Breaking from the laboratory – On line and at line characterization of particles

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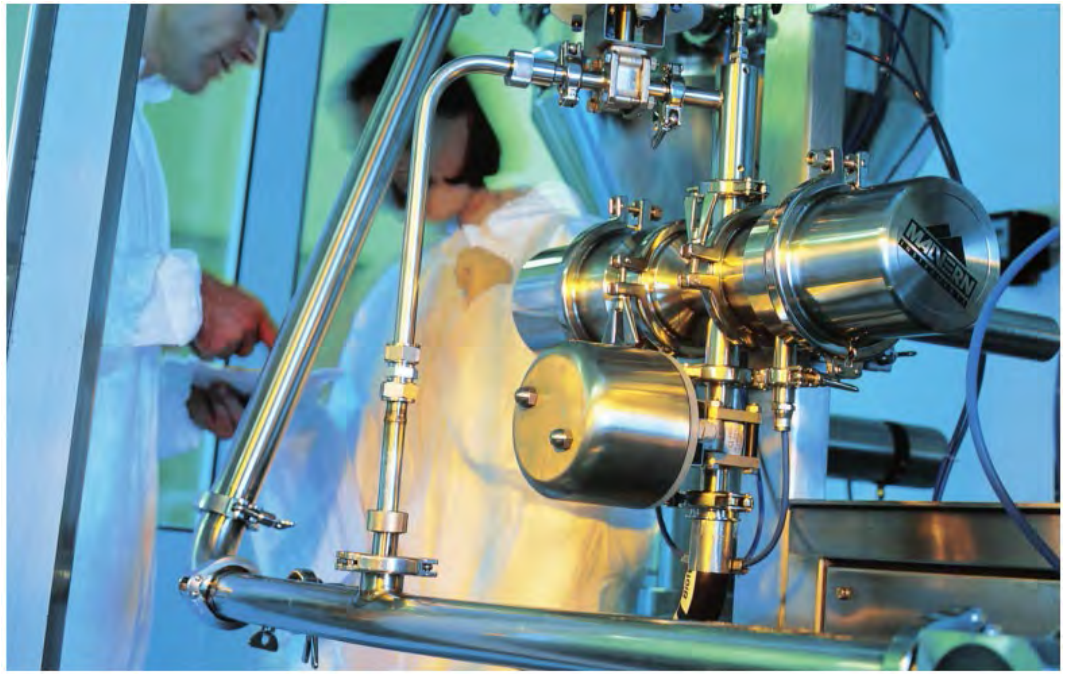
Reason to go online

- High return on investment
- Reduced energy consumption
- Automated control
- Intelligent troubleshooting
- Fast, effective process optimization
- Smarter process development
- More complete plant utilization
- Instant upset detection
- Market leading product quality
- Reducing risk

Smarter Process Development

- On-line control enables fast product development
- Pilot plants are expensive to run. Accelerating the early stage tests saves money
- From g/h to t/h as fast as possible without risks



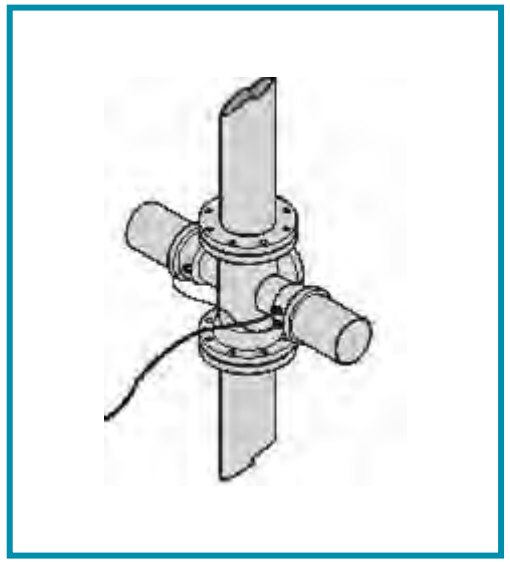
Reduced Risk

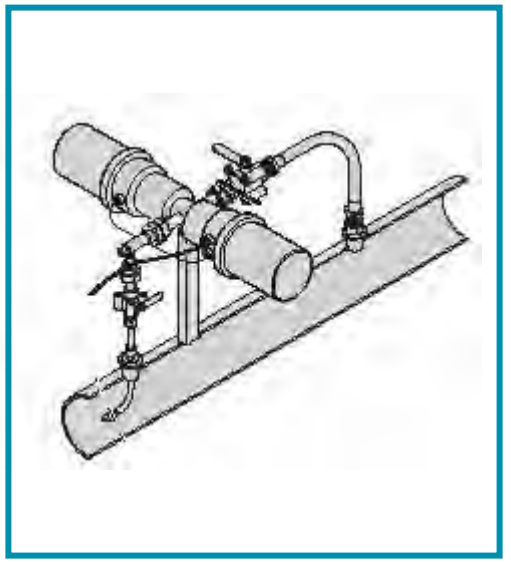
- Sample extraction and work-up presents a potentially significant health and safety risk
- Eliminate operator variability – during sampling and measurement
- Measure larger and continuous sample volumes – a vastly higher proportion of the process stream
- Automate the complete analytical cycle

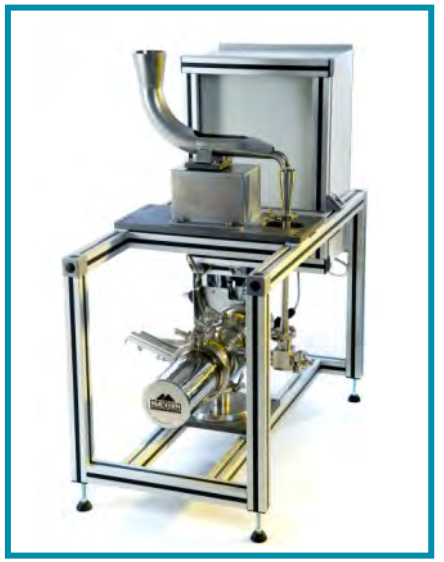
Sample extraction and handling is not always simple!

Process probes- In-line, on-line or at-line?

- IN Line
- ON Line
- AT Line







< 20kg/h

>100 kg/h

Typical Process Applications

- What are the “processes”?
- Size reduction and particle creation
- Milling / Micronising / Emulsification
- Spray drying / Atomisation / Granulation and coating

PAT (Process Analytical Technology)

Malvern Panalytical
a spectris company

Inline Particle Sizing can play an important role to

R&D

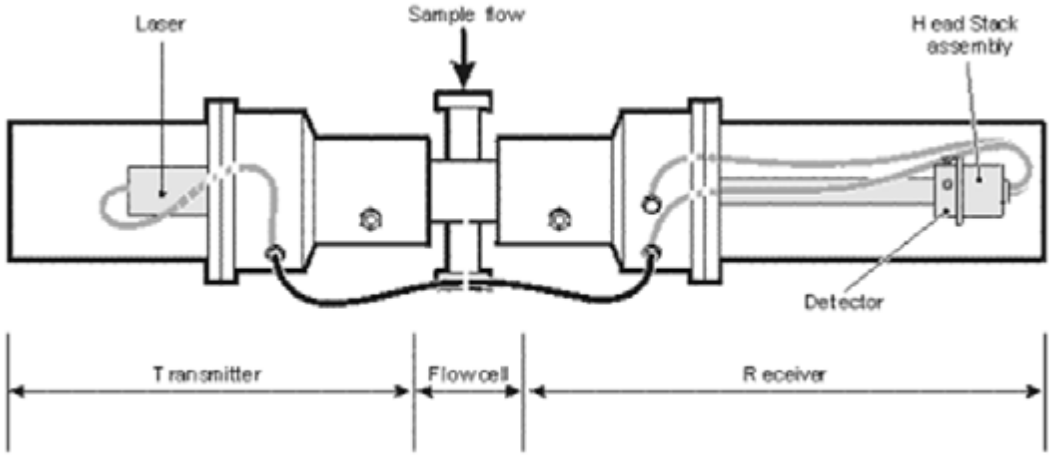
- Improve process understanding and transparency
- Generate and verify process models
- Monitor and control critical process parameters
- Reduce time for process development and up-scaling

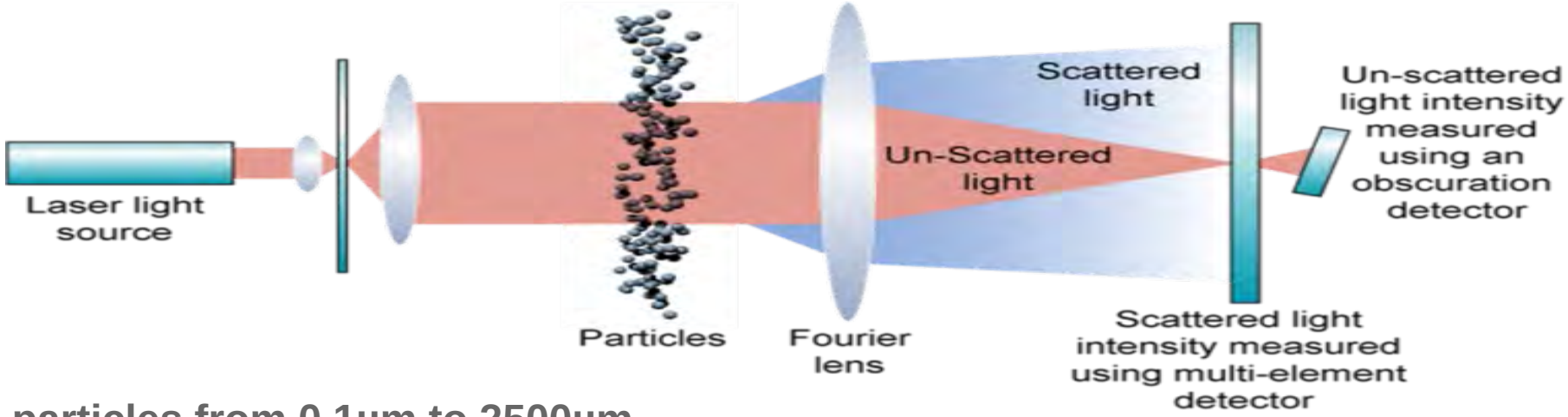
Production

- Monitor product quality in real-time
- Enable more efficient processes
- Increase process safety
- Direct control of processes
- Reduce number of Lab analyses – and costs

Inline Particle analysis can open a window to your process

Insitec - Introduction

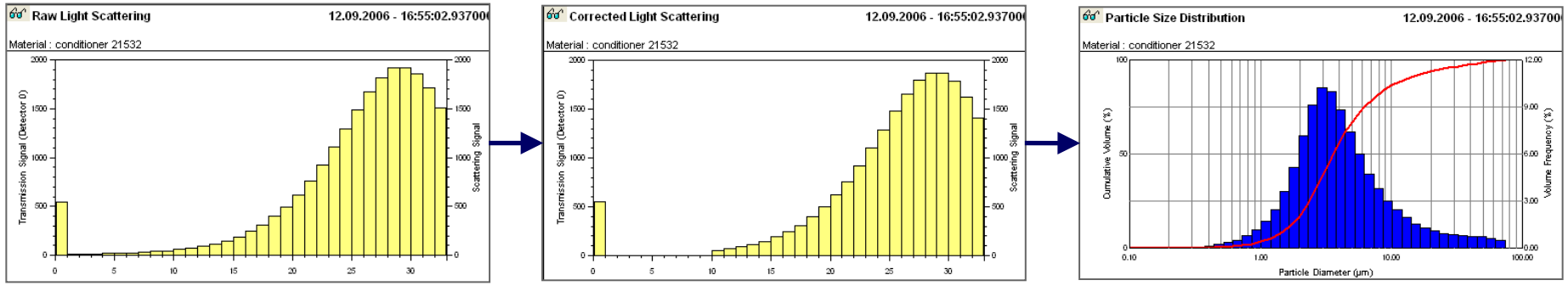




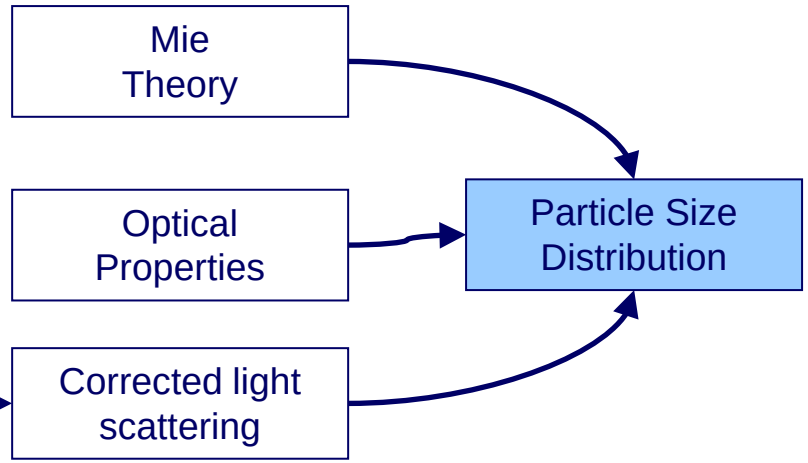
Can measure particles from 0.1µm to 2500µm

Insitec - *Result presentation/ interpretation*

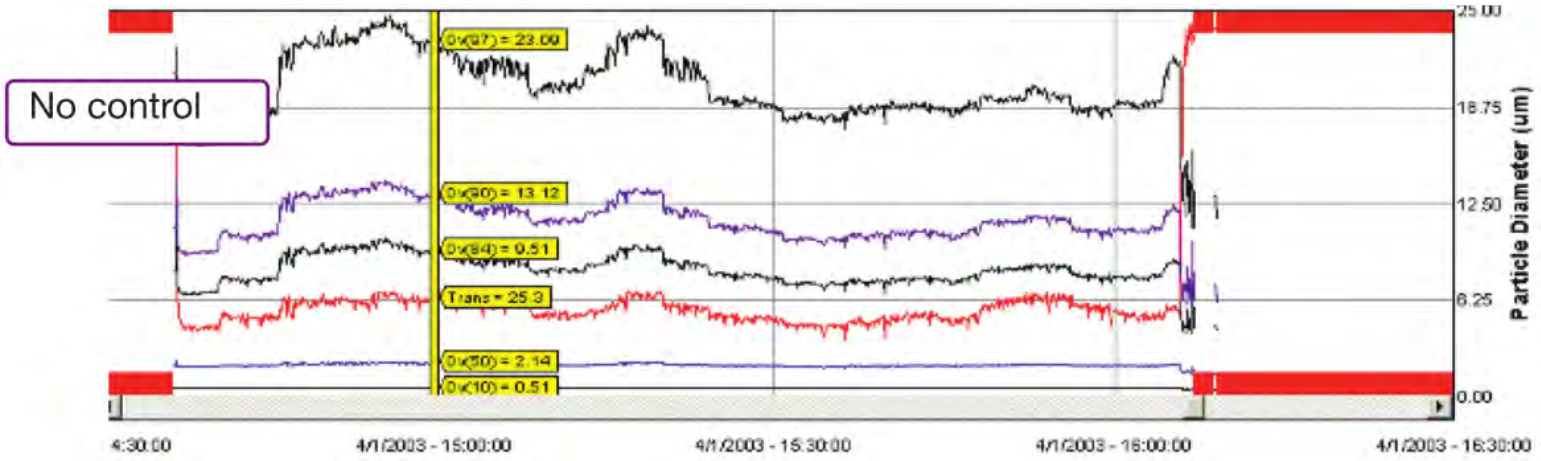
RTSizer

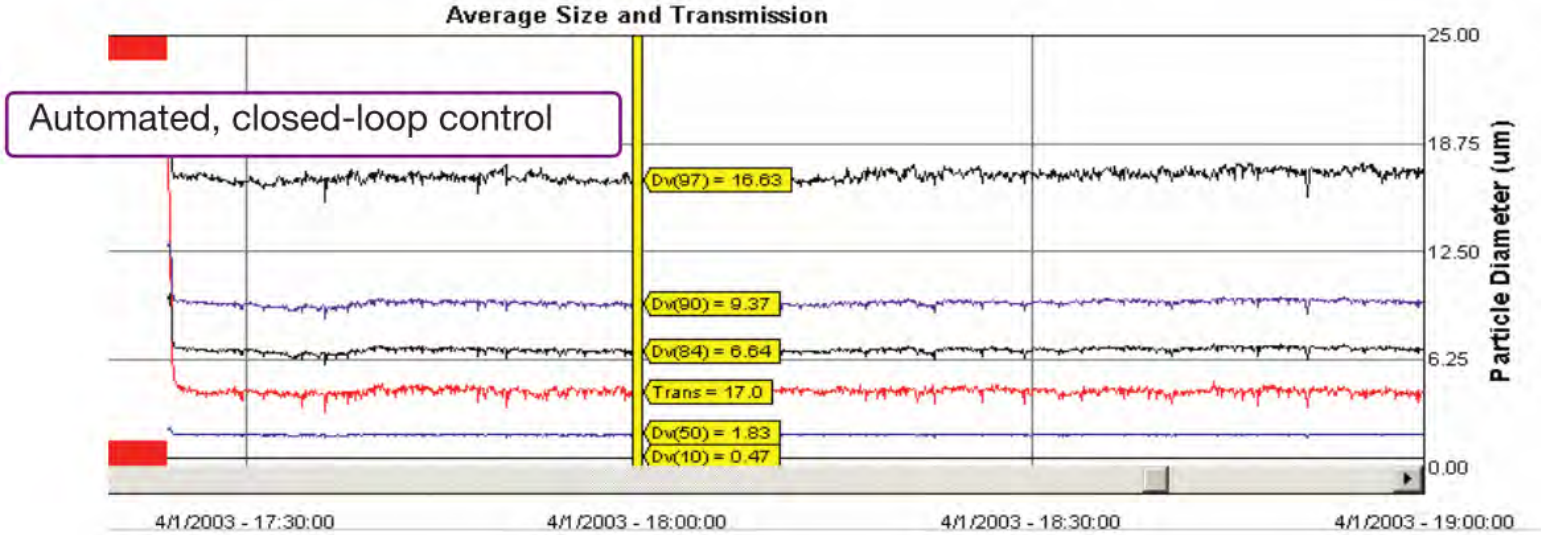


	Raw light scattering
-	Dark Background
-	Light Background
-	Threshold
-	Killed rings
x	Instrument geometry
=	Corrected light scattering



Automated Control

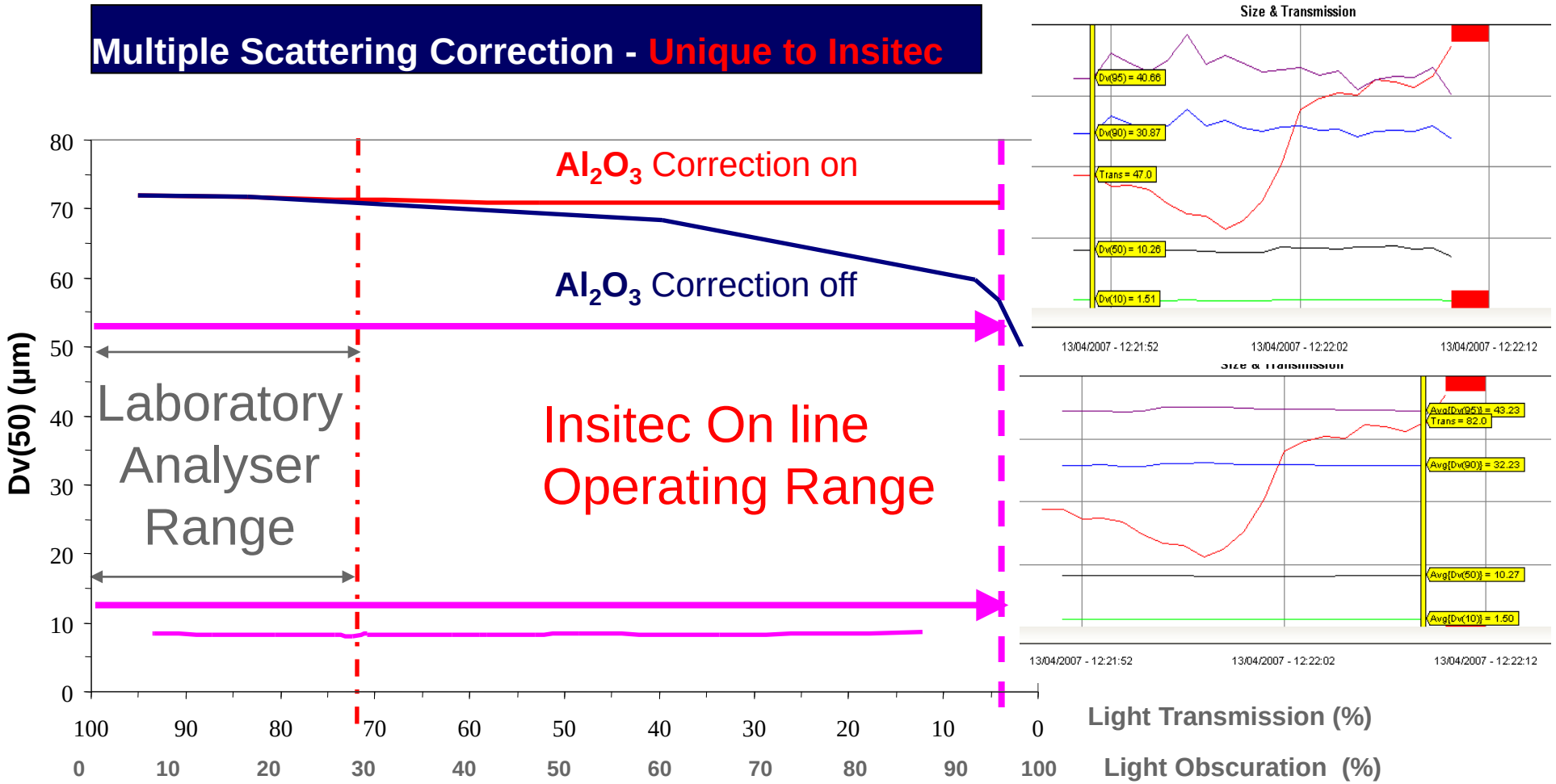




Multiple Scattering Correction

Insitec can operate continuously without errors caused by process fluctuations

Multiple Scattering Correction - Unique to Insitec



Products and solutions

- **Insitec** on-line dry
  - Particle size and distribution 0.1-2500um
  - Real time analysis
  - Fully automated
  - Integration with plant control

Gas or dust zoned hazardous environments - The world's first ATEX intrinsically safe on-line particle size analyzer (zones 0, 1, 2 and 20, 21 and 22)

Customised Configurations

- **Insitec** on-line wet
  - Particle size and distribution 0.1-2500um
  - Real time / auto batch analysis
  - Fully automated
  - Integration with plant control

High Sample Concentration - Insitec LPS

- Real-time continuous or at-line batch measurement
  - Emulsions
- Innovative patented approach to dilution
  - Able to dilute process streams continuously
  - Only uses diluent to power diluter, with no moving parts, and easy cleaning
  - Full automation available

LPS – Liquid Process Sizer

Automated MS3000

PAT4 nano
Real-time Nanoparticle Characterization

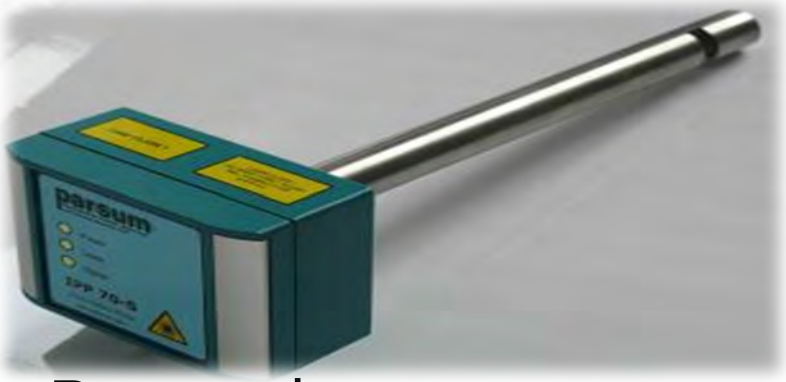
EU funded project as part of a consortium developing a range of PAT tools to help end users fully understand their processes, scheduled to last 3 years

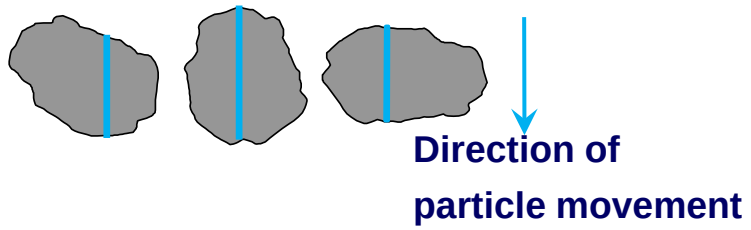
Developing MS3000AT as part of this project to monitor particle size reduction and particle growth processes for nano materials in a range of industries including Pharma

For more information please see

Website: www.pat4nano.com

Parsum

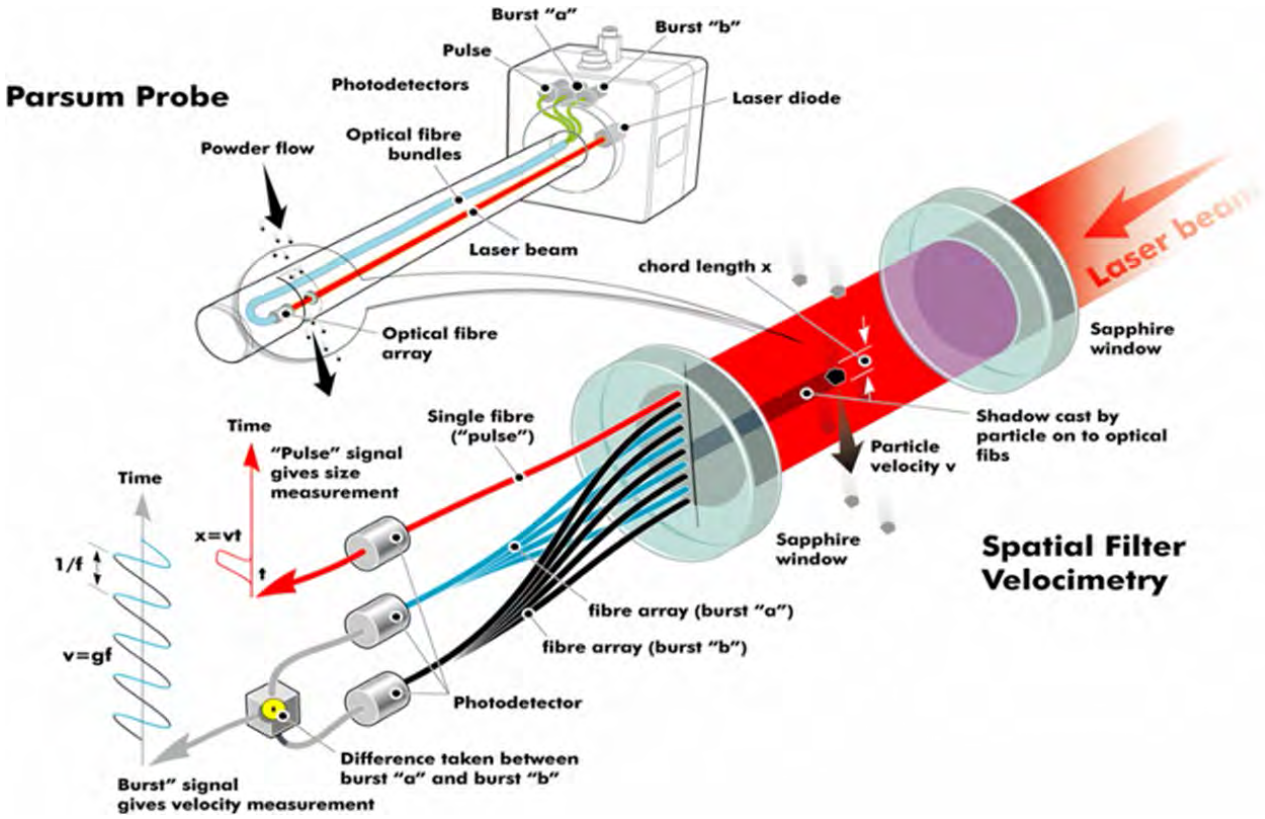




- Patented measurement technique.
- Chord length ≡ The link between two points on the perimeter of the measured particle projection face.

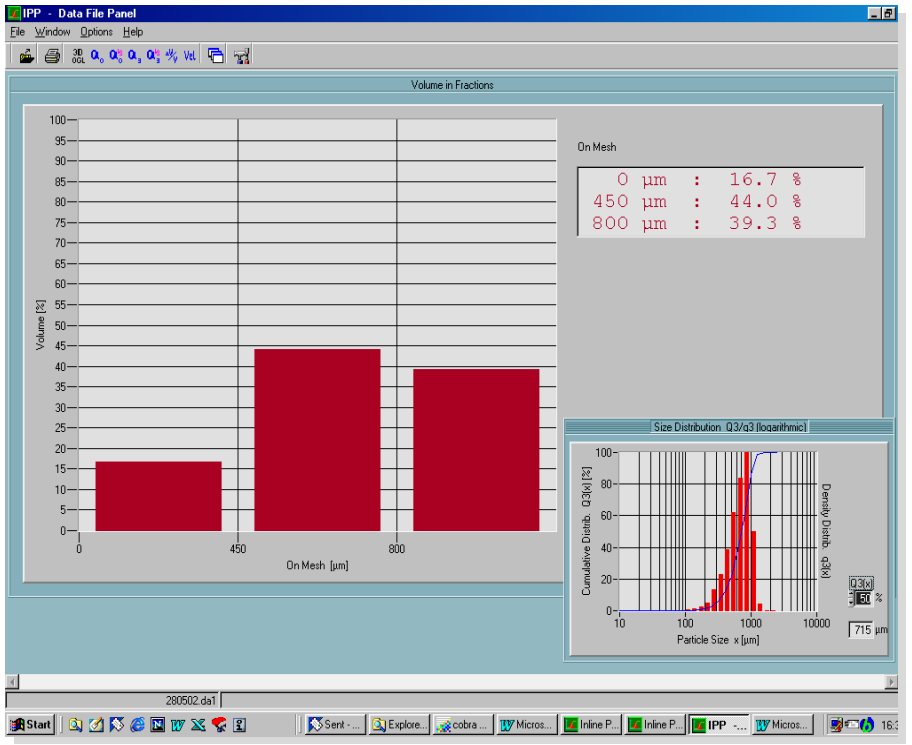
Solutions for In-Process Control …continued - Parsum

Measuring Principle

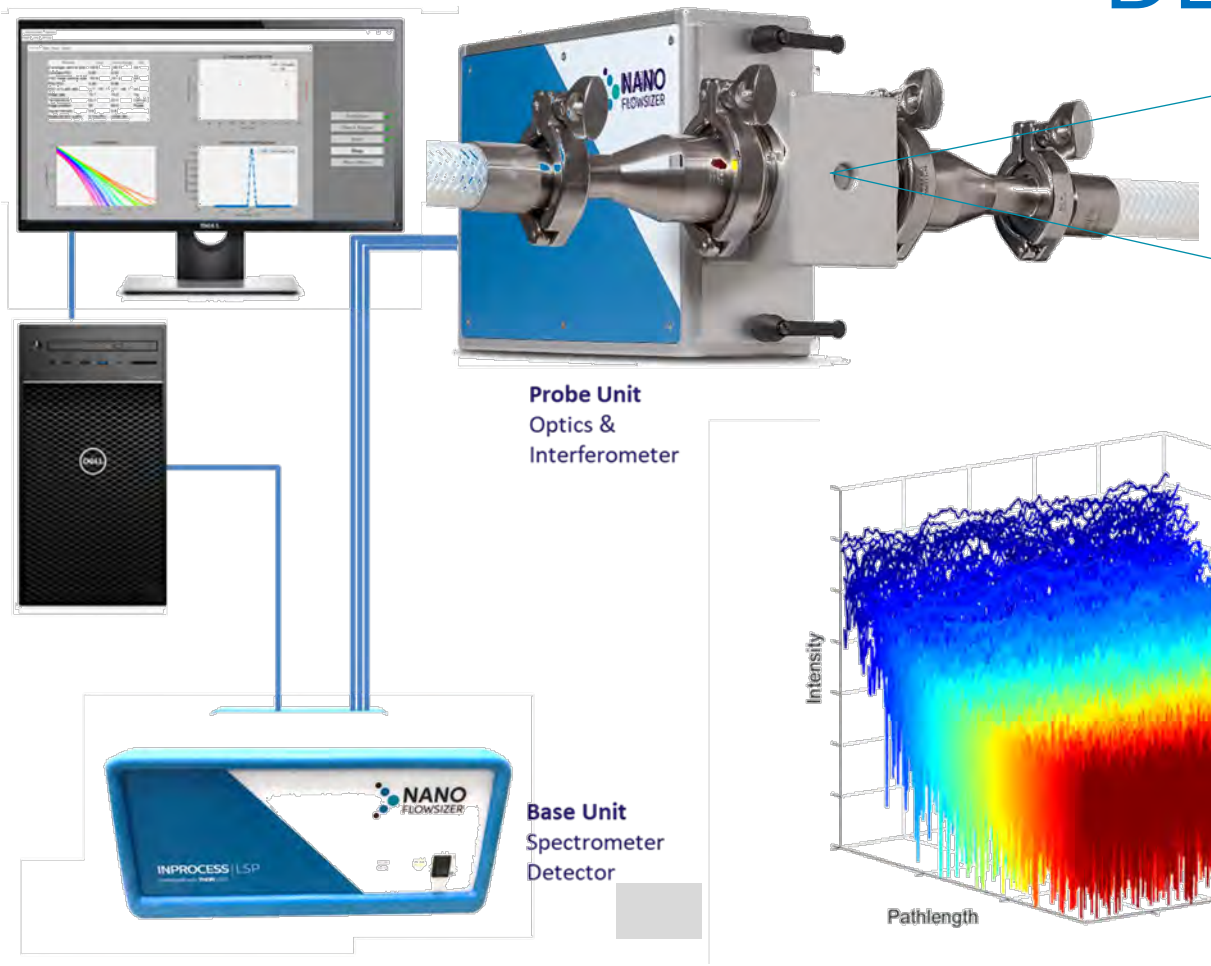


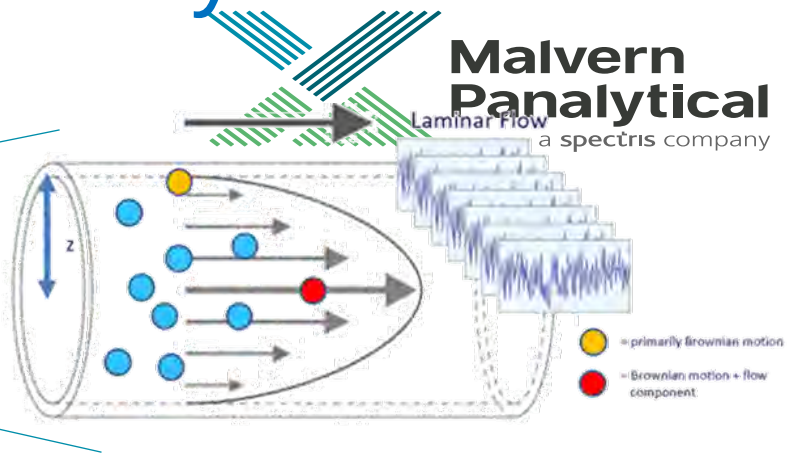
Process monitoring of phosphonate production

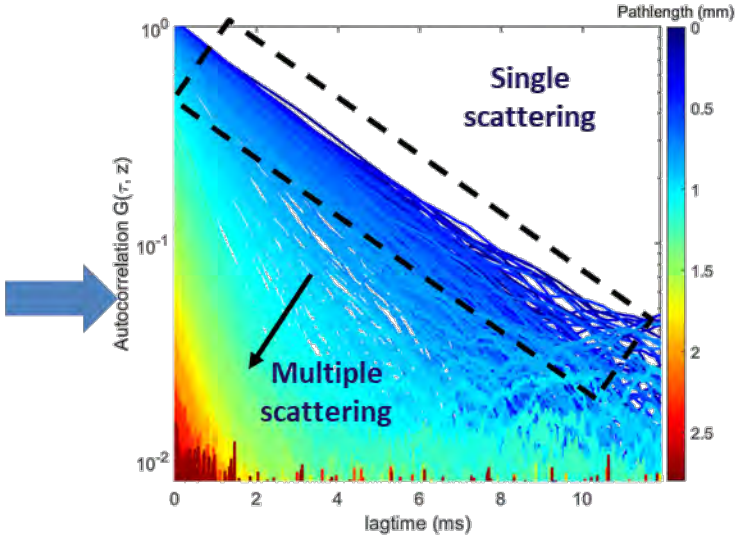
- Product: Phosphonate for detergent manufacture
- Plant: GLATT Continuous fluid bed granulator
- Size Range: 300um to 2mm
- Installation location: Gravity discharge after Rotary Valve
- Line Diameter: 40cm
- Product specification 450 to 800um
- Customer Objective
  - To reduce recirculation of off-spec material
  - To inform operator of % within spec
  - To reduce requirement for sieve measurement
- Equipment: IPP 50-S, SZ 11



NanoFlowSizer Technology: Spatially Resolved - DLS



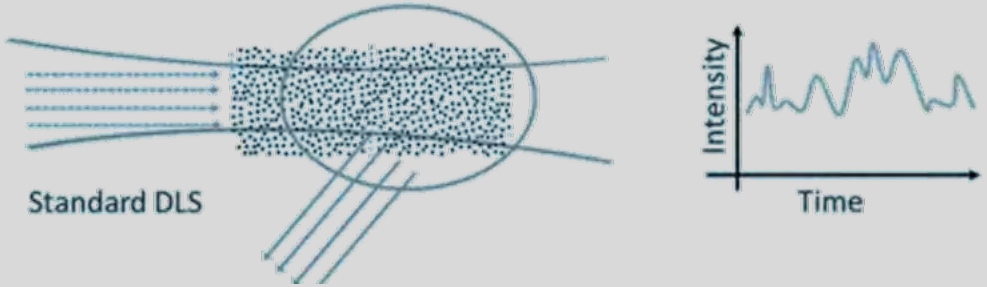




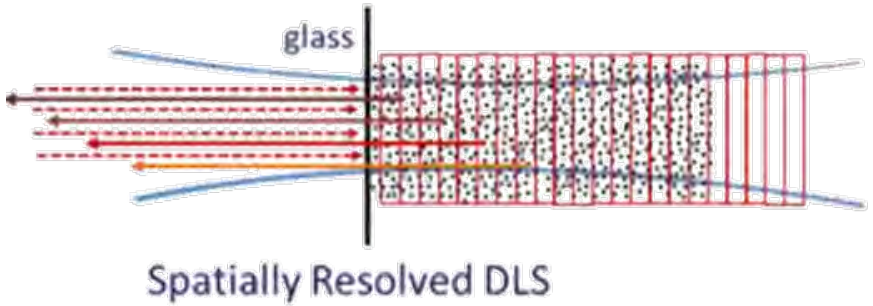
Conventional DLS versus Spatially Resolved DLS

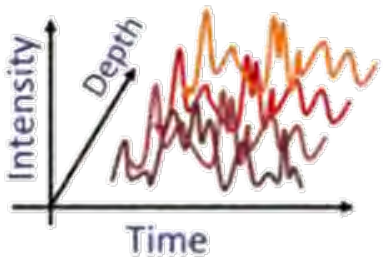
(conventional) DLS:

- **Single scattering**
- **Only low turbid suspensions can be measured**

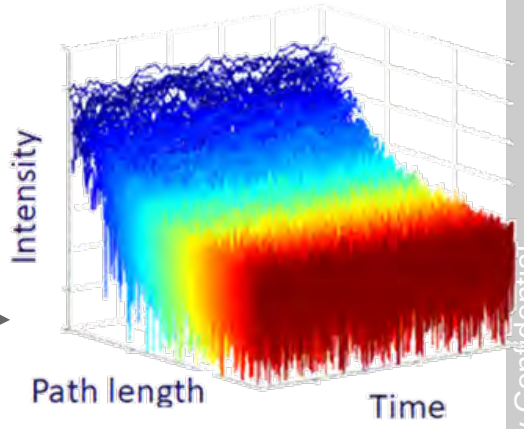


Spatial-Resolved DLS: *Depth (pathlength) resolved scatter data by low coherence interferometry*



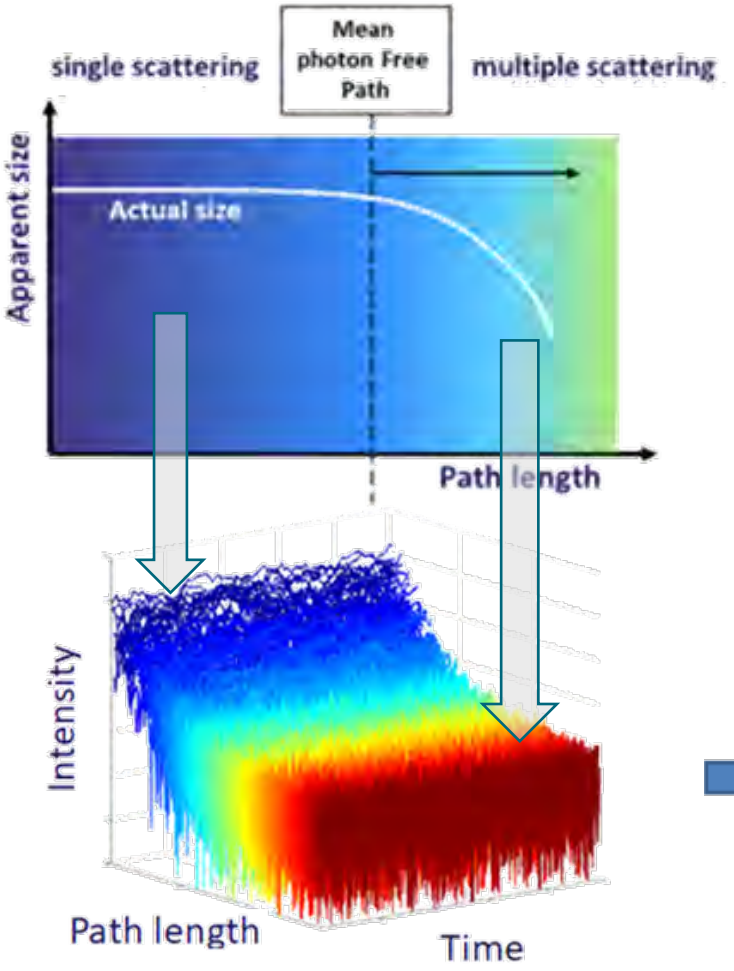


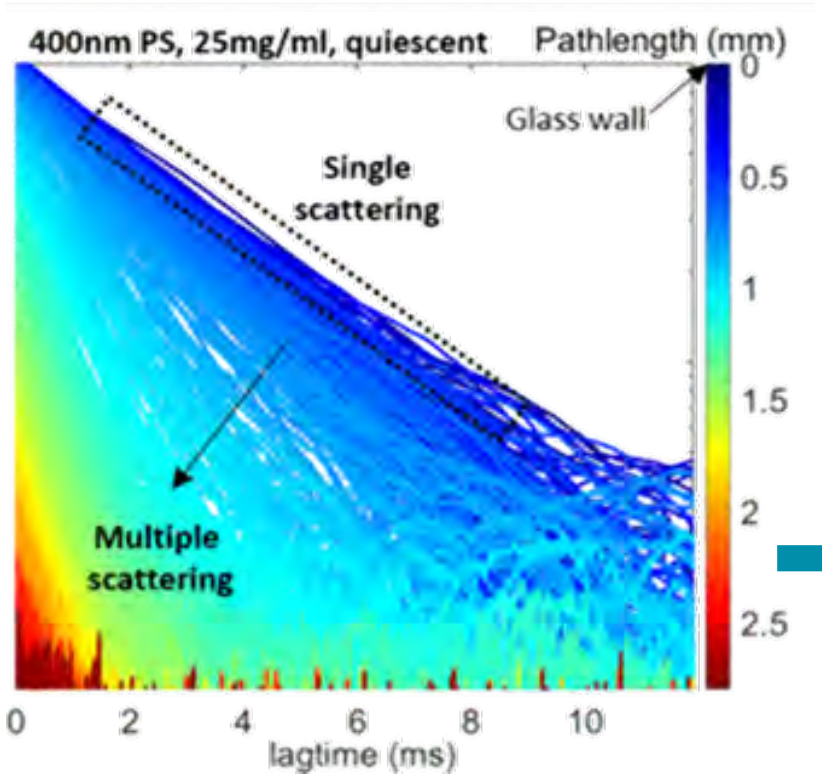
- **Back scattering (180°)**
- **Spatial resolved data** up to pathlength of ± 3mm
- **± 1000 scatter patterns** recorded **simultaneously**

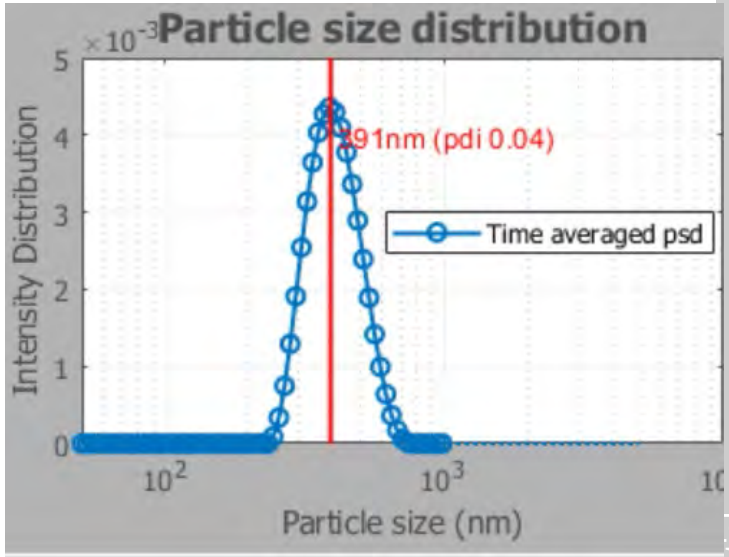


Measuring turbid samples

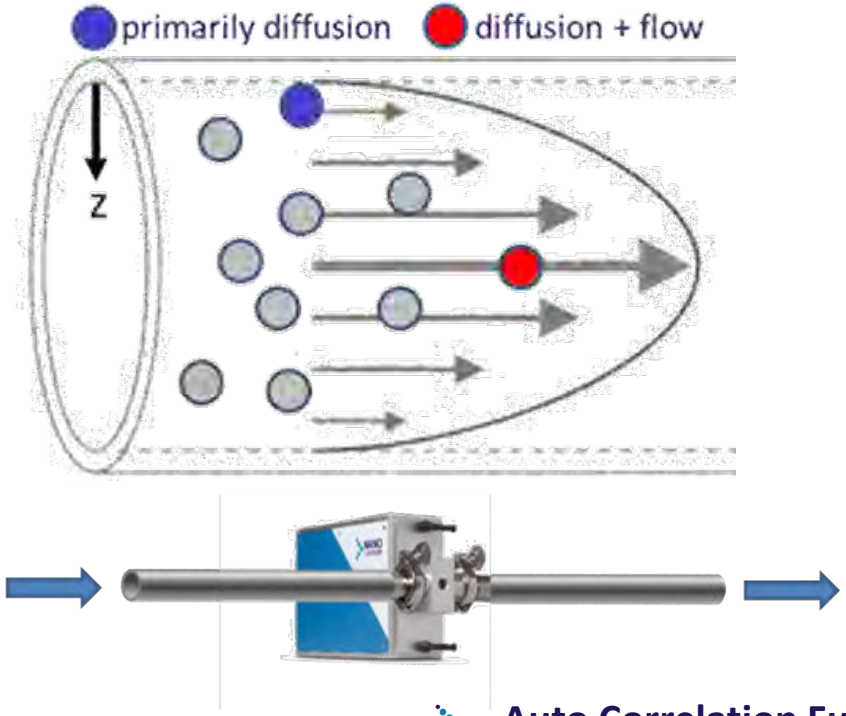
- **Multiple scattering data filtered (SR-DLS)**
- **Single & Multiple scattering regimes diagnosed automatically**
- **<u>Advantage: no dilution needed for turbid samples</u>**

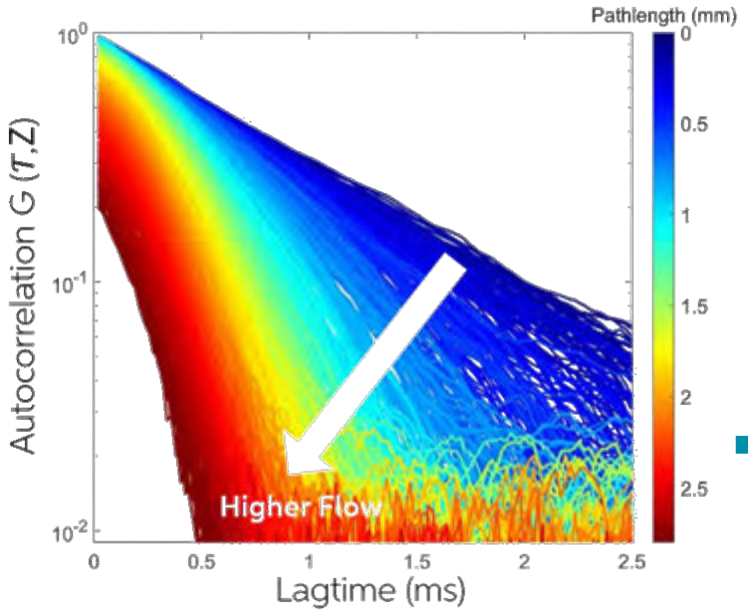


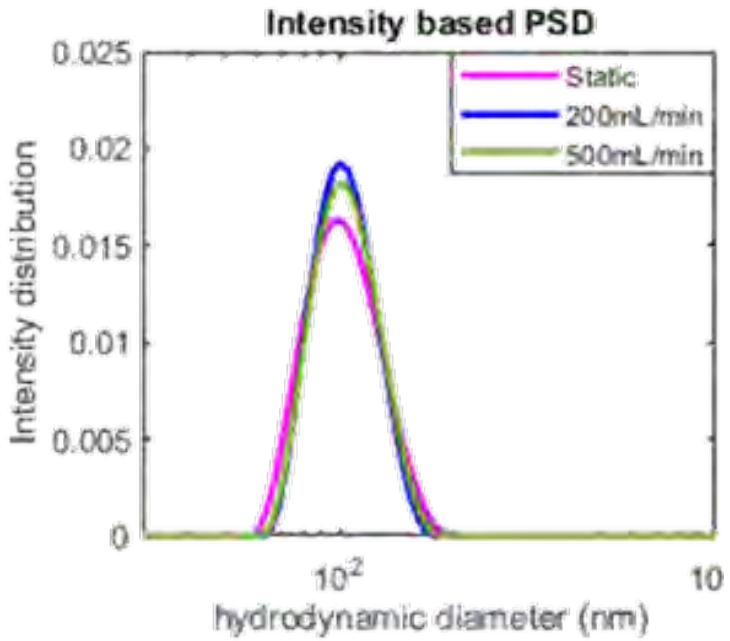




Measuring samples in Flow





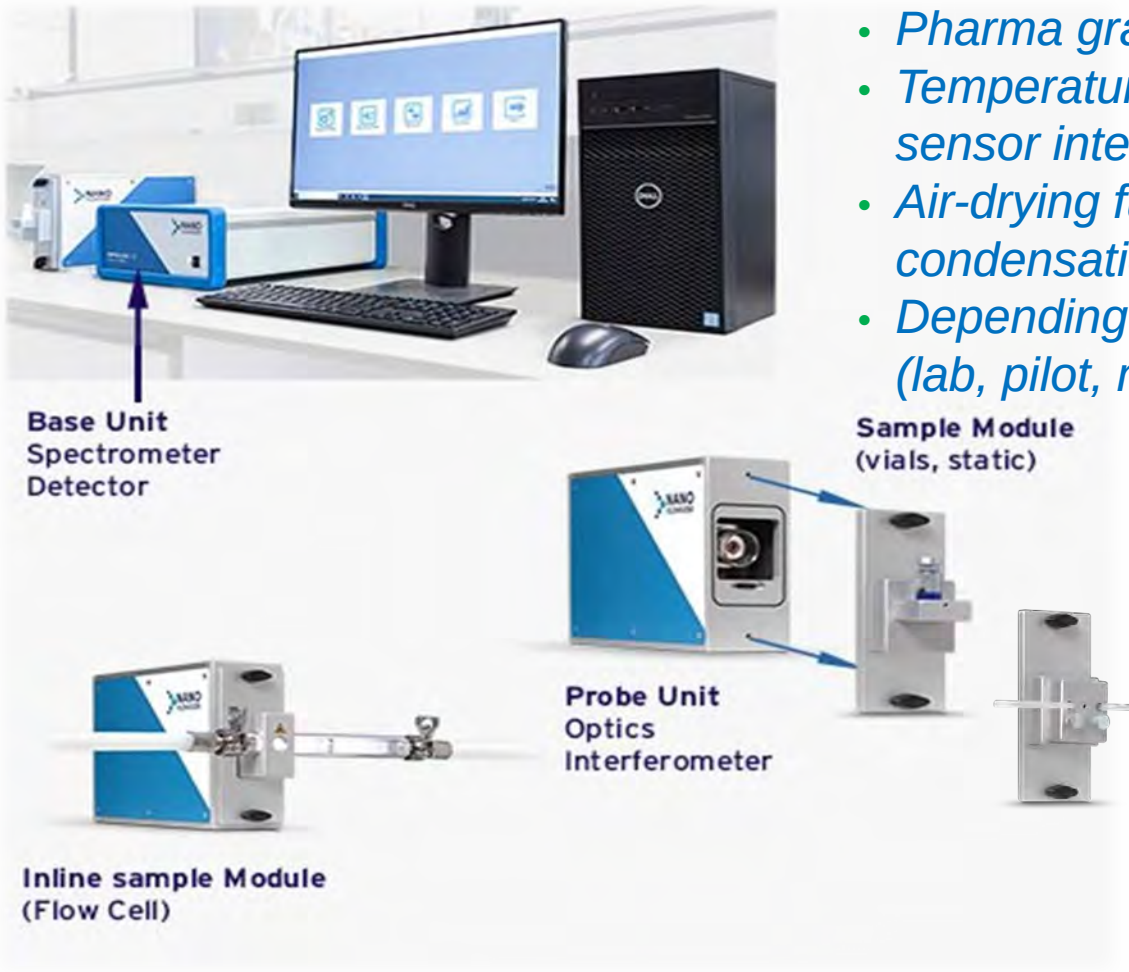


- **Auto Correlation Functions contain information on diffusion and local flow speed.**
- **Flow measured and corrected for => size analysis from diffusive part of ACF**
- **Flow-independent size, No prior knowledge of flow needed. NFS indicates if flow is within range.**

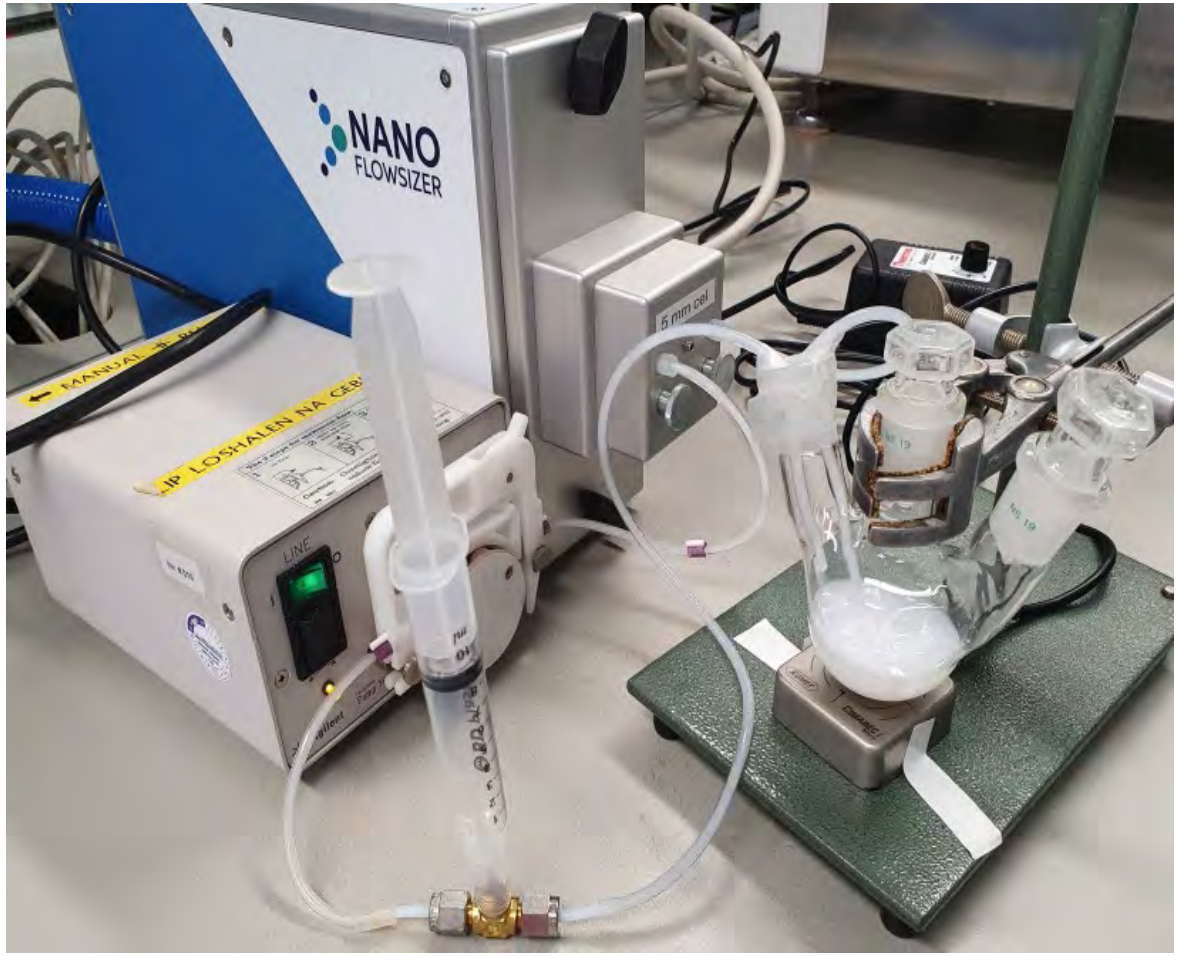
Spatially Resolved Dynamic Light Scattering Instrumentation

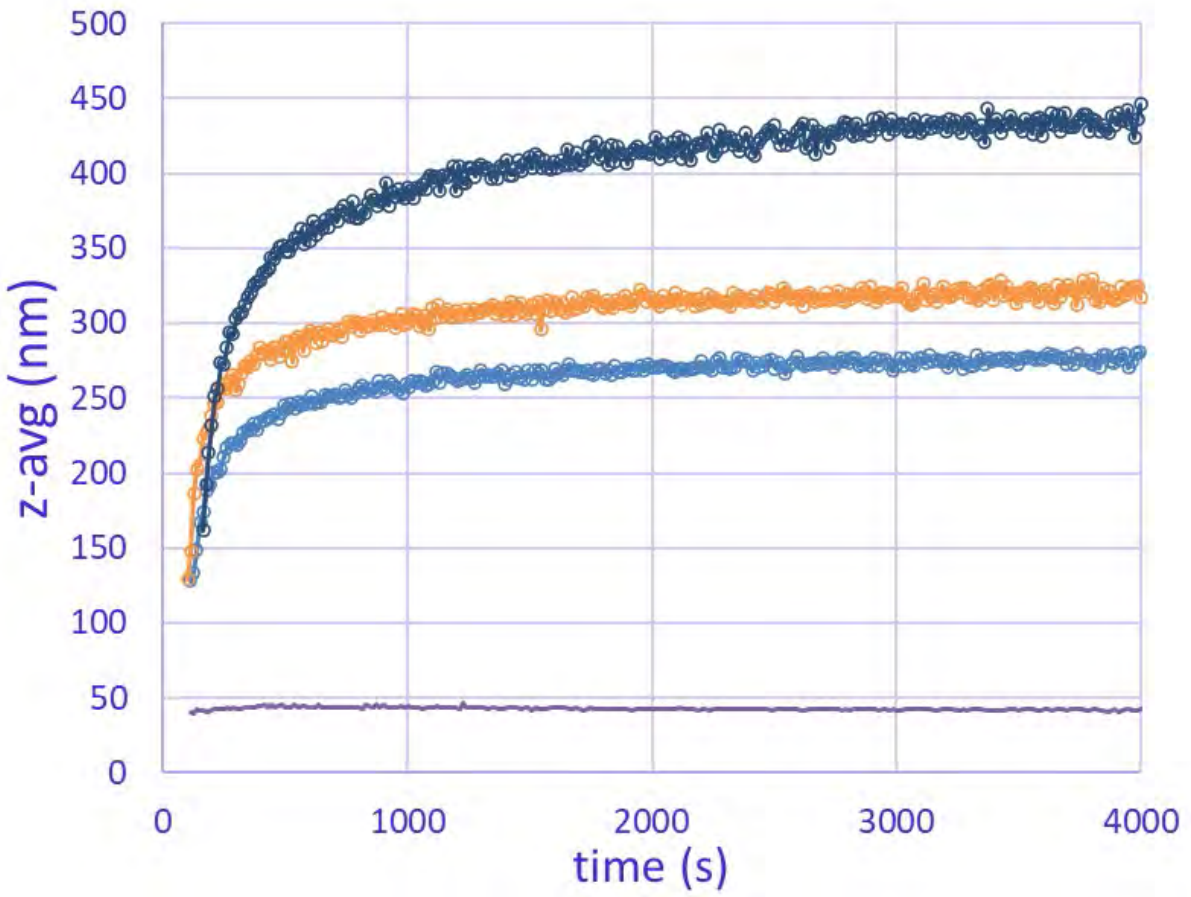
MODULAR FOR VARIOUS SCALES

- *Non-invasive Inline configurations*
- *Pharma grade flow-cells*
- *Temperature & Module recognition sensor integrated*
- *Air-drying functionality to prevent condensation*
- *Depending on scale & flow speeds (lab, pilot, manufacturing)*



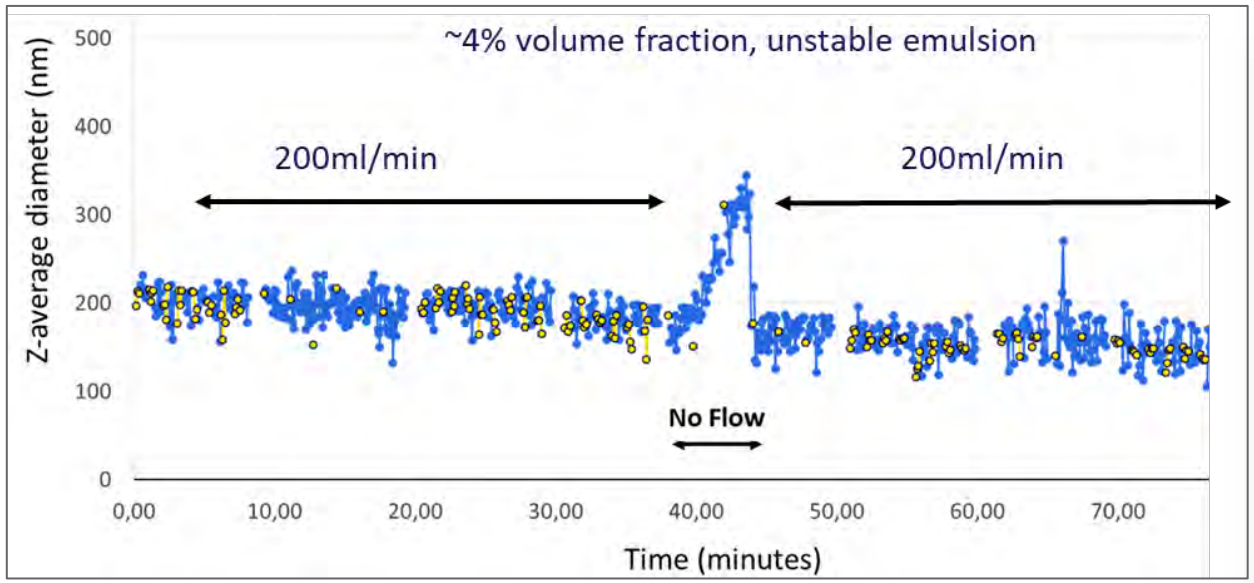
TiO_2 Synthesis: Online Micro-Flow-Cell





Inline droplet size of unstable nano-emulsion

- **Unstable, turbid emulsions: challenge for standard sampling**
- **NFS with 2” Flowcel integrated in homogenization loop**
- **Continuous flow + flow interruption**



Measure, control and optimize your production process inline

SOPAT

Smart Online Particle Analysis Technology

- Inline
- Precise
- Real-time

What is SOPAT?

- Inline photo-optic particle size measurement system
- Quantitative data based on real images from the process
- Differentiates particles, droplets, bubbles, etc… in size and shape

SOPAT hardware

- Particle size range 0.5 – 20,000 µm
- Several optics and probe lengths
- Up to 1200 bar, 700°C, pH 0 – 14

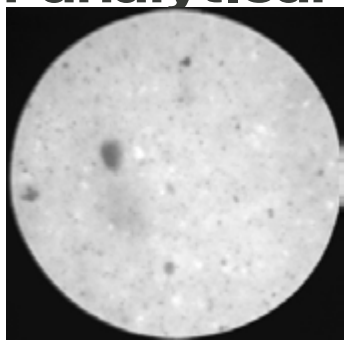
SOPAT software

- Automated image analysis
- For low and high concentrations
- Communication with PCS

What You Get

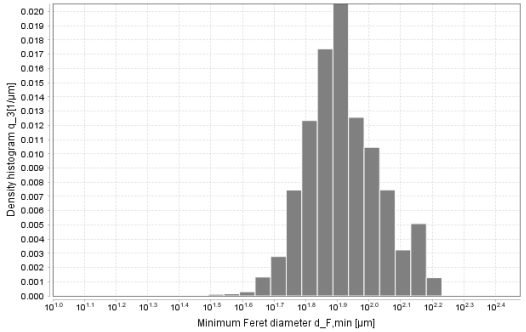
- Live view of particles in your system
  (for immediate optical control and for future reference)

  automated image analysis

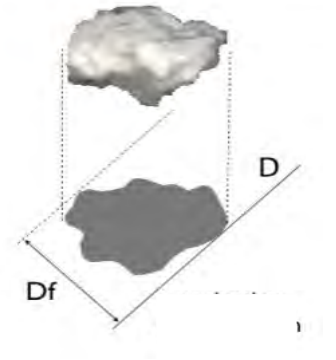


- Reliable monitoring of the particle size distribution
  (and all corresponding characteristic values)

  data export to Excel

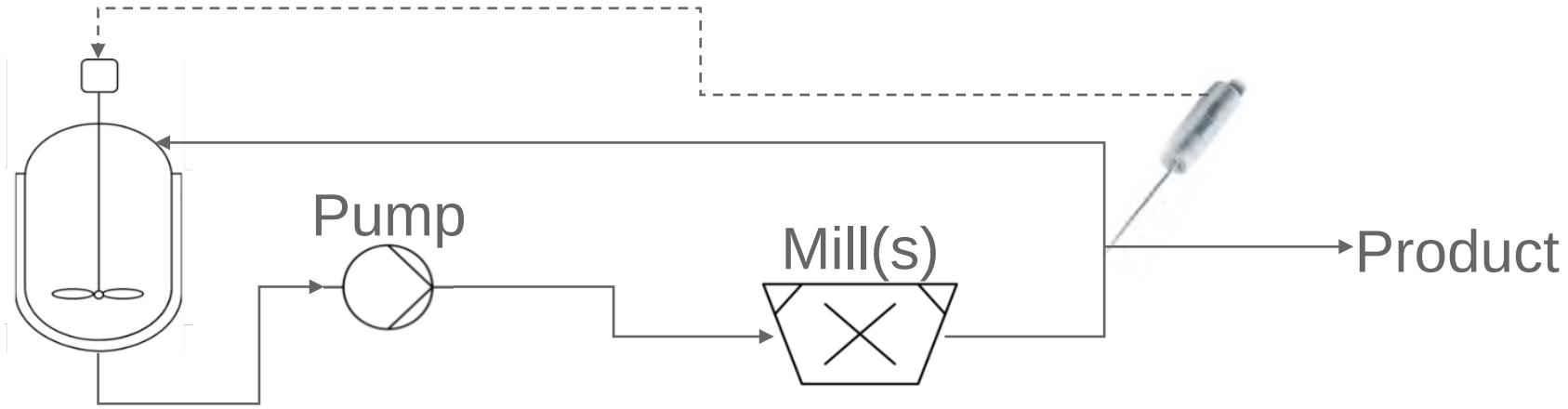


- Quantitative information on particle shape and morphology
  (additional information for better product assessment)



Example of a Typical Installation

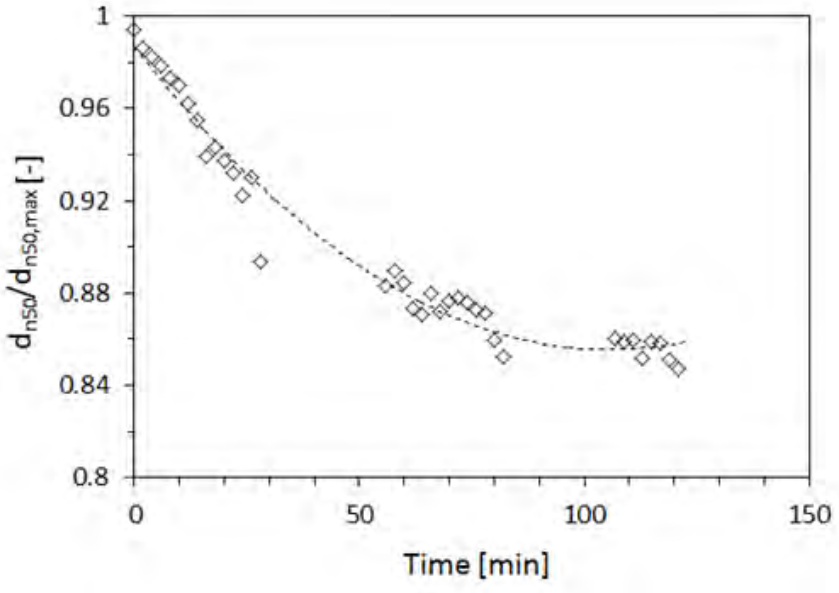
Process Flow Diagram for a Grinding/Crushing Process:



Customer benefits

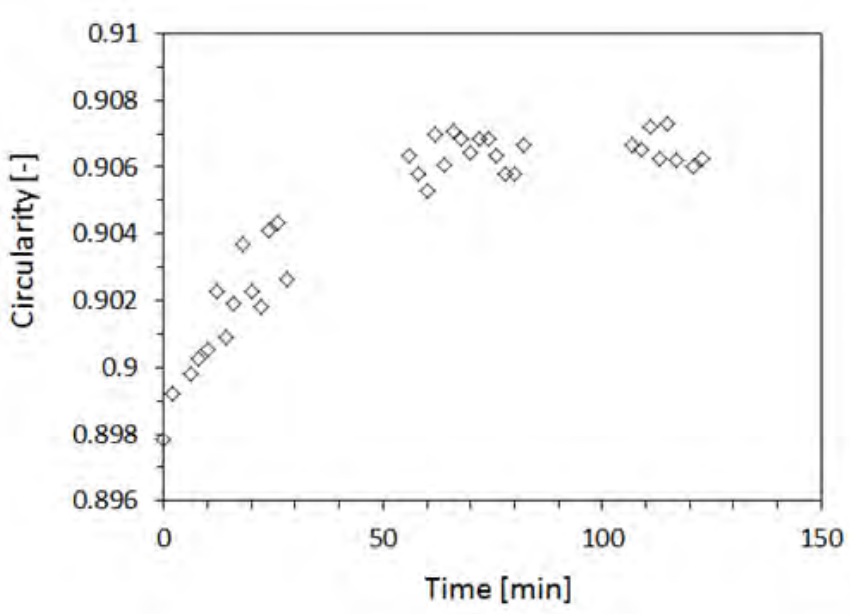
- Consistent product quality (*here: particle size*)
- Online product quality adjustments (*via control loop*)
- Optimized throughput (*reduced dead times*)

Example of Results and Impact



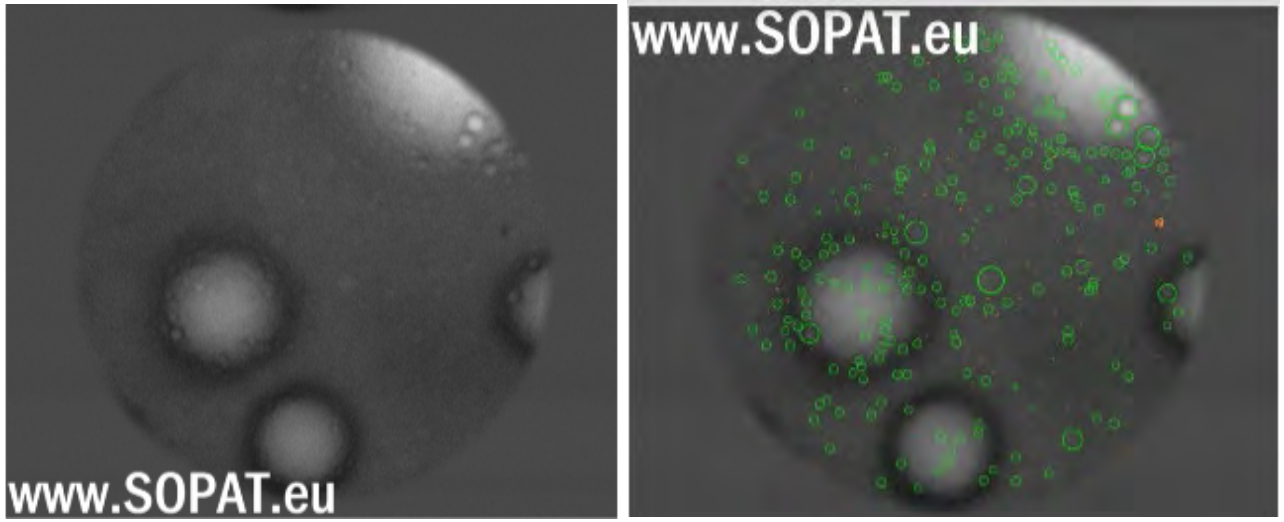
- Dimensionless number based on median diameter as a function of *time*
- Monitors *crushing* of particles
- Detects steady state

- Particle *circularity* over time
- Monitors *rounding* of particles
- Detects steady state



Nystatin Cream (NC) Analysis

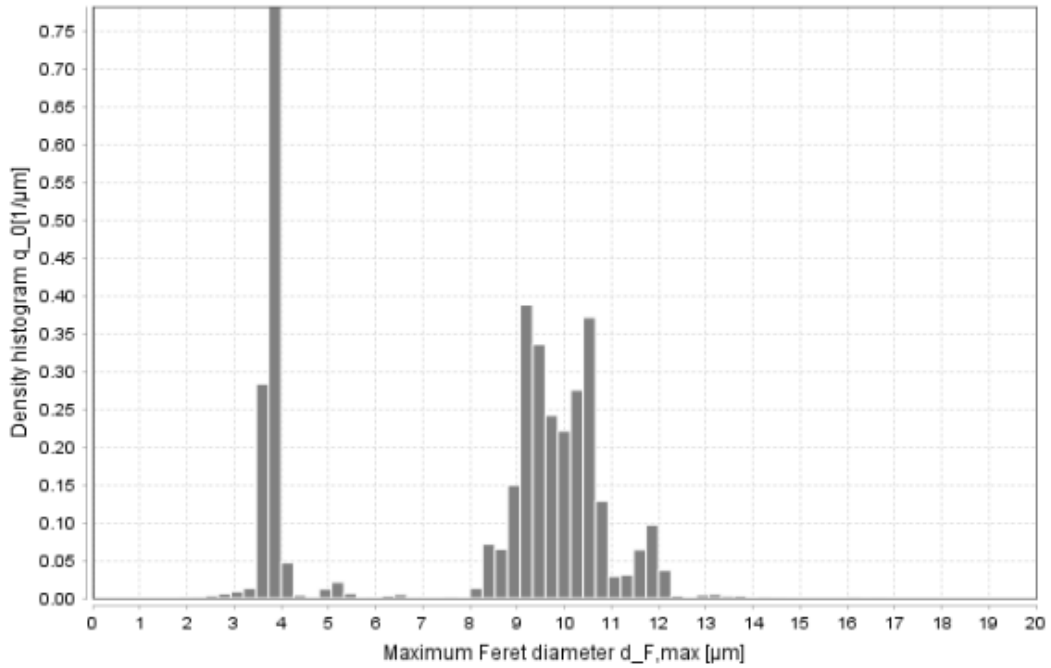
Microscopic probes MM1 and SOPAT-Ma were used to analyze emulsion samples.



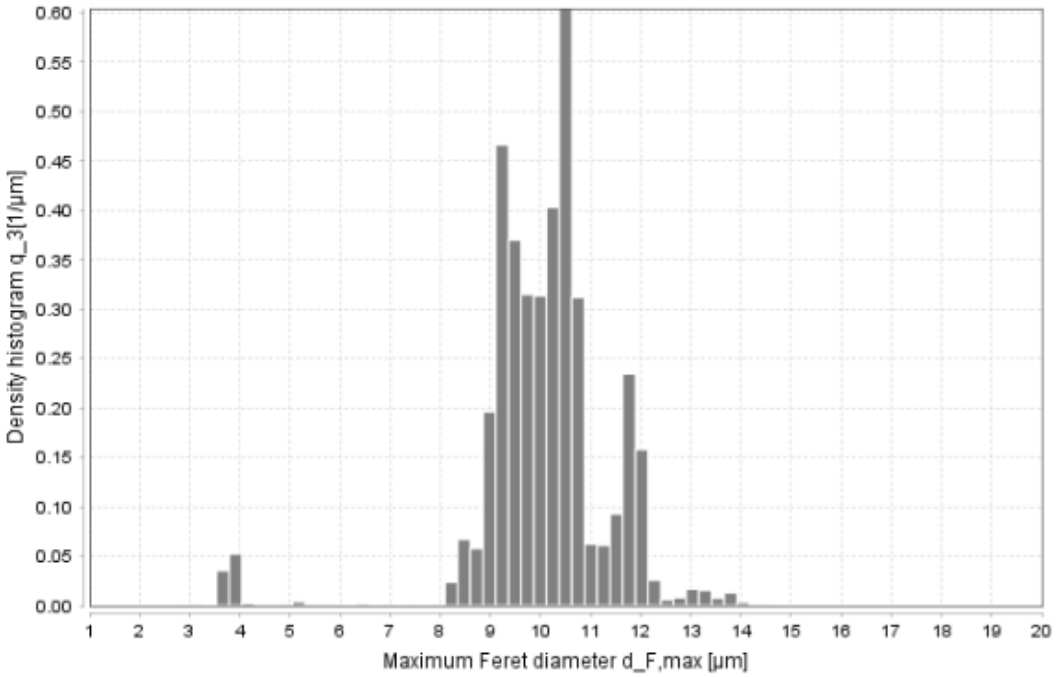
SOPAT software differentiates between solid and liquid particles; globules detected are encircled in green and solid particles in orange (right image).

Particle Size Distribution of NC

Number density



Volume density



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Developing MS3000AT as part of this project to monitor particle size reduction and particle growth processes for nano materials in a range of industries including Pharma

For more information please see

Website: www.pat4nano.com

Thank you to…

- Tina and the PAS team at MP
- Parsum, In Process BV and SOPAT for slides and discussion
- All involved in PAT4Nano for being a source of interesting samples and opportunities