The Application of exposure science to the life cycle

This research is funded by U.S. EPA - Science To Achieve Results (STAR) Program Grant # RD833322

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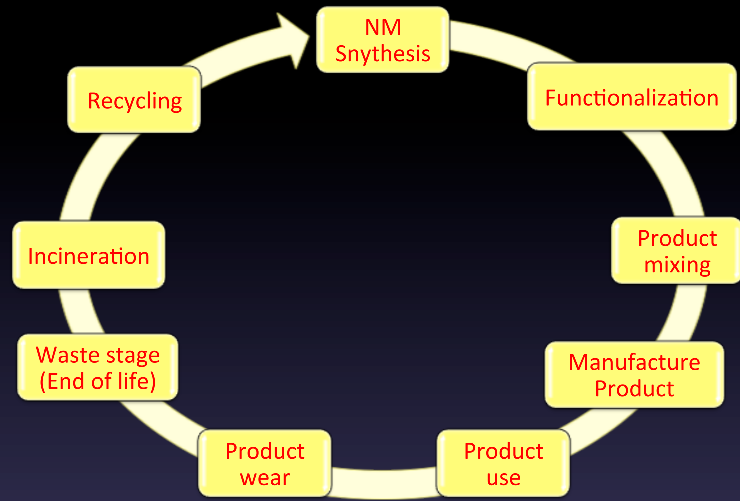
DOE BER
Grant number: DE-FG02-08ER64613



Paul Westerhoff, PhD, PE, BCEE

Arizona State University (Tempe, AZ)

A true story
Two men walk into my office…

A worker claiming to be exposed to nanomaterials and feeling sick and unable to work any more

A lawyer asking what diseases do nanoparticles cause in workers

Joking aside: We don't really know how to help
Despite over a decade of research

Guiding Questions for Presentation

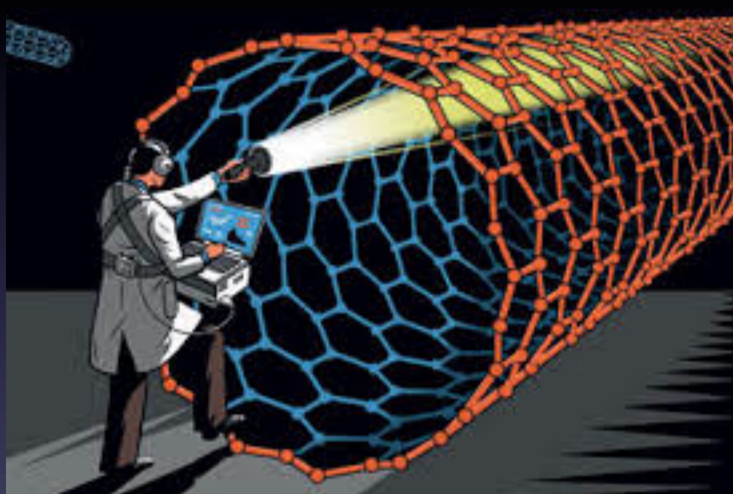
What is the state of the science in nano exposure?

What data & methods are available for releases from products across the life cycle?

What tools are being used to detect & quantify exposures?

What are the data telling us?

What is the state of the science in nano exposure?



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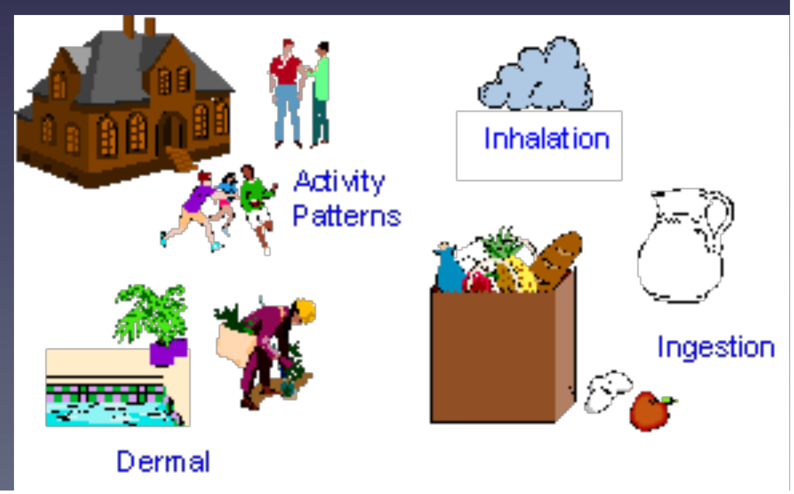
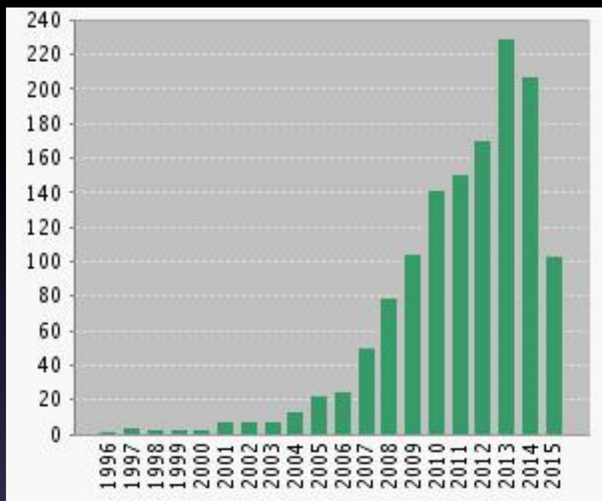
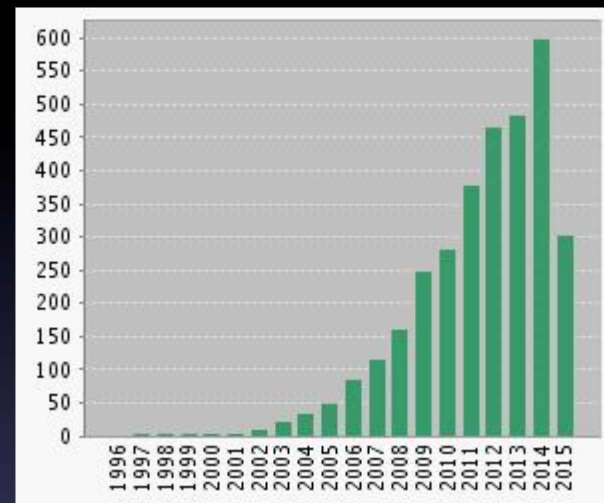


Publication Trends:
What's in a title?

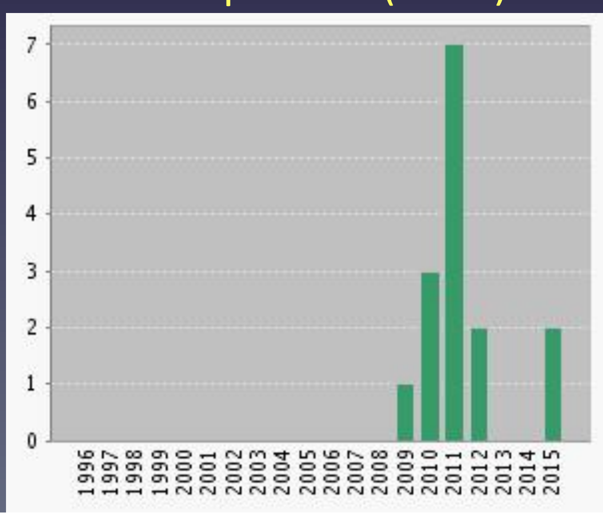
Nano* + Exposure (n=1375)



Nano* + Toxic* (n=5,270)



Nano* + Epidem* (n=16)



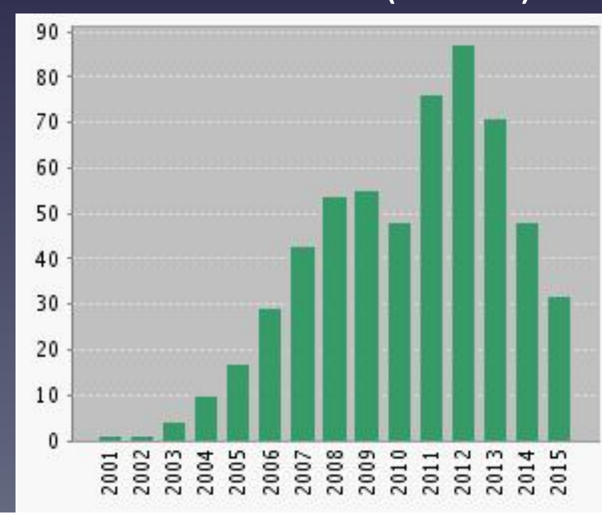
Focus on workers (most prior to 2012)

None related to consumers

One provactive hypothesis title:

Type 1 diabetes epidemic in Finland is triggered by zinc-containing amorphous silica nanoparticles

Nano* + Risk (n=576)



2010 Workplace Exposure Challenge

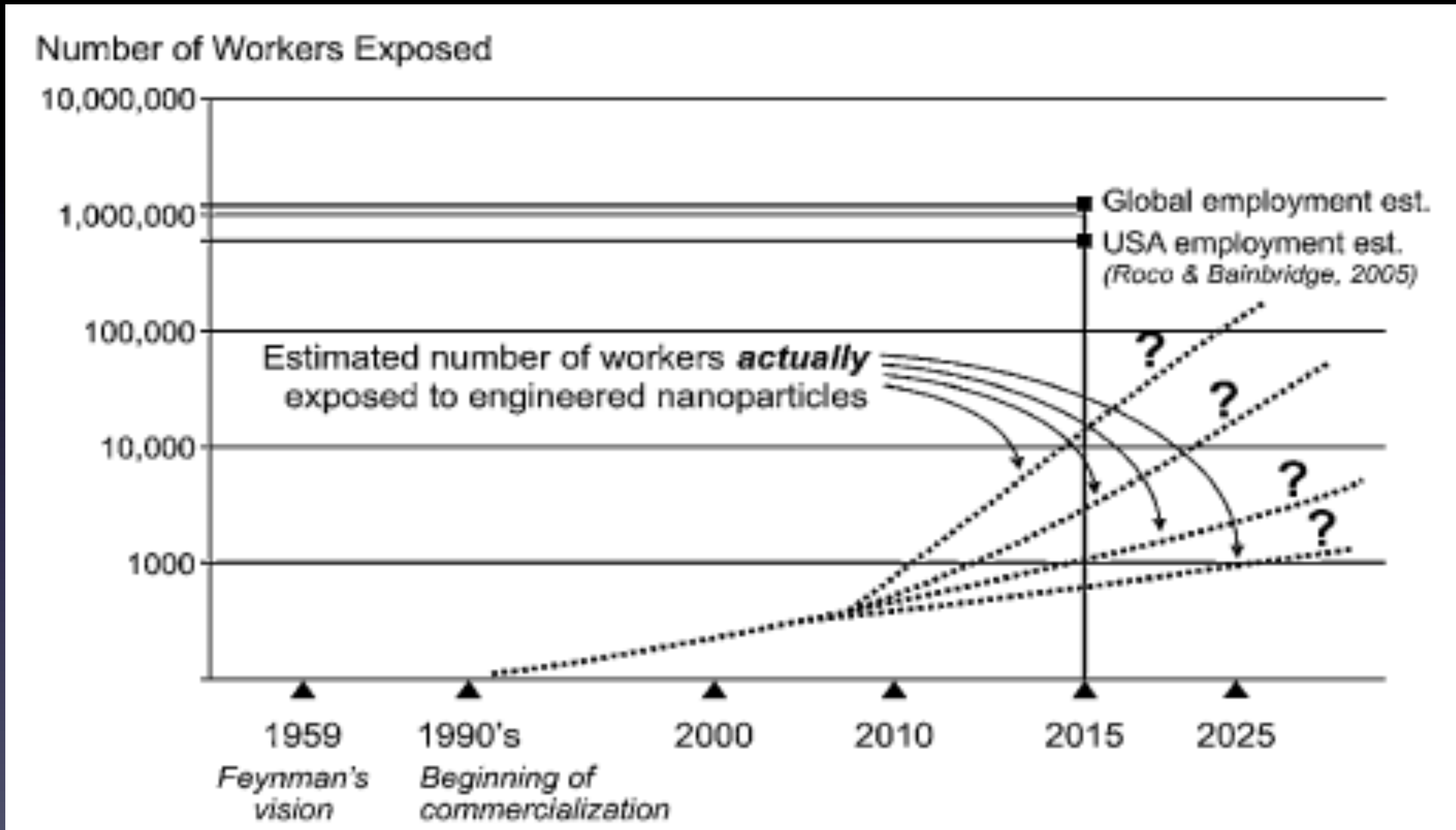


Fig. 4. Dilemmas in identifying workers exposed to engineered nanoparticles.

D.B. Trout, P.A. Schulte / Toxicology 269 (2010) 128–135

Based upon all these publications - Have we made Progress?

National Nanotechnology Initiative

ENVIRONMENTAL, HEALTH, AND SAFETY RESEARCH STRATEGY

National Science and Technology Council
Committee on Technology

Subcommittee on Nanoscale Science, Engineering, and Technology

OCTOBER 2011

1. Develop NM measurement infrastructure
2. Human exposure assessment
3. Human health
4. Environment
5. Risk Assessment & management methods

2008 NNI-EHS Strategy Priority Areas for Human Exposure Assessment

1. Characterize exposure among workers — C-
2. Identify population groups and environments exposed to ENMs — C
3. Characterize exposure to the general population from industrial processes and industrial and consumer products containing ENMs — D
4. Characterize health of exposed populations and environments — D
5. Understand workplace processes and factors that can determine exposure to ENMs — A

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2011 Human Exposure Assessment research requirements

- Develop methods or approaches to identify sources, characterize exposure scenarios, and measure actual exposure to NMs **B-**
- Collect data and information on the life cycle and variables affecting exposure to NMs **C+**
- Collect data and develop databases for health surveillance and exposure to NMs **D**
- Develop models to estimate exposures to specific NMs **D**

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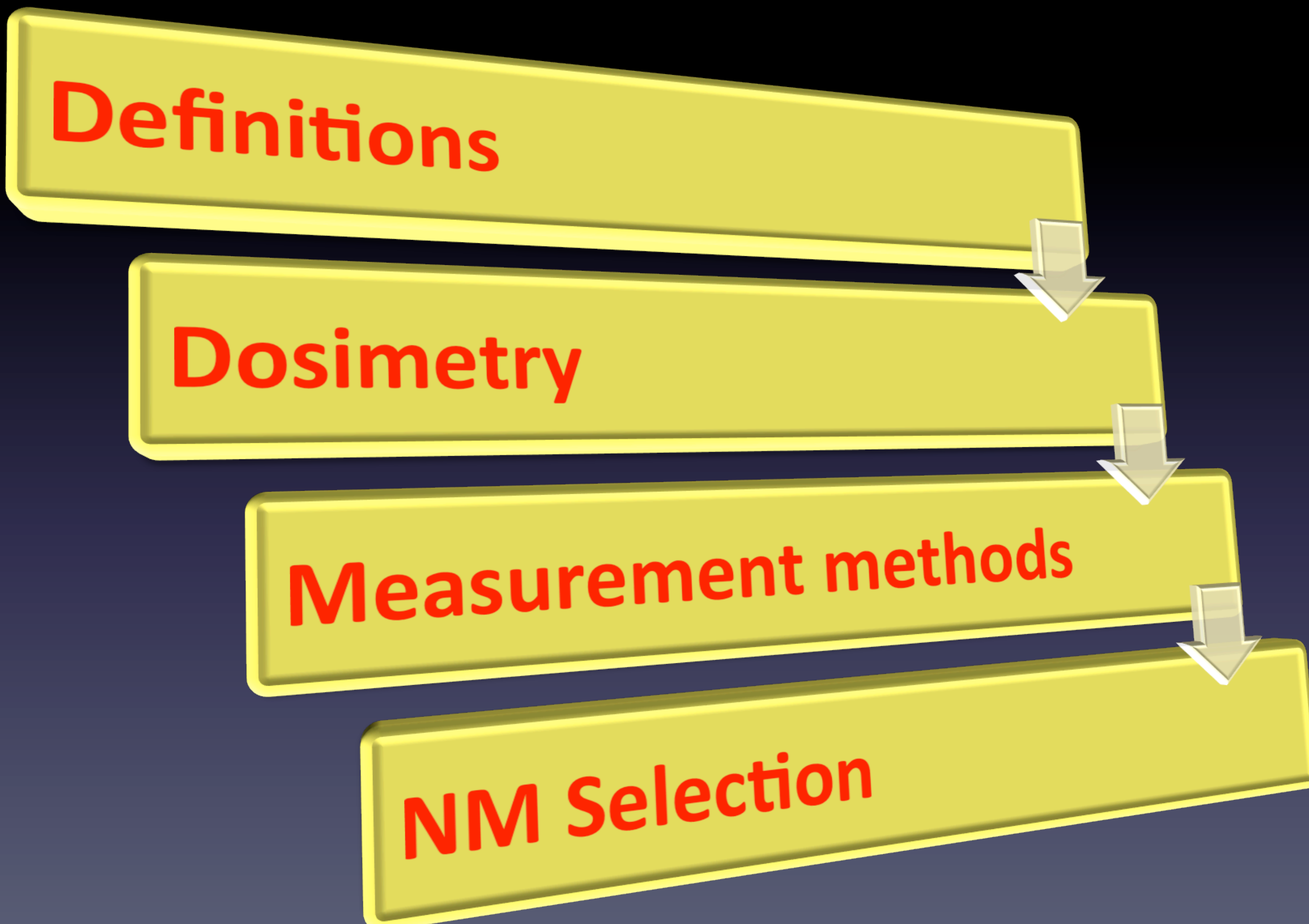
Factors Influencing Lack of Progress in Exposure Assessments



Definition of Nano Remains an Issue

- Common definition
  - Less than 100 nm in at least 1 dimension
  - Should have unique properties
- EU Regulation on **Cosmetics** (EU/1223/2009):
  - Nanomaterial means an *insoluble or biopersistent and intentionally manufactured* with … on from 1 to 100 nm
- EU Regulation on **food labelling** (EU/1169/2011)
  - Engineered NM means any *intentionally produced material* … dimensions on the order of 100 nm or less…, including structures, agglomerates or aggregates, which may have size > 100 nm but retain properties that are characteristic of the nanoscale (high SA, don't exist in non-nanoform)
  - [under consideration]: …*intentionally manufactured material*, containing particles, in an unbound state or as an aggregate or agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is 1 to 100 nm
- EU Regulation on **Biocidal products** (EU/528/2012)
  - NM means *natural or manufactured* active substances or non-active substances containing particles…50% or more of the particles in the number size distribution, one or more external dimensions is 1 to 100 nm (including fullerenes, FLG, CNT)

Dosimetry is a challenge

Units

- Mass concentration is the historical metric for exposure assessments
- Nano specific considerations:
  - Number concentrations
  - Size and concentrations
  - Surface area concentration
  - Aspect ratio

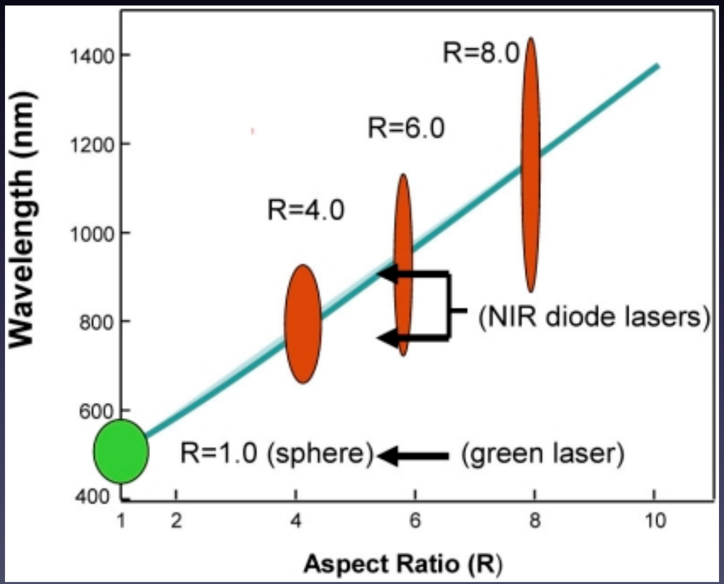
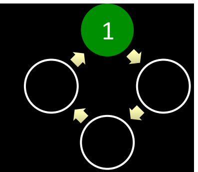
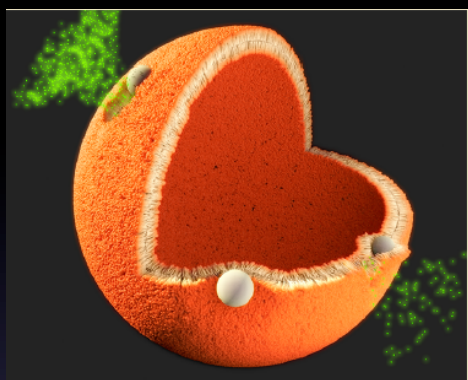
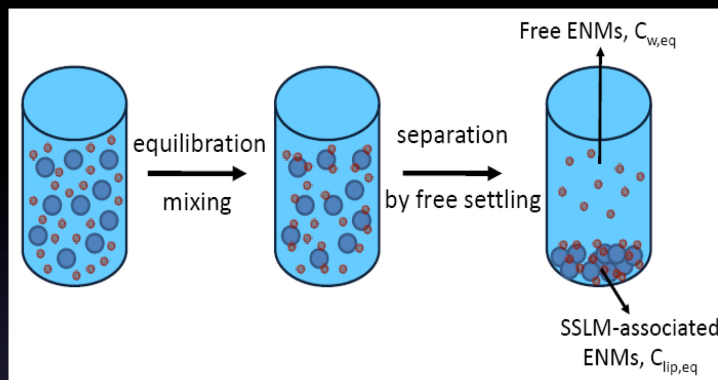


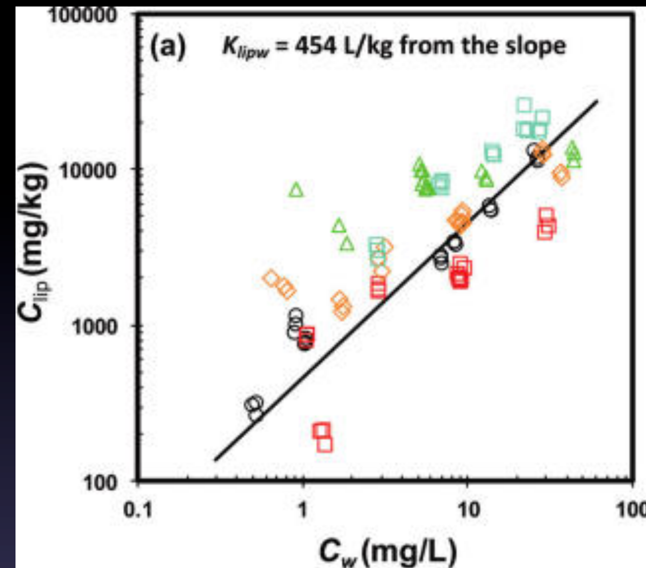
***Figure 1.** The resonant wavelength is redshifted from the visible (for spherical nanoparticles, with R=1) to near-IR (for nanorods, with R > 1). R: Aspect ratio. NIR: Near-IR. Lin SPIE Newsroom*

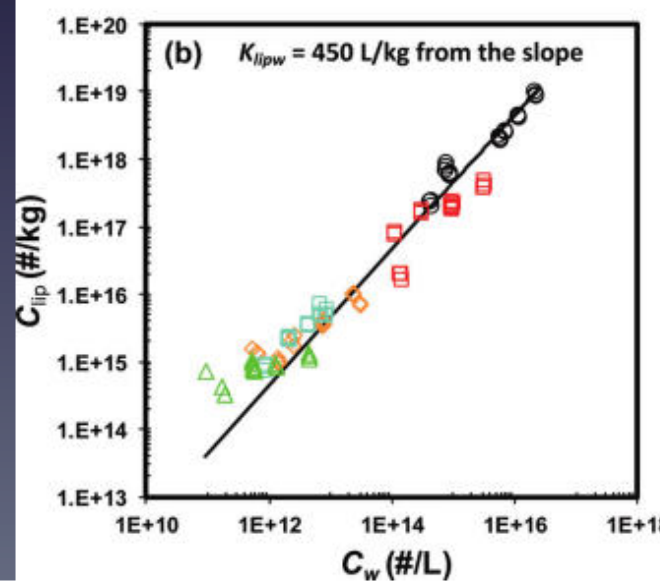


Example Dosimetry
Au-NP / Lipid Distributions





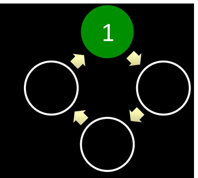




Particle number may be better than mass concentrations as a predictor

It's difficult to control dosimetry at same mass & # concentrations for different sized nanoparticles

Hou et al., ES&T, 2012, 46, 1869-1876



What concentration levels are potentially a concern?

External Dosing

(*in vivo* aquatic organisms)

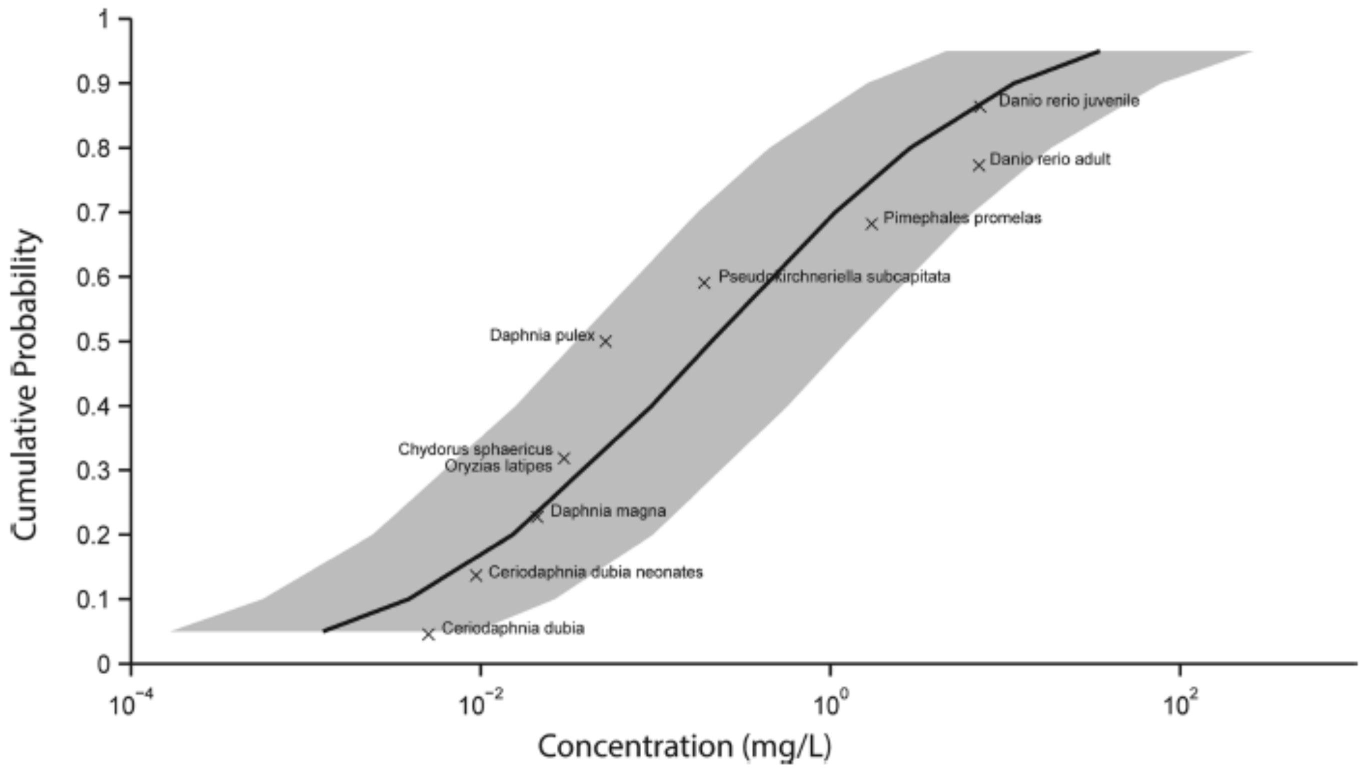


Figure 1. Species sensitivity distribution for uncoated n-Ag, based on 10 species. The 95% confidence interval is shown by the gray shaded area around the curve, which indicates a range in values of about 1 order of magnitude.

Garner et al., Environ. Sci. Technol. 2015, 49, 5753–5759

Surface Functionality & Ionization Broaden Range of Toxicity Concern

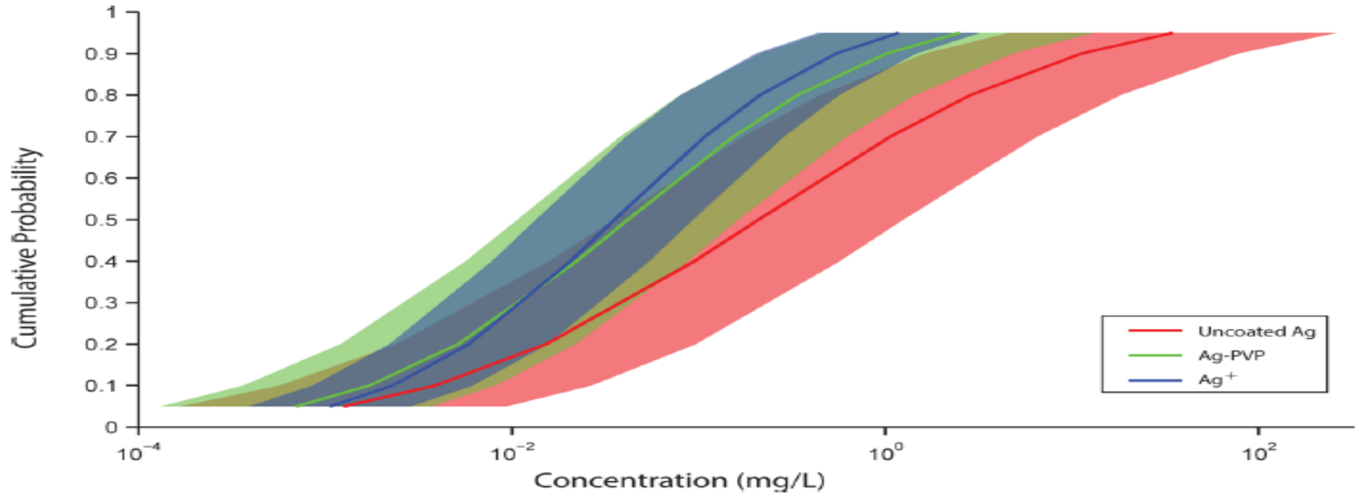


Figure 2. Comparison of silver SSDs, including uncoated n-Ag, PVP-coated n-Ag, and Ag^{+} derived from dissolving AgCl and $AgNO_3$. The 95% CI for each curve is depicted by the corresponding shaded area.

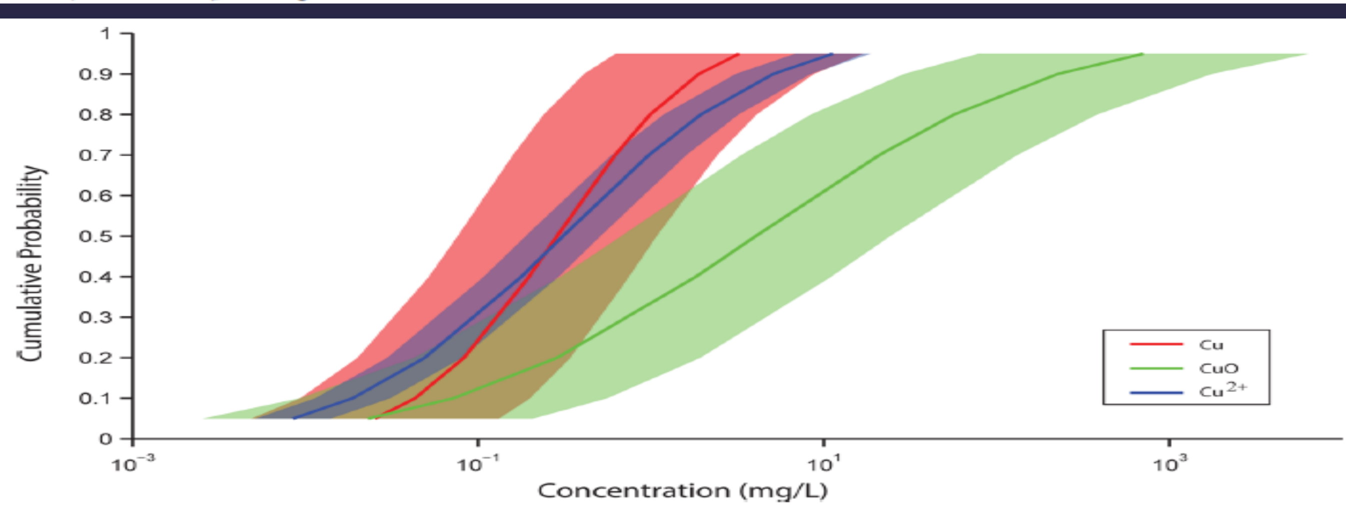


Figure 3. Comparison of copper SSDs, including n-Cu, n-CuO, and Cu^{2+} derived from dissolving $CuCl_2$, $Cu(NO_3)_2$, or $CuSO_4$. The 95% CI is depicted as the shaded region in color corresponding to each curve.

Garner et al., Environ. Sci. Technol. 2015, 49, 5753–5759

Two forms of Carbon

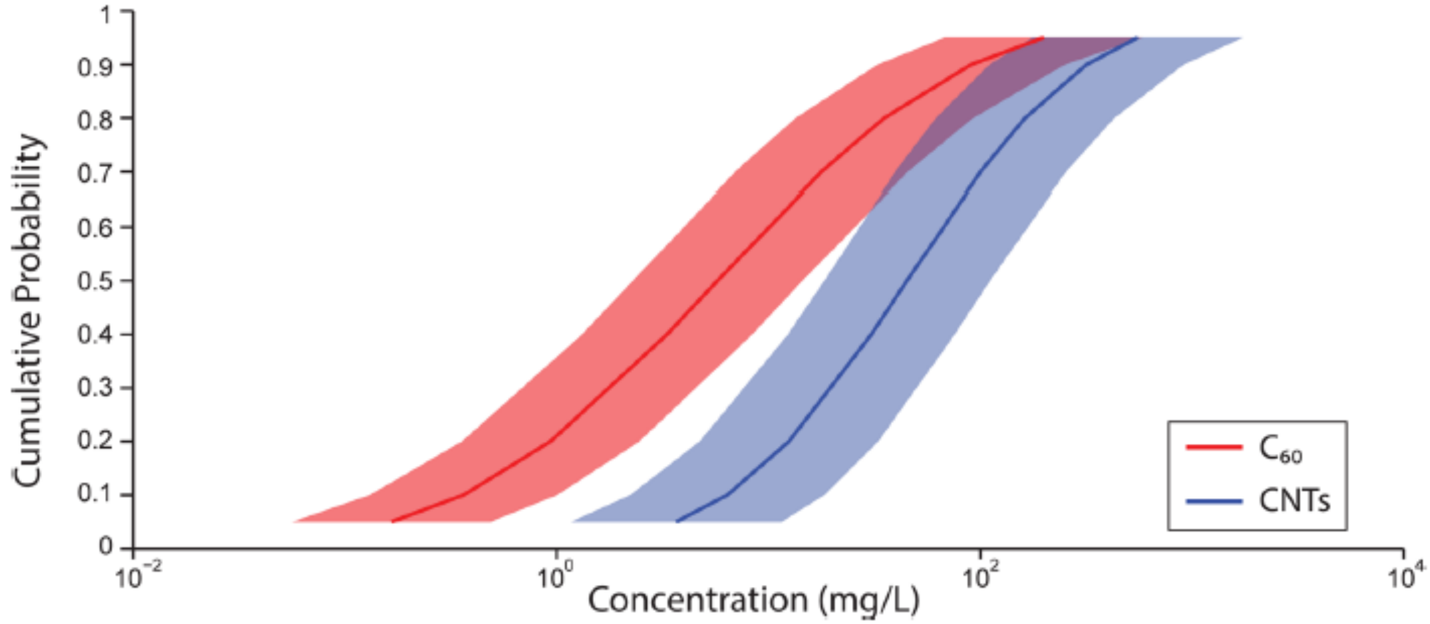


Figure 5. Comparison of carbonaceous nanoparticle SSDs, including n-C_{60} and CNTs. The shaded region around each curve depicts the 95% CI.

Garner et al., Environ. Sci. Technol. 2015, 49, 5753−5759

Example of Advances in human Toxicity & exposure ranges (μg/mL) being tested

"High-Throughput Screening Platform for Engineered Nanoparticle-Mediated Genotoxicity Using CometChip Technology" by Watson et al., ACS Nano 8:3:2188 (2014)

Genotoxicity profiles were observed:

- ZnO > Ag > Fe2O3> CeO2 > SiO2 in TK6 cells at 4 h
- Ag > Fe2O3 > ZnO > CeO2 > SiO2 in H9T3 cells at 24 h

- Toxic metals in ionic form are toxic in nano-form

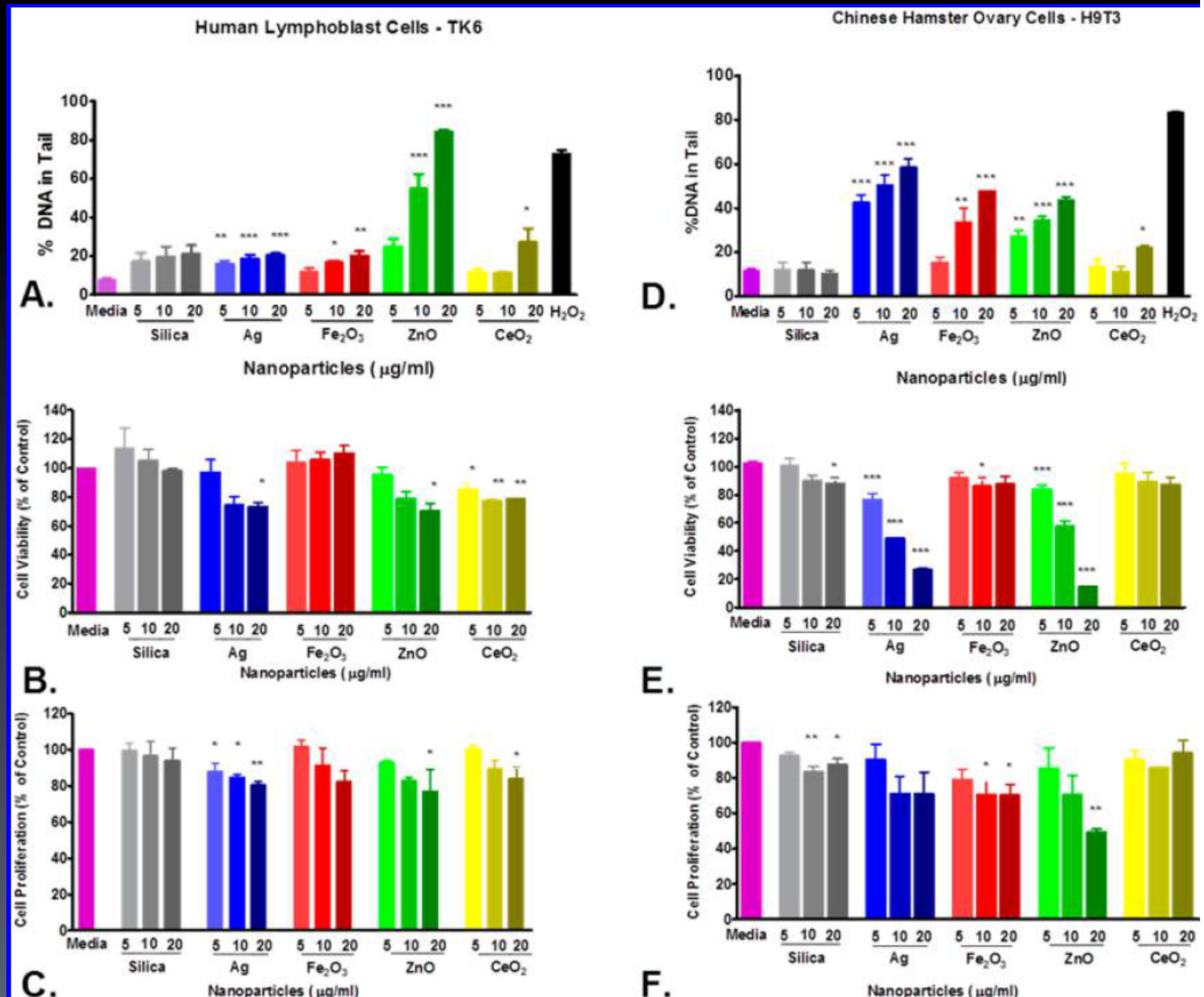


Figure 3. Evaluation of TK6 cells seeded at a density of 1 × 10^6 cells/well and H9T3 cells seeded at a density of 1 × 10^4 cells/well exposed to 5, 10, and 20 μg/mL of ENPs where (A,D) DNA damage, (B,E) cellular viability, and (C,F) CyQuant NF assessments were performed 4 and 24 h post-exposure, respectively. Data represent an average of three or more

Field is moving toward integrated strategies for *in vitro* dosimetry

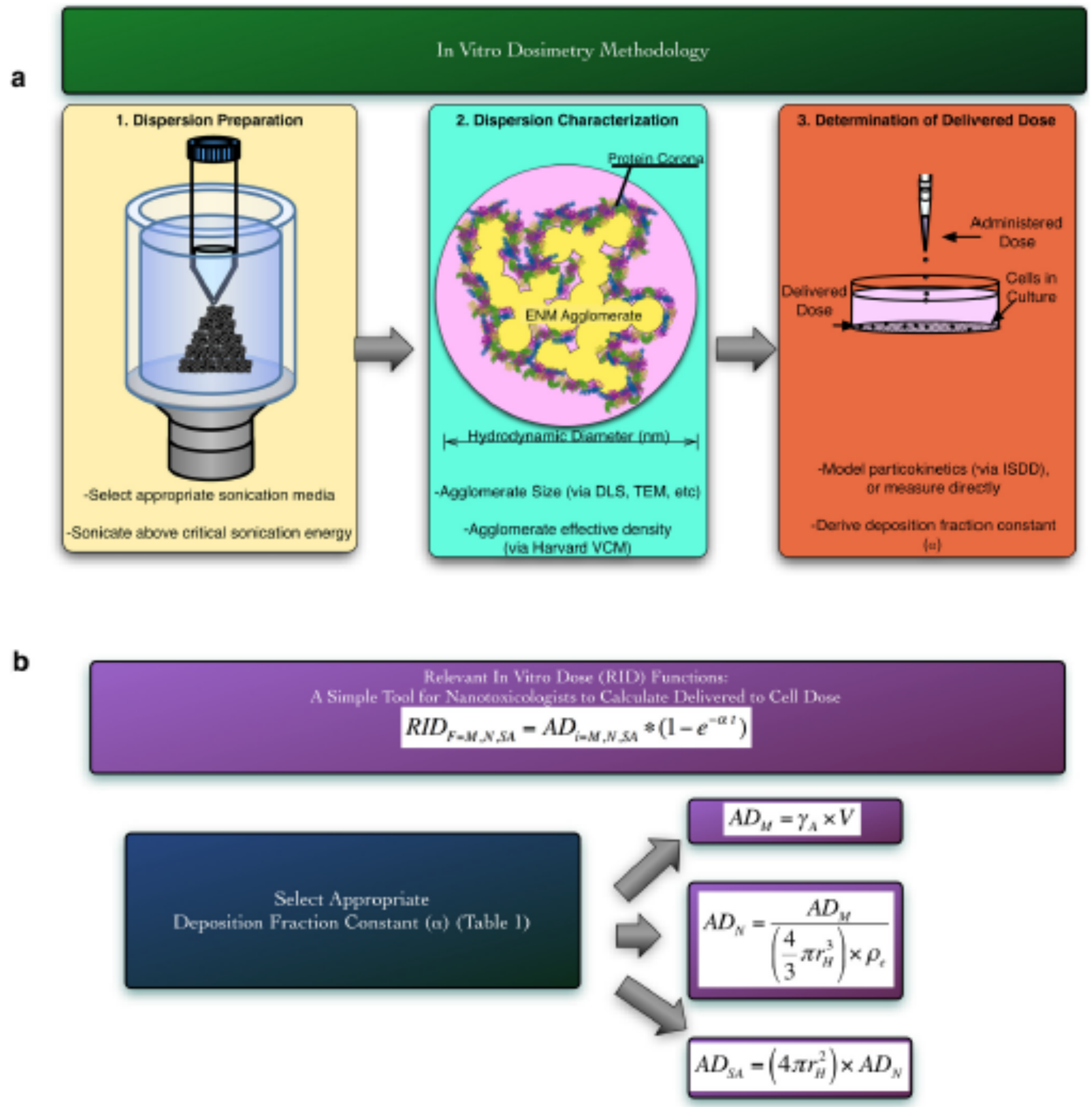


Figure 1 Schematic Map for proposed integrated In Vitro Dosimetry Methodology. a, Proper dispersion preparation requires selection of appropriate sonication media (such as DI H_2O for metal oxide ENMs), and sonication above the critical sonication energy required to break ENMs down to the smallest possible agglomerates that are stable over time. Characterization of dispersion characteristics including agglomerate diameter and agglomerate effective density allow for accurate modeling of particokinetics in vitro, and determination of delivered dose metrics and the deposition fraction constant. **b**, Relevant In Vitro Dose functions (RIDs) provide a simplified tool for nanotoxicologists to quickly estimate delivered dose values for the ENMs investigated in this manuscript. Selection of the appropriate deposition fraction constant (α, listed in Table 1), allows nanotoxicologists to directly calculate relevant in vitro doses (RID) for any exposure duration, including delivered ENM mass (RID_M, µg), delivered particle number (RID_N, #), and delivered surface area (RID_{SA}, cm^2), using the equations listed below. t is exposure duration (h), γ is ENM mass concentration (µg/ml), V is media volume applied to cells (ml), r_h is hydrodynamic radius (cm, listed in Table 1), and ρ_E is agglomerate effective density (g/cm^3, listed in Table 1).

Cohen et al. Particle and Fibre Toxicology 2014, 11:20

Internal Dose Assessment

- SNO Special Workshop on Nanoceria
- Accumulation, target organs, and issues of clearance;
  - After IV infusion, nanoceria rapidly translocates from the blood to the liver, spleen, and bone marrow, from which clearance is slow
  - Appreciable entry of nanoceria into brain parenchyma was not seen with ≥ 5 nm ceria, but was observed in the cerebellum with a 2.9 nm ceria.
  - Ce^{3+}/Ce^{4+} ratio of NPs can change

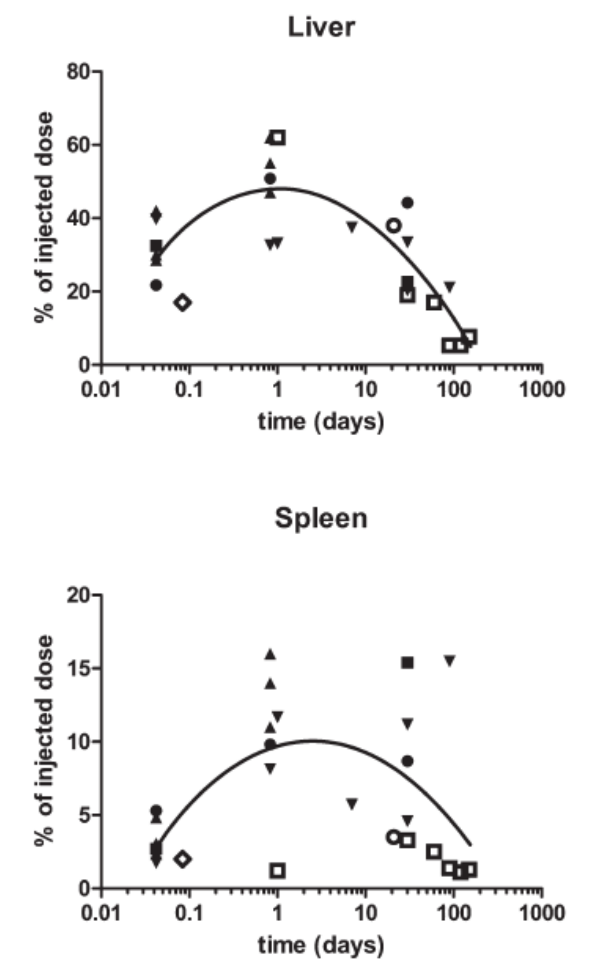


Fig. 1 The percentage of the injected dose in the liver and spleen after intravenous nanoceria administration of various sizes, shapes, doses, and surface-coatings. ● = five nm, polyhedral, citrate-coated,

Yokel et al., Environ. Sci.: Nano, 2014, 1, 406

What data & methods are available for releases from products across the life cycle?

Global, product-line & local life cycles

Release studies

Analytical methods for exposures

NM Type & Flux Through Society
Global Life Cycle Assessment
(The BIG 10 nanomaterials)

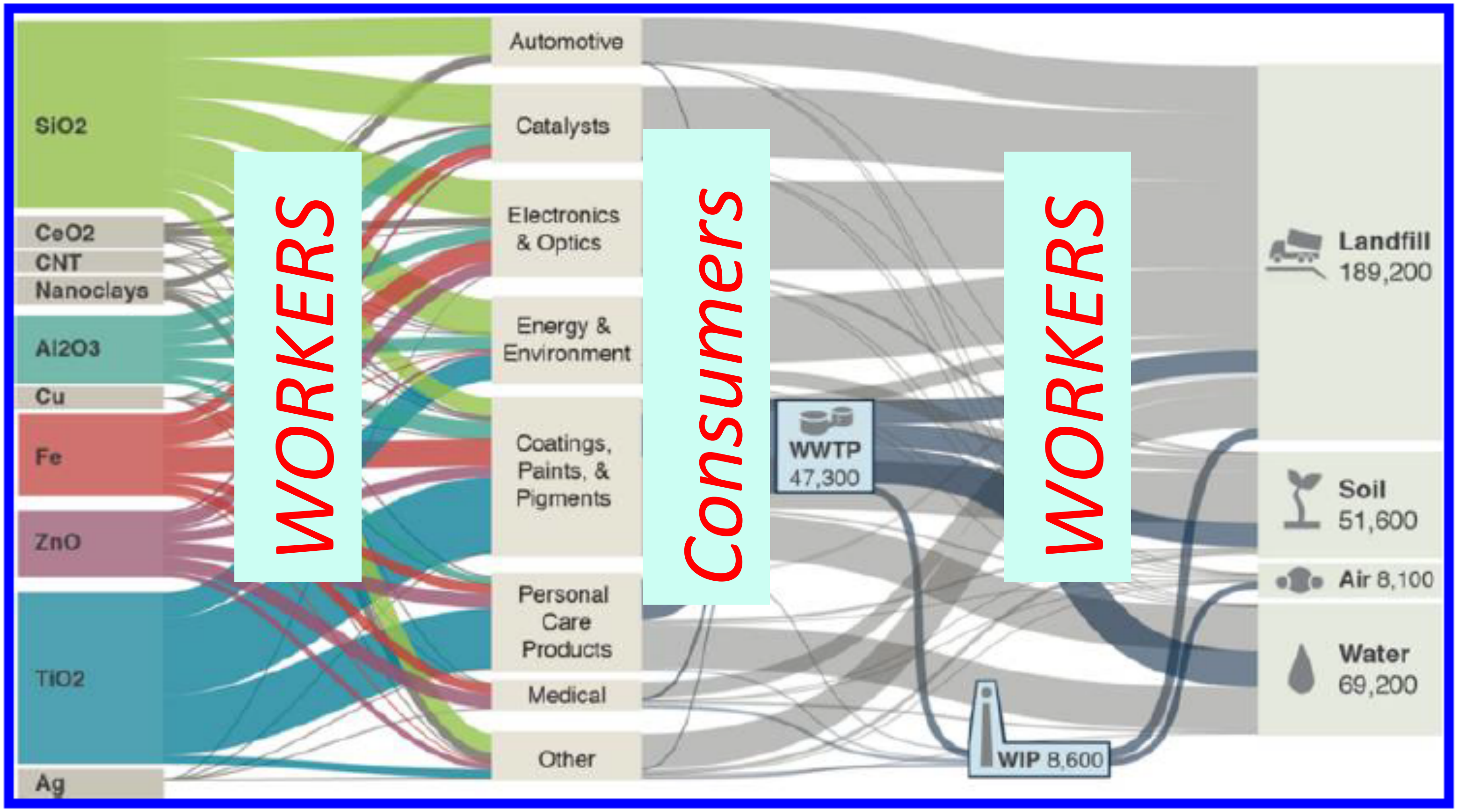
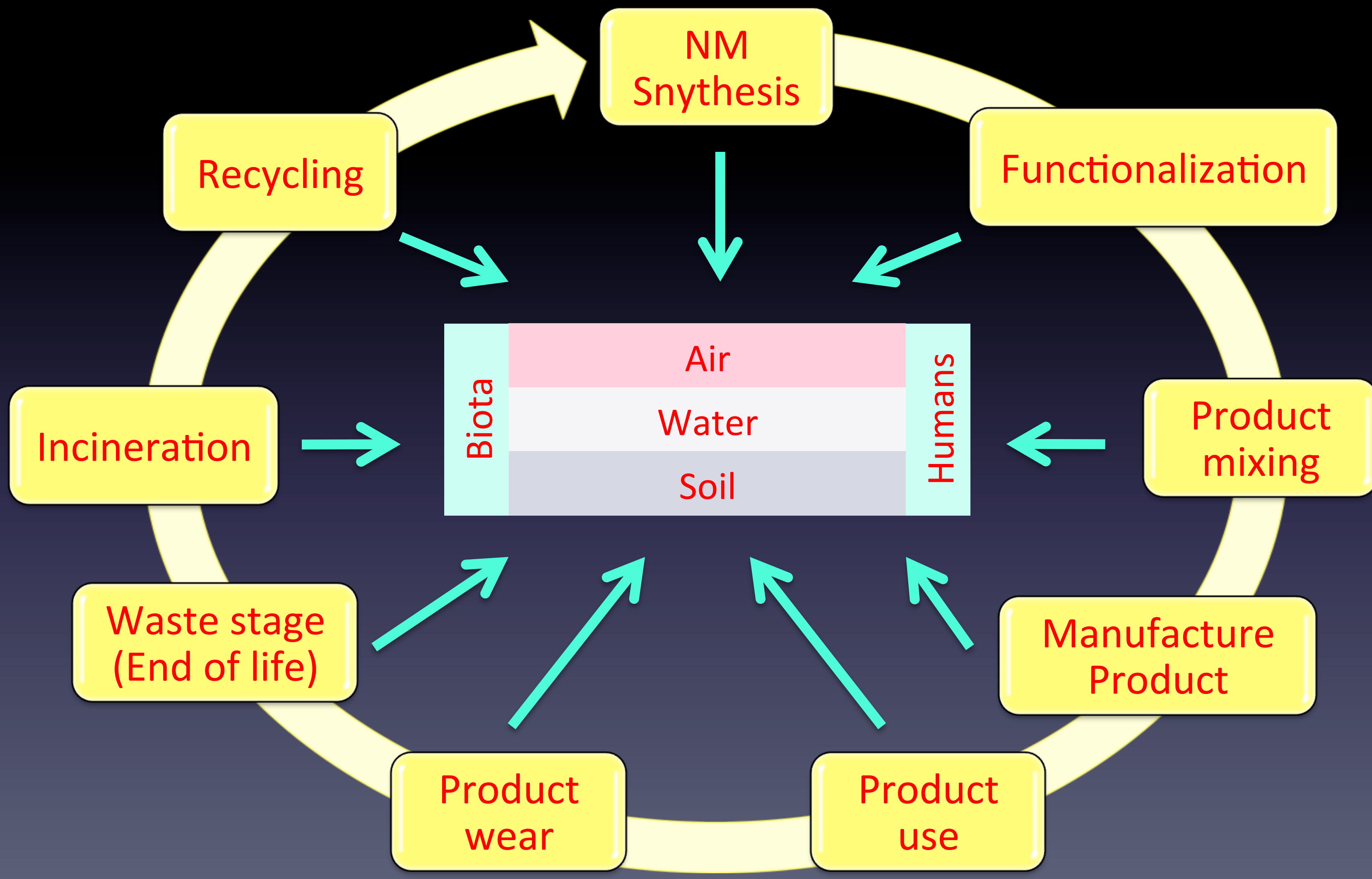


Figure 1. Estimated global mass flow of ENMs (in metric tons per year) from production to disposal or release, considering high production and release estimates as of 2010. Production data are from ref 14, without modification.

Keller and McFerran, J Nanopart Res (2013) 15:1692

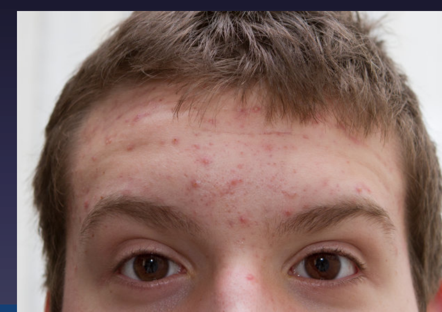
Life cycle / Value Chain Perspective



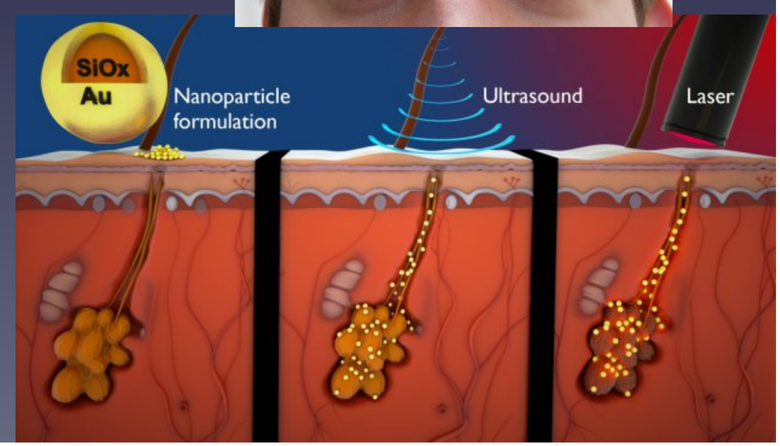
NM Applications are Very Diverse

Nano ZnO
“transparent”
sunscreen

Nano-silver in Bandages & socks



Nano-sized “additives”



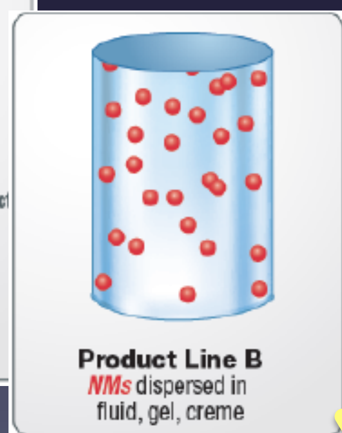
LCnano Product Lines include

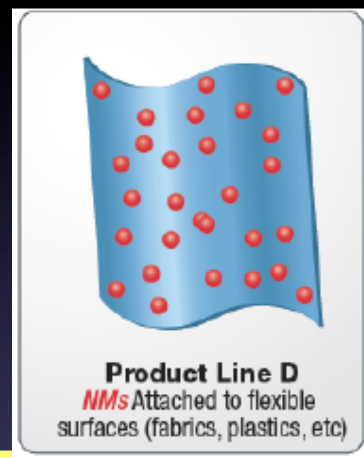
NM Functionality & Application

Reactive NMs

CeO_2 in Polishing Agents

TiO_2 in Foods

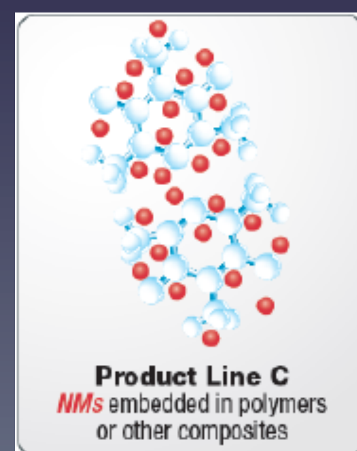




Ag^0 clothing

"Free" NMs

Embedded NMs



SiO_2 in floor coatings

SiO_2 in Foods

Passive NMs

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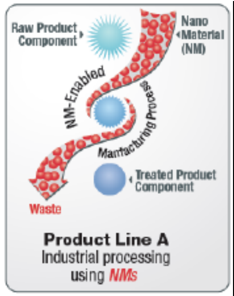
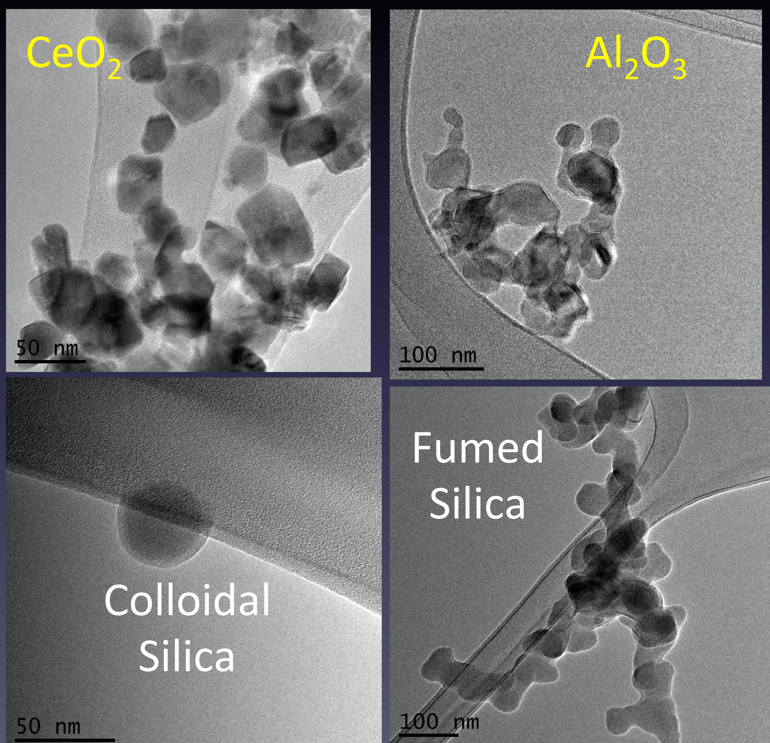


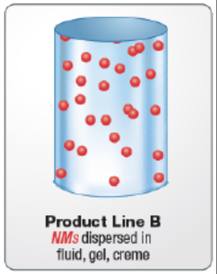
Product Line A – Polishing Agents

Chemical-Mechanical Polishing (CMP) fluids



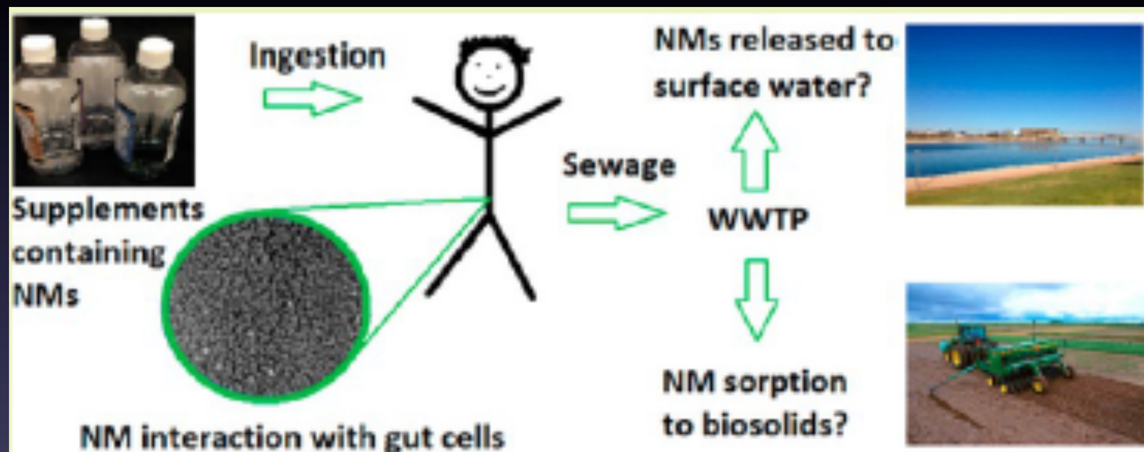
Physical, Chemical, and In Vitro Toxicological Characterization of Nanoparticles in Chemical Mechanical Planarization Suspensions Used in the Semiconductor Industry: Towards Environmental Health and Safety Assessments, Env. Sci: Nano (2015)

- >5500 tons per year of CMP nanoparticles are used
- Mass balances for a city with a FAB suggests 0.1-1 mgNP/L is realistic at WWTPs
- Semiconductor industry concerns:
  - Workplace exposure & monitoring
  - Polishing of III/V materials
  - On-site industrial treatment designed to remove Cu, As, F, etc in wastestreams & not CMP nanoparticles



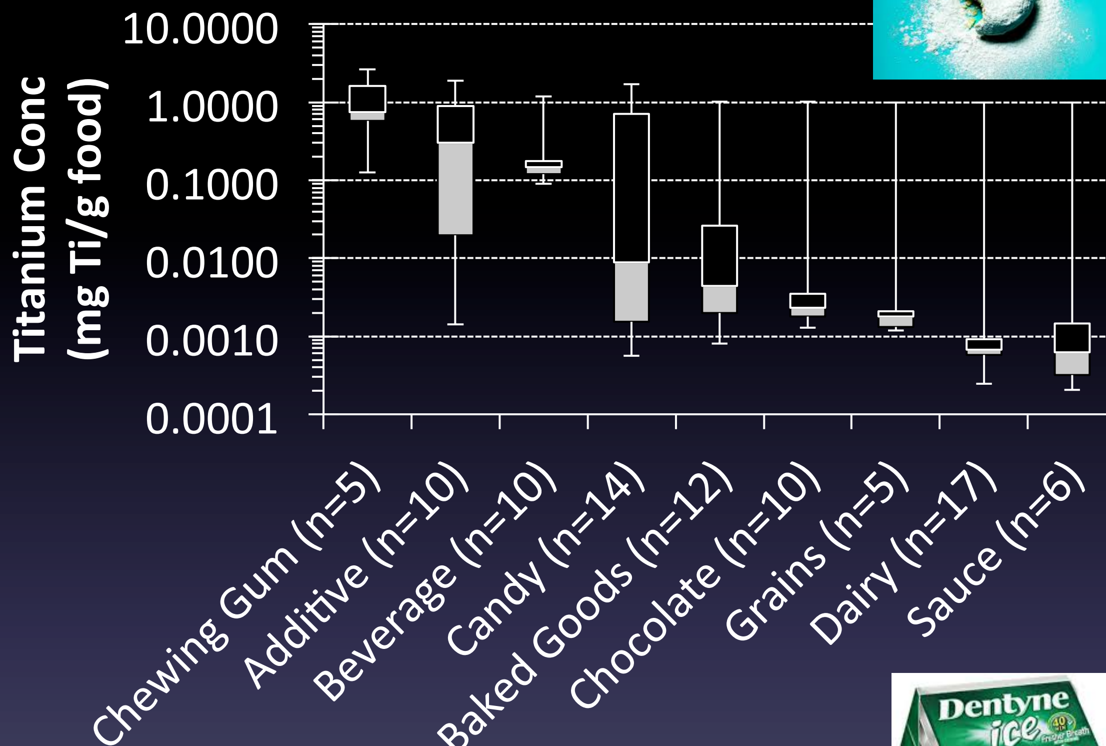
Product Line B
Nanomaterials in foods

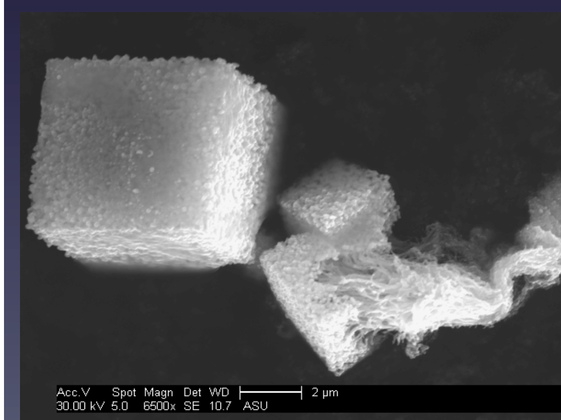
- Nanomaterials added to food for a variety of reasons:
  - Texture
  - Anti-caking
  - Color
  - Oxygen barrier
  - Abrasives
  - Antimicrobial
- Little confirmed occurrence data exists

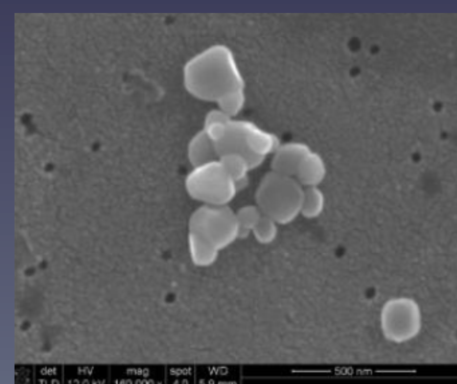


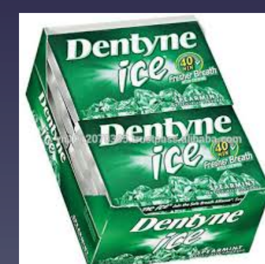
ACS Sustainable Chem. Eng. 2014, 2, 1616−1624

Nanomaterials Dispersed in Products







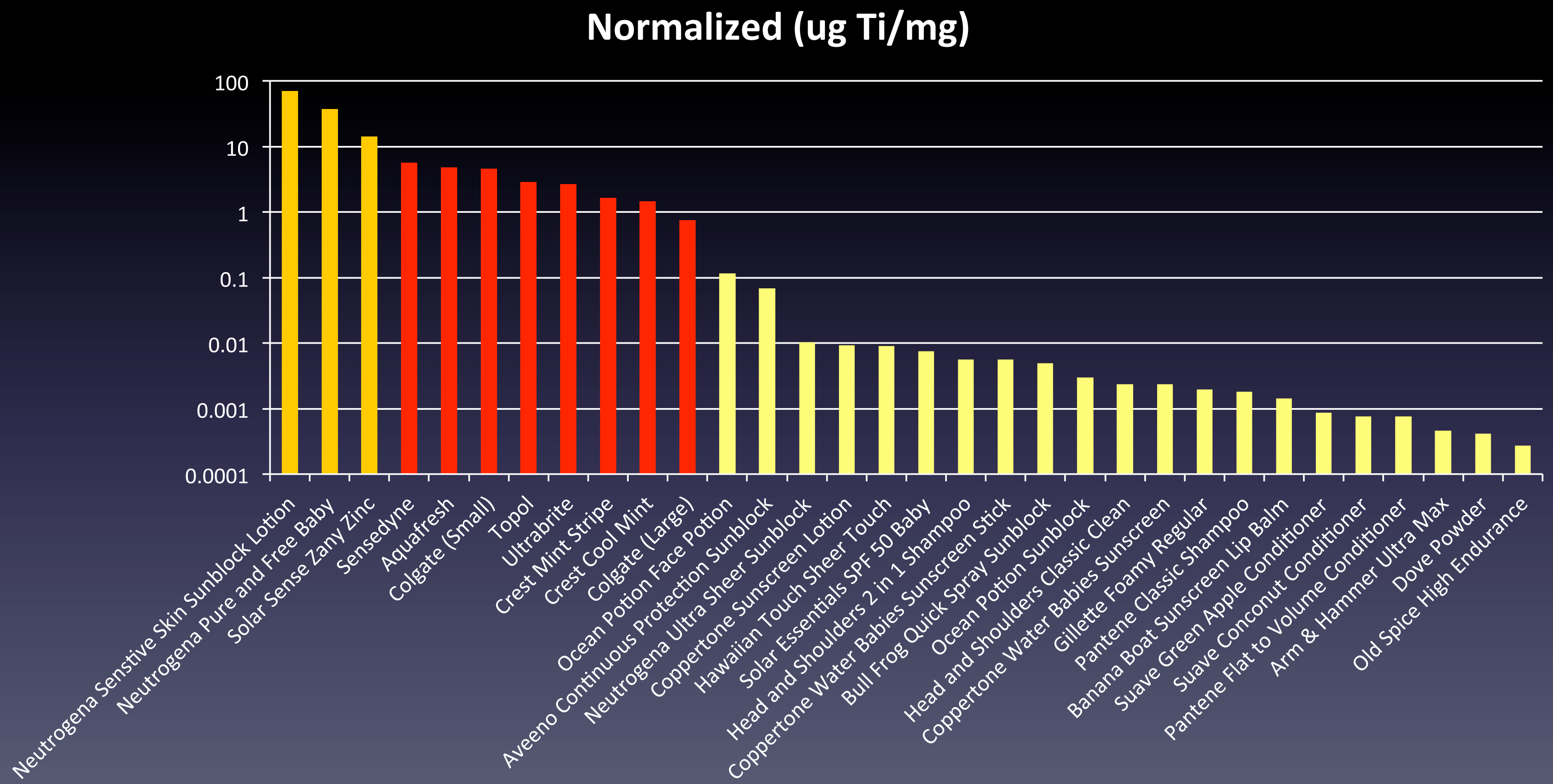


Silver in Shampoo

Weir et al., ES&T (2012)

Benn et al., J. Environmental Quality, 39:1-8 (2010)

Products harness different functional properties (whitening, hydroscopic, quantum confinement) of nano-TiO_2

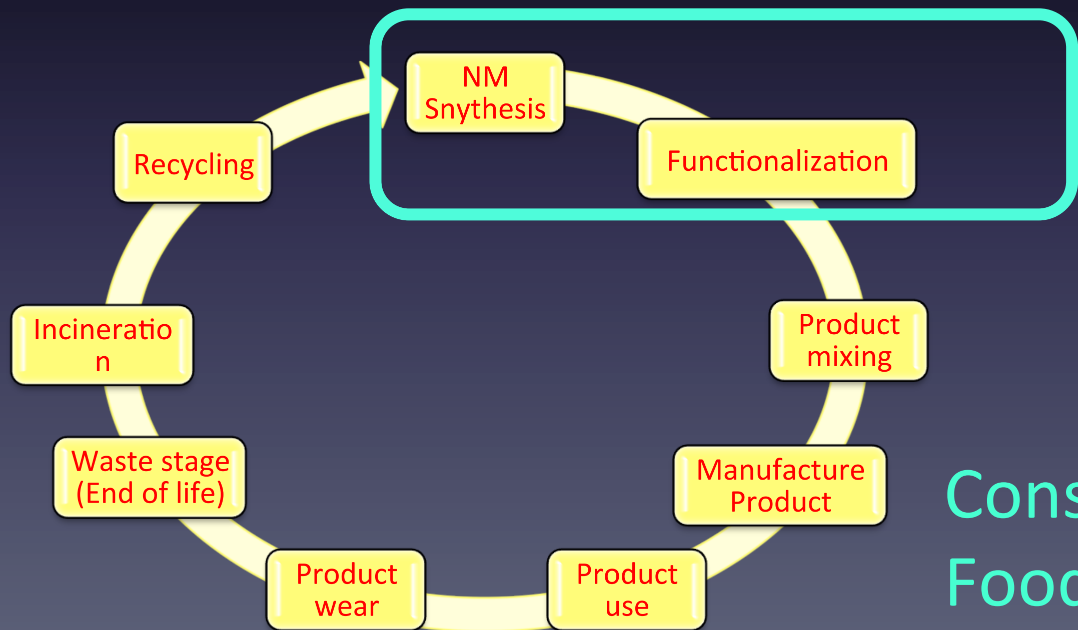


Orange: Sunscreen with Ti listed on label

Red: Toothpaste with Ti listed on label

1000's of foods…. Test them all?

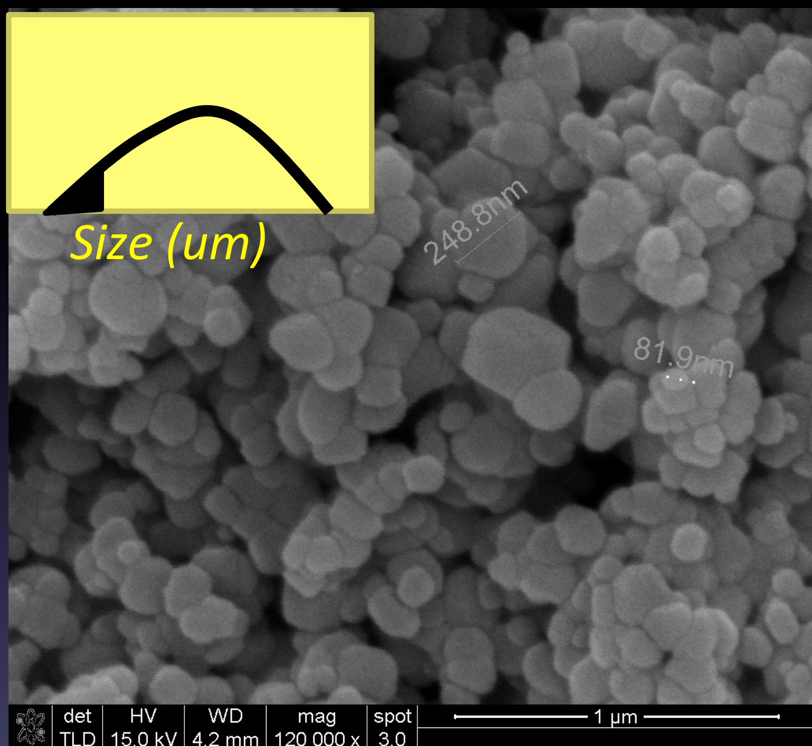
Follow them through the life cycle (value chain)

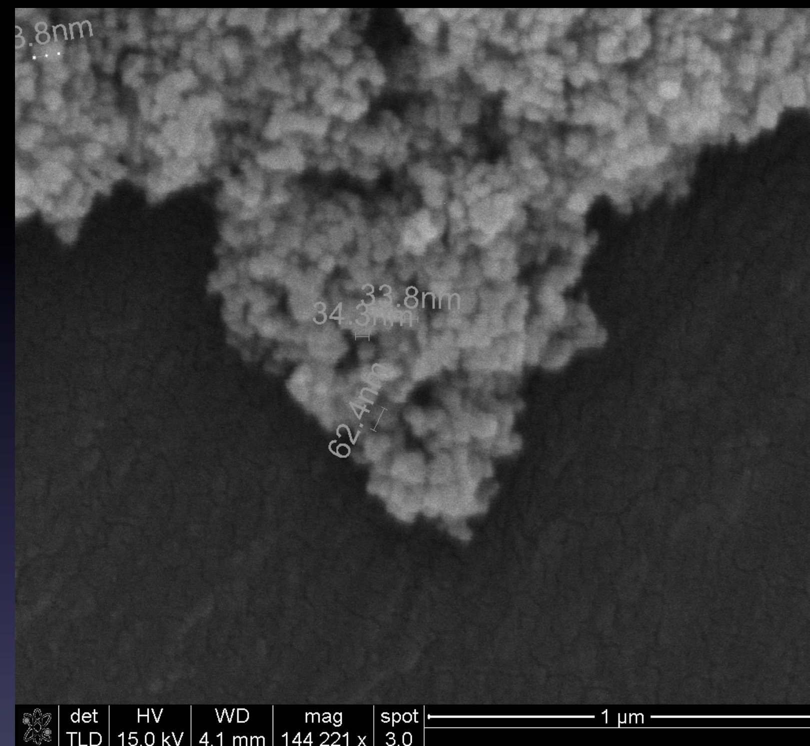


Consumer Foods (< 10)

Consumer Foods (1000's)

Titanium Dioxide



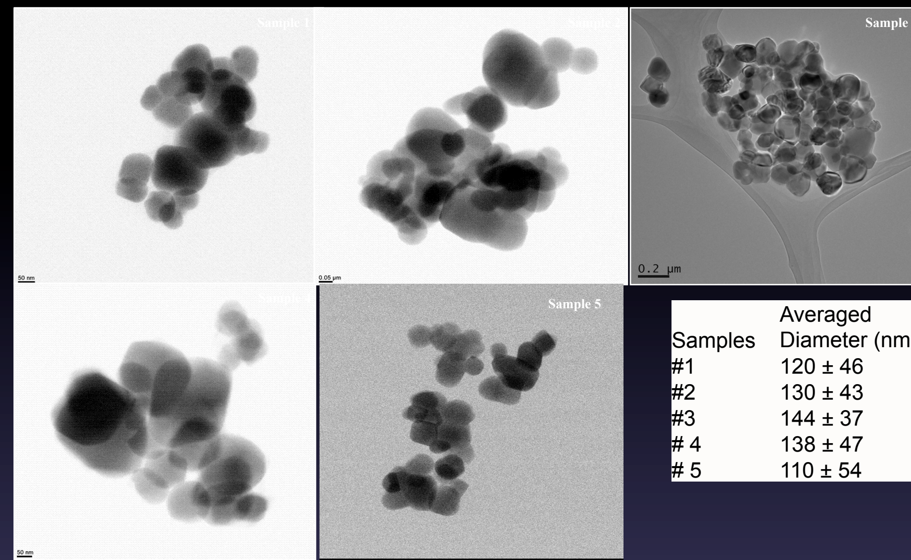


- E171 is food-grade color additive
- Contains a distribution of sizes (100-200 nm average)
-~30% less than 100 nm
- EASILY dispersed in water

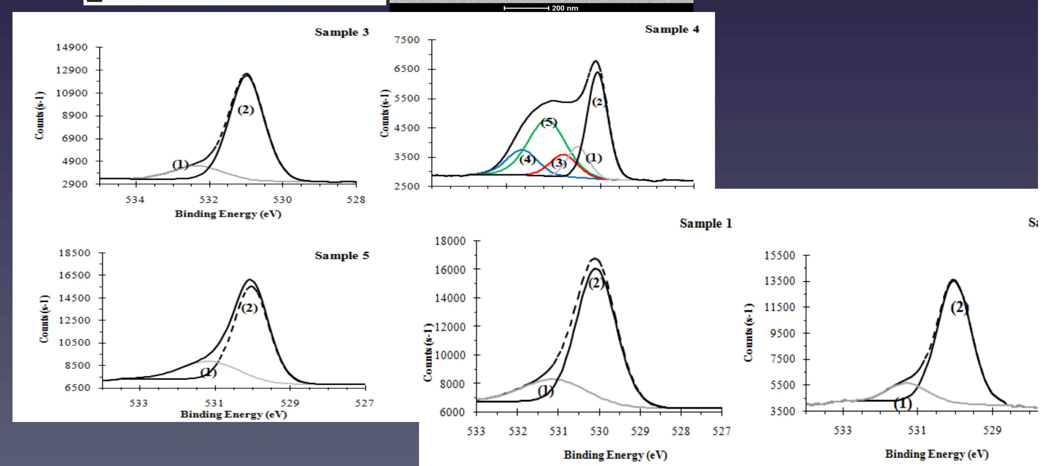
- P25 is a catalyst or catalyst support
- Individual NPs < 100 nm
- NOT EASILY dispersed in water
-Used in concrete & coatings

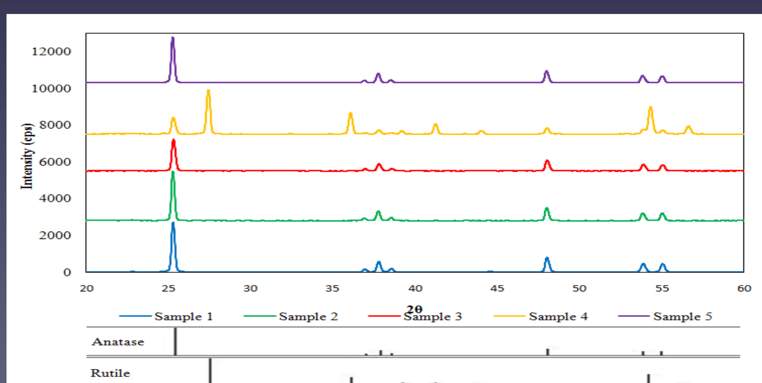
Bulk additives are easy to characterize

- *Go to suppliers instead of food grade products*
- Can assess fundamental properties of NPs
- Example: food grade TiO_2 contains P-surface groups & is primarily anatase



Samples	Averaged Diameter (nm)
#1	120 ± 46
#2	130 ± 43
#3	144 ± 37
# 4	138 ± 47
# 5	110 ± 54





Yang, et al., *ES&T*, 48:11:6391-6400 (2014)

Truth in labeling?

Function = Impact bacterial community in the gut

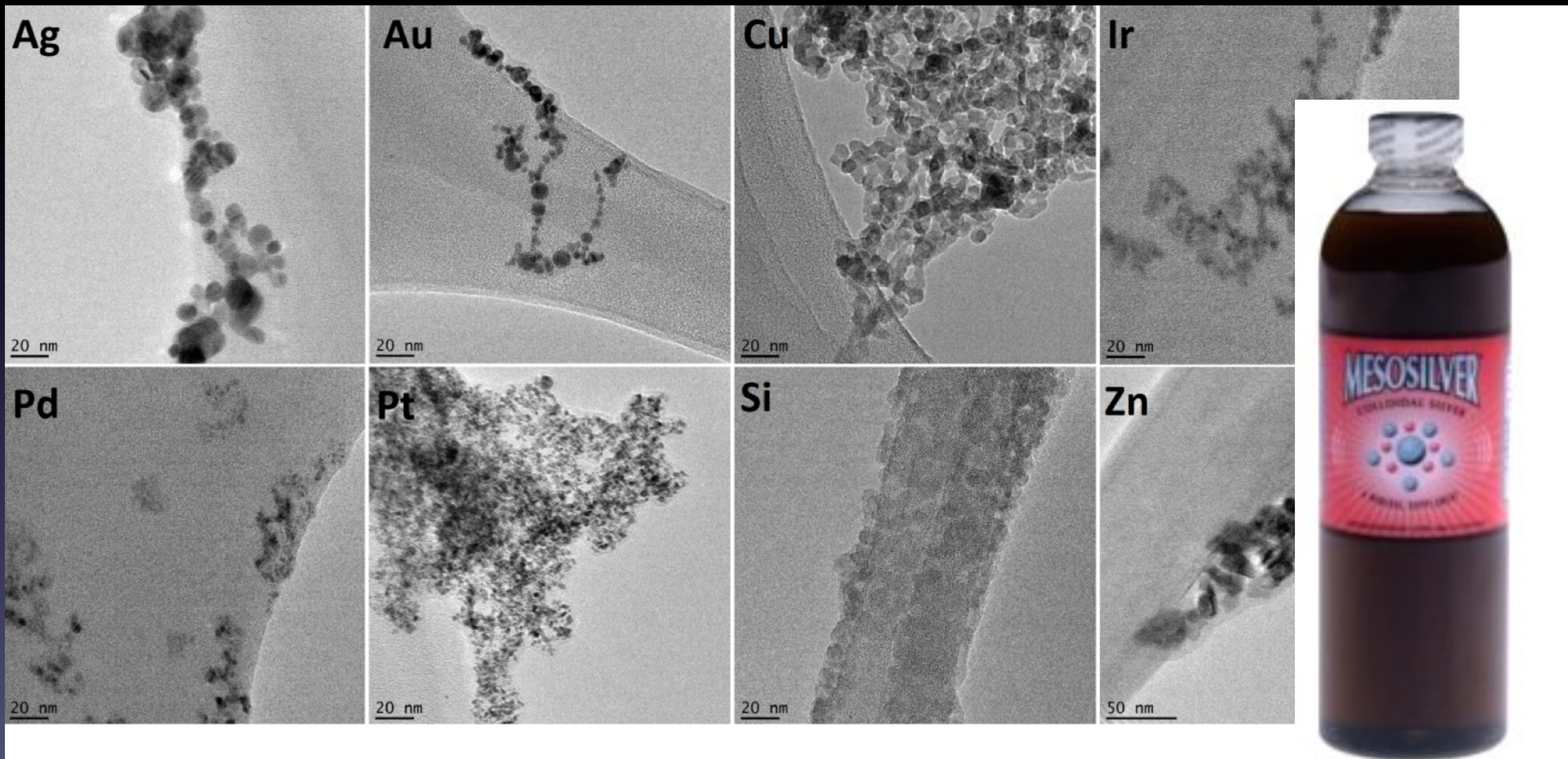


Figure 1. Representative TEM images of NMs found in supplement drinks.

TEM is a powerful – but expensive analytical tool

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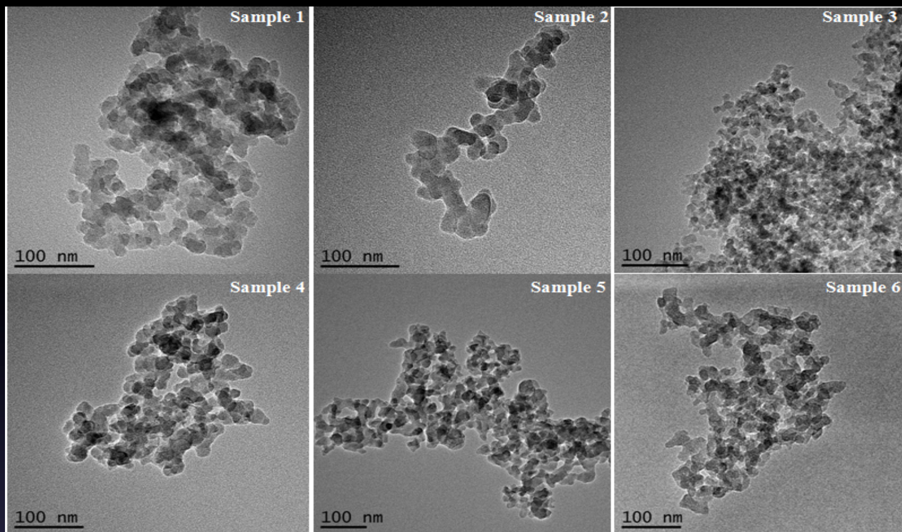
What happens to NMs are “use phase”?



Foods Claim Containing Silica

Transformations of NMs impact Exposures & Hazards

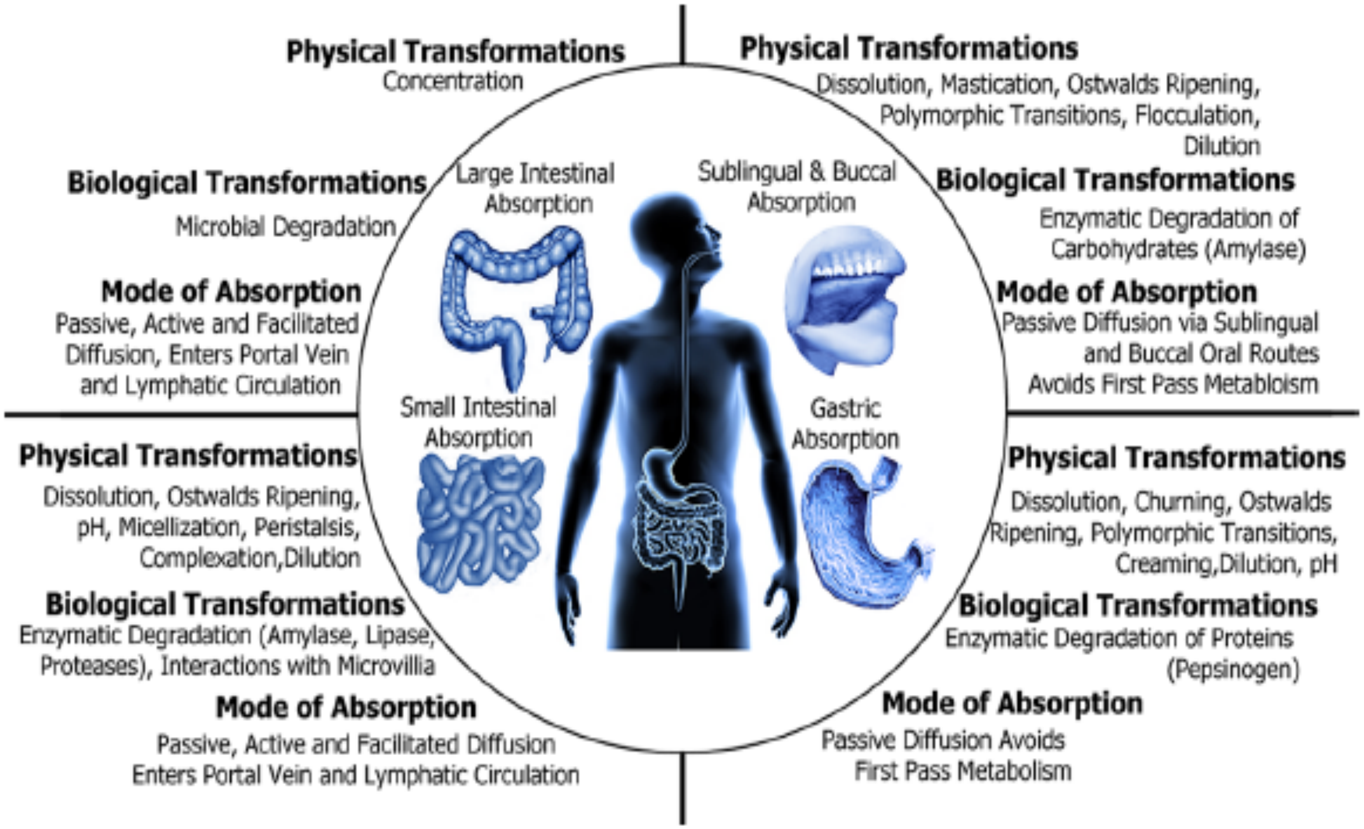
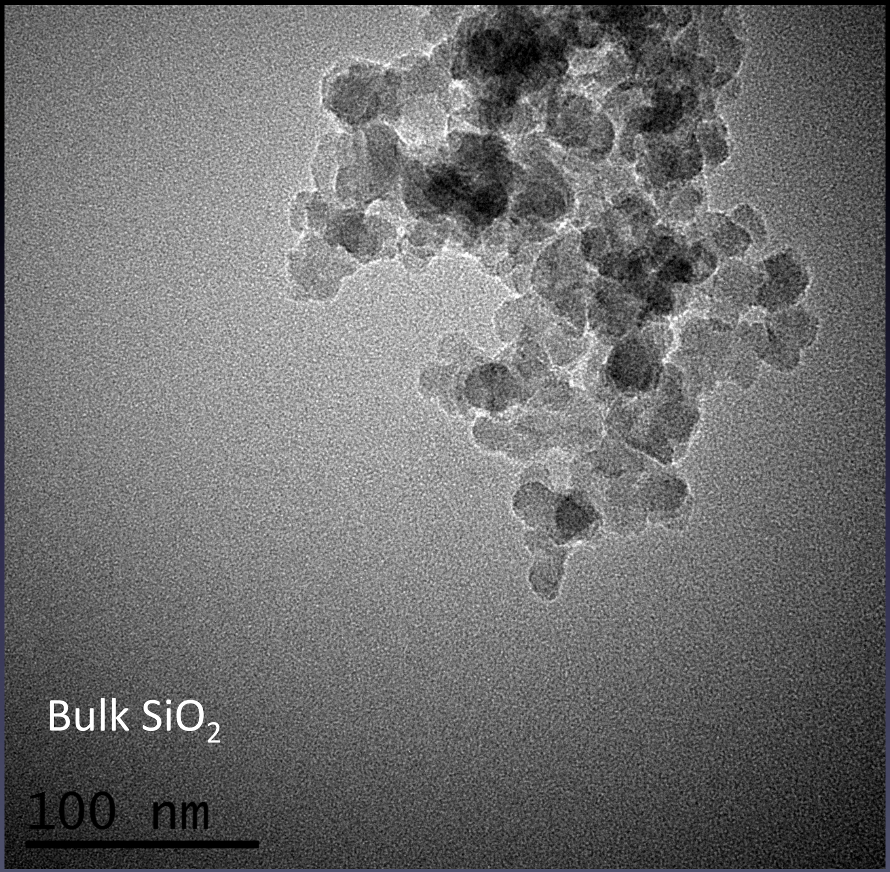
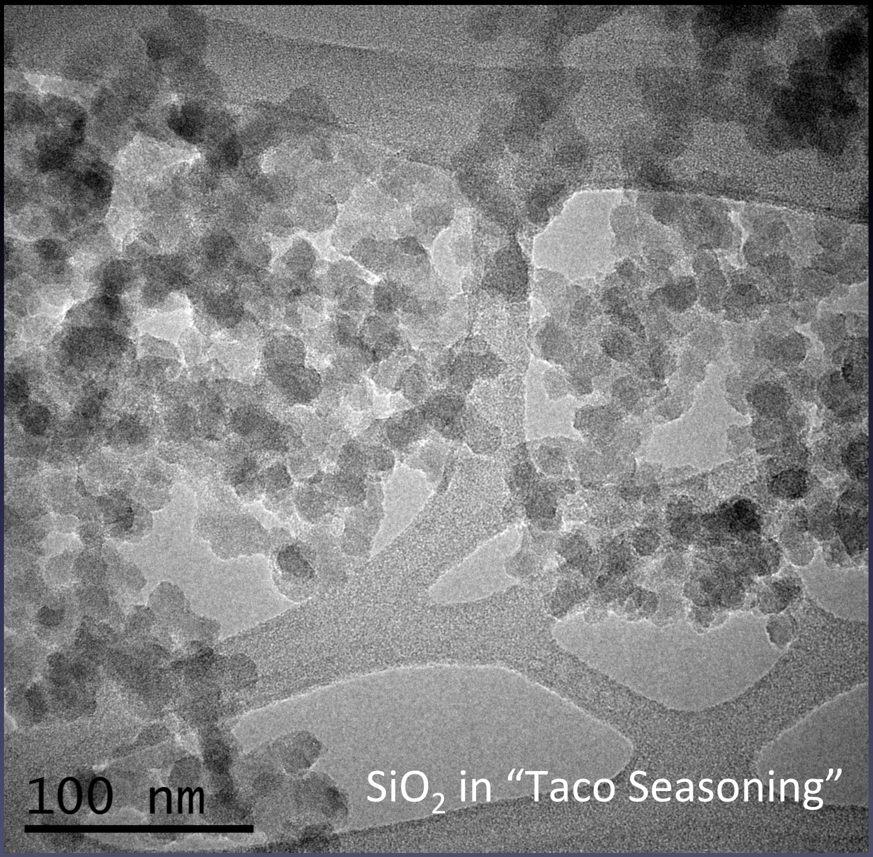


Figure 4. Endogenous modifications to nanomaterials within the alimentary tract during transport from time of consumption to excretion.

Transmission Electron Microscopy (TEM) on Bulk Food-grade Silica & a "real" Food

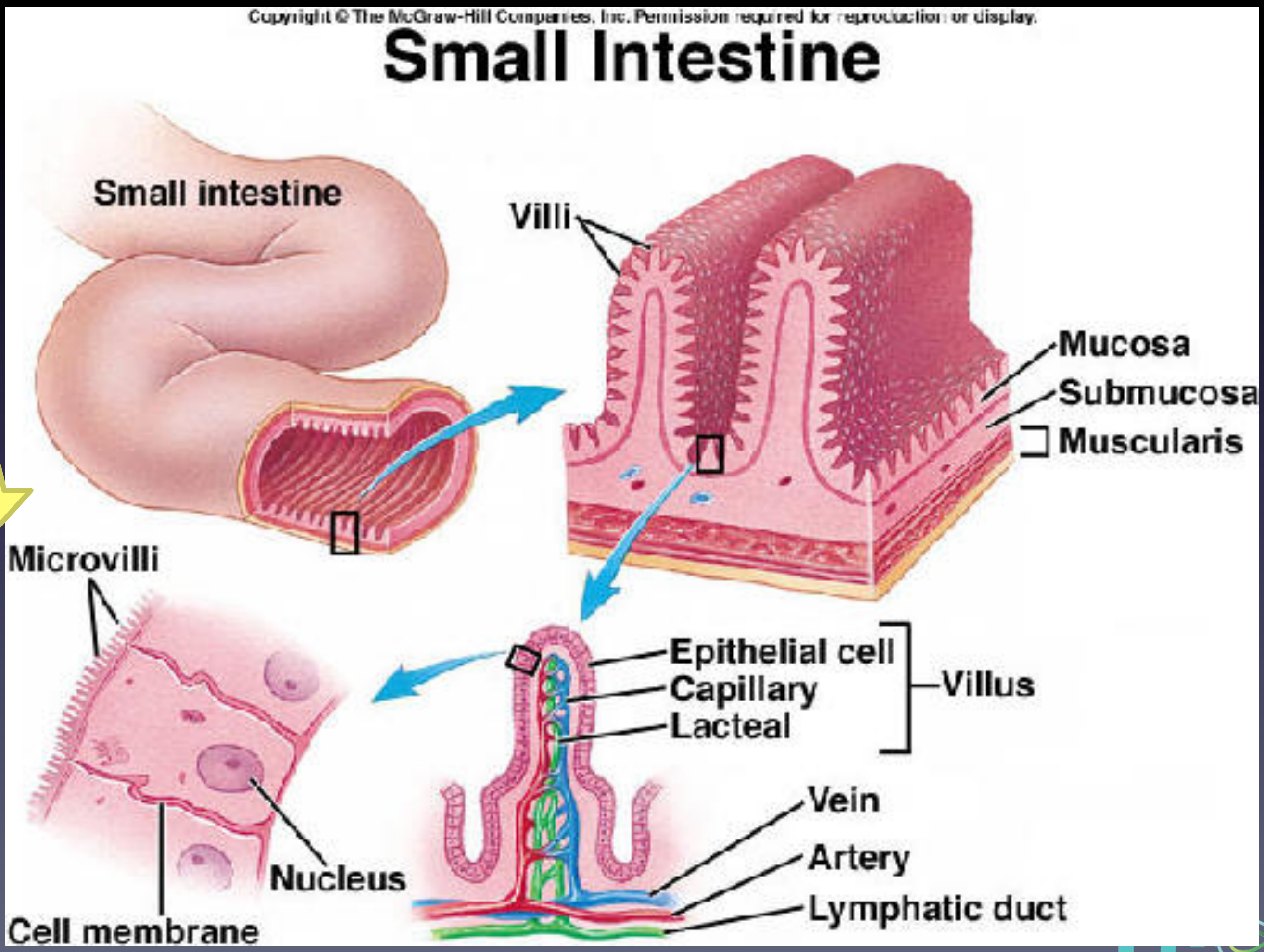




→ Nano silica present in foods

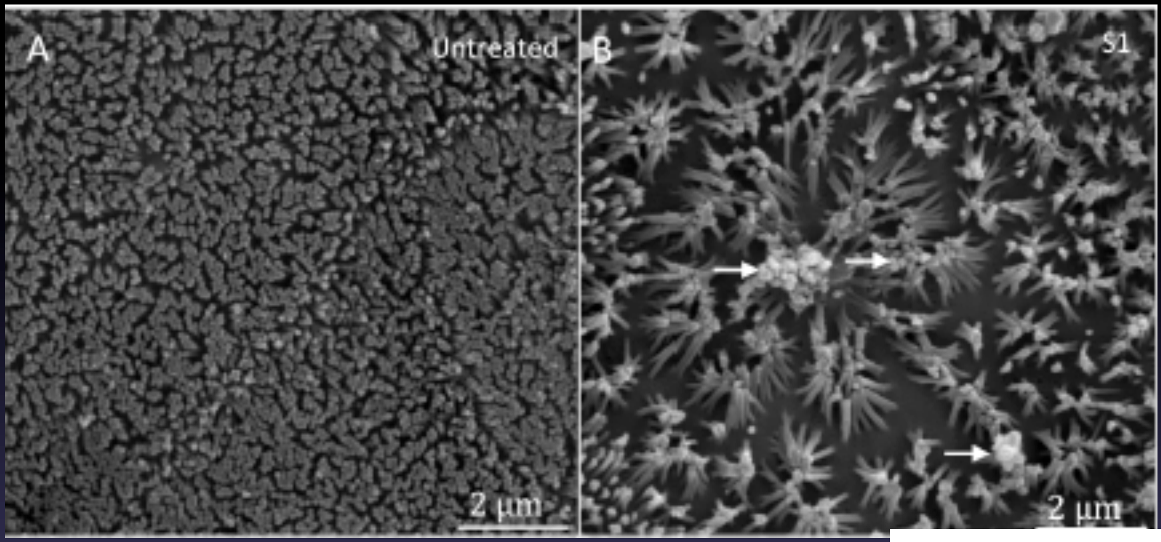
LC nano

Humans are part of NM life cycles
Inhibition Study on Microvilli

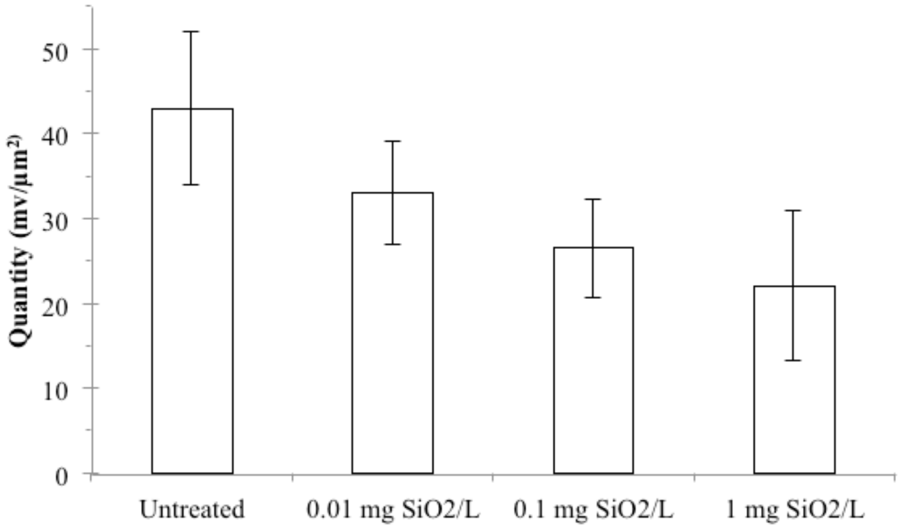


Caco-2BBe1 cells were purchased from ATCC (Manassas, VA; CRL-2102)

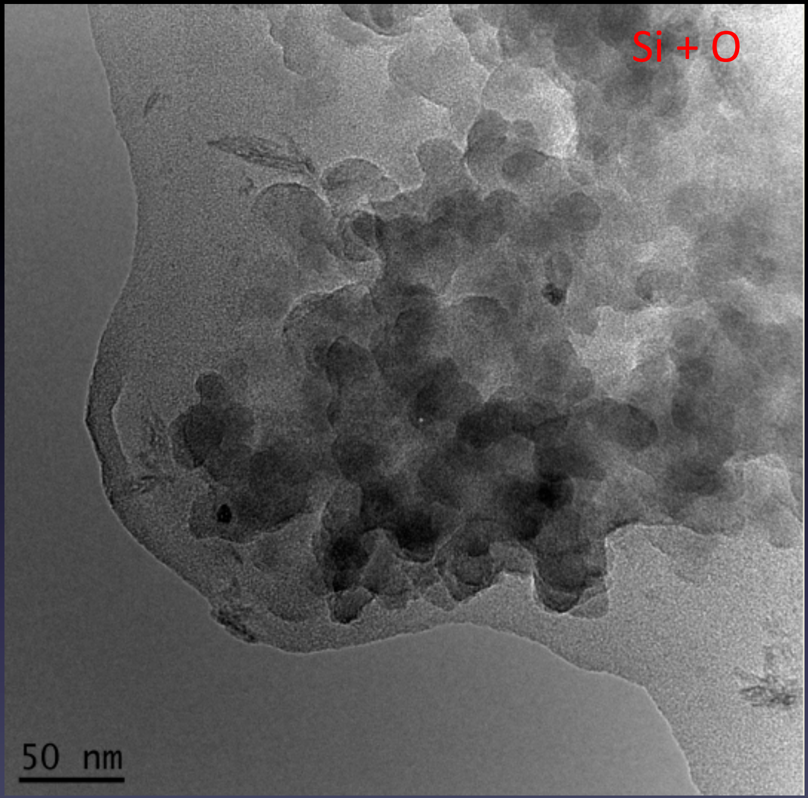
Food-grade Silica Inhibited Growth of Microvilli



Disruption of the brush border at 0.01 mg/L



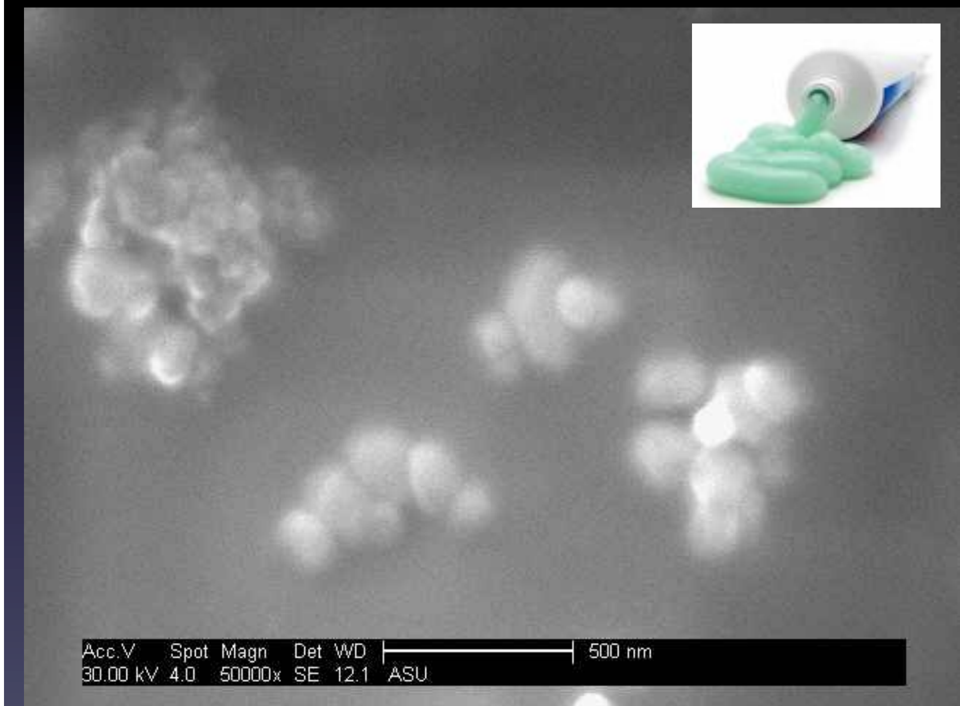
Post Use-Phase:
From Foods to Wastewater



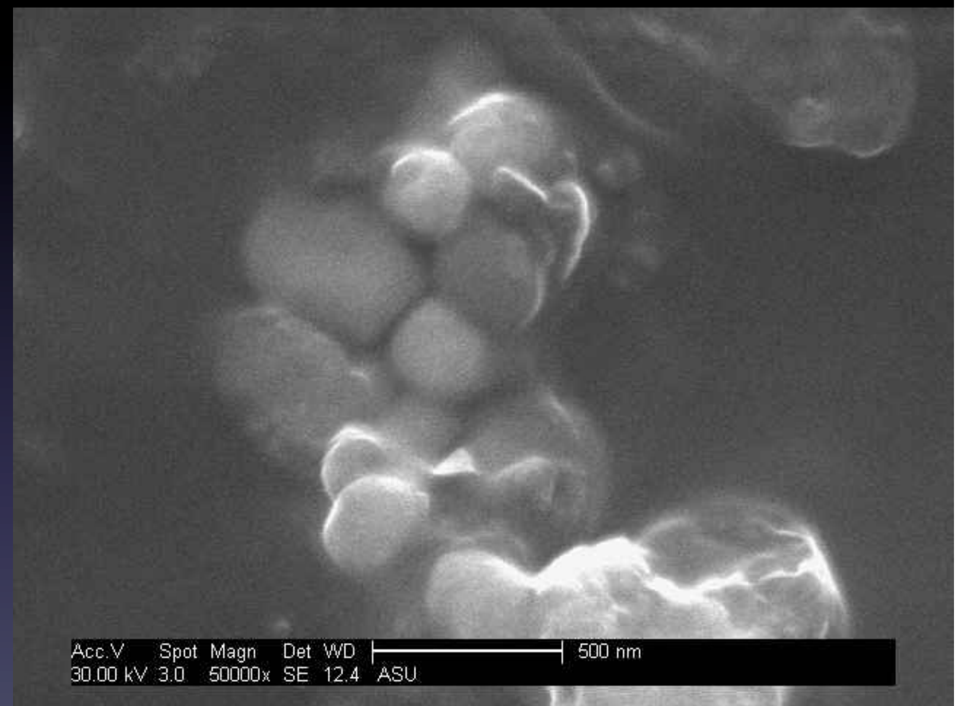
- Method: Cloud point extraction + TEM
- Presence in the influent of wastewater treatment plants.
- No aggregates of SiO_2 observed in effluent of WWTP.

	Influent wastewater (mg/L)	Secondary effluent (mg/L)	Final effluent (mg/L)	Recycled sludge (mg/g)	Final Biosolid (mg/g)
Silicon	108 ± 2	298 ± 3	211 ± 16	3698 ± 236	8480 ± 127

TiO_2 in commercial products are similar to TiO_2 extracted from biosolids

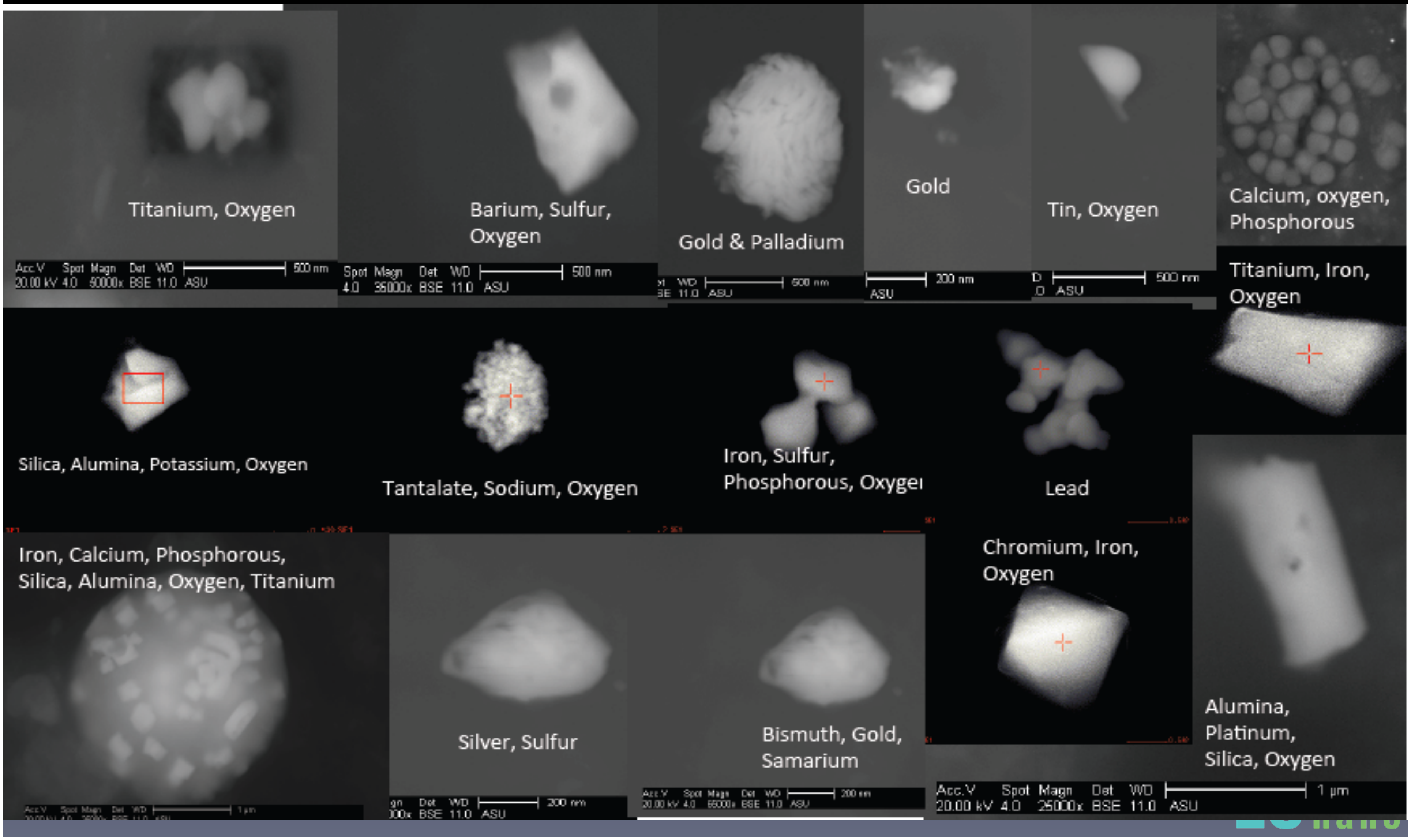


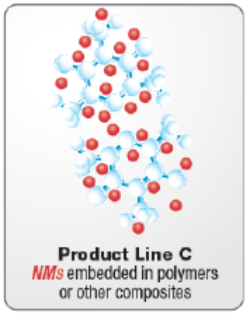
TiO_2 in Toothpaste



TiO_2 in Biosolids

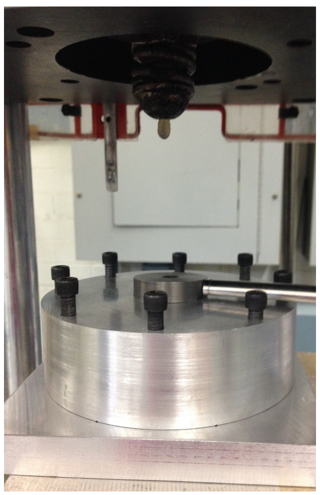
Nano-scale objects found in Biosolids

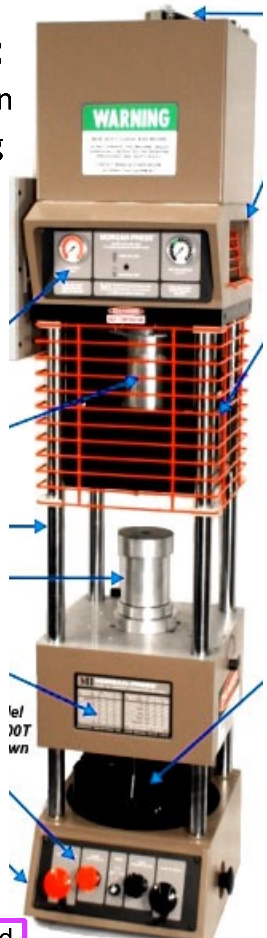




Product Line C probably has most NM release studies by many groups

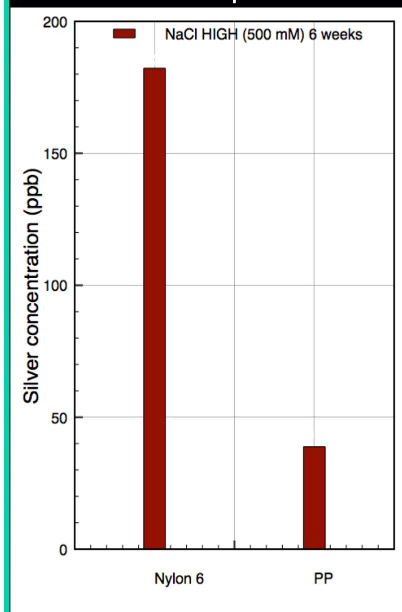
Injection Molding:
The most common modern method of manufacturing parts



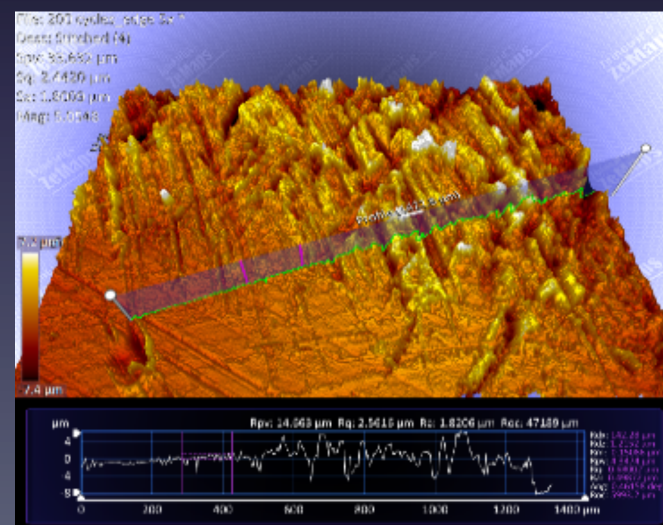


AgNP - Polypropylene from mold

6 weeks exposure time



Higher Silver release from Nylon 6 (absorbs ~10% water) than Polypropylene (<1%).



Top: abraded polycaprolactone polymer
Bottom: optical profilometry analysis

Example Summary & Bias on Hazard

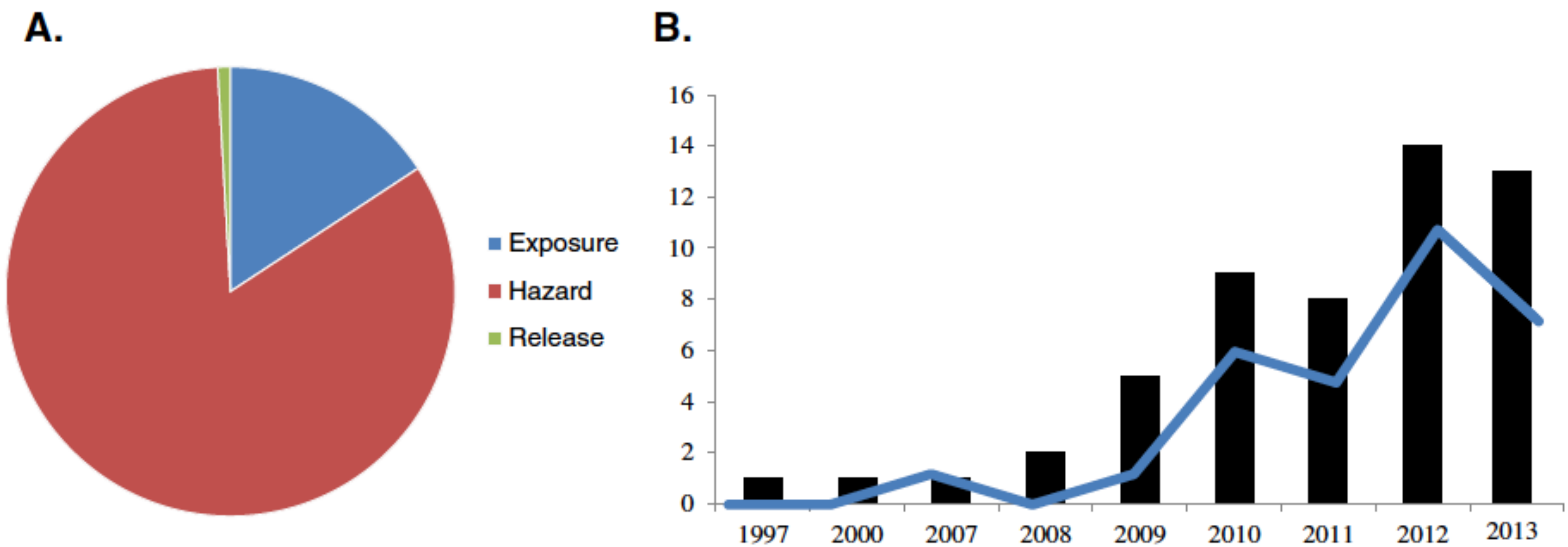
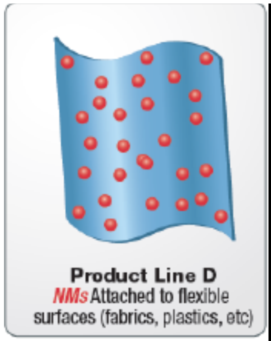


Figure 1 Published literature on release form nanocomposites. The "nanorelease" picture in terms of how many research articles have been published. **(A)** Using the ICON online database of nanotechnology environmental health and safety research, we report the number of articles identified by the "exposure" and "hazard" search terms, and compare these to the release studies we identified through multiple search engines. Considerable attention has been directed toward examining intrinsic hazards (83%) of nanomaterials, and less on potential exposure (16%) and least on release from nanocomposite (0.8%). **(B)** Since the first nanorelease study we identified in 1997, understanding release from solid, non-food nanocomposites has received increasing attention (bars) and an increasing number of these studies have been rigorous experiments (line).

Froggett *et al. Particle and Fibre Toxicology* 2014, **11**:17



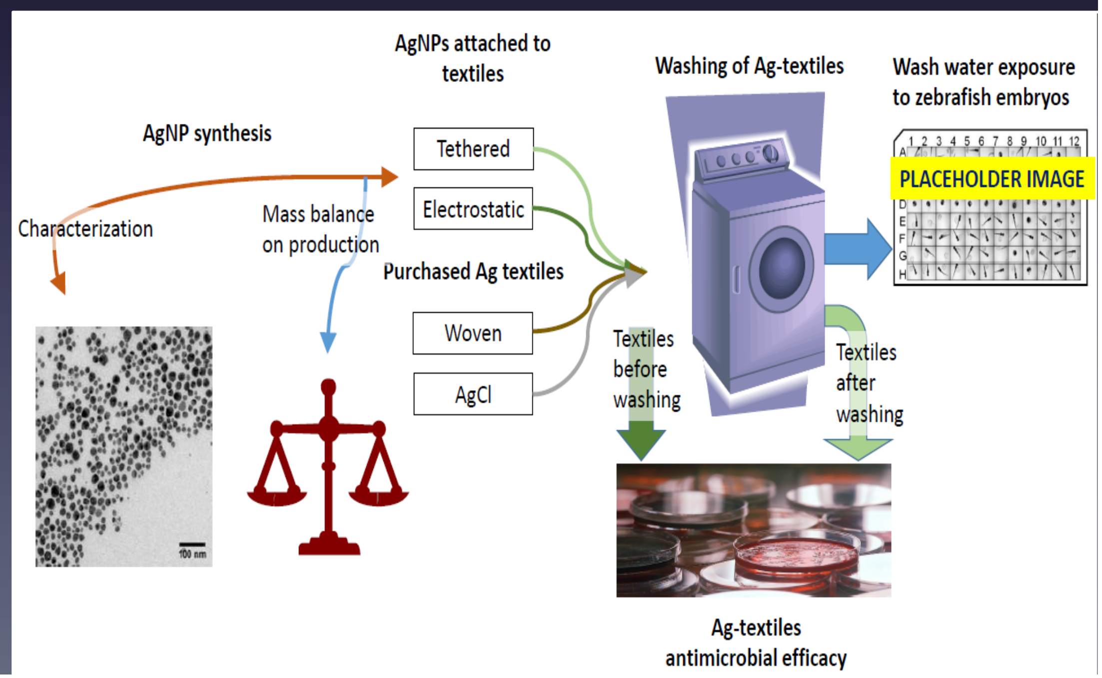
Product Line D
Nano-enabled fabrics

- Why (efficacy)?
  - Anti-microbial (no stink)
  - Flame Retardant
  - Self cleaning

LOADING and CHEMISTRY
(Different types and amounts of Ag)

PERFORMANCE
(Antimicrobial activity)

RELEASE
(AgNPs and Ag^+)

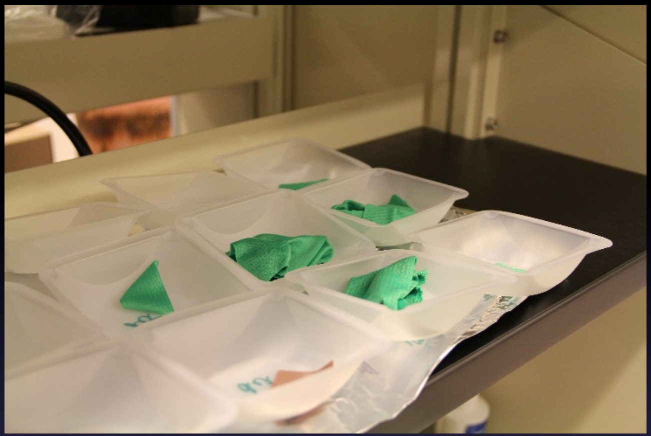


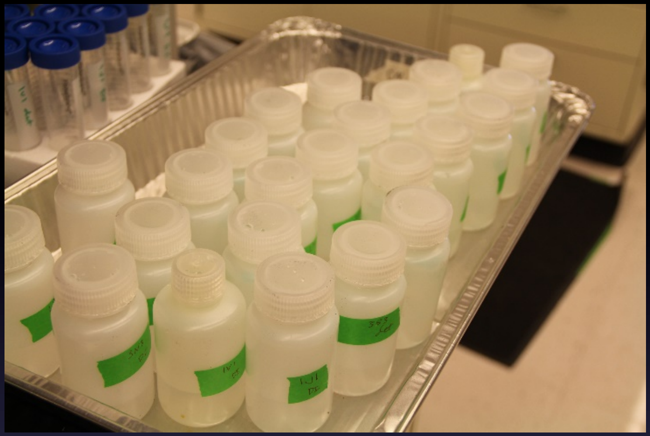
Comparison of 4 Ag-Treated fabrics

Silver loadings and attachment chemistry

Shirt	X-static (X)	Linked*On* (L)	Non-Linked (N)	Polygiene (P)
Ag content (ppm)	~4000 ppm	~24 ppm	~1 ppm	~16 ppm
Ag “bonding”	Ag-coated fibers woven in to shirt	AgNPs bound by proprietary linker	Non-covalent bonding of AgNPs to shirt	Ag solution added to shirt

Simulated Use: Washing Methods





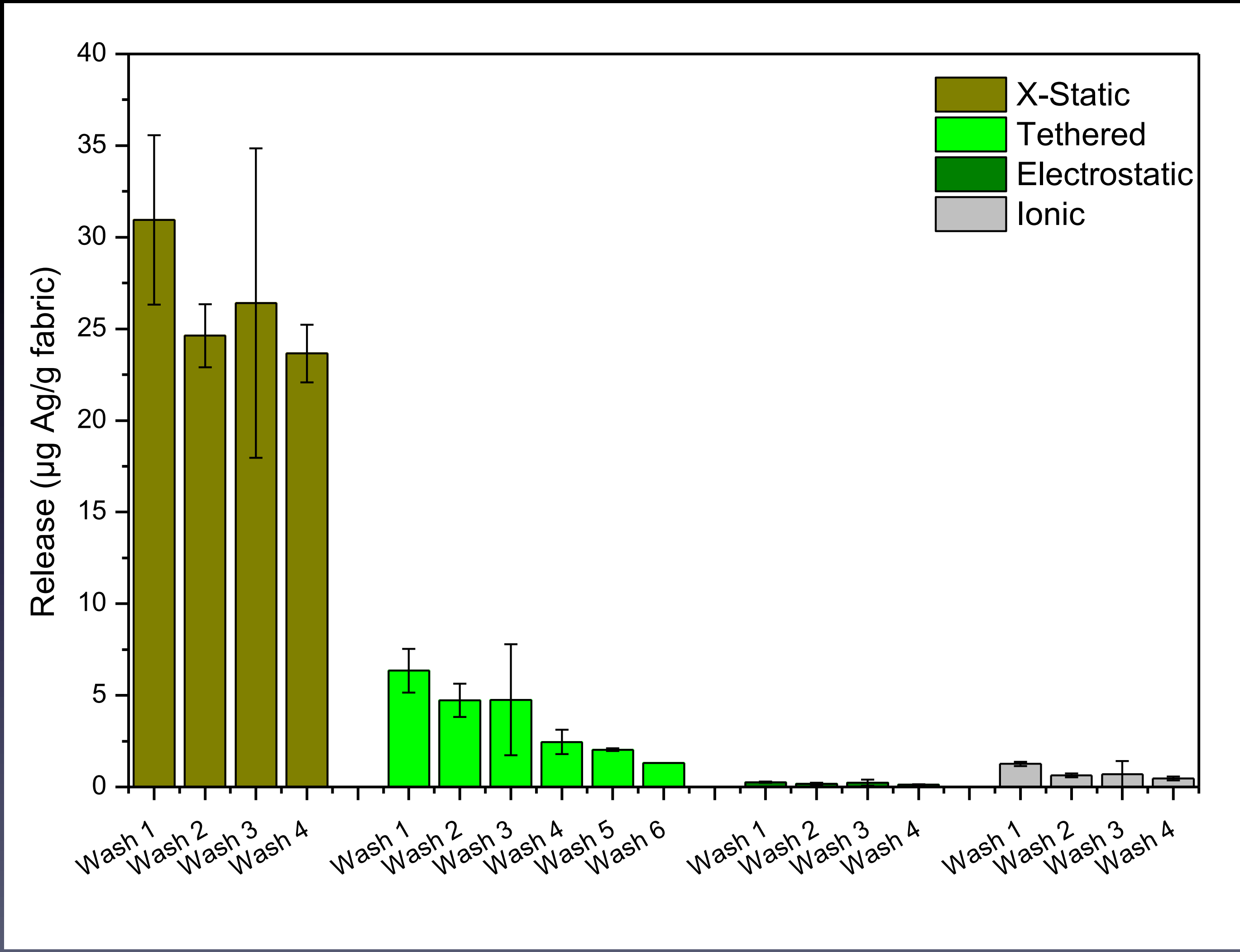
1. Triplicate fabric swatches (~2 g each) were placed in 125 mL polyethylene bottles with 50 mL liquid

2. Two matrices:
- **DI water (DI)**
- **DI + detergent* (DI + Det)**

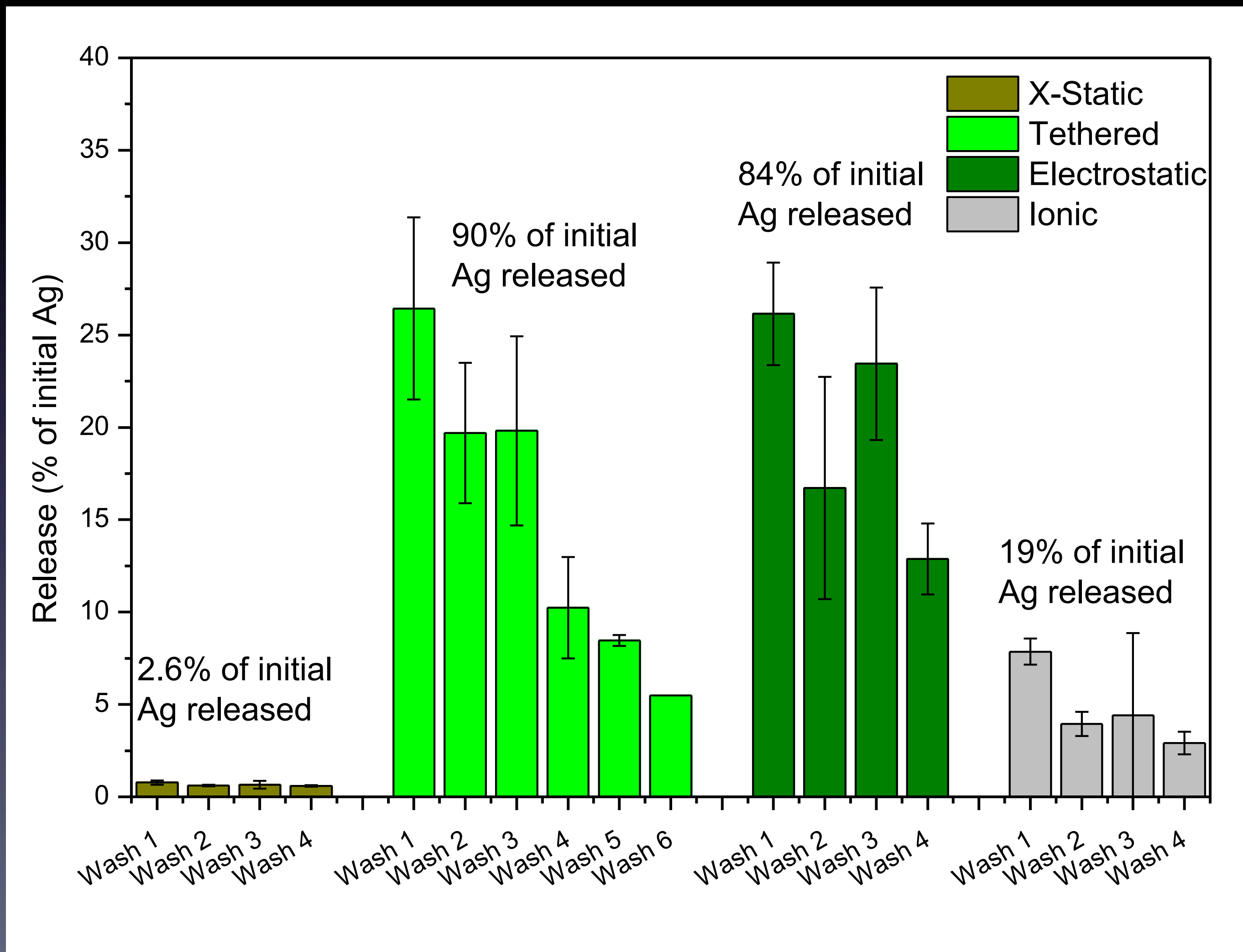
*** American Association of Textile Colorists and Chemists standard detergent without optical brightener**

Rotated in mixer for 30 minutes at 40 rpm
Included glass beads for additional agitation

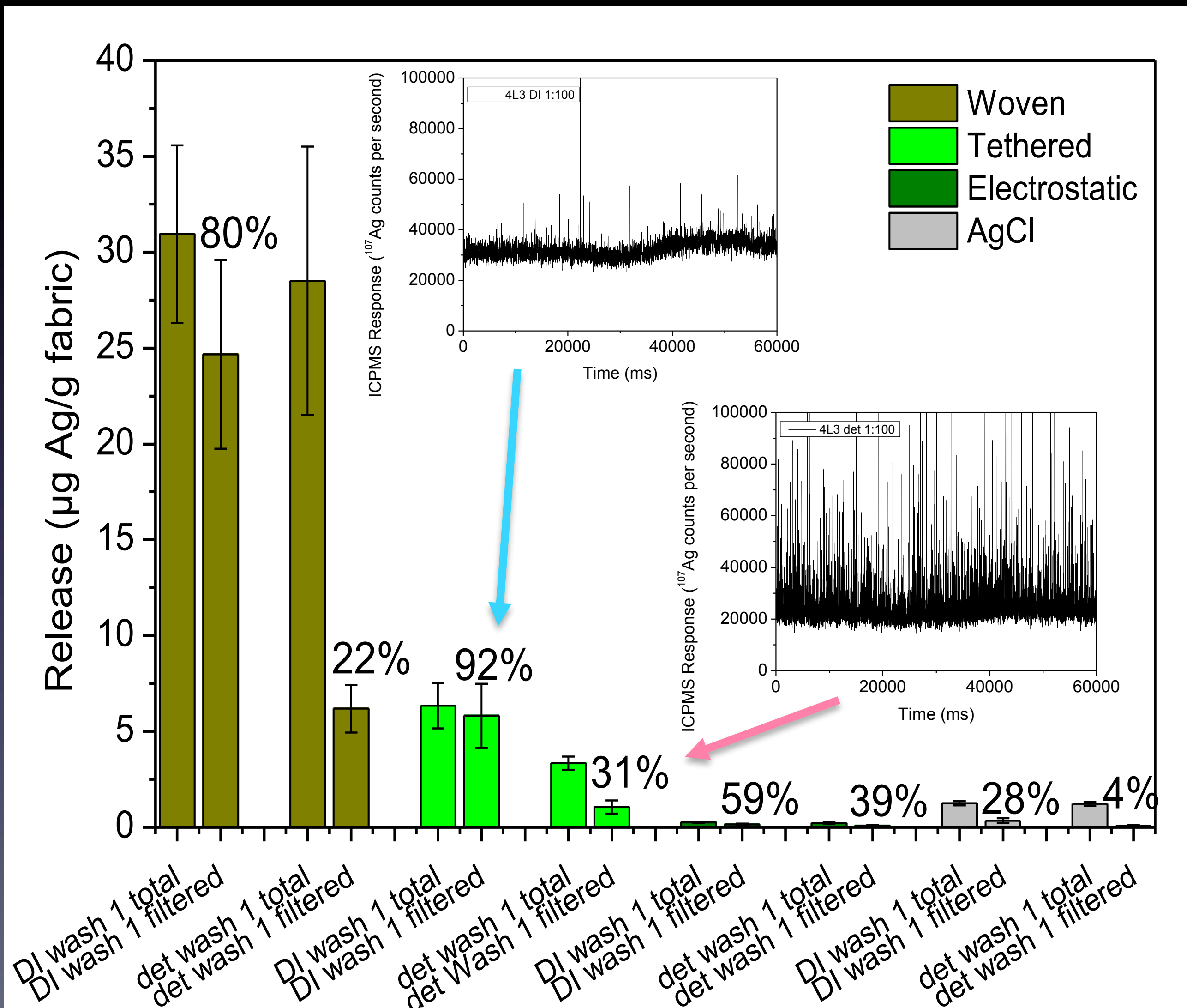
Extent of Ag release in DI

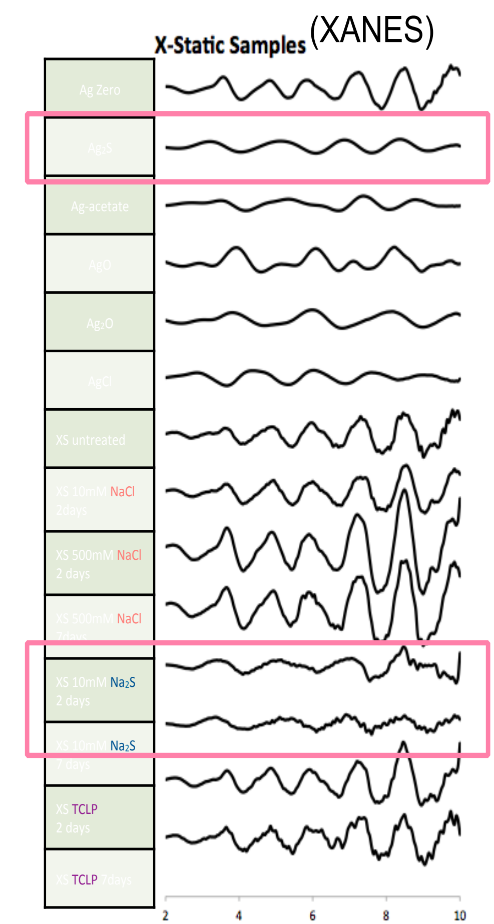


Release of Ag as % of initial load



Silver is released as ionic silver but can re-precipitate to form new nanoparticles

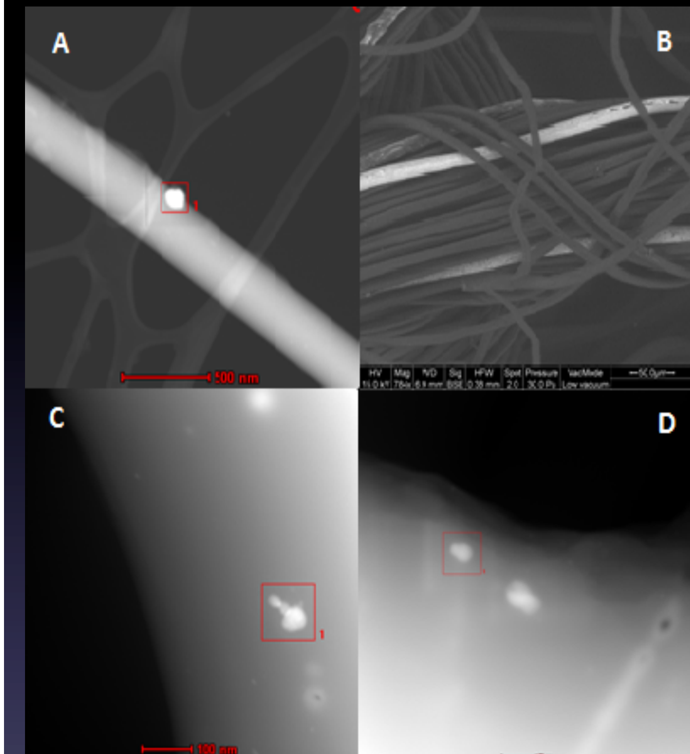




X-Static samples showed some changes:

- NaCl and TCLP: No reactions
- Na_2S: Rapidly transforms to Ag_2S

TEM images and Nano-Enabled Textiles



SEM image of woven textile (A&B)
TEM image of tethered textile (C)
TEM image of AgCl textile (D)

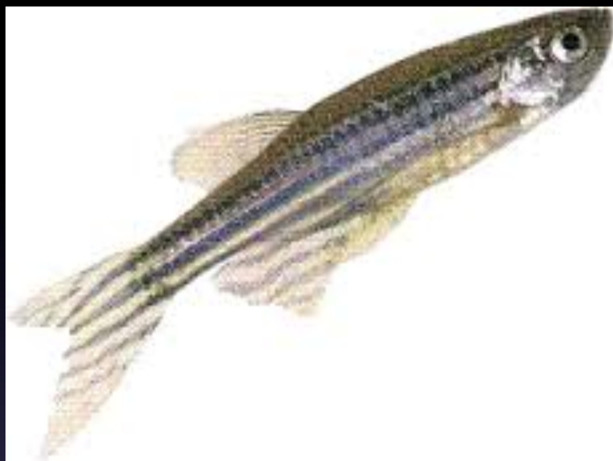
Effect of Washing on Ag-NP in Fabrics

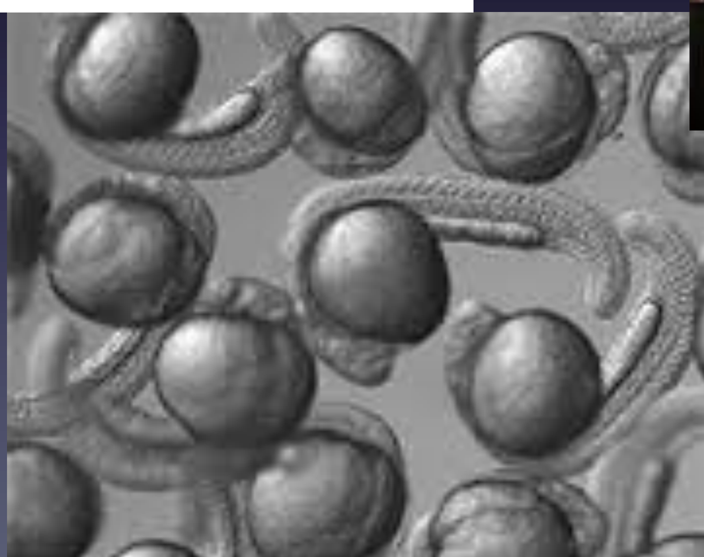
DUNE SCIENCE Linked*On*

DUNE SCIENCE Linked*On*, *DI + Detergent washed, 4 washing cycles*

DUNE SCIENCE Linked*On*, *DI washed, 4 washing cycles*

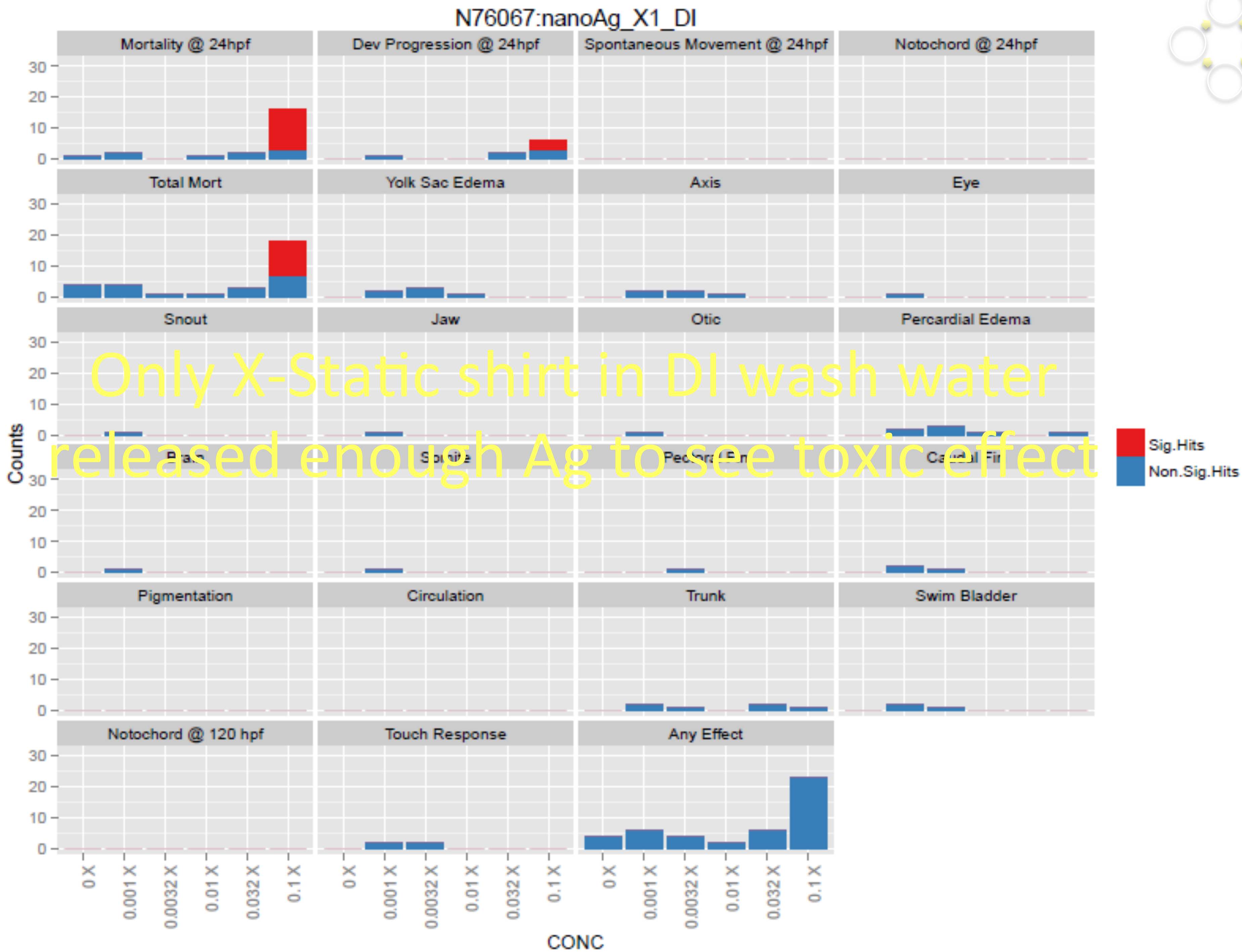
High Throughput Toxicity Testing





Tethered AgNP shirt wash water shows no significant effect

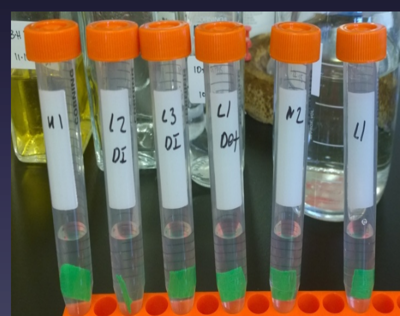
$[Ag]_{aq}$ = 306 ug/L

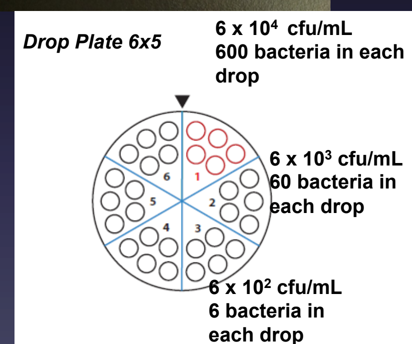

N76067:nanoAg_X1_DI
Mortality @ 24hpf
Dev Progression @ 24hpf
Spontaneous Movement @ 24hpf
Notochord @ 24hpf
Total Mort
Yolk Sac Edema
Axis
Eye
Snout
Jaw
Otic
Percardial Edema
Pigmentation
Circulation
Trunk
Swim Bladder
Notochord @ 120 hpf
Touch Response
Any Effect
Counts
0
10
20
30
0 X
0.001 X
0.0032 X
0.01 X
0.032 X
0.1 X
CONC
Sig.Hits
Non.Sig.Hits
Only X-Static shirt in DI wash water released enough Ag to see toxic effect

Toxic effects observed in detergent wash solutions

Nano-Enabled Product ***EFFICACY*** is critical to assess (but not easy)

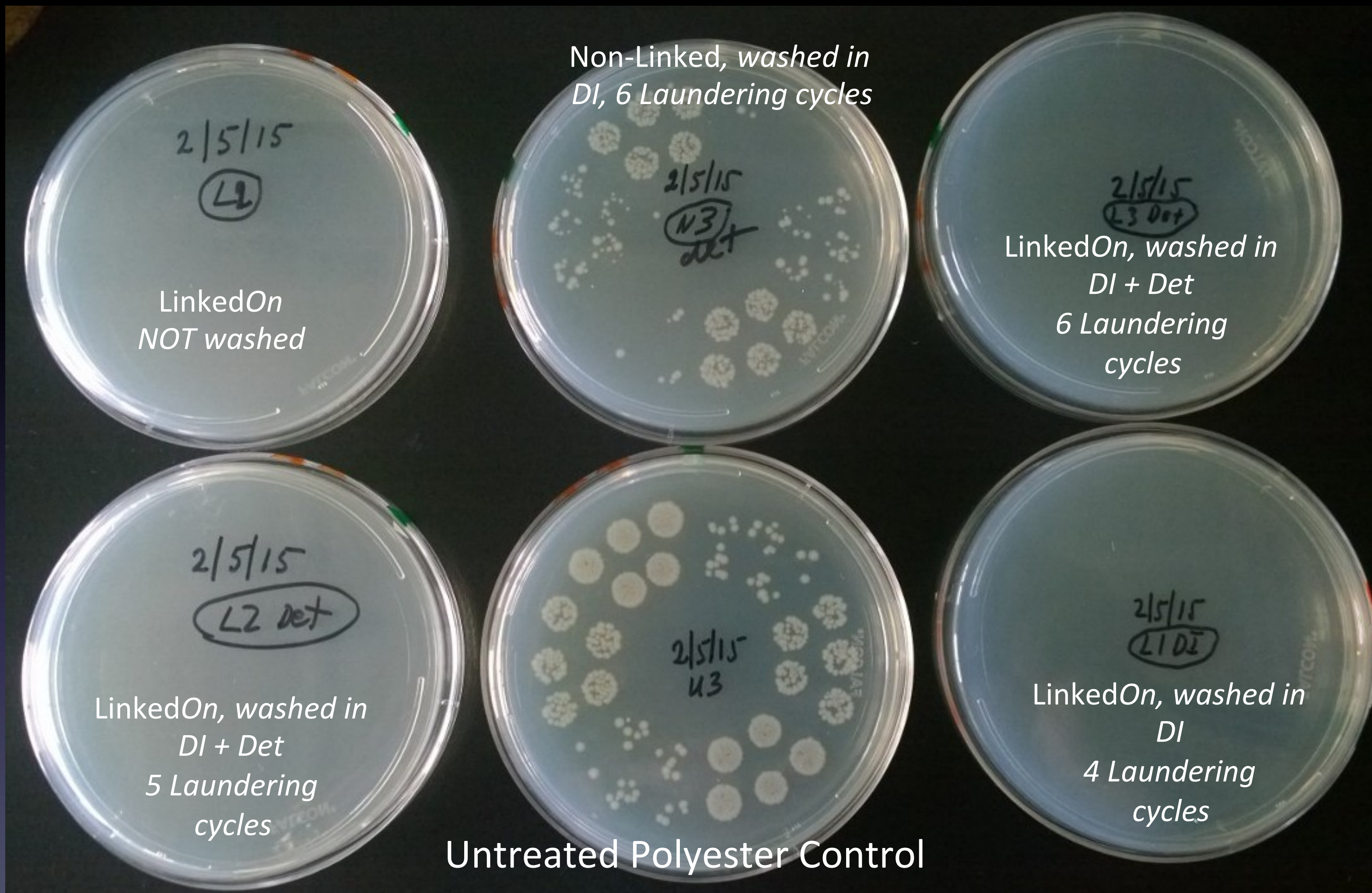
AATCC 100 - Antimicrobial Fabric Test



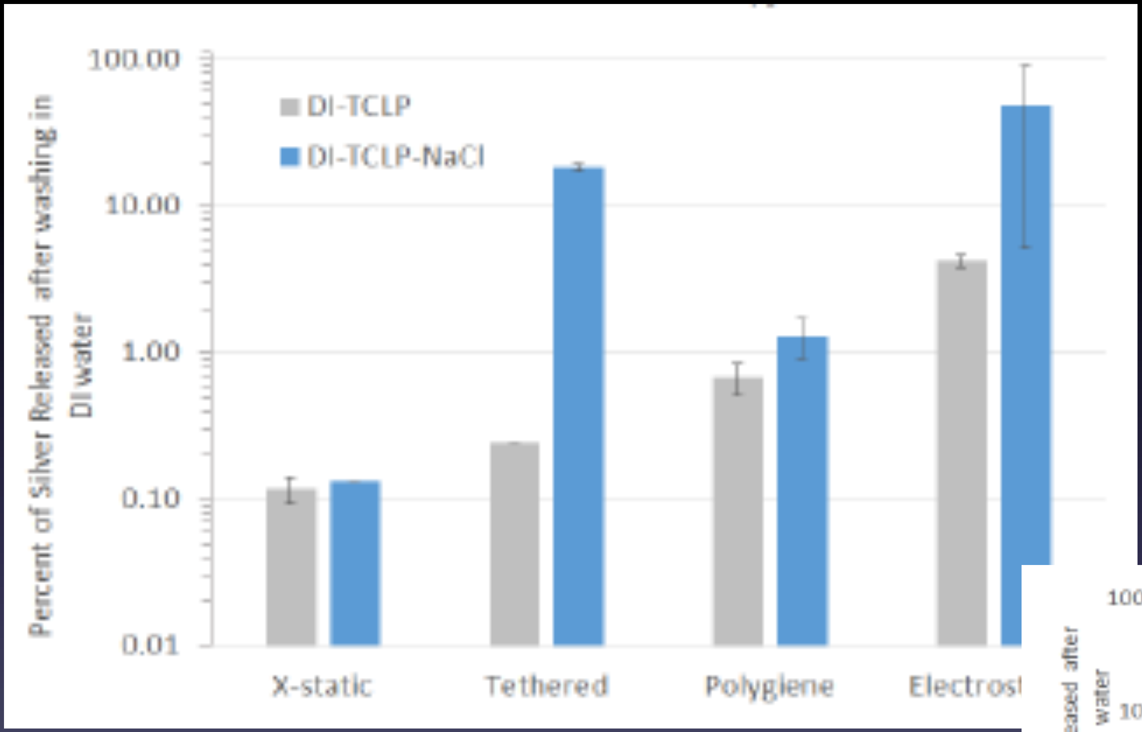


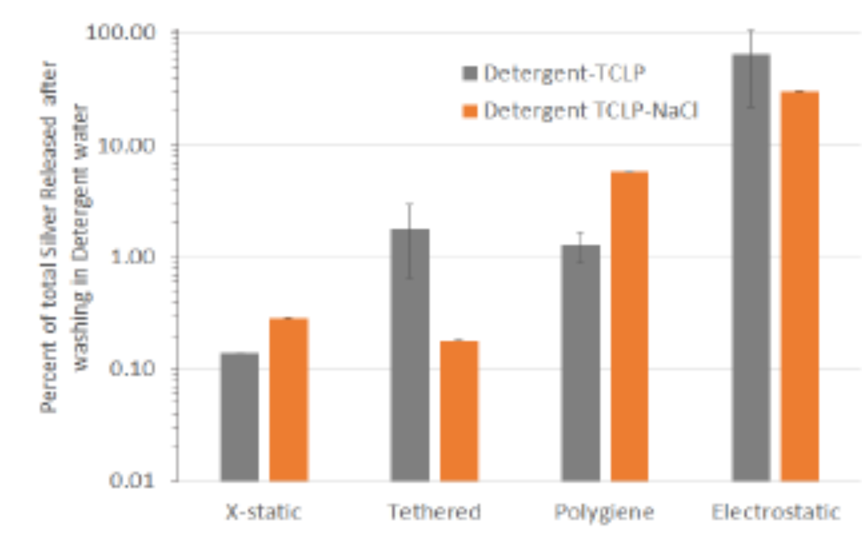
- Equal weight swatches cut from test fabrics. Place into sterile Petri dishes. Inoculate bacteria culture. Incubate for 24 hr at 37 °C.
- Achieved high level of reproducibility

LinkedOn and Non-Linked Fabrics



End of Life
Amount of silver released during TCLP



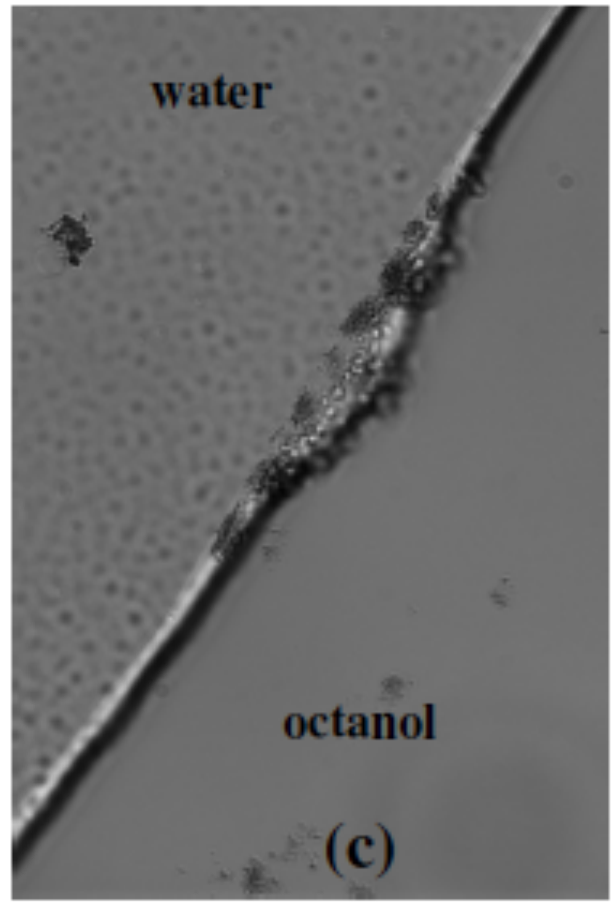


TLCP Tests conducted after washing 4 x

Modeling paradigms

- NMs accumulate at interfaces whereas chemicals move through interfaces

$$\Delta E = \frac{r^2\pi}{\gamma_{AB}}\left[\gamma_{AB} - (\gamma_{PA} - \gamma_{PB})\right]^2$$



Conventional chemicals

PCB
$\log K_{ow}$
NO_x
EDTA
K_H
K_D
Cu
PAH
Hg
speciation
$\log K_{lipw}$
dichlofenac

Nanomaterials

nC_{60}
Nano-Ag
?
K_D
Nano-TiO_2
α
CNT
$\log K_{lipw}$

Hristovski et al., JESH-A (2011); Westerhoff & Nowack, ACR (2013)

2

Nano-Metrology is An Evolving Science

Complexity across lifecycle challenges analytical methods (e.g., Foods)

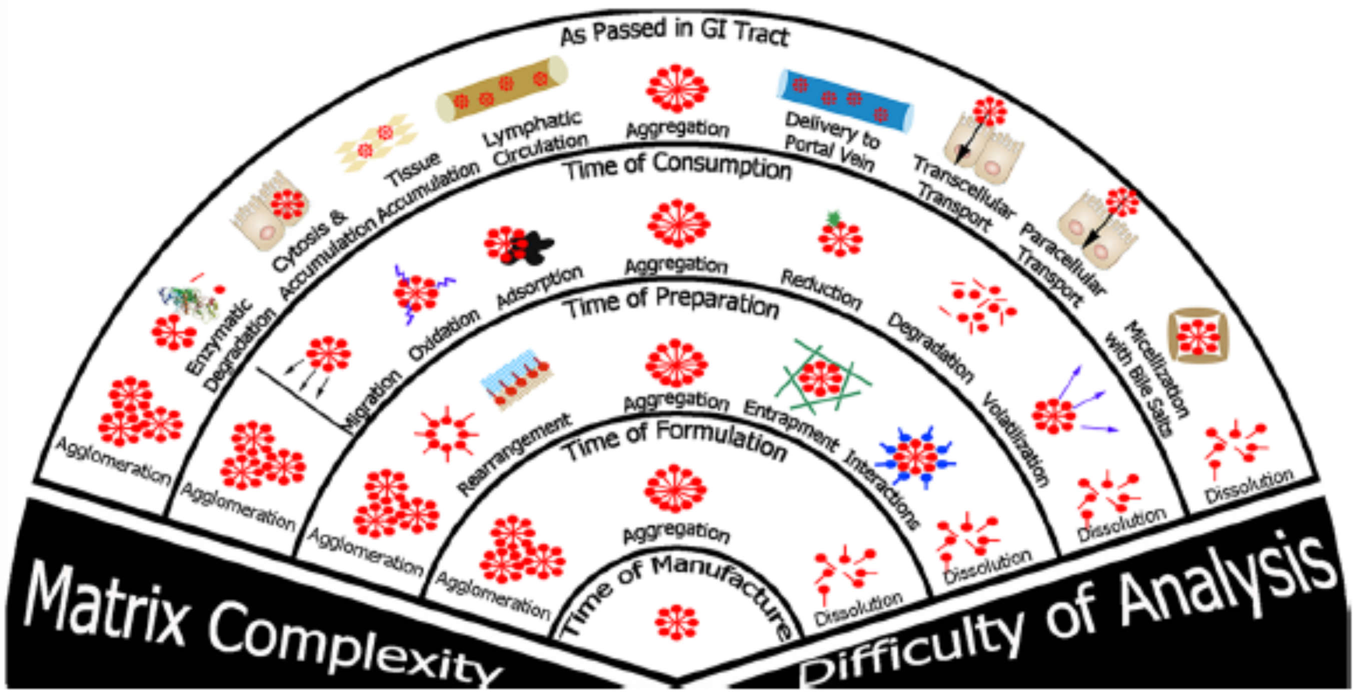


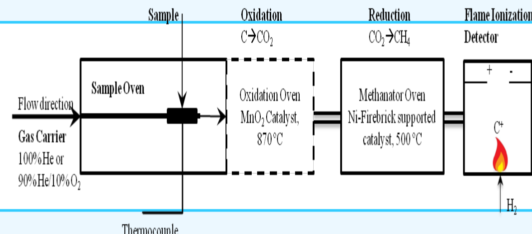
Figure 2. Potential modes of destabilization through the lifecycle of a nanomaterial from the time of manufacture to potential biological interactions in the alimentary tract and the complexity/difficulty of sample quantification and detection. GI, gastrointestinal.

Szakal et al., ACS Nano, 8:4:3128 (2014)

LC nano

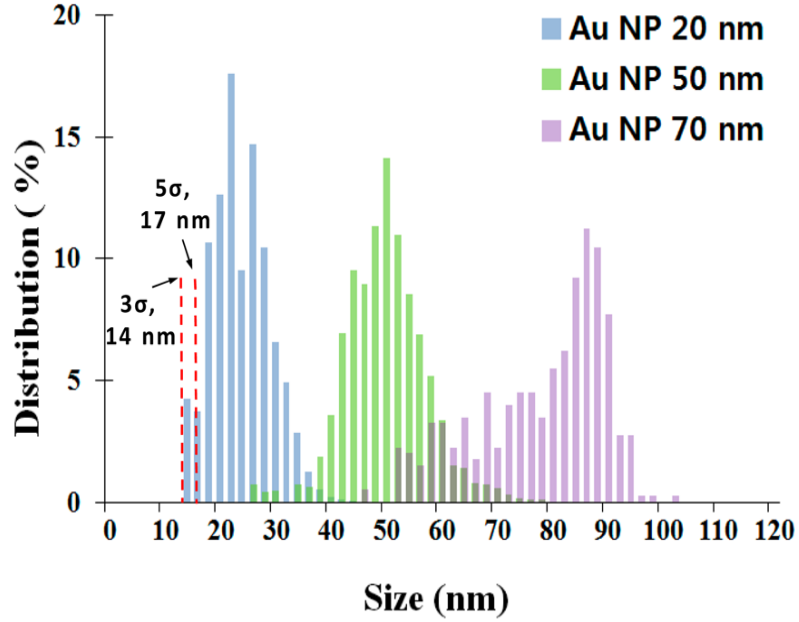
Common Direct NM Detection

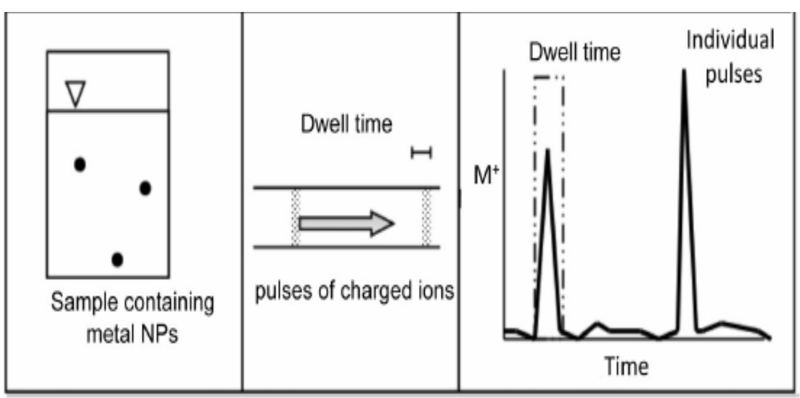
Method	NM Type	Generalized Detection Limit Comments
Light scattering (UV/VIS)	any	**> 1 mg/L** in water **0.05 mg/L** with HPLC of NM extract
ICP-MS (better than ICP-AES) TOF-MS (emerging)	metals	**> 10 ppt** in water (total metal conc) Ability to get size, # and concentration dosimetry (sp- , FFF-, centrifugal – ICP-MS)
LC-MS	C60	**~ 1 ppt**
Thermal combustion or Microwave thermal analysis	MWCNT SWCNT	**~ 1 ppb**
Isotopes	^{14}C Metal isotopes	**< 1 ppb** by Scintillation counting Isotopic ratios

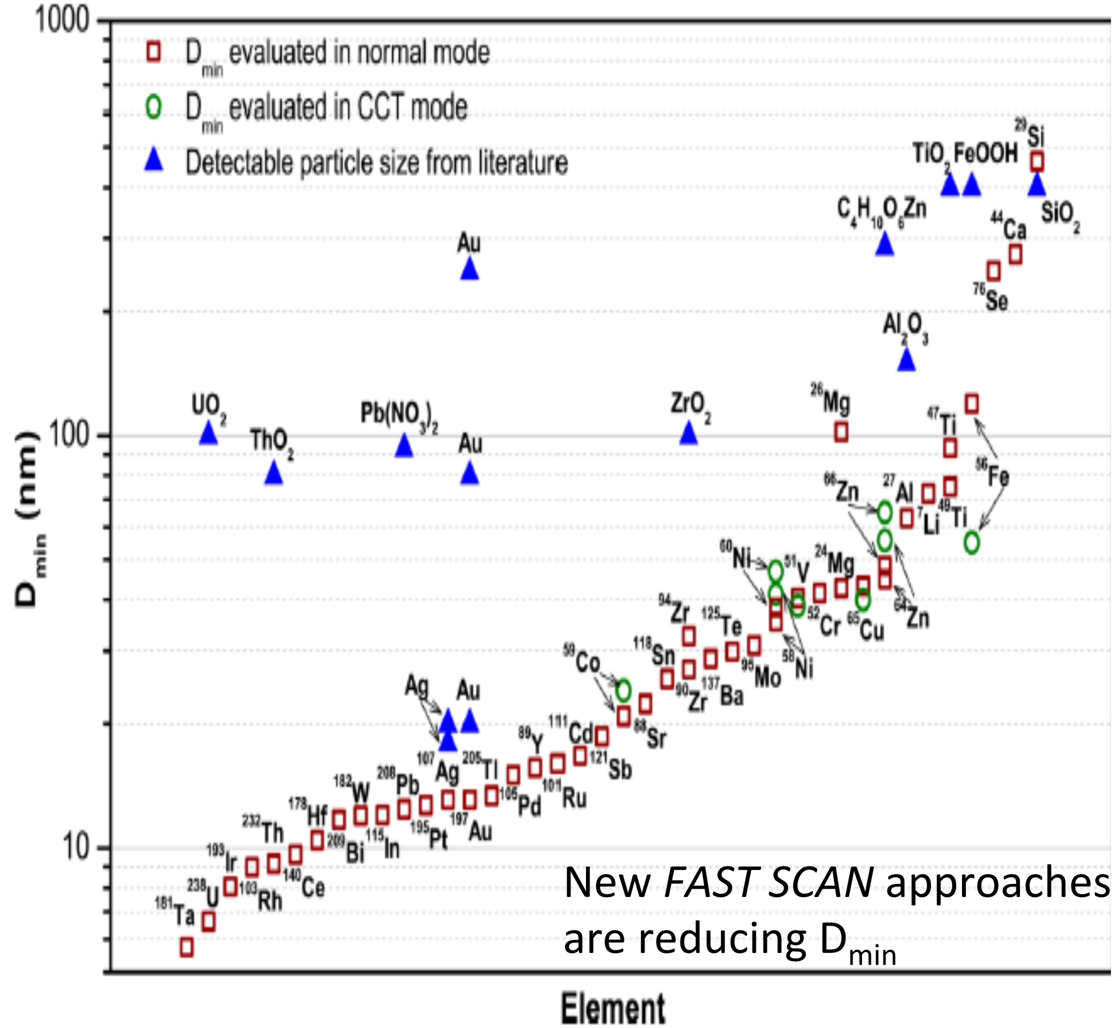


Single Particle (sp)ICP-MS

Minimum Size Detection Depends Upon Element



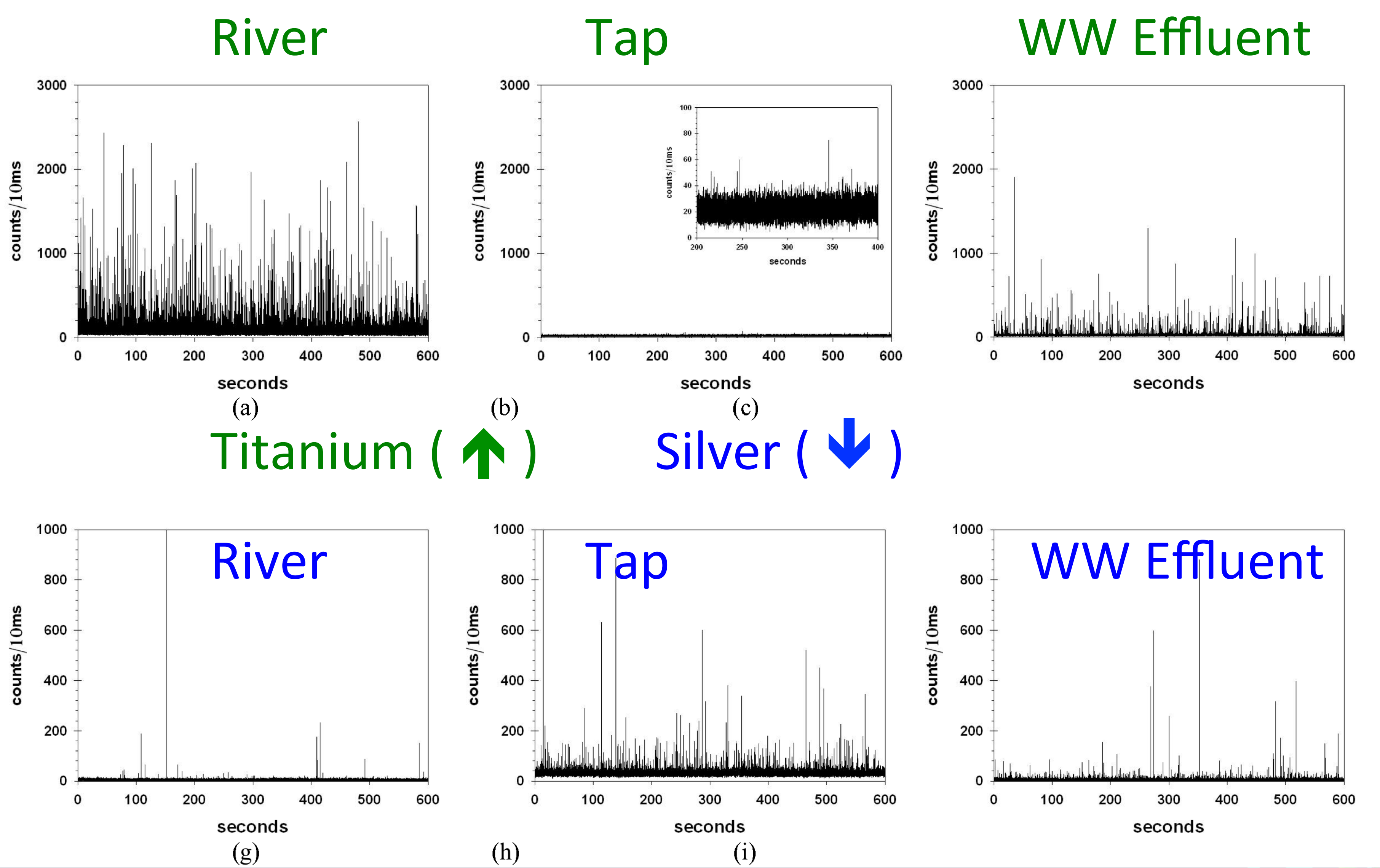




New *FAST SCAN* approaches are reducing D_{min}

spICP-MS Examples in Water

Background (Incidental & Nature) and Engineered NMs



Lee et al. (in-prep)

It's a matter of perspective…

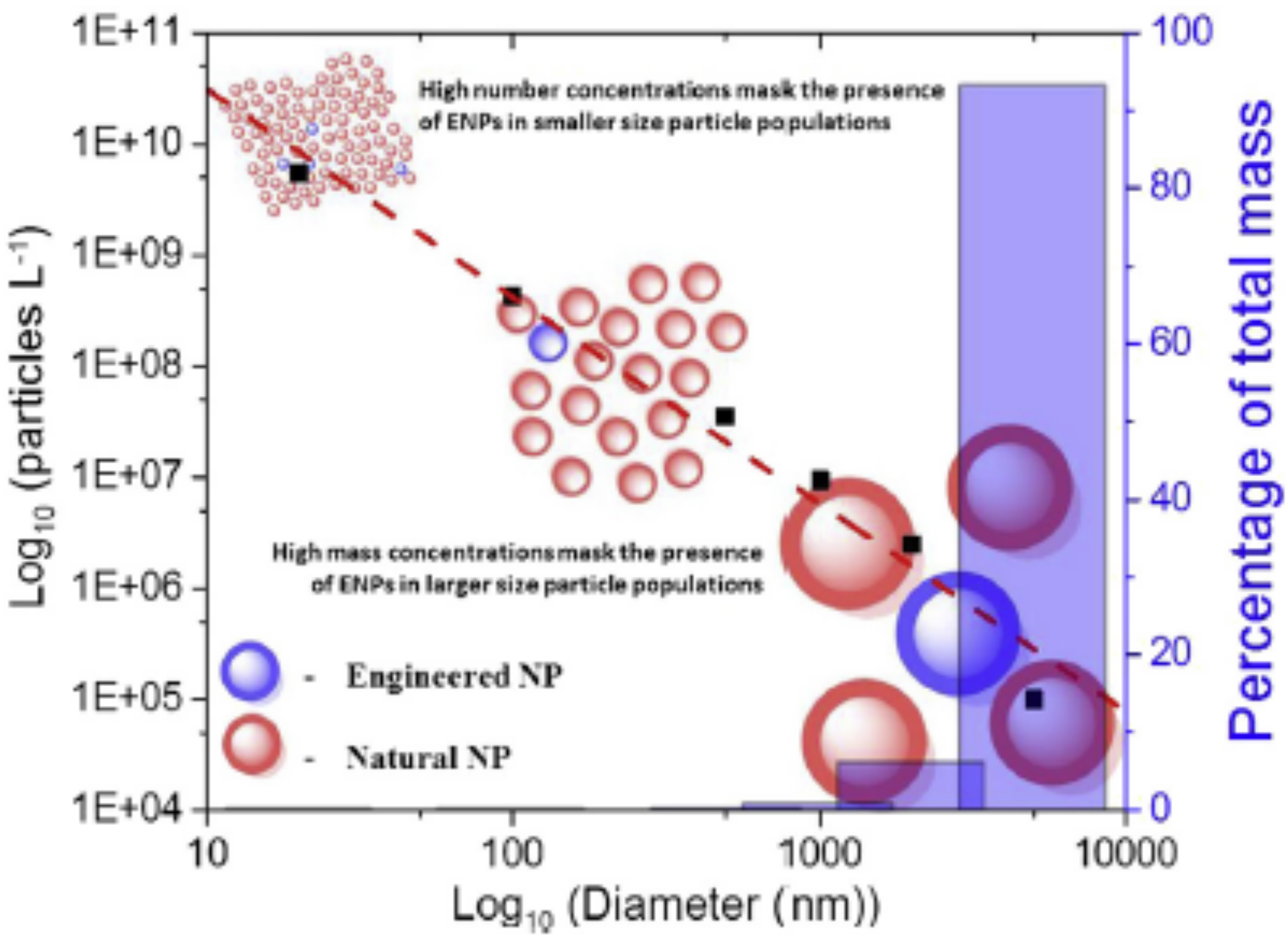


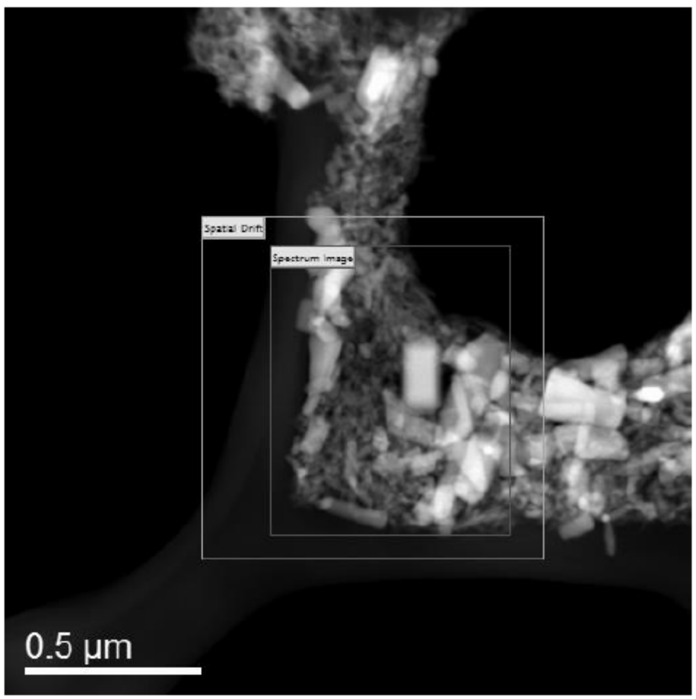
FIGURE 7 Considerations for PSDs when examining particles in natural waters. *Data from Harris (1977)*[94].

Ranville & Montano, Chap. 3 in *Characterization of nanomaterials in complex environmental and biological media (Eds. Baalousha & Lead, 2015)*

TEM can inform “what” to look for in water phases

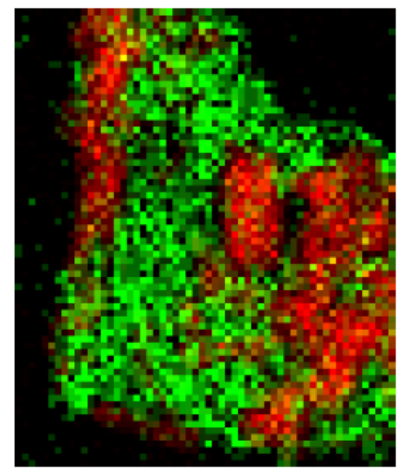
Seeing is Believing?

Sunscreen



Ti

Zn



Ti in green,
Zn in red

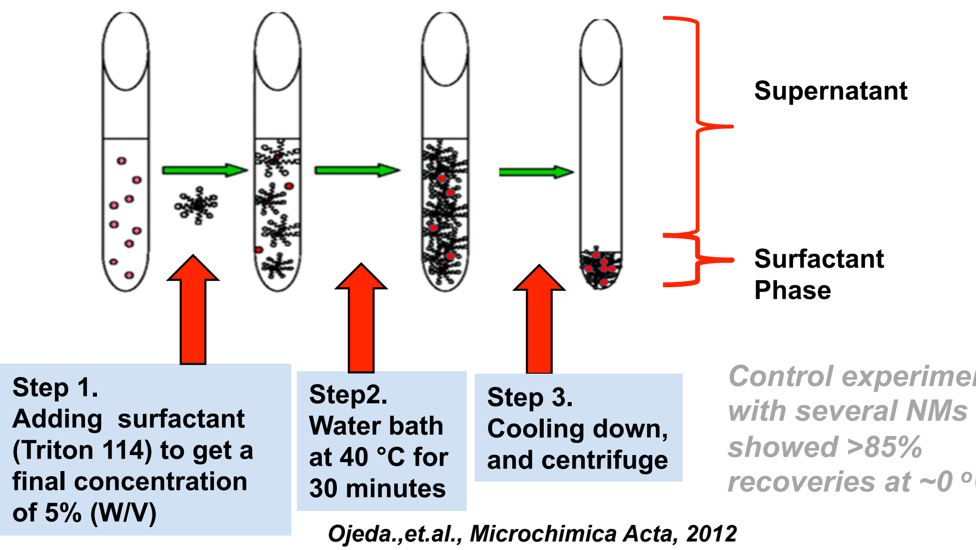
Sample Prep is Challenging

Can I put a donut in
your TEM instrument?

Examples of Sample Preparation

- Solids Digestion for biological samples (NaOH, ProteinaseK, Solvable, acids, oxidants)
- Extraction from liquid samples:
  - High speed centrifugation
  - Filtration
  - **Centrifugal Ultrafiltration**
  - Extraction (**Cloud point extraction,** Solvents)

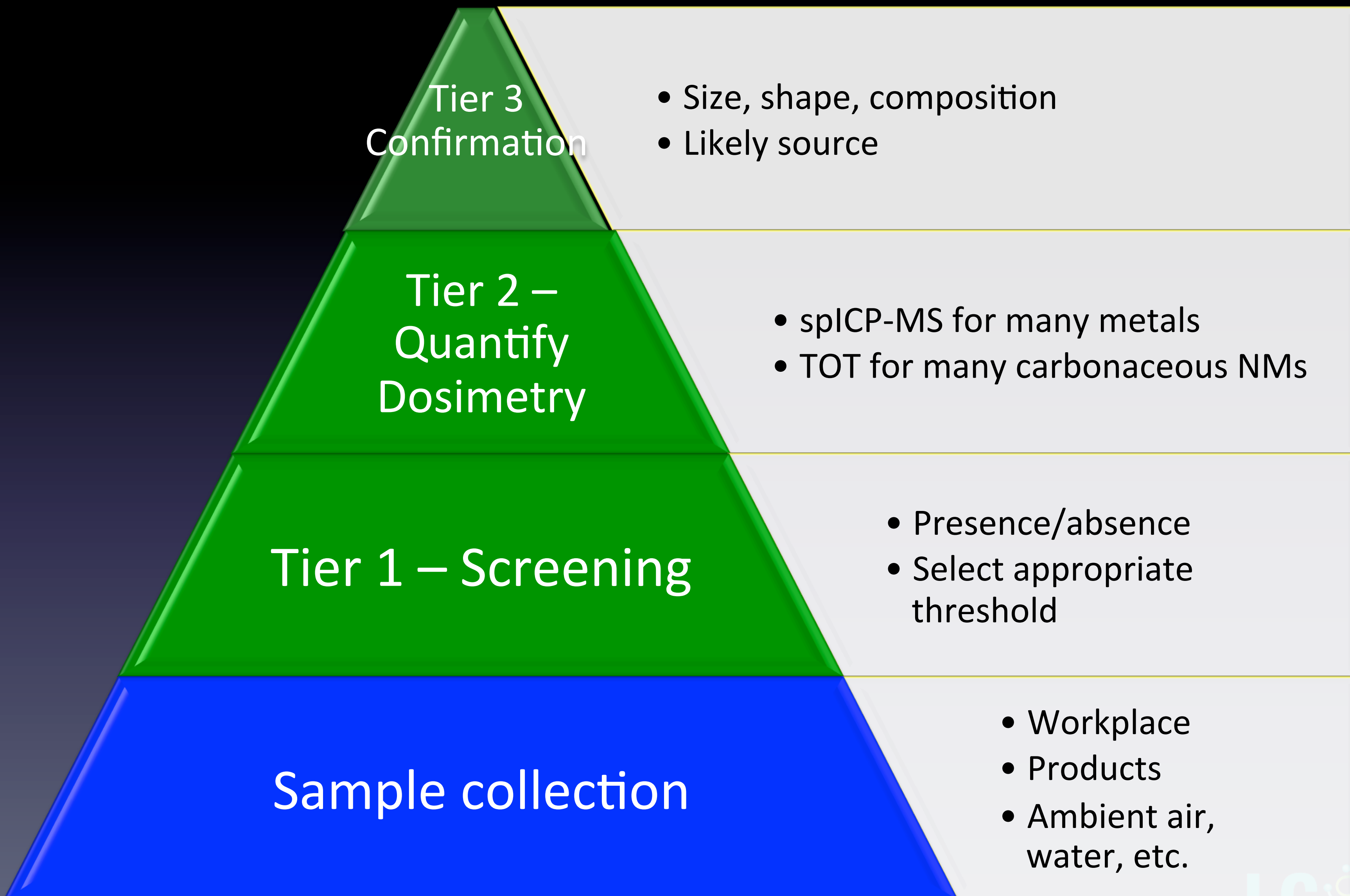
Cloud Point Extraction



Control experiments with several NMs showed >85% recoveries at ~0 °C

Ojeda.,et.al., Microchimica Acta, 2012
Hartmann et al., Anal. Chem, 2014

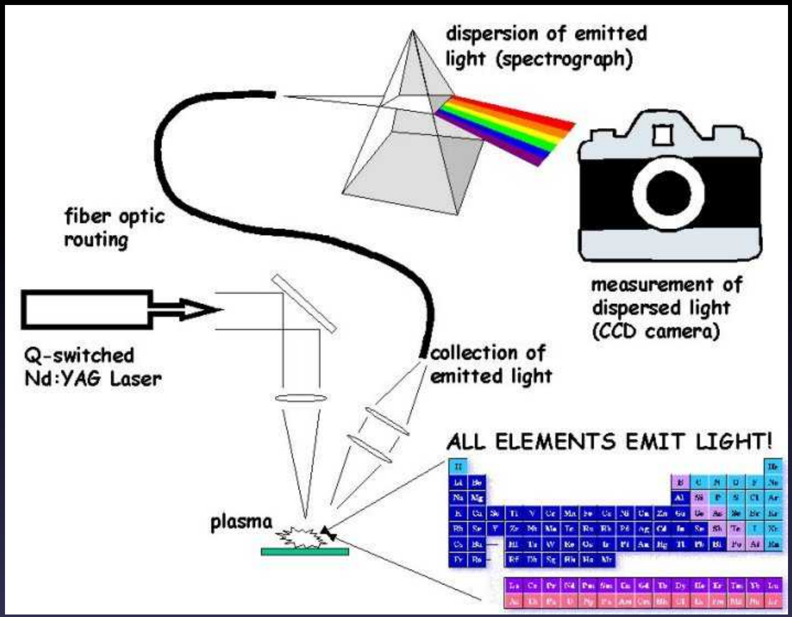
Tiered Exposure Analytical Approaches



Presence/Absence Examples

- Laser Induced Breakdown Spectroscopy (LIBS) or X-Ray fluorescence spectroscopy (XRF)

- Pro's
  - Fast
  - Commercial systems available
  - Semi-quantitative
  - Able to differentiate elements
  - Used in air pollution already
- Cons
  - No sizing information
  - ~0.01% detection limits (may be ok?)



Source: US Army Research Laboratory

Preliminary study:
- LIBS confirmed presence/absence of TiO_2 or SiO_2 in food samples (n~20), fabrics and plastics
- Results confirmed by ICP-MS & TEM

Example: Lab Exposure to NMs

- Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods

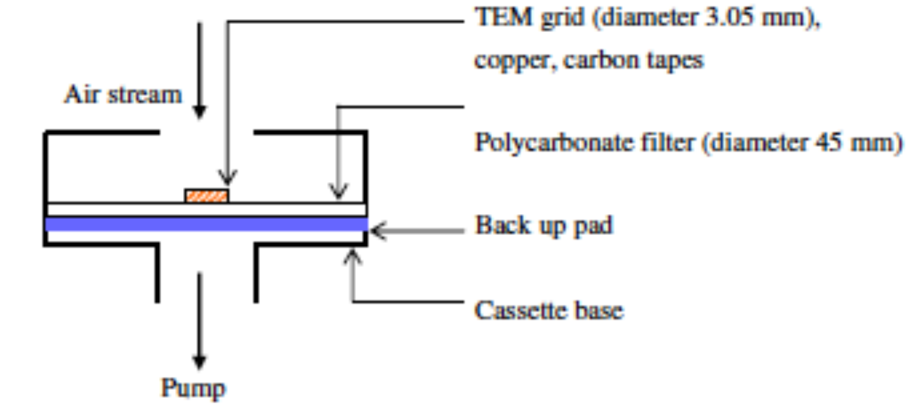


Fig. 3 Design of the TEM grid sampler

J Nanopart Res (2009) 11:147–161

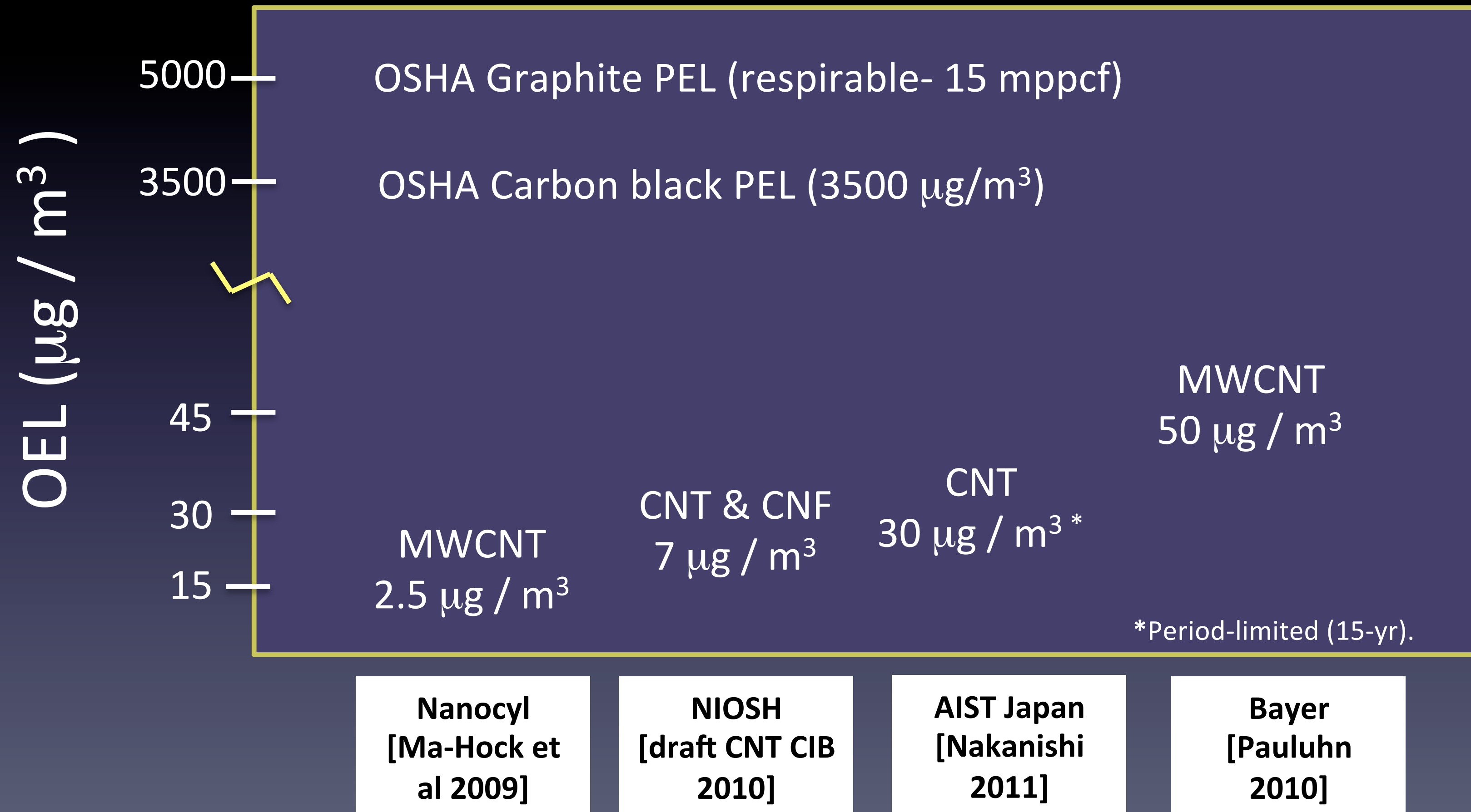
"Results found that the handling of dry powders consisting of nano-sized particles inside laboratory fume hoods can result in a significant release of airborne nanoparticles from the fume hood into the laboratory environment and the researcher's breathing zone."

Laura Hodson / NIOSH

OELs for Carbon Nanotubes

> Workers who could receive the greatest benefit from medical screening include the following:
>
> - Workers exposed to concentrations of CNT or CNF in excess of the REL (i.e., all workers exposed to airborne CNT or CNF at concentrations above 1 μg/m³ EC as an 8-hr TWA).

NIOSH Current Intelligence Bulletin 65 (2013) "Occupational Exposure to Carbon Nanotubes and Nanofibers"



Adapted from L. Hodson / NIOSH

BSI—0.01 f/ml [benchmark exposure limit-BEL] for high aspect ratio nanomaterials (1/10th asbestos OEL).

LC nano

What is the data telling us?

- There are a BIG10 high volume NMs today: SiO_2 > TiO_2> Fe-Ox > ZnO > Al_2O_3 > CeO_2 > nano-clay> CNT > Ag ≈ Cu
- Definition of "nano" keeps shifting
- Product labeling of NMs inadequate

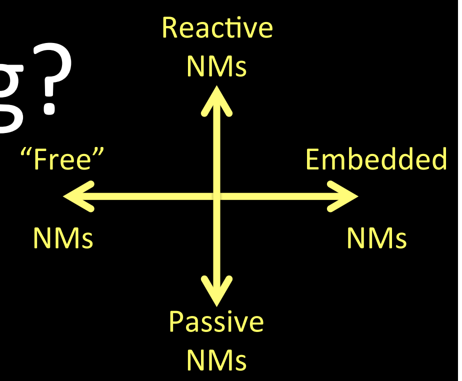
- Does use of NMs reduce exposure to chemical pollutants?
- Who is responsible for "transformed" or non-pristine NMs?

What do we know?

Exposure measurements & models

- We can characterize feedstocks & pristine NMs
- Analysis of NMs in complex matrices remain largely purview of research labs
- Manufacturers use both dry and wet NM feedstocks
- Difficult to distinguish engineered NMs from incidental or natural colloids
- Mechanistic models including NM transformations are well developed (but not validated)
- Few human studies track NM bio-distribution, bio-availability or bio-accumulation or adverse outcomes released from consumer products

What should we be doing?



- Assess TiO_2 & SiO_2 NMs:
  - Should we remove these from concern?
  - Do we really understand their consumer exposures?
  - Are there sensitive consumer population or nano-specific adverse outcomes?
- Apply FUNCTIONAL uses for NMs in products as a guiding tool for life cycle exposures
  - Measure unique properties (optical, thermal, antimicrobial, magnetic, etc)
  - Group products & exposure scenarios around functional uses
- Design studies across the life cycle of NMs to validate models
  - Validate assumption that pristine NMs can be seen as precursors
  - Assess human exposures (workers, consumers) to measured NM exposure levels (inhalation, oral, dermal), within biological fluids (nasal, urine, blood) and health outcomes
- Implement monitoring programs (Ti, Ag, Ce for NHANES) & discovery nano-specific biomarkers

LC nano

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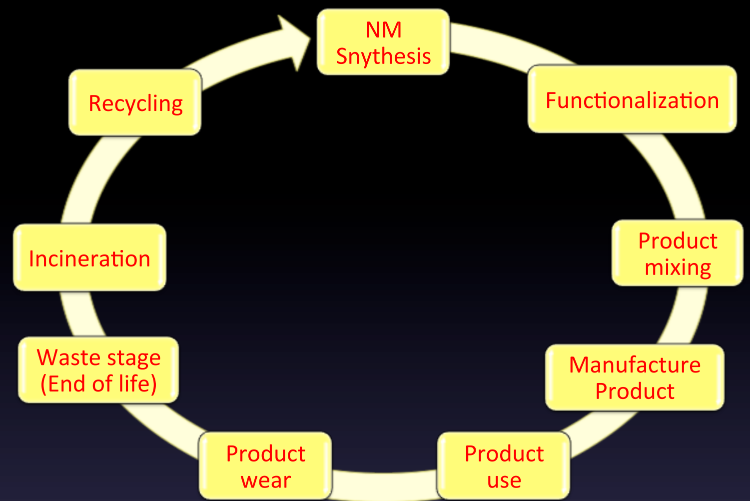

- Key collaborators
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  - Many current PhD students & post-docs