Particle Analysis Systems + Lumetics LINK™

INTRODUCTION

LINK is the software solution for automated analytical data import, analysis, and reporting. LINK scans network locations for new measurement files, extracts all useful data, and copies this data directly to a centralized database. The powerful analysis user-interface allows datasets to be aggregated, grouped, and visualized in the form of charts/tables/images. User-customizable analysis templates deliver rapid and error-free data visualization, with the ability to be replicated across many studies and shared within your organization.

All instrument settings and parameters calculated by the instrument software are copied to the LINK database, including full underlying raw data curves. Sample metadata may be easily assigned and incorporated within the analysis to integrate various product/process variables. LINK has been demonstrated to deliver time savings more than 90% and provide a highly affordable fully automated data management and analysis solution.

PARTICLE CHARACTERIZATION & ANALYSIS SYSTEM DETAILS & APPLICATIONS

Particles may be classified in several ways using many different techniques. Particle characterization is the process of identifying various particles by particle shape, size, surface properties, charge properties, mechanical properties, and microstructure. Particle size analysis, particle size measurement, or simply particle sizing is the collective name of the technical procedures, or laboratory techniques which determines the size range, and/or the average, or mean size of the particles in a powder or liquid sample.

LINK may be utilized to assist directly in the following Particle Analysis application areas:

- Study Summarizations:
  - Formulation Optimization Studies
  - Stability Studies
  - Orthogonal and Complimentary Technique Comparisons and Overlays
- Advanced Analysis and Development:
  - Particle Classification (e.g. Protein vs. Silicone Oil)
  - Morphological Parameter Filter Development
  - SFactor Filter Development and Application
- QA/QC:
  - System Suitability Test Conformance/Trending
  - USP 788/787 Conformance/Trending
  - Particulate Investigations

PARTICLE ANALYSIS SUPPORTED INSTRUMENTS

LINK currently supports multiple instruments specific to particle classification systems, including:

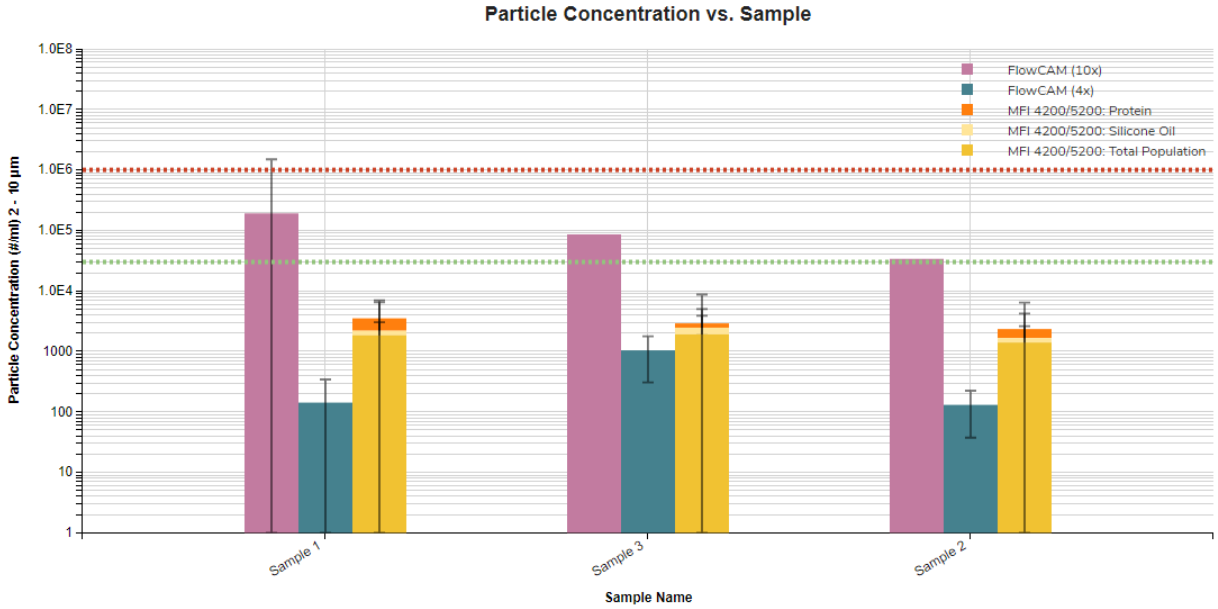
- Flow Microscopy – FlowCAM, MFI
- Static Imaging – Eyecon, HORIZON, Keyence VHX
- Raman/LIBS – Hound, Morphologi G3
- Resonant Mass Measurement (RMM) – Archimedes
- Nanoparticle Tracking Analysis (NTA) – NanoSight
- Dynamic Light Scattering (DLS) – DynaPro, LiteSizer, ZetaSizer
- Light Obscuration (LO) – Accusizer SPOS, HIAC, Klotz, PAMAS
- Static Light Scattering (SLS) – MasterSizer
- Total Holographic Characterization (THC) – xSight
- Coulter Counter – MultiSizer, Spectradyne nCS1

INSTRUMENT SUPPORT DETAILS – FLOW MICROSCOPY: MFI (Protein Simple) & FLOWCAM (Fluid Imaging)

MFI is an image-based particle analysis that combines the direct imaging capabilities of digital microscopy with the precise control of microfluidics. Images of the sample are captured as it passes through the flow cell's sensing zone. Every particle in every image is then analyzed to create a database of particle count, size, transparency, and morphology (or shape). FlowCAM rapidly counts and images particles in a fluid stream to characterize the particles using a variety of measurements.

LINK supports MFI and FlowCam output data for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Count/Concentration vs. Particle Morphology Parameters. With a customizable import method, LINK includes settings for particle thumbnail imports, sub-populations, custom particle parameter calculations, and dilution factor.

Fig 1. Column Chart dashboard visualizing MFI data with subpopulations and FlowCAM measurement files plotting raw data for Particle Concentration vs. Sample Name with error bars and limit lines.



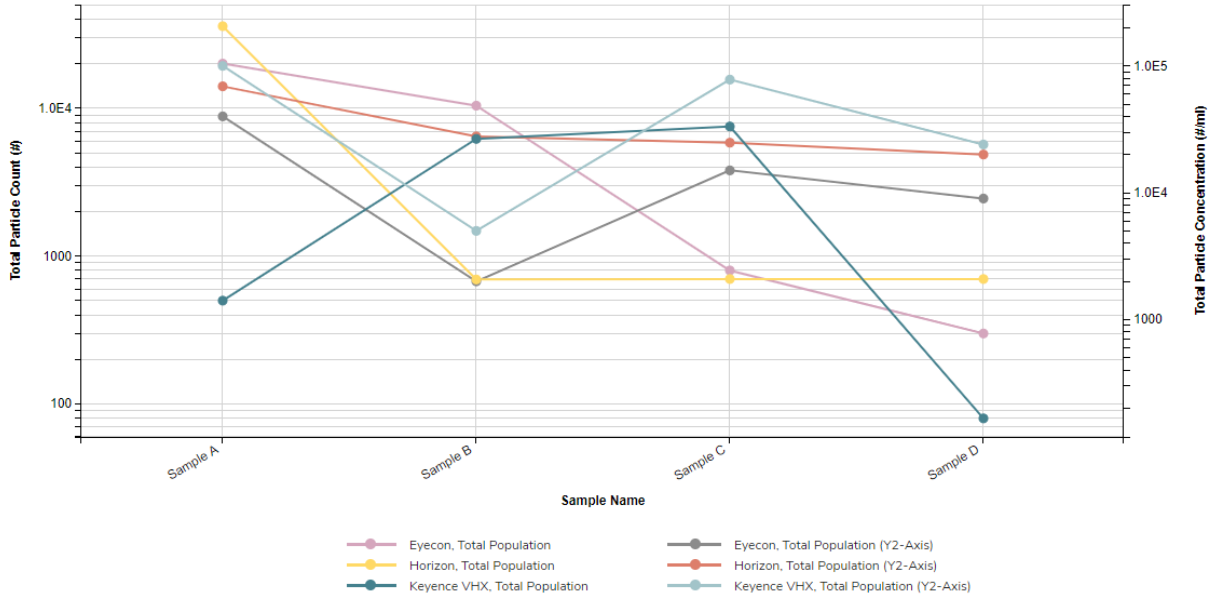
INSTRUMENT SUPPORT DETAILS – STATIC IMAGING: HORIZON (Halo Labs) & EYECON (Innopharma) & VHX-7000 (Keyence)

HORIZON system provides quantitative subvisible particle analysis. The HORIZON system is powered by a highly sensitive Backgrounded Membrane Imaging (BMI) technology. LINK supports HORIZON output data for instrument/analysis settings, parameters, calculations, and raw data curves for Particle count or concentration vs. morphology. With a customizable import method, LINK includes settings for particle thumbnail imports, sub-populations, custom particle parameter calculations, and dilution factor.

The Eyecon is a particle analyzer for the analysis and profiling with non-product contact that generates real-time on-screen images, particle size and shape information. LINK supports Eyecon output data for instrument/analysis settings, parameters, calculations, and raw data curves for Dv10, Dv50, Dv90, an Eccentricity vs. Elapsed Time & Volume Fraction (Cumulative) vs. Particle Diameter.

Keyence VHX is a 4K Ultra-High Accuracy Microscope for advanced measurement capabilities for inspection and failure analysis. LINK supports Keyence output data for instrument/analysis settings, parameters, calculations, and raw data curves for Particle count/concentration vs. particle diameter/area/circularity/perimeter. With a customizable import method, LINK includes settings for sub-populations and custom particle parameter calculations.

Fig 2. Column Chart dashboard visualizing Static Imaging measurement files plotting data for Total Particle Concentration & Count vs. Sample Name in the form of line + marker rather than columns.

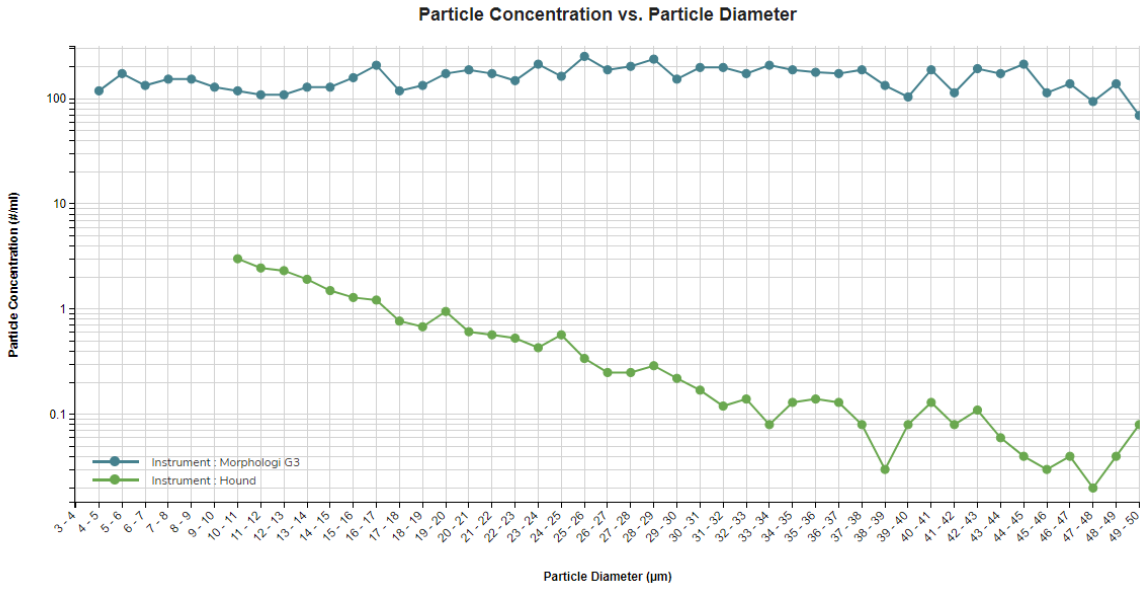


INSTRUMENT SUPPORT DETAILS – RAMAN/LIBS: HOUND (UnChained Labs) & MORPHOLOGY G3 (Malvern Panalytical)

Hound combines microscopy and Raman and Laser-Induced Breakdown Spectroscopy (LIBS) to forensically identify particles by their chemical and elemental fingerprints. The Morphologi G3 provides an advanced particle characterization tool for the measurement of particle size and particle shape from 0.5 microns to several millimeters.

LINK supports Hound and Morphologi G3 output data for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Count/Concentration vs. Particle Morphology Parameters. With a customizable import method, LINK includes settings for sub-populations, custom particle parameter calculations, and dilution factor.

Fig 3. Histogram dashboard visualizing Hound and Morphologi G3 measurement files plotting raw data for Particle Concentration vs. Particle Diameter.

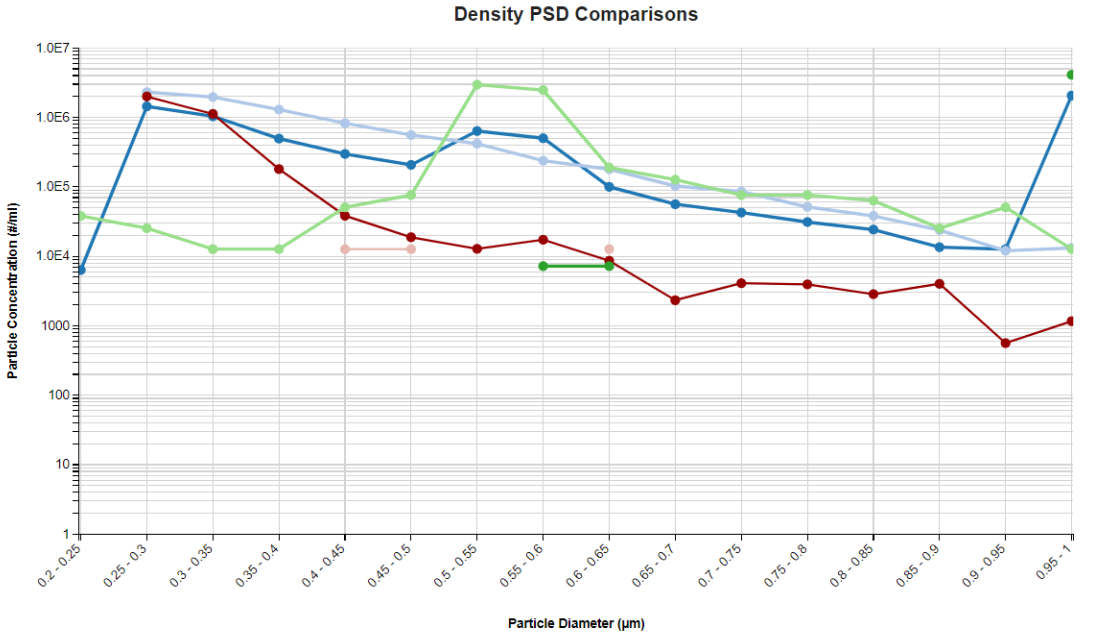


INSTRUMENT SUPPORT DETAILS – RMM: ARCHIMEDES (Malvern Panalytical)

Archimedes harnesses the technique of resonant mass measurement to detect and count particles in the size range 50nm - 5µm* and to measure particle mass and size.

LINK supports Archimedes for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Concentration vs. Particle Size. With a customizable import method, LINK includes settings for particle coincidence adjustments, buoyance sub-populations and dilution factor.

Fig 4. Histogram dashboard visualizing Archimedes measurement files plotting binned raw data curves for Particle Concentration vs. Particle Diameter.

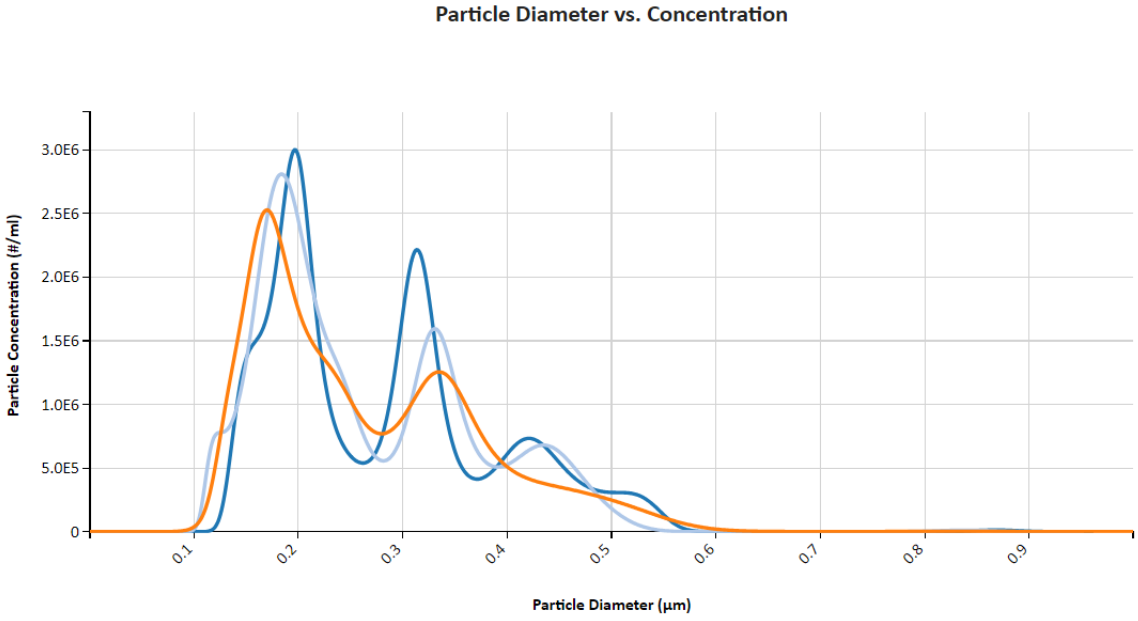


INSTRUMENT SUPPORT DETAILS – NTA: NANOSIGHT (Malvern Panalytical)

NanoSight instruments utilize Nanoparticle Tracking Analysis (NTA) to characterize nanoparticles in solution. They provide high resolution nanoparticle size, count-based concentration, and aggregation measurements while a fluorescence mode provides specific results for suitably labelled particles. With real time monitoring, subtle changes in the characteristics of particle populations are provided with all of these analyses confirmed by visual validation.

LINK supports NanoSight for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Count/Concentration vs. Particle Size.

Fig 5. Line Chart dashboard visualizing NanoSight measurement files plotting raw data curves for Particle Concentration vs. Particle Diameter and split by Sample Name.



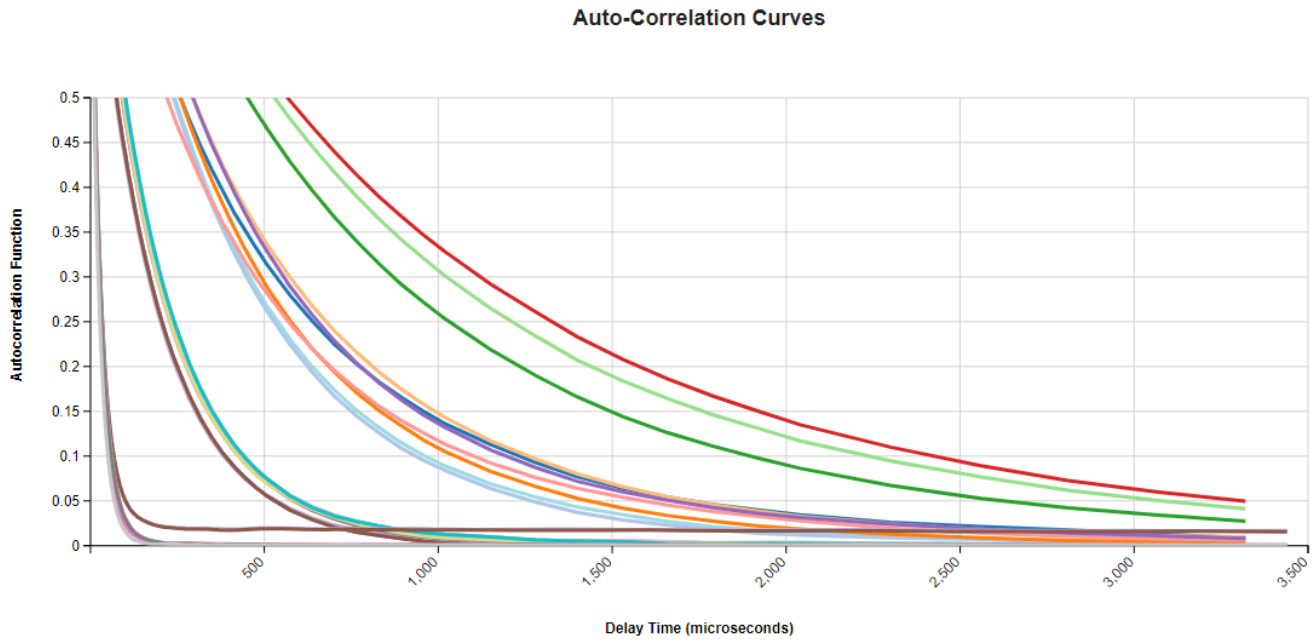
INSTRUMENT SUPPORT DETAILS – DLS: DYNAPRO (Wyatt) & LITESIZER (Anton Paar) & ZETASIZER (Malvern Panalytical)

DynaPro is a unique cuvette based DLS instrument used for the analysis of proteins, promiscuous inhibitors, micelles, quantum dots, liposomes, metallic nanoparticles and more. LINK supports DynaPro for instrument/analysis settings, parameters, calculations, and raw data curves for Intensity & Mass vs. Particle Size and Autocorrelation vs. Delay Time

Litesizer is an instrument for characterizing nano- and microparticles in dispersions and solutions. It determines particle size, zeta potential, and molecular mass by measuring dynamic light scattering (DLS), electrophoretic light scattering (ELS), and static light scattering (SLS). LINK supports LiteSizer for instrument/analysis settings, parameters, calculations, and raw data curves for Intensity & Mass vs. Particle Size and Autocorrelation vs. Delay Time.

Zetasizer instrument is used to measure particle and molecular size from less than a nanometer to several microns using dynamic light scattering; zeta potential and electrophoretic mobility using electrophoretic light scattering; and molecular weight using static light scattering. LINK supports ZetaSizer for instrument/analysis settings, parameters, calculations, and raw data curves for Intensity & Mass vs. Particle Size and Autocorrelation vs. Delay Time and Total Counts vs. Zeta Potential.

Fig 6. Line Chart dashboard visualizing DLS measurement files plotting raw data curves for Autocorrelation vs Delay Time.



INSTRUMENT SUPPORT DETAILS – LO: HIAC (Beckman Coulter) & ACCUSIZER (Entegris) & KOLTZ & PAMAS

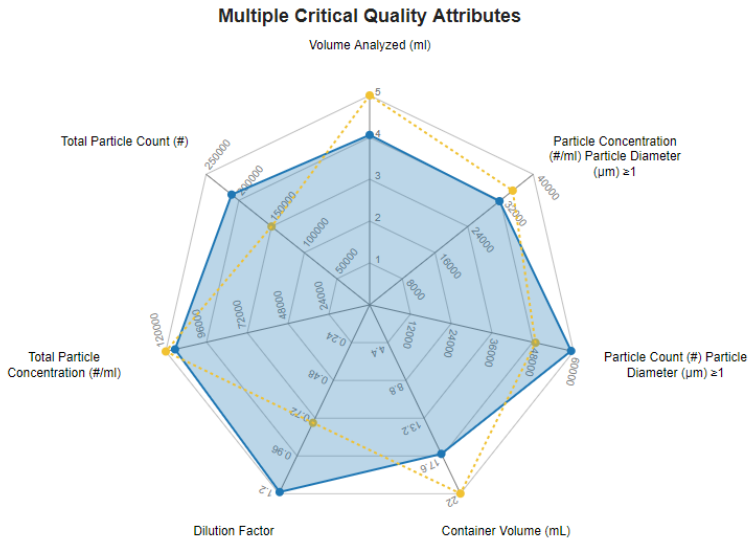
HIAC is an aerosol particle counter where a stream is drawn through a chamber with a light source (either Laser Based Light or White Light). When a particle is illuminated by this light beam, it is redirected or absorbed. This allows for sizing and counting of individual particles.

AccuSizer is a comprehensive portfolio of high accuracy and resolution liquid particle counters that determine particle size and concentration of your suspensions. AccuSizer utilizes the SPOS technique, where particles in liquid suspension flow through a photozone, light is either absorbed or refracted due to the physical presence of the particle or it can be scattered at some oblique angle. Klotz is engaged in laser technologies and devices for particle measuring and develops, manufacture and tests the complete product range of optical and electronic components.

PAMAS particle counters measure solid particulate contamination of liquids and control the efficiency of filters and the cleanliness of liquids. Particles circulating at high speed and pressure in the liquids of turbines, power plans, gearboxes and offshore applications are capable of damaging mechanical parts of the system.

LINK supports HIAC, Accusizer, Klotz, and PAMAS instruments for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Concentration vs. Particle Size.

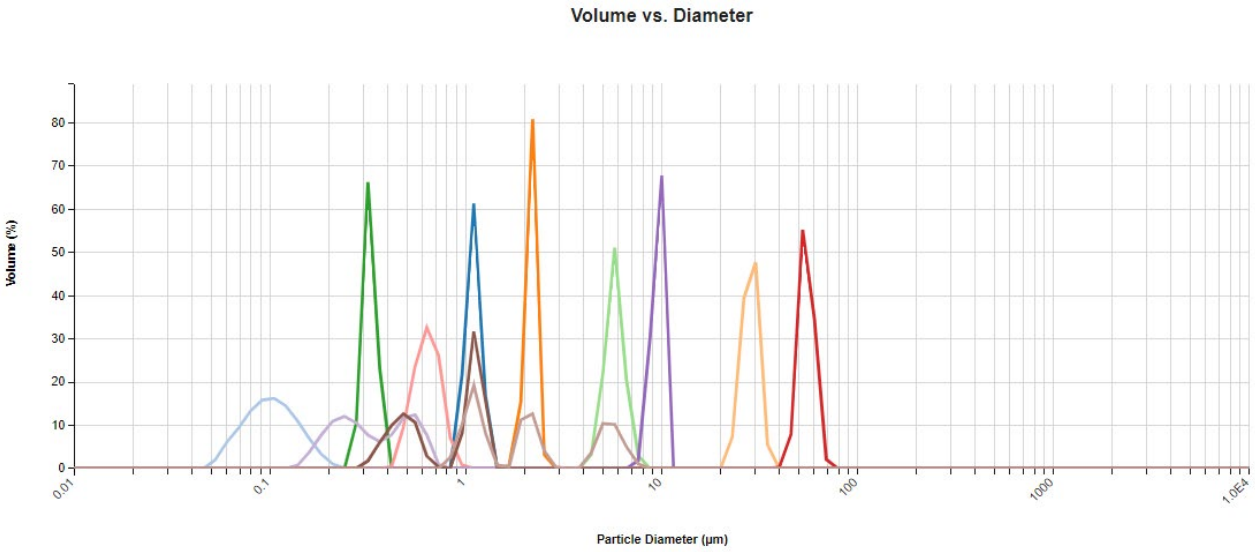
Fig 7. Radar Chart dashboard plotting Multiple Critical Quality Attributes from Light Obscuration measurement files.



INSTRUMENT SUPPORT DETAILS – SLS: MASTERSIZER (Malvern Panalytical)

The Mastersizer laser diffraction particle size analyzer delivers accurate particle size distributions for both wet and dry dispersions. LINK supports MasterSizer for instrument/analysis settings, parameters, calculations, and raw data curves for Volume (%) & Number (%) & Mass (%) vs. Particle Size.

Fig 8. Line Chart dashboard visualizing MasterSizer measurement files plotting raw data curves for Volume (%) vs. Particle Diameter and split by Sample Name.



INSTRUMENT SUPPORT DETAILS – THC: XSIGHT (Spheryx)

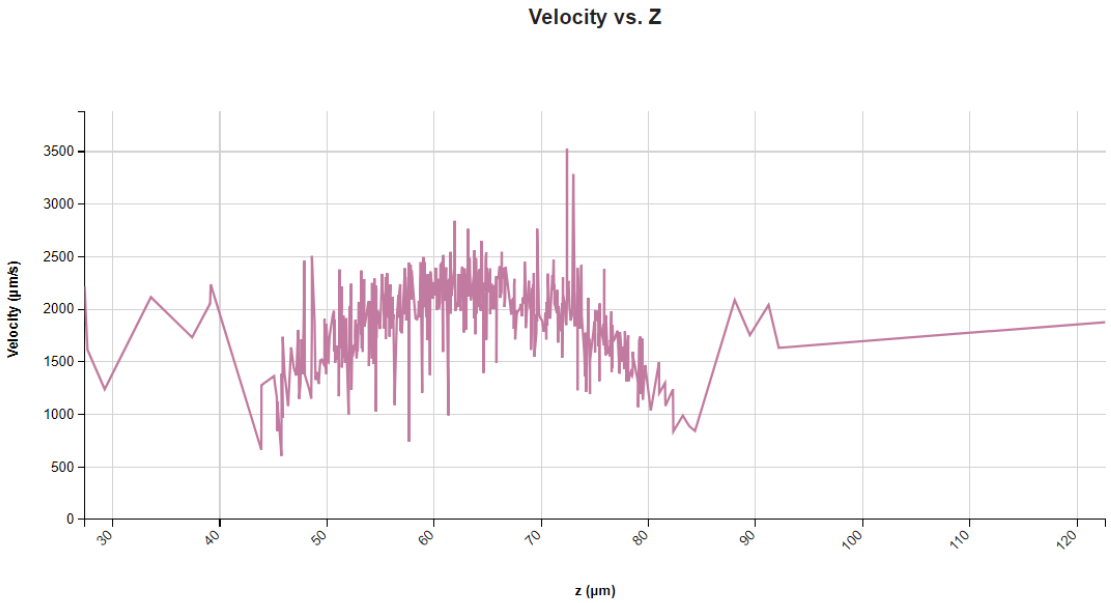
The xSight system is a total holographic characterization technology that non-invasively yields a wealth of information with precise, reliable and accurate quantitative measurements of suspended particles in complex samples. This technology has the unique ability to distinguish different distributions in multi-component suspensions – even when they are the same size.

LINK supports xSight for instrument/analysis settings, parameters, calculations, and raw data curves for:

- Count/Concentration/Count per Container vs. Particle Diameter
- Count/Concentration/Count per Container vs. Refractive Index
- Count/Concentration/Count per Container vs. Time
- Average Refractive Index vs. Particle Diameter
- Velocity vs. Z

With a customizable import method, LINK includes settings for Sub-populations and particle thumbnail import specifications.

Fig 9. Line Chart dashboard visualizing xSight measurement files plotting raw data curves for Velocity vs. Z.

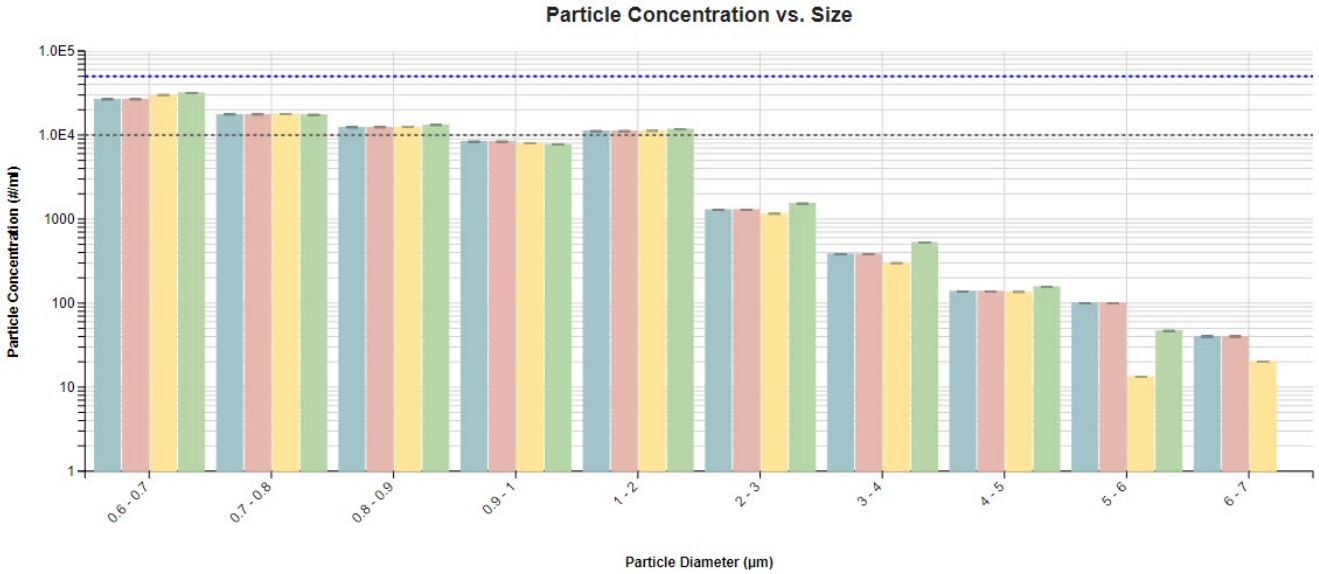


INSTRUMENT SUPPORT DETAILS – COULTER COUNTER: MULTISIZER (Beckman Coulter) & SPECTRADYNE

MultiSizer is a highly versatile particle counting and characterization system. It uses the Coulter principle to detect particles via electrical zone sensing, regardless of the particle's nature or optical properties. The Spectradyne nCS1 employs a novel implementation of the resistive pulse sensing method to count and size nanoparticles quickly and with high resolution. Sizing precision of ±3% is typically achieved, with measurement rates up to 10,000 particles/s.

LINK supports MultiSizer and Spectradyne output data for instrument/analysis settings, parameters, calculations, and raw data curves for Particle Count/Concentration vs. Particle Size.

Fig 10. Histogram dashboard visualizing Archimedes measurement files plotting binned raw data curves for Particle Concentration vs. Particle Diameter.



VISUALIZATIONS – LINK ANALYSIS

LINK's dynamic analytical suite will aggregate data and provide visualization tools to suit your specific needs. Imported Separation Systems measurement data can be analyzed using the LINK platform's customizable charts, tables, calculations, images etc. User-customized analysis templates deliver rapid and error-free data visualization with the ability to be exported as a word report to share across your organization. All particle data can be visualized separately, as well as overlaid in the same chart and tables.

Fig 11. Tabular Summaries

Measurement Summary Table – Measurement Results

Sample Name	Conc. < 0.2 µm	Conc. 0.2-0.5 µm	Conc. 0.5-1 µm	Conc. ≥ 1 µm	Conc. 2-10 µm	Conc. ≥ 10 µm	Conc. ≥ 25 µm	Pdi Width (d.nm)	Z-Average (d.nm)	Zeta Potential (mV)
Sample A	3,399,587,397	15,998,721	5,150,634	1,209,563	280,231	4,951	883	1	2	-33
Sample B	3,273,099,475	17,587,519	3,264,007	546,721	11,682	877	199	29	79	-36
Sample C	407,361,551	155,739,164	720,176	76,608	21,348	783	68	22	50	

Measurement Summary Table – Instrument Settings

Sample Name	Total (#/ml)	Total Protein (#/ml)	Total Silicone (#/ml)	% Protein	% Silicone
Sample A	5,562	3,078	1,143	58.0%	22.0%
Sample B	7,630	3,186	1,479	49.9%	21.5%
Sample C	33,513	20,651	2,535	46.4%	17.5%

Fig 12. Critical Quality Attribute vs. Sample Metadata

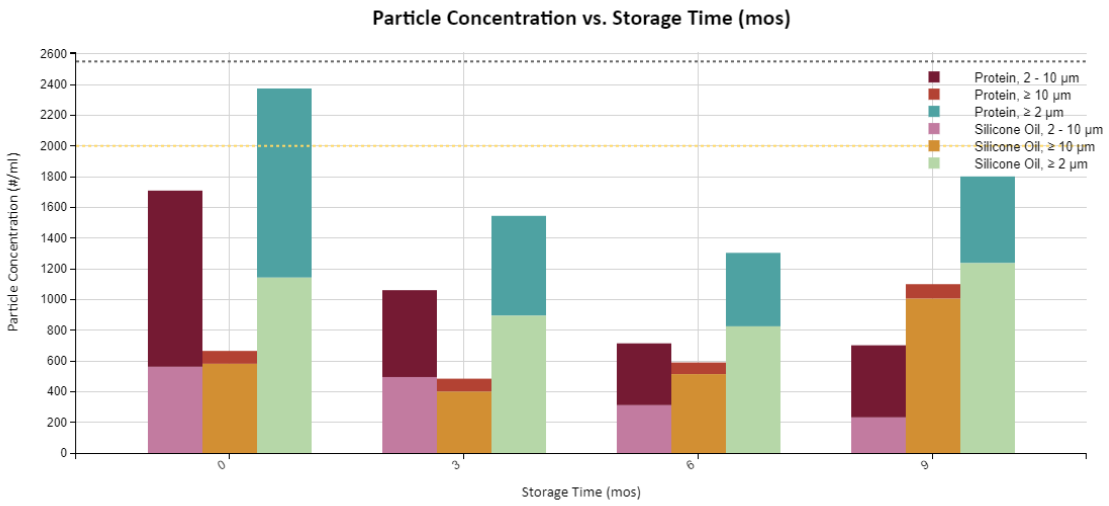


Fig 13. Multiple Critical Quality Attribute Visualization

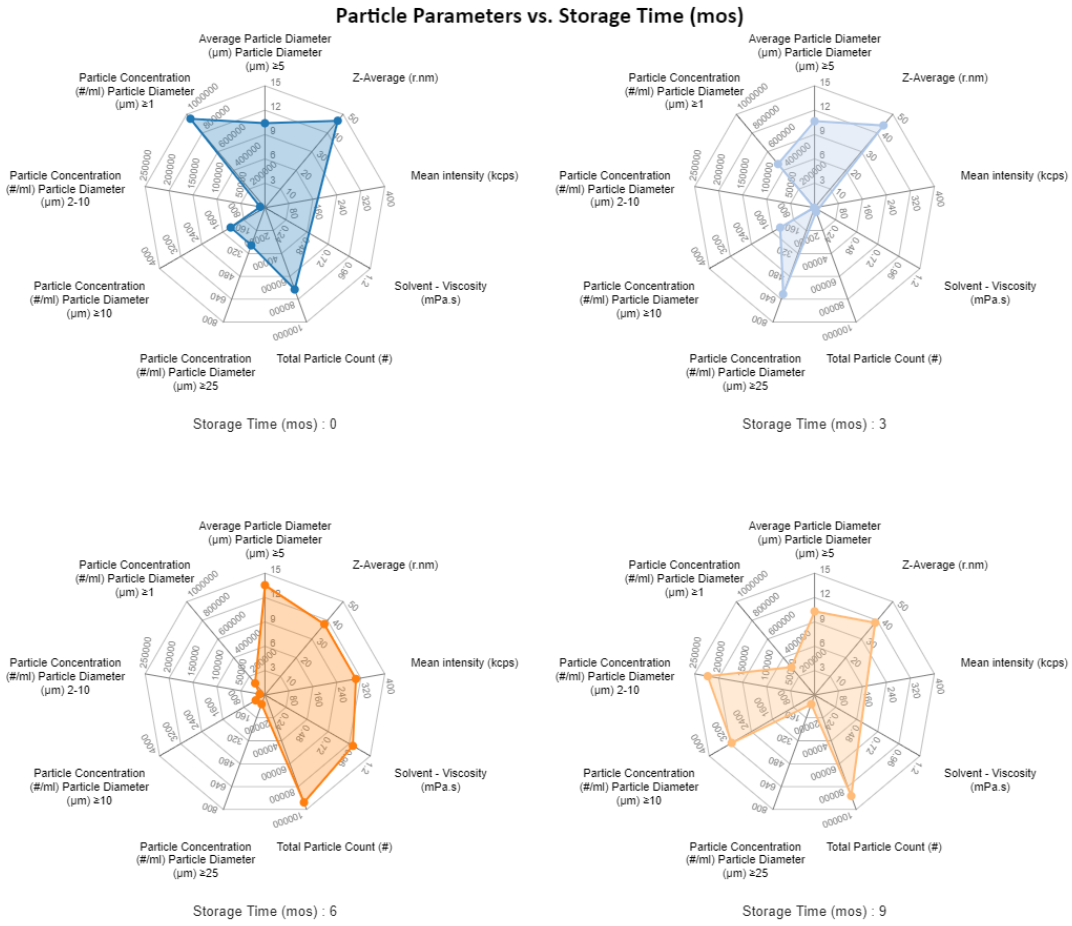


Fig 14. Multi-Factor Visualization

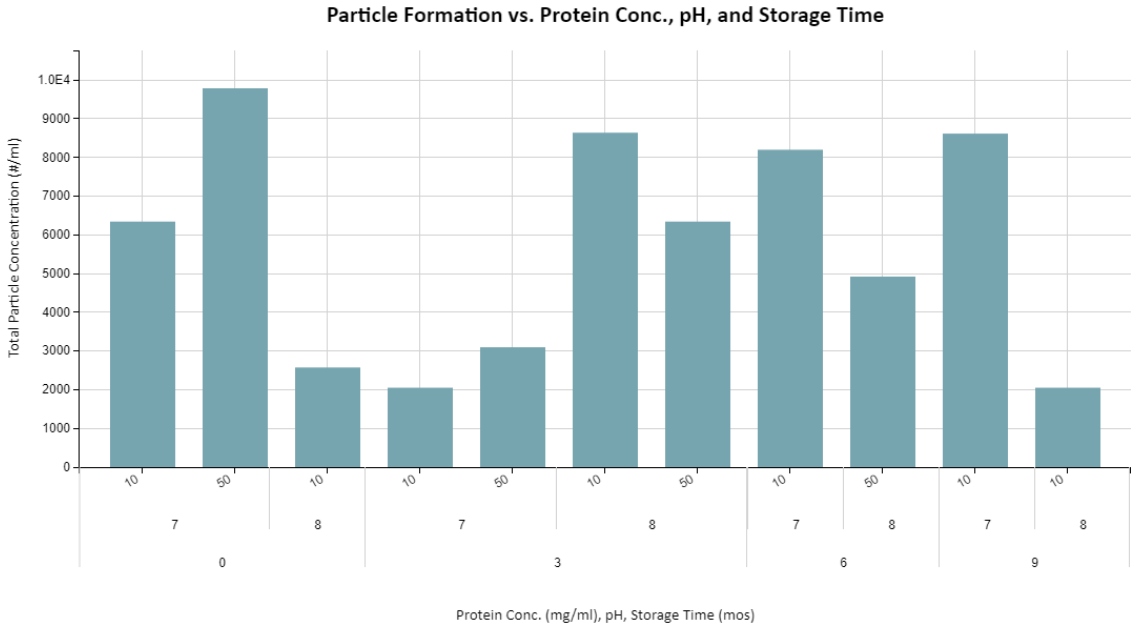


Fig 15. Raw Curve Data

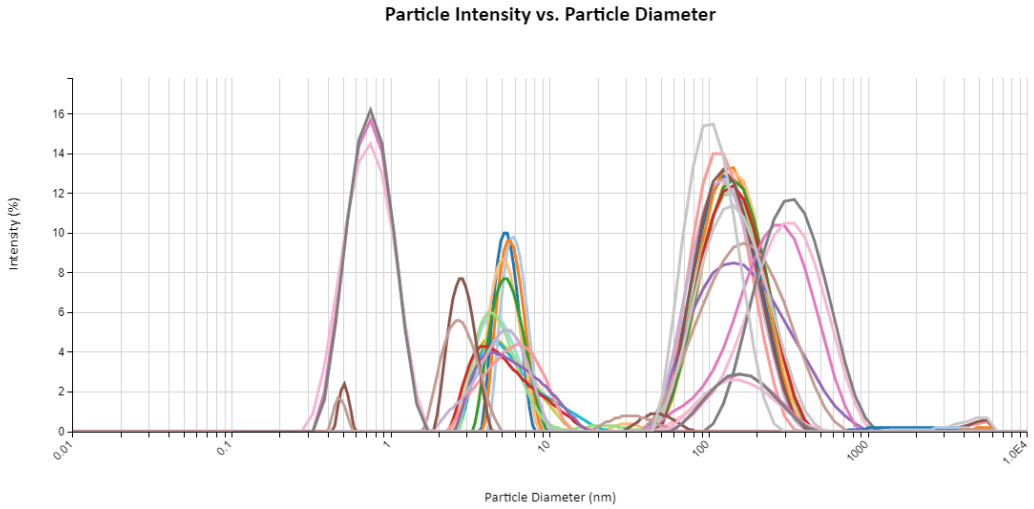


Fig 16. Complimentary Technique Comparisons

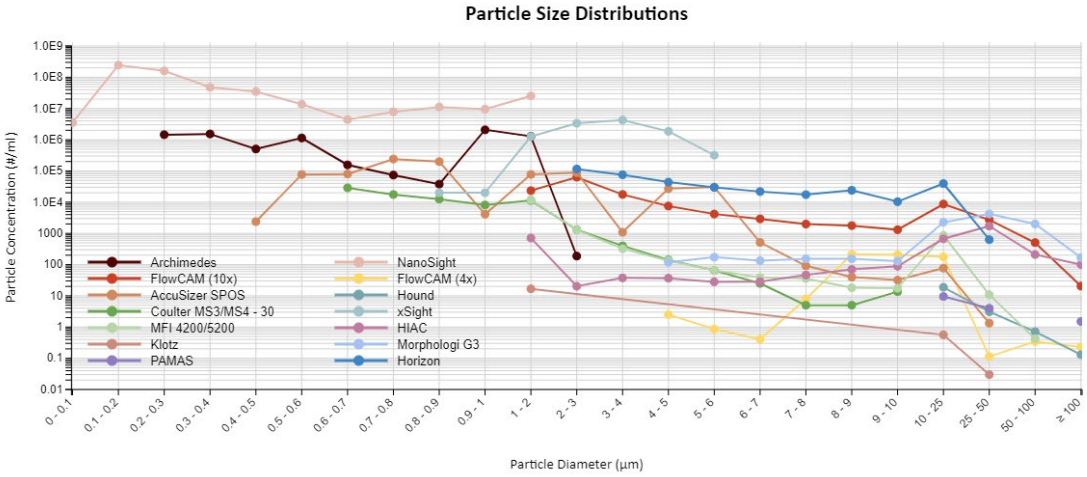


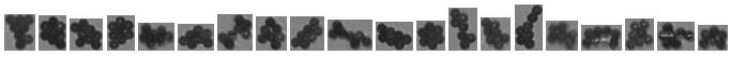
Fig 17. Particle Images

Particle Images

FlowCAM (10x) VS Series/PV-100/8100, ECD ≥10 AND ECD < 25

FlowCAM (4x) VS Series/PV-40/8100, ECD ≥10 AND ECD < 25

Horizon, ECD ≥10 AND ECD < 25



MFI 4200/5200, ECD ≥10 AND ECD < 25

PARTICLE ANALYSIS DASHBOARDS

LINK contains an extensive built-in dashboard library from LINK version 2.4.0.210401 and later. This function contains specific pre-created dashboards for all instruments and application groups.

CONTACT LUMETICS

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