ISO/FDIS 23484:2022(E)

ISO/TC 24/SC 4/WG 10

Secretariat: BSI

Date: 2023-02-16

Determination of particle concentration by small-angle X-ray scattering (SAXS)

2022-12-08

Edited DIS - MUST BE USED FOR FINAL DRAFT

Détermination de la concentration de particules par diffusion des rayons X aux petits angles (SAXS)

FDIS stage

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Published in Switzerland

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Foreword

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This document was prepared by Technical Committee ISO/TC 24, *Particle characterization including sieving*, Subcommittee SC 4, *Particle characterization.*

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Introduction

Small-angle X-ray scattering (SAXS) is a well-established method to obtain structural information on inhomogeneities in materials at the nanoscale, typically between 1 nm and 100 nm, and is thus perfectly suited for nanoparticulate systems. Under certain conditions, the upper limit can be extended to 200 nm and beyond. For sufficiently monodisperse spherical particles, the observed oscillations of the scattered intensity as a function of the momentum transfer, which is directly related to the scattering angle and the wavelength of the incident X-rays, enable the size determination of nanoparticles. In order to determine their concentration in a liquid (also called suspending medium, solvent or matrix), the absolute differential scattering cross section has to be determined, thus the ratio of the scattered intensity to the incident intensity. Assumptions on the particle shape are required, which can be based on microscopic techniques like electron microscopy. Furthermore, the electron density difference between the particles and the liquid needs to be known.

The concentration of nanoparticles, thus particles in the size range between about 1 nm to 100 nm, is one of the most important parameters for nanoparticle use in industry, medicine and research, and is expected to become relevant as well for regulatory purposes, especially in the pharmaceutic sector. The application of SAXS for the determination of the mean particle size and size distribution has been described in ISO 17867:2020. This document covers the extension to obtain the nanoparticle concentration as well from SAXS measurements. User-friendly commercial SAXS instruments are available worldwide from several manufacturers for both routine and more sophisticated analyses, and state-of-the-art research instruments are available at synchrotron radiation facilities.

As in all particle size measurement techniques, care is required in all aspects of the use of the instrument, collection of data, and further interpretation. Therefore, there is a need for a document that allows users to obtain good inter-laboratory agreement on the accuracy and reproducibility of the technique.

Since all illuminated particles present in the X-ray beam are measured simultaneously, SAXS results are ensemble and time averaged across all the particle orientations which are present in the sample.

Determination of ~~the~~ particle concentration by small-angle X-ray scattering (SAXS)

~~2~~1 Scope

This document deals with the application of small-angle X-ray scattering (SAXS) for the measurement of the particle concentration in suspensions. In this document, only the concentration of sufficiently monodisperse spherical particles is treated, which means that the width of the size distribution ~~should~~is typically ~~be~~ below about 50 % of the mean diameter. Here, the differential scattering cross section can be calculated based on the form factor, which depends only on the momentum transfer *q* and the particle radius *r*. Furthermore, this document is limited to dilute systems. A dilute system in the sense of SAXS means that particle interactions are absent. In case of long-range interactions (Coulomb forces between the particles), special care ~~has~~needs to be taken and a reduction of the concentration ~~might~~can be necessary.

~~3~~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 17867~~:2020~~, *Particle size analysis — Small angle X-ray scattering (SAXS)*

~~4~~3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

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

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

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

3.1
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: A particle can move as a unit.

Note 3 to entry: This ~~general particle~~ definition applies to nano-objects.

[SOURCE: ISO/TS 80004-6:2021~~(en)~~, 3.9]

3.2
particle size
linear dimension of a *particle* ~~(3.1)~~(3.1) determined by a specified measurement method and under specified measurement conditions

Note 1 to entry: Different methods of analysis are based on the measurement of different physical properties. Independent of the particle property actually measured, the particle size can be reported as a linear dimension, e. g. as an equivalent spherical diameter.

[SOURCE: ISO/TS 80004-6:2021~~(en)~~, 4.1.1]

3.3
particle size distribution
distribution of *particles* (3.1)(3.1) as a function of *particle size* (3.2)(3.2)

Note 1- to- entry:- Particle size distribution may be expressed as cumulative distribution or a distribution density (distribution of the fraction of material in a size class, divided by the width of that class).

[SOURCE: ISO/TS 80004--6:2021(en),, 4.1.2]

3.4
suspension
heterogeneous mixture of materials comprising a liquid and a finely dispersed solid material

[SOURCE: ISO/TS 80004-6:2021(en),, 3.13]

3.5
concentration
amount-of-substance of a component divided by the volume of the system

[SOURCE: ISO 18113-1:2022(en),, 3.2.12]

3.6
particle number concentration
number of particles per unit of volume of suspension

[ADOPTED: ISO 29464:2017(en), 3.2.131]

Note 1- to- entry:- The particle number concentration can also be given as number of particles per unit of mass of suspension. Literature values for the density of the liquid can be used for the conversion as, in most cases, the low content of particles for which this document is applicable will not affect the sample density significantly.

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[SOURCE: ISO 29464:2017, 3.2.131]

4 Symbols and abbreviations

The symbols and abbreviations used in this document are listed in Table 1.

Table 1 — Symbols

Symbol	Description	Unit (with prefix)
C	Particle number concentration	l^{-1}
$\bar{d}_{ln}$	Median of lognormal size distribution	nm
$\bar{d}_{num}$	Number-weighted mean particle diameter	nm
f_1, f_2	Atomic scattering factors	-
$g_{num}(r)$	Number-weighted particle size distribution	-
I_{out}	Primary beam intensity with sample	-
I_{in}	Primary beam intensity without sample	-
$I(q)$	Scattered intensity (or scattering intensity)	-
M	Molar mass	g/mol
N	Number of particles	-
N_A	Avogadro constant	mol^{-1}
$P(q, r)$	Particle form factor as functions of q-value and particle radius, r	-
q	Momentum transfer or q-value, magnitude of the scattering vector given by $q = (4\pi / \lambda) \sin \theta$	nm^{-1}
q_{min}	Minimum accessible q-value	nm^{-1}
q_{max}	Maximum accessible q-value	nm^{-1}
r	Particle radius	nm
r_e	Thomson radius	fm
$S(q,r)$	Structure factor as functions of q-value and particle radius, r	-
T	Transmission	-
t_o	Optimum sample thickness	mm
V	Volume of particle	nm^3
w	Sample thickness	mm
Z	Number of protons	-
λ	Wavelength of the incident X-rays in vacuum	nm
μ	Linear absorption coefficient	mm^{-1}
ρ	Mass density	g/cm^3
ρ_e	Electron density	nm^{-3}
ρ_{e_P}	Electron density of particles	nm^{-3}
ρ_{e_L}	Electron density of the liquid	nm^{-3}
$\Delta\rho_e$	Electron density difference	nm^{-3}
σ	Standard deviation of Gaussian size distribution	nm
$\frac{d\Sigma}{d\Omega}(q)$	Differential scattering cross section per volume	$cm^{-1}\ sr^{-1}$