We have previously covered the major instrumental components of an ICP mass spectrometer; now let’s turn our attention to the technique’s most common interferences and what methods are used to compensate for them. Although interferences are reasonably well understood in inductively coupled plasma–mass spectrometry (ICP-MS), it can often be difficult and time-consuming to compensate for them, particularly in complex sample matrices. Having prior knowledge of the interferences associated with a particular set of samples will often dictate the sample preparation steps and the instrumental methodology used to analyze them.

Interferences in ICP-MS are generally classified into three major groups — spectral, matrix, and physical. Each of them has the potential to be problematic in its own right, but modern instrumentation and good software, combined with optimized analytical methodologies, has minimized their negative impact on trace element determinations by ICP-MS. Let us take a look at these interferences in greater detail and describe the different approaches used to compensate for them.

**Spectral Interferences**

Spectral overlaps are probably the most serious types of interferences seen in ICP-MS. The most common type is known as a polyatomic or molecular spectral interference, which is produced by the combination of two or more atomic ions. They are caused by a variety of factors, but are usually associated with either the plasma and nebulizer gas used, matrix components in the solvent and sample, other analyte elements, or entrained oxygen or nitrogen from the surrounding air. For example, in the argon plasma, spectral overlaps caused by argon ions and combinations of argon ions with other species are very common. The most abundant isotope of argon is at mass 40, which dramatically interferes with the most abundant isotope of calcium at mass 40, whereas the combination of argon and oxygen in an aqueous sample generates the 40Ar16O interference, which has a significant impact on the major isotope of Fe at mass 56. The complexity of these kinds of spectral problems can be seen in Figure 1, which shows a mass spectrum of deionized water from mass 40 to mass 90.

Additionally, argon can also form polyatomic interferences with elements found in the acids used to dissolve the sample. For example in a hydrochloric acid medium, 40Ar combines with the most abundant chlorine isotope at 35 amu to form 40Ar35Cl, which interferes with the only isotope of arsenic at mass 75, while in an organic solvent ma-
Spectroscopy

Figure 2. Relative isotopic abundances of the naturally occurring elements, showing all the potential interferences.

Oxides, Hydroxides, Hydrides, and Doubly Charged Species

Another type of spectral interference is produced by elements in the sample combining with H, O, or OH (either from water or air) to form molecular hydride (H), oxide (O), and hydroxide (OH) ions, which occur at 1, 16, and 17 mass units higher than its mass (2). These interferences are typically produced in the cooler zones of the plasma, immediately before the interface region. They are usually more serious when rare earth or refractory-type elements are present in the sample, because many of them readily form molecular species (particularly oxides), which create spectral overlap problems on other elements in the same group. Associated with oxide-based spectral overlaps are doubly charged spectral interferences. These species are formed when an ion is generated with a double positive charge, as opposed to a normal single charge, and produces a peak at half its mass. Like the formation of oxides, the level of doubly charged species is related to the ionization conditions in the plasma and can usually be minimized by careful optimization of the nebulizer gas flow, rf power, and sampling position within the plasma. It can also be impacted by the severity of the secondary discharge present at the interface (3), which was described in greater detail in Part IV of the series (4).

Table II shows a selected group of elements, that readily form oxides, hydroxides, hydrides, and doubly charged species, together with the analytes that are affected by them.

Tutorial
Isobaric Interferences

The final classification of spectral interferences is called “isobaric overlaps,” produced mainly by different isotopes of other elements in the sample that create spectral interferences at the same mass as the analyte. For example, vanadium has two isotopes at 50 and 51 amu. However, mass 50 is the only practical isotope to use in the presence of a chloride matrix, because of the large contribution from the 35Cl interference at mass 51. Unfortunately mass 50 amu, which is only 0.25% abundant, also coincides with isotopes of titanium and chromium, which are 5.4% and 4.3% abundant, respectively. This makes the determination of vanadium in the presence of titanium and chromium very difficult unless mathematical corrections are made. Figure 2 — the relative abundance of the naturally occurring isotopes — shows all the naturally occurring isobaric spectral overlaps possible in ICP-MS (5).

Ways to Compensate for Spectral Interferences

Let us look at the different approaches used to compensate for spectral interferences. One of the very first ways used to get around severe matrix-derived spectral interferences was to remove the matrix somehow. In the early days, this involved precipitating the matrix with a complexing agent and then filtering off the precipitate. However, this has been more recently carried out by automated matrix removal and analyte preconcentration techniques using chromatography-type equipment. In fact, this method is preferred for carrying out trace metal determinations in seawater because of the matrix and spectral problems associated with such high concentrations of sodium and magnesium chloride (6).

Mathematical Correction Equations

Another method that has been successfully used to compensate for isobaric interferences and some less severe polyatomic overlaps (when no alternative isotopes are available for quantitation) is to use mathematical interference correction equations. Similar to inter-element corrections (IECs) in ICP-optical emission spectroscopy, this method works on the principle of measuring the intensity of the interfering isotope or interfering species at another mass, which ideally is free of any interferences. A correction is then applied by knowing the ratio of the intensity of the interfering species at the analyte mass to its intensity at the alternate mass.

Let’s take a look at a real-world example of this type of correction. The most sensitive isotope for cadmium is at mass 114. However, there is also a minor isotope of tin at mass 114. This means that if there is any tin in the sample, quantitation using 114Cd can only be carried out if a correction is made for 114Sn. Fortunately Sn has a total of 10 isotopes, which means that at least one of them will probably be free of a spectral interference. Therefore, by measuring the intensity of Sn at one of its most abundant isotopes (typically 113Sn) and ratioing it to 114Sn, a correction is made in the method software in the following manner:

Table I. Some common plasma, matrix, and solvent-related polyatomic spectral interferences seen in ICP-MS.

<table>
<thead>
<tr>
<th>Element</th>
<th>Matrix/Isotope</th>
<th>Solvent/Matrix</th>
<th>Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>39K</td>
<td>H2O</td>
<td>38ArH</td>
<td></td>
</tr>
<tr>
<td>40Ca</td>
<td>H2O</td>
<td>40Ar</td>
<td></td>
</tr>
<tr>
<td>56Fe</td>
<td>H2O</td>
<td>44Ar4O</td>
<td></td>
</tr>
<tr>
<td>80Se</td>
<td>H2O</td>
<td>80Ar80Ar</td>
<td></td>
</tr>
<tr>
<td>51V</td>
<td>HCl</td>
<td>50Cl2</td>
<td></td>
</tr>
<tr>
<td>75As</td>
<td>HCl</td>
<td>74Ar74Cl</td>
<td></td>
</tr>
<tr>
<td>28Si</td>
<td>HNO3</td>
<td>44N44N</td>
<td></td>
</tr>
<tr>
<td>44Ca</td>
<td>HNO3</td>
<td>44N44N40Ar40Ar</td>
<td></td>
</tr>
<tr>
<td>55Mn</td>
<td>HNO3</td>
<td>54Ar54N</td>
<td></td>
</tr>
<tr>
<td>40Ti</td>
<td>H2SO4</td>
<td>40S40S</td>
<td></td>
</tr>
<tr>
<td>52Cr</td>
<td>H2SO4</td>
<td>52S52S</td>
<td></td>
</tr>
<tr>
<td>64Zn</td>
<td>H2O</td>
<td>64S64S32P32P</td>
<td></td>
</tr>
<tr>
<td>65Cu</td>
<td>H3PO4</td>
<td>65P65P</td>
<td></td>
</tr>
<tr>
<td>24Mg</td>
<td>Organics</td>
<td>12C12C</td>
<td></td>
</tr>
<tr>
<td>52Cr</td>
<td>Organics</td>
<td>52Ar52C</td>
<td></td>
</tr>
<tr>
<td>65Cu</td>
<td>Minerals</td>
<td>65Ca65Ca</td>
<td></td>
</tr>
<tr>
<td>64Zn</td>
<td>Minerals</td>
<td>64Ca64Ca</td>
<td></td>
</tr>
<tr>
<td>65Cu</td>
<td>Seawater</td>
<td>65Ar65Na</td>
<td></td>
</tr>
</tbody>
</table>
Total counts at mass 114 = $^{114}\text{Cd} + ^{114}\text{Sn}$

Therefore $^{114}\text{Cd} = \text{total counts at mass } 114 - ^{114}\text{Sn}$

To find out the contribution from $^{114}\text{Sn}$, it is measured at the interference-free isotope of $^{118}\text{Sn}$ and a correction of the ratio of $^{114}\text{Sn}/^{118}\text{Sn}$ is applied:

Which means $^{114}\text{Cd} = \text{counts at mass } 114 (^{114}\text{Sn}/^{118}\text{Sn})/ (^{118}\text{Sn})$

Now the ratio ($^{114}\text{Sn}/^{118}\text{Sn}$) is the ratio of the natural abundances of these two isotopes (0.65%/24.23%) and is always constant

Therefore $^{114}\text{Cd} = \text{mass } 114 - (0.65%/24.23\%) \times (^{114}\text{Sn})$

or $^{114}\text{Cd} = \text{mass } 114 - (0.0268) \times (^{114}\text{Sn})$

An interference correction for $^{114}\text{Cd}$ would then be entered in the software as: $- (0.0268) \times (^{114}\text{Sn})$.

This is a relatively simple example, but explains the basic principles of the process. In practice, especially in spectrally complex samples, corrections often have to be made to the isotope being used for the correction — these corrections are in addition to the analyte mass, which makes the mathematical equation far more complex.

This approach can also be used for some less severe polyatomic-type spectral interferences. For example, in the determination of V at mass 51 in diluted brine (typically 1000 ppm NaCl), there is a substantial spectral interference from $^{35}\text{Cl}^{16}\text{O}$ at mass 51. By measuring the intensity of the $^{37}\text{Cl}^{16}\text{O}$ at mass 53, which is free of any interference, a correction can be applied in a similar way to the previous example.

**Cool/Cold Plasma Technology**

If the intensity of the interference is large, and analyte intensity is extremely...
low, mathematical equations are not ideally suited as a correction method. For that reason, alternative approaches have to be considered to compensate for the interference. One such approach, which has helped to reduce some of the severe polyatomic overlaps, is to use cold/cool plasma conditions. This technology, which was reported in the literature in the late 1980s, uses a low-temperature plasma to minimize the formation of certain argon-based polyatomic species (7).

Under normal plasma conditions (typically 1000–1400 W rf power and 0.8–1.0 L/min of nebulizer gas flow), argon ions combine with matrix and solvent components to generate problematic spectral interferences such as $^{39}$ArH, $^{40}$Ar, and $^{40}$Ar$^{16}$O, which impact...
the detection limits of a small number of elements including K, Ca, and Fe. By using cool plasma conditions (500–800 W rf power and 1.5–1.8 L/min nebulizer gas flow), the ionization conditions in the plasma are changed so that many of these interferences are dramatically reduced. The result is that detection limits for this group of elements are significantly enhanced (8).

An example of this improvement is seen in Figure 3, which shows a spectral scan of 100 ppt of 56Fe (its most sensitive isotope) using cool plasma conditions. It can be clearly seen that there is virtually no contribution from 40Ar16O, as indicated by the extremely low background for deionized water, resulting in single-figure parts-per-trillion (ppt) detection limits for iron. Under normal plasma conditions, the 40Ar16O intensity is so large that it would completely overlap the 56Fe peak.

Cool plasma conditions are limited to a small group of elements in simple aqueous solutions that are prone to argon-based spectral interferences. It offers very little benefit for the majority of the other elements, because its ionization temperature is significantly lower than a normal plasma. In addition, it is often impractical for the analysis of complex samples, because of severe signal suppression caused by the matrix.

**Collision/Reaction Cells**

These limitations have led to the development of collision and reaction cells, which use ion–molecule collisions and reactions to cleanse the ion beam of harmful polyatomic and molecular interferences before they enter the mass analyzer. Collision/reaction cells are showing enormous potential to eliminate spectral interferences and make available isotopes that were previously unavailable for quantitation. For example, Figure 4 shows a spectral scan of 50 ppt As in 1000 ppm NaCl, together with 1000 ppm NaCl at mass 75, using a dynamic reaction cell with hydrogen/argon mixture as the reaction gas. It can be seen that there is insignificant contribution from the 40Ar35Cl interference, as indicated by the NaCl baseline. The capability of this type of reaction cell to virtually eliminate the 40Ar35Cl interference now makes it possible to determine low ppt levels of mono-isotopic 75As in a high chloride matrix — previously not achievable by conventional interference correction methods (9). For a complete review of the benefits of collision/reaction cells for ICP-MS, refer to part 9 of this series (12).

**Matrix Interferences**

Let’s now take a look at the other class of interference in ICP-MS — suppression of the signal by the matrix itself. There are basically two types of matrix-induced interferences. The first and simplest to overcome is often called a sample transport effect and is a physical suppression of the analyte signal, brought on by the matrix components. It is caused by the sample’s impact on droplet formation in the nebulizer or droplet-size selection in the spray chamber. In the case of organic matrices, it is usually caused by a difference in sample viscosities of the solvents being aspirated. In some matrices, signal suppression is caused not so much
by sample transport effects, but by its impact on the ionization temperature of the plasma discharge. This is exemplified when different concentrations of acids are aspirated into a cool plasma. The ionization conditions in the plasma are so fragile that higher concentrations of acid result in severe suppression of the analyte signal. Figure 7 shows the sensitivity for a selected group of elements in varying concentrations of nitric acid in a cool plasma (13).

Internal Standardization
The classic way to compensate for a physical interference is to use internal standardization. With this method of correction, a small group of elements (usually at the parts-per-billion level) are spiked into the samples, calibration standards, and blank to correct for any variations in the response of the elements caused by the matrix. As the intensity of the internal standards change, the element responses are updated every time a sample is analyzed. The following criteria are typically used for selecting the internal standards:

- They are not present in the sample
- The sample matrix or analyte elements do not spectrally interfere with them
- They do not spectrally interfere with the analyte masses
- They should not be elements that are considered environmental contaminants
- They are usually grouped with analyte elements of a similar mass range. For example, a low mass internal standard is grouped with the low mass analyte elements and so on up the mass range
- They should be of a similar ionization potential to the groups of analyte elements so they behave in a similar manner in the plasma
- Some of the common ones reported to be good candidates include Be, Sc, Co, Ge, Y, Rb, In, Tm, Lu, Re, and Th.

A simplified representation of internal standardization is seen in Figure 8, which shows updating the analyte response curve across the full mass range, based on the intensities of low, medium, and high mass internal standards. It should also be noted that internal standardization is also used to compensate for long-term signal drift produced by matrix components slowly blocking the sampler and skimmer cone orifices. Even though total dissolved solids are kept below <0.2% in ICP-MS, this can still produce instability of the analyte signal over time with some sample matrices.

Space-Charge Interferences
Many of the early researchers reported that the magnitude of signal suppression in ICP-MS increased with decreasing atomic mass of the analyte ion (14). More recently it has been suggested that the major cause of this kind of suppression is the result of poor transmission of ions through the ion optics due to matrix-induced space charge effects (15). This has the effect of defocusing the ion beam, which leads to poor sensitivity and detection limits, especially when trace levels of low mass elements are being determined in the presence of large concentrations of high mass matrices. Unless any compensation is made, the high-mass matrix element will dominate the ion beam, pushing the lighter elements out of the way. Figure 9 shows the classic space charge effects of a uranium (major isotope 238U) matrix on the determination of 'Li, 'Be, 23Mg, 54Mn, 87Rb, 115In, 137Cs, 205Tl, and 208Pb. The suppression of low mass elements such as Li and Be is significantly higher than with high mass elements such as Tl and Pb in the presence of 1000 ppm uranium.

There are a number of ways to compensate for space charge matrix suppression in ICP-MS. Internal standardization has been used, but unfortunately doesn’t address the fundamental cause of the problem. The most common approach used to alleviate or at least reduce space charge effects is to apply voltages to the individual ion lens components. This is achieved in a number of ways but, irrespective of the design of the ion focusing system, its main function is to reduce matrix-based suppression effects by steering as many of the analyte ions through to the mass analyzer while rejecting the maximum number of matrix ions. Space charge effects and different designs of ion optics were described in greater detail in part V of this series (16).

References