Challenge

Achieving lowest detection limits to accurately and precisely calibrate an ICP-MS at parts per quadrillion (ppq) concentration levels.

Solution

An ICP-MS with market-leading sensitivity and efficient interference removal using the patented integrated collision reaction cell (iCRC) for accurate quantification of lowest concentrations.

Achieving Lowest Detection Limits in ICP-MS to Calibrate at ppq Levels

Introduction

ICP-MS, mass spectrometry with inductively coupled plasma is a powerful multi-element technique to quantify elements at lowest concentrations. ICP-MS is capable to analyze almost the entire periodic table of elements in various matrices. In the determination of trace and ultratrace concentrations, not only the instrument performance but also the laboratory environment and correct sample handling are crucial factors. This application note highlights the capabilities of the PlasmaQuant MS Elite family in the accurate and precise determination of lowest quantities of analytes.

The limit of detection (LOD) is defined as the lowest quantity that can be distinguished from a blank with a certain confidence level. The instrument detection limit is typically defined as the concentration of an analyte, which gives a signal equal to measurement above the blank solution. This equals a probability of about 1% for a false positive error (α) meaning 1% chance of assigning a signal originating from the blank to an analyte. However, at this concentration there is a 50% chance of assigning an analyte signal to the noise (false negative error (β) = 50%). For that reason and to minimize the false negative errors, the limit of quantification (LOQ) is often estimated as the concentration which leads to a signal as high as 10x noise of the blank solution measurement above the blank intensity. Hereby the factor 10 is historically established and commonly chosen in analytical chemistry. At this concentration the relative imprecision of the method is 5%. However, different factors may be used depending on statistical demands. The relationship between noise, limit of detection and limit of quantification is schematically shown in Figure 1.

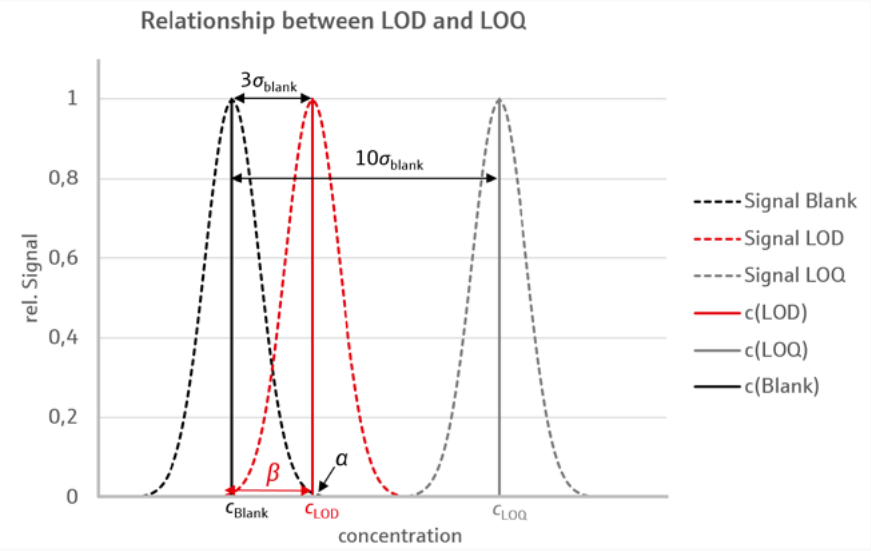

Figure 1: Relationship between noise, limit of detection (LOD) and limit of quantification (LOQ). The parameter α denotes the concentration at which the probability of assigning a blank signal (black) falsely to an analyte equals 1% (false positive error). At this concentration there is a 50% chance of assigning an analyte signal (red) to the noise (β, false negative error).

Theoretical considerations

The noise of the signal is typically assumed to be the standard deviation of the measurement. The limit of detection can be calculated using the 3 sigma method:

$$c_{LOD} = \frac{3\,\sigma_{blank}}{\text{Sensitivity}}$$

with σ_{blank} being the standard deviation of the blank signal. As a first approximation, the standard deviation scales with the square root of the intensity ($\sigma \propto \sqrt{\text{Intensity}}$). More in detail, noise in ICP can be described by a double stochastic Poisson process. Different noise sources (e.g. plasma flickering noise, counting statistics noise) add up to total noise. Counting statistics noise, also called Poisson noise, has its origin in the ion transmission from the ICP ion source to the detector and is often assumed to scale with the square root of the blank intensity (Poisson noise, $\sigma_{Poisson} \approx \sqrt{I_{blank}}$). The second noise source is often called plasma flickering noise ($\sigma_{flickering}$) and is normally assumed to be 0.5% of the blank signal ($\sigma_{fl} = 0.005 \cdot I_{blank}$). It consists of many different individual noise sources which all contribute to the excess variance of the Poisson process.[1] The limit of detection can then be calculated by:

$$c_{LOD} = \frac{3\,\sigma_{blank}}{\text{Sensitivity}} \quad \text{with } \sigma_{blank} \approx \sqrt{(\sigma^2_{poisson} + \sigma^2_{flickering})}$$

For the reason that the blank solution is typically contaminated to some extend with the element of interest the intensity (I) resulting from the contamination can be calculated by:

$$I_{contamination} = c_{contamination} \cdot \text{Sensitivity}$$

Hereby, the contamination of the blank solution with the analyte of interest depends on many factors such as the elemental abundancy, the purity of the used chemicals and flasks, the usage of clean room conditions etc.

For a contamination of 0.1 ng/L (ppt) and a sensitivity of $1.5 \cdot 10^6$ cps (counts per second) per µg/L (ppb) the resulting signal from the contamination is 150 cps. The total intensity of the blank is the sum of the contamination and the continuous background (cb):

$$I_{blank} = I_{contamination} + I_{cb}$$

The continuous background is typically <1 cps. Therefore, it has only a minor influence even at low contamination levels of only 0.1 ng/L. As the intensity of the blank solution is mainly determined by the contamination of the blank and as the absolute noise of the blank increases with increasing signal, the reduction of contaminations due to chemicals, tubes and the manufacturing process strongly improves the LODs.

To highlight the influence of sensitivity, noise and contamination the following Table 1 lists a short comparison of LODs under different circumstances considering the above mentioned calculations (3 sigma method). The continuous background was set to 1 cps. More detailed information regarding the relationship between sensitivity, noise and contamination of the blank solution can be found in the publication "When Sensitivity Does Matter".[2]

Table 1: Comparison of limits of detection calculated for different sensitivities and contamination of the blank solution.

Sensitivity [cps/ppt]	150	1500	150	1500	150	1500
Contamination [ppt]	1.0	1.0	0.1	0.1	0.01	0.01
Intensity blank [cps]	151	1501	16	151	2.50	16
LOD [ppt]	0.246	0.079	0.080	0.025	0.032	0.008

At equal blank contamination, a sensitivity advantage of a factor of 10 enables to achieve significantly lower LODs compared to low sensitive ICP-MS instruments (sensitivity advantage of the PlasmaQuant MS Elite family: 5-15x). When comparing the expected LOD for high sensitivity (1500 cps/ppt) at 1ppt contamination of the blank and the LOD for a 10 times lower sensitivity (150 cps/ppt) but a 10 times cleaner blank solution (contamination: 0.1 ppt) it can be noticed that comparable LODs can be achieved. This shows the capability of a 10x more sensitive ICP-MS to tolerate 10x higher contamination levels while still achieving competitive LODs. This is especially important since a major source of contamination is the sample preparation and the chemicals involved as well as the laboratory environment in general. These sources are independent from the instrument used and increase the LOD significantly for low sensitive instruments.

Influence of lab environment, purity of chemicals and flask material on the limit of detection

The contamination of the blank solution has a big impact on the resulting limit of detection as described in theoretical considerations. For this reason it is highly important to minimize contaminations as much as possible. The origin of the contamination depends on the element and its abundancy. Different strategies are common to minimize elemental contaminations during sample preparation.

When not in use, flasks are conditioned with an acid solution (e.g. 1% HNO_3) in order to leach out elements present in the flask material and to equilibrate surface processes. Hereby, glass flasks must be avoided for trace metal analysis as the glass surface is chemically not inert and can lead to reactions and ad-/desorption processes. Polymer flasks, especially ones made out of perfluoroalkoxy alkane polymers (PFA) are chemically inert and are proven for the quantification of ultra-trace amounts of elements. Additionally, the purity of the used chemicals directly affects the background concentration of all solutions and therewith the achievable limit of detection. Chemicals with certificates specifically produced for trace metal analysis should be used if possible.

Another source of contamination are particles present in the air. They have an elemental composition, which can differ, with regard to the location of the lab. Especially at dusty environments such as mining sites, elevated backgrounds can be expected for certain elements. The best way to minimize those contaminations is to have the instrument and sample preparation located in a clean room. However, this is not possible as construction and maintenance of a clean room is very expensive. A cheap and effective way to minimize this kind of problems is to use a flow box for sample preparation and autosamplers covered with a dust box including a HEPA filter.

Figure 2: Flowbox used for sample preparation generating a semi-clean room atmosphere.[3]

Materials and Methods

Samples and Reagents

All samples and standards were prepared using high purity reagents. The standards and blanks were made with deionized water <0.055 µS/cm (ELGA Lab), 1% HNO_3 (Merck) as this is frequently used to stabilize the elements.
Calibration solutions were prepared from a multi-element stock solution. A calibration with at least five data points was created with the lowest standard having a concentration close to the limit of quantification.

Instrumentation

A PlasmaQuant MS Elite S, Micro Mist (0.4 mL/min) nebulizer, Scott-type double-pass spray chamber and a Fassel torch with 2.4 mm injector were used for the analysis.
All experiments were performed under non-clean room conditions.
The limit of detection was calculated using the 3 sigma method (see, Theoretical considerations).

Instrument settings and method parameters

Elements, which are not subject to polyatomic interferences were measured in no gas mode. Argon based interferences were removed by injecting hydrogen as a reaction gas via the integrated collision reaction cell (iCRC) as hydrogen is more powerful in removing this type of interferences compared to helium which was used for the removal of all other polyatomic interferences. The patented BOOST technology was used to retain sensitivity on a high level when injecting hydrogen into the iCRC for interference removal. The resulting low limits of detection enabled precise and accurate analyses.
Table 2 lists the method parameters used.

Table 2: Methode parameters.

Parameter	Specification
Plasma Gas Flow	7.5 L/min
Auxiliary Gas Flow	1.50 L/min
Nebulizer Gas Flow	1.08 L/min
Spray Chamber Temperature	3 °C
RF Power	1220 W
Sampling Depth	5.0 mm
Scan Mode	Peak hopping – 1 pt/peak
Dwell Time	50 ms
Scans per Replicate	20
No. of Replicates per Sample	10
iCRC Gas	He, H_2
BOOST Voltage	10 V

Results and Discussion

The instrument detection limits (IDL) obtained from the calibration curves were calculated by performing a noise analysis of the measured blank solution (three sigma method) as described in theoretical considerations and are listed in Table 3.

Table 3: Instrument detection limits in ng/L for a 1% HNO_3 matrix.

Element	no gas	H_2	He	Element	no gas	H_2	He
^{7}Li	0.5	2.5	3.0	^{115}In	0.01	0.03	0.05
^{9}Be	0.4	0.7	1.2	^{120}Sn	0.1	n. m.	n. m.
^{11}B	6.9	17	21	^{121}Sb	0.04	n. m.	n. m.
^{23}Na	25	13	25	^{125}Te	0.4	1.4	0.9
^{24}Mg	1.1	2.0	2.3	^{133}Cs	0.05	0.09	0.2
^{27}Al	0.9	2.4	3.8	^{138}Ba	0.07	0.07	0.10
^{44}Ca	n.m.	23	79	^{139}La	0.02	n. m.	n. m.
^{45}Sc	3.5	n. m.	n. m.	^{140}Ce	0.01	n. m.	n. m.
^{49}Ti	0.6	n. m.	n. m.	^{141}Pr	0.006	n. m.	n. m.
^{51}V	2.3	0.8	2.6	^{146}Nd	0.03	n. m.	n. m.
^{52}Cr	6.1	0.5	6.1	^{147}Sm	0.03	n. m.	n. m.
^{55}Mn	0.7	0.8	0.9	^{153}Eu	0.01	n. m.	n. m.
^{56}Fe	n. m.	1.6	n. m.	^{157}Gd	0.03	n. m.	n. m.
^{57}Fe	571	76	91	^{159}Tb	0.004	n. m.	n. m.
^{59}Co	0.1	0.4	0.1	^{163}Dy	0.02	n. m.	n. m.
^{60}Ni	22	10	18	^{165}Ho	0.003	n. m.	n. m.
^{63}Cu	0.4	0.7	0.5	^{166}Er	0.009	n. m.	n. m.
^{66}Zn	1.6	2.1	3.2	^{169}Tm	0.004	n. m.	n. m.
^{69}Ga	0.1	0.4	0.4	^{172}Yb	0.02	n. m.	n. m.
^{75}As	5.4	1.9	n. m.	^{175}Lu	0.003	n. m.	n. m.
^{78}Se	15	13	n. m.	^{178}Hf	0.02	n. m.	n. m.
^{85}Rb	0.1	0.9	0.3	^{181}Ta	0.005	n. m.	n. m.
^{88}Sr	0.04	0.05	0.06	^{182}W	0.02	n. m.	n. m.
^{89}Y	0.01	n. m.	n. m.	^{185}Re	0.01	n. m.	n. m.
^{90}Zr	0.05	n. m.	n. m.	^{193}Ir	0.01	n. m.	n. m.
^{93}Nb	0.02	n. m.	n. m.	^{195}Pt	0.04	n. m.	n. m.
^{95}Mo	0.1	n. m.	n. m.	^{197}Au	0.03	n. m.	n. m.
^{98}Mo	0.1	n. m.	n. m.	^{202}Hg	0.4	n. m.	n. m.
^{101}Ru	0.06	n. m.	n. m.	^{205}Tl	0.03	0.03	0.05
^{103}Rh	0.008	n. m.	n. m.	^{206,7,8}Pb	0.04	0.03	0.07
^{105}Pd	0.05	n. m.	n. m.	^{209}Bi	0.01	0.01	0.02
^{107}Ag	0.03	0.1	0.1	^{232}Th	0.02	n. m.	n. m.
^{112}Cd	0.06	0.1	0.1	^{238}U	0.01	n. m.	n. m.

Legend: n. m. = not measured

Calibration

At very low concentrations, interferences resulting from the matrix or plasma may lead to apparent too high signals. As the interference is an element specific offset for a given matrix and method, the deviation of measured and true concentration increases with decreasing analyte concentration. For that reason, many regulations require the first calibration standard near the limit of quantification to prove the linearity and correctness of the calibration function in this low concentration range. Four representative calibration curves with the lowest standard close to the limit of quantification are shown in Figure 3. The obtained minor deviations of the individual standards from the regression function prove the reliability and performance of the instrument. The outstanding sensitivity results in a very high precision minimizing noise and uncertainties and enables the accurate calibration at very low parts per trillion (ppt) concentrations.

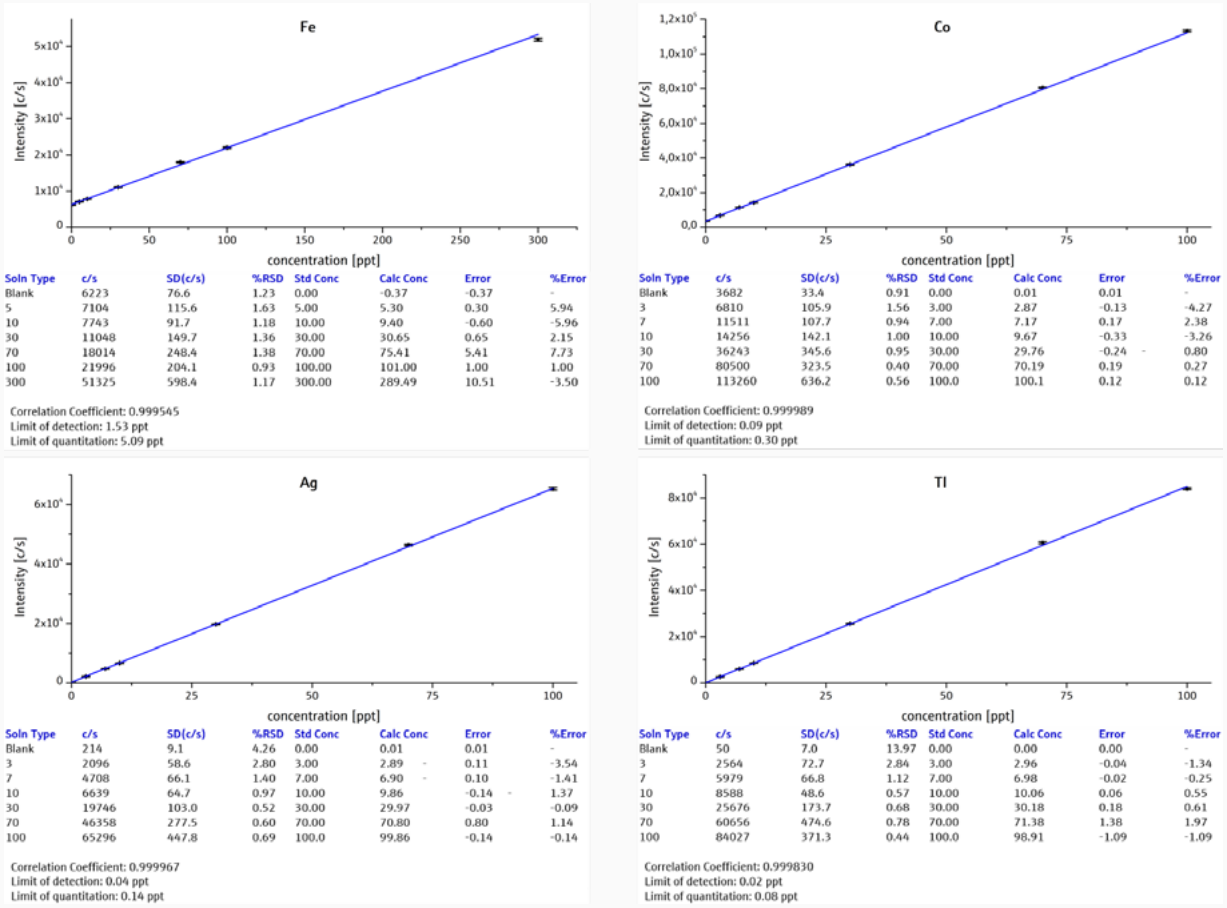

Figure 3: Representative calibration graphs.

Due to the market-leading sensitivity of the PlasmaQuant MS instruments and the low background resulting in an unmatched signal to noise ratio, lowest limits of detection of up to only a few parts per quadrillion (ppq) are achieved. This enables to accurately and precisely calibrate at concentrations in the low ppq range as required, e.g. for ultra-trace analysis of rare earth elements. Four representative calibration curves using calibration standards with 50 pg/L to 1000 pg/L (ppq) are shown in Figure 4.

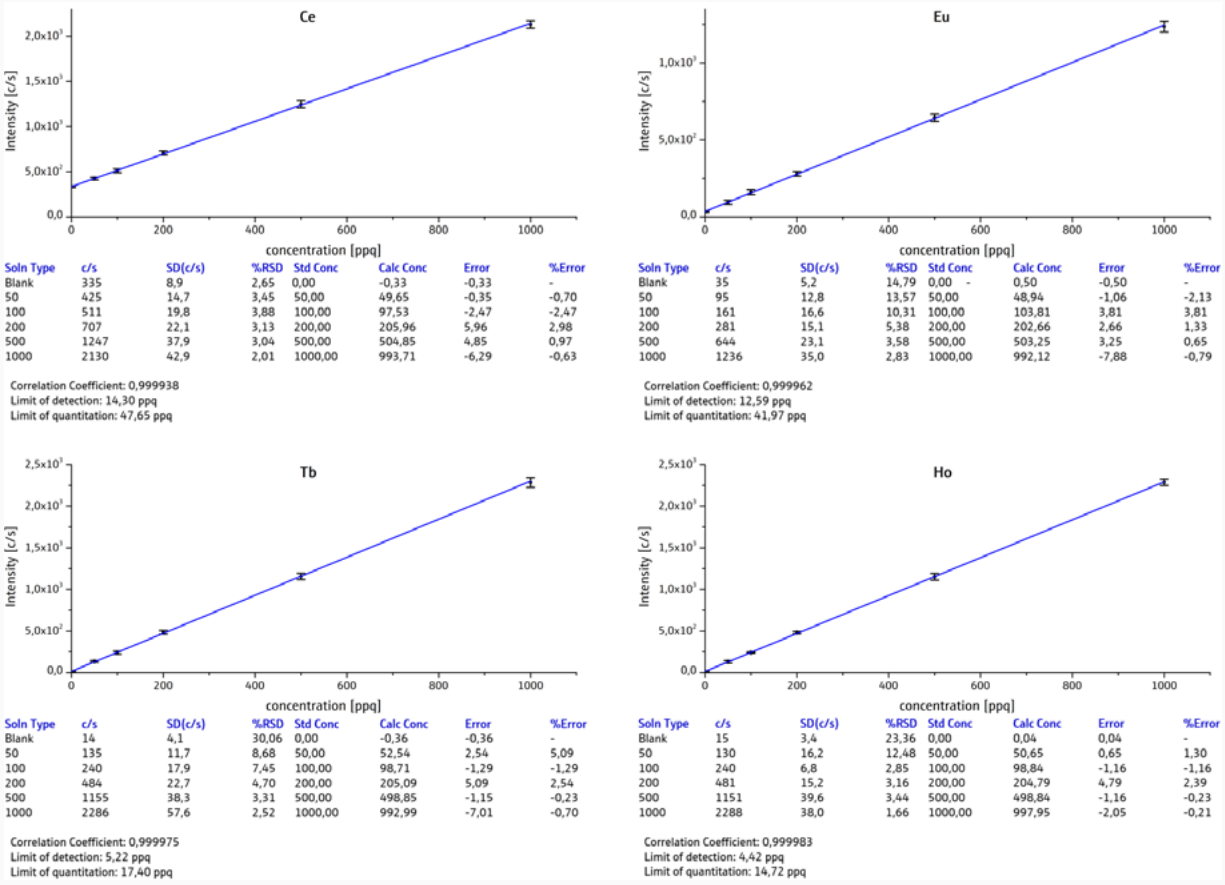

Figure 4: Representative calibration graphs of rare earth elements with concentrations in the parts per quadrillion (ppq) range.

Conclusion

Within this study the instrument detection limits were determined for the matrix 1% HNO_3 as this matrix is established for sample acidification. The instrument detection limits listed are the concentrations, which can be detected at best conditions in a standard, non-clean room environment. Hereby, the contamination of the blank solution is the determining factor for the limit of detection for elements having a relatively high abundance. This highlights the necessity for high purity reagents and a clean lab in order to minimize contaminations as much as possible. Furthermore, factors such as treatment of the used lab equipment (e.g. leaching of flasks) are highly important. For typically low abundant elements, such as rare earth elements, the instrument sensitivity is key for achieving lowest limits of detection. The superior sensitivity of the PlasmaQuant MS Elite S leads to outstanding limits of detection of down to a few pg/L. The robust design allows to accurately calibrate the instrument even at low parts per quadrillion (ppq) concentrations close to the limit of quantification making the PlasmaQuant MS series the ideal solution for the robust and correct quantification of smallest amounts of elements.

References

[1] A. Ulianov et al., *THE ICPMS SIGNAL AS A POISSON PROCESS: A REVIEW OF BASIC CONCEPTS*, Journal of Analytical Atomic Spectrometry, 30, **2015**, 1297-1321.
[2] S. Elliot et al., *ICP-MS: WHEN SENSITIVITY DOES MATTER*, Current Trends In Mass Spectrometry, 40, **2007**, 36-43.
[3] https://www.spetec.de/downloads/brochure_CleanBoy.pdf

This document is true and correct at the time of publication; the information within is subject to change. Other documents may supersede this document, including technical modifications and corrections.

Headquarters
Analytik Jena AG
Konrad-Zuse-Strasse 1
07745 Jena · Germany

Phone +49 3641 77 70
Fax +49 3641 77 9279

info@analytik-jena.com
www.analytik-jena.com

Version 1.0
en · 12/2020
© Analytik Jena AG | Pictures ©: Analytik Jena, p1-Istock/YvanDube