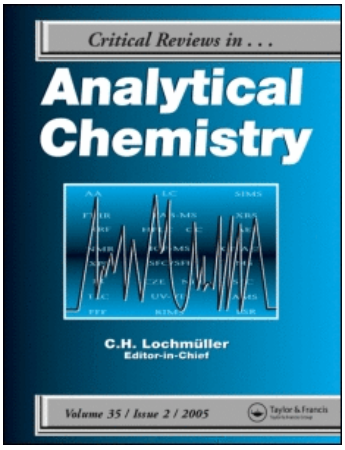

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RECENT DEVELOPMENTS IN IONIZATION PROCESSES RELATED TO ANALYTICAL METHODS IN MASS SPECTROMETRY

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INTRODUCTION

The recent literature has been surveyed to review and correlate developments in ionization processes of interest to the analytical chemist. Electron impact methods are discussed in the overwhelming number of publications on mass spectrometry. The need has been to improve sensitivity of detection for many applications and research interests have been directed to the detection and identification of materials down to the pico-gram level, both by direct analysis and in conjunction with gas chromatography. Many publications have appeared that have widened the scope of spark source mass spectrometry. The use of the electrical detection in this field has increased the precision and accuracy of analysis. Rapid surveys of elemental analysis in such diverse areas as biochemistry, pollution control, and geology have become much more convenient by this method.

The most important single item of information that the mass spectrometrist wants is the molecular weight of the sample being examined. In many cases the electron impact spectrum does not exhibit a molecular ion. Both chemical ionization and field ionization mass spectrometry give a spectrum with an intense molecular ion or the molecular ion plus or minus one hydrogen atom. Although advances have been made in the stability of emitters and in the sensitivity of field ionization mass spectrometry, chemical ionization methods appear to be most useful, especially when used in a mode that gives both information about the molecular weight and a sufficient number of ion fragments to aid in structure determination.

The examination of solid materials by mass spectrometer surface analysis techniques has been the subject of both technological and theoretical advances. Publications have appeared concerning new instruments, experimental methods, and a theoretical basis for the calculation of the analytical results.

I. GENERAL ANALYTICAL METHODS

Electron impact methods are the most frequently used techniques of analytical mass spectrometry. They are applied whenever it is possible to introduce the sample to be analyzed into the ion source as a gas either directly or by vaporization from a solid probe. A number of new applications of electron impact methods have recently been published.

A. Electron Impact Methods in Reactive Systems

Chemical mapping of O and OH radicals in low pressure and atmospheric pressure flames has been reported previously. Hastie[1] has recently described a mass spectrometer system for the measurement of the reactive intermediates in the CH_4-O_2 and CH_4-O_2-N_2 flames at atmospheric pressure. The sample from the flame passes through a conical system into an evacuated chamber kept at 10^{-3} to 10^{-4} torr and then into another chamber at 10^{-7} torr which contains a chopping wheel for modulating the molecular beam and a quadrupole mass spectrometer. A complete analysis of all species in excess of 10^{-5} mole fraction is obtained. Detection of free radicals in this system requires the use of low ionizing electron energies, and appearance potential curves have been studied to differentiate H^+ from H and the fragmentation of H_2 and CH_3^+ from CH_3 and the fragmentation of CH_4. The technique has good precision, but it suffers from the lack of information on the sensitivities of the radical species so that ion intensities cannot be translated into absolute concentrations.

Another application is the sampling of plasmas. In this area, one must consider the additional problem of many ionization processes contributing to the resulting mass spectra. Vasile and Smolinsky[2] have sampled reactive plasmas of vinyltrimethylsilane (VTMS) and argon or helium. The mass spectra of the VTMS-helium and VTMS-argon differ, and both spectra obtained in the plasma differ from the conventional electron impact spectrum of VTMS. The proposed mechanism for the variation in the spectra is as follows: in the plasma

$$C_2H_3\text{–}Si(Me)_3 + e \rightarrow C_2H_3\text{–}Si(Me)_3{}^* + e \quad (1)$$

$$C_2H_3\text{–}Si(Me)_3{}^* \rightarrow C_2H_3 \cdot + \cdot Si(Me)_3 \quad (2)$$

The $Si(Me)_3$ radical can be ionized by low energy electrons, creating a more intense ion at this mass when the discharge creating the plasma is on. Another case of probing plasmas is the analysis of sputter gas atmospheres. The formation of new compounds in the plasma is detected by the mass spectrometer. During the sputtering of metals in the presence of argon, water vapor is desorbed from the surfaces.[3] When a nonreactive metal such as platinum is sputtered, the desorbed water is dissociated into H and OH, and the spectrum due to the recombination of the radicals is observed in the mass spectrometer. When a reactive metal such as tantalum is sputtered, the oxygen reacts with the tantalum, and hydrogen is observed in the mass spectrometer. Sputtering in the presence of nitrogen leads to the formation of ammonia[4] due to the reaction of nitrogen either with hydrogen from the dissociation of water in the plasma or with the water vapor directly. Visser[5] has compared the performance of a cycloidal and quadrupole mass spectrometer for plasma studies. Both instruments can accept an energetically nonuniform ion beam. In the cycloidal mass spectrometer, the resolution was destroyed at 10^{-4} torr; however, with the quadrupole mass spectrometer, at pressures of 10^{-2} torr, although sensitivity decreased, resolution did not deteriorate and noise did not become serious.

With a time of flight mass spectrometer, the mass analysis of ions sampled continuously from external sources such as shock tubes, gas discharges, and thermal ions from flames has been shown to give rise to spurious satellite peaks in addition to peaks which would occur if the ions were internally generated. DiValentin and Dove[6] have shown that these satellite peaks are artifacts which are caused by the interaction of the draw-out pulse and the continuous stream of incoming ions. They have analyzed the problem theoretically, and the computer generated spectra are in good agreement with the position of the satellite peaks and in fair agreement with their intensity. They suggest methods both for identifying the spurious peaks and for suppressing them.

Nishijima and Murotani[7] have extended the usefulness of an apparatus which Nishijima[8] had designed for the dual purpose of the analysis of the energy of ions desorbed from a tantalum target by an electron beam and for Auger electron spectroscopy. In the initial apparatus, the ions were passed through an electric sector for energy

analysis only. By pulsing the electron beam, the time of flight of the ions could be calculated and the masses identified.

Using a time of flight mass spectrometer, Freese et al.[9] have increased the efficiency of detection and measurement of vaporized metal atoms formed by the pulse heating of pure metals. Cryogenic pumping, which is accomplished by an ion source that is surrounded by surfaces at liquid nitrogen temperature, reduces the partial pressure of contaminants such as C_2H_4, C_2H_2, CO_2, and water. As a result of the reduced pressure of the contaminants, the peak height of the Mg^+ ion is increased in the experiment reported. In addition, they used a reduced electron energy (30 eV); this gave a maximum in the Mg ionization efficiency curve, whereas the efficiency of ionization of the hydrocarbons is at about ½ of the maximum at 30 eV. This increase in sensitivity by a factor of >100 has made it possible to make quantitative measurements of elemental vapor densities as a function of temperature. Experiments on pulse heating graphite and various metals by laser beams were also carried out in this work.

B. Temperature Effects on Fragmentation

The effect of the temperature of the ion source on the fragmentation patterns of hydrocarbons in mass spectrometry was noted by Fox and Hipple.[10] They noted that the effect of temperature varied with the molecular weight and degree of branching of the hydrocarbons studied. Stevenson[11] also noted this temperature effect and explained why (a) the specific intensity of all of the ions in the spectrum decreased as the temperature increases, and (b) the intensities of the parent ions decrease more rapidly than those of the fragment ions. Strict attention to this problem is necessary for the accurate interpretation of analytical data from mixture analyses. In a good analytical mass spectrometer, the source temperature is controlled within narrow limits. Komarov et al.[12] have applied the temperature effect on the fragmentation pattern in order to differentiate the structure of isomers that exhibit otherwise similar cracking patterns. The mass spectrometer source was made of *molybdenum* and the source temperature could be varied from 150 to 950°C.[13] The source was designed so that the gas sample underwent a large number of collisions with the heated walls before ionization. To check the possibility that the samples were being pyrolyzed, appearance potential measurements of the fragments were made to determine whether or not they were free radicals or fragment ions. However, the problem of isomerization of the samples at high temperature remains and must be studied further before the technique can be applied to analytical problems. Data are reported on several groups of isomers.

Brodskii et al.[14] have indicated an analytical procedure and methods of calculation for the quantitative analysis of complex mixtures of hydrocarbons introduced by a solid probe into the mass spectrometer ion source. Mass spectra are recorded during the evaporation, and the total ion current is monitored. Comparison of the results is made with the same sample introduced via a heated inlet system and molecular leak. The results show that good quantitative analyses can be made with solid probe introduction. Kankare[15] has described a simple temperature programmer for use with the direct insertion probe. This can be used in conjunction with measurements of the integrated ion current or for controlled temperature program pyrolyses. Although Kankare plots total ion current and runs spectra, there is no reason why this apparatus should not be used with a rapid switching technique.

Seiler and Knödgen[16] have observed that quantitative measurement of small samples by the integrated ion current techniques[17] with a calibrating standard that is introduced simultaneously from a sample reservoir[18] failed to give satisfactorily reproducible results with sample sizes in the 10^{-10} to 10^{-11} mole range. By simultaneously evaporating the sample and standard from the probe it was possible to obtain results that were reproducible to ±10% for samples in the subnanogram range. A switching device alternately measures the selected masses of the sample and standards at 6 to 7 Hz while the material in the probe is flash evaporated into the ion source. The presence of extraneous material in amounts as much as 100 times the sample being measured did not affect the analysis so long as the extraneous material did not give interfering ion fragments at the mass being monitored.

The technique of integrating ion currents to obtain quantitative analyses has been used by Van Leuven[19] for the microanalysis of organic compounds. Gas chromatography has been used in conjunction with an oxygen combustion for the analysis of C, H, and N. By using a quadrupole

mass spectrometer with peak selection it has been possible to monitor all the above elements as well as sulphur and the halogens. The repetition rate of the mass measurements is eight times per second. The output signals from the mass spectrometer are integrated in a computer. By programming in the weight of the sample, the complete analysis is printed out within a few minutes after the combustion. The analytical results are compared to standards and the results, in particular those for fluorine, are impressive.

C. Determination of Molecular Weights

A method of determining the molecular weight of compounds is suggested by Jardine et al.[20] A combinatorial computer program is used to combine the fragment ions and may be useful when the spectrum does not extend to the molecular ion. The assumption is that the parent molecule ion fragments into either two, three, or four fragments. The program determines the probability of possible values of the molecular weight by the summation of the masses of the fragment ions in groups and by the summation of the probability of occurrence of these ions. The sum of the probabilities should be a maximum and equal to one at the molecular weight of the sample. It is advantageous to introduce an estimate of the molecular weight into the computer in order to limit the number of calculations. About 50 compounds were studied; the correct molecular weight was generally obtained, but at times it was in error by as much as 15 mass units. Also, in the tabulation of probabilities in several of the examples, the maximum did not appear to be very sharp.

D. Analysis of Lunar Samples

The examination of the lunar samples returned by Apollo 11 has been an impetus to obtaining maximum sensitivity of mass spectrometer analyses.[21]

Analyses were carried out on the rare gases extracted from lunar samples and on the vapor phase evolved by heating lunar samples from ambient to about 500°C. For the rare gases, a 60° magnetic deflection mass spectrometer was operated with a sensitivity of about 2×10^{-10} cc/mV for He, Ne, and Ar and 3×10^{-13} cc/mV for Kr and Xe. The mass spectrometer was operated under static vacuum conditions, and isotope analysis was possible for all the rare gas samples. For the analysis of carbonaceous material obtained by programmed heating of the sample, a Hitachi RMU 6-E mass spectrometer with a high efficiency ion source and a high-gain electron multiplier was employed. The presence of pyrolyzable organic material was established by the abundance of ions at mass 78 and 91. The intensity of these ions increased as the temperature was raised. The levels of organic matter observed were calculated to be in the range of 0.2 to 0.5 ppm. The problem of carbonaceous contamination due to handling of the samples remains open. A more extensive report on the search and characterization of lunar organic compounds was subsequently published.[22] Lunar samples from Apollo 11, 12, and 14 were also studied by a programmed thermal treatment, and the evolved gases were analyzed with a quadrupole mass spectrometer.[23] Carbon monoxide was observed in this study but was believed to be due to the reaction of N_2O and C in the mass spectrometer.

Raitt et al.[24] have described a Langmuir probe for measuring the composition, temperature, and density of the positive ion plasma in the ionosphere. The probe was mounted on the satellites ESRO-1A and ESRO-1B. The resolution of the mass spectrometer is low, but it was possible to make density measurements of H^+, He^+, and O^+.

The lifetime of mass spectrometer ion source filaments in the presence of oxygen is of great importance in airborne probes. This problem has been investigated by Mauersberger and Olson.[25] They selected filaments of 97% tungsten and 3% rhenium in a hairpin mount for this study. Below residual pressures of 10^{-9} torr (the composition of the residual gases is not specified), there were no significant changes in the diameter of the filament over an 8-month test period and it was concluded that evaporation of the metallic substances did not contribute to the deterioration of the filament. In the pressure range of 10^{-5} to 10^{-4} torr of pure oxygen, reaction with the metal gave a linear relationship between lifetime and filament diameter. However, it has been found that reactions of oxygen which lead to a pumping effect in the mass spectrometer cause errors in the measurement of the partial pressure of oxygen at pressures less than 10^{-8} torr.[26] Experiments were carried out with rhenium, tungsten, and thoriated iridium filaments. The pumping effect was found to be dependent on the emission current at which the filament was operated. Reducing the emission

current from 1 mA to 80 μA decreased the pumping effect and increased the limit of detection of oxygen from 10^{-7} to 5×10^{-9} torr-1. Intermittent rather than continuous sampling further increased the limit of detection to 5×10^{-12} torr-1. The problem of accurate oxygen analysis was considered by von Zahn,[27] who concluded that the O/O_2 ratios measured by rocket-borne mass spectrometers are low, possibly by a factor of 4, due to the loss of atomic oxygen by trapping at the walls and recombination to N_2O and CO_2. The assumption of no loss of atomic oxygen led to a low value of the O/O_2 ratio in the treatment of the data from the Aerobee rocket flight in 1965.[28] The recombination and surface reaction problem was considered carefully in the treatment of the data of Ogo 6 by Hedin et al.[29]

E. Negative Ion Mass Spectrometry

Negative ion mass spectrometry can be used in the analytical laboratory to complement positive ion mass spectrometry for chemical analysis, isotope analysis, and structure determination. The major difficulties in working with negative ion mass spectra have been that the negative ion mass spectra are usually considerably less intense than positive ion spectra and that the negative ion spectra exhibit a large degree of energy dependence. Tang et al.[30] have developed a Cs impact source for the production of negative ion mass spectra. Negative ions are produced by a charge transfer process between a beam of Cs atoms and the target molecules. When the energy of the Cs atom is greater than 150 eV, the mass spectra are relatively insensitive to the Cs energy. A series of molecules was studied, and it was found that the intensity of the parent negative ion produced by Cs impact is greater than the sensitivity of the negative ions produced by conventional electron impact methods.

Ito et al.[31] have studied the negative ion mass spectra of a series of dicarboxylic acids. They demonstrated that these molecules give intense $[M]^-$, $[M-H]^-$, $[M-H_2O]^-$, and $[M-COOH]^-$ ions. These are useful in the determination of molecular weights in the cases where the positive ion spectra are more complex and do not give molecular ions. Metastable decompositions of negative ions have been studied by Bowie and Hart[32] by the use of "metastable defocusing"[33] with a Hitachi RMU 7-D double focusing mass spectrometer. The mechanism of multiple metastable ion decomposition of negative ions was deduced. Collision excitation with nitrogen introduced into the field-free region of the mass spectrometer was used to differentiate between the metastables formed by simple cleavage or rearrangement.

Svec and Flesch[33a] have constructed a mass spectrometer for the simultaneous measurement of positive and negative ions. A back-to-back ion source from which positive and negative ions can be extracted into two 15-cm 60° analyzer tubes enables the simultaneous measurement of the positive and negative ion spectra of a sample. The instrument has not been used for analytical work; however, it is useful in the determination of thermodynamic properties. Flesch et al.[33b] have determined bond dissociation energies, heats of formation, electron affinities for CrO_2Cl_2 and CrO_2F_2, and all their ionic and neutral fragments.

F. Thermal Ionization

Cameron et al.[34] have developed a thermal ionization procedure for the analysis of lead in the nanogram range. The technique is an adaptation of one developed by Akishin et al.[35] for the thermal ionization analysis of lead from a silica-zirconia matrix. Cameron and co-workers have found that silica gel alone was as satisfactory as the silica-zirconia matrix and furthermore was much easier to prepare in a pure form. They placed 1 mg of the silica gel on the "V" filament; the lead sample as lead nitrate was deposited on the gel, dried with an infrared lamp, and then moistened with 1 μl of phosphoric acid. Lead ions in sufficient intensity for satisfactory analysis are produced in the 1100 to 1300°C temperature range. A 10-ng sample gave a current of about 10^{-13} A for at least 20 min which, in the case of the mass spectrometer used, was sufficient for 10 runs. Corrections for voltage sweep and count loss were made by comparisons with standard samples, and the results of the isotope analysis compared with samples run in other laboratories are very good. The same technique has also been used successfully for the thermal ionization analysis for small samples of tellurium, thallium, bismuth, and polonium. Arden and Gale[36] have developed the chemistry for the separation of lead in quantities as low as 10 ng from natural silicates by a procedure of sequential anodic and cathodic electrolysis. The separation is better than 95% efficient. They have applied this technique to samples of geochronological interest such as silicates, sphenes, and meteorites. The lead

isotope analysis was carried out by thermal ionization according to the procedure of Cameron et al.[34] The results of analyses for the lead isotopes and the amount of lead compare very well with the certified values for USGS Rock Standard BCR-1.

G. Rapid Switching Techniques

Sweeley et al.[37] introduced rapid switching between peaks (the accelerating voltage alternator method) for the mass spectrometer analysis of unresolved or partially resolved peaks from a gas chromatography column. By switching rapidly between selected mass peaks, it was possible to analyze a mixture of penta-*O*-trimethylsilyl-D-glucopyranose and its d_7 analog over a series of sample mixtures ranging from 0.55 to 1.12 μg and concentrations of glucose d_7 from 1.35 to 45%. The error in these determinations was less than 10%.

When the mass spectrometer is used as a detector for gas chromatography, the rapid switching and recording of a number of peaks of a mass spectrum gives the analyst a mass fragmentogram of the gas chromatography effluent. The technique was proposed by Hammar et al.[38] for the identification of chlorpromazine and its metabolites in human blood. The mass numbers selected for the fragmentogram can be either the molecular ions or characteristic fragment ions. By the use of this technique, $10^{-1.2}$g of chlorpromazine could be detected. Koslow et al.[39] have applied mass fragmentography to the quantitative assay of norepinephrine and dopamine. For a quantitative assay, an internal standard must be used to compensate for unpredictable losses due to handling and in the gas chromatography column. The ideal internal standard would be the same compound as that being analyzed but labeled with heavy isotopes on the fragments selected for the mass fragmentographic analysis. Since these were not available, Koslow et al. used the closely related compounds α-methylnorepinephrine and α-methyldopamine as internal standards. Measurements were made on 0.1-mg tissue samples, and the sensitivity was about 0.5 pmol; the response of the method was linear up to 200 pmol.

Samuelson and Hamberg[40] used multiple ion detection with a deuterated carrier for the GC/MS analysis of prostaglandin E_1 (PGE_1). The PGE_1 was converted to the methyl ester and methoxime derivative. This derivative was combined with the corresponding methoxime-d_3 derivative in ratios of protium to d_3 of 1:1000 to 8:1000. Analysis of the mixtures gave a linear relationship between the ratio of the two forms and the composition of the injected sample. Holland et al.[41] have elaborated this technique with a computer control of the beam focusing along with real time data collection and immediate presentation of the results. The automatic optimization of the beam obviates the necessity of manually refocusing the peaks as the magnetic field changes due to heating effects. Tests show that the system will accommodate a change of 0.25 amu from the optimum focus within 3 to 5 scan cycles. In general, the precision of the data is better than 1% when tested on the analysis of fatty acid methyl esters and isotope ratios. Since the ultimate sensitivity of the method is many orders of magnitude greater than that achieved by sample introduction with a solid probe, this appears to be a most promising technique in analysis for biochemical and pollution problems.

II. ISOTOPE ANALYSIS

The early measurements of isotope abundances by the Aston mass spectrograph[42] suffered from the difficulty in comparing line intensities on photographic plates. The measurements made by the method of Dempster[43] involved measuring the individual ion currents with an electrometer. In spite of these experimental problems, by 1924, Aston[44] was able to publish a list of 12 elements whose isotopic composition had been determined by mass spectrometry. Silver, for example, had "two nearly equally intense lines" (Ag^{107}–51.82%, Ag^{109}–48.18%). These data were not sufficiently accurate as a basis for precision atomic weights or isotope tracer work. By 1942, Aston[45] had listed isotopes for practically all the elements, but the abundances listed were measured either by photometry of plates or by the individual measurement of ion currents by electrometers. Acquisition of precise data by plate photometry suffered from the problem of precise measurements of intensities from photographic plates, and the data obtained by the second method suffered from the sequential recording of the ion beams and changes in gas flow and instrumental drift between the measurement of isotope peaks.

The most significant development in the precise measurement of small differences in isotope

abundance ratios was the adaptation of the Nier mass spectrometer to a dual ion collection system by McKinney et al.[46] Two ion beams were simultaneously focused on separate collectors, and a recording potentiometer was used to detect the ratio of the intensity of the beams. Furthermore, the modification included two independent inlet systems which permitted the rapid exchange of the sample and reference gases in the mass spectrometer. Data are presented as the differences in permils of the ratio between the sample and the standard working gas, i.e.,

$$\delta = \left(\frac{R_{sample}}{R_{standard}} - 1\right)1000 \quad (3)$$

Where the instrument is used for O^{18} analysis, R_{sample} and $R_{standard}$ are the ratios of $CO^{16}O^{18}$ to CO_2^{16} for the unknown sample and reference gas; differences to a precision of 0.2 per mil of the oxygen isotope ratio are achieved.

More recently, a dual collection instrument has been used by Horton[47] to measure the ratio of the boron isotopes in boron trifluoride. The instrument simultaneously collected the $B^{10}F_2^+$ and $B^{11}F_2^+$ ions, and the ratio of isotopes was measured to a standard deviation of 0.0014. A dual collector system has been developed for the AEI MS2[48] to measure the abundance ratio of $^{87}Sr/^{86}Sr$. The strontium is ionized by thermal ionization. The average ratio and standard deviation of 10 replicate analyses is 0.7126±0.0003. The error introduced in dual collection isotope measurements due to tailing from adjacent peaks was investigated. It was determined that sample and filament mounting must be carried out carefully and reproducibly and that the pressure in the mass spectrometer tube must be below 0.2 μtorr to obtain reproducible results. In addition, interference from tailing must be kept negligible or constant for precise isotope measurement or comparison of ratios.

Where the mass spectrometer is equipped with peak matching capability, Dodson[49] has shown that with minor modifications, isotope ratios can be measured with a precision of 0.2 to 0.5%. A strontium isotope analysis gave ratios of 0.3004 and 0.9460 by peak matching and 0.3006 and 0.9459 by chart measurement. It is pointed out that the use of expanded-scale recording could increase the precision to 0.02%.

Using a quadrupole mass spectrometer and two data acquisition techniques — a multiple ion monitor-integrator system and the mass fragmentography program of the data system — Caprioli et al.[50] have determined isotope ratios of rare gases and normal and O^{18} enriched pentaglucose. The isotope ratios of argon, krypton, and xenon were determined both from a reservoir and as a GC effluent. The precision of the analyses ranges from about ±1% in the 1- to 10-at% range to ±0.15% in the 10- to 100-at% range. The accuracy of the analyses from the gas chromatography effluent is actually better than that from the reservoir.

A large quadrupole mass spectrometer[51] has been used to analyze xenon isotopes, and the results are in good agreement with the data by Nier with an electromagnetic instrument. The work involved the redetermination of the relative abundances of the 11 isotopes of terrestrial xenon. A magnetic resonance mass spectrometer[52] has been described that can measure an He^3/He^4 ratio of about 10^{-8} with a sample of 10^{-5} cc at SC with an accuracy of ±2%.

By use of a "static" mass spectrometer, Merrill[53] was able to measure xenon and krypton isotopic ratios in gas samples of xenon or krypton of about 10^{10} atoms. These instruments are of importance in the measurement of small geochemical samples.

The production of H_3^+ in a hydrogen discharge was shown to exist by Thompson, and the mechanism was considered by Smyth.[54] In his mass spectrometer search for the isotopes of hydrogen, Bleakney[55] considered that H_3^+ is formed at a rate proportional to the square of the pressure of H_2, whereas HD^+ would vary linearly with the pressure. The presence of H_3^+ has been a continuing nuisance over the years in the determination of H_2/HD ratios. Analysts have measured the mass 2/3 ratio at a series of pressures, and the data were extrapolated to zero pressure to determine the H_2/HD ratio of the sample.

Beavis[56] has reexamined the problem with several mass spectrometers in his laboratory and has concluded that the relative amounts of H_3^+ ions produced are strongly dependent upon electrical operating conditions in the ion source and only slightly pressure dependent, so that variation of the source settings can lead to the observation of H_3^+ by one investigator and none by another investigator who might be using the same type of analyzer. Fuchs[57] has studied the formation of

H_3^+ in paraffin spectra at 70 eV and has shown that the H_3^+ ion is the result of the decomposition of multiply charged ions in hydrocarbons. Regardless of the source or mechanism of formation of H_3^+, in isotope analysis, the pressure effect problem should be investigated by every analyst in order to determine whether it will lead to spurious data from his instrument.

Precision isotopic analysis of solids by thermal ionization methods (see Section I.F) has been reported by several investigators. Riley[58] has measured the ratio of Re^{185}/Re^{187} to 1 part per thousand with a thermal ionization source. The Bureau of Standards group[59,60] have determined the absolute isotope abundance ratios and atomic weights of magnesium and chromium by surface emission mass spectrometry.

Catanzaro[61] has found that a triple-filament source consisting of rhenium-ribbon sample filaments and a platinum-ribbon ionizing filament gives greater precision for the isotope ratios of lead than the single-filament PbS or PbC_2O_4 methods. Stable total lead ion signals of 4×10^{-13} A for a 20-μg sample to 6×10^{-11} A for a 500-μg sample were obtained using a 12-in. radius of curvature single focusing mass spectrometer equipped with a Z lens that increased source efficiency by a factor of 4. $PbCl_2$, $Pb(NO_3)_2$, and $Pb(OH)_2$ were investigated as the sample mounting media; $Pb(OH)_2$ was found to give the most stable signal. Their 10 analyses of a reference sample gave 95% confidence limits (per analysis) of 0.054% for Pb^{204}/Pb^{206}, 0.023% for Pb^{207}/Pb^{206}, and 0.071% for Pb^{208}/Pb^{206}. These precisions are better by a factor of 2 to 8 than data obtained by the single-filament methods and by the gas analysis technique using $Pb(CH_3)_4$.

Svec and Anderson[62] combined thermal ionization and dual collection techniques in a mass spectrometric measurement of the lithium isotopes. A number of lithium salts were investigated, but LiI was found to give the best results. A 10-μg sample is adequate for the analysis, and the precision in the Li^6/Li^7 measurement is better than 1 part in 1000.

For the measurement of large isotopic abundance ratios such as 10^8:1, a tandem double focusing mass spectrometer has been built,[63,64] and a peak/valley ratio of 10^7/1 was demonstrated for the Sm^{148}-Sm^{149} separation.

A. Isotope Ratio Calculations

The method of calculating the relative abundance of isotopes in molecular species has been described by Margrave and Polansky[65] and by Riedel.[66] Margrave and Polansky have reviewed the elementary probability theory associated with the calculation of the abundances of isotopic species and have given a sample calculation for the calculation of the isotopic peaks for BCl_3. Riedel describes a matrix method for the calculation of isotopic peak heights that is readily carried out with a desk calculator. A simple calculation for nitrobenzene is completely worked out. Brauman[67] has presented a computer program for calculating the monoisotopic spectrum from the isotopic cluster using least squares techniques. Boone et al.[68] have described a computer program to convert the entire or selected portion of a low resolution mass spectrum of a compound having the elemental composition $C_wH_xB_yO_z$ into the corresponding complete or partial monoisotopic mass spectrum. Carrick and Glockling[69] have presented a computer program for determining both the mass and the relative abundance of an ion that contains up to ten atoms, three of which may be polyisotopic elements. A more general calculation of the ionic formulae and the monoisotopic spectra of low resolution spectra is presented by Crawford.[70] Crawford's method encompasses the general case of a molecule with many elements with no restriction on the number of elements that may be isotopic.

McLaughlin and Rozett[71] have reported a computer technique which calculates a least squares fit monoisotopic spectrum, restricted to positive solutions, from polyisotopic spectra. The method can be used for the determination of isotope abundances and the calculation of the cluster of isotope peaks due to any formula. The advantage to the analyst is that these calculations can lead to the detection of impurities in mass spectra. The isotope cluster analysis applied to the spectrum reported as $B_{20}H_{26}$ by McLaughlin et al.[72] showed that the spectrum actually resulted from a mixture of $C_9B_{10}H_{28}$ and probably $C_9B_9H_{29}$. It would be interesting to see this analysis confirmed by high resolution mass spectrometry.

There are a number of situations where direct analysis of isotopically tagged compounds is not feasible. The compound may lack a sufficiently intense parent peak, or the instrument may lack a solid introduction system or high mass capability. In these cases, it is necessary to degrade the compound, separate the isotopically tagged species, and analyze it directly.

Günther et al.[73] have described a method for

measuring the N^{15} content of organic and inorganic compounds. The compound is degraded with CuO and CaO at 650°C in an evacuated glass tube, and the nitrogen isotopes are analyzed. Proksch[74] reports a similar method in the application of mass and emission spectrometry to the analysis of nitrogen isotopes in biological materials. Samples are treated in a vacuum Dumas apparatus, CuO is used to oxidize the organic matter, and CaO is used to absorb all reaction products except nitrogen gas.

Fong et al.[75] have reevaluated the pyrolysis conditions for the production of CO and CO_2 for O^{18} determination from a series of organic compounds. $SnCl_4$ appears to be the preferred sensitizer for obtaining better yields of CO_2, and pyrolysis at 500°C and 1 hr is recommended.

The preparation of sulfur dioxide for the assay of the sulfur isotopes by combustion of the sample with copper oxide has been reported by Fritz et al.[76] This procedure overcomes the drawback of the possibility of introducing impurities via oxygen combustion and avoids the procedure of the conversion of sulfur to the hexafluoride. The hexafluoride method,[77,78] which is capable of handling very small samples, has the drawback of requiring the use of extremely reactive fluorinating reagents.

Deuterium analysis methods in organic chemistry have been reviewed by Cox and Willcott,[79] who discuss other analytical methods besides mass spectrometry. Gaffney et al.[80] have discussed the isotopic analysis of compounds directly from the gas chromatograph. This is a tempting shortcut to save extensive sample preparation and purification if adequate precautions are taken to ensure that isotopic fractionation between the leading and tailing edge of the gas chromatographic peak does not create a serious problem.

An analysis of the accuracy of isotope analysis has been made by Mook and Grootes.[81] All corrections – voltage gradient of the input resistors, resolving power of the mass spectrometer, contamination of the sample, background and memory, and additional masses on the collector of the higher abundance isotope in the case of dual collection and isotopic molecules of equal mass – are discussed in detail.

B. Isotope Dilution

The isotope dilution method was utilized by Rittenberg[82] for the quantitative analysis of specific products in complex mixtures. The method requires that a known amount of the isotopically enriched compound be mixed with the mixture to be analyzed and only a small sample of the desired material separated in the pure state for analysis. The yield of the separation is not important. The usefulness of the method depends on the precision of the isotopic analysis. The degradation of the tagged compound to a small molecule followed by analysis with an isotope ratio mass spectrometer is more precise than calculation of the isotope ratio from the total spectrum of a large molecule.

Curtius et al.[83] studied metabolic pathways in vivo using stable isotopes and isotope dilution analysis. Deuterated tyrosine and leucine were given orally, and the deuterium contents of the metabolites were measured. Nanogram samples were separated by gas chromatography and analyzed directly by mass spectrometry; the LKB 9000 system was used.

Crocker and Hart[84] have utilized the isotope dilution method to determine the amount of fission product xenon in uranium ceramics and have reduced the error of the determination from the ±10 to 25% obtained by gas measurement to ±3%.

A procedure for the anodic separation of lead as PbO_2 is described by Barnes.[85] The method is applicable for quantities from <10 ng to 10 μg and is applicable to the work of geochronologists, environmentalists, and clinical chemists. The efficiency of the separation was checked by isotope dilution and mass spectrometry.

Tsuge et al.[86] have extended the isotope dilution method to metals; the metal is analyzed as a volatile coordination compound. They have applied the technique to the microdetermination of zirconium in geological and lunar samples. The volatile tetrakis (1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato) Zr^{IV} was used in the determination. The method requires samples of 10 to 40 mg, and the zirconium can be detected in the ppm range. The volatile chelate can be analyzed with an ordinary mass spectrometer. The $^{90}Zr\ (fod)_3^+$ and $^{91}Zr\ (fod)_3^+$ ions are used to measure the isotope ratios. The same technique has been applied to chromium in geological samples with Cr^{III}-trifluoroacetyl acetonate.[87] Further examples of the use of the isotope dilution method with metal ions are discussed under the topic of spark source mass spectrometry; however, the greater accuracy and precision

of the electron impact method should make this approach more desirable when available.

III. CHEMICAL IONIZATION

The development of chemical ionization methods in which the mass spectra of the ions of interest are formed by ion-molecule reactions is due to the studies of Munson and Field.[88] The advantage of chemical ionization is that the spectra produced are much simpler than those from electron impact. A small amount of sample is mixed with a large amount of reagent gas (the ratio being about 10^{-3}), and the mixture is introduced into the ionization chamber at a pressure of about 1 torr. Under these conditions, one is assured that (a) the electrons will ionize predominantly the reagent gas, and (b) the ions thus formed will react with other molecules of the reagent gas and sample molecules. Methane and isobutane were the reagent gases initially used in CIMS; however, hydrogen, nitrogen, rare gases, and ammonia have also been used. The selection of the reagent gas depends on the features of the chemical ionization spectrum desired. A number of reviews have been written on chemical ionization mass spectrometry[89-96] which outline the instrumentation and the results of the use of the method.

Modifications of mass spectrometers for chemical ionization work primarily require: (a) sources with slits sufficiently small so that the source can be pressurized to 1 torr or higher, (b) the addition of sufficient pumping capacity to the source region so that the pressure in the analyzer section is kept in the 10^{-5}-torr region to avoid peak broadening due to collisions, and (c) the insulation of components in order to avoid high voltage flashovers due to the higher pressures.

Yinon[97] has discussed the various aspects of hardware and instrumentation modifications required to modify a mass spectrometer for chemical ionization. In addition, a number of papers have appeared dealing specifically with the modification of specific mass spectrometers for CI work, for the MS9,[98-100] Consolidated 21-110B,[101] and the MS12.[102] All authors report that after the mass spectrometer has been modified to operate in the CI mode, it has a sensitivity comparable to operation in the EI mode and that there is no loss of resolution compared to normal operation of the mass spectrometer.

Bonner et al.[103] have shown that an alternative to the high pressure chemical ionization source is a three-dimensional quadrupole ion storage trap (Quistor) mounted in place of the conventional ion source of a quadrupole mass spectrometer. Ion storage for 3.5 msec of a mixture of methane (2×10^{-4} torr) and methanol (5×10^{-7} torr) gave a peak at mass 33 due to reaction $CH_5^+ + CH_3OH \rightarrow CH_4 + CH_3OH_2^+$.

Chemical ionization sources have also been proposed which eliminate the necessity for filament operation in the presence of oxidizing gases, organic compounds and water vapor at high pressures, high electron energy, and emissions, all of which shorten filament life. McEwen[104] has proposed a filamentless CI source using a Townsend discharge for ion production. The sensitivity obtained with the discharge is at least as good as the filament method and allows the use of oxidizing reagent gases. For most of the reagent gases studied by the discharge method, the CI spectra obtained were identical to those from the filament method of ionization. Hoegger and Bommer[105] use argon ions produced in a high frequency electrodeless discharge to interact with the selected reagent gas that is added downstream past the discharge zone. Ion-molecule or charge transfer reactions between Ar^+ and the reagent gas form the primary reagent ions; these, in turn, react with the sample to form the chemical ionization spectrum. In practice, the reagent gas is added until the Ar^+ peak has disappeared; then the sample gas is added. Further work with this type of source will show whether the complexity of titrating the Ar^+ is worth the saving of filaments.

A technique that proposes to provide the advantages of both CI and EI mass spectrometry has been suggested by Hunt and Ryan[106,107] and by Arsenault.[108] Since CI spectra are ideal for molecular weight determination, and since EI spectra often do not contain a molecular peak but generally contain sufficient fragment ions to elucidate structure and differentiate isomers, a system that creates a sum of the two spectra is proposed. In mixtures of a rare gas (argon or helium) and water (>100/1), at about 0.5 torr, both *m/e* 19 (H_3O^+) and the rare gas ions are formed. The H_3O^+ ion protonates most organic molecules, leading to abundant M + 1 ions. With the rare gas ions, electron transfer leads to sample ions that undergo extensive fragmentation. The reactions taking place are

$$He + e \rightarrow He^+ + 2e$$

$$He^+ + P \rightarrow He + P^+ \rightarrow \text{fragmentation of P} \quad (4)$$

and

$$H_2O + e \rightarrow H_2O^+ + 2e \quad (5)$$

or

$$He^+ + H_2O \rightarrow H_2O^+ + He$$

$$H_2O^+ + \xrightarrow[H_2O]{} H_3O^+ + P \rightarrow (P+1)^+ + H_2O \quad (6)$$

For example, argon-water CI spectra are shown to be able to differentiate pentabarbital 2 from the 1 isomer. The molecular weight is identified from the P + 1 ion, and the isomer identification is made from the fragmentation ions. Peak matching against a fluorocarbon standard is not affected since proton transfer from H_3O^+ to fluorocarbons does not occur. The only ions produced in the fluorocarbon spectrum result from electron transfer reactions between the rare gas ion and PFK, and the PFK spectrum is essentially identical to that obtained in the EI mode. Another advantage can be found in the application of this procedure in GC/MS work; water vapor can be added to the helium carrier gas after it leaves the chromatograph and before it enters the mass spectrometer so that molecular weights and structural information can be obtained on a single sample.

Addition of 1,2-diaminoethane and 2-aminoethanol-1 to the isobutane reactant gas has been used to modify the reactivity of isobutane. The use of these additives results in the formation of reactant ions of different acidity which promotes selective protonation or complex formation of the sample analyzed.[109] Among the many other analytical applications of CIMS have been the identification of alcohols where the parent peak is small or nonexisting[110] and the identification of noncannabinoid phenols in marijuana smoke.[111] The isobutane CI mass spectra of 48 commonly used drugs have been reported by Milne et al.[112] In his review of CIMS, Foltz[112a] has given a number of illustrative examples of the methods for identifying drugs and drug metabolites, phospholipids, and macrolide antibiotics.

Chemical ionization mass spectra of a series of explosives – RDX, HMX, 1,3,5-TNB, 2,4,6-TNT, and PETN – have been determined using hydrogen as a reagent gas.[113] These studies are of value both for analytical purposes and for the elucidation of processes leading to detonation.

CIMS has also been applied to the study of inorganic compounds. A series of boron hydrides[114] have been analyzed by CIMS. The CIMS spectra show that the compounds with dihydro terminal groups, B_2H_6, B_4H_{10}, and B_5H_{11}, are ionized by dissociative proton transfer and hydride abstraction to form $(M - 1)^+$ ions, and the compounds with a monohydro terminal group, B_5H_9 and B_6H_{10}, react with a number of hydrocarbons to form $(M + 1)^+$ species as well as higher molecular weight complexes containing carbon.

The combination of the simplified CIMS spectra and the volatile coordination compounds with the ligands 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dione (H(fod)) and 2,2,6,6-tetramethylheptane-3,5-dione (H(thd)) is used to separate and analyze the lanthanide elements.[115] Separation of the lanthanide chelates is carried out by gas chromatography. Relatively little fragmentation takes place when isobutane is used as the reagent gas, so the only peaks in the CI mass spectrum are the isotope peaks of the ligand and metal. CIMS[116] using methane as a reagent gas has been applied to the characterization of a series of arene chromium tricarbonyls (where Ar = benzene, toluene, fluorobenzene, chlorobenzene, mesitylene, and methyl benzoate) and molybdenum complexes. Comparisons are made between the gaseous, ionic, and solution behavior of the compounds.

IV. SPARK SOURCE MASS SPECTROMETRY

The potential of utilizing spark source mass spectrometry for the determination of trace and ultratrace concentrations was noted by Dempster[117-119] in connection with the development of his mass spectrograph isotope studies. The introduction of electrical recording in spark source instruments as either an alternative or a supplement to photographic recording has increased the speed and convenience of obtaining data from these instruments. Gorman et al.[120] used a spark source instrument with electrical recording to analyze Cr and Ni in stainless steels. By measuring the individual ion currents as a fraction of the total ion current, variations due to fluctuations of the spark source were essentially eliminated, and

precision in the analyses between 0.01 to 0.5% was obtained. Hannay's[121,122] mass spectrograph of the Mattauch type was capable of both photographic and electrical detection of bulk impurities in solids of 0.1 ppm and surface contaminants of less than a monolayer. The potential of this instrument in the growing field of semiconductors was recognized by Hannay.

An analysis of the precision and accuracy of SSMS using electrical detection has been made by Bingham and Elliot.[123] The advantages of rapid scanning, dynamic range, and immediate availability of results are stressed. Rapid semiquantitative surveys of samples can be made in a short time with on-line computer acquisition and processing of electrically recorded spark source mass spectra.[124] An interpretation algorithm based on a chemist's thought processes checks multiply charged ions, isotope patterns, overlapping spectra, and complex ions. Examples of the analysis of a copper sample and water pollution sample are given.

A further improvement in electrical detection of spark source mass spectra is the simultaneous ionbeam collection by Conzemius and Svec.[125] The dual collector system serves two purposes: It can be used for the measurement of isotope abundances, or one collector can be used instead of the total ion monitor in analytical work. When heterogeneous pellet samples are used as electrodes, there are fluctuations in the total ion beam due to variation in the concentration of major ions as sample and pelletizing material are vaporized. The system was tested in a study using electrodes of the heterogeneous Nd_2O_3-graphite pelleted sample. The $^{142}Nd^+$ ion current was focused on the collector slit and alternately referenced against the other Nd^+ isotope ion currents on the second slit and against the total ion monitor. Referencing against the second collector slit gave data for the relative intensity of $^{142}Nd^+$ whose precision was better by a factor of 15 than the data obtained when referencing against the total ion current monitor. Data are also presented for the abundances of the dysprosium isotopes and show a deviation of $<0.5\%$.

Magee and Harrison[126] have described an apparatus for magnetic peak switching in spark source mass spectrometry. They pointed out that electric peak switching introduces a number of problems: voltage effects on the mass spectra, the resulting uncertainties in sensitivities, and the effect of the varying ion energies on the electron multiplier gain. Electrostatic scanning also covers a more limited mass range than magnetic scanning. On the other hand, magnetic peak switching with a fixed accelerating voltage and precise integration techniques allows a large number of elements to be measured against precise sensitivity factors.

Improved precision and accuracy in SSMS with electrical detection and peak switching have made it advantageous to be able to switch rapidly between sample and standard electrode. This is accomplished[127] by dual electrode mounts. Thus, sample and standard can be rapidly switched without breaking the vacuum system, which certainly speeds up the analysis and improves the accuracy.

The areas in which spark source mass spectrometry has been applied have widened considerably due, in part, to ingenious instrument modifications. The modification of the source by the addition of a sample cooling system permits the analysis of liquid samples. Cherrier and Nalbantoglu[128] report on the analysis of impurities between about 0.01 and 1500 ppm in mercury, phosphoric acid, and nitric acid by this method. The spark method of analysis has also been applied to solutions of Mg, Ni, Cd, Pb, and some rare earth chlorides; in addition, aqueous solutions containing known amounts of KOH, HF, and HClO have also been analyzed.[129] The drop of test liquid was placed in a gold crucible and frozen in liquid nitrogen in preparation for the analysis. Sensitivity factors for this type of analysis were studied and should be a simpler matter than in regular spark source analysis since the analyst is dealing with a matrix (water) which is identical for all samples.

Gregory[130] has used a DC rather than a radio frequency source and improved his instrument resolution to 24,000. With this improved resolution, he has identified the interfering ions in the elemental analysis of ashed blood samples and compiled a list of ions that can be analyzed without interference.

Grundoboni[131] has compared the results obtained by spark source mass spectrometry and atomic absorption spectrophotometry for six elements (Mn, Ni, Cr, V, Cu, and Zn) in coal ash. Although some comparisons deviate by a factor of two for the two methods, in general, the agreement between the two methods is quite good. The absolute detection limits of the above elements are

estimated to be between 0.03 and 0.1 ppm. Relative standard deviations of 6 to 15% were obtained for the mass spectrometer data, compared to 2 to 3% for the atomic absorption values.

An accuracy of about 10% was obtained by Jackson and Strasheim[132] in the analysis of nonconducting geological samples in silver or graphite matrices using a low voltage discharge source. Careful control of conditions allows the analysis of elements that range in concentration over two orders of magnitude. Three international standards are analyzed, and the mass spectrometric results for major and minor elements are compared with other analytical methods.

The spark source technique was applied by Schmidt et al.[133] to determine the diffusion coefficients of iron, niobium, nickel, silicon, and titanium in vanadium at 1600, 1700, and 1800°C. The diffusion couple is mounted over the high voltage plate in the source, and 16 sampling sites separated by about 0.9 mm are analyzed along the couple. The high sensitivity of the mass spectrometer allows the experiment to be carried out with a low concentration of solute. Ions were measured electrically with a wide mass range dual beam collector.

The application of spark source mass spectrography to geological samples and similar materials has been studied by Nichols et al.[134] Precision of ±5% was obtained by following a carefully developed procedure of electrode preparation and sparking. The effect of sensitivities, selective volatilization from the electrodes, matrix effects, and the formation of multiply charged ions is thoroughly discussed. Tabular data comparing the mass spectrographic analysis of geochemical standard rock with other analytical methods is given. Mass spectrometer data is compared with neutron activation, optical spectrography, and colorimetric and chemical analysis.

Keene[135] has applied spark source mass spectrography to the analysis of iron and low-alloy steel. The instrument was calibrated by determining the relative ionization factors for each element in iron so that quantitative results could be guaranteed. Twenty-four elements have been determined in different samples, and in general, the spectrometer results are in reasonable agreement with the nominal values of the standards. With a few exceptions, given coefficients of variations are between 15 and 35%, but sulfur, phosphorus, arsenic, and lead showed larger deviations.

In a brief survey of spark source mass spectrometry, Brown et al.[136] have discussed recent instrumental advances and applications of spark source mass spectrometry. Electrical detection techniques, log-ratio exponential scanning for rapid survey analysis, computer data acquisition, and peak switching are discussed. Applications to coal ash, water analysis, metallurgy, and biological samples are noted, and examples of the analyses are tabulated.

Spark source mass spectrometry at a high level of sensitivity has been used to characterize the materials in art objects and artifacts.[137] Small samples of drillings are compressed into an electrode, and pigment samples are mixed with silver in a vibrator and then compressed. Interesting information about ancient metallurgy and pigment formulation has been obtained.

For the many applications that require photoplate recording, the problems of obtaining accurate quantitative information from photoplates continue to be studied. Schuy and Franzen[138] have reviewed and critically assessed the known methods of photoplate evaluation up until 1966. They have examined all parts of the calibration function – e.g., time, transmission factors, background effects, and sensitivity of the photoplate to ion current. They have concluded that mathematical treatments are available to enable the spectroscopist to attain results that have a precision of 0.01 to 0.02 relative standard deviations.

Ordzhonikidze et al.[139] have carried out a series of replicate determinations of the impurities in a sample of molybdenum. It is concluded that the precision of the results is to a considerable extent dependent on the method used to calibrate the photoemulsion. Four methods are examined, and the empirical method of Hull[140] for the calibration of the transmission curve gives the highest precision. Relative standard deviations between 0.05 and 0.15 were obtained.

Fergason and Young[141] have described a method for the treatment of the photoplate lines which is based on three parameters: (1) the maximum absorption of the line, (2) background in the vicinity of the line, and (3) total area under the densitometer tracing of the line. The method is checked out by treatment of spectra of the tin isotopes. The procedure reduces the quantity of data that must be taken for the Hull method and successfully corrects photoplate data for line width variations.

The manual treatment of photoplate data is extremely tedious, and computer methods must be applied. Burdo[142] has described a densitometer computer system for storage and treatment of transmittance data and for calculating calibration curves for the integration of intensities and the evaluation of elemental concentrations.

Magee and Harrison[143] have investigated the variation of the sensitivity factor with the variation in the spark gap. In graphite matrices, changes of up to a factor of three were observed. Methods of controlling the spark gap have been published. The maintenance of a controlled gap is important in all spark source mass spectrometry,[144,145] but particularly so with the increased precision and accuracy which are possible using electrical detection methods.

A further development by Conzemius and Svec to ensure optimum electrode geometry is a device to maintain an optimum illumination angle along with the spark gap control.[146] By careful control of these factors, the precision they obtained for the isotope abundances for the dysprosium isotopes is impressive.

In addition to the many other special problems encountered in spark source mass spectrometry, the problem of meaningful sensitivity factors is one of the major impediments in obtaining accurate quantitative analyses by this technique. Short and Keene[147] have studied ionization corrections in the determination of solids and have made the following observations: (1) Ionization corrections may depart significantly from unity. (2) The sensitivity factor is affected by the matrix; a high value for a particular element in one matrix does not ensure a high value in another matrix. (3) No correlation was observed between the ionization corrections determined and the volatility of either a particular element or the matrix or the relation between the two. (4) Cooling of the electrodes did not produce any significant change in sensitivity factors. Thus, the absolute accuracy of the mass spectrometer results must be suspect unless the sensitivity factor of a particular impurity is determined and used as a standard in the same matrix that is used for the analysis of the unknown.

Keene[135] has examined the sensitivities of a series of elements in iron and alloy steels where the range of impurities was between 0.001 and 0.1%. Hamilton and Minski[148] have extended this study by comparing the sensitivities of impurities in a number of certified materials. They compared their data with data obtained in other laboratories with both the same and different instruments. They found that the variations ranged from 20 to 90%. The study included the effect of different matrices on the sensitivity factors.

Conzemius and Svec[149] have computed relative sensitivity factors for rare earth elements on the basis of empirical models relating sensitivities to fundamental chemical and physical properties. The calculated relative sensitivities show the same trend as the experimental ones, but the deviations of the calculated sensitivities are quite large for analytical applications.

Another instrumental advance that has increased the limit of detection is the use of cryopumps. This has made it possible to detect oxygen in metals and semiconductors.[150,151] The lowering of the pressure of the residual gases in the instrument permits sufficiently low blanks so that meaningful results of <1 ppm can be obtained for oxygen, nitrogen, and carbon. This has overcome the problem noted by Keene,[147] who was only able to obtain order of magnitude values for these elements.

V. FIELD IONIZATION MASS SPECTROMETRY

A recent book by Beckey[152] covers all the work in the area of field ionization mass spectrometry published prior to 1968 and some work published up to 1970.[153]

The field ion sources that have been used in most of the published work have been based on razor blade emitters. Although razor blade emitters have satisfactory sensitivity, the sensitivity is further improved by sensitization with a number of organic reagents.[154-156] Anbar and Aberth[157] have described a recently developed field ionization source that consists of an array of about 100 points spaced 25 μm apart and deposited by evaporation techniques over an area of 2 mm^2. This source ionized most organic compounds with an efficiency of 10^{-4} to 5×10^{-3}, which produced ion currents in the range 10^{-9} to 10^{-8} A – currents which are readily measured in the mass spectrometer.

FIMS has been applied to the analysis of mixtures and has given satisfactory quantitative results in this application. Liitmaa et al.[158] point out, however, that in field ionization, the ion intensity does not follow the simple linear relationship with pressure that is observed in EI mass

spectrometry, and that a simple correction does not appear possible.

On first glance, the generation of only parent molecule ions in the mass spectrum would appear to simplify the analysis of mixtures because each constituent contributes only one single mass number to the ion beam. The use of FIMS, however, requires the application of auxiliary methods to distinguish between isomers in the sample. FIMS has a great potential in routine analysis in clinical and biochemical work where the molecular weight is sufficient to identify the compound of interest.

The absence of fragmentation and H/D scrambling[159] makes FIMS analysis of isotopically labeled compounds an ideal method since only the molecular ion peak is obtained. This method is not troubled by the loss in sensitivity that is experienced in attempting to obtain only parent peaks by the use of low electron accelerating voltages in an EI source.

Games et al.[160] have used a combination of FI and EI mass spectrometry together with on-line data acquisition and high resolution to examine the alkaloids obtained from the seeds of *Erythrena princeps*. The FI spectra gave the molecular ions whose precision mass could be determined for elemental analysis, and the EI spectra were used in structure assignment.

Schulten et al.[161] have used high resolution FIMS in a study of bacterial pyrolysis products. They obtained about 200 lines on a photoplate. Without additional information, the system could not separate isomers and provided only elemental analysis. Additional information regarding the structures was obtained from metastables. Migahed et al.[162] also used metastable peaks to distinguish between the FI spectra in their study of the acetylpyridine isomers.

The application of FIMS has not been limited to the study of volatile compounds. Colby and Evans[163] have demonstrated that analytically useful information can be obtained when a strong electrostatic field interacts with a conducting liquid meniscus. Liquid metals are introduced into the ion source through hollow needles. Spectra for a GaInSn alloy and Cerrolow, a quinternary alloy, are given in their paper.

In spite of the progress made in the application of FIMS and the fact that several mass spectrometer manufacturers are supplying field ionization sources, field ionization has not come into routine use in analytical laboratories. On a routine basis, the time-consuming problem of emitter conditioning and sensitivity calibration has impeded the general acceptance of the technique.

VI. FIELD DESORPTION MASS SPECTROMETRY

In general, in electron impact, chemical ionization, and field ionization mass spectrometry, the sample must be introduced into the ion source as a gas. In the case of molecules which are difficult to volatilize, this may require sufficient thermal energy to cause excessive fragmentation and result in the absence of a molecular ion. This difficulty is overcome by FDMS, in which the sample is applied to an electrode by treating the electrode with a solution of the sample. Sample sizes are in the order of 10^{-8} g. The technique offers great promise to workers who wish to analyze sugars, carbohydrates, glycosides, nucleosides, and peptides.

The technology of FDMS follows closely that of FIMS with regard to electrode design and sensitization. Schulten and Beckey[164] have reported that the microneedles on the electrodes have a much higher stability when they are formed by high temperature activation. Under these conditions, spectra can be taken without the destruction of the microneedles. FD spectra are presented for a number of substances as a function of temperature. Sodium acetate with the emitter temperature at 300°C gives only an Na^+ ion. At 500°C, it gives a complex ion $CH_3\text{-}C^{+}\!\!\begin{smallmatrix}ONa\\ONa\end{smallmatrix}$ at *m/e* 105, a quasi-molecular ion $[M + 1]^+$ at *m/e* 83, and the fragments: $[NaO]^+$ at *m/e* 39, $[CH_3\text{-}C{\equiv}O]^+$ at *m/e* 43, and $[CH_3COOH]^+$ at *m/e* 60. At temperatures above 500°C, the peaks at masses 83 and 105 disappear, and peaks at masses 28, $[CO]^+$ and 15, $[CH_3]^+$ appear. These peaks are undoubtedly due to the pyrolysis of the sodium acetate at these elevated temperatures. It seems reasonable to assume that FDMS can be applied to other organic acid salts. EI and FI spectra of perfluorokerosine and perfluorotributylamine are compared; the FI spectra give peaks to higher masses, and the high mass peaks are of greater intensity. Thus, these substances are useful in identifying high mass FD spectra.

For certain types of samples, an indirect heating of the anode by IR radiation[165] gives reduced

molecular fragmentation and more intense molecular ions or protonated molecular ions at a lower anode temperature than direct heating of the anode. Barofsky and Barofsky[166] report that initiating activation with benzonitrile is more reliable when the wire emitter surface is roughened under controlled conditions by alternate oxidation and reduction in a hydrogen/hydrogen-water atmosphere.

FDMS has been studied with a quadrupole mass analyzer.[167] The quadrupole mass analyzer has the advantage of a rapid scan rate, which is important since the sample duration is between several seconds and several minutes. It also has the capability of accommodating an energy spread of 10 eV, thus permitting the use of activated anodes with an energy distribution of half-width 2 to 4 eV. Schulten and Beckey[168] have used a modified CEC 21-110B for FDMS work. The instrument was equipped with a micromanipulator for positioning the emitters, and the authors were able to study the components of nucleic acids at a resolution of 15,000 to 25,000.

VII. PHOTOIONIZATION MASS SPECTROMETRY

Photoionization methods in mass spectrometry have been used mainly in appearance potential and ion-molecule studies. In appearance potential work,[168a] a photon beam in conjunction with a monochromator permits irradiation of the sample by an almost monoenergetic beam. This leads to an ionization efficiency curve whose fine structure can be determined. In ion-molecule studies,[168b] a wavelength of very small energy spread can be selected to produce the primary ion for the reaction. Since the wavelength can be selected to prevent fragmentation of the primary ion, identification of the products is vastly simplified.

For analytical applications the main advantage of photoionization is in the study of compounds that are unstable and undergo pyrolysis in a hot filament type source. Beynon et al.[168c] have designed a windowless photon source consisting of an open-ended capillary which directs the radiation into the ionization chamber for use on the line-of-sight inlet port of the MS 9. A stream of gas is passed through the capillary, a DC source activates the discharge, and the pressure in the ionization region is kept low by differential pumping. Hydrogen, helium, and neon were found to give the most intense photoion beam under the discharge conditions used. Total ion production is roughly in the ratio H:Ne:He = 15:4:1. In the mass spectrum of fluothane, the hydrogen discharge gives a pattern of an intensity comparable to a 10-μA beam of 21-eV electrons. The photoion spectrum, however, has a more intense parent ion and shows less fragmentation.

VIII. MASS SPECTROMETER SURFACE ANALYSIS

Spark source mass spectrometry is the preferred method for the bulk analysis of solids. An effort is usually made to remove the surface layers of the sample, which may not be representative of the bulk sample, before the spectra are recorded. When the analysis of the surface layer is desired, one of the methods of secondary ion mass spectrometry must be used. In SIMS, ionization of the surface layer is achieved by bombardment with a beam of ions that have been accelerated to energies between 2 and 20 keV. This bombardment causes the emission of photons, electrons, neutral atoms, and positive and negative ions from the sample target. The emitted ions are analyzed by a mass selector in order to obtain the composition at or near the surface. Either a single selected mass, a portion of the spectrum, or the whole mass spectrum can be monitored. Several variations in the technique of SIMS exist depending on the information desired and the instrumentation used. The mass analysis is accomplished by either quadrupole, single focusing, or double focusing mass spectrometers.

A chemical and isotopic analysis of the monolayer can be made by using a primary ion current density so low that there is no destruction of the first layer of the solid.[169] Currents of 10^{-9} A-cm^{-2} are used for the bombardment; however, to obtain sufficient signal for measurement, a target area of 0.1 cm^2 is required. An ultra high vacuum is also required to reduce continuing contamination of the surface by residual gases. Sensitivity is in the ppm range, and the detection limit is 10^{-6} of a monolayer for many species. SIMS is the only surface analysis technique with which isotope analysis and the analysis of carbon and hydrogen compounds can be obtained.

The low intensity bombardment of the surface allows time dependence studies to be made on the sample. Sputtering rates can be kept low enough

that 10^{-4} of a monolayer can be examined and the depth that anion complexes exist can be determined. The technique is valuable in the study of surface reactions and catalysis problems.

The use of a more intense beam of primary ions permits the study of concentration profiles in a diameter of 300 μm.[170,171]

The ion microprobe mass spectrometers[170] are analogous to the electron microprobes. A finely focused beam of primary ions of argon, nitrogen, or oxygen of high intensity and focused to 1 μm bombards the sample, and the secondary ions are conducted into a double focusing mass spectrometer. The primary ion beam is formed in a high intensity duoplasmatron source. A refinement of the ion microprobe technique is to mass select the primary beam so that the bombarding ions consist of only one species, thus eliminating ions formed from impurities in the gas and background species in the vacuum system.

During the examination of the surface, the primary ion beam of 1 to 2 μm is moved across a sample surface about 300 μm in diameter in much the same way as the beam in a TV tube, and a magnified image of a single element is produced. By repetition of the process, successive images give a three-dimensional characterization of the sample. Scanning in the positive or negative mode is possible.

In the direct imaging mass analyzer of Castaing and Slodzian,[172,173] an area of 10 to 300 μm is bombarded with a beam of primary ions (Ar^+, H^+, etc.) with an energy of 10 keV. The secondary ions are focused by an electrostatic lens through a magnetic analyzer, reflected by an electrostatic mirror, and then focused through a second magnetic analyzer. The ion image is converted to an electron image which can then be recorded in a number of ways. The system gives both mass and energy analysis and also image magnification. The lens system simultaneously acquires all the points in the secondary ion image. By constant bombardment of the surface in the direct imaging technique, surface agitation is produced which prevents reaction of the surface with the residual gas in the system. This is an advantage over the scanning ion microprobe technique in which material is removed from only one spot during imaging and the remaining area may react with residual gases.

The atom probe field ion microscope, developed by Müller,[174] is a combination of a field ion microscope and a mass spectrometer of single atom detection sensitivity. With this instrument, an atomically resolved image of the sample specimen is obtained. The surface area that is to be analyzed is lined up with the tip and the probe hole in the image screen. As the voltage for imaging the tip is increased, the particle leaves the surface by field evaporation and is mass analyzed in a time of flight or magnetic deflection mass spectrometer.

Several papers have recently appeared on the conversion of the RGA quadrupole mass spectrometer for use in secondary ion studies.[175-177] When using a quadrupole mass spectrometer in secondary ion studies, it is necessary to suppress the neutrals and high energy sputtered or backscattered ions which would produce a high background noise. The ion energies are selected by an electrostatic analyzer so that they are in the 4-eV range. Thomas and de Kluizenaar[176] present composition profiles of aluminum and stainless steel, and Schubert and Tracy[177] present an analysis of Ga-As and a depth profile study of thin films of $Al_xGa_{1-x}As$.

Šroubek[178] has described a simple method of focusing and filtering secondary ions. The sample is positioned in an off-axis configuration with respect to the quadrupole mass filter. The positive ions that are deflected onto the entrance slit of the mass spectrometer are determined by the bias on a simple deflector plate. The off-axis positioning of the sample has the additional advantage of preventing nonfilterable particles from reaching the electron multiplier.

Zwangobani and MacDonald[179] have built a secondary ion mass spectrometer incorporating an oscillating electron beam ionizer with high ionization and extraction efficiencies around a quadrupole mass analyzer. Analysis of secondary ions and neutrals can be carried out for studies of sputtering and radiation damage.

Rüdenauer[180] has compared quadrupole and magnetic mass spectrometers for secondary ion studies. The quadrupole is simpler to operate, has a linear mass scale and fast switching capability, and is in general lower priced, undoubtedly a compelling reason for its use in the homemade SIMSs listed above. The double focusing mass spectrometer with a carefully matched secondary ion source can detect bulk elements in the 10^{-2}-ppb region and has the advantage of high resolution which is valuable in separating inorganic

ions from hydrocarbon and background peaks. Furthermore, the peak matching capability of the double focusing instrument is useful in identifying molecular ion clusters sputtered from the sample surface. To take advantage of the quadrupole, it is necessary to design an energy analyzer that is matched to the energy spread acceptable by the mass spectrometer. The sensitivity of a 10-cm quadrupole decreases from 1 ppb for the lighter elements to 1 ppm for the heavier elements, whereas the sensitivity of a magnetic instrument is 1 ppb and is independent of mass.

Barrington et al.[181] have described an ion microprobe mass spectrometer in which secondary ions are focused into a double focusing mass spectrometer. A comparison is made of the analysis of a graphite and a platinum sample by the ion microprobe, spark source, neutron activation, and emission spectroscopy. The mass spectrometer methods give the highest sensitivity, but the various methods are quite divergent in the analytical results obtained.

The quantitative analysis of C, N, and O in tantalum films sputtered on glass has been studied by Morabito[182] using Auger electron spectroscopy and secondary ion mass spectrometry. The calibration was carried out on standards with electron microprobe analysis which provided quantitative information about the C, N, and O in the tantalum above the 5-atom % level. Extrapolation of the SIMS data indicated that detection limits for oxygen and carbon were in the ppm range and for nitrogen in the 0.1% range.

The theoretical study of the surface ionization process has received considerable attention. Schroeer[183-185] has proposed a model for the ionization process by inert gas ions which is applicable to the sputtering of metals that are either clean or covered with, at most, one layer of adsorbed gases. The model assumes that the sputtered atoms leave the surface initially as neutral atoms and are then ionized by quantum mechanical transitions of the atoms' valence electrons to the top of the conduction band of the metal. Defining S^+ as the ratio of the number of sputtered ions to the number of bombarding ions and S as the ratio of the number of sputtered atoms to the number of bombarding ions, the $R = S^+/S$ = the probability of ionization. The theory leads to the value for $R = (A/\Delta E)^2 (\hbar v/a\Delta E)^n$. $\Delta E = I - \phi$ where I is the ionization energy of the sputtered atom, ϕ is the work function of the surface, v is the average velocity after sputtering, A is the surface binding energy before sputtering (= sublimation energy), and a is the thickness of the surface. For pure metals, using a = 1.4Å, n = 2.5, and values of S derived from the literature, the equation yields values of R within a factor of 3 of the experimentally determined values. The model has been extended to a metal with varying concentrations of impurities. The analyst measures Y^+, the apparent sputtering yield, and $Y^+ = C_i R S_m$ where C_i is the concentration of the impurity and S_m is the sputtering yield of the major metal, i.e., the matrix. In this case, the value of R takes the form

$$R = \left[\frac{A_i + A_m}{2(I_i - \phi_m)}\right]^2 \left[\frac{\hbar v_m 2m_m}{(m_m + m_i)(I_i - \phi_m)a}\right]^n \qquad (7)$$

where the symbols retain the meanings defined above; the subscript m refers to the matrix, the subscript i to the impurity, m_m refers to the mass of the matrix atom, and m_i refers to the mass of the impurity atom. The model was tested by sputtering Fe with known concentrations of varying impurities (0.01 to 10% of Mo, Ni, Cu, C, Mn, and Cr). Using the same values for n and a as above, agreement within a factor of 5 (except 8 for C) was obtained between the calculated values and the known concentrations. Šroubek[186] has also arrived at a similar expression for R in which he includes a continuum of states below the Fermi level. The consideration of level crossings leads to a square root dependence of R on the velocity of the sputtered atoms. The calculated values by this treatment are in closer agreement to experimental values than those obtained by Schroeer's equation.

A very satisfactory theoretical treatment, based on thermodynamics, which gives excellent checks with standard samples bombarded with reactive ions has been presented by Andersen and Hinthorne.[187] The theory is based on a thermal equilibrium model of the sputtering ion region. The relative number of positive, negative, and neutral atoms and oxide molecules – that is, the total number of atoms of the element M – is given by: $n_M = n_{M^+} + n_{M^-} + n_{M^0} + n_{MO} + n_{MO_2}$. The concentrations of the varying species are calculated by using the Saha-Eggert ionization equation. All the terms in the equation are available in the literature, and the effective temperature and electron density are obtained by the use of standard

samples. A computer program has been devised such that if the temperature and electron density are given and the singly charged positive ion intensities of all the elements observed in the mass spectrum are entered, the corrected analysis of the sputtering region is obtained. Results are given for a range of materials – insulators, semiconductors, and metals – and the reported results are quite impressive. The major and minor elements are generally within 10% relative error of the analyses determined by wet chemical techniques. It is suggested that as a minimum, the method should give analyses within a factor of two for any trace element in any matrix with a minimum knowledge of the sample. Tables of data are given for the analysis of minerals, alloys, and gasses.

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