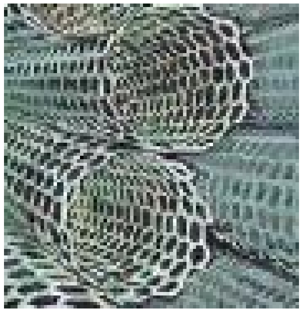
Agilent Technologies

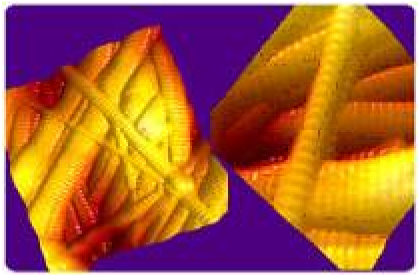
Metrology Needs for Nano-EHS

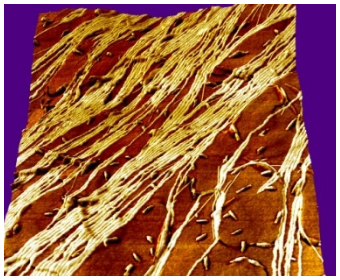
An Instrument Manufacturers Perspective

Prepared for

Nanoparticle Air Monitoring Workshop







Presented by:

Craig Wall Ph.D.
Product Manager – Agilent AFM,
Nanomeasurements Division

March 2-3, 2009

Perspective as an instrument manufacturer of metrology and characterization equipment

1- What should I measure (geometry, chemical composition/reactivity, isomers/chirality, physical properties) that is relevant to addressing nano-EHS needs

2- What standards should I use to calibrate my instruments and compare results

3- What models are appropriate for in vitro and in vivo diagnostics and how do they relate to question #1

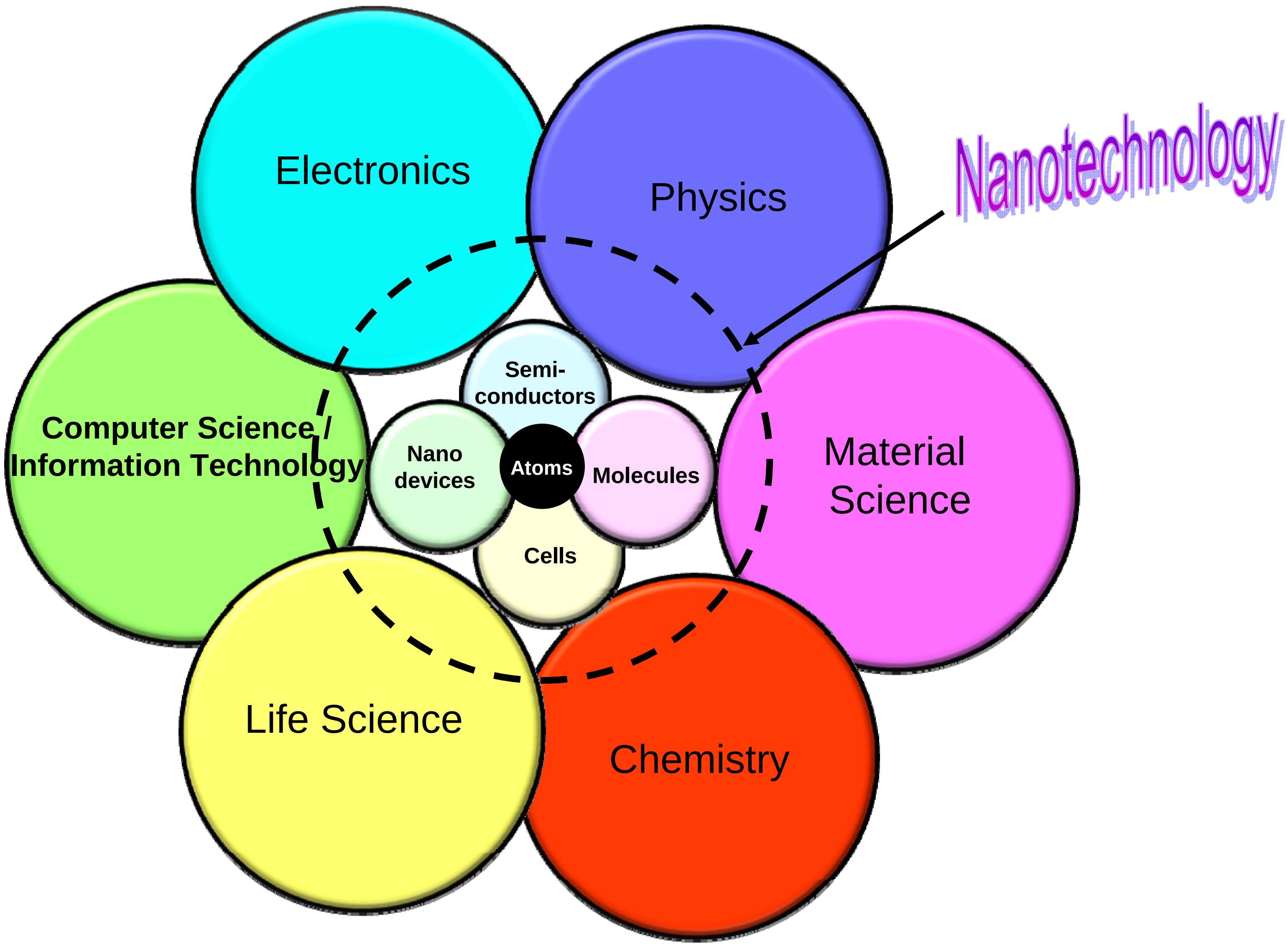
4- Because of the nano-nature of the materials what are relevant dosimetry/workplace exposure monitoring methods

5- What models are appropriate for product life cycle/product use with respect to consumer exposure and how do they relate to questions #1-3

Answering these questions will allow Agilent and other instrument manufacturers to provide a necessary link in the nano-EHS chain.

The ability to precisely measure and predict the effects of nanomaterials on the safety, health, and the environment at the subnanoscale and molecular scale will ensure human safety and enhance quality of life.

Nanotechnology – Spanning the Disciplines



Nanomaterials in the workplace

Nano-particles & organic contaminants

- adsorption, concentration, facilitated transport

Nano-particles & toxic metals

- adsorption, concentration, facilitated transport

Nano-particles & Acids and bases

- surface hydroxylation/activation

Adsorbed organics & adsorbed metals

- complexation, retention of contaminants

Nano-pores & trace level toxic volatiles

- Kelvin effect, pore condensation

Nanomaterials in the News

To see whether nanotubes mimic asbestos' toxicological behavior, Donaldson's team injected 50 µg of MWNTs into the abdominal cavity of mice and observed their effect on the mesothelial layer of cells that line the cavity.

They found that when MWNTs were straight and longer than 20 µm, they caused the same type of inflammation and granuloma, or scar formation, as asbestos. The response is predictive of mesothelioma, Donaldson says, although no such cancer was observed in this study. In contrast, shorter MWNTs, tangled nanotube aggregates, and nanoparticulate carbon black didn't cause any inflammation or granuloma formation, further indicating that the toxicity is a function of size and shape, not chemistry (Nat. Nanotechnol., DOI: 10.1038/nnano.2008.111).

Chemical & Engineering News May 26, 2008 Volume 86, Number 21 p. 9

Nanomaterials in the News

Alderson and other speakers at the conference noted that a major problem FDA and other regulatory agencies have is that these nanomaterials have different toxicity characteristics than the same chemical composition has in bulk forms. This is changing the paradigm for how toxicity is measured, according to several speakers. For nanomaterials, it is not only the mass of the dose that determines the toxicity, but also probably the surface area of the particles, the particles' surface charges, and even their solubility, the speakers explained.

These differences are not just theoretical, Scott E. McNeil said at the conference. McNeil, director of the Nanotechnology Characterization Laboratory for the National Cancer Institute, said his group is studying nanomaterials that might be used against cancers because of their interesting surface chemistry and the multifunctional capabilities of multiple surface charges on particles.

There is still much to learn about how these nanoparticles react, McNeil said. "It is a daily occurrence in our labs that one of our standard assays doesn't work because of the unusual properties of these materials."

This unusual behavior is one of FDA's concerns because the agency relies on bioassays to determine a product's safety, Alderson said. One of FDA's major questions is about the biocompatibility of nanomaterials and whether the in vitro and in vivo tests the agency relies on will remain valid.

Chemical & Engineering News March 17, 2008 Volume 86, Number 11 pp. 32-34

Capabilities and Barriers

Individual Particle Techniques

Microscopy
(SPM, SEM, TEM)

Nanoprobe (multi-probe)

EDS, WDS

Electron Diffraction

Ensemble Techniques

Photon based Spectroscopy
(FT-IR, RAMAN, NMR)

X-ray
(scattering, spectroscopy)

Mass Spectrometry

Reverse Chromatrography

Metrology Standards

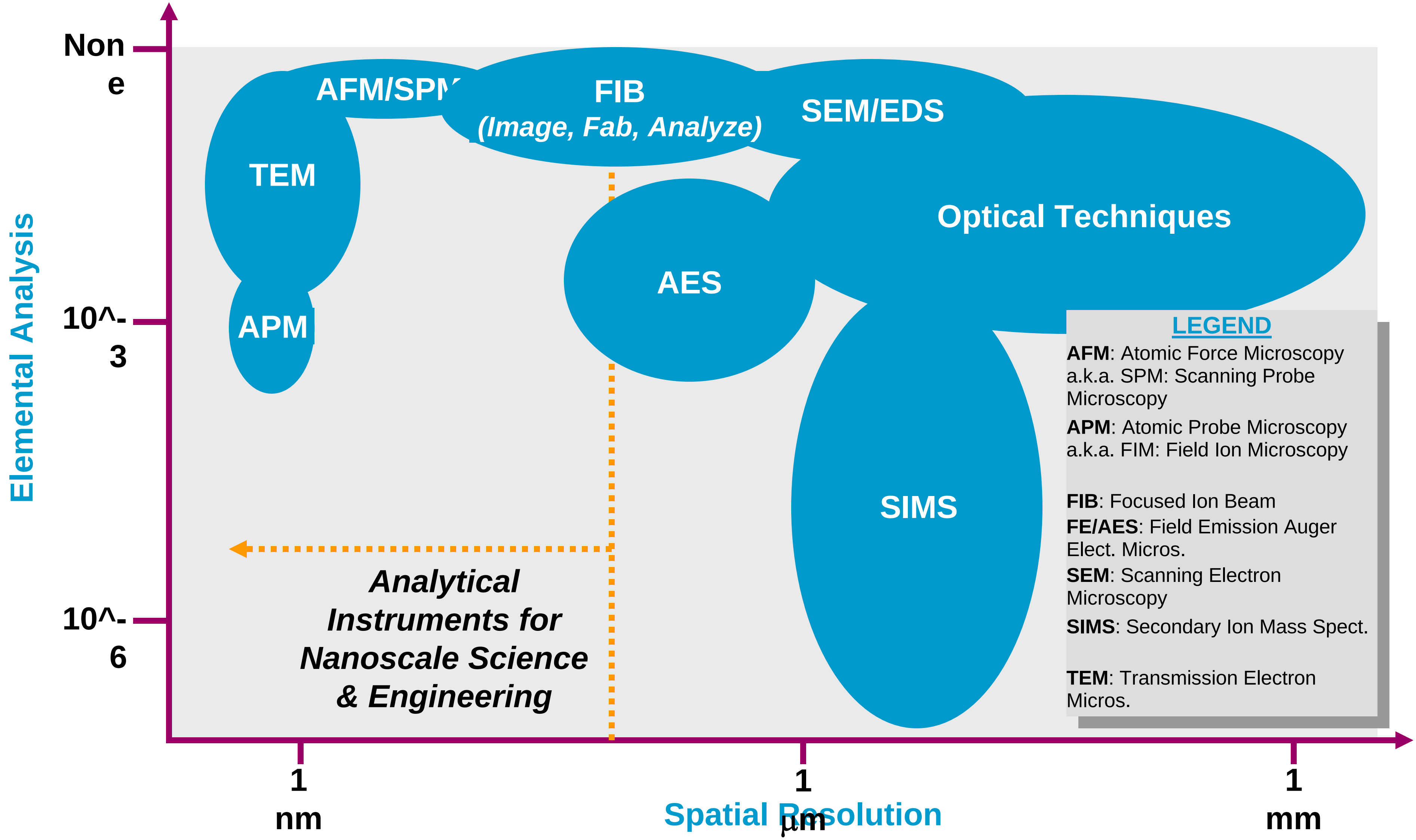
3-DCharacterization Standards

Dispersion and Distribution

Interfacial Interactions

Interphase Properites

The Nano-Analytical Tool Universe

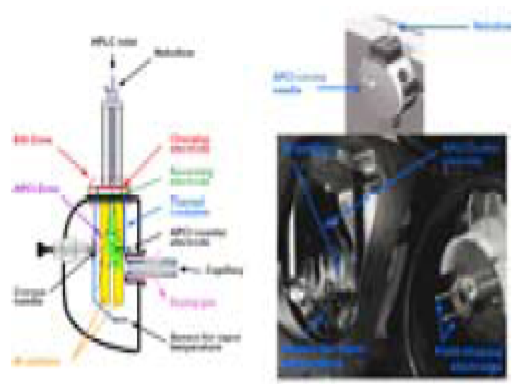


Source: Modified from Charles Evans & Associates, Analytical Resolution versus sensitivity diagram.

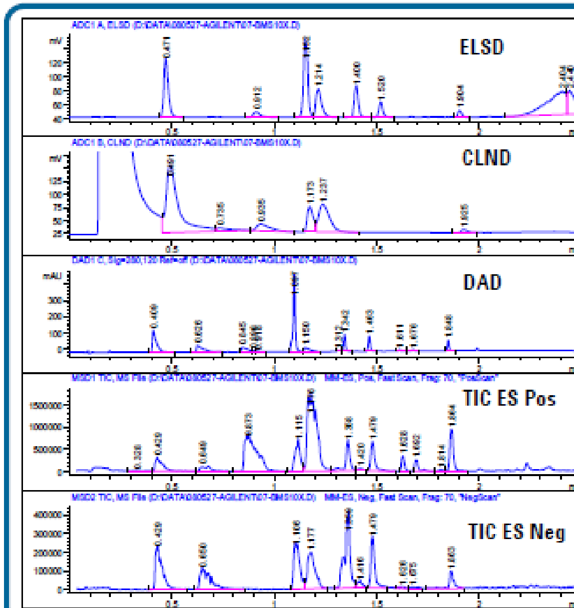
LC-MS Techniques for coated particles

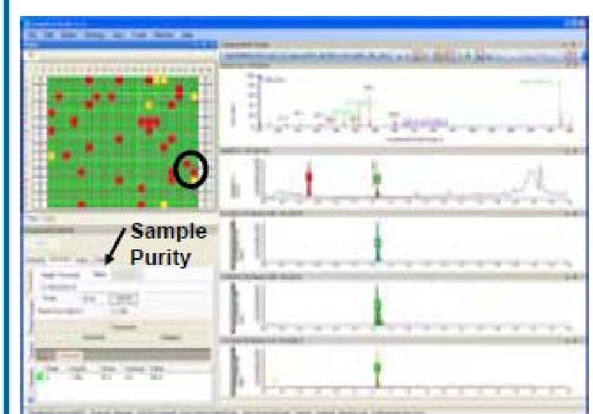
LC/DAD/CLND/ELSD/MS System

The Multimode Source Design

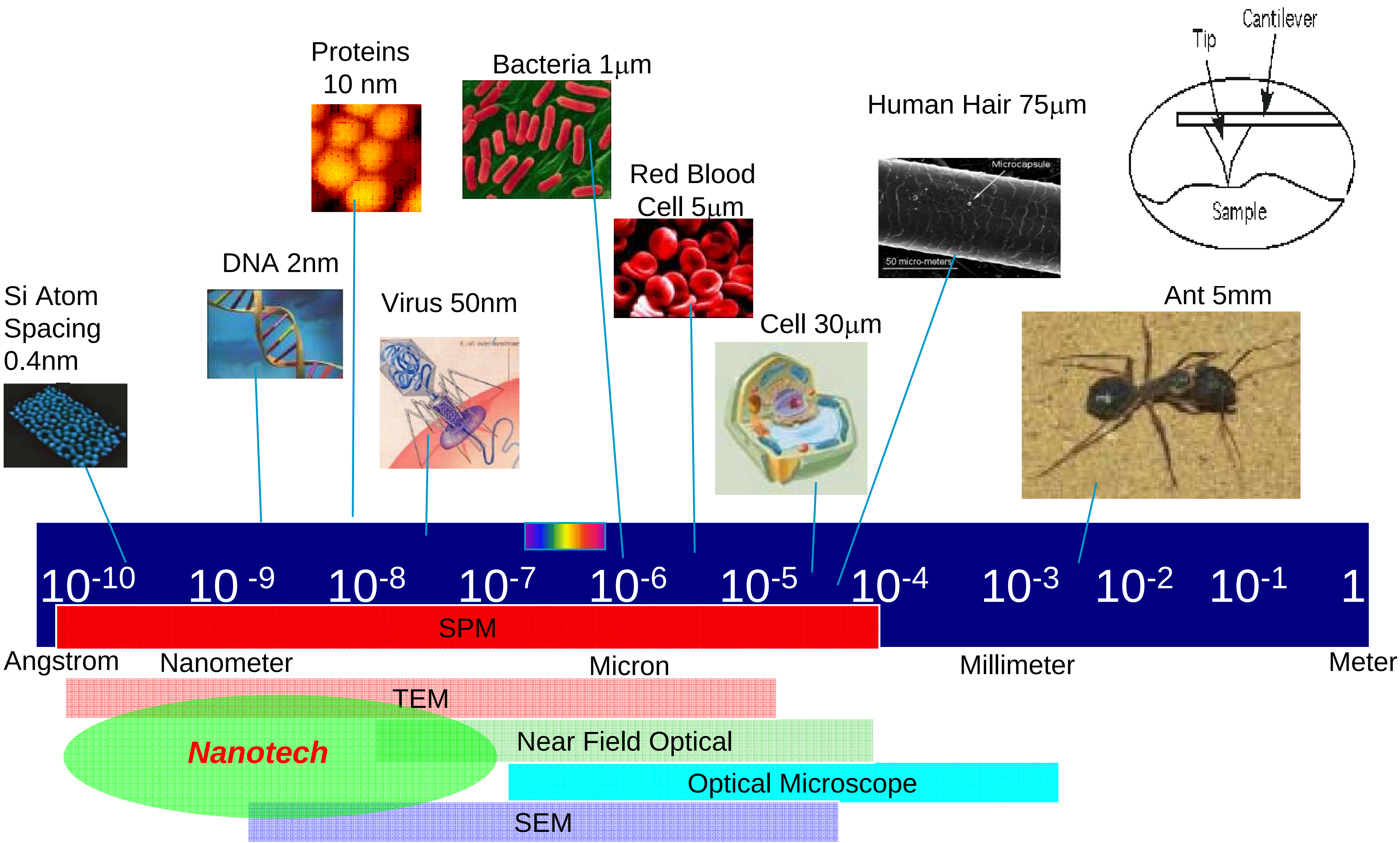


Fast Chromatography for Evaluaton Mixture

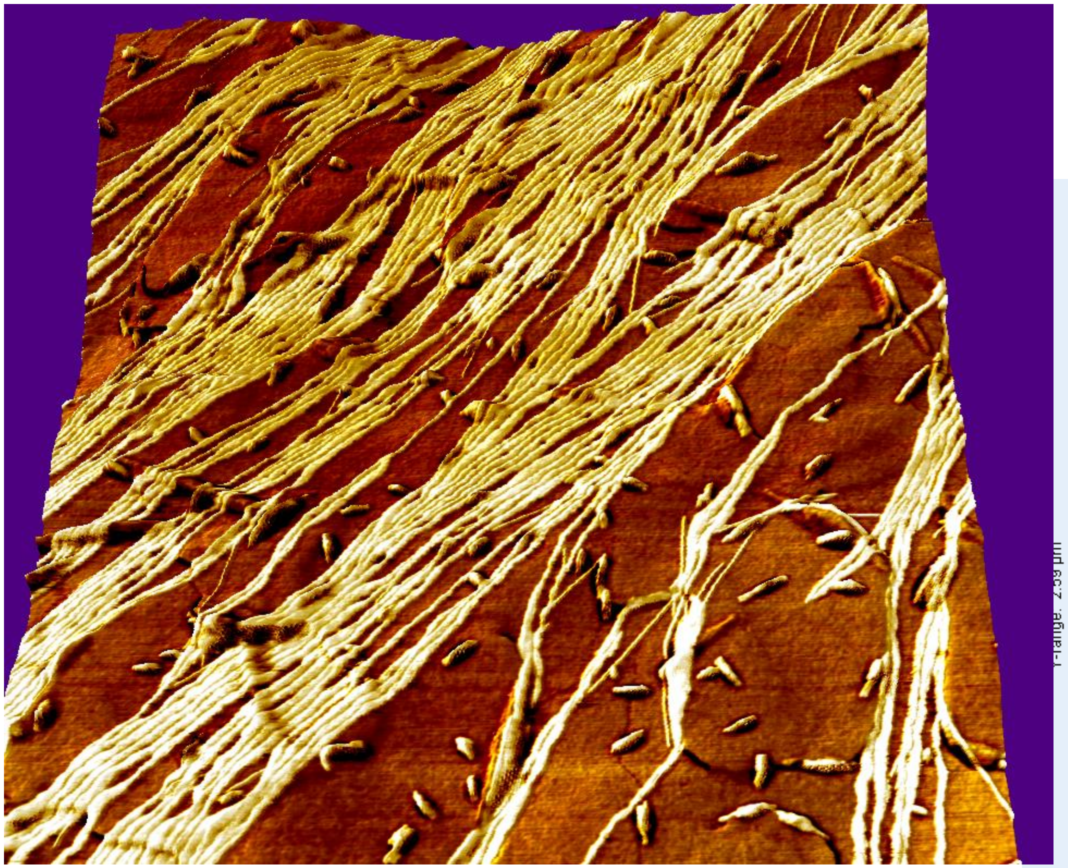




Imaging Techniques: Scales

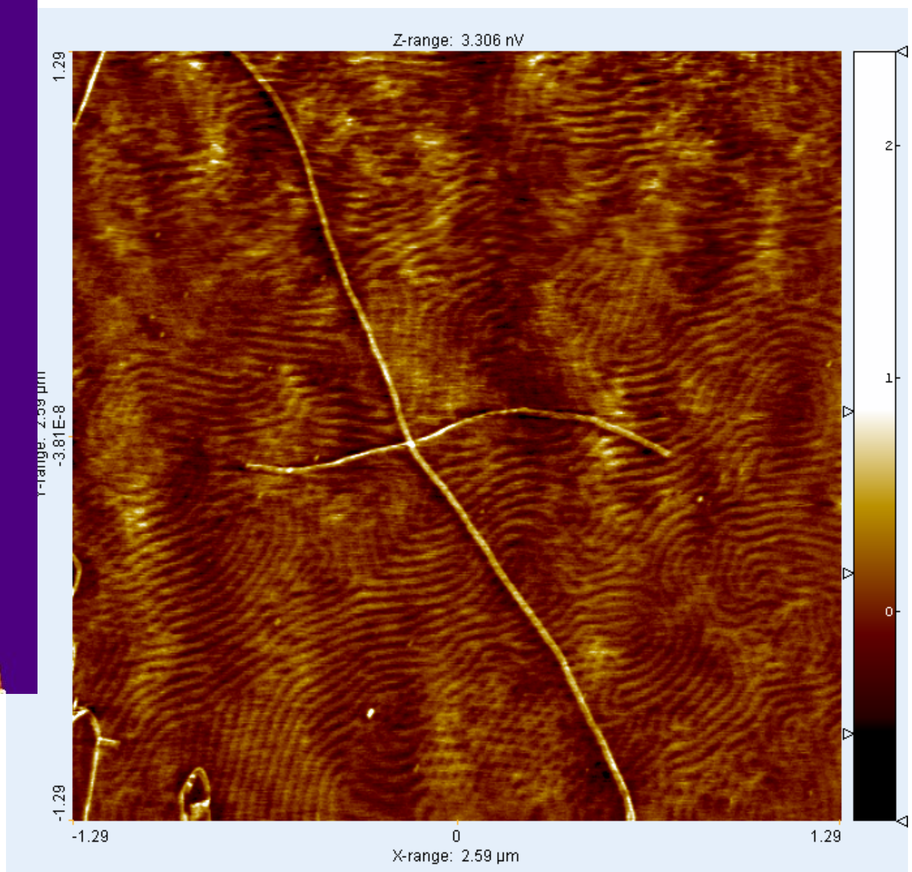


SPM Microscopy



SWCNT Cast From Solution

70:30 Reactively blended SEBS:PP



NMR and RAMAN Spectroscopy

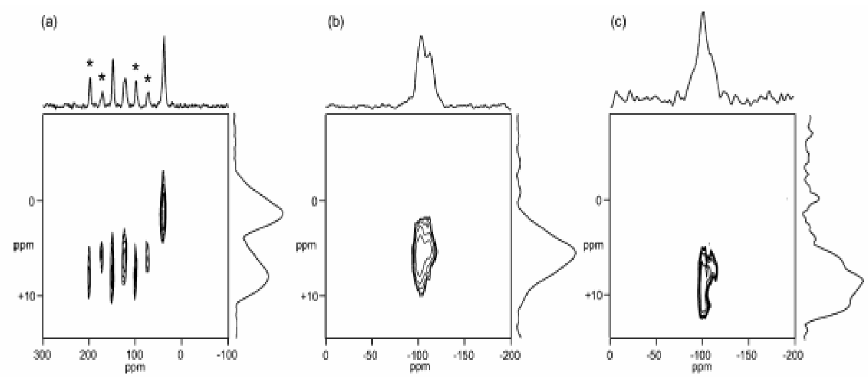


Figure 6. (a) Part of a WIM-24 high-resolution proton−carbon-13 correlation spectrum of the P4VP/silica nanocomposite recorded with the parameters described in the text and carbon-13 (top) and proton (right) skyline projections. Spinning sidebands are marked in the carbon-13 projection with asterisks. (b) Part of a LG-CP high-resolution proton−silicon-29 correlation spectrum of the dried pristine Nyacol silica sol recorded with the parameters described in the text and silicon-29 (top) and proton (right) skyline projections. (c) As for part b but for the P4VP/silica nanocomposite recorded with the parameters described in the text and silicon-29 (top) and proton (right) skyline projections.

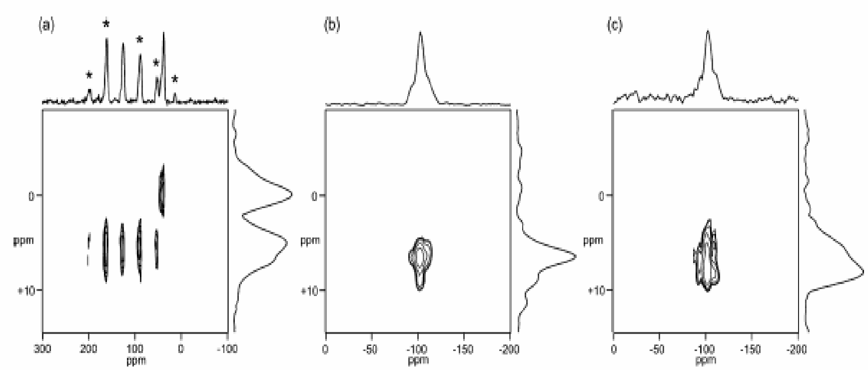


Figure 7. (a) As for Figure 6a but for the PS/silica nanocomposite. (b) As for Figure 6b but for the dried pristine IPA-ST sol. (c) As for Figure 6c but for the PS/silica nanocomposite.

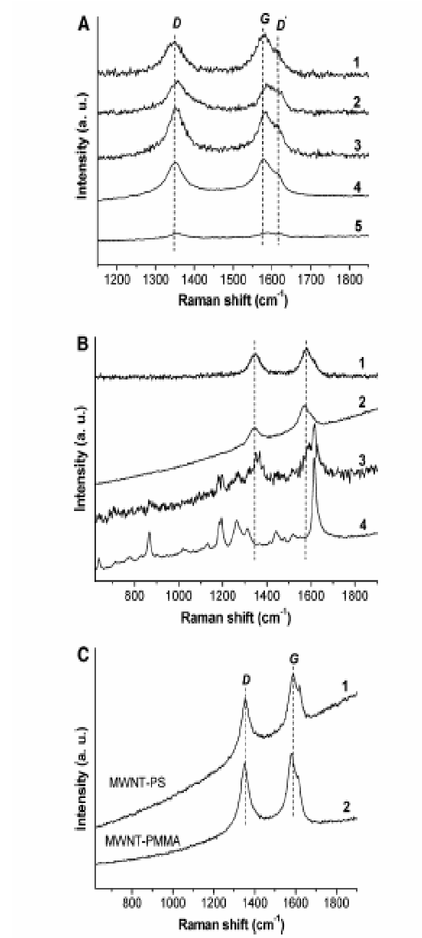


Figure 7. (A) Raman spectra of crude MWNTs (1), MWNT-COOH (2), MWNT-NH_2 (3), NTPU1 (4), and NTPU3 (5). (B) Raman spectra of crude MWNTs (1), mixture sample Mix-1 with 30 wt % of polyurea (2), mixture sample Mix-2 with 72 wt % of polyurea (3), and neat polyurea (4). (C) Raman spectra of MWNT-PS with 85 wt % of polystyrene (1) and MWNT-PMMA with 80 wt % of PMMA (2).

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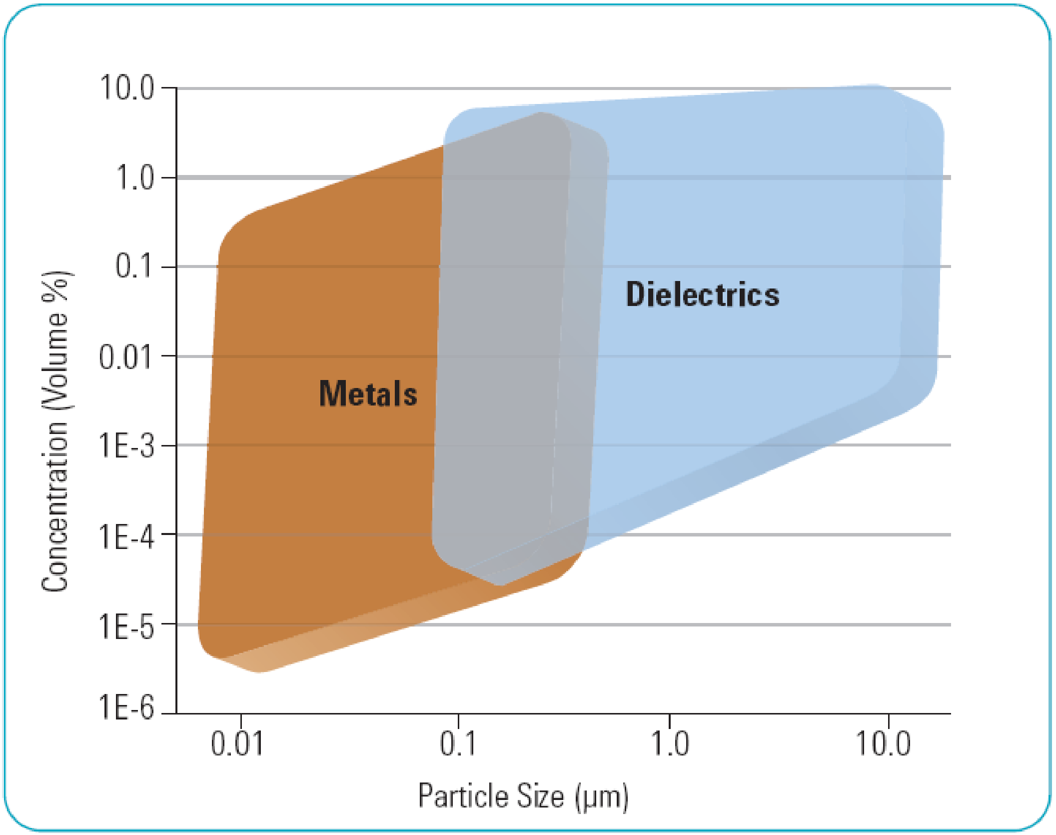
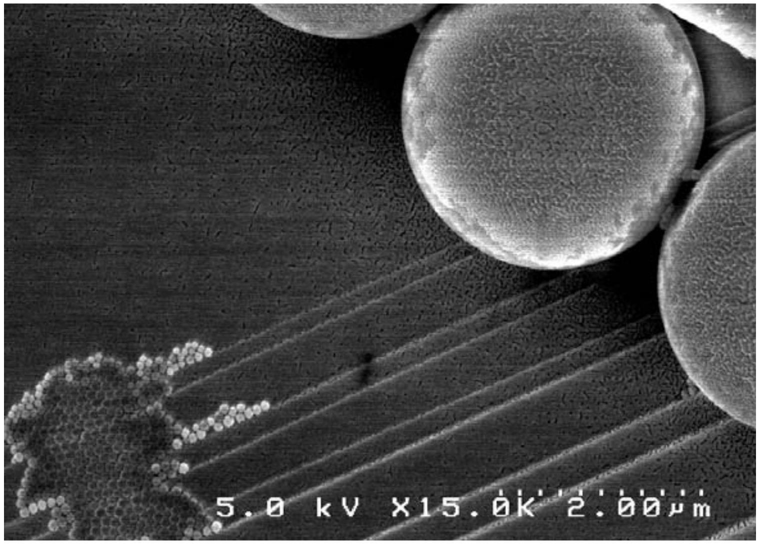
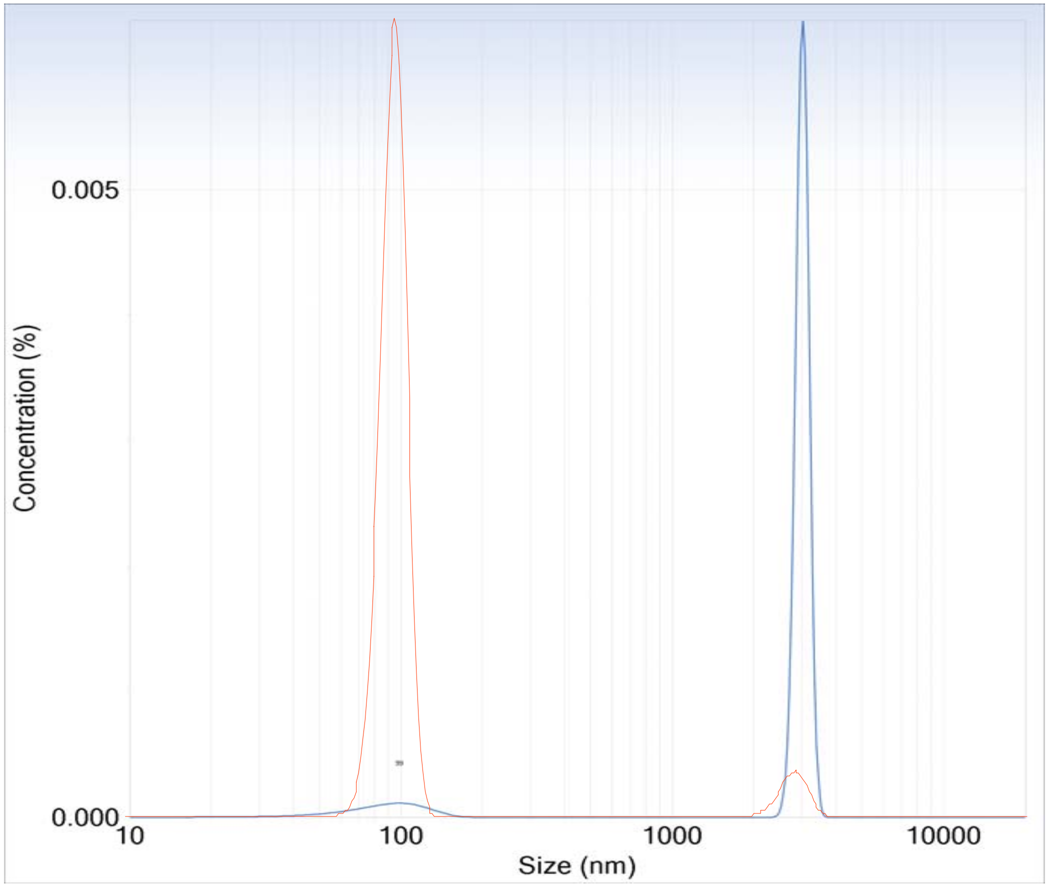
Particle Size Analysis

1. Improve particle size resolution
2. Wide range of particle size and concentration
3. Fast – measurements in seconds



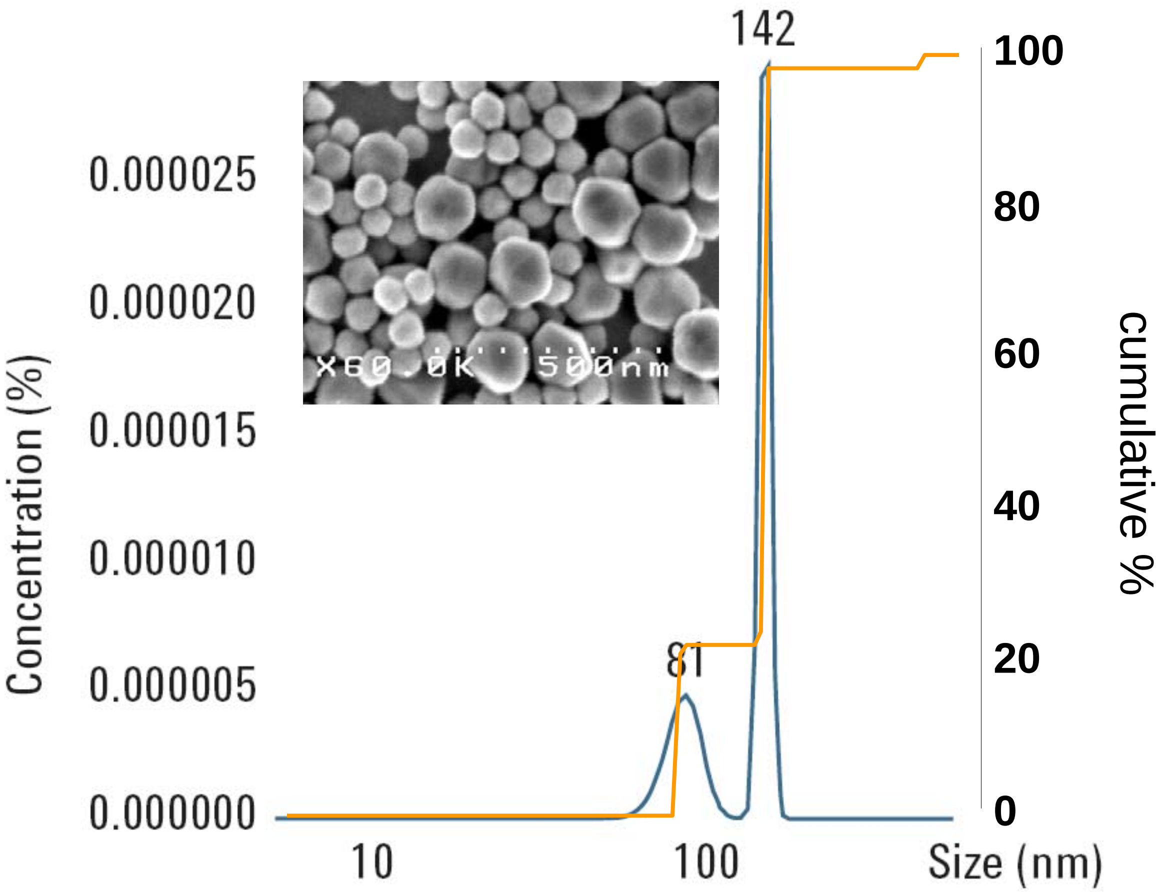
Small mode detection





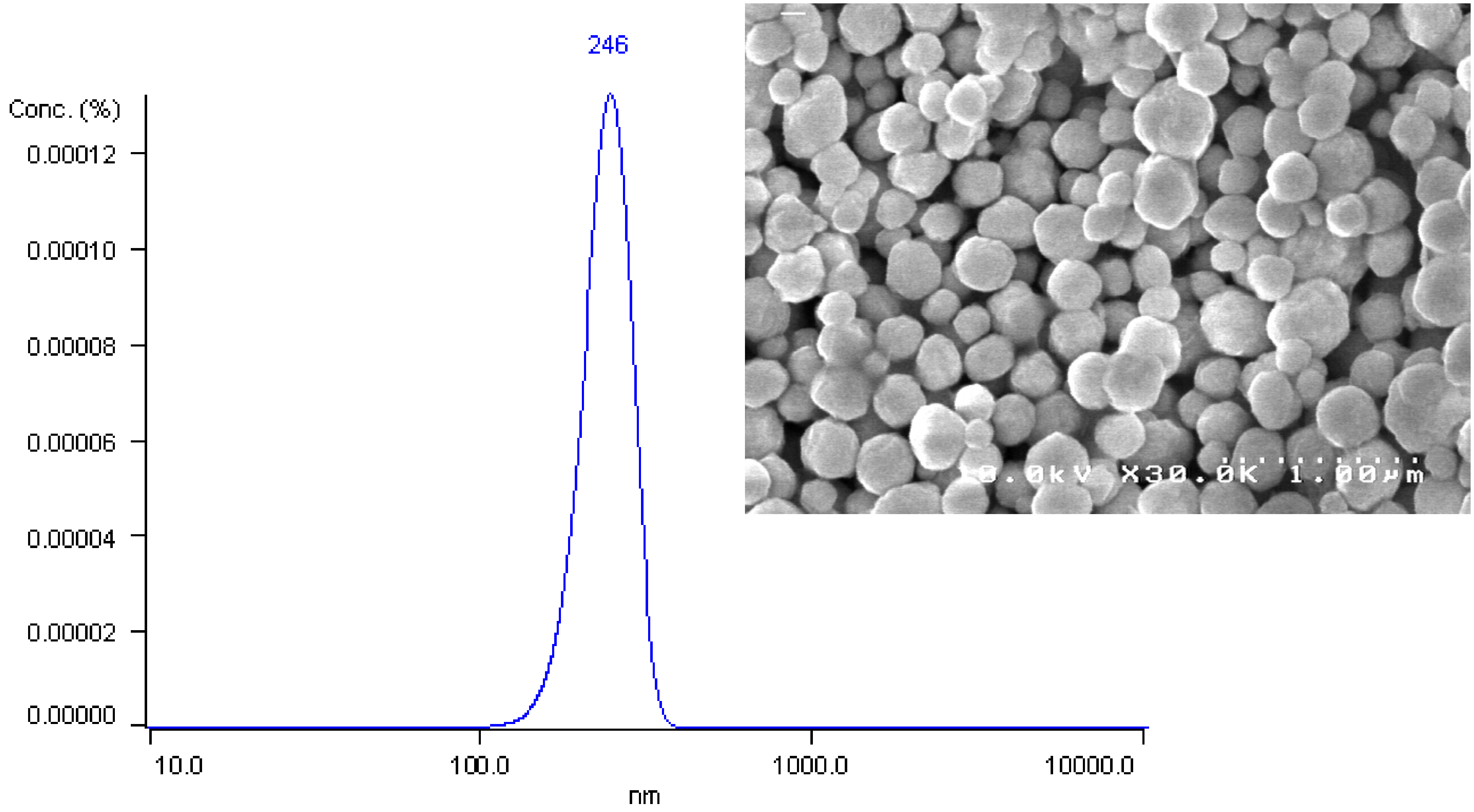
Gold

1:3 mixture of 80 nm and 150 nm

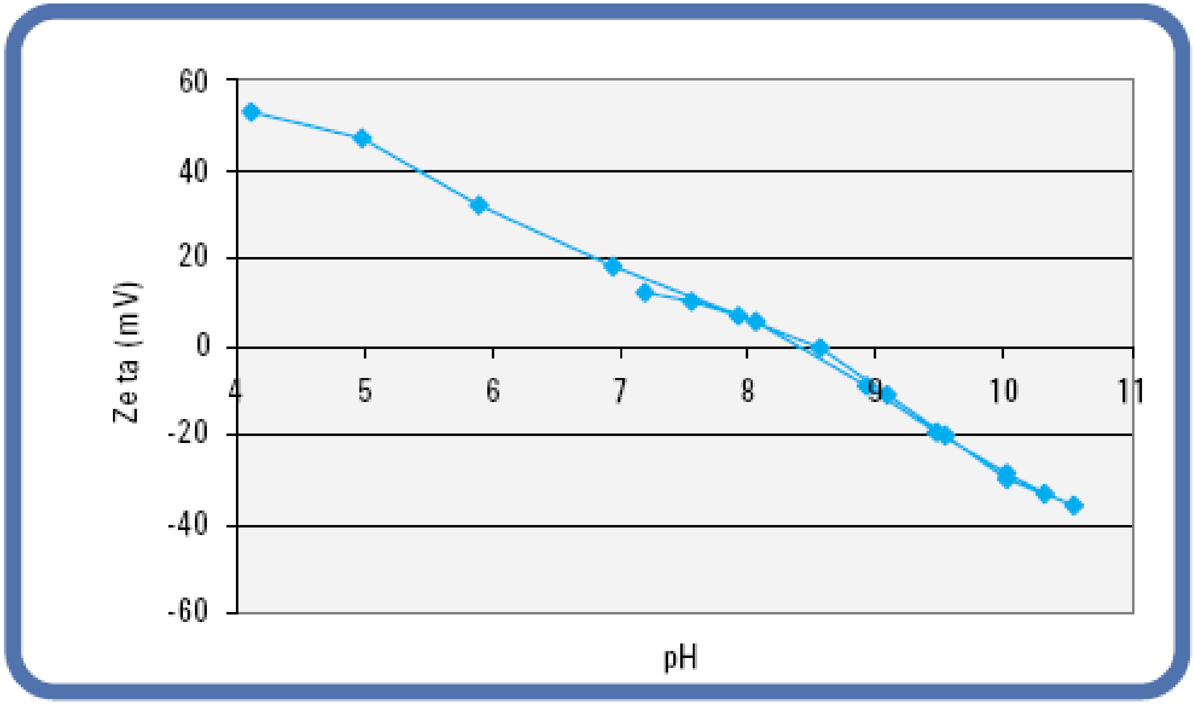


Concentration ~ 0.0003 %v/v

Broader distribution Ni sample



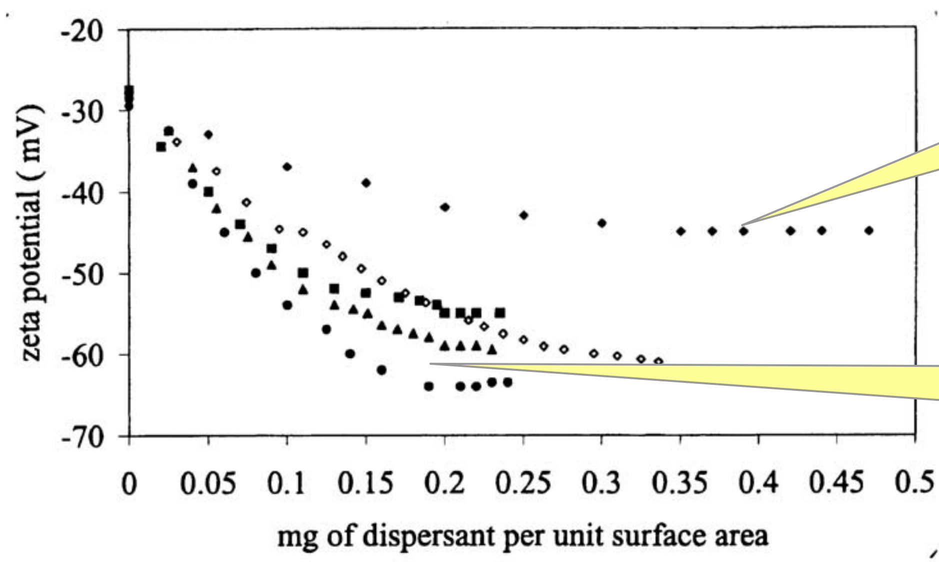
Isoelectric point determination



IEP near 9 shows this TiO_2 has Al_2O_3 coating

Optimum dispersant dose

Choosing the best dispersant



Complete surface coverage when zeta levels off (0.35 mg/m^2)

These dispersants only require 0.2 mg/m^2

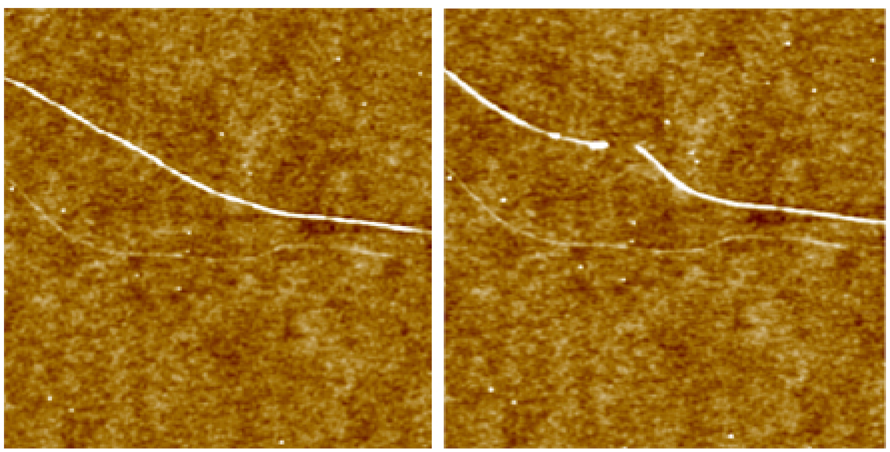
Measurements by Greenwood et al[1] using five commercial dispersants on alumina

[1]Greenwood, R. (2003) "Review of the measurement of zeta potentials in concentrated aqueous suspensions using electroacoustics" *Advances In Colloid And Interface Science* **106** 55-81

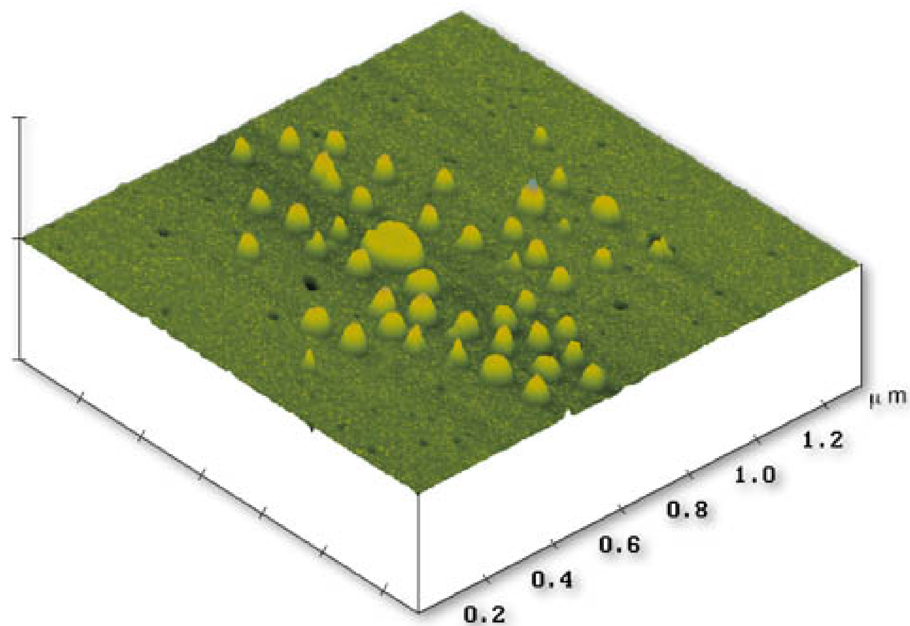
Advantages of AFM

… when you really need to *see* your nanoparticles

- Measure particles individually – at nanometer size
- Physical/chemical characterization
- Shape
- Structure

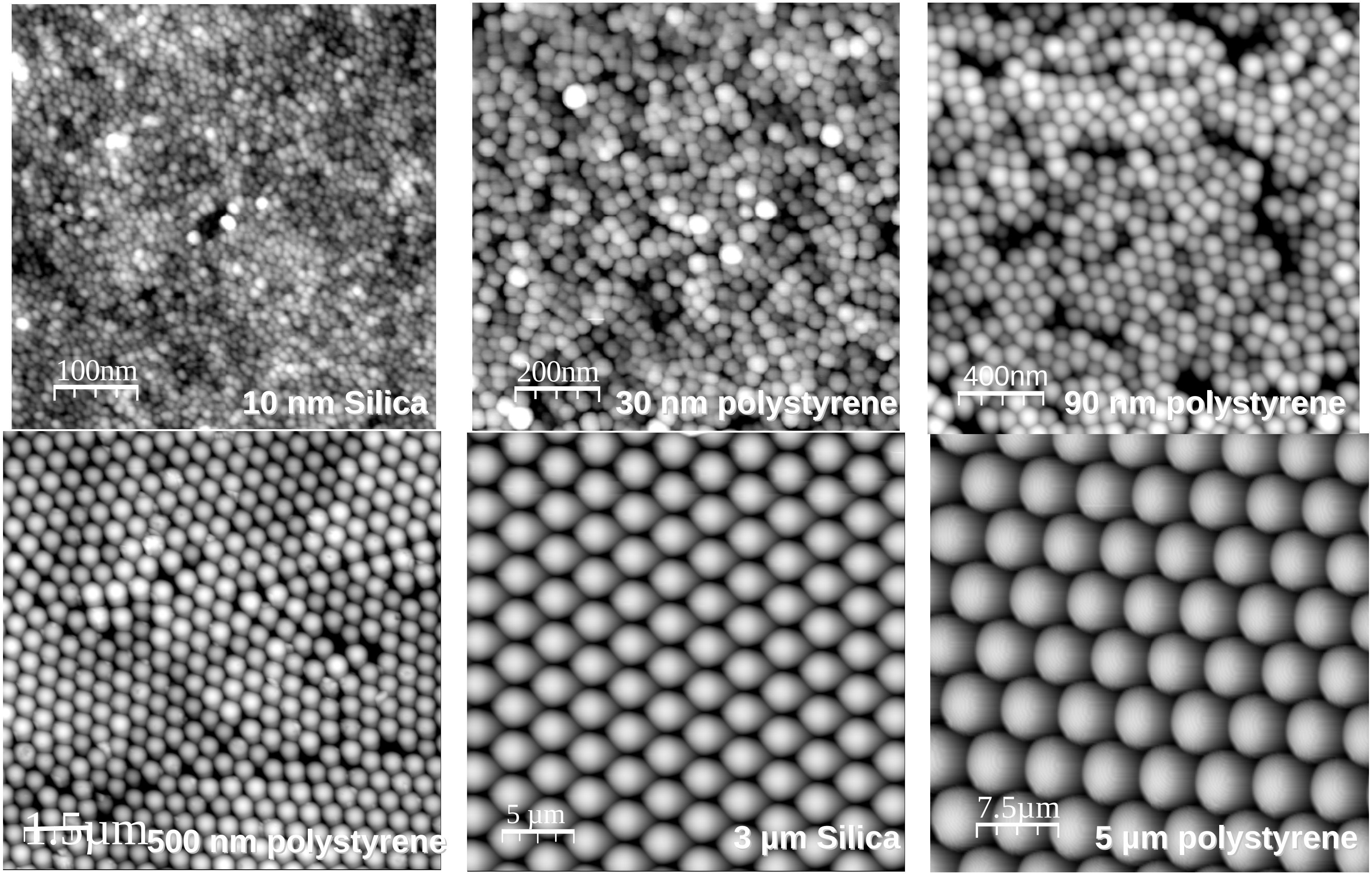


Carbon nanotubes before and after a precision 100 nm cut



MAC mode image of liposomes in pH 7.0 buffer

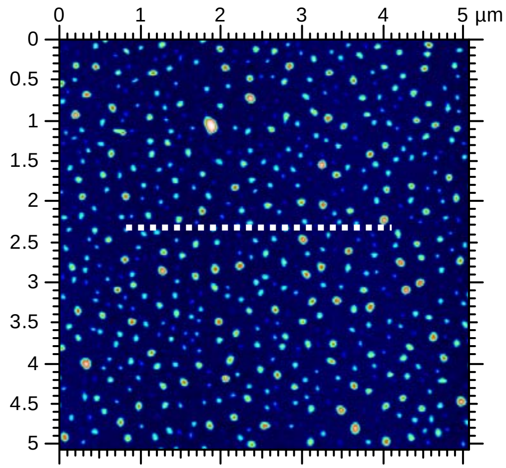
Size characterization of close packed nanoparticles

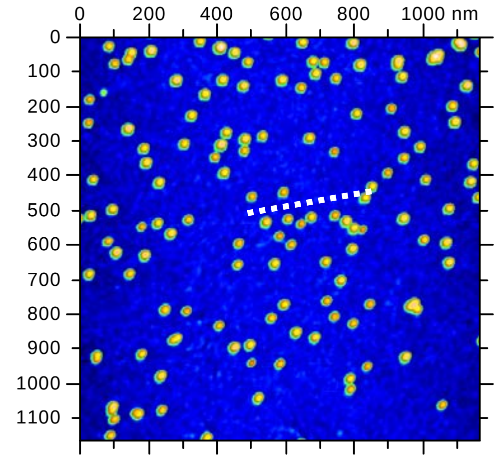


Size characterization on isolated nanoparticles

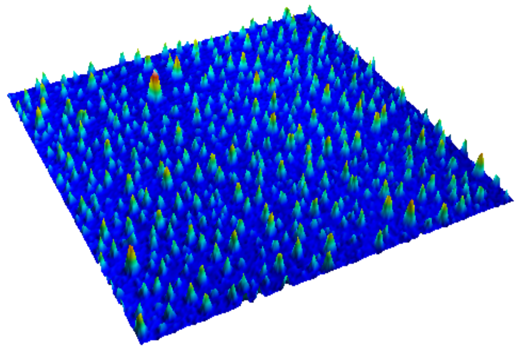
Subcellullar structures (Yeast Lysates) | Au nanoparticles

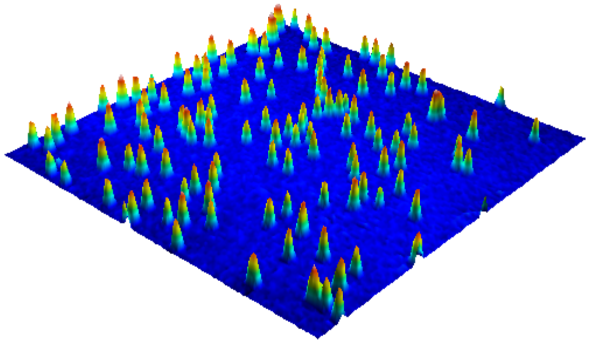
Topography



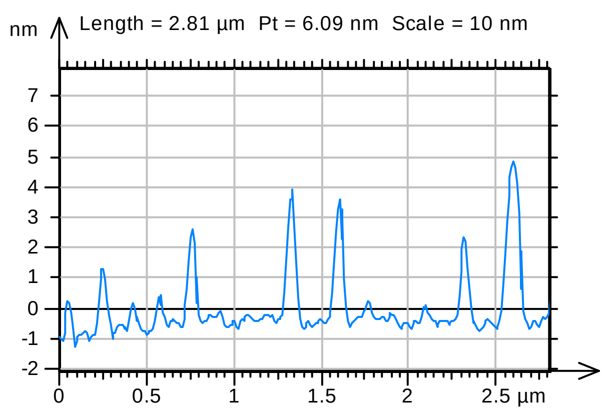


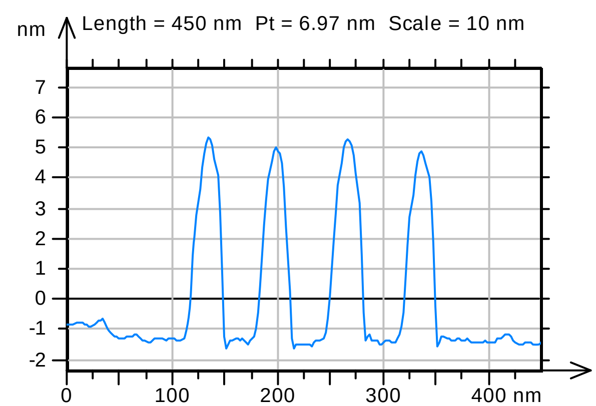
3D view



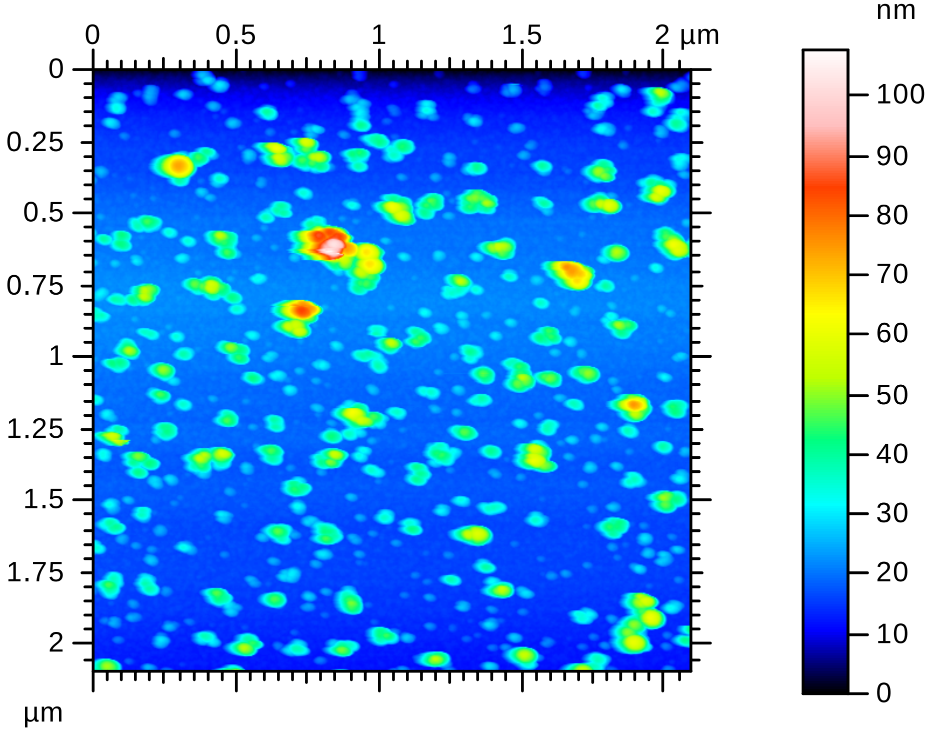


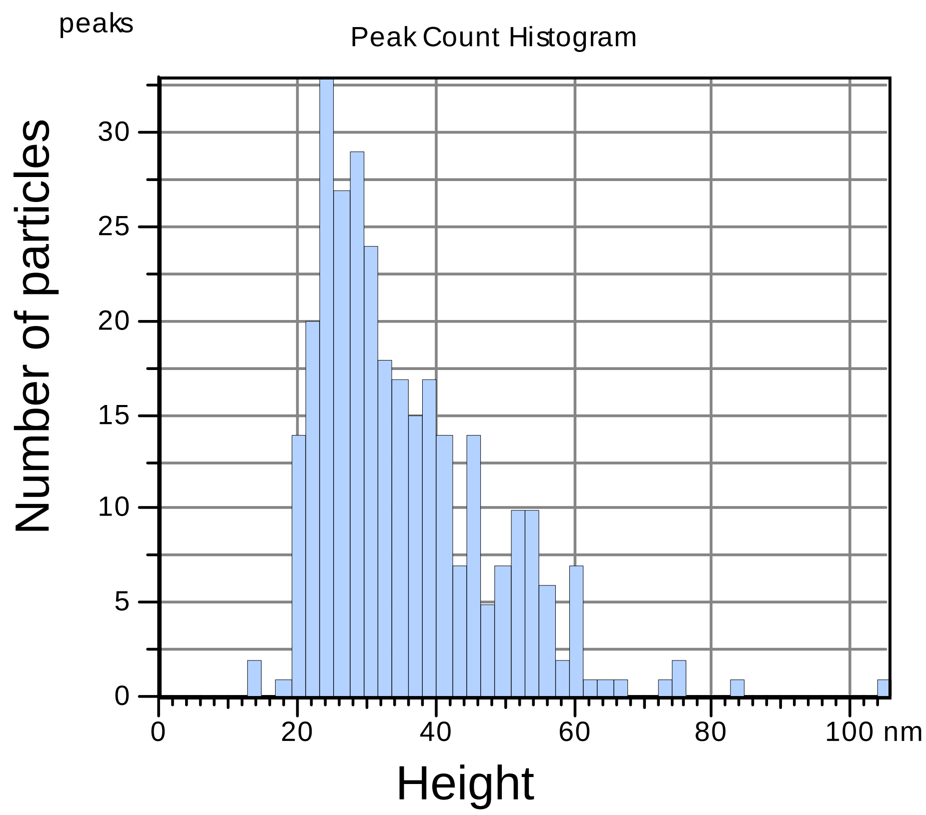
Height





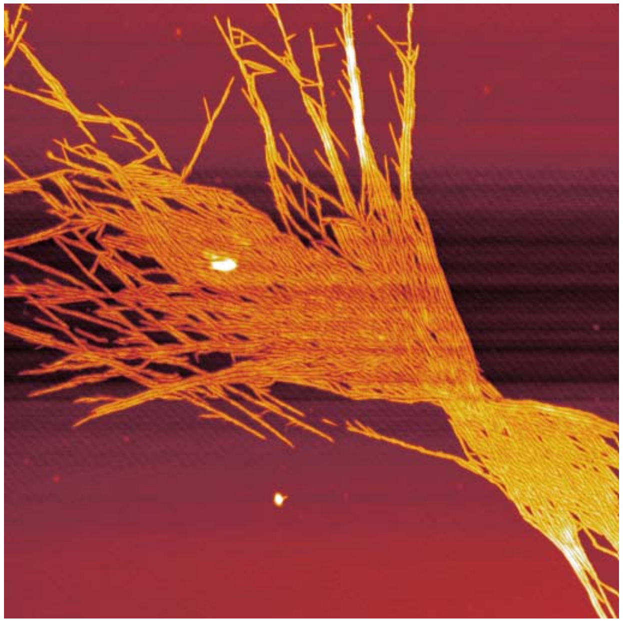
Quantitative analysis of polydisperse sample
25 nm Al_2O_3





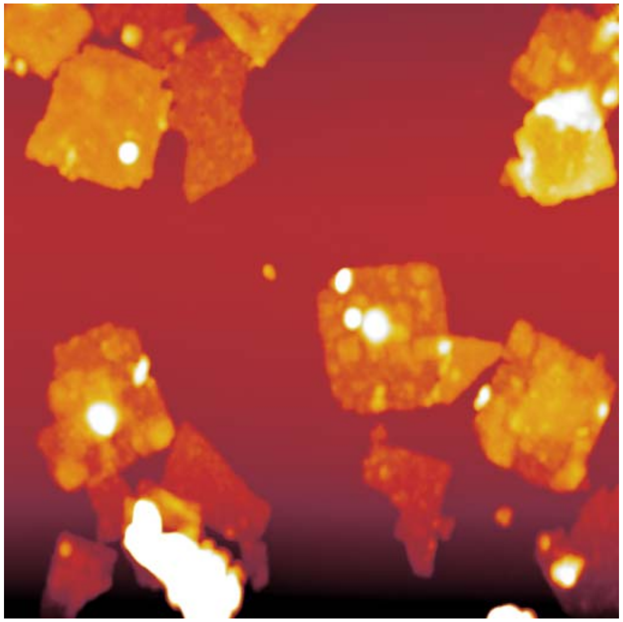
Nanoparticle shape

Silicon Nitride nanopowder



Scan size: 3.6x3.6 um

Yttrium Oxide nanoparticles

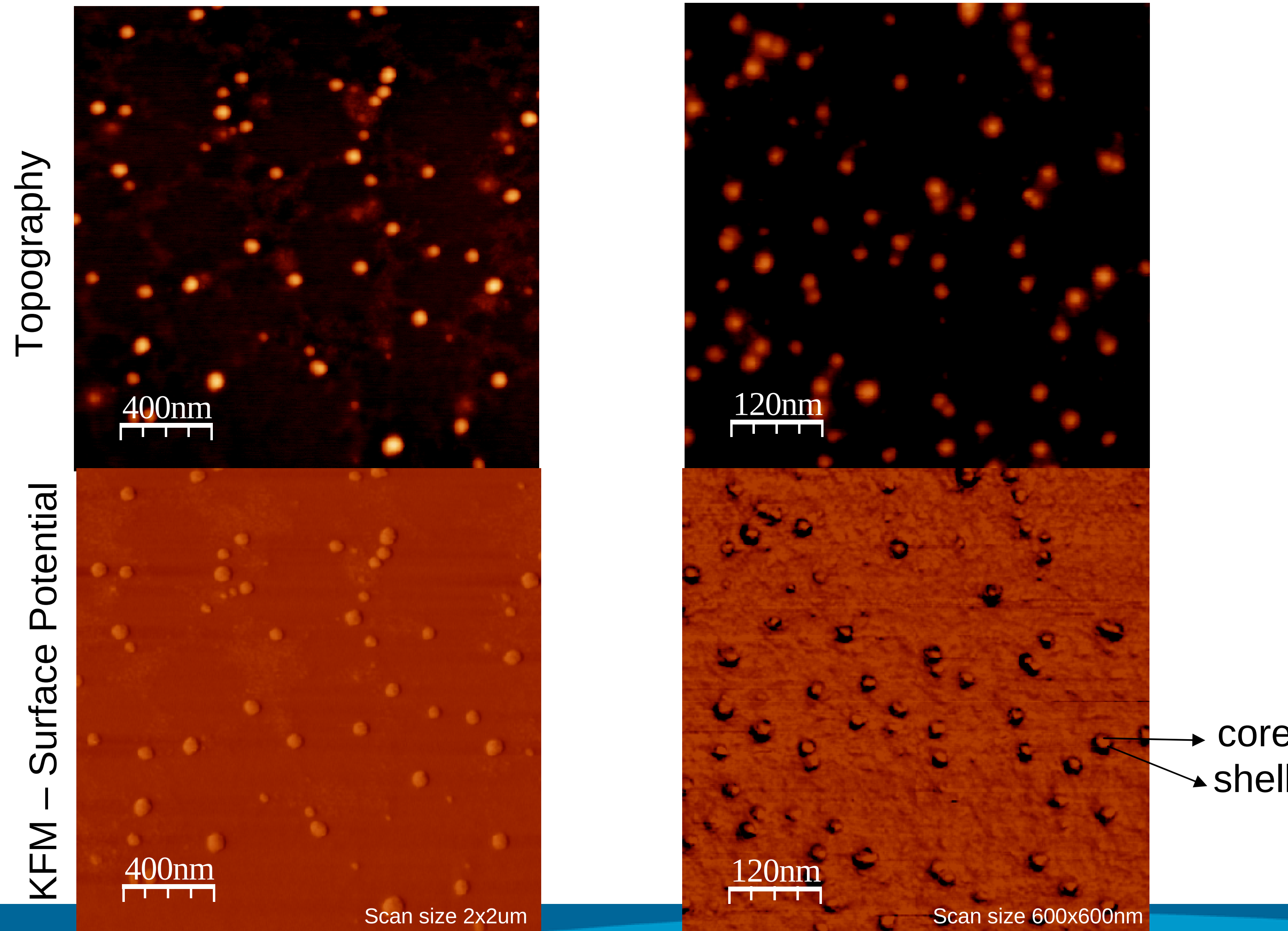


Scan size 2x2 um

Nanoparticle structure

15 nm Au nanoparticle

Poly-lysine coated 5nm Au



Nanomaterials & EHS

Life-cycle analysis

- Expect zero or very low consumer exposure for EPM products
- Waste handling (including research waste)

What is properly handled within existing industry practices for handling hazardous materials

- Damage mechanisms don't change, but density of active sites does
- Utilize existing expertise on naturally occurring or incidental ultrafine particles
- High level of diligence in electronics industry

Workplace monitoring and exposure controls, OSHA protocols

- Personal Protective Equipment

What's new

- Waste stream monitoring (can't see nanoparticulates)
- Airborne exposure monitoring for nanoparticles

Materials of interest

- Nanotubes, nanowires, and nanoparticles
  - Carbon, boron nitride, GaN, …

Metrology Deliverables/Needs

- Establishment of metrological, predictive capabilities, and globally-accepted standards for manufacturing, modeling, and measurements of materials and their properties.
- Accurately and reproducibly measuring and predicting the dimension, structure, and chemistry of nanomaterials, and their interactions with the view of environmental and health effects.
- Development of instrumentation, metrologies, and models for reliably quantifying the concentration, dispersion, and reactivity of varied-shape nanoparticles in the workplace.
- Providing accurate measurement at the nanometer scale and to relate such measurements to macro-scale properties especially focused on in vitro diagnostics.

Acknowledgements

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•Dr. Tom Campbell (ADA)

•Danielle Chamberlin (Agilent)

•Patrick O’Hagan (Agilent)

•Wayne Duncan (Agilent)

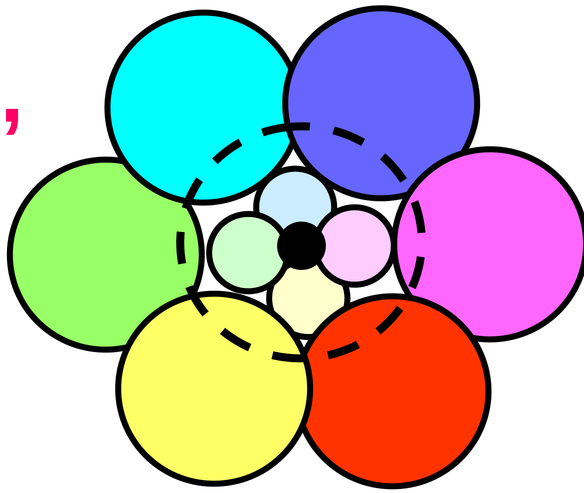
Agilent Technologies

Helping our customers to …

be novel,

Explore,

be first

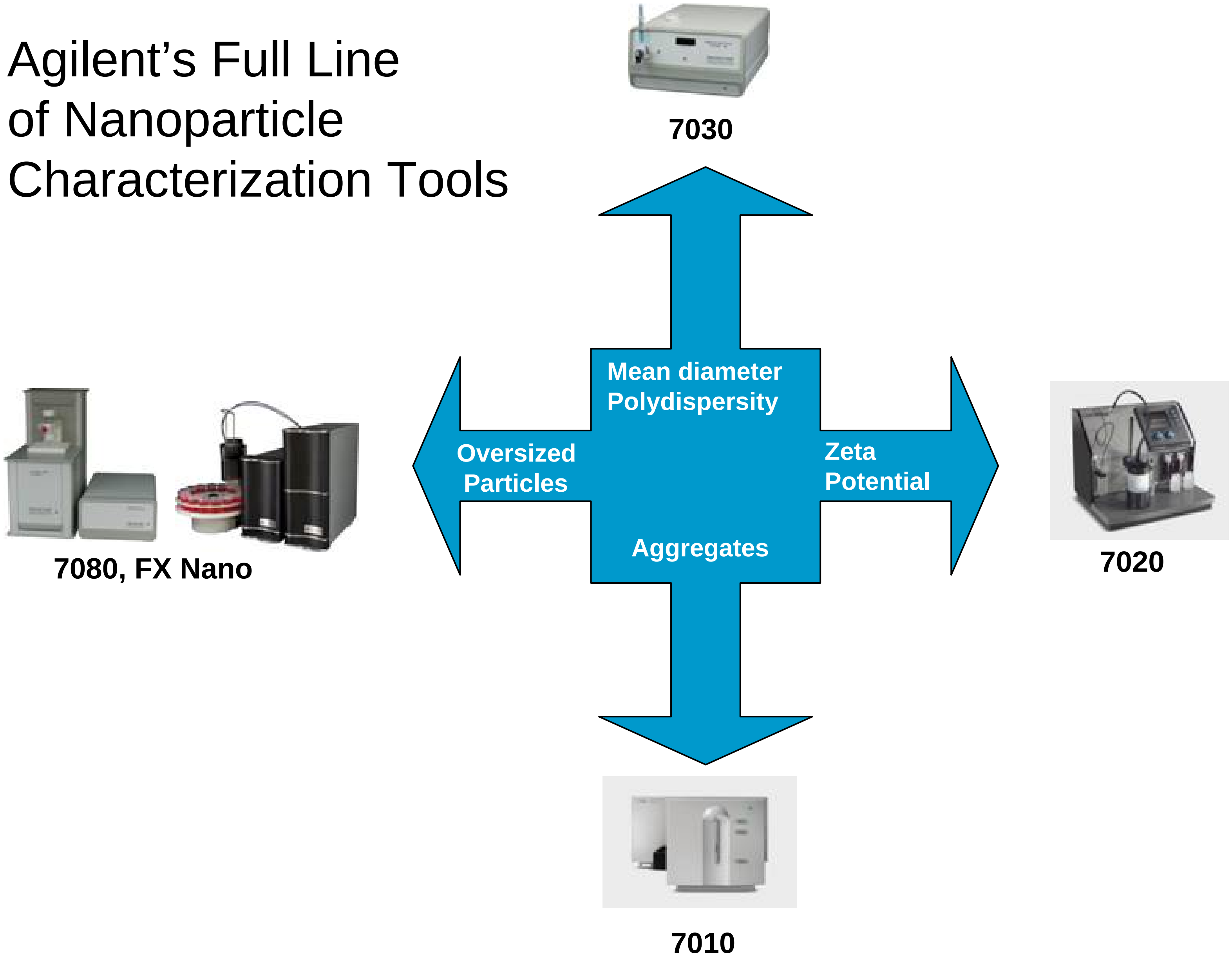


Backup Materials

Particle Analysis Techniques

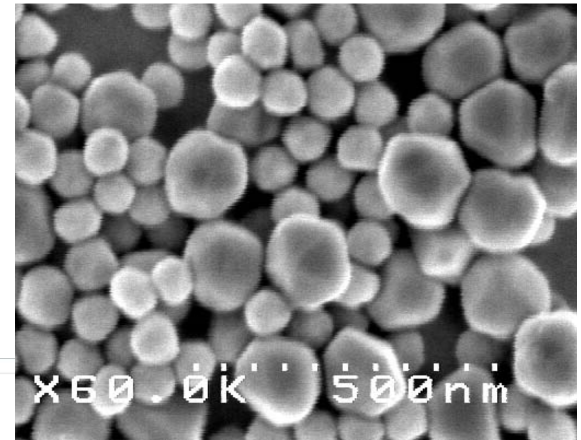
Technique	Common Applications	Characteristics	Comparison with AFM
Laser Light Diffraction	Powders	Ensemble technique. Commonly used in chemical and pharmaceutical industries. Fraunhofer and Mie light scattering are the basic principles of operation. Typical range: 1µm to 1000µm	Morphological information limited to aspect ratio. No surface information. Imaging of individual particles impossible. Range excludes particles <1µm, but, unlike AFM, can measure particles with much larger diameters (>10µm).
Dynamic Light Scattering	Powders	Ensemble technique. Also commonly used in chemical and pharmaceutical industries. Relies on Brownian motion of particles in a liquid medium to determine particle size. Typical range: 50nm to 1µm	Morphological information limited to aspect ratio. No surface information. Imaging of individual particles impossible. Sample must be dispersed in liquid, which can alter particle characteristics. Range is comparable to AFM, but fails to span the gap to measure in the 1µm to 10µm range.
Sedimentation	Powders	Ensemble technique. Level of obscuration of visual light or X-ray signal determines particle size distribution. Typical range: >0.1µm.	No morphological information. No surface information. Imaging of individual particles impossible. Range excludes particles <100nm. Sample must be dispersed in liquid.
Coulter Counting	Powders	Single particle technique. Established technique for particle counting. Provides measurement based on volume displacement. Typical range: >0.5µm.	No morphological information. No surface information. Imaging of individual particles impossible. Range excludes particles <0.5µm. Sample must be dispersed in electrolytic liquid.
DMA + CNC	Aerosols	Ensemble technique. DMA creates monodisperse stream of particles; relies on mass-based charge to isolate particles within a specified size range. CNC grows small particles to a size large enough to detect with other techniques, such as light scattering. Typical range: >10nm	No morphological information. No surface information. Imaging of individual particles impossible. CNC alters particles before they are measured.
Light Microscopy	Powders and Aerosols	Single particle technique. Typical range: >1µm.	Resolution limited by light wavelength; Range excludes particles <1µm.
SEM	Powders and Aerosols	Single particle technique. Compositional information can be obtained with EDS. Typical range: 50nm to 1cm.	Sample preparation can be complex Generally must be performed at vacuum. Costly equipment.
TEM	Powders and Aerosols	Single particle technique. Compositional and crystallographic information can also be obtained. Typical range: 5nm to 500µm.	Since e-beam is transmitted through sample, image is 2D projection of sample. Sample preparation can be very complex. Must be performed under vacuum. Costly equipment.

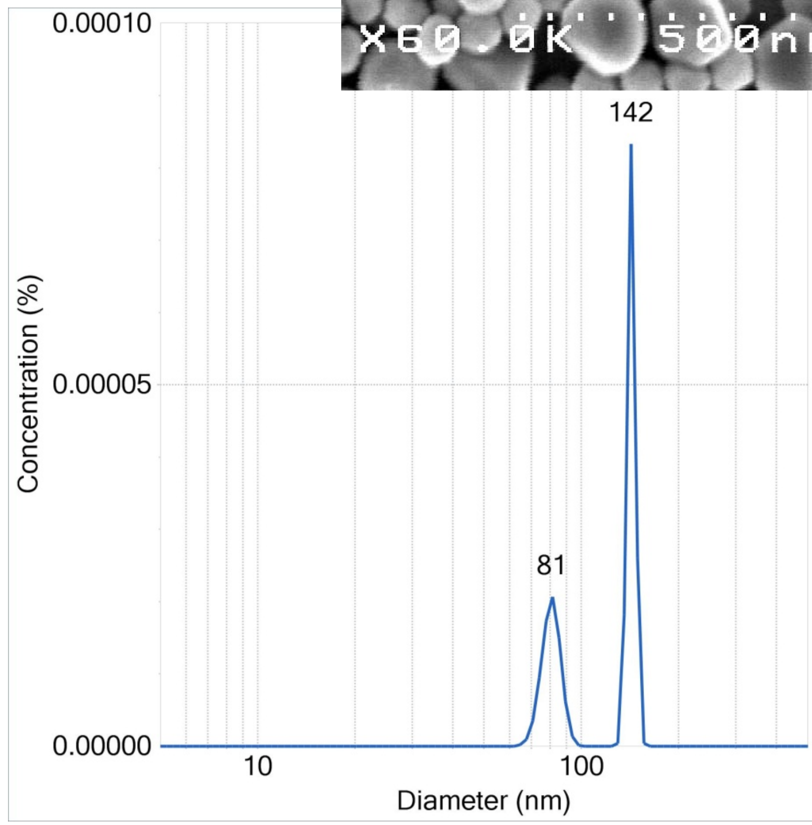
Agilent's Full Line of Nanoparticle Characterization Tools



7010 Particle Size Spectrophotometer

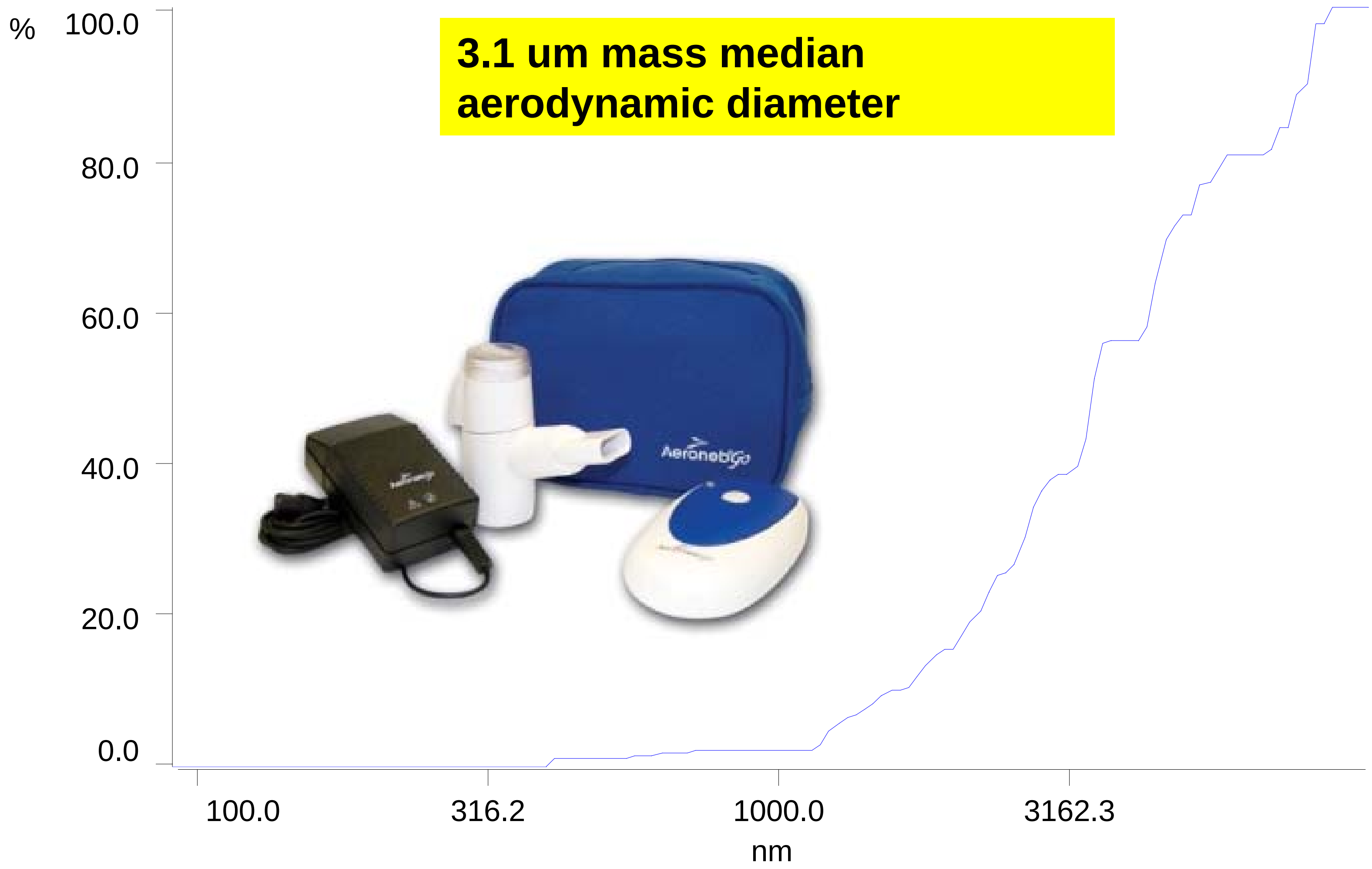
1:3 mixture of 80 nm and 150 nm Gold particles



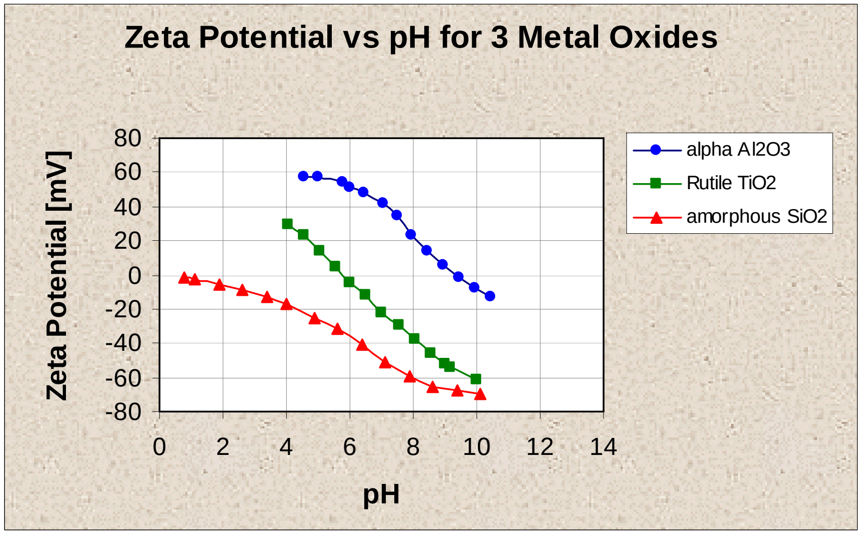


- Size Range: 5 nm to 15 microns
- Higher resolution and better concentration information than DLS or SLS
- Takes only seconds to obtain data
- Works at high concentrations
- Also can be used for UV-Vis Spec.

Measurement of aerosol – nebulized water



7020 ZetaProbe



•Size Range: 1 nm to 50 microns

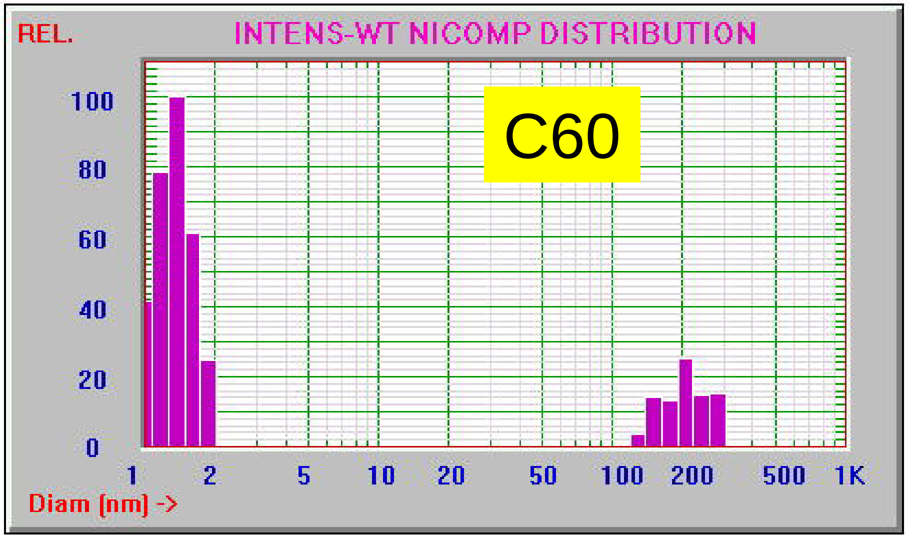
• Measures zeta potential without dilution in polar and non-polar solvents and on nano- and micro-sized particles

• Unique autotitration capability. Allows for accurate IEP determination

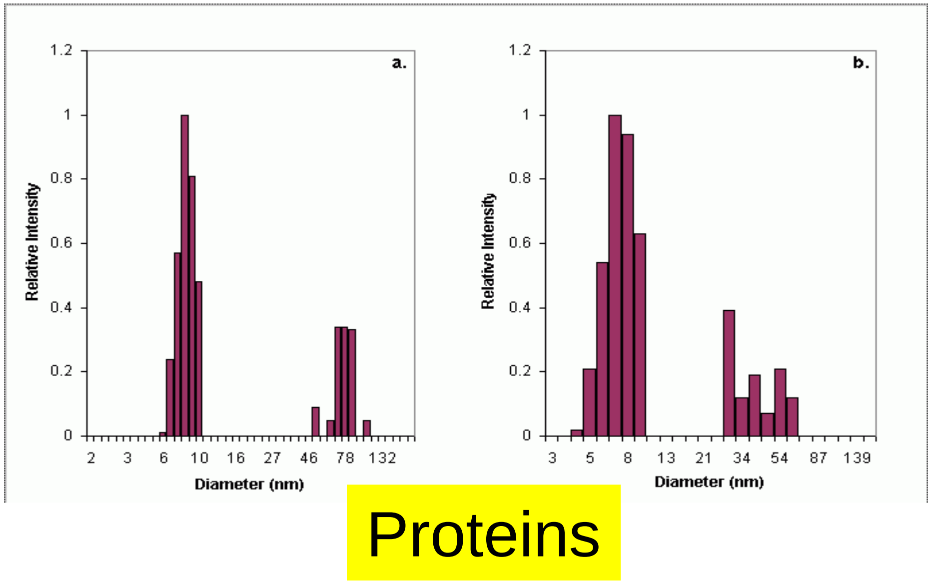
• Multi-frequency electroacoustic technique automatically corrects for particle size

Autotitration allows the measurement the iso-electric point of a dispersion.

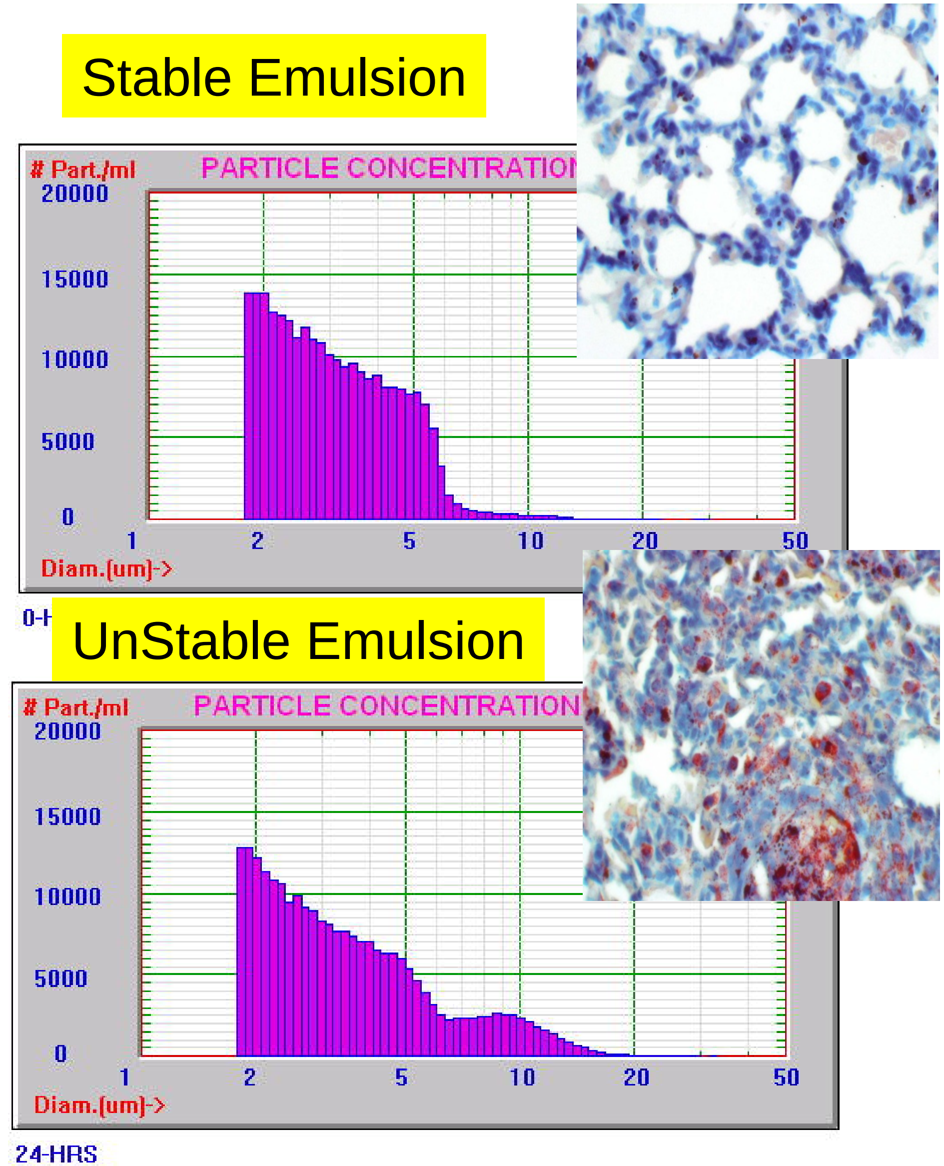
7030 Nicomp



- Size Range: 0.5 nm to 10 microns
- Based on DLS, a commonly known method
- Can be combined with Zeta Potential Analysis in one box
- Compared to other DLS tools, the 7030 has a more flexible hardware



7080 AccuSizer



- Size Range: 0.5 to 2500 ums
- Utilizes Single Particle Optical Sizing or SPOS
- Sizes & counts the BIG particles in tails
- Has high resolution
- Complements DLS and SLS