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BSI Standards Publication

Nanotechnologies — Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation

bsi.

National foreword

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The UK participation in its preparation was entrusted to Technical Committee NTI/1, Nanotechnologies.

A list of organizations represented on this committee can be obtained on request to its committee manager.

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English Version

Nanotechnologies - Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation (ISO/TS 21362:2018)

Nanotechnologies - Analyse des nano-objets par fractionnement par couplage flux-force asymétrique et à force centrifuge (ISO/TS 21362:2018)

Nanotechnologien - Analyse von Nanoobjekten mit Hilfe von Asymmetrischer-Fluss-Feldflussfraktionierung und zentrifugaler Feldflussfraktionierung (ISO/TS 21362:2018)

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European foreword

The text of ISO/TS 21362:2018 has been prepared by Technical Committee ISO/TC 229 "Nanotechnologies" of the International Organization for Standardization (ISO) and has been taken over as CEN ISO/TS 21362:2021 by Technical Committee CEN/TC 352 "Nanotechnologies" the secretariat of which is held by AFNOR.

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Endorsement notice

The text of ISO/TS 21362:2018 has been approved by CEN as CEN ISO/TS 21362:2021 without any modification.

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 229, *Nanotechnologies*.

Introduction

The capacity to isolate and analyse diverse populations of nano-objects and their agglomerates or aggregates, often suspended in, or extracted from, complex matrices, is critical for applications ranging from materials discovery and nanomanufacturing to regulatory oversight and environmental risk assessment. Furthermore, the ability to characterize these analytes with minimal perturbation of their natural or native state is highly desirable. The list of available techniques capable of achieving such objectives is relatively short, and while all techniques have advantages and disadvantages, and no single technique is solely adequate or appropriate for all possible applications and materials, a group of related separation techniques known collectively as field-flow fractionation (FFF), conceptually proposed by J. Calvin Giddings in 1966[1], offers many advantages for nanotechnology applications. In FFF, the analyte, suspended in a liquid medium, is fractionated by the application of a field (e.g. flow, centrifugal, electric, thermal-gradient, magnetic) perpendicular to the direction of flow of the analyte and mobile phase eluting through a thin defined channel. Separation occurs when the analyte responds to the applied field, such that populations with different response sensitivities reach equilibrium positions (i.e. in equilibrium with diffusional forces) higher or lower in the laminar flow streamlines perpendicular to channel flow, thus eluting differentially.

Among the FFF variants, asymmetrical flow FFF (variously abbreviated in the literature as AF4, A4F, AFFFF, AfFFF or AsFlFFF) and centrifugal FFF (abbreviated as CF3, also called sedimentation FFF and abbreviated as SdFFF), are available commercially and have been most widely adopted in the nanotechnology field (for convenience and simplicity, the abbreviations AF4 and CF3 are used throughout this document). AF4 is arguably the most versatile technique with respect to the wide range of applications, materials and particle sizes to which it has been applied. Symmetrical flow FFF (fFFF), the original "flow-based" technique as first described in 1976[2], has been supplanted commercially by AF4, introduced in 1987[3], due to several advantages, including a simpler channel design, the ability to visualize the sample through a transparent top channel wall, and reduced analyte band width. The theory and application of CF3 as it is presently applied was described by Giddings and coworkers in 1974[4], although a centrifugal field-based FFF system was first developed and tested independently by Berg and Purcell in 1967[5]. Other FFF field variants, such as thermal, electrical and magnetic, provide unique capabilities, but have been limited in the scope of their applications vis-à-vis nanotechnology or commercial availability.

Where FFF was once predominantly the domain of specialists, these instruments are now commonly and increasingly utilized in government, industry and academic laboratories as part of the nano-characterization toolbox. Two factors are driving this increase in nanotechnology utilization: maturation of commercial instrumentation and versatility with respect to coupling a wide range of detectors to FFF systems. In the latter case, recent developments have led to the use of highly sensitive elemental detectors (e.g. inductively coupled plasma mass spectrometer or ICP-MS), which offer enhanced characterization and quantification for many materials. Additionally, traditional concentration or sizing detectors, such as ultraviolet-visible (UV-Vis) absorbance, fluorescence, multi-angle light scattering (MALS) and dynamic light scattering (DLS), yield online data for eluting populations, and theoretically provide more accurate information than obtainable using off-line measurements of unfractionated polydisperse systems. The measured retention time of an eluting peak can also be used to determine the hydrodynamic size by AF4 based on theoretical relationships or calibration with a known size standard. CF3 has the unique capacity to rapidly separate species of the same size but differing in density.

Although FFF based techniques have the capacity to separate and characterize analytes over an extremely broad size range, from about 1 nm up to tens of micrometers, this document focuses primarily on materials in the nanoscale regime and their associative structures. The basic underlying principles, experimental approach, and hardware described here can be more broadly applied.

While this specification includes the most common online detection schemes for nano-object analysis, other less common forms of detection have been utilized or reported in the literature, including differential refractometry (primarily used for macromolecular analysis), particle tracking analysis, graphite furnace atomic absorption spectrometry, single particle ICP-MS, and small-angle X-ray scattering. This number is likely to grow in the future, as new techniques emerge and existing ones are modified and evaluated for coupling to FFF.

In order to develop and validate methods for application of FFF to the analysis of nano-objects and their agglomerates or aggregates, and to properly report experimental results and conditions in order to enable reproducibility across laboratories, it is critical to specify key parameters to be controlled and reported. These parameters encompass all aspects of FFF methodology, including sample/analyte, instrumentation, fractionation, calibration, qualification, performance specifications, measurement uncertainty, and data analysis. This document identifies the key parameters and lays out a general approach to method development for AF4 and CF3.

General references and further reading on FFF theory and practise, as well as AF4 and CF3 applications to nanotechnology, can be found in the Bibliography[6]-[18].

Nanotechnologies — Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation

1 Scope

This document identifies parameters and conditions, as part of an integrated measurement system, necessary to develop and validate methods for the application of asymmetrical-flow and centrifugal field-flow fractionation to the analysis of nano-objects and their aggregates and agglomerates dispersed in aqueous media. In addition to constituent fractionation, analysis can include size, size distribution, concentration and material identification using one or more suitable detectors. General guidelines and procedures are provided for application, and minimal reporting requirements necessary to reproduce a method and to convey critical aspects are specified.

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/TS 80004-1, *Nanotechnologies — Vocabulary — Part 1: Core terms*

ISO/TS 80004-2, *Nanotechnologies — Vocabulary — Part 2: Nano-objects*

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

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/TS 80004-1, ISO/TS 80004-2, ISO/TS 80004-6 and the following apply.

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

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

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

3.1
nano-object
discrete piece of material with one, two or three external dimensions in the nanoscale (from approximately 1 nm to 100 nm)

Note 1 to entry: Generic term for all discrete nanoscale objects.

[SOURCE: ISO/TS 80004-2:2015, 2.2, modified — In the definition, "(from approximately 1 nm to 100 nm)" has been added. Note 1 to entry has been changed.]

3.2
nanoparticle
nano-object with all external dimensions in the nanoscale where the lengths of the longest and the shortest axes of the nano-object do not differ significantly

Note 1 to entry: If the dimensions differ significantly (typically by more than 3 times), terms such as nanofibre or nanoplate may be preferred to the term nanoparticle.

[SOURCE: ISO/TS 80004-2:2015, 4.4]

