NANOPHOX | PCCS

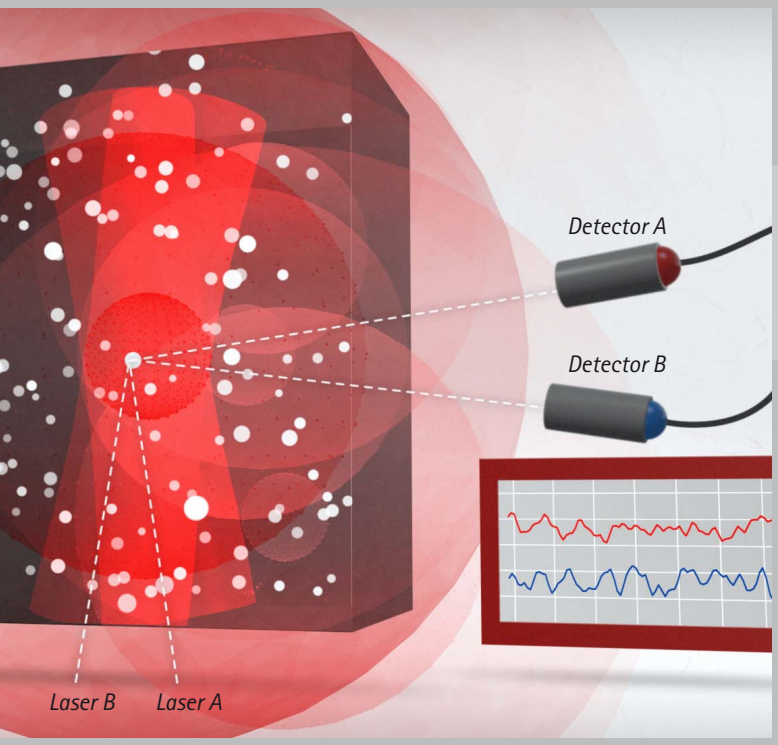
Particle Measurement | Laboratory

Size and Stability | 0.5 nm to 10,000 nm

Sympatec develops, manufactures, sells, services and supports a range of best instruments for particle size and shape analysis for laboratory and process applications to customers worldwide. With continuous innovations Sympatec makes a prominent contribution to ❱ laser diffraction, ❱ image analysis, ❱ ultrasonic extinction and ❱ photon cross-correlation spectroscopy.

Clear Signals from Opaque Suspensions

Measuring Nanoparticles in Liquids



Trend Nanotechnology

The size reduction of materials plays a central role for the development of innovative products. Applications based on ➔ nanoparticles can lead to advances in the improvement of properties and functionalities of disperse systems.

In pharmacy and biochemistry nanoparticles serve as API carriers or can be charged with molecules for targeted drug delivery. Polymers applied for steric stabilisation or ions serving as electrostatic stabilisation modify the size of the nanoparticles. For fine tuning of their properties and to study the functionality in its natural environment, reliable and efficient technologies and appropriate measuring instruments are required.

Dynamic Light Scattering (DLS)

DLS is a robust, simple and non-contact method for the measurement of particle size and particle size distributions from the nanometre to the submicron range. With high sensitivity it is ideally suited for detection of size changes as a function of time. Process modifications occurring in seconds may be traced in real time.

Within a measuring time of just a few minutes a very high number of particles is captured guaranteeing representative results. Its independence of particle properties, which are difficult to assess or measure (e.g. refractive index, absorption coefficient and material density), constitutes additional advantages for DLS. In the nanometre range these properties largely depend on size. In particular for coated, porous or alloyed particles they are difficult to determine.

For DLS analysis the hydrodynamic diameter is measured through optical detection of the ➔ Brownian molecular motion of particles in a liquid. The thermally agitated liquid molecules collide with the particles causing a random movement or diffusion.

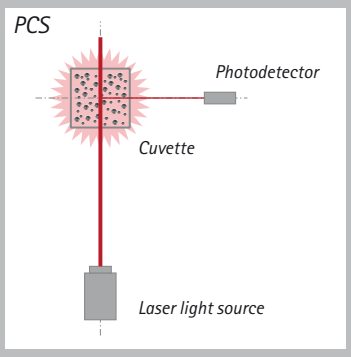
According to the ➔ Stokes-Einstein equation the diffusion velocities are inversely proportional to the size of the particles.

$$D(x) = \frac{k_B \cdot T}{3 \cdot \pi \cdot \eta \cdot x}$$

PCS as conventional technology

The principle of DLS traditionally is realised with Photon Correlation Spectroscopy (PCS). A laser is transmitted through the sample. With the help of a photodetector the scattered light intensity is monitored over time and then ➔ autocorrelated. The particle size distribution can be calculated with the correlation function.

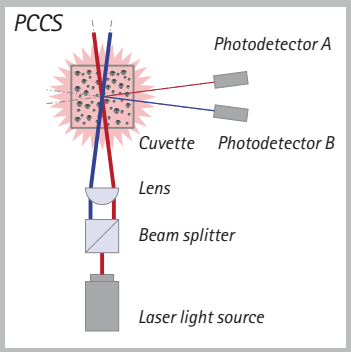
The size analysis with PCS is only valid for single scattered light. Samples of high solids concentration show a large proportion of ➔ multiple scattered light and the method reaches its limitations. To avoid incorrect data on particle distributions and to generate reliable measuring results, samples have to be diluted to a high ratio. In this way significant modifications of the particle properties are likely to occur.



PCCS as key technology

By applying an innovative light scattering technique using Photon Cross-Correlation Spectroscopy (PCCS) we are able to provide concurrent measurements of particle size and stability in opaque suspensions and emulsions.

The outstanding technical features of 3D cross-correlation are the acquisition of two separately generated scattered light intensities and its cross-correlation. The single scattered light proportion is thus separated from the multiple scattered part. A single laser beam is split into two separate beams of identical intensity and superimposed in one sample. Two independent scattering waves are then recorded with one detector for each wave, thus ensuring the exact signal interpretation.



➔ **Nanoparticles** *according to ISO definition are objects with 3 dimensions in the nano range between approx. 1 nm to 100 nm.*

➔ **Brownian molecular motion** *is the thermal motion of particles in liquids. It is measured for determination of the particle size.*

➔ **Stokes-Einstein equation** *establishes the correlation between viscosity η and temperature T of the liquid and the size x of the assumed spherical particles and its velocity. This defines the diffusion coefficient D(x) which serves for calculation of the hydrodynamic particle diameter x. k_B is the Boltzmann constant. If*

Nanoparticle Measurement in Primary Condition

NANOPHOX with PCCS

As a professional pioneer of PCCS we are offering the first table top instrument based on Photon Cross-Correlation Spectroscopy (PCCS). With this we consequently follow our strategy of developing innovative instruments which measure the sample as close as possible to its original state. PCCS opens possibilities for analysis of nanoparticles in suspensions and emulsions with hundreds of times higher solids concentrations than ever before.

The application of cross-correlation technology allows the calculation of the particle size distribution by eliminating the effect of multiple scattering. The amplitude of the cross-correlation function, which depends on the multiple scattering, provides direct measurement of changes in particle number and size. Differentiating measurements of agglomeration and sedimentation behaviour thus become feasible.

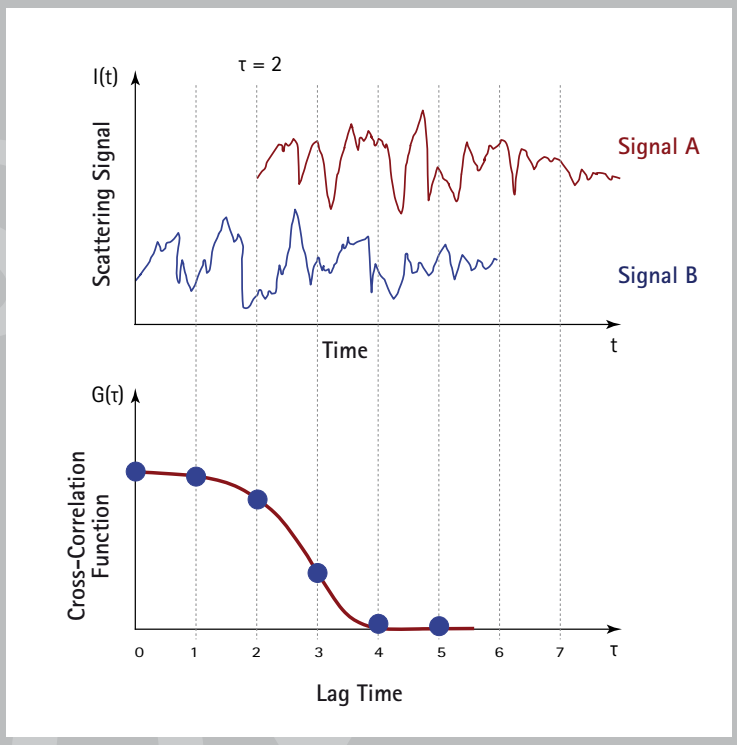
NANOPHOX is ideally suited for research and development as well as for industrial quality control.

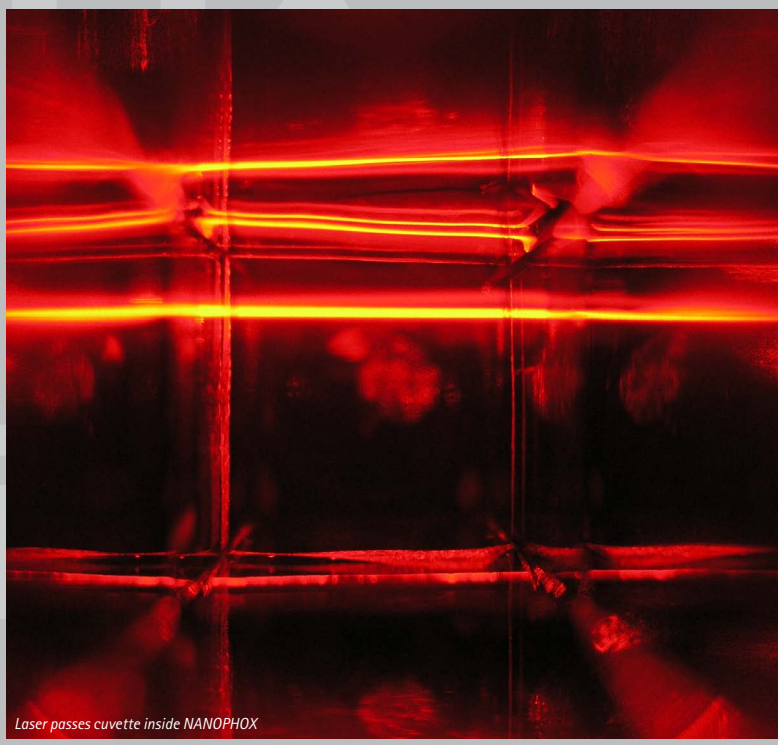
Reliable results made simple
NANOPHOX helps to reach the target quickly. Elaborate sample preparation is not required as even samples of high concentrations often need no dilution. The results are less sensitive against potential contaminations which for strongly diluted samples tend to significantly influence the particle distribution. Automatic positioning of the cuvette and precise setting of the laser intensity for optimization of the measuring signal is straightforward and user-friendly, helping to make the measurement process fast and simple.

» Small, smaller, nano ... with high sensitivity to reproducible results! «

Extended application range
NANOPHOX covers the vast particle size range of 0.5 nm to 10,000 nm. The size analysis is independent of concentration and masters high concentrations up to approximately 20 % by volume. Using a 30 mW semiconductor laser and Avalanche photo diodes minimum sample concentrations of just 0.0001 % by volume are measurable. This remarkably broad concentration range is possible due to the combination of PCS and PCCS in a single instrument.

With a precisely controlled temperature range from 0°C to 90°C the behaviour of nanodispersions can be observed or influenced, respectively. NANOPHOX proves its specific performance for stability analysis of steric or electrostatic stabilising in high-concentrated nanodispersions. No matter if the particles have been stabilised with electric charges, polymers or surfactants, NANOPHOX reliably provides information on aggregation or agglomeration behaviour. Thus new opportunities for characterization in previously uncharted fields, such as particle-particle interactions and changes in dynamic viscosity, are easily accessible.

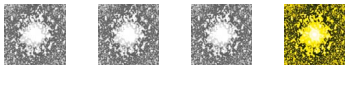



Laser passes cuvette inside NANOPHOX

[3] *viscosity and temperature remain unchanged, fine particles move faster than coarse particles.*

➔ **Autocorrelation:** *The scattered signal is correlated with itself at different points in time (a comparison of the time lagged and the original function).*

➔ **Multiple scattered light** *occurs if the incident laser light is scattered more than once by particles and disturbs the scattering wave on its way to the detector.*



Nanoparticles in a Unique Concentration Range

Who is Closer to the Original?

Dilution Series | Stability Analysis

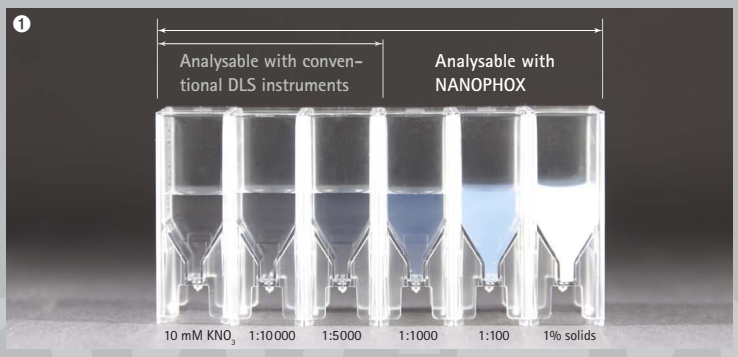
Dilution series | PCS and PCCS

High solids concentrations induce ➔ photons to be scattered more than once. Distorted results and misinterpretations are the consequence. When measuring with PCS sample dilution reduces the multiple scattering. We have conducted tests with 100 nm DLS reference material over a wide concentration range showing the performance of PCCS. ❶ Five different latex samples illustrate a spectrum extending from the undiluted original suspension with 1 % solids content to a dilution ratio of 1:10,000.

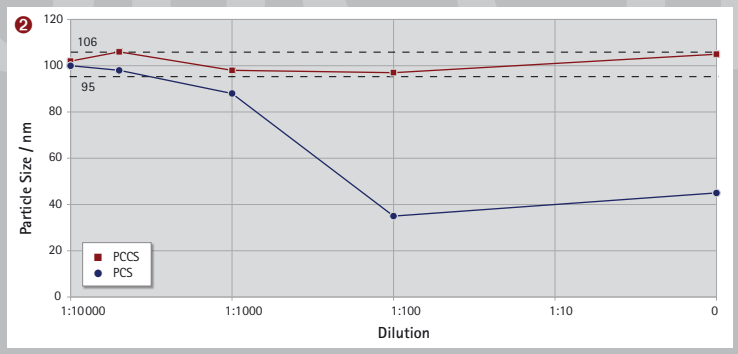
❷ For measurements performed on the NANOPHOX in the PCCS mode the hydrodynamic diameter ranges within the specifications between 97 and 106 nm, independent of the dilution. Meanwhile the PCS results remarkably deviate from the specifications for dilution ratios of 1:1,000 and above. Particle size cannot be determined reliably without dilution.

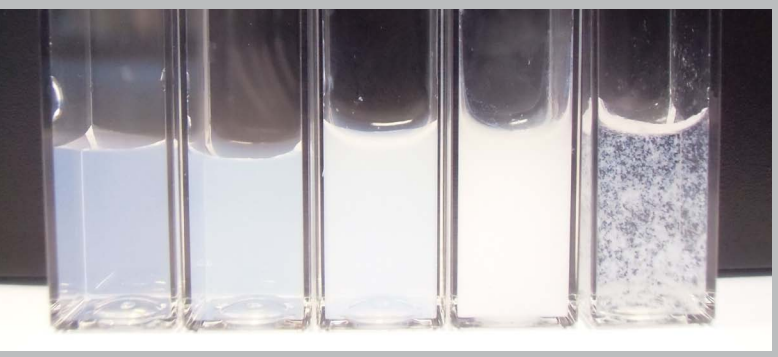
For correct results no dilution of the latex sample is required when using PCCS. The application of cross-correlation significantly enhances the concentration range for samples which can be measured with dynamic light scattering. Unwanted sample dilution can be avoided and particle size measurements in the original concentration of the respective application are possible.

❶

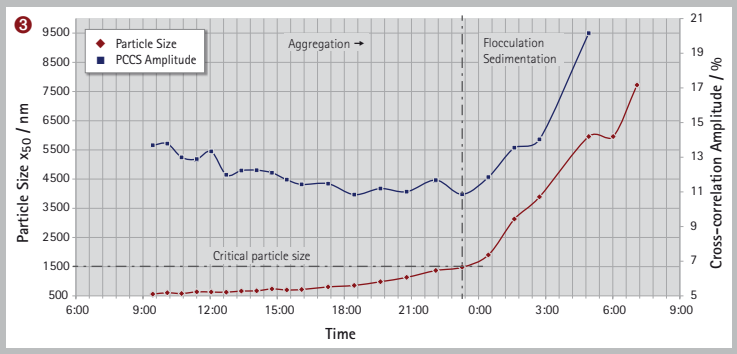


❷





❸



Stability analysis

Stability is a vital factor for the production and storage of nano-dispersions. It provides information about the duration of use for a product under optimum storage conditions.

The stability of an emulsion or suspension is significantly affected by the chemical environment of the particles such as the pH-value, ionic strength, surfactant or polymer concentration.

❸ The time-dependent aggregation of a 500 nm latex suspension in a 0.15 molar NaCl solution is shown as an example. With progressing aggregation the sample becomes more turbid until it flocculates. The amount of coarse particles and its ➔ scattering efficiency increases. The cross-correlation amplitude decreases with increasing multiple scattering. Once the coarse particles reach a critical size so that sedimentation occurs, the particle concentration decreases and with this the fraction of multiple scattered light. The cross-correlation amplitude increases.

With the time dependent measurement of the cross-correlation amplitude and the mean particle diameter, PCCS captures aggregation and sedimentation kinetics. PCS cannot provide such information. The example impressively proves the interaction of two instable processes which NANOPHOX can measure directly, sensitively and reliably.

➔ **Photons** *or light particles are elementary particles of the electromagnetic field. They are „components" of electromagnetic radiation.*

➔ *Scattering theory describes the* **scattering efficiency** *of a particle as scatter diameter. It depends on the particle diameter with the 6th power (C–x⁶). Doubling the particle diameter yields a 64 times bigger scattering efficiency and is valid for the Rayleigh regime.*

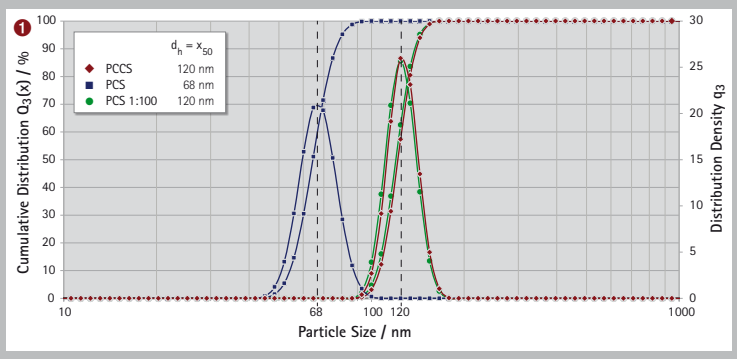
Precise Results without Dilution | High Sensitivity for Size Change

Ophthalmic emulsion

In pharmaceutical applications particulate systems are applied as drug carrier. Its precise characterization is a basic condition for the approval of the product. Pharmaceutical emulsions such as eye drops are subject to numerous quality characteristics, one of which is the droplet size of the disperse phase within the emulsion.

Droplets being too fine or too coarse may reduce the efficiency or may become a risk for the eye. The ophthalmic emulsion analysed in this example is a white, very turbid homogeneous liquid. With the PCCS technology the sample can be measured without dilution. ❶ The result shows the expected mono-modal size distribution with a mean diameter of 120 nm. When measuring this sample in PCS mode the size distribution shows a mean diameter of just 68 nm and clearly remains below the expected specifications. The strong deviations can be explained by the influence of multiple scattering. Only after dilution to a ratio of 1:100 in pure water the size distribution of the droplets is correctly determined.

NANOPHOX measures the sample in its original condition, minimising the effect of sample contamination. Dilutions which might change the chemical properties can be discounted. Based on the robust and easy to use measuring method, the instrument is ideally suited for production and quality control of pharmaceutical emulsions.



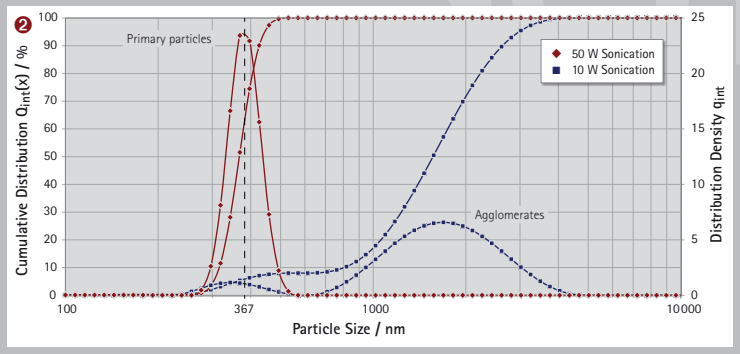
Alumina powder

A variety of nano and micro particles are synthesized by dry production processes. For numerous industrial applications of alumina powders the particles have to be prepared as suspensions before introducing them for efficient product improvements. This introduces the challenge of preparing stable dispersions. Agglomerates may affect the functionality of the product.

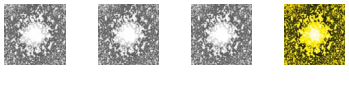
❷ For measurement of the dispersion quality a suspension was prepared of 0.05 % by weight alumina powder in water and treated with an ultrasonic probe. The energy input of 50 W yields a monomodal distribution with a diameter of 367 nm. Reducing the ultrasonic power to 10 W provides a significantly worse dispersion quality. A remarkable portion of coarse agglomerates can be observed in the measured particle size distribution together with a reduced fraction of primary particles.

The strengths of NANOPHOX can be found in the broad concentration range and the sensitive resolution of bimodal particle distributions. It also very reliably indicates size changes.

With PCCS the result is independent of particle concentration and permits measurements of dispersion quality even in suspensions of high concentrations.



➔ *Further typical applications for NANOPHOX are polymer emulsions, colloidal silica, ink, pigments and the research of nanomaterials in general, specifically for the automotive industry, electronics, pharma, mechanical engineering, environmental protection and energy.*

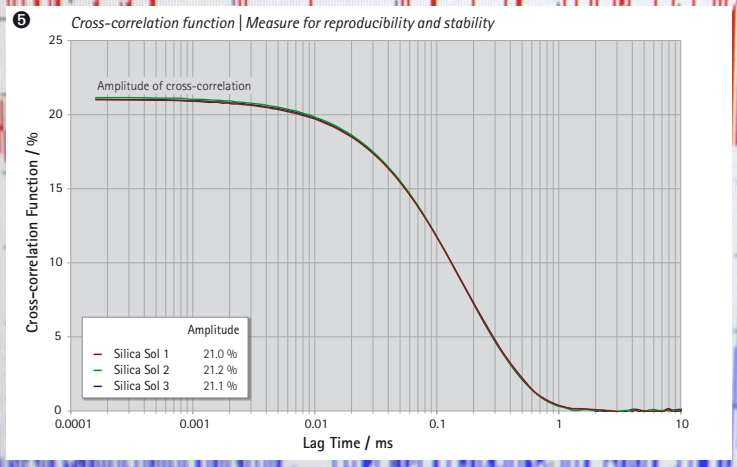


WINDOX Software

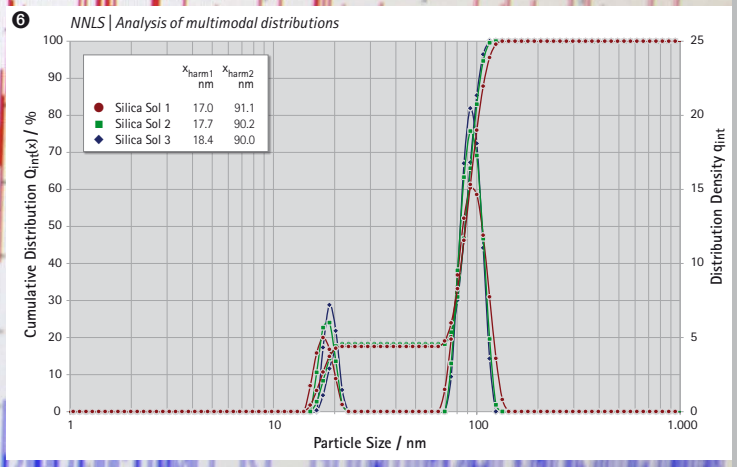
Measuring Process and Results

Preparation | Measurement | Evaluation

❺ *Cross-correlation function | Measure for reproducibility and stability*



❻ *NNLS | Analysis of multimodal distributions*



Sympatec's WINDOX software is realised on contemporary Windows® based operator interfaces and multi-user, multitasking database infrastructure. From a single control window all functions are addressed offering intuitive solutions for reliable measurement operations.

After ❶ filling the cuvette, the sample is ❷ loaded into the NANOPHOX which takes one hand only. A simple mouse click ❸ starts the measurement.

The signal yield can be optimized fully automatically or manually. As the measuring signals are presented in real time, changes or quality of measurement can be observed directly. After each run the raw data is stored in the database automatically. This allows for later input of evaluation parameters and the re-evaluation of the measurement without additional analysis.

❹ WINDOX provides graphical presentations and reports, which can be selected from a variety of formats or user defined and arranged with extensive editing options. Data browser and filter functions allow the retrieval and presentation of already available analysis data.

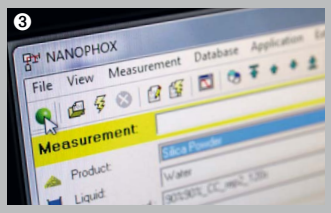
❺ The cross-correlation function, representing reproducibility and stability, is used to calculate the particle size distribution. In addition to the classic ➔ 2nd Cumulant evaluation WINDOX offers a distinctly more efficient ❻ Non Negative Least Square (NNLS) evaluation algorithm. The NNLS mode reliably presents polydisperse or ➔ bimodal samples with up to 256 size classes directly as volume or intensity based distribution. A diversity of characteristic values such as the arithmetic or harmonic mean values (x_{harm}) of single modes is directly available.

With its open structure, programming facilities and data management our WINDOX software is ideally suited for flexible applications in production as well as research. It also meets the requirements of regulated industries. For users in pharmaceutical sector the software comprises all elements to allow full compliance with the demands of 21 CFR Part 11.

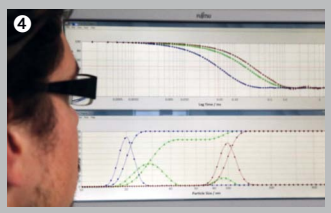
❶

❷

❸



❹



➔ **2nd Cumulant evaluation** *provides a mean diameter and a polydispersity index (ref ISO 22412:2008). It cannot present a particle size distribution.*

➔ *A* **bimodal sample** *comprises two particle fractions (modes) of different size distributions.*

Pulverhaus

Brand Home of Sympatec's Premium Instruments

Development of Innovative Methods for Particulate Systems Characterization

Laser Diffraction | Image Analysis | Ultrasonic Extinction | PCCS

Perspective

"A classic is timeless and at the same time ahead of its time."

The variety of disperse products requires innovative and sustainable technologies to master the challenges in today's research, development, quality and production control.

With dry dispersion we have introduced product orientation and adaptation to laser diffraction.

The HELOS sensor family and a great range of dispersing units – spear-headed by RODOS – offer you premium performance. Our laser diffraction instruments allow for a significant extension of your particle knowledge concerning size and size distributions.

New questions and desires inevitably arise with unbowed progress. Power of innovation consequently remains key to future developments.

Today, if we encounter application limits of laser diffraction e.g., in suspensions of high optical concentration, we offer efficient solutions with ultrasonic extinction (NIMBUS).

If particle shape becomes of interest, we provide a great spectrum of powerful solutions with high-speed dynamic image analysis (QICPIC family). Now even sophisticated fibre analysis is amongst the range of multifaceted particle shape aspects.

And in case particles predominantly belong to the nanometre range, we have brought the unique Photon Cross-Correlation Spectroscopy (PCCS) to market with Sympatec's NANOPHOX.

By nature, we also keep an eye on the production of disperse systems when developing methods of particle characterisation. Hence, you may also trustfully address us in case process control becomes an issue. Laser diffraction with MYTOS, ultrasonic extinction with OPUS and dynamic image analysis with PICTOS are hundredfold approved process applications from Sympatec.

Designed with a consistent technological basis, our in-, on-, at-line systems reliably deliver results that are perfectly comparable to those of our laboratory instruments – most accurate, reproducible and at the shortest measuring times.

As "Particle People" we originate from the powder technology field. This is why we have a natural approach to process engineering and the production of disperse systems. The collective particle expertise of our physicists, mathematicians, computer scientists, engineers, electronic and mechanic technicians is built into our instruments.

Your particles in the best of hands with us.

Particle Measurement and Know-how from Pulverhaus

Several Thousand Installations

At Particle Professionals Worldwide

Sales | Service and Partner Organisations

Sympatec

Headquarter
Pulverhaus Clausthal
Germany Centre & North
+49 5323 717 0

Germany South & Alps
Southeastern Europe
Augsburg
+49 8231 605 7991

Germany East | Eastern Europe
Leipzig
+49 341 942 3510

Germany West
Pulverhaus | Krefeld
+49 2151 978 100 | 101

Nordic
Vimmerby SE
+46 4964 0220

Switzerland
Basel
+41 61 303 1040

BeNeLux
Etten-Leur NL
+31 76 503 1634

Commonwealth of
Independent States (CIS)
Ekatarinburg RU
+7 905 801 8759

United Kingdom
Bury GB
+44 161 763 5757

France
Orsay
+33 1 6918 1955

Korea
Seongnam
+82 31 706 4783

China Head Office
Suzhou
+86 512 6660 7566

China Beijing Region
Beijing
+86 10 6831 5728

Head Office North America
USA Northeast & Canada
Pennington NJ
+1 609 303 0066

USA Middle Atlantic
Columbia MD
+1 410 299 1746

USA Southeast
Charlotte NC
+1 704 519 5379

USA Midwest
Patricksburg IN
+1 812 859 3699

USA West
Fort Collins CO
+1 267 886 3455

India
Mumbai
+91 22 6770 9181

Partner

Your personal contact

worldwide partners

Sympatec GmbH – System | Partikel | Technik
Am Pulverhaus 1, 38678 Clausthal-Zellerfeld
Germany

Contact
+49 5323 717 0
sales@sympatec.com

www.sympatec.com