INTRODUCTION

Common to all experiments in mass spectrometry is the creation of gas-phase ions. Electron impact (EI) ionization is a familiar method for creating ions from volatile gas-phase molecules (M). In EI ionization, fast-moving electrons remove an electron from the neutral molecule to create the odd-electron molecular ion M⁺. Another common ionization method is chemical ionization (CI). Here, an ion-molecule reaction between the sample molecule and a reagent ion such as CH₃⁺ or NH₄⁺ results in proton transfer to M to form [M + H]⁺. In each of these methods, the sample molecule is originally in the gas phase. The volatilization process must create these gas-phase sample molecules without sample decomposition or reorganization.

For non-volatile sample molecules, other ionization methods must be used and have been developed over the past 20 years. These methods include fast atom bombardment (FAB), (static) secondary ion mass spectrometry (SIMS), liquid secondary ion mass spectrometry (LSIMS), laser desorption and electrospray ionization. The diversity of approaches defies tidy organization, but most methods can be classified into desorption ionization (DI) or nebulization ionization methods. In DI, the unifying aspect is the rapid addition of energy into a condensed-phase sample, with subsequent generation and release of ions into the mass analyzer. In EI and CI, the processes of volatilization and ionization are distinct and separable; in DI, they are intimately associated. Table 1 compares some aspects of various ionization methods used in mass spectrometry, placing DI in perspective with other methods available to the analyst. In nebulization ionization, an aerosol spray is used at some point to separate sample molecules and/or ions from the solvent liquid that carries them into the source of the mass spectrometer. These ionization methods include thermospray and electrospray ionization. Since this paper is focused on DI processes, nebulization methods will not be discussed further.

This paper will first consider general aspects of DI hardware (the mechanics), followed by a brief description of sample preparation and ionization mechanisms. Issues of interest include energy input and energy transfer, in addition to ionization, association and dissociation reactions. Although detailed elements of the mechanisms of ionization may still be debated, DI source conditions and sample attributes are easily manipulated so that high-quality data can generally be obtained. DI methods tend to produce even-electron ions such as protonated molecules [M + H]⁺ or cationized molecules such as [M + Na]⁺; these stable ions undergo only a minimum amount of fragmentation.

The development of DI methods amplified the impact of mass spectrometry many fold. The inherent restrictions in EI an CI that limited applications to volatile sample molecules constituted severe limitation especially in the field of biochemical chemistry. DI was applied immediately with great enthusiasm to a wide range of analytical problems, and the field of mass spectrometry has flourished as a result. In their infancy, DI methods were relegated to the periphery of mass spectrometric research, pursued and developed by those for whom the inability to deal with non-volatile samples in the ion source constituted an analytical challenge. Progress was dependent on the solution of problems related to sample handling and ion transport through substantial pressure and potential gradients. Non-volatile samples, regardless of their molecular mass, were difficult samples to handle. Figure 1 shows the positive-ion plasma desorption mass spectrum recorded in the mid-1970s for tetrodotoxin and chiriquitoxin.⁴ The mass of the tetrodotoxin is only 320, but the non-volatility rendered the molecule resistant to EI and CI methods of analysis prevalent at the time. The impact of the new capabilities of plasma desorption (PD) for the determination of molecular mass for these samples was enormous. Such leading work for PD and other desorption ionization methods foretold of extensive applications to problems in biochemical and natural products analysis, since sample volatility was no longer required.

† Editor's Note: This is the first of several 'Tutorial' articles which will appear this year in the Special Features section of the journal. These tutorials will describe fundamental aspects and applications of mass spectrometry with the general reader, not the author's peer group, in mind. The aim will be to cover some specific areas of mass spectrometry in a manner in which a teacher might present the subject in a graduate level course. Although these articles are normally invited, comments and suggestions from readers are welcome. Please address these to the Special Features Coordinator; Graham Cooks, Dept of Chemistry, Purdue University, W. Lafayette, IN, USA, 47907. Further, as a special offer to readers, copies of the figures of this 'Tutorial' article, as color slides, are available free of charge on request from the editor-in-chief's office. Supplies are limited and slides will be sent out in the order requests are received.

CCC 1076-5174/95/020233-08
© 1995 John Wiley & Sons, Ltd.

Received 18 December 1994
Revised 26 December 1994
Accepted 27 December 1994
Table 1. Summary of attributes for ionization methods in mass spectrometry (adapted from Ref. 1)

<table>
<thead>
<tr>
<th>Ionization method</th>
<th>Ionization agent</th>
<th>Source pressure (Torr)</th>
<th>Spectral character</th>
<th>Typical application</th>
</tr>
</thead>
<tbody>
<tr>
<td>EI</td>
<td>70 eV electrons</td>
<td>~10⁻⁶</td>
<td>Reproducible</td>
<td>Volatile samples of low molecular mass; structural elucidation</td>
</tr>
<tr>
<td>Chemical ionization</td>
<td>Gas-phase reagent ions</td>
<td>~1</td>
<td>Protonated</td>
<td>Volatile samples of low molecular mass; molecular mass determination</td>
</tr>
<tr>
<td>DI (LSIMS, FAB, PD)</td>
<td>Energetic atoms, ion or photons used as incident particles</td>
<td>~10⁻⁸</td>
<td>Intact molecular ions generated through acid-base or redox reactions</td>
<td>Non-volatile samples of medium to high molecular mass</td>
</tr>
<tr>
<td>Nebulization ionization (electrospray, thermospray)</td>
<td>Electric field gradients and thermal energy within a microdroplet spray</td>
<td>1–760</td>
<td>Intact molecular ions (some with multiple charges); minimum fragmentation</td>
<td>Non-volatile samples with medium to high molecular mass</td>
</tr>
<tr>
<td>GD</td>
<td>Energetic plasma electrons and ions</td>
<td>0.1–10</td>
<td>Atomic ions and stable metal oxides, some cluster ions</td>
<td>Inorganic and atomic samples</td>
</tr>
<tr>
<td>ICP</td>
<td>Energetic plasma electrons</td>
<td>760</td>
<td>Atomic ions and stable metal oxides,</td>
<td>Inorganic and atomic samples</td>
</tr>
</tbody>
</table>

DI methods grew in influence with amazing quickness. As this description of DI unfolds, the reader may perceive parallels that foreshadow current research in nebulization ionization. It is this repetitive pattern of development in mass spectrometry that renders broad historical examination of the field worthwhile. General references organized according to the various methods are collected at the end of the paper.³⁻²³

MECHANICS OF DESORPTION IONIZATION

The most common methods of desorption ionization are particle-induced desorption, FAB, LSIMS, PD and photon-induced desorption (such as matrix-assisted laser desorption ionization (MALDI)). Instrumental details of implementation of these ionization methods have evolved in diverse directions specific to various applications (Table 2). In FAB and LSIMS, the incoming particle is a neutral atom, single ion or small cluster of ions. These particles are moving with a velocity imparted by acceleration through a potential difference of 5000–35000 V. In FAB, these particles are, for example, Xe atoms that are first ionized and then neutralized to give a neutral atom beam. The velocity corresponds to 2.2 × 10⁵ m s⁻¹ for a cesium ion accelerated through 35 keV, as commonly used in LSIMS. If we assume an interaction time of 0.1 ns as the particle initially impacts the surface, the power is about 6 × 10⁻⁵ W. This value varies with the mass of...
Table 2. Summary of desorption ionization methods in mass spectrometry (adapted from Ref. 1)

<table>
<thead>
<tr>
<th>Method</th>
<th>Primary particle incident particle</th>
<th>Primary particle flux</th>
<th>Support matrix</th>
<th>Common mass analyzer</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMS</td>
<td>keV ions (Ar⁺, Cs⁺)</td>
<td>10⁻¹⁰ A cm⁻²</td>
<td>None</td>
<td>Any</td>
<td>Surface sensitive; weak and transient signal</td>
</tr>
<tr>
<td>Secondary ion mass spectrometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSIMS</td>
<td>keV ions (Ar⁺, Cs⁺)</td>
<td>10⁻⁶ A cm⁻²</td>
<td>Non-volatile liquid (glycerol, nitrobenzyl alcohol)</td>
<td>Any</td>
<td>Intense, stable signal; time variation of mass spectra</td>
</tr>
<tr>
<td>Liquid secondary ion mass spectrometry</td>
<td>(Ar⁺, Cs⁺)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAB</td>
<td>(keV) atoms (Ar⁺, Xe⁺) equivalent</td>
<td>10⁶⁻¹⁰⁷ W cm⁻²</td>
<td>None</td>
<td>Time-of-flight</td>
<td>Applied to elemental analysis</td>
</tr>
<tr>
<td>Fast atom bombardment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LD Laser desorption</td>
<td>UV/visible/IR photons</td>
<td>10⁶⁻¹⁰⁷ W cm⁻²</td>
<td>Time-of-flight</td>
<td>Applied to high-mass biomolecular samples; gives predominantly molecular ions</td>
<td></td>
</tr>
<tr>
<td>MALDI Matrix-assisted laser desorption ionization</td>
<td>IV/visible/IR photons</td>
<td>10⁶⁻¹⁰⁷ W cm⁻²</td>
<td>Solid crystalline matrix with high absorbance at wavelength used</td>
<td>Time-of-flight</td>
<td></td>
</tr>
<tr>
<td>PD Plasma desorption</td>
<td>MeV ions (fission fragments)</td>
<td>10³ particles cm⁻² s⁻¹</td>
<td>None</td>
<td>Time-of-flight</td>
<td>High efficiency, low absolute signal level</td>
</tr>
</tbody>
</table>

the particle and its velocity. Although higher incident particle masses and higher velocities have recently been used to generate higher-quality mass spectra, the total power to initiate desorption and ionization remains about 10⁻⁵ W. However, as the impact area is small, the power density generated by a single particle is perhaps 10⁶ W cm⁻². Incident particles in FAB and LSIMS are generated in filament ionization sources or plasma discharge sources; the technology is simple and straightforward. These sources, biased as either ion or atom emitters, are conveniently connected to sector, quadrupole and time-of-flight mass spectrometers. In FAB and LSIMS, the initial particle impact is thought to generate instantaneously a series of collisions within the sample that can lead to the ejection of atomic and molecular species from the impact region—this is a process called sputtering (Fig. 2).

In plasma desorption, the incident particle is an MeV energy ion generated from radioactive decay of a nuclide such as ²⁵²Cf or extracted from a particle accelerator. In the case of ²⁵²Cf fission, the exact identities and masses of the fission fragments that cause each desorption event are not known because pairs of fission particles are produced with a range of masses (where

Figure 2. Simple illustration of an instantaneous collision cascade generated as a result of primary particle impact in desorption ionization mass spectrometry.
the sum of the masses of the pair is 252). For particles from accelerators, specification of the mass and charge state of the incident particle is an inherent part of ion formation and extraction. The total kinetic energy available in plasma desorption is much higher than in LSIMS and FAB owing to the higher particle mass and higher velocity. In PD, interactions of the primary particle with the sample molecules begin as electronic interactions, whereas impulsive ‘billiard-ball’ dynamics prevail in LSIMS and FAB from the beginning. The source of the MeV incident particle can be a small sealed disk that contains the radionuclide. Spontaneous fission releases two high-energy particles that travel in opposite directions. One of these particles starts the timing circuit of a time-of-flight mass spectrometer while the other fission fragment passes through the sample prepared as a thin film on a support foil.

MALDI has also been developed primarily using time-of-flight mass analyzers. The short (1–10 ns) laser pulse that creates the ions from the sample provides a natural ‘start’ signal for the mass analyzer. Lasers of several different wavelengths have been used, with the most popular being nitrogen lasers with a wavelength of 337 nm and IR lasers with a wavelength of 10.6 μm. The sample is uniformly mixed with an energy-absorbing matrix that mediates both the desorption and ionization processes (see the next section). For a nitrogen laser the laser power may be 5–20 W, although only a small fraction of this power is used to create ions. The efficiency of transformation of laser power into sample ion current depends on the form of the sample and its surroundings. With reasonable values of molar absorptivity and interaction length, during the laser pulse a total of perhaps 10⁻⁷ W may be available for desorption and ionization (focused into a very small spot size, the power density increases by orders of magnitude (see Table 2)). In MALDI with UV photons, initial energetic interactions are clearly not of the ‘billiard-ball’ type, but reflect electronic interactions. However, as the energy propagates through the condensed-phase medium, collision dynamics assume a more substantial role. With IR photons in MALDI, direct vibrational excitation occurs on irradiation.

SAMPLE PREPARATION

Sample preparation must take into account the specific instrumental details that may limit sample amount and volatility. For instance, there are variations in FAB and LSIMS sources as they are fitted to quadrupole, ion trap, sector, time-of-flight or Fourier transform ion cyclotron resonance mass spectrometers. Films of solid inorganic or organic samples may be analyzed with D1 mass spectrometry, but sample preparation as a solution for LSIMS and FAB is far more common. The sample molecules are dissolved in a low-vapor-pressure liquid solvent, usually glycerol or nitrobenzyl alcohol. Other solvents have also been used for more specialized applications. Key requirements for the solvent matrix are sample solubility, low solvent volatility and muted acid–base or redox reactivity. Differential sample solubilities can lead to sampling bias, as when the component of a mixture with the highest surface activity appears with enhanced ion abundances in the initial mass spectra recorded from the solution mixture. Solvent molecule reactivity can be manifest in the presence of sample–solvent cluster ions, substitution reactions that involve the solvent molecule and reduction and oxidation reactions of the sample or solvent molecules. Various solvents have been ranked in terms of their redox susceptibility, although the ordering also depends on the sample, the other partner in the redox couple. Even in the absence of specific sample-solvent interactions, the solvent produces its own mass spectrum. Background subtraction can reduce the contribution of this background mass spectrum, but since the ion abundances of the background and the sample do not remain constant, background subtraction in FAB and LSIMS cannot be performed with the same confidence as in EI and CI mass spectrometry. Continuous-flow FAB (in which the sample solution is brought into the source of the mass spectrometer in a flow stream of 5–10 μl min⁻¹) eliminates the task of discrete sample solution preparation and reduces the contribution of solvent spectral background.

In PD, liquid matrices have also been used, but most samples are prepared as a thin-film solid. A solution of the sample in a volatile solvent is sprayed onto a thin support, forming a thin, homogeneous film after solvent evaporation. This supported sample film is placed near the disk containing the radionuclide so that at least some fraction of the emitted MeV particles will pass through the supported sample. Most fission fragments will not be emitted in the appropriate geometry or time window (mass analysis of the ions created from one event has to be completed before the start of the next cycle), so the sample ion flux created in plasma desorption is typically low.

In MALDI, co-crystallization of the sample and the energy-absorbing support matrix is sought through careful control of rate of solvent evaporation from the solution mixture deposited on an inert surface. The ratio of the matrix to the sample is an important parameter for successful MALDI analysis; the matrix-to-sample ratio can range between 1000:1 and 5000:1. Some MALDI instruments allow the user to target specific crystals or areas of high sample density on the surface for analysis. Without a targeting capability, a random distribution of laser shots across the surface is used, with the summed and averaged mass spectra recorded. A number of matrices function well in MALDI. Although a good matrix material has several important characteristics, a high molar absorbance at the laser wavelength used in paramount. As UV absorbance spectra are often broad, this requirement is readily met by aromatic compounds with extended electron conjugation, such as cinnamic acid and sinapinic acid (think of sunscreen!). Other MALDI matrices developed for specific applications are regularly reported in the research literature. Here, MALDI mirrors FAB, in that much early development work was marked by study of different liquid matrices, their properties and their specific applications. In FAB and LSIMS, however, a well mixed sample solution is homogenous. In MALDI, the distribution of crystals across the surface is clearly heterogeneous. Limited amounts of sample available for analysis place a further burden-
some requirement on the selection of the correct MALDI matrix. As in FAB and LSIMS, most reported MALDI analyses use a few common, well characterized support matrices.

In summary, sample preparation for the common DI methods varies greatly. In PD, spraying a thin film of sample onto the support is simple. The sample ion flux is low, however, and extended signal integration times may be necessary. In FAB and LSIMS, the special 'art' of sample preparation in the selection of a solvent matrix, and then manipulation of the mass spectral data afterwards to minimize its contribution, still predominates. In MALDI, some commercial instruments use carousels or plates that hold up to 100 individual small samples stages on which a mixture of energy-absorbing matrix and sample is deposited. Acquisition of a MALDI mass spectrum can usually be completed within 1 min with relatively simple-to-operate instruments that can be directly operated by end users of the data.

**MECHANISMS OF DESORPTION IONIZATION**

Elucidation of the detailed mechanism of an ionization technique is difficult and all too often postponed when the method is applied with success to the problem at hand. In DI, the mechanism appears far more complex than was first believed, and even what we 'understand' now will probably be regarded as limited in a few years. Clearly, we cannot define the mechanism of FAB/LSIMS or the mechanism of MALDI. If we design experiments to decide between two sharply divided models of desorption ionization, we fail to appreciate the balance of several different ionization processes, and how that balance shifts as the sample environment and instrumental parameters are changed. There are two central mechanistic issues. The first is the movement of sample molecules or ions from a condensed phase into the vacuum and the second is the transformation of those molecules into ionic form.

In FAB and LSIMS, ions are generated from a total of 1–2 µl of a solution spread across a surface area of 25–50 mm². At the minimum, the solution contains two components (the sample and the solvent), and may contain many more. Particle bombardment sets the molecules of the solution into motion, and some fraction of molecules and molecular aggregates may achieve a velocity that allows them to break solution bonds and leave the surface. The inherent vapor pressure of the solvent (often about 10⁻³ Torr (1 Torr = 133.3 Pa) at room temperature) results in the evaporation of single solvent molecules. However, concerted motion of larger aggregates induced by the particle bombardment can result in the 'evaporation' of aggregates that contain tens, hundreds and perhaps thousands of molecules. Within these aggregate droplets are molecules/ions of the sample itself. Solvent intermolecular forces are diminished and redirected in droplets and, as a result, the rate of solvent evaporation is increased. Droplet desolvation commences immediately in the selvedge, the intermediate pressure region between the surface of the condensed phase and the vacuum. As time passes after the initial impact event, the simple collision cascade in Fig. 2 is replaced by a more complicated process of the surface in which these large aggregate droplets are transferred into the gas phase and then undergo successive desolvation reactions to lead to sample ions extracted into the mass spectrometer (Fig. 3). Without the intervention of an ionization process, all of the neutral solvent and the occasional sample molecules would simply diffuse through the vacuum. Ionization occurs in the initial cascade, and in acid–base and redox reactions that occur as sample molecules move into the vacuum away from the surface. The usual ions seen in FAB and LSIMS spectra are even-electron protonated or deprotonated molecules ([M + H]⁺ or [M − H]⁻) and cationized molecules [M + cat]⁺ in the positive-
ion mass spectra. A cation can be something as ubiquitous as Na$^+$ or K$^+$, or transition metal cations such as Fe$^+$ or Ag$^+$.

How ionization occurs in FAB and LSIMS can be established with more certainty than precisely when it occurs. Within the sample solution, usual condensed-phase acid–base reactions occur along with additional photolytic (most ion and neutral particle sources produce a broad spectrum of light) and bombardment-induced reactions. Furthermore, molecules are subject to reaction in an electrochemical environment that includes multiple potentials and evanescent redox partners, including electrons generated by the bombardment itself. Ions may be formed in distinctive beam-induced processes. Finally, ions and molecules must survive passage through a so-called selvedge region. The selvedge is phenomenologically defined as the boundary above the surface beyond which no ion–molecule reactions occur, and past which only unimolecular dissociation reactions occur. In this region, the pressure drops from that of the condensed phase to that of the free vacuum of the mass spectrometer source and ions and molecules may undergo association and dissociation reactions both with each other and with other solution components as well as the matrix.

As a matter of common experience, samples that can be prepared in a performed ionic state tend to give high-quality DI mass spectra. A fascinating area of research is the design of experiments that document ionization and evaporation processes in FAB and LSIMS. Investigators are getting a clearer idea of the processes involved in the transition which brings a group of highly energized, rapidly expanding set of molecules from the impact region to a cooler, more interactive plume of sample molecules and ions in the selvedge. In addition, the results of these studies influence our understanding of spray and aerosol ionization methods and, indeed, suggest that basic processes of ion formation are more similar than disparate.

In MALDI, the high ratio of support matrix to sample (e.g. 5000:1) means that the laser photons statistically encounter matrix rather than sample molecules (Fig. 4). The photon energy (UV or IR) must ultimately be dispersed as vibrational energy within the sample. As the matrix/sample crystalline structure becomes energized, crystal integrity and surface binding forces are diminished. Ions are created by acid–base reactions, perhaps between the sample and excited states of the matrix molecules. The matrix molecules desorb, leaving the ions (some still associated with matrix molecules) free of the surfaces. The ions are then extracted by an instrument potential into the selvedge where they undergo association and dissociation reactions both with each other and with other solution components as well as with the matrix.

**Prospects**

Advances in ionization methods can be expected to evolve from the present focus on hardware design and implementation to future interpretive strategies that attempt to produce a shift in the basic information derived from mass spectrometry. The classical pattern is that the ions in the mass spectrum (the molecular ion and its lower mass fragments) provides information about molecular structure, and the intensity of the ion signal is proportionately related to sample amount. With new ionization methods where multiply-charged molecular ion species can be produced, the pattern of ion masses and abundances at higher $m/z$ values than that of the ionized molecule ion must also be considered. The distribution of both fragment and cluster ions in mass spectrometry is used in a much broader sense to learn about the chemistry of the sample and its interactions. For example, the distribution of the ions formed during clustering can reflect the thermochemistry and the kinetics of that reaction, that is, the mass.
spectrum reflects the reactivity of the ion. Similarly, electrospray ionization can be used to probe non-covalent interactions between some large biomolecules and their substrates and changes in the mass spectrum often reflect changes in experimental conditions, i.e. changes in ionic strength, pH or the presence of co-factors in the solution from which the sample is obtained. We are finally beginning to realize that ions can be characterized not only by their mass-to-charge ratios, but also by their chemical reactivity with a host of specific reagents. In considering the mass spectrometer as a miniature chemical reactor, new areas of exciting research are opened up that will sustain the field for some years to come.

It is intriguing to consider whether or not MALDI mass spectrometry would have made such a rapid and significant impact on the field of bioanalytical mass spectrometry if concurrent and independent improvements in time-of-flight mass analysis had not occurred. The explosive growth of MALDI supports the adage that ‘new instrumentation begets new chemistry’. This is relevant to this paper because this new instrumentation has changed the scope and application of DI. In FAB, LSIMS and MALDI, little advantage has been taken of the demonstrated ability to focus the particle or laser beam to a small spot and to image (via mass spectrometric data) the surface of a three-dimensional sample. Sample preparation methods presume that the goal is a homogeneous sample. Much of the real world, however, is composed of samples as they reside (or are prepared) on surfaces as diverse as thin-film supports, planar chromatography media or biological surfaces. The rapid growth of scanning-tunneling microscopy and atomic force microscopy reminds us of the scope of use for spatially resolved information. The visual impact of spatially resolved mass spectral information cannot be underestimated. Imaging capabilities developed in hardware will be bolstered by new methods for sample preparation, reaction and manipulation that rely on specific, designed chemistry. Immobilization is a method with considerable natural precedent, and we would be wise to take advantage of it.

The sensitivity of mass spectrometric instrumentation will continue to increase. Specialized instruments already routinely and meaningfully detect the presence of just a few ions. It is likely that limits of detection will continue to decrease at the current rate of an order of magnitude per decade. During the same time, we will focus renewed attention on the precise and accurate determination of ionic mass. Fourier transform ion cyclotron resonance mass spectrometers offer an extraordinary capability for exact mass measurement of ions trapped for long periods within the cell of the instrument. If the masses of all the ions in the mass spectrum can be measured with an accuracy perhaps ten times better than is now possible, how will this change the process by which we interpret a mass spectrum? We can speculate that accurately determined mass differences between ions will be used to elucidate dissociation or association reactions. The principal issue then will be to acquire a specific link between the ions in a reaction sequence. This forged link is the core of mass spectrometry/mass spectrometry experiments. Major increases in sensitivity will be needed to support imaging experiments with DI in which the spatial distribution of ions in the x–y plane are followed with resolutions of a few tens of microns, and the total ion current obtained is a few hundreds of ions.

The bipartite challenge is therefore to create and transport small populations of ions into the mass analyzer of choice, and to devise the reaction chemistry necessary to force them to reveal their exact structural and reactive nature. These are not small problems, and the solutions will involve significant attention and efforts of investigators for years to come. If our reach does not exceed our grasp, then what is mass spectrometry for?

REFERENCES


General references

Desorption ionization


FAB/LSIMS


Plasma desorption


MALDI