High sensitivity analysis of SiO$_2$ nanoparticles using the Agilent 8900 ICP-QQQ in MS/MS mode
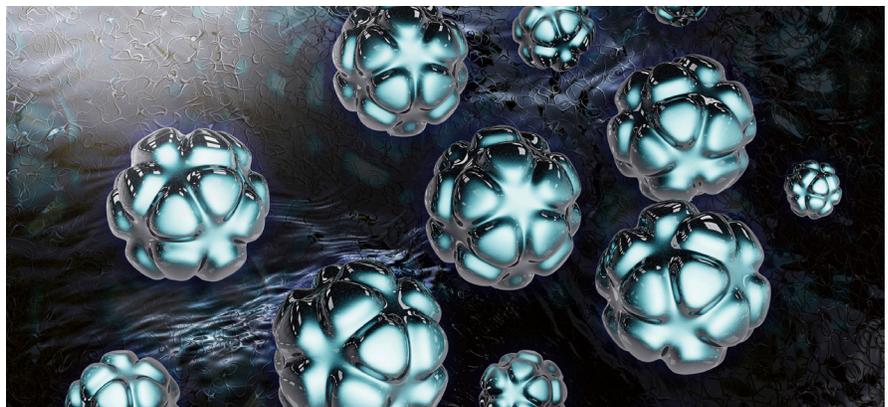
Application note

Materials, environmental, food

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Introduction

Nanomaterials are increasingly used in industrial processes, manufactured goods, medicines, and consumer products such as cosmetics, sunscreen, and food. The measurement of nanoparticles (NPs) is the focus of attention because the fate of NPs in the environment and the potential for toxic effects once absorbed into the body are not yet well understood.

ICP-MS is a well-established technique for measuring the elemental content of materials; the relatively recent development of Single Particle acquisition mode (spICP-MS) now provides a powerful method to characterize the NP content of a sample. spICP-MS is used to record the target element signals generated from individual NPs in the solution analyzed, allowing simultaneous determination of the number, concentration, and size of particles present, as well as the dissolved element concentration. This approach has been developed by many researchers [1-4], and modern ICP-MS instruments can now offer automated acquisition and calibration approaches to support NP characterization. Current ICP-MS systems use short dwell times and acquire data continuously for a single isotope with no

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settling time between measurements. This enables the detection of smaller particles because, while the total background counts over the dwell period are reduced proportionally, the signal from the particle plume is not reduced. However, if the dwell time is shorter than the duration of the plume, which is typically around 0.5 ms, then the analyte signal is also reduced with decreasing dwell time. This increases the error in the counting statistics. It is important to maintain statistically valid count rates by using the highest possible sensitivity (signal-to-noise) and an appropriate dwell time.

There are many challenges in measuring NPs accurately by conventional quadrupole ICP-MS, particularly the ability to distinguish the background signal from the signal generated from a small particle. Consequently, it is not surprising that much of the work reported thus far has concentrated on elements such as silver and gold, which are relatively easy to measure by ICP-MS. These elements have high sensitivity, are not typically affected by interferences, and are normally absent from natural samples, making it easier to measure smaller particles.

In practice, however, many natural and engineered NPs are based on elements that are much more difficult to measure by ICP-MS, for example, iron, sulphur, titanium and silicon-based NPs. For these elements, there are potentially intense polyatomic interferences from the sample matrix or plasma background, and in some cases sensitivity is low due to low ionization or the necessity to measure a minor isotope. As silicon dioxide (SiO_2) NPs are used for a variety of applications including paints, coatings, adhesives, food additives, polishing microelectronic devices etc., there is a clear requirement for them to be monitored. However, Si measurement by ICP-MS is not easy since the major isotope of Si (^{28}Si – 92.23% abundance) is interfered by the background polyatomic ions CO and N_2. The interferences can be addressed using reaction chemistry in the collision/reaction cell of an ICP-MS, and for controlled and consistent reaction processes, a tandem mass spectrometer instrument such as the Agilent 8900 Triple Quadrupole ICP-MS (ICP-QQQ) is required.

The 8900 ICP-QQQ uses two quadrupole mass filters (Q1 and Q2), with an octopole reaction cell located between them, to provide a double mass selection capability, commonly termed MS/MS. MS/MS provides an elegant approach for solving even the most challenging cases of spectral overlap, and can also offer a clear insight into the cell processes. ICP-QQQ allows the successful determination of the most problematic elements such as Si.

In this work, SiO_2 NPs were measured in spICP-MS mode using MS/MS on the Agilent 8900 ICP-QQQ, equipped with Single Nanoparticle Application Module software. The capabilities of the instrument for the measurement of SiO_2 are discussed.

Experimental

Reference materials and sample preparation
SiO_2 NP reference materials with nominal diameters of 50 nm, 60 nm, 100 nm, and 200 nm were purchased from nanoComposix (San Diego, USA). All the reference materials were diluted to a particle concentration of between 40 and 1000 ng/L with deionized (DI) water, and sonicated for 5 min to ensure sample homogeneity. In order to check the potential impact of the CO interference on the ^{28}Si signal, a SiO_2 NP solution containing a carbon matrix of 1% ethanol was also prepared using the same procedure. A Si ionic standard of 5 μg/L was prepared with DI water and used to measure the elemental response factor.

Instrumentation
An Agilent 8900 ICP-QQQ (#100, Advanced Applications Configuration) was used throughout. The instrument was equipped with standard nickel sampling and skimmer cones, a glass concentric nebulizer, quartz spray chamber and quartz torch with 1 mm injector. 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 ^{28}Si in fast Time Resolved Analysis (fast TRA) mode, using a dwell time of 0.1 ms (100 μs) per point with no settling time between measurements. The ^{28}Si signal was measured on-mass in MS/MS mode, where both quadrupoles (Q1 and Q2) were set to m/z 28. Hydrogen cell gas was used to eliminate any on-mass polyatomic interferences such as $^{12}C^{16}O$ and $^{14}N_2$. The general settings of the Agilent 8900 ICP-QQQ are detailed in Table 1.

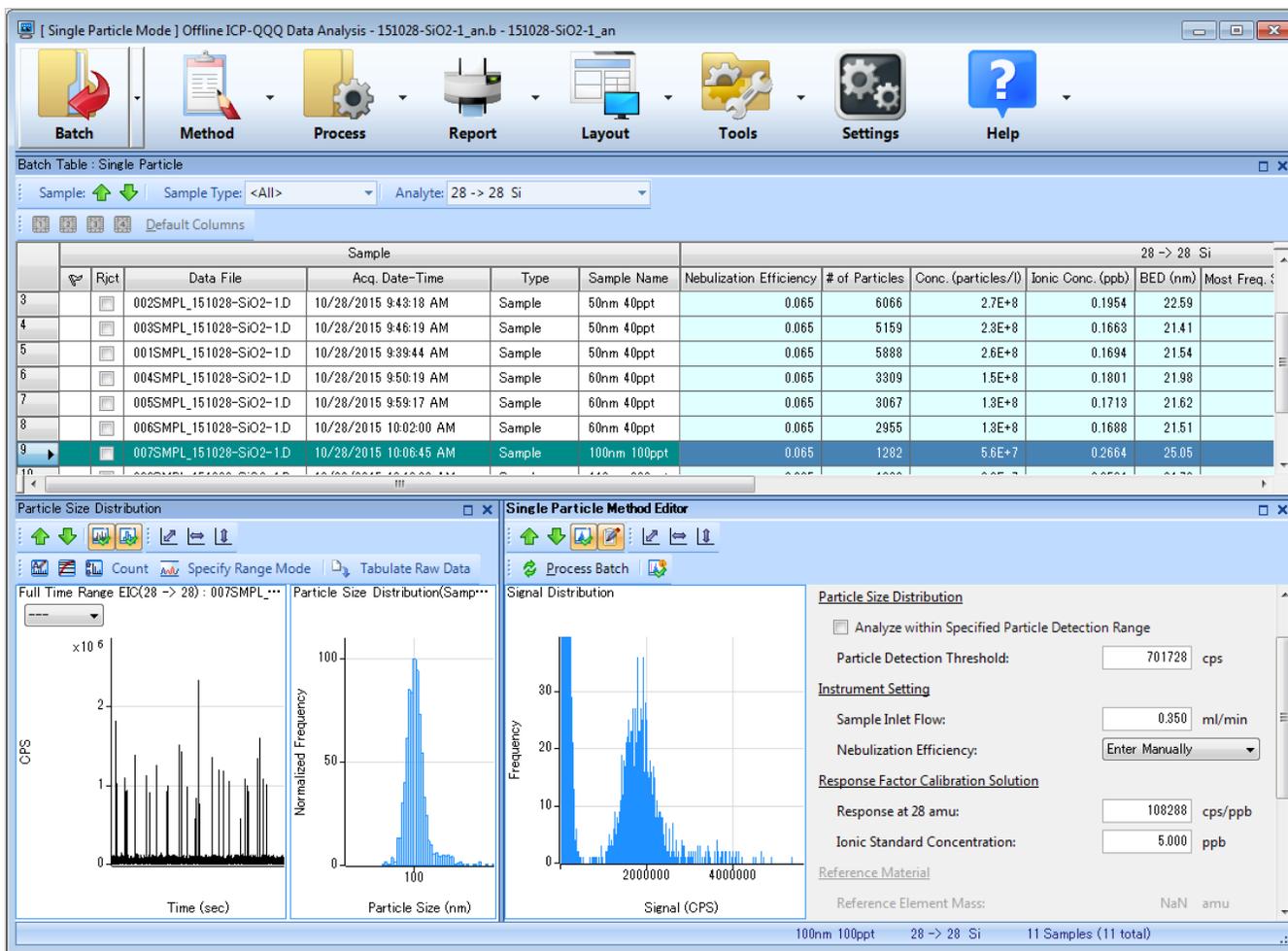**Figure 1.** Data view from the Single Nanoparticle Application Module software

Table 1. ICP-QQQ operating parameters

Parameter	Value
RF power	1550 W
Sampling depth	7 mm
Carrier gas	0.76 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	28 for Q1 and Q2
Cell gas	Hydrogen
Cell gas flow rate	2.0 mL/min (for water samples) 3.0 mL/min (for 1% ethanol samples)

The optional Single Nanoparticle Application Module of the ICP-MS MassHunter software was used for method setup and data analysis. Sample results for an entire batch are summarized in the 'Batch at a Glance', which displays detailed graphical results for the selected sample, permitting visual confirmation and optimization of particle threshold and method settings if needed (Figure 1).

Results and discussion

Nebulization efficiency
In order to convert the signals measured with spICP-MS to the particle content of the original sample, it is necessary to calculate or measure the nebulization efficiency. The nebulization efficiency is the ratio of the amount of analyte entering the plasma to the amount of analyte delivered to the nebulizer, and is usually calculated by measuring a reference material of known particle size. However, well characterized CRMs are usually very expensive, making them unsuitable for use in routine analysis. In this work, we obtained the nebulization efficiency in two ways. First, measuring the sample uptake mass (g/min) coming into the nebulizer and the drain mass (g/min) coming out of the spray chamber. The difference between them corresponds to the mass of the sample aerosol being delivered to the torch, and the nebulization efficiency can be calculated from the mass delivered to the torch divided by the sample uptake mass. Another way to obtain nebulization efficiency is calculating from the size of an Au NP reference material. Both methods gave the same nebulization efficiency value (0.065) using the operation conditions in Table 1.
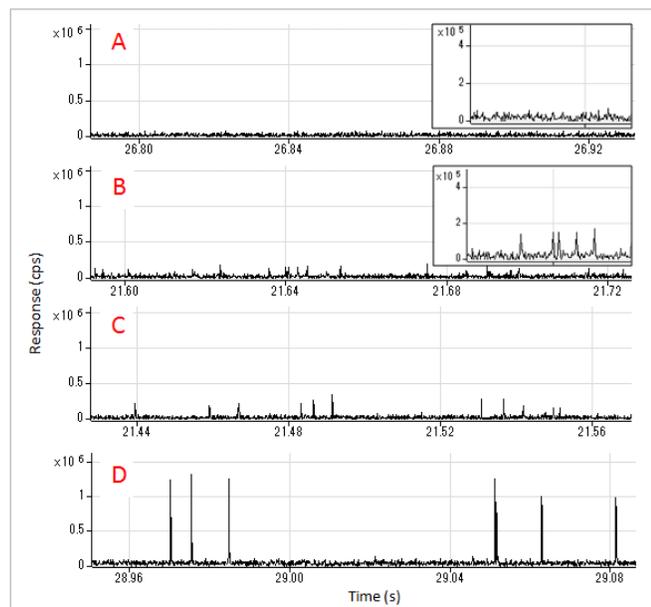

Figure 2. SiO$_2$ single nanoparticle events acquired using fast TRA mode with 0.1 ms dwell time. A DI water. B 50 nm. C 60 nm. D 100 nm. Inset: zoomed in A and B.

Time resolved signals of SiO$_2$ NPs
TRA measurement of NPs by ICP-MS produces a narrow signal peak for each particle that passes through the plasma, with the peak intensity being proportional to the particle mass. The typical signals measured in DI water (without particles) and in solutions containing SiO$_2$ particles with diameters of 50 nm, 60 nm and 100 nm are shown in Figure 2. Fast TRA mode allows multiple measurements to be made during the signal peak from a single particle, so the shape and duration of the ion plume from each NP can be identified. The Single Nanoparticle Application Module of ICP-MS MassHunter includes the calculations to convert signal intensity to particle diameter (assuming spherical particles). Due to the high sensitivity and the effective interference removal of the Agilent 8900 ICP-QQQ, small 50 nm SiO$_2$ particles provided clear peaks (Figure 2B) that were easily distinguished from the baseline signal and the low background signal observed in DI water (Figure 2A).

Analysis of SiO$_2$ NPs
The frequency distribution plots of the signals obtained from SiO$_2$ nanoparticles are shown in Figure 3. The particle concentrations prepared for 50 nm, 60 nm and 100 nm particle were 40 ng/L, 40 ng/L and 100 ng/L respectively. The particle signals were clearly distinguished from the background (dissolved, ionic component) signals, although the background and particle signals were partially overlapped for the 50 nm particles (shown in Figure 3B). From these results we can estimate that the practical detection limit for the particle diameter was below 50 nm. The background equivalent diameter (BED) was 22 nm for the 50 nm particle analysis.

The intensity of the pulse generated by a single nanoparticle is a function of the mass of the nanoparticle and hence of its size. Assuming SiO$_2$ particles are spherical, the particle mass m_p for a particle of diameter d is given by:

$$m_p = \frac{4}{3}\pi\left(\frac{d}{2}\right)^3\rho \qquad [1]$$

where ρ is the density of SiO$_2$. This equation means that the particle mass, or the signal from one NP, is proportional to the cube of the particle diameter.

Table 2. Particle size and particle concentration determination for SiO_2 nanoparticles

Nominal size (nm)	Measured particle size			*Reference particle size obtained by TEM (nm)	Prepared particle concentration (ng/L)	Measured particle concentration (ng/L)
	Median (nm)	Mode (nm)	Mean (nm)			
50	49	50	50	46.3 ± 3.1	40	49
60	61	62	62	57.8 ± 3.5	40	45
100	99	100	102	97.0 ± 4.8	100	92
200	200	204	200	198.5 ± 10.5	1000	956

*Certificate values supplied by nanoComposix

The results for the size analysis of different SiO_2 NP solutions are shown in Figure 4. The plots confirm that all the SiO_2 particle sizes could be determined accurately, including the 50 nm NPs, which can be distinguished from the background signal as a result of the removal of polyatomic interferences in MS/MS mode with H_2 cell gas, combined with the high sensitivity of the 8900 ICP-QQQ. All the size distributions demonstrated a Gaussian distribution, as indicated by the supplier of the SiO_2 NPs. The results for median, mode and mean particle sizes agreed well with the reference sizes obtained by TEM (Table 2). Also, the measured particle concentration agreed well with the prepared particle concentration, although the result of 50 nm was slightly higher due to overlapping from the background signal.

Figure 5 shows the plot of the mean signal intensity measured by spICP-QQQ versus the particle diameter determined by TEM. The logarithmic plot has a slope of 2.84, which is in good agreement with the theoretical cube relationship between diameter and mass indicated in the previous equation [1].
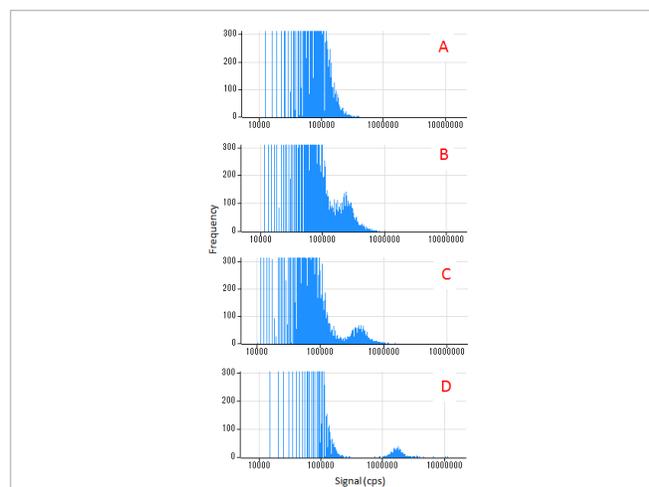

Figure 3. Frequency distribution for SiO_2 nanoparticle signals. A DI water. B 50 nm (40 ng/L). C 60 nm (40 ng/L). D 100 nm (100 ng/L)
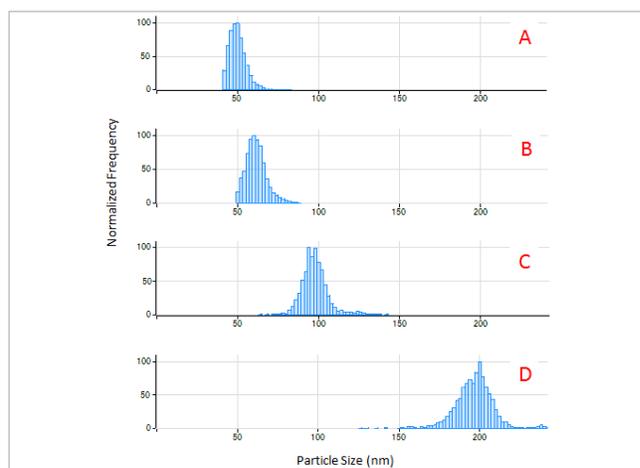

Figure 4. Particle size distribution calculated for SiO_2 nanoparticles. A 50 nm. B 60 nm. C 100 nm. D 200 nm
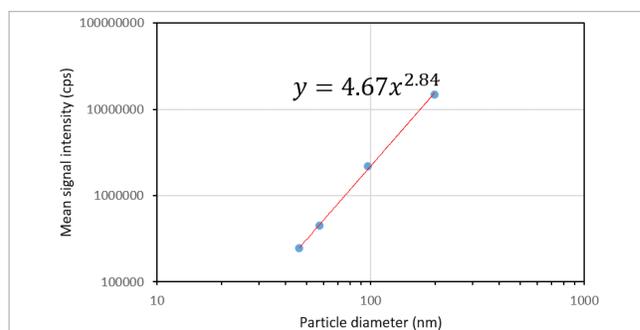

$$y = 4.67x^{2.84}$$

Figure 5. Relationship between particle diameter (by TEM) and mean signal intensity (by spICP-QQQ).

Removal of carbon interference

Real samples such as biological fluids and tissues, food matrices, pharmaceutical ingredients, organic solvents, etc. contain carbon matrices which cause a $^{12}C^{16}O$ polyatomic ion interference on ^{28}Si. The 8900 ICP-QQQ in MS/MS mode with hydrogen cell gas can eliminate this interference effectively. The particle size distribution for a mixed solution of the 100 nm and 200 nm SiO_2

NPs measured in a sample containing 1% ethanol is shown in Figure 6. Despite the high concentration of carbon, the size distribution for each group of particle sizes was consistent with the result obtained by TEM, and the different particle sizes were separated with excellent resolution. This result suggests that the spICP-QQQ technique can resolve matrix interferences to allow accurate determination of particle sizes for SiO_2 nanoparticles in real sample matrices.
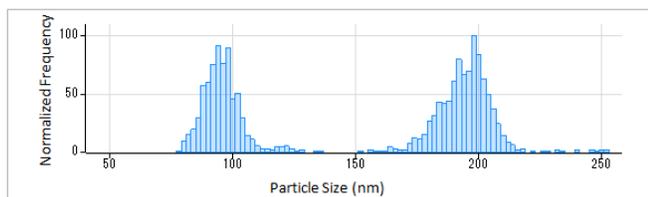

Figure 6. Size distribution results of 100 nm and 200 nm SiO_2 NPs in 1% ethanol

Conclusions

The Agilent 8900 ICP-QQQ operating in MS/MS mode with H_2 cell gas was used successfully for the determination and characterization of SiO_2 nanoparticles. MS/MS operation effectively eliminated polyatomic ions which interfere with Si analysis at *m/z* 28, delivering low background signals and excellent sensitivity, even in the presence of a high level of carbon matrix. The dedicated Single Nanoparticle Application Module for ICP-MS MassHunter software was used to calculate the particle sizes, providing accurate results for individual NP reference materials and mixed solutions. The spICP-QQQ method provides fast analysis times, excellent detection limits for particle size and concentration, and accurate results for SiO_2 particles less than 100 nm.

References

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