Solutions for Macromolecular and Nanoparticle Characterization

WYATT TECHNOLOGY

A Word from Dr. Philip Wyatt, Founder and CEO

It is my great pleasure to welcome you to the pages of this booklet which describe Wyatt Technology and its products.

For most of my adult life, I've led companies developing and producing light scattering instruments—as well as a few other analytical devices. From commercializing the very first scientific instruments incorporating lasers and microprocessors to overseeing the introduction of the very first multi-angle light scattering (MALS) detectors, I've been at the nexus of some remarkable organizations. Wyatt Technology is a private family business—not beholden to outside shareholders, private equity ownership or short-term profitability. Our first commitment is to our customers, and our mission to delight them. But in order to do this, our second pledge is to our employees who enable us to indulge in this old-fashioned approach to customer service. Without the team of extraordinarily talented, diverse and passionate people we have, we could not have thrived for the past 35 years.

More than two decades ago, I established what has become one of the crown jewels of Wyatt Technology—a course we call Light Scattering University (LSU). This class, which typically runs three days, is taught monthly by our distinguished technical staff and designed to ensure that our customers get the most out of their Wyatt instruments.

I take enormous pleasure in personally interacting with our participants during lunches and dinners, not to mention leading them through our Light Scattering Instrument Museum with a highly-personalized tour. LSU really is the starting point for our successful, life-long relationships with our customers.

I would love to have you visit us here in Santa Barbara by enrolling in an LSU class, or by planning a visit to see our company and our manufacturing facilities, as well as meeting our incredible people. In the meantime, I hope that the following pages will help you learn more about our products, which have been referenced in nearly 13,000 peer-reviewed scientific papers, used by Nobel laureates and installed in most major academic and corporate macromolecular characterization laboratories in the world.

Wyatt Technology

SEC-MALS Products for HPLC & UHPLC

Molar Mass, Size, Conformation, Intrinsic Viscosity, Polydispersity

Dynamic & Electrophoretic Light Scattering Products

Size, Zeta Potential, Stability, Polydispersity

Field Flow Fractionation & CG-MALS Products

Complex Fluids

Biomolecular Interactions

Training, Service & Support

This Time, It's Personal

For more than thirty-five years, we've operated as one of the very few remaining family-owned businesses in the analytical instrument industry.

After all, we aren't just a literal family, we're a metaphorical one, too. All of our customers and staff are considered part of the extended family, and we take the work of our customers personally; when they succeed, we couldn't be prouder.

Through almost four decades, Wyatt Technology has grown—not by acquisition—but organically, by focusing on our customers and their science. We drive our accomplishments by developing and manufacturing our own hardware and software and remaining committed to our mission of delighting our customers. Assisting researchers with cutting-edge macromolecular and nanoparticle characterization tools is our passion, which we personalize through peer-level customer contact, Light Scattering University lunches and dinners and unprecedented relationship-building.

We invite you to join our family and experience our refreshingly different corporate philosophy of emphasizing *you!*

Clifford D. Wyatt, Executive Vice President (left)
Dr. Philip J. Wyatt, Chief Executive Officer (center)
Geofrey K. Wyatt, President (right)

OUR MISSION

Wyatt Technology delights its customers by providing outstanding analytical tools, as well as unparalleled levels of personal service, to support life-enhancing macromolecular and nanoparticle science.

Growth & Cutting-Edge Technological Innovation

2010

2017 DynaPro Plate Reader III, with true molar mass capability, launched
2017 miniDAWN TREOS II, with field-serviceability and upgradeability to µDAWN, introduced
2017 DAWN HELEOS II wins Scientist's Choice Award® from SelectScience for Instrument of the Year
2017 Wyatt Technology expands headquarters by 50% to 45,000+ square feet
2016 Completely re-engineered ViscoStar III revealed
2014 First MALS detector for UHPLC, the µDAWN, featured
2011 Tibbetts Award for exemplifying notable lifetime achievements in innovation
2010 Mobius zeta potential instrument, first with flow through and pressurized capabilities, introduced

2000

2009 Wyatt Technology wins Company of the Year, presented by South Coast Business & Technology
2008 Scientist Magazine Award: Best Places to Work in Industry—also awarded in 2009, 2010 and 2012
2007 miniDAWN TREOS introduced with front panel computer
2007 Calypso (Composition-Gradient) system introduced for reversible and irreversible interactions
2005 R&D 100 Award for Optilab rEX RI detector
2005 DAWN HELEOS (18-angle) instrument introduced with front panel computer
2005 First DynaPro Plate Reader for automated DLS measurements introduced
2004 Optilab rEX (Extended Range) array diode RI detector arrives

1990

2004 Wyatt Technology acquires assets of Protein Solutions
2004 Wyatt Technology China office formed
2004 ViscoStar viscometer enters the market
2004 ASTRA GPC software with 21 CFR Part 11 compliance released
1999 DAWN EOS (18-angle Enhanced Optical System) introduced with solid state laser
1995 Optilab DSP (Digital Signal Processing) RI detector comes to market
1994 Major sensitivity improvements arrive with the DAWN DSP (Digital Signal Processing)
1993 Wyatt Technology Europe formed in Germany
1992 miniDAWN (3-angle) GPC detector introduced with solid state laser
1989 ASTRA 1.0 GPC software released

1980

1988 Optilab differential refractive index detector line acquired from Perstorp Analytical, Sweden
1986 First high temperature (150°C) DAWN F instrument placed
1985 DAWN B (Batch-mode) instrument introduced
1984 AMOCO Production Company orders 1st DAWN 16-angle GPC detector
1983 SC Johnson & Son orders 1st DAWN F with 7-angle flow-through detector
1982 Wyatt Technology formed with $50,000 contract to detect toxicants in drinking water

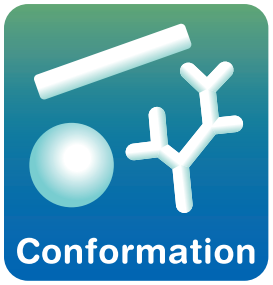
Wyatt Technology's Rich History

In 1970, Wyatt Technology's founder, Philip Wyatt, and some of his colleagues, formed a company that developed the world's very first multi-angle light scattering instruments using a laser as the light source. In addition, they developed instrumentation that was the first to incorporate microprocessors.

Since those days, Dr. Wyatt has been spearheading the definition and redefinition of state-of-the-art analytical instrumentation at Wyatt Technology. The company's light scattering lore runs deep, and with a team of now more than 130 people, including 25+ Ph.D.'s, we ensure that Dr. Wyatt's expertise is multiplied and perpetuated.

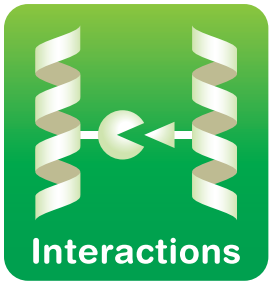
What can I measure?

Absolute molecular weight
from 200 to 1,000,000,000 g/mol

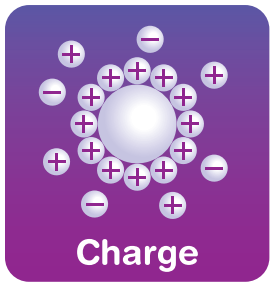


Shape, structure and
branching parameters

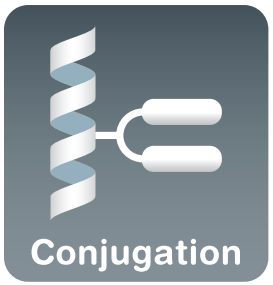
RMS radius from 10 to 500 nm
and hydrodynamic radius
from 0.2 to 5,000 nm



Binding affinity from pM to mM
and absolute stoichiometry
of complex interactions

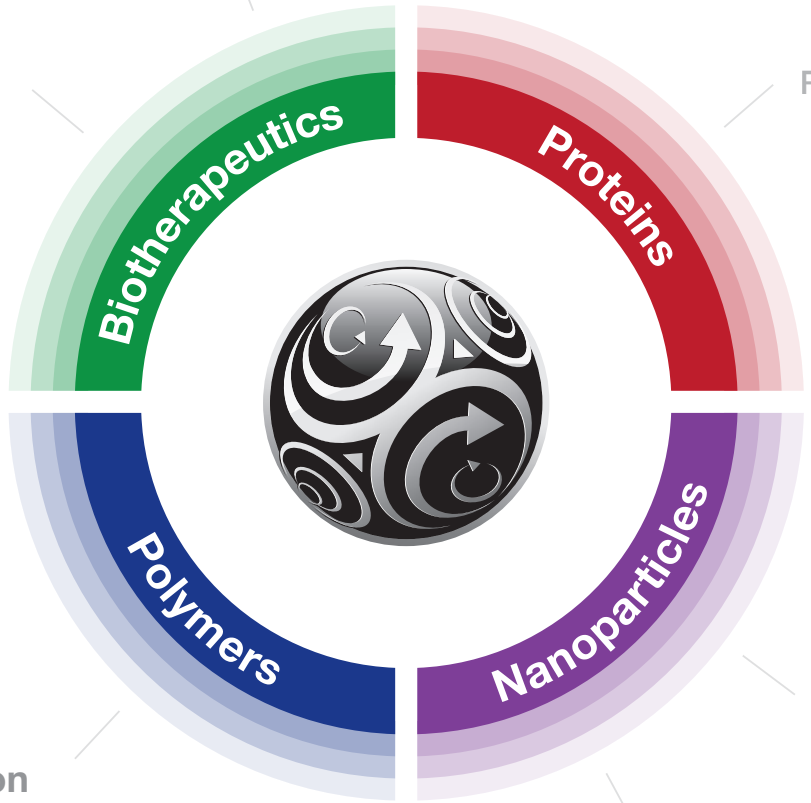


Zeta potential and net molecular
charge for particles from 2 nm
to 100 µm



Molecular weight and fraction
of each constituent in a binary
conjugate

What can I analyze?



Native Properties
Oligomeric State
Glycoproteins
Membrane Proteins

Aggregation
Impurities & Fragments

Conjugation
PEGylation
Protein-polysaccharides

Solution Quality
Purification
Reagent Qualification

Formulation Screening
High-concentration mAbs
Colloidal and Thermal Stability

Interactions
Affinity & Stoichiometry
Self-associations
Hetero-associations

Mass and Size Distributions
Reaction Monitoring
Degradation Kinetics

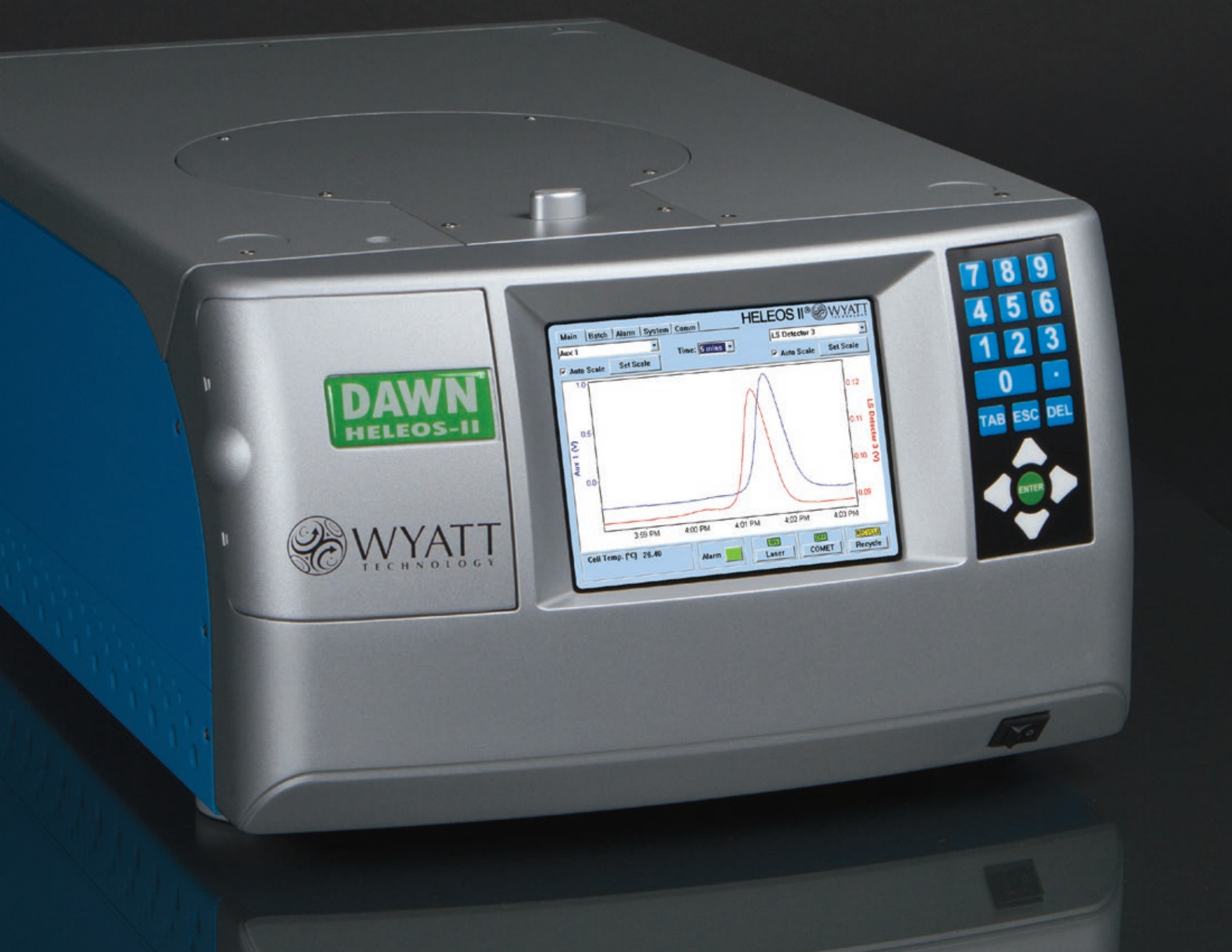
Shape and Structure
Size Distributions
Number Distributions

Process Development
Liposomes, Viruses, VLPs
Separation of Complex Fluids

Conformation
Mark-Houwink-Sakurada Parameters
Branching

Copolymers
Composition Ratio
dn/dc

Zeta Potential
Engineered and Environmental Nanoparticles
Drug Delivery Nanoparticles


DAWN
HELEOS-II
WYATT
TECHNOLOGY
HELEOS II
WYATT
Main
Batch
Alarm
System
Comm
Aux 1
Time: 5 mins
LS Detector 3
Auto Scale
Set Scale
Auto Scale
Set Scale
1.0
0.5
0.0
Aux 1 (V)
0.12
0.11
0.10
0.09
LS Detector 3 (V)
3:59 PM
4:00 PM
4:01 PM
4:02 PM
4:03 PM
Cell Temp. (°C) 26.40
Alarm
Laser
COMET
Recycle
7 8 9
4 5 6
1 2 3
0 .
TAB ESC DEL
ENTER

SEC-MALS Products

For HPLC & UHPLC

Characterize molar mass, size and conformation

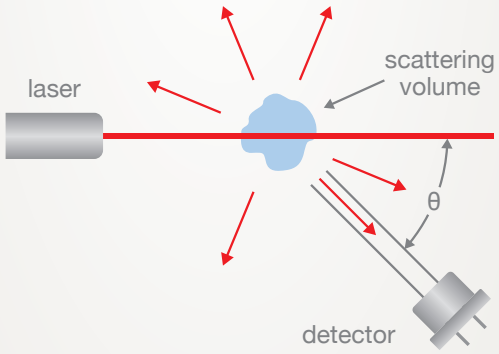
MALS

multi-angle light scattering

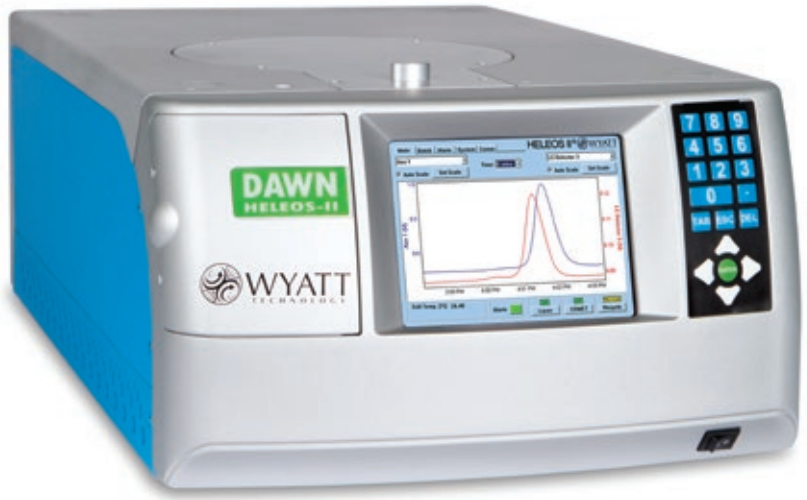
Based on first principles, MALS determines the molar mass and size of macromolecules and nanoparticles in solution.

Characterize:

- Peptides and proteins
- Conjugated proteins
- Polymers and copolymers
- Nanoparticles
- Virus-like particles
- Liposomes and exosomes



Multi-angle light scattering determines molar mass from the scattered intensity and the molecular radius from the angular scattering pattern.

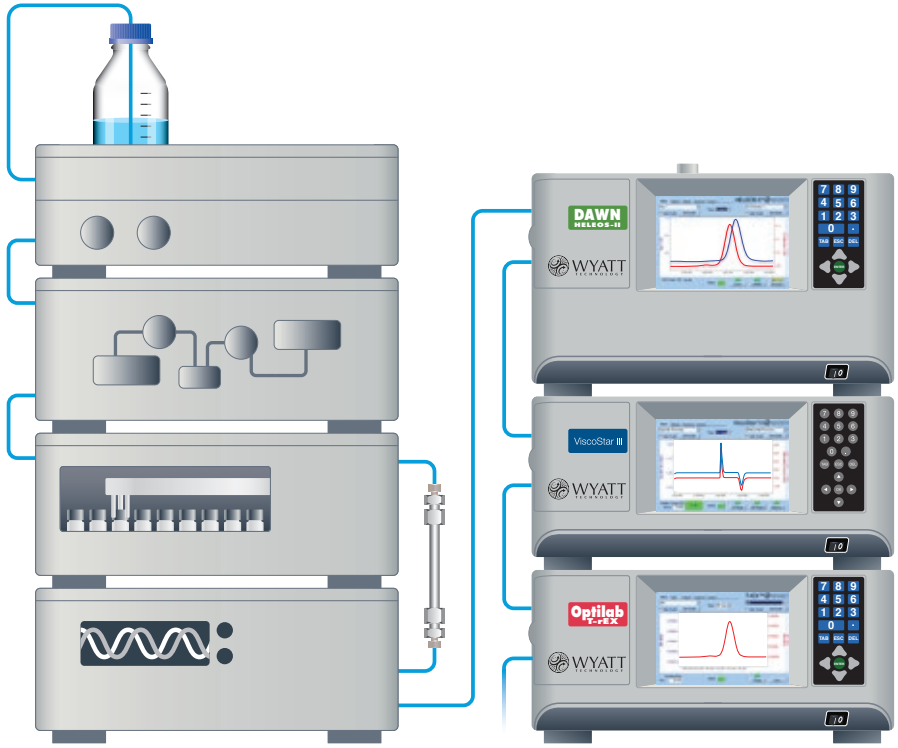


DAWN

Premier family of MALS detectors

Choose between HELEOS II for the highest sensitivity and widest measurement range or TREOS II for fundamental analysis of proteins and small polymers. Also available is µDAWN, uniquely suited for UHPLC.

SCIENTISTS' CHOICE AWARDS 17 WINNER



Wyatt's MALS detectors interface to most industry-standard HPLC, GPC and FPLC systems.

	DAWN HELEOS II	miniDAWN TREOS II	µDAWN
Description	The premier SEC-MALS detector for absolute molar mass and size, offering the highest sensitivity	The best in fundamental multi-angle light scattering	The only MALS detector uniquely designed for UHPLC with superb sensitivity
Applications	Peptides, proteins and polymers; plus viruses, vesicles and nanoparticles up to 500 nm in radius	Peptides, proteins small polymers, small viruses, VLPs and nanoparticles	Peptides, proteins and small polymers compatible with UHPLC
Molar Mass Range	200 Da to 1 GDa	200 Da to 10 MDa (proteins) or 1 MDa (polymers)	200 Da to 10 MDa (proteins) or 1 MDa (polymers)
Molecular Size Range (MALS — r_g)	10 to 500 nm	10 to 50 nm	10 to 50 nm
Molecular Size Range (DLS — r_h)	Flow: 1 to 300 nm Batch: 0.5 nm to 1 µm	Flow: 1 to 40 nm Batch: 0.5 nm to 1 µm	Flow: 1 to 30 nm Batch: N/A
Compatible with	HPLC only	HPLC Upgradeable to UHPLC	UHPLC HPLC adapter available
Flow Cell	Standard and high-temperature flow cells	Standard flow cell	Micro flow cell
Detectors	18 angles	3 angles	3 angles
MALS Sensitivity: BSA in Aqueous Buffer	0.2 µg typical, 30 cm GPC column	0.5 µg typical, 30 cm GPC column	70 ng typical, 15 cm UHPLC-SEC column
MALS Sensitivity: 100 kDa Polystyrene in THF	10 ng typical, 30 cm GPC column	25 ng typical, 30 cm GPC column	3.5 ng typical, 15 cm UHPLC-SEC column
Temperature Control	Ambient; heated/cooled -15°C to +150°C; Ultra-high: Room temp. to +210°C	Ambient only	Ambient only
Options	Temperature control, Fluorescent polymer configuration, WyattQELS embedded DLS, COMET cell cleaning	Upgradeable to UHPLC configuration, WyattQELS embedded DLS, COMET cell cleaning	HPLC Compatibility Kit, WyattQELS embedded DLS (COMET cell cleaning is already included)

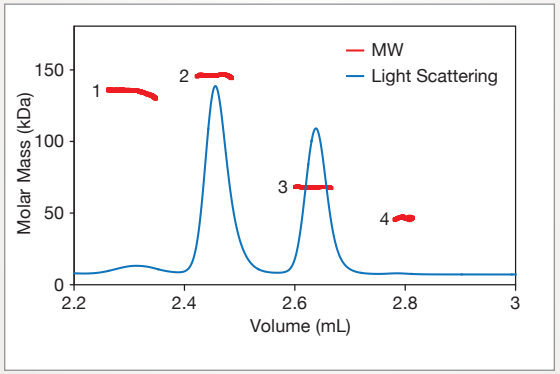
SEC-MALS

size exclusion chromatography combined with multi-angle light scattering

SEC-MALS is an absolute method that does not rely on column calibration for analyzing:

- Molar mass
- Size distributions
- Oligomeric state
- Conformation
- Polymer branching

SEC-MALS combines MALS, intrinsic viscosity (IV) and differential refractive index (dRI) instruments with SEC separation.



Even though Peak 1 elutes earliest, MALS shows that it does not have the largest molar mass for this example of protein aggregates and fragments.

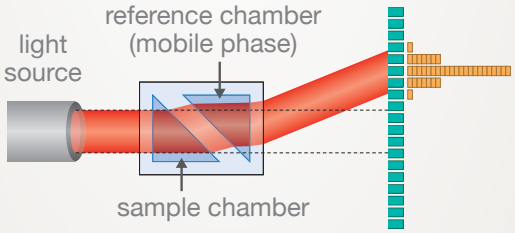
dRI

differential refractive index

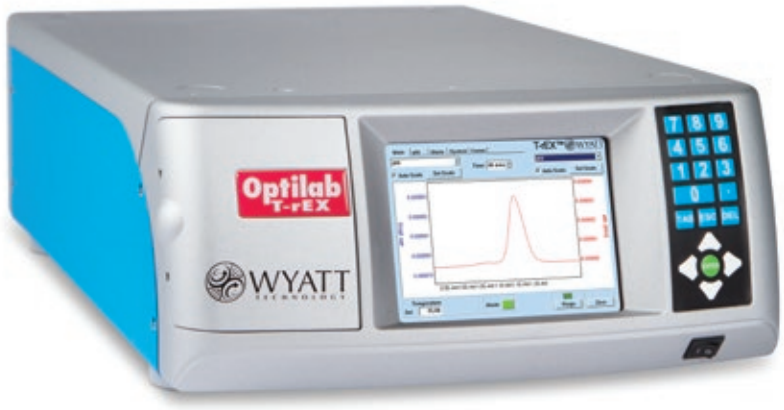
dRI is a universal concentration measurement technique that does not depend on chromophores or fluorophores.

Optilab online dRI instruments are used in:

- MALS analysis of molar mass
- Intrinsic viscosity determination for polymer conformation and branching
- Triple-detection characterization of copolymers and protein conjugates
- Basic quantitation of chromatographic peaks
- Measurement of *dn/dc* in different mobile phases
- Determination of solvent absolute refractive index



The Optilab's 512-detector array means it can reliably quantify a tiny peak at the nanogram level superimposed on a milligram-level peak!



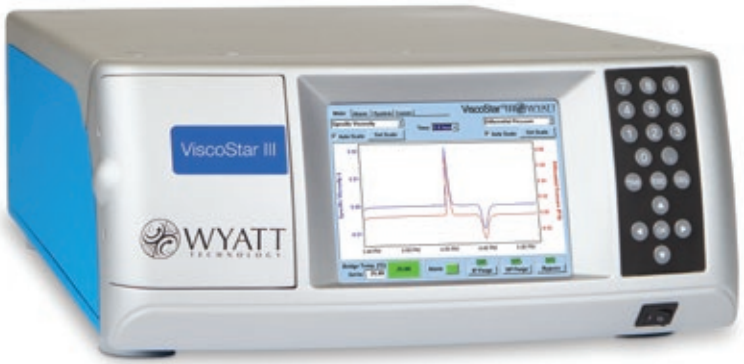
Optilab

Extended dRI measurement range

The only RI detector designed to operate at the same wavelength as the MALS detector for *dn/dc* measurements, the Optilab is available in a variety of configurations depending on your application. It can also measure the absolute refractive index (aRI) of the solvent.

R&D 100

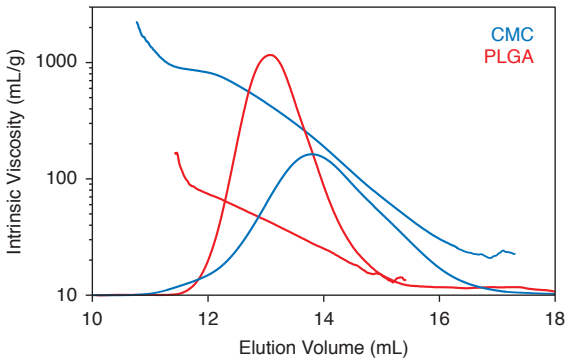
	Optilab T-rEX	Optilab T-rEX HC	Optilab UT-rEX
Description	dRI detector for standard HPLC, offering the highest sensitivity and dynamic range	dRI detector for CG-MALS, protein purification and other high-concentration analyses	dRI detector for UHPLC, offering the highest sensitivity and dynamic range
Application	Quantify a few ng/mL up to 25 mg/mL	Measure proteins up to 180 mg/mL	UHPLC
dRI Range	-4.7×10^{-3} RIU to $+4.7\times10^{-3}$ RIU (refractive index unit)	-2.6×10^{-3} RIU to $+3.4\times10^{-2}$ RIU	-4.7×10^{-3} RIU to $+4.7\times10^{-3}$ RIU
Dynamic Range	12,000,000:1	23,000,000:1	6,000,000:1
dRI Sensitivity	0.75×10^{-9} RIU	1.5×10^{-9} RIU	1.5×10^{-9} RIU
aRI Range	1.2 to 1.8	1.2 to 1.8	1.2 to 1.8
aRI Sensitivity	±0.002	±0.002	±0.002
Temperature Control	4°C to 65°C	4°C to 65°C	4°C to 65°C



ViscoStar

Unsurpassed differential viscometer

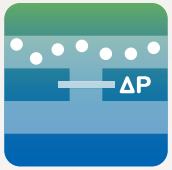
Incorporating patented thermal bridge balancing, as well as proprietary technology to suppress pressure pulse noise and temperature gradients, the ViscoStar III offers the best performance in differential viscosity measurements.



Widest Range of Polymer Intrinsic Viscosity

Intrinsic viscosities of poly(lactic co-glycolic acid) in THF and carboxymethyl cellulose in aqueous mobile phase measured with ViscoStar III and Optilab T-rEX from tens to thousands of mL/g.

	ViscoStar III
Description	The ultimate differential viscometer for GPC
Applications	Polymers below ~ 1 MDa for conformational analysis; all polymers for Mark-Houwink-Sakurada parameters
Sensitivity	0.1 µg of 100 kDa polystyrene in THF
Dynamic Range	135,000:1
Drift	2.5 Pa/hr
Temperature Control	4°C to 70°C
Capillary Bridge Tuning	Automated thermal tuning
Pump Pulse Suppression	Full impedance matching of the capillary bridge and proprietary software algorithms
Delay Column Options	8.1, 5.4 or 2.7 mL standard; 16.2 mL optional



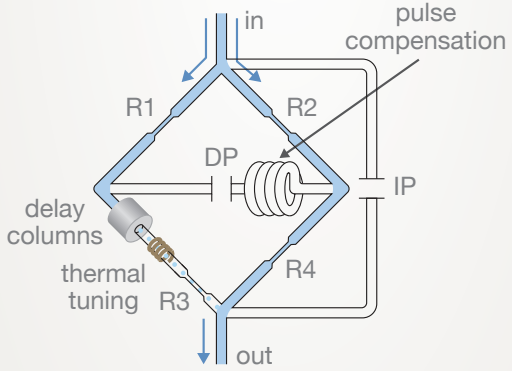
IV

intrinsic viscosity

Differential viscometers are used in conjunction with SEC to measure the specific and intrinsic viscosities of polymer solutions.

Combined with a MALS instrument, SEC-MALS-IV determines:

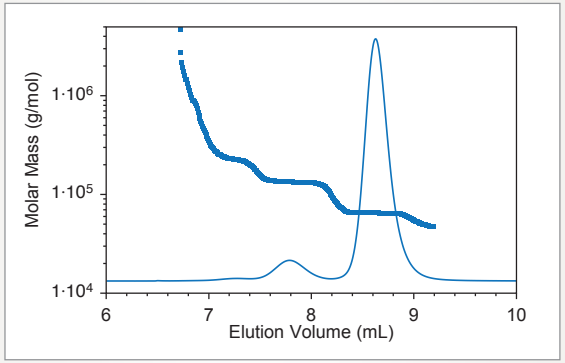
- Intrinsic viscosity
- Conformation
- Branching analysis
- Hydrodynamic radius
- Mark-Houwink-Sakurada parameters



Without delay columns, the impedance of the capillary bridge would be fully balanced. The pulse compensation element matches the additional impedance of the delay columns, eliminating the effect of pump pulses on the DP transducer.

ASTRA

advanced software
for macromolecular and
nanoparticle characterization



Absolute molar mass analysis

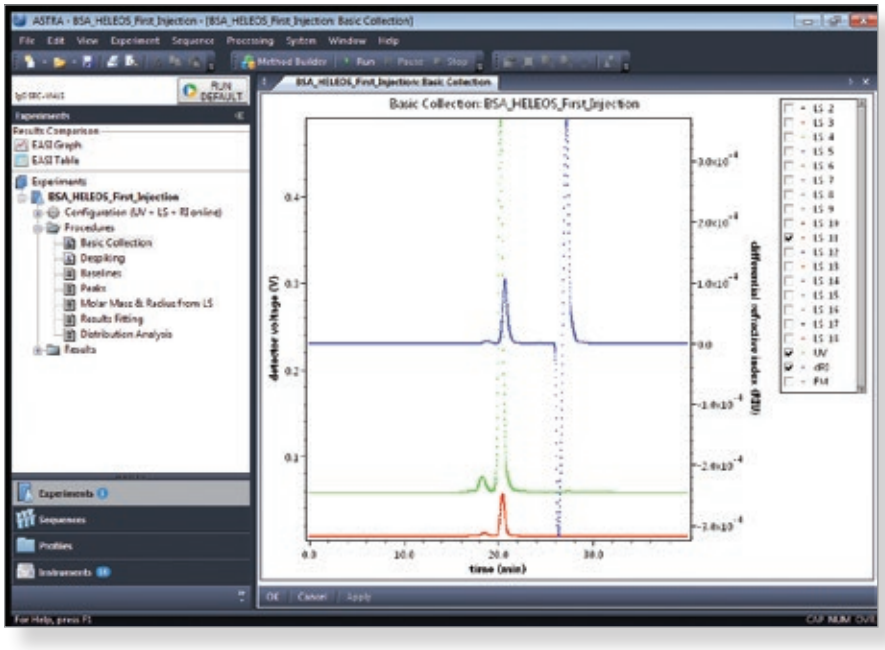
ASTRA's Band Broadening Correction accounts for interdetector dispersion to match signals from each detector in the chromatographic elution series.

This algorithm is responsible for proving uniform molecular weights across the BSA monomer, dimer and trimer peaks.

ASTRA

The premier software for analyzing macromolecules and nanoparticles by multi-angle light scattering

ASTRA integrates MALS, UV, refractive index, dynamic light scattering and intrinsic viscosity data for comprehensive characterization of the physical properties of materials in solution/suspension.



ASTRA provides absolute determination of:

- Molar mass and size
- Conformation, shape and conjugation ratio
- Differential and cumulative distributions; moments of the distribution and polydispersity
- Intrinsic viscosity and Mark-Houwink-Sakurada parameters
- Number density of nanoparticles

Compile key results:

ASTRA gives you a quick and easy overview of your most important results in one compact table.

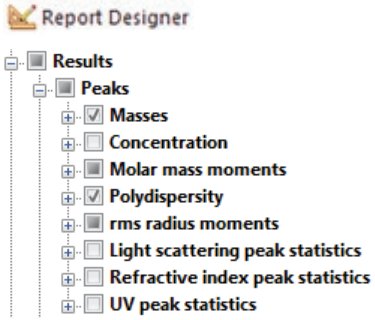
Sequence1: Configuration | 978TS - Aq1: Distribution Analysis | EA

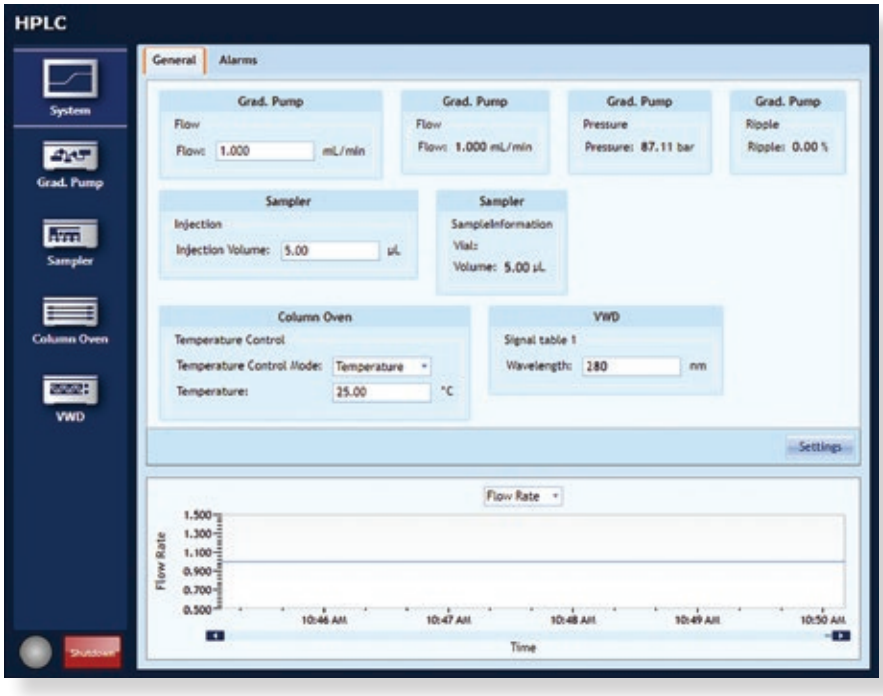
Experiments: Peaks: Scalars:

	Peak 1		
	Mw (kDa)	Calculated mass (µg)	Mass fraction (%)
978TS - Aq1	65.4 (±0.6%)	196.84	100.0
Average	65.4	196.84	100.0
Standard deviation	n/a	n/a	n/a
% Standard deviation	n/a	n/a	n/a
Minimum	65.4	196.84	100.0
Maximum	65.4	196.84	100.0

Customized reports:

ASTRA provides customized reporting options so you can export exactly the information you need. It even allows you to customize the report with your company's logo and descriptive text.





Optional HPLC Control Module provides:

- Full digital synchronization between your HPLC pump, autosampler, UV, light scattering and other detectors
- A single software solution for control, acquisition and analysis to minimize user error
- The ability to include HPLC modules and Wyatt detectors in a common experiment configuration

Regulatory Compliance

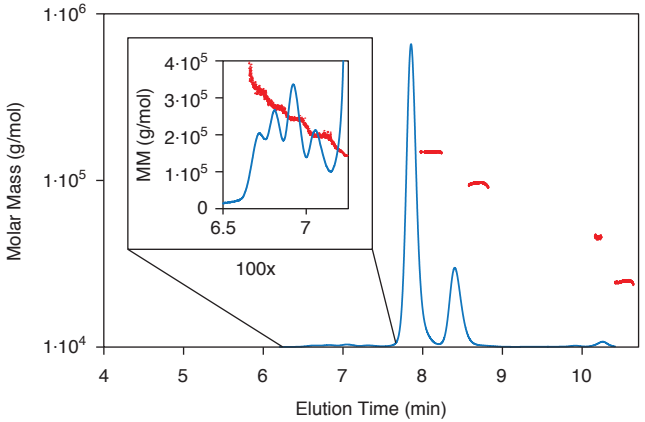
Following industry standards, ASTRA offers an optional 21 CFR Part 11 compliance package, including IQ/OQ documents and procedures.

ASTRA's Security Pack includes:

- Administrator, researcher, technician and guest access levels
- Full audit trails
- Electronic signatures
- Sign-in/sign-out during a run
- Secure SQL server database
- Local or remote database connectivity
- Data integrity validation
- Full IQ/OQ procedures and documentation validation

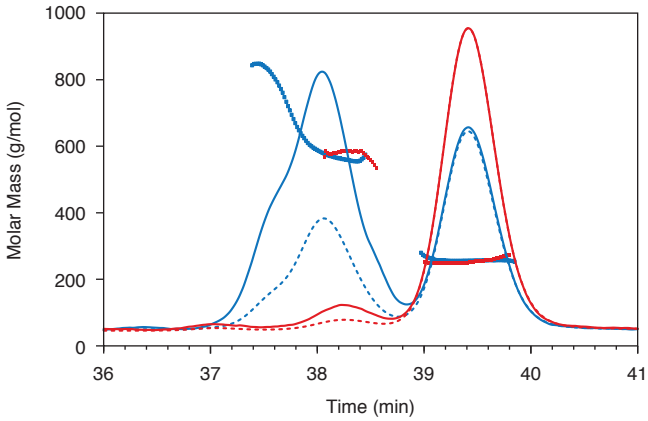
SEC-MALS Applications

Aggregates and Fragments



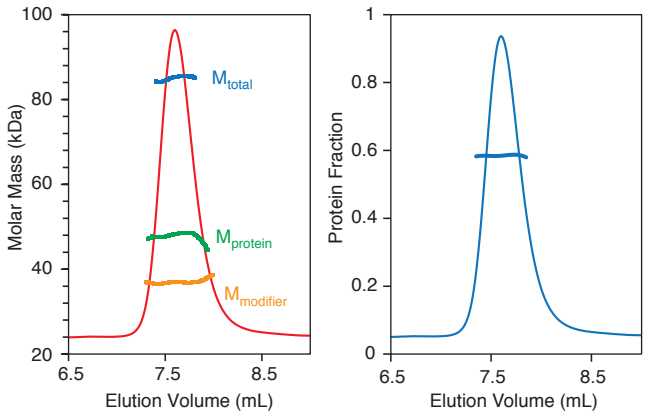
The power of UHPLC for separating aggregates and fragments combines with MALS to unequivocally identify small quantities of impurities in an IgG sample. Each of the aggregate peaks shown in the 100x inset represent a fraction of one percent of the monomer total mass yet is well-quantified by µSEC-MALS.

Small Polymers and Peptides



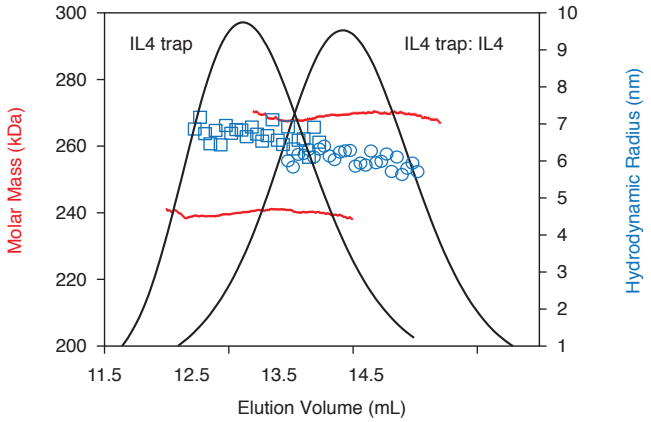
Methylene diphenyl 4,4'-diisocyanate (MDI) has a molar mass of 250 Da and will readily form oligomers in THF. The superior sensitivity of the HELEOS and TREOS is essential in characterizing molecules like MDI that have such low molar masses.

Protein Conjugate and Copolymer Analysis



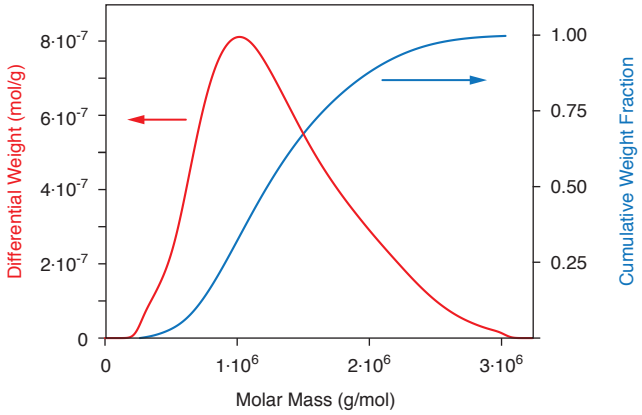
ASTRA's Protein Conjugate algorithm makes use of data from MALS, UV and RI detectors to characterize conjugated proteins and copolymers. This analysis determines the molecular weights of the protein, modifier and complete conjugate as well as average extinction coefficient and *dn/dc*.

Protein Complexes and Conformations



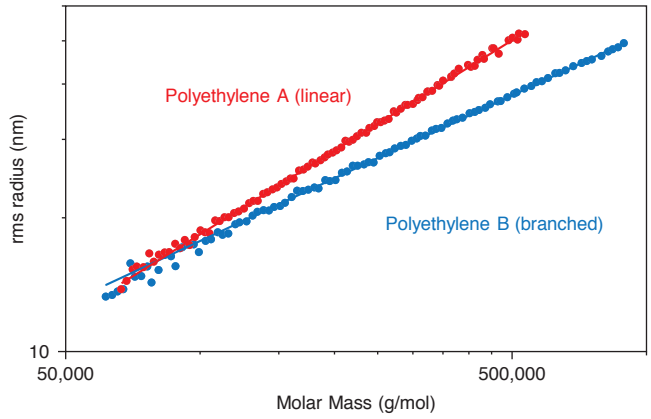
Pure interleukin 4 trap (IL4-trap) elutes earlier than the IL4 : IL4-trap complex, despite its lower molecular weight. MALS MW analysis (small red symbols) indicates the expected MW values. Online DLS rh data (open blue symbols) show the reason for the late elution: IL4 stabilizes the trap to form a compact IL4 : IL4-trap complex.

Molar Mass and Size Distributions



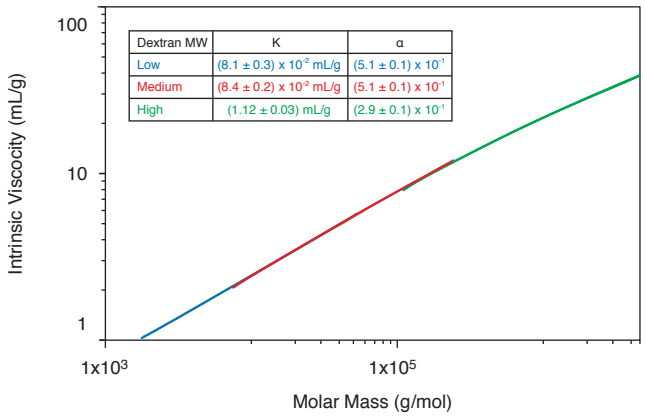
In addition to plotting the molar mass and size determined by multi-angle light scattering over a chromatogram or fractogram, ASTRA can convert the data into distributions. These graphs show differential and cumulative distributions of molar mass as measured for hyaluronic acid.

Polymer Branching



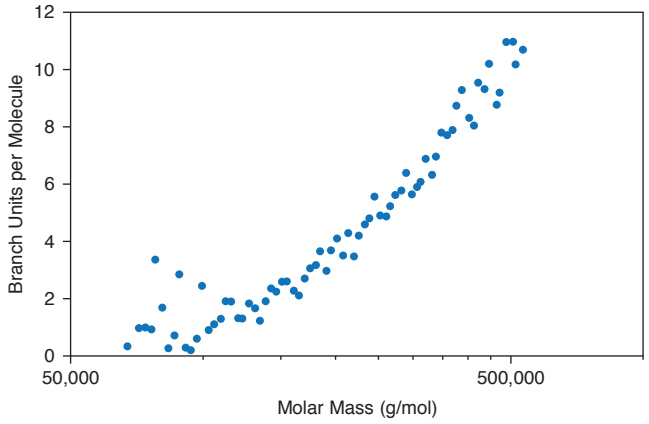
A MALS instrument measures rms radius vs. molar mass to reveal a polymer's branching properties. Here, the branching of Polyethylene B is apparent by its significantly lower slope in relation to Polyethylene A, which is known to be linear.

Conformational Change with MW



A Mark-Houwink-Sakurada (MHS) plot shows intrinsic viscosity as a function of molar mass—revealing the polymer conformation. The MHS plots of low, medium and high MW dextrans, shown here, indicate conformational change with increasing molar mass of the molecules.

Branching Calculations



ASTRA compares linear and branched polymers to determine branching ratios. The data in the top chart (Polymer Branching) were further analyzed to yield the average number of branching units per molecule and the dependence of this value on molar mass.


DynaPro
Plate Reader III
WYATT
TECHNOLOGY
Wyatt DynaPro Plate Reader III
DASHBOARD
CHART
CAMERA
EVENTS
SYSTEM
Temperature
25.00 °C
GOOD
Set Point: 25.00 °C
Count Rate
6.17e5 Hz
Well Position
A07
Quick Controls
Laser
Door
OPEN DOOR
Auto Correlation Function
Correlation Function
Delay Time (s)
7 8 9
4 5 6
1 2 3
0 .
TAB ESC DEL
OK

DLS & ELS Products

Measure in Cuvettes and Well Plates

Characterize size, zeta potential and stability

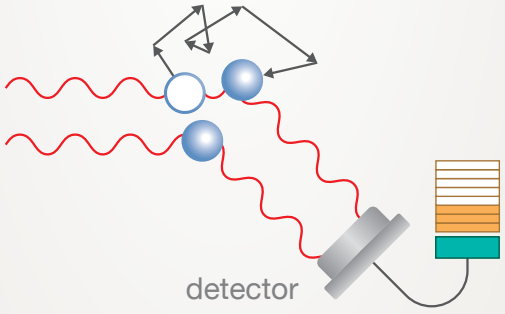
DLS

dynamic light scattering

DLS determines the diffusion coefficients, size and size distributions of particles in a fluid by measuring the light intensity fluctuations arising from their Brownian motion.

In addition to basic sizing applications for sub-micrometer macromolecules and nanoparticles, DLS measures:

- Quality
- Aggregation
- Stability
- Propensity for aggregation



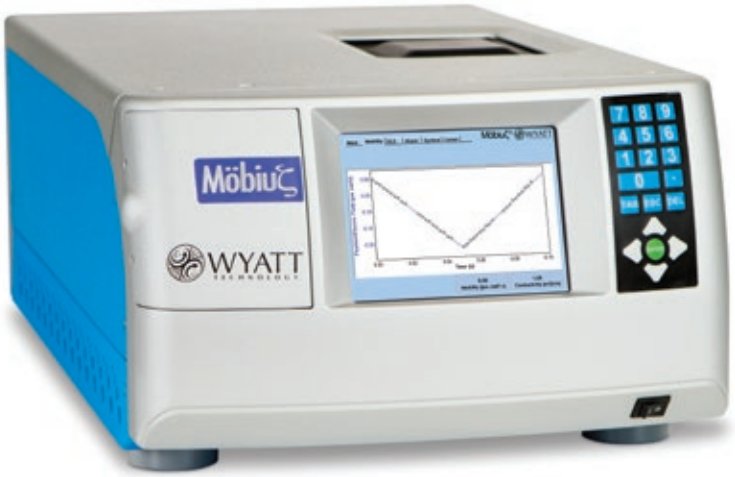
Brownian motion of sub-micrometer particles gives rise to intensity fluctuations in the scattered light. The rate of fluctuation is analyzed to determine the diffusion coefficient.

DynaPro

Unrivaled DLS/SLS detection

Perform fully automated DLS and SLS with the breakthrough Plate Reader III in standard 96, 384 or 1536 well plates or use the NanoStar cuvette-based instrument for minimum sample volume and maximum results.

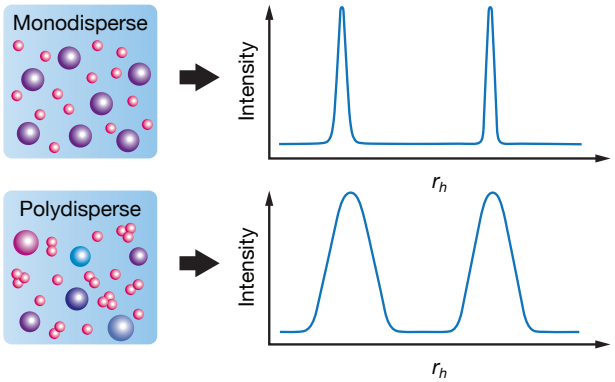
	DynaPro Plate Reader III	DynaPro NanoStar	WyattQELS
Description	Automated DLS measured directly in standard microwell plates	Traditional cuvette-based DLS, just better	Embedded DLS module for any Wyatt MALS detector
Application	High-throughput screening and other automated measurements of multiple samples	Low-volume, high-quality size and MW measurements for precious samples. Also supports online measurements	Online DLS for high-resolution size distributions, simultaneous with MALS MW analysis
Plate Scan Time	As little as 1.5 hours for a 384 well plate	n/a	n/a
Hydrodynamic Radius Range (r_h)	0.5 nm to 1 µm	0.2 nm to 2.5 µm	Flow: see page 11 Batch: 0.5 nm to 1 µm
Sensitivity (r_h)	0.125 mg/mL lysozyme	0.1 mg/mL lysozyme	0.1 mg/mL lysozyme
Molar Mass Range	1000 g/mol to 10^6 g/mol	1000 g/mol to 10^6 g/mol	n/a
Minimum Sample Volume	4 µL (1536 well plate), 10 µL (384 well plate), 60 µL (96 well plate)	1.25 µL (quartz cuvette), 4 µL (disposable cuvette)	Flow: n/a DAWN microCuvette: 10 µL Flow cell: 300 µL
Temperature Control	4°C to 85°C	-15°C to +150°C	Depends on MALS detector



Möbius

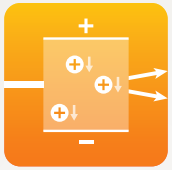
Most versatile zeta potential detector

Configurable in batch or automated flow mode for high throughput applications, Möbius is the only zeta potential detector offering a pressurized flow cell for measurements in high-salt buffers.



DLS determines size distributions without fractionation, providing polydispersity estimates as well as hydrodynamic radii.

	Möbius
Description	Superior zeta potential and DLS instrument for the most sensitive batch and flow mode measurements
Application	Size and zeta potential from proteins to micron-sized particles; manual or automated
Hydrodynamic Radius Range (r_h)	0.2 nm to 5 µm (flow cell), 0.2 nm to 200 nm (dip cell, quartz cuv.), 0.2 nm to 250 nm (disp. cuv.)
Sensitivity	0.1 mg/mL lysozyme
Size Range (r_h) for Zeta Potential	2 nm to 50 µm
Sensitivity for Zeta Potential	1 mg/mL lysozyme (flow cell), 5 mg/mL BSA (dip cell)
Minimum Sample Volume	45 µL (DLS, quartz cuv.), 65 µL (ELS, quartz cuv.), 180 µL (flow cell)
Temperature Control	4°C to 70°C
Automation	Analyses can be automated with an HPLC autosampler and pump
Additional Options	• Pressurized flow cell • Fluorescence-blocking filter • Dip electrode cell • Disposable cuvette for DLS



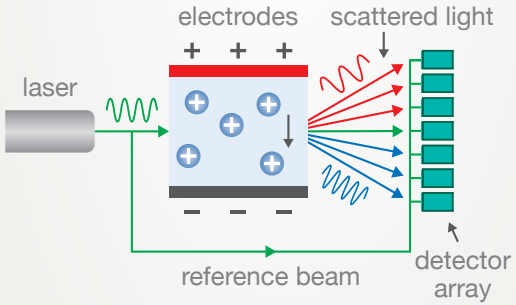
ELS

electrophoretic light scattering

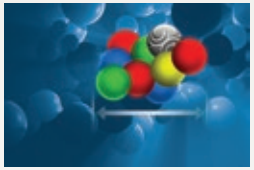
ELS determines the zeta potential and electrophoretic mobility of particles in a fluid by measuring their velocity under an applied electric field. In addition to determining r_h from DLS, the net charge on a particle is also calculated.

ELS measures:

- Stability against flocculation of colloids
- Electrostatic contribution to stability of protein formulations isoelectric point in native formulation buffer

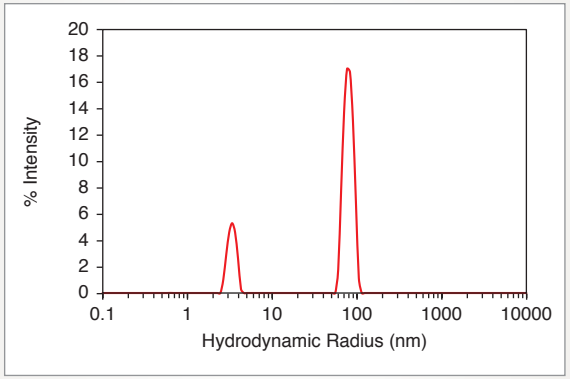


Wyatt's Massively-Parallel Phase Analysis Light Scattering (MP-PALS) utilizes low voltage and multiple low-noise, high-dynamic range detectors to achieve the highest sensitivity without damaging fragile samples.



DYNAMICS

comprehensive software for dynamic and electrophoretic light scattering



Size distributions from sub-nanometers to micrometers

Dynamic light scattering determines size distributions without any separation. This regularization graph shows the presence of an 80 nm nanoparticle in a protein solution.

Essential Size and Zeta Potential

Intuitive yet powerful, DYNAMICS gives you access to all the information needed to ensure correct and thorough analysis of Dynamic Light Scattering (DLS) and Electrophoretic Light Scattering (ELS) data:

- Autocorrelation function from raw DLS data
- Size distributions
- Datalog table of all parameters, results and goodness-of-fit indicators
- Raw electrophoresis data for zeta potential analysis

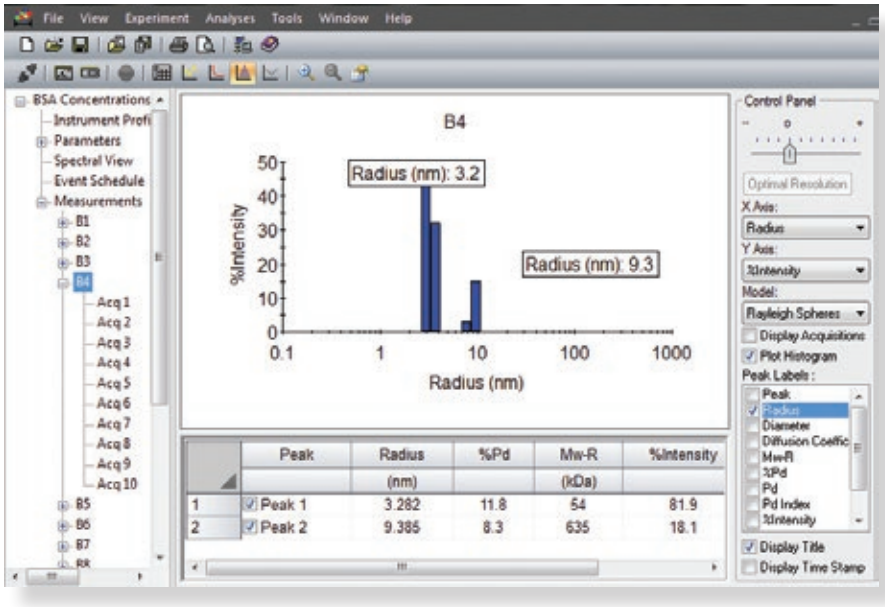
From Mobility to Stability

Collect, display and analyze batch Dynamic Light Scattering (DLS), Phase Analysis Light Scattering (PALS), and Static Light Scattering (SLS) measurements.

Size and Size Distributions
Average size from cumulants, distributions from regularization, polydispersity index. Analyze by %Intensity, %Mass or %Number.

Zeta Potential or Net Charge
Electrophoretic mobility for nanoparticles or proteins vs. pH or salt concentration.

Molar Mass
Average solution molecular weight from SLS or estimated from DLS.



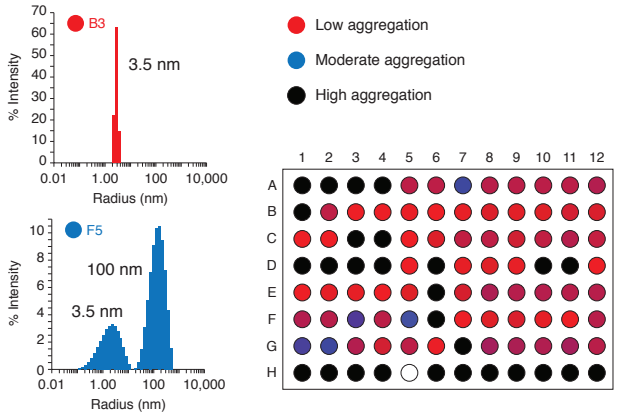
DYNAMICS Regularization View offers many ways to analyze and display multimodal size distributions.

Parametric Analysis
Determine dependence on temperature, concentration or time for stability analysis.

Full Automation
For ease of use, DYNAMICS allows you to program the temperature profiles, samples to measure in the plate (DynaPro Plate Reader), or autosampler sequence (Möbius).

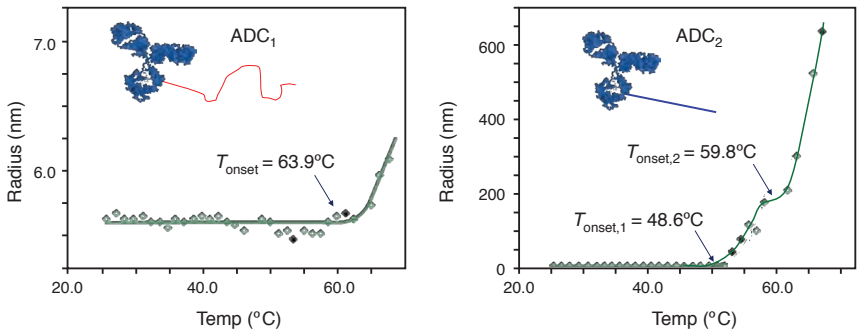
DLS Applications

Aggregation in a 96 Well Plate



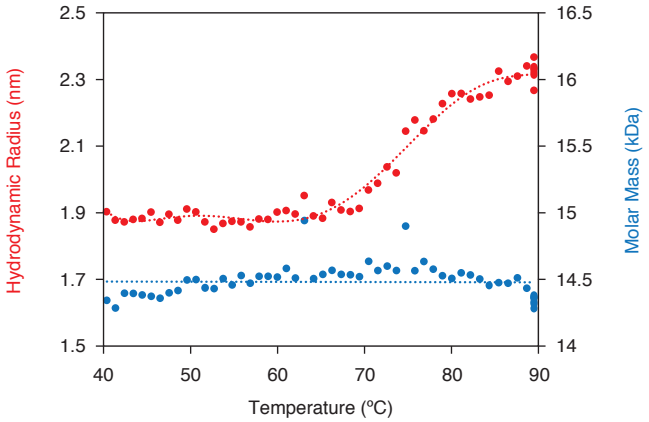
The SpectralView feature in DYNAMICS supports color-coded visualization of the results of a plate scan, which might include hundreds of samples. Here the visualization represents the degree of aggregation for a rapid, intuitive assessment of the optimal formulation.

Conformational Stability



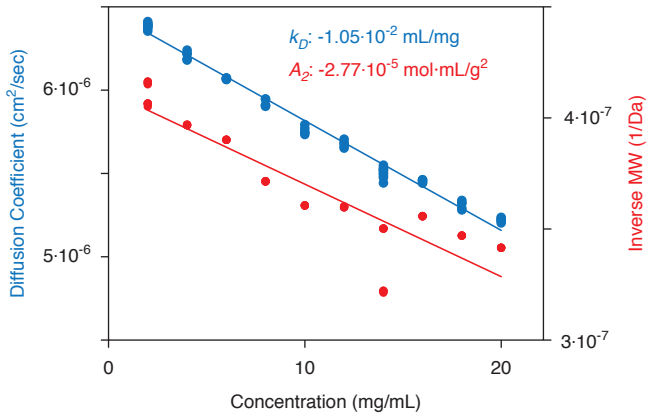
Conjugating the same monoclonal antibody and drug via different linkers can have significant impact on stability. Here, ADC_2 exhibits two thermal transitions, one at 60°C, similar to ADC_1, while the other is near 50°C. DLS highlights the degree of thermally-induced aggregation, negligible in ADC_1 yet rapid and extensive in ADC_2.

Protein Unfolding



DLS size analysis reveals the thermally induced denaturation of lysozyme with T_m=69.8°C. The molar mass determined from static light scattering (SLS) distinguishes between pure unfolding (no change in molar mass) and aggregation (increased molar mass).

Aggregation Propensity



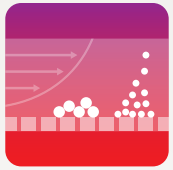
Non-specific protein-protein interactions, important for selecting and optimizing biotherapeutic candidates and formulations such as IgG, are characterized by means of a concentration series. Both static light scattering (A_2) and dynamic light scattering (k_D) may be used.


Wyatt Technology Europe GmbH
Eclipse S/N 4001
IP 192.168.254.101 MAC 00-01-05-08-33-41
ECLIPSE
SEPARATION SYSTEM
DUALTEC
WYATT
Calypso-II
WYATT
TECHNOLOGY
PUMP 1
PUMP 2
PUMP 3

FFF & CG-MALS Products

Technologies for Extended Characterization

Characterize complex fluids and interactions



FFF

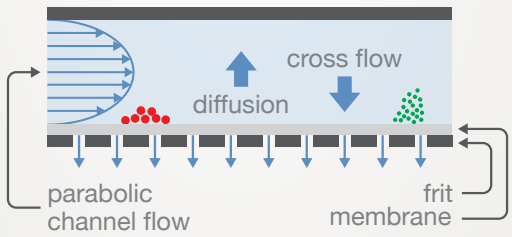
field-flow fractionation

Flow-FFF is a powerful separation technique over a size range of 1 to 10,000 nm. Having very low surface area and no stationary phase, Flow-FFF generates very little shear and is an excellent choice when non-ideal sample-surface interactions are a concern. MALS, DLS and dRI detectors are placed downstream of the separation channel for complete characterization.

Flow-FFF fractionates and characterizes:

- Colloids and nanoparticles
- Macromolecules and assemblies
- Complex fluids

Asymmetric Flow Field-Flow Fractionation (AF4) Flat Channel



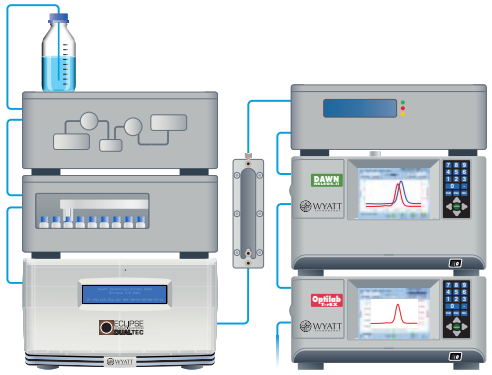
FFF separation power can be tuned by changing the ratio of cross flow to channel flow.

Eclipse

Advanced Flow-FFF technology

Offered as the DualTec or AF4, Eclipse is a sophisticated system for performing analytical and semi-preparative separations over a wide range of analytes. Eclipse leverages industry-leading HPLC modules along with Wyatt's novel single-pump technology.

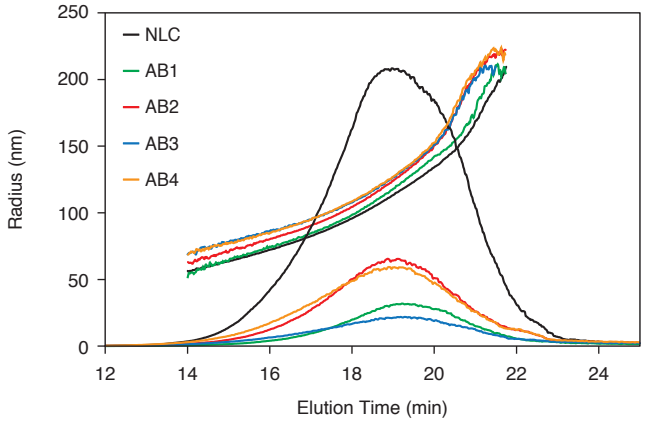
	Eclipse DualTec	Eclipse AF4
Description	Advanced Flow-FFF technology for the most versatile separations	Optimal for the specialized frit-injection channel or semi-preparative use
Tip Injection	For HF5	No
Dual-channel Switching	Any two of SEC, AF4, HF5	Optional
Metal-free Flow Path	For ICP-MS	No
Temperature-controlled Separations	4°C to 90°C *	4°C to 90°C *
Channel Options		
Analytical AF4	Long and Short Channels 1 to 100 µg injections	
Disposable Hollow Fiber	pg to low µg injections	No
Semi-preparative	No	mg separations
Frit-inlet	No	For aggregation-prone samples



*With the ThermosPro temperature regulation chamber

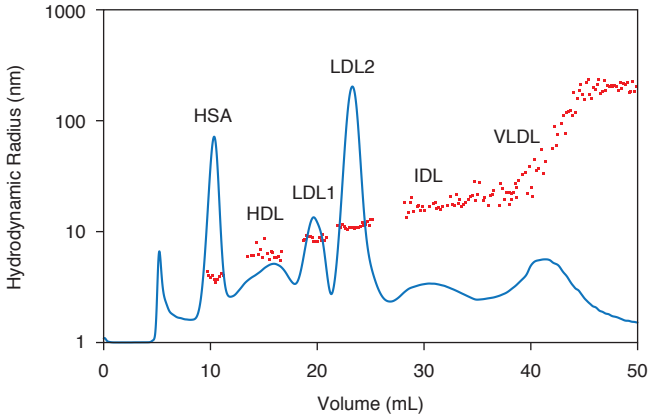
FFF Applications

High Resolution for Nanotherapeutics



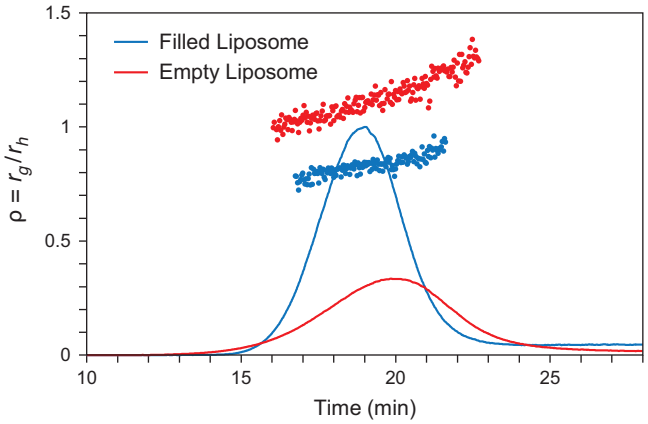
FFF-MALS analysis of a nanolipid complex (NLC) and microsilver-loaded NLC formulations with varying concentrations of NLC and microsilver. All formulations show a higher radius than the pure NLC, proving the adsorption of silver ions. Size reproducibility is better than 1%.

Blood Serum Components



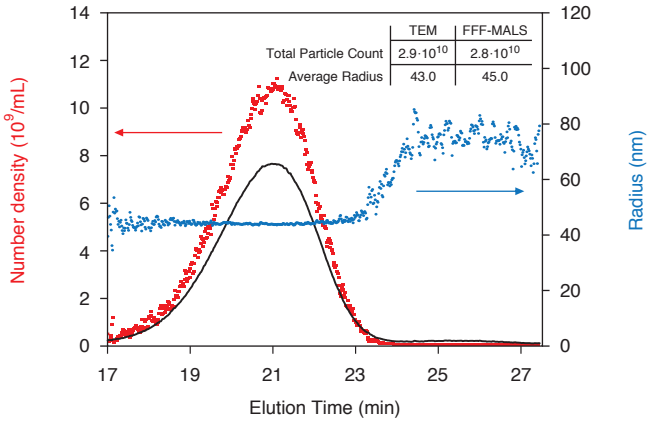
FFF-MALS-DLS separation of whole serum with distinct peaks for serum albumin, IgG and various types of lipoproteins. Sizes (r_h) were determined by online DLS embedded in the MALS detector. MALS also determines molar masses of each peak and for species larger than ~10 nm, rms radius (r_g).

Particle Shape Factor



ASTRA's Burchard-Stockmayer plot shows the shape factor $\rho = r_g/r_h$, i.e. the ratio of rms radius (measured by MALS) to hydrodynamic radius (measured by DLS). The shape factor is indicative of the shape or structure of a nanoparticle and is determined across the FFF fractogram.

Nanoparticle Number Densities



FFF-MALS provides quantitative, high-resolution size distributions with large particle ensembles that compare well with imaging techniques. This adenovirus analysis indicates the number density in billion/mL at each elution time along with the radius. The LS fractogram is overlaid in black. A small fraction of dimers is evident.

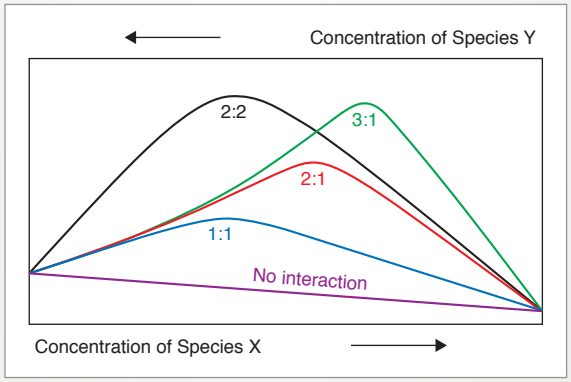
CG-MALS

composition-gradient multi-angle light scattering

CG-MALS is a label-free, immobilization-free technique for characterizing:

- Protein-Protein interactions
- Protein-DNA complexes
- Other macromolecular interactions

CG-MALS characterizes biomolecular interactions from first principles by measuring the change in the weight-average molar mass (M_w) of a solution as a function of concentration and composition.



CG-MALS analyzes the light scattering signals from composition gradients to calculate K_d and absolute stoichiometry. It can differentiate between complexes with the same stoichiometric ratio but different overall number of bound monomers.

Calypso

Composition-gradient stop-flow system for biomolecular interactions and reaction kinetics

- K_d from pM to mM
- Reaction times from seconds to hours
- Self- and hetero-associations
- Interfaces with DAWN, miniDAWN and Optilab instruments for automated MALS and concentration measurements.

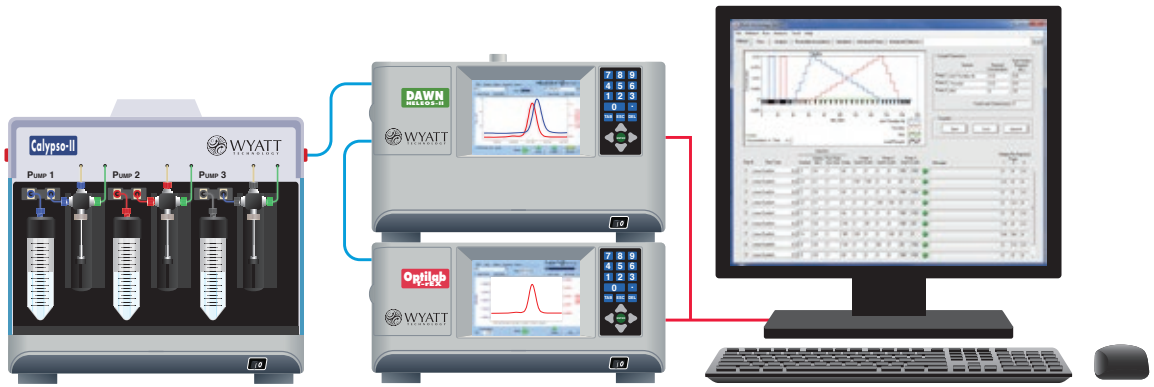
CALYPSO Software

Comprehensive set of association models covering simple to complex interactions

- Versatile, easy-to-use method programming for multiple gradient types, system preparation and post-experiment cleanup
- Simulation capabilities for experiment design and interpretation

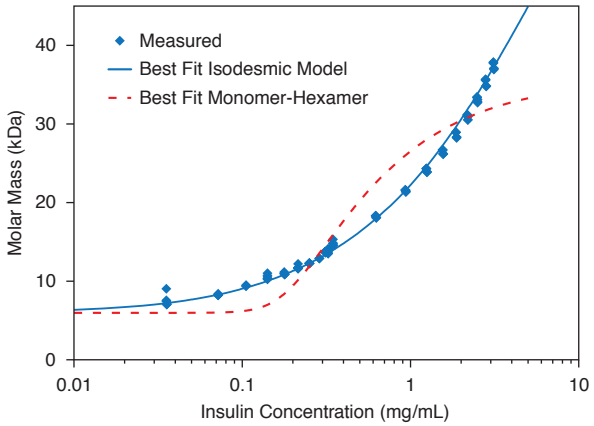
Versatile association model design for:

- Standard homodimer, heterodimer and progessive self-association
- Multivalent interactions and multiple oligomers in equilibrium
- Simultaneous self- and hetero-association
- High-concentration proteins
- Non-specific interactions of cosolutes



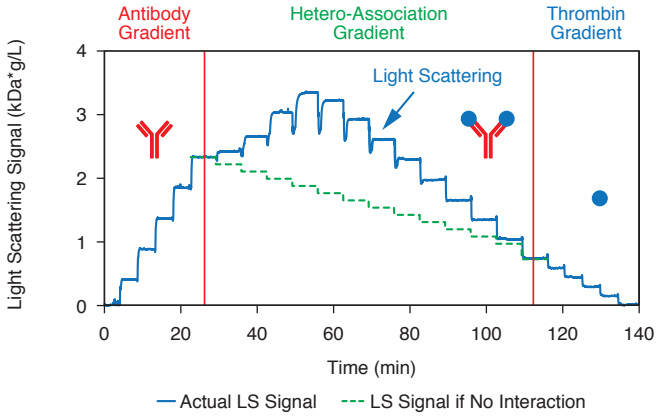
CG-MALS Applications

Insulin Self-Association



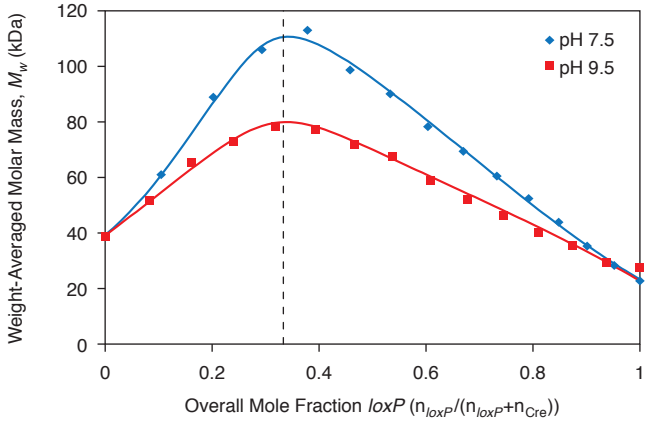
CG-MALS analyzes self-association by measuring the weight-average molar mass over a concentration series. In the absence of zinc, insulin is found to self-associate isodesmically (progressively) with a K_d of 52 µM. A monomer-hexamer model fits poorly and can be ruled out.

Antibody-Antigen Binding



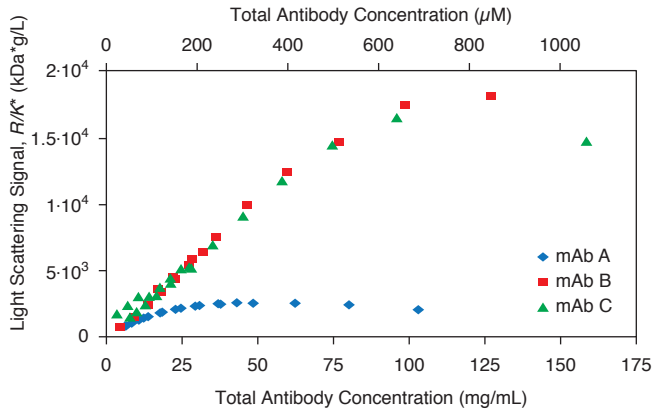
A Calypso stop-flow measurement of antibody-antigen interactions. Here the CALYPSO software found that thrombin binds to an anti-thrombin monoclonal antibody with K_d=9 nm at two equivalent, non-cooperative binding sites on the mAb and no self-association.

Cooperative Binding vs. pH



Cre recombinase binds to the *loxP* DNA segment in a pH-dependent manner. CG-MALS determines that at pH 7.5, each *loxP* binds two Cre molecules with positive cooperativity, and the 2:1 complex dimerizes to form a synapse tetramer; while at pH 9.5, cooperativity and synapsis are lost.

High-Concentration IgG



mAbs A, B and C exhibit widely varying viscosities at high protein concentration, a consequence of differing degrees of self-attraction. CG-MALS is one of very few techniques capable of analyzing protein self-interaction at high concentrations. For these mAbs, self-interaction correlates well with viscosity.

Support Contracts

continued service and support

Maximize productivity with world-class service:

Gold Service Contract

- On-site preventative maintenance and basic repair services
- Loaner units available should an instrument require factory repair
- Service without delays: All parts and labor included
- Comprehensive, first priority technical and application support by phone, email and screen sharing sessions

Silver Service Contract

- Priority factory preventative maintenance and repair services
- Loaner units based on availability
- Factory service without delays: All parts and labor included
- Comprehensive, priority technical and application support by phone, email and screen sharing sessions

Service & Support

Customer Service

Our team of support specialists and application scientists will help you get the most out of your Wyatt instruments. All new Wyatt instruments come with a full year of unlimited telephone and e-mail support.

Wyatt Technology is committed to your continued success by offering two levels of comprehensive service contracts: Gold and Silver. We also offer installation, preventative maintenance and qualification (IQ/OQ), as well as training and consulting.

In our online support center, you'll find a wealth of technical notes, application guides, software and instrument firmware downloads, manuals, tutorials, training videos and more.

We look forward to meeting you at Light Scattering University!

Application Support

Our dedicated and helpful application scientists with diverse backgrounds at Wyatt Technology are not only enthusiastic about our technologies, but also curious about your applications. Whether you're working with synthetic polymers, polysaccharides, therapeutic proteins or nanoparticles, we're committed to helping you solve real world problems.

We're also the liaison between you and our product development team, ensuring continuous improvements of our instruments and software to meet your application needs.

Our newly expanded application lab in Santa Barbara showcases our state-of-the-art static and dynamic light scattering instruments, either stand-alone or connected to HPLC, UHPLC and field flow fractionation systems.

We welcome customers and collaborators from around the world to visit our lab!

Dr. Sigrid Kuebler
Director of Customer Service
Joined Wyatt Technology 2006

Dr. Michelle Chen
Director of Analytical Services
Joined Wyatt Technology 1996

Light Scattering University

Demystify light scattering and get the most out of your Wyatt instruments

"I wanted to thank you for the tremendous training experience with the Wyatt staff. It has been the most remarkable and useful training session that I've ever completed. Truly first class."

Dr. InKwan Han,
Merck & Co. Inc.

Highlights of LSU

Many trainees come away from LSU inspired with new ideas for how light scattering can solve some of their analytical challenges. One of the most popular aspects of LSU is the opportunity to meet and work with the scientists and engineers behind the products, as well as get acquainted with support staff that they usually only contact over the phone.

Another not-to-be missed session (available only in Santa Barbara) is the Light Scattering Museum tour, led by Dr. Philip Wyatt, the inventor and pioneer of MALS detectors.

LSU

light scattering university

Often described by participants as the best instrument user training they have ever attended, Light Scattering University (LSU) is an intensive experience that combines hard work, good food and a friendly atmosphere.

You'll learn about:

- Light scattering theory and applications
- How to interpret your data
- Instrument best practices
- History of light scattering

Dr. Sophia Kenrick
Dean of Light Scattering University
Joined Wyatt Technology 2010

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Global Offices

North and South America
(Corporate Office)
Wyatt Technology Corporation
6330 Hollister Ave.
Santa Barbara, California 93117
USA
Tel: +1 805 681 9009
info@wyatt.com
www.wyatt.com

Northeast Applications Lab
18 Commerce Way, Suite 2850
Woburn, MA 01801
USA
Tel: +1 805 681 9009 x212
info@wyatt.com
www.wyatt.com

Germany, Austria, BeNeLux, Czech Republic (and all other Eastern European countries), Scandinavia, Switzerland
Wyatt Technology Europe GmbH
Hochstraße 12a
D-56307 Dernbach, Germany
Tel: +49 2689 925 0
info@wyatt.eu
www.wyatt.com

China
Wyatt Technology China
RM 2302 Building 7 Jin Hui Jia Yuan
No. 58
Xi Zhi Men Bei Street
Hai Dian District
Beijing, China
Tel: +86 10 8229 2806
info@wyatt.com.cn
www.wyatt.com.cn

France, Portugal and Spain
Wyatt Technology France
45 rue Adolphe Coll
FR-31300 Toulouse, France
Tel: +33 (0)5 34 55 99 28
wtf@wyatt.com
www.wyatt.com

United Kingdom and Ireland
Wyatt Technology UK Ltd.
Gothic Building
Chauntry Mill
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CB9 8AZ
United Kingdom
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Greece
N. Asteriadis S.A.
Tel: +30 2310 260 331
info@asteriadis.gr

India
Spinco Biotech Pvt., Ltd.
Tel: +91 44 4567 8900
info@spincotech.com

Israel
Danyel Biotech Ltd.
Tel: +972 8 936 6066 x225
amit@danyel.co.il

Italy
Alfatech S.p.A.
Tel: +39 010 46 99 369
info@alfatechspa.com

Japan
Shoko Science Co., Ltd.
Tel: +81 45 913 6688
ei.tsuruta@shoko-sc.co.jp

Korea
In Sung Chroma-Tech Co., Ltd.
Tel: +82 2 2644 1991
is@insung.net

New Zealand
Shimadzu Scientific Instruments
Pty. Ltd.
Tel: +64 9 839 7100
info@shimadzu.com.au

Poland
Polygen Sp. z o.o.
Tel: +48 322388 195
krystynan@polygen.com.pl

Taiwan
Systematic Instruments Co., Ltd.
Tel: +886 2 8227 8822
sysemail@ms21.hinet.net

Turkey
Bilim Lab.Cih.San.Tic.Ltd.Sti.
Tel: +90 216 575 08 54
oguzhan@bilimlab.com.tr

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W1000B | October 2017

WYATT TECHNOLOGY

6330 Hollister Avenue
Santa Barbara, CA 93117
Tel: +1 (805) 681-9009
Fax: +1 (805) 681-0123
Web: www.wyatt.com