Fundamentals of nanoparticle analysis by ICP-MS

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ICP-MS Software Product Manager
Agilent Technologies
Agenda

Nanoparticle Definition and Overview
Survey of Analytical Techniques
ICP-MS Based Techniques – benefits and limitations of each
Single Particle ICP-MS – important considerations
Single Particle ICP-MS – some results
   Precision
   Accuracy
   Matrix effects
What are nanoparticles and where do they come from?

Particles with at least one dimension in the nano-scale (1-100nm) $10^{-9}$ m

**Natural Sources**

Produced by redox reactions, weathering, mining, volcanos, dust storms…

**Unintentionally produced NPs**

Emitted to air, water and soil from combustion, wear, metal polishing and metal working, electric motors etc.

**Engineered NPs**

Synthesized for a specific purpose by design
Official definition(s)

In 2008 the International Organization for Standardization (ISO) defined a nanoparticle as a discrete nano-object where all three Cartesian dimensions are less than 100 nm.

But in 2011 the Commission of the European Union endorsed a more detailed, but wider-ranging definition:

- A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an 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.
Relative size of nanoparticles (log scale)

Nanoparticles are order(s) of magnitude smaller than single human or bacterial cells
Why are nanoparticles so important?

Novel physical and chemical characteristics

- Very large surface area to volume ratio \(\rightarrow\) large role of intermolecular (surface) forces
  - Increased solubility
  - Increased vapor pressure (lower melting temperature)
  - Very high surface energy
  - High absorption of EM radiation (photovoltaic cells, sunscreen)

Ability to cross biological membranes
Uses of Engineered Nanoparticles

Consumer goods
Pharmaceuticals and Medical Research
Semiconductor manufacturing
Foods and Food packaging
Ceramics
Superconductors
Electronics
Agriculture
Defense
...
Nanoparticles in the environment - considerations

- Environmental health and safety concerns of nanoparticles
  - Potential to be released into environment
  - May be toxic to beneficial microbes
  - Potential impact on aquatic species
  - Poorly characterized toxicity to humans

- Analytical needs
  - Chemical composition
  - Size and size distribution
  - Mass/number concentration
  - Agglomeration state
  - Shape
  - Surface area/charge
  - ......

How many of these needs can ICP-MS related methods meet?
Methods for NP characterization

• **Imaging** methods (TEM, SEM, AFM) are often definitive for detection, shape and size determination. Not quantitative nor representative.

• **Spectroscopic/optical** methods (UV-Vis, dynamic light scattering) simple, but subject to interferences. No elemental information.

• **Hyphenated techniques** (Chromatographic (or other online) separation coupled with ICP-MS detection). Allow representative samples, provide good particle size resolution, high elemental sensitivity but no information on individual particles.

  - FFF-ICP-MS
  - CE-ICP-MS
  - HPLC-ICP-MS

• **Single particle ICP-MS**
Methods for NP characterization

- Transmission Electron Microscopy (TEM)

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent size and shape characterization for individual particles</td>
<td>Time consuming preparation</td>
</tr>
<tr>
<td>Capability to detect very small particles</td>
<td>Subject to preparation artifacts</td>
</tr>
<tr>
<td></td>
<td>No elemental information</td>
</tr>
</tbody>
</table>

![TEM images showing individual particles and clusters.](image-url)
Methods for NP characterization

- Field Flow Fractionation - ICP-MS

The “separation force” can be
- Hydraulic Pressure Gradient Crossflow (AF4)
- Centrifugal
- Thermal
- …

Courtesy PostNova Analytics
Methods for NP characterization

- FFF - ICP-MS

**Benefits**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Good sensitivity for small particles when number concentration is high enough</td>
<td>Sensitivity dependent on particle number concentration</td>
</tr>
<tr>
<td>Multi-element capability</td>
<td>No information on individual particles</td>
</tr>
<tr>
<td>Applicable over wide range of particle sizes</td>
<td>Relatively long run times</td>
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</table>

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
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<tr>
<td></td>
<td>Can’t determine dissolved (ionic) concentration</td>
</tr>
</tbody>
</table>

Fig. 4. Overlaid fractograms of silver nanoparticle mixtures recorded with UV/vis detector (upper) and ICP-MS (lower, not-smoothed signal). The nominal concentration of each fraction corresponds to 580 μg L⁻¹. Numbers above the peaks represent the size of each fraction in nm.
Using ICP-QQQ to enable detection of sulfur coated polystyrene nanoparticles which contain no metals

Sulfur is typically difficult to detect by ICP-MS due to significant interference from $O_2$ on all S isotopes (32, 33, 34). ICP-QQQ can completely eliminate those interferences.

The same techniques can be used to determine other “difficult” elements for traditional ICP-MS such as Si and Ti.

Isotopic information is preserved, permitting isotope dilution quantification.

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**FFF-ICP- 8800 MS detection of S-coated PS nanoparticles (100 and 200 nm) via S detection**

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$H_2 + O_2$ mode:
4.5 ml/min $H_2$ and 45% of $O_2$

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Agilent Technologies
Methods for NP characterization

- **CE - ICP-MS**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Relatively short analysis time</td>
<td>Limited sample size may limit sensitivity</td>
</tr>
<tr>
<td>Minimal matrix interferences</td>
<td>Not as well characterized as other techniques</td>
</tr>
<tr>
<td>Multi elemental capability</td>
<td></td>
</tr>
<tr>
<td>May provide ionic concentration information</td>
<td></td>
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</tbody>
</table>
## CE-ICP-MS compared with TEM

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>ICP-MS</td>
<td>Agilent 7500ce</td>
</tr>
<tr>
<td>CE</td>
<td>Agilent HP3D CE System</td>
</tr>
<tr>
<td>CE-ICP-MS interface</td>
<td>Agilent CE-ESI-MS sprayer kit</td>
</tr>
<tr>
<td>Capillary</td>
<td>60cm x 75µm id fused silica</td>
</tr>
<tr>
<td>Running buffer</td>
<td>10mM tris, 10mM H$_3$BO$_3$, 10mM NaB$_4$O$_7$ (pH 9.0)</td>
</tr>
</tbody>
</table>
Methods for NP characterization

- Single Particle - ICP-MS
  - Each nanoparticle gives a transient signal (a plume of ions generated from the particle)
  - Use Time Resolved data acquisition and analysis
  - Particle concentration, particle diameter, composition and size distribution are obtained

Nanoparticle sample

Signal from one nanoparticle event

Signal intensity (cps) vs Time (s)
## Single Particle ICP-MS

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple and fast</td>
<td>Minimum detectable particle size is determined by analyte sensitivity/background (not possible to gain sensitivity by pre-concentrating samples)</td>
</tr>
<tr>
<td>Minimal sample preparation (maybe filtration and dilution)</td>
<td>Internal standardization is difficult due to neutral pH of samples</td>
</tr>
<tr>
<td>Provides mean particle size and size distribution</td>
<td>Relatively narrow optimum range of particle number concentrations</td>
</tr>
<tr>
<td>Provides elemental information</td>
<td>Limited to 1-2 elements</td>
</tr>
<tr>
<td>Provides particle number concentration and mass concentration</td>
<td></td>
</tr>
<tr>
<td>Provides dissolved ionic concentration</td>
<td></td>
</tr>
</tbody>
</table>
Some important concepts for single nanoparticle analysis (Dwell Time matters, determining the optimum)

- **Long Dwell Time (> 3-5ms)**

  Integrated signal for entire dwell time creates a single intensity value for that “scan” including any nanoparticle peaks plus background due to ionic concentration, spectral interferences and instrument background.

  Spectrum shown at right

  Important Considerations:
  - Correct dilution factor is critical to avoid multiple peaks per scan
  - Background contribution to total signal increases with increasing dwell time.
Some important concepts for single nanoparticle analysis

However...as the dwell time becomes shorter, the nanoparticle signal will begin to decrease with the background, but the potential problem with overlapping peaks is still not solved. **Correct dilution is still important.**

- Just shortening the dwell time alone does not solve the problem
- Need a way to integrate signal over multiple scans to:
  - Accurately quantify signal from single particle
  - Help identify overlapping peaks

<1ms
Microsecond Scanning with no Settling Time
- Short Dwell Time (<<1ms)

• Peak Integration Mode

Single nanoparticle event

Duration for one NP event (0.5-1msec)

“Peak Integration Mode” is automatically enabled by sNP Data Analysis software when dwell time is <1ms
Effects of Dwell Time on Measured Particle Number as a Function of Particle Number Concentration

At low particle number concentration, long dwell times (5-10ms) still give good results, but as particle number increases, particle coincidence results in undercounting of particles at longer dwell times.

100 - 200µs give similar results over a range of particle concentrations.

Important: Dwell times between 0.2ms and 1ms are not useful.
- Too long for peak integration mode
- Too short to capture entire peak reliably
What about very short dwell times (<100µs)?

**Minimum Particle Size and ionic concentration**

- Minimum Detectable Particle Size is limited by signal/background
- Particle signal decreases as the cube of the diameter so high sensitivity is critical to achieve good particle signal precision
  - 30nm particle generates 1/8 the response of a 60nm particle
  - 15nm particle generates 1/64 the response of a 60 nm particle
- Background signal doesn’t decrease with particle size
- 1 detected background count at 10µs dwell time = 100,000cps! Background precision (minimum detectable particle size and ionic concentration) are compromised.
- Particle signal precision decreases with decreasing dwell time
- 100µs dwell time is a good compromise between background precision and sufficient points to define the nanoparticle peak shape (~5 -10 points/peak)
Effect of Sensitivity on Background Equivalent Diameter (minimum detectable particle diameter)

- A reduction in sensitivity by 8x should result in a doubling in minimum detectable particle size (Background Equivalent Diameter)

- Especially critical for low response or high background elements such as Au, Si, Ti, Fe.

**Example:**

- **NIST 30nm Au reference material**
- **Typical Agilent 7900 response factor for Au (~200,000 cps/ppb)**
- **BED = 3.2nm**
Effect of Sensitivity on Background Equivalent Diameter (minimum detectable particle diameter)

- A reduction in sensitivity by 8x should result in a doubling in minimum detectable particle size (Background Equivalent Diameter)
- Especially critical for low response or high background elements such as Au, Si, Ti, Fe.

Same Data Set, but response factor changed manually

Au response factor was manually divided by 8 and BED recalculated

BED = 6.3nm
Fast TRA on Agilent 7900 (100µs dwell time, no settling time)

10,000 data points per second
600,000 data points per minute
Workflow for NP characterization

ICP-MS TRA data

Response vs frequency

- Analyte response factor > Mass of analyte in particle
- Nebulization efficiency (calculated from reference material)
- Analyte density
- Analyte mass fraction in sample particle

Size distribution

- Tabulate and Report

Workflow:

1. Input
2. Calculate
3. Tabulate and Report
Complex process simplified by Method Wizard

Method setup – 3 easy steps

1 – Select Analysis Mode, 2 - Click on analyte element(s), 3 – Select Reference Material

After sample sequence analysis, Data Analysis is automatically performed. No additional user input is required.
Precision and Accuracy (NIST 8012 and 8013)

<table>
<thead>
<tr>
<th>Sample (Prepared concentration)</th>
<th>Observed Concentration (particles/L)</th>
<th>Observed Concentration (ng/L)</th>
<th>Observed Particle Size (nm)</th>
<th>Reference Particle Size obtained by TEM (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIST 8013 Nominal 60nm (100 ng/L)</td>
<td>$2.62 \times 10^7$</td>
<td>103</td>
<td>55</td>
<td>56.0 ± 0.5</td>
</tr>
<tr>
<td>NIST 8012 Nominal 30nm (10 ng/L)</td>
<td>$2.34 \times 10^7$</td>
<td>10.5</td>
<td>28</td>
<td>27.6 ± 2.1</td>
</tr>
</tbody>
</table>

Relative Standard Deviation (%) n = 5

<table>
<thead>
<tr>
<th></th>
<th># of Particles</th>
<th>Concentration (particles/L)</th>
<th>Concentration (ng/L)</th>
<th>Ionic Concentration (ppb)</th>
<th>BED (nm)</th>
<th>Particle Size (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60nm particles (50ppt)</td>
<td>3.7%</td>
<td>3.7%</td>
<td>2.8%</td>
<td>4.7%</td>
<td>1.6%</td>
<td>0.1%</td>
</tr>
<tr>
<td>30nm particles (30ppt)</td>
<td>3.3%</td>
<td>3.3%</td>
<td>3.1%</td>
<td>2.0%</td>
<td>0.7%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>
Analyzing mixtures of different particle sizes

Fig. 2 Nanoparticle events acquired using fast time resolved analysis mode with 0.1 ms dwell time. A – wide scale. B – Zoomed in 30 nm and 60 nm Au NPs.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Observed concentration (particles/L)</th>
<th>Observed concentration (ng/L)</th>
<th>Prepared total concentration (ng/L)</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 nm (NIST 8013) 50 ng/L + 30 nm (NIST 8012) 5 ng/L</td>
<td>4.78 x10^7</td>
<td>57.6</td>
<td>55</td>
<td>105%</td>
</tr>
<tr>
<td>60 nm (NIST 8013) 80 ng/L + 30 nm (NIST 8012) 2 ng/L</td>
<td>5.13 x10^7</td>
<td>86.1</td>
<td>82</td>
<td>105%</td>
</tr>
</tbody>
</table>

Fig. 6 Size distribution results of Ag NPs. A – 20 nm, B – 40 nm, C – 60 nm, D – 100 nm, E – mixture of 20, 40, 60, 100 nm.

M. Yamanaka et al, European Winter Plasma Conference Poster, 2015
Effect of dissolved (ionic) analyte plus matrix on sNP calculations

Spiked sample (NIST 60nm Au + 1ppb ionic Au into Tap Water analyzed using same calibration 20 hours later

- Particle number and number concentration unaffected
- Particle mass concentration unaffected
- Ionic concentration recovery = 100%
- Particle size calculation unaffected
- BED increased from ~5nm to ~16nm due to ionic background
Q&A Session

Your questions…