



Webinar Series

Principles of Particle Size Reduction and Characterization

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About Microfluidics

A World of Difference



Who We Are

- Founded in 1983 outside Boston, MA
- 3,000 processors in 50 countries
- Technology Center (virtual tour online)

Our Technology

- Uniform particle size reduction
- Cell disruption with high protein recovery
- Bottom-up nanoparticle creation
- Continuous crystallization



*LV1 Low Volume
(1 ml capable) processor*



*M-110P "plug n' play"
benchtop lab model*



*M-110EH-30
pilot/production scale*



*M-700 series commercial
production*



Tiny Particles, **BIG RESULTS**

More than Machines

Microfluidics Technology Center

- State-of-the-art nanotechnology research lab
- Processes over 100 applications every year
- Uniquely diverse range of application experience

Lab Services

- Proof of Concept testing
- Process development
- Scaleup consulting
- MRT evaluations



Customer Success Story

“The engineers in the Microfluidics Technology Center were extremely friendly and knowledgeable, and helped us to understand the effects of varying pressure and interaction chamber types on our product. By using **HORIBA particle size analyzers** in the lab, they were able to show us **results after each pass**.”

This work was very valuable as it will help us **reduce production time** and **save cost** when we prepare to scale up. In fact, we were so pleased with the performance of the Microfluidizer processor that we **purchased an additional M-110P benchtop unit** for our internal research and development projects.”

Piyush Patel, Ph.D., Director of Formulation and Analytical Development, Cephalon, Inc.

What We Do Best

- Nanoemulsions
- Encapsulation (liposomes, polymers, emulsions)
- Cell disruption
- Dispersions
- Deagglomeration

Example: Oil-in-water emulsion (oil and water)

Method One: Roto/stator mixer



Method Two: Microfluidizer



Select Applications

Pharmaceutical

- Vaccines and adjuvants
- Cancer therapeutics
- Inhalables
- Parenterals
- Antibiotics
- Anesthetics

Biotechnology

- *E. coli*
- Yeast
- Algae
- Mammalian
- Plant
- Insect
- Bacteria
- Fungi



Chemical	Energy	Nutraceutical/Food	Cosmetics
<ul style="list-style-type: none">• Carbon nanotubes• Coatings and inks• Sealants/waxes• LCD pigments• Resins/polymers• Adhesives/lubricants	<ul style="list-style-type: none">• Fuel cells• Photovoltaics• Batteries• Biodiesel	<ul style="list-style-type: none">• Functional foods• Vitamins• Fish oil (<i>omega-3</i>)• Weight loss powders• Flavors• Controlled release	<ul style="list-style-type: none">• Emulsions/creams• Skin treatment• Sunscreen• Makeup/mascara• Waxes/lipstick• Fragrances

Benefits of Uniform High Shear Processing

Smaller Nanoparticles

- Greater bioavailability
- Targeted drug/actives delivery
- Naturally optimized product quality (touch/feel/color/odor)

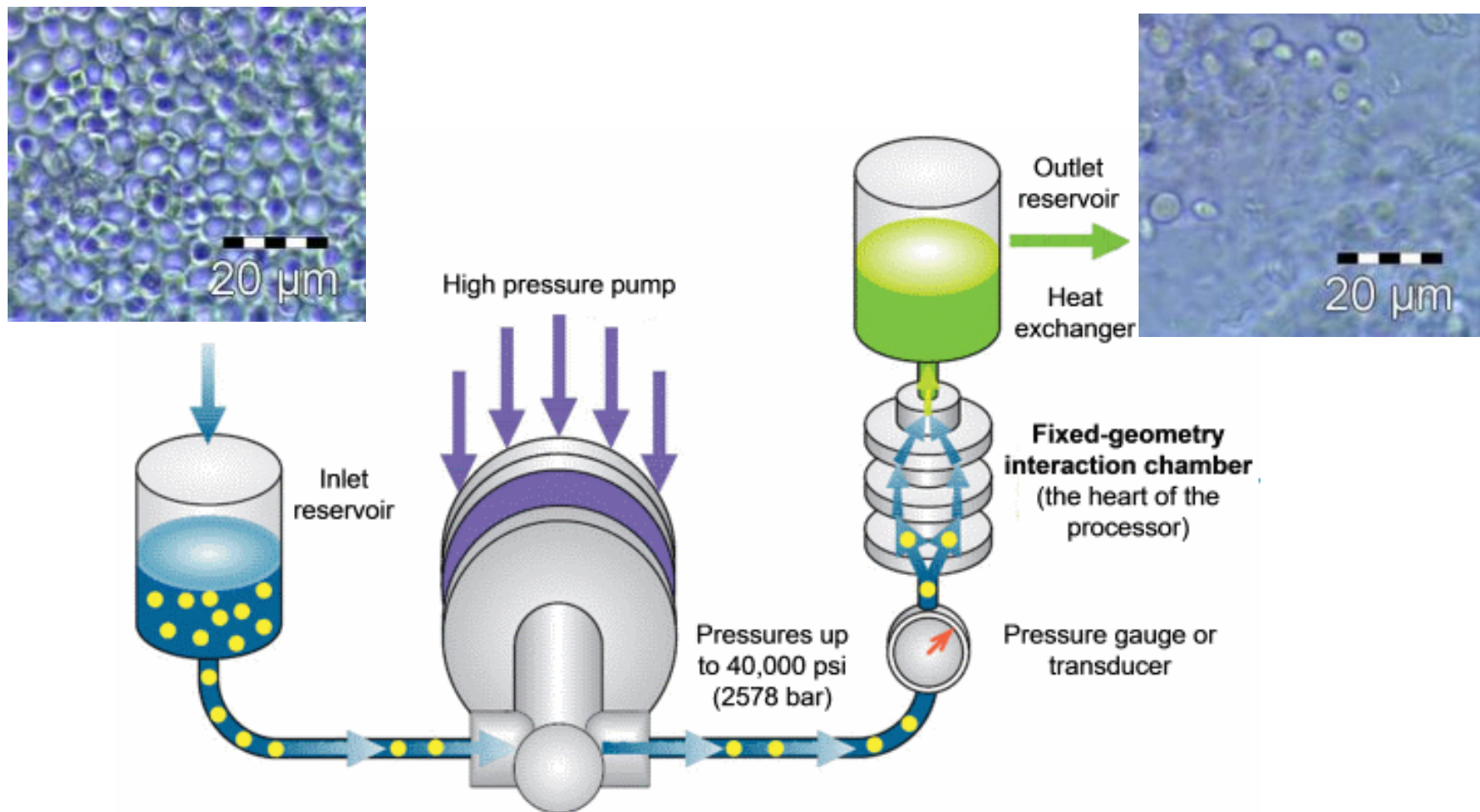
Narrow Particle Size Distribution

- Prolonged shelf life
- Uniform product characteristics
- Simplified downstream processing (e.g. sterile filtration < 200 nm)

Return on Investment

- Scaleup guaranteed
- Higher yield after cell rupture
- Less energy (passes, operation, cleaning)
- No contamination
- Continuous production & less raw materials

Microfluidizer® Processor



Heart of the Technology

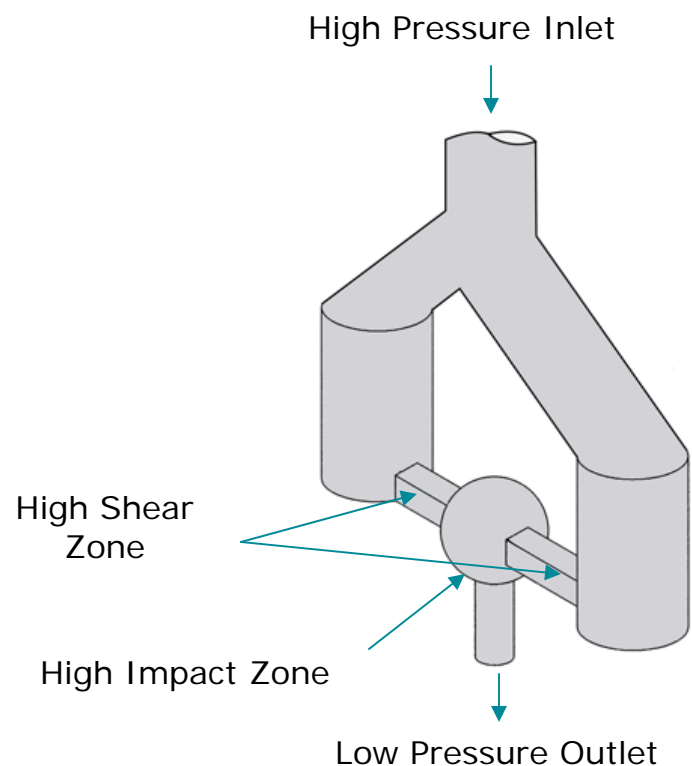
Fixed-Geometry Interaction Chamber

- Microfluidics exclusive
- Generates incredibly high shear and impact forces
- Precisely engineered microchannels
- Repeatable and scalable results
- Diamond or ceramic construction

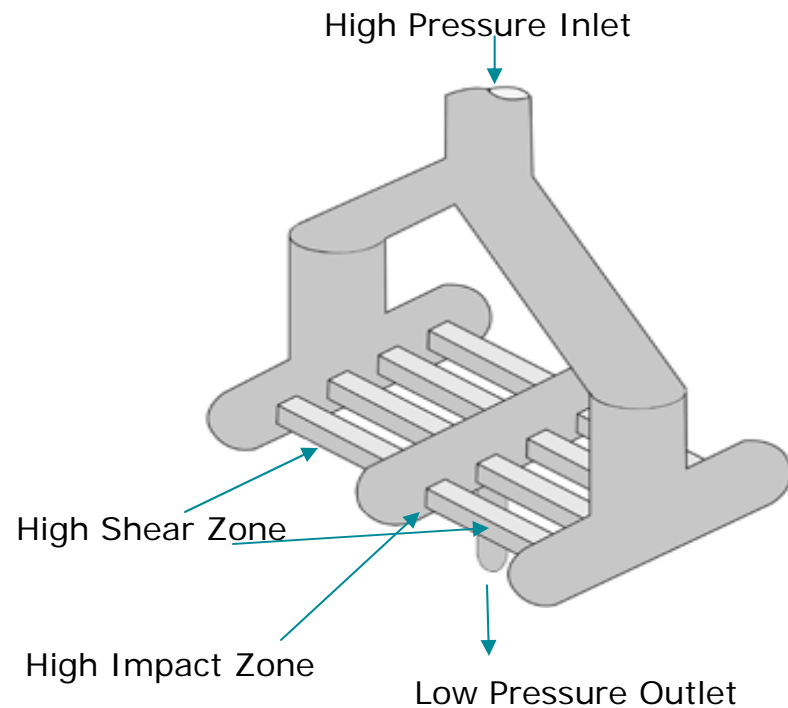


Interaction Chamber

“Y” Single-slotted

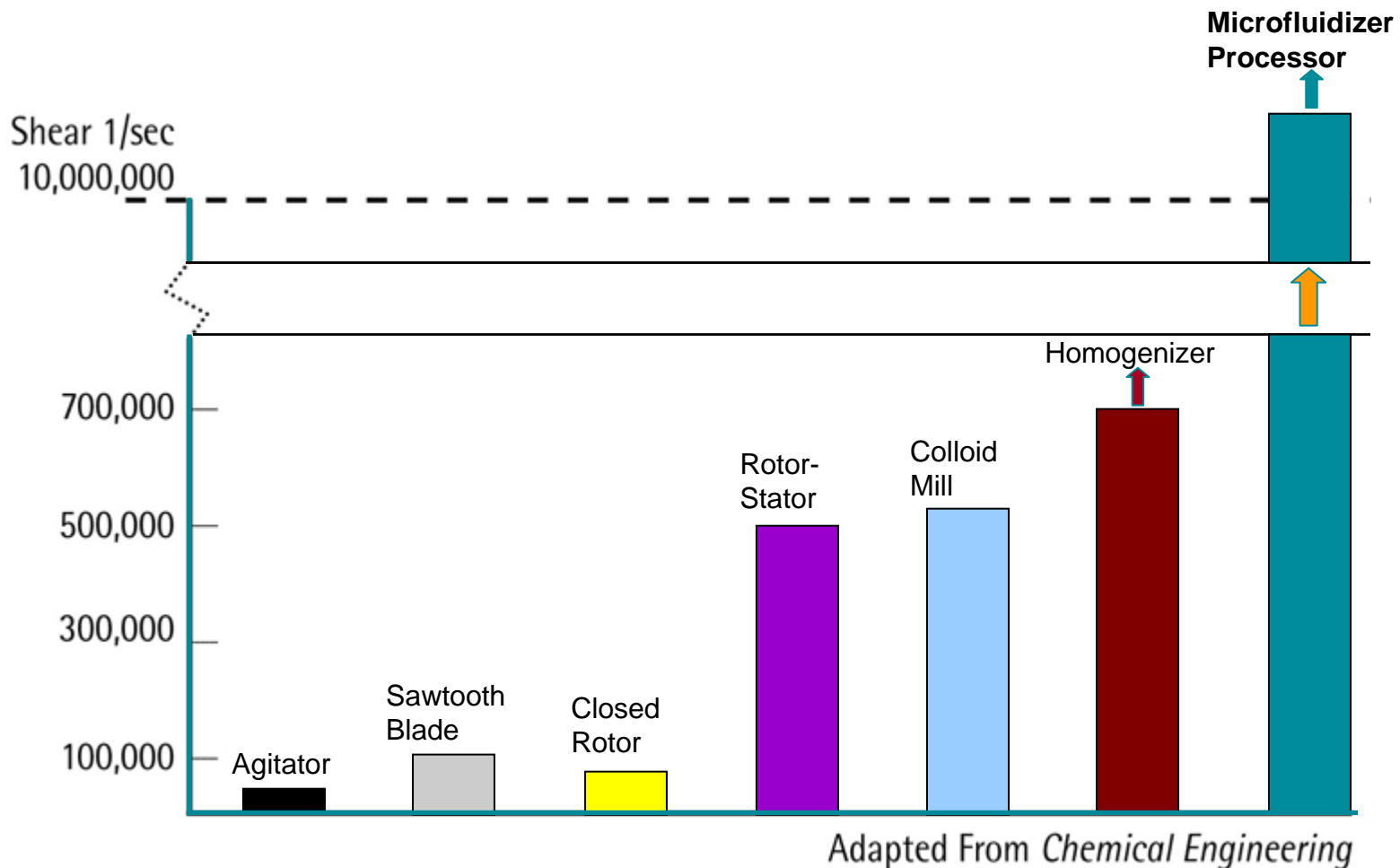


“Y” Multi-slotted



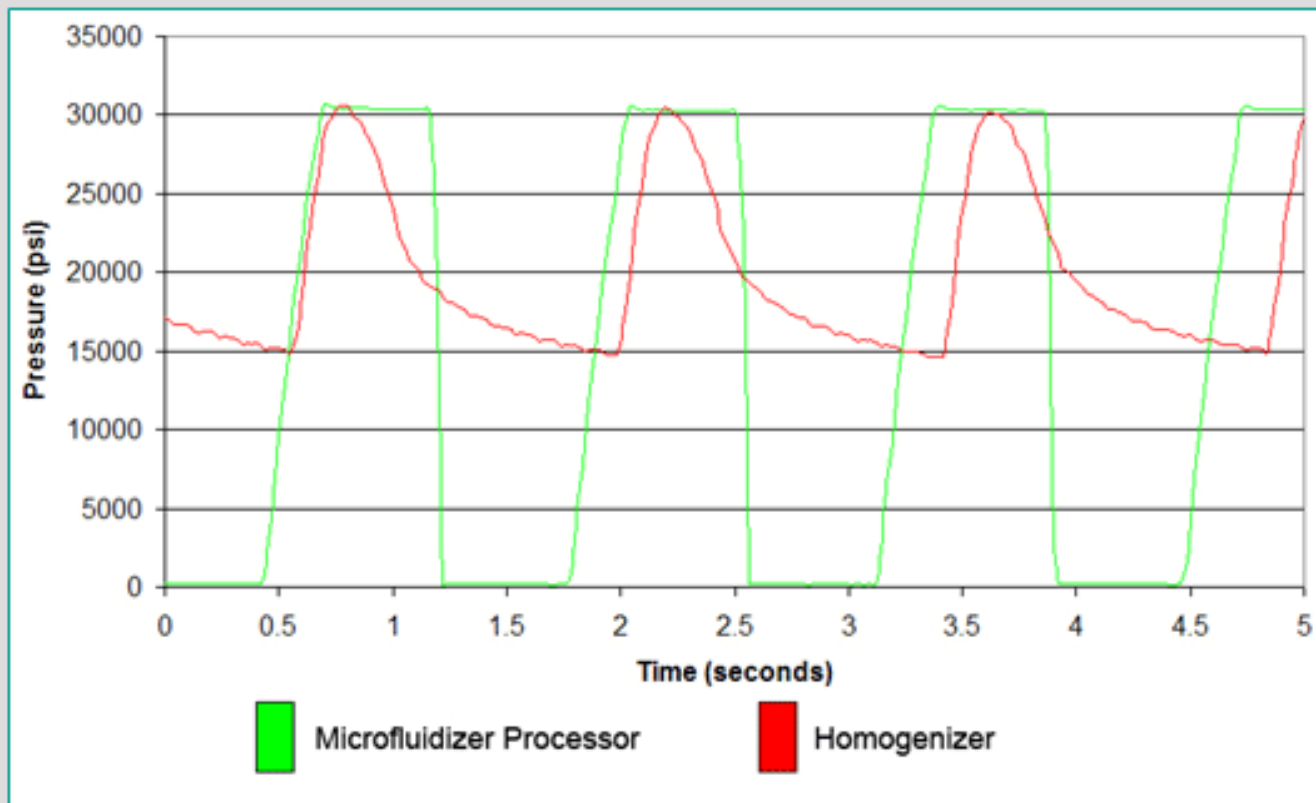
- Channel velocities over 400 m/s
- Channel minimum dimensions typically 50-300 microns
- Shear rates up to 10^7 s^{-1} ; controllable mixing in the 25-50 nm scale
- Constant mixing conditions for entire batch
- Demonstrated scalability to tens of liters per minute

Shear Rates for Various Technologies



Constant Pressure Ensures Minimal Energy Input

Case in Point: *Pressure profiles while processing*



The homogenizer operates at maximum pressure for mere moments – approximately 7% of each cycle. Conversely, the Microfluidizer processor applies constant processing pressure for most of the power stroke, leading to a more uniform shear field.

Case Study: Microfluidizer vs. Homogenizer



- Oil-in-water emulsion to be used as a vaccine adjuvant
- Processed three identical batches on each technology

Critical Quality Criteria	Leading Homogenizer	Microfluidizer Processor
Average Particle Size	185 nm after 15 passes (best achieved)	141 nm after 3 passes
Goal: < 150 nm	✗	✓
Polydispersity	43.1% above 200 nm	0.51% Above 200 nm
Goal: < 10% above 200 nm	✗	✓
Active Concentration	15% loss of actives	1% loss of actives
Goal: < 2% loss of actives	✗	✓
Filter Area Required Per Liter of Product	640 cm ²	17 cm ²
	The leading homogenizer required 38 times more filter area	

Based on these results, Corixa switched from their leading homogenization equipment to a Microfluidics production environment

Data courtesy of **Jedd Taylor**, Corixa (now GlaxoSmithKline)

Common Mechanical Methods of Cell Rupture

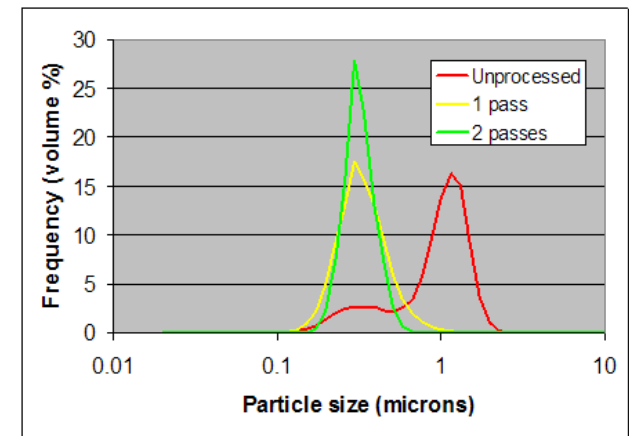
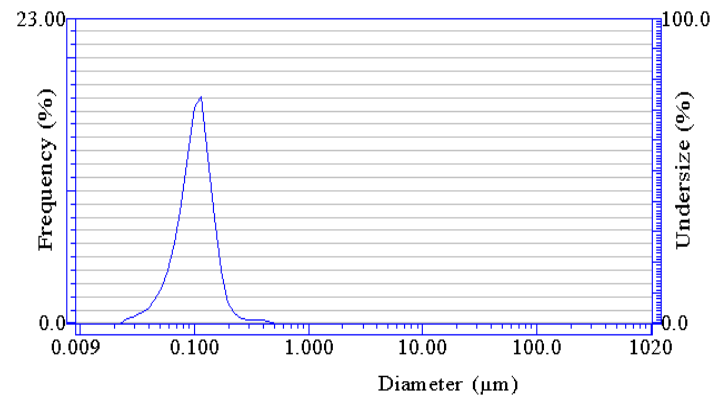
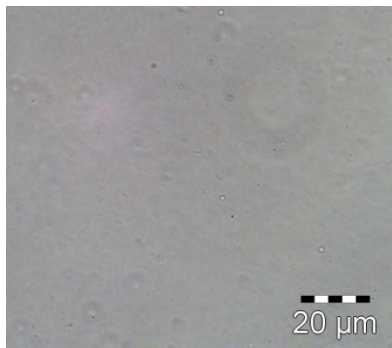
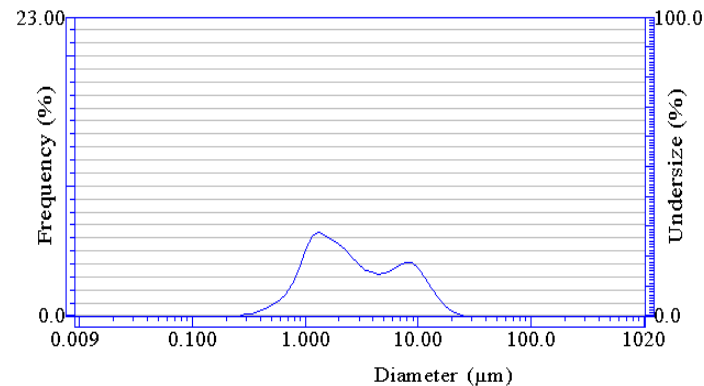
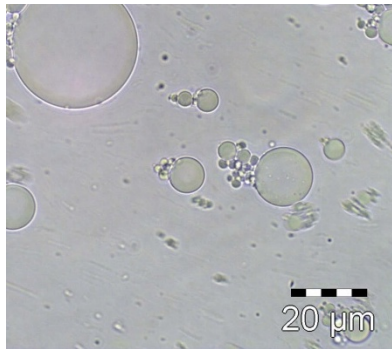
	Microfluidizer	Homogenizer	Sonicator	Bead Mill
Continuous	Yes	Yes	No	No
Scalable	Yes	Limited	No	Yes
Optimal Temp Control	Yes	Yes	No	No
Contamination Free	Yes	Yes	Yes	No
Minimum Volume	1ml*	10 ml	1ml	1 ml
Shear Rate Potential	Highest	High	High	Medium



* Now available with the **LV1 Low Volume** Microfluidizer processor

Ophthalmic Drug Delivery

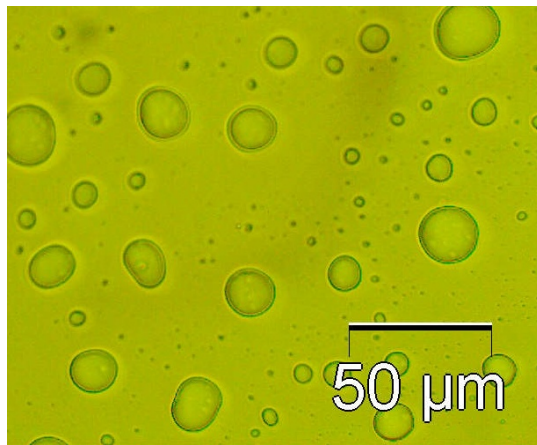
Particle size reduction – Ophthalmic drug delivery



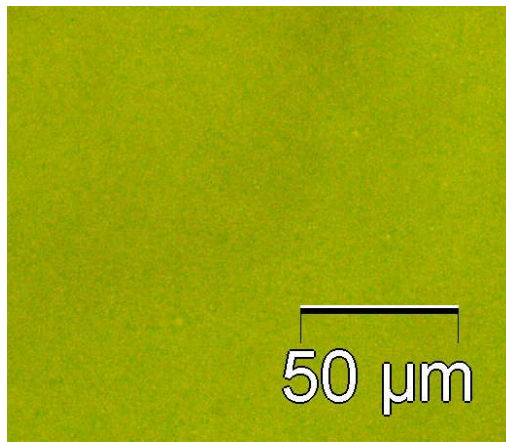
Median particle size (D50) after 1 pass @ 24,000 psi: **96 nm**

O/W Emulsion - Fish Oil Encapsulation

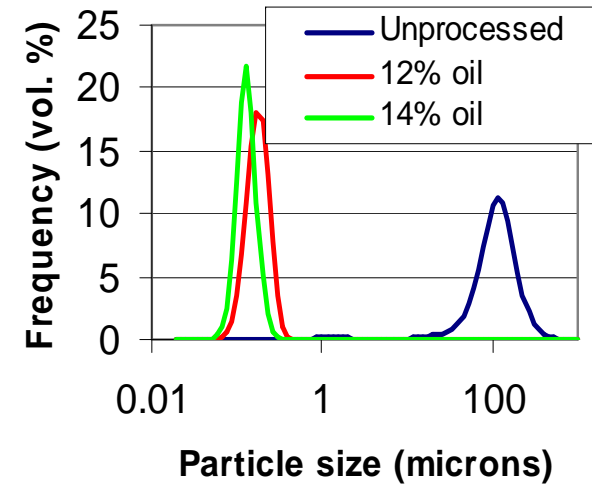
- Fish oil contains Omega 3 fatty acid, which is an essential nutrient.
- By encapsulating the fish oil, the undesirable taste can be reduced substantially and the oil is protected from oxidation



Before



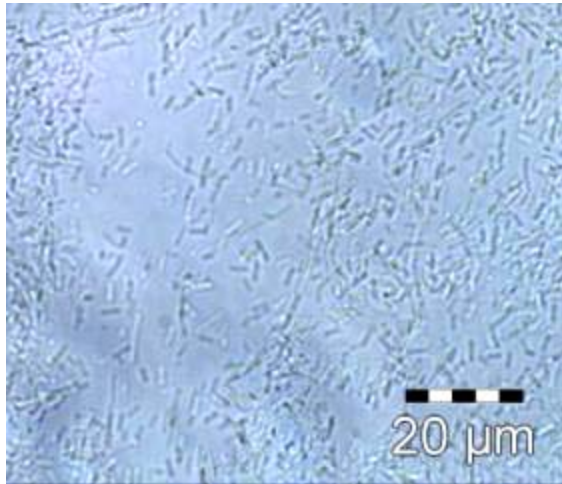
After



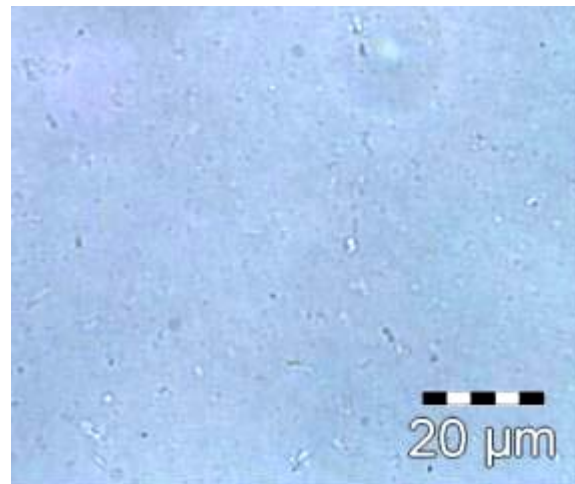
Median particle size of 12% fish oil emulsion after processing: **0.163 μm**

Median particle size of 14% fish oil emulsion after processing: **0.119 μm**

Cell Disruption - *E. Coli*



BEFORE



AFTER

Process pressure: 18,000 psi (1241 bar)

Chamber: H10Z (100 microns)

Shear rate: $5.58 \times 10^6 \text{ s}^{-1}$

Reaching A New Low (...Volume)

New! LV1 Low Volume Processor

- Only high shear processor to operate on samples as small as **1 ml**
- Superior replacement for obsolete French press, limited ultrasonicator
- Fully scalable to lab, pilot and production volumes

New! LA-950 with MiniFlow Attachment

- 35 to 55 ml volume requirements
- Resistant to organic solvent
- Auto fill pump and auto-drain facilities



Low volume products are ideal for companies and universities working with precious or limited materials



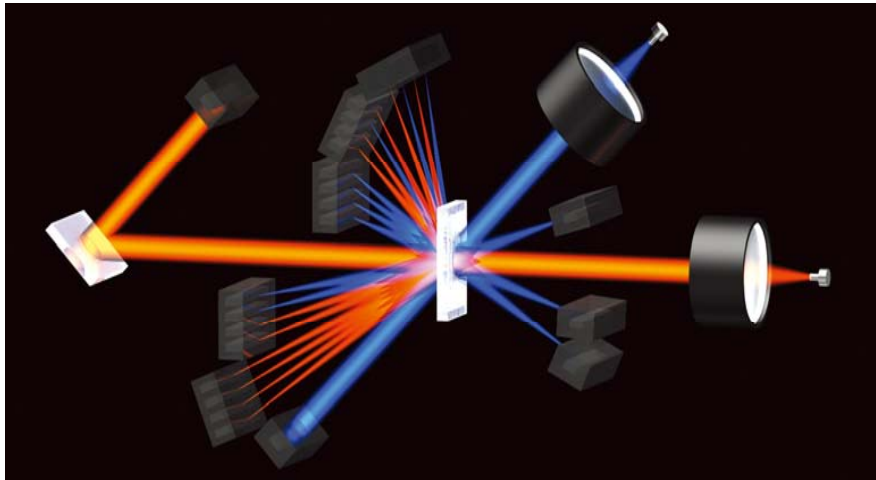
Monitoring Particle Size Reduction

- Want wide dynamic range, before + after
- Ability to measure down to nanoparticle range
 - Less than 100 nm
- Fast, easy to use
- Small sample volume required
- HORIBA LA-950 ideal for this application



Laser Diffraction

Particle size 0.01 – 3000 μm

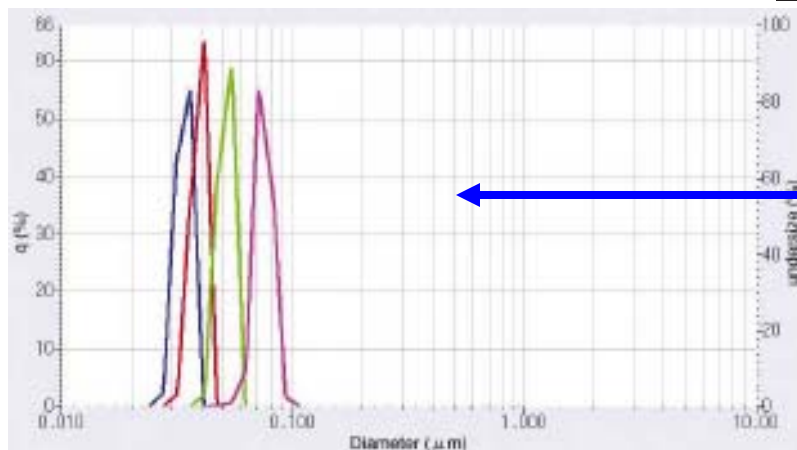
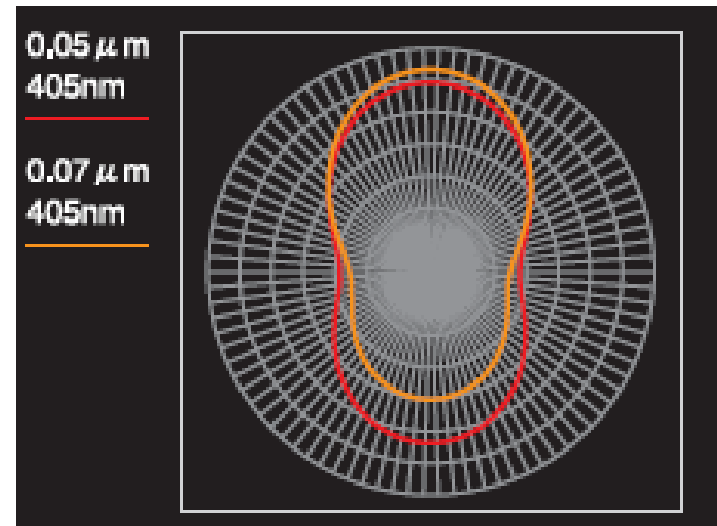
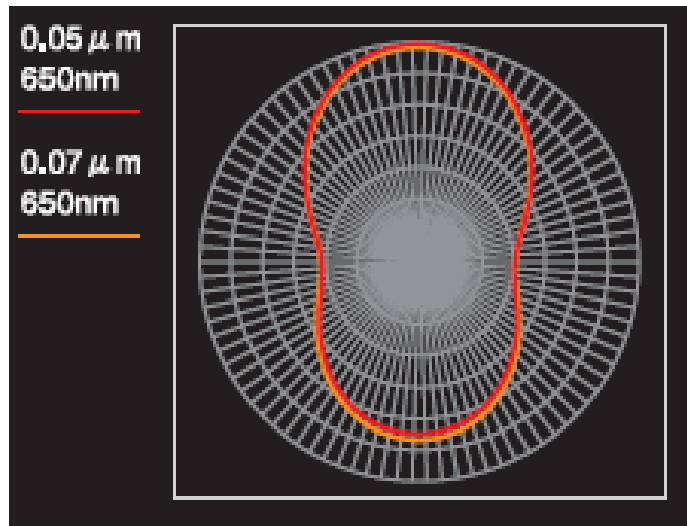


Laser Diffraction

- Particle size 0.01 – 3000 μm
- Converts scattered light to particle size distribution
- Quick, repeatable
- Most common technique
- Suspensions & powders

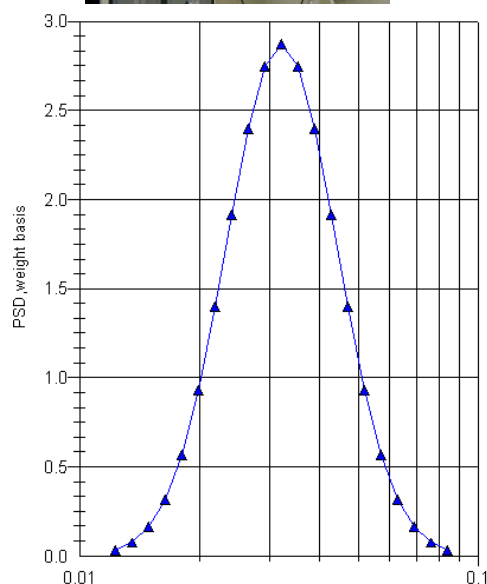
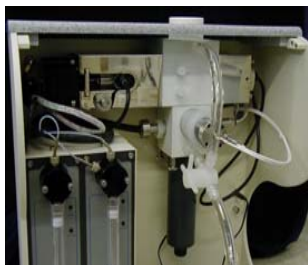


Low End Sensitivity



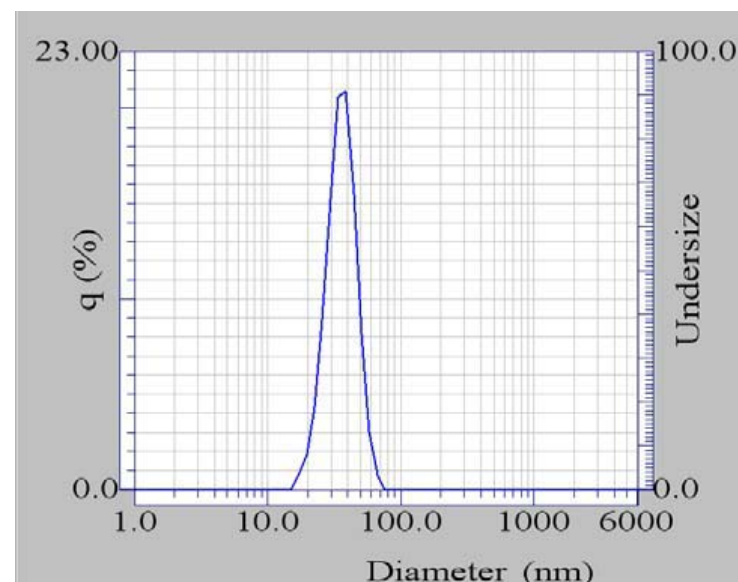
30, 40, 50, 70 nm
latex standards

30 nm Colloidal Silica*



Mean Size : 0.0321(μm)

Figure 1: Typical particle size analysis for LUDOX TM on the DT-1201



Mean Size : 34.1(nm)

Figure 3: Typical particle size analysis for LUDOX TM on the LB-550

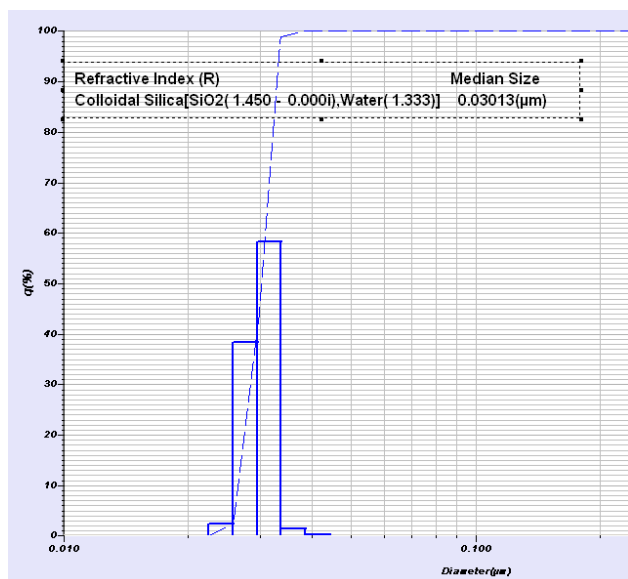
*see TN156 "Colloidal Silica as a Particle Size and Charge Reference Material on www.horiba.com/us/particle

Low End Sensitivity

■ Sensitivity: small particle detection

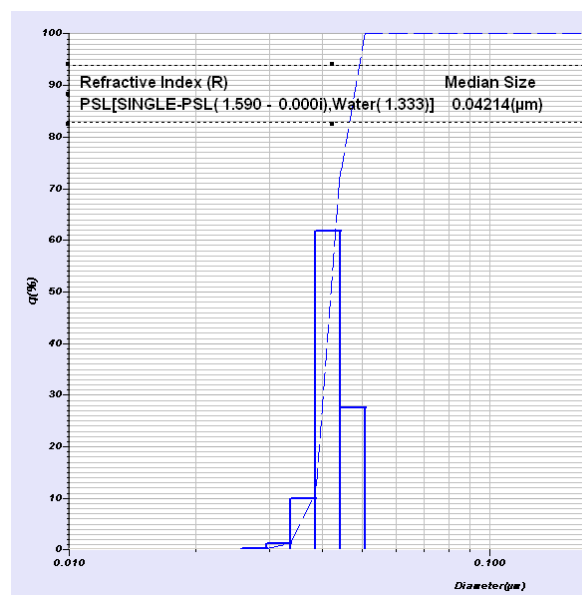
30 nm silica

S.P.Area : 2.0183E+6(cm²/cm³)
 Mean Size : 0.02990(μm)
 Variance : 5.0313E-6(μm²)
 Median Size : 0.03013(μm)
 Mode Size : 0.0302(μm)
 Skewness : -0.2901

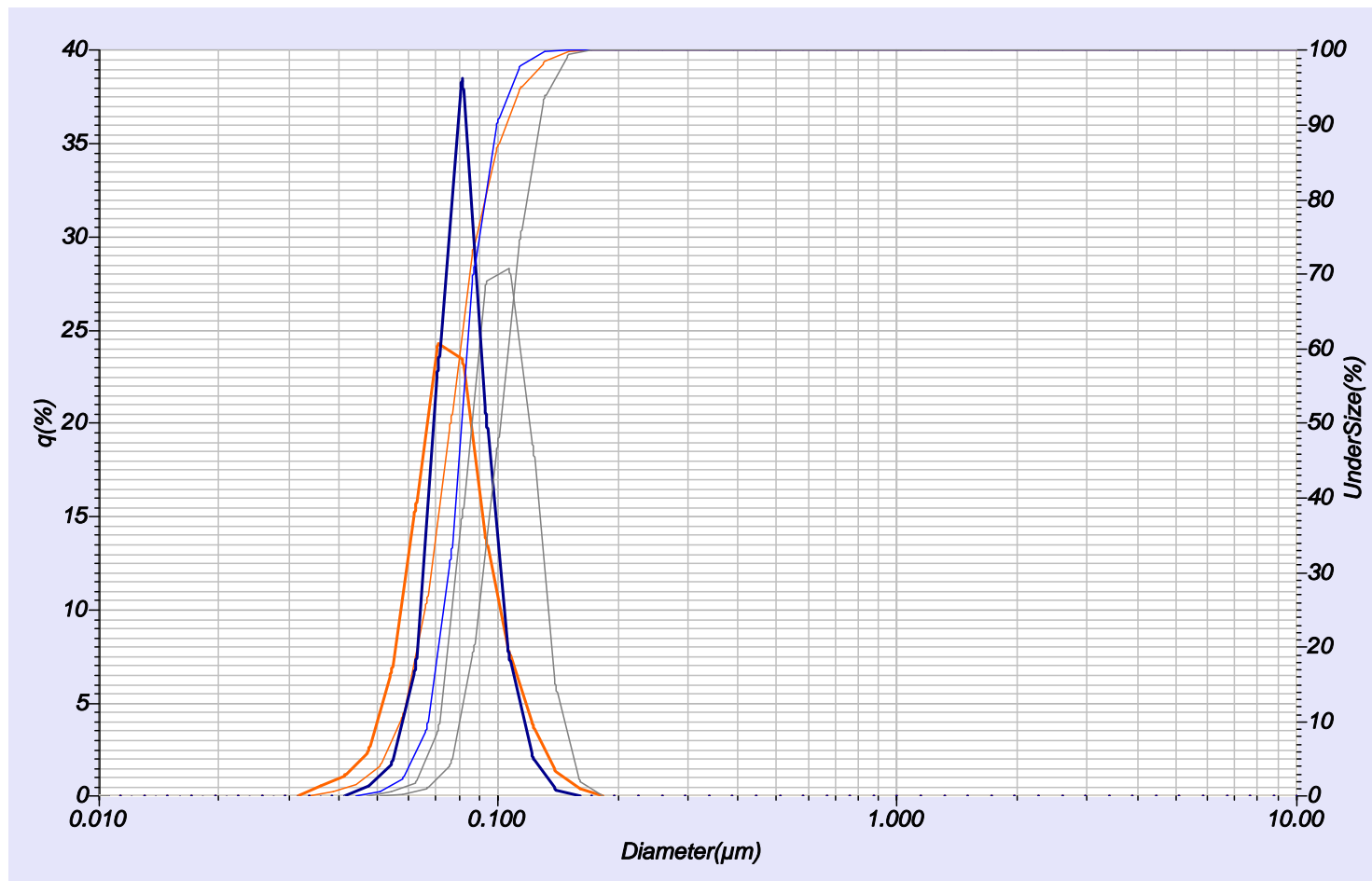


40 nm latex

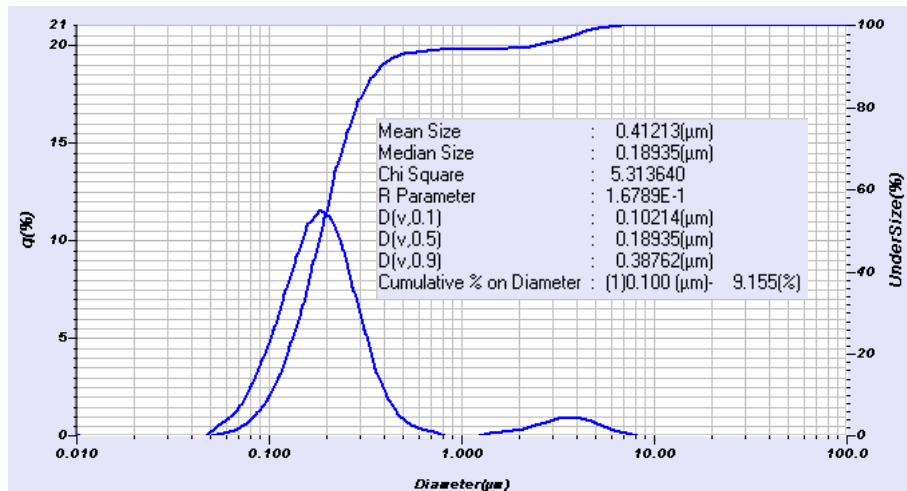
S.P.Area : 1.4253E+6(cm²/cm³)
 Mean Size : 0.04241(μm)
 Variance : 1.2759E-5(μm²)
 Median Size : 0.04214(μm)
 Mode Size : 0.0422(μm)
 Skewness : -0.1514



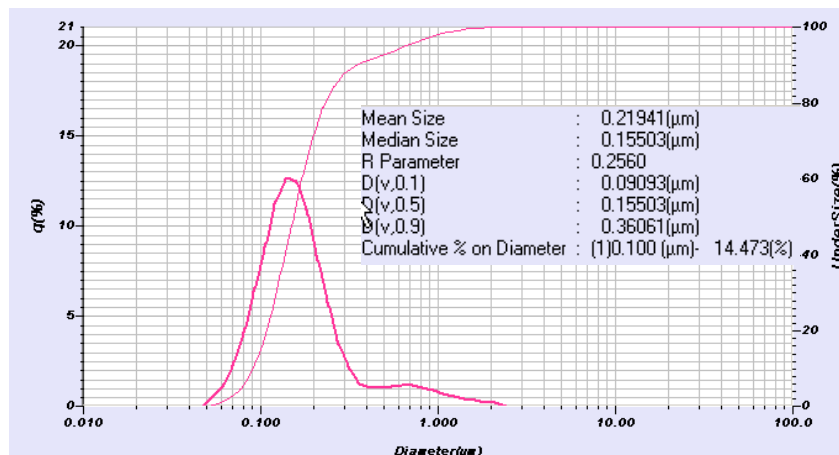
Low End Sensitivity: Pigments



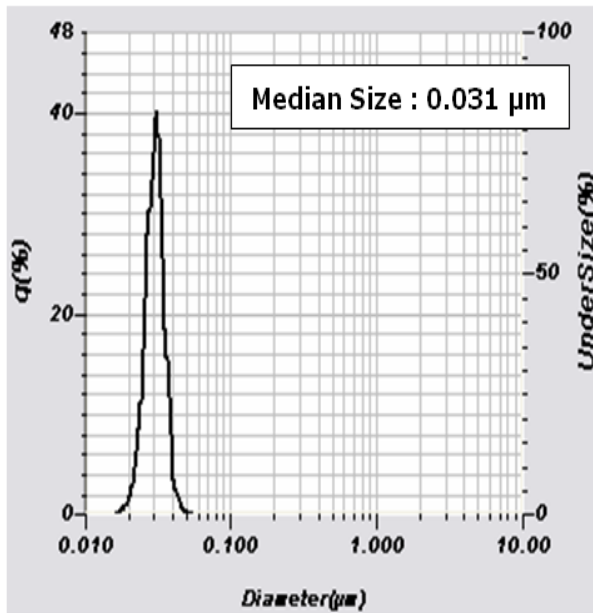
Low End Sensitivity: Cosmetics



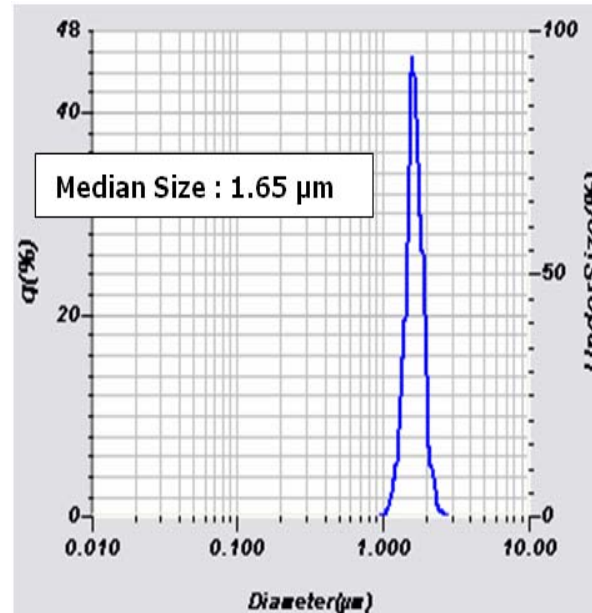
- Some (unfounded?) concerns with particles <100nm
- LA-950 good at determining sub 100nm particles
- Software set to display % under any given size
- Data shown left is for skin cream and TiO₂ suspension



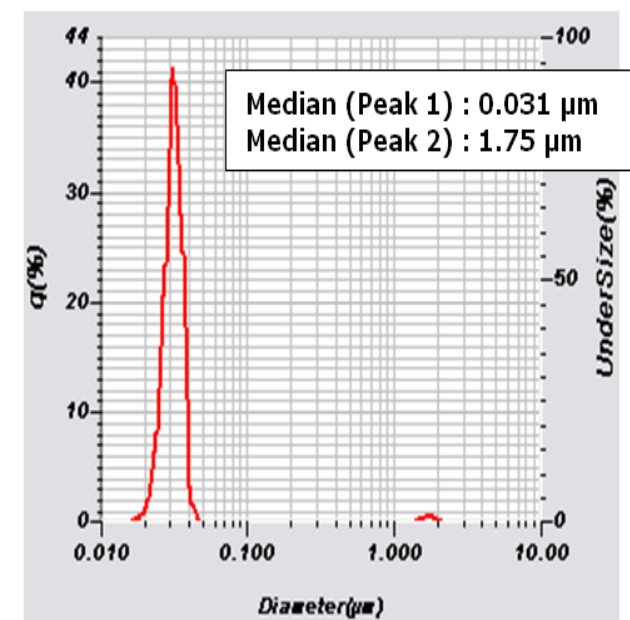
Detecting Second Population



Small silica



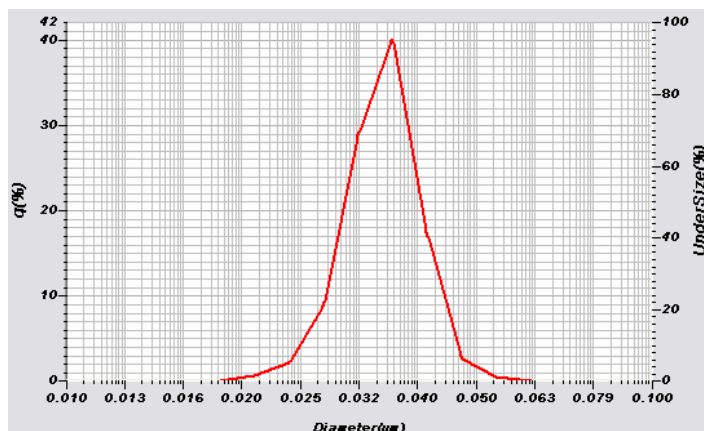
Geltech dopant



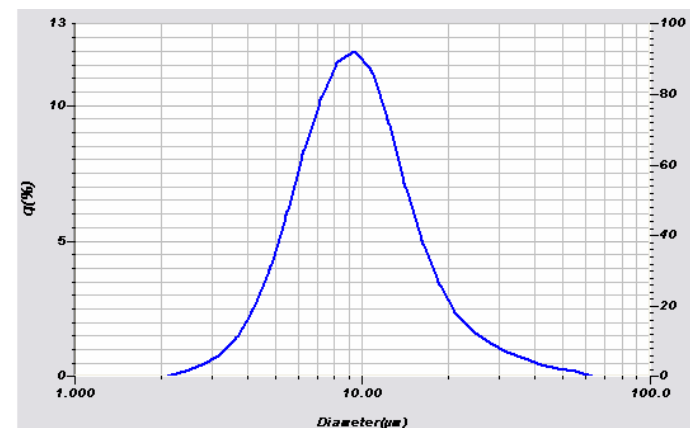
Finding 0.05% dopant

- Highest sensitivity system for detecting second population
 - Large particles or smaller particles

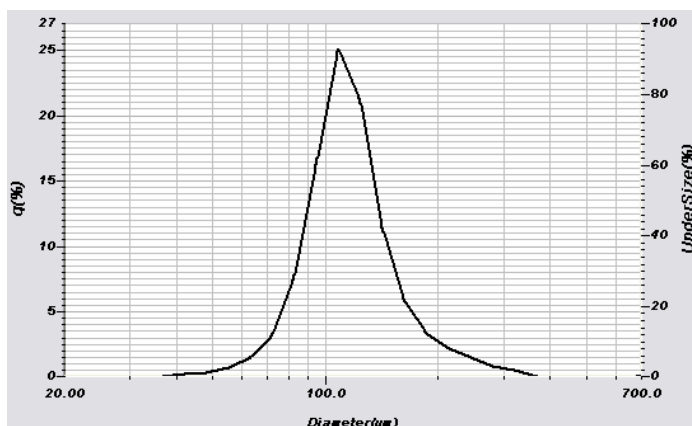
Small Sample Volume (MiniFlow)



Colloidal Silica (weak scatterer)
 Median (D50): **35 nm**
 Sample Amount: **132 mg**



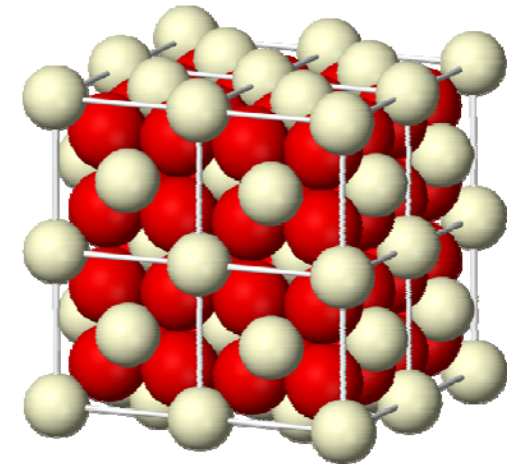
Magnesium Stearate
 Median (D50): **9.33 μm**
 Sample Amount: **0.165 mg**



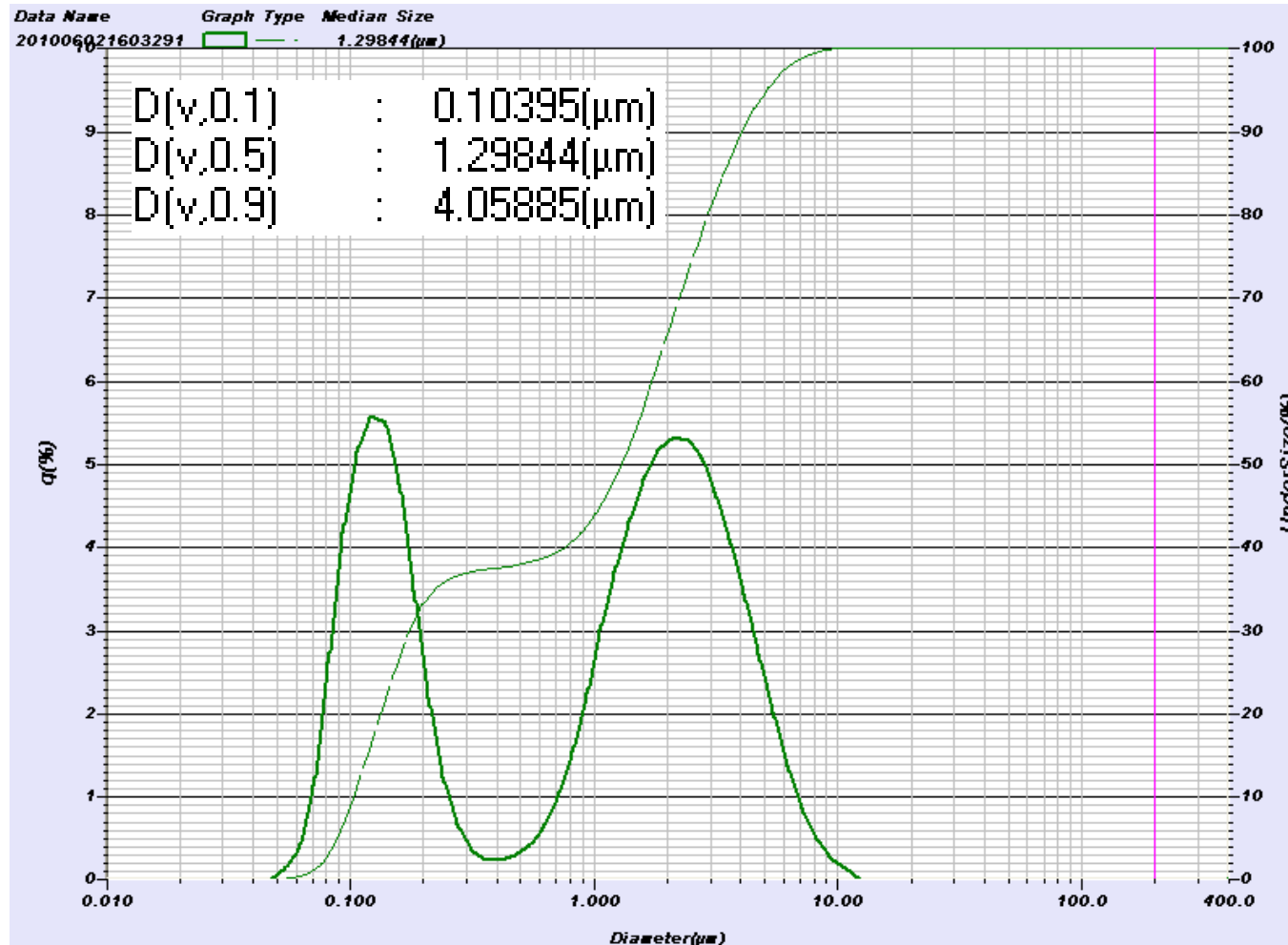
Bio-degradable Polymer
 Median (D50): **114 μm**
 Sample Amount: **1.29 mg**

Ceria

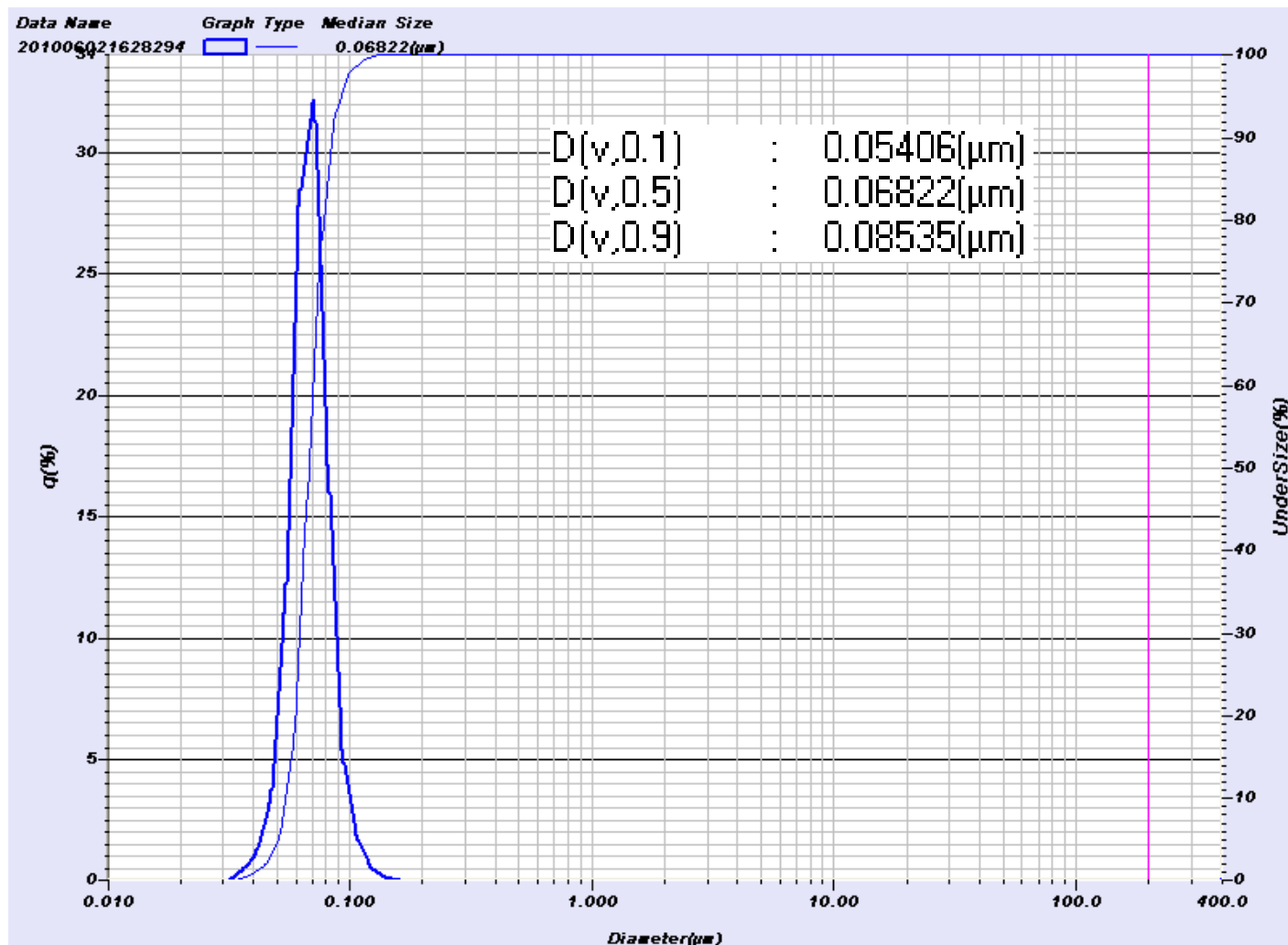
- Cerium (IV) oxide: CeO_2
- Used in ceramics, catalysts, CMP slurries
- In doped form used for solid oxide fuel cells
- Particle size is important for all of these applications
- Size reduction by M-110P Microfluidizer, particle size analysis by LA-950



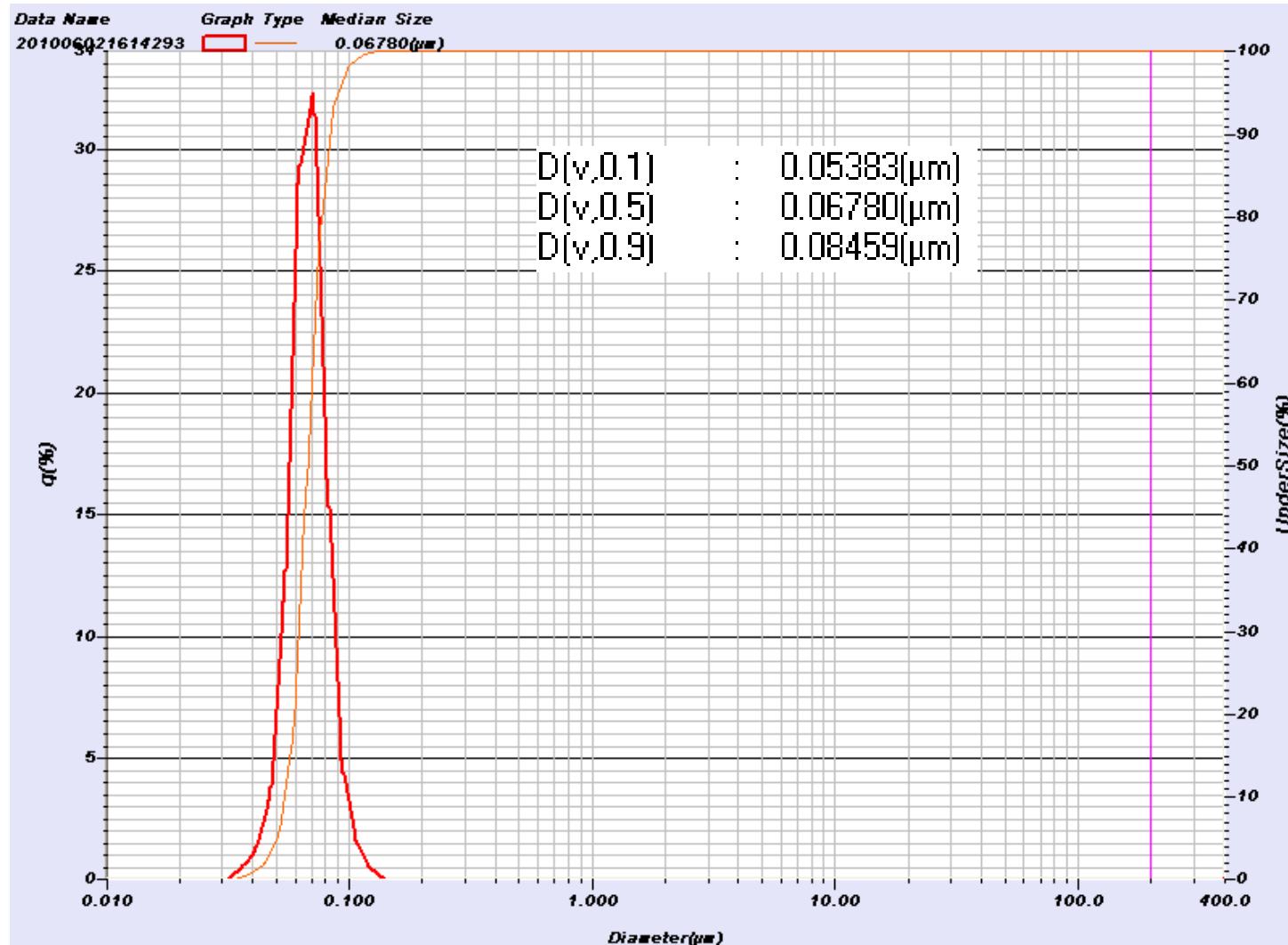
Ceria: Unprocessed



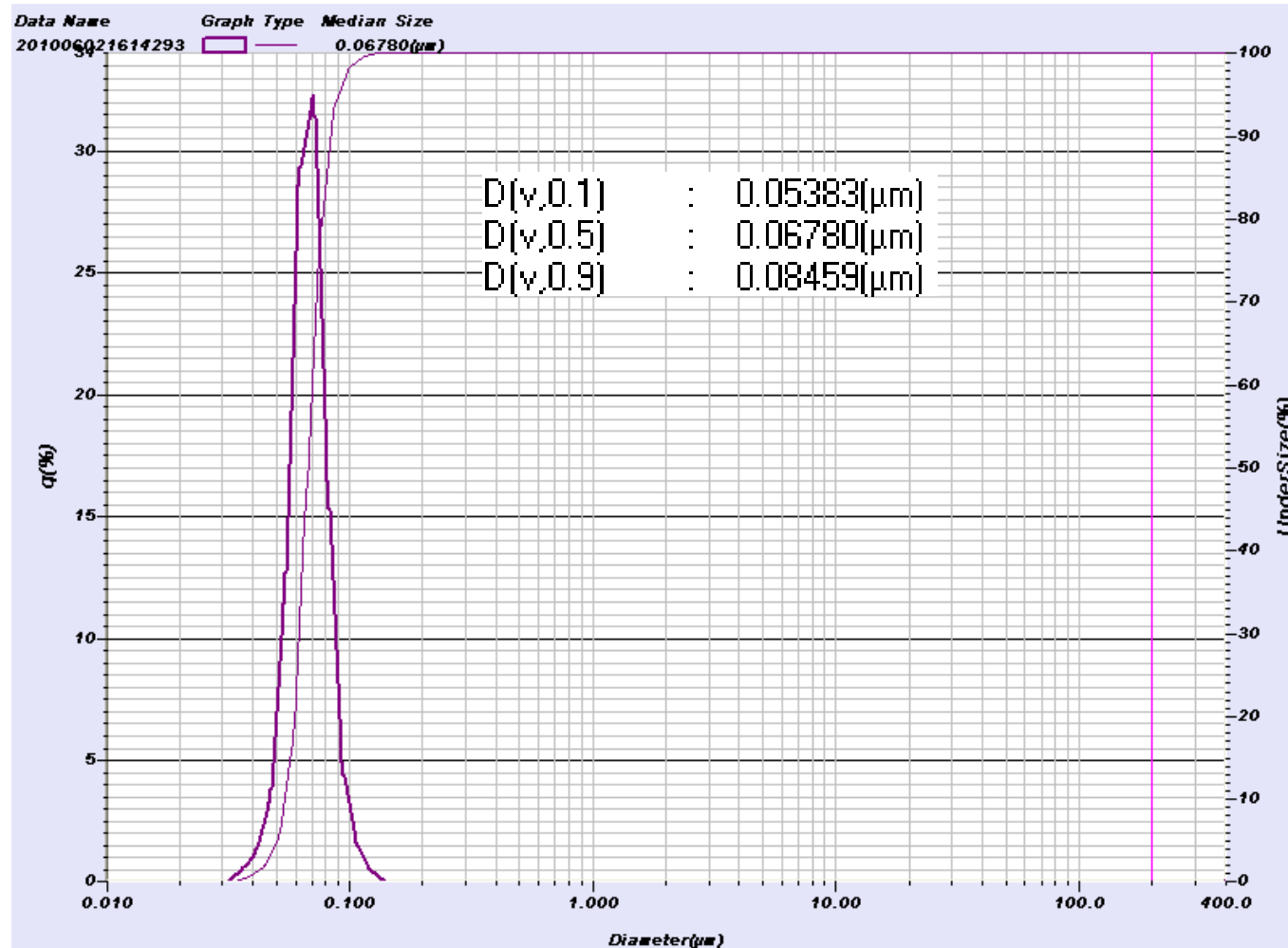
Ceria: 1 Pass



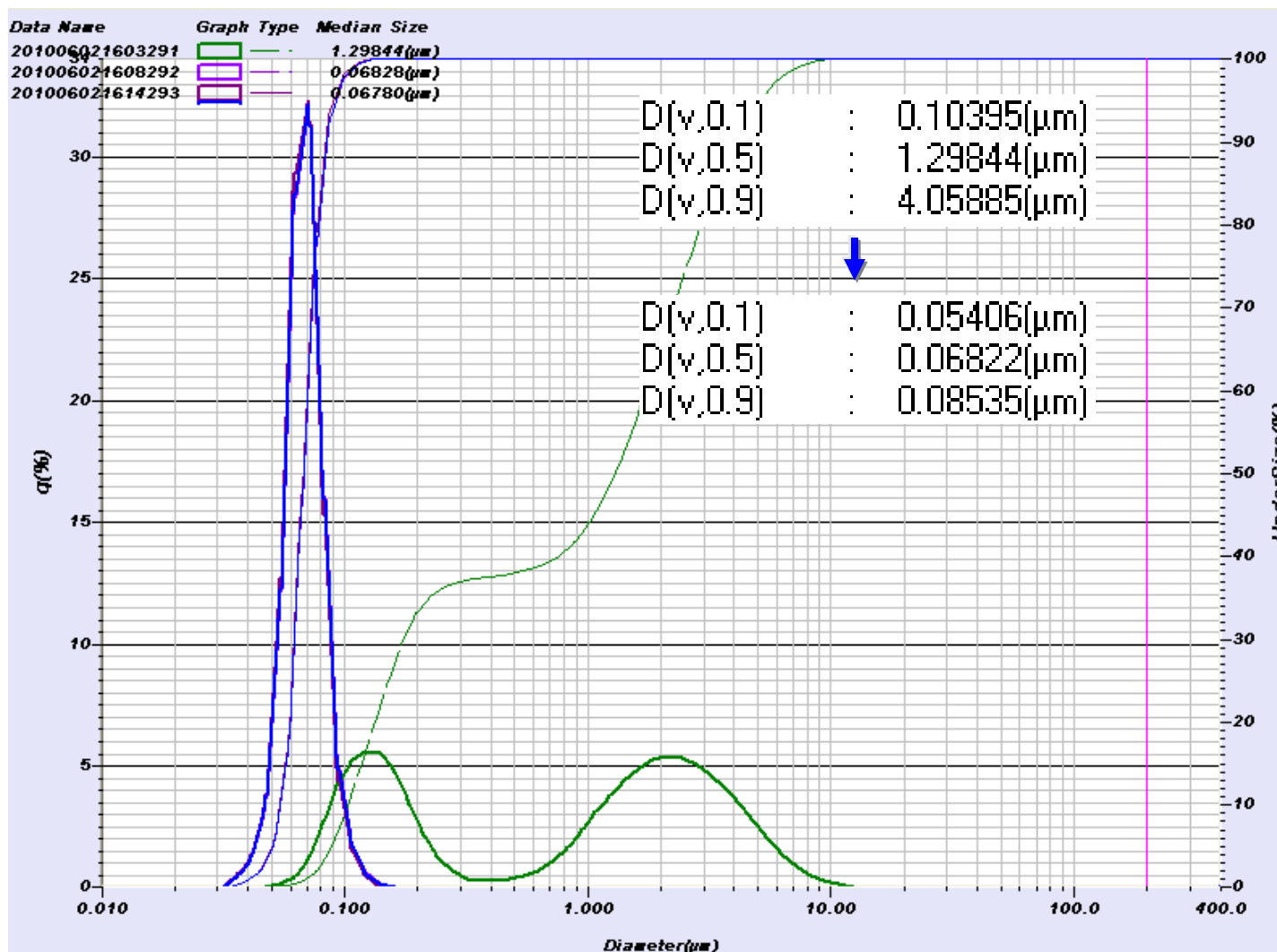
Ceria: 2 Passes



Ceria: 3 Passes

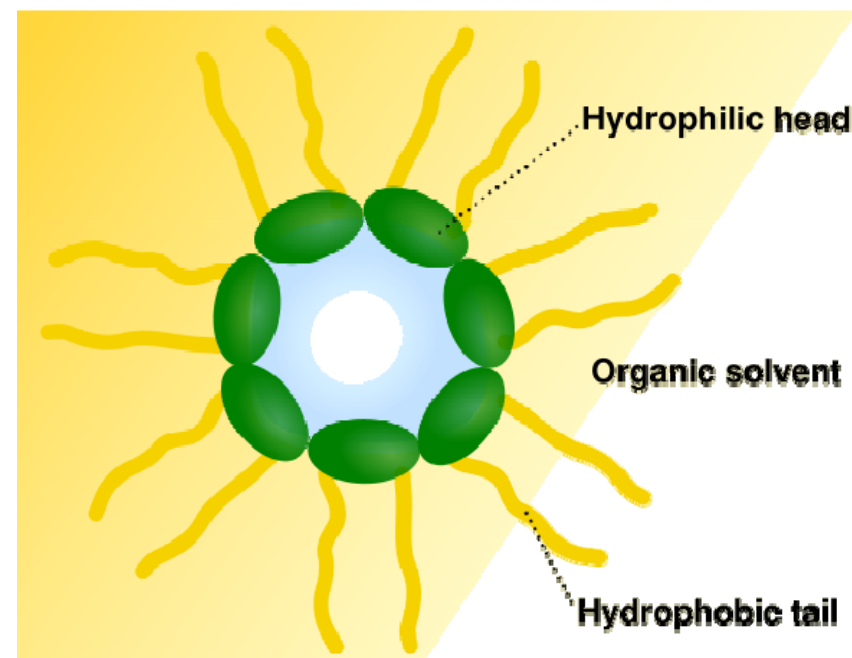
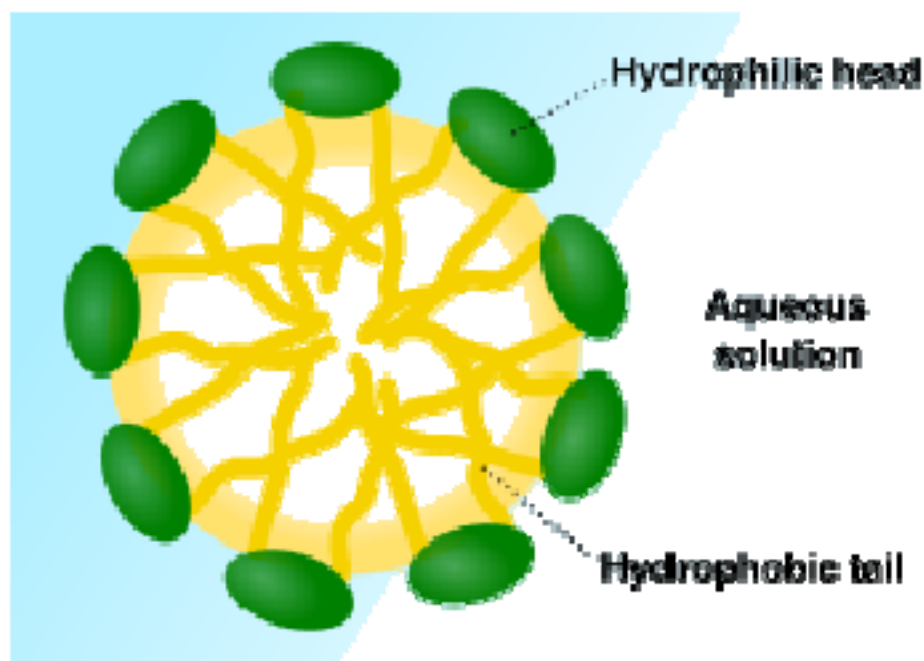
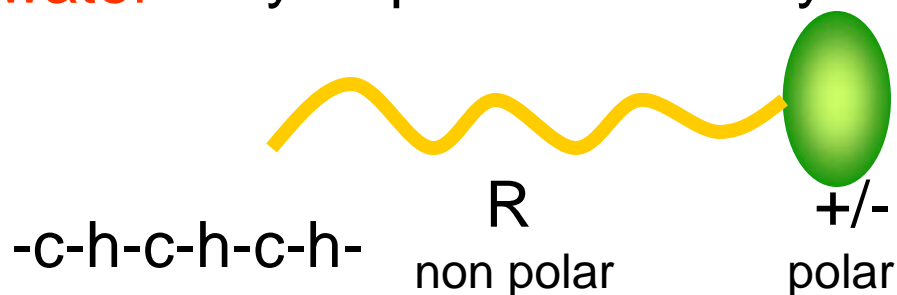


Ceria: Before, After Processing

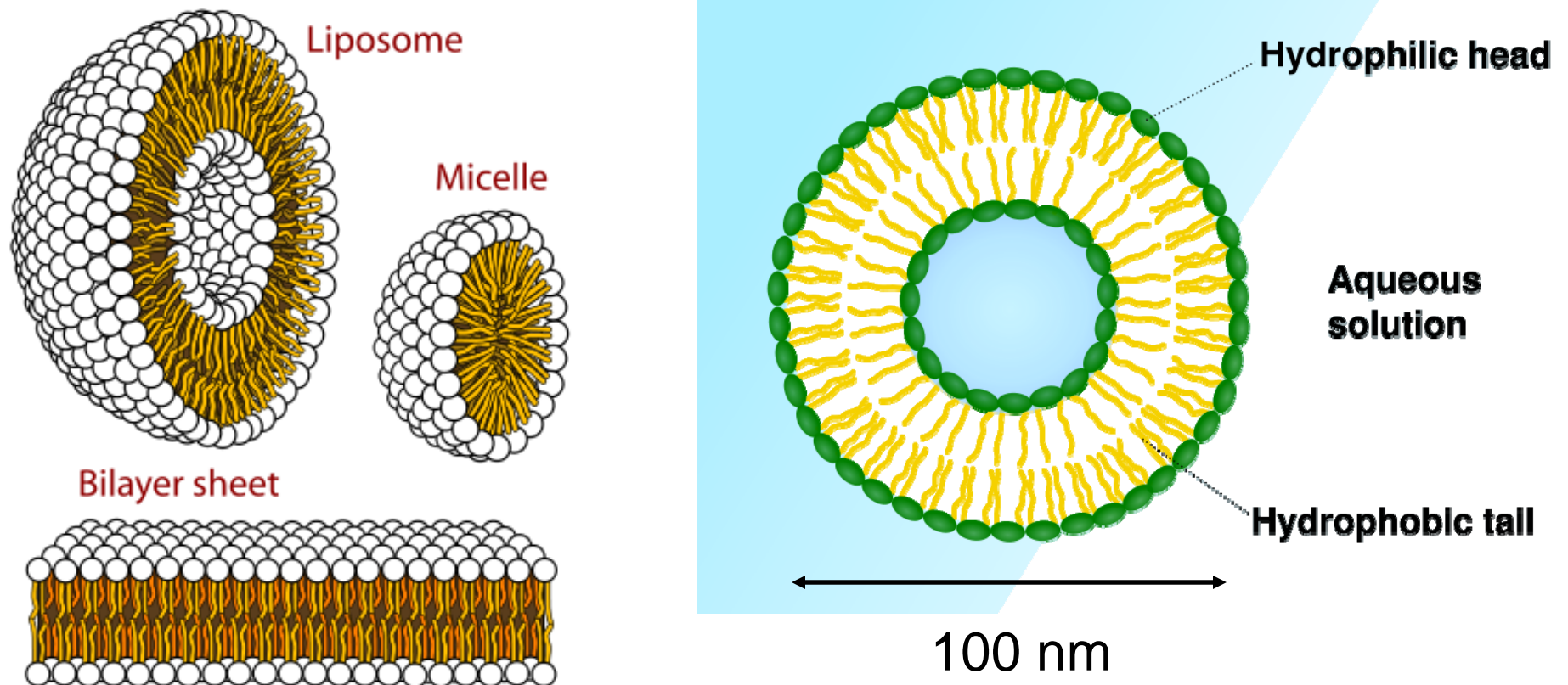


Self Assembly: Micelles

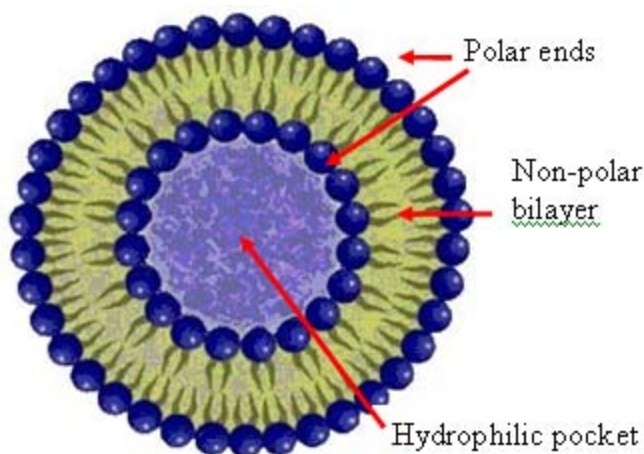
hates water Hydrophobic tail Hydrophilic head loves water



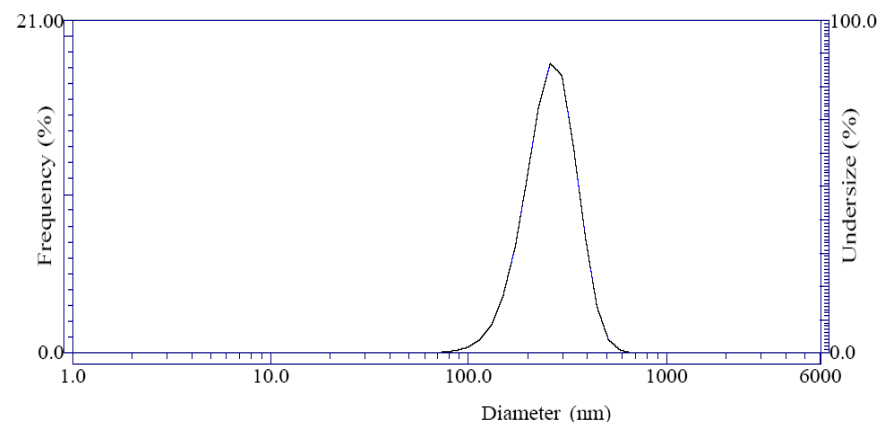
Liposomes



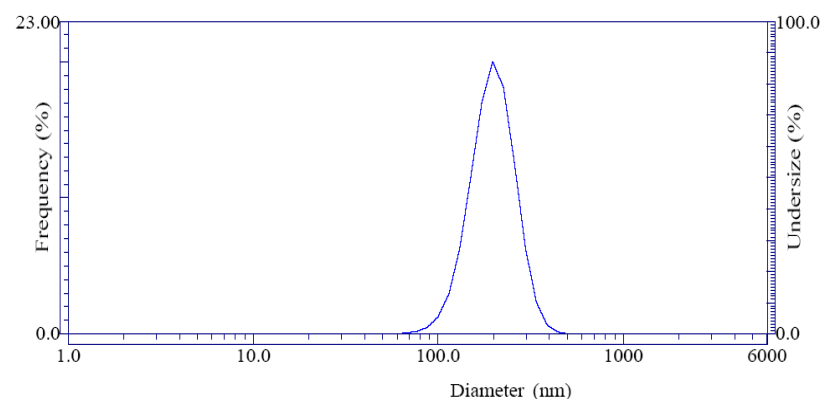
DLS Application : Liposomes



LB-550 DLS System



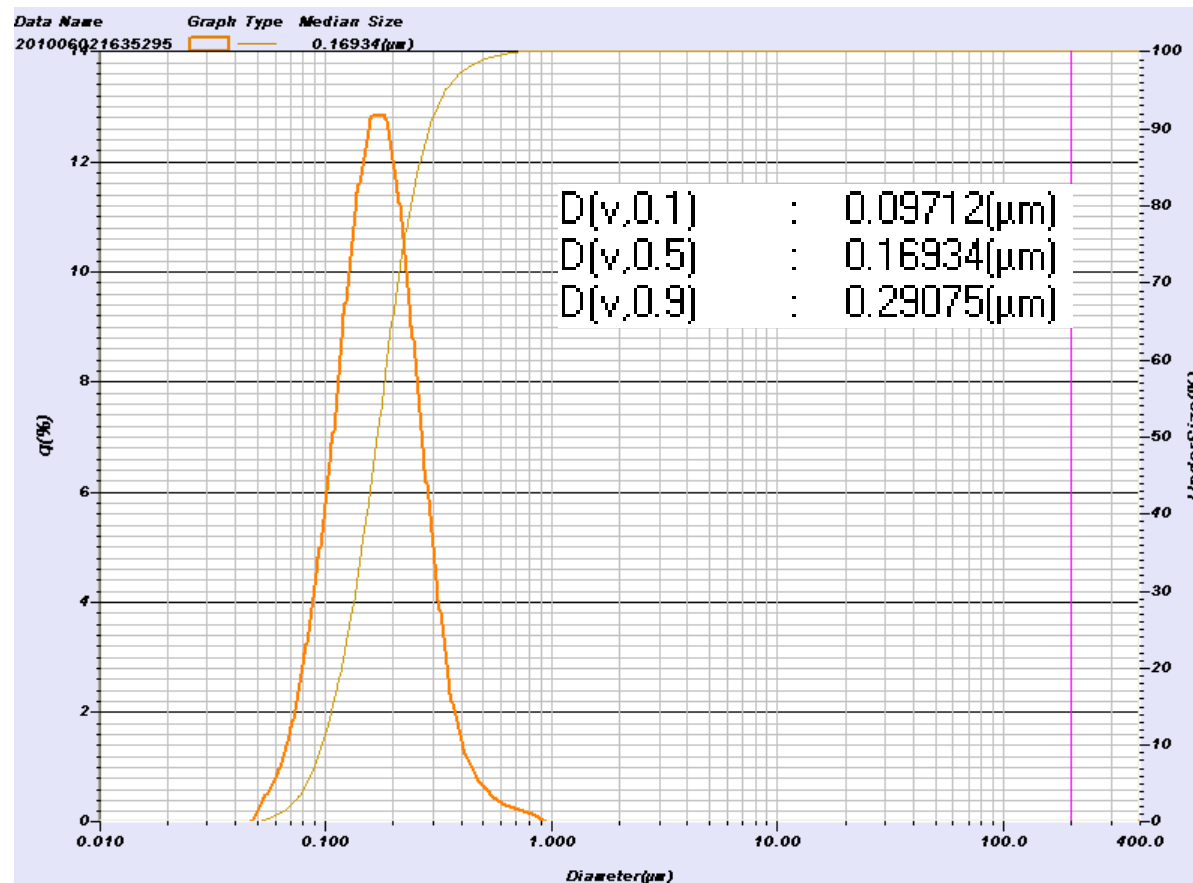
Liposome particle size after 5 passes through a 100 mm membrane ~ 250 nm



Liposome particle size after 20 passes through a 100 mm membrane ~ 150 nm

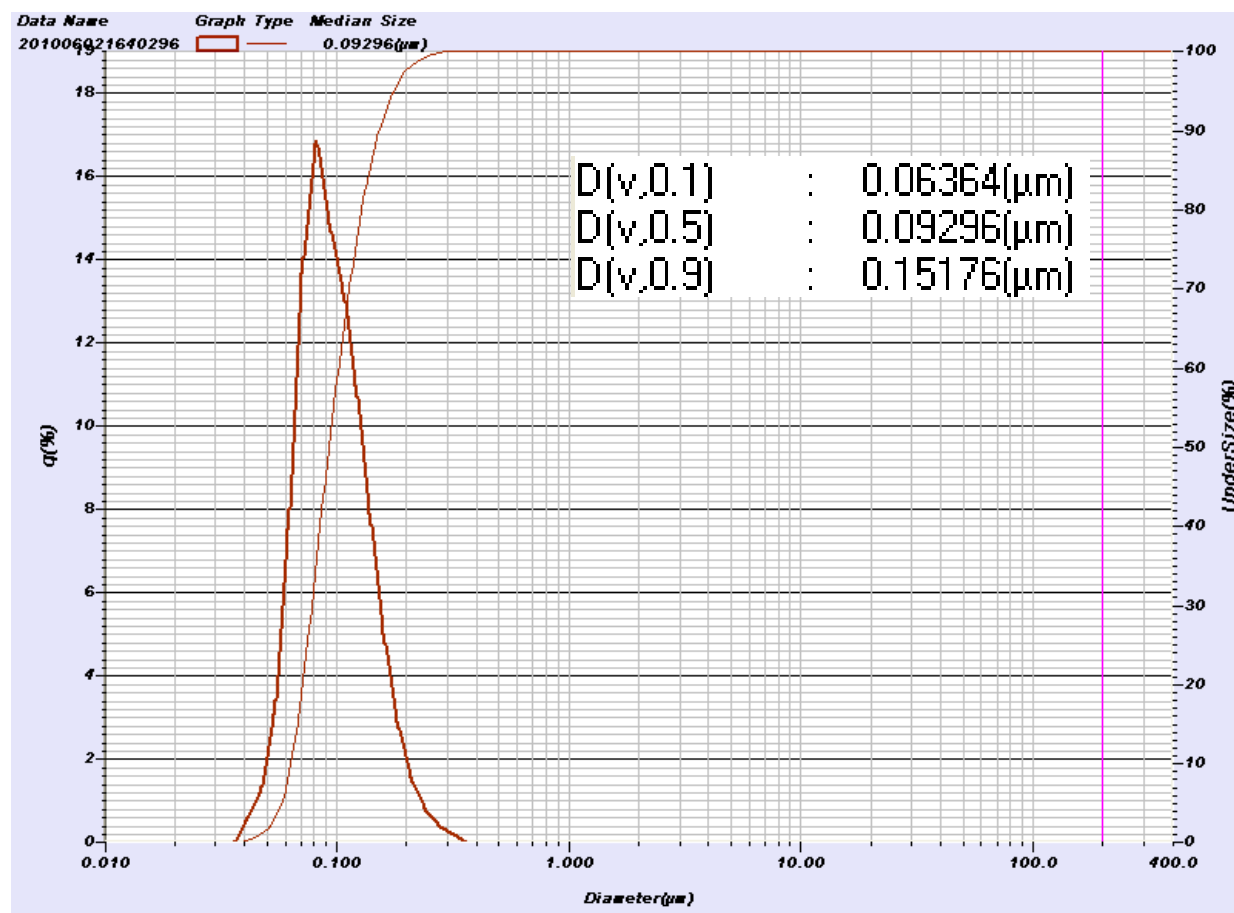
Liposome: Unprocessed

Measured on LA-950



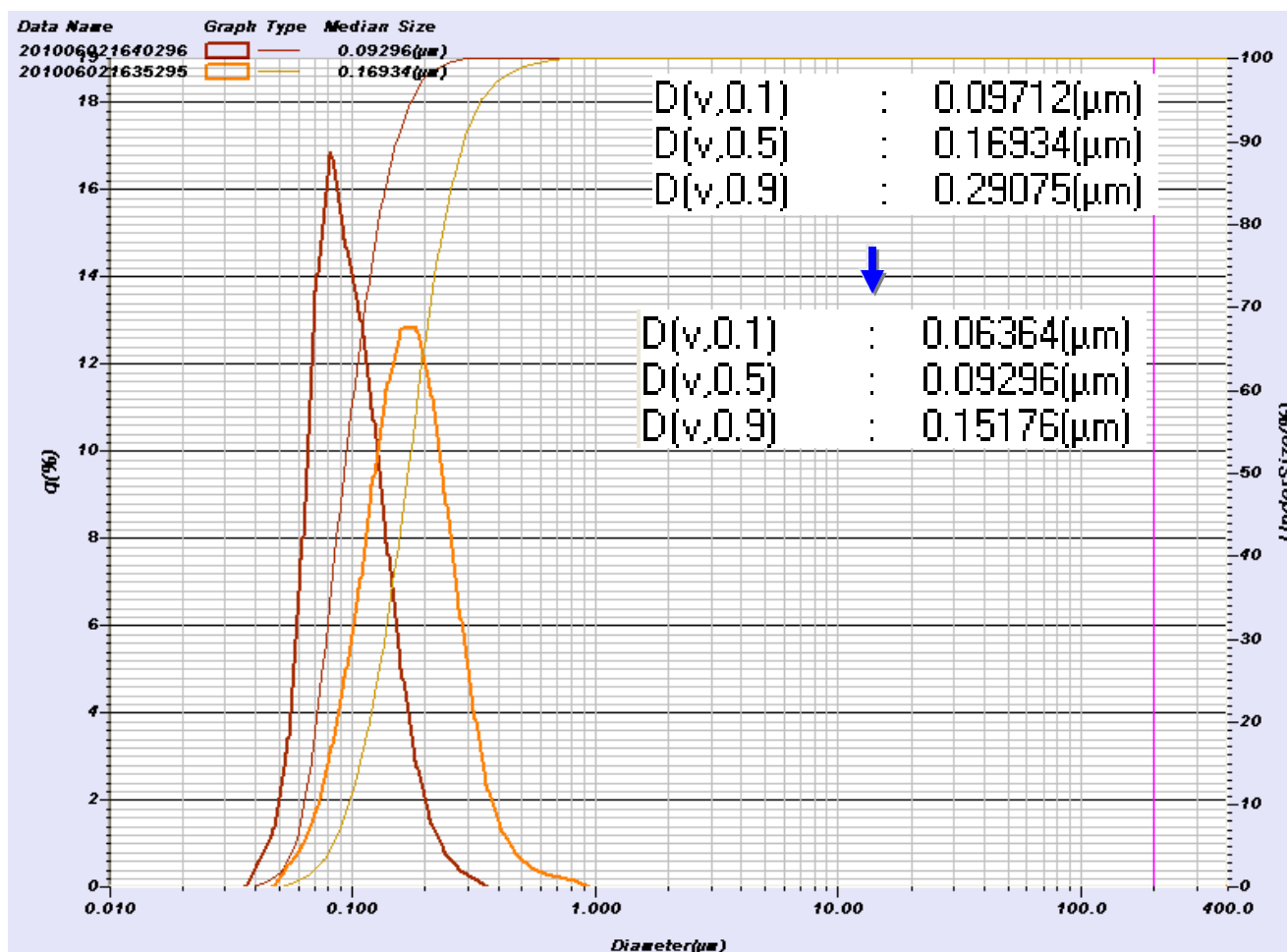
Liposome: Processed by Microfluidizer

Measured on LA-950



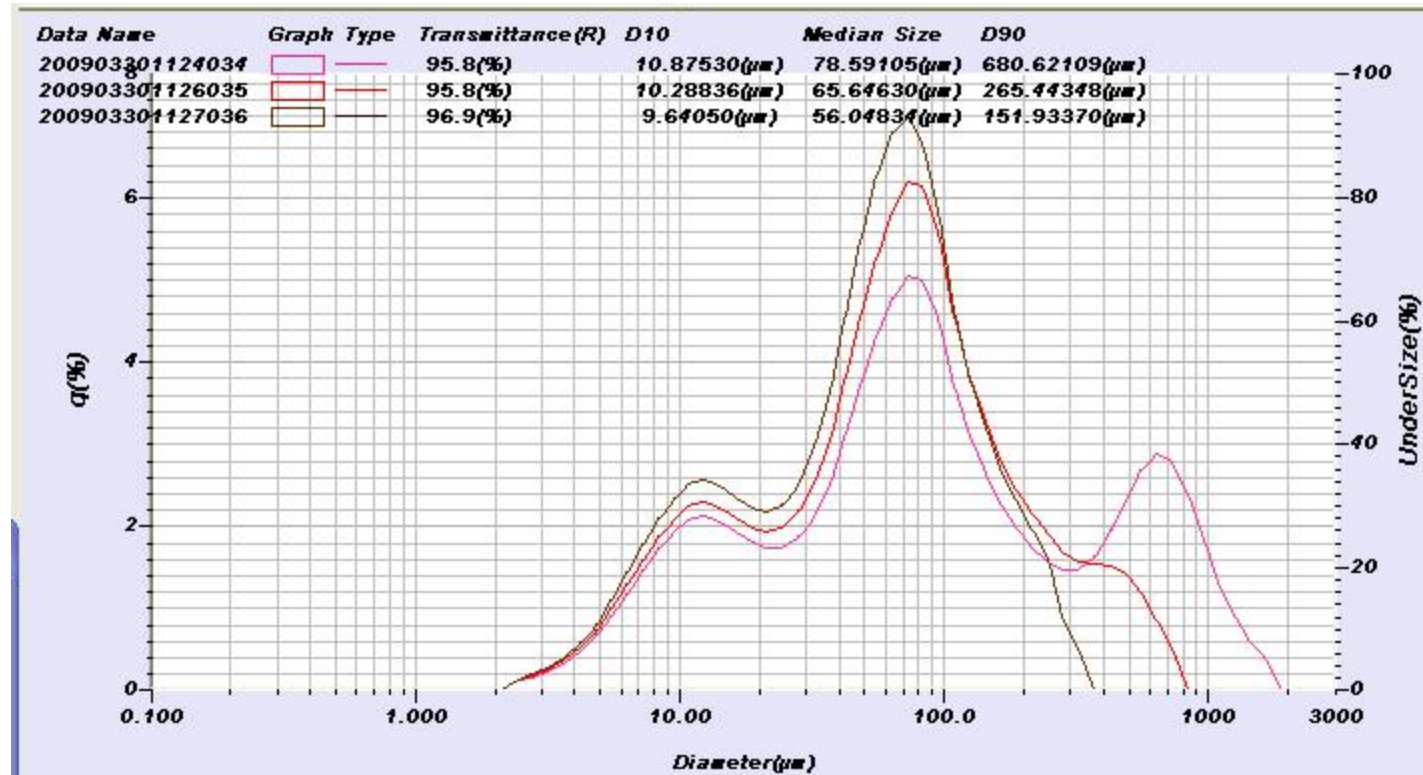
Liposome: Before, After

Measured on LA-950



Not Always Small Particles

Dry Powder Feeder: API



Laser Diffraction

- Most popular method
 - Wide dynamic range, wet and dry, automation
- LA-950 unique ability to measure 30 nm – 3000 μm
- Unique Method Expert software
- Unique USP & ISO calculations
- Best small particle detection, smallest sample volume requirements



Summary

- Microfluidics excels at particle size reduction technology
 - No other technology generates such small, narrow distributions
- HORIBA LA-950 excels at analyzing particles in this size range
 - Highest sensitivity, smallest sample volume
- Microfluidics and HORIBA have been partners for > 15 years
- Thanks for your attention

To Learn More

www.microfluidicscorp.com

www.horiba.com/us/particle



Microfluidics

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MICROFLUIDIZER PROCESSORS WHAT WE DO APPLICATIONS SERVICES WHY MICROFLUIDICS? RESOURCES ABOUT

Tiny Particles, Big Results

Microfluidizer® high shear fluid processors are the gold standard in nano-enabled applications for uniform particle size reduction, cell disruption and bottom-up nanoparticle creation - with scaleup guaranteed. Discover why 17 of the top 20 global pharmaceutical companies innovate with Microfluidics technology.

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Microfluidics Proof of Concept Testing Improves Customer Product Quality and Scaleup Efficiency by Optimizing Nanomaterial Processing

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Microfluidics is in business to help our customers change the world. Make the most of your processor with value-added services and incentive programs. [Explore Offerings](#)

M-110P BENCHTOP MODEL IMPROVED

With simplified usage controls, cooler operation, and reduced weight and noise, the new M-110P is setting gold standards all over again.

UPDATED! UPCOMING WEBINARS

Our educational Webinar Series continues with particle size reduction and characterization, customer case studies and chemical industry applications. [Register today](#) or access the archive.

ACADEMIC RESEARCH COLLABORATION (ARC)

New university program makes cutting-edge nanomaterials processing equipment more accessible and valuable for academic research. See the [innovation incentives](#)



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Particle Characterization

Home > Scientific > Products > Particle Characterization

Particle Characterization

HORIBA designs, manufactures, and supplies state of the art particle characterization instruments.

Every instrument across the five business segments must meet stringent requirements before the HORIBA name is attached. The Particle Characterization group of analyzers has incorporated this principle into each new design since entering the business in 1979. Relentless innovation united with high performance to attain the ultimate goal: a new standard in usability.

Particle Characterization Products

HORIBA offers instruments for particle size, particle shape, zeta potential, and surface area analysis. Measurable particle size range is from 1 nanometer to 30 millimeters, at concentrations ranging from 1 ppm to 50 vol% with shape determination available starting at 1 micrometer. A range of analytical techniques are employed including laser diffraction (Mie Theory), dynamic light scattering, acoustic and electroacoustic spectroscopy, and dynamic and static image analysis. (measuring both particle size and shape information).

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