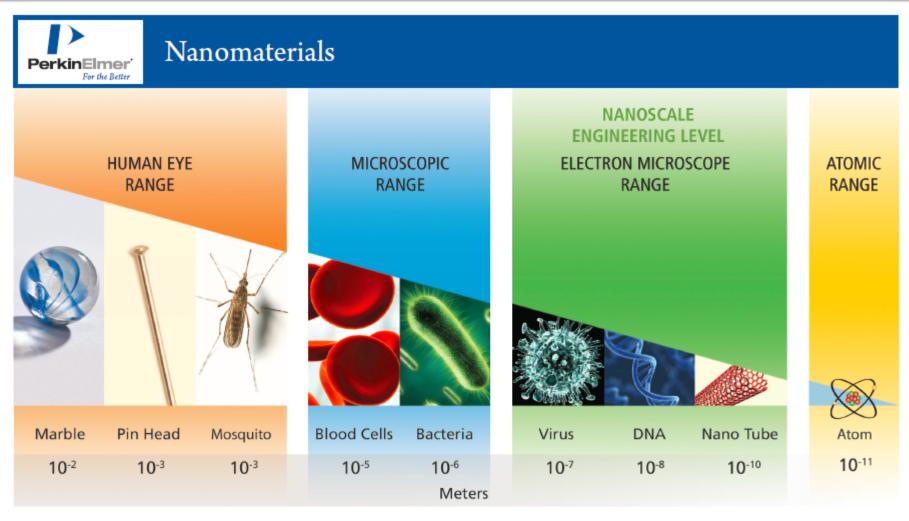
Single Particle ICP-MS

Detection of Metal-Based Nanoparticles in Complex Environment Matrices May 3, 2016



HUMAN HEALTH • ENVIRONMENTAL HEALTH © 2014 PerkinElmer

Engineered NanoParticles (ENP's)



This poster compares the nano-region to things we know, such as a pin, insect and cells to provide a visual perspective. Nanotechnology is the science and technology of precisely manipulating the structure of matter at the molecular level.

For Nanomaterial Applications, please visit www.perkinelmer.com/nano

PerkinElmer, Inc. 940 Winter Street Waltham, MA 02451

HUMAN HEALTH | ENVIRONMENTAL HEALTH

Engineering at an Atomic Scale



Where are ENP's found?



Environmental

- Fate studies
 - Drinking water
 - Surface water
 - Water treatment
- Remediation studies
- Bioavailability studies
- Bioaccumulation studies
- Distribution in the ecosystem



Consumer

- •Health and Fitness
- Energy
- •Foods and Beverages
- Fabrics and Textiles
- Paint
- Semiconductor
- •Automotive
- •Appliances
- •Electronics and computer
- •Sunscreen
- •Nanocomposite materials

Everywhere



Biological/ Biomedical

- Early diagnosis
- Cancer treatment (Pt)
- Drug design and delivery
- Toxicological studies
- Anti-Microbial (Ag)



How do Nanoscale Materials Impact the Environment?



"Nanoparticles: Regulating a Tiny Problem with Huge Risks"

Columbia Journal of Environmental Law

- The continuing advancement of nanotechnology represents a tremendous opportunity for society because of the unique traits that nanoscale materials possess.
- Unfortunately, the same physical traits that give nanotechnology its economic and scientific value also make it a potentially dangerous emerging form of pollution that is particularly difficult to regulate under current law.
- Regulatory regime that could prove to be more successful in confronting the environmental risk posed by nanoparticles.

http://www.columbiaenvironmentallaw.org/articles/nanoparticles-regulatinga-tiny-problem-with-huge-risks

Toxicity Testing Costs on Nanomaterial Regulation

- Information about the toxicity of nanoparticles is important in determining how nanoparticles will be regulated. In the U.S., the burden of collecting this information and conducting **risk assessment** is placed on regulatory agencies without the budgetary means to carry out this mandate.
- We show for the United States that costs for testing existing nanoparticles ranges from \$249 million for optimistic assumptions about nanoparticle hazards (i.e., they are primarily safe and mainly require simpler screening assays) to \$1.18 billion for a more comprehensive precautionary approach.
- At midlevel estimates of total corporate R&D spending, and assuming plausible levels of spending on hazard testing, the time taken to complete testing is likely to be very high (34–53 years) if all existing nanomaterials are to be thoroughly tested.

Jae-Young Choi[†], Gurumurthy Ramachandran[‡] and Milind Kandlikar^{*§} Division of Health Policy and Management and Division of Environmental Health University of Minnesota, Minneapolis, Minnesota 55455 *Environ. Sci. Technol.*, 2009, 43 (9), pp 3030–3034



Nanoparticles Present Sustainable Way to Grow Food



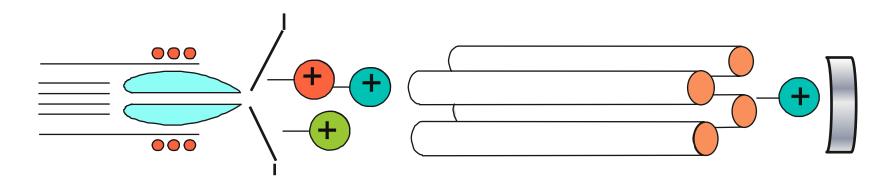
- Scientists are working <u>diligently</u> to prepare for the expected increase in global population -- and therefore an increased need for food production-- in the coming decades. A team of engineers at Washington University in St. Louis has found a sustainable way to boost the growth of a protein-rich bean by improving the way it absorbs much-needed nutrients.
- Ramesh Raliya, a research scientist, and Pratim Biswas, the Lucy & Stanley Lopata Professor and chair of the Department of Energy, Environmental & Chemical Engineering, both in the School of Engineering & Applied Science, discovered a way to reduce the use of fertilizer made from rock phosphorus and still see improvements in the growth of food crops by using zinc oxide nanoparticles.

PerkinElmer Nanometrology Portfolio



Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

The quantitative determination of <u>elements</u> using <u>mass spectrometry</u> of ions generated in an <u>inductively coupled plasma</u>.



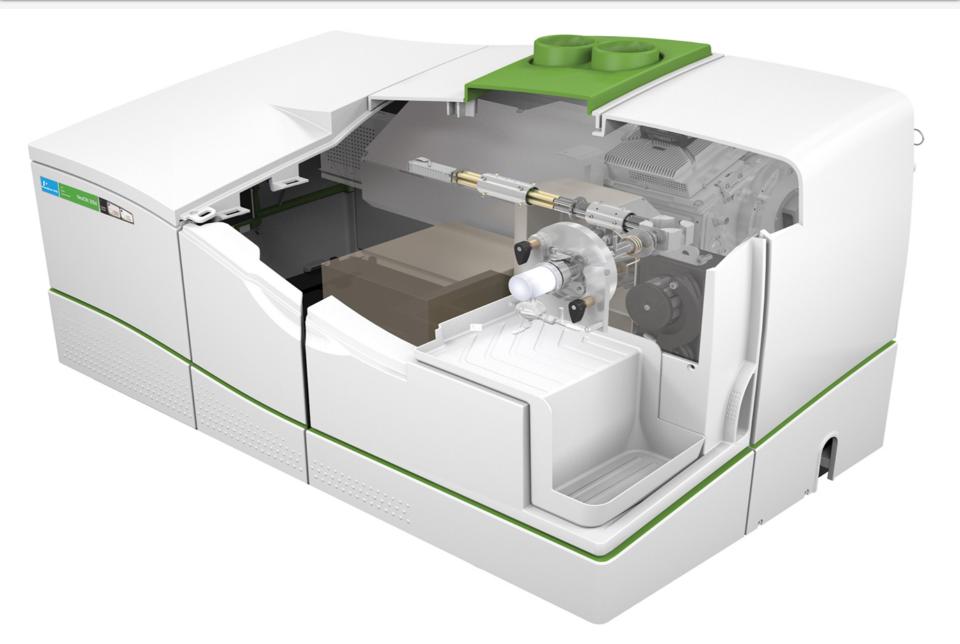
ICP-MS Detection Limits and Isotopes



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NexION ICP-MS



Sample Introduction System

- Continuous Flow
- 0.25 ml/min liquid uptake rate
- Concentric nebulizer with low dead volume connections

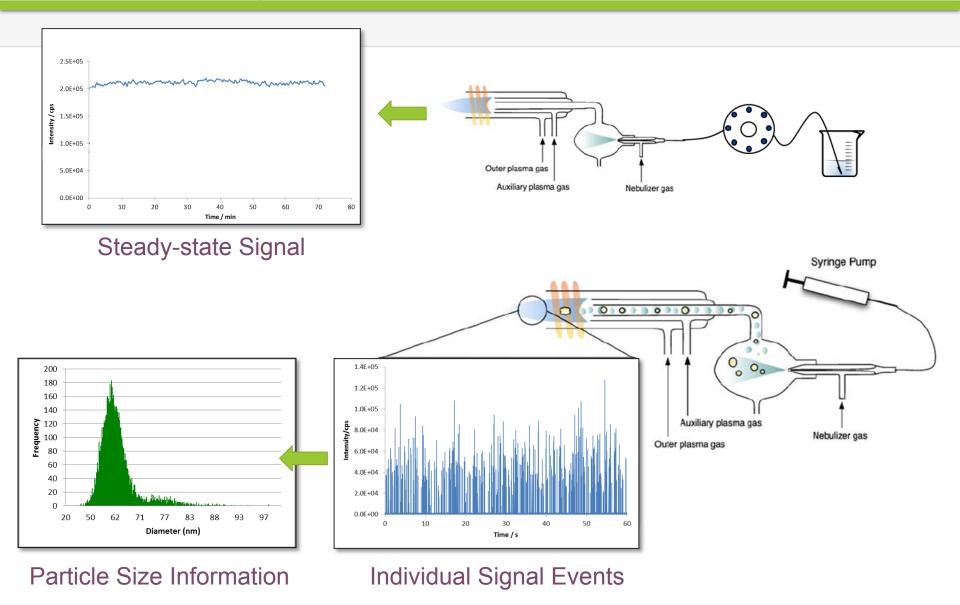


Mass Spectrometry Enhancements allow for new types of measurements to analyze Nanoparticles in Environmental Samples

- New advancements in ICP-MS technology allow the measurement of individual inorganic nanoparticles .
- Technique allows for the differentiation between ionic (M⁺) and particulate signal (nanoparticles) in a wide variety of matrices without any prior separation.
- It is element specific, and provides composition, ionic and particle concentration, size and size distribution.
- Allows the analysis of nanoparticles at low concentrations (as low as 50 particles/mL).
- Time Studies: Tracks nanoparticles' fates in the environment.
- Requires operating the instrument in a different manner than when analyzing dissolved elements.



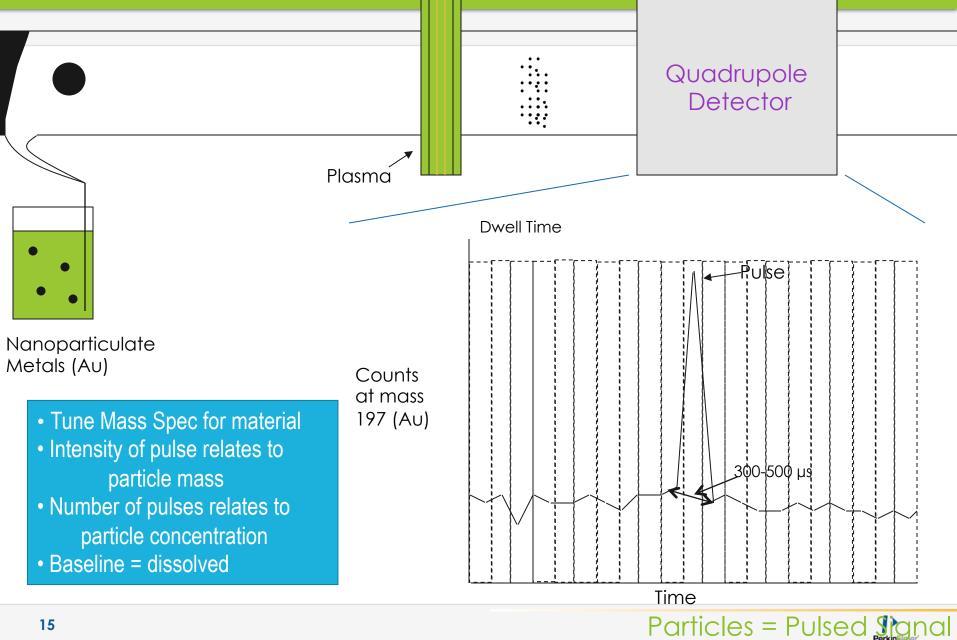
Concept of Single Particle-ICP-MS



¹⁴ Differentiation between Dissolved and Particles Signals



ICP-MS Schematic of General Analysis for Nano Metals



Fast Continuous Data Acquisition

Time

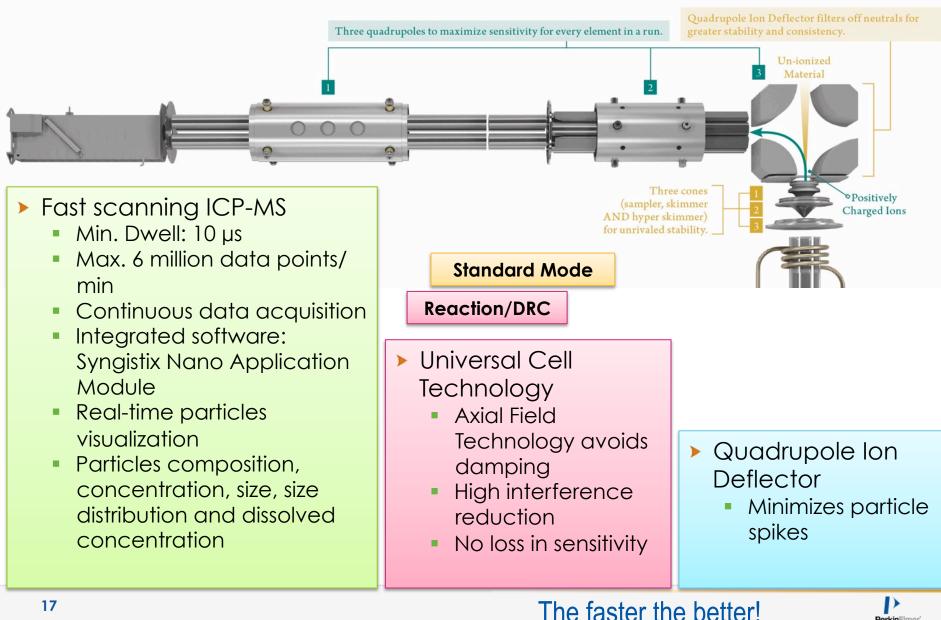
Fast Continuous Data Acquisition = No Settling Time

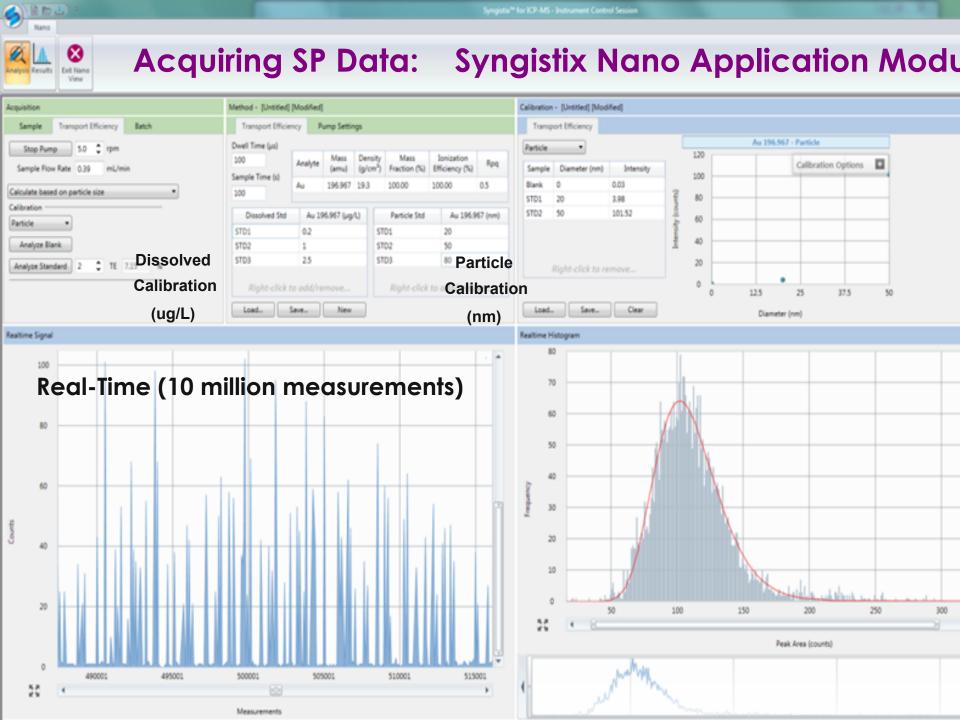
Dwell Time Shorter than the Particle Transient Time

NexION 350 Single Particle Mode



Hardware Meets Software





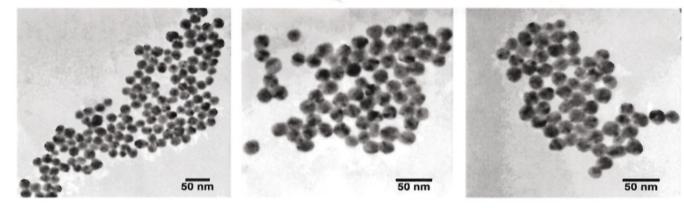
20 nm PELCO Citrate NanoXact Silver Nanoparticles Lot#: DAC1212

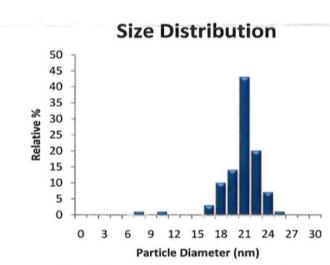
www.TedPella.com

20 nm PELCO[®] Citrate NanoXact[™] Silver

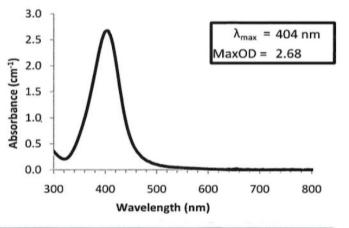
Lot Number: DAC1212

Diameter (TEM):	19.9 nm	Hydrodynamic Diameter:	N/A
First Standard Deviation:	2.4 nm	Zeta Potential:	N/A
Coefficient of Variation:	12.3 %	pH of Solution:	8.0
Mass Concentration (Ag)	0.020 mg/mL	Particle Surface	Sodium Citrate
Particle Concentration	4.7E+11 particles/mL	Solvent:	Aqueous 2mM Citrate



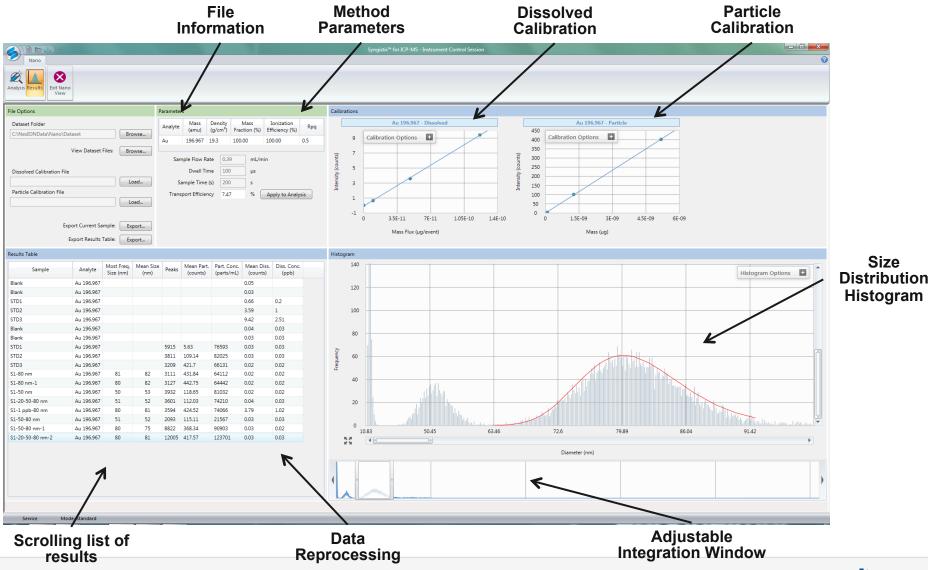






19

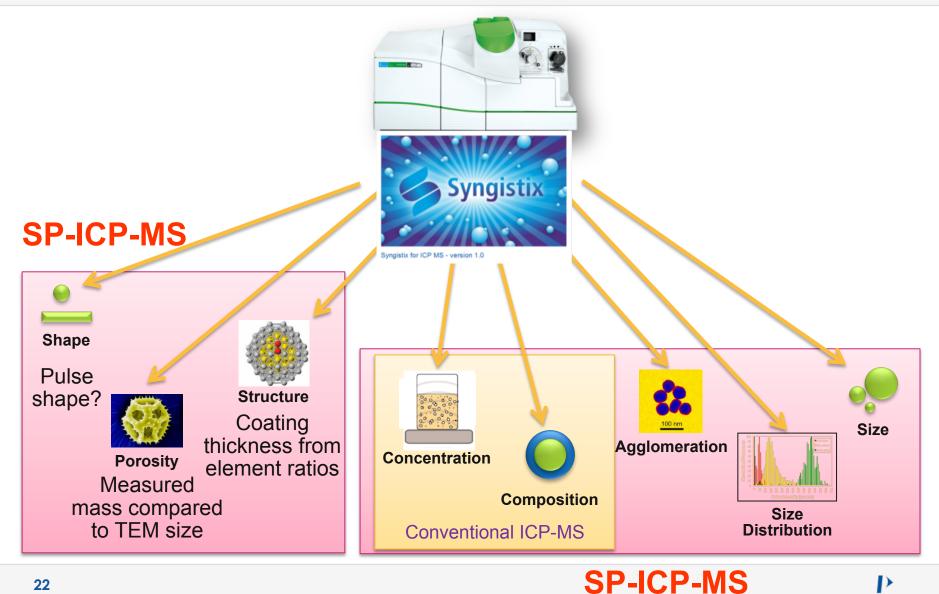
Syngistix Nano Application Module – Results Tab



Syngistix Nano Application Module – Results Tab

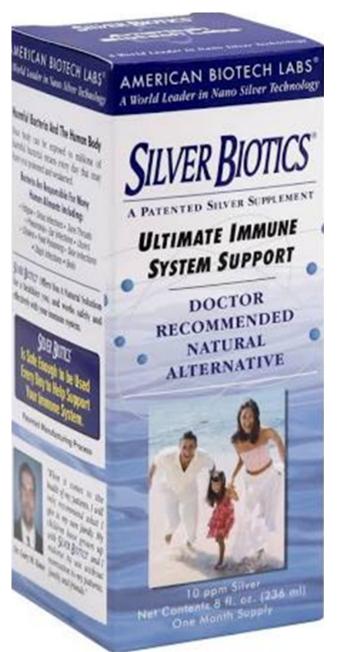
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rt Results T	able:	Expo	ort		Sa	mple	Anal	yte Size (nm)	•	Peaks	Mean Part. (counts)	Part. Conc. (parts/mL)	Mean Diss. (counts)	Diss. Conc. (ppb)
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Analysis Results														
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Nanoparticle Characterization by Single Particle ICP-MS



Goal: Characterize Silver Nanoparticles in Dietary Supplements

- Silver NPs are most commonly used in consumer products
 - Large surface area enhances reactivity and efficiency of Ag's microbial properties
 - Label claim "Ag NPs fortify the immune system".
- Measure and characterize Ag NPs in three dietary supplements
 - Ionic and particulate Ag
 - Particle size and size distribution
 - Particle concentration
 - Dissolved Ag concentration



0.08mg Ag/day

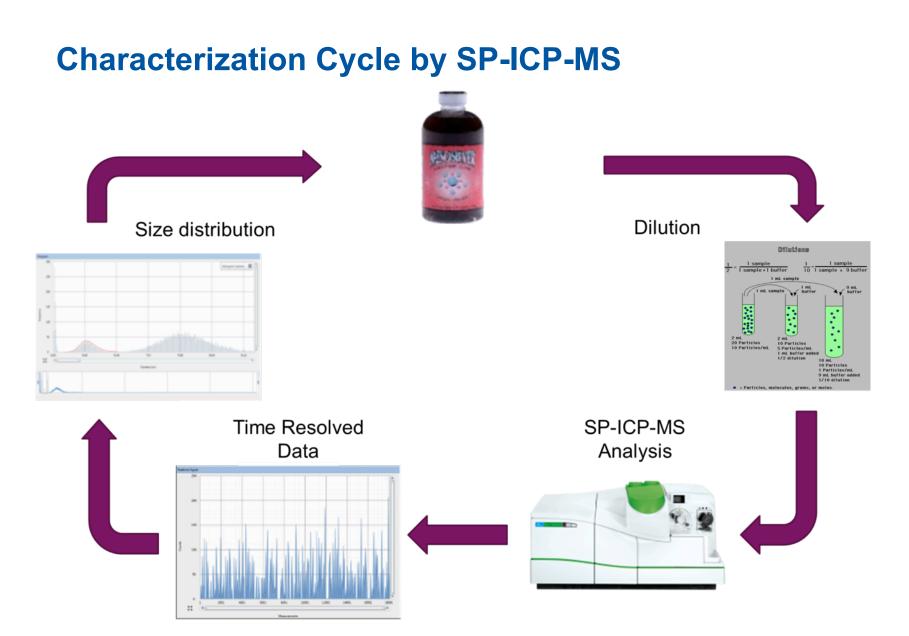
SP-ICP-MS Experimental

- Samples
 - Purchased in local health food store
- Sample Preparation
 - Dilute in deionized water
 - Dilution factor depends on particle concentration in sample
 - Sonicate
- NexION 350 Instrumental Parameters Parameters

I alametei	value5
SP-ICP-MS Instrument	PerkinElmer NexION 350 ICP-MS
Nebulizer	Meinhard
Spay Chamber	Baffled Cyclonic, Glass
Injector	2.0 mm id Quartz
Plasma Power	1600 W
Aux Flow	1.1 L/min
Neb Gas Flow	1.05 L/min
Sample Uptake Rate	0.4 mL/min
Silver Isotope	107 amu
Dwell Time	50 µs
Quad Settling Time	Zero
Sample analysis time	60 s
	PerkinElmer



Values

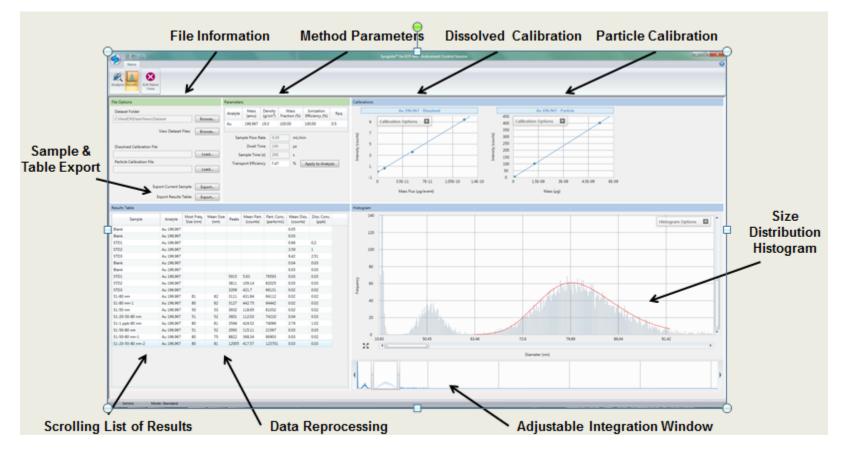


Dilute down to about 100,000 Particles/mL



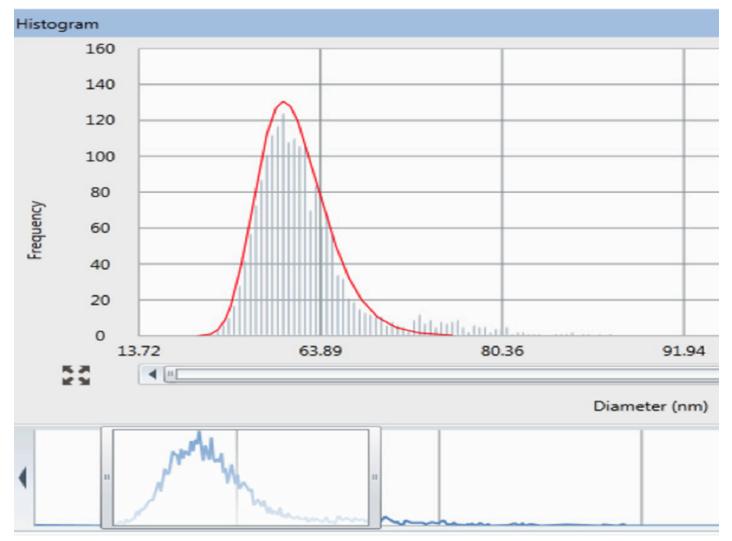
Data Analysis: Syngistix Nano Application Module

- Dissolved and particle concentrations
- Particle size and size distribution
- Nanoparticle composition



Method Validation

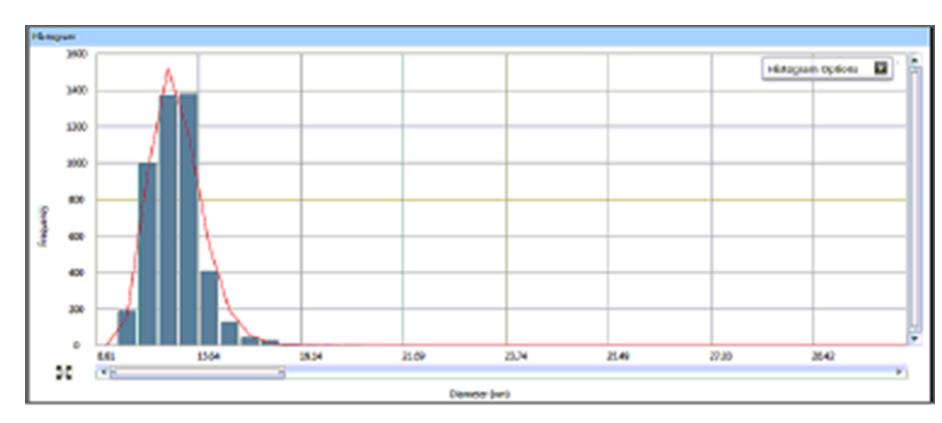
Analyze 60 nm Ag NP standard as Unknown



Size distribution centered on 60 nm



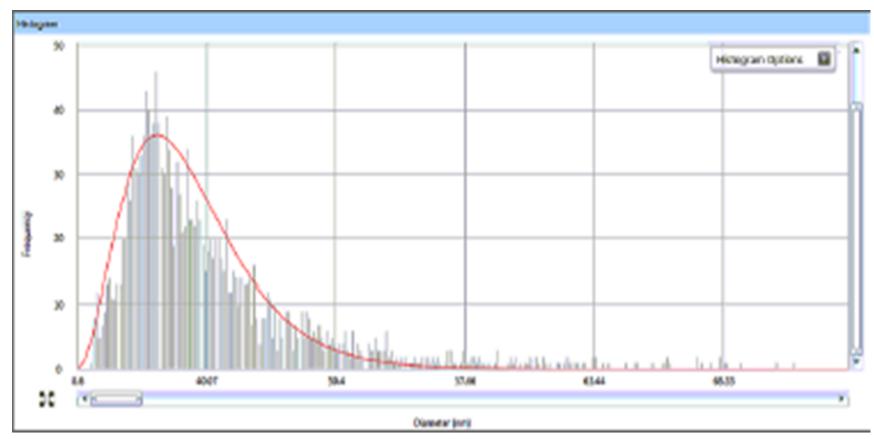
Results: Sample 1



Size distribution centered around 15 nm

Log-normal fitting algorithm selected

Results: Sample 2



Size distribution centered around 33 nm

Log-normal fitting algorithm selected

Results Summary

Sample ID	Mean Size (nm)	Most Frequent Size (nm)	Particle Concentration (particles/mL)	Dissolved Concentration (mg/L)
Sample #1	14	14	3.0E+10	9.5
Sample #2	39	33	2.1 E+9	21.9
Sample #3	53	59	2.7E+10	48.1
50 nm Standard	43	48	2.4E+10	-

- Samples are distinctly different
 - Particle size, particle concentration, & dissolved concentration
- 50 nm Ag Standard run as a control check
 - Most frequent size agrees well with the known value
 - Measured particle concentration agrees well with certificate value
 - Certificate: 2.5E+10 particles/mL



APPLICATION NOTE



ICP - Mass Spectrometry

Authors: Lee Davidowski, Ph.D. Chady Stephan, Ph.D. PerkinElmer, Inc.

Shelton, CT

Characterization of Silver Nanoparticles in Dietary Supplements by Single Particle ICP-Mass Spectrometry

Introduction

A nanopartcile is defined as a small object, between 1 and 100 nanometers in size, that behaves as a whole unit with respect to

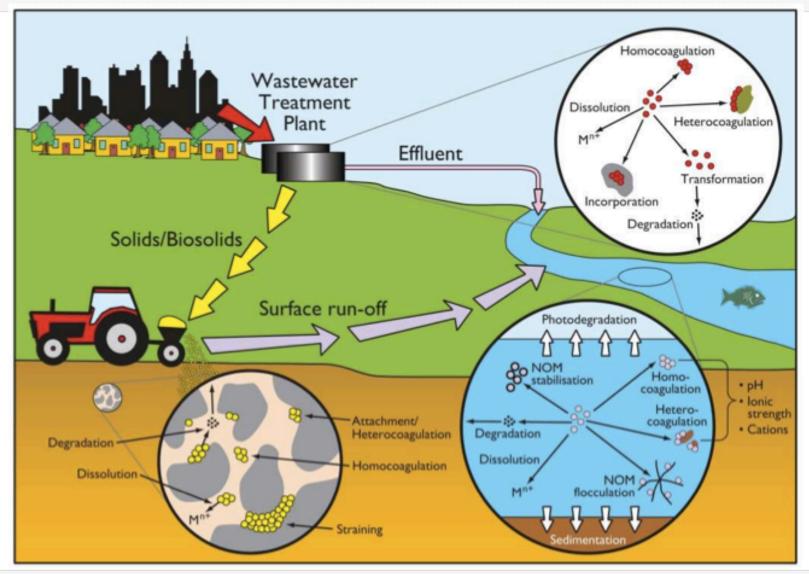
its transport and properties. Because of their small size and large surface area, nanoparticles can exhibit different chemical and physical properties from the bulk material. Nanoparticles have found their way into a large number of consumer products. As of 2013, it is estimated that there are over 1300 different consumer products which feature nanoparticles. Silver nanoparticles (AgNPs) are the most frequently found element in all varieties of consumer products (>23%)¹. Manufacturers of consumer products use AgNPs due primarily to their known antimicrobial properties. Because of their very small size, AgNPs have high surface areas yielding high reaction rates, increasing the efficacy of silver as an antimicrobial.

The use of colloidal and nano silver is directly marketed to the public in such forms as odorless clothing, mildew-resistant shower curtains, food containers and food cutting boards and are even being promoted for direct human consumption as dietary supplements to fortify one's immune system.

More Information

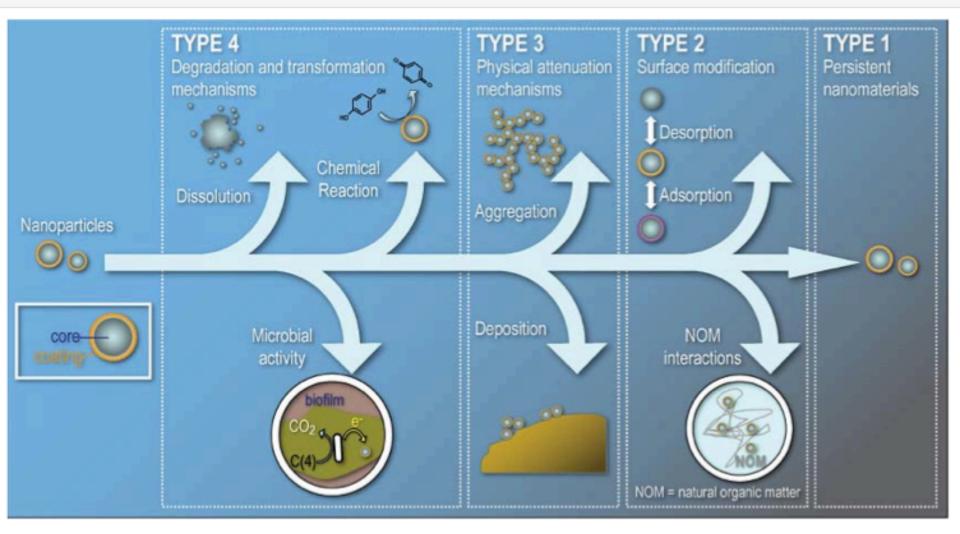


Environmental Samples



G. Batley, SETAC Berlin 2012

Environmental Transformation of ENP's



Alvarez P.J.J., V. Colvin, J. Lead and V. Stone (2009). Research Priorities to Advance Eco-Responsible Nanotechnology. ACS Nano 3(7): 1616-1619

Tracking Nanoparticles in Waste Water



APPLICATION NOTE

ICP – Mass Spectrometry

Authors: Mehrnoosh Azodi Subhasis Ghoshal McGill University

Chady Stephan

PerkinElmer, Inc. Shelton, CT

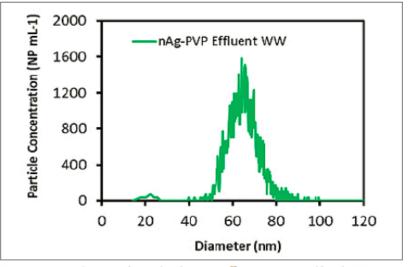


Figure 2. Measured Ag particle size distribution in effluent wastewater diluted 1000 times.

Measurement and Analysis of Silver Nanoparticles in Wastewaters with Single Particle ICP-MS

Introduction

The drastic increase in production and consumption of engineered nanoparticles (ENPs) has raised the concern and questions about their release into the environment and

potential harm to aquatic and terrestrial species. The characteristic properties of nanoparticles, such as small size and high specific surface area and reactivity, make them desirable for their use in various products.

Silver (Ag) nanoparticles are among the most commonly used nanoparticles in consumer products due to their antimicrobial properties. Therefore, it is expected that Ag ENPs will find their way into the environment, necessitating a way to accurately and rapidly detect and characterize them in a variety of environmental matrices. Work has already been performed demonstrating the ability to successfully characterize Ag ENPs in a variety of water samples¹⁻³ and biological media which may be exposed to Ag ENPs in the environment⁴.

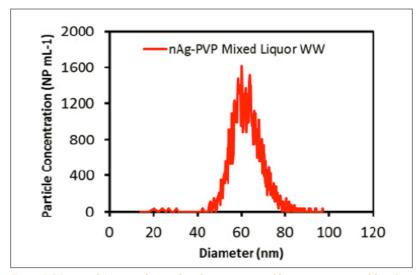
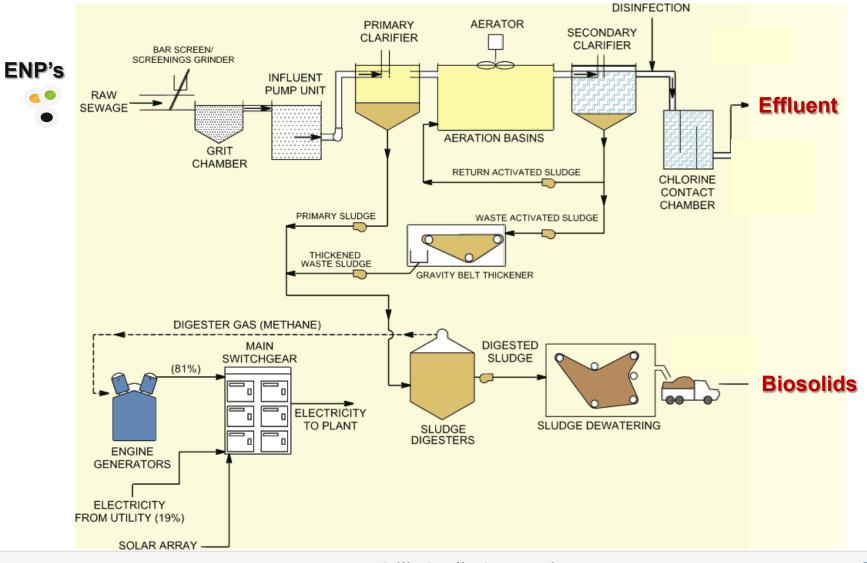


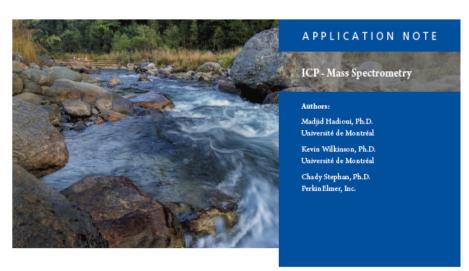
Figure 3. Measured Ag particle size distribution in mixed liquor wastewater diluted 1000 times.

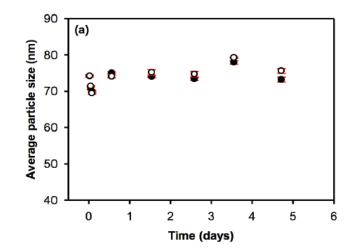
Nanoparticles in Wastewater Treatment Plants

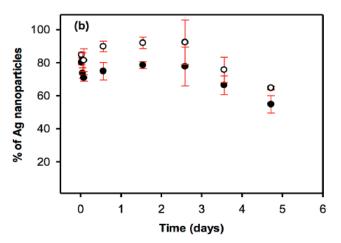


McGill Collaboration

Tracking Transformation of Silver Nanoparticles in Surface Water







Assessing the Fate of Silver Nanoparticles in Surface Water using Single Particle ICP-MS

Introduction

During the last decade, the production and use of engineered nanomaterials (ENIMs) have experienced a drastic

increase, resulting in a potential risk of their release into the environment. Therefore, the study of their impact on the environment becomes crucial. The appropriate ecological risk assessment and management of ENMs in the environment requires quantitative measurements of both exposure and effects' that should, ideally, be performed by in situ analysis and give physicochemical characterization. However, most analytical techniques are not suitable for environmental matrices since nanoparticle concentrations are typically very low².

Some studies on the persistence, aggregation and dissolution of metal nanoparticles in natural freshwaters and synthetic complex waters were recently published^{p-3}. Historically, particle size has been measured by dispersive light scatter (DLS) and tunneling electron microscopy (TEM), while dissolved content has been measured by ultrafiltration. These common techniques have known limitations for measuring low concentrations in the presence of colloidal species in complex waters.

University of Montreal Collaboration

Tracking Nanoparticles Dissolution



APPLICATION NOTE

ICP - Mass Spectrometry

Denice Mit

James P. Rasville

Department of Chemistry and Geochemistr Colorado School of Mines Golden, CO USA

Chady Stephan Perkinfilmer, Inc. Shelton, CT

Quantitative Evaluation of Nanoparticle Dissolution Kinetics using Single Particle ICP-MS: A Case Study with Silver Nanoparticles

Accurate data on engineered nanoparticle (DNP) environmental behavior and the interolay

between ENP size, dissolution rate, apglomeration, and interaction with the sample matrix is ortical to appropriately characterize the risks these novel materials may pose to environmental health. The advancement of the single particle ICP-MS STechMS technique is a great benefit for the study of ENPs in natural systems at environmentally relevant (ngt.) concentrations. Revious studies may have obscured environmentally-relevant transformations because of artificially high ENP concentrations used in the experimental. Therefore, the SP-ICP-MS method is at the forefront to game the type of information most relevant for environmental risk assessments, namely the precise tracking of changes in ENP size, associated dissolved metal concentrations and determining polydispensity of an EMP sample, all at lute concentrations in complex solutions. Because dissolution rate is surface-rese controlled, the time to complex molection is highly dependent on the initial and (potentially stable) intermediate particle sizes. By measuring the change in particle size, as well as the evolution of Agriagi in solution, using SP4/CP-MS, potential pitfalls related to loss of Agr to experimental materials and to other environmental surfaces, such as supended sediments or biota in the case of complex matrices, may be avoided.



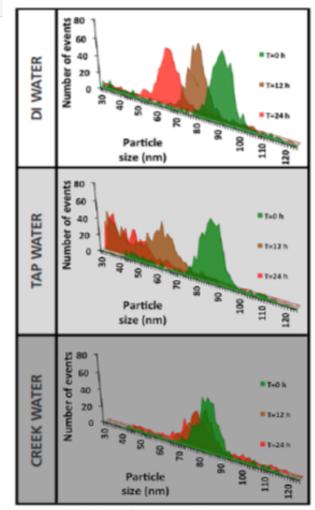


Figure 2. Particle size distribution of Ag ENP suspended in various water chemistries [D], tap, and creek waters) over 24 h. Evidence of decreasing particle diameter with ime through particle oxidation and dissolution in some samples (e.g. DI and tap raters) with less change in particle size observed in other samples, (e.g. creek water).

Quantitative dissolution of Nanoparticles – App note

Bioaccumulation/Bioavailability of Ag Nanoparticles



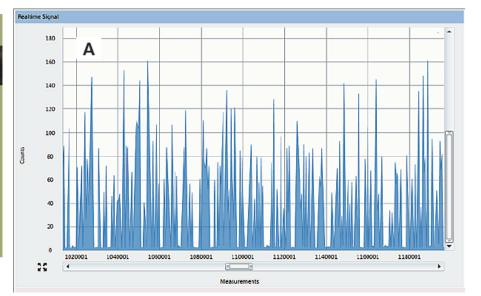
APPLICATION NOTE

ICP - Mass Spectrometry

Authors: Evan Gray Christopher P. Higgins Department of Civil an

Engineering James F. Ranville

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Analysis of Nanoparticles in Biological Tissues using SP-ICP-MS

Introduction

The use of engineered nanoparticles (ENPs)

in consumer products is well documented and has raised concern of the eventual fate and potential toxicity of these materials at the end of their consumer-product life^{1,2}. It is likely that these materials will eventually find their way into environmental systems through food packaging and manufacturing, food products or waste disposal². The analysis of ENPs is focused on three metrics: particle size, particle number, and particle mass distributions. Each of these metrics is very important for assessing environmental effects, and utimately the risk associated with the use of these materials in consumer products. While established methods exist for the determination of mass distributions of metals in tissue samples, few robust methods have been developed to detect and characterize nanomaterials, especially particle number and size distributions⁴.

- L. variegatus was digested using the TMAH procedure, allowing for SP-ICP-MS analysis of tissues.
- The pulses observed in Figure 2A, can clearly be observed above a very low Ag+ background.

Bioavailability of Gold Nanoparticles in Tomato Plants



APPLICATION NOTE

ICP - Mass Spectrometry

Authors

Yongbo Dun¹², Weilan Zhang¹, Xingmao Ma²³, Honglan Shi¹³, Chady Stephan⁴

¹Department of Chemistry, Missouri University of Science and Technology

¹Center for Single Nanoparticle, Single Cell, and Single Molecule Monitoring (CS¹M), Minsouri University of Science and Technology ²Department of CHill and Environmental Bagiasering, Southern Illinois University ⁴PedenEinser, Inc.

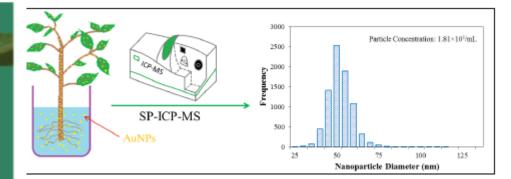


Table 1. NexION 300/350D Instrumental and Analytical Parameters.

Parameter	Value
Nebulizer	Concentric (glass)
Nebulizer Flow	1.08 L/min
Spray Chamber	Baffled Cyclonic (glass)
ICP RF Power	1600 W
Analyte	Au
Mass	197 amu
Dwell Time	0.1 ms
Settling Time	0 ms
Sampling Time	100 sec
Number of Data Points Acquired	1 million per sample
Au Density	19.3 g/cm ³

Gold Nanoparticle Uptake by Tomato Plants Characterized by Single Particle ICP-MS

Introduction

With the increasing use of engineered nanoparticles (ENPs) in a variety of products and processes, there is concern about the release of ENPs into and impact on the environment. One aspect of the environmental into and indicate or ENPs environmental into an environmental interest of the environmental into an environmental interest of the environmental into an environmental interest of the environ

impact of ENPs that must be explored is their uptake by plants, as ENPs can make their way to plants via migration through water and/or soil. If ENPs end up in food crops, this is a potential pathway to human exposure.

The challenge arises in how to measure ENPs in plant materials and, more specifically, in sample preparation. To our knowledge, current sample preparation techniques have limited capability to conserve the concentration and characteristics of nanoparticles INP1 income they enter plant tissues, as they mainly depend on acid digestion. These limitations can be avoided by careful choice of the ENP extraction procedure and performing the analysis with single particle ICP-MS (SP4CP-MS), the combination of which will preserve the particle size information, allow for rapid analysis of a large number of samples, and yield results on the particle size. concentration, and size distribution.

Rapid Analysis of Nanoparticles in Drinking Water



APPLICATION NOTE

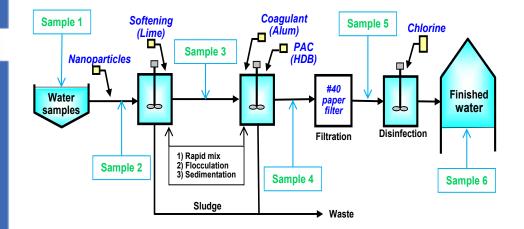
ICP - Mass Spectrometry

Authors

Ariel R. Donovan¹³, Honglan Shi¹³, Onig Adams²³, Chady Stephan⁴

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²Department of Criti and Environmental Engineering, Utah State University
⁴PerkinElines. Inc.



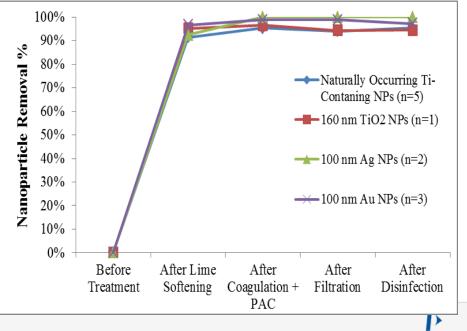
Rapid Analysis of Silver, Gold, and Titanium Dioxide Nanoparticles in Drinking Water by Single Particle ICP-MS

Introduction

ticles in Drinking Single Particle ICP-MS The discharge of industrial waste and from discarded consumer products. Although

the concentration of NPs is expected to be low in environmental systems, their impact on human health is unknown. Therefore, the need exists to determine NPs in drinking water systems.

Because of its unique ability for rapid, sensitive and element-specific analysis, single particle CP-MS (SP-ACP-MS) is an ideal tool for measuring Ms in drinking water systems. This work will highlight the efficiency of drinking water treatment systems in removing silver (Ag), gold (Au), and thanum dioxide (TiO) nanoparticles using SP-ACP-MS as the sole analytical technique.



Effectiveness of Three Water Treatment Plants at Removing TiO₂ Particles and Dissolved Titanium

Plant #	Treatment Pre vs. Post	Most Frequent Size (nm)	Particle Concentration (Particles/mL)	Dissolved Concentration (ug/L)
1	Pre	170	432.000	18
	Post	< 65	<	1
2	Pre	150	451,000	12
	Post	< 65	<	1
3	Pre	160	425,000	11
	Post	< 65		< 0.5

Toxic Substances Control Act (TSCA) Section 8(a) TSCA Modernization Act, December 17, 2015

- Gives EPA broad authority to require manufacturers and processors of chemical substances to maintain records or report data to carry out TSCA mandates.
 - Regulations can be tailored to meet needs via chemical-specific rules or information can be obtained via use of standardized reporting rules.
 - Examples of Section 8(a) reporting rules are a Preliminary Assessment Information Rule (PAIR)(40 CFR part 712) and the Chemical Data Reporting Rule (CDR)(40 CFR part 711).

https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act

Control of Nanoscale Materials under the Toxic Substances Control Act

Regulatory Approach

To ensure that nanoscale materials are manufactured and used in a manner that protects against unreasonable risks to human health and the environment, EPA is pursuing a comprehensive regulatory approach under TSCA including:

- Premanufacture notifications (PMN's) for new nanomaterials
- An information gathering rule on new and existing nanomaterials
- Mandated by section 5 of the Toxic Substances Control Act (TSCA), EPA's New Chemicals program helps manage the potential risk to human health and the environment from chemicals new to the marketplace. The program functions as a "gatekeeper" that can identify conditions, up to and including a ban on production, to be placed on the use of a new chemical before it is entered into commerce.



Goals of Issuing this TSCA Section 8(a) Proposed Rule

- Ensure that EPA has basic information on nanoscale materials currently in commerce to:
 - Increase understanding of what nanoscale materials are in commerce;
 - Inform EPA efforts to characterize risk; and
 - Enhance the ability to assess risks and make appropriate risk management decisions.
- EPA would review the data submitted for all nanoscale materials subject to the rule.
- EPA would consider whether further actions or additional data are needed.

A Major Issue in Utilizing TSCA to Regulate ENP's are the Exceptions:

- Any Food and Food Additive
- Drugs
- Cosmetics
- "Devices"

The above are beyond EPA's reach and most fall under the authority of the FDA, but so far FDA has ruled nanoparticles to be identical to the bulk material.

Guidance documents issued

On June 24, 2014, FDA issued **three final guidance documents** related to the use of nanotechnology in regulated products, <u>incuding cosmetics and food substances</u>. **c. Toxicity Testing Section**

On August 5, 2015, FDA issued **one final guidance document** related to the use of nanotechnology in <u>food for animals</u>.



ISO TC229 Nanotechnologies

Technical Working Groups: JWG1 – Terminology and Nomenclature JWG2 – Measurement and Characterization WG3 – Health, Safety and Environment WG4 – Material Specifications Other Groups: CAG – Chairman's Advisory Group TG2 – Consumer and Societal Dimensions TG3 – Sustainability

Selected Published Standards:

- ISO/TS 13830:2013: Nanotechnologies Guidance on Voluntary Labelling for Consumer Products Containing Manufactured Nano-Objects
- ISO/TS 80004-8:2013: Nanotechnologies Vocabulary Part 8: Nanomanufacturing
- ISO/29701:2010: Nanotechnologies Endotoxin Test on Nanomaterial Samples for In Vitro Systems – LAL Assay
- ISO/TS 11308:2011: Nanotechnologies Characterization of Single-Wall Carbon Nanotubes Using Thermogravimetric Analysis

Selected Work Items Currently Under Development:

- **ISO/DTR 18196:** Nanotechnologies Measurement Technique Matrix for Nano-Objects
- ISO/DTS 19590: Nanotechnologies Nano-Objects Detection and Characterization Using Single-Particle ICP-MS
- ISO/DTR 19601: Nanotechnologies Nano-Object Aerosol Generators for Inhalation Toxicity Studies

SP-ICP-MS for Nanomaterials



Environmental

- •Fate studies
- Drinking water
- •Surface water
- Water treatment
- Remediation studies
- •Bioavailability studies
- •Bioaccumulation studies
- Distribution in the ecosystem



Consumer

- •Health and Fitness
- Energy
- Food and Beverage
- Textiles
- Paint
- Semiconductor
- Automotive
- •Electronics and computesr •Sunscreen
- •Nanocomposite materials

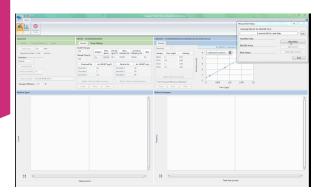




Biological/Biomedical

- Early diagnosis
- Cancer treatment
- Drug design and delivery
- •Toxicological studies

Single Particle ICP-MS Syngistix™ Nano Application Module



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