Single particle analysis using the Agilent 7700x ICP-MS

Application note

Materials

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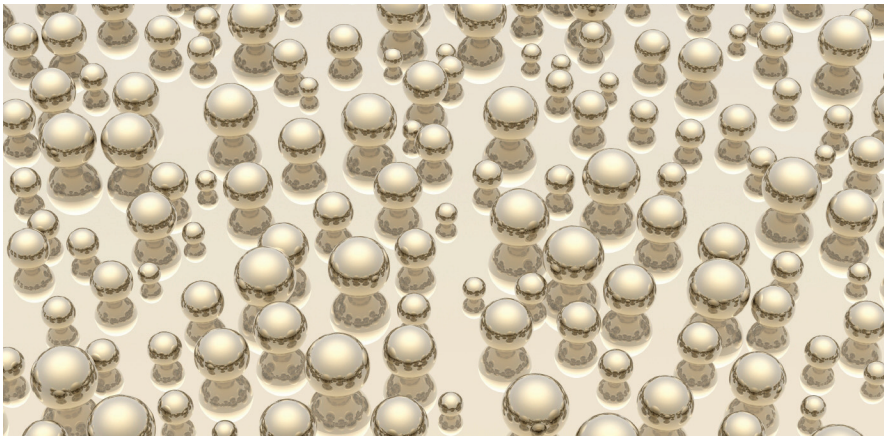

Introduction

Nanoparticles (NPs) are defined as ultrafine particles with one dimension between 1–100 nm [1]. Because of their small size, they have a very large surface area relative to their weight, so they often react quite differently from a bulk solid or dissolved material of the same composition. For this reason they may offer novel and interesting properties for a broad range of applications. Current and potential applications for NPs range from food additives, cosmetics and pharmaceuticals, to biocidal packaging, fuel cell technology and electronics. But while their use is constantly increasing, questions and concerns have been raised about their safety and their health impact. For this reason, there is an urgent need to develop analytical methods that are suitable for the particular evaluation of NPs. These methods need to be appropriate to the specific properties of nanoparticles,

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and so should allow not only the determination of the NPs mass concentration, but also the evaluation of their size and size distribution.

An interesting approach for the characterization of NPs has been developed by Degueldre et al. [2] based on elemental determination using Inductively Coupled Plasma Mass Spectrometry (ICP-MS). If samples containing NPs are introduced at a low flow rate and the number of particles in the solution is sufficiently low, analysis using ICP-MS in time resolved mode makes it possible to collect the intensity for a single particle as it is vaporized and atomized in the plasma. Then, each measured data point can be correlated to the size and mass fraction of a unique NP. This method of NP characterization is called Single Particle ICP-MS (SP-ICP-MS) analysis. The key feature of this analysis lies in the capacity of the ICP-MS to distinguish the data collected for each individual NP. For this reason, care must be applied in the sample dilution (particle number in solution) and in the selection of the integration time [3–5]. For a given content of NPs in the sample following its dilution, the integration time of the ICP-MS should be:

- Long enough to collect the entire signal from one NP and avoid the partial measurement of the particle, which would lead to an underestimation of its size. This point is also important in ensuring that the NP signal can be accurately discriminated from the background signal [4],
- Short enough to avoid the measurement of two NPs in a single integration period, which would lead to an overestimate of the size of the NPs, and an underestimate of the particle number [3, 5].

In the present work the analysis of various NPs has been carried out using the Agilent 7700x in SP-ICP-MS mode. Initially, the analysis of gold standards from NIST was used to evaluate the method for the detection of NPs sizes. Then, the method was applied to the characterization of samples containing gold and silver NPs.

Experimental

Instrumentation

Measurements of NPs were performed using the Agilent 7700x ICP-MS. The samples were introduced directly into the ICP-MS system using the standard peristaltic pump with Tygon pump tubing (internal diameter of 1.02 mm), and ASX-520 autosampler.

Analyses were performed in time resolved analysis (TRA) mode using an integration time of 3 ms for all measurements. While the integration times used in the literature vary, they are typically around 5 ms, and a maximum integration time of 10 ms is recommended [3–6] to avoid the double-counting mentioned previously.

A rinse solution containing 1% nitric acid was used to ensure sample washout between each analysis.

The general settings of the 7700x system are detailed in Table 1.

Table 1. General settings of the 7700x ICP-MS

Parameter	Value
RF power	1550 W
Carrier gas	1.05 L/min
Spray chamber temperature	2 °C
Nebulizer pump	0.1 rps
Sample depth	8.0 mm
Integration time	3 ms
Acquisition time	60 s
Mass monitored	^{107}Ag or ^{197}Au

Data analysis

Details of approaches used for data processing and interpretation for SP-ICP-MS analysis can be found in the literature [3–6]. In the present work, a dedicated spread sheet developed by the National Institute of Food Safety in the Netherlands (RIKILT) was used for data conversion. Briefly, the custom spreadsheet uses the distribution plot of the signal intensities to allow the NP signals to be discriminated from the background (due to instrument noise and the signal from the dissolved component of the element in solution). The sensitivity of the ICP-MS (cps per µg/L) for the element of interest can be calibrated using conventional (non-NP) measurement of a standard solution, and so the signal peaks from the NPs can then be converted into the mass concentration of the element measured. The density of the material/element of interest is then entered into the spreadsheet, allowing the volume of each NP to be calculated. Based on the assumption that the NPs are spherical, the cube root of the NP volume can then be used to calculate each NP's diameter, allowing a size distribution plot to be generated, from which the median NP size is calculated. For the accurate conversion from intensities to particle sizes, the nebulization efficiency of the ICP-MS must be established, as well as the sensitivity for the target element. A sequence of analysis for samples containing NPs will therefore include at least the measurement of:

- A reference material with known NP particle size (for the evaluation of the nebulization efficiency)
- An ionic (dissolved) solution made from the same material as the unknown NP (for the determination of the ICP-MS sensitivity)
- The unknown sample(s)

Ultimately, the SP-ICP-MS analysis and custom spreadsheet calculations are able to determine the number of particles present in the sample, their size distribution, the median size of the NPs population and the mass concentration for the element that the NP is composed of.

Sample preparation

Gold nanoparticle reference materials (RMs) NIST 8012 and NIST 8013, with reference values of 30 and 60 nm respectively, were purchased from NIST (Gaithersburg, MD, USA). Unknown gold or silver NP samples with different sizes were provided by different NP producers.

The nanoparticle samples were diluted with water using polypropylene vials. Sample dilution was performed on the day of the analysis in order to avoid sample degradation. Before dilution of the samples and prior to their analysis, all solutions were placed in an ultrasonic bath for 15 min to ensure that the samples were fully homogenized.

The gold NP standard at 60 nm (NIST 8013) was diluted to 5 ng/L Au concentration, for the evaluation of nebulization efficiency.

Ionic solutions of gold and silver were diluted to 1 µg/L for the evaluation of the system sensitivity for each element.

Each NP sample was diluted to ensure the measurement of between 200–2000 particle events per minute by SP-ICP-MS. This point is important to correctly measure the full signal from only one nanoparticle within each TRA integration. For this application, using the typical sample flow rate of the 7700x ICP-MS, the above particle number per minute correlates to approximately 10^7 particles per liter, which equates to an elemental concentration of between 5–500 ng/L, depending on the size and composition of the NPs.

Results and discussion

Analysis of gold nanoparticles

In order to evaluate the suitability of the ICP-MS method, a preliminary analysis of the reference NPs was performed. The gold NP standard (NIST 8012), which has a reference diameter of around 30 nm, was used for this purpose. A typical TRA acquisition for single NP measurement on the 7700x ICP-MS is shown in Figure 1. From this raw data, the background signal was eliminated by the custom spreadsheet, and the remaining intensities were converted into particle size to give the distribution pattern shown in Figure 2. From this size distribution plot, the median size was calculated to be 26.9 nm. This measured size is in good agreement with the reference value shown on the investigation report, which is 24.9–28.4 nm, depending upon the technique used for the measurement. The three replicate analyses of this sample gave a relative standard deviation of 0.5%, demonstrating the good repeatability of the 7700x SP-ICP-MS method.

The particle number in the diluted sample was estimated at 1.6×10^7 particles/L and the mass concentration for Au was 3.2 ng/L.

It should be noted that the data in Figure 2 show that no NPs were detected at a higher size range than the expected group in the 30 nm region. In particular around the 38 nm region where the signal should appear if a particle containing a cluster of two NPs was measured, the number of events measured is less than 2% of the total number of NPs detected. This observation suggests that the sample preparation approach was successful in ensuring that the measured NPs were distributed homogeneously, and were not present as an agglomeration of particles in the diluted sample. The absence of a significant number of particle events at a size greater than 30 nm also confirms that the chosen acquisition parameters did not lead to the measurement of more than one NP in each TRA integration period. Therefore, the integration time selected in the method was suitable for the discrete analysis of each individual NP introduced in the system.

For a better evaluation of the developed method and to demonstrate that the method is able to discriminate NPs of a larger size, a mixture of gold NPs at 30 nm (NIST 8012) and 60 nm (NIST 8013) was also analyzed.

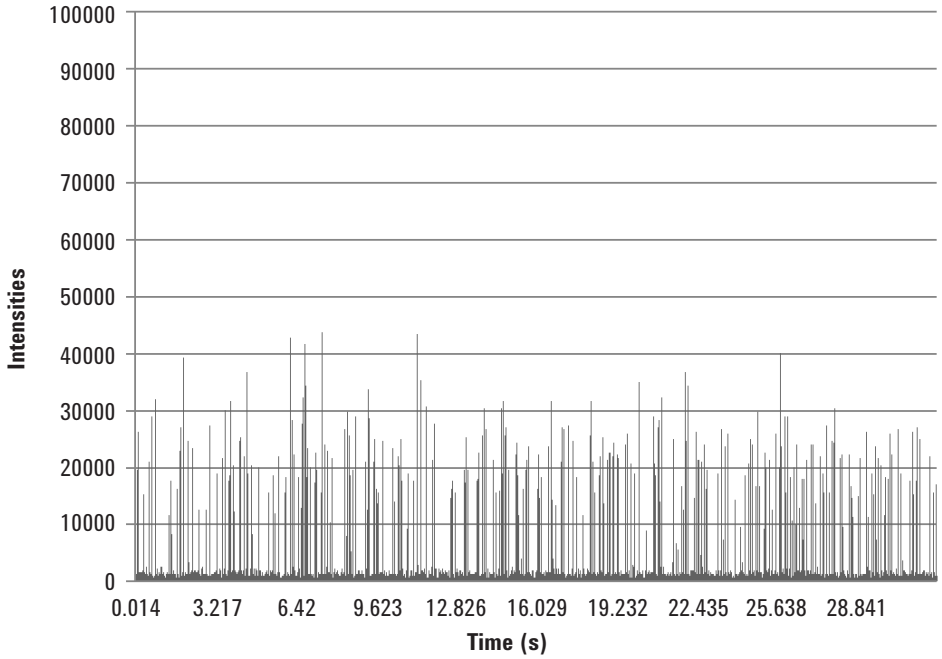

Figure 1. Typical TRA measurement of Single NPs. Example of the measurement of 30 nm gold NP standard (NIST 8012).

The result of this analysis is displayed in Figure 3. As can be seen, the method was clearly able to identify the presence of the two different NP sizes, with no overlap between the two different populations. The method has therefore been shown to have sufficient resolution to detect and discriminate between mixtures of different NP sizes within a single sample.

Following the analysis of the NIST NP RMs, the remaining gold nanoparticle samples were measured as unknowns. Au NPs with a nominal particle size of 40 and 15 nm were analyzed as separate samples, and the median particle size was found to be 38 and 16 nm respectively. The results for the characterization of those samples can be seen in Table 2.

Table 2. Results for the analysis of unknown gold NPs

Theoretical size	40 nm	15 nm
Experimental size	38 nm	16 nm
Particles number	5.5×10^7 particles/L	6.4×10^6 particles/L
Element concentration	3.7 ng/L	0.3 ng/L

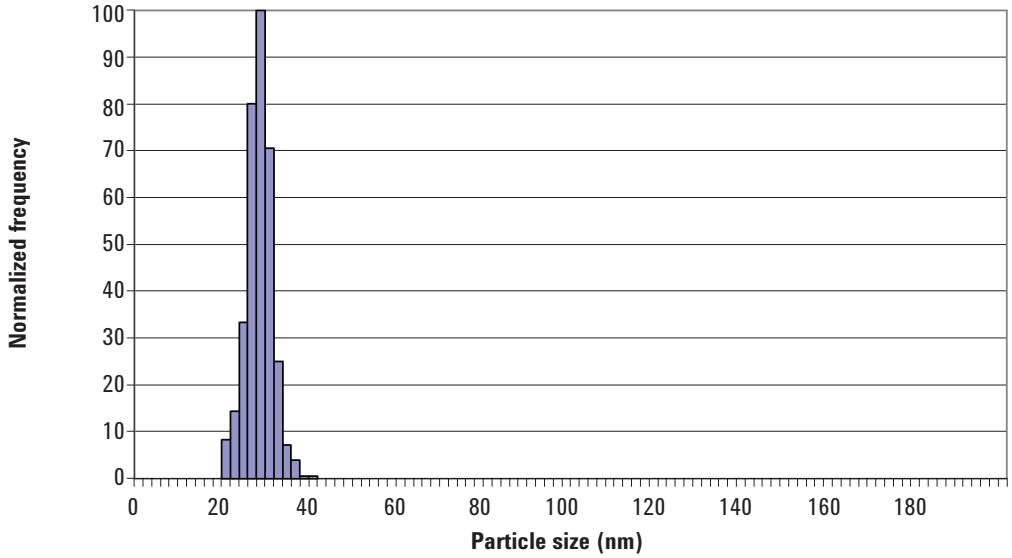

Figure 2. Particle size distribution for a 30 nm gold NP standard (NIST 8012)

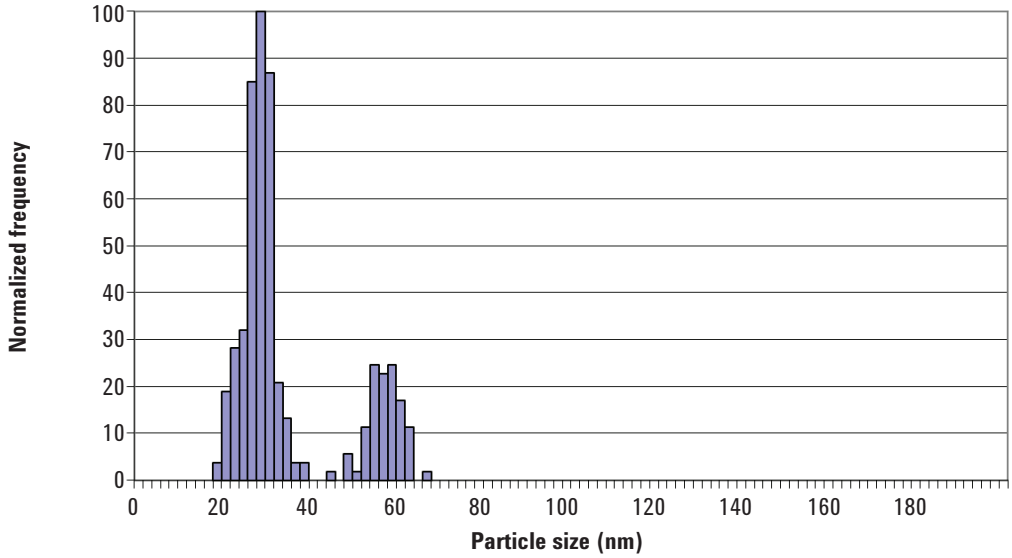

Figure 3. Particle size distribution for a mixture of 30 nm and 60 nm gold NP standards (NIST 8012 and 8013)

Analysis of silver nanoparticles

After the development of the gold nanoparticles method, the same procedure was applied to the analysis of silver NPs. A sample with indicative particle size of 20 nm was analyzed.

The analysis of the 20 nm NPs led to a median size of about 18 nm, in good accordance with the indicative value (Figure 4). The number of particles was found to be 1.1 x 10^7 particles/L and the silver concentration was calculated to be 0.4 ng/L. However, the detection of this NP size was near the limit of the method, as the signal distribution for the NPs was close to the background signal measured by the ICP-MS.

Conclusions

The present work illustrates the suitability of the Agilent 7700x ICP-MS for the analysis of single nanoparticles. The method has been successfully applied to the analysis of gold and silver NPs with sizes ranging from 15–60 nm. The SP-ICP-MS method provided the size distribution, median size, number of particles and the elemental concentration of a given NP sample.

Additional work may be required to fully validate the SP-ICP-MS measurement and data analysis approach, in particular to validate the calculations used when converting the measured intensities into NP sizes. To complement the results obtained by the SP-ICP-MS analysis, additional approaches should be used, such as Scanning Electron Microscopy (SEM) or the coupling of Field Flow Fractionation (FFF) devices with ICP-MS.

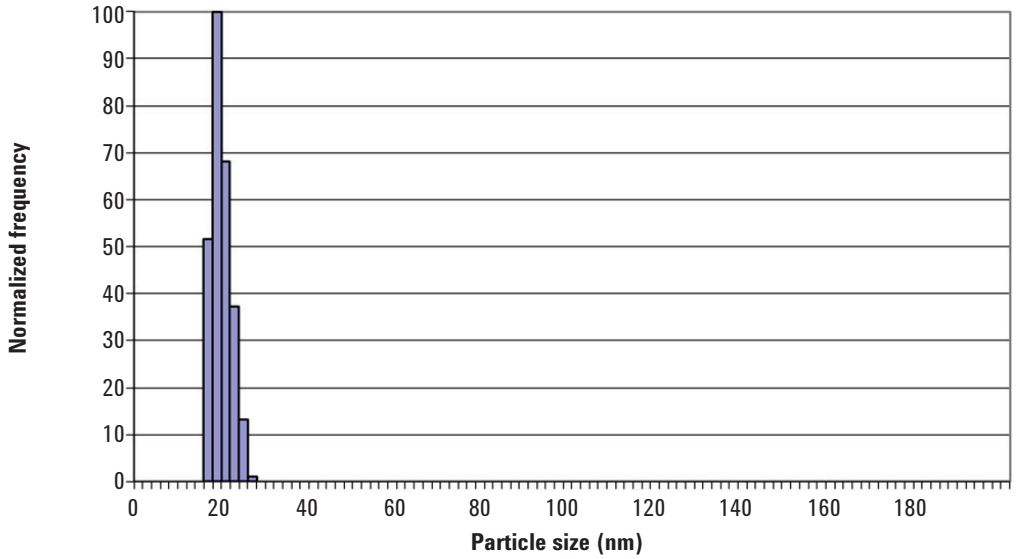

Figure 4. Particle size distribution for unknown silver NPs with indicative size of 20 nm

The next challenges for SP-ICP-MS analysis will be to apply the method to real samples which include a matrix that could create interferences, and to use the method for the measurement of nanoparticles containing elements such as titanium, iron or silicon, which are more challenging for ICP-MS due to the potential for spectral interferences.

Acknowledgements

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References

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