



Breakthrough in Nanoparticle Tracking Analysis (NTA)

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Outline



Background

Technology overview

Validation results

Product details

Established Technologies



- Dynamic Light Scattering (DLS)
- Nanoparticle Tracking Analysis (NTA)
- Transmission Electron Microscopy (TEM)
- Flow Cytometry (FC)

Unmet Needs



- Visualization of polydisperse particles
- Accurate & reproducible measurement of:
 - Particle number concentration
 - Particle size distribution
 - Particle kinetic processes

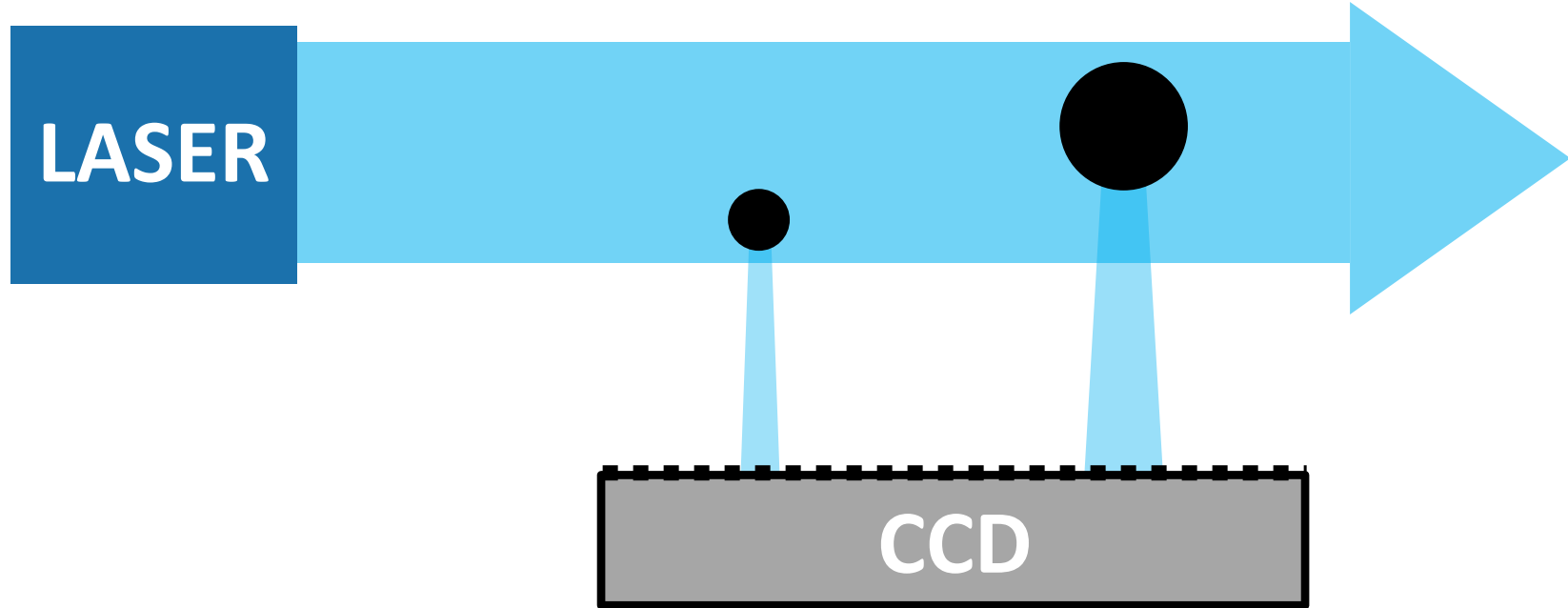
Technology



Light Scattering 101

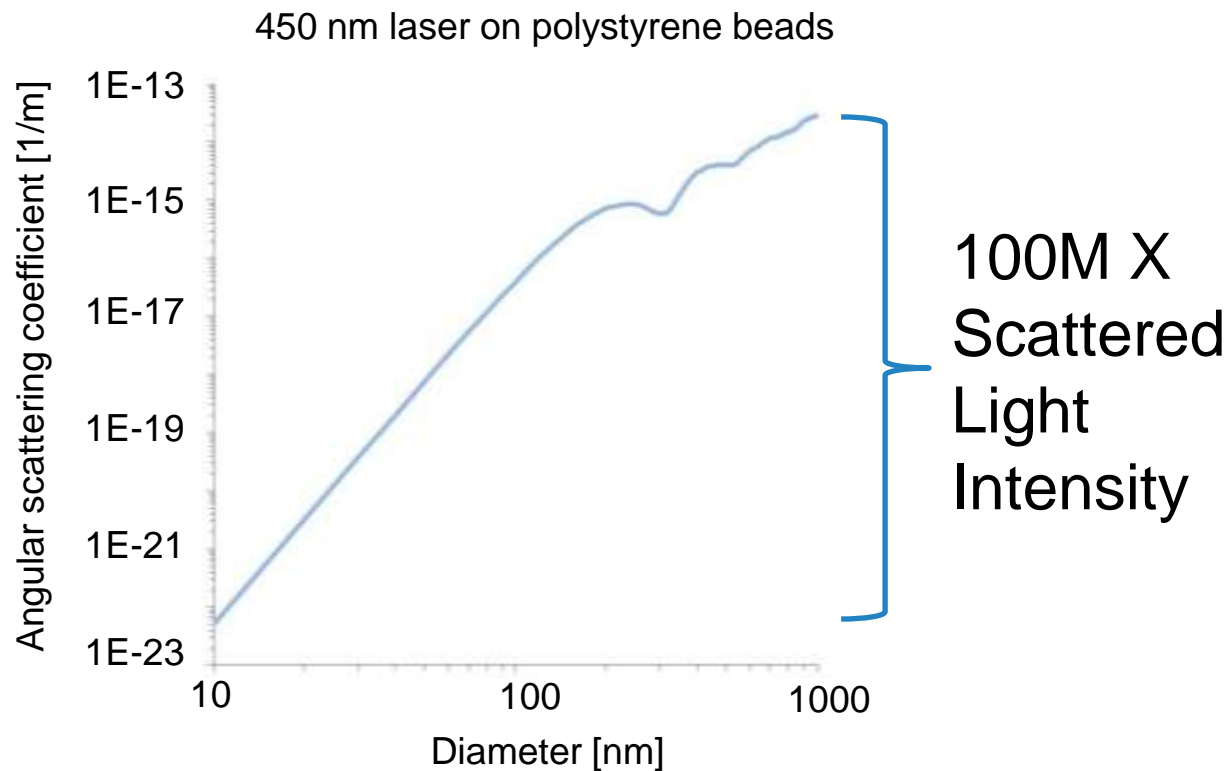


In Brownian motion, particle movements are related to their size:



& movements are measured by tracking scattered light in videos

Problem



Problem & Effects



100M X Scattered Light Intensity

- DLS – large particles skew results
- NTA – different sized particles co-existing can't be seen

Problem is Well Known



INTERNATIONAL
STANDARD

ISO
19430

Particle size analysis — Particle tracking analysis (PTA) method

“Sample polydispersity affects the ability to track and therefore analyse different size fractions in the particle number-size distribution. ... In a polydisperse sample large particles scatter a lot more than small particles making it difficult to detect or track small size particles.”

Reference Customer



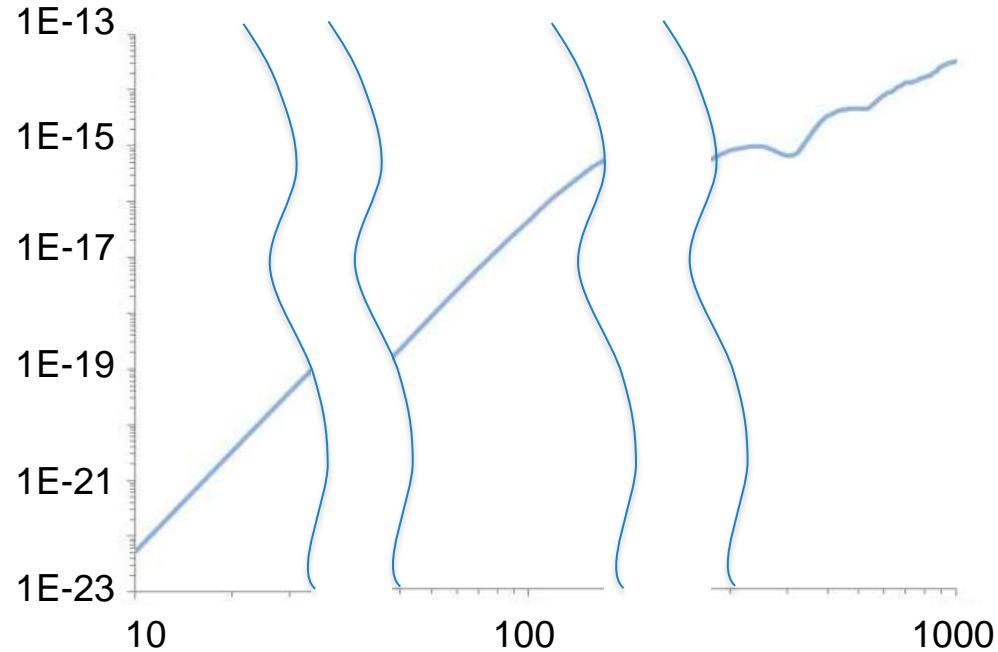
Dr. Sadik Eisner,

Director, OHSU's Center for Early Cancer Detection Research

“In our tests leading up to the purchase of our ViewSizer™ 3000, **we confirmed this easy to use bench top instrument meets all our needs for visualizing, sizing and counting nanoparticles** such as live viruses, exosomes, silver, RNA, and YAG”

“The ViewSizer™ 3000 is **the first product we've found that can effectively characterize particles in polydisperse samples** and its unmatched visualization of all particles, even in complex samples, removes elements of mystery associated with other methods.”

The Solution

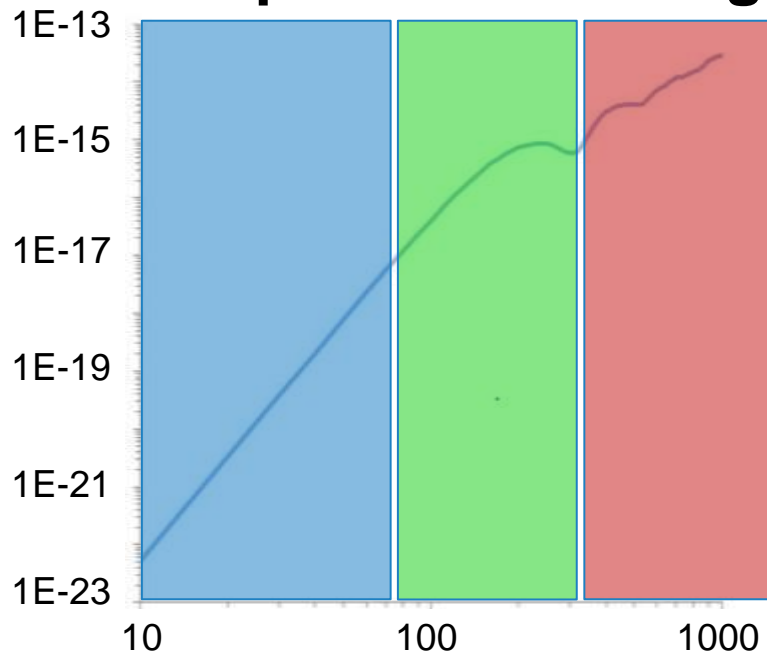


Break the problem into manageable segments

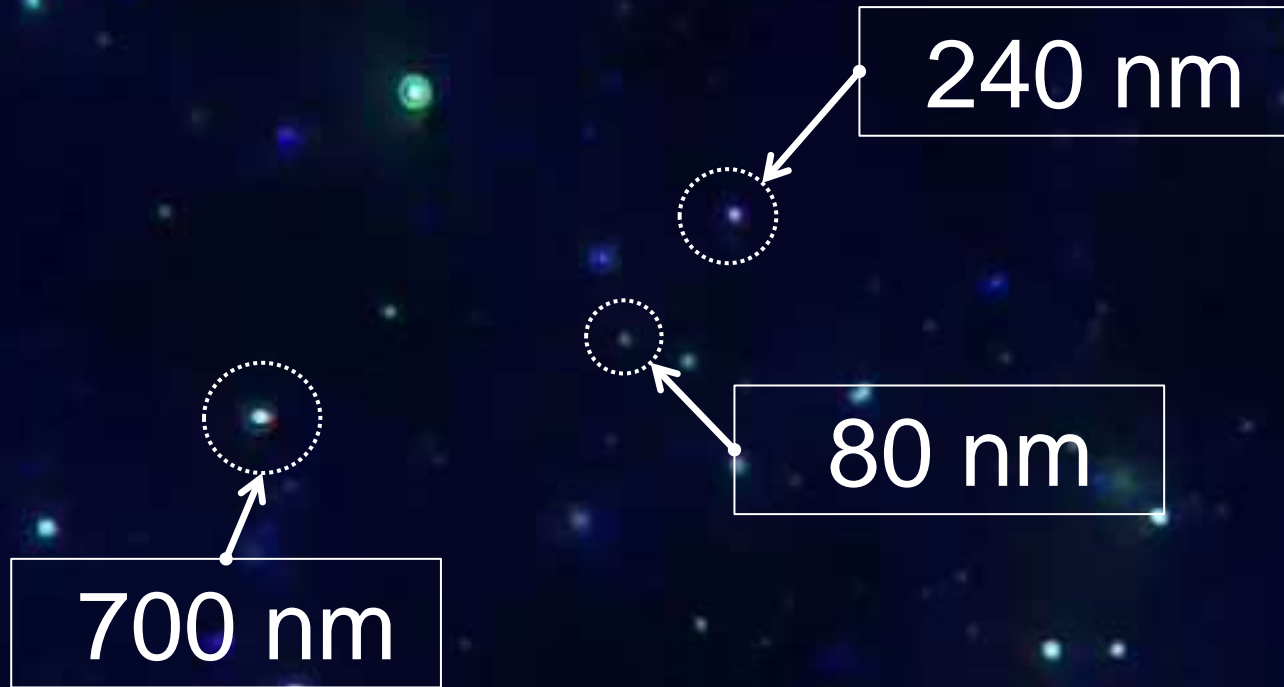
The MANTA Solution



(Most Advanced Nanoparticle Tracking Analysis)



Simultaneous Multispectral Particle Analysis



MANTA can measure a wide range of nanoparticle sizes simultaneously

Customer Comments



“Wow, I can see all my particles!”

“Amazing, I didn’t think this was possible!”

“Oh my god, I love this!”

“I can’t do my research without MANTA.”

“Our other instruments can’t do this.”

“Are you sure that’s the right price?”

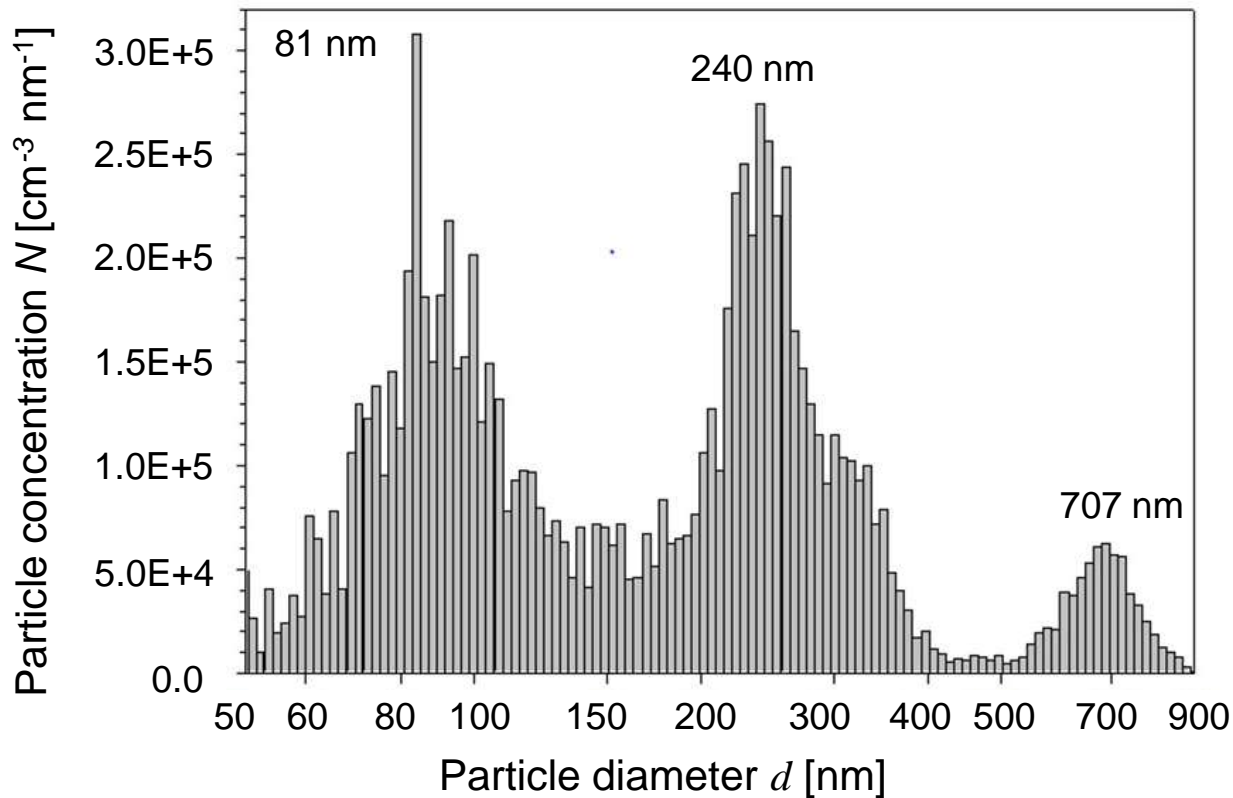
Validation



Polydisperse: resolution



Standard
Polystyrene
Beads



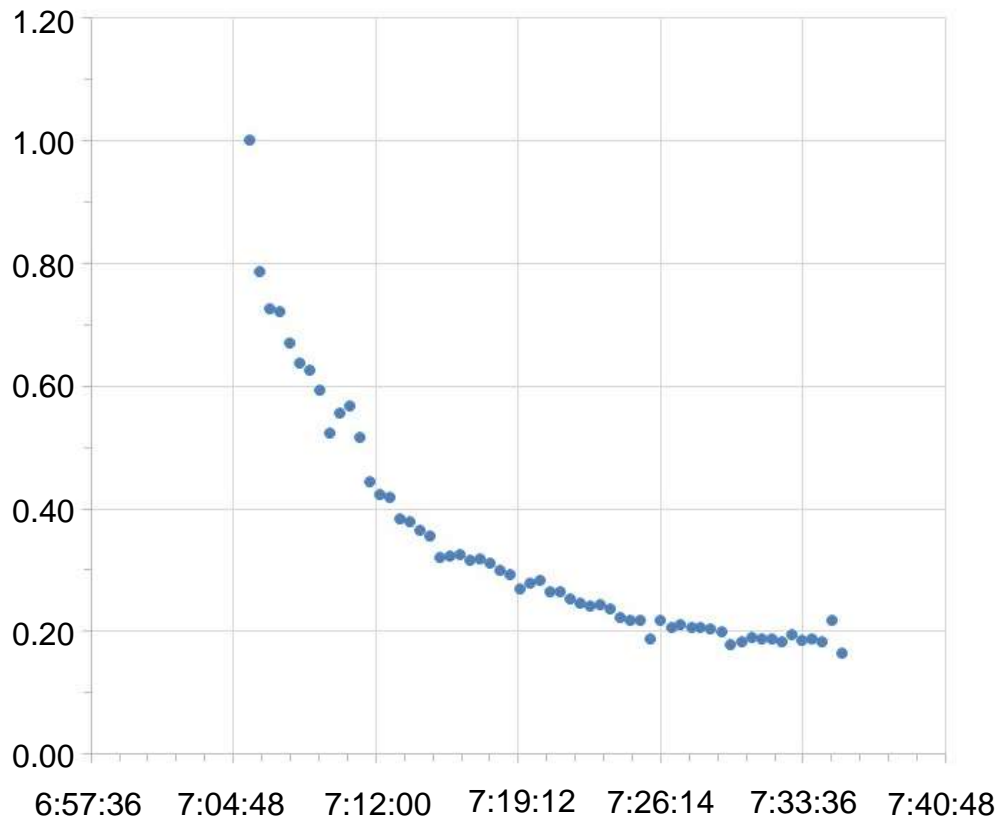


Visualization and measurement of nanoparticle dissolution rates

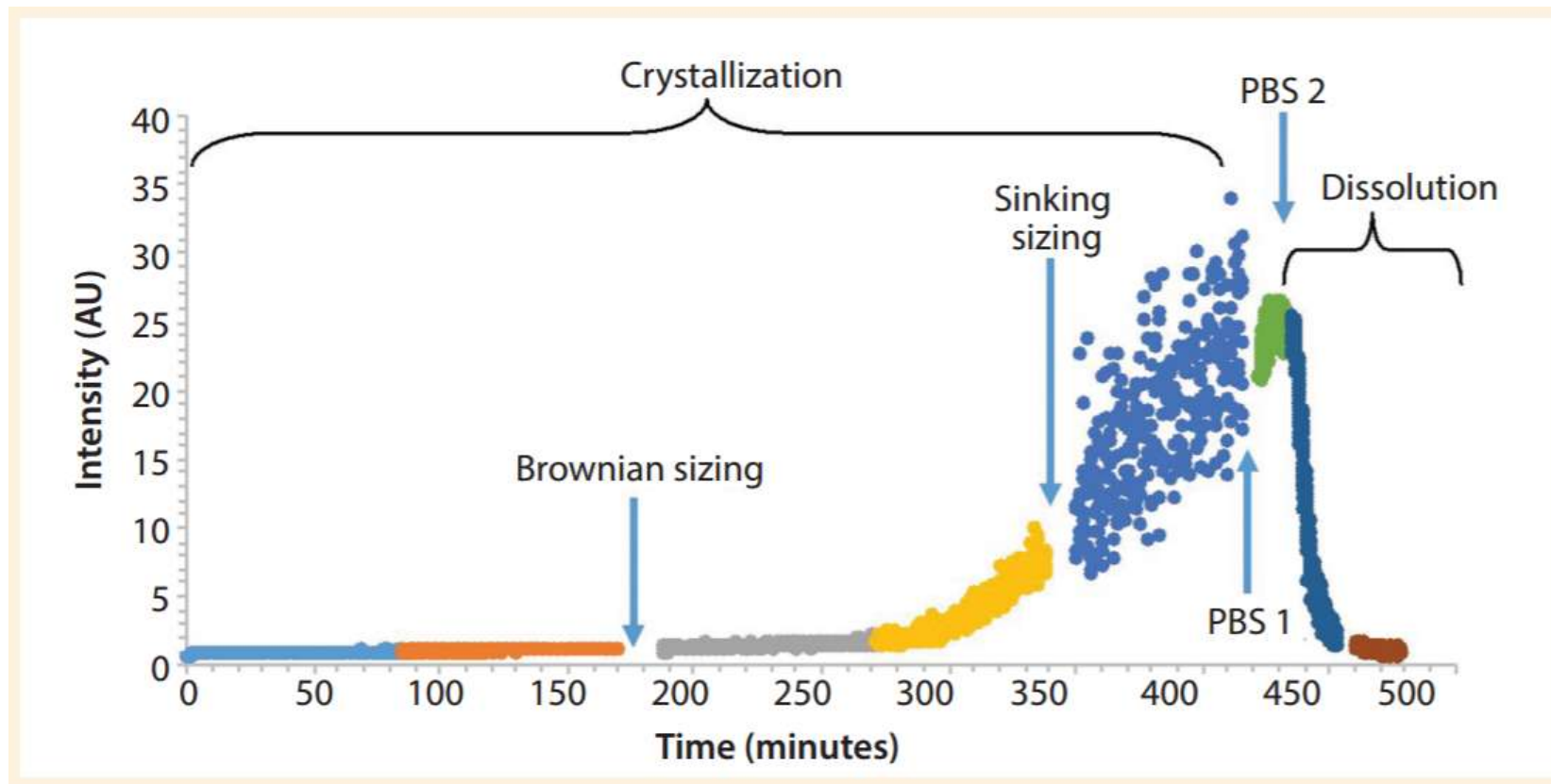
Nanoparticle Dissolution Rate



Scattered
Light
Intensity



Crystallization & Dissolution Rates



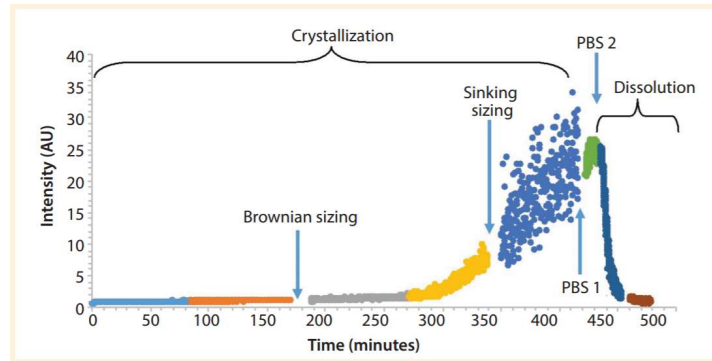
Recent Publication

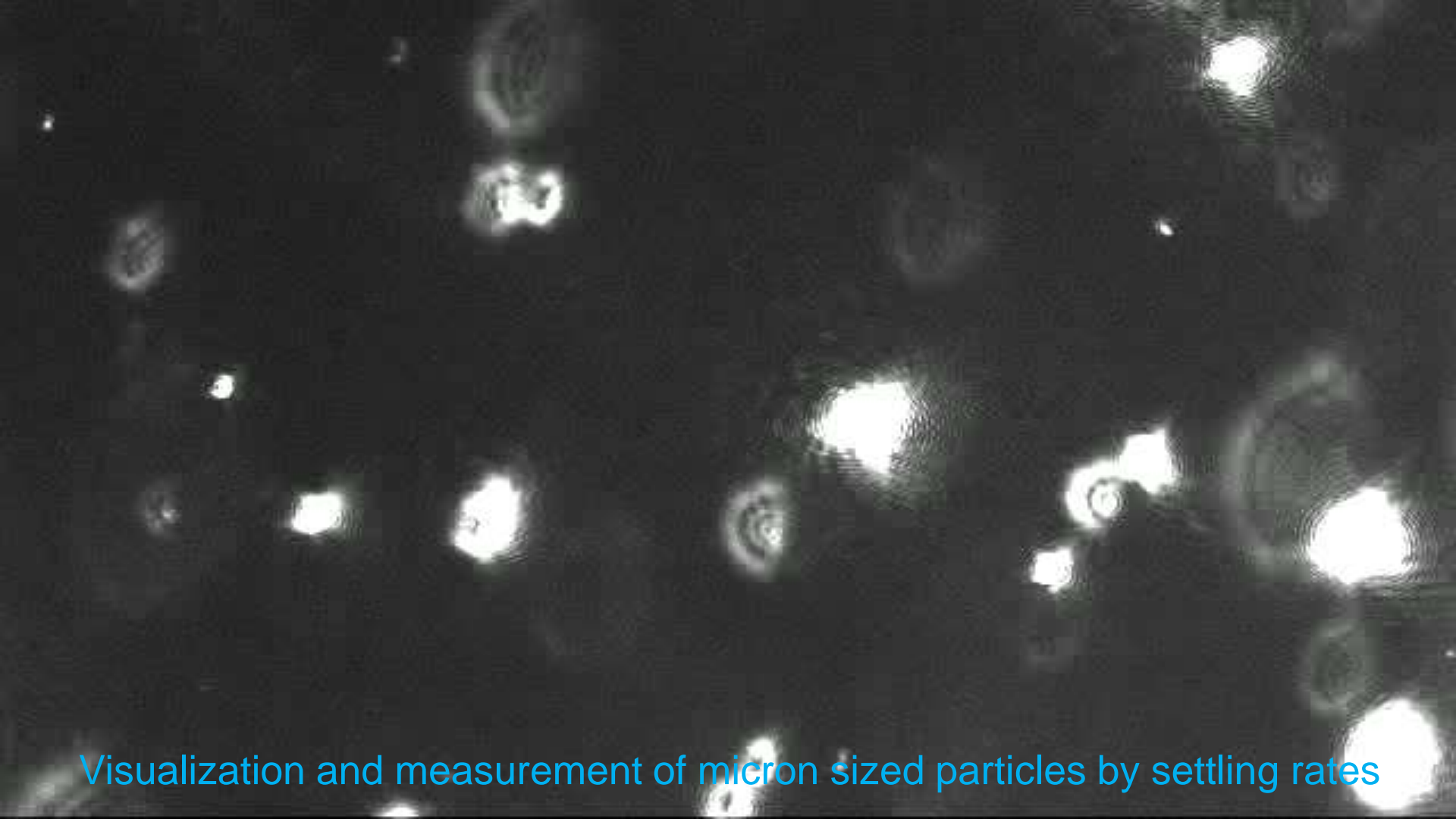


“Biological Characterization Using Protein Crystal Measurements”

BioProcess International March Issue

<http://www.bioprocessintl.com/>

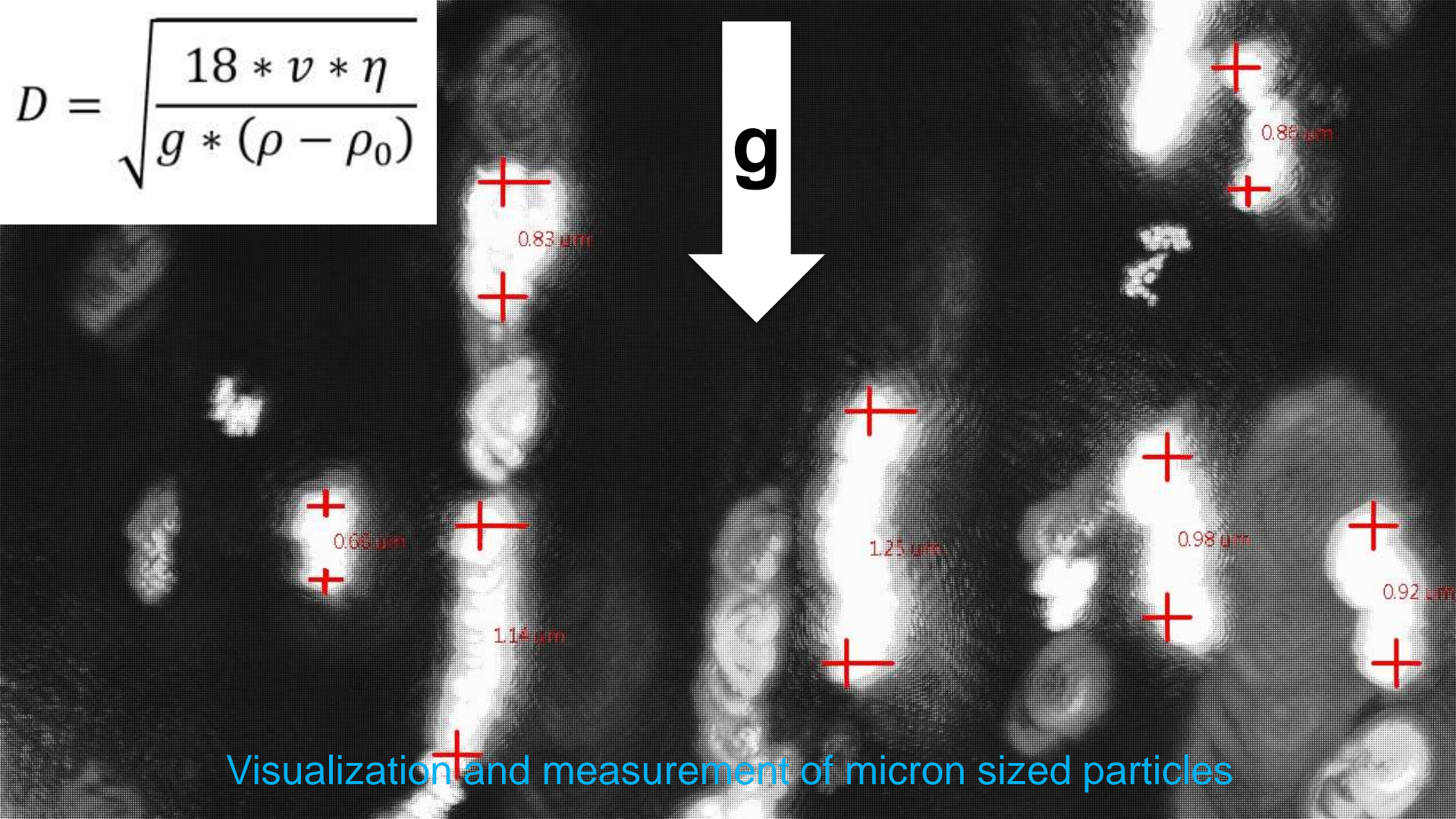




Visualization and measurement of micron sized particles by settling rates

$$D = \sqrt{\frac{18 * v * \eta}{g * (\rho - \rho_0)}}$$

g



Visualization and measurement of micron sized particles

Protein Aggregates are Important



ELSEVIER

Contents lists available at [ScienceDirect](#)

Journal of Pharmaceutical Sciences

journal homepage: www.jpharmsci.org



Rapid Communication

Subvisible Particle Content, Formulation, and Dose of an Erythropoietin Peptide Mimetic Product Are Associated With Severe Adverse Postmarketing Events



Joseph Kotarek ¹, Christine Stuart ¹, Silvia H. De Paoli ¹, Jan Simak ¹, Tsai-Lien Lin ², Yamei Gao ³, Mikhail Ovanosov ¹, Yideng Liang ¹, Dorothy Scott ¹, Janice Brown ⁴, Yun Bai ⁵, Dean D. Metcalfe ⁵, Ewa Marszal ^{1,*}, Jack A. Ragheb ^{6,*}

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³ Office of Vaccines Research and Review, [Center for Biologics Evaluation and Research, US Food and Drug Administration](#), Silver Spring, Maryland 20993

⁴ Office of New Drug Quality Assessment, [Center for Drug Evaluation and Research, US Food and Drug Administration](#), Silver Spring, Maryland 20993

⁵ National Institute of Allergy and Infectious Diseases, [National Institutes of Health](#), Bethesda, Maryland 20892

⁶ Office of Biotechnology Products, [Center for Drug Evaluation and Research, US Food and Drug Administration](#), Silver Spring, Maryland 20993

Visualization of Protein Aggregates

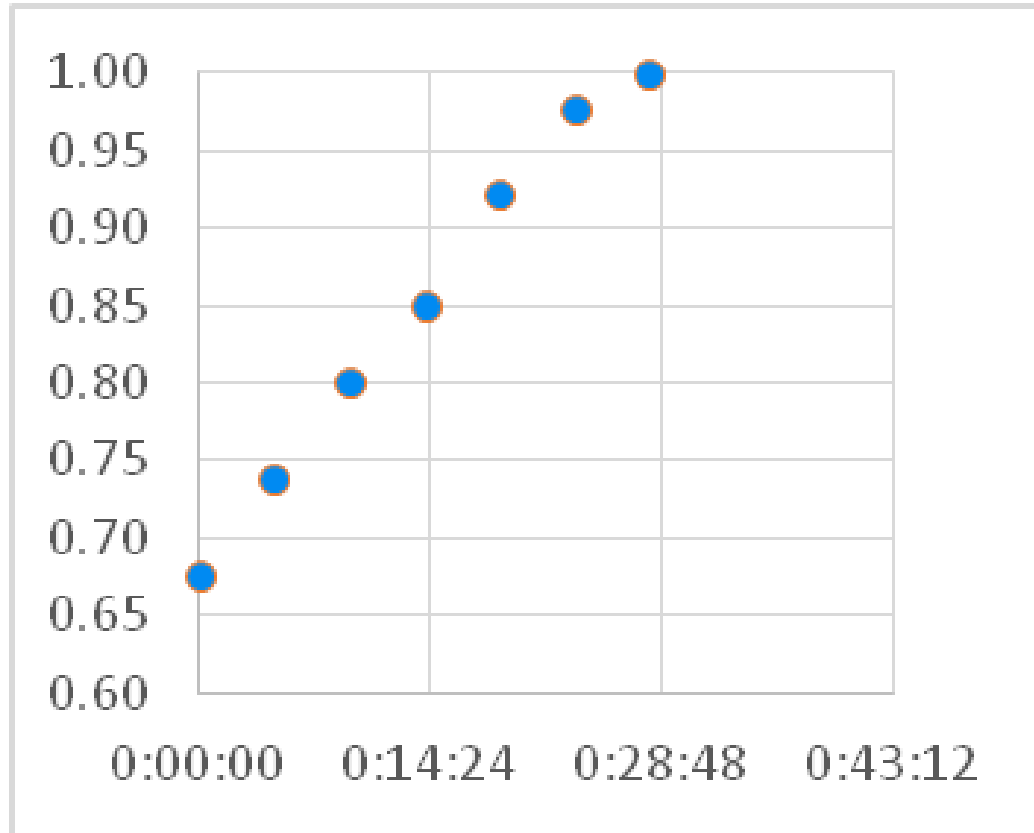


“If the proteins aggregate in your biologic and you can’t visualize them, do they still aggregate?”

Monitoring Protein Aggregation



Scattered
Light
Intensity



Successfully Tested Samples



polystyrene w/ and w/o PEG coating, silica, silver, 316L stainless, gold, sand, CaO, YAG, SiO₂, carbon, PMMA

sea water, rain water, tap water, wine, urine, blood plasma, milk, ammonia

small molecule APIs, protein aggregates, silicon oil, protein crystals, liposomes, exosomes, vesicles, micelles, lactalbumin, RNA, rolled DNA, viruses, emulsions, polymeric API carriers, bacteriophages, self-adjuvanted protein

$\Sigma = 36$ as of March 2017

Product



Introducing



MANTA ViewSizer™ 3000 INSTRUMENTS



ViewSizer™ 3000



- Elegant technology
 - Only 3 inputs needed
 - Sample (in a cuvette)
 - Temperature (controlled to customer's set point)
 - Viscosity (from literature, or measured by ViewSizer™)
- Absolute method, no calibration standards req'd

Specifications



Range of Particle Sizes Measured *	10 nm to 15 μ m
Minimum Sample Volume	0.4 mL
Typical Sample Concentration	5×10^6 to 2×10^8 particles/mL
Sample Temperature Range (Controlled)	5 °C to 50 °C, +/- 0.1 °C (-15 °C to 110 °C available)
Dimensions	55 cm W x 66 cm D x 35 cm H
Weight	27 kg
Operational Environment	15 °C to 30 °C with < 85% RH

* Sample dependent

Competition



Customer Requirements

DLS

NTA



Particle Visualization



Particle Concentration



Particle Size Distribution



Particle Kinetic Processes



Summary



Breakthrough technology

New & better particle characterization

Happy customers & partners

Stronger Together



HORIBA





Thank You

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