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INTERFERENCE REMOVAL

Inductively Coupled Plasma Mass Spectrometry

Smart Note

Complete and comprehensive interference removal in ICP-MS: Can this be achieved?

Which interferences are generally of concern?

Amongst the interferences commonly observed in Inductively Coupled Plasma Mass Spectrometry (ICP-MS), polyatomic interferences are the most common. These interferences mainly result from recombination of ions and neutral species formed when a sample enters the plasma. The formation of such interferences occurs mostly in the transition through the interface region, connecting the plasma (formed under atmospheric pressure) and the high vacuum region of the mass spectrometer. The most abundant polyatomic interferences are observed in the mass range between *m/z* 40–100. Prominent examples are $^{40}Ar^{16}O^+$ on ^{56}Fe, $^{40}Ar^{38}Ar^+$ on ^{78}Se and $^{80}Ar_2^+$ on ^{80}Se. Depending on the sample type and preparation strategy, other elements can also create significant overlaps, such as chlorine based interferences (if HCl is used for sample preparation or chloride is present at high concentration in the sample) on vanadium ($^{35}Cl^{16}O^+$ on ^{51}V), chromium ($^{35}Cl^{16}O^1H^+$ on ^{52}Cr) and arsenic ($^{40}Ar^{35}Cl^+$ on ^{75}As).

Polyatomic interferences can be removed by pressurizing the collision/reaction cell (CRC) with helium as an inert collision gas and applying kinetic energy discrimination (KED). As all ions travel through the helium-filled cell, they undergo a series of collisions with helium atoms and lose some of their original kinetic energy. As polyatomic species have a larger size (i.e., collisional cross section), they undergo more collisions and suffer more kinetic energy loss than analyte ions of the same mass. As a result, the majority of these polyatomic ions are unable to pass from the cell into the analyzer quadrupole and so are separated from the target analyte.

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However, as all precursor ions travel along in the ion beam, polyatomic interferences can be formed not only in the interface region, but also in other parts of the mass spectrometer, such as inside the collision / reaction cell (CRC) itself. An active mechanism to minimize formation of polyatomic interferences downstream in the mass spectrometer, such as a low mass cut off, is highly beneficial to further reduce backgrounds and enable the highest accuracy and lowest possible detection limits.

Are there other interferences to worry about?

Doubly-charged interferences are normally less often of concern in ICP-MS analysis, however, they may impact some key, regulated analytes. Doubly-charged interferences can be formed by all elements that have a 2nd ionization potential lower than the ionization potential of argon (i.e., below 15.76 eV). As all mass spectrometers detect ions on the basis of their mass to charge ratio (*m/z*) rather than their isotope mass, doubly-charged ions are detected at half their nominal mass. Two important analytes should be specifically considered regarding these interferences: monoisotopic arsenic ($^{75}As^{+}$) can be biased from $^{150}Nd^{++}$ or $^{150}Sm^{++}$, and the most commonly analyzed isotope of selenium, $^{78}Se^{+}$, can suffer from interferences created by $^{156}Dy^{++}$, and more severely, $^{156}Gd^{++}$. A key problem with these interferences is that they are actually increased under the kinetic energy discrimination (KED) conditions used to remove polyatomic interferences, because they carry a higher kinetic energy compared to single-charged analytes appearing at the same mass and are therefore preferentially transferred into the mass spectrometer.

Where are doubly-charged interferences of concern?

Doubly-charged interferences are of concern when accurate and reliable determination of contaminants like arsenic or selenium is required, and samples may contain lanthanide group elements, even at low concentrations. This can be the case for plant materials which have been grown on soils with naturally occurring amounts of lanthanides, or for biological samples, such as urine or serum, where gadolinium containing contrast agents have been administered for magnetic resonance imaging purposes. A false positive result for either element can be observed already at lanthanide concentration levels of less than 10 $\mu g \cdot L^{-1}$ in the analyzed solution. Good examples for the presence of lanthanides as potential interferents are the standard reference materials NIST 1515 (Apple Leaves) and NIST 1573a (Tomato Leaves), produced by the National Institute for Standards and Technology in the U.S. NIST 1515 contains approximately 17 $mg \cdot kg^{-1}$ of neodymium and 3 $mg \cdot kg^{-1}$ of gadolinium (dry weight), which translate to approximate concentrations of 85 $\mu g \cdot L^{-1}$ and 15 $\mu g \cdot L^{-1}$, respectively, in the measured solution (assuming a 200-fold dilution through sample preparation).

Can doubly-charged interferences be addressed when using single quadrupole ICP-MS?

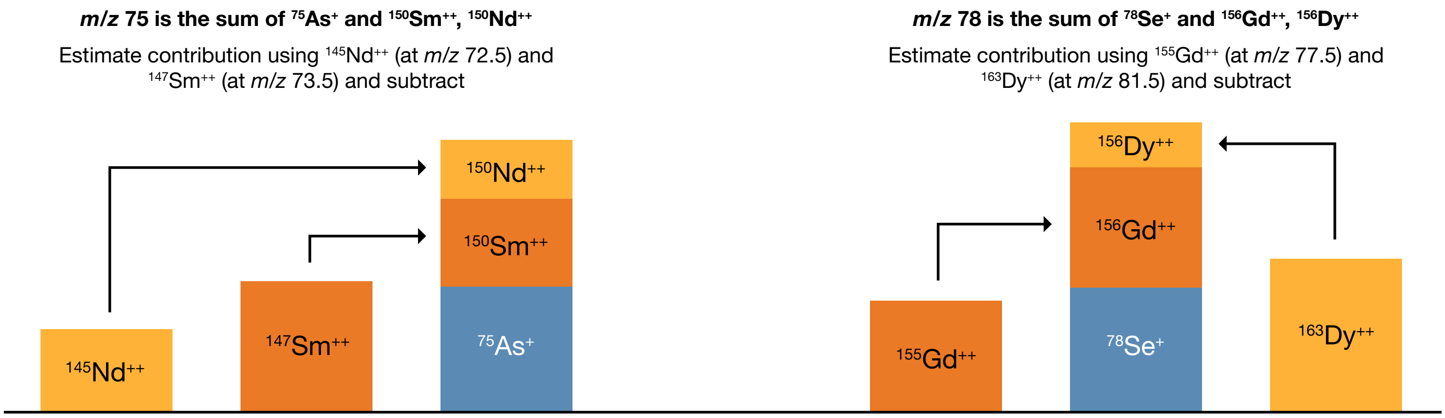
There are ways to account for these interferences to some degree with single quadrupole-based ICP-MS instruments, such as the Thermo Scientific™ iCAP™ RQ ICP-MS. This instrument can use mathematical correction equations to correct for doubly-charged ion interference. If analysis can be accomplished with sufficient mass resolution (at least better than 0.5 amu) to resolve a specific non-interfered isotope of the interfering element, natural isotopic abundances can be used to estimate the contribution to the intensity caused by the interfering isotope of the same element and mathematically correct for it. For example, a measurement of $^{145}Nd^{++}$ at a mass to charge ratio of 72.5, fully resolved from the adjacent $^{72,73}Ge^{+}$ signals (used for example as an internal standard) allows estimation of the contribution of $^{150}Nd^{++}$ at *m/z* 75 using the following formula:

$$I\,[^{75}\mathrm{As}]_{\mathrm{corr.}} = I\,[^{75}\mathrm{As}]_{\mathrm{meas.}} - I\,[m/z\ 72.5]_{\mathrm{meas.}} \times 0.6747$$

With the factor 0.6747 derived from the relative isotopic abundances of ^{150}Nd and ^{145}Nd, (5.6% and 8.33%), respectively.

Similar equations can be set up for the other elements mentioned previously. Figure 1 shows a schematic of the underlying process.

These equations can be easily set up in a LabBook or Template in the Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution™ Software. Calculation of the correction can be toggled on and off directly in the LabBook to allow for an easy comparison of results. Each instrument in the Thermo Scientific™ iCAP™ Qnova Series ICP-MS can achieve the required resolution, as shown in Figure 2.



m/z 75 is the sum of $^{75}\text{As}^{+}$ and $^{150}\text{Sm}^{++}$, $^{150}\text{Nd}^{++}$

Estimate contribution using $^{145}\text{Nd}^{++}$ (at m/z 72.5) and $^{147}\text{Sm}^{++}$ (at m/z 73.5) and subtract

m/z 78 is the sum of $^{78}\text{Se}^{+}$ and $^{156}\text{Gd}^{++}$, $^{156}\text{Dy}^{++}$

Estimate contribution using $^{155}\text{Gd}^{++}$ (at m/z 77.5) and $^{163}\text{Dy}^{++}$ (at m/z 81.5) and subtract

Figure 1. Process of mathematical correction of doubly-charged interferences using a half mass measurement for arsenic (left) and selenium (right).

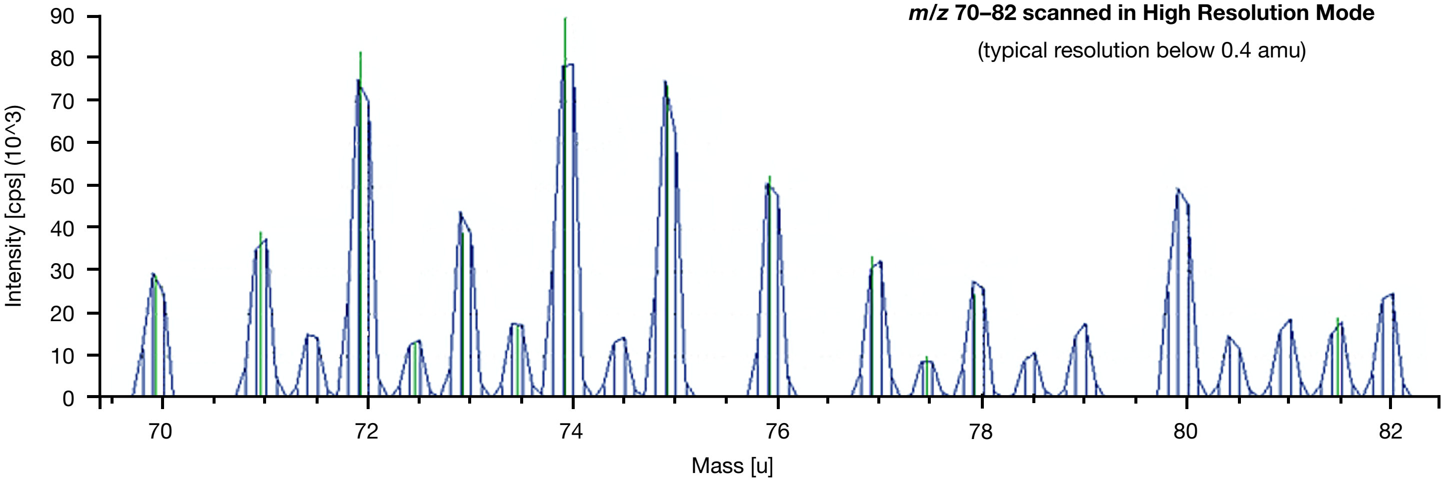


Figure 2. Survey scan spectrum between m/z 70–82 acquired on an iCAP RQ ICP-MS using high resolution. The analyzed solution contained germanium, arsenic, selenium and a mixture of different lanthanides. Please note that some signals appear at half mass (i.e., 72.5 u) and are still baseline resolved from all other signals.

However, increasing the resolution of the quadrupole mass filter also means that some ions of the analyte of interest will not reach the detector, and hence, a reduction of the sensitivity is observed compared to standard resolution (typically around 0.7 amu). This can negatively impact the detection limits and may become critical when analyzing samples with demanding quantification limits, such as baby foods.

Are there limitations to this approach?

Mathematical correction primarily accounts for the contribution of the interference but does not remove it. This leads to the need to define an appropriate working range in which half mass correction provides accurate and reliable results during method validation. To investigate the working range of this approach, a series of solutions containing 5 $\mu g \cdot L^{-1}$ of either arsenic or selenium were spiked with different amounts of the interfering lanthanides prior to analysis. Neodymium and samarium would affect the results for arsenic, whereas gadolinium and dysprosium create interferences for selenium, as described above. The results are summarized in Table 1.

Table 1. Results of the analysis of solutions containing either 5 µg·L-1 arsenic or selenium, spiked with different concentrations of lanthanides as interferences; with and without mathematical correction. All measurements were made using He KED mode on an iCAP RQ ICP-MS.

Arsenic			Selenium		
5 µg·L^{-1} of Arsenic	**Without correction [%]**	**With correction [%]**	**5 µg·L^{-1} of selenium**	**Without correction [%]**	**With correction [%]**
+ 10 µg·L^{-1} Nd	108.2	101.2	+ 10 µg·L^{-1} Dy	101.7	101.3
+ 50 µg·L^{-1} Nd	138.1	102.7	+ 100 µg·L^{-1} Dy	108.2	104.2
+ 10 µg·L^{-1} Sm	105.4	99.0	+ 5 µg·L^{-1} Gd	161.8	103.4
+ 50 µg·L^{-1} Sm	130.8	99.2	+ 10 µg·L^{-1} Gd	215.2	95.4
+ 10 µg·L^{-1} Sm and Nd	114.1	100.4	+ 50 µg·L^{-1} Gd	635.3	42.7
+ 100 µg·L^{-1} Sm and Nd	143.9	104.3	100 µg L^{-1} Gd	1178.2	-114.3

For arsenic, the control of doubly-charged interferences is possible up to a concentration of 100 µg·L^{-1} of each interferent, even if both are present at the same time (corresponding to the maximum concentration tested here). Whereas an increasing false positive is observed starting from a concentration of 10 µg·L^{-1} when no correction is applied, the use of mathematical correction does account for them in an acceptable manner. For selenium, the results are significantly different. Whereas dysprosium does not heavily contribute as an interference (^{156}Dy is only 0.06% abundant in nature), gadolinium is a cause for concern. Significant false positives are detected without correction already at a gadolinium concentration of 5 µg·L^{-1}, and correction of these interferences using the approach described is still feasible at this level. At higher concentration levels, starting at approximately 10 µg·L^{-1}, the correction leads to a reduced recovery of the measured concentration of selenium in solution, returning a severe false negative at concentrations exceeding 50 µg·L^{-1}. The reason for this overcorrection is related to the nature of the correction factors, which only take into account natural isotopic abundances, and do not account for effects occurring inside the mass spectrometer, leading to a small, but observable deviation between the natural isotope ratio and the measured isotopic ratio. This causes drastic effects when the contribution of the correction becomes large compared to the signal of the analyte, which is more severe in the case of selenium, having generally a low sensitivity in ICP-MS due to its elevated ionization potential, and lower abundance of the ^{78}Se isotope (in contrast to monoisotopic arsenic, having a similar ionization potential).

Are there other ways to overcome these interferences in case they are present in a sample?

As an alternative to mathematical correction, these interferences can be resolved using a triple quadrupole-based ICP-MS system, such as the Thermo Scientific™ iCAP™ TQe ICP-MS, operated with a reactive gas, such as oxygen. In this case, $^{75}As^+$ reacts with O_2 to form $^{91}[^{75}As^{16}O]^+$, while the interferences ($^{150}Sm^{++}$ and/or $^{150}Nd^{++}$) do not react and are hence, eliminated in the third quadrupole. Because the mass of the analyte is changed by the reaction taking place inside the CRC, this process is also often referred to as a mass shift reaction. Triple quadrupole ICP-MS has proven to be able to fully eliminate interferences derived from doubly-charged ions of the lanthanides at much higher concentration levels.

Using this approach, all other polyatomic interferences are also effectively suppressed, as shown in Figure 3.

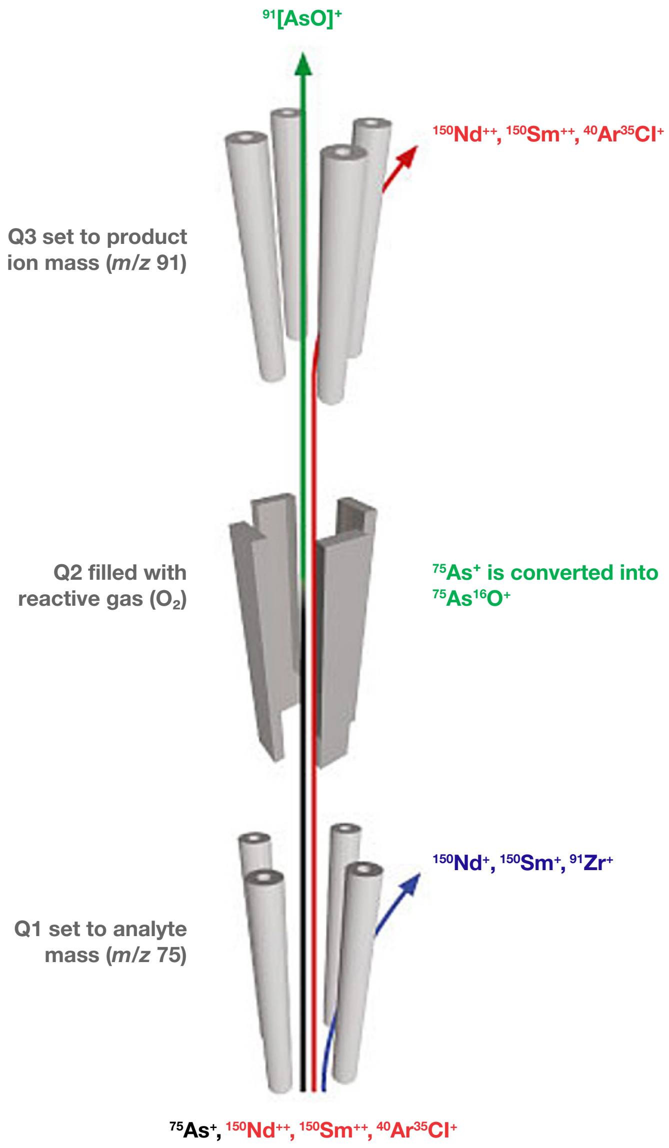


Figure 3. Mass shift reaction with O_2 to eliminate all potential interferences on arsenic.

To highlight the potential of triple quadrupole ICP-MS for the removal of these interferences, a baby food sample was analyzed before and after spiking with different amounts of the lanthanide elements. For baby food, permissible levels for toxic elements are set to the lowest thresholds to ensure their absence because of the large negative impact these elements can have on healthy child development. This in turn means that even the lowest amounts of arsenic in particular, need to be analyzed with high accuracy and confidence. The results are summarized in Table 2.

Table 2. Results obtained for the analysis of a baby food sample for arsenic and selenium, spiked with two different concentrations of a mixture of the lanthanide elements as potential interferents. All measurements were made on an iCAP TQe ICP-MS, operated in SQ-KED mode and TQ-O_2 mode.

	SQ-KED mode		TQ-O_2 mode	
	^{75}As [µg·L^{-1}]	^{78}Se [µg·L^{-1}]	^{75}As [µg·L^{-1}]	^{78}Se [µg·L^{-1}]
Original sample	0.034 ± 0.06	0.029 ± 0.01	0.028 ± 0.003	0.015 ± 0.009
Spiked with 20 µg·L^{-1} REE	1.00 ± 0.02	6.46 ± 0.2	0.027 ± 0.004	0.015 ± 0.004
Spiked with 50 µg·L^{-1} REE	2.44 ± 0.1	16.22 ± 0.5	0.034 ± 0.003	0.021 ± 0.007

Table 2 shows that, again, the results in SQ-KED mode are influenced by the presence of doubly-charged ions and return false positive data. Based on the results shown previously, mathematical correction would be feasible for arsenic, but lead to a potential false negative result for selenium. In TQ-O_2 mode, access to the most abundant isotope of selenium, ^{80}Se (49.20% abundant in nature) is possible and is the default selection of the Reaction Finder Method Development Assistant. To enable like for like comparison on the same interferences, identical isotopes were chosen for both single and triple quadrupole based modes. The ^{80}Se isotope is not accessible when using single quadrupole ICP-MS, due to overlap with the intense $^{40}Ar_2^+$ interference. Access to the ^{80}Se isotope, combined with the generally higher sensitivity achieved with mass shift measurements of Se, leads to a significant improvement of the detection limits achievable for this element.

Are there any other advantages of using triple quadrupole ICP-MS?

There are other interferences that can cause unexpected bias on key contaminants. For example, the results obtained for mercury can be positively biased in the presence of even small amounts of tungsten in He KED mode, due to the formation of WO^+ interferences which affect all the major Hg isotopes. Although these interferences are polyatomic in nature and so would be expected to be reduced in He KED mode, they are still transmitted to a large extent because the relative size difference between analyte and interference is much smaller for heavy elements. This means that KED becomes much less efficient for polyatomic interference removal at higher masses. In contrast, triple quadrupole ICP-MS provides an effective alternative for removing these interferences by, in this case, reacting away the WO^+ interferences as higher oxides of W and allowing Hg to be measured directly on its isotope masses.

Conclusion

Interferences remain a challenge in ICP-MS. Single quadrupole ICP-MS instruments, using a generic interference removal mechanism (He KED), can remove the most commonly found polyatomic interferences efficiently enough for most applications. However, other interferences remain that may become a problem in specific samples, depending on the nature of the sample and the concentration of the interfering species. If not recognized and appropriately accounted for, these interferences can unexpectedly cause incorrect results, leading to the need to troubleshoot and re-analyze the affected samples. The use of triple quadrupole ICP-MS is a simple way to overcome these challenges completely, offering opportunities to further improve detection limits, enhance data quality and increase sample throughput.

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