APPLICATION NOTE

ICP-Mass Spectrometry

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Analysis of NIST® Gold Nanoparticles Reference Materials Using the NexION 300 ICP-MS in Single Particle Mode

Introduction

Engineered nanomaterials (ENs) refer to the process of producing and/or controlling materials that have at least one dimension in the size range of 1 to 100 nm. They often possess different properties compared to bulk materials of the same composition, making them of great interest to a broad spectrum of industrial and commercial applications.

Recent studies have shown that some nanoparticles may be harmful to humans. A 2009 study in the Journal of Nanoparticle Research showed that zinc oxide nanoparticles were toxic to human lung cells in lab tests even at low concentrations (Weisheng et al., 2009).[1] Other studies have shown that tiny silver particles (15 nanometers) killed liver and brain cells in laboratory rats. At the nano scale, particles are more chemically reactive and bioactive, allowing them to easily penetrate organs and cells (Braydich-Stolle *et. al.*, 2005).[2]

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To better understand the impact of nanoparticles, several key characteristics need to be assessed, such as concentration, composition, particle size, shape and other nanoparticle surface characteristics (Figure 1). Given these requirements, several analytical instruments must be used to characterize the material. Table 1 lists the key characteristics and many of the current analytical technologies that can be applied.

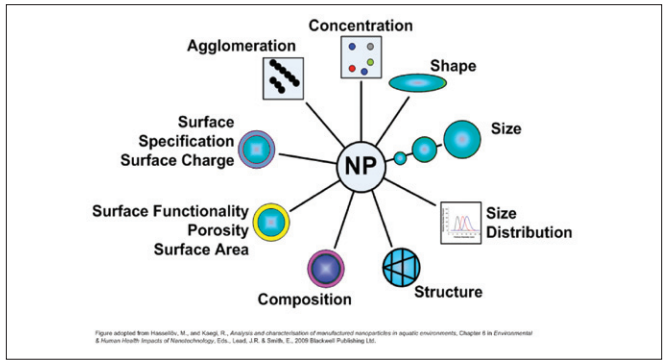

Figure 1. Key parameters to characterize nanomaterials (Hasselhov, 2009).[3]

Table 1. **Nanomaterial characteristics and applicable analytical technologies.**

Analytical Technique		Nanomaterial Characteristic								
		Concentration	Particle Size	Particle Size Distribution	Surface Charge	Surface Area	Shape	Agglomeration	Structure	Composition
Inductively Coupled Plasma-Mass Spectrometry	ICP-MS	●								●
Single Particle ICP-MS	SP-ICP-MS	●	●	●				●		●
Field Flow Fractionation + ICP-MS	FFF-ICP-MS	●	●				●	●		●
Liquid Chromatography/Mass Spectrometry	LC/MS	●								●
Optical Spectroscopy - UV/Vis	UV/Vis	●								●
Fluorescence Spectroscopy	FL	●	●					●		●
Turbidity			●	●				●		
Scanning Electron Microscopy	SEM		●	●			●	●	●	
Transmission Electron Microscopy (+EDX)	TEM		●	●		●	●	●	●	●
Atomic Force Microscopy	AFM		●	●	●	●	●	●		
Confocal Microscopy			●	●			●	●	●	
Field Flow Fractionation	FFF		●	●			●	●		
Dynamic Light Scattering	DLS		●	●			●	●		
Static Light Scattering	SLS		●				●	●		
Laser-Induced Plasma Spectroscopy	LIPS		●							
Dialysis			●	●						
Electrophoresis and Capillary Electrophoresis			●	●	●					
Ultrafiltration			●	●						
Centrifugation			●	●				●		
Filtration			●	●						
Nanoparticle Tracking Analysis	NTA		●	●				●		
Hydrodynamic Chromatography	HDC		●	●						
Laser-Induced Breakdown Detection	LIBD		●	●				●		
Size Exclusion Chromatography	SEC		●	●						
Selected Area Electron Diffraction	SAED		●	●					●	
Zeta Potential by DLS					●					
Molecular Gas Absorption (BET)					●	●				
X-ray Photoelectron Spectroscopy	XPS				●	●				●
X-ray Diffraction	XRD								●	
Thermogravimetric Analysis	TGA									●
Quartz Microbalances										●
Differential Scanning Calorimetry	DSC									●
Dynamic Mechanical Analysis	DMA									●
Fourier Transform-Infrared Spectroscopy	FT-IR									●
FT-IR Imaging									●	●
Raman Spectroscopy									●	●
TGA Coupled with Gas Chromatography/Mass Spectrometry	TGA-GC/MS									●
Electron Energy Loss Spectroscopy	EELS (+EDX)									●

Inductively coupled plasma mass spectrometry (ICP-MS) is one of the leading analytical techniques capable of measuring and assessing many of these key characteristics of metal-containing particles.[4] Low detection limits are critical in determining small concentrations of particles in a liquid as well as examining the characteristics of a single particle. Additionally, flexibility of the parameters, such as dwell time and speed of the electronics, can influence the quality of data collected. This work explores the capability of modern ICP-MS to measure the key characteristics of metal manufactured nanoparticles.

Experimental

All work was performed using a NexION® 300 ICP-MS (PerkinElmer, Shelton, CT, U.S.). In Standard mode, composition and concentration measurements were collected. Single Particle mode analysis (SP-ICP-MS) allows the differentiation between soluble and nanoparticles analyte signal, measuring nanoparticles size (if shape is known or assumed) and assessing agglomeration and/or size distribution. Coupled to a size-separation technique (i.e. field flow fractionation [FFF] and liquid chromatography [LC]), ICP-MS is capable of addressing size, size distribution, surface charge and surface functionality.

The NexION 300 ICP-MS is equipped with a high-speed mass analyzer which has a scan rate that exceeds 5000 data points/sec, a read speed that exceeds 3000 points/sec, a slew speed of 1.6 million amu/sec, and a detector capable of integrating ionic signals at a dwell time as short as 100 µs with a settling time of only 50 µs. Combined with a unique ion path design (Triple Cone Interface [TCI] and Quadrupole Ion Deflector [QID]), the NexION 300 ICP-MS, in SP-ICP-MS mode, is crucial in assessing nanoparticle fate, transformation and transportation in different matrices (i.e. environmental, biological, food, etc.).

All samples were measured in triplicate (three separate dilutions) under the conditions stated in Table 2.

Gold nanoparticle standard reference materials (RM 8011, RM 8012 and RM 8013 – NIST®, Gaithersburg, MD, U.S.) were used to represent samples.

The gold particles were suspended in a solution of deionized water at a concentration of 2 x 10^5 particles/mL. In order to avoid dissolution of the gold nanoparticles, acid was not added.

Table 2. **NexION 300 ICP-MS operational conditions.**

Parameter	Value
Instrument	NexION 300Q ICP-MS
Nebulizer	Concentric PFA-ST
Spray Chamber	Baffled Cyclonic
Torch and Injector	Glass Torch and Glass Injector
Power (W)	1600
Plasma Gas (L/min)	17
Aux Gas (L/min)	1
Neb Gas (L/min)	1.03
Sample Uptake Rate	0.3 (mL/min)
Sample Tubing	Standard (Orange/Green)
Dwell Time	0.2 ms
Settling Time	0.05 ms

All data was collected at *m/z* 197, the only isotope for gold, at a 0.2 ms dwell time. The fast electronics of the system allowed a short settling time of 0.05 ms to be used, thus allowing more data to be collected for each particle. Results for 60-nm gold nanoparticles (RM 8013) are shown in Figure 2. Each peak represents the instrumental response for each integration point.

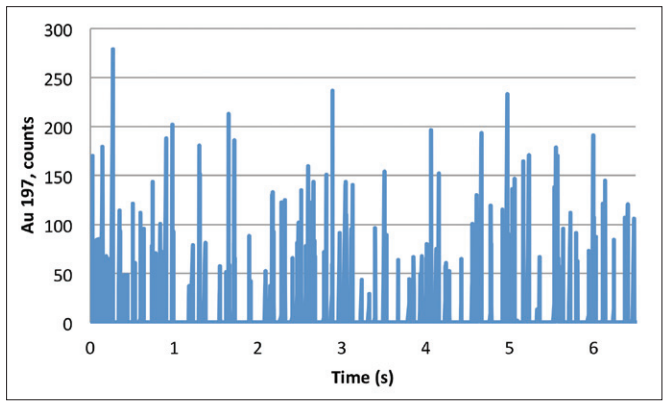

Figure 2. General pattern of obtained signal when measuring nanoparticles in Single Particle-ICP-MS mode.

To obtain additional information from the data collected, mathematical examination of the data was necessary. Since the mathematical calculations fall outside the scope of this paper, please refer to Laborda *et. al.*[5] Figure 3 shows the intensity distribution for RM 8011 (10 nm gold nanoparticles) with a measured median intensity of 9.01 counts.

These results can be replicated as shown by the close agreement of the three replicate dilutions in blue, red and green.

Similarly, Figure 4 shows the intensity distribution for RM 8012 (30 nm gold nanoparticles) with a measured median intensity of 20.02 counts. The median intensity indicates the size of the particle and will be shown later as a way to calibrate this determination.

Figure 5 shows the intensity distribution for RM 8013 (60 nm gold nanoparticles) with a measured median intensity of 42.18 counts. A second small peak is seen in this figure and can be attributed to two particles being introduced into the plasma at the same time.

By applying a cumulative distribution function to the analyzed RMs, we can plot the cumulative distribution vs. counts of the different RMs analyzed to obtain the plots shown in Figure 6. The cumulative distribution function describes the probability that a real-valued random variable *x* with a given probability distribution *f(t)* will be found at a value less than or equal to *x* and is defined by the following equation:

$$P(x) = \int_{-\infty}^{x} f(t)dt$$

The median is the halfway point, where the *P(x)* is equal to 0.5, where *t* is the dwell time.

The intensity of the pulses generated by a single nanoparticle is a function of the number of atoms in the nanoparticle, and hence its size. The plot of the median intensity, calculated at *P(x)* = 0.5 versus the nanoparticle diameter of the NIST® standards, is shown in Figure 7 (Page 5).

Nanoparticle diameter limit of detection (LOD) was related to the capability of a nanoparticle to produce a pulse with a number of counts equal to three times the standard deviation of the background. This limit of detection depends on the transmission efficiency of the ion plume generated from each nanoparticle through the spectrometer. Under the operational conditions stated in Table 2 (0.2 ms dwell time and 0.05 ms settling time), a detection limit of 2.56 nm of gold nanoparticle was obtained.

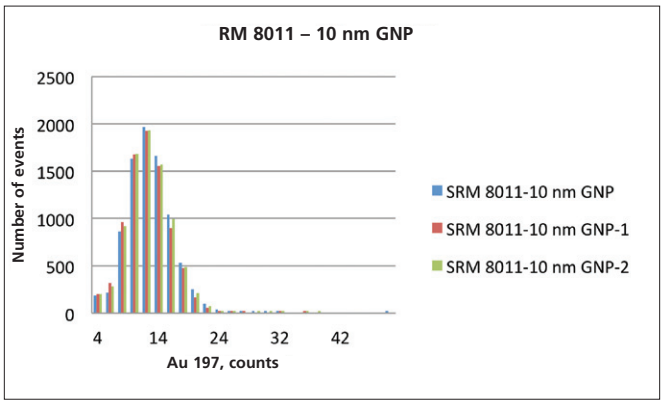

Figure 3. Cumulative statistics – events vs. counts – for SRM 8011 (10 nm gold nanoparticles).

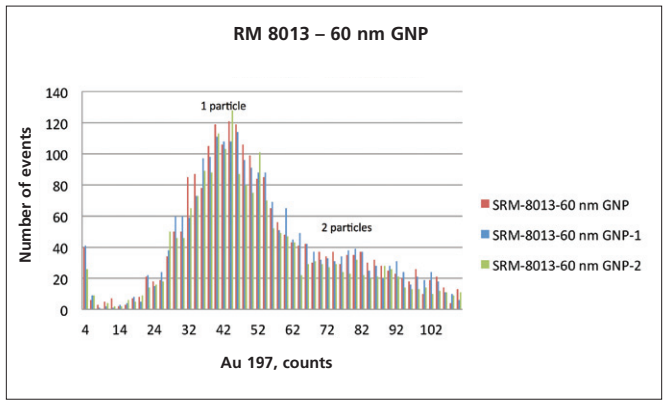

Figure 5. Cumulative statistics – events vs. counts – for SRM 8013 (60 nm gold nanoparticles).

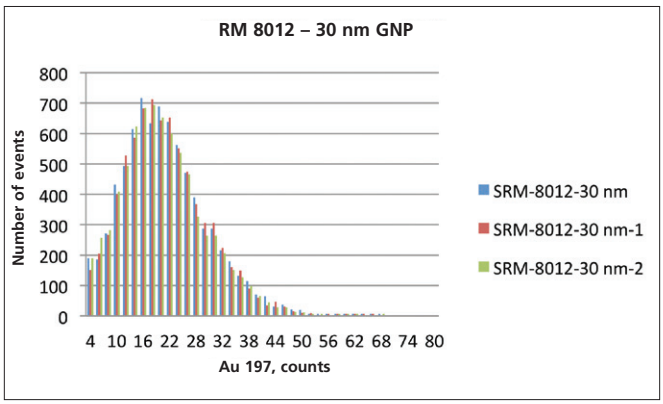

Figure 4. Cumulative statistics – events vs. counts – for SRM 8012 (30 nm gold nanoparticles).

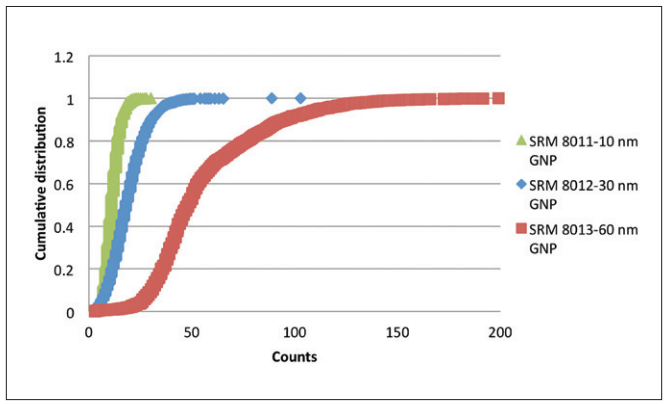

Figure 6. Cumulative distribution vs. counts of the various NIST® SRMs (8011, 8012, 8013) gold nanoparticles.

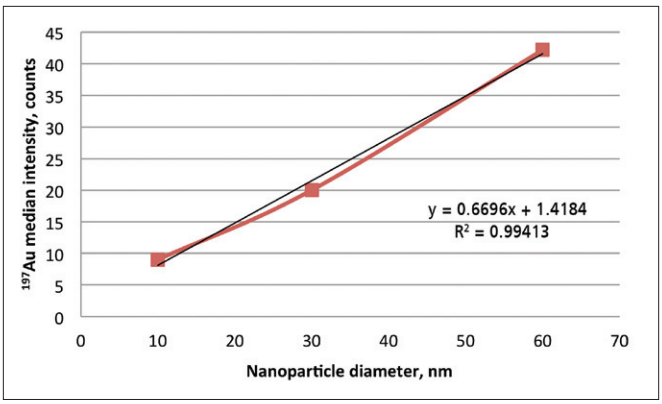

Figure 7. Median intensity counts vs. NIST® RMs nanoparticle diameter.

Conclusion

ICP-MS is rapidly becoming the elemental measurement technique of choice for assessing the manufacturing and environmental life cycle of engineered nanoparticles. In Standard mode, an ICP-MS provides accurate composition and concentration measurements. In Single Particle mode (SP-ICP-MS), it allows the differentiation between ionic and particulate signals, measures particle sizes (if shape is known), and explores agglomeration and size distribution. Modern instruments, with ultra-fast electronics that enable the fastest data rates to capture nanoscale events, can provide advantages in the collection of more data per unit of time, with greater precision. This data is important in characterizing nanoparticles used in food and consumer products. Additionally, SP-ICP-MS is growing into the analytical technique of choice used in exploring the fate, transformation and effects of manufactured nanomaterials in the environment.[6]

References

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