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Publishable Executive Summary

The present document shows a summary of the most relevant characterization techniques used to measure particle sizes and size distribution. These techniques are classified in three main approaches depending on the particle size distribution (PSD) analysis, which are ensemble, separation and counting methods. Each of the methods explained in the present document are based on different physical principles and present their own advantages and limitations. Only few of the techniques reviewed are valid for online/inline analysis.

Relevant characterization techniques for nanoprocesses monitoring

Many tools based on different physical principles are currently available to measure particle sizes in the range of 1 nm to hundreds of microns. They can be classified in three main approaches with regards to particle size distribution (PSD) analysis: ensemble, separation and counting methods.

1. Ensemble methods

In these ensemble methods, the particles over a range of sizes are measured all at once, without any separation or individual counting (Figure 1).

Figure 1. Principle of PSD measurement by ensemble methods.

In general, ensemble methods are often "easy" and "simple" to operate. Dilution of samples is needed (to avoid multiple signals). Ensemble methods need limited to extended sample information such as shape, viscosity, density (distribution) and light absorption. Often a broad size range can be measured, but with extreme low resolving power. The data (automated) evaluation is complex: PSD is modelled and results depend on the model used (including dn/dc). Among the ensemble methods, the following ones can be distinguished:

1.1   Dynamic light scattering (DLS) / Quasi-elastic light scattering (QELS)[1]

Off-line monitoring technique to measure mono and polydisperse nanoparticles. The hydrodynamic size of the particles is measured by determination of the diffusion coefficient. Both the size and size distribution (polydispersity) of particles undergoing Brownian motion are analysed. The analysis is carried out in a cuvette.

The minimum measurable size depends on the laser wavelength and power, sensitivity of the detector, sample concentration and scattering signal (scattering difference between dispersant and continuous phase). Typically, from few nm up to micron range depending on the particles.

The concentration range for measurements is obtained as the range where the average Z value stays nearly constant. Too low or high concentrations may give distortions / bad results. Usually 1-10 mg/mL as a starting point. Concentration study is done for particle system. The pH range that can be measured depends on the cuvette to be used.

The accuracy is negatively affected by non-spherical particles due to the determination of the equivalent spherical hydrodynamic diameter. Photon correlation function gives implicit information about the particles hydrodynamic radius. Measurement time ranges from few seconds up to few minutes.

In conclusion, it is a fast, non-destructive and simple method that needs small sample quantity with no (or low) previous sample information. However, it has an extremely low resolving power, average sizes more than PSD are measured, and small quantities of nanoparticles are hidden in the large quantity, apart from small particles being hidden by large ones due to higher scattering given by the larger particles.

Commercially available equipments: Zetasizer by Malvern Panalytical, DynaPro Plate Reader by Wyatt Technologies, nanoPartica by Horiba, VASCO[TM] nanoparticle size analyzer by Cordouan,

Mobius by Wyatt Technology, Nanophox by Sympatech GmbH, NanoLab 3D by LS Instruments, Light Sizer by Anton Paar GmbH, NANO-Flex by Colloid Metrix GmbH, IG-1000 by Shimadzu.

1.2 Static light scattering (SLS) / Multi-angle light scattering (MALS)[2]

Off-line monitoring technique to measure particles dispersed in a liquid.

It uses Mie-Theory to compute the mean spherical diameter using information of backscattered and transmitted light. Size, concentration and hydrodynamic diameter measured during sedimentation.

The measurable nanoparticles size goes from 10 nm ~ 1 mm, and the concentration range up to 95% v:v. The pH range that can be measured depends on the cuvette to be used.

Not suitable for strongly absorbing (e.g. metallic) nanoparticles with certain plasmon resonance frequencies. Size range depends on optical setup and detector angles. It is possible to measure at very high concentrations (SMLS). Since scattering depends on the refractive index (RI) of the particles, this information may be required.

In summary, it is a fast, non-destructive and simple technique to measure broad dynamic range (10 nm to millimeter). However, it has a low resolving power (whole PSD is represented by limited set of data points), the accuracy depends on parameters (RI, absorption/optical properties, shape) and large particles overshadow small particles very easily.

Commercially available equipments: Zetasizer by Malvern Panalytical, DAWN (Wyatt Technologies), Partica Series by Horiba, PN3609 by Postnova.

1.3 Laser Diffraction[3]

Off-line monitoring technique to measure particles dispersed in a liquid or dry powders. Strictly speaking a form of static light scattering, with a focus on the evaluation of low angle scattering or forward scattering detection applying Fraunhofer approximation and Mie theory.

It measures size and size distribution, with a measurable particle size range of 10 nm to ~5 μm, and the concentration range up to 95 % v:v. The pH range that can be measured depends on the cuvette to be used.

It cannot be used for very concentrated or low concentrated samples and whole dielectric function of particles may be required.

Commercially available equipments: Partica by Horiba, Mastersizer by Malvern Panalytical, Analysette 22 NeXT by Fritsch, SYNC particle analyzer by Microtac MRB, LS13 320XR particle size analyzer by Beckman, Bettersizer 2600 by 3P Instruments, SALD by Shimadzu, HELOS by Sympatec.

1.4 Acoustic spectroscopy[4]

Off-line and in-line technique to measure concentration, size, and size distribution.

The basic concept is to measure the frequency-dependent attenuation or velocity of ultrasound as it propagates through a heterogeneous sample, e.g. colloids, dispersions and emulsions. There are two main types of vibrations: free and forced. Free vibrations are the natural or normal modes of vibration for a substance. Forced vibrations are caused by some sort of excitation to make the analyte resonate beyond its normal modes. Both acoustic and electroacoustic spectroscopies are linked to a sound propagation through a heterogeneous system such as a suspension or an emulsion. An acoustic spectrometer measures only the changes in the properties of the sound wave,

whereas an electroacoustic spectrometer deals with connection between electrodynamic phenomena and the sound wave pressure field.

The measurable nanoparticles size goes from ≈10 nm to ≈3 mm, and the concentration range up to 50 % v:v (so no dilution is needed for concentrated samples). The measurement is not affected by stirring and/or pumping of the sample. However, it is required that the properties of the systems to be analyzed are well defined, such as density, thermal expansion coefficient, heat capacity and heat conductance of the particles and liquid separately.

Commercially available equipments: Ultrasizer by Malvern Instruments, DT by Dispersion Technology Inc.

1.5   Photon Density Wave spectroscopy (PDWS)[5]

In-line fiber-optical technique to quantify the absolute optical properties, i.e. the absorption and the reduced scattering coefficient, of highly turbid liquid systems. The absorption coefficient is related to the concentration of light absorbing species in the dispersion. The reduced scattering coefficient is related to the size of the light scattering particles, droplets, or cells in a dispersion. Particle size analysis is built upon Mie theory and theories for dependent light scattering. For the absolute determination of the optical coefficients, the refractive index of the dispersion is required. For particle size analysis, volume fraction of the scatterers as well as refractive index of the dispersed and the continuous phase are needed.

PDWS requires turbid systems, i.e. dispersions exhibiting multiple light scattering. In detail, at a given experimental measurement wavelength, light scattering should be stronger than light absorption. Depending amongst others on size, volume fraction, and refractive index at a given wavelength, liquid dispersions often exhibit light scattering in the particle diameter range of approx. 50 nm to 500 μm – which is the typical sizing range of PDWS. Scatterer volume fraction accordingly should be at least 0.01.

PDWS provides a time resolution in the sub-minute regime, thus it is suitable for many industrial reactions but not for extremely fast processes. Since PDWS is suited for high concentrations of disperse material (> 40 vol%), it does not require sampling and dilution but can be directly implemented into processes. Implementation is based on a purely fiber-optical process probe without focussing optics. In conjunction with the low optical emission intensities of approx. 15 mW, PDWS process probes can be applied directly in ATEX environments. The probe material can be changed to deal with the process pH.

Commercially available equipments: Spectrometer by PDW Analytics.

1.6   Turbidity spectrometry[6]

In-line monitoring technique to measure size, concentration and material composition of particles dispersed in a fluid.

The system under analysis is illuminated with a broadband light source typically in the VIS and NIR regions. The scattering or absorption spectra are collected respectively in reflection (i.e. back scattering) or transmission (i.e. forward scattering) configuration by means of a spectrophotometer. Careful analysis of turbidity spectra based on Mie or Rayleigh theory algorithms provides the mentioned particles properties.

The technique is based on the principle that particles-light interaction is strongly dependent on scatterers size, material, relative refractive index with respect to medium, and illumination light wavelength. Below particles concentration of 10 % multiple scattering processes are negligible, on the other hand for higher concentrations additional strategies are required to recover information. Turbidity spectrometry enables measurement of particle sizes ranging from 60-70 nm to tenths of microns, depending on particles material. The measurements are not affected by stirring and/or pumping of the sample. Additionally, with advanced analytical techniques, it can provide basic information on particle size distribution, the presence of aggregates and basic shapes of scatterers.

Because of the relative simplicity of the experimental apparatus and speed of measurements (spectra integration time of 1-10 msec), it is particularly suitable for in-line and real-time nanoparticles characterization.

Commercially available equipments: From our knowledge, no commercial equipments are on the market.

2. Separation methods

In these methods, the particles are separated into size classes before measurement (Figure 2).
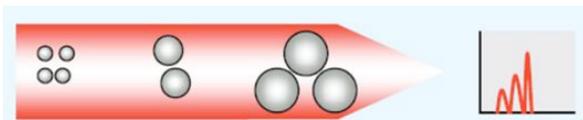
Figure 2. Principle of PSD measurement by separation methods.

Separation/classifying methods are often "easy" and "simple" to operate for routine, but can be very advanced for complex samples. Dilution of samples is needed to avoid multiple signals. Limited to extended samples information is needed (shape, viscosity, density, light absorption). All the separation technologies provide extreme high resolution and a very accurate description of multimodal nanoparticles dispersions. However, the upper size range is around 1-2 µm. The data (automated) evaluation is complex: based on calibration and separation, which results in a more accurate PSD. Still particle shape is assumed to be spherical and used for PSD determination.

2.1   Analytical centrifugation[7]

Off-line technique to measure particle size distribution.

Analytical centrifugation (AC) is chosen here as the generic term for a number of centrifugal sedimentation techniques, some of which are also known as centrifugal liquid sedimentation (CLS), analytical ultracentrifugation (AUC) or differential centrifugal sedimentation (DCS). Together, this is a versatile family of methods with broad diameter range (1 nm to 5 000 nm) and high resolution. The nanoparticles are forced to move through a predominantly aqueous medium inside an AC measuring cell under a centrifugal force of 500 to 500 000 × g (rotor speed 100 rpm to 60 000 rpm). Sedimentation causes fractionation to take place, because the larger particles move faster. The sedimentation velocities of the different fractions are measured with refractive index, ultraviolet (UV) -absorption or light scattering/turbidity detectors. The diameters of the different fractions can be calculated from the difference in sedimentation velocity, i.e. the complete particle size

distribution, according to Stokes' law. The resolution of the AC method is so high because, according to Stokes, velocity is proportional to the square of particle diameter.

The AUC particle size distribution method can give spurious results if particle size is too high, i.e. if the particles form a sediment too quickly or if they display a broad chemical heterogeneity (i.e. no uniform particle density).

Commercially available equipments: Disc Centrifuge by CPS Instruments. LUMISizer by LUM GmbH.

2.2   HydroDynamic Chromatography

Off-line technique to measure particle size distribution. Even if there have been some examples in which this techniques has been used on-line, the setup is not robust.

HydroDynamic Chromatography (HDC) can be applied to separate particles based on their size. The principle is based on the separation of particles by eluting them according to particle size (in a (ionic) surfactant solution to preserve stability of waterborne resin particles) using a parabolic flow profile. The origin of this profile can be flow through a capillary (CHDF), or through packed columns of spherical particles which has a parabolic flow profile in the interstitial channels between the column particles (HDC).

Depending on the column used: the separation range is between 5-1000 nm (upper range is 500 nm for 8 μm column particle size, while the upper range is 1000 nm for 12 μm column particle size). The use of a capillary column (so-called Capillary HydroDynamic Fractionation, CHDF) is fundamentally the same as HDC using packed columns.

In conclusion, this is a moderately simple technique that can provide highly resolved PSD, but which requires dilution of samples in emulsified medium, a previous calibration and the refractive index of the nanoparticles and whose particle size range is limited to 1-2 μm.

Commercially available equipments: CHDF3000 by Matec Applied Sciences

2.3   Field-flow fractionation (FFF)[8]

This is a fractionation technique that uses a field-flow (thermal, electrical, flow or other) to separate the particles by size. Coupled with a detector can provide size, size distribution, concentration (with an additional detector), and chemical composition (with an additional detector).

The separation technique is based on applying a field to a liquid suspension typically passed along a thin and flat channel in order to cause separation of the particles present in the liquid, dependent on their different interactions with the applied field. Hollow fibre separations are also commercially available. The field can be, for example, gravitational, centrifugal, flow, electrical or magnetic; flow FFF is the most widely used and commercialized FFF sub-technique. Flow FFF separates according to hydrodynamic size. Using a suitable detector after or during separation allows determination of the size, size distribution and concentration of nano-objects. Channel flow is parabolic under operational conditions, with particles moving at different rates depending on the location within the parabolic flow profile.

Lower size limit depends on particle density and the FFF method used but is typically 2 nm to 5 nm. Size can only be determined accurately by calibration, retention time, or by secondary detection.

Distributions that range from the nm scale to greater than 1 μm will not be properly separated, as the elution order inverts above roughly 1 μm. Sample required to be dispersed in liquid.

The most significant drawback of FFF, is the lack of a single procedure which allows the routinely analysis of particle size mixtures (each sample requires its own settings with respect to injection, focusing and elution before an optimal separation is obtained).

Commercially available equipments: DAWN/Eclipse FFF-MALS by Wyatt Technology, AF2000MT by Postnova analytics.

3. Counting methods

Particles are counted one at a time in these methods (Figure 3).
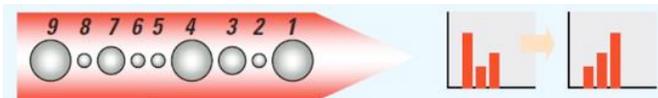
Figure 3. Principle of PSD measurement by separation methods.

Counting methods are often more advanced to operate, but give very accurate data (PSD, shape) for very complex samples. Advance dilution and/or fixation of samples/particles is needed but very limited samples information is needed (shape, viscosity, density, light absorption). The size range varied from mid nanometers up to thousands of microns and have an extreme high resolving power. Image of each particles separately can be made (and the use of some technologies, "chemical" information can be obtained). To create 'readable' distribution results, a well-trained expert is required. These approaches are capable to measure the PSD of complex/multimodal distributions including images of each particle.

3.1   Particle Tracking Analysis (PTA) / Nanoparticle Tracking Analysis (NTA)[9]

Off-line monitoring technique to measure samples in liquid suspension. The hydrodynamic size of the particles is measured by determination of the diffusion coefficient of particles undergoing brownian motion in a liquid. Particle concentration and size distribution are also measured.

The measurable particle size range is from ~10 nm up to ~2 μm. Lower limit is given by signal to noise ratio, whereas the upper limit is given due to sedimentation since the particles undergo brownian motion.

The concentration range for measurement is from 10^6 to 10^8 particles / mL.

Particles need to be in suspension and the optical contrast (RI of Particles / RI Suspension) should not be ~1, otherwise the refraction signal could be very low or non measureable at all. Time increments are ~30 ms. It can be combined with syringe pump to measure fluorescently labeled particles under flow conditions.

Commercially available equipments: ViewSizer by Horiba, ZetaView by Particle Metrix, Malvern Nanosight NS300 by Malvern Panalytical.

3.2   Scanning electron microscopy (SEM)[10]

Off-line monitoring technique to measure conductive samples, non-conductive samples (requires sample preparation), or hydrated or biological Samples (Environmental SEM (ESEM)).

It is able to obtain information on nanoparticles size, size distribution, shape, chemical composition and crystal properties (use of different detectors in the SEM for the last two cases). However, size

distribution measurement requires a high number of images recorded to obtain statistically relevant data.

The measurable nanoparticles size goes down to 50 nm and up to millimeter range. The measurable concentration range varies, but in high concentrations it may be difficult to distinguish between agglomerated and aggregated particles.

The particle size distribution can be obtained using software. It is possible to image hydrated or biological specimens using higher pressures. This requires additional hardware (ESEM). Non-conductive sample may require carbon coating or use of lower operation energy and low pressure gas. The use of a SEM sometimes requires more sample preparation time (special samples e.g. non-conductive etc.) and training to operate especially to interpret images in different scanning modes and to sort out artifacts. Beam damaging can occur on high acceleration voltages and may therefore alter the sample especially when focusing very small zones.

Commercially available equipments: SEM microscopes by ZEISS, FEI or Hitachi.

3.3   Transmission electron microscopy (TEM)[11]

Off-line monitoring technique to measure electron transparent thin sample layer (less than 100 nm).

It is able to obtain information on nanoparticles size, size distribution, shape, chemical composition (requires X-ray spectroscopy) and crystal information. As in the case of SEM, size distribution measurement requires a high number of images recorded to obtain statistically relevant data (software available for automatic counting).

The measurable nanoparticles size goes from atomic to millimetre range. It requires electron dense samples to reach high enough optical contrast. It is generally not possible to distinguish between agglomeration and aggregation in samples.

Similar to the SEM, the electron beam damaging may alter the sample. Sample preparation is essential and has an extremely high impact on results. Measurements usually take long time for statistical relevant data to be obtained.

Commercially available equipments: TEM microscopes by ZEISS, FEI, JEOL, Phillips or Hitachi.

3.4   OptoFluidic force induction (OF2i)[12]

On-line monitoring technique to measure samples in (continuously) flowing liquid suspensions.

The hydrodynamic size of particles is measured by the introduction of optical forces altering particle pathways and the subsequent determination of resulting trajectories which contain size and shape information. Software containing Mie theory, boundary element methods and particle tracking algorithms are used for converting particle data. Concentrations, size and size distributions (D-values) are extracted.

The measurable nanoparticle size range is from ~20 nm to ~20 μm (sample dependent).

Measurement statistics are obtained by scanning ~10^4 particles/min continuously (lag time: < 20 s for characterization statistics data-stream).

Continuous measurement requirements: Sample stream of optimal > 0.7 mL/min with concentrations > 10^7 objects/mL (minimal ~5 μL/min with minimum of 10^5 objects/mL). Concentrated samples (> 10^{10} objects/mL) will be continuously diluted.

Particles need to be in suspensions, and the optical contrast (RI of Particles / RI of Suspension) should be > 1 (positive optical contrast). Since induced forces depend on the optical contrast, refractive index information may be required for absolute value determination. Continuous supply of dilution media may be required (~50 mL/min, concentration dependent).

Commercially available equipments are under development by BRAVE Analytics GmbH.

3.5   Light obscuration (LO)[13]

Online and offline monitoring technique to measure dilute streams of particles in liquid suspensions.

It is possible to obtain particle size distribution for particles in the size range of 150 nm up to 400 µm. The detectable sizes strongly depend on the samples dilution. For this method to work, samples need to be diluted so that particles pass the optical region one at a time, avoiding collisions. While there are offline monitoring possibilities there exist also online versions including LO.

Particles sizes below 1 µm are usually detected using "Light Scattering" (LS) where different processes occur such as scattering, absorption or refraction. These physical processes depend on the particles scattering cross-sections. When particles are separated prior the scattering event, a single particle light scattering (SPLS) operation mode can be obtained for high resolution and achieving broader dynamic range.

The light obscuration for particles sizes above 1 µm is measured and detected using LO. Here, the amount of extinction is measured and compared to a calibration curve. Advantage of this technique is that the particles are measured once at a time and inherently increase the accuracy of the measurement building statistics with each particle at a time.

The measurement of both particles below 1 µm and above requires a setup with appropriate detectors.

The concentration limitation for the mentioned size region is 10,000 particles/mL with a recommended flow rate of 30 mL/min. The calibration can be performed for different flow rates as needed. Size accuracy is listed as ~2% where the count accuracy is ~10%.

Commercially available equipments: SPOS by Entegris, iSpect by Shimadzu, Multisizer Beckman Coulter, PSA300 by Horiba, LUMISpoc (SPLS) by LUM GmbH

3.6   Particle Visualisation Method (PVM)[14]

Online/Inline particle monitoring technique using high resolution microscope probes to measure a variety of samples e.g. creams, emulsions, bubbles, droplets etc.

The microscope probe defines the measured particle size regime where different probes cover regions from 0.5 µm up to 30,000 µm. The sample temperature may reach from -50°C up to 450°C, and maximum pressure of 320 bar.

High speed measurements can be performed up to few m/s flow speeds.

This technique also works for very low/high dispersed phase fractions.

Automated cleaning and evaluation process implemented in software reduces error by manual operation.

Commercially available equipments: Probe and ProbeControl by Sopat, PVM Particle View / FBRM Particle Track by Mettler Toledo,

3.7   Tunable Resistive Pulse Sensing (TRPS)[15]

Tunable Resistive Pulse Sensing (TRPS) measures nanoparticles suspended in electrolytes on a particle-by-particle basis as they pass through a nanopore. The transient current pulse caused by a particle traversing the pore is directly proportional to particle volume, enabling a highly precise and repeatable measurement of size to be achieved; in ideal conditions TRPS offers sub nm resolution of diameter. TRPS provides a calibrated measurement of the true size and concentration distribution of nanoparticles. The range of sizes measured by TRPS is 40 nm to 10 μm and the concentration range is $1x10^5$-$1x10^{11}$ part/mL.

Commercially available equipments: qNano Gold by Izon.

Conclusions

The present document shows a summary of the relevant characterization techniques for particle size and size distribution measurement (Figure 4). Currently, there exist many tools available to measure particle sizes in the range of 1 nm to hundreds of microns. These methods can be classified in three main approaches depending on the particle size distribution (PSD) analysis. These methods are ensemble, separation and counting methods. Each of the methods explained in the present document are based on different physical principles and present their own advantages and limitations. As a result of limitations in their physical approaches, only a few of the techniques reviewed can be implemented online/inline. Attempts of adapting common technologies for in/online measurement are available e.g. Brownian motion based DLS approaches: IPAS by Colloid Metrix GmbH, NanoFlowSizer by InProcess LSP or scattering based laser diffraction systems for powder characterization: Mythos by Sympatec GmbH or Insitic by Malvern Panalytical. Due to their physical approaches, realtime nano-characterization as an in/online approach is hardly achievable, and therefore it can be concluded that the approaches addressed within NanoPAT, i.e. PDWS, Turbidity Spectromety and OptoFluidic Force Induction are the most promising ones.
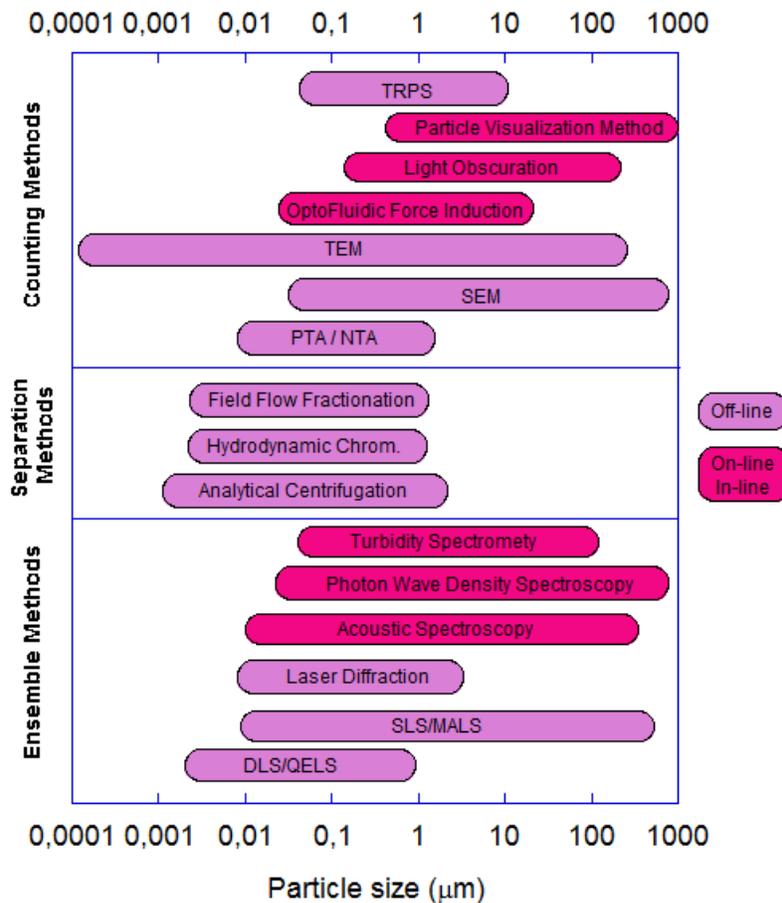
Figure 4. Size ranges measured by the different techniques.

Table 1: Pending activities

Description of pending work that was not achieved at the time of submitting the deliverable	None
Time at which the result is expected	N/A
Place where it will be reported	N/A

Bibliography

[1]   ISO 22412, ISO 13321

[2]   ISO 13320, ISO/TR 13097

[3]   ISO TR 18196-20106

[4]   ISO 20998-1, ISO 20998-2

[5]   R. Hass, M. Münzberg, L. Bressel, O. Reich, "Industrial applications of Photon Density Wave spectroscopy for in-line particle sizing." Appl. Optics, Vol. 52, pp. 1423-1431, 2013.

[6]   G. Crawley, M. Cournil, D. Di Benedetto "Size analysis of fine particle suspensions by spectral turbidimetry: potential and limits" *Powder Technology* 91 (1997) 197-208.

         B.N. Khlebtsov, V.A. Khanadeev, N.G. Khlebtsov "Determination of size, concentration and refractive index of silica nanoparticles from turbidimetry" *Langmuir* 24(16) (2008) 8964–8970.

[7]   ISO 13318-1, ISO 13318-2, ISO 13318-3.

[8]   J. Gigault, J.M. Pettibone, C. Schmitt, V.A. Hackley, "Rational strategy for characterization of nanoscale particles by asymmetric-flow field flow fractionation: A tutorial." *Anal. Chim. Acta.* 809 (2014) 9–24.

[9]   ISO 13321, ISO 19430, ASTM E2834

[10]   ISO 13067, ISO 16700, ISO 22493, ISO 24173, ISO/TS 10798

[11]   ISO 25498, ISO 29301, ISO/TS 10797, ISO/TS 11888

[12]   under development, based on: Hill, C. Optofluidic force induction (OF2i) - Platform technology for particle characterization and active manipulation in microfluidic environments *(Doctoral dissertation). 2018, Medical University Graz*

[13]   https://www.entegris.com/en/home/resources/technical-information/glossary/light-obscuration.html [visited 09/2020]

[14]   https://www.sopat.de [visited 09/2020]

[15]   https://www.izon.com [visited 09/2020]