

Nano Particle Size Analyzer

SALD-7500nano



High-sensitivity Measurement of Nano Particle Size Distribution

A powerful new tool for research and development in nanotechnology and life sciences, and for measuring fine bubbles.

|| Evaluation of the dispersion and aggregation characteristics of particles is realized with a wide measurement range and in real time.

|| The SALD-7500nano was developed to provide accurate and high-sensitivity measurement of low concentration or high-light absorption nano particles. It achieves sensitivity in the nano area about ten times higher as compared to conventional instruments. In addition, low concentration samples of less than 1 ppm can be measured.

|| Enables measurement of fine bubbles (micro bubbles from 100 nm to 60 μm), and allows real-time tracing of the changes in the bubble diameter.

|| This system enables the evaluation of sub-visible particles included in biopharmaceuticals. Special options can be added to create an aggregation analysis for biopharmaceuticals.

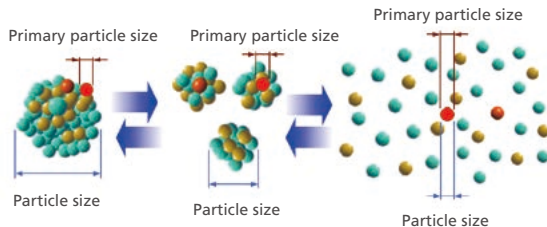


Nano Particle Size Analyzer

SALD-7500nano

Wide Measurement Range: 7 nm to 800 μm From primary particles to sub-visible particles and contaminants

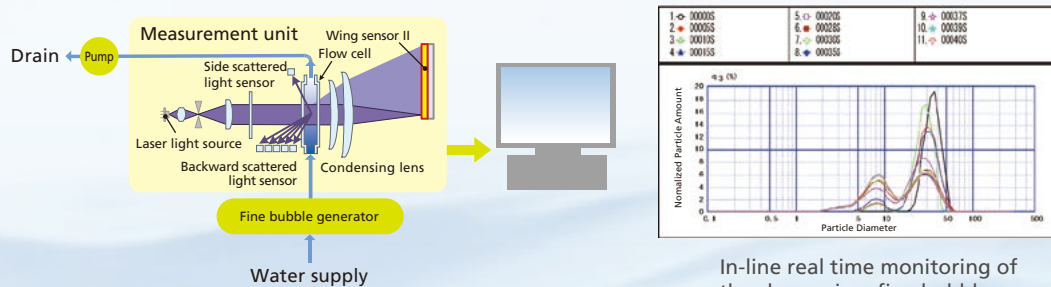
- Changes in particle size across the 7 nm to 800 μm measurement range can be continuously measured using a single light source, single optical system and single measurement principle.
- Since a primary particle and an aggregate and contaminant can be measured with one system, the aggregation properties by a dispersion condition can be checked.



The evaluation of the dispersion and aggregation characteristics of the particles is realized with a wide measurement range and in real time.

1-Second Minimum Serial Measurement Time. Real time monitoring

- By incorporating a single light source, which does not require switching, and the wide-angle detection method, the measurement time can be reduced to a minimum of 1 second. In addition, the particle size distribution can be displayed in real time at 1-second intervals.
- Serial observations of the dispersion, cohesion or dissolution reaction processes are possible at 1-second intervals, and these results can be saved. Functions for statistical processing and 3D display of the particle reaction processes offer multifaceted analyses and evaluations.
- Connecting the flow cell directly to the fine bubble generator enables in-line real-time monitoring of the changes in fine bubbles.



Measure Concentrations from 0.1 ppm to 20 %

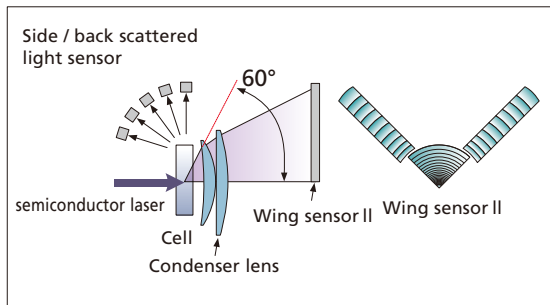
- Compared to other instruments, the SALD-7500nano permits measurements across an extremely broad concentration range of 0.1 ppm to 20 %.
- The particle size of fine particles, particularly nano particles, varies with the concentration. The dispersion and coagulation of nano particles can be observed while altering the concentration.
- Accurate analysis of samples in which the particle size distribution changes with dilution is possible, as measurements can be conducted on the undiluted solution or after minimal dilution. For example, commercial hand creams, face creams, and rinses can be measured with hardly any pretreatment.

Measurement of Small Sample Amounts

- Drainage of a small quantity of a suspension liquid is adequate since the SALD-BC75 batch cell permits analysis of a volume of just 5 cm^3 . Most organic solvents can be used.
- A combination of the SALD-HC75 high-concentration measurement unit with special glass slides featuring a shallow indentation permits measurement on just 15 micro liters.

Features of SALD-7500nano

Single detection face continuously captures forward-scattered light up to a 60° angle



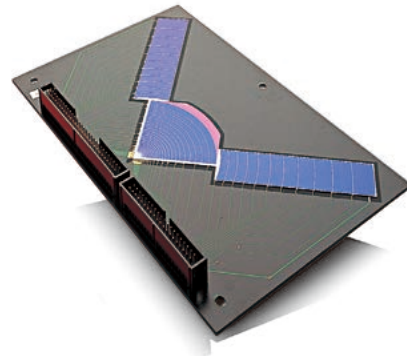
SLIT optical system

The target particle size range is seamlessly covered using a single measurement principle, single optical system, and single light source. Additionally, because the SALD-7500nano does not incorporate multiple optical systems that create discontinuities in the data, accurate particle size distribution measurements are possible across the entire measurement range using a single standard. The application of the SLIT* optical system, based on sophisticated scattered light intensity tracing technology, smashes conventional wisdom to continuously capture forward-scattered light at up to a wide 60° angle on a single detector face. This achieves high resolution in the fine particle region.

*SLIT (Scattered Light Intensity Trace)

High-Resolution/High-Sensitivity Wing Sensor II

High-Resolution/High-Sensitivity Wing Sensor II forward diffracted/scattered light is detected by a “wing sensor II”, a 78-element sensor developed using semiconductor manufacturing technology of the highest level. This sensor can detect greatly fluctuating small-angle forward scattering light with a high level of resolution and wide-angle scattering light of a low optical intensity with a high level of sensitivity. Also, side scattered light is detected by 1 sensor element and back scattered light is detected by 5 sensor elements. Accurately capturing light intensity distribution patterns with a total of 84 sensor elements enables the high-resolution, high-precision measurement of particle size distributions over a wide particle diameter range.

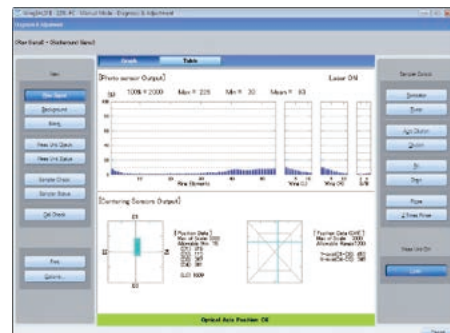


More Stable Optical System

The Omnidirectional Shock Absorption Frame (OSAF) fully isolates all elements of the optical system from shocks and vibrations. This eliminates concerns about adjusting the optical axis.

Built-in Self-Diagnostic Functions Ensure Easy Maintenance

These analyzers incorporate powerful self-diagnostic functions. The output signals sent by the sensors and detecting elements and the instrument operating status can be checked, facilitating easier maintenance. Using the Operation Log function, detailed information about, for example, the instrument usage status and contamination of the cells is included with all the measurement data, making it possible to investigate the validity of measurement data obtained in the past.



Laser diffraction method ISO 13320 and JIS Z 8825-1 compliant

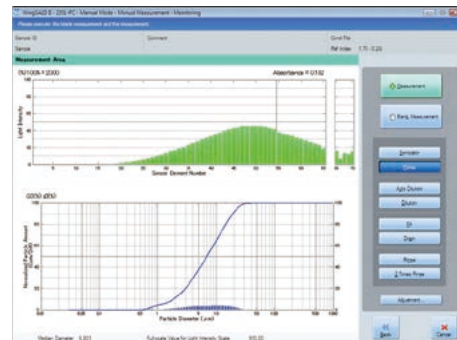
The SALD-7500nano complies with ISO 13320 and JIS Z 8825-1 laser diffraction and scattering standards.

Validation possible with JIS standard particles

System performances can be confirmed using a MBP1-10 standard particle specified in JIS Z 8900-1. These samples have a broad particle size distribution, which is specified by the JIS standard. Using these samples allows verifying that the instrument is always accurate.

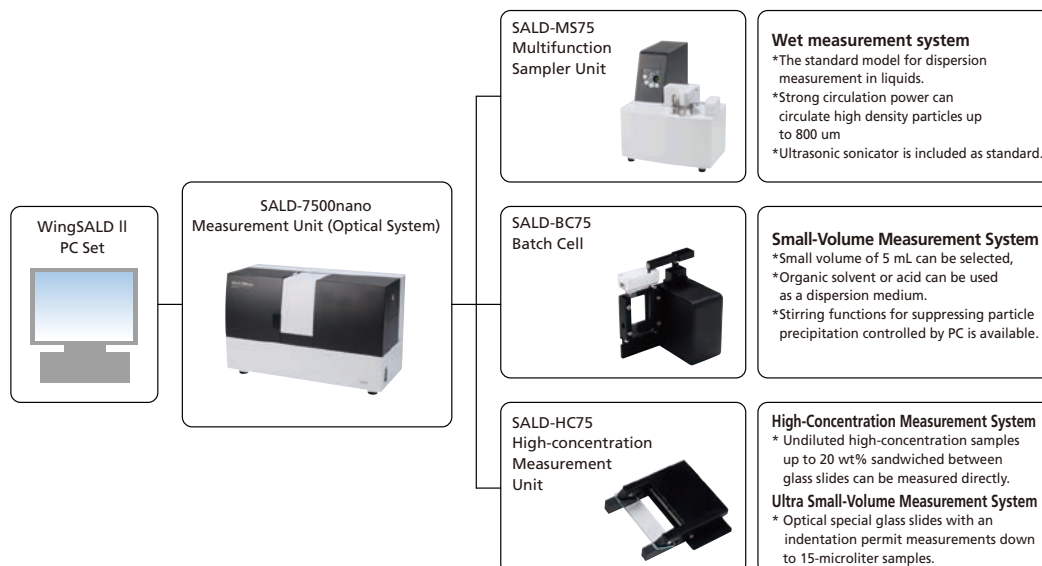
Allows verifying the validity of measurement results by referencing light intensity distribution data

Since light intensity distribution data (raw data) and measurement results (particle size distribution data) can be displayed on the same screen, measurement results can be verified while viewing both data sets. This allows users to verify whether the detection signal level (particle concentration) is appropriate, and to confirm the validity of measurement results from multiple aspects, such as in terms of the distribution width and the presence of aggregates and contaminants.



Wide application applicability

The system configuration can be optimized to address various uses, purposes, measurement objects, environments and conditions.



Software Features

Eliminates the mistake or trouble of selecting refractive indices

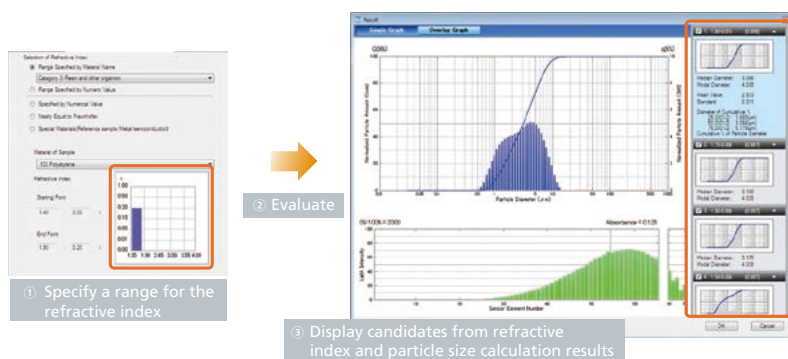
Automatic Refractive Index Calculation Function

Selecting a refractive index was an unavoidable part of using the laser diffraction method, where generally a published value was entered, but such values were not necessarily appropriate, considering the effects of particle composition and shape. Therefore, tedious trial and error processes were used to select refractive indices.

WingSALD II solves such problems by being the world's first software to include a function that automatically calculates an

appropriate refractive index based on the LDR (light intensity distribution reproduction) method.

Top 5 of the refractive index candidates (from No. 1 to No. 5) are displayed with the evaluation point, and the particle size distribution calculated by the refractive index is also displayed as a thumbnail. An appropriate refractive index can be selected referring to the evaluation point and the thumbnail. The refractive index of the main material can be selected from the list.



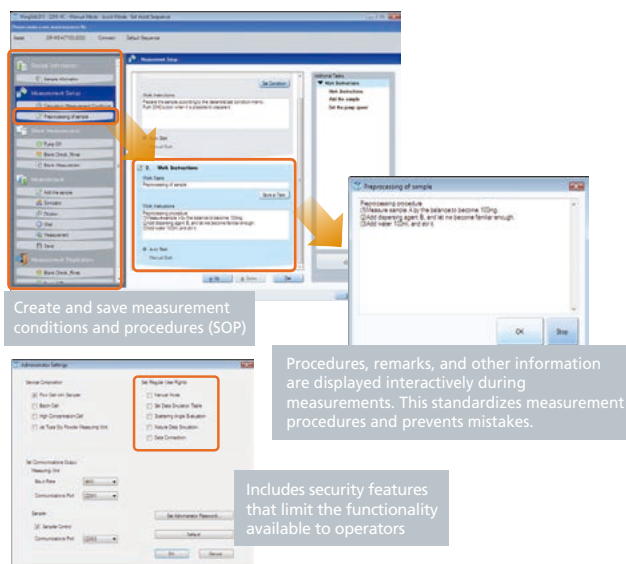
Note: The LDR method automatically calculates an appropriate refractive index based on consistency between the actual measured light intensity distribution and one reproduced (recalculated) from particle size distribution data. This method was developed by Shimadzu and published in two technical papers. It is sometimes called the "Kinoshita Method", in academic communities, after the name of Shimadzu's engineer.

Assist function decreases operational error to ensure more accurate measurement

Measurement Assistant Functions: allow preparing SOPs to ensure measurements are always performed using the same conditions and procedures.

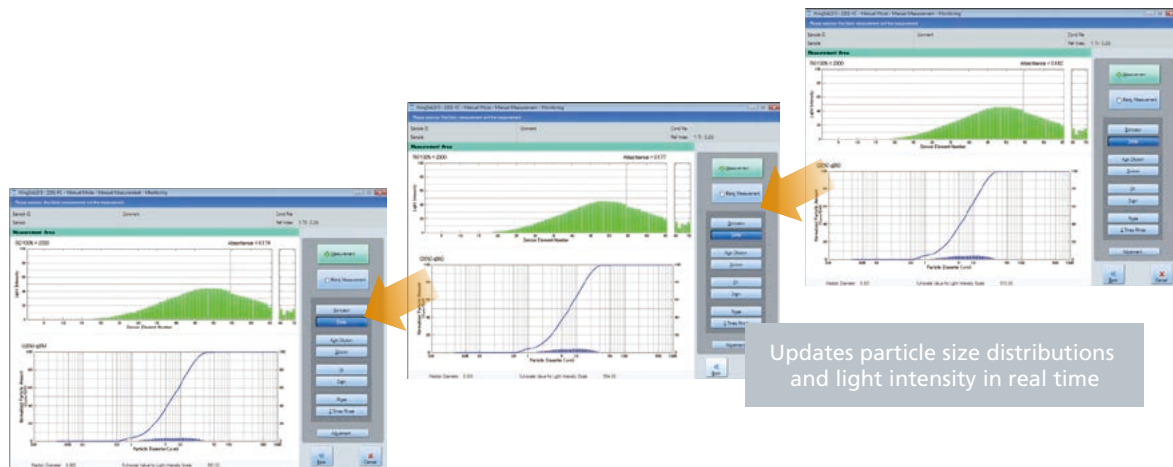
Creating, saving, and sharing measurement conditions and procedures, including pretreatment methods and conditions, ensures measurements are performed using the same conditions and procedures, even if performed by a different operator or at a different location or plant, and allows safely comparing data. Furthermore, when the measurement assistant function is used, measurement instructions for the operator are displayed on the screen. This enables even inexperienced operators to perform measurements correctly. In addition, administrators and operators can be assigned different operating privileges to ensure security.

Note: SOP is an acronym for Standard Operating Procedure.



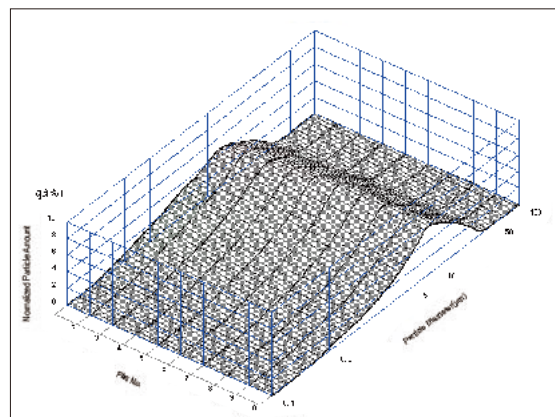
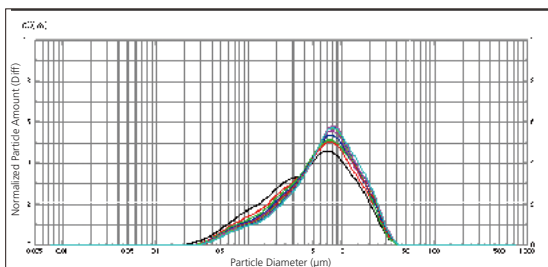
Particle size distribution data and light intensity distribution data can be displayed in real-time

This means that changes in the sample over time or shifts in the dispersion status can be monitored in real time. Since both the light intensity distribution data, which is the raw data, and particle size data can be monitored simultaneously, both data sets can be compared to monitor any changes in the status of samples.



Continuous measurement of 1-second interval particle size changes

Changes in particle size distributions and particle diameters are measured continuously, at intervals as short as 1 second, and the results are saved. Furthermore, the results can be subjected to multifaceted analysis and evaluation using functions such as 3D graphing. For example, the reaction processes that occur when particle groups disperse, aggregate, or dissolve can be monitored



This is an example of light intensity distribution data and particle size distribution data for the dissolution process of calcium carbonate. It shows how dissolution progresses from smaller diameter particles and how the normalized amount of large particles increases.

Software Features

Measurement data from multiple facets – Extensive assortment of data analysis applications included standard –

The following data analysis applications are included standard.

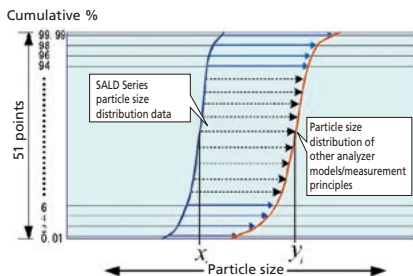
Evaluation of Scattering Angle

Graphs the components of scattered light intensity at each angle. Taking advantage of the features of the highly integrated photodiode array, it allows evaluating low-angle scattered light with high resolution.

Application Fields: Evaluating the scattering characteristics of films and sheets

Data Emulation Function

Based on SALD series measurement results, this function allows emulating measurement results obtained using other models and measurement principles. This ensures data compatibility with previous measurement methods.



- 99.99 % 1st emulation expression: $\log y_1 = (\log x_1) \times a_1 + b_1$
- 98 % 2nd conversion expression: $\log y_2 = (\log x_2) \times a_2 + b_2$
-
- ith conversion expression: $\log y_i = (\log x_i) \times a_i + b_i$
-
- 2 % 50th conversion expression: $\log y_{50} = (\log x_{50}) \times a_{50} + b_{50}$
- 0.01 % 51st conversion expression: $\log y_{51} = (\log x_{51}) \times a_{51} + b_{51}$

51 conversion expressions can be obtained at the cumulative % points (0.01 %, 2 %, 4 % 96 %, 98 %, 99.98 % on vertical axis) to express the relationship between the particle size distribution data measured by SALD-7500nano and that measured by another instrument or technology.

102 parameters a_i ($i = 1, 2, \dots, 51$) and b_i ($i = 1, 2, \dots, 51$) used in 51 conversion expressions can be stored as a parameter table, which can be used for emulations.

This emulation function may be able to reduce some problems when an old particle size analyzer is upgraded to a new instrument.

The same samples must be measured by two instruments in order to develop the parameter table for emulations.

Mixture Data Simulation Function

Allows simulating particle size distributions using any mixture ratio of multiple particle size distributions. This makes it possible to determine the optimal mixture ratio for obtaining the desired particle size distribution, without the trouble of repeatedly measuring the particle size distribution of sample mixtures.

Data Connecting Function

Allows combining the measurement results for two different measurement ranges at any particle size point to create a single particle size distribution. For example, sieve data for particles above 2000 μm can be combined with SALD series data for particles below 2000 μm to create a wide-ranging particle size distribution, which is required for civil engineering, disaster prevention, and environmental fields.

More efficient processing of multiple sets of data

Multiple sets of data can be stored as a group. In addition to organizing the data, it makes redisplaying and reanalyzing it easier. Data can be loaded as a group and displayed or analyzed at the same time, rather than having to load each set of data separately.

System Structure

An evolved nano particle size analyzer for accurate evaluation of nano particles

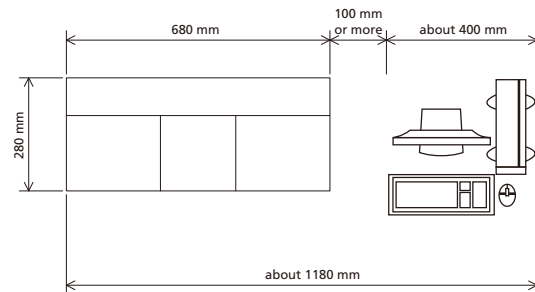
Measurement unit SALD-7500nano

- Violet semiconductor laser (wavelength: 405 nm) is used for the light source. Maintenance, such as gas replacement, is unnecessary.
- The detector incorporates 78 elements at the front, 1 element at the side, and 5 elements at the back for a total of 84 elements. Additionally, high-sensitivity light receptors that support violet semiconductor laser wavelengths are adopted with all detectors.
- The fixed parts of the cell and cell holder can be pulled out at the front of the unit using a slide mechanism. This makes it easy to mount and replace cells, and to perform maintenance.
- WingSALD II software is supplied as standard. It offers versatile data processing and simple, high-speed operation to suit every purpose and processing requirement.

Add optional units to the SALD-7500nano to design a wide range of systems.



Measurement unit SALD-7500nano



The batch cell and the high-concentration measurement unit can be set in the measurement unit.

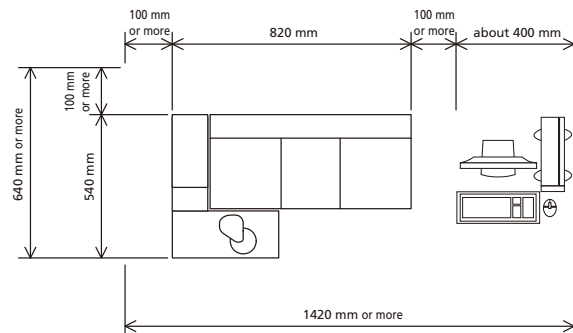
Small-volume Measurement System (SALD-7500nano and SALD-BC75)

High-Concentration Measurement System (SALD-7500nano and SALD-HC75)

Ultra Small-Volume Measurement System (SALD-7500nano and SALD-HC75 and "Glass Slides with Indentation")

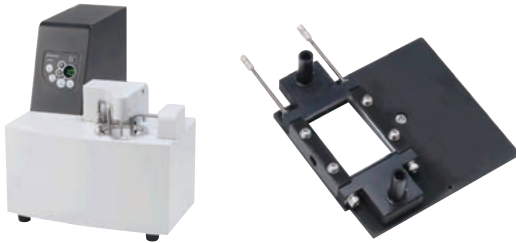


Wet Measurement System
SALD-7500nano and SALD-MS75



System Structure

Easy Measurement under PC Control Sampler SALD-MS75



- Groups of particles are dispersed in a liquid medium and measured as they are circulated between the flow cell, which is placed in the measurement unit, and a dispersion bath in the sampler.
- The dispersion bath incorporates a stirrer and an ultrasonic sonicator. A pump delivers the dispersed suspension to the flow cell.
- The pump is specially designed to ensure both liquid medium and the particles are circulated.
- It can be controlled from a PC.
- Most organic solvents can be used as dispersion media.

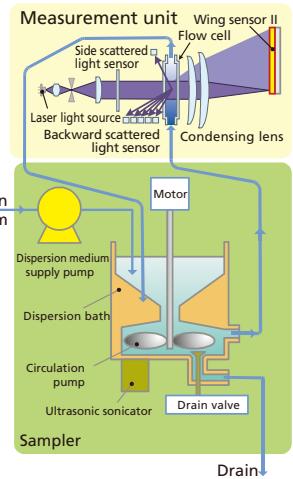
Solvent Resistance

Solvent	Solvent Resistance	Solvent	Solvent Resistance	Solvent	Solvent Resistance
Acetone	Applicable*note2	Xylene	Applicable*note2	Isopropyl Alcohol	Applicable
Isopropyl Alcohol	Applicable	Cyclohexane	Applicable*note2	Hexane	Applicable
Ethyl Alcohol	Applicable	Cyclohexane	Applicable*note2	Benzene	Applicable*note2
Ethylene Glycol	Applicable	Toluene	Applicable*note2	Methyl Alcohol	Applicable

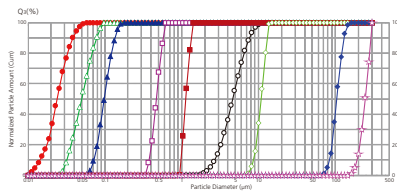
Note1 Solvent resistance toward materials used in the passageways of SALD-MS75. Solvent resistance values are representative, and are not certified.

Note2 Only applicable for liquid pump. Not applicable for liquid supply pump.

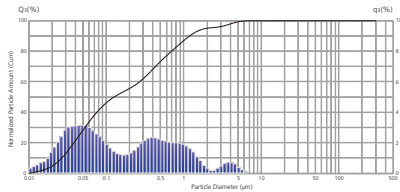
Note3 Ultrasonic cleaning instruments are needed for the measurement of reference sample.



Measurement data



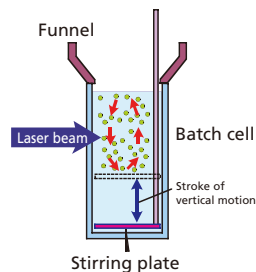
Variety of small and large sample particles



Carbon nano tube

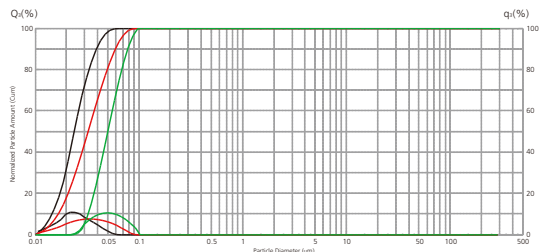
Ideal for Measurement with Small Amounts of Organic Solvent

Batch Cell SALD-BC75

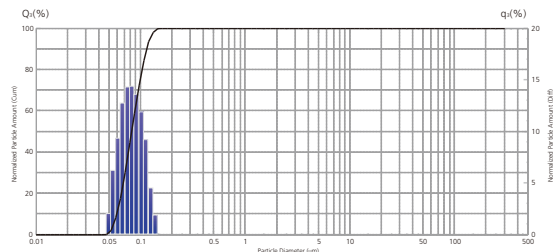


- Measurement is possible with a small amount of sample (i.e., measured particles) and liquid medium (i.e., dispersion medium).
- The capacity of the batch cell is only 5 cm³ so waste treatment for the suspension can be performed with relatively small amounts.
- The vertical motions of the stirring plate prevent sedimentation of the particles.
- The funnel reduces the possibility of sample spillage.
- A tetrafluoroethylene resin funnel is provided to reduce the possibility of suspension getting on the hands of the user. It also prevents the cell surface from becoming dirty.

Measurement data



Polystyrene Latex (20 nm, 30 nm, 50 nm)

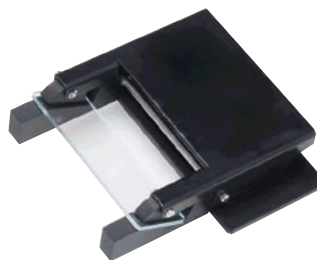
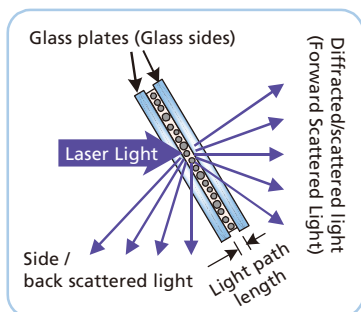
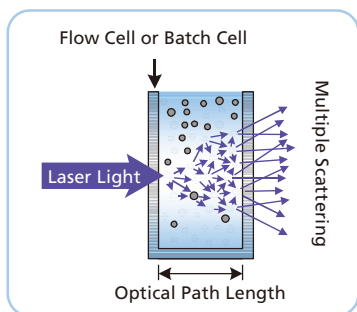


Silica particle

Measurement Samples without Dilution

High-Concentration Measurement Unit: SALD-HC75

- High-concentration samples can be measured using the laser diffraction method.
- Measurement is possible by simply holding the high-concentration sample particles to be measured between two glass slides.
- Samples for which the particle size distribution would be changed by dilution can be measured in their original state, or with the minimum required level of dilution, and a true image of the measurement object can be obtained.
- Commercial hand creams, face creams, and rinses can be measured with hardly any pretreatment.



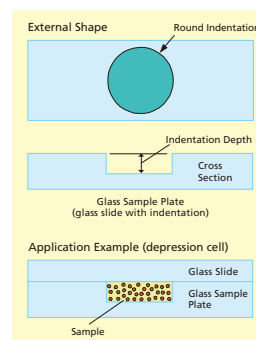
If a standard flow cell or batch cell is used to measure a sample at a high concentration, the long light pathlength results in multiple scattering, making it difficult to obtain accurate measurements. With this system, however, it is possible to hold the

high-concentration sample particles between two glass slides, which shortens the length of the light paths, avoids the negative effects of multiple scattering and makes accurate measurement possible.

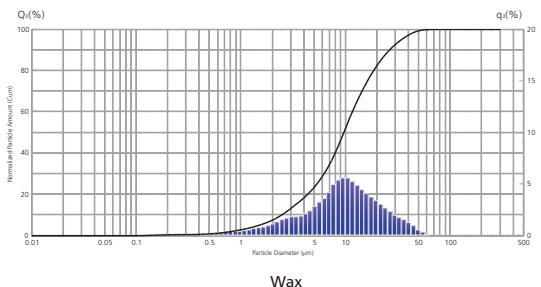
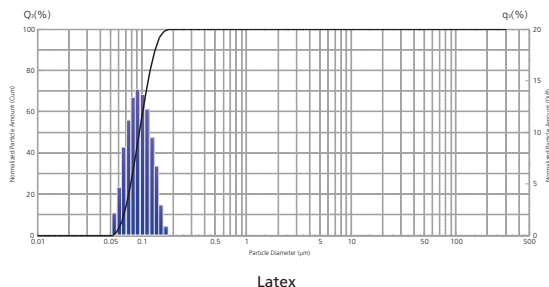
Glass sample plates (glass with indentation) (Option)

Effective for measuring samples with relatively low concentrations, or expensive samples that can only be used in small amounts.

P/N	Name	Indentation depth	Number	Sample volume	Particle concentration (% by weight)
346-62295-01	Glass sample plate (0.1 mm)	0.1 mm (100 μm)	10	0.03 cm ³	A few hundred ppm to a few percent
346-62295-02	Glass sample plate (0.2 mm)	0.2 mm (200 μm)	10	0.06 cm ³	
346-62295-03	Glass sample plate (0.3 mm)	0.3 mm (300 μm)	10	0.09 cm ³	
346-62295-04	Glass sample plate (0.4 mm)	0.4 mm (400 μm)	10	0.12 cm ³	
346-62295-05	Glass sample plate (0.5 mm)	0.5 mm (500 μm)	10	0.15 cm ³	
346-62295-06	Glass sample plate (0.05 mm)	0.05 mm (50 μm)	10	0.015 cm ³	
347-60002	Glass sample plate set	0.05 to 0.5 mm, two each	12 in total		



Measurement Data



Specifications

Hardware

General Specifications

Measurement principle	Laser Diffraction Method
Measurement range	7 nm (0.007 μm) to 800 μm (when using sampler) 7 nm (0.007 μm) to 400 μm (when using batch cell) 30 nm (0.03 μm) to 280 μm (when using high-concentration sample unit)

Note 1: The measurement range varies according to the shape etc. of the particle.

Measurement unit: SALD-7500nano (P/N 347-61710-42 [115V], 347-61710-44 [230V])

Light source	Semiconductor laser (Wavelength 405 nm)
Light detector	Detector elements for violet semiconductor laser Total 84 elements (78 forward, 1 side, 5 back)
System compliance	Class 1 Laser Product, CE
Required power supply	AC 100 V \pm 10 %, 1 A, 50/60 Hz
Dimensions & weight	Approx. W680 x D280 x H430 mm, Approx. 32 kg
Operation environment	Temperature: 10 to 30 °C, Humidity: 20 to 80 % (no condensation)

Note 2: Reference sample and USB cable (2 m) supplied as standard

Note 3: Ultrasonic cleaning instruments are needed for the measurement of reference sample.

Sampler: SALD-MS75 (P/N 347-61711-42 [115V], 347-61711-44 [230V])

Dispersing bath	Capacity: 100 / 200 / 300 mL
Sonicator	Frequency: about 32 kHz, output: about 40 W
Liquid pump	Radial pump, maximum flow rate 2000 cm^3/min
Liquid pump material	Stainless (SUS 304, SUS 316), Tetrafluoroethylene (PTFE), Perfluoroelastomer (FEP)
Liquid supply pump	Diaphragm pump, maximum flow rate: 750 cm^3/min
Liquid supply pump material	Polypropylene
Flow cell	Quartz glass
Required power supply	AC 100 V \pm 10 %, 2 A, 50/60 Hz
Dimensions & weight	Approx. W390 x D520 x H430 mm, Approx. 18 kg
Operating environment	Temperature: 10 to 30 °C, Humidity: 20 to 80 % (no condensation)

Note 4: USB cable (2 m) supplied as standard

Batch Cell: SALD-BC75 (P/N 347-61712-42)

Cell material	Quartz glass
Required liquid volume	Approx. 5 cm^3
Stirrer mechanism	Up-and-down movement of blade
Dimensions & weight	Approx. W100 x D120 x H140 mm, Approx. 0.8 kg
Operating environment	Temperature: 10 to 30 °C, Humidity: 20 to 80 % (no condensation)

High-concentration Measurement Unit: SALD-HC75 (P/N 347-61713-42)

Cell material	Borosilicate glass
Required liquid volume	Approx. 0.15 cm^3
Dimensions & weight	Approx. W20 x D100 x H9 mm, Approx. 0.2 kg
Operating environment	Temperature: 10 to 30 °C, Humidity: 20 to 80 % (no condensation)



WingSALD II

Measurement and Data Display Functions	
Measurement of Particle Size Distribution	Allows measurements using measurement assistant function (interactive process based on SOP) and manual mode
Automatic Calculation of Refractive Index	Automatic calculation by Light Intensity Distribution Reproduction (LDR) method based on specified substance name or range
Real-time Display	Particle size distribution / Light intensity distribution simultaneous display
Recalculation of Particle Size Distribution	Max. 200 data batch calculation or individual data calculation
Display of Particle Size distribution Data	Max. 200 data overlay graph or individual data graph
Display of Light Intensity Distribution	Max. 200 data overlay graph or individual data graph
Diagnostics/Adjustments	Self-diagnostic functions, Cell check functions
Statistical Data Processing	Max. 200 data (Max. 200 data overlay graph)
Time Series Analysis	Max. 200 data
3-Dimensional Graph	Max. 200 data
Data Transfer via Clipboard	Image Output, Text Output
Data Sorting	Sort by file name, sample ID, sample number, or refractive index.
Output Conditions	
Particle Size Distribution (μm) Number of Divisions	Fixed 101 / 51 divisions / Optional (can be set by user) 51 divisions
Particle Mass Distribution (%) Number of Divisions	Fixed 51 divisions, Optional (can be set by user) 51 divisions
Dimension of Particle Amount	Count, length, area or volume
Expression of Cumulative Distribution	Undersize, oversize
Expression of Data Frequency	q , $q / \Delta x$, $q / \Delta \log x$
Smoothing Level	10 Level
Distribution Function Fitting	Rosin-Rammler distribution, logarithmic Gaussian distribution
Data Shifting	± 10 levels
Report Functions	Batch output possible by selecting single data (template 6), overlay data (template 5), statistical data, time-series data, or 3D data
Data Analysis	
Scattering Angle Evaluation	Max. 200 data overlay graph or individual data graph
Data Conversion Function	Emulation of particle distribution data by other instruments or measuring principles
Mixing Simulation Function	Max. 6 points
Data Connection Function	2 data connections
Continuous Measurements Function	Measurement interval: 1 second min., Save up to 200 data points

Note 5: The Light Intensity Distribution Reproduction (LDR) method calculates the refractive index from the conformity between the measured light intensity distribution pattern and the light intensity distribution data reproduced (calculated) from the particle size distribution data. LDR is a proprietary method developed by Shimadzu. Two papers have been published on this method. It is sometimes called the "Kinoshita Method" at academic conferences.

PC Requirements (reference)

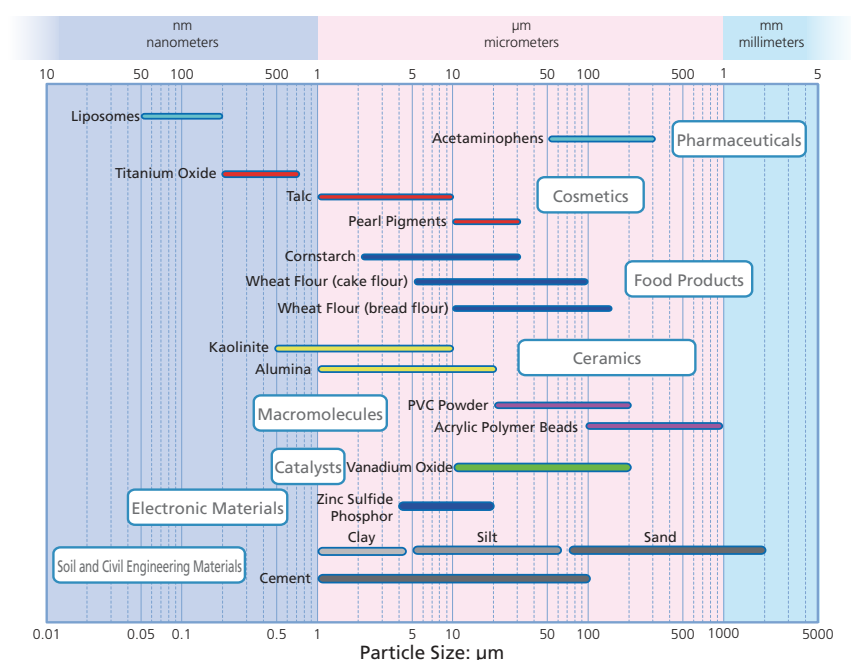
The software is included standard on a CD-R with the SALD system (optical system). Install the software on a PC that meets the following specifications.

OS	Windows 7 (32 bit version)
CPU	Pentium Dual-Core 2.5 GHz min
MEMORY	2 GB min
HDD	Min 1 GB of free space required
CD-ROM Drive	Required software installation
Serial Port	USB×1 (required 2 USB ports for using sampler via PC)
Display	SXGA (1280×1024 pixel) min.
Printer	Must be compatible with operating system

Particle Size Analyzer Applications

Particle size distribution is one of the main factors determining the characteristics of powders and particles, which are used in a wide variety of fields for a wide range of objectives and applications. In some cases, they are used directly as pharmaceuticals, catalysts, additives, or binders while in other situations they are used as raw ingredients. In either case, the

particle size distribution can have a major effect on the characteristics desired for a given application or objective, or on the performance and quality of a final product. Consequently, measuring the particle size distribution is essential to stabilize and/or improve the characteristics, performance, or quality of powders or particles.



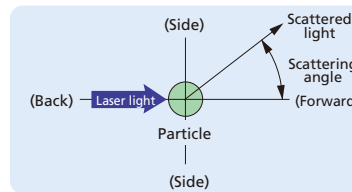
Shimadzu particle size analyzers are used in a wide variety of fields for a wide range of purposes and applications.

1. Nano particles	Nano particles are expected to provide benefits as a result of the special properties related to their size. Particle size analyzers provide an extremely important tool for developing methods to maintain good dispersion characteristics by ensuring contaminants and aggregates are identified and screened out.
2. Pharmaceuticals	The smaller the particles, the larger their specific surface area and the more quickly they dissolve. In the case of particles in medical injection, the particle size determines how they pass through or penetrate capillaries and blood vessel walls and which parts of the body they reach. This has a major influence on the efficacy and side effects of pharmaceuticals.
3. Cosmetics	For lipstick, mascara, and eye shadow, subtle differences in color and shine are controlled by differences in the particle size distribution. The smoothness or UV light-blocking properties of creams also vary depending on the particle size distribution.
4. Food Products	Many food products include powdered ingredients. The mouth, tooth, and tongue feel and other characteristics of bread, cakes, pasta, etc. depend on the particle size distribution. Also, controlling the particle size distribution in beverages is important to ensure consistent quality. For example, smaller particle sizes are used in milk and lactic acid beverages to prevent differences in concentration and taste between the upper and lower portions of the container.
5. Ceramics	The strength, density, hardness, heat resistance, water and air permeability, and other characteristics of ceramics depend not only on the type of ingredient particles, but also significantly on the particle size distribution.
6. Macromolecules	When particles are used as ingredients in pipes, films, and sheets, the particle size distribution can affect the strength and light permeability of the final product.
7. Catalysts	Though chemical reactivity is affected by the specific surface area and pore structure, given the same material, the chemical reactivity can be controlled by varying the particle size distribution.
8. Electronic Materials	The manner and degree to which particle size affects electronic materials differ depending on the application and material. However, the quality control of particle size distribution is increasingly required to ensure higher and more consistent quality of the final product.

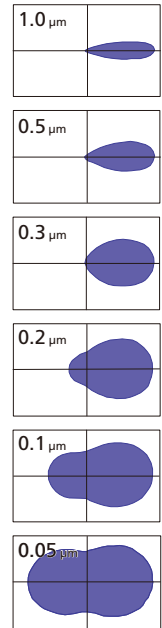


There is a one-to-one correspondence between the particle diameter and the light intensity distribution pattern.

When a particle is irradiated with a laser beam, light is emitted from the particle in every direction. This is "scattered light". The intensity of the scattered light varies with the scattering angle and describes a spatial intensity distribution pattern, known as the "light intensity distribution pattern". If the particle diameter is large, the scattered light emitted from the particle is concentrated in the forward direction (i.e., the direction of the laser beam), and fluctuates intensely in an angular range too small to be represented in a diagram. Compared to the light emitted in the forward direction, the intensity of all other light is extremely low. As the particle diameter becomes smaller, the pattern of the scattered light spreads outwards. As the particle becomes even smaller, the intensity of the light emitted to the side and backwards becomes higher. The light intensity distribution pattern becomes gourd-shaped and spreads out in every direction. Therefore, there is a one-to-one correspondence between the particle diameter and the light intensity distribution pattern. This means that the particle diameter can be ascertained by detecting the light intensity distribution pattern.



Diffraction / Scattering by Particle



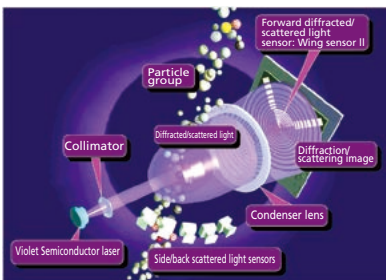
Relationship between particle diameter and Light Intensity Distribution pattern

Violet Laser Allows Accurate Measurements of Ultra-Small Particles.

The light intensity distribution pattern varies little relative to the particle size distribution when the particle size drops to several tens of nanometers. This is the reason for the minimum limit of detection of the laser diffraction method. A violet laser creates clearer differences in the light intensity distribution pattern at ultra-small particle sizes than a red laser. Consequently, a violet laser is used to enhance the measurement performance for ultrafine particles of the order of several tens of nanometers.

Measurement is performed on particle groups.

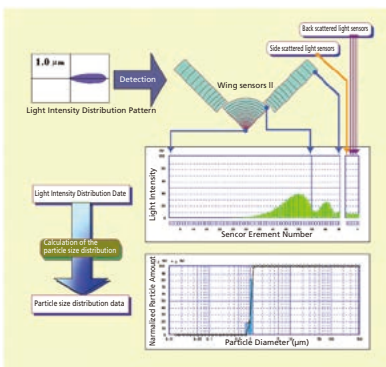
Particle size distribution measurement is not performed on individual particles, but rather on particle groups made up of a large number of particles. Particle groups contain particles of different sizes, and the light intensity distribution pattern emitted by a group is composed of all the scattered light emitted from all the individual particles. The particle size distribution, in other words, what particle sizes are present in what proportions, can be obtained by detecting and analyzing this light intensity distribution pattern. This is the basic principle behind the laser diffraction method.



Optical system in SALD-7500nano

Optical System in SALD-7500nano

The laser beam emitted from the light source (semiconductor laser) is converted into a thick beam with a collimator and this is directed at the particle group. The scattered light emitted from the group in a forward direction at up to a 60° angle is concentrated with a lens, and concentric scattering images are formed at a detecting plane positioned at a distance equal to the focal length. This is detected with the Wing sensor II in which light-receiving elements are arranged concentrically. The scattered light emitted to the side and backwards is detected with side and back scattered light sensors. The light intensity distribution data can be obtained by detecting scattered light data of all directions.



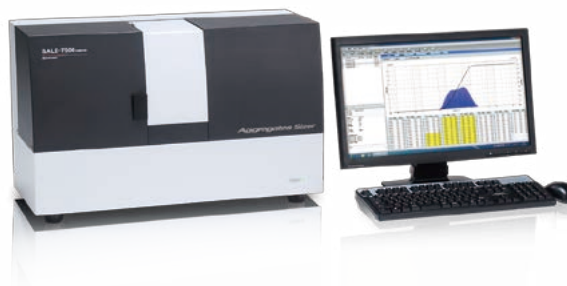
Flow of Light Intensity Detection and Data Processing

With the SALD-7500nano, particle size distributions are calculated using the light intensity distribution data. The overall flow of detection and data processing is shown in the diagram to the left. The whole range of operations from the detection of scattered light intensity distribution patterns to the calculation of the particle size distribution is executed as one process, and the particle size distribution data is output. Recalculation of particle size distributions can be performed by using the previously detected and saved light intensity distribution data and selecting a refractive index that is different from the time of measurement.

Aggregation Analysis System for Biopharmaceuticals

Aggregates Sizer

The Aggregation Analysis System for Biopharmaceuticals is created by adding a special option to the SALD-7500nano Nano Particle Size Analyzer. It permits the quantitative evaluation of sub-visible particles (SVP) in the sub-visible region (100 nm to 10 μ m). Despite the ability of sub-visible particles (SVP) to cause fatal side effects in humans, such as anaphylaxis, they have been little studied and no analytical method has been established for them. This system offers the following three features.



1 Quantitatively evaluates SVP range aggregate concentrations

The Aggregates Sizer is able to measure aggregates of a wide range of particles sizes, from 7 nm to 800 μ m, as part of a particle size distribution (displayed with particle quantities totaling 100 %). Furthermore, aggregate concentrations in the SVP (sub-visible particle) range, from 100 nm to 10 μ m, can be evaluated quantitatively (in terms of μ g/mL or number/mL).

Evaluation range of particle size: 40 nm to 20 μ m

Concentration display range: 40 nm to 20 μ m

2 Measures aggregates with high sensitivity

The Aggregates Sizer is over ten times more sensitive than Shimadzu's previous SALD series (SALD-7100) particle size analyzers. This means that even micro sample quantities can be measured accurately using disposable cells for 0.4 mL sample quantities.

3 Quantitatively evaluates aggregation processes at intervals as short as one second

Changes (sizes and quantities) in aggregates can be confirmed quantitatively as a concentration (unit: μ g/mL) at intervals as short as one second. This allows observing the status at various intermediate stages, not just at two stages, before and after such changes, which allows evaluating rates of change. Using a batch cell (5 mL sample capacity), aggregation processes can be observed as samples are mechanically stimulated.

4 Evaluates effect of temperature on aggregation process

Aggregates Sizer TC temperature control system can evaluate protein aggregates under a constant temperature (20 $^{\circ}$ C to 42 $^{\circ}$ C). It enables the evaluation of protein aggregation depending on the temperature.

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