









HIGH PERFORMANCE PARTICLE SIZER— THE FIRST SYSTEM TO COMBINE HIGH SENSITIVITY WITH A HIGH CONCENTRATION CAPABILITY



#### **Compact and versatile**

N T R O D U C T I O N

The Malvern HPPS covers a wider application range than three conventional dynamic light scattering systems. The patented technology incorporated in the Non-Invasive Back-Scatter optics (NIBS<sup>™</sup>) enables high sensitivity and high concentration measurements over an exceptionally wide size range from 0.6nm to 6000nm diameter.

- A higher sensitivity than a dedicated instrument for samples as dilute as 0.1ppm
- The high concentration range of back-scatter optics up to 20 vol% to simplify sample preparation
- A wider range of applications than covered by a classical dynamic light scattering system



### The widest application range

Using a single instrument, requiring a minimum of bench space, you can conduct particle size measurements on:

- Small particles such as solutions of proteins and peptides, micelles and viruses, organic and inorganic nano-particles
- Samples at concentrations up to 20 vol%, equivalent to 40 wt% for silica, can be measured with little or no dilution preserving their original nature
- A range of sample sizes from sub-nanometer to as high as 6 microns diameter
- Highly absorbing samples such as inks, dyes and pigments
  - Malvern's HPPS is a uniquely flexible analytical tool for particle size measurement across an unmatched range of concentrations and sizes.

# The advantages of Non-Invasive Back-Scatter technology — NIBS<sup>m</sup>

Non-Invasive— the sample is contained in disposable plastic or glass cuvettes

Back-Scatter— optics allow concentrated samples to be measured

#### Reduced sample preparation the simplest way to measure

It is often preferable to measure samples with minimal or no dilution.

- There is less risk of changing the sample if it is measured at or close to its original state
- Measurements of larger particles are improved as the higher number of particles in the measurement volume reduces intensity fluctuations

# The highest sensitivity for the measurement of solutions of proteins and polymers

The novel optics arrangement maximises the detection of scattered light while maintaining signal quality. This provides the exceptional sensitivity that is required for measuring the size of molecules smaller than 1000Da.

### He-Ne gas laser as light source for the best results

Laser diodes suffer from higher beam dispersion and poorer phase coherence, resulting in lower measurement repeatability.

He-Ne Laser



#### Features:

- Automatic adjustment to optimise settings for all sample types using auto cell-positioning
- Automatic adjustment of laser attenuator with a dynamic range of 300,000:1 to cover an intensity range of an amazing 3 x 10<sup>7</sup>:1
- Precision cell temperature control 10°C 55°C with 10°C 90°C option
- High efficiency avalanche photodiode detector as standard for the highest sensitivity
- Laser power monitor and transmission detector for sample and system diagnostics
- Stable He-Ne laser to ensure result repeatability



### Extended concentration range due to automatic cell positioning

The optimum measurement position in the cell depends on the sample concentration. This is close to the cell centre for small and dilute samples to maximise the observation volume, near the cell wall for more concentrated samples to minimise the distance light has to travel through the sample.

Diode Laser

Laser Detector

# Sub nanometer particles and molecules in solution

### Applications requiring exceptionally high sensitivity

- Protein interaction and conformation studies
- Protein screening for aggregates prior to crystallisation experiments
- Surfactant micelle size measurement
- Molecular size measurement of proteins and polymers
- Where only exceptionally small quantities of sample are available



### Size measurement of Cholesterol, 387Da

For particles smaller than a diameter of 2.0nm, the scattered light intensity is very low, even at concentrations as high as 20mg/ml. These materials are the ultimate test of an instrument's sensitivity. Prior to crystallisation studies, it is important to determine that the solution contains no aggregates.

Measurements of Cholesterol in butanone at a 20mg/ml gives a typical hydrodynamic diameter of 0.64nm.

This measurement is so demanding that there are few, if any, previous values for verification. The size measured matches a simple calculation of the size of a spherical molecule of molecular weight 387Da.



### Lysozome, 0.1mg/ml

Lysozyme monomer has a molecular weight of 14,400 and a hydrodynamic diameter of 4.1nm. This can be measured effectively even at 0.1mg/ml concentration with a measurement time of just 300 seconds.

### Measurement of highly absorbing samples. Phenolphthalein at pH 9.5

Coloured samples can be highly absorbing, greatly reducing the intensity of scattered light.

Back-scattering optics minimise the distance that the illuminating and scattered light has to pass through the sample, so minimising absorption.

Phenolphthalein has a molecular weight of just 318 Daltons, but the combination of high sensitivity and back scattering optics enables the HPPS to measure the hydrodynamic diameter at pH 9.5 as 0.6nm.



# Measurement with minimal or no dilution



The back-scatter optics of the HPPS enables measurements to be made at very high concentrations. For many samples where all particles are below 100nm and 20%w/v, the results will be directly comparable with measurements after dilution. However surface charge characteristics and hydrodynamic interactions at high concentration can influence the size measured.

In cases where the particles show significant interactions, but cannot be diluted, measurements are still possible and the results can be used to monitor sample changes.



### 100nm Silica at 40% mass concentration

Knowledge of the size of the silica particles used in polishing slurries is important as it affects the substrate removal rate as well as the surface finish.



Measured value

Silica samples at these high concentrations are opaque. Attempts to do measurements in a system using a classical 90° scattering angle, will give erroneous results, even with short path length cells, due to the presence of multiple scattering. This is shown by the result on the graph at cell position 4, which gives an apparent size of 22nm for the 100nm sample. The HPPS back-scatter optics minimises multiple scattering by automatically measuring close to the cell wall with concentrated systems.

The graph shows that by measuring close to the cell wall, i.e. at the left of the graph, a result of 104nm is obtained, within 4% of the result found after the extensive dilution required for measurement in a classical DLS system.

# The effect of pH on the size of silica at 20% mass concentration

At high concentrations the hydrodynamic diameter and particle size distribution of silica is very dependent on the pH of the dispersant. Measurement at a range of pH's clearly shows the change in diameter. The repeatability is excellent even at the smallest size of 1.1nm.



# Automated set-up and measurement

Minimal training is required as most aspects of the instrument set-up, including cuvette position, attenuator setting, data acquisition, analysis and results display take place with no operator intervention.

Standard Operating Procedures ensure consistent measurements are made. During the measurement the data quality can be assessed from the live count rate and data display.

P Editor			
cumentation Material/Solvent Measurement cycles			
Details			
Experiment Name:			
200 nm Latex			
Comments:			
Test sample of known size.			
	ОК	Cancel	7 Help
			3 Tich

#### **Result reports**

ern HPPS - [test.db]

Layout

1

Ele Edit Yew Measure Configure Icols Help

A report is simply produced by highlighting a record, then selecting the appropriate report 'tab'. Each report contains measurement conditions, sample parameters, the mean size and a graph of the distribution, as well as the modes and percentages of each peak for multi-modal distributions.

- I X

0 🗃 🖬 🚳 👗 📭		8 % <b>?</b>		
Records Result Analysis				
Sample Name	Measured on	Notes	Actual Te	
mte	05/06/2001 12.19.00	Attn= 4, 2.11E-003;x= 0.750;ICPT=0.96;Solv=		
mtc	05/06/2001 12:19:00	Attn= 4, 2.11E-003;x= 0.750;ICPT=0.96;Solv=		
mtc1	05/06/2001 12:30:30	Attn= 4, 2.11E-003;x= 0.750;ICPT=0.95;Solv=		
mtc2	05/06/2001 14.42.56	Attn= 4, 2.11E-003;x=-1.750;ICPT=0.75;Solv=		
mtc2	05/06/2001 14.56.37	Attn= 4, 2.11E-003;x=-1.750;ICPT=0.76;Solv=		
Klebasol 30R25	05/06/2001 15.12.37	Attn= 8, 2.83E-002;x=-1.750;ICPT=0.87;Solv=		
Klebasol 30R25	05/06/2001 15.15.49	Attn= 8, 2.83E-002;x=-1.750;ICPT=0.87;Solv=		
Klebasol 30R50	05/06/2001 15.21.29	Attn= 4, 2.11E-003;x= 0.000;ICPT=0.95;Solv=		
Klebasol 30R50	05/06/2001 15:24:21	Attn= 4, 2.11E-003;x= 0.000;ICPT=0.95;Solv=		
Klebasol Mix	05/06/2001 15.33.24	Attn= 6, 1.19E-002;x= 0.750;ICPT=0.99;Solv=	1	
800nm 0.1%	08/06/2001 16.16.02	Attn= 6, 1.19E-002;x=-1.750;ICPT=0.94;Solv=		
Lysozyme 2mg/ml	12/07/2001 18:08:51	Attn=14, 1.00E+000,x=-1.750;ICPT=0.27;Solv=		
Lysozyme 2mg/ml	12/07/2001 18.15.04	Attn=14, 1.00E+000;x=-1.750;ICPT=0.28;Solv=		
Lysozyme 0.1mg/ml	12/07/2001 18:29:34	Attn=14, 1.00E+000;x= 0.750;ICPT=0.06;Solv=		
Lysozyme 0.05mg/ml	13/07/2001 09.27.35	Attn=14, 1.00E+000;x=-0.750;ICPT=0.03;Solv=		
No Sample Name supplied	06/08/2001 12:32:38	Attn=12, 2.67E-001 x= 0.750;ICPT=0.98;Solv=		
Klebasol 30R50	07/08/2001 15.46.54	Attn=12, 2.67E-001;x= 0.750;ICPT=0.98;Solv=		
No Sample Name supplied	07/08/2001 17.16.00	Attn=12, 2.67E-001 x= 0.750;ICPT=0.99;Solv=		
No Sample Name supplied	08/08/2001 09.39.42	Attn=12, 2,67E-001 x= 0,750;ICPT=0.98;Solv=		

#### Measurement data access

Sample data and results are stored as individual records in database files for easy recall, display and printing.



#### Data analysis

The size distribution algorithm is suitable for samples with a wide range of distributions from narrow monomodal to polydisperse and multimodal.

# **Technical Specifications**

Parameter	Specification		
Size range*	0.6nm to 6000nm hydrodynamic diameter		
Sensitivity	0.1mg/ml of Lysozyme monomer		
Molecular weight range*	$10^3 - 10^7$ Daltons		
Concentration range*	0.00001 vol% (0.1ppm) to 20 vol%		
Sample volume required	12 microlitres minimum to 3ml maximum		
Measurement Technique	Dynamic light scattering		
Patents Granted	German Patent 19725211		
	US Patent 6016195		
	Japanese Patent 2911877		
Correlator specifications	Minimum sample time 125ns, maximum number of data channels 560, symmetric normalization		
Laser	He-Ne, 3.0mW. 633nm		
Product laser class	Class 1 compliant, EN 60825-1:94		
Laser attenuation	Automatic, transmission 100% to 0.0003%		
Laser power monitor	Silicon photodiode		
Detector	Avalanche photodiode, $Q.E > 50\%$ at 633nm		
Temperature control range (standard)	10°C to 55°C		
Extended temperature control range	10°C to 90°C Optional at extra cost		
Temperature Control	Thermo-electric Peltier heater/cooler element		
Dimensions	280mm(w) x 240mm(h) x 520mm(d)		
	Weight ~16kg		
Power Requirements	AC 90-240V, 50/60Hz		
Power Consumption	Max 50W		
Ambient operating conditions	Temperature 15°C - 40°C		
	Humidity 20 – 70% non-condensing		
Operating system compatibility	Windows NT4, 2000		
Minimum computer requirements	Pentium PC 266MHz, 1 Free PCI slot (32-bit, 5V), 64MByte RAM, 10MByte free hard disk space, 1024 x 768 screen resolution, CD-ROM drive, 3.5" disk drive, Windows NT4 or 2000 operating system		

System	Part number	Specification
Malvern HPPS	HPP5001	Temperature range: 10°C to 55°C
Malvern HPPS-ET	HPP5002	Temperature range: 10°C to 90°C
(extended temperature control range)		

\*Actual specifications will depend on the exact nature of the sample and dispersant

NIBS<sup>™</sup> is a registered trade mark of ALV-Laser Vertriebsgesellschaft mbH, Langen, Germany

Malvern Instruments Ltd, reserves the right to change specifications without prior notice.

### Malvern service and support

#### Validation and traceability

Malvern Instruments seeks innovation not only in product design and development, but in every area of business. As many of our systems are used in highly regulated environments, product validation and R&D traceability are key commitments to our customers. We have therefore invested to achieve ISO9001 with TickIt accreditation and are able to provide full traceability of changes in software and design.

#### **Applications** expertise

Malvern Instruments' trained specialists are available on the ground in more than 50 countries around the world to assist with applications development and advise on and analyze difficult samples. We have our own laboratory facilities with extensive applications experience derived both from our own work and that of our extensive user base. Malvern's own Applications Laboratories in the UK as well as North and South America, Europe and Asia routinely run thousands of customer samples each year. We can offer advice on how to measure difficult materials, optimise sample dispersion and eliminate causes of error in sample preparation.

#### **Remote diagnosis**

Our innovative approach to customer service is illustrated by the development of after-sales remote diagnostics. Malvern Instruments' service specialists can access and control instruments worldwide via modem links in order to minimize downtime and improve payback.

#### Ongoing development

In many industries, particle size analysis has become a key QC parameter. The need to obtain data as close to the production line as possible and to react to that data as quickly as possible, is becoming increasingly important. Malvern Instruments applies its expertise to meeting this challenge through continued research and applications development.

Trends in regulatory requirements are watched closely and we are developing the tools to support customers in electronic data protection and submission.

For a full description of all Malvern Instruments' products, services and support contact your nearest office.

**Malvern Instruments Limited Enigma Business Park Grovewood Road** Malvern Worcs **WR14 1XZ** U.K. Tel: +44 (0)1684 892456

Fax: +44 (0)1684 892789

Malvern Instruments Inc. **10 Southville Road** Southborough MA 01772 U.S.A. Tel: +1 (508) 480-0200 Fax: +1 (508) 460-9692

**Malvern Instruments Japan** SORIO-3, 6th Floor 2-2-1 Sakaemachi Takarazuka, Hyogo 665-0845 Japan Tel: +81 (0)797 85 5060 Fax: +81 (0)797 85 5657

Malvern Instruments S.A. Parc Club de L'Université 30. Rue Jean Rostand 91893 Orsay Cedex France Tél: +33 (1) 69 35 18 00 Fax: +33 (1) 60 19 13 26

**Malvern Instruments GmbH Rigipsstraße 19** 71083 Herrenberg Germany Tel: +49 (0) 7032 97770 Fax: +49 (0) 7032 77854

Malvern Instruments Nordic AB Box 15045, Vallongatan 1 **750 15 UPPSALA** Sweden Tel: +46 (0) 18 55 24 55 Fax: +46 (0) 18 55 11 14

#### www.malvern.co.uk

MRK420-03

