Frontiers and Standardization Trends of Particle Measurement and Analysis Technology

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This report summarizes the frontiers of measurement and analysis technologies related to particle size, which is a fundamental and extremely important Physico-chemical property of fine particles, with a focus on compliance with regulations in Europe, where leading technical standards are being introduced, as well as recent topics in standardization. In the case of particle size measurement in air, the calibration of detectors, which is directly related to the regulations, and in the case of particle size measurement in liquid, the number-based size distribution, which is the basis of the EC definition of nanomaterials, were introduced, including attempts to obtain international equivalence by using various measurement methods.

Introduction

The specific properties of atomic and molecular ensembles have been used for a long time. It is not easy to identify the beginning, but it is widely known that some stained glass elements that had a great influence on medieval European architecture use fine particles of color.

As the progress of measurement and analysis techniques has led to reports that fine particles exhibit properties that differ from those of their atomic (microscopic) and bulk (macroscopic) constituents, along with their size, research and development in the area of mesoscopic science and cluster science have been actively promoted for the understanding and active use of these characteristics.

Many effects of size on properties in both chemical and physical fields have been reported, for example, the catalytic activity of platinum particles varies depending on particle size, and the effects of size on the properties have been noted. In addition to composition and structure, the importance of size (spatial spread) parameters have been highlighted. The concept of nanotechnology was proposed in the mid-1970s for the expression and application of new physical and chemical properties based on size. Since then, research and development on nanotechnology has been promoted in various countries, starting with the National Nanotechnology Initiative in the United States, and many products using nanotechnology are now found around the world. On the other hand, there is a need to establish reliable particle size measurement and analysis techniques, as there is also a demand to evaluate the effects of specific physical and chemical properties that are based on size on health and the environment.
In this report, the trend of standardization is outlined, focusing on measurement technology to obtain accurate particle size and distribution.

Definition of nanomaterials in Europe

On June 10 2022, the European Commission (EC) issued a final recommendation[1] on the definition of nanomaterials. The recommendation amends the official definition of nanomaterials for use in regulations (2011/696/EU) issued in 2011. While ISO had previously specified the size and structure of individual objects (ISO/TS8004-1), the EC definition includes the size range and distribution of the number of objects in a specific quantity, which is a more advanced definition when dealing with real materials. However, the difficulty in determining the size distribution including the constituent particles of the aggregate has caused confusion to both material manufacturers and measurement experts. For the effective use of nanomaterials definition, large-scale projects such as NanoDefine were promoted in the European Union (EU) and an intensive research was conducted by the Joint Research Center (JRC) of the EC. The final recommendations, which have improved the practicality based on the findings obtained

through them, are as follows. The full definition of new nanomaterials is quoted below, considering the possibility of their use in various regulations in the future.

(1) 'Nanomaterial' means a natural, incidental or manufactured material consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates, and where 50% or more of these particles in the number-based size distribution fulfil at least one of the following conditions:
   (A) one or more external dimensions of the particles are in the size range 1 nm to 100 nm.
   (B) the particle has an elongated shape, such as a rod, fibre or tube, where two external dimensions are smaller than 1 nm and the other dimension is larger than 100 nm;
   (C) the particle has a plate-like shape, where one external dimension is smaller than 1 nm and the other dimensions are larger than 100 nm.

In the determination of the particle number-based size distribution, particles with at least two orthogonal external dimensions larger than 100 μm need not be considered.
However, a material with a specific surface area by volume of < 6 m^2/cm^3 shall not be considered a nanomaterial.

(2) For the purposes of point (1), the following definitions apply:

   (A) 'particle' means a minute piece of matter with defined physical boundaries; single molecules are not considered 'particles'
   (B) 'aggregate' means a particle comprising of strongly bound or fused particles
   (C) 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual

Measurand and measurement procedure

In the report published by JRC in 2012 titled "Measurement methods required to implement EC Definitions for Nanomaterials",[2] the currently used particle size measurement methods are classified into three categories: ensemble methods (DLS, SAXS, etc.) to obtain overall information on a certain amount of sample as the size measurement method of nanoparticles, counting methods (TEM, SEM, AFM, etc.) to measure each component separately, and fractionation methods (FFF, CLS, SEC, etc.) to evaluate each size of separated fractions. The introduction of the classification is an excellent analysis of measurement methods. Based on the characteristics of each method, the use of multiple measurement techniques will not only enable the acquisition of the necessary information accurately, but will also enable new analytical evaluations. It is important to accurately grasp and understand the applicability and the measured values.

Even if the same particle size is measured, the details of the measured quantity often vary depending on the method used (method dependent). The main reason for the method dependence is the difference in the physical phenomena used. In order to compare the results of counting nanomaterials individually with the results of evaluating them as averaged value in a space (ensembles), it is necessary to examine the details of each measurement principle. Furthermore, even with the same counting method, there is a difference (Method dependent), for example, the equivalent circle diameter in TEM and the electric mobility equivalent sphere diameter obtained by DMAS. By utilizing the difference in measurement quantity, applications such as obtaining a quantitative index of particle shape from the relationship between mean particle diameter and particle size distribution can be expected.

Moreover, it is known that the results of the same measurement method differ according to the measurement procedure (protocol dependent). The main reason for the procedural dependence is that the quantity of measurement actually detected depends on the measurement parameters. For example, when the palm is slowly immersed in the water, this action may cause the hand to feel mainly water temperature or water viscosity. If the palm of the hand was used to hit the surface of the water quickly, the main sensation of the hand would be the surface tension of the water. This means that simply changing the speed of movement of the hand used for detection (measurement parameters) has changed the amount of measurement detected (physical quantity).

It is paramount to consider the physical phenomena used, the measurement procedures applied, and the condition of the object, and to ensure that the instrument is properly calibrated and that the measurement procedures are validated in order to achive accurate measurement analysis of particle sizes.

Airborne particle measurement and standardization trends

The state in which tiny particles are suspended in the gas phase is called an aerosol. In particular, the composition, size, and quantity of particulate matter suspended in the air have been monitored for a long time from the viewpoint of environmental protection and occupational safety. Measurements of large particles, such as PM2.5, are

carried out by using inertial forces to remove coarse particles using impactors or cyclones, and then by collecting particles from a constant volume of the atmosphere with a filter and evaluating their mass. The particulate concentration evaluated by these methods is expressed as mg/m3 and is called the mass concentration. Together with the idea that the toxicity of particles increases with the total mass of the exposed particles, the aerosol of large particles is better evaluated by mass, and the European automobile emission regulations for particulate matter were limited to mass standards only until Euro5 in 2009. As the amount of particulate matter contained in exhaust gases decreased due to the advancement of material collection technology, it became necessary to evaluate the quantity standards for monitoring more dilute particles. Introduced in 2011, Euro5^{+} introduced a number standard in addition to the mass standard for particulate matter in diesel exhaust emissions. The number of solid particles in the exhaust gas is measured by the particle counter after removing the volatile component particles by heating dilution. The Condensation Particle Counter (CPC) is usually used as a particle counter.

In principle, CPC has an excellent property to provide stable detection efficiency for a wide range of particle sizes, but with decreasing particle size, the detection efficiency decreases rapidly. This is mainly due to insufficient particle growth due to the adsorption of atmosphere molecules onto the surface of the fine particle at the lower detection limit. For this reason, the detection efficiency of particles near the lower limit of detection is specified for use in regulation. The detection efficiencies of the particles regulated in Euro5^{+} /Euro6 and planned to be introduced in Euro7 are shown in Table 1.

Table 1 Requirements of particle detection efficiencies under European vehicle emissions controls

	Year	Particle Detection Efficiencies
Euro5^{+}	2011	50%±12%@23 nm Over 90%@41 nm (SPN23)
Euro6	2014	
Euro6a	2017	
Euro7	2025	65%±15%@10 nm Over 90%@15 nm (SPN10)

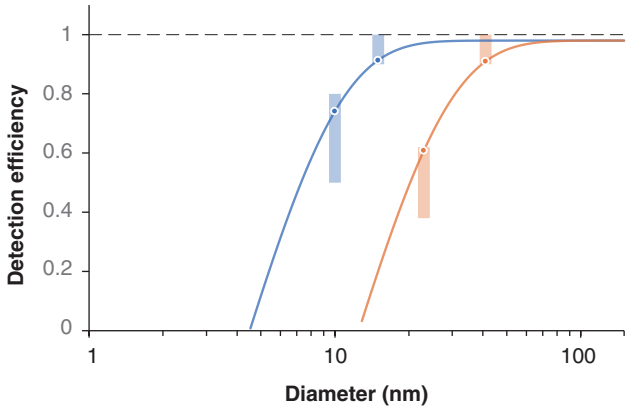


Figure 1 Requirements of particle detection efficiencies under European vehicle emissions control (indicated by bands) and typical detection efficiency curves of a CPC. Orange is for SPN23, blue is for SPN10 (planned).

It should be noted that Euro7, which is scheduled to be introduced in 2025, is considering extending the lower limit from the number of solid particles with a particle size of 23 nm or greater to the number of solid particles with a particle size of 10 nm or greater.

Figure 1 shows each demand value (indicated by band) and a typical CPC detection efficiency curve. Both SPN23 and SPN10 require advanced calibration to meet the required values.

The uncertainty of the detection efficiency calibration of CPC and the standard Faraday-cup aerosol electrometer has already been reported.[3] Figure 2 shows the general calibration scheme of CPC.

In the particle generator, it is necessary to generate a stable number of particles at the target particle size. The electrospray method, which generates small and uniform sized droplets, is often used for particle generation. When using a capillary with an inner diameter of 25 μm , the droplet diameter is about 150 nm to 200 nm. In the calibration of detection efficiency of CPC for measuring automobile exhaust emissions, poly-alphaolefin (Pole-α-Olefin:PAO) dissolved in alcohol is usually used. The detection efficiency of CPC is also affected by the chemical properties of the particles, especially near its lower limit. PAO, a hydrocarbon, can be expected to provide detection efficiency comparable to that of particulates in automobile exhaust gas. By adjusting the concentration of PAO solution, the size of PAO particles after the evaporation of alcohol solvent can be controlled.

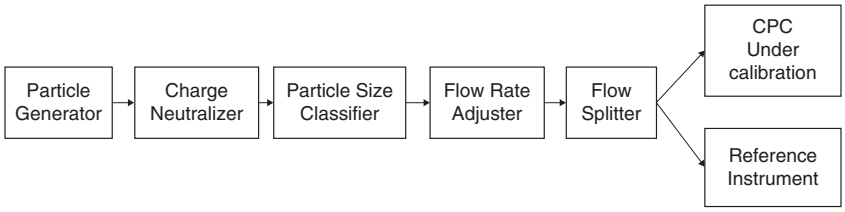


Figure 2 Schematic representation of the CPC calibration setup.

The droplet is electrically neutralized and the solvent-volatilized particles are monodispersed to the size used for checking the detection efficiency in the Particle Size Classifier. The solvent evaporation must be completed and the particle size must be stable before it is introduced into the particle size fractionator, and the verification is one of the key factors for accurate detection efficiency. The differential mobility analyzer (DMA) is used for the particle size fractionator. Since the particle size value in the device is the horizontal axis of Figure 1, it is necessary to fully understand and minimize the uncertainty. Based on a detailed analysis of the uncertainty of the DMA particle size calibration, the AIST has been examining the supply of DMA size calibration with sufficient uncertainty from both the calibration with DMA reference equipment and the calibration via the reference material.

Recently, the miniaturization and uniformity of droplets generated from inkjet nozzles has dramatically improved due to the demand for improved print quality. The inkjet technology capable of producing minute and uniform droplets has been widely applied in various fields such as pharmaceutical manufacturing. It is also widely used in the field of measurement analysis for examples, sample preparation by ICP-MS, ionization of samples, and spray drying method.

The Inkjet Aerosol Generator (IAG) is being developed to establish a single dispersion particle count standard.[4] In order to utilize this method, it is necessary to study the stability of the produced nuclei and the precipitation of impurities in the nucleation, which is caused by the increase of the contamination opportunity of the solution due to the complicated path, especially when generating small particles.

Since the number of particles generated in IAG can be controlled digitally, it is possible to calibrate the detection efficiency by directly connecting the IAG and CPC in the grain size region where the size, stability and reproducibility of the particles produced are sufficiently evaluated. IAG has already been used to calibrate an OPC(Optical Particle Counter). ISO 21501-4, Determination of particle size distribution - Single particle light interaction methods - Part 4: light scattering airborne particle counter for clean spaces is currently being developed in ISO/TC 24/SC 4 and will be added to the IAG as one of the calibration methods. As of July 2022, the addendum is in DAMD state, but will be issued as Amd in 2023.

The use of IAG greatly simplifies the calibration set-up of Figure 2, and it is expected that a calibration system with increased portability will be developed depending on the required measurement conditions and accuracy, and that a standard embedded measurement system with a calibration system built into the measurement system will be realized.

In addition, IAG is expected to use biomaterials and markers in the solution as a reference for the composition and functionality of the particles produced.

Dispersed particles in liquid and standardization trends

The measurement and analysis methods of dispersed particles in liquid vary widely, including the measurement method of dispersed particles on solid surfaces. For this reason, differences in measurement results due to the differences in measurement volume described in Chapter 3 are often considerable. JRC published a report[5] in 2019 as points to consider in the assessment of particulate materials according to the European Commission's Recommendation on a definition of nanomaterial. The report includes results of evaluating particle sizes using various methods for European reference materials with different dispersion properties. It is reported that the difference between the measurement methods is small for samples with spherical particles close to monodisperse, whereas the difference between the measurement methods is significant for samples with large particle size distributions. This is because the underlying physical principle of each measurement usually only works for ideal sample systems with monodisperse particle sizes.

In real materials, due to the spread of the particle size distribution, attention must be paid to realize a reliable measurement and analysis of particle size. Results of DLS and LD, the typical ensemble methods for samples with bimodal particle sizes, are introduced. The sample used is a 1:1 (mass based) mixture of PSL (PolyStirene Latex) standard particles with a particle size of 70 nm and 180 nm. SEM images of each PSL standard particle are shown in Figure 3.

It is shown that both PSL particles are spherical and have extremely sharp particle size distribution. Given that the density of PSL is constant regardless of particle size, there

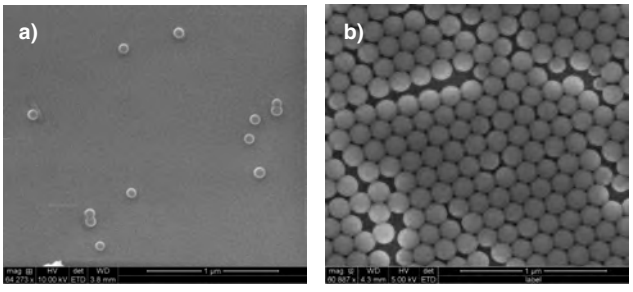


Figure 3 Electron micrographs of PSL reference particles.
a) d = 70 nm, b) d = 180 nm

are about 17 times as many 70 nm PSL particles in the mixed solution adjusted at a mass ratio of 1:1 as there are 180 nm PSLs on number basis.

Figure 4 shows the particle size distribution of particles in mixed solutions evaluated by DLS and LD. In Figure 4, a unit of vertical axes of two measurements is different, but the size distribution of the two peaks cannot be reproduced in both measurements. This is because the intensity of the light scattered from the particles is proportional to the sixth power of the particle size, so strong scattered light from large particles can shield the effect of weak scattered light from small particles.

Although DLS and LD have excellent features as ensemble methods, for accurate analysis of materials with wide particle size distribution, it is necessary to compose the results obtained by dividing them into multiple fractions with narrow particle size distribution. A case has been reported that the combination of Field-Flow Fractionation and DLS reproduce a particle size distribution of bimodal samples adequately.[6]

As the definition of nanomaterials in EC is based on the size distribution of the particles on a number basis, verification of the reproducibility of measurements across laboratories and countries for number-based concentrations is being conducted in various frameworks. The largest case is a comparison of gold nanoparticle number concentrations between laboratories conducted by the Versailles project on Advanced MAterials and Standards (VAMAS), with the participation of 50 research institutions from around the world.[7] A gold nanoparticle with a particle size of 30 nm dispersion in water was used for the sample. Preliminary studies by CLS and SEM showed that the gold nanoparticles stabilized by citric acid of the sample are almost spherical and have very narrow particle size distribution. Measurement methods used for comparison were SAXS, CLS, UV-Vis, PTA, and spICP-MS. The results was discussed by comparing the counting method (PTA and spICP-MS) and population-averaging methods (SAXS, UV-Vis and CLS).

What is interesting about the results is that the population-averaging method shows high reproducibility between laboratories. The relative standard deviations of SAXS, CLS, and UV-Vis reported were 2.6%, 11%, and 1.4%, respectively. The Ensemble method, in particular, showed high reproducibility in the evaluation of the sample at the ideal number concentrations, beyond the laboratory. This is attributed to the relatively simple and robust measurement set-up and a measurement protocol of the method. CLS is considered technically more complicated and requires more detailed calibration. In contrast, the reported inter-laboratory reproducibility of the counting method were significantly lower than those by a population-averaging method. Inter-laboratory reproducibility of the spICP-MS and PTA are 46% and 68%, respectively, whilest an intra-laboratory reproducibility of those are about 12% in relative standard deviation. The reason for the poor reproducibility between laboratories was considered including the effect of the dilution process at a sample preparations, but no clear interpretation has been reached. In order to improve the inter-laboratory reproducibility by counting method, it has been pointed out that standardization of the measurement and data processing procedures including sample preparation is important. In flamework of the meter convention, pilot studies and international key comparisons using monodisperse gold nanoparticle dispersants and bimodal gold nanoparticle dispersants are being carried in the CCQM (Consultative Committee for Amount of Substance : Metrology in Chemistry and Biology). It is expected that a metrology and analysis base with higher accuracy and international consistency for the number concentration measurement of nanoparticles will be established.

The international standardization of particulate measure-

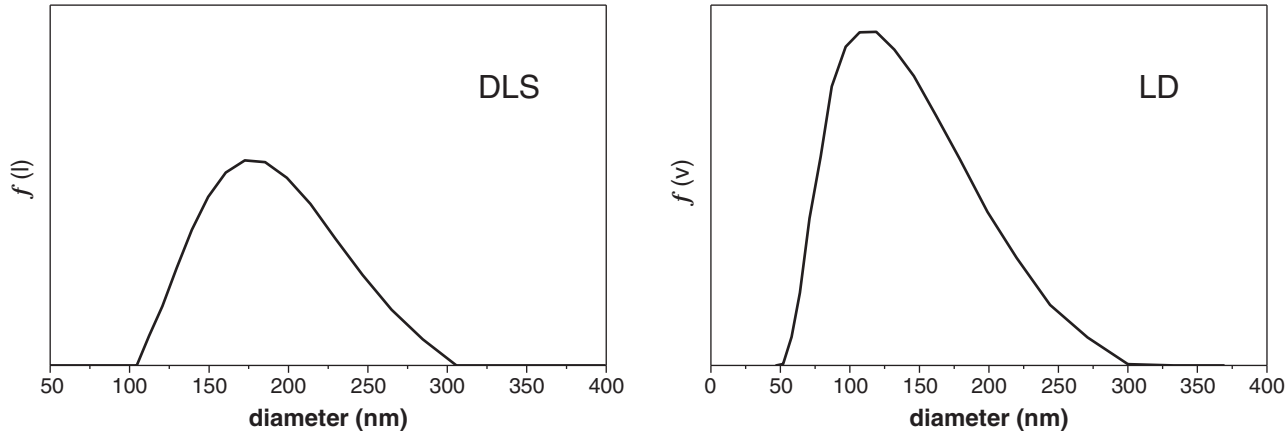


Figure 4 Particle size distributions of bimodal reference sample evaluated by DLS and LD.
DLS(Dynamic Light Scattering), LD(Laser Diffraction)

ment and analysis is mainly carried out in the ISO TC 24/SC 4 or ISO TC 229/JWG 2 (for AFM measurement techniques, ISO TC 201/SC 9). The PTA and spICP-MS methods, which are important for measurement and characterization of a number-based size distributions of nanoparticle, already have international standards (ISO 19430:2016, ISO/TS 19590:2017, respectively). Both have been updated on a regular basis and are currently undergoing revisions with recent technical progresses.

At the usage of counting method for particle number concentration, PTA has a higher potential to simplify a measurement protocol by automation, compared to the microscopic method. It is expected that the PTA can be applied to a in line usage.

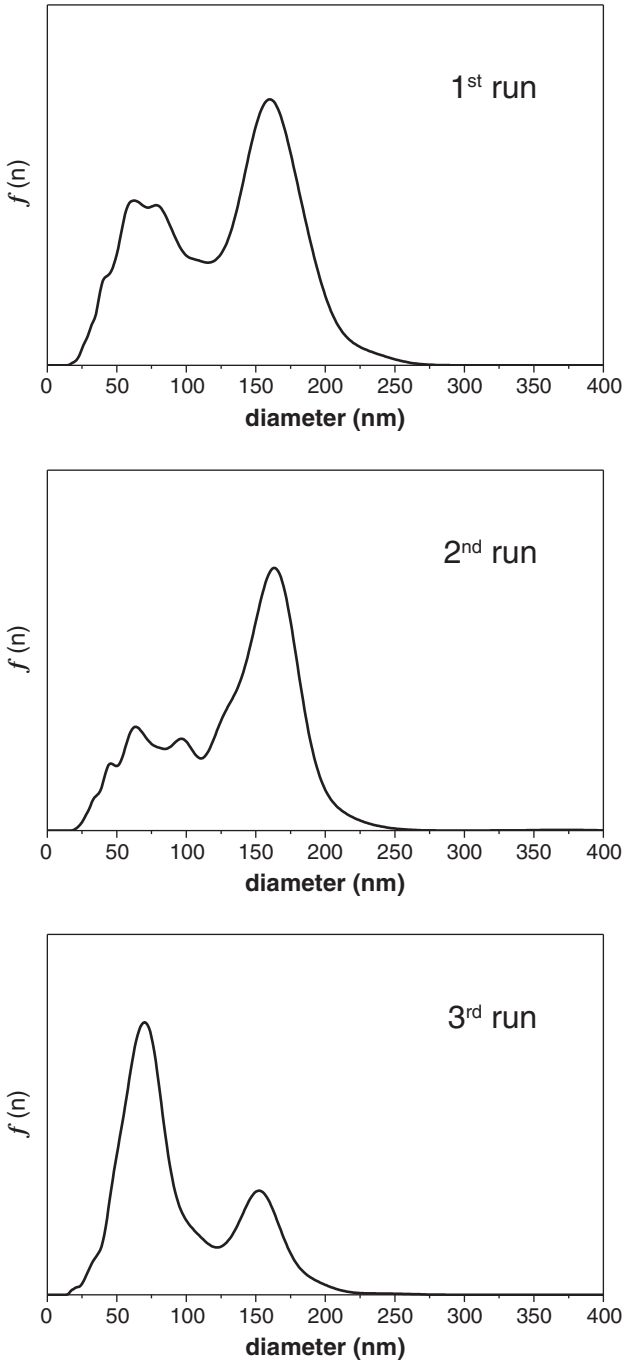


Figure 5 Number based particle size distribution evaluated by PTA method for a bimodal reference sample.

Figure 5 shows measurement results of a mixture of the standard particles of PSL with a particle size of 70 nm and 180 nm with a mass ratio of 1:1 by PTA.

The size distribution shows that it is bimodal, but the concentration axis varies from measurement runs. Particle size distribution by sigle run does not reflect the number concentration at the preparation. Since the particles in an area to measure by PTA is far fewer than the whole sample as similar in other microscopic methods, it is important to confirm that the data accumulation is statistically significant as in other microscopy methods.

The selection of specific surface areas is first used to determine the conformity of EC to the nanomaterials definition, but if the final decision is doubtful, measurement analysis by an electron microscope is required to confirm the constituent particles of the aggregate. In the use of electron microscopes, it is necessary to use statistically correct standardized procedures for the sample preparation and the analysis of results. ISO 21363:2020 (Nanotechnologies - Measurements of particle size and shape distributions by transmission electron microscopy) can be used for TEM, and ISO 19749:2021 (Nanotechnologies - Measurements of particle size and shape distributions by scanning electron microscopy) can be used for SEM. .

These international standards are also cited in OECD Test Guideline 125 (Nommaterial Particle Size and Size Distribution of Nanomaterials, 30 June 2022).

Conclusion

The recent topics on particle measurement/analysis technology and standardization were summerized, mainly in response to European regulations, where leading technical standards are introduced. Since 2011, when the first edition of the definition of nanomaterials was proposed by EC, the detailed understanding of particulate measurement/analysis and the improvement in the reliability of the measurement results have been remarkable.

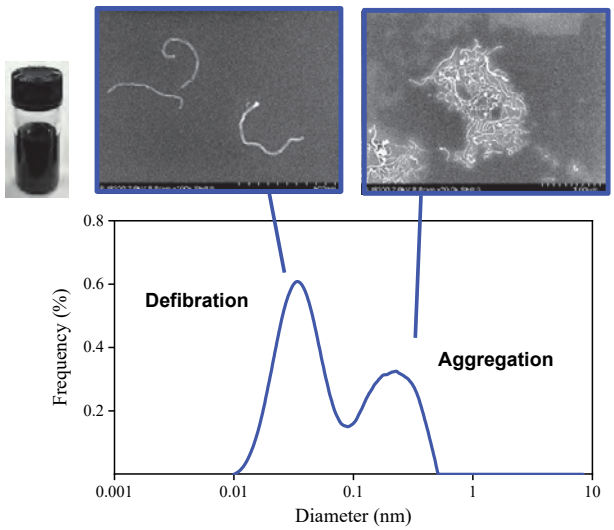
In 2021, AIST has established a cooperative research laboratory, HORIBA Institute for Particle Analysis in AIST TSUKUBA(HIPAA), in the national metrology institute of Japan (NMIJ). Major aims of the HIPAA is to develop a world leading particle measurement systems and put them into practical use. The activity has been started with the themes of developing a particle measurement system to comply with stricter environmental regulations, and an analysis and evaluation system for nanomaterial charac-

teristics. In the development of particle measurement systems, an important knowledge is being obtained for the accuracy improvement and system simplification for smaller particles measurement in areas such as PM2.5 and automobile exhaust particles, where further tightening of regulations is expected in the future to solve environmental issues. On the other hand, in the development of a system for analysis and evaluation of nanomaterial properties, a detailed study using carbon nanotubes and cellulose nanofibers through comparisons with microscopic observation is being performed in order to establish reliable applications for centrifugal particle size distribution measurement systems. Results have been obtained that lead to high-resolution particle size analysis by centrifugal sedimentation, which is difficult to achieve with conventional scattering methods (Figure 6). Furthermore, in promoting the utilization and practical application of these results, it is expected that results will be created to expand the fields of application by taking characteristics of the cross-disciplinary nature of particle measurement technology.

In recent years, DX (Digital Transformation) has been promoted worldwide, aiming to generate new knowledge by accumulating measurement and analytical data. The principle of FAIR (Findable, Accessible, Interoperable, and Reusable) has been proposed for sharing data that is important in DX. The details of FAIR principles have been discussed in various communities, but it is important that the data should be stored with sufficient metadata, accessible and understandable in standard ways, and that the traceability of the data is clearly described.

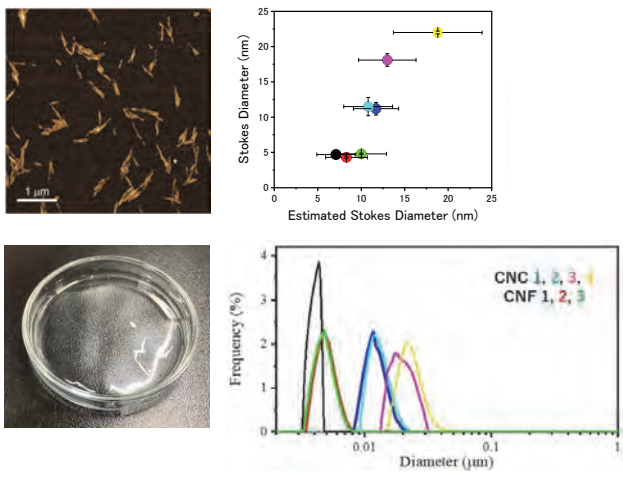
Application development of Centrifugal Nanoparticle Analyzer in HORIBA Institute for Particle Analysis in AIST TSUKUBA

a)



a) Carbon Nano Tube : Particle size distribution and electron microscope images.

b)



b) Nanocellulose: Particle size distribution and correlation with AFM.

Centrifugal Nanoparticle Analyzer

Since fine particles are used in a wide range of technical fields, information required for measurement and analysis of particles is diverse. Reliable shared data, stored and accumulated with sufficient metadata based on a detailed understanding of measurement and analysis techniques, is expected to lead to breakthrough applications of fine particles via DX. It is hoped that the use of excellent instrumentation and well-studied measurement protocols will enable cross-field interoperability of measurement results, leading to the understanding and utilization of noble characteristics of fine particles.

* Abbreviation for measurement method
  AFM(Atomic Force Microscopy),
  CLS(Centrifugal Liquid Sedimentation),
  CPC(Condensation Particle Counter),
  DMA(Differential Electrical Mobility Analyzer),
  DLS(Dynamic Light Scattering),
  ICP-MS (Inductively Coupled Plasma – Mass Spectroscopy),
  LD(Laser Diffraction),
  PTA(Particle Tracking Analysis),
  SAXS(Small-Angle X-ray Scattering),
  SEM(Scanning Electron Microscopy),
  spICP-MS(Single Particle ICP-MS),
  TEM(Transmission Electron Microscopy),
  UV-Vis(Ultra Violet - Visible)

* Editorial note: This content is based on HORIBA's investigation at the year of issue unless otherwise stated.

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