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GEOSTANDARDS and GEOANALYTICAL RESEARCH

Back to Basics Review

Quadrupole ICP-MS: Introduction to Instrumentation, Measurement Techniques and Analytical Capabilities

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The low detection limits and multi-element capability of inductively coupled plasma-mass spectrometry (ICP-MS) makes it an attractive option in a wide range of environmental, medical, biological, industrial and archaeological applications. Quadrupole ICP-MS is used to determine element concentrations in a diverse range of sample types, often very different from the geological applications for which ICP-MS was originally developed. Whilst modern instruments are robust and capable of a high degree of automation, it is essential that users of both instrumentation and data are aware of the strengths and limitations of the technique. Many people who are now involved with the operation and application of ICP-MS instruments are not specialists in the field, as was usually the case amongst early operators. This back-to-basics review is aimed at the novice user and includes a guide to ICP-MS instrumentation and performance. Whilst solids, liquids and gases can all be measured by ICP-MS, discussion of sample introduction is limited to liquids. Requirements for producing good quality data, including aspects of sample preparation, calibration, and methods of interference limitation are also discussed.

Keywords: inductively coupled plasma-mass spectrometry, ICP-MS, introduction, review, instrumentation.

Les limites basses de détection et la fonctionnalité multi-élémentaire font de la spectrométrie de masse couplée à une torche à plasma (ICP-MS) une technique d'analyse attrayante pour un large éventail d'études environnementales, médicales, biologiques, industrielles et archéologiques. Ce type d'instrument est utilisé pour déterminer les concentrations des éléments chimiques contenus dans une vaste gamme de types d'échantillons, souvent très différents de ceux provenant des études géologiques pour lesquelles la technique ICP-MS a été originellement développée. Parce que les instruments modernes sont robustes et pourvus d'un degré élevé d'automatisation, il est essentiel que les utilisateurs de la technique ICP-MS et des données qu'elle produit soient conscients de ses atouts et limites. Beaucoup de personnes qui sont aujourd'hui impliqués dans le fonctionnement des ICP-MS et dans leurs applications ne sont pas des spécialistes du domaine alors que c'était habituellement le cas durant la période de développement de cette technique. La présente revue qui vise l'utilisateur novice au travers d'un retour aux bases comprend un guide de la technique ICP-MS et de ses performances. Alors que les solides, les liquides et les gaz peuvent tous être mesurés par ICP-MS, la discussion de l'introduction de l'échantillon est ici limité aux liquides. Les conditions pour la production de données de bonne qualité, y compris les aspects de la préparation de l'échantillon, de la calibration, ainsi que ceux des méthodes de limitation des interférences sont également discutées.

Mots-clés : spectrométrie de masse couplée à une torche à plasma, ICP-MS, introduction, revue, instrumentation.

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Inductively coupled plasma-mass spectrometry (ICP-MS) is accepted as the most powerful multi-element analytical technique available today, capable of true multi-elemental determinations within minutes. Since publication of the first ICP-MS mass spectra almost 30 years ago (Houk *et al.* 1980, Gray 1993), the number of commercial ICP-MS instruments sold worldwide has risen to over 5000. The low detection limits and multi-element capability of ICP-MS makes it an attractive option in a wide range of environmental, medical, biological, industrial and archaeological applications, amongst others. Whilst modern instruments are robust and highly automated, it is essential that users of both instrument and data are aware of the strengths and limitations of the technique. This review is aimed at the novice user and includes a guide to the instrumentation, both from a theoretical and practical perspective, plus the requirements for producing good quality data, including calibration, and methods of interference limitation. This review focuses on quadrupole ICP-MS, which incorporates a quadrupole mass spectrometer, although comparison is made to high resolution magnetic sector field (SF) ICP-MS. While solids, liquids and gases can all be measured by ICP-MS, discussion of sample introduction is limited to liquids. Some aspects of sample preparation are also discussed, although a complete discussion of appropriate sample preparation methods is beyond the scope of this article.

The basic principle of ICP-MS is elemental differentiation on the basis of atomic mass. While atoms of a given element may have different atomic masses, or isotopes, the isotopic composition of each element is well studied and, therefore, is easily predicted (Coplen *et al.* 2002, Bohlke *et al.* 2005). Mass spectrometry (MS) cannot differentiate between neutral atoms. Therefore, atoms must first be ionised to form positively charged particles by removal of an electron. In ICP-MS, this ionisation step is carried out using an inductively coupled plasma (ICP), which comprises a highly ionised phase at a very high temperature.

Instrumentation

The components of an ICP-MS instrument are shown in Figure 1. A sample travels through six main steps during an analysis:-

- The sample is converted into a suitable form for introduction into the plasma
- The sample is ionised in the plasma
- Ions are extracted from the plasma
- Ions are focussed and transported to the mass spectrometer
- The mass spectrometer is used to separate the ions based on mass-to-charge ratio (m/z)
- Ions are counted to quantify the amount of each in the original sample.

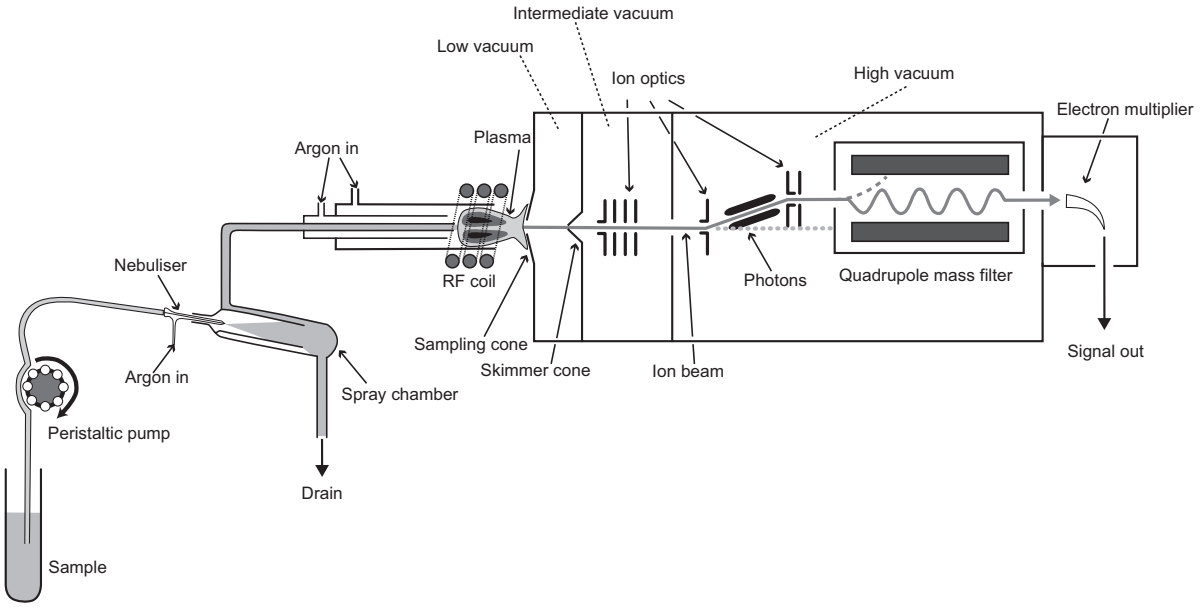

Figure 1. Schematic diagram of the major components of an ICP-MS instrument.

Sample introduction into the plasma

A wide variety of techniques have been developed for the introduction of solids, liquids and gases into ICP-MS instrumentation (Campbell 1992, Jarvis 1992, Günther *et al.* 1999, Sing 1999, Kántor 2001, Russo *et al.* 2002, Mora *et al.* 2003, Günther and Hattendorf 2005, Nakahara 2005). However, discussion in this review will be limited to liquids, the most common sample types analysed by ICP-MS. It is important that samples are introduced to the ICP in small volumes that are finely dispersed as otherwise the plasma may become unstable or even be extinguished. Normally a nebuliser is used to disperse the solution into a fine, gas-borne aerosol and a spray chamber is used to remove larger droplets from the aerosol (Mora *et al.* 2003). The most commonly used nebulisers are pneumatic, where the aerosol is formed by the action of a high-speed gas jet over a tip of a small orifice. Common pneumatic nebulisers include the concentric (Meinhardt) nebuliser, the crossflow nebuliser and the Babington or v-groove nebuliser. Each has varying efficiency, sensitivity and resistance to blocking (Sharp 1988a). Conventional nebulisers typically operate at a flow rate of ~ 1 ml min^{-1}, although micro-flow nebulisers with flow rates of 0.2-0.5 ml min^{-1} are often used to analyse smaller volume samples. High efficiency "total consumption" nebulisers have recently been introduced, in which the entire aerosol is injected into the plasma (Bjorn *et al.* 2002, Nam *et al.* 1994). These also operate at lower solution uptake rates (10-100 μl min^{-1}) than conventional systems. Total consumption nebulisers have better signal to noise ratios, but poorer precision, attributed to high white noise and pump noise.

Although some nebuliser types self aspirate without external pumping, most are operated in conjunction with a peristaltic pump, ensuring a constant flow of liquid irrespective of solution viscosity or the vertical distance that the liquid must be lifted. Pumping also means that liquid uptake is independent of nebuliser gas flow and the nebuliser can be operated at the flow rate for its optimum performance. However, pumping fluctuations may introduce noise into the signal, which should be minimised by using a narrow bore sample introduction tubing and replacing it regularly before it becomes damaged or flattened (Jarvis *et al.* 2003).

Pneumatic nebulisers produce aerosols with a broad distribution of droplet diameters up to 100 μm and only about 1% of droplets are small enough (< 10 μm) to be efficiently ionised (Browner and Boorn 1984). A spray chamber is used to screen the aerosol to remove unsuitably large droplets through gravity or inertia. Spray chambers require good temperature and pressure stability, low washout time (ideally less than two minutes) and should not suffer from significant memory effects (Sharp 1988b). Some elements in particular, such as iodine, boron and mercury can be retained on glassware and therefore require special precautions or conditions to ensure efficient washout (e.g., Vanhoe *et al.* 1993, Al-Ammar *et al.* 2000, 2001, Jarvis *et al.* 2003, Li *et al.* 2006).

A further function of the spray chamber is to remove solvent from the aerosol, which improves ionisation efficiency. Elemental signals may be up to three times higher using a spray chamber cooled to 2 °C than with the spray chamber at ambient temperature (~ 18 °C) because less energy is used vaporising the solvent (Linge and Jarvis 2010). Matrix ions (such as H and O, in the case of H_2O) also serve as a source of ions for the formation of interfering polyatomic species (Hutton and Eaton 1987). Table 1 shows that the proportion of H- and O-based polyatomic interferences is reduced by between 2 and 4 times when the spray chamber is operated at 2 °C rather than ambient temperature (~ 18 °C). For many years aerosol desolvation was achieved using a water-cooled spray chamber, but on most modern instruments the spray chamber is fitted with Peltier cooling. Alternately, membrane desolvation can decrease some polyatomic interferences by one or two orders of magnitude (Tao and Miyazaki 1995), but is less suitable for volatile elements such as Se or Hg (Tubaro *et al.* 1999).

Table 1.
The effect of spray chamber temperature on the measured "concentration" of selected polyatomic ions containing O and H. Concentrations (μg l^{-1}) have been calculated and standardised using the signal for 10 μg l^{-1} Co. The proportion of H- and O-based interferences is reduced by between 2 and 4 when the spray chamber is operated at 2 °C compared with ambient temperature (18 °C)

m/z	Spray chamber at 2 °C (μg l^{-1})	Spray chamber at 18 °C (μg l^{-1})
17 ($^{16}O^{1}H$, ^{17}O)	17700	39900
18 ($^{1}H_2{}^{16}O$, ^{18}O, $^{17}O^{1}H$)	17600	55500
32 ($^{16}O_2$, ^{32}S)	2220	3490
41 ($^{40}Ar^{1}H$)	49100	180000
56 ($^{40}Ar^{16}O$)	103	223
57 ($^{40}Ar^{16}O^{1}H$)	1.45	5.34
80 ($^{40}Ar^{2}$)	211	620

Table 2.
Distribution of elemental ionisation energies for singly- and doubly-charged ions at 1 eV intervals, adapted from Jarvis *et al.* (2003). Elements that have low ionisation energies (e.g., U) may be 100% ionised, but the degree of ionisation decreases as the elemental ionisation energy becomes closer to that of Ar. For example, only ~ 30% P and only ~ 0.1% N will be ionised

Ionisation energy (eV)	Singly-charged ions	Doubly-charged ions
‹ 7	Li, Na, Al, K, Ca, Sc, Ti, V, Cr, Ga, Rb, Sr, Y, Zr, Nb, In, Cs, Ba, La, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu, Hf, Tl, Ra, Ac, Th, U	
7–8	Mg, Mn, Fe, Co, Ni, Cu, Ge, Mo, Tc, Ru, Rh, Ag, Sn, Sb, Ta, W, Re, Pb, Bi	
8–9	B, Si, Pd, Cd, Os, Ir, Pt, Po	
9–10	Be, Zn, As, Se, Te, Au	
10–11	P, S, I, Hg, Rn	Ba, Ce, Pr, Nd, Ra
11–12	C, Br	Ca, Sr, La, Sm, Eu, Tb, Dy, Ho, Er
12–13	Xe	Sc, Y, Gd, Tm, Yb, Th, U, Ac
13–14	H, O, Cl, Kr	Ti, Zr, Lu
14–15	N	V, Nb, Hf
15–16	Ar	Mg, Mn, Ge, Pb
› 16	He, F, Ne	All other elements

As an alternative to pneumatic nebulisation, the ultrasonic nebuliser uses the vibration of a piezoelectric transducer to break up a surface film into aerosol droplets. Ultrasonic nebulisers are highly efficient. Aerosol production is completely independent of gas flow and greater aerosol can be transported at lower nebuliser gas flow rates. Detection limits are usually an order of magnitude better than with pneumatic nebulisers (Fassel 1986). However, the higher efficiencies also result in greater solvent loading to the plasma and desolvation is essential. Ultrasonic nebulisers are expensive and their added complexity means they may be less reliable than simple pneumatic nebulisers.

Sample ionisation in the plasma

Once the sample has been converted to a suitable aerosol, it is injected into the ICP for ionisation. A plasma is a highly ionised gas composed of ions, electrons, and neutral particles, usually at high temperature. An ICP is a plasma in which the transfer of energy to create and maintain the ionised gas is carried out via electromagnetic induction – that is, by using time-varying magnetic fields.

Although many gases can be used to produce a plasma, argon is the most appropriate gas for ICP-MS because it is relatively inert and does not form stable compounds. The ionisation energy of argon (15.2 eV) ensures that most elements will be ionised in an argon-based plasma (Table 2), although the degree of ionisation decreases as the ionisation energy of an element becomes closer to that of argon. For a number of elements (e.g., Ba and Ce), the energy required to remove a second electron (second ionisation energy) is also lower than the first ionisation energy of argon. Therefore, some proportion of these elements will be doubly-charged ions instead of singly-charged.

The ICP is supported within a quartz torch that consists of three concentric tubes. The torch is mounted inside a water-cooled copper coil that supplies the magnetic field that transfers energy to the plasma. A radio frequency (rf) generator (usually 1000-1500 W) produces an alternating current within the coil, oscillating at either 27 or 40 MHz (Uchida and Ito 1994), and inducing an intense electromagnetic field around the tip of the torch. Argon gas (~ 15 l min^{-1}) flows tangentially between the outer and middle tubes, while a lower auxiliary flow (~ 1 l min^{-1}) is passed between the middle and central injector tubes. A high-voltage spark produces free electrons that are accelerated in the oscillating magnetic field, causing collisions and ionisation of the argon gas and plasma formation at the open end of the quartz torch. The sample is introduced into the plasma via the injector tube at sufficient velocity to punch a hole through the centre of the plasma discharge. Each droplet is desolvated, and vaporised to a gas (Olesik *et al.* 1997). Compounds become atomised and, finally, individual atoms are ionised. Production of analyte ions, or signal, can be optimised by altering the five variables associated with the plasma; the nebuliser, plasma and auxiliary gas flow rates, the rf power supplied to the plasma, and the distance between the torch and the point where ions are extracted for measurement. The relationship between rf power and nebuliser gas flow results in the highest signal being achieved when the energy for ion

formation is balanced against the residence time of the aerosol in the plasma (Vaughan *et al.* 1987).

The ion extraction interface

Transferring ions from atmospheric pressure in the extremely hot ICP, into a high vacuum region which houses the mass spectrometer presented several challenges when the instrument was first designed (Gray 1993). Ions are normally sampled through to a two-stage interface (Gray and Date 1983, Niu and Houk 1996). The first stage comprises a sampler cone with a small orifice about 1 mm diameter, in direct contact with the plasma. The sampler cone tip is normally made of nickel, although platinum tipped cones may be used for some applications. Altering the distance of the quartz torch from the sampler cone alters sampling depth and changes the region in the plasma from which ions are sampled.

After passing through the sampler cone, the plasma gas expands as a supersonic jet into a lower pressure region of between 1×10^{-2} and 1×10^{-1} kPa. The central section of the jet then flows through a second skimmer cone, located directly behind the sampler cone. Skimmer cones are also nickel or platinum and have a smaller orifice than the sampler cone (~ 0.4-0.7 mm). After long periods of use a residue may build up around both the sampler and skimmer orifices, particularly when measuring samples with high total dissolved solids (TDS). These residues can change the geometry of each orifice, and therefore alter how ions are extracted from the plasma (Douglas and Kerr 1988). It is extremely important to clean both cones regularly in order to maintain their correct geometry. Cones that have bent or damaged tips must be discarded for the same reason.

The plasma has a net positive potential compared to the grounded sampler cone. If this potential is high enough, an electronic discharge will arc between the plasma and the cone (Gray and Date 1983) resulting in the formation of ions from the sampler cone itself. As well as decreased cone lifetime, secondary discharges also cause high background levels of ions of the cone material, of species such as photons, metastable argon atoms and fast electrons, and a greater production of doubly-charged ions. Secondary discharge can be minimised by grounding the coil at the centre, resulting in a low positive potential in the plasma (Niu and Houk 1996). More recently, a "shield" comprising a grounded platinum strip that sits between the torch and the coil electrically decouples the coil and plasma (Sakata and Kawabata 1994, Tanaka *et al.* 1991) Electrons from the coil preferentially pass into the grounded shield, minimising secondary discharges and ensuring the kinetic energy of the ions is much more uniform. A shielded torch has also demonstrated lower polyatomic ion concentrations for ArH^+ and ArO^+ (Nonose *et al.* 1994).

Ion focussing and transmission

Despite the high sensitivity of ICP-MS, transmission losses are significant. Niu and Houk (1996) calculate that only one analyte ion out of every 50000-500000 in the plasma actually reaches the detector. The lenses that focus and transport ions to the mass analyser are typically a series of metal pates or rings, each with a specific voltage. The lens stack may be located in the high vacuum region or directly behind the skimmer in order to "pull" the ions from the interface region. The exact dependence of the signal on the voltage of each lens will depend on the design and arrangement of the lens stack. Each lens voltage should be checked as part of the daily instrument set-up in order to optimise signal for the analysis being carried out. It is prudent to clean the lens stack routinely every few months or if signal becomes compromised.

The lens stack also removes neutral species and photons from the ion beam that would otherwise be registered as additional ion counts by the detector (Lafreniere *et al.* 1987). A circular disk, or photon stop, may be incorporated into the lens stack in the direct line of the ion beam. Applying a voltage to the photon stop will deflect ions around the disk, while stopping photons or neutral species. More recently, manufacturers have offset the entrance of the mass analyser from the plasma, directing the ion beam through a chicane. This offset ion lens is generally more efficient than the photon stop, leading to better detection limits even when transmission is constant (Hu *et al.* 1993).

Ions of different mass respond to changes in lens voltage in different ways and it is impossible to optimise the voltage on the lenses such that all ions are transported with the same efficiency (Hu *et al.* 1993, Vaughan and Horlick 1990b). Ion lens voltages are generally optimised to give maximum sensitivity for isotopes in the middle of the mass range ($m/z \sim 125$), with transmission of heavier and lighter elements sacrificed. In addition the total number ions that can be compressed into an ion beam is limited by the

"space-charge" effect, caused by mutual repulsion of positive ions in the ion beam. High ion densities cause the ion beam to expand, with lighter ions more likely to be deflected and lost than heavier ions (Douglas 1992, Gillson *et al.* 1988, Niu and Houk 1996, Tanner 1992). The space charge effect can be exacerbated when the sample has a "heavy" matrix, or high TDS. This leads to increases in the ion density of the beam, which causes further expansion, or defocusing of the ion beam. The presence of heavier matrix elements, such as uranium may have significantly greater effect on the amount of light elements that are extracted compared to lighter matrix elements like calcium or sodium (Jarvis *et al.* 2003, Linge and Jarvis 2010).

Ion separation

To quantify each element, the ions must be separated from the ion beam and counted. A mass spectrometer is able to distinguish between different ions based on mass-to-charge ratio (m/z). The most common mass spectrometer used in ICP-MS is the quadrupole mass filter, consisting of four metal rods that are suspended in parallel to, and equidistance from, the ion beam (Figure 2). Each rod is electrically connected to the rod directly opposite and voltages are applied to both rod pairs. Ions entering the quadrupole travel down the central axis and the voltages applied to the rods cause the ions to oscillate. The magnitude of the oscillations are influenced by both the mass and charge of the ion. Extreme oscillations cause the ion to be ejected from the stable transmission region, striking the rods or the inside of the quadrupole housing. The rod voltages are optimised to ensure that only ions of a single m/z have a stable path and exit the quadrupole and the mass filter must be switched to sequentially filter for each m/z of interest. This switching process is very rapid and data collection can be collected for the range 0-300 amu in about 100 ms.

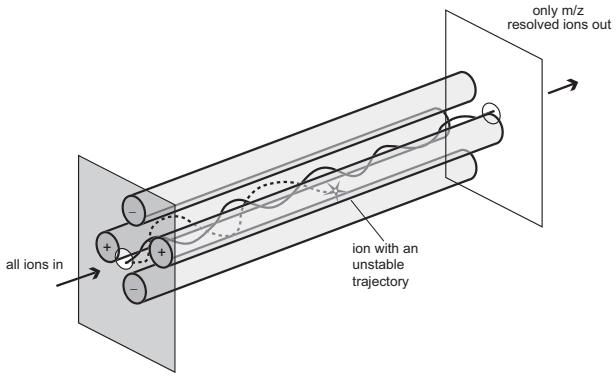

Figure 2. Schematic diagram of a quadrupole mass filter, the most common mass spectrometer used in ICP-MS. Voltages applied to the rods cause the ions entering the quadrupole to oscillate. Extreme oscillations cause the ions to be ejected from the stable transmission region, striking the rods or the inside of the quadrupole housing. Only ions of a single m/z have a stable path and exit the quadrupole.

Most quadrupole filters are designed to resolve routinely to 1 amu but can usually resolve ~ 0.5 amu. Increasing resolution changes the normally asymmetric, smooth topped peaks into sharp, angular peaks. Measurement of sharper, over-resolved peaks is typically less precise and signal intensity is reduced as fewer ions are counted. If resolution is decreased to › 1 amu, overall peak size and signal intensity increases but it becomes more difficult to separate adjacent peaks. Related to resolution is abundance sensitivity - the contribution to an analyte peak from the tail or leading edge of adjacent peaks. An abundance sensitivity of 10^6 means that a peak of 1 million counts per second (cps) at m/z = x-1 would contribute 1 cps at m/z = x. Abundance sensitivity is normally better at the high mass side (~ 10^7) than the low mass side (~ 10^6) because of peak asymmetry.

The quadrupole is always maintained at a high vacuum to limit interferences with the mass filtering process and to protect the quadrupole. When an ICP-MS instrument is not in operation, the turbo pumps that create the high vacuum remain running and a slide valve fits across the entrance to the high vacuum chamber to minimise particles entering and maintain vacuum. When in operation, the slide valve is retracted to allow a clear path. However the contact between the plasma and the sample cone means that only ions from the plasma can enter.

Another mass spectrometer used in commercial ICP-MS instruments is the high resolution magnetic sector field (SF) ICP-MS (Feldmann *et al.* 1994, Ekman *et al.* 2009). Here, ions are separated using both m/z, using a laminated magnet, and kinetic energy, using an electrostatic analyser (ESA). A magnetic field is applied perpendicularly to the ion beam and forces the ions into a circular motion, with a radius based on the magnetic field, m/z and the velocity of the ions. Only ions travelling along a particular arc will pass through a narrow slit and enter the detector. Because the curvature applied by the magnet is dependent on kinetic energy, the ESA can be used to focus ions to a

particular position at the exit slit. Mass resolution can then be controlled by modifying the width of the slit at the detector. The highest resolution achievable by a typical SF-ICP-MS is 10000, meaning it can resolve differences in m/z to 0.01-0.001 amu. In comparison a quadrupole mass filter can resolve to ~ 0.5-1 amu.

In the simplest mode, varying the magnetic field strength will focus ions with different m/z on the slit in front of the detector. Varying the magnetic field is a relatively slow process, however, and therefore scanning through the whole mass table can take over 300 ms (compared to 100 ms for the quadrupole mass filter). Faster analysis can be achieved by also employing the ESA for mass discrimination. In this case, the magnet can be set at a fixed magnetic field strength, while the ESA modifies the kinetic energies in the ion beam, effectively scanning m/z at a much faster rate. This method can only be used to scan through about 10 m/z units higher or lower than the m/z at which the magnet has been fixed, however. Traditionally the ESA has been placed before the magnet, however more recent magnetic sector instruments use a "reverse" geometry in which the ESA is behind the magnetic sector, which means that high ion currents are reduced during magnetic mass filtering before energy analysis, which improve noise and abundance sensitivity (Jakubowski *et al.* 1998).

Ion counting

Individual ions are counted by pulse counting, where each ion is converted into a discrete electrical pulse. The number of pulses is related to the number of analyte ions present in the sample and can be converted into an absolute concentration by comparing the signal from a sample with that from a calibration reference sample.

The two main pulse counting detectors used in ICP-MS instruments both employ electron multiplication. The channel electron multiplier is an open glass cone coated with a semi conductor type material that generates electrons from ions hitting its surface (Kurz 1979). The front of the cone is biased at a negative potential and the far end is kept at ground, attracting positive ions. As each ion hits the front surface, one or more secondary electrons are formed and are attracted towards the grounded end. As these electrons hit the surface of the tube, more electrons are formed and the process continues to form a discrete pulse of many millions of electrons. The discrete dynode electron multiplier works in a similar manner, but electron multiplication is carried out on a series of discrete flaps, or dynodes. The discrete dynode electron multiplier may be placed off axis from the ion beam to minimise the background from stray radiation and neutral species. In this case, each ion follows a curved path before striking the first dynode. The discrete dynode electron multiplier is considered to have more uniform detection efficiency and less secondary ion feedback than the channel electron multiplier (Shchemelinin *et al.* 1999).

The number of counts that can be registered by each detector is limited by the electron multiplication process. An ion will not be counted if it hits the detector during electron multiplication of the previous ion. Typically ~ 20-30 ns, this "dead time" is a fundamental limitation of the electron multiplier (Vanhaecke *et al.* 1998). When ion counts are high, the dead time may be used to correct the signal for missed ions. Pulse counting detectors are typically linear between 0 and 10^6 cps. Most modern quadrupole ICP-MS instruments are fitted with a dual-stage electron multiplier, in which the ions can be measured as an analogue signal when the ion count rate rises above a certain "trip" level.

ICP-MS data and figures of merit

The data resulting from the analysis of a sample consists of the number of ions counted at fixed m/z (or channels), as selected by the operator. Normally the total ions counted are converted to ions counted per second (cps) to give counts which are independent of counting time at each channel. The operator may chose to count ions at a single channel for each isotope (i.e., peak hopping), or to count at multiple channels across each m/z (i.e., peak scanning). Measuring multiple channels (normally 6 or more) of all m/z produces a full mass spectrum. Often detection of certain masses, such as m/z = 40, will be blocked. This protects the detector from wear if large signals from argon gas peaks such as ^{40}Ar were measured. A small section of a typical mass spectrum is illustrated in Figure 3, and shows both the counts measured at individual channels (Figure 3a), and the peaks obtained by integrating the channels together (Figure 3b). Compared to many other analytical techniques, element identification in ICP-MS is relatively easy and visual examination of a spectrum indicates which elements are present in that sample. Elements that have multiple isotopes produce predictable peak patterns based on isotopic abundance. Figure 3b shows that peaks measured for the four natural Pb isotopes (^{204}Pb, ^{206}Pb, ^{207}Pb and ^{208}Pb) are

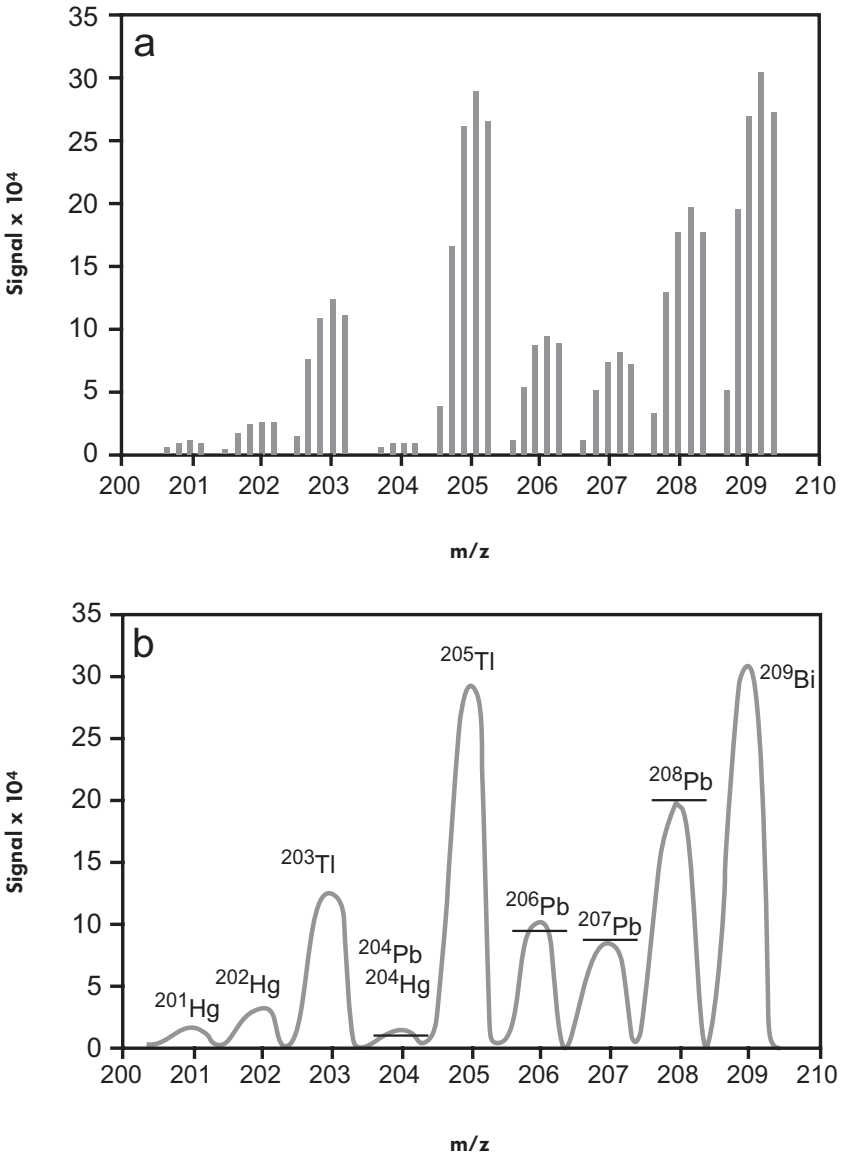

Figure 3. A mass spectrum for Pb, Tl, Bi and Hg (10 μg l^{-1}) showing m/z = 200-210. In (a), the spectrum was produced by measuring a fixed number of channels over each m/z. In (b), the channels were integrated into peaks. It can be noted that Pb isotopes at m/z = 204, 206, 207 and 208 produce peaks in the same proportion as their natural abundance, apart from m/z = 204, which may be overestimated because of the influence of ^{204}Hg.

in the same proportion as their natural abundance (1.4%, 24.1%, 22.1% and 52.1% respectively), although m/z = 204 may be overestimated because of measurement of ^{204}Hg. If the peaks for a given element deviate from the normal pattern, it is likely that the m/z of at least one of the isotopes is experiencing interference and further investigation is required.

The analyte signal depends on how many ions are counted by the detector and this is influenced by a number of factors. The total number of atoms available in the sample will depend on the abundance of the isotope measured. The percentage of atoms that are ionised depends on the ionisation energy of the element. However, even when these factors are corrected, elements of differing mass do not produce the same signal for the same concentration. Coupled with inherent mass bias caused by ion extraction and transmission, the ICP has a high degree of spatial resolution and ions are not homogeneously spaced throughout (Niu and Houk 1996). Most ICP-MS instruments will be set up to give optimised sensitivity in the middle mass range, and lower signal at higher and low masses, such as illustrated in Figure 4.

Background signals in ICP-MS are usually negligible, in the region of a few counts. However, even minor reagent contamination can result in significant "blank" signals being recorded. Generally laboratory grade reagents are not sufficiently pure and even high purity reagents can produce an elevated background. For example, sodium is present as a contaminant in high purity deionised water and nitric acid (Linge and Jarvis 2010). Some background signals may be derived

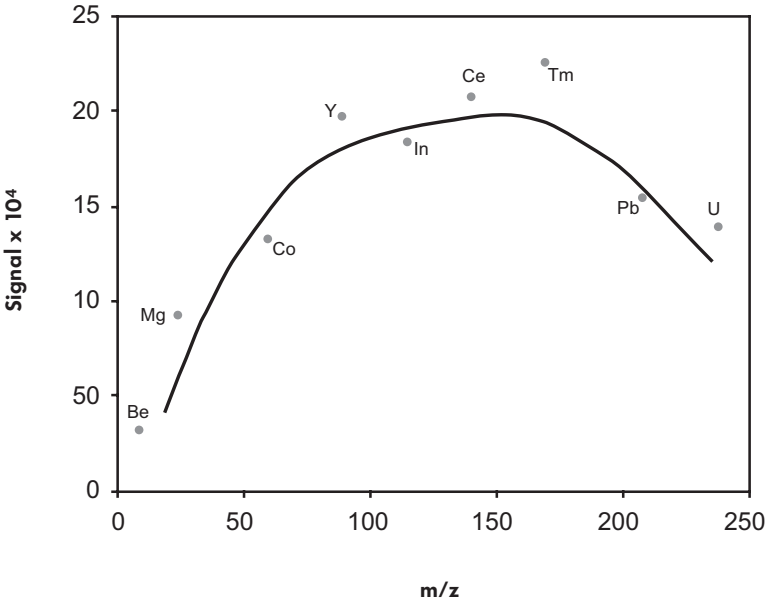

Figure 4. Signal response of a series of isotopes (^{9}Be, ^{24}Mg, ^{59}Co, ^{89}Y, ^{115}In, ^{140}Ce, ^{169}Tm, ^{208}Pb, ^{238}U) typically used in ICP-MS instrument set-up. Signal response has been corrected for both abundance and ionisation energy. Signal has been optimised for mid-range masses, with some signal loss at both the high and low mass ends. There is a greater signal loss at the low mass end than the high mass end because of ion competition.

from the instrument itself, such as elevated Ni from the nickel sampler and skimmer cones. Extremely high background signals, such as that measured at ^{56}Fe, usually indicates a polyatomic ion interference. Many masses below m/z = 80 have significant background counts due to the formation of polyatomic ions. Background signals must be measured and subtracted from the sample integrals.

Another important consideration is quantifying the limit of detection for each element to confirm the signal measured in a real sample is statistically different from that measured in the blank. The limit of detection is calculated using the standard deviation of replicate measurements of the blank (s_B) (Potts 2003, Skoog *et al.* 1990) and limits of detection are generally poorer for isotopes that have a high background signal. The lower limit of detection (LLD) is the concentration equivalent to $3s_B$. Although often quoted for quantitative data, the LLD represents the limit of when a concentration can be qualitatively distinguished from the blank. The smallest value that can be quantitatively recognised is characterised by the limit of determination (LoD), the concentration equivalent to $6s_B$. Data with legal, commercial or statutory implications are most often compared to the limit of quantitation (LoQ), the concentration equal to $10s_B$. Typical LLD for quadrupole ICP-MS are listed in Table 3.

Table 3.
Typical lower limits of detection (LLD, μg l^{-1}) for ICP-MS calculated using the standard deviation of five replicates of a 2% v/v HNO_3 blank, and a 10 μg l^{-1} multi-element standard solution. Typically LLD for most elements is sub μg l^{-1}. Elemental sensitivity and background contamination levels can change daily, however, and therefore LLD should be calculated using the blank solution measured for every analysis

Al	0.15	I	0.03	Sm	0.0039
Sb	0.0042	Ir	0.0054	Sc	0.016
As	0.022	Fe	1.5	Se	0.63
Ba	0.012	La	0.0005	Ag	0.0049
Be	0.0013	Pb	0.0064	Na	0.94
Bi	0.0016	Li	0.01	Sr	0.0063
B	0.066	Lu	0.0006	Ta	0.0014
Br	2.2	Mg	0.083	Te	0.052
Cd	0.038	Mn	0.014	Tb	0.0017
Ca	2.7	Hg	0.073	Tl	0.0008
Ce	0.0004	Mo	0.012	Th	0.0019
Cr	0.054	Nd	0.0015	Tm	0.0006
Co	0.0045	Ni	0.019	Sn	0.013
Cu	0.016	Nb	0.0027	Ti	0.084
Dy	0.0022	Pd	0.02	W	0.0026
Er	0.0005	P	1.4	U	0.0006
Eu	0.0016	Pt	0.0037	V	0.0034
Gd	0.0017	K	3.1	Yb	0.0009
Ga	0.022	Pr	0.0005	Y	0.0007
Au	0.065	Re	0.0012	Zn	0.28
Hf	0.002	Rh	0.0015	Zr	0.004
Ho	0.0006	Rb	0.0032		
In	0.0012	Ru	0.005		

Comparison to other analytical techniques

Quadrupole ICP-MS has many similarities to other optical spectrometry techniques that also measure concentration using atom properties, such as atomic absorption or atomic emission spectrometry (Willard *et al.* 1988). Quadrupole ICP-MS can also be compared to high resolution SF-ICP-MS. Representative LLDs for

Table 4.
Typical LLD (μg l^{-1}) for selected elements in water by flame atomic adsorption spectrometry (FAAS), electrothermal (or graphite furnace) atomic adsorption spectrometry (ETAAS), inductively coupled plasma-atomic emission spectrometry (ICP-AES), quadrupole ICP-MS, and SF-ICP-MS

	FAAS[a]	EAAS[a]	ICP-AES[a]	ICP-MS[b]	SF-ICP-MS
Ag	0.9	0.001	0.2	0.005	0.0004[c]
Al	20	0.01	0.2	0.2	0.0004[c]
As	0.02	0.08	2	0.02	0.001[d]
Au	50	0.1	0.5	0.06	0.0008[c]
Ba	8	0.04	0.01	0.01	0.0007[c]
Br	-	-	-	2	0.08[f]
Ca	0.5	0.01	0.0001	3	0.0015[c]
Cd	0.5	0.0002	0.07	0.04	0.0005[c]
Ce	8	0.04	-	0.0004	0.000014[e]
Co	2	0.008	0.1	0.004	0.00014 (M)[c]
Cu	1	0.005	0.04	0.02	0.0002[c]
Dy	50	-	4	0.002	0.000008[e]
Fe	3	0.01	0.09	1	0.0009 (M)[c]
Hf	2000	-	10	0.002	0.00012[g]
I	-	-	-	0.03	0.05[f]
In	20	0.02	0.4	0.001	0.0002[c]
K	1	0.004	30	3	0.0004 (H)[c]
La	2000	0.5	0.1	0.0005	0.000018[e]
Mg	0.1	0.0002	0.003	0.08	0.0002[c]
Na	0.2	0.004	0.1	0.9	0.0003[c]
Pb	10	0.007	1	0.006	0.00012[c]
Pt	40	0.2	0.9	0.004	0.0014[c]
Ru	70	-	30	0.005	-
Th	-	-	3	0.002	0.00002[g]
U	-	30	1.5	0.0006	0.00001[g]

[a](Willard *et al.* 1988); [b](Linge and Jarvis 2010); [c](Jakubowski *et al.* 1998); [d](Wildner and Hearn 1998); [e](Field and Sherrell 1998); [f](Bu *et al.* 2003); [g](Yu *et al.* 2000).
(M) analytes measured using medium resolution mode (M/ΔM = 3000).
(H) analytes measured using high resolution mode (M/ΔM = 8000).

flame atomic absorption spectrometry (FAAS), electrothermal (or graphite furnace) atomic absorption spectrometry (ETAAS), inductively coupled plasma atomic emission spectrometry (ICP-AES), quadrupole ICP-MS, and SF-ICP-MS are compared in Table 4. Similar LLD to those achievable by ICP-MS are produced by some other techniques, particularly ETAAS. However, both FAAS and ETAAS lack the multi-element capability of ICP-MS. Linear signal response from both FAAS and ETAAS is also limited to a few orders of magnitude or less (Kirkbright and Sargent 2006), compared to the potential of linear calibration over seven to nine orders of magnitude from ICP-MS. Furthermore, both techniques are less robust than ICP-MS because the atomisation methods used (flame and electrothermal vaporisation) are much more matrix sensitive.

Both ICP-MS and ICP-AES are capable of measuring many elements in a single analysis and both use an ICP to atomise and excite the sample. However, while ICP-MS measures ions produced in the plasma, ICP-AES measures the intensity of light emitted from atoms excited by the plasma at wavelengths that are specific to each element (Thompson and Walsh 2003). ICP-AES is more resistant to high TDS and samples require less dilution. Measurements usually have better precision (‹ 0.5%) than can normally be achieved for trace element analysis by ICP-MS (2-5%) and ICP-AES is therefore suited to measuring major element concentrations. However, the wide range of possible wavelengths can result in a complicated spectrum compared to that produced by ICP-MS. ICP-MS produces lower and more consistent LLDs compared to ICP-AES, where LLDs can vary over many orders of magnitude. Finally, while all these techniques can measure elemental concentrations, ICP-MS is the only technique that can also be used to make isotopic measurements as well.

Typically, SF-ICP-MS is more sensitive than quadrupole ICP-MS and exhibits less electronic noise and lower backgrounds. In most cases, the limiting factor of

SF-ICP-MS detection limits is laboratory contamination via reagents, laboratory equipment and the sample introduction system and extensive cleaning procedures may be require to measure ultra-low concentrations (Field and Sherrell 2003, Krachler 2007). SF-ICP-MS also offers the opportunity to separate the analyte signal from spectral interferences in some cases (Jakubowski *et al.* 1998, Townsend 1999, Moor and Kobler 2001, Castro *et al.* 2008). The major drawbacks for SF-ICP-MS are significantly higher acquisition and operating costs as well as the slower scan speed of instruments compared to ICP-QMS. Typically SF-ICP-MS will be used to determine a limited group of analytes, rather than for multi element determinations (Field and Sherrell 1998, Jakubowski *et al.* 1998, Wildner and Hearn 1998, Yu *et al.* 2000, Bu *et al.* 2003).

Interferences

Interferences in ICP-MS are classed as either spectroscopic or non-spectroscopic (Evans and Giglio 1993). Spectroscopic interferences arise when different ions with the same m/z are counted together. In such cases attributing the entire signal only to the analyte of interest results in an overestimation in concentration. In most cases, spectroscopic interferences are simple to predict when the operator is familiar with typical mass spectra and they do not vary with time.

Types of spectroscopic interferences

The most problematic spectroscopic interference is an isobaric overlap, when two elements have isotopes nominally of the same mass. For example Cr and Fe both have an isotope of 54 amu. While the exact masses differ (^{54}Fe = 53.939612 amu compared to ^{54}Cr = 53.938882 amu), the quadrupole mass analyser can not resolve this tiny difference in mass (0.00073 amu) and ions counted at m/z = 54 may be either Fe or Cr. Counting at a mass free from isobaric overlap (e.g., ^{52}Cr or ^{57}Fe) will give a measurement free from this interference. Indium is the only element that has an isobaric overlap on all isotopes. However, the interference from ^{115}Sn on the major isotope ^{115}In is usually negligible unless the sample contains significant amounts of Sn. Measuring a free isotope of the interfering element (e.g., ^{118}Sn) will indicate whether the contribution to the analyte (e.g., ^{115}In) is significant.

Polyatomic ions, or adduct ions, are formed by the combination of two or more atoms and, again, the quadrupole mass analyser cannot distinguish between a polyatomic, and an atomic ion if they have the same nominal m/z. The most significant polyatomic ions are formed from the most abundant isotopes of argon, atmospheric gases, and the solvents or acids used during sample preparation (Tan and Horlick 1986, Jarvis *et al.* 2003). Despite the combinations possible, polyatomic ion formation is generally insignificant above m/z = 80 (May and Wiedmeyer 1998). The background spectra of solutions of deionised H_2O, HNO_3, HCl and H_2SO_4 (Figure 5a, b, c and d, respectively) are all dominated by peaks at m/z = 56 (^{40}Ar^{16}O) and m/z = 80 (^{40}Ar^{40}Ar). The spectrum from deionised H_2O is otherwise free from major interference, as is that from HNO_3 apart from a peak at m/z = 54 (^{40}Ar^{14}N). For HCl, Cl, O and H produce significant peaks between m/z = 51 (^{35}Cl^{16}O) and m/z = 54 (^{37}Cl^{16}O^{1}H), while Ar and Cl combine to produce peaks at m/z = 75 (^{40}Ar^{35}Cl) and 77 (^{40}Ar^{37}Cl). These peaks all overlap with the only otherwise interference free isotopes of V (m/z = 51), As (m/z = 75), and Se (m/z = 77). For H_2SO_4, polyatomic peaks occur at m/z = 48 (^{32}S^{16}O), 49 (^{32}S^{16}O^{1}H and ^{33}S^{16}O), 50 (^{33}S^{16}O^{1}H and ^{34}S^{16}O), 64 ($^{32}S_2$ or ^{32}S$^{16}O_2$), and 72 (^{40}Ar^{32}S). Avoiding the use of S or Cl based acids during sample preparation is necessary for the accurate determination of some elements. The other major type of polyatomic interferences is caused by refractory oxides, which result from incomplete dissociation, or recombination in cooler plasma regions, particularly in the boundary layer around the sampler cone (Vaughan and Horlick 1990a). Unlike polyatomic ions formed from Ar and elements in the atmosphere and solvent, refractory oxide ions exist for elements that have high oxide bond strengths like Ce and Ba, producing an interference at 16 (M^{16}O), 32 (M$^{16}O_2$) or even 48 (M$^{16}O_3$) mass units above the M peak.

Doubly-charged ions may form for elements whose second ionisation energy is less than the first ionisation energy of argon (15.2 eV, see Table 2). With z = 2, these will be counted with singly-charged ions of half their mass. For example whilst ^{136}Ba^{+} will be counted at m/z = 136, ^{136}Ba^{2+} will be counted with ^{68}Zn^{+} at m/z = 68. As previously discussed, secondary discharge between the plasma and the sampler cone, can increase doubly-charged ions to higher than predicted (Douglas 1992).

Refractory oxide and doubly-charged ions are both influenced by the plasma operating parameters (Vaughan and Horlick 1986, Gray and Williams

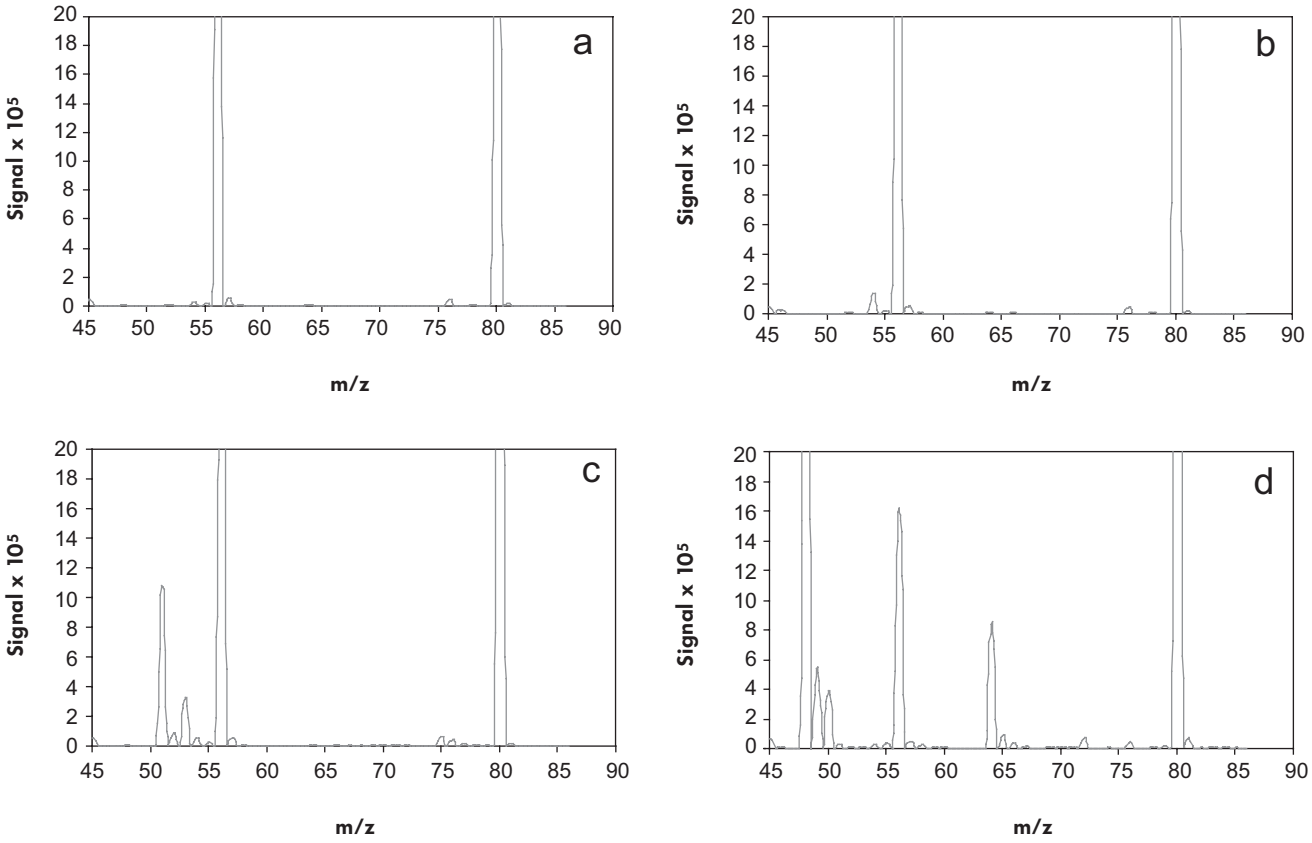

Figure 5. Background spectra produced from different solution matrices: (a) de-ionised H_2O, (b) 0.3 mol l^{-1} HNO_3, (c) 0.3 mol l^{-1} HCl and (d) 0.3 mol l^{-1} H_2SO_4. The spectra have been normalised for the effect of each matrix on absolute signal.

1987a, b, Linge and Jarvis 2010). Refractory oxides are particularly influenced by nebuliser gas flow because molecules have less residence time within the plasma as the flow rate increases and are less likely to fully dissociate. Conversely doubly charged ions decrease with increasing nebuliser flow, as the lower residence time means that fewer ions are likely to become doubly charged. Fortunately the gas flow at which both refractory oxide ions and doubly-charged ions are minimised is roughly coincident with optimum analyte signal.

Attenuating spectroscopic interferences

In principle, any isobaric overlap can be corrected by calculating the relative contribution of the interfering analyte, based on signal of another isotope at an interference free m/z. However, mathematical correction is subject to error, particularly when multiple steps are applied. The magnitude of this error depends on the absolute signal and the contribution subtracted. Mathematical correction can be extended to polyatomic interferences as well (Aries *et al.* 2000, Raut *et al.* 2005). However it is extremely important that no contributions to the peak signal are overlooked and that the sample matrix is well characterised. Furthermore, changes in instrument performance during the analysis must be assumed to affect analyte ionisation and polyatomic formation in the same way, which may not be the case.

Adding another gas such as nitrogen, oxygen, air, helium, and hydrogen to the argon plasma gas feed can significantly change the fundamental properties of the ICP, altering or minimising inherent polyatomic interferences. Nitrogen in particular has been found useful for increasing signal and decreasing Ar and O-based interferences (Lam and Horlick 1990). Nitrogen-argon plasmas are more energetic and hotter than argon-only plasmas, attributed to the higher thermal conductivity of nitrogen leading to more efficient energy transfer within the plasma. Addition of other gases to the plasma does lead to the formation of new interferences, however. For example, addition of N_2 leads it an increase in background peaks that can be attributed to N^+, N_2^+, NO^+ and ArN^+, as well as ClN^+ if the

sample matrix has significant concentrations of Cl (Hill *et al.* 1992). It may also lead to an increased overall background from increased photon emission in the interface. An alternative approach to minimising polyatomic interferences is operating under "cool" plasma conditions, where the ICP is operated at a much lower RF power (500-800 W instead of 1100-1500 W) and higher nebuliser gas flow rates. Under these conditions, many argon-related ions, including ArH^+, Ar^+, and ArO^+, are greatly reduced in intensity and the background spectrum becomes dominated by NO^+, O_2^+, and H_2O^+ or H_3O^+, if sample aerosols are not desolvated. Cool plasma conditions improve sensitivity for a very specific group of elements, most notably Ca, Fe and K, and was first demonstrated by Jiang *et al.* (1988) for $^{39}K^+$ and $^{41}K^+$, which are normally dominated by $^{38}Ar^1H^+$ and $^{40}Ar^1H^+$. Fewer ions are extracted from a "cool" plasma and therefore space charge effects are also less severe. However, because of the lower plasma temperature, elements with ionisation potentials › ~ 8 eV have significantly lower sensitivity and ion-molecule interactions (such as NO^+ and O_2^+ charge transfer reactions) become important ionisation mechanisms (Holliday and Beauchemin 2002). With higher nebuliser flow rates, cool plasmas more prone to secondary plasma discharge (Jiang *et al.* 1988, Tanner 1995) and coil grounding or a shielded torch is essential in order to operate in this mode (Sakata and Kawabata 1994, Niu and Houk 1996).

In the late 1990s a new technique for interference reduction emerged - the collision or reaction cell (Bandura *et al.* 2002, Tanner *et al.* 2002), based on the collision cell used in organic tandem mass spectrometry (Douglas 1989, Rowan and Houk 1989, Eiden *et al.* 1997). In "cell" ICP-MS, the ion beam passes through a cell filled with a specifically chosen gas before entering the mass spectrometer. Interfering species are removed through interactions with the gas, whilst analyte ions pass through to the mass spectrometer to be detected. While cell designs vary, they all comprise a multipole ion guide inside a small chamber. The ion guide is made up of a fixed number of parallel rods equidistant from the ion beam, similar to the quadrupole mass analyser itself. Multipole guides currently in use include the quadrupole (four rods), the hexapole (six rods) or the octopole (eight rods). The cell is generally positioned after the ion lenses and just before the mass analyser. Without a gas flow into the chamber, cell instruments operate in normal ICP-MS mode with the cell acting as an ion guide only.

Although "collision cell" and "reaction cell" are often used interchangeably in the literature, classification of an ICP-MS cell as either collision or a reaction cell is largely determined by type of multipole ion guide used. The number of rods in the ion guide determines the area of the ion stability region. It is smallest in a quadrupole ion guide but becomes larger as the multipole order increases. Despite the small region of ion stability, the quadrupole ion guide can also selectively transmit ions based on m/z, allowing only a narrow bandwidth of ions though the guide and enabling mass-selective ejection of precursor or product ions. Cells with quadrupole ion guides are therefore generally known as reaction cells as unwanted reaction products from reactive gases can be identified and rejected before mass separation and ion detection (Tanner and Baranov 1999). Hexapole and octopole ion guides have higher transmission and lower selectivity and are better suited to more selective gas-molecule interactions. These are normally termed collision cells, operating under lower gas pressures than reaction cells and under non-thermal conditions, where ions have higher kinetic energies (Tanner *et al.* 2002).

Collisions between ICP-generated ions and cell gas molecules may induce numerous processes including energy transfer, molecular fragmentation, charge transfer, or chemical reaction. Collisions with a non-reactive cell gas like He will cause the ion to lose kinetic energy. Polyatomic ions are larger than single analyte ions and are thus more likely to collide with the gas atoms and lose more kinetic energy. Ions with a low kinetic energy can be prevented from entering the quadrupole mass analyser by kinetic energy discrimination and this is an important mechanism for removal of polyatomic interferences, particularly in collision cells (Hattendorf and Günther 2004, McCurdy and Woods 2004). Collisions transferring kinetic energy to internal bonds within the molecule can also cause molecular fragmentation, or collisionally induced dissociation (Tanner *et al.* 2002). Initially collisionally induced dissociation was considered an important mechanism for interference reduction, however it is unlikely to contribute significantly because of the inefficiency of the process (Bandura *et al.* 2001, Tanner *et al.* 2002). Collision cells have also been operated with xenon as collision gas for both Se (Schaumloffel *et al.* 2007) and S (Profrock *et al.* 2003) determination.

A number of gases have also been used for chemical reaction in cell ICP-MS, including H_2, O_2, NH_3, CH_4, NO, CO_2 and C_2H_4 (Eiden *et al.* 1997, Bandura

et al. 2001, 2006). Only H_2 is routinely used in collision cells, although use of O_2 has also been reported (Izmer *et al.* 2003). The simplest reaction to occur is charge transfer. Reactions involving the transfer of a charged or uncharged hydrogen atom are also significant since the transfer is usually fast. Other reactive gases induce oxidation or clustering. Clustering reactions, in particular, can produce analytical complications if cluster products are not controlled and are only really appropriate for use in reaction cells where the quadrupole ion guide can be used to filter unwanted reactants or products. In most cases, a gas will be chosen that selectively reacts with the interfering ion, leaving the analyte background free. However, better analytical results are sometimes achieved when the gas targets the analyte ion and the reaction product is measured instead. For example, rather than minimising interferences at m/z = 31 and 32, ^{31}P and ^{32}S have been measured by monitoring $^{31}P^{16}O^+$ and $^{32}S^{16}O^+$ at m/z = 47 and 48 using a reaction cell employing O_2 (Yang and Jiang 2004).

It is usually impossible to predict every reaction that will take place within the cell, particularly for samples of unknown composition. Reference data for specific ion-molecule reactions is often incomplete or unavailable (Koyanagi *et al.* 2005). Therefore, interference optimisation using cell ICP-MS normally still relies on empirical studies rather than theoretical calculations. The most appropriate method of interference removal will depend on the type of cell being used. For example, $^{40}Ar^{16}O^+$ is efficiently removed in a reaction cell using NH_3 (Tanner and Baranov 1999), but in a collision cell, a combination of He and H_2 is more appropriate (Niemela *et al.* 2003). Further information about the operation of collision and reaction cells, as well as ion-molecule interactions can be found in several excellent reviews of the topic (Tanner *et al.* 2002, Koppenaal *et al.* 2004, Koyanagi *et al.* 2005).

Non-spectroscopic interferences

Unlike spectroscopic interferences, non-spectroscopic interferences usually affect whole sections of the mass range and can be broadly categorised as suppression/enhancement effects and signal drift. Suppression or enhancement effects arise from changes in sample transport to the plasma, ionisation in the plasma, or transmission of the ion beam, all of which directly affect the number of ions reaching the detector. Suppression is often seen in samples with a high level of TDS. All of the elements present in solution are ionised by the ICP, regardless of whether they require determination. Excessive matrix may result in an offset between the signal from samples and synthetic calibration solutions and can also result in a loss of light ions from the ion beam (Tan and Horlick 1987). Most matrix effects can be minimised by matrix matching calibration solutions to samples, dilution or, in more complex cases, by chemically separating the analytes from the matrix before analysis (Moller *et al.* 1992, Arslan and Paulson 2002, Bruzzoniti *et al.* 2003, Jarvis *et al.* 2003, Daniels and Arslan 2007).

High solvent loadings cool the central argon stream, which subsequently decreases desolvation, atomisation and ionisation efficiencies (Longerich 1989). An excess of easily ionisable elements, such as Na, may have the same effect (Olivares and Houk 1986). The introduction of organic solvents into a plasma can cause either signal enhancement or suppression. Small concentrations of carbon may lead to improved signal for elements with high ionisation potentials, possibly through charge transfer from carbon ions to neutral analyte atoms (Hu *et al.* 2004). However, high solvent concentrations cool the central channel resulting in signal loss. High organic solvent loadings also lead to carbon deposition on the sampler cone. Oxygen is added in such cases to oxidise the excess carbon to CO_2.

In addition to signal suppression, high TDS may also cause drift in signal over time caused, to a great extent, by deposition of material on the sampler and skimmer cones, and on the ion lenses (Linge and Jarvis 2010). Deposition on the cone orifices alters cone geometry and substantially affects the ion extraction process. Ideally, samples should be diluted so that the matrix does not cause suppression, normally when TDS ‹ 200-300 $\mu g\ ml^{-1}$, and drift can be corrected using either internal standards or external drift correction procedures. In cases where sample dilution is undesirable, it may be appropriate to use a flow injection system to "inject" small volumes of each sample into the plasma (de Castro and Tena 1995) and increasing ICP power may also help attenuate suppression in such cases (Makishima and Nakamura 1997). Alternatively, a rapid loss of signal at the start of the analysis period can be avoided by equilibrating the instrument to steady state before analysis by aspirating a solution of similar composition to the sample matrix.

Calibration and quantitative analysis

Calibration

Like most other analytical techniques, ICP-MS is a comparative method. Calibration is required to generate concentrations from raw instrumental data, most commonly by comparing the signal of unknown solutions to external calibration solutions. The calibration curve produced can be fitted by least squares regression to a straight line (Skoog *et al.* 1990, Potts 2003), often over many orders of magnitude. Since the ICP is such a robust ion source, calibration can usually be achieved by using a series of synthetic solutions prepared in a matrix of 2% v/v HNO_3. As an example, Svantesson *et al.* (2002) demonstrated that calibration using inorganic standard solutions of proteins and biomolecular compounds samples by ICP techniques was possible for sufficiently dilute samples with no matrix matching. The dilution factor at which suppression disappears, and at which signals are comparable to synthetic calibrator solutions, can be determined by measuring a representative sample at several dilutions (Linge and Jarvis 2010).

Sometimes dilution to avoid signal suppression leads to concentrations falling below the detection limit. Two other methods that can be used for calibration are standard addition (Jarvis *et al.* 2003) and isotope dilution (Heumann 1988, 2004, Zeisler *et al.* 2006). Both of these approaches are more labour intensive than external calibration and better suited to measurement of a few elements only. For standard addition, two or more (and preferably three or more) sample aliquots are spiked with increasing concentrations of the element of interest. Measuring the unspiked sample and spiked aliquots provides each sample with its own matrix matched calibration curve. The signal of the unaltered sample is plotted directly on the y-axis, while concentration in the original sample is the value of the intercept of the line of best fit with the x-axis. Samples may require analysis using external calibration first to determine the approximate concentration present. Preparation of spikes for multi-element determinations are complex. While standard addition compensates for matrix effects, it does not compensate for instrument drift (Salin *et al.* 2004).

Isotope dilution is the most accurate and precise method of measuring concentration and uses the ratio of two isotopes of the element of interest (Heumann 1988). An enriched isotopic spike is added to the sample to alter the natural isotopic ratio. Elemental concentration is calculated using the natural isotopic ratio, the measured ratio and the quantity of the sample and the spike. Altering the ratio to near unity gives best precision and therefore, like standard addition, the sample may need to be first analysed using external calibration to estimate the sample concentration and investigate the presence of polyatomic interferences. Instrumental mass bias must be monitored to ensure that the ratio is not biased and a correction made if necessary. Isotope dilution requires only one analysis per sample and equilibrating the spike at the earliest possible stage of sample preparation ensures that any subsequent analyte loss does not affect measurement accuracy. Isotope dilution is often used in speciation studies (Rodriguez-Gonzalez *et al.* 2005). However, it can only be used for elements that have at least two stable isotopes. It requires the use of extremely pure and concentrated isotopic reference samples, which are expensive and difficult to obtain. While the method compensates for non-spectroscopic interferences and drift, it cannot account for spectroscopic interferences.

Measurement accuracy

Measurement accuracy should be estimated by considering both the precision and trueness of the measurement (ISO 1994). While sometimes used interchangeably, these terms represent distinct data properties. Precision refers to the closeness of agreement between multiple test results. Precision may be measured as repeatability, when factors such as operator, equipment used, and calibration are kept constant to give a measure of the effect of random error. In ICP-MS analysis, this is determined by repeated measurements over a short period of time, usually less than five minutes. Repeatability is often quantified as relative standard deviation (RSD), equal to the standard deviation of replicate measurements expressed as a percentage of the mean. In practice, ICP-MS analysis will normally include three replicate measurements carried out consecutively, producing a repeatability of between 2-5% RSD. Precision of analysis can also be measured as reproducibility, in which case analytical conditions such as operator, equipment and temperature may all be varied, giving an estimate for maximum variability. Trueness may be defined as the percentage variation from the true value and is a measure of the systematic error in a measurement. Strictly, trueness for an unknown sample can never be determined as, by definition, the true concentration is unknown. In practise, trueness is normally estimated through analysis of a certified

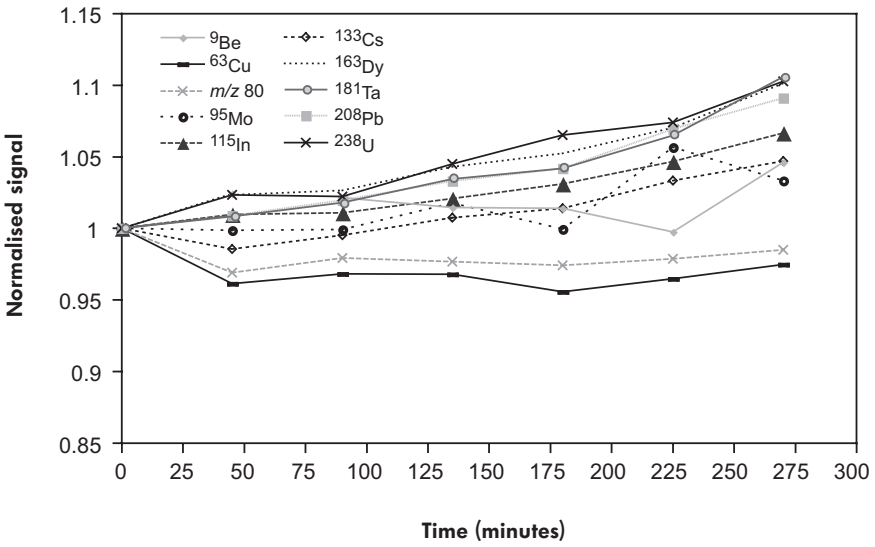

Figure 6. Normalised signals for isotopes from across the mass range, measured over four hours. Whilst most isotopes except ^{63}Cu show a gradual increase in signal, the signal response varies significantly between isotopes. The signal for the ^{40}Ar^{40}Ar^{+} dimer also does not increase, indicating that internal standardisation using this dimer would be inaccurate in this case.

reference material (CRM) along with the unknown samples (Kane 2001). A CRM is a material of proven homogeneity that has been rigorously analysed by a wide variety of techniques, often by laboratories worldwide (Kane 2004, Zeisler *et al.* 2006). Reference materials are available for many samples types, including geological, environmental and biological, amongst others. However the work required to prepare and validate CRMs means they are expensive and are often certified for only a few elements. Reference materials for the sample type of interest may not be available, in which case a CRM of similar composition may need to be used, although this will compromise the confidence with which trueness can be evaluated (Kane 2002).

Drift correction

Long-term instrumental drift is also usually monitored and corrected. Two methods used for drift correction are internal standardisation and external drift correction. Internal standardisation, the most commonly used method, monitors drift by measuring the signal of an element added to all calibration solutions and samples at the same concentration, the internal standard. Analyte signals are corrected on the basis of changes in the internal standard signal. As well as long term drift, short-term signal fluctuations and unidentified matrix suppression effects may also be corrected. However, there is an inherent assumption that the element chosen as the internal standard accurately reflects signal changes for all other elements (Wangen *et al.* 1991). Ideally, the internal standard will have a similar ionisation energy and mass as the analytes it is being used to standardise (Vanhaecke *et al.* 1992). Indeed, poor selection of an internal standard can produce results that are less accurate than if no drift correction had been applied (Salin *et al.* 2004). Internal standard selection can be difficult for multi-element analysis because element properties vary widely and the choice of an internal standard is limited to elements not present in significant amounts in the sample. Common choices include In, Rh and Ga, as these element are not usually present in samples in high concentrations. Figure 6 demonstrates normalised signal changes for a range of isotopes over four hours. In this example, the signal increases for the majority of isotopes. However the degree to which each increases does differ and is roughly related to the mass of the isotope. Using ^{115}In as an internal standard would correct the general trend but would also cause an underestimate in the signal of low mass isotopes such as ^{9}Be and an overestimate for high mass isotopes such as ^{238}U. Furthermore, as ^{63}Cu does not demonstrate the same trend, Cu concentrations corrected by ^{115}In would be grossly underestimated. Multi-element determinations can benefit from using several internal standards, although the choice is still limited to elements not present in the sample. As an alternative, the analyst may choose to use an element already present in the sample if concentration data is already to hand. This simplifies sample preparation, but the element chosen will not necessarily be any more appropriate for internal standardisation. The use of a gas or polyatomic ions produced in the plasma, such as the ^{40}Ar^{40}Ar^{+} dimer (Chen and Houk 1995), has been trialled but such ions are produced by very different mechanisms to analyte ions. In Figure 6 the ^{40}Ar^{40}Ar^{+} dimer shows dramatically different signal behaviour

to the analytes and results standardised by this dimer would be less accurate than those standardised by ^{115}In.

The alternative to internal standardisation is external drift correction. Here signal drift is monitored by analysing a specific drift monitor solution, normally a mid-range calibration solution, regularly throughout the run. Therefore the drift behaviour of each element is measured and corrected individually and nothing is added to the samples. The major assumption of external drift correction is that signal drift is linear, although non-linear correction has also been applied (Cheatham *et al.* 1993). Sharp changes in signal, which may be caused by extreme matrix changes, for example, will not be corrected accurately and external drift correction cannot monitor unidentified matrix suppression effects. In most cases, however, instrumental drift can be approximated as a linear change if the drift monitor is measured often enough, normally every 5-10 samples.

Considerations for analysis

A complete discussion of appropriate sample preparation methods for ICP-MS analysis is beyond the scope of this article, but further information can be found in these recommended texts: Jarvis *et al.* (2003), Potts (2003) and Vanhoe (1993). The ideal sample matrix will avoid solvents or acids that cause spectroscopic interferences, where possible, and be dilute enough to minimise non-spectroscopic interferences. Freshwater or rainwater samples will normally require no sample preparation other than ensuring elements are preserved during storage (Abbu *et al.* 2000, Gomez Ariza *et al.* 2000). Complex liquid samples, such as seawater and effluent, will usually require dilution, digestion or chemical separation to mitigate matrix effects. Solid samples will require digestion. Total sample digestion for ICP-MS will often be undertaken by alkali fusion or HF acid digestion (Jarvis *et al.* 2003, Potts 2003). Many partial digestions also exist, such as the sequential extraction schemes used on soils and sediments (e.g., Tessier *et al.* 1979). The high TDS and carbon content of the extractants used in these schemes can produce solutions that are extremely difficult to measure by ICP-MS, however, and their use should be approached with caution.

Sample blanks, vital for identifying contamination and the determination of LLD, can be prepared by processing empty vials through the preparation procedure. If available, appropriate reference materials should also be included to determine accuracy. Calibration by external calibrators will require one or more standard solutions to be measured at the same time as the samples. Calibration solutions should span the range of concentrations expected in the samples. If calibration solutions are not matrix matched to the samples, dilution experiments should be carried out to ensure that suppression does not influence the final measured concentrations. Calibration by either standard addition or isotope dilution will require the addition of pure and concentrated spike solutions to multiple and identical volumes of each sample, ideally before sample preparation.

The volume of sample required for an analysis is determined by the nebuliser flow rate, the time required to introduce the sample into the ICP, and the time required to complete the analysis. Flow rates are normally set for optimum nebuliser performance and will vary between nebulisers, but are generally less than 1 ml min^{-1}. Combined uptake and analysis times are normally of the order of 2-3 minutes per sample and so usually 10 ml is more than sufficient for an analysis. The ICP-MS can also be optimised for analysis of smaller samples. The easiest step is to shorten uptake time by minimising the length of tubing between the sample and the ICP. Alternately, micro-flow and total consumption nebulisers with flow rates of 100 μl min^{-1} and lower can be used for micro-samples (Todoli and Mermet 2006).

Analysis by ICP-MS is normally carried out in either scanning or peak jumping mode. In scanning mode, multiple data points are collected for each isotope of interest (up to 10-20 per peak) so that the entire peak is defined (e.g., as demonstrated in Figure 3). Collecting a complete spectrum from m/z = 0 to 250 allows the analyst to obtain an overview of the elements present in a sample very quickly. The other advantage of scanning mode is that data is collected for both the isotopes of immediate interest, as well as the wider mass range for archival purposes. This additional information can be very useful in identifying interfering isotopes not initially considered and to ensure that peak shape and mass calibration have not changed.

In peak jumping mode, data is only collected for those isotopes of interest, often at only one channel at the centre of each peak. Peak jumping mode is generally quicker than scanning mode and can provide

greater signal and lower uncertainty because only the largest part of the peak is counted (Denoyer 1992). However, it is important that the mass calibration is stable as the limited channels collected means it is impossible to determine whether changes in peak shape or position occur.

Analysis time, normally 20-60 seconds, will depend on the number of isotopes being measured, the number of channels or points measured for each isotope peak, the length of time spent counting at each channel (dwell time), and the number of times the quadrupole cycles through the mass range (the number of sweeps). The time required to scan and settle the quad at each channel is normally small but data quality may be compromised if more time is spent switching between isotopes than counting signal. For multi-element determination, where the quadrupole must switch between isotopes frequently, the use of fewer sweeps with longer dwell times will normally optimise the duty cycle. In certain cases, such as the measurement of isotope ratios, increasing the number of sweeps and decreasing dwell times improve precision. Normally, however, only a few isotopes are measured in such cases and therefore the time spent scanning and settling is less significant.

Analyses must be repeated to measure instrumental precision but the large numbers of replicates required for a true Gaussian distribution is usually impractical. In routine analysis each sample will normally be measured three times, although five or more replicates are preferred for blank solutions, as these are used to estimate the LLD.

An analytical experiment usually begins with measurement of blank solutions, to avoid contamination by more concentrated samples and allow early identification of contamination issues. Ideally calibration solutions will be freshly prepared, span the range of expected concentrations in the samples, and be analysed in order of least to highest concentration to minimise the effect of sample carryover. Instrument sensitivity may vary slightly from one day to another and so calibration data are generated for each analytical run. Instrumental drift is monitored during the run to ensure that drift is not excessive, as this might indicate faulty operation. If external drift correction is being undertaken, then the drift monitor should be measured regularly, normally every 5-10 samples. The first drift monitor is measured just after the blank solution and before the calibration solutions and the last analysis of the run must be a drift monitor. Measurement precision should also be checked regularly. Individual cases of poor precision may indicate faulty sample introduction for that sample and identification during the run allows the measurement to be repeated.

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