PARTICLE SIZE ANALYSIS BY LASER LIGHT DIFFRACTION

The method is based on the ISO standards 13320, 9276-1(1998) and 9276-1/AC1 (2004). Figure 2 of this chapter is based on Figure 1 of JIS Z 8825 (2013).

INTRODUCTION

The laser light diffraction technique used for the determination of particle-size distribution is based on the analysis of the diffraction pattern produced when particles are exposed to a beam of monochromatic light. Historically, the early laser diffraction instruments only used scattering at small angles. However, the technique has since been broadened to include laser light scattering in a wider angular range and application of the Mie theory, in addition to the Fraunhofer approximation and anomalous diffraction.

The technique cannot distinguish between scattering by single particles and scattering by clusters of primary particles, i.e. by agglomerates or aggregates. As most particulate samples contain agglomerates or aggregates and as the focus of interest is generally on the size distribution of primary particles, the clusters are usually dispersed into primary particles before measurement.

For non-spherical particles, an equivalent sphere-size distribution is obtained because the technique assumes spherical particles in its optical model. The resulting particle-size distribution may differ from those obtained by procedures based on other physical principles (e.g. sedimentation, sieving).

This chapter provides guidance for the measurement of size distributions of particles in different dispersed systems, for example, powders, sprays, aerosols, suspensions, emulsions, and gas bubbles in liquids, through analysis of their angular light-scattering patterns. It does not address specific requirements of particle size measurement of specific products.

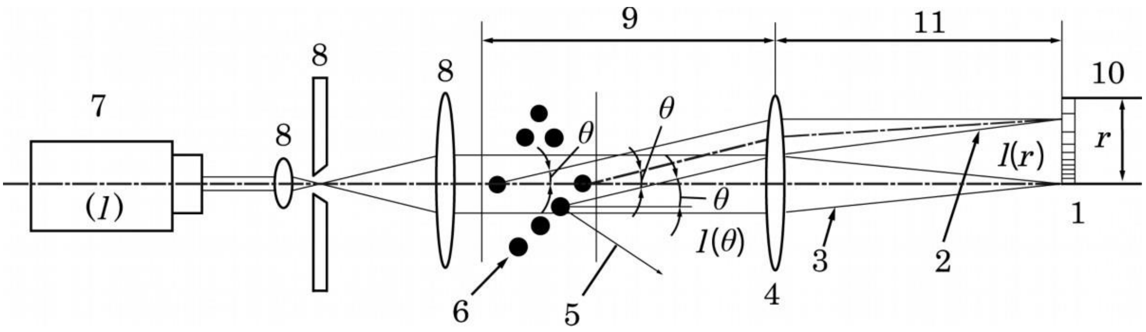
PRINCIPLE

A representative sample, dispersed at an adequate concentration in a suitable liquid or gas, is passed through a beam of monochromatic light, usually a laser. The light scattered by the particles at various angles is measured by a multi-element detector. Numerical values representing the scattering pattern are then recorded for subsequent analysis. These scattering pattern values are then transformed, using an appropriate optical model and mathematical procedure, to yield the proportion of total volume to a discrete number of size classes, forming a volumetric particle-size distribution.

INSTRUMENT

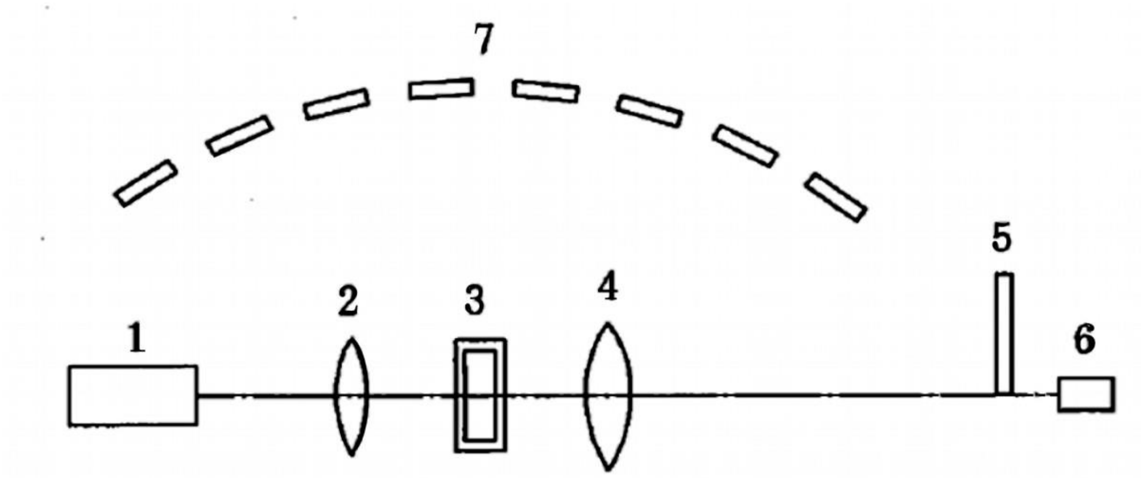
The instrument is located in an environment where it is not affected by electrical noise, mechanical vibrations, temperature fluctuations, humidity or direct bright light.

An example of a Fourier set-up of a laser light diffraction instrument is given in Figure 1. Other optical arrangements as shown in figure 2 may be used.



1. Obscuration detector
2. Scattered beam
3. Direct beam
4. Fourier lens(es)
5. Scattered light not collected by lens (4)
6. Particle ensemble
7. Laser light source
8. Beam processing optics
9. Working distance of lens (4)
10. Multi-element detector
11. Focal distance of lens (4)

Figure 1. - *Example of a Fourier set-up of a laser light diffraction instrument*



1. Laser light source
2. Reverse Fourier lens(es)
3. Measurement cell or zone
4. Fourier lens(es)
5. Low-angle detector(s), either bespoke design or pixel array
6. Transmission or obscuration detector
7. High-angle detector array

Figure 2. - *Example of optical arrangements in laser light diffraction instrument*

The instrument comprises light source(s), beam processing optics, a sample measurement zone (or cell), a Fourier/reverse Fourier lens, and a multi-element detector for measuring the scattered light pattern. A data system is also required for deconvolution of the scattering data into a volumetric size distribution and associated data analysis and reporting.

The particles can enter the laser beam in 2 positions. In the Fourier set-up the particles enter the parallel beam before the collecting lens and within its working distance. In the so-called reverse Fourier set-up, the particles enter after the collecting lens and thus, in a converging beam. The advantage of the Fourier set-up is that a reasonable path length for the sample is allowed within the working distance of the lens. The reverse Fourier set-up requires small path lengths but enables the measurement of scattered light at larger angles.

The interaction of the incident light beam and the ensemble of dispersed particles results in a scattering pattern with different light intensities at various angles. The total angular intensity distribution, consisting of both direct and scattered light, is then focused onto a multi-element detector by a lens or a series of lenses. These lenses create a scattering pattern that, within limits, does not depend on the location of the particles in the light beam. Hence, the continuous angular intensity distribution is converted into a discrete spatial intensity distribution on a set of detector elements.

It is assumed that the measured scattering pattern of the particle ensemble is identical to the sum of the patterns from all individual scattering particles present in random relative positions. Note that only a limited angular range of scattered light is collected by the lens(es) and, therefore, by the detector.

DEVELOPMENT OF THE PROCEDURE

The measurement of particle size by laser diffraction can give reproducible data, even in the sub-micron region, provided the instrument used and the sample tested are carefully controlled to limit variability of the test conditions (e.g. dispersion medium, method of preparation of the sample dispersion).

It is applicable to particle sizes in the range of approximately 0.1 µm to 3 mm. With special instrumentation and conditions, the applicable size range can be extended above 3 mm and below 0.1 µm.

Sampling. The sampling technique must be adequate to obtain a representative sample of a suitable volume for the particle-size measurement. Sample splitting techniques such as rotating riffler or the cone and quartering method may be applied.

Evaluation of the dispersion procedure. A preliminary examination of the sample is carried out visually or with the aid of a microscope, to estimate its size range and particle shape. The dispersion procedure must be adjusted to the purpose of the measurement. The purpose may be such that it is preferable to deagglomerate clusters into primary particles as far as possible, or it may be desirable to retain clusters as intact as possible. In this sense, the particles of interest may be either primary particles or clusters.

For the development of a procedure it is highly advisable to check that comminution of the particles does not occur, and conversely, that dispersion of particles or clusters is satisfactory. This can usually be done by changing the dispersing energy and monitoring the change of the particle-size distribution. The measured size distribution must not change significantly when the sample is well dispersed and the particles are neither fragile nor soluble. Moreover, if the manufacturing process (e.g. crystallisation, milling) of the material has changed, the applicability of the procedure must be verified (e.g. by microscopic comparison).

Sprays, aerosols and gas bubbles in a liquid are measured directly, provided that their concentration is adequate, because sampling or dilution generally alters the particle-size distribution.

In other cases (such as emulsions, pastes and powders), representative samples may be dispersed in suitable liquids. Dispersing aids (wetting agents, stabilisers) and/or mechanical forces (e.g. agitation, sonication) are often applied for deagglomeration or deaggregation of clusters and stabilisation of the dispersion. For these liquid dispersions, a recirculating system is most commonly used, consisting of an optical measurement cell, a dispersion bath usually equipped with a stirrer and ultrasonic elements, a pump, and tubing. Non-recirculating, stirred cells are useful when only small amounts of a sample are available or when special dispersion liquids are used.

Dry powders can also be converted into aerosols through the use of suitable dry powder dispersers, which apply mechanical force for deagglomeration or deaggregation. Generally, the dispersers use the energy of compressed gas or the differential pressure of a vacuum to disperse the particles to an aerosol, which is blown through the measurement zone, usually into the inlet of a vacuum unit that collects the particles. However, for free flowing, coarser particles or granules the effect of gravity may be sufficient to disperse the particles adequately.

If the maximum particle size of the sample exceeds the measuring range of the instrument, the material that is too coarse can be removed by sieving and the mass and percentage of removed material are reported. However, after pre-sieving, note that the sample is no longer representative, unless otherwise proven.

Optimisation of the liquid dispersion. Liquids, surfactants, and dispersing aids used to disperse powders must:

– be transparent at the laser wavelength and practically free from air bubbles or particles;

– have a refractive index that differs from that of the test material;

– be non-solvent for the test material (pure liquid or pre-filtered, saturated solution);

– not alter the size of the test material (e.g. by solubility, solubility enhancement, or recrystallisation effects);

– favour easy formation and stability of the dispersion;

– be compatible with the materials used in the instrument (such as O-rings, gaskets, tubing, etc.);

– possess a suitable viscosity to facilitate recirculation, stirring and filtration.

Surfactants and/or dispersing aids are often used to wet the particles and to stabilise the dispersion. For weak acids and weak bases, buffering of the dispersing medium at low or high pH respectively can assist in identifying a suitable dispersant.

A preliminary check of the dispersion quality can be performed by visual or microscopic inspection. It is also possible to take fractional samples out of a well-mixed stock dispersion. Such stock dispersions are formed by adding a liquid to the sample while mixing it with, for example, a glass rod, a spatula or a vortex mixer. Care must be taken to ensure the transfer of a representative sample and that settling of larger particles does not occur. Therefore, a sample paste is prepared or sampling is carried out quickly from a suspension maintained under agitation.

Optimisation of the gas dispersion. For sprays and dry powder dispersions, a compressed gas free from oil, water and particles may be used. To remove such materials from the compressed gas, a dryer with a filter can be used. Any vacuum unit should be located away from the measurement zone, so that its output does not disturb the measurement.

Determination of the concentration range. In order to produce an acceptable signal-to-noise ratio in the detector, the particle concentration in the dispersion must exceed a minimum level. Likewise, it must be below a maximum level in order to avoid multiple scattering. The concentration range is influenced by the width of the laser beam, the path length of the measurement zone, the optical properties of the particles, and the sensitivity of the detector elements.

In view of the above, measurements must be performed at different particle concentrations to determine the appropriate concentration range for any typical sample of material. (Note: in different instruments, particle concentrations are usually represented by differently scaled quantities, e.g. obscuration, optical concentration, proportional number of total mass).

Determination of the measurement time. The measurement time, the reading time of the detector and the acquisition frequency, is determined experimentally in accordance with the required performance of the analytical procedure. Generally, the measurement time is chosen to allow a large number of detector scans or sweeps at short time intervals.

Selection of an appropriate optical model. Most instruments use either the Fraunhofer or the Mie theory, though other approximation theories are sometimes applied for calculation of the scattering matrix. The choice of the theoretical model depends on the intended application and the different assumptions (size, absorbance, refractive index, roughness, crystal orientation, mixture, etc.) made for the test material. If the refractive index values (real and imaginary parts for the used wavelength) are not exactly known, then the Fraunhofer approximation or the Mie theory with a realistic estimate of the refractive index can be used. The former has the advantages that it is simple and it does not need refractive index values; the latter usually provides less-biased particle-size distributions for small particles. For instance, if the Fraunhofer model is used for samples containing an appreciable amount of small, transparent particles, a significantly larger amount of small particles may be calculated. In order to obtain traceable results, it is essential to document the refractive index values used, since small differences in the values assumed for the real and imaginary part of the complex refractive index may cause significant differences in the resulting particle-size distributions. Small values of the imaginary part of the refractive index (e.g. 0.01 i - 0.03 i) are often applied to allow the correction of the absorbance for the surface roughness of the particles. It is noted, in general, that the optical properties of the substance to be tested, as well as the structure (e.g. shape, surface roughness and porosity), bear upon the final result.

VALIDATION

Typically, the validity of a procedure may be assessed by the evaluation of its specificity, linearity, range, accuracy, precision and robustness. In particle-size analysis by laser light diffraction, specificity as defined by ICH is not applicable as it is not possible to discriminate between different components in a sample, nor is it possible to discriminate agglomerates from dispersed particles unless properly complemented by microscopic techniques. Exploring a linear relationship between concentration and response, or a mathematical model for interpolation, is not applicable to this procedure. Rather than evaluating linearity, this procedure requires the definition of a concentration range within which the result of the measurements does not vary significantly. Concentrations below that range produce an error due to a poor signal-to-noise ratio, while concentrations above that range produce an error due to multiple scattering. The range depends mostly on the instrument hardware. Accuracy is confirmed through an appropriate instrument qualification and comparison with microscopy, while precision may be assessed by means of a repeatability determination.

The attainable repeatability of the procedure mainly depends on the characteristics of the material (homogeneity – representative sampling, milled/not milled, robust/fragile, width of its size distribution, etc.), whereas the required repeatability depends on the purpose of the measurement. Mandatory limits cannot be specified in this chapter, as the repeatability (independent sample preparations) may vary appreciably from one substance to another. However, it is good practice to aim at acceptance criteria for repeatability such as $s_{rel} \leq 10$ per cent [$n = 6$] for any central value of the distribution (e.g. for x_{50}). Values at the sides of the distribution (e.g. x_{10} and x_{90}) are oriented towards less stringent acceptance criteria such as $s_{rel} \leq 15$ per cent [$n = 6$].

For any characteristic parameter (e.g. x_{10}, x_{50}, x_{90}) that is below 10 µm the acceptance criteria may be doubled.

Robustness may be tested during the selection and optimisation of the dispersion media and forces. The change of the dispersing energy may be monitored by the change in the particle-size distribution.

MEASUREMENT

Precautions. The main sources of variation are the characteristics of the test material, sample preparation conditions, and the individual analyst’s technique. Efforts are made to reduce contributions from these sources.

The instructions given in the instrument manual are followed:

– never look into the direct path of the laser beam or its reflections;

– earth all instrument components to prevent ignition of solvents or dust explosions;

– check the instrument set-up (e.g. warm-up, required measuring range and lens, appropriate working distance, position of the detector, no direct bright light);

– in the case of wet dispersions, avoid air bubbles, evaporation of liquid, schlieren or other inhomogeneity in the dispersion ; similarly, avoid improper mass-flow from the disperser or turbulent air-flow in the case of dry dispersions ; such effects can cause erroneous particle-size distributions.

Measurement of the light scattering of dispersed sample(s). After proper alignment of the optical parts of the instrument, a blank measurement of the particle-free dispersion medium must be performed using the same procedure as that used for the measurement of the sample. The background signal must be below an appropriate threshold. The detector data are saved in order to subtract them later from the data obtained with the sample. The dispersed sample is then measured according to the procedure developed.

For each detector element, an average signal is calculated, sometimes together with its standard deviation. The magnitude of the signal from each detector element depends upon the detection area, the light intensity and the quantum efficiency. The co-ordinates (size and position) of the detector elements together with the focal distance of the lens determine the range of scattering angles for each element. Most instruments also measure the intensity of the central (unscattered) laser beam. In this case the ratio of the intensity from the sample to that from a blank is inverse correlated to the proportion of scattered light and hence the particle concentration.

Conversion of scattering pattern into particle-size distribution. This deconvolution step is the inverse of the calculation of a scattering pattern for a given particle-size distribution. The assumption of spherical particle shape is particularly important as most algorithms use the mathematical solution for scattering from spherical particles. Furthermore, the measured data always contain some random and systematic errors, which may vitiate the size distributions. Several mathematical procedures have been developed for use in the available instruments. They contain some weighting of deviations between measured and calculated scattering patterns (e.g. least squares), some constraints (e.g. non-negativity for amounts of particles), and/or some smoothing of the size distribution curve.

The algorithms used are specific to each make and model of equipment, and are proprietary. The differences in the algorithms between different instruments may give rise to differences in the calculated particle-size distributions.

Replicates. The number of replicate measurements (with individual sample preparations) to be performed depends on the required measurement precision. It is recommended to set this number in a substance-specific procedure.

REPORTING OF RESULTS

The particle-size distribution data are usually reported as cumulative undersize distribution and/or as density distribution by volume. The symbol x is used to denote the particle size, which in turn is defined as the diameter of a volume-equivalent sphere. Q3(x) denotes the volume fraction undersize at the particle size x. In a graphical representation, x is plotted on the abscissa and the dependent variable Q3 on the ordinate. Most common characteristic values are calculated from the particle-size distribution by interpolation. The particle sizes at the undersize values of 10 per cent, 50 per cent, and 90 per cent (denoted as x_{10}, x_{50}, and x_{90} respectively) are frequently used. x_{50} is also known as the median particle size. It is recognised that the symbols d or D are widely used to designate the particle size, thus the symbol x may be replaced by d or D.

Moreover, sufficient information must be documented about the sample, the sample preparation, the dispersion conditions, and the cell type. As the results depend on the particular instrument, data analysis program, and optical model used, these details must also be documented.

INSTRUMENT QUALIFICATION

Use the instrument according to the manufacturer's instructions and carry out the prescribed qualifications at an appropriate frequency, according to the use of the instrument and substances to be tested.

Operation qualification. Laser diffraction instruments, although assuming idealised properties of the particles, are based on first principles of laser light scattering. Thus, calibration is not required. However, it is still necessary to confirm that the instrument is operating correctly. This can be undertaken using any certified reference material (CRM) that is acceptable in industrial practice, which is characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty (u_{crm}) and a statement of metrological traceability.

The entire measurement procedure is examined, including sample collection, sample dispersion, sample transport through the measurement zone, the measurement and deconvolution procedure. It is essential that the total operational procedure is fully described.

Certified reference materials (CRMs) consist of spherical or non-spherical particles having homogeneous particle density and optical properties. They shall have a known distribution over an appropriate size rage such that for example the x_{90} / x_{10} ratio is at least 1.5. The real and imaginary part of the complex refractive index are specified for the material if the Mie theory is to be applied in data analysis.

Preferably, these particles have certified values from laser light diffraction analysis. The use of reference values from methods other than laser light diffraction may cause a significant bias. The reason for this bias is that the different principles inherent in the various methods may lead to different sphere-equivalent diameters for the same non-spherical particle.

Although the use of CRMs is preferred, other well-defined reference materials may also be employed. They consist of substances of typical composition and particle-size distribution for a specified class of substances. Their particle-size distribution has proven to be stable over time. The results must comply with previously determined data, with the same precision and bias as for the CRM.

The response of a laser diffraction instrument is considered to meet the requirements if the average value of x_{50} from at least 3 independent measurements does not deviate by more than 3 per cent from the certified range of values of the reference material. I.e. when a certified size of a reference material is stated as a range rather than a single value, that range is expanded by the relevant percentage to determine the criterion for measurement. The average values for x_{10} and x_{90} must not deviate by more than 5 per cent from the certified range of values. For any characteristic parameter (e.g. x_{10}, x_{50}, x_{90}) that is below 10 µm the acceptance criteria may be doubled.

Performance Qualification. In addition to the operation qualification, the performance of the system must be qualified at regular time intervals or as frequently as appropriate. This can be undertaken using any suitable reference material as mentioned in the previous paragraph.

The qualification of the system is based on the concept that the equipment, electronics, software and analytical operations constitute an integral system, which can be evaluated as an entity. Thus the entire measurement procedure is examined, including sample collection, sample dispersion, sample transport through the measurement zone, and the measurement and deconvolution procedure. It is essential that the total operational procedure is fully described.

In general, unless otherwise specified in the individual monograph, the response of the system is considered to meet the requirements if the x_{50} value does not deviate by more than 10 per cent from the range of values of the reference material. If optionally the values at the sides of the distribution are evaluated (e.g. x_{10} and x_{90}), then these values must not deviate by more than 15 per cent from the certified range of values. . For any characteristic value (e.g. x_{10}, x_{50}, x_{90}) that is below 10 µm the acceptance criteria may be doubled.

NOTE: Stricter requirements for instrument operation qualification are prescribed in the corresponding section.