**Atomic Spectrometry Update: Review of Advances in Atomic Spectrometry and related techniques**

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**SUMMARY OF CONTENTS**

**Strapline:** *This review of XXX references covers developments in ‘Atomic Spectrometry’ published in the twelve months from November 2015 to November 2016 inclusive. It covers atomic emission, absorption, fluorescence and mass spectrometry, but excludes material on speciation and coupled techniques which is included in a separate review. It should be read in conjunction with the previous review and the other related reviews in the series.A critical approach to the selection of material has been adopted, with only novel developments in instrumentation, techniques and methodology being included.*

*There do not seem to be novel developments that really stand out this year. However, there has been steady progress in understanding of how particles behave as they transit through the ICP, and how this affects ionisation and matrix interferences. Allied to advances in single particle analysis by nebulisation ICP-MS, this promises to yield useful information about the composition of nano-particles. The development of element tagging approaches for ICP-MS has slowed considerably, largely due to the dearth of available standards for biological assays, but some advances have been made in this area which point the way forward. The number of stable isotope systems which are now examined routinely by ICP-MC-MS has grown over the period of the review. Such methods may eventually lead to new insights into isotopic fractionation effects that result from environmental and biological processes which involve these elements. There have been several novel developments in instrumentation, such as ambient desorption ionisation, using a variety of modified sources and liquid electrode plasmas for AES. These hold out some promise as low-cost sources that may be incorporated into miniaturised systems of the future.*

**1. Sample Introduction**

* 1. **Liquids**
     1. **Sample pre-treatment.**
        1. *Solid phase extraction.* Traditional methods of SPE involve ion exchange or chelating substrates to separate the charged ions of the analyte from the matrix. A somewhat different approach has been taken by Farzin *et al*.1, who used *thymine-rich oligonucleotides to preconcentrate Hg2+*. This mercury-specific DNA contained seven Hg2+ binding sites; binding causing it to fold into a hairpin structure. In practice, the biotinylated DNA was first bound to strepdavidin coated magnetic beads (MBs). To this mixture a digested blood or urine sample was added, resulting in binding of Hg2+ to the DNA. The DNA was then released from the strepdavidin, the MBs separated and the DNA denatured to release the Hg2+. Subsequent analysis by CV-AAS yielded an LOD of 0.05 µg L-1 and an enhancement factor of 280.

A novel take on SPME was reported by Asiabi *et al*.2, who developed an *electrochemical method* based using a stainless steel capillary tube coated internally with polypyrrole doped with polyethyleneglycoldimethacrylate (PPy-EGDMA). The sample solution was passed through the PPy-EGDMA electrode tube and Se (anionic form) extracted by applying positive potential of 0.8 V. Desorption into 150 µL of 0.1 mol L-1 NaCl was effected by applying a negative potential, and the analyte then eluted in 3.0 mol L-1 HCl for determination by HG-AAS with an LOD of 0.004 µg L-1. The method was validated by the analysis of several tap and wastewater samples and was deemed free from interferences by coexisting ions commonly found in natural waters.

*Microfluidic sample preparation and introduction systems* have become increasingly common for MS assays of organic compounds, in the form of chip-based assays. However, they have struggled to gain a routine foothold when coupled with atomic spectrometry. Nevertheless, Zhang *et al*.3 have developed a device for the microextraction of Bi from HepG2 cell lysate, followed by Bi determination by ICP-MS. Polyglycidylmethacrylate trimethylolpropane triacrylate (poly (GMA-co-TRIM)) monolithic columns were fabricated *in situ* on a PDMS chip. The 2.5 cm x 50 µm x 500 µm columns were surface modified with EDTA to allow SPE from 100 µL of cell lysate solution. The LOD was 0.21 ng mL-1.

*1.1.1.2 Liquid phase extraction.* An overview of the combination of *LPME techniques with GFAAS* was reported by de la Calle *et al*.4. The high sensitivity of GFAAS is significantly enhanced by its association with a variety of miniaturised solvent extraction approaches. LPME-GFAAS thus represents a powerful combination for determination of metals, metalloids and organometallic compounds at trace and ultra-trace levels. The various LPME modes that are used with GFAAS were described with a discussion of the relevant experimental parameters. The main issues found when coupling LPME and GFAAS, as well as those strategies reported in the literature to solve them, were summarised. Relevant applications published on the topic so far were included.

*1.1.1.3 Elemental tagging.* The use of elemental tags, or intrinsic hetero-atoms, for the *quantitation of proteins, peptides and nucleic acids* has been an area of research which has matured into a routine procedure. A number of approaches have been adopted, usually involving ICP-MS as the analytical technique, often coupled with LC for separation. The target compound is usually determined by quantitation of an element which is either already part of the molecule (e.g. the metal moiety in an enzyme or seleno-protein), or which is incorporated by means of a bio-conjugate reaction, in single or multiple steps (*e.g.* a sandwich immunoassay for nucleic acids or bio-conjugate tagging of a peptide). Quantitation can then be performed either by straightforward calibration or by ID-MS. Elemental tagging was reviewed (61 references) by Swart and Jakubowski5 in the context of the *metrological requirements for routine clinical analysis*. They rightly focussed on the requirement for traceable standards and described the role of the Metrology for Metalloproteins (HLT05) project, which was part of the European Metrology Research Programme (EMRP), dealing with: iron containing proteins transferrin (TRF) and HGB; Zn-superoxide dismutase (SOD1) and ceruloplasmin (CER); and the seleno-proteins glutathione peroxidase (GPX1) and selenoprotein P (SEPP). They focussed on advances, since 2012, in the development of traceable standards for the routine determination of these compounds in a clinical setting, and concluded that ID-MS methods, for which isotopically enriched standards have been specifically synthesised, came closest to completely traceable methods. However, they also conclude that MS-based techniques are still too complex for routine clinical analysis. Another review by Maes *et al*.6 focussed exclusively on the *quantitation of phosphoproteins*, largely using ICP-MS but also by parallel use of molecular and elemental mass spectrometry. Most of the applications require the use of coupled LC-MS techniques, but some analyses using LA-ICP-MS were also included. Their main conclusions were that determination of individual phosphoproteins in real biological samples is extremely challenging because it requires high-resolution separation and detection at extremely low levels, though new instrumental techniques such as ICP-QQQ-MS may be up to the challenge. In this regard they highlighted the potential of using stable isotope labelled peptides for ID-MRM-MS, for absolute quantitation in complex matrices. In contrast, Lee *et al*.7 have quantified the hGH protein by analysing the total amount of sulfur by ID-ICP-MS then subtracting the contribution from impurities after separation using SEC. This seems like a very simple approach compared to the various tagging methods now employed, but the authors claimed traceability to SI and their results agreed well with the standard method of acid hydrolysis and analysis of component amino acids using LC-MS.

*The use of isotopically labelled standards* which have been synthesised from scratch, e.g. by a cell culture method, are preferred. This approach was adopted by Hermann *et al*.8, who synthesised 34S-labelled cysteine and methionine *in vivo,* using a yeast

fermentation method, for IDA quantification of cysteine and methionine by ICP-QQQ-MS. Enrichment to 96.3% and 98.5%, and LODs of 1.0 and 0.56 µmol L-1, were achieved for cysteic acid and methionine sulfone, respectively. The IDA method was validated for the absolute quantification of lysozyme and ceruloplasmin protein standards after hydrolysis to individual amino acids. Deitrich *et al*.9 synthesised 76Se-enriched peptides for use as calibrants in the ID-ICP-QQQ-MS determination of selenoprotein P (SEPP1) after tryptic digest to release the individual peptides. Key to this was equilibration of the spike with the peptides during sample digestion and subsequent chromatographic separation so that the peptides specific to SEPP1 could be determined. In a subsequent paper, some of the same workers10 took this approach a step further by synthesising a standard and spike of the complete SEPP1 protein by cell-free *E. coli* protein synthesis, where Se was introduced in the form of selenomethionine. This was used to determine SEPP1 in human plasma by ID-HPLC-ICP-MS. The (as in the previous study? – you cannot say again as this is the first mention of these RMs) method was validated by analysis of BCR-637 and SRM 1950. In keeping with a metrological approach, they performed a number of different types of analysis to validate the method, including both species-specific and species-unspecific IDA of the intact proteins, and comparison with post-column, species-specific IDA of the Se-peptides. A complete uncertainty budget was also calculated with a coverage factor of k=2. These combined approaches give confidence in the method such that, for example, the analysis of BCR-637 resulted in the sum of the individual Se species totalling to 80 ng g-1, compared with total Se of 79.6 ng g-1 and a certified value for total Se of 79 ng g-1.

Specificity of the target protein or peptide in the aforementioned studies was achieved by chromatographic separation. However, another way of achieving this is by means of an immunoassay type approach wherein an isotopic tag is applied to a specific target molecule. Research in this area has been reviewed (58 references) by Liu *et al*.11, who focussed on tagging with stable isotopes *via* antibody–antigen or nucleic acid probe vectors; multiplexing to enable determination of multiple analytes in a single shot; and absolute quantitation of biomolecules. A novel example of using a nucleic acid probe is described by Chen *et al*.12, who utilised a *hairpin DNA beacon probe*. The probe contained numerous thymine bases which formed a thymine-Hg2+-thymine connection, such that Hg2+ was sandwiched in the hairpin of the folded DNA strand. The presence of a complementary DNA sequence ( the target molecule) resulted in hybridisation and release of the Hg2+ which was detected using CVG-AFS with reduction by SnCl2. Determination of single and double stranded DNA, and proteins yielded LODs as low as 0.2 and 0.3 nM. The protein thrombin was also determined, with a LOD of 0.08 nM, using a thrombin specific aptamer to enable specificity. An additional advantage of this approach is that multiple Hg2+ ions are released for every target molecule, thereby amplifying the analytical signal. This is even more pronounced when nanoparticles, containing thousands of metal atoms per target molecule, are used as tags. For example, Liu *et al*.13 used an immunoreaction of caspase-3, primary antibody and gold NP labelled IgG; then subsequent determination by ICP-MS after release of the gold NPs from the immune-complex. An LOD of 0.42 ng mL−1 (0.31 nM) was obtained for caspase-3. A similar approach was adopted by Xu *et al*.14 for the determination of human IgG, but this time by labelling with CuO nanoparticles and determination by GFAAS. They achieved an LOD of 0.19 ng mL-1, which is comparable to ICP-MS.

A variation on this amplification method was reported by Lian *et al*.15 who also used a sandwich immunoassay for the determination of an organophosphorylated acetylcholinesterase adduct (OP-AChE), which is a biomarker for exposure to organophosphate pesticides and nerve agents. The OP-AChE target compound was captured from the sample matrix by chelation with TiO2 coated magnetic nanoparticles (TiO2-MNPs), which were then selectively recognised by an anti-AChE antibody attached to a protein cage nanoparticle (PCN). The PCN was packed with lead phosphate which could be released, after separation from the sample matrix, and determined by ET-AAS. The LOD was 2 pM, which is below the average AChE concentration in human plasma and erythrocytes (c.a. 0.12 nM and 3 nM respectively). This compared well with an LOD of 0.02 nM obtained using elctrochemical detection.

*1.1.1.3 Other methods*. The sample preparation step is often considered to be the most critical, and is often the longest step in any procedure. Consequently, a great deal of effort has gone into finding ways to speed it up and make it more efficient. Matusiewicz and Slachinski16 have reported a novel idea whereby a pressurised flow system using electromagnetic induction heating was used for the continuous, off-line solubilisation of slurries (3% m/V) of biological tissue, milk powder and lichen. The system was operated at 120 °C and 3.5 bar. Measurement by MIP-OES for trace and minor elements yielded average recoveries of 99.2%.

**1.1.2 Nebulisation.** The fabrication and use of a *disposable low cost microfluidic chip as sample introduction system for ICP-MS* was described by Verboket *et al*.17. The chip produces monodisperse aqueous sample droplets in PFH. The size and frequency of the aqueous droplets can be varied in the range of 40 to 60 µm and from 90 to 7,000 Hz, respectively. The droplets are ejected from the chip with a second flow of PFH and remain intact during the ejection. A custom-built desolvation system removes the PFH and transports the droplets into the ICPMS. The resultant signals were found to be very stable, with a narrow intensity distribution, showing the monodispersity of the droplets. The analytical capability of the system was demonstrated for the determination of Fe in single bovine red blood cells. Extending the capabilities of the system through the integration of additional microfluidic modules is possible.

Gold NPs were used by Kanaki and Pergantis to *determine the transport efficiency (TE%) of microflow and nanoflow nebulisers in ICP-MS*18. An aqueous suspension containing 60 nm gold NPs (a NIST reference material) was introduced to an ICP-MS operating in single particle mode (short dwell times and dilute samples) for the detection of individual NPs. Various flow rates ranging from 500 nL min-1 to 10 mL min-1 using various modified pneumatic nebulisers were tested and transport efficiencies were determined. In addition, the overall system sensitivity was determined for both gold NP suspensions and dissolved metal solutions. The method suggested has the potential to allow comparisons of TE% for the various micro-/nano-flow systems currently in use and those in development.

*Single particle (sp) ICP-MS* has proven to be a powerful technique for the detection and characterisation of aqueous dispersions of metal-containing nanomaterials. Combining high-throughput with the specificity of a single particle counting technique and the elemental specificity of ICP-MS, spICP-MS is capable of rapidly providing researchers with information pertaining to size, size distribution, particle number concentration, and major elemental composition with minimal sample perturbation. Recently, advances in data acquisition, signal processing, and the implementation of alternative mass analysers (e.g., time-of-flight) has resulted in a wider breadth of particle analyses and made significant progress toward overcoming many of the challenges in the quantitative analysis of NPs. A useful review by Montano *et al*. provides an overview of spICP-MS development from a niche technique to application for routine analysis, a discussion of the key issues for quantitative analysis and examples of its further advancement for analysis of increasingly complex environmental and biological samples19. *Asymmetrical flow field-flow fractionation (AF4) coupled with spICP-MS* is considered to be a valuable tool for separating, characterising and quantifying engineered nanoparticles for their risk assessment and evaluation in terms of environmental exposure. Optimisation of a system for this purpose was described by Lee *et al*.20. Application of the same technique to the determination of silver NPs in the environment was also described by Huynh *et al*.21. The results obtained indicated that AF4-spICPMS is capable of detecting and quantifying silver NPs and other engineered metal NPs in environmental samples. However, the authors concluded that further studies are needed before AF4-spICPMS can become a routine analytical technique.

**1.1.3 Thermal vapourisation.** A method based on a *tungsten boat furnace vapouriser*, tungsten sample cuvettes and ICP-OES was developed for the direct determination of Si, P, and S in silver NPs22. The novel aspect of the proposed method was the suggestion that the entire sample in each batch is vapourised, which enables simultaneous measurement of the emission of both the analyte and the Ag matrix. Since the Ag NPs are sufficiently pure, the contribution of impurities to the sample measurements can be considered negligible. This allows the sample mass in each aliquot to be estimated from the analytical results rather than time consuming weighing procedures used previously. An additional advantage is that pretreatment and/or predigestion are unnecessary. The sample throughput was approximately 35 batches per hour and LODs for Si, P, and S in the silver NPs (dry powder) were found to be 15, 4.2, and 62 µ g , respectively. The method was proposed for rapid screening and accurate analysis of silver NPs, especially for industrial applications.

A *heated torch integrated sample introduction system* (hTISIS) has been used for direct injection of bioethanol into ICP-OES for the determination of metals and metalloids23. Two injection modes (continuous liquid aspiration and air-segmented FI analysis) were evaluated. The matrix effects caused by ethanol-water mixtures were removed by operating the hTISIS at 400 ºC in segmented injection. It was also demonstrated that the system could be operated in continuous mode at 200 ºC with complete interference removal. Twenty eight samples with bioethanol contents between 55% and 100% were analysed and recoveries from 80% to 120% were obtained for 18 analytes. The analyte concentrations determined were in agreement with those obtained using a preconcentration reference method. LODs from 3 ng mL-1 for Mn to 500 ng mL-1 for Ca were obtained.

**1.2. Vapour generation**

**1.2.1. Chemical Vapour Generation**. Butcher24 has reviewed advances made in instrumentation and applications of CVG coupled with AFS over the period 2014 and 2015. Advances in the development and application of diffusive gradients in thin films, photochemical vapourisation and novel atom cells were highlighted.

D’Ullivo25 has presented *a comprehensive review (90 references) of the mechanism of CVG* using tetrahydridoborate (THB), with the aim of producing a reaction model for aqueous CVG of metal and semimetal species. This was attempted by combining current knowledge of reaction mechanisms in analytical CVG with the literature on the synthesis of nanoparticles using aqueous THB and applications in catalytic hydrolysis for hydrogen production. The author outlines the current state of knowledge to be: hydrides are formed by direct transfer of hydrogen from borane species to the analyte atom; then hydrogen transfer takes place through an analyte–borane complex; and the final volatile hydrides are formed stepwise via the formation of intermediate hydrido-metal complexes. Depending on the stability of the final hydride, it can decompose to release the element in the zero valent state. Alternatively, it is possible that the intermediate hydrido-metal complex could release the element. Focussing predominantly on CVG of arsenic species, the author developed a ‘non-analytical’ reaction model in which took into account some additional possibilities, *viz*: the CVG of polynuclear and mononuclear substrates; formation of by-products by reaction with intermediate hydrido-metal complexes; competition between hydride formation and condensation reactions when. A further conclusion was that when the analyte:borane ratio is several orders of magnitude, the rate of condensation decreases the rate of formation of hydrides and intermediate hydrido-metal complexes increases. Under these conditions the non-analytical reaction model reduces to the simpler analytical one.

Novak *et al.*26 investigated *a planar DBD as an atom cell for CVG-AAS* and compared it with the more commonly used QTA. The advantage of the DBD is that it is relatively compact and requires only a 25 kHz, HV power supply operated at 17 W. The DBD was evaluated using argon, nitrogen, helium and hydrogen as discharge gases, for the atomisation of the hydrides of As. LODs of 0.16 ng mL-1 and 0.15 ng mL-1 were obtained using the DBD and QTA respectively. Matrix interferences caused by other hydride-forming elements Bi, Sb and Se were absent below 500 ng mL-1. Interestingly, when oxygen was added to the gas flow at 7 mL min-1 it was possible to pre-concentrate arsine in the DBD, which was subsequently volatilised when the oxygen flow was stopped. A pre-concentration efficiency of c.a. 100 % was observed for pre-concentration periods of up to 300 s, thereby lowering the LOD to 0.012 ng mL-1.

A DBD has been used by Li *et al*.27 to generate volatile species for AFS detection. They investigated the effect of adding a non-ionic surfactant to the sample on the generation of volatile Cd and Hg species, in a method which they called DBD-plasma CVG. They found that the addition of Triton X-114 resulted in approximately 5-fold improvements in the fluorescence signals for Cd and Hg, with respective LODs of 2.4 and 4.5 ng L-1. They postulated that the surfactant increased the reaction rate and transport efficiency of ‘plasma assisted chemical reactions’ which produced the volatile species, though no empirical evidence of this was presented. Pyrolysis has also been used combined with CVG-AFS to improve efficiency of volatile Cd generation.28 The sample was pyrolysed at ~500 °C in the presence of sodium formate to yield volatile Cd species. Thiourea was also added to enhance the efficiency and eliminate interference due to Cu. An LOD of 0.38 ng for 0.17 mL of sample was achieved.

*Ionic liquids have also been used to modify CVG reactions*, the aim generally being to enhance sensitivity or reduce interferences. Wen *et al*.29 investigated solid reductants of LiAlH4, SnCl2 or THB in a room temperature ionic liquid (IL) for CVG-AFS. Analyte ions were extracted from the aqueous phase into the IL by LLE then directly mixed with the solid reductant to generate volatile species of AsIII, HgIII and SbIII. Interferences from Cu, Fe, Ni, Zn and Pb were generally absent at concentration between 2.5 and 20 mg L-1. Compared to conventional CVG-AFS, absolute LODs for As, Hg and Sb were 62, 24, and 96-times lower respectively, but concentration LODs were higher because of the 10 µL sample size. A similar approach was adopted by Zeng *et al*.30 using LLE into a fluorine-free IL, but with thermospray FF-AAS as the method of detection. Complexation of Bi and Se with dithizone and APDC, respectively, facilitated extraction into 1-octyl-3-methylimidazolium perchlorate, where solid KBH4 was used to generate volatile species. LODs for Bi and SeIV were 8.3 and 4.8 ng mL-1, respectively.

**1.2.2. Photochemical Vapour Generation**. The PVG technique has been developed over the last few years as an alternative means of vapour generation, using an organic acid in the presence of intense UV radiation to generate free radicals, rather than the powerful reducing agent that are used in conventional CVG. Formic or acetic acid are generally the preferred reagents for use in PVG to generate volatile species of the transition metals as well as the more usual hydride-forming elements. Despite these advantages it has not been widely used for the analysis of real samples with complex matrices, presumably because of the effect of chemical interferences. However, Gao *et al*.31 reduced interferences in the direct analysis of seawater by using Plackett-Burman and central composite design optimisation. The optimal condition was a mixture of 20% (v/v) formic and 20% acetic acid (v/v), which yielded the same PVG generation efficiencies for As(III), As(V), MMAs and DMAs with a 3pg g-1 LOD using ICP-MS. The method was validated for the determination of As in CASS-5 and NASS-6 CRMs using a one point gravimetric standard addition with internal standard. In a second paper by the same authors32 they used PVG to generate volatile Cu species for determination in digests of biological samples by ID-MC-ICP-MS. Interestingly, they found that copper-containing species were initially retained on the reactor wall during a ‘loading’ phase then, following a purge of the line with air (‘drying’), could be desorbed in the presence of a plug of 60% formic acid to yield volatile species. They speculated that, on passing through the PVG reactor, Cu2+ ions may be transformed to Cu(CO)+, then the high temperature and UV irradiation during ‘drying’ caused reduction to volatile Cu. Unfortunately, the formation of an unstable intermediate volatile Cu during the ‘drying’ stage resulted in a measurement precision of near 30%, so further work is necessary before this becomes a viable method.

Coutinho *et al*.33 developed a PVG method for the determination of Co in biological samples using a 50% formic acid solution, UV radiation at 254 and 185 nm, and ICP-OES detection. They initially encountered strong matrix interferences but these were reduced with longer irradiation times and >50-fold dilution factor, to achieve between 90% and 110% recoveries for analyses of CRMs TORT-2 and TORT-3.

Wang *et al*.34 investigated the effect of ferric species as ‘enhancers’ for the determination of inorganic As by PVG-AFS. They found that 15 mg L−1 of ferric chloride plus 20% acetic acid combined with 4% formic acid and 30 s UV irradiation resulted in a 10-fold signal enhancement, and yielded an LOD of 0.05 µg L−1.

**1.2.3. Electrochemical Vapour Generation**. There has been very little novel research in this area over the review period, though Novakova *et al*.35 have coupled EVG with an Ir-treated GF, in a flow-through system, to generate and pre-concentrate volatile Cd species. A number of different cathode materials and electrolytes were evaluated for EVG, with HCl (0.5 mol dm-3) and H2SO4 (2.0 mol dm-3) found to be optimal for the anolyte and catholyte respectively. Operating at 1.5 A and with 5x10-4 mol dm-3 Triton X-100 present, the LOD was 1.0 ng ml−1 (1.5 ng absolute).

**1.3 Solids**

**1.3.1 Direct methods**

*1.3.1.1 Glow discharge.* GD-OES is a well-established analytical technique used in the analysis of solid, conducting materials. Though primarily of interest as a depth profiling technique on samples with varying layers of both conducting and non-conducting materials, it is also capable of rapid bulk analysis of homogenous, solid samples. *An interesting overview of the technique* itself and its application to nuclear materials was described36. An *atmospheric pressure glow microdischarge* (µAPGD) generated between a small-sized He nozzle jet anode and a flowing liquid cathode was coupled with USN for OES in a preliminary study by Greda *et al*.37. The spatial distributions of the emitted spectra from the novel coupled USN-µAPGD system and the conventional µAPGD system were compared. In the µAPGD, the maxima of the intensity distribution profiles of the atomic emission lines Ca, Cd, In, K, Li, Mg, Mn, Na and Sr were observed in the near cathode region, whereas, in the case of the USN-µ APGD, they were shifted towards the anode. In the novel system, the intensities of the analytical lines were boosted from several(2-fold?) to 35-fold. The LODs of metals achieved with the USN-µ APGD-OES method were in the range from 0.08 µg L-1 for Li to 52 µg L-1 for Mn.

An interesting coupling of a *GD in pulsed mode (PGD) as secondary source for excitation/ionisation of the material provided by LA* was investigated using OES38. Emission properties of the LA-PGD plasma in each temporal region (prepeak, plateau or afterglow) of the GD pulse were evaluated for analytical lines of different elements. Resonant atomic lines showed higher emission intensity in the prepeak region compared to non-resonant lines. Non-resonant lines showed higher enhancement of the emission intensity in the afterglow region. The coupled LA-PGD system offered better linear correlation coefficients using a set of glass standards for calibration as well as lower LOD (by at least a factor of two) when compared to LIBS.

**1.3.2 Indirect methods.**

*1.3.2.1 Laser ablation.* Laser sampling in analytical spectrometry has long prevailed as it does not require sample pretreatment, large samples or cause contamination. However, it suffers from a series of drawbacks such as elemental fractionation, matrix effects and a shortage of matrix-matched reference materials for most samples of interest. To correct these undesired effects and achieve better analytical performance, it is vital to be conscious of when and how they occur, to what extent the various parameters involved influence them, and what means can be applied to minimise them. Zhang *et al*. provide *a review summarising the recent research work involving elemental fractionation and matrix effects in laser sampling approaches*39. To date, SP-ICP-MS has generally been restricted to direct NP introduction using nebulisation or microdroplet generation systems. Benesova *et al*.40 have developed a system where *gold NPs are introduced into ICP-MS by substrate-assisted laser desorption (SALD)* directly from a suitable absorbing plastic surface using a commercial ablation cell. In SALD, desorption of individual NPs is mediated using a frequency-quintupled Nd:YAG laser (213 nm) operated at a relatively low laser fluence. The method was demonstrated on a reference material, 56 nm gold NPs with a transport efficiency of 61% and commercially available 86 nm gold NPs. The feasibility of the technique for NP detection and characterisation was discussed and the results obtained compared well with those obtained using conventional nebuliser spICP-MS.

Laser ablation is a promising technique for the *direct analysis of polymer samples*, however, the lack of available reference materials and the presence of matrix dependent effects means that internal standardisation is necessary for quantitative analysis. Deiting *et al*.41 investigated: the correlation between the C released during the ablation process; the 13C signal detected by ICP-MS; and its use as an internal standard. In the study, twenty-one virgin polymer materials were ablated and the released C determined and correlated with the corresponding integrated 13C signal. A direct relationship between the ablated carbon and 13C signal was observed, demonstrating the potential ability to overcome at least some of the matrix dependent and transport effects which occur during the LA of virgin polymers.

A *near-field LA system* was developed for the analysis of inorganic solid samples in the nanometer resolution range42. The instrument is based on the coupling of a nanosecond Nd:YAG laser with an AFM. The technique uses a tip enhancement effect obtained by the interaction of laser radiation with the conductive tip of the AFM maintained at a few nanometers above the sample surface. By applying this technique to conducting Au and semiconducting silicon samples, a lateral resolution of 100 nm was demonstrated. With a single laser pulse, craters of about 100 nm in diameter and a few nanometers in depth were obtained. A multi-parametric study was carried out in order to understand the effect of different experimental parameters (laser fluence, tip-to-sample distance, sample and tip nature) on the near-field LA efficiency, crater dimensions and amount of ablated material. Numerical simulations of the localised heating with a home-made 3-D code provided a good explanation for the nanometer-sized crater diameters obtained in the experiments.

*LA was successfully applied to the analysis of low molecular weight solids separated on standard TLC plates43*. The ablated sample was ionised using a flowing atmospheric pressure afterglow source. The laser pointer used was capable of ablating organic compounds directly from the TLC spots and the LOD was estimated to be 35 ng cm-2 of a pyrazole derivative.

Over the last decade, the application of *LA-ICP-MS in bioimaging* has steadily increased. In the time covering this review, a significant number of publications describing the approach have appeared. Gundlach-Graham and Gunther44 provided *a review describing trends in fast, high resolution elemental imaging by LA-ICP-MS*. They reported that the recently developed low dispersion LA cells can deliver quantitative transport of ablated aerosols within 10 ms and provide enhanced sensitivity compared to conventional LA cells because the analyte ion signal becomes less diluted during aerosol transport. Combining these low dispersion cells with simultaneous ICP-MS can help to overcome the instrumental limitations of elemental imaging to deliver faster, higher resolution analyses. A review by Van Malderen *et al*. covers *developments in the design of LA cells, the associated transport tubing assembly and their coupling to ICP-MS instrumentation*45. Recently developed low dispersion ablation cell designs have reduced the pulse response duration for a single laser shot to <10 ms, using the criterion of the full peak width at 1% of the height of the maximum signal intensity. The evolution towards these low dispersion systems was described and reported to have been profoundly influenced by: an understanding of processes driving the initial dispersion; of the design aspects of the cell and tubing that influence transport-induced dispersion and transport efficiency; and of limitations imposed by the temporal resolution of ICP-MS instruments. Rapid response LA-ICP-MS systems greatly benefit throughput and sensitivity, which are key parameters in 2D and 3D imaging at high lateral resolution. As noted earlier, the analysis and imaging of biological material has come to the forefront as a key application of LA-ICP-MS and the review described the impact of the technical developments in LA-ICP-MS systems on emerging applications, including multiplexed metal-tagged antibody detection (for immunohistochemistry), NP and compound hypo- and hyperaccumulation, and (intra-) cellular/histological studies.

The incorporation of cooling to the LA cell allows elemental imaging of soft and semi-soft samples, specifically biological tissues to be carried out. Hamilton *et al*.46 described the evaluation of a *custom single Peltier-cooled ablation cell* for this purpose. Use of the cell was successfully applied to the analysis of three different biological tissues as spatially resolved images of mapped elements were obtained whilst maintaining the structural integrity of the tissues.

A *combination of LA-ICP-MS and LIBS was used for laterally resolved elemental analysis of biological samples47*. LIBS was used to overcome the inability of LA-ICP-MS to detect bulk components such as H or O. In addition to those elements, some other elements that are difficult or impossible to investigate using LA-ICP-MS (e.g. F, N, Cl), can be detected by LIBS. In the described work, tandem LA/LIBS (the simultaneous use of LIBS and LA-ICP-MS) was applied to the analysis of biological samples, with the purpose of moving towards the possibility of the complete analysis of the elemental composition of a human tumour sample. The results obtained showed good correlation with histological staining and the distribution images obtained were deemed to provide a useful basis for further medical interpretation.

Bishop *et al*. used *triple quadrupole-ICP-MS* (instead of the commonly-used single quadrupole) for elemental bioimaging using LA48. The triple quadrupole ICP-MS was found to reduce the polyatomic interferences that can restrict the sensitivity of biologically important elements such as Fe.

*1.3.2.2 Thermal vapourisation.*Mao *et al*. developed a system for *solid sampling ETV using a tungsten coil* to trap Zn and Cd at room temperature49. The analytes were simultaneously vapourised and carried into an ICP-MS for detection. Grain samples were analysed and LODs of 1 pg Zn and 0.1 pg Cd obtained. The vapourised and trapped species of Zn and Cd were also found to be predominantly atoms through investigation using AFS and XPS.

**2. Instrumentation, Fundamentals and Chemometrics**

**2.1 Instrumentation**

**2.1.1 Sources.** The established sources used for atomic spectrometry are the Flame, ICP, GF, MIP, and GD. These have been used successfully for many years as atom/ion cells for OES, AAS, AFS and MS, and have reached a level of maturity where truly novel variations are infrequent. However, there have been a number of developments of note during the review period*. A novel ICP has been developed* by Schwartz *et al*.50, who used microwave frequency (2.45 GHz), rather than the traditional radiofrequency, at 1 kW power generated by the magnetron from a microwave oven. Rather than an induction coil they used a dielectric resonator ring made from an advanced ceramic which did not require water cooling. The plasma could be sustained in air or nitrogen and tolerated the direct introduction of a number of organic solvents which would typically be introduced into an ICP using a concentric quartz nebuliser. LODs, obtained using an ultrasonic nebuliser, were in the range 0.03 –70 ppb which is broadly comparable with other MIP and ICP-OES systems. A particular advantage of using the dielectric resonator rather than an induction coil is that there was no net electric potential, which eliminated the possibility of capacitive coupling. This improved plasma homogeneity and would be useful if used as an ion source for MS. The major disadvantage of the source was the higher molecular background below 400 nm compared with an argon ICP, largely due to the fact of using air and nitrogen as the plasma gas. In addition, while there was no evidence of severe matrix effects, a more in-depth evaluation of this particular aspect would be necessary before making comparisons with other low-cost alternatives to the ICP. In another attempt to address the ‘cost of argon’ issue, Tirk *et al*.51 developed an *ICP-OES interface in which all of the argon supplied to the torch was recycled* and fed back to the outer gas flow, resulting in decreased argon consumption from 14 to 1.4 L min-1. They removed water and particulate matter produced by the hot plasma by trapping in a pipe filled with molecular sieve material. *Texc*, *Trot* and *ne* were similar to traditional ICP-OES torches. The LODs were degraded by a factor of 5, which the authors attributed to a non-optimal viewing zone caused by increased pressure in the enclosed plasma interface. Nevertheless, this may still be acceptable in parts of the world where Argon is prohibitively expensive and the shortcomings will most likely be overcome in any case.

Periodically, there is a flurry of research into ion *sources which are capable of generating anything from the molecular ion of an organic molecule through to elemental ions*. The latest iteration of this is the development of ambient desorption ionisation (ADI) sources and variations on them, which can operate on solid samples at atmospheric pressure. One such has been reported by Evans-Nguyen *et al.*52, who used a *modified MPT for ADI from solid samples* placed in the gap between the source and the interface of an ion-trap MS. The MPT was operated at 300 W and with an argon flow rate of 68 L min-1[sic], according to the paper. This was sufficient to desorb and ionise the matrix elements direct from samples such as a coin but less successful for the determination of minor elements deposited on a filter paper. When a metal mesh substrate was used instead of filter paper amounts of Ba and Cs at 100 ng and 1 ng respectively were detected. In comparison, the same conditions were used to produce limited fragmentation of the gunshot residue (GSR) methyl centralite (100 ng) and the explosive RDX (1 µg), and application that would be useful for the simultaneous determination of firearm discharge residue components on forensic swabs. A similar set-up, called matrix assisted plasma atomisation emission spectrometry (MAP-AES) has been reported by Yuan *et al*.53, who used the tail plume of a surfatron to desorb and ionise elements from salt solutions deposited on a filter paper. LODs were between ~2 and ~60 ng mL-1 for a number of transition elements.

Another investigation into ADI, this time using a GD as the source, has been undertaken by Marcus *et al*.54. They used a 75 μm i.d. × 125 μm o.d. fused silica capillary, mounted coaxially within a 500 μm i.d. × 700 μm o.d. stainless steel capillary, surrounded by a helium sheath gas flow of 0.6 L min−1. A 5% (v/v) aqueous HNO3 solution was passed through the capillary and a liquid electrode plasma generated upon application of a 60 mA, ∼850 V d.c. power supply. This was used to volatilizs, ionise and excite Cu and Ni species from samples such as metallic thin films, dry solution residues, and bulk materials, with detection by OES for qualitative analysis. Given that the thermal temperature of the plasma does not exceed 300 °C they speculated that there is likely to be a vapour phase chemical process occurring, possibly related to the presence of H3O+ or the formation of volatile metal salts (with which this reviewer speculates there may be similarities with matrix modification used to influence volatility in GF-AAS?).

*A softer approach to ionisation* was taken by Klute *et al.*55 who investigated a helium DBD source, doped with CHClF2 at between 750 ppb and 150 ppm as anayte. The DBD was initiated by a square-wave voltage with a rise-time within 0.01μs and peak-to-peak voltages up to 4 kV, at a frequency of 20 to 40 kHz. Spatiotemporal measurements of the plasma emission showed that, during a single voltage duty cycle, the plasma evolved from a soft to dissociative ionisation source. The LODs for CHClF2 were 0.7 and 1.2 ppb using the Cl 912 and the F 739 nm lines, respectively.

In a novel study, Nakadi *et al*.56 described a method for *isotopic analysis using high resolution continuum source GF-AAS*. What made this approach different was that they chose to deliberately generate diatomic species of Br from solid samples (CaBr being the preferred diatom) which have much larger isotopic shifts in their molecular spectra compared to their atomic spectra. The species were generated using a matrix modifier comprised of 500 mg L-1 palladium NP and a 10 g L-1 Ca solution in HNO3 (5% v/v). The molecular transitions of Ca79Br and Ca81Br which yielded greatest sensitivity, resolution and precision were observed at 600.492 nm and 600.467 nm respectively. The method was used for the IDA of Br in PVC-H-07-A and NIST SRM 1573a tomato leaves. Direct solid sampling was adoptedand the method yielded good agreement with the certified value and 4–8% RSD precision. The LOQ was estimated to be 60 ng for 20 µL liquid samples, or 30 µg g-1 for solid samples using a sample mass of 2 mg.

*A chip based LEP-OES system* has been further developed by workers in Japan.57 The principle of this micro-plasma device is based on Joule heating, caused by application of a pulsed-DC voltage to an electrolyte confined in a microchannel. The vapour bubbles formed as a result contained microplasmas which were capable of exciting atomic emission of elements dissolved in solution. The techniques lends itself readily to microfabrication on a chip, however, one of the problems is low sensitivity because the PDMS material used has poor light transmission close to the UV. One way round this is to fabricate chips from quartz, but this is difficult and expensive, so an alternative approach was adopted whereby the chip design included a channel for inclusion of a Pb-selective SPE resin for pre-concentration. In a further refinement, a pneumatic membrane micro-pump was also incorporated. In this way, an LOD of 0.4 ng mL-1 was obtained for Pb.

**2.1.2 Spectrometers.** A number of publications have appeared in which workers attempt to couple various plasma sources with a range of mass spectrometers. In the first of these, the group of Hieftje *further developed their ICP-DOF-MS system by inclusion of an IonCCD camera as a detector*.58 The method of DOF-MS is conceptually similar to TOF-MS, except that in TOF-MS, the time an ion takes to traverse a known distance is measured. In DOF-MS the distance travelled in a known time is measured by detecting ions simultaneously along a focal plane by means of a spatially selective detector. An IonCCD camera is a direct-charge integrating, linear-array detector that provides position-sensitive detection of ions. Key figures of merit for a 5.1 cm long IonCCD detector were: mass resolution (FWHM) = 800-950; dynamic range >=103; IR precision >= 0.008% RSD for 1 ppm solutions of Pb, Eu and Ag with less than 1s integration and zero mass bias. This is comparable to TOF-MS in performance. Another paper from the same group59 reported on the *performance of ICP-Zoom-TOF-MS*. This combined both conventional, constant-energy acceleration (CEA) and constant momentum acceleration (CMA) modes in a single instrument. Respective figures of merit for resolution, LOD and IR precision were 1200, 0.02 ppt and 0.2% RSD for CEA mode, and 1900, 0.8 ppt and 0.2% RSD for CMA mode. When the repetition rate was increased from 10 to 43.5 kHz for CMA the precision was improved to 0.09% RSD for the same integration time, albeit for a narrow m/z range.

In a completely different type of study,60 the same research group have investigated the use of interference filters with a10 nm bandpass in conjunction with solution-cathode GD-OES. The idea was to develop a low-cost instrument. This computer-controlled filter wheel instrument provided RSDs between 0.5 and 4.6%, linear ranges of between 1.5 and 4.9 orders of magnitude, and LODs that ranged from 0.5 to 450 ppb for the alkali and alkaline earth metals. The LODs were between 2 and 43 times higher than the case with a traditional spectrometer and the instrument suffered from interferences caused by background emission due to the sample matrix, which could not be easily corrected.

Ion trap mass spectrometers have been used extensively in organic MS, but the difficulty of coupling them with many plasma sources means that they have found less favour for elemental analysis. However, if these problems can be overcome, their compact size and ability to perform MSn in a single unit offers definite advantages. Hoegg *et al*.61 have coupled a *liquid-sampling, atmospheric pressure GD to a commercial ion trap* instrument with the specific purpose of evaluating it for IRMS measurements of U isotopes. An IR precision of ~0.1% RSD was achieved, but this was degraded to 1%-3% RSD for low-abundance species. However, as the intention was also to use this as a field deployable instrument, this was deemed satisfactory. Jiang *et al*.62 coupled an MPT with a commercial linear ion trap MS instrument, for the determination of Cd and Zn as both positive M(NO3)·nOH·mH2O and negative M(NO3) ions. The MPT was operated at 50 W with a total gas flow of ~1300 mL min-1 argon. Spectra obtained in positive ion mode were too complex to be used for quantitative analysis, but negative ion spectra were simpler and allowed quantitation, with LODs of 10 µg L-1.

**2.2 Fundamentals**

**2.2.1 Fundamental constants.** For those wishing to know the most recently evaluated isotopic abundances**, t**he Commission on Isotopic Abundances and Atomic Weights of IUPAC has published a revised table of the *isotopic compositions of the elements*.63 The IUPAC have also updated the standard atomic weights of nineteen of the elements,64 four of them resulting from recent determinations of isotopic abundance in terrestrial materials. The project for the accurate determination of Avogadro’s constant and definition of the kilogram is still ongoing, with HR-ICP-MS playing a significant role. The molar mass of 28Si-enriched crystal AVO28 was determined using virtual element IDMS, which was able to resolve interferences, such as 28Si1H from 29Si, in medium mass resolution mode. An average molar mass of 27.97696905 g mol-1 was obtained.

Diagnostic studies require a ready source of fundamental data. New *measurements of the oscillator strengths* of Mo(II)65, 66 and V(II)67 lines were additions to this database. De Podesta *et al*.68 have revised an earlier estimate (2013) of the Boltzmann constant made by measuring the speed of sound in argon. They partly based this on a separate measurement of the molar mass of argon, by making precision comparison measurements of the IRs found in gravimetrically prepared argon against the ratios of Ar isotopes found in atmospheric air. A revised estimate of the Boltzmann constant of kB = 1.380 647 53(125) × 10−23 J K−1,with an uncertainty (k = 1) of 0.91 parts in 106, was computed.

**2.2.2 Diagnostics**

*2.2.2.1 Plasmas.* This reviewer has been a long-time fan of the ongoing work of Bogaerts and co-workers, on *computational modelling of the ICP*, which has been given a timely overview.69 Their approach has been particularly insightful into the behaviour of particles and droplets as they pass through the ICP, both with and without an MS sampling cone present. Their latest two publications described investigations into the behaviour of copper droplets as they pass through the ICP to the MS sampling cone. In the first of these papers70 they used the computational model to study the effects of axial injection position (*i.e.* on and off axis), droplet diameter and mass loading flow rate. They found that droplets injected on-axis were more likely to travel in a straight path through the plasma, with less radial movement and consequently better transport to the sampling cone. Their calculations also predicted an optimum copper droplet diameter of <10 µm (for the particular operating conditions under study) to ensure complete evaporation before entering the sampling orifice. In addition, they found that mass loadings of <100 µg s-1 did not affect the plasma temperature whereas higher loadings of up to 500 µg s-1 caused significant cooling. Consequently evaporation occurred closer to the sampler cone, thereby reducing the probability of ionisation. In the second study71 they built on this work by investigating what happens to the ion clouds formed from the copper droplets, and found that the ion clouds behaved similarly to the droplets, *i.e.* on-axis droplets formed ion clouds closer to the sampler with less radial diffusion. This resulted in a significantly higher fraction of Cu+ ions entering the sampler orifice (i.e., 90% vs 48% in the case of off-axis injection). Increasing the carrier gas rate from 0.4 to 0.6−0.8 L min-1 resulted in a higher ion density at the sampler, with the highest Cu+ fraction entering the sampler at 0.6−0.8 L min-1, but higher gas flows caused too much cooling to increase the ion density further. They also found that an applied power of 1400 W was optimal because it moved the ion cloud closer to the sampler and improved sampling efficiency.

While computational models are all very well, it is important to obtain confirmatory evidence by empirical study. Chan and Hieftje72 used time-resolved, 2D *imaging of the load-coil region of an ICP* to study the behaviour of single 50 µm diameter droplets as they passed through that region. Three wavelengths were observed in order to elucidate the effects on plasma conditions: 309.0 nm OH molecular band; 656.3 nm H(I) emission; and 696.5 nm Ar(I) emission. In the region of the droplet they observed plasma shrinkage due to a thermal pinch effect and heating upstream for up to 4 ms after passage of a vapourising droplet. They speculated that hydrogen from the droplet played a role in these effects due to its higher thermal conductivity compared with argon. They also observed significant plasma cooling up to 6 mm downstream from the droplet location, and a significant change in plasma impedance which lasted for 10 ms. As a consequence, if the droplet introduction rate is higher than 100 Hz, the perturbation in plasma impendence is unlikely to return to a steady-state level before arrival of the next droplet.

Further downstream of the ICP-MS sampling interface, single particle analysis requires fast detection of the transient signals, which might only last between 200 and 400 µs. Most instrument electronics have minimum dwell times of between 50 and 100 µs which limits the counting time and hence sensitivity for the analysis of particles less than 10 nm in diameter. A further problem is that the linear dynamic range is limited to *c.a.* 150 counts per 50 µs dwell time, thus making the detection of fast transient signals something of a challenge. Shaw and Donard73 have overcome this problem by using a magnetic sector ICP-MS instrument with GHz ppm-1 sensitivity, using dwell times of a low as 10 µs. They achieved this by incorporating a physical attenuation grid, after the MS but before the detector, to reduce the intensity of the ion beam. Hence, it was possible to use a discrete dynode electron multiplier in pulse counting mode even for large ion counts. They used this system to monitor solutions of gold NPs of between 5 and 60 nm in diameter, with fast data acquisition up to 105 Hz and capable of measuring signals in excess of 3 x 107 cps. In a related study, Strenge and Englehard74 developed a home-built data acquisition (DAQ) unit to address some of these problems in single-particle ICP-MS. The unit was capable of 5 µs dwell times during continuous data acquisition for virtually unlimited measurement time. Samples containing gold NPs with nominal sizes of 10nm and 30 nm at different particle number concentrations were analysed using this system and compared with a standard DAQ. They found that the increased time resolution almost eliminated errors in monitoring single particle ion clouds, such as particle coincidence and split-particle events.

*Temperature measurements and spatial diagnostics* have long been favoured techniques for plasma characterisation, so inevitably some of the new miniaturised plasmas have now received this treatment. Krahling *et al*.75 determined *Te* and *ne* in a liquid electrode DBD using Stark broadening of Sr(II) 407.771 nm, Sr(II) 421.552 nm and Sr(I) 460.733 nm lines. They determined *ne* to be between 0.8 and 1.6 x 1016 cm−3 and *Te* > 1.1 eV. Unsurprisingly, Boltzmann plots of the OH rotational distribution deviated from thermal equilibrium. Kuklya *et al*.76 studied a low temperature He/N2 DBD used for ambient ionisation. They mapped the spatial distribution of various species in the plasma, but made particular mention of the decrease in N2+, thought to be an important intermediate for the formation of H3O+ and also proton transfer ionisation of analyte species. However, there was an excess of NO in a 0.6% nitrogen plasma, suggesting that charge transfer reactions involving NO+ formed by Penning ionisation might be significant in this type of plasma, though no empirical evidence was presented in the paper.

Burger and Hermann77 presented a method for the measurement of *Stark broadening of atomic and ionic lines* in a plasma produced by UV nanosecond laser ablation of calcium sulfate in argon at near atmospheric pressure. Spectral lines from Ca, O2 and several impurity elements were observed, simultaneously with the Hα transition, over a 6,000 to 14,000 K temperature range. The uniform nature of the ablated plasma aided the reproducible measurement of Stark broadening and the use of an echelle spectrometer of large resolving power allowed the recording of a large number of spectral lines. Borggren *et al*.78 have used diode lasers to excite fluorescence in a pre-mixed, low pressure, methane-air flame, thereby facilitating a two-line ratio method of temperature measurement using In as the thermometric species. The stated advantage was that it afforded 2D planar imaging with a spatial resolution of 210 µm, normally only possible with high power, pulsed lasers.

Sometimes, direct visual observation confirms the intuitive. Yu *et al*.79 used a *high-speed camera to study* an argon MPT source at various power and flow rates. This design mimics that of the more traditional ICP, so the observation that the cone shaped plasma has a rotational motion of *c.a.* 100 Hz follows; as does the conclusion that this helps stabilise it in the presence of a central sample introduction gas flow.

*2.2.2.2* **Graphite furnaces.** *A full 3D nonstationary numerical model of various graphite ETAs* was developed by Tsivilskiy *et al*80. The model was based on the solution of a heat equation within solid walls of the atomiser with a radiative heat transfer and numerical solution of a full set of Navier-Stokes equations with an energy equation for a gas. The governing equations for the behaviour of a discrete phase, *i.e.* atomic particles suspended in a gas (including gas-phase processes of evaporation and condensation), are derived from the formal equations for molecular kinetics by numerical solution of the Hertz-Langmuir equation. A number of types of instrument, including a standard heated ETV and a double-stage tube-helix atomiser were used to test the model. The experimental verification of computer calculations was carried out by a method of shadow spectral visualisation of the spatial distributions of atomic and molecular vapours in an analytical space of an atomiser.

**2.2.3 Interferences.** Since the introduction of ICP-MS over 30 years ago interferences have been a perennial problem. Lum and Yeung81 have reviewed methods used to overcome spectral interferences in ICP-MS, over the last 10 years. They mainly covered recent developments in instrumentation and sample introduction, with an emphasis on the latter. In the case of instrumentation, the crossover of MSn techniques from the organic to the inorganic analysis domain has been significant. The latest approaches involve the use of a triple quadrupole (ICP-QQQ-MS), which has two quadrupole mass analysers in series, separated by an octopole reaction system cell. In a similar way to organic MS, the first quadruple transmits a parent ion which is subject to collision induced dissociation (CID) in the octopole to produce daughter ions. These are then subject to kinetic energy discrimination or chemical resolution before transmission to the second quadrupole. In this way, a variety of approaches can be adopted to reduce spectral interferences. For example, Sugiyama and Shikamori82 used ICP-QQQ-MS to remove spectral interferences on Ag, Au, Ir, Os, Pd, Pt, Rh and Ru by using NH3 to form product ions. Removal of interference was achieved either by selectively reacting NH3 with the interfering species, or by a reaction with the analyte ion to shift its mass away from the interference. The method was tested by measuring 1 ng g-1 of the noble metals spiked into a solution containing 10 µg g-1 each of Cu, Hf, Mo, Nb, Ni, Pb, Rb, Sr, Ta, W, Y, Zn, Zr and the REEs.

Hattendorf *et al*.83 have studied interferences caused by doubly-charged, polyatomic Ar interferences in ICP-MS. They focussed on the unexpected interference at m/z 63 and 64 caused by ArSr2+ and its effect on Zn and Cu IRA. They found that the same mass concentration of Sr altered the measured 63Cu:65Cu and 64Zn:66Zn isotope ratios by between −0.036 ‰ and −0.95‰. In addition, they also observed effects on IRs caused by: BaAr2+ on Sr+; MgAr2+ on S+; and CaAr2+ on Ca+. Wet sample introduction and lower carrier gas flow rate was found to reduce the interferences, but the authors noted that matrix removal prior to analysis may be a requirement to ensure accurate IRs.

Cheung *et al.*84 continued a recent theme which focussed on prediction of matrix interferences in ICP-OES. However, in the paper they used the temporal nature of ICP-TOF-MS to monitor the time-dependent ratio of two ion signals, and used it to indicate and correct for mass-dependent matrix interferences. By injecting a discrete sample solution they were able to monitor the time-dependent dispersion of the aerosol. In the absence of matrix interference all species yielded the same concentration profiles, with matching signal profiles. However, in the presence of a matrix this was not the case, and signal ratios could be monitored to detect this. They studied the 51V+:55Mn+, 59Co+:107Ag+, 55Mn+:208Pb+, and 52Cr+:208Pb+ ratios and found that the ion pairs having the largest mass difference were best to flag up matrix interferences caused by heavy matrices such as Ba and U. In addition, the dilution factor necessary to minimise the interference could be identified by the point at which the ratio became constant.

* 1. **Chemometrics**

Novel research on the application of chemometrics to analytical atomic spectrometry continues to be sparse. Novaes *et al*.85 reviewed (152 references) the application of multivariate optimisation for ICP-OES. They covered a range of methods, such as various types of Factorial, Central-composite, Placket-Burman, Doehlert and Simplex optimisations. These were applied to sample preparation, sample introduction and instrument optimisation. However, the review only covered the relatively recent literature, with an emphasis on secondary sources in certain areas, as evidenced by the omission of key papers from the early development of ICP-OES.

In a somewhat philosophical paper, Andersen86 commented on the origin of uncertainty in analytical measurements. He examined the question of why some laboratories produce excellent results while others do not; and whether is it down to human error or inherent failings in the system. He suggests that lack of compliance can be explained largely by the latter rather than the former, and concluded that a consensus value should include any outliers. While this reviewer does not agree entirely with this anaylsis, it does hold out hope for the ‘ordinary’ practising analyst.

**3 Laser-based atomic spectrometry.**

Key fundamental studies and instrumental developments (published in 2016) in laser-based atomic spectrometry are highlighted in this section, following on from progress in this area reviewed in previous years. Atomic spectrometry techniques where the laser is used as either an intense energy source or a source of precise wavelength (e.g. LIBS, LIF, LAAS and CRDS) are considered. Studies related to LA-ICP-MS and LA-ICP-AES are reviewed in section 1. The use of lasers for fundamental studies of the properties of atoms, or for thin film deposition, is not reviewed.

**3.1 Laser induced breakdown spectroscopy (LIBS).**

LIBS is one of the most widespread techniques in which the laser is used as an energy source to induce an optical plasma. This section describes the latest instrumental developments and fundamental studies related to LIBS, and some important new areas of application. There have been several reviews covering LIBS in the areas of sample preparation,87 nuclear fusion technology,88 agriculture,89 and soil carbon.90 Labutin *et al*.91 presented a review that summarised nearly two decades of studies on femtosecond (fs)-LIBS. It covered the advantages of fs-LIBS, including low ablation thresholds, high-spatial resolution, and rapid analysis of samples. It also addressed limitations of the technique and different approaches to overcome such constraints, while retaining the unique possibilities of fs-LIBS. Development and applications of LIBS in Asia were recently summarised and discussed by Wang *et al*.92

**3.1.1 Fundamental studies.** Several reports of *methods to measure, evaluate and minimise noise sources, spectral interferences and matrix effects in LIBS* were published. Tognoni *et al*.93 presented an introductory review on signal and noise sources in LIBS. Careful design of the experimental setup and of the measurement protocol was considered to be essential to reduce the spectral fluctuations. Different signal normalisation strategies were also discussed together with the use, if available, of appropriate internal standards. In this context, Mao *et al*.94 investigated the limitations of LAMIS in the presence of measurement noise (e.g. source flicker, photon shot) and spectral interferences, and ways to minimise their impacts using PLS regression. In calibrations with matrix-matched standards, spectral interferences were found to affect precision but not accuracy. In particular, it was found that the precision of 13C isotope abundances degraded from ~1‰ RSD, in the absence of spectral interference, to up to ~20‰ in the presence of multiple interfering peaks that were 1000x stronger than the molecular bandhead of the analyte. Additionally, Judge *et al*.95 investigated, experimentally and theoretically (e.g. using ATOMIC code), the matrix effects observed in LIBS emission spectra of binary mixtures of Na–Cu and Mg–Cu pressed powders. They found that the presence of Cu increased Na(I) and Mg(I) emission intensities but decreased Mg(II) intensity. The presence of Cu was thought to induce an increase of the plasma electron density at short delay times (< 1µs), which enhanced the recombination processes.

*Several workers investigated plasma shielding effects and ablation processes at different operating conditions*, such as underwater, ambient gas, pressure and temperatures). In particular, Pishdast *et al*.96 investigated, experimentally and numerically, the influence of plasma shielding induced by Nd:YAG laser irradiance at various pressures (ranging from 5 to 1000 mbar) and different atmospheres (*e.g*. Ar, He, Ne, and air), on the behavior of radiation intensity, SBR, and expansion of the plasma. Strong enhancement of Cu atomic emission lines due to increasing plasma temperature and density was observed at increasing laser irradiance, but saturation was observed at values above 5 GW cm-2. Simulation and experimental values of plasma plume expansion velocity, obtained using the absorption and scattering of a continuous He–Ne probe laser beam, showed that plume velocity was enhanced at increasing laser irradiance until it saturated due to plasma shielding and a reduction in effective laser target interaction. Temporal evolution of pressure, density, *Te*, *Tion* and velocity of different layers of plasma, were numerically calculated using hydrodynamic equations to confirm the experimental results.

El-Saeid *et al*.97 studied the effect of very low sample temperature (77 K) on LIBS spectral behavior and plasma parameters, under both atmospheric pressure and vacuum conditions. From the analysis of bronze alloy samples, it was observed that analyte emission and ablation rates were reduced when the samples were at low temperature. Plasma *ne* and *Te* were lower at low temperature and increased under vacuum conditions. LIBS analysis under extreme temperature conditions might be of interest for applications in planetary exploration. Laser ablation under vacuum conditions was also studied by Oderji *et al*.98, who developed a model to describe the laser ablation of W, based on the non-equilibrium mechanism of explosive partial sublimation in the superheated zone of the sample surface. Vacuum conditions simulated the situation within a fusion reactor. During the irradiation of W only a portion of the lattice bonds were thought to be broken so a mixture of atoms and particles was generated. The mass of ablated particles was measured using two quartz crystal deposition monitor sensors located at different angles to the normal of the target surface, and compared with a theoretical estimate obtained using a heat conduction equation. The results suggested that ablated particles were free to disperse whereas atoms formed vapour plume which produced rarefaction waves on expansion on a vacuum.

*Underwater LIBS has become a hot topic*. Gavrilovic *et al*.99 investigated the spatial and temporal evolution of an underwater LIBS plasma, formed on an aluminium target, using fast photography, Schlieren imaging, shadowgraphy, and optical emission spectroscopy. Observation revealed that the plasma rapidly expanded and decayed immediately after the single laser pulse. The optical emission was characterised by an intense continuum component and large line-widths. However, at longer delays (> 5 µs) another plasma phase, starting from the backward reheated target and lasting over tens of microseconds from the laser pulse, was observed. This secondary plasma, confined inside the expanded vapour cavity, was found to have significantly lower electron densities, resulting in emission spectra with an almost continuum-free component. Goueguel *et al*.100 reported the use of underwater LIBS for direct *in situ* measurements of CaCO3 dissolution at elevated pCO2 (e.g. up to 350 bar, which equates to depths of about 3500 m). Dissolution of CaCO3 was observed at increasing pCO2 (from 50 to 150 bar) but then remained nearly constant at higher pressures, which may be related to changes in pH. The authors thought that this method might provide a practical way to perform real-time measurements of elements released during carbonate dissolution resulting from the degradation of cement seals in geologic CO2 storage.

*LIBS methods have been developed for the analysis of aerosols*. Boudhib *et al*.101 demonstrated that calibration-free LIBS measurements provided accurate results for the compositional analyses of aerosols in a helium flux. The LIBS plasma was considered to be in partial LTE, in which the population number densities of plasma species, except He atoms and ions, followed Boltzmann equilibrium distributions. The authors claimed that this method could be applied to all types of low density aerosols, where reabsorption of spectral lines from vapourised atoms is negligible in the cold plasma peripheral zone.

**3.1.2 Instrumentation.** Novel, low-cost approaches have been investigated to improve IR measurements and to monitor the spatial and temporal evolution of plasma species. For instance, Morgan *et al*.102 demonstrated the use of a compact Fabry–Perot etalon, integrated with a moderate resolution Czerny–Turner spectrometer, to achieve the resolution needed for the LIBS measurement of uranium enrichment (235U:238U) in ambient air. Spectral line widths of about 10 pm were achieved for the U(II) 424.437 nm emission line, which is enough to discriminate natural from the highly enriched uranium. The authors considered this to be inexpensive and effective alternative to high resolution Czerny– Turner or echelle spectrometers for detection of U isotopes, which could lead to the development of portable, low-cost, and high-resolution LIBS instruments with isotopic measurement capability. Negre *et al*.103 showed the high potential of UV-LIBS (266 nm) for the classification and identification of plastic materials. They used a simplified detection system based on an intensified CCD camera associated with narrowband filters. The spatial distribution and evolution of the molecular species (e.g. C2 and CN) in the ablation plume exhibited different behaviours for different polymers. Differences in the spatial distribution and temporal evolution were related to different formation pathways of radicals in the ablation plumes (*e.g.* fragmentation versus recombination). Moreover, it was demonstrated that the presence of additives did not affect the classification capabilities. The authors concluded that these additives might improve the laser absorption efficiency and reduce the penetration depth into the polymer.

*Tandem-LIBS has been investigated as a way to improve analytical figures of merit*. Viljanen *et al*.104 developed microwave assisted LIBS (MW-LIBS) working at atmospheric pressure conditions without employing an enclosed cavity. Signal enhancement was achieved by using integration times of hundreds of microseconds. The external microwave field was coupled into the plasma using a novel and simple near-field applicator. The experimental set-up was developed to avoid the complex process of sample loading and to provide improved temporal and spatial resolution. Jarvinen *et al*.105 employed electrodynamic balance trap (EDB)-LIBS to investigate the analysis of single water droplets, containing known amounts of Al, Mn and Pb. The dependence of signal on the level of analyte preconcentration was evaluated by varying the water content and the exact position of the particles. Emission signals became saturated after 6 s (*i.e.* after total evaporation) because even a small amount of water in the particle resulted in a significant reduction in the LIBS signal. Emission signals were also reduced when the trapped particle was out of the focal position. The authors scanned the particles across the focal spot of the laser beam, with a resolution of a few micrometers. This was claimed to provide means to improve the sensitivity and reproducibility of single particle LIBS analysis.

**3.1.3 Novel LIBS approaches.** *New LIBS methods for 3D bio-imaging* have recently been developed, opening new research fields in medicine and biology. Gimenez *et al*.106 developed a quantitative method with 3D capability to image NPs in the tissue of whole organs. They achieved detectability at the ppm level and resolution of 100 μm2. The distribution of Gd-based NPs, used in image-guided radiotherapy, in mouse kidney was investigated. Emission spectra, covering the range 315 to 345 nm, was recorded for each laser shot to simultaneously measure Ca, Gd and Na emission lines. The high scanning speed of LIBS, compared to other techniques such as µ-XRF or LA-ICP-MS, allowed 3D investigations to be conducted on large biological samples within reasonable time periods.

*Determination of trace amounts of halogens in solid samples* by LIBS is a challenging task due to the low excitation efficiency of these elements. Alvarez-Llamas *et al*.107 developed an atmospheric-air LIBS method, based on the detection of CaF molecular emission bands, for the determination of trace amounts of F in solid samples. Samples of copper, containing F concentrations between 50 and 600 μg g-1 and variable amounts of Ca, were used to demonstrate the linear relationships between CaF emission signal and F concentration. LODs for F determination in atmospheric-air LIBS were improved by more than 1 order of magnitude.

Several approaches for *direct LIBS liquid analysis* were published during the review period, highlighting the increased interest in this research field. Zhong *et al*.108 developed an ultrasonic nebuliser to improve LIBS capabilities for direct liquid quantitative analysis. An operational procedure was designed to enhance LIBS stability and repeatability for the analysis of Pb-containing solutions. A linear calibration curve, up to a Pb concentration of about 4000 µg g-1, for the background normalised Pb(II) emission line at 220.35 nm was obtained. De Giacomo *et al*.109 demonstrated the use of NELIBS for microdrop analysis at the sub-ppm level using single shot mode. The emission intensity of Ag(I) 328.1 nm, Li(I) 670.8 nm, and Pb(I) 405.7 nm increased when a microdrop (e.g. aqueous, protein and human serum solutions) was deposited on a glass substrate covered with gold NPs. The authors thought that the enhancement was due to field enhancement caused by coupling of the electromagnetic field of the laser with that induced on the NP surface plasmon. Other effects such as adsorption of analytes on the NP surface and increase of particle number density in the plasma phase might also have had an influence. These promising results highlight the potential capability of NELIBS on future medical and forensic science applications. The wavelength dependency of NELIBS was investigated by Sherbini *et al*.110 Three wavelengths from a Nd:YAG laser, at 1064 nm, 532 nm and 355 nm, were employed for the LIBS analysis of ZnO nanomaterial and bulk material. Enhanced emission signals and lower laser fluence thresholds were observed for the nanomaterial. The authors considered that lower laser fluence thresholds were due to a reduction in the bulk thermal conduction length to the size of the nanoparticles. Moreover, laser radiation dependent threshold fluence was found to vary with wavelength as 1/λ2.

**3.2 Laser-induced fluorescence (LIF).**

Harilal *et al*.111 demonstrated 2D absorption–emission mapping of LIF Al transitions from a laser induced plasma at atmospheric pressure conditions. A narrow band, tunable continuous wave laser was employed as a LIF excitation source to increase the intensity and persistence of emission from selected atomic transitions at 394.40 nm and 396.15 nm. Line broadening effects, such as Stark broadening, were negligible because LIF utilises the ground-state population which persists longer when the plasma is cooler. This method, based on 2D fluorescence spectroscopy of the laser induced plasma, enhanced the capability of fluorescence spectroscopy by combining the information of both the excited and ground-level populations.

**3.3 Laser atomic absorption spectroscopy (LAAS).**

A novel tunable diode laser atomic absorption spectroscopy (TDL-AAS) instrument was developed by Qu *et al*.112 for the detection of K under optically thick conditions, produced when the product of atomic line strength and absorption path length gives rise to high absorbance. Line broadening and analyte concentration were simultaneously obtained by least-square fitting of simulated and measured absorption profiles. This K gas sensor was found to provide fast, robust, calibration-free, *in situ* measurements over 6 orders of magnitude. Hence, it was considered to be well suited for diagnostics and process monitoring in combustion and gasification applications.

**3.4 Cavity ringdown spectroscopy (CRDS).**

CRDS provides sensitive light absorption measurements for applications in trace gas detection, spectroscopy, and reaction kinetics. Sadiek *et al*.113 developed a new continuous wave IR-CRDS setup, equipped with a tunable narrow-bandwidth high power OPO laser system. They used this to investigate the saturation dynamics and working limits of the novel saturated-absorption CRDS approach. Transient dynamics of absorption saturation were observed to depend on the interaction of the absorbing molecule with the buffer gas, the overall relaxation and the empty cavity decay rate. This CRDS approach was able to provide the absorption spectrum of several lines with different intensities, and to exhibit linear response with respect to sample concentrations.

**4 Isotope Analysis**

Measurement of IR continues to shift in emphasis as instrumental advances are disseminated across the mass spectrometric community. In particular, high-impedance resistors have been utilised in studies of U-Pb chronology as well as in the examination of low-concentration samples for mass-dependent fractionation. The range of ‘stable’ isotope systems continues its inexorable spread across the mass range between lithium and uranium. At the high-mass end there are continued developments in nuclear forensic applications for uranium and plutonium.

**4.1 Reviews**

Although TIMS is perhaps an instrument on the wane relative to MC-ICP-MS for IR determination, Aggarwal*et al.114* provided a review of TIMS usage in nuclear science. The main conclusion was that it is a technique which complements plasma-source and AMS instrumentation in nuclear forensic analysis, but no direct comparison was made between the techniques. Primarily, the advantage of TIMS stems from low backgrounds and low polyatomic interferences, but other techniques are leading the way in terms of sensitivity, mass fractionation stability and comparable inter-element fractionation coefficients.

This year Goderis *et al.115* provided a significant review of isotopes in cosmochemistry. It covered the range of radiogenic, mass-dependent and mass-independent IR variation and provided very useful tables of information on the key isotopes of interest. Of particular interest was a schematic figure that depicted the key processes responsible for each stable isotope deviation and a comprehensive reference list across the subject area.

Horsky *et al.116* evaluated the *uncertainty of Sr isotope measurements* by calculating the combined uncertainties inherent in three different instrumental mass fractionation strategies: internal normalisation to 86Sr:88Sr; sample-standard bracketing; and using Zr as a fractionation proxy. A conclusion from comprehensive propagation modelling was that natural variation in normalisation parameters expands relative uncertainties by a factor of two, meaning that instrumental fractionation corrections become the major contributor to overall uncertainty. *Correction for mass fractionation* and application of double spike protocols requires complex mathematical calculations. To assist with this, Zhang *et al.117* produced a Matlab-based program named “IsotopeMaker”. This software provided a solution to all double spike systems, both radiogenic and stable, with four or more isotopes. It was also aimed at users of laser ablation MC-ICP-MS for whom it will perform data reduction and correct for interferences in Sr, Nd and Hf isotope determinations.

**4.2 Isotope Dilution Analysis**

A study by Isnard *et al.118* utilised a 127I spike to quantify the 129I present in synthetic samples. This work used Te as an internal standard to determine instrumental mass bias following blank and interference correction. Results indicated that 129I could be determined to better than 0.7% and may lead to a new determination of the 129I half-life. Liu *et al.*119 also investigated 129I measurement, this time by AMS. They also used stable 127I as an addition with a niobium matrix powder for the AMS sputter target and found that it produced consistent results for rapidly screening a wide variety of materials, including seaweed and sediment. Pagliano *et al.*120 investigated methods to define the curvature that can be inherent in ID calibrations. They demonstrated that the exact curvature could be defined from a three-parameter function known as the Padé *et al.*121 approximant. This method was found to eliminate errors induced by applying linear functions to nonlinear calibration curves.

**4.3 Isotope Ratio Analysis**

**4.3.1 New developments.** Tandem ICP-MS was investigated as a method for Sr isotope determination by Bolea-Fernandez *et al.*122. This study used an ICP-QQQ-MS instrument with a CH3F–He mixture in the octopole reaction cell. Sr+ ions reacted with the CH3F which enabled measurement of the 86-87-88Sr isotopes at m/z 105,106 and 107 respectively. A key feature of this analysis was the non-reactivity of Rb so there was no interference from to from 87RbF+. As such, this technique opened the way for Sr isotope determination without prior chemical separation, providing the level of precision delivered by ICP-MS is appropriate for the purpose.

Laser ablation produces transient signals that often result in an IR drift through the course of measurements. Claverie *et al.*123 examined the relationship between detector response times on MC-ICP-MS and drift in IR. Detector response times were noticeably different between Faraday-Faraday combinations, in particular when signals changed rapidly at the start of ablation. By minimising the regression coefficient between coincident detector signals through an acquisition they were able to calculate the time lag between the detectors (or the order of 150 ms between ion counting and Faraday detectors). This produced a consistent 235U:238U ratio during the course of ablation of uranium particles. The method could be applied routinely to any LA IR analysis.

The effect of LA transient signals on IR was also investigated by Kumura *et al.*124. These workers examined the effect of changes in the intensity of Pb signal on the Pb IR generated by differences in the response of Faraday amplifiers. The study utilised the recently introduced 1013 Ω resistors and made comparisons with 1012 Ω and multiple ion counting detector combinations. After detector-amplifier response time correction, data generated using1013 Ω resistors for 208Pb:206Pb in the 1.7 ppm Pb BHVO-2G reference glass achieved precisions of +/- 0.2% (2 sd). This was demonstrated to be a 2–3 fold improvement in precision relative to the 1012 Ω amplifiers. Zircon U:Pb geochronology by TIMS was the subject of a study by von Quadt *et al.*125. The study used 1013 Ω resistors to measure all isotopes except 204Pb which was assigned to an axial electron multiplier detector. Collector gains were completed using an Nd isotope standard. Results indicated that the high-impedance equipped Faraday collectors were capable of reproducibility at the 0.01% level.

**4.3.2 Geological studies.** Klaver *et al.*126 used 1013 Ω resistors during the measurement of Pb isotopes by solution MC-ICP-MS. This study used a 207Pb–204Pb double spike to correct instrumental mass fractionation and examined sample quantities down to 5 ng Pb. At this concentration the precision achieved was similar (<+/-0.002 for 206Pb:204Pb in NIST SRM 981) to that using 1011 Ω resistors on high concentration samples. It was noted that the limiting factor in low-level Pb isotope determination was minimising and correcting for the procedural and instrumentatal blank contributions.

Lead IR measurement by both 265 nm femtosecond and 213 nm nanosecond LA was investigated by Ohata *et al.*127. Instrumental mass fractionation on the MC-ICP-MS was corrected by introducing the SRM 981 reference solution via desolvation and a dual-sample introduction system. Both laser systems produced consistent results and demonstrated that application of a fractionation determined from the coincident solution measurement gave accurate Pb IR.

*Calibration schemes for determination of Pb:U during zircon geochronology by SIMS* were evaluated by Jeon *et al.*128. Of the various Pb/UO calibration schemes tested with reference zircon 91500, Pb/UO-UO2/UO showed the smallest mean uncertainty. The use of this scheme demonstrated that precision was much improved, but the age determined was not changed significantly. Sharp *et al.*129 investigated the mass bias corrections used in the U-Pb dating of uraninite by SIMS. They found that the level of mass bias varied as a function of Pb content of the mineral analysed, and developed a three-point calibration protocol based on different reference materials to correct bias in unknown materials. Errors in age determination were found to be as much as 130 Ma in uraninite of ~500 Ma.

*Thallium isotope measurement* was the focus of a study by Nielsen *et al.*130. They examined the Tl-isotope variation across the chain of Aleutian volcanoes and found that ε205Tl changed to heavier ratios toward the west. This was taken to reflect the nature of the sedimentary material being subducted – more continental or mantle derived to the east and more pelagic or MnO-bearing to the west.

**4.3.3 Stable isotope ratio studies.** An issue with *sample-standard bracketing as a method for correcting instrumental mass fractionation* is the potential for matrix differences between the unknown and the reference standard. This has been found to be a particular problem with Li isotopes. Lin *et al.*131 examined the background and memory effects of Li during MC-ICP-MS analysis and concluded that high Li instrumental backgrounds caused apparent fractionation differences between sample and standard. After rinsing the aspiration system with 5% NaCl they found that backgrounds were reduced by up to 70 times. This effectively eliminated the need to match sample and standard acid concentration or Li concentration as fractionation remained stable between measurements.

In order to remove the matrix prior to MC-ICP-MS analysis, Van Hoecke *et al.*132 devised a cation exchange scheme with 0.28 M HCl loading of <100 ng Li and elution of 0.5 ml fractions. This resulted in an external precision of +/- 0.2‰ for both carbonate and clay fractions of sedimentary material.

Magnesium is an abundant element in many geological materials, so Mg IR variation is a potential target for LA. Dai *et al.*133 coupled a femtosecond laser to MC-ICP-MS and investigated Mg isotope variation in geological reference materials in glass form. They concluded that reproducible δ25Mg and δ26Mg could be achieved by referencing to a solution standard providing the concentration ratio of the sample:standard was in the range 0.4–3.0 δ26Mg. The reproducibility was reported to be within ~+/- 0.2 for BCR-2G and BIR-1G. Vogl *et al.*134 characterised the absolute Mg isotope composition and atomic weights of European Reference Materials and related these to NIST SRM 980. Fractionation laws used to correct Mg isotope ratios were found to produce systematic bias, with the exponential law found to induce the smallest.

Sulfur isotopes have been traditionally measured by electron-ionisation gas source mass spectrometers. Typically these achieve δ34S reproducibility of +/-0.2‰ but require mg levels of analyte. Because of the lower amount of sulfur required, Albalat *et al.*135 have investigated using MC-ICP-MS for δ34S on medical samples. Their study demonstrated that subtle variations in δ34S (+/- 0.1‰) can be achieved with concentrations of approximately 300 ng ml-1. The medical application showed that there are detectable differences in sulfur IR between patients with and without liver cancer. Fu *et al.*136 also used MC-ICP-MS to measure sulfur isotopes, but via LA. The study examined a range of solid sulphide reference materials with the aim of enhancing sensitivity by optimising operational conditions and improving precision of sulfur IR. Their instrument was tested with standard cones as well as ‘X’ skimmer and ‘Jet’ sampling cones in combination with varied addition of Ar make-up gas and N2. Laser ablation is known to produce fewer hydride interferences compared with solution-based sample introduction, but these were still present in mass scans across the sulfur peaks in their study. Addition of 4 ml min-1 N2 was found to suppress hydride formation and, combined with measurement at medium resolution (~5000), resulted in stable δ33S and δ34S with precision of ~ +/-0.4 (2 SD). A useful assessment was made of the relationship between signal intensity and measurement precision for each of the cone combinations, which provided a good guide to what can be achieved with different sulfur concentrations. Hauri *et al.*137 demonstrated the potential for sulfur isotope measurement by nano-SIMS. These workers were able to demonstrate long-term reproducibility of metal sulphide analysis of +/-0.4 for δ33S. The technique was then used to demonstrate that measurements by nano-SIMS were capable of distinguishing mass-independent fractionation of sulfur isotopes generated by microbial sulfate reduction in the neoarchaean (~2.7 Ga).

*The potential for high precision K IR measurements* was examined by Li *et al.*138. They used single-focusing ICP-MS with a collision cell that removed ArH+ at m/z 41 by reaction with He and D2 gas. Following cation chromatographic purification, the measurements resulted in precision of +/- 0.02% (2 sd) for 41K:39K on samples including rock reference materials and plant samples.

Measurement procedure and *fractionation correction of Ca isotopes* was the subject of a study by Naumenko-Dezes *et al.*139 They used TIMS to measure Ca SRM 915 and found that a modified exponential law fractionation correction produced internally consistent Ca IR across the mass range. It resulted in valid results across the range of fractionation conditions, including when the filament was strongly depleted following extensive ionisation.

Vanadium IR were investigated by Nielsen *et al.*140 using MC-ICP-MS. At medium resolution (~4000) and with a combination of 1010 Ω and 1012 Ω resistors they achieved an external reproducibility of +/-0.15‰ δ51V. This is similar performance to previous low resolution methods, but they used as little as 200 ng V per analysis.

Larsen *et al.*141 studied *Cr IR measurements to quantify mass-dependent and mass independent fractionation* from a chemical separation viewpoint. They identified the magnitude of stable isotope fractionation generated by the elution characteristics of CrIII species (Cr3+, CrCl2+, CrCl2+, CrCl3) and devised a chromatographic procedure that resulted in Cr recoveries in excess of 95%.

A study by Finlayson *et al.*142 set out to *improve the precision of Fe IR* in geological measured by MC-ICP-MS. Like many Fe isotope studies, these workers used a 57Fe–58Fe double spike to correct for instrumental mass fractionation. However, a novel aspect was the use of ion counting to measure 60Ni, to enable a more accurate determination of the isobaric 58Ni. This improved the reproducibility of 56Fe threefold. Further improvement was also made by the detection of transient NeAr polyatomic interference by the ion counting detector.

A method for Cu isotope measurement in geological materials was investigated by Hou *et al.*143. These authors deployed *NIST SRM 944 gallium as an internal mass fractionation standard*. Fractionation of 65Cu:63Cu in bracketed standards was quantified using 69Ga:71Ga and their average value corrected the Cu fractionation in the samples.

In order to understand the biogeochemical processes operating on Zn in seawater Samanta *et al.*144 developed an MC-ICP-MS protocol using a 67Zn–68Zn double spike added to the seawater prior to processing. Results indicated that there is a systematic change in Zr isotopes with ocean depth which were attributed to variation in biological activity.

Louvat *et al.*145 have examined the systematics of Br isotope measurement by MC-ICP-MS using high- and low-resolution mode, and made a comparison between three different introduction systems: spray chamber, direct injection and desolvation. Results in low resolution mode were found to produce higher precision than high resolution providing the 40Ar2H+ isobaric interference was minimised by tuning the mass spectrometer. Br solutions and salts gave reproducible δ81Br to better than +/- 0.25‰. Alternatively, Ma *et al.*146 used positive ionisation TIMS to determine Br isotopes from Cs2Br+ ions and reported an external reproducibility of < 0.18 ‰ δ81Br.

Molybdenum isotopic measurements of geological samples were investigated by Liu *et al.*147 using MC-ICP-MS. The accuracy of Mo isotopes was compared following fractionation correction by double spiking and sample-standard bracketing. Both methods were found to give comparable results, but the double spike method produced better results for samples with less than 500 ng g-1 Mo. External precision for samples with between 10 and 100 ng g-1 Mo was found to be better than +/- 0.04% for δ98:95Mo. Nagai *et al.*148 investigated the potential for negative ionisation TIMS to measure Mo isotopes, by generating MoO3- ions from a rhenium filament loaded with La(NO3)3. Following a correction for oxygen isotope interferences they claimed that this method resulted in a 1.3 to 2.7 fold improvement in reproducibility, of +/- 10 μ 95Mo, where μMoi = [(iMo/96Mo)sample/(iMo/96Mo)std - 1] x 106: normalized to 98Mo/96Moi = 1.413173 by using the exponential law. Worsham *et al.*149 also measured Mo isotopes by negative TIMS and found that careful oxide correction resulted in ~2.4 times improvement in the precision of μ97Mo.

A technique for measuring Ru stable IR was developed by Hopp *et al.*150. This utilised a 98Ru–101Ru double spike added prior to sample digestion to accommodate instrumental mass fractionation and chromatographic fractionation. An effective separation method was performed by cation exchange followed by distillation of volatile Ru oxides. Analysed rock standards demonstrated that an external precision of +/-0.05 ‰ for δ102:99Ru could be measured using MC-ICP-MS, and that this level of precision was sufficient to confirm that variations of approximately 1‰ δ102:99Ru existed between Ru standard solutions and natural chromite crystals.

Saji *et al.*151 reported Nd isotope measurements using MC-ICP-MS that examined mass-dependent isotope compositions of geological, meteoritic and reference materials. The high precision achieved (<3.5 ppm on all Nd isotope pairs) and high chemical recovery allowed a comparison of mass-dependent effects and potentially revealed the effects of a 146Nd nucleosynthetic anomaly.

Tungsten IR in reference materials were the analytical focus of Abraham *et al.*152. Following three-step anion chromatography, W isotopes were measured in high resolution by MC-ICP-MS, in a 0.2 M HNO3–0.1 M HF solution. Mass fractionation was accounted for using a 180W–183W double spike. External reproducibility of rock reference materials was determined to be +/- 0.05‰ of the δ186W parameter. Trinquier *et al.*153 used negative ionisation TIMS to measure W isotopes as WO3-. A problem was a mass-dependent oxygen isotope variation on the oxide ions at 182W and 184W. Corrections could be made on the 183W:184W ratio, but this assumed the tungsten ratio is itself constant. A method was employed to simultaneously monitor the 18O:16O and the W IR on an individual integration basis.

Mercury isotope analysis by MC-ICP-MS was the subject of a study by Rua-Ibarz *et al.*154. They investigated the effect of sample introduction using both pneumatic nebulisation and CV generation. Using combined sample-standard bracketing and Tl as mass fractionation correction, they were able to provide a long-term precision of better than 0.006 %. Cold vapour generation was found to enhance Hg signal intensity by a factor of 20 compared to pneumatic nebulisation.

**4.3.4 Nuclear forensics.** During nuclear fission one product is 93Zr but this is difficult to measure because of the isobaric interference from 93Nb. Martschini *et al.*155 used a multi-anode ionisation chamber in AMS to separate 94Zr from 94Mo. They predicted that this would result in a reduction of 93Nb interference and enable measurement of 93Zr:Zr ratios below 10-9.

Esaka *et al.*156 used *ICP-MS to measure individually dissolved U and Pu particles*. They demonstrated that 240Pu:239Pu, 241Pu:239Pu and 242Pu:239Pu can be determined accurately in particles with U:Pu ranging from 1 to 70, provided a correction is made for 238UH. It was not possible to measure 238Pu:239Pu with good precision due to the high blank on m/z 238. Konegger-Kappel *et al.*157 measured Pu isotopes of particle samples by LA-MC-ICP-MS. They targeted material originating from the Chernobyl reactor and determined average values for 240Pu:239Pu and 242Pu:239Pu that were comparable with previously published data for the contamination incident. Hedberg *et al.*158 also evaluated nuclear forensic measurements of U particles but used multi-ion counting SIMS. They achieved precision for 235U:238U of 0.1% (1 sd) on reference materials with 10% 235U and ~1.5% on ratios with the minor isotopes 234U and 236U in the U010 reference material.

Plutonium IR were determined by Isselhardt *et al.*159 using RIMS. This technique has the potential to allow isobar-free analysis of heavy elements without chemical purification. Tests with Pu deposited on metal surfaces yielded overall precision of 240Pu:239Pu better than 1.5% (2 sd).

*High-resolution ICP-OES has been used to examine U and Pu isotopes* by Krachler *et al.*160. They demonstrated the potential for this technique to quantify 238Pu, 239Pu and 242Pu. In addition161 this was shown to be an alternative to MC-ICP-MS for 234U:238Pu age dating. Buompane *et al.*162 examined the potential for measuring 236U-238U by AMS using uranium carbide relative to uranium oxide as molecular ions. Results indicated that when UC- ions are injected 238U backgrounds were significantly reduced relative to UO- or UC2-.

Paul *et al.*163 investigated *new ionisation techniques for* *TIMS analysis of U and Pu*. They used a polymeric material as sorbent to concentrate the actinides. These polymer sorbents were grafted to rhenium filaments by melting before measurement to determine U and Pu concentration. The advantage of this method was seen as providing a single-step preparation with reduced exposure of analytical personnel to radiation.

**5. Glossary of Abbreviations**

Whenever suitable, elements may be referred to by their chemical symbols and compounds by their formulae. The following abbreviations may be used without definition. Abbreviations also cover the plural form.

|  |  |
| --- | --- |
| 3D | three dimensional |
| AA | atomic absorption |
| AAS | atomic absorption spectrometry |
| ADI | ambient desorption ionisation |
| AES | atomic emission spectrometry |
| AF | atomic fluorescence |
| AF4 | asymmetric flow field-flow fractionation |
| AFM | atomic force microscopy |
| AFS | atomic fluorescence spectrometry |
| APDC | ammonium pyrrolidine dithiocarbamate |
| APGD | atmospheric pressure glow discharge |
| CCD | charge coupled detector |
| CCP | capacitively coupled plasma |
| CRM | certified reference material |
| CRS | cavity ringdown spectroscopy |
| CS | continuum source |
| CV | cold vapour |
| CVG | chemical vapour generation |
| DBD | dielectric barrier discharge |
| DC | direct current |
| DDW | distilled deionised water |
| DL | diode laser |
| DLTV | diode laser thermal vapourisation |
| DMA | dimethylarsenic |
| DOF-MS | distance of flight mass spectrometry |
| DOTA | 1,4,7,10-tetraazacyclo-dodecane n,n′,n″,n′′′-tetra acetic acid |
| EDB-LIBS | electrodynamic balance trap laser induced breakdown spectroscopy |
| ES-MS | electrospray mass spectrometry |
| ETV | electrothermal vapourisation |
| ETV-AAS | electrothermal vapourisation atomic absorption spectrometry |
| ETV-ICP-MS | electrothermal vapourisation inductively coupled plasma mass spectrometry |
| EVG | electrochemical vapour generation |
| FAPA | flowing atmospheric pressure afterglow |
| FF | flame furnace |
| FI | flow injection |
| FWHM | full width at half maximum |
| GD | glow discharge |
| GD-MS | glow discharge mass spectrometry |
| GD-OES | glow discharge optical emission spectrometry |
| GF-AAS | graphite furnace atomic absorption spectrometry |
| HG-AAS | hydride generation atomic absorption spectrometry |
| HG-AFS | hydride generation atomic fluorescence spectrometry |
| HPLC-ICP-MS | high performance liquid chromatography inductively coupled plasma mass spectrometry |
| HR | high resolution |
| hTISIS | heated torch integrated sample introduction system |
| HV | high voltage |
| ICP-AES | inductively coupled plasma atomic emission spectrometry |
| ICP-DOF-MS | inductively coupled plasma distance of flight mass spectrometry |
| ICP-MS-MS | inductively coupled plasma multicollector mass spectrometry |
| ICP-MS | inductively coupled plasma mass spectrometry |
| ICP-MS/MS | triple quadrupole inductively coupled plasma mass spectrometry |
| ICP-OES | inductively coupled plasma optical emission spectrometry |
| ICP-QMS | inductively coupled plasma quadrupole mass spectrometry |
| ICP-QQQ-MS | inductively coupled plasma triple quadrupole mass spectrometry |
| ICP-TOF-MS | inductively coupled plasma time-of-flight mass spectrometry |
| ID | isotope dilution |
| IDA | isotope dilution analysis |
| ID-ICP-MS | isotope dilution inductively coupled plasma mass spectrometry |
| ID-MRM-MS | isotope dilution multiple reaction monitoring mass spectrometry |
| ID-MS | isotope dilution mass spectrometry |
| IL | ionic liquid |
| IRMS | isotope ratio mass spectrometry |
| LA | laser ablation |
| LA-ICP-MS | laser ablation inductively coupled plasma mass spectrometry |
| LA-MC-ICP-MS | laser ablation multicollector inductively coupled plasma mass spectrometry |
| LAMIS | laser ablation molecular isotopic spectrometry |
| LC | liquid chromatography |
| LEP | liquid electrode microplasma |
| LIBS | laser induced breakdown spectroscopy |
| LIF | laser induced fluorescence |
| LOD | limit of detection |
| LPME | liquid phase microextraction |
| LTP | low temperature plasma |
| MALDI | matrix-assisted laser desorption ionisation |
| MC-ICP-MS | multicollector inductively coupled plasma mass spectrometry |
| MIP | microwave induced plasma |
| MMA | monomethylarsenic |
| MNP | magnetic nano-particle |
| MPT | microwave plasma torch |
| MW-LIBS | microwave assited libs |
| MW-LIBS | microwave assisted LIBS |
| Nd:YAG | neodymium doped:yttrium aluminum garnet |
| ne | electron number density |
| NELIBS | nanoparticle enhanced libs |
| NP | nano-particles |
| od | outer diameter |
| OPO | optical parametric oscillator |
| PDMS | polydimethylsiloxane |
| PFH | perfluorohexane |
| PLS | partial least squares |
| PN | pneumatic nebuliser |
| ppb | parts per billion (10-9) |
| ppm | parts per million (10-6) |
| ppq | parts per quadrillion (10-15) |
| ppt | parts per trillion (10-12) |
| PVG | photochemical vapour generation |
| Q | quadrupole |
| QTF | quartz tube furnace |
| RF | radiofrequency |
| RIMS | resonance ionisation mass spectrometry |
| RSD | relative standard deviation |
| RVM | relevance vector machine |
| SALD | substrate assisted laser desorption |
| Sat-CRDS | Saturated-absorption CRDS |
| SBR | signal-to-background ratio |
| SBR | Signal to background ratio |
| SCGD | solution cathode glow discharge |
| SNR | signal-to-noise ratio |
| SP | single particle |
| SPME | solid phase microextraction |
| TDLAAS | tunable diode laser atomic absorption spectroscopy |
| Te | electron temperature |
| Tgas | gas temperature |
| TIMS | thermal ionization mass spectrometry |
| Tion | ionization temperature |
| TOF | time-of-flight |
| Trot | rotational temperature |
| UV | ultraviolet |
| VG | vapour generation |

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