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SPECIAL FEATURE: PERSPECTIVE

Elemental Analysis by Inductively Coupled Plasma Mass Spectrometry with Sector Field Instruments: a Progress Report

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Inductively coupled plasma mass spectrometry (ICP-MS) for elemental analysis has been dominated since its introduction by instruments with quadrupole filters for mass separation. Although considerably impeded by isobaric ion interferences, ICP-MS with quadrupoles has nevertheless matured to become the most prominent MS technique for element analysis with widespread applications, providing extremely low detection limits in combination with true multi-element capabilities. Some years ago, a second generation of double-focusing ICP-MS instruments was introduced, offering the chance to overcome interference problems by high mass resolution. The special features of these instruments for elemental analysis are discussed and the progress achieved in analytical performance is demonstrated by selected examples, emphasizing speciation as a field in which organic and inorganic aspects come close together. © **1998 John Wiley & Sons Ltd.**

KEYWORDS: elemental analysis; inductively coupled plasma mass spectrometry; sector field; quadrupole

INTRODUCTION

Elemental analysis today

With the rapidly increasing industrial development in the second half of this century, elemental analysis has received more attention and the responsibility for securing high quality standards for industrial products in particular as well as for quality of life in general. The main driving force in this development is the continuously increasing demand for quantitation with lower detection limits, down to previously inaccessible levels in both trace analysis and micro analysis. On the one hand this requirement arose from the general experience, mainly in material sciences, that physical properties may be changed drastically by extremely low concentrations of certain elements in many matrices of technical interest. Therefore, elemental analysis gained a significant role in research and development as well as in support of manufacturing in the branches of industry concerned. With the increasing social awareness of the problems, risks and hazards connected with new materials, fabrication processes and products, inorganic analytical chemistry on the other hand began to play a major role in risk assessment and environmental control. Thus elemental analysis is now simultaneously applied for technical innovation and development of new products as well as for control of their risks and consequences.

In real applications the most challenging requirements for analytical detection power arise in the semiconductor industry and refer not only to metal and semiconductor starting materials but even more to the chemicals applied in the fabrication processes for etching, rinsing, etc. A special problem in this field is the determination of Ra, Th and U, which may be deleterious for electronic circuits by inducing soft errors due to α-radiation.

The analytical determination of radioactive elements, as just mentioned, is an intriguing special task, because their presence in nuclear waste of any kind is of great environmental significance, even at very low concentrations. Here we are leaving general trace element determination for quality control and crossing over to environmental risks. In this field, elemental analysis is an indispensable requirement in many applications such as pollution studies for water, soil and air. The medical interest in trace element studies, concerning both toxic trace elements and the essential elements, is obvious. Striking examples are the investigations of the consequences of the increasing environmental pollution by Pt from automotive exhaust catalysts, medical waste from cancer therapy and artificial fertilizers in agriculture.

The determination of Pt in environmental samples is challenging owing to the low concentrations involved, and is further aggravated by the requirement for speciation, because the real environmental risks can only be estimated when taking into account the bioavailability

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of the different species in which the element may be present. In the speciation of organic compounds—a really demanding task with a very wide field of applications—the frontiers between inorganic and organic analysis are increasingly becoming obliterated, because coupling of element detection with chromatographic separation of the molecular species involved may lead to registration of analytical signals with respect to selected elements for inorganic species and for organics, at least when real samples are under investigation.

The demand for lower detection limits has stimulated the development of many techniques for elemental analysis, among which electrochemistry without doubt excels as far as detection limits are concerned. Lower detection limits, however, lead, more or less unintentionally, to the consequence of further intricacy owing to an increase in the number of elements that have to be considered. This in turn leads to increased interest in analytical techniques that permit true multi-element analysis while simultaneously retaining the maximum detection power. This special demand can be satisfied by instrumental techniques, among which mass spectrometry (MS), after a long period of stagnation, has now become a widespread high-performance tool.

Development of elemental MS

The long predominance of atomic emission spectrometry (AES) over MS in elemental analysis was due to the formerly unsolved basic dilemma in elemental MS. On the one hand the method has unique advantages: in comparison with AES the mass spectra exhibit only a limited number of lines, which can easily be identified and contain relevant analytical information on all elements which may be constituents of the sample under investigation. On the other hand, there is the problem of ablation from the sample of material representative of the composition of the sample and of transforming the ablated material into an ion beam which can be mass separated and detected by a mass spectrometer. For volatile organic materials, this is usually not a problem: evaporation with subsequent electron ionization with low energies is in most cases sufficient and can easily be performed by simple means. In contrast to organic substrates, however, this is a difficult obstacle to overcome for most inorganic solids, in particular metals, for which the relevant thermodynamic properties are much more demanding as far as the development of suitable ionization sources is concerned.

Basically there are two different approaches for the generation of the required ion beam. The straightforward approach is its direct production from a solid sample by means of electric discharges, sputtering by surface bombardment or any other means involving electrical, thermal and mechanical processes in a more or less complex interaction which still eludes any satisfactory theoretical description of the frequency distribution of the ionization states involved. Hence absolute quantitation is unsatisfactory and can only be performed by using sensitivity factors derived from appropriate standards, which in many cases are not available. The alternative approach corresponds in some way to the famous Gordian knot: the solid sample is disintegrated by solution, but at the severe risk of introducing contamination from the chemicals used in the necessary steps which may include digestion and extraction. During the stagnation phase of elemental MS, there was no suitable ionization technique available for solid or liquid analysis, except the sophisticated technique of thermal ionization which, however, is restricted to a minority of elements.

Any consideration of the preferred approach in an analytical task has to take into account also the question of quantitation. Solution analysis offers the advantage of external calibration by means of standards as well as by standard addition techniques. Additionally, solution avoids the problem of local inhomogeneities which are always crucial in direct analysis of solids. External calibration by standards is much more demanding for the analysis of solids, because the complex interactions in the atomization and ion formation processes mean that standards must be similar to the sample under investigation in physical and crystallographic properties and surface structure as well as chemical composition. The latter is a general problem for solids, in particular when concentrations down to the ultratrace level must be determined, but not so for solutions.

The duality of the approaches of direct solid analysis or solution analysis as just discussed is reflected in developments since the early 1980s, when a renaissance of MS in elemental analysis occurred. New ion source techniques were introduced: (i) glow discharge mass spectrometry (GDMS) for direct bulk analysis and additionally for surface and depth analysis in the μm region, (ii) sputtered neutral mass spectrometry (SNMS) for direct surface and depth analysis in the nm region and (iii) inductively coupled plasma mass spectrometry (ICP-MS), a procedure which uses the alternative of solution analysis. The last method has meanwhile found widespread application, not only in the field of solution analysis but also for the direct analysis of solids by micro-sampling with laser ablation.

The development of GDMS and ICP-MS, although proceeding in parallel, showed a remarkable difference. The first commercial instruments in the field of GDMS were double-focusing devices based on magnetic sector field mass analyzers, whereas the regime of ICP-MS was dominated for a long time by low-resolution instruments which used quadrupole filters for mass analysis (the acronym ICP-QMS will be used henceforth whenever the discussion is restricted to ICP-MS with quadrupole filters as mass analyzers; correspondingly, the acronym ICP-SFMS will be used when sector field instruments are intended). Of course, from the beginning there were the idea, expectation and hope for an ICP-MS instrument with high mass resolution in a reasonable price range not too far above that of the quadrupole instruments. However, neglecting instruments of a first generation in a nearly exclusive price class, it took until the mid-1990s for the second generation of commercial high mass resolution ICP-MS instruments, specifically designed for elemental MS, to appear. This development provided a new, strong impetus to the application of ICP-MS, and the consequences will be

outlined in this paper after a short survey of some important aspects of conventional ICP-QMS from an analytical point of view, but neglecting the physical details.

ANALYTICAL QUADRUPOLE ICP-MS: AN ASSESSMENT

Instrumentation

In the inductively coupled plasma (ICP) as used for excitation in AES and for ionization in MS, an electrical flame, the plasma, is produced by inductive coupling of high-frequency energy to a working gas flow, usually argon. An aerosol of a nebulized analyte solution is injected into the center of the plasma where the aerosol droplets are vaporized and ionized. The plasma is operated at atmospheric pressure; however, for mass separation by electromagnetic forces it is, of course, necessary to increase the mean free path lengths of the ions up to the geometrical dimensions of the housing, which means that the pressure must be reduced to high vacuum conditions. This is achieved by differential pumping in an interface region as illustrated in Fig. 1. In the first stage of the interface, ions are sampled from the plasma flow by an entrance orifice, the so-called 'sampler,' and transferred to the mass analyzer volume by a second orifice, the so-called 'skimmer.' This is the crucial region of the whole system. An increase in the orifice diameter provides higher ion yields but also a higher gas load on the pumping system; smaller diameters, on the other hand, reduce the demands for the pumping system, but only at the price of lower ion yields while simultaneously increasing the risk of influences from cool boundary layers around the aperture on the composition of the plasma and the resulting ion species. Further problems in the interface include the risk of secondary discharges, ablation of the orifice materials and clogging of the sampler or skimmer by salt or carbon deposits. A certain problem area in the QMS arrangement is also the ion optical system. This lens system usually includes a Bessel box with center beam stop which is employed for energy filtering and also serves to shield the detection system from photons and high-energy particles, while shaping the ion beam for optimum acceptance by the subsequent quadrupole filter. In most cases analog and digital detection by a Faraday collector and an electron multiplier device, respectively, are provided, which in combination provide a dynamic range of about nine orders of magnitude for detection.

Nebulization

A special part of the ICP-MS instrument is the nebulization system, which is required to produce an aerosol from the analyte solution for sample introduction into the ICP. In order to permit maximum atomization efficiency and minimum loss by droplets which are too large to be vapourized completely, the size distribution should be restricted to droplet diameters less than (about) 5 μm. Pneumatic nebulizers are standard and occur in many varieties, among which the Meinhard type is probably the most prominent. However, it suffers from a low overall efficiency of about 1–2% for a typical sample uptake rate of 1 ml min^{-1}, so much

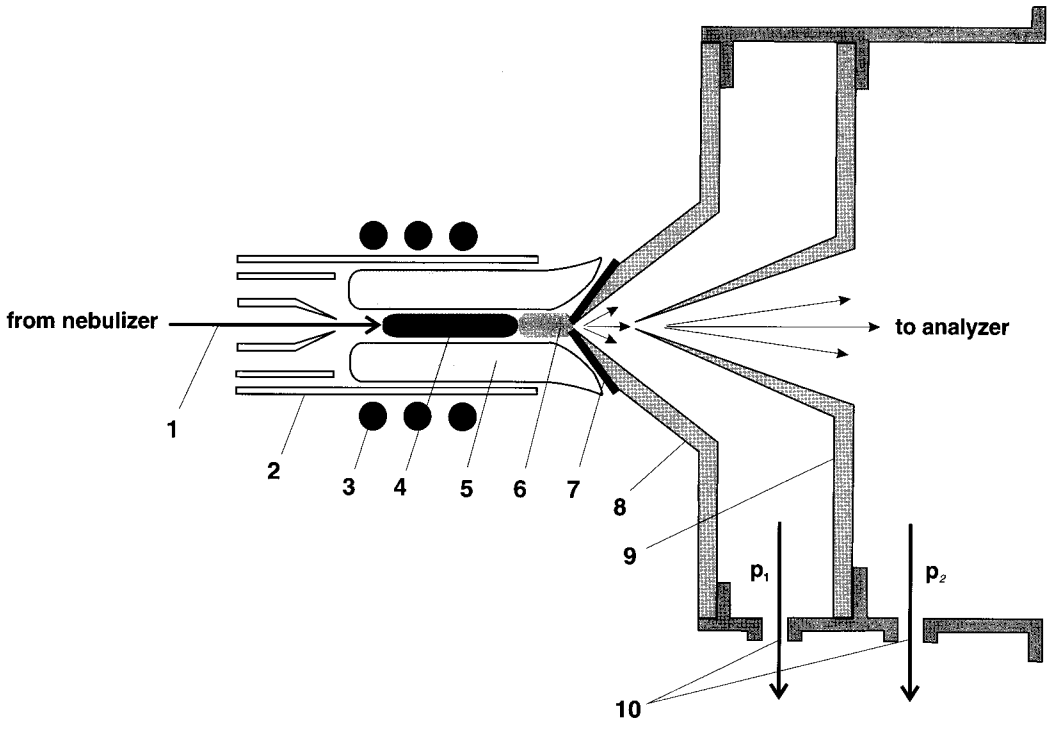

Figure 1. Schematic illustration of the plasma and interface region. 1 = Aerosol; 2 = plasma torch; 3 = induction coil; 4 = vaporization region; 5 = induction region; 6 = ionization region; 7 = boundary layer; 8 = sampler orifice; 9 = skimmer orifice; 10 = differential pumping.

research effort has been aimed at high-efficiency, low-cost devices which maximize sensitivity and power of detection. Among different high-efficiency nebulization techniques, ultrasonic nebulization (USN)[1] and hydraulic high-pressure nebulization (HHPN)[2] excel in performance. As an additional advantage, HHPN is more tolerant of a high salt load or high analyte viscosity. However, the high water load to the plasma often leads to the additional requirement for a desolvation system which combines heating and cooling stages for reduction of the solvent load. The higher efficiency of these nebulization systems is, of course, an advantage that improves sensitivity and detection limits by more than an order of magnitude for a majority of elements, so that the choice of the nebulizer system strongly influences the final performance of the analytical procedure.

Interferences

The basic problem in elemental MS is not only production of an ion beam which represents the composition of the sample but also ensuring that the recorded spectrum represents, as far as possible, nothing else but the sample under investigation. The appearance of any contamination from the sample preparation, in particular chemical pretreatment, or from residual gases and products of any plasma reactions may be deleterious for the reliability of an analytical procedure and the accuracy of its results. This is valid for direct analysis of solids by GDMS and for solution analysis by ICP-MS, but is of considerably greater significance in solution analysis owing to higher risks during the more comprehensive sample preparation. Furthermore, source operation in the open atmosphere may lead to a greater variety of spectroscopic interferences. We can, of course, never totally get rid of these interferences; therefore, care is always required in order to avoid misinterpretation and erroneous results.

Strictly, 'spectroscopic interference' means the coincidence of contributions from different species in one signal, which is to say in one unresolved spectral line in the case of MS. In ICP-QMS we are dealing with instruments that usually exhibit unit resolution. Therefore, it has become common practice to speak of interferences more generally in the case of different species with the same nominal mass, whether or not the signals are resolved in a spectrum.

Spectroscopic interferences may be subdivided into different types. First we have the isobaric interferences from atoms with a different number of protons but the same total of nucleons. This is not too great an impediment, because for all elements, except In, there is at least one isotope free of any isobaric interference. In most cases, however, this will not be the isotope of the highest abundance, so that the detection limit will be worsened by the selection of a minor isotope. The most annoying example of an isobaric interference is the coincidence of ^{40}Ar and ^{40}Ca. A similar type of quasi-isobaric interference is caused by ions of mass m with multiple (z) charges which appear in the spectrum according to their m/z ratios, with both quadrupoles and magnetic sector fields. A prominent example of this type is the couple $^{28}Si^+$ and $^{56}Fe^{2+}$.

The most significant type of interference, in both number and as in intensity, is caused by a variety of molecular ions. These are hydrides, oxides, etc., molecules of the argide type and clusters of any abundant components including organic species, a particular problem when organic solvents are involved. Recognizing and eliminating these moleculars interferences may become crucial to the success of the analysis. Important examples are, to give only a few, the interference of $^{15}N^{16}O^+$ and $^{14}N^{16}O^1H^+$ with $^{31}P^+$, of $^{40}Ar^{16}O^+$ with $^{56}Fe^+$ and of $^{40}Ar^{35}Cl^+$ with $^{75}As^+$. The appearance of a majority of these molecular interferences not only depends on the sample itself and the working gas of the discharge, but also on the chemicals used in sample pretreatment, in particular the solvents. Table 1 compiles selected examples indicating also possible origins of the constituents. It should be mentioned that mass resolution values in this case are theoretical ones calculated from the mass differences, whereas in practical examples the 10% valley definition is always used.

Finally, it should also be mentioned that highly abundant neighboring signals, mainly caused by the matrix or the working gas of the discharge, may also contribute to a disturbance of the true analytical signal which, particularly with the low-resolution instruments, may become a problem. When operated at low mass resolution, the 'abundance sensitivity' of ICP-SFMS instruments is about an order of magnitude lower than that of ICP-QMS instruments, but can be considerably improved by an increase in the resolution.

The significance of the interference problem varies, of course, with the matrix under investigation. Simple aqueous solutions with low salt loads may be easy to analyze. Analysis of metals after solution by acids has its special problems. Quantitative multi-element analysis of complex materials such as blood or ceramics may lead to a variety of unforeseen interferences. Special attention must also be paid to the interference

Table 1. Some typical interferences in elemental analysis by ICP-MS and the theoretically required resolution

Atomic ion	Molecular ion	Required resolution	Origin
$^{24}Mg^+$	$^{12}C_2^+$	1605	C (including organic)
$^{28}Si^+$	$^{14}N_2$	958	HNO_3
$^{28}Si^+$	$^{12}C^{16}O^+$	1557	C (including organic)
$^{31}P^+$	$^{14}N^{16}O^1H^+$	968	H_2O, Ar
$^{31}P^+$	$^{15}N^{16}O^+$	1458	HNO_3
$^{32}S^+$	$^{16}O_2^+$	1801	H_2O
$^{44}Ca^+$	$^{12}C^{16}O_2^+$	1281	C (including organic)
$^{48}Ti^+$	$^{32}S^{16}O^+$	2519	H_2SO_4
$^{51}V^+$	$^{35}Cl^{16}O^+$	2572	HCl
$^{52}Cr^+$	$^{35}Cl^{16}O^1H^+$	1671	HCl
$^{52}Cr^+$	$^{40}Ar^{12}C^+$	2375	C (including organic), Ar
$^{54}Cr^+$	$^{40}Ar^{14}N^+$	2054	HNO_3, Ar
$^{54}Fe^+$	$^{40}Ar^{14}N^+$	2088	HNO_3, Ar
$^{56}Fe^+$	$^{40}Ar^{16}O^+$	2502	H_2O, Ar
$^{64}Zn^+$	$^{32}S^{16}O_2^+$	1952	H_2SO_4
$^{64}Zn^+$	$^{32}S_2^+$	4264	H_2SO_4
$^{75}As^+$	$^{40}Ar^{35}Cl^+$	7775	HCl, Ar
$^{96}Mo^+$	$^{40}Ar^{56}Fe^+$	13043	Ar

problem when organic compounds are involved as, e.g. in ICP-MS analysis of chromatographic fractions. A typical example of this kind is the interference of $^{40}Ar\,^{12}C^+$ with $^{52}Cr^+$, the latter being the main isotope of an element which is of great interest in the field of element speciation. This example is chosen here to show what spectra recorded by QMS and SFMS look like. Figure 2 shows a mass spectrum obtained by ICP-QMS covering the region in which Cr appears and also a moderate-resolution SFMS spectrum at 52 u that allows the isobaric ions to be separated.

Many attempts have been made to cope with interference problems, as reviewed recently.[3] Mixed gas plasmas were investigated, collision or reaction cells were additionally employed with different gases and more recently the cold plasma approach has found some attraction.[4] However, none of these techniques realizes a general solution to the problem; at most they offer a chance to get rid of several problems from a group of interferences or for selected elements in special cases so that, in conclusion, the interference problem is still the most significant weakness of ICP-QMS.

For reasons of completeness, it should be mentioned that in addition to these spectral interferences, non-spectral interferences, generally addressed as matrix effects, can also be an obstacle for ICP-MS. For example, a concentration of 50 ppm of a heavy element can cause a 10–20% depression of the analytical signal of a light element, and at 1000 ppm the loss of sensitivity may even amount to a factor of 50. This phenomenon, which nowadays is often interpreted in terms of space charge effects in the interface region, results in calibration non-linearities with increasing concentration of major sample constituents.[5] The general experience with such effects can be summarized in the statement that elements of greater mass usually exert stronger influences of this type whereas light elements are usually affected more strongly. A common technique to cope with such non-linearities is internal standardization by selected elements such as Be, Sc, Co, Y, Rh, In, Hf and Bi. Monoisotopic elements not present in the sample are preferable as standards; similarity to the elements of main analytical interest in various properties such as mass, ionization energy and oxide formation is desirable.

In conclusion, the unique combination of advantages of ICP-MS for elemental analysis—extremely low detection limits for (nearly) all elements down to the ppt region and true multi-element capabilities in a quasi-simultaneous procedure—should be recalled. On the basis of permanent 'learning by doing,' the analytical community has learned to live with the above-mentioned deficiencies. The unique combination of advantageous features has had convincing analytical benefits in many fields of application. This success, together with the awareness that considerable improvements can be expected from high-resolution instruments, is the reason why the appearance of such instruments has been awaited for many years.

ANALYTICAL SECTOR FIELD ICP-MS: GENERAL ASPECTS

Enhancement of the mass resolution means reduction of the interference problem, but it cannot be a panacea against spectroscopic interferences in general, because the mass resolution will always be limited. As an example, consider the determination of As in the presence of the nearly inevitable $^{40}Ar\,^{35}Cl^+$ ion as illustrated in Fig. 3. This is probably the most significant example in which a resolution of about 10^4 is required.

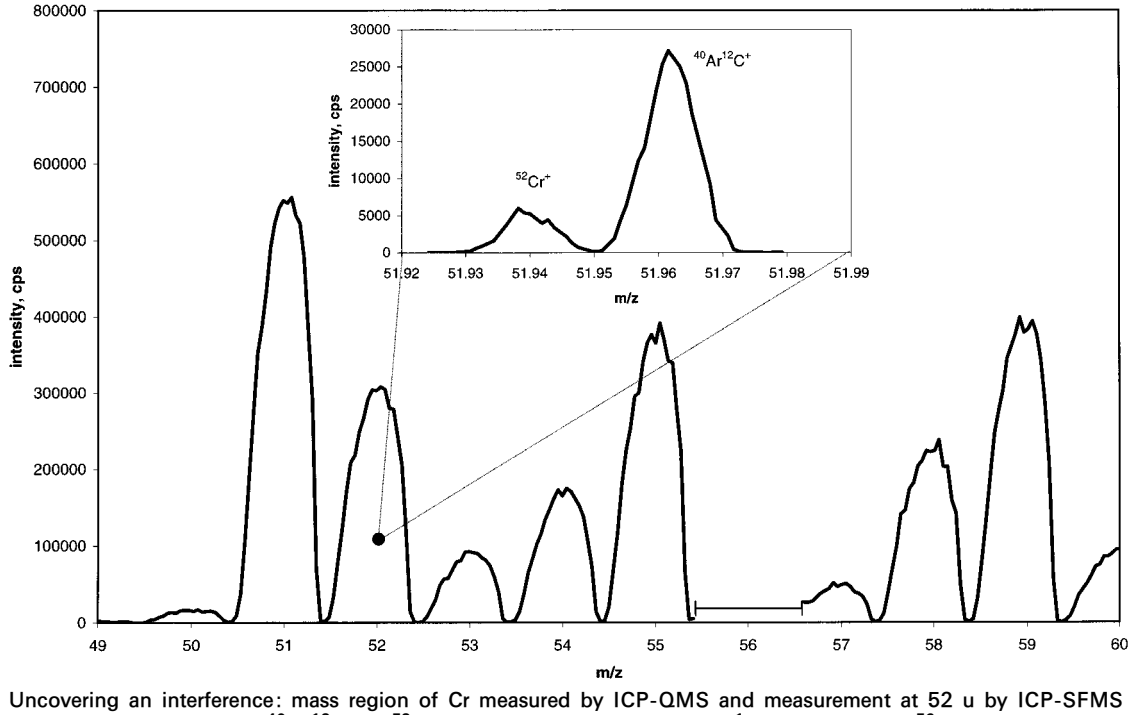

Figure 2. Uncovering an interference: mass region of Cr measured by ICP-QMS and measurement at 52 u by ICP-SFMS ($R = 3000$) showing the strong interference from $^{40}Ar\,^{12}C^+$ to $^{52}Cr^+$ (Cr concentration 0.2 ng ml^{-1}). Registration of ^{56}Fe was suppressed for overload protection.

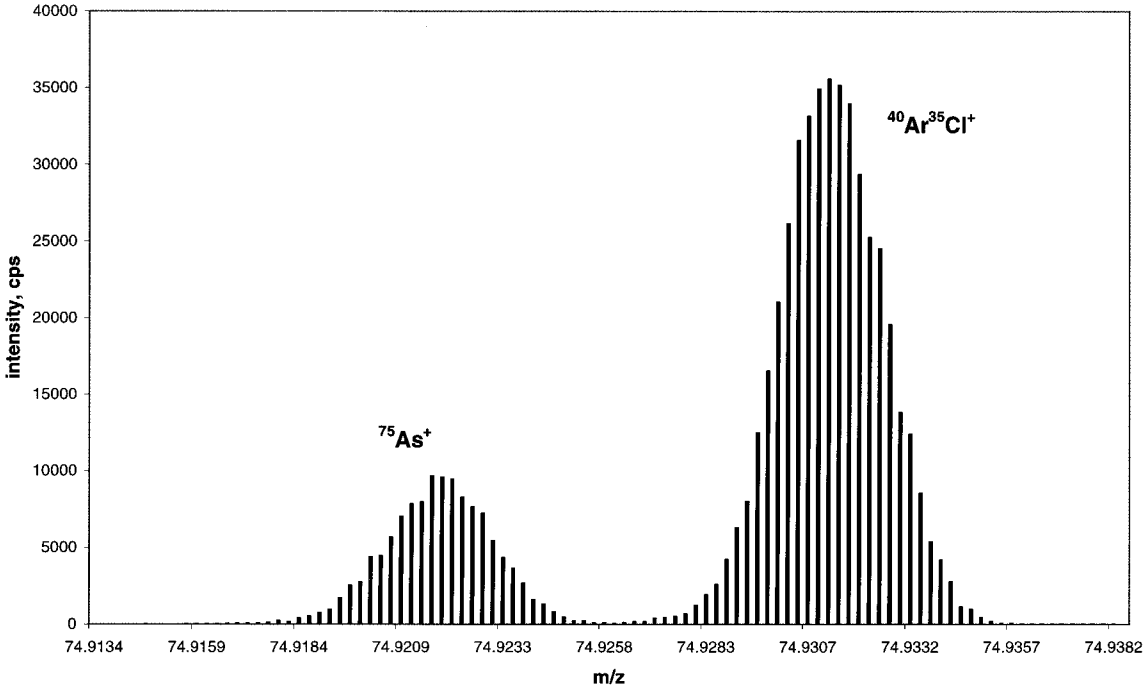

Figure 3. Interference of $^{40}Ar^{35}Cl^+$ with $^{75}As^+$ measured with a resolution $R = 13\,000$, from a determination of 10 ng ml^{-1} As in 1.0% HCl (courtesy of Finnigan MAT, Bremen, Germany).

However, with $R = 10^4$ the separation of $^{40}Ar^{56}Fe^+$ from $^{96}Mo^+$ remains a problem, and there are some cases in which even a resolution of $R = 10^5$ may not help, e.g. the interference of $^{40}Ar^{51}V^+$ with $^{91}Zr^+$. In conclusion, a great majority of the interferences of analytical significance can be overcome by a resolution of $R \geqslant 10^4$.

In performance evaluation we have to take into account a further influential parameter. In practice, an increase in the mass resolution is achieved by a reduction in the widths of beam defining slits, and this in turn leads to a decrease in ion transmission, which for instance amounts to about one order of magnitude when the resolution is increased from 300 to 3000. In spite of the general familiarity with the basic trade-off of mass resolution for ion transmission, its significance for elemental analysis will nevertheless be illustrated here. The example chosen is the interference of $^{40}Ar^{16}O^+$ with $^{56}Fe^+$, the major isotope of this important element. Figure 4 shows ICP-SFMS signals for the region of 56 u recorded with resolution R varying from 300 up to 2500. A small Fe signal can be observed even in the highest resolution scan, but the drastic intensity reduction due to the resolution increase is also obvious. One should be aware that there are other argide interferences also.

Higher mass resolution always has to be paid for by a decrease in sensitivity and detection limits. Hence the

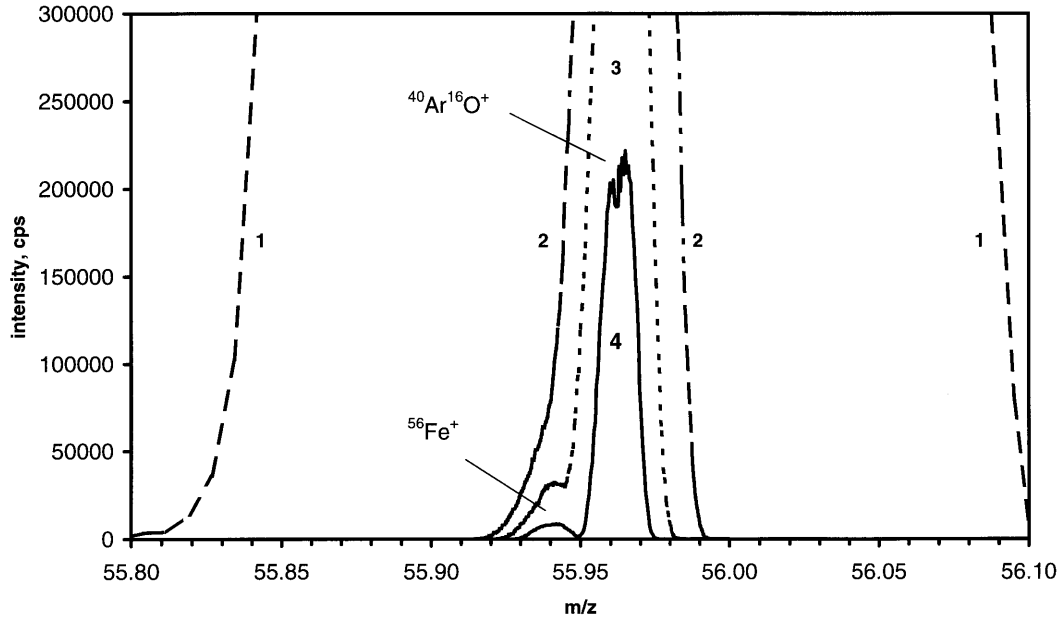

Figure 4. ICP-SFMS measurement of the region of 56 u with varying mass resolution. An Fe concentration of 20 ng ml^{-1} can finally be determined on the low-mass tail of the extremely abundant $^{40}Ar^{16}O^+$ molecule. R = (1) 300; (2) 1500; (3) 2000; (4) 2500.

dilemma arises of whether higher mass resolution or higher ion transmission is of greater priority for an analytical task. Ultimate detection limits can only be realized with low or moderate resolution using sector field instruments, and these instruments are therefore often operated under conditions which come close to ICP-QMS as far as the resolution is concerned. This is the reason why it is generally preferable to characterize ICP-MS with high-resolution instruments as ICP-SFMS (sector field) and not as ICP-HRMS (high resolution).

The technical demands and the economic risks in the development of an instrument specially designed for ICP-SFMS are the reasons why progress was so slow in this field. The Plasmatrace I (VG/Fisons, Winsford, UK), was the only instrument of the first generation, and the introduction of ICP-SFMS with a specifically designed double-focusing MS analyzer as a high-performance extension of the conventional ICP-QMS had to wait until the early 1990s. Four manufacturers now offer a selection of such instruments: the Element (Finnigan MAT, Bremen, Germany), the Plasmatrace II (Micromass, Manchester, UK), the JMS-Plasmax 2 (Jeol USA, Peabody, MA, USA) and the Plasma 54 (VG Elemental, Winsford, UK; Micromass), and two new instruments with improved performance features have been announced: the Axiom (VG Elemental) and the Isoprobe (Micromass). Technical details are beyond the scope of this paper and can be found in the manufacturers' brochures. It should merely be pointed out that the Plasma 54, the Isoprobe and also the Axiom were especially developed for high-precision isotope ratio measurement with a multi-collector system. Furthermore, it may be of interest in this context that only in the Element instrument is the acceleration voltage applied to the analyzer system, so that operation of the ICP and interface is possible without any high-voltage hazards.

Figures of merit

The primary aims of elemental analysis are (i) quantitative determination of the elemental composition of a sample and (ii) calculation of a detection limit which provides an estimate of the upper limit possible when the presence of an element is not established. Elemental concentrations are determined from a calibration line, the slope of which is the sensitivity. Determination of a detection limit involves, in addition, repeated measurement of a blank sample at the spectral position of the analytical signal. Concerning sensitivity, it is an advantage of SFMS that the ion transmission generally does not depend on the mass whereas QMS exhibits an increasing sensitivity loss above 100 u. The sensitivity of ICM-SFMS instruments is in the region of 10^7–10^9 cps per $\mu g\ ml^{-1}$ (cps = counts per second). A sensitivity of 10^8 cps per $\mu g\ ml^{-1}$ has also been achieved with an ICP-QMS instrument of the most recent generation.[6] Generally, however, SFMS instruments are superior when operated at low resolution and are comparable overall to QMS when operated at moderate resolution.

Extremely low background noise below 1 count s^{-1}, which is an order of magnitude lower than with quadrupole instruments, is a further major advantage of ICP-SFMS instruments. This generally offers the chance to achieve detection limits below 1 pg ml^{-1}, but which in many practical applications cannot be realized owing to too high blank values. A typical example is the appearance of a high blank value for Ni, which is inevitable when the interface cones are made of this metal. The use of Pt cones is a frequently applied alternative. In conclusion, the higher transmission and lower background of SFMS permit an improvement in the detection limits for low-resolution operation that may amount to up to three orders of magnitude in comparison with QMS as long as blank values do not prohibit this.

Precision is particularly relevant for isotope ratio measurement. The most important limiting factors arise from fluctuations in aerosol generation, nebulization and plasma instabilities. These effects can only be be overcome with real simultaneous operation in multi-collector arrangements. The limitations due to source noise, however, remain the most serious.

APPLICATIONS

Reduction of interferences

Basically, two types of applications may be discerned that suffer severely from interferences. In the analysis of pure and ultrapure metals, in particular as starting materials for 'high-tech' products, the analytical performance is limited for a variety of elements by spectral overlap at least for the most abundant isotope of the element in question. This is particularly valid for the semiconductor industry. On the other hand, in complex matrices, the wide variety of components may give rise to unforeseen interferences as a source of systematic errors; typical cases of this type are, for instance, the analysis of sea water, serum or urine and also of ceramics of refractory oxide mixtures.

For steel analysis, ICP-MS offers a particular chance to analyze non-metallic elements such as P and S together with the metal components. These elements can have a strong influence to the properties of steel even at low concentration levels ($\mu g\ g^{-1}$). Owing to intense interferences, detection limits are poor in QMS. With SFMS, however, detection limits for the solid in the $ng\ g^{-1}$ range are generally achieved. Even for phosphorus, which is not a desired element in steel, the concentration has to be determined according to increasing quality demands down to the low $ng\ g^{-1}$ range. The determination of P by ICP-MS requires a resolution of about 1500 owing to interferences from $^{15}N\,^{16}O^+$ and $^{14}N\,^{16}O^1H$, as demonstrated in Fig. 5. In comparison with the conventional determination of P by absorption spectrophotometry, which is laborious and time consuming, the determination by ICP-SFMS is a fast, multi-element alternative, as has been shown in recent work.[7]

In a study concerning the analysis of high-purity standard reference metals (Cd, Cu, Ga, Zn), mean detection limits of about 15 pg ml^{-1} were obtained for 30 elements; the corresponding mean value for the solids was 3.5 $ng\ g^{-1}$.[8] An interesting finding was the observation of a matrix-induced interference, which in

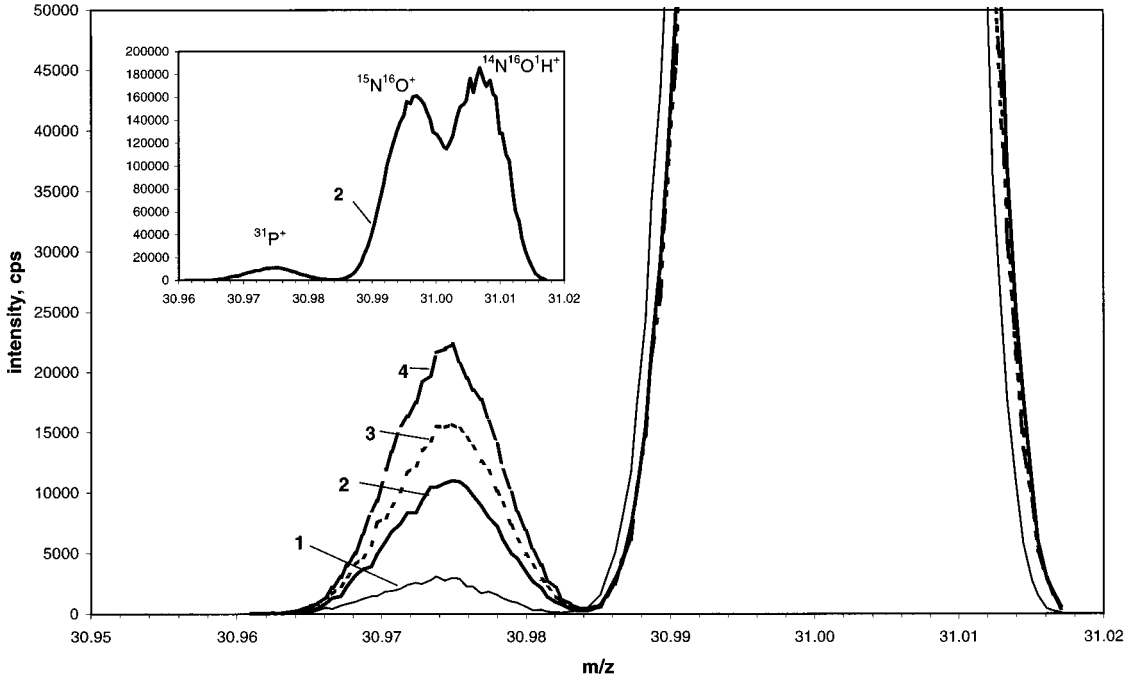

Figure 5. Determination of ^{31}P in the presence of abundant interferences using ICP-SFMS with standard addition for calibration. $R = 2100$ (inset). 1 = Blank; 2 = sample; 3 = sample + 1.63 ng ml^{-1}; 4 = sample + 3.26 ng ml^{-1}.

ICP-QMS would have resulted in a matrix effect. The isotope concerned was $^{151}Eu^+$, for which an interference from $^{40}Ar^{111}Cd^+$ became apparent with Cd as matrix. This demonstrates that ICP-SFMS is a useful tool for securing accuracy, as in particular required in the analysis of standard reference materials, by the elucidation of contributions from interferences, even if unforeseen.

Human serum, as well as whole blood, urine and tissue, represents the type of complex matrix for which analysis by ICP-QMS suffers from more interferences than usual. In addition to the contributions from more common species such as argides and oxides, the presence of a variety of elements in serum (C, Na, P, S, Cl, K, Ca) gives rise to many unusual interferences, and the apparent concentration, i.e. the element concentration corresponding to the signal intensity of the interferent, of these species can be as high as the μg ml^{-1} level. It has been shown that for some important trace elements (e.g. Fe, Cu, Zn), a reliable determination in their typical concentration range is nevertheless possible, whereas an accurate determination with ICP-QMS is more or less impossible for others (Ti, V, Cr, Ni).[9]

Really difficult examples of complex matrices are ceramics, soils and rocks. Digestion of such samples usually requires a mixture of acids, so that the risk of interferences from contamination is multiplied according to the number of components. To consider one case in more detail, the signal of $^{48}Ti^+$ often suffers considerably from the interference of $^{32}S^{16}O^+$ owing to the application of H_2SO_4 in the mixture used for digestion of powdered materials such as SiC, whereas the minor abundant isotopes of Ti are also more or less obscured. Figure 6 shows results from the calibration for Ti in 2.5% H_2SO_4 solution. With respect to the mass difference, a resolution of 2518 should be sufficient for signal separation; in practice, however, a resolution of nearly 5000 is required, owing to the high abundance of the interfering molecular ion.

Ultimate detection limits

The performance of ICP-SFMS in recent work on the determination of Pd and Pt in urine illustrates its application to environmental effects of automotive catalyst exhaust.[10] A detection limit of about 0.05 pg ml^{-1} could be obtained, which is comparable to those of an extremely sensitive adsorptive voltammetric procedure and definitely below the results obtained with any other technique. Further improvement may be achieved by even more careful control of blanks and removal of interferences by using suitable sample preparation techniques. Based on this work, the authors recommend the application of the standard addition procedure for quantitation in order to correct for non-spectroscopic interferences associated with high matrix concentrations.

The excellent performance of ICP-SFMS as a multielement technique becomes particulary obvious in purity analysis of the type required in the semiconductor industry. Recently a comparative study of the determination of ultratrace components in GaAs has shown that solution analysis by ICP-SFMS permits detection limits for the solid in the low ng g^{-1} range. This value is as good as in GDMS, the alternative direct technique, in spite of the dilution in the liquid analyte.[11] This result, however, could only be achieved by demanding efforts to avoid contamination. A further example of a typical application in this field has already been presented in Fig. 3. In this case, the analytical task was the determination of 10 ng ml^{-1} of As in 1.0% HCl. It may be estimated from Fig. 3 that detection limits in the sub-ppb region could be realized. The most impor-

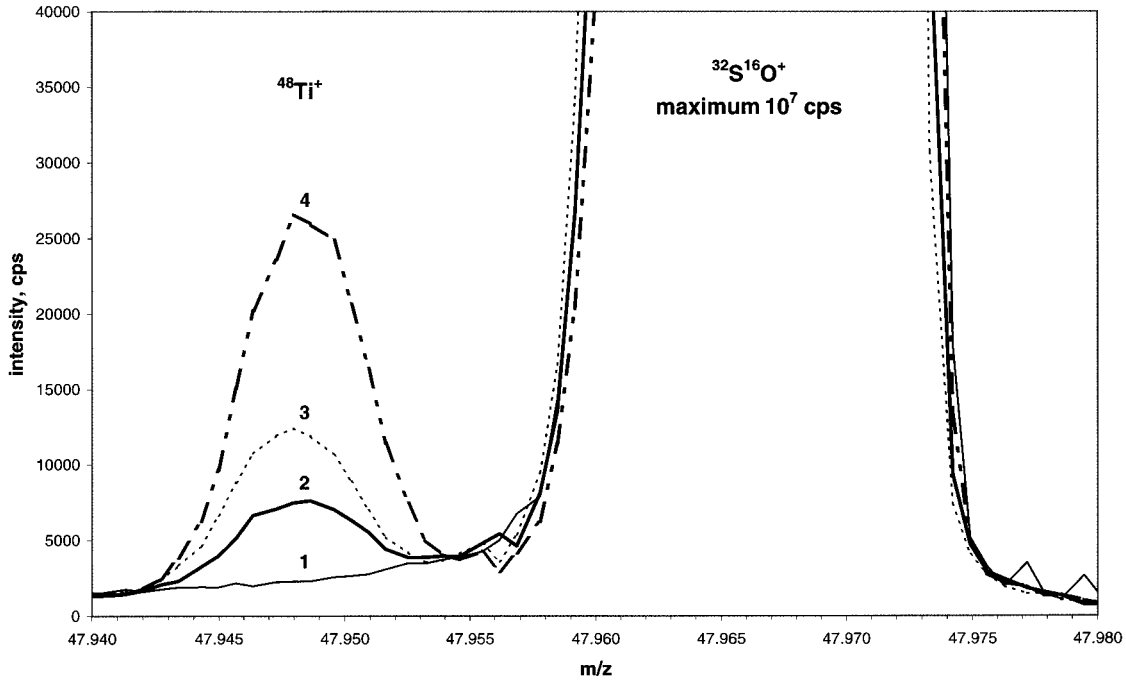

Figure 6. Determination of $^{48}Ti^{+}$ in 2.5% H_2SO_4 solution resulting in a strong interference from $^{32}S\,^{16}O^{+}$. Owing to the highly abundant interference together with low mass tailing of the molecular peak, a resolution of $R = 5000$ is necessary instead of 2520 as calculated from the mass difference. 1 = Blank; (2) = 1 ng ml^{-1}; 3 = 2 ng ml^{-1}; 4 = 5 ng ml^{-1}.

tant application of ICP-SFMS in the semiconductor industry, one in which it really excels, is the multi-element analysis of solvents and other liquid reagents. As an example, Fig. 7 shows detection limits from the analysis of semiconductor grade sulfuric acid obtained using a pneumatic nebulizer and various resolving powers. The values are mainly concentrated within two orders of magnitude with a mean of about 5 pg ml^{-1}.

An impressive example of ultimate detection limits can be taken from early work in this field by Yamasaki *et al.*,[12] who investigated the determination of ultratrace elements in terrestrial water. In comparison with the preceding example, one has to take into account that this work was performed utilizing the higher efficiency of USN instead of pneumatic nebulization. Detection limits (DL) calculated from three times the scatter of the blank signal were presented for 50 elements with four different mass resolution settings. A compilation of the results is given in Fig. 8. Generally the DL values of the elements are in the sub-pg ml^{-1} region with the exception of only a few. For the transition elements which were measured with $R = 3000$, the DL values are at a level of 100 fg ml^{-1}. Arsenic was the only element to require a mass resolution of $R > 7500$, and a DL of 10

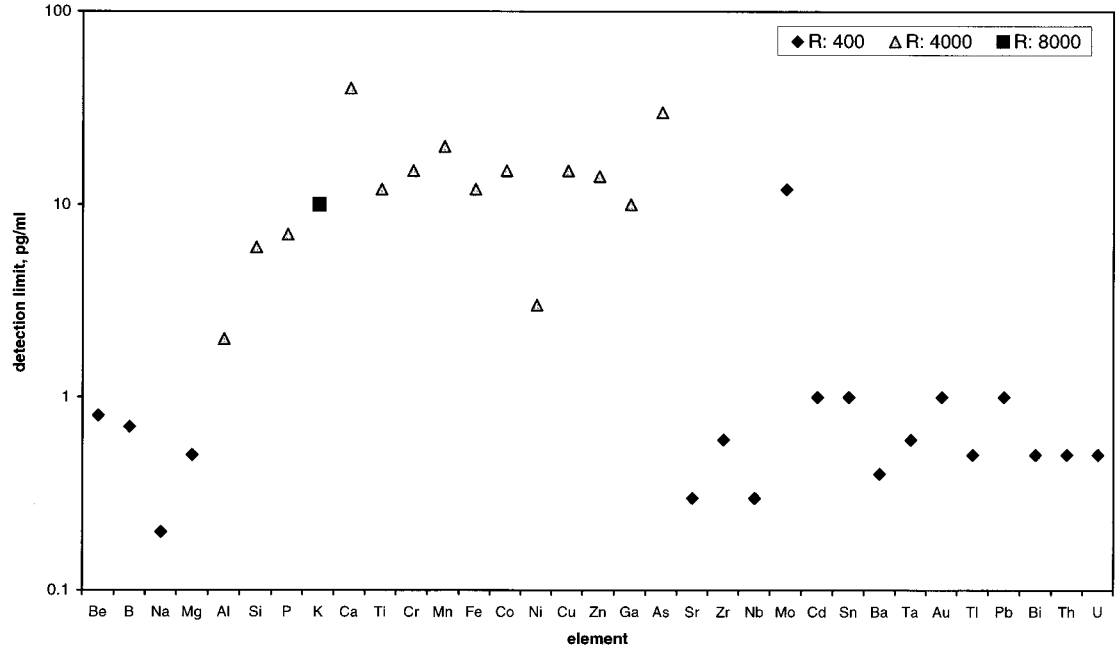

Figure 7. Detection limits from an ICP-SFMS analysis of semiconductor-grade sulfuric acid with various settings of the mass resolution R using a pneumatic nebulizer (courtesy of VG Elemental, Winsford, UK).

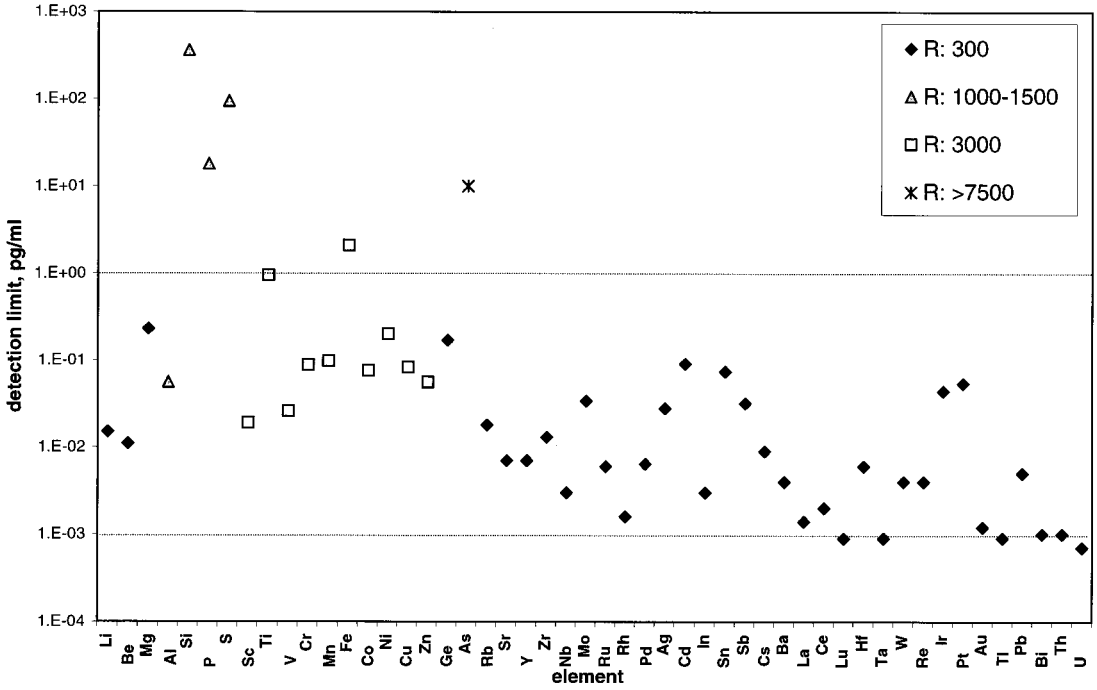

Figure 8. Representation of detection limits in ICP-SFMS determinations with various settings of the mass resolution *R* using an ultrasonic nebulizer, as reported by Yamasaki *et al.*[12]

pg ml^{-1} resulted. Presumably unrivalled is the determination of a DL for ^{235}U: a value of 0.07 fg ml^{-1} was achieved in a 1 h measurement of a blank solution. In spite of extreme precautions, limitations arise mainly from blank values.

Another application in which ultimate detection limits are sought is the determination of radioactive nuclides. Reliable monitoring is necessary owing to their high environmental risk potential. In the work of Kim *et al.*,[13] ICP-SFMS was successfully employed for the determination of some long-lived radionuclides (^{99}Tc, ^{226}Ra, ^{232}Th, ^{237}Np, ^{238}U, ^{239}Pu, ^{240}Pu). With application of USN, detection limits in the region of 1–10 fg ml^{-1} were obtained, corresponding to activities in the low nBq region. For reasons of comparison, this required ~2.5 min using ICP-SFMS, whereas with conventional radiometric techniques at least 1 day is necessary to register about 100 counts per gram of sample material.

Isotope ratio measurement

Notwithstanding the basic superiority of thermal ionization mass spectrometry (TIMS), ICP-MS instruments also provide isotope ratio measurements and thus application of the isotope dilution technique. The capabilities are sufficient for many applications and, in particular, for tracer studies in biological matrices. ICP-MS is certainly superior to TIMS as far as sample preparation demands and analysis time are concerned. In comparison with ICP-QMS, the performance is improved by SFMS, which must be attributed mainly to improved counting statistics. A relative standard deviation (RSD) of 0.04% with low resolution has been demonstrated, for instance, for Mg and Pb.[14] Lead contents of 0.02–9.7 ng g^{-1} were determined with respect to their isotope ratios with an average RSD of only 0.14%. The improvement achieved by ICP-SFMS has also been demonstrated in ratio measurements of the radioisotopes ^{240}Pu and ^{239}Pu, which were performed in a 21 pg ml^{-1} Pu solution with a precision of 2% and a deviation of 0.8% from the certified value.[15] With a resolution of 3000 an RSD of <0.1% was obtained for the determination of the $^{63}Cu/^{65}Cu$ ratio in 10 replicate measurements.[16] ICP-SFMS may furthermore be attractive for studies of the uptake and excretion of stable tracers in the human body in order to avoid radiation hazards from radiotracers on the one hand and cost and time consumption associated with TIMS or even accelerator MS on the other.[17] The performance of ICP-SFMS may become competitive with TIMS by utilization of multicollector arrangements with truly simultaneous detection.

CURRENT TRENDS

Instrumental developments

As can be seen from the preceding selection of application examples, the appearance of ICP-SFMS instruments has provided a strong impetus for new and demanding analytical applications. Beyond this, the rapid increase in new and sometimes exciting analytical experiences has a strongly stimulating effect for the whole field of ICP-MS. The performance features of the new instruments and their acceptance in the analytical community are the basis for a rapid increase in applications. The commercial success in turn is stimulating commercial competition, as demonstrated by the appearance of instruments of the second generation in rapid succession.

The progress in elemental analysis which has been achieved with the appearance of ICP-SFMS instruments has even resulted in a certain interest in still

higher mass resolution. In pioneering work, an ICP-MS instrument achieving $R = 120\,000$ has been described.[18] A further promising approach to SFMS instruments is possible by a return to the old Mattauch–Herzog geometry as the basis for truly simultaneous detection.[19] Once this was utilized mainly with photoplates in spark source instruments for the analysis of solids, and a revival now seems possible with the ICP as source by application of an array detector. An arrangement of this type can be expected to offer the highest sensitivity for simultaneous multi-element operation and also convincing precision for isotope ratio measurements.

Considerable activity in instrumental and methodological endeavors can also be observed in the field of ICP-QMS, probably as a result of mutual challenge. An example of a new technique is the 'cold plasma' approach, which is especially suited to improve in 'clean' solutions and semiconductor-grade chemicals the detection limits for K, Ca and Fe.[20] Another approach used with increasing frequency is the inclusion of collision cells that are useful in the reduction of argide-type interferences.[21]

Recent work with the aim of developing high-resolution quadrupoles has shown promising results.[22] With a newly developed system, it was possible to resolve $^{40}Ar^{16}O^+$ from $^{56}Fe^+$. The quadrupole analyser was operated in the second stability region which minimized the sensitivity losses normally appearing with high-resolution settings of quadrupoles. Ion trap analyzers offer another alternative to conventional quadrupole mass filters, and high mass resolution can be obtained as is well known in organic MS. Ions can also be stored in a commercially available ion trap operated as a reaction cell, which has been successfully exploited for the destruction of polyatomic ions.[23]

As a further MS technique, time-of-flight mass analysis is also under investigation for ICP-MS. It has been demonstrated that a mass resolution $R > 1000$ can be obtained. Additionally, the high time resolution of these instruments makes them well suited to follow fast transient signals, as has been demonstrated in an application with electrothermal evaporation.[24]

In conclusion, in the early days of ICP-MS the development was mainly influenced by unsatisfied demands from the application of AES. Typical users of this method were the first to become interested in ICP-MS and its analytical applications and to develop it to the maturity it has now reached. The current trends, however, demonstrate that typical tools of organic MS such as collision cells, ion traps and time-of-flight instruments now are increasingly being considered as new and promising components for further development.

Hyphenated methods

The increase in performance and in the field of applications is a reason to consider ICP-SFMS also for elemental detection in 'hyphenated' techniques. In particular, this involves coupling with various chromatographic procedures utilizing the on-line capabilities of modern high-efficiency nebulization techniques. Basically the settling time of the magnet limits scan speed and repetition frequency of ICP-SFMS instruments. With the improved performance of modern laminated magnets, however, ICP-SFMS instruments are finding increasing interest as detection systems to be coupled not only with different sample introduction techniques for direct analysis of solids, mainly electrothermal vaporization and laser ablation, but also for liquid chromatography and gas chromatography. In response to the increasing demand for speciation, the capabilities of ICP-SFMS in combination with different chromatographic techniques are under investigation in several research groups. The capabilities for measurement of transient signals do not reach the excellent time resolution of ICP-QMS; however, they will be sufficient for many applications of ICP-SFMS as a detection method in analytical procedures. In speciation, ultimate detection limits are in many cases of greater priority, so that research in this field will increasingly be undertaken with ICP-SFMS instruments for element-specific detection.

As an early example of processing of transient signals for only a few seconds duration by ICP-SFMS, the coupling of an ICP-MS instrument for element detection with a capillary gas chromatograph has been reported.[25] The aim of this investigation was the simultaneous multi-element speciation of organic pollutants in water from a harbor basin. Xe was added as internal standard and detected continuously together with Sn, Hg and Pb. The widest mass span to be covered by peak hopping in the multiple ion detection procedure was from ^{120}Sn up to ^{208}Pb. All isotopes taken into account could be measured three times a second, and the results obtained were satisfactory with respect to precision and accuracy.

The basic advantage of ICP-SFMS of exhibiting true multi-element capabilities is specifically applied to the task of multi-species analysis, which opens up a new field because more conventional speciation techniques are usually restricted to one element only. In an investigation by ICP-MS of Pt-treated plants, on-line coupling with size-exclusion chromatography gave multi-element determinations of indicator elements and enabled conclusions to be drawn about the nature of the fractions observed in combination with size-exclusion chromatography.[26] As an example from this investigation which was performed with both low and high mass resolution, a strong correlation was observed between the elements Pt and S for one of the organic fractions. As far as resolution is concerned, the measurements demonstrate a background reduction and an improvement in signal-to-noise ratio by SFMS in comparison with QMS when applied for recording a mass-specific chromatogram. As far as the interrelation between organic and inorganic MS is concerned, the correlation of the signals for Pt and S is a clear hint that we are dealing here with a protein fraction, probably a phytochelatine. In another fraction, the correlation between Pt and Ca indicates an exchange mechanism for Ca and Pt in polygalacturonic acids as a consequence of the Pt stress. In a further recent investigation of DNA adducts, the quantitative determination of all observed species was possible by evaluation of the phosphorus signal detected with ICP-SFMS.[27] These are first preliminary

examples that multi-element analysis by ICP-MS can be a useful tool for the interpretation and quantitative determination of complex organic species by measurement of indicator elements. Simple quantitation by standard addition allows the lack of suitable organic standards to be overcome. It may be foreseen that elemental analysis by ICP-SFMS will become a versatile tool, even for many typical organic applications.

CONCLUSION

It was a primary aim of this progress report to demonstrate through several examples that ICP-SFMS has rapidly gained a significant role in elemental analysis. It is an important high-perforance tool for many application fields, such as materials science, environmental analysis, the electronics industry, nuclear technology, biology and medicine. As always, success has many origins: high mass resolution, extremely low noise, ultimate detection limits, satisfactory precision and acceptable cost. Increasing acceptance leads to increasing competition: further reductions in costs can be expected, and more research and development should result in innovations leading to improved performance and versatility. Established concepts and techniques from organic MS, e.g. the application of ion traps and time-of-flight analyzers, are being introduced into inorganic MS. The future will probably bring more similarities between organic and inorganic MS and also an enhanced interrelation that is fruitful for both. In the fields of speciation for metals and non-metals in biomolecules, the frontiers are already being obliterated. Both fields can complement each other and both stand in a certain need of each other to satisfy the permanent demand to identify and determine more and more complex substances in lower concentrations with higher precision and accuracy.

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