Analysis of 10 nm gold nanoparticles using the high sensitivity of the Agilent 8900 ICP-QQQ

Application note

Materials, environmental, food

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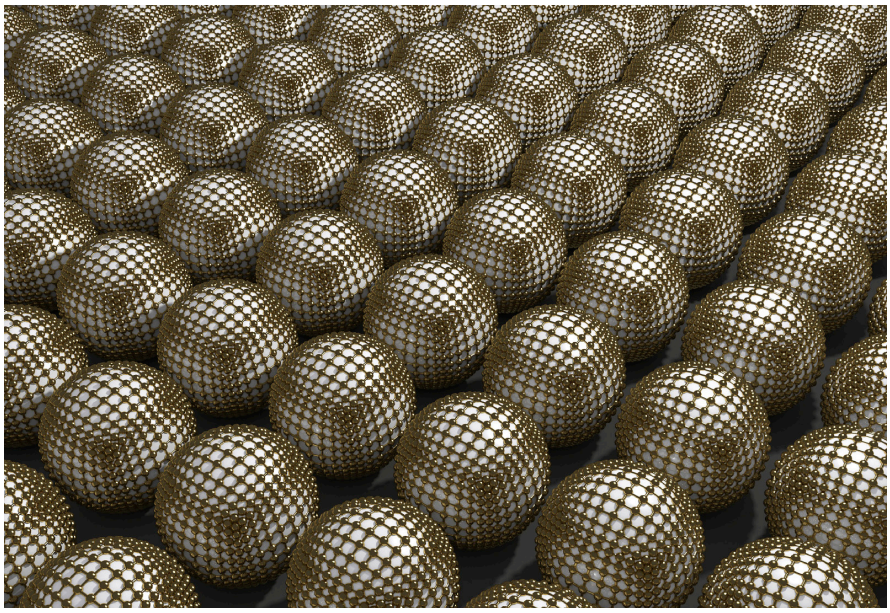

Introduction

According to the European Commission (EC) Recommendation (2011/696/EU) a nanomaterial, for regulatory purposes, is 'natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm' [1]. Materials with external dimensions or internal structures on the nanometre scale develop unique properties that are not present in the materials' macroscale form.

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Gold nanoparticles (NPs) have a broad range of uses: they are increasingly used in medical applications to deliver drugs, or as biomarkers in the diagnosis of tumors or heart disease. Industrial and technology applications range from plastics, coatings and textiles to organic photovoltaics, electronic chip manufacturing, catalyst applications, and fuel cells. They are even used in colorimetric sensors designed to test whether foods are safe for consumption [2].

Gold, in common with silver, is a relatively easy element to measure by ICP-MS as it is not affected by common spectral interferences. This means ICP-MS is highly suitable for characterizing the gold based nanoparticle content of samples, as it is easy for the signal generated from the nanoparticles to be distinguished from the background signal [3]. The NP number concentration of a sample can be determined using the ICP-MS in Single Particle acquisition mode (spICP-MS), where the ICP-MS measures the signal generated by each NP as it passes through the plasma [4]. Dedicated software facilitates automated acquisition and calibration approaches to support calculation of the particle number, concentration, and size distribution of the NPs in a sample [5].

However, the detection of very small particles (<20 nm) remains challenging for spICP-MS, due to the low signal generated from such particles. The measured signal in spICP-MS is based on the number of ions present in an individual particle, which is proportional to the mass of the particle. But particle mass decreases as the cube of the diameter, so a factor of 2 reduction in particle diameter (for example from 60 nm to 30 nm) results in an 8x reduction in mass and therefore signal. Likewise, a 15 nm particle will generate only 1/64 the signal of a 60 nm particle. It is clear from this that an instrument with very high sensitivity combined with very low background is essential to support detection and analysis at smaller particle sizes.

The Agilent 8900 Triple Quadrupole ICP-MS (ICP-QQQ) has low background (<0.2 cps) and sensitivity up to Gcps/ppm, making it suited to small particle detection. In addition, the 8900 can operate with a very short (0.1 ms) dwell time, which supports very fast time resolved analysis (TRA) acquisitions and leads to an improvement in the signal-to-noise ratio.

In this study, 10 nm gold nanoparticles (Au NPs) were measured in spICP-MS mode using the Agilent 8900 ICP-QQQ with Agilent's Single Nanoparticle Application Module software option. The performance of the instrument for the measurement of peak signals from individual small NPs is described.

Experimental

Reference materials and sample preparation

Three Au NP reference materials were used in the investigation: NIST 8011 with a nominal diameter of 10 nm (8.9 ± 0.1 nm determined by Transmission Electron Microscopy (TEM)), NIST 8012 with a nominal diameter of 30 nm (27.6 ± 2.1 nm determined by TEM) and NIST 8013 with a nominal diameter of 60 nm (56.0 ± 0.5 nm determined by TEM).

Stabilization of ionic gold standard

In order for the signals measured in spICP-MS to be converted into particle size, it is necessary to know the specific sensitivity (counts per second per unit concentration) for the element of interest. To determine this specific element sensitivity, an ionic standard is prepared using the same element as the one in the target NP sample, in this case, gold. However, ionic gold isn't sufficiently stable for this purpose, even in an acidified solution. As an alternative, L-cysteine can be used as an effective stabilizer of ionic gold because of the formation of a chemical bond between the L-cysteine thiol group and the gold surface [6]. In this work, both the gold ionic solution and Au NP samples were prepared in solutions that contained 0.01% L-cysteine, ensuring the stability of the Au ionic standard, and providing a consistent matrix for all solutions.

Intermediate diluted solutions were prepared with 1% ethanol in deionized water to ensure the stabilization of NPs in solution. Final solutions were diluted to a Au concentration of between 0.2 and 50 ng/L (ppt) using 0.01% L-cysteine. A gold ionic standard of 100 ng/L was prepared with 0.01% L-cysteine and used to determine the elemental response factor for Au.The nebulization efficiency was determined by 'the particle size method' [7]. In this method a sample (reference) with known particle size is introduced into the ICP-MS in order to calculate the nebulization efficiency. Here, NIST 8013 Au NP reference material was used as the reference particle size (56 nm by TEM).

Instrumentation

An Agilent 8900 ICP-QQQ (#100, Advanced Applications configuration) was used for all measurements. The instrument was equipped with a standard glass concentric nebulizer, quartz spray chamber, a quartz torch with 1.0 mm i.d. injector, and standard nickel sampling and skimmer cones. Samples were introduced directly into the ICP-MS with the standard peristaltic pump and pump tubing (1.02 mm i.d.). Analyses were performed by measuring ^{197}Au in fast TRA mode, using a dwell time of 0.1 ms (100 µs) per point, with no settling time between measurements. The Au signal was measured in Single Quad mode with no cell gas in the collision/reaction cell (CRC). The general settings of the Agilent 8900 ICP-QQQ are detailed in Table 1.

Table 1. ICP-QQQ operating parameters.

Parameter	Value
RF power	1550 W
Sampling depth	7 mm
Carrier gas	0.78 L/min
Sample uptake rate	0.35 mL/min
Spray chamber temp.	2 °C
Dwell time	0.1 ms
Settling time	0 ms
Acquired mass number	197
Acquired time	60 s
Cell gas	(No gas mode)

Single Nanoparticle Application Module

All aspects of method setup and data analysis were carried out using the fully integrated Single Nanoparticle Application Module option of the ICP-MS MassHunter software. The Method Wizard guides the analyst through the automated creation of the method, including setting up suitable acquisition parameters, entering reference material values, and defining data analysis parameters. The "Batch at a Glance" data table summarizes sample results for an entire batch, while detailed graphical results are displayed for each selected sample, allowing results to be viewed and compared, or method settings to be optimized if necessary (Figure 1).

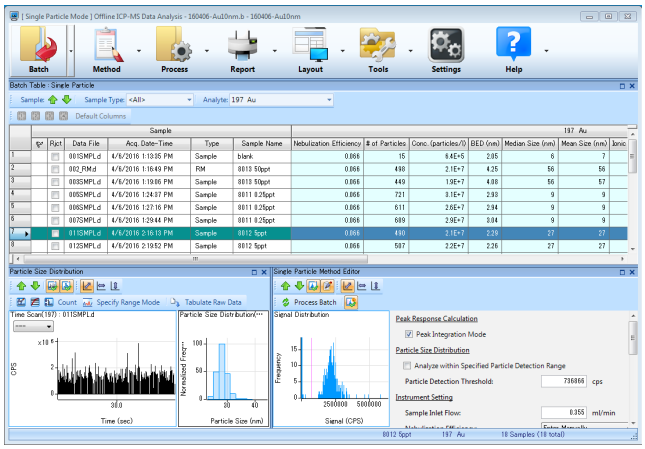

Figure 1. Data view from the Single Nanoparticle Application Module of ICP-MS MassHunter. Final batch results are reported in tabular and graphical formats.

Results and discussion

Time resolved signals of 10 nm Au NPs

The narrow signal pulse generated from each particle that is ionized in the plasma is collected in fast TRA mode. The ion intensity is proportional to the mass of the target element in the original particle, allowing for the determination of the particle size, assuming spherical particles. Representative TRA signals measured in A, a blank solution (0.01% L-cysteine without Au NPs), and B, a solution containing 10 nm Au NPs are shown in Figure 2. Due to the high sensitivity and low background of the Agilent 8900 ICP-QQQ, small 10 nm Au NPs provided clear peaks (Figure 2B) that were easily distinguished from the signal observed in the blank solution (Figure 2A).

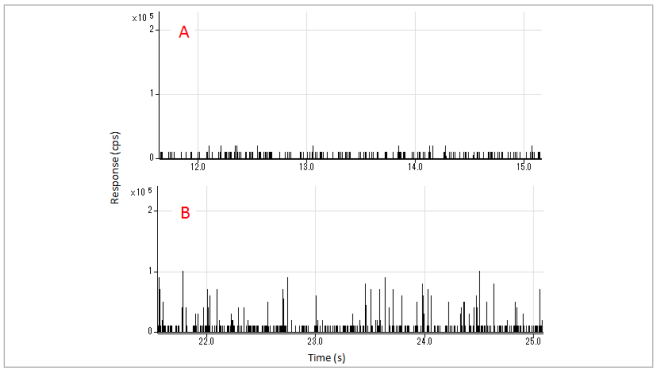

Figure 2. Au single nanoparticle events acquired using fast TRA mode with 0.1 ms dwell time. A: Blank (0.01% L-cysteine). B: 10 nm Au NP.

Analysis of Au NPs samples

Solutions containing gold NPs with particle sizes of 10 nm, 30 nm and 60 nm were prepared at concentrations of 0.25 ng/L, 5 ng/L and 50 ng/L, respectively. The solutions were measured using fast TRA acquisition on the Agilent 8900 ICP-QQQ, and the frequency distribution plots of the signals are shown in Figure 3. The particle signals were clearly distinguished from the background signal (shown in Figure 3A), even for the 10 nm particles (Figure 3B), confirming the high sensitivity capability of the 8900 ICP-QQQ. From Figure 3B, we can estimate that the practical detection limit of the particle diameter is around 30,000 cps (equivalent to ~6.5 nm). The background equivalent diameter (BED) was estimated to be 3 nm, based on the analysis of the 10 nm particle standard.

Figure 4 shows the results for the particle size analysis of the different Au NP solutions. The plots confirm that all of the Au NP sizes could be determined accurately, including the 10 nm NPs. All of the size distributions demonstrated a Gaussian distribution, as indicated in the 'Report of Investigation' supplied by NIST. Figure 4D shows the calculated particle size distribution for a mixture of 10, 30 and 60 nm Au NPs, demonstrating that multiple particle sizes could be analyzed accurately and with good resolution in a mixed solution. The results for the median, mode and mean particle sizes for all three standards agreed well with the reference sizes obtained by TEM (Table 2).

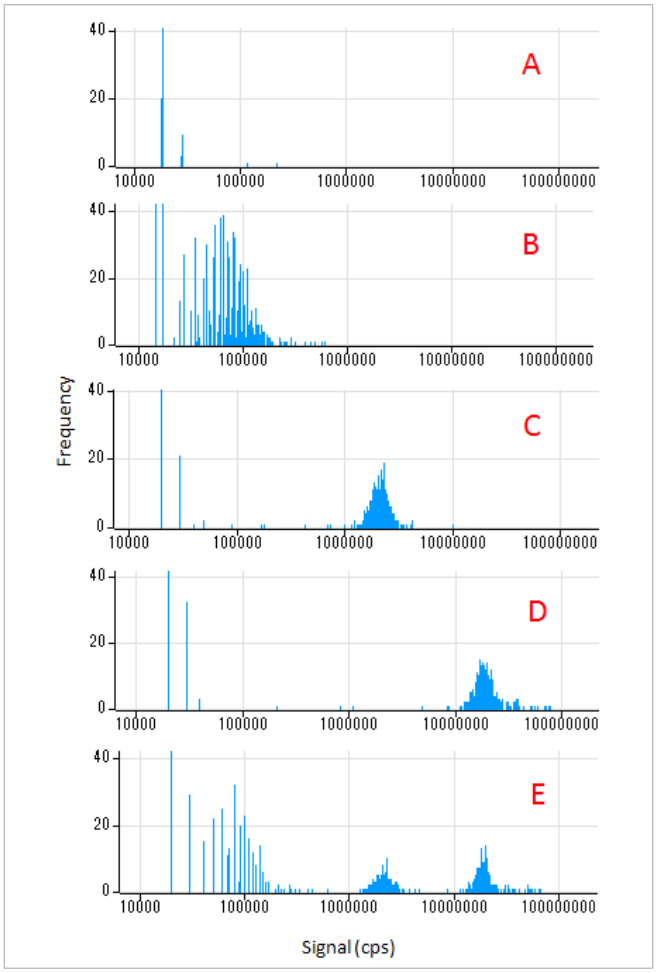

Figure 3. Frequency distribution for Au NP signals. A: blank (0.01% L-cysteine). B: 10 nm. C: 30 nm. D: 60 nm. E: mixture of 10, 30 and 60 nm.

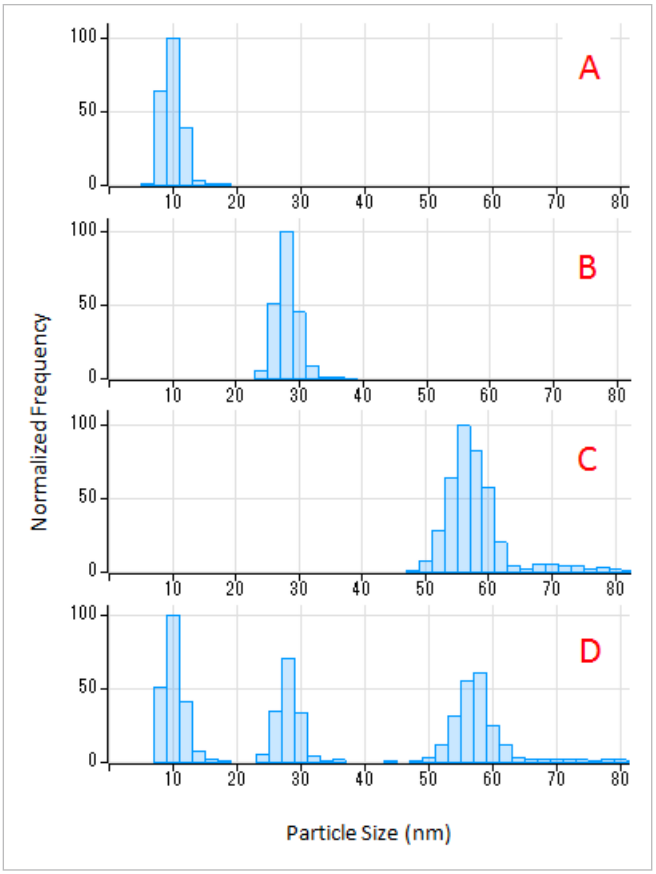

Figure 4. Particle size distribution calculated for Au NPs. A: 10 nm. B: 30 nm. C: 60 nm. D: mixture of 10, 30 and 60 nm.

Table 2. Particle size and particle concentration determination for Au NPs.

Nominal size (nm)	Measured particle size (n=10)						*Reference particle size obtained by TEM (nm)
	Median		Mode		Mean		
	Size (nm)	RSD (%)	Size (nm)	RSD (%)	Size (nm)	RSD (%)	
10	9.0	3.3	10	0.0	9.2	3.3	8.9 ± 0.1
30	26.9	0.3	28	0.0	27.0	0.3	27.6 ± 2.1
60	56.1	0.3	56	1.8	57.2	0.4	56.0 ± 0.5

*Values supplied by NIST

Conclusions

The low background and high sensitivity of the Agilent 8900 ICP-QQQ make it suitable for single particle analysis of solutions containing the smallest-sized nanoparticles. The size and composition of gold NP solutions were characterized from 10 nm up to 60 nm with good accuracy. The estimated practical detection limit of the particle diameter was 6.5 nm and BED was 3 nm. Accurate particle size analysis was performed with good resolution for a mixed solution containing 10, 30 and 60 nm NPs.

The entire process of nanoparticle determination is facilitated by the optional Single Nanoparticle Application Module for ICP-MS MassHunter software. The method provides quick and accurate results for Au nanoparticles down to 10 nm diameter.

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