Courtesy of A. G. Brenton and co-workers, reproduced with permission © Wiley (*117*)]

redistribution: What is the geometry of a complex, and with what structure does it grow? How does a weakly bound adduct influence the radiationless decay of its electronically excited partner? What is the rate of energy flow into and consequent scission of a weak van der Waals linkage? Although occasionally complicated by fragmentation, MPI-MS approaches (*98*), including newer ion-dip–detected stimulated-emission pumping methods (*99*), complement more established laser-induced fluorescence (LIF) probes (*100*) of these and other issues relating to small complexes. With growing cluster size, the spectrum-structure connection becomes less distinct, but broader issues of energetics (*101*) and collective ordering (*102*) remain.

For larger molecular clusters, interesting new efforts have targeted excitation transport (*103*) and chemical reactions (*104*) within pure and mixed aggregations, as well as the dynamics of charge localization (*105*) and evaporation (*106*). Representative of these types of studies is work on $(Ar)_nHCO_2^-$, $n = 10$ to 130. With the use of a reversed-geometry mass spectrometer and both laser and collisional dissociation, the formate anion was shown to occupy surface sites on the argon cluster, as did its fragmentation products. Some channels of dissociation observed in the isolated ion are closed to the cluster, but new channels open up (*107*).

Elemental clusters have long been regarded as an important testing ground for theories of bonding and electronic structure (*108*). New experiments on large alkali-metal clusters extend the reach of TOF reflectron spectrometry to unprecedented masses and resolution (*109*). Motivating such studies on very large systems is the issue of the size at which an atomic assembly fully assumes the properties of the bulk. This question has been explored in extreme terms for Na_n clusters with n as great as 21,000, where it is found that structural effects persist, with the formation of super shells in systems as heavy as 500,000 daltons (*110*).

The structure and dynamics of monomer and small cluster cations. The electronic structure and radiationless dynamics of monocations have been areas of longstanding interest to chemists, astrophysicists, and others. Results obtained from ionic collisions (*111*) and photoelectron spectroscopy (*112*), together with more recent photoelectron-photoion and fluorescence coincidence methods (*113*), have provided a broad source of information on a wide range of systems. In special cases, highly detailed structural and dynamical data has been supplied by laser photofragment spectroscopy (*114*), as well as by cation emission and LIF spectroscopy (*115*). Adding to this established base has been a great deal of new effort on several fronts. With improved precision, inelastic scattering methods show fine structure that reflects ion internal states (*116, 117*). For example, improvements in kinetic-energy resolution have allowed inelastic scattering measurements to be used to assign product states with high precision. The C^+-N_2 system gives results shown in Fig. 4, and further improvement in resolution is anticipated (*117*). Note that the advantages of the technique include access to very high energy species and immunity from spectroscopic selection rules.

Velocity-modulated infrared (IR) absorption spectroscopy probes ion rovibrational structure at high resolution (*118*). In addition, new information on the structure and dynamics of ground state and electronically excited monomer and small cluster cations is now emerging from ion photodissociation spectroscopy, while threshold, or zero–kinetic-energy, photoelectron spectroscopy resolves photoionizing transitions to discrete cation internal states with laser bandwidths. Representative of these latter two classes of experiment, which combine laser radiation with mass or electron spectroscopy, are studies of IR transitions in cluster ions of $(H_2)_n$ about H_3^+ (*119*), $(H_2O)_n$ about H_3O^+ (*120*), $(NH_3)_n$ about NH_4^+ (*121*), and $(CH_3OH)_n$ about Cs^+ (*122*). Photodissociation is used in each case to detect absorption. For hydrogen and cesium-methanol clusters, one-photon IR excitation is accompanied by vibrational predissociation, which channels signal on-resonance to a monitored lower mass. For ammonia clusters, a second IR photon, which in this case originates from a high-power YAG-pumped pulsed dye laser, stimulates dissociation.

Photodissociation of cation monomers and clusters with optical photons provides spectroscopic and dynamical information about electronically excited states (*123*), and, for clusters, about the interactions between a chromophore and its environment (*124*). For benzene monomer, photodissociation of resonantly prepared cations has provided a means to study the unimolecular decomposition rates of rotationally selected metastable excited states (*125*). Resonant two-photon photodissociation has provided a means to register the sharp structure of nondissociative excited states in monomeric CO_2^+, N_2O^+, CS_2^+, CH_3I^+, $C_6H_6^+$, and $C_6H_5F^+$ (*126*), as well as in heterodimer ions such as $C_6H_5F^+ \cdot Ar$ and $C_6H_5Cl^+ \cdot Ar$ (*127*).

Excitation spectra for larger molecular cluster ion systems are broad, like their atomic cluster cation counterparts. However, substantial information on molecular cluster structure and dissociation dynamics can be found in fragmentation patterns and kinetic energy releases. For example, energy and angular distributions for product CO_2^+ from photofragmentation of $(CO_2)_3^+$ suggest that photodissociation proceeds by sequential loss of CO_2 monomers (*128*). Larger $(CO_2)_n^+$ clusters appear to absorb a photon and always eject near six CO_2 monomers, regardless of the size of the parent cluster. This observation supports a picture in which photon energy absorbed by a $(CO_2)_2^+$ core at the center of the cluster degrades to thermal energy, which migrates to the surface, where it dissipates by monomer evaporation (*129*). Interestingly, the same mechanism, with the same number of CO_2 monomers ejected, appears to apply to $Br_2^- \cdot (CO_2)_n$ clusters (*130*), indicating that evaporative dissipation is independent of interior composition. Core-relaxation times for photoexcited $I_2^- \cdot (CO_2)_n$ have been measured directly by picosecond pump-probe experiments, which indicate an accelerated vibrational relaxation time in the cluster condensed phase, owing perhaps to the presence of a path of irreversible energy flow in monomer evaporation (*131*).

Zero–kinetic-energy (ZEKE) photoelectron spectroscopy provides a means to register ion internal-state structure at the frequency resolution of the photoionizing light source (*132*). When this light source is a laser, and particularly when double resonance is involved, this resolution is sufficient to resolve rotational-level structure. This method, which derives from the long-established technique of threshold photoelectron spectroscopy, detects the states of the ion as successive photoionization thresholds to which very high Rydberg series converge. It is the electrons from these Rydberg states, within a wavenumber or so of threshold, that are detected by a delayed extraction field pulse of about 1 V/cm. In some cases, a continuous reverse bias in the range of 100 mV is used to sweep away all prompt electrons formed by direct ionization. Use of this method, both as a general probe of ion structure and as a means of assessing partial cross sections for electron ejection, has expanded since its introduction as a probe of rotationally selective threshold photoionization in NO and benzene (*133*). New experiments have used vacuum ultraviolet (VUV) lasers to probe threshold intensities of rotational resolved transitions from neutral ground states to O_2^+ (*134*), HCl^+ (*135*), and N_2O^+. Progressions of vibrational thresholds reflect the interatomic potential in $Xe_2{}^+$ (*136*). Two-color two-plus-one experiments in HCl reveal structure associated with upper and lower spin-orbit thresholds from rovibronically selected intermediate states (*137*).

Future Prospects

By selectively describing developments in MS and its use in laser spectroscopy, we have sought to highlight some broad trends in these fields of research. From this perspective it is as tempting as it is dangerous to extrapolate. We can be confident about two things: MS will continue to draw from an expanding base of knowledge in physical chemistry to increase its reach, and progress in a number of areas of physical chemistry will be paced by developments in MS.

For example, we can expect that tunable VUV laser methods, which are finding increasing use in high-energy atomic and molecular spectroscopy, will be adapted as routine sources for species-specific high-resolution threshold photoionization in analytical MS. Similarly, tunable dye-laser photodissociation will widely supplement collisional methods as means for depositing precise amounts of energy in MS/MS experiments. Conversely, the benefits of high resolution at large *m/z* ratios will be increasingly made use of in chemical physics, particularly cluster science. New sources that provide for the routine volatilization of very large molecules and clusters of biological and materials interest will open new avenues in spectroscopy and photophysics and invite the dynamical study of a new generation of ion-fragmentation and ion-molecule reactions.

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