TITLE

NANOPARTICLE SUSPENSIONS – COUNTING AND SIZING NANOPARTICLES VIA SINGLE PARTICLE INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY

1 OBJECTIVE AND SCOPE

1.1 Objective

The objective of the method is the determination of the number and mass concentration, and the size of inorganic nanoparticles in an aqueous suspension.

1.2 Scope

The procedure is applicable for the determination of inorganic nanoparticles, metal and metal oxides (e.g. Ag, Au, TiO_2, CeO_2, etc.), with size ranges of 20 to 1000 nm in aqueous suspensions. Typical mass concentrations that can be determined are in the range of 1 to 1000 ng/L. In addition to the particle concentrations, ionic concentrations can also be determined. The aqueous suspensions can be diluted digests of food or tissue samples or diluted environmental water samples.

2 DEFINITION

SP-ICP-MS : Single particle inductively coupled plasma mass spectrometry.
Nanoparticle : A particle with at least one dimension in the range of 1 to 100 nm.
Dwell time : The time during which the ICP-MS detector collects and integrates incoming pulses. Following integration the total counts are registered as one data point, expressed in counts, or counts per second.

3 PRINCIPLE

The sample, an aqueous suspension, is introduced continuously into a standard ICP-MS system that is set to acquire data with a high time resolution (i.e. a short dwell time is used). Following nebulization, a fraction of the nanoparticles enter the plasma where they are atomized and the individual atoms ionized resulting in a cloud of ions. This cloud of ions is sampled by the mass spectrometer and since the ion density in this cloud is high, the signal pulse is high compared to the background signal if a high time resolution is used. A typical run time is 60 seconds and is called a time scan. The mass spectrometer can be tuned to measure any specific element, but due to the high time resolution only one m/z value can be monitored during a run. The data are exported as a CSV file and imported in Excel to calculate the number and mass concentration, and the size and size distribution of the nanoparticles.
The number of pulses detected per second is a directly proportional to the number concentration of nanoparticles in the aqueous suspension that is being measured. To calculate concentrations, the nebulization efficiency has to be determined first using a reference particle.
The intensity of the signal pulse is directly proportional to the mass of the detected nanoparticle, and thereby to

the nanoparticle's diameter to the third power (i.e. assuming a spherical geometry for the nanoparticle). Calibration is performed using ionic standard solutions of the measured element analyzed under the same condition.

4 CHEMICALS AND REAGENTS

4.1 Chemicals

4.1.1 Sodium dodecylsulphate, SDS, $C_{12}H_{25}NaO_4S$ (e.g. Sigma)

4.1.2 Sodium citrate $C_6H_5Na_3O_7$-$2H_2O$ (e.g. AnalaR)

4.1.3 Nitric acid, 70% (trace analysis grade, e.g. Fisher Chemical)

4.1.4 Standard materials

4.1.4.1 Gold nanoparticles: NIST reference material 8013 consisting of a suspension of gold nanoparticles with a mass concentration of 50 mg/L stabilized in a citrate buffer. These particles have a spherical shape and a diameter of 60 nm.

4.1.4.2 As an alternative for 4.1.4.2., silver nanoparticles: BioPure suspension EAW 1093 of silver nanoparticles with a mass concentration of 1000 mg/L stabilized in a citrate buffer. These particles have a spherical shape and a diameter of 60 nm.

4.1.4.3 Ionic standard solutions: Ionic standard solutions of the element that will be measured. Any well-defined commercially available ionic standard solution will do (e.g. Merck).

4.2 Reagents

4.2.1 Stock standard of 60 nm gold nanoparticles (50 µg/L)

Pipet 50 µL of the gold reference standard 8013 (4.1.4.1) to 25 mL MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a final mass concentration of 50 µg/L. Mix thoroughly and store at room temperature in amber glass screw necked vials. This intermediate standard is stable at room temperature for at least one month. Prior to use place the standard in an ultrasound bath for 10 minutes

4.2.2 Working standard of 60 nm Gold nanoparticles (50 ng/L)

Prepare the working standard by pipetting 50 µL of the stock standard (4.2.1) to 25 mL of MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a final mass concentration of 50 ng/L. Mix thoroughly and store at room temperature in amber glass screw necked vials. Although this standard is stable for several days, it is prepared daily.

4.2.3 Stock standard of 60 nm Silver nanoparticle (1 mg/L)

Pipet 50 µL of the silver standard EAW 1093 (4.1.4.2) to 25 mL MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a mass concentration of 1 mg/L. Mix thoroughly and store this intermediate standard in amber glass screw necked vials. Protected from light this intermediate standard is stable at room temperature for at least two weeks. Prior to use place the standard in an ultrasound bath for 10 minutes

4.2.4 Working standard of 60 nm Silver nanoparticle (50 ng/L).
Pipet 50 µL of the stock standard (4.2.3) to ca. 25 mL of MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a mass concentration of 1 µg/L. Prepare the working standard by pipetting 2.5 mL of this standard into a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a final concentration of 50 ng/L. Mix thoroughly and store the working standard at room temperature in amber glass bottles. Protected from light this standard is stable for 24 hours and is prepared daily.

4.2.5 Stock standards of ionic solutions of the particle's elemental composition (100 µg/L).
Assuming the supplied ionic standard solution (4.1.4.3) has a concentration of 100 mg/L, pipet 50 µL of the standard to 25 mL MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water resulting in a concentration of 100 µg/L. Mix thoroughly and store this intermediate standard in amber glass screw necked vials. Protected from light this intermediate standard is stable at room temperature for at least two weeks.
(NOTE: recalculate for ionic standard solutions having different concentrations)

4.2.6 Working standards of ionic solutions of the particle's elemental composition (0.2 – 5 µg/L).
According to table 1 pipet the volumes of the stock standard (4.2.5) to ca. 25 mL of MilliQ water in a 50 mL glass measuring flask and fill to the mark with MilliQ water. Mix thoroughly. Together resulting working standards in table 1 form a calibration curve. Store the working standard at room temperature in glass bottles. Protected from light this intermediate standard is stable at room temperature for the period indicated in table 1.

Table 1: Volumes for the preparation of the working standards of the ionic stock solution.

Volume of the stock standard (4.2.5) diluted to 50 mL MilliQ water	Ionic concentration of the working standard (4.2.6)	Stability of the ionic working standard in glass
2.5 mL	5 µg/L	2 weeks
1 mL	2 µg/L	2 weeks
0.5 mL	1 µg/L	2 weeks
0.25 mL	0.5 µg/L	1 week
0.1 mL	0.2 µg/L	1 week

4.2.7 Rinsing fluid for the ICP-MS sampling system.

Dilute the concentrated nitric acid (4.1.3) to a strength of ~3% by adding 400 mL of nitric acid to 7600 mL MilliQ water in a 10 L plastic container.

5 EQUIPMENT

5.1 Inductively coupled plasma mass spectrometer (e.g. Thermo Fisher Scientific, model X-SERIES 2)

5.2 Vortex mixer (e.g. Fisher Scientific Genie 2 model G-560)

5.3 Analytical balance (e.g. Mettler Toledo)

5.4 Ultrasonic bath (e.g. Branson 3510)

6 PROCEDURE

6.1 General

This procedure describes the determination of the number and mass concentration, and the size of nanoparticles in diluted aqueous suspension. If the sample matrix is different, a pre-treatment is required to produce an aqueous suspension. Dilution is often required to avoid violation of the “single particle rule” (i.e. more than one particle arriving at the detector in one dwell time). Using a dwell time of 3 ms, a maximum of 20,000 particles can be registered per minute, however, to satisfy the “single particle rule”, the number of peaks in the time scan should not exceed ca. 2000 per minute (as a guidance, a suspension of 60 nm gold particles with a mass concentration of 300 ng/L at an ICP-MS input flow of 0.5 mL/min and a nebulization efficiency of 3% will result in this number of peaks).

6.2 Safety precautions

Protective clothing is required. Wear a lab coat, safety glasses, and gloves. Use reagents in an efficient fume hood. Handle acids wearing gloves and safety glasses. Each chemical should be treated as a potential health hazard and exposure to these chemicals should be minimized.

6.3 Sample dilution

In general the number of peaks in a time scan should not exceed 10% of the maximum number of peaks based on the dwell time (6.1). For the instrumental settings used in this procedure (6.5.1) a particle number concentration in the range of $2x10^6$ to $2x10^8$ particles/L results in useful measurement data. As a guidance table 2 gives the corresponding mass concentrations for different types and sizes of particles.

Table 2. Mass concentration ranges of different types of nanoparticles at number concentrations of $2x10^6$ to $2x10^8$.

Particle composition	Particle size

	30 nm	60 nm	120 nm
Gold (Au)	1 – 100 ng/L	5 – 500 ng/L	20 – 2000 ng/L
Silver (Ag) Cerium oxide (CeO_2)	0.5 – 50 ng/L	2 – 200 ng/L	10 – 1000 ng/L
Titanium dioxide (TiO_2) Iron oxide (Fe_2O_3) Zinc oxide (ZnO)	0.2 – 20 ng/L	1 – 100 ng/L	5 – 500 ng/L

If no information or estimation of the possible nanoparticle concentration in a sample or aqueous extract are available a 10,000 times dilution is recommended as a starting point. Based on the observed number of peaks in the analysis of the diluted sample the dilution can then be adapted. Dilutions are made in MilliQ water or, if stabilisation is required, in 5 mM sodium citrate or 10 mM SDS in MilliQ water.

6.4 Amount of sample

For the instrumental settings used in this procedure (6.5.1) the minimal required sample volume after dilution is 5 mL.

6.5 Description procedure

6.5.1 Settings of the ICP-MS system

Use the best settings as provided by the supplier of the ICP-MS system. If no such settings are given, the following settings can be used:

- Forward power : 1400 W
- Nebulizer : standard type
- Gas flows : plasma, 13 L/min
  nebulizer, 1.1 L/min
  auxiliary, 0.7 L/min
- Rinsing liquid flow rate : 1 mL/min
- Sample flow rate : 0.5 mL/min
- Data acquisition : time resolved analysis mode
- Dwell time : 3 ms
- Total acquisition time : 60 s
- Ion monitoring : Gold, Au, m/z 197
  Silver, Ag, m/z 107
  Titanium, Ti, m/z 48

Iron, Fe, m/z 56
Cerium, Ce, m/z 140

(NOTE: In case of low m/z values as for Ti (48) and Fe (56), interferences by polyatomic ions such as SO and ArO may cause background levels rendering small particles invisible. In that case the use of a collision cell or dynamic reaction cell can improve the results).

A 3% nitric acid solution is used to rinse sampling system, tubing etc. of the ICP-MS before and in between runs.

6.5.2 Checking the performance of the ICP-MS system

The instrument has a performance check and an autotune function which are designed to replace the manual checks and tuning procedures and the short term stability test. See SOP A1078 to carry out the performance check. If the criteria of the performance check are not met, a tuning, autotune or manual tune, is performed to optimize the instrument.

Special attention should be paid to the cleanliness of the sample introduction system of the ICP-MS. If high nanoparticle concentrations have passed through the tubing this may result in continuous background levels. On the other hand, if high concentrations of other type of samples have passed through the tubing this can cause adsorptions giving erroneous results when determining the nebulization efficiency and measuring true samples. If unsure, change the tubing, or better reserve a set of tubing for SP-ICP-MS.

6.5.3 Determination of the nebulization efficiency.

The nebulization efficiency is determined using a known nanoparticle standard. In this procedure the 60 nm gold particle is used (6.5.3.1). If not available, the 60 nm silver particle or any other well-known nanoparticle can be used, the procedure is the same. If no particles are available an alternative, but less accurate volumetric method can be used (6.5.3.2).

6.5.3.1 Determination based on a nanoparticle standard of known size and concentration

Calculate the particle number concentration in working standard (4.2.2) using the equation:

$$C_p = \frac{C_m}{m_p}$$

Where: C_p = particle number concentration (mL^{-1}); C_m = mass concentration of the particle suspension (g/mL); m_p = mass per particle (g). The mass of a 60 nm gold nanoparticle is 2.2×10^{-15} g and with a mass concentration of 50 ng/L this results in a particle concentration C_p = 22,730 ml^{-1}.

Analyze the working standard (4.2.2) using the settings according to the procedure (6.5.1) and determine the particle flux in the plasma, i.e. the number of particle peaks per second in the time scan. Calculate the nebulization efficiency using the following equation:

$$\eta_n = \frac{60\ q_p}{C_p\ V} \times 100\%$$

Where: η_n = nebulization efficiency (%); q_p = particle flux in the plasma (s^{-1}); C_p = particle number concentration (mL^{-1}); V = sample flow (mL/min). With a standard type of nebulizer, η_n is expected to be in the order of 2 - 3%.

6.5.3.2 Determination based on a nanoparticle standard of known size

If a nanoparticle standard is available of which only the size is known, the nebulization efficiency can be determined if a series of ionic standards 4.2.6, table 1) of the same element as the nanoparticle is analyzed in the same series.

Analyze the working standard of the particle suspension (4.2.2 or 4.2.4, or other) and the working standards of the ionic solutions (4.6.2, or other) using the settings according to the procedure (6.5.1). Using linear regression determine the correlation coefficient of the calibration line. The correlation coefficient should be >0.99. The particle mass concentration of the working standard of the particle suspension is calculated as follows:

$$C_m = \frac{\sum I_p}{RF_{ion}}$$

Where: C_m = mass concentration of the particle suspension (µg/L); I_p = particle signal intensity minus background intensity in the time scan (cps); RF_{ion} = ICP-MS response for ion standaard (cps/µg/L).

Use the determined value for C_m and the data of the analysis of the working standard of the particle suspension to determine the transport efficiency as in 6.5.3.1.

6.5.3.3 Determination based on flow measurements

Rinse the ICP-MS sample introduction system with Milli-Q water for 5 minutes. Check that the tubing is filled completely, without air bubbles, and is not leaking. Weigh an empty Greiner vial and a Greiner vial containing 50 mL of MilliQ water to 0.01 g accurate. Place the Greiner vial with the MilliQ water in the ICP-MS autosampler and attach the waste tubing from the spray chamber to the empty Greiner vial. Make sure that the sipper and waste

tubing are completely filled with liquid. With the plasma ignited, place the sipper into the Greiner vial in the autosampler and start the peristaltic pump. After 30 min the peristaltic pump is stopped, the sipper is removed from the Greiner vial in the autosampler, and the waste tubing is removed from the Greiner vial collecting the waste liquid. Weigh both Greiner vials to 0.01 g accurate and calculate the nebulization efficiency as follows:

$$\eta_n = \left(1 - \frac{W_{out}}{(W_{in_0} - W_{in_{30}})}\right) \times 100\%$$

Where: η_n = nebulization efficiency (%); W_{out} = weight of collected waste water (g); W_{in_x} = weight of nanoparticle suspension in the Greiner vial after x min (g).

(NOTE: Keep in mind that this method is less accurate than 6.5.3.1 since relatively small differences are determined from large numbers)

6.5.4 Determination of the linearity of the response

Analyze the working standards of the ionic solutions (4.2.6) using the settings according to the procedure (6.5.1). Using linear regression determine the correlation coefficient of the calibration line. The correlation coefficient should be >0.99

6.5.5 Determination of the blank level of the ICP-MS

Analyze three blank samples, MilliQ, or the water used for sample dilution using the settings according to the procedure (6.5.1). If the detection limit is defined as less than 1% false negatives then it can be shown that the number of particles observed in the measuring period should not exceed 10. The number of observed particles in the blank should not exceed 10.

6.5.6 Analysis of aqueous suspensions

Prepare the instrument for analysis and set up an injection list according to SOP A1078. Blanks, ionic calibration standards and/or nanoparticle standards are included in the analyses sequence at the start, after every 10 samples, and at the end of the sample sequence to verify instrument performance over the course of the run. The calibration curve of the ionic standards is included only at the start of the sequence and at the end of the sequence if no more than 5 series of 10 samples are analyzed. A typical sample sequence looks like as follows:

1 MilliQ
2 Ionic standard 0.2 µg/L
3 Ionic standard 0.5 µg/L

4 Ionic standard 1 µg/L
5 Ionic standard 2 µg/L
6 Ionic standard 5 µg/L
7 Nanoparticle standard 2x10^7 particles/L (for 60 nm gold this is ~50 ng/L, for 60 nm silver ~25 ng/L)
8 MilliQ
9 Sample 1
10 Sample 2
11 Sample 3
12 Sample 4
13 Sample 5
14 Sample 6
15 Sample 7
16 Sample 8
17 Sample 9
18 Sample 10
19 MilliQ
20 Ion standard 2 µg/L
21 Nanoparticle standard 2x10^7 particles/L (for 60 nm gold this is ~50 ng/L, for 60 nm silver ~25 ng/L)
22 MilliQ
23 Sample 11
24 Etcetera….

(NOTE: If uncertain about the quality or concentration of the samples, each sample may be followed by a blank MilliQ water to check for memory effects or blank development.)

6.5.7 Data conversion

Currently there is no software to process SP-ICP-MS data. Therefore, the ICP-MS raw data of the complete sample sequence is exported as a CSV file and imported in Microsoft Excel for data processing. To do so using the Thermo Xseries 2, do as follows:

- In the “experiment” screen, click on the “results” tab
- Select the “numerical results” tab
- Click on the “time” tab to block all numerical results columns
- Right mouse click and select “Export CSV file”
- Save the CSV file in a corresponding directory.

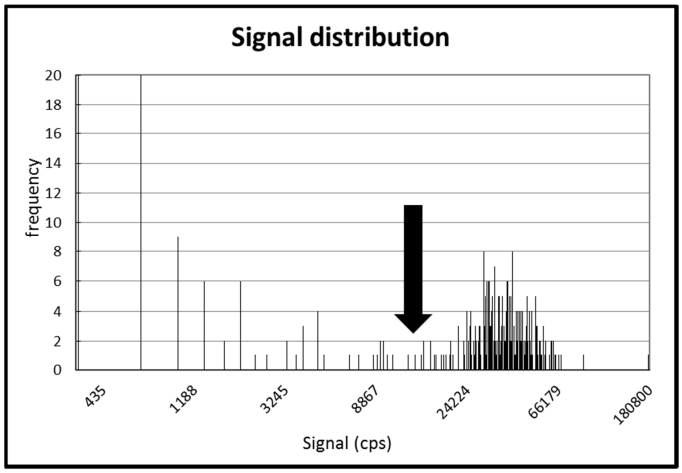
- Split the data in the CSV file for the individual samples. A special Excel macro is available to import the CSV file and organize the numerical data into separated columns per sample.

7 RESULTS

7.1 Calculations

Calculations are performed in the Single Particle Calculation (SPC) spreadsheet by entering the converted ICP-MS data and the required information (see appendix 1). The converted ICP-MS data is shown as a “Time scan” and as a “Signal distribution”. The latter is used to differentiate the particles from the background (instrument noise and ions). The ICP-MS response that separates the particles from the background is found as a minimum in the graph (see figure 1). This minimum is visually determined and entered in the spreadsheet as the “limit for particle detection”.

Figure 1. Signal distribution graph plotting the frequency of the ICP-MS response in data points as a function of the ICP-MS response. ICP-MS responses left from the minimum depict background and ions, those right from the minimum particles.



The spreadsheet consists of a “Calibration” and a “Sample” worksheet. The “Calibration” worksheet (Appendix 1) requires the following information:

- Administrative data (dates, file names and operator)
- The converted ICP-MS data of the nanoparticle working standard (4.2.2) to determine the nebulization efficiency (use the “paste special” “values” option to enter these data)
- The instrument settings (sample inlet flow and dwell time)

- The composition of the nanoparticle working standard to determine the nebulization efficiency (element, element density, particle mass concentration, particle diameter, limit for particle detection)
- The ICP-MS response of the ionic working standards (4.2.6) for calibration (element and ICP-MS response from linear regression)

The "Sample" worksheet (Appendix 2) requires the following information:

- Administrative data (dates, file names and operator)
- The converted ICP-MS data of the sample (use the "paste special" "values" option to enter these data)
- The composition information of the target particle (particle composition, molar mass ratio and density)
- The calibration data (limit for particle detection, other information is collected from the "Calibration" worksheet)

7.1.1 Calculation of the nebulization efficiency.

The nebulization efficiency η_n is calculated in the "Calibration" worksheet using the entered information of the nanoparticle working standard (4.2.2) and the equation presented in 6.5.3.1.

7.1.2 Calculation of the ICP-MS response

Calculate the ICP-MS response from the calibration line of the ionic working standards (4.2.6) using linear regression. The ICP-MS response is the slope of the calibration function expressed as cps/µg/L and entered in the "Calibration" worksheet.

7.1.3 Calculation of particle concentration and size in a sample

Following the input of the required data in the "Calibration" and "Sample" worksheet, the particle concentration and size are calculated and presented in the "Results" section and the "Size distribution" graph in the "Sample" worksheet. The following formulae are used in these calculations:

- Calculation of the particle number concentration:

$$C_p = \frac{N_p}{\eta_n} \times \frac{1000}{V}$$

Where C_p = particle number concentration (L^{-1}); N_p = number of particles detected in the time scan (min^{-1}); η_n = nebulization efficiency; V = sample input flow (mL/min).

- Calculation of the mass of the individual particles in the sample:

$$m_p = \frac{I_p\ t_d}{RF_{ion}} \times \frac{V\ \eta_n}{60} \times \frac{M_p}{M_a}$$

Where m_p = particle mass (ng); I_p = particle signal intensity in the sample (cps); RF_{ion} = ICP-MS response for ion standard (cps/µg/L); t_d = dwell time (s); V = sample flow (mL/min); η_n = nebulization efficiency; M_p = molar mass nanoparticle material; M_a = molar mass analyte measured. To calculate the particle mass concentration the masses of all individual particles are summed:

$$C_m = \frac{\sum m_p}{\eta_n \times V \times 1000}$$

Where C_m = particle mass concentration (ng/L); m_p = particle mass (ng); η_n = nebulization efficiency; V = sample flow (mL/min).

- The particle size, expressed as the particle's diameter (and assuming a spherical particle shape) is calculated as follows:

$$d_p = \sqrt[3]{\frac{6\ m_p}{\pi\ \rho_p}} \times 10^4$$

Where: d_p = particle diameter in the sample (nm); m_p = particle mass (ng); ρ_p= particle density (g/mL). The "Results" section gives the mean particle diameter while the diameters of the individual particles are plotted in the "Size distribution" graph.

7.1.4 Calculation of ionic concentration in a sample

The ionic concentration in the aqueous sample is calculated as follows:

$$C_{ion} = \frac{I_{bg}}{RF_{ion}}$$

Where C_{ion} = ionic concentration (µg/L); I_{bg} = background intensity in the sample (cps); RF_{ion} = ICP-MS response for ion standard (cps/µg/L). Note that if small nanoparticles are not recognized and isolated during data processing these will be in the background intensity and will be unjust quantified as ionic material.

- Calculation of the mass of the individual particles in the sample:

7.2 Criteria

7.2.1 Nebulization efficiency

The nebulization efficiency (6.5.3.1 and 6.5.3.2) should be higher than 1.0%. If the nebulization efficiency is <1.0% check the nebulizer, its position and the nebulization gas flow to increase the nebulization efficiency.

7.2.2 Linearity of calibration curve

The correlation coefficient of the calibration curve (6.5.4) should be >0.99. If the correlation coefficient is <0.99 check the instrument and the ionic working standards for calibration (4.2.6) and repeat the calibration.

7.2.3 Blank samples

The number of particles detected in the blank samples (6.5.5) shall not exceed 10 particles. If the number of observed particles is >10 check the instrument, especially the tubing in the sample introduction system. Repeat the blank analysis.

7.2.4 Number of detected particles

In general, the number of detected particles in the time scan of a nanoparticle standard or sample extract should not exceed 10% of the maximum number of samples that can be detected. Using a dwell time of 3 ms, the number of detected particles in the time scan should not exceed 2000. If this number is exceeded the aqueous sample extract should be diluted and re-analysed.

7.3 Final results

The final results of the determination are given in the “Results” section and the “Size distribution” graph in the “Sample” worksheet.

8 REGISTRATION

8.1 Lab journal

Dates, project number, sample numbers, sample sequences and followed procedures are recorded in the lab journal. Deviations from existing procedures as well as any sample preparation methods for which currently no

standard operating procedures are available are recorded in the lab journal. The lab journal should also contain a note where the raw data and processed data can be found.

8.2 Electronic data

The raw data acquired by the ICP-MS and the converted data after processing with Excel should be stored on the appropriate location on the U-disc.

LITERATURE

Gold colloid analysis by inductively coupled plasma-mass spectrometry in a single particle mode. C. Degueldre, P.Y. Favarger, S. Wold. Anal. Chim. Acta 2006, 555, 263–268.

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An approach to the natural and engineered nanoparticles analysis in the environment by inductively coupled plasma mass spectrometry. M.S. Jiménez, M.T. Gómez, E. Bolea, F. Laborda, J. Castillo. Int. J. Mass Spectrom. 2011, 307, 99– 104.

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Development and validation of single particle ICP-MS for sizing and quantitative determination of nano-silver in chicken meat. R. J.B. Peters, Z. Herrera-Rivera, G. van Bemmel, H.J.P. Marvin, S. Weigel, H. Bouwmeester. Anal. Bioanal. Chem., 2014, 16, 3875-3885.

Single particle ICP-MS combined with a data evaluation tool as a routine technique for the analysis of nanoparticles in complex matrices. R. J.B. Peters, Z. Herrera-Rivera, M. van der Lee, H.J.P. Marvin, H. Bouwmeester, S. Weigel. J. Anal. At. Spectrom., 2015, DOI: 10.1039/C4JA00357H.

APPENDIX 1 - Calculation spreadsheet – Calibration worksheet

CALIBRATION FILE

ADMINISTRATION	
Date:	A
Project:	B
Particle standard:	C
Data file:	D
Ion standard:	E
Data file:	F
Operator:	G

INPUT (paste special; values)

scan no	signal (cps)
1	0
2	0
3	0
4	0
5	0
6	0
7	0
8	0
9	0
10	0
11	0
12	0
13	0
14	0
15	0
16	0
17	0
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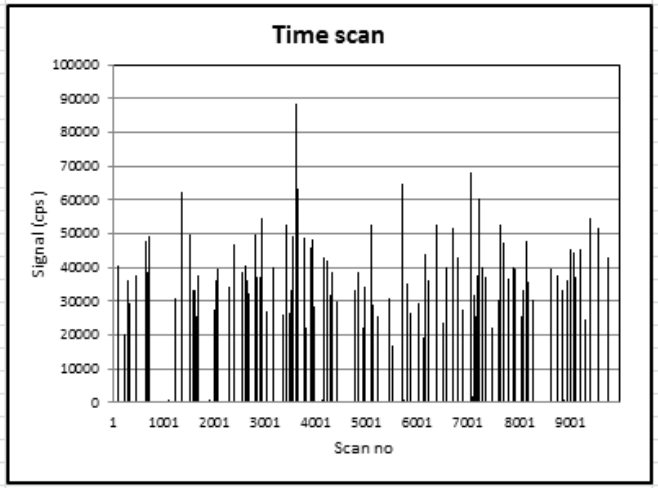
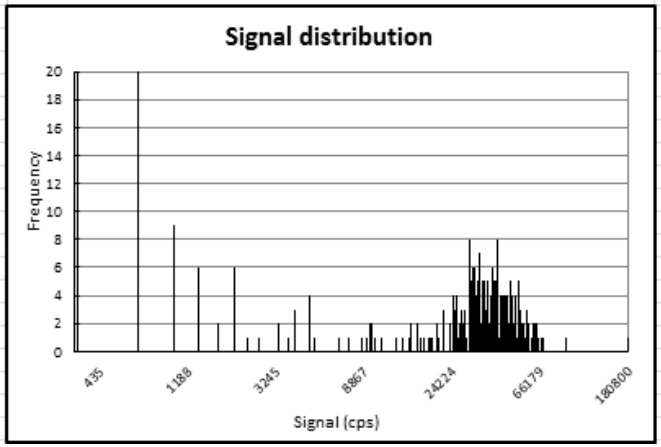
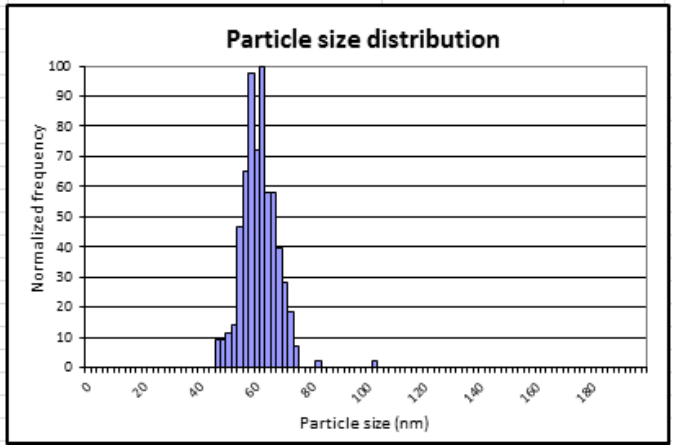
26	0
27	0
28	0
29	0





INSTRUMENT SETTINGS AND CALIBRATION DATA		
Instrument settings:		
ICPMS sample inlet flow	0.5	ml/min
ICPMS dwell time	3	ms
Determination of nebulization efficiency:		
elemental composition of standard particle	Au	
element density	19.3	g/ml
standard particle mass concentration	50	ng/l
standard particle diameter	60	nm
calculated standard particle mass	2.18	fg
limit for particle det.	15000	cps
detected number of particles	275	#/min
calculated transport efficiency	0.024	
Determination of ion response target element:		
Elemental composition op target particle	Au	
ICPMS response to ion standard of target analyte	10500	cps/(µg/L)

Check results		
Concentration (particle numer)	2.3E+07	particles/L
Concentration (mass)	50	ng/L
Particle size	60	nm



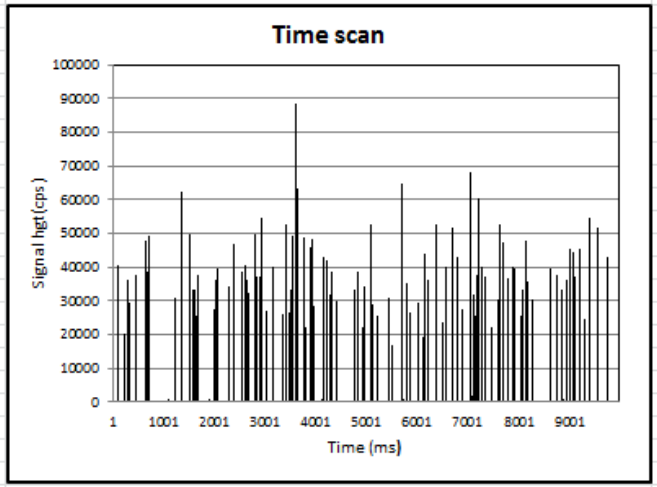
APPENDIX 2 - Calculation spreadsheet – Sample worksheet

SAMPLE FILE

ADMINISTRATION	
Date:	A
Project:	B
Particle standard:	C
Data file:	D
Ion standard:	E
Data file:	F
Operator:	G

INPUT (paste special; values)

dwell time event	signal (cps)
1	0
2	0
3	0
4	0
5	0
6	0
7	0
8	0
9	0
10	0
11	0
12	0
13	0
14	0
15	0
16	0
17	0
18	0
19	0
20	0
21	0
22	0
23	0
24	0
25	0
26	0
27	0
28	0
29	0



INSTRUMENT SETTINGS AND CALIBRATION DATA		
Instrument settings:		
ICPMS sample flow	0.5	ml/min
ICPMS dwell time	3	ms
Properties of target particle:		
elemental composition of target particle	Au	
molar mass particle/molar mass analyte	1	
particle density	19.3	g/ml
Calibration data:		
transport efficiency	0.024	
ICPMS response ion standard	10500	cps/(µg/L)
limit for particle detection	15000	cps
number of particles detected	275	

Results		
Particle concentration (number-based)	2.3E+07	particles/L
Particle concentration (mass-based)	50	ng/L
Particle size	60	nm
Ionic concentration	<100	ng/L