Technical Specification

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Nanotechnologies — Characterization of nano-objects using single particle inductively coupled plasma mass spectrometry

Nanotechnologies — Caractérisation des nano-objets par spectrométrie de masse à plasma induit en mode particule unique

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Foreword

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This document was prepared by Technical Committee ISO/TC 229, *Nanotechnologies,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 352*, Nanotechnologies,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO/TS 19590:2017), which has been technically revised.

The main changes are as follows:

— general restructuring;

— expansion of text on the test method;

— inclusion of considerations regarding method precision and measurement uncertainty;

— updates to normative and bibliographical references.

Any feedback or questions on this document should be directed to the user’s national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Following the introduction of single particle inductively coupled plasma mass spectrometry (spICP-MS) by Degueldre in 2003,[1] the technique has increasingly been used for nano-object characterization due to its high sensitivity, elemental specificity, the fact that often minimal sample preparation is needed and the development of much improved instrumentation, along with user-friendly data analysis software.

In spICP-MS, a very diluted suspension containing nano-objects is introduced continuously into an ICP-MS system with the intent that the ion cloud from one particle at a time arrives at the detector, set to acquire data with a high time resolution (i.e. dwell time). Following the nebulization, a fraction of the nano-objects enter the plasma where they are atomized, and the individual atoms ionized. Every atomized particle results in a cloud of ions which is then sampled by the mass spectrometer. The mass spectrometer can be tuned to measure any specific element. Typically, only one mass-to-charge value per single particle will be monitored with a quadrupole-based MS instrumentation. However, the technique can also be used with time-of-flight (TOF) mass spectrometers, allowing simultaneous multi-element and multi-isotope detection.

The number of events detected in each run (time scan) is directly proportional to the number of nano-objects in the suspension introduced but necessitates calibration of the sample transport efficiency to calculate the particle number concentration. Several available approaches to measure the transport efficiency are described in detail in this document. The intensity of the measured signal is directly proportional to the mass of the measured element in the nano-object, which can be derived following appropriate calibration of the instrument's response factor, also described in this document. For particles of known geometry, composition and density, the mass can be related to particle size. Most of the currently available, commercial data analysis software assumes spherical geometry; particle diameter is proportional to the cubic root of the mass of element(s) in a spherical nano-object. In addition to nano-object characterization with spICP-MS, mass concentrations of dissolved element present in the same sample can also be determined from the same data, if a good separation between the dissolved and particulate fraction is achieved. This represents one of the key advantages of the technique.

spICP-MS was once predominantly the domain of specialist laboratories, but with recent developments in commercially available hardware and software, the technique is now more commonly used and increasingly popular for high-throughput analysis as well as high accuracy reference measurements.

Further information on spICP-MS can be found in ISO/TS 24672, and References [1], [2], [3], [4] and [5].

Nanotechnologies — Characterization of nano-objects using single particle inductively coupled plasma mass spectrometry

1 Scope

This document specifies parameters, conditions and considerations for the reliable detection, characterization and quantification of nano-objects in aqueous suspension by spICP-MS.

Particle number concentration, particle mass, particle mass concentration, particle spherical equivalent diameter, and number-based size distribution are considered the main measurands, but the technique also allows for determination of the dissolved element mass fraction in the sample. This document provides general guidelines and procedures related to spICP-MS application, and specifies minimal reporting requirements.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 18115-1, *Surface chemical analysis — Vocabulary — Part 1: General terms and terms used in spectroscopy*

ISO/TS 80004-6, *Nanotechnologies — Vocabulary — Part 6: Nano-object characterization*

ISO/TS 80004-8, *Nanotechnologies — Vocabulary — Part 8: Nanomanufacturing processes*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/TS 80004-6, ISO/TS 80004-8, ISO 18115-1 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
nano-object
discrete piece of material with one, two or three external dimensions in the nanoscale

[SOURCE: ISO 80004-1:2023, 3.1.5]

3.2
nanoscale
length range approximately from 1 nm to 100 nm

[SOURCE: ISO 80004-1:2023, 3.1.1]

3.3
particle
minute piece of matter with defined physical boundaries

Note 1 to entry: A physical boundary can also be described as an interface.

Note 2 to entry: This general particle definition also applies to nano-objects.

[SOURCE: ISO 80004-1:2023, 3.2.1]

3.4
nanoparticle
NP
nano-object with all external dimensions in the nanoscale

Note 1 to entry: If the dimensions differ significantly (typically by more than three times), terms such as "nanofibre" or "nanoplate" are preferable to the term nanoparticle.

[SOURCE: ISO 80004-1:2023, 3.3.4]

3.5
agglomerate
collection of weakly or medium strongly bound particles where the resulting external surface area is similar to the sum of the surface areas of the individual components

Note 1 to entry: The forces holding an agglomerate together are weak forces, for example, van der Waals forces or simple physical entanglement.

Note 2 to entry: Agglomerates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO 26824:2022, 3.1.2]

3.6
aggregate
particle comprising strongly bonded or fused particles where the resulting external surface area is significantly smaller than the sum of surface areas of the individual components

Note 1 to entry: The forces holding an aggregate together are strong forces, for example, covalent or ionic bonds, or those resulting from sintering or complex physical entanglement.

Note 2 to entry: Aggregates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO 26824:2022, 3.1.3, modified — Note 1 to entry has been adapted.]

3.7
spICP-MS
single particle inductively coupled plasma mass spectrometry
method using inductively coupled plasma mass spectrometry whereby a dilute suspension of nano-objects is analyzed, and the ICP-MS signals collected at high-time resolution, allowing particle-by-particle element detection at specific mass peaks and number concentration, size and size distribution to be determined

3.8
dwell time
time during which the ICP-MS detector accumulates signal corresponding to an individual reading along the time scan

Note 1 to entry: Following integration, the total ion count number per dwell time is registered as one data point, expressed in counts or counts per second.

3.9
transport efficiency
ratio of detected particle events to particles introduced

Note 1 to entry: Depending on the solvent and analyte combination used, transport efficiency can be considered equal to nebulization efficiency.

3.10
nebulization efficiency
ratio of the amount of nebulized sample reaching the plasma to the amount of the sample introduced

Note 1 to entry: It is often used interchangeable with "transport efficiency".

3.11
time scan
total acquisition time
duration of one replicate measurement

Note 1 to entry: This is typically set as 1 min, but can be extended to few minutes in order to increase the number of registered particle events.

3.12
event
signal intensity registered by mass spectrometer caused by the ion cloud from a single particle, aggregate or agglomerate

3.13
BED
background equivalent diameter
spherical equivalent diameter of the smallest particle that can be detected with spICP-MS

Note 1 to entry: Assuming spherical geometry, for particles of known chemical composition and density, the corresponding background equivalent diameter can be calculated (see 5.3) from the mass of the smallest particle that can be detected with spICP-MS, which in turn is determined by the instrument sensitivity along with the background signal, for the given dwell time.

3.14
particle number concentration
number of particles in the specific mass of a suspension

Note 1 to entry: Particle number concentration is typically expressed as g^{-1} or kg^{-1}.

Note 2 to entry: It can also be expressed per volume, e.g. L^{-1}.

Note 3 to entry: To convert between units, the density of the suspension must be determined.

3.15
m/z
mass-to-charge ratio
positive absolute value of the quantity formed by dividing the mass of an ion by the unified atomic mass unit and by its charge number

[SOURCE: ISO 18115-1:2023, 20.1]

4 Abbreviated terms

For the purposes of this document, the following symbols and abbreviations apply.

BIPM CCQM	Bureau International des Poids et Mesures Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology
DI	delegated institutes
DMF	dynamic mass flow
EM	electron-multiplier
ICP-MS	inductively coupled plasma mass spectrometry

ILC	interlaboratory comparison
IS	internal standardization
LOD	limit of detection
LOQ	limit of quantification
NMI	national measurement institute
PTA	particle tracking analysis
PHD	pulse-height distribution
QCM	quality control materials
Q-MS	quadrupole mass spectrometers
RM	reference materials
RTM	representative test material
SF-MS	sector-field mass spectrometers
TE	transport efficiency
TEM	transmission electron microscopy
TOF	time-of-flight
TRA	time resolved analysis
ULOQ	upper limit of quantification
ULOQsize	upper size limit of quantification
VAMAS	Versailles Project on Advanced Materials and Standards

5 Principles of operation

5.1 Introduction to spICP-MS

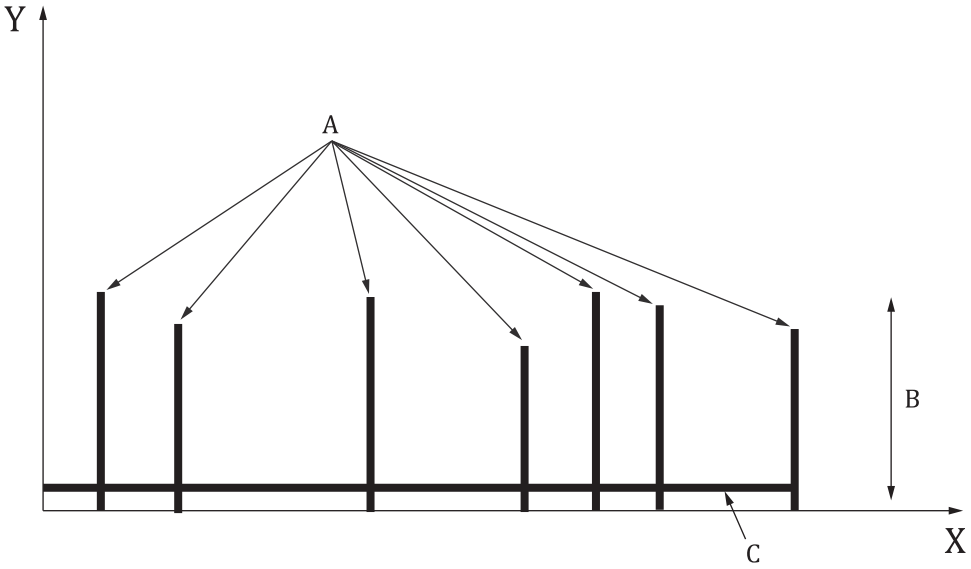
Since the introduction of spICP-MS by Degueldre in 2003,[1] the technique has increasingly gained popularity for nanoparticle analysis due to its high sensitivity, elemental specificity, often minimal sample preparation and the development of much improved instrumentation with fast, continuous data acquisition and software able to handle the large amount of data produced during spICP-MS experiments.[2]

In spICP-MS, a very dilute particle suspension is introduced into the instrument to minimize the possibility of more than one particle being detected in a single event (e.g. 2 or 3 particles). The inductively coupled plasma atomizes and ionizes the constituent analyte, generating discrete pulses of ions above the continuous background signal at a corresponding mass-to-charge ratio (m/z), lasting a few hundred microseconds. If the MS detector is set to acquire data with dwell times in the range from microsecond to low millisecond, individual or so called "single" particle events (signal intensity spikes) can be detected.

The number of events detected in each analysis window (time scan) is directly proportional to the number of nano-objects in suspension introduced into the ICP-MS, whilst the intensity of the measured signal is directly proportional to the mass of the measured element within the nano-object.

NOTE 1 Constituent particles as well as aggregates are counted as single objects, and in some cases, it can be challenging to resolve the two.

In addition, the mass concentrations of dissolved element fraction present in the sample alongside nano-objects can be determined from the same data, as illustrated in Figure 1.



Key

X time
Y event intensity, counts
A particle number-based concentration
B element mass per particle (~size)
C dissolved fraction

Figure 1 — Measurement principle of spICP-MS

The number of detected events in the time scan is related to the particle number concentration, whilst their intensity is related to the mass of element in the particles, which in turn can be converted to particle size. A dissolved element appears as constant background signal.

However, to obtain accurate particle number concentration and size values with spICP-MS, it is necessary to establish what portion of the acquired nano-objects is actually detected as particle events. This is a key parameter in spICP-MS analysis, called the transport efficiency ($\eta_{transport}$). The terms "transport efficiency" and "nebulization efficiency" are often used interchangeably and are related to sample introduction and nebulization processes in atomic spectrometry.

NOTE 2 Reference [3] suggested transport efficiency is a combination of nebulization and transmission efficiencies. In this regard, nebulization efficiency is the amount of introduced liquid actually converted into a spray and reaching the plasma (i.e., 100 % in case of a total consumption nebulizer). While the transmission efficiency is the extent of this spray effectively reaching the detector, i.e. after being desolvated, vaporized, atomized, ionized, passed into the mass spectrometer, and then collected on the ion-detector after mass separation. However, the issue of the different ionization, extraction, transmission and detection of particles versus dissolved elements can also be addressed alternatively from a calibration approach,[4] where the efficiency of these processes is included as a detection efficiency ($K_{\text{ICP-MS}}$) in Formula (1):

$$Y_{\text{R}} = K_{\text{R}}\, X^{\text{M}} = K_{\text{intro}}\, K_{\text{ICP-MS}} K_{\text{M}} X^{\text{M}} \tag{1}$$

where