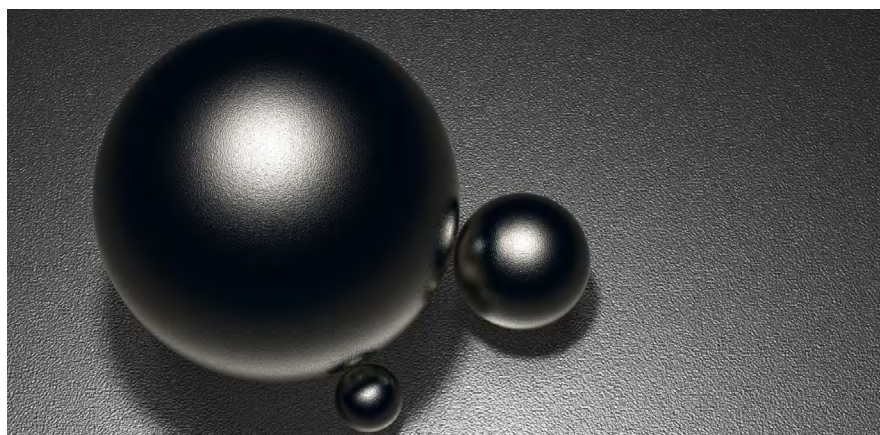# Single particle analysis of nanomaterials using the Agilent 7900 ICP-MS

Application note

Materials, Environmental

Authors

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Introduction

Nanoparticles (NPs) are common components in a wide range of materials in industries from high technology electronics, optics, and medical devices, to food additives, pharmaceuticals, cosmetics and environmental sciences. Nanomaterials occur naturally, but the rapid expansion in their use is due to the development of manmade or engineered nanoparticles (ENPs). As the health impact of these relatively new materials is not yet fully understood and concerns have been raised about their safety, there is an urgent requirement to develop analytical methods that are capable of identifying and characterizing NPs. Such methods should not only measure the total concentration of the analyte(s), but also be able to identify if particles are present in the sample, and characterize their size and number [1].

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The flexibility of ICP-MS means that it can be used as an elemental detector for separation techniques such as Field Flow Fractionation (FFF) [2] or can be used to measure individual particles in the sample [3]. The latter mode is referred to as single particle (SP-ICP-MS) mode.

For SP-ICP-MS mode to be successful, samples containing NPs need to be introduced at a low flow rate and the number of particles in the solution needs to be sufficiently low. Operating the ICP-MS in time resolved analysis (TRA) mode makes it possible to collect the intensity for a single particle as it is vaporized and ionized in the plasma. The signal intensity at each measured data point can then be correlated to the size and mass fraction of the NP. The key feature of SP-ICP-MS analysis lies in the capacity of the ICP-MS to distinguish the data collected for each individual NP, and to separate the NP signals from the baseline (due to the instrument background, any interferences, and the dissolved component of the element in the solution). To achieve this, care must be applied in the sample dilution (particle number in solution) and in the selection of the integration time [3–5]. Sample dilution (and integration time) should be selected to ensure that no more than around 1 in 10 of the measured data points contains a particle. The remaining measured points are used to give an accurate background measurement, which is essential to allow the particle signals to be accurately discriminated from the dissolved elemental or electronic background.

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 (one particle's signal being split between two ICP-MS data points), which would lead to an underestimate of the particle size and an overestimate of the particle number. Sufficiently long integration time 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].

To satisfy both of these requirements, the typical recommended integration (or dwell) times used in previous studies are in the range from 1 to 10 ms per point.

With the latest generation of ICP-MS systems such as the Agilent 7900, shorter dwell times (below 1 ms) can be used, and the settling time between measurements has been eliminated. This allows an alternative measurement approach to be used, where the ICP-MS acquisition rate is fast enough to make several individual measurements during the signal pulse from the cloud of ions from one particle arriving at the detector. This allows integration of the signal from a single particle, akin to the measurement of a very short-lived chromatographic peak.

In a previous study of nanoparticles, we used an Agilent 7700x ICP-MS [6]. In this work, we evaluate the performance of the Agilent 7900 ICP-MS for the measurement of individual NP peak signals. The 7900 ICP-MS features a new orthogonal detector system that has a fast integration time of 100 µs, zero settling time between TRA readings, and an overall acquisition speed in TRA mode that is 30x faster than the 7700x, permitting fast transient signal measurement.

Experimental

Instrumentation
All measurements were performed using the Agilent 7900 ICP-MS equipped with a standard sample introduction system consisting of a MicroMist nebulizer and Scott type double pass spray chamber. Samples were introduced directly into the ICP-MS using an ASX-520 autosampler with the standard peristaltic pump and tubing (i.d. 1.02 mm).

Analyses were performed in TRA mode using an integration time of 3 ms or 0.1 ms (100 µs) per point depending upon the experiment. Total acquisition time was fixed at 60s for all analyses. The general settings of the 7900 ICP-MS are given in Table 1.

Data analysis
Details of approaches used for data processing and interpretation of SP-ICP-MS analysis can be found in the literature [2–7]. In this work, a dedicated spread sheet developed by the National Institute of Food Safety in the Netherlands (RIKILT) was used for data conversion of the measurements made at an integration time of 3 ms.

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

Table 1. 7900 ICP-MS operating parameters

Parameter	Value
RF power	1550 W
Carrier gas	1.05 L/min
Make-up gas	0.10 L/min
Spray chamber temperature	2 °C
Nebulizer pump	0.1 rps
Sample depth	8.0 mm
Oxide ratio	1.5%
Integration time	3 ms or 100 µs (see text)
Acquisition time	60 s
Mass monitored	^{107}Ag or ^{197}Au

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)

For complete characterization of the nanoparticle content of a given sample, 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 material (RM) NIST 8013 with a reference value of about 60 nm particle diameter was purchased from NIST (Gaithersburg, Maryland, USA). Silver NP samples with particle sizes from 10 to 100 nm were acquired from Sigma-Aldrich (Saint-Louis, Missouri, USA).

The nanoparticle samples were diluted with water in polypropylene vials. Sample dilution was performed on the day of the analysis in order to avoid sample degradation. Before dilution of the samples and again prior to their analysis, all solutions were placed in an ultrasonic bath for 10 min to ensure that the samples were fully homogenized.

The gold NP standard at 60 nm (NIST 8013) was diluted to 50 ng/L Au concentration, for the evaluation of the nebulization efficiency to be used in the data conversion from raw signal to NP size.

An ionic solution of silver was diluted to 0.5 µg/L and used to determine the ICP-MS system sensitivity for Ag.

The silver nanoparticle samples were diluted to concentrations between sub-ng/L and 400 ng/L depending upon the size of the NPs. As a general rule, the smaller the nanoparticle size, the higher the dilution needed to reduce the number of particles in solution to the correct level for optimum measurement (i.e. so that approximately 1 in 10 measurements will contain a NP).

Results and discussion

Single particle analysis at 3 ms

The first analysis was performed using an integration time of 3 ms, which is typical of the range of timing used in the literature [3-7].

Figure 1 shows a TRA acquisition of a solution containing 40 nm Ag NPs measured using the 7900 ICP-MS. 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 the size distribution plot, the median size was calculated at 40 nm. This measured size is in good agreement with the 40 ±4 nm value provided by the supplier, which is verified using Transmission Electron Microscopy (TEM) analysis. The particle number in the diluted sample was estimated to be 3.4×10^7 particles/L and the mass concentration for Ag was 13 ng/L.

A summary of the results for the analysis of different Ag NP samples containing different NP sizes is shown in Table 2. In all the cases, the 7900 ICP-MS results agree with the specification values provided by the NP manufacturer.

It is worth noting that in comparison to the previous work carried out using a 7700x ICP-MS [3], the superior sensitivity offered by the 7900 ICP-MS enables the measurement of lower NP sizes. The sensitivity of the 7900 ICP-MS determined on the day of the analysis was 600 counts per femtogram of silver.

In addition, the design of the new orthogonal detector system reduces the impact of the electronic background (noise) on the NP analysis allowing the measurement of silver down to few attograms in SP-ICP-MS mode which represents NPs sized between 7 to 9 nm.
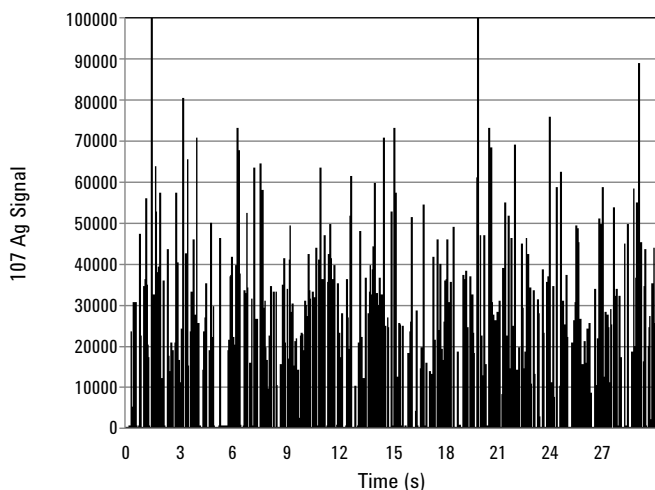
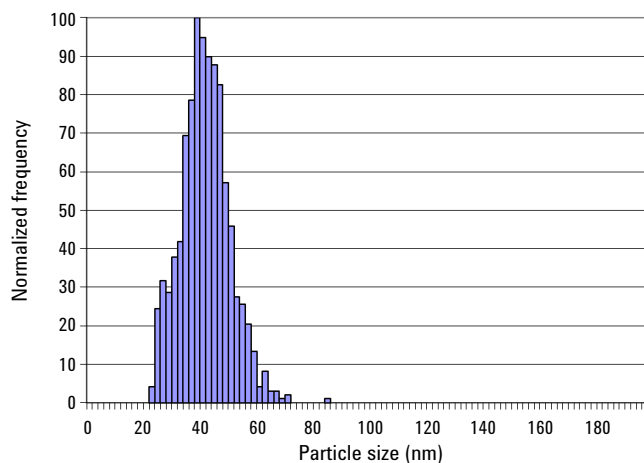**Figure 1.** Measurement of 40 nm Ag NPs acquired using SP-ICP-MS mode

Figure 2. Particle size distribution for a 40 nm Ag NP sample

Table 2. Results of particle size (diameter), particle number and element concentration for the analysis of Ag NPs

Supplier's specification (nm)	10 ±4	20 ±4	40 ±4	60 ±8	100 ±8
Experimental size (nm)	9	18	40	55	103
Number of particles (particles/L)	1.8×10^7	3.9×10^6	3.4×10^7	1.5×10^7	5.2×10^7
Element concentration (ng/L)	0.07	0.2	13	14	424

Single particle analysis with 100 µs integration time

As mentioned previously in the text, the new fast TRA feature of the 7900 ICP-MS enables SP-ICP-MS analysis with an integration time of 100 µs. This short integration time enables the measurement of several data points across the signal pulse from the ion cloud created as a single NP passes through the plasma (Figure 3), as opposed to an integration time of 3 ms, where the entire signal pulse from an individual NP is contained in one TRA measurement reported as single intensity.

Different Ag NP samples were analyzed using an integration time of 100 µs. For each set of data, the integration of each NP peak has been realized. The background signal (due to instrument noise and the signal from the dissolved component of the element in solution) was eliminated by the custom spreadsheet allowing the median signal for each NP to be identified. It is possible therefore to study the relationship between NP size with its signal obtained by ICP-MS.
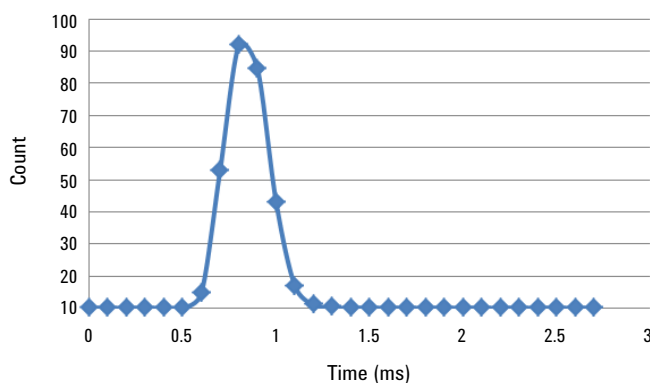
Figure 4 shows the plot of the median signal against Ag NP size. A trend line has been calculated using Microsoft Excel to show the experimental relationship between the two parameters.

As can be seen, the NP diameter is proportional to the cube root of its signal (number of atoms) which is in agreement with the theory of SP-ICP-MS analysis [7, 8] assuming spherical particles. The excellent linearity obtained between the NP signal versus its size also confirms that each NP sized between 10 and 100 nm is completely ionized when introduced to the 7900 ICP-MS, which is in good agreement with the expectation that the ICP is able to fully decompose and ionize solid particles that are smaller than ~100 nm diameter.

Figure 3. Measurement of one single 100 nm Ag NP with 100 µs integration

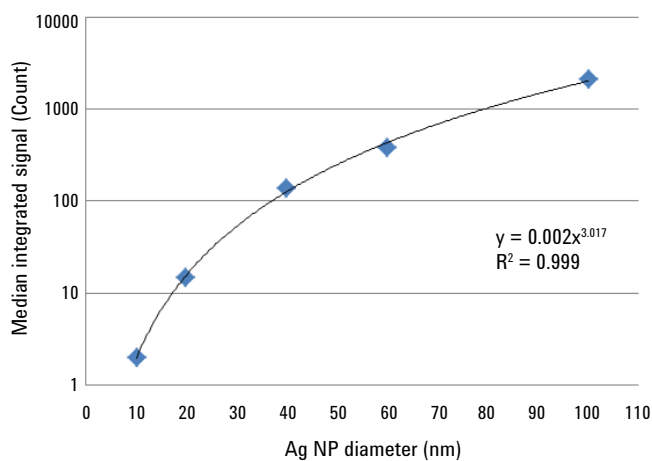$y = 0.002x^{3.017}$
$R^2 = 0.999$

Figure 4. Plot of the median integrated signal against the NP size accompanied by the calculated trend line.
Note: the median signal is plotted on a log scale for ease of visualization.

Conclusions

The new Agilent 7900 ICP-MS has shown excellent analytical performance for this challenging application due to its superior detector, fast TRA acquisition mode, and improved sensitivity and background compared to the previous generation ICP-MS. The results confirm the suitability of the 7900 ICP-MS to characterize single Ag NPs with a size range from 10 to 100 nm. For research purposes, it is also possible to lower the integration time down to 100 μs in order to increase the number of data points acquired per single NP. The SP-ICP-MS method described can provide size distribution, median size, number of particles and the elemental concentration of given NP samples.

Acknowledgements

References

1. ISO TS 80004-1:2010: Nanotechnologies - Vocabulary - Part 1: Core terms

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