NanoEHS Landscape (mid 2016)

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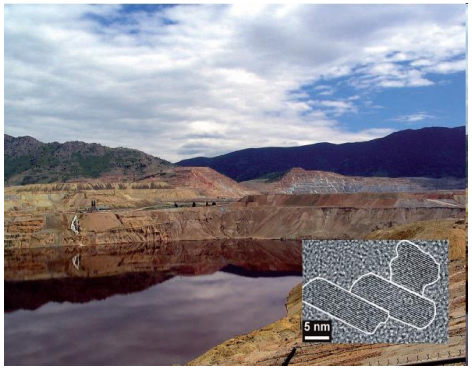
CEINT
Center for the Environmental Implications of NanoTechnology

Carnegie Mellon University

NSF EF-0830093/1266252

Key Questions to ask about Risk



Exposure → **Risk Characterization** ← **Hazard**

- Where do nanomaterials accumulate?
- Who is exposed?
- What form of the NM are we exposed to?
- What exposure concentration is expected?

- What are the acute, chronic, and accumulative effects?
- What is the internal dose?
- How does transformation affect toxicity?

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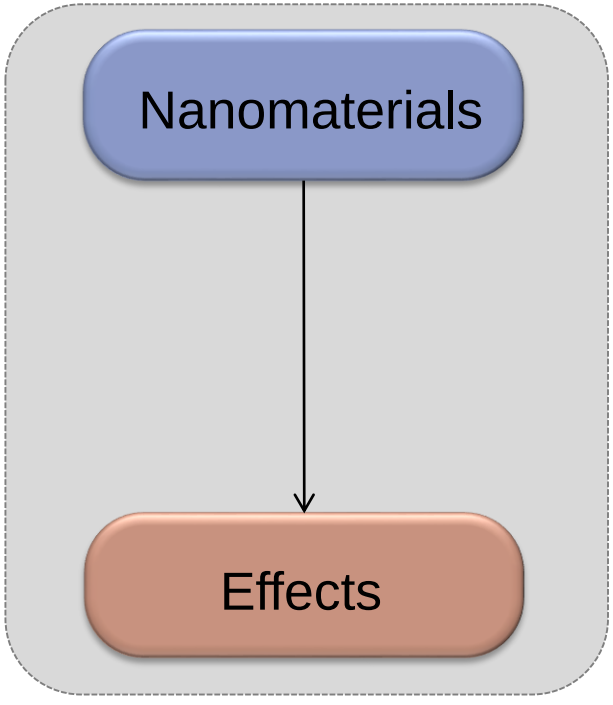
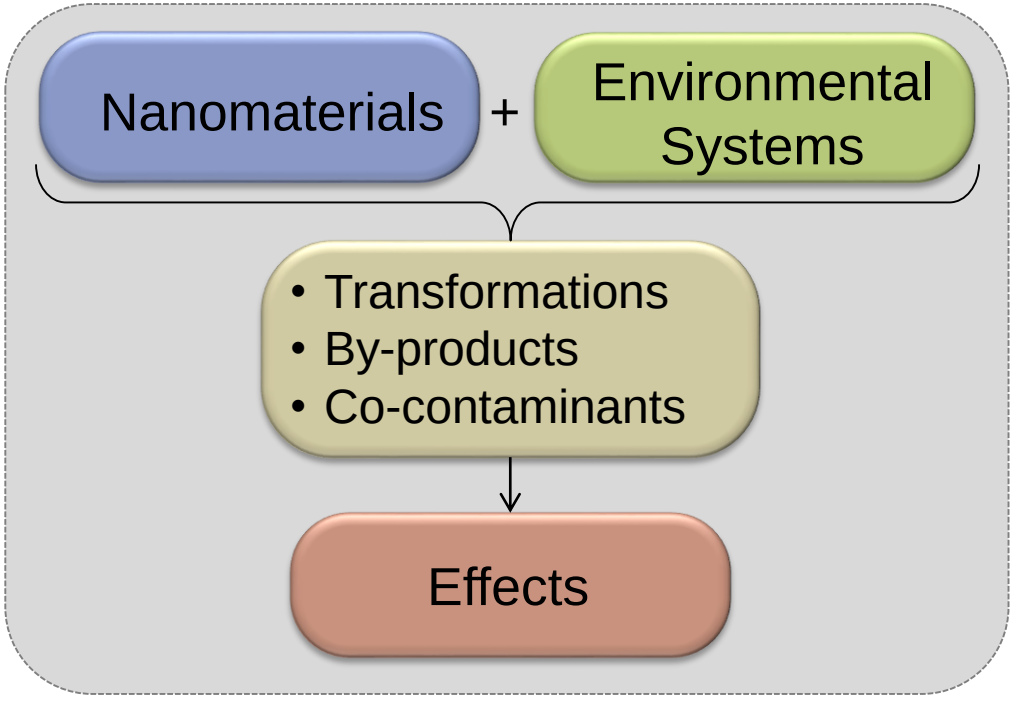
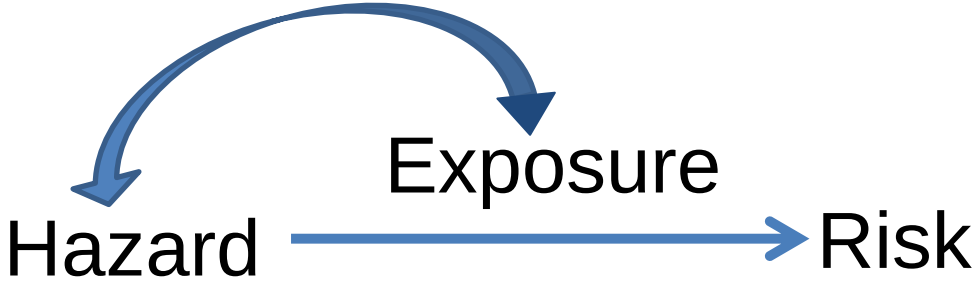
Exposure and Hazard are Inseparable





Exposure x Hazard
= Risk



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Nanomaterials are Dynamic

- Rates of processes are needed (not equilibrium)

$$\frac{dn_{k_i}}{dt} = \pm\alpha\beta n_i \gamma_j - k_{dissolution} n_k + k_{formation} n_k + k_{transformation} n_k + k_{biouptake} n_k + k_{depuration} n_k$$

- Settling
- Aggregation
- Deposition

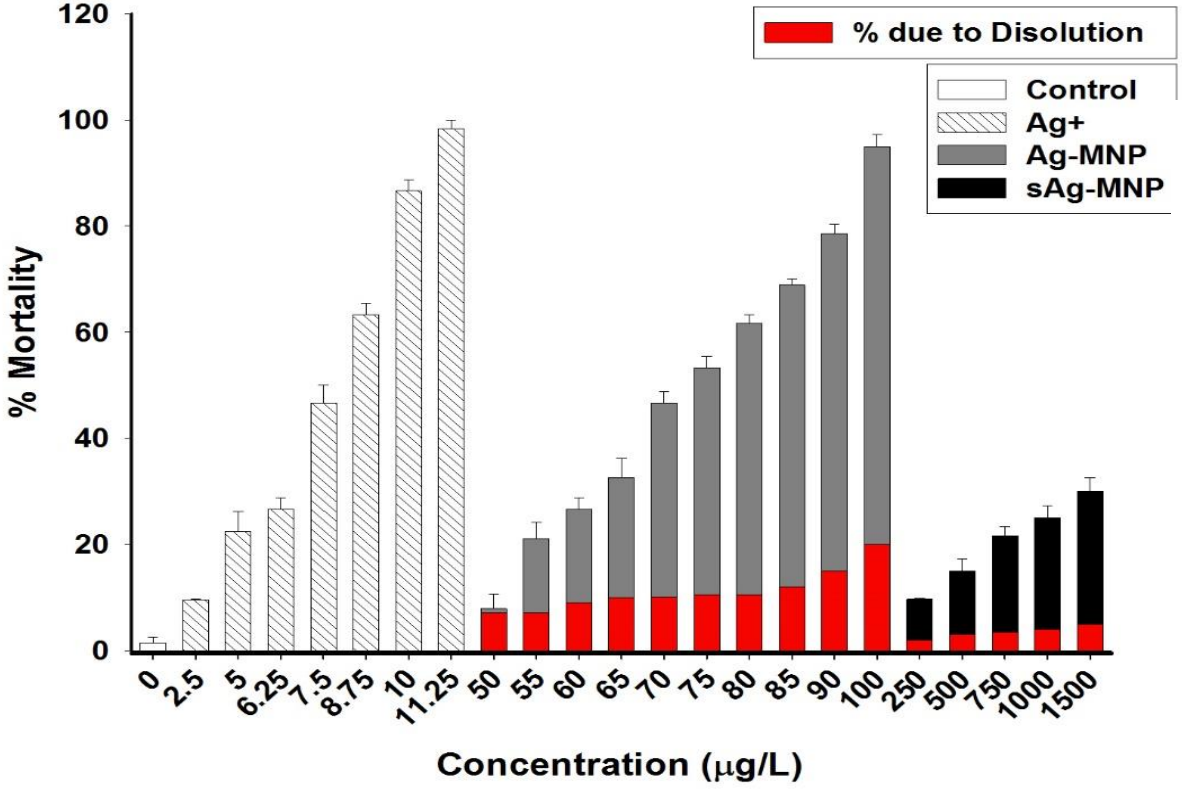
- Precipitation
- Bioproduction

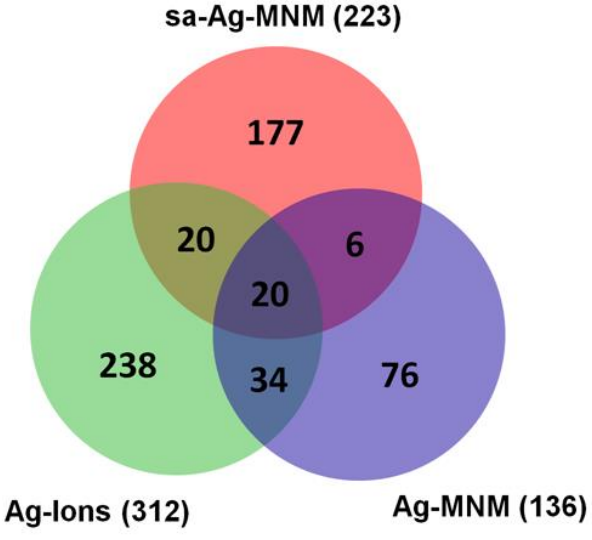
- Sulfidation
- Complexation
- Hydroxylation
- Oxidation/ Reduction …

- Transformation and aggregation affect reactivity, fate, toxicity and persistence
- System properties cannot be ignored

Evidence exists for particle-specific effects

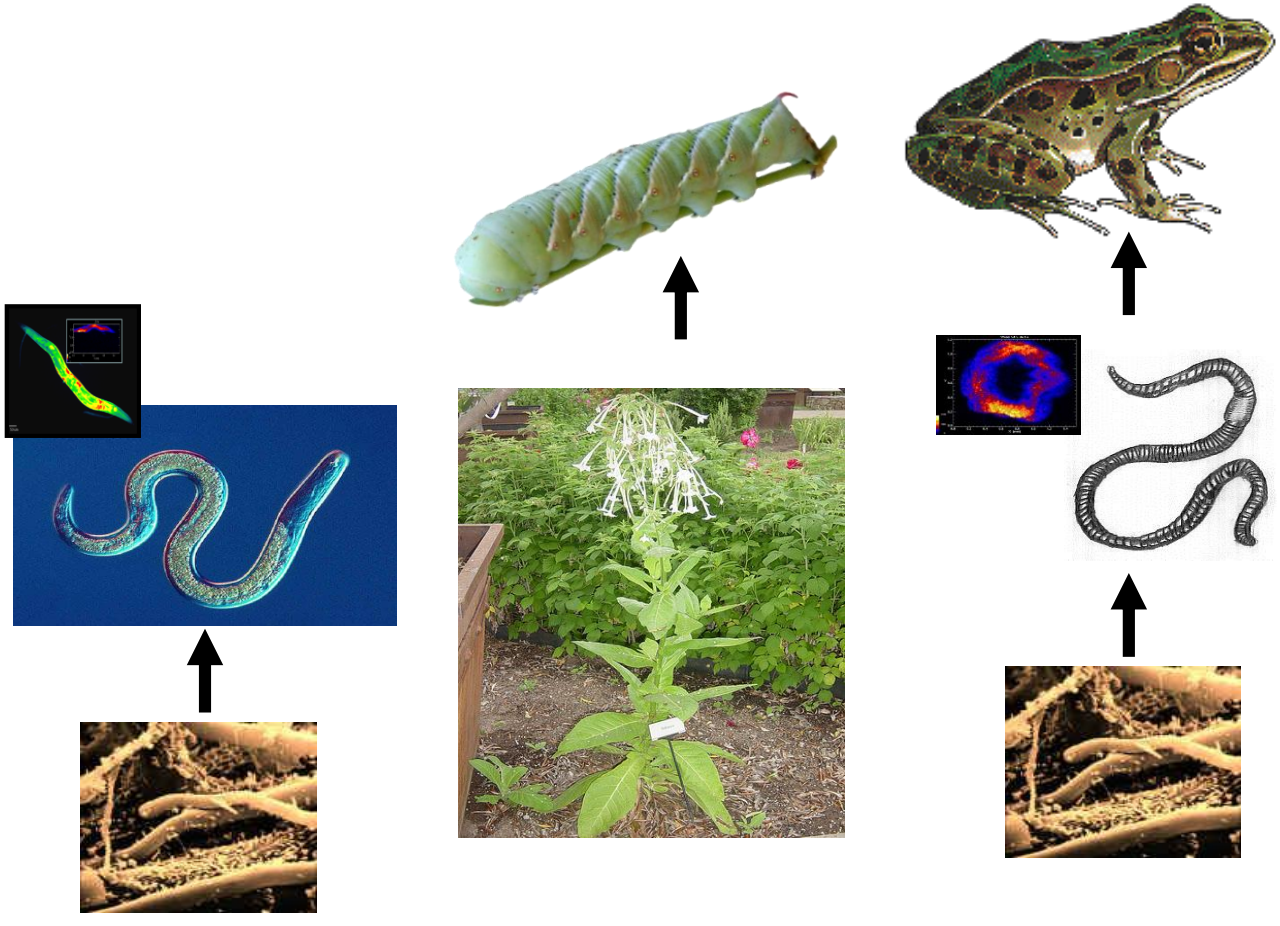
Ag NP toxicity to *C. elegans*

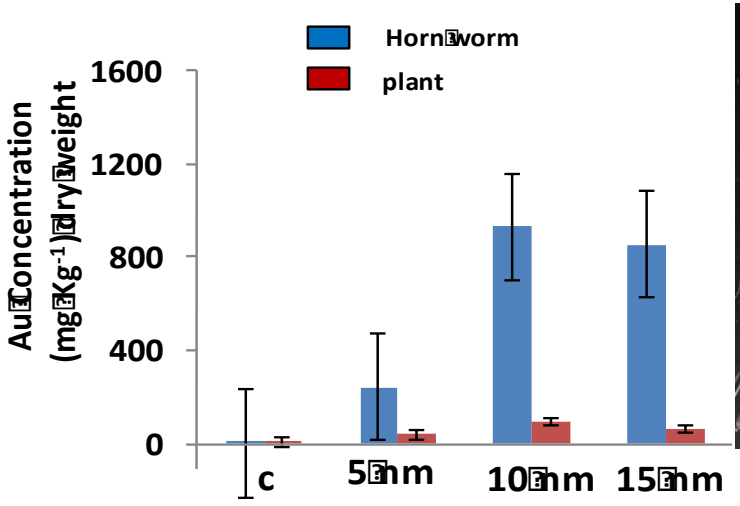




Starnes et al., 2015, 2016, Env. Pollut.

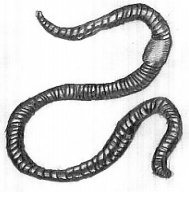
Trophic transfer of nanoparticles occurs



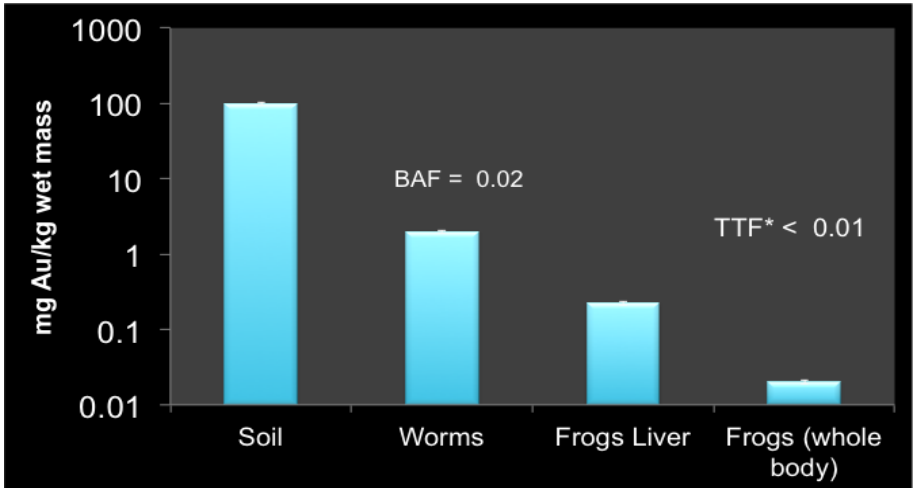


Judy et al., 2011. *Environ. Sci. & Technol.*

Bioaccumulation



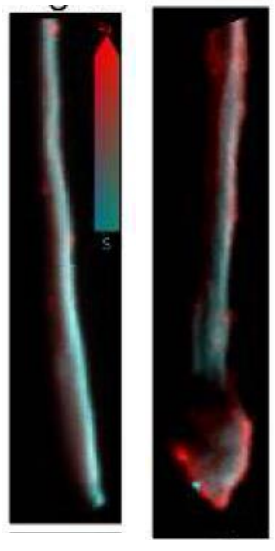
Trophic Dilution



Unrine et al. 2012 Environ. Sci & Technol.

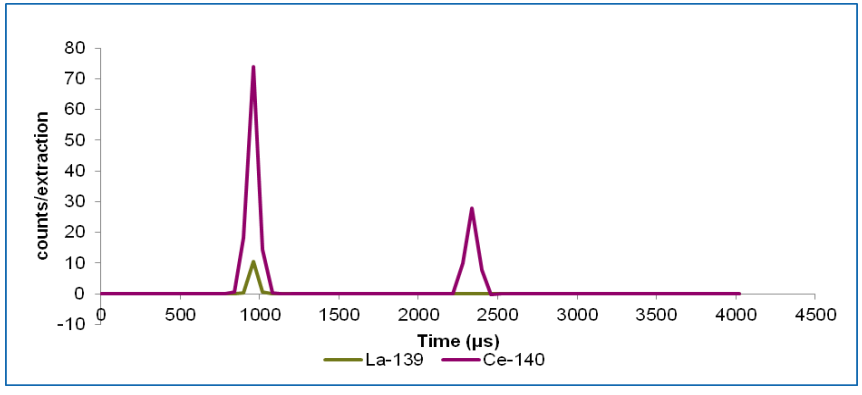
We can identify and measure some nanomaterials in complex matrices

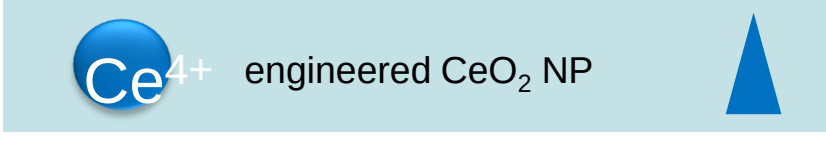
- Needed for regulatory purposes
- Needed for determining dose
- Improves mechanistic knowledge

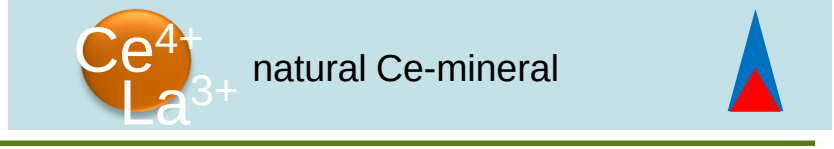


Stegemeier et al., 2015 *ES&T 49* (14) 8451

SP-ICP-MS

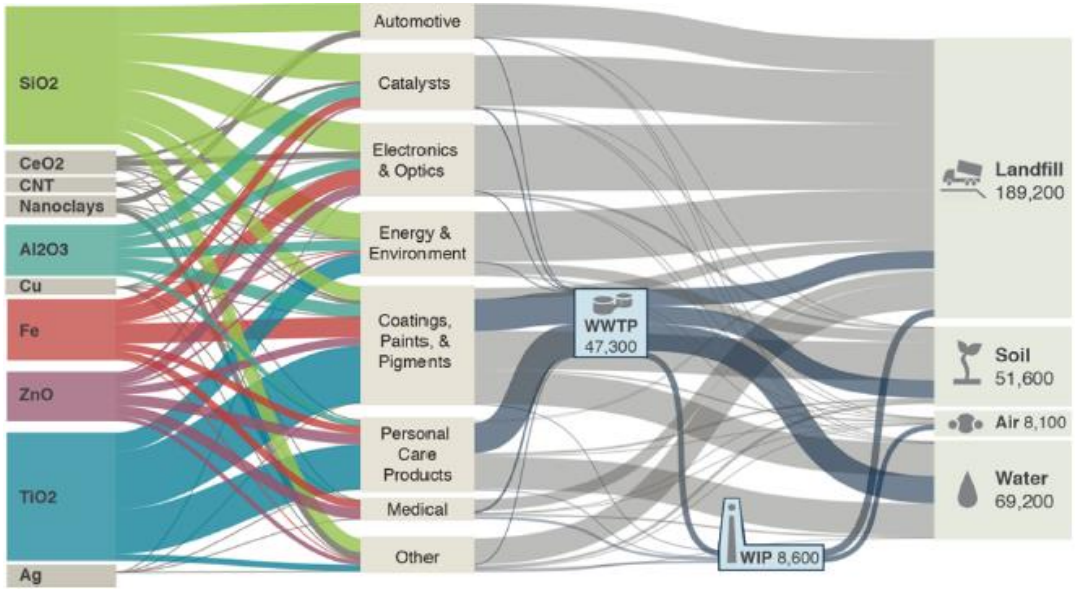




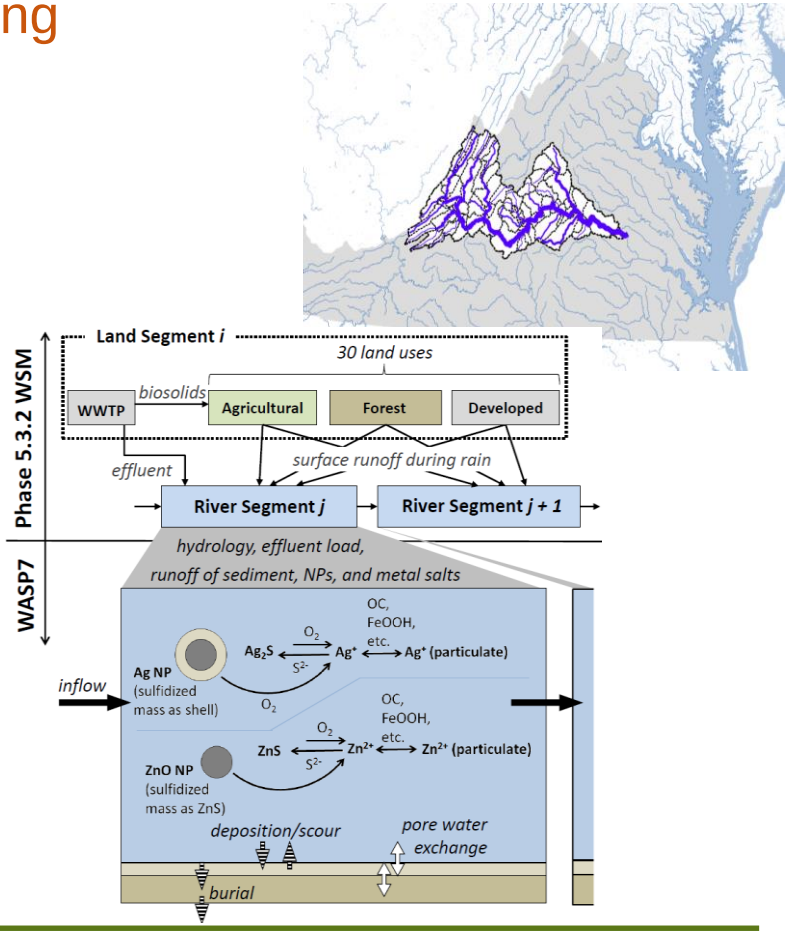


We have nanomaterial environmental fate and exposure models

- Determined key parameters describing ENM behaviors
- Second generation of models emerging
- Sign of maturing field



Keller & Lazareva *Environ. Sci. Technol. Lett.* 2014, 1, 65−70



Dale et al. 2015 *ES&T* 49 (12), pp 7285

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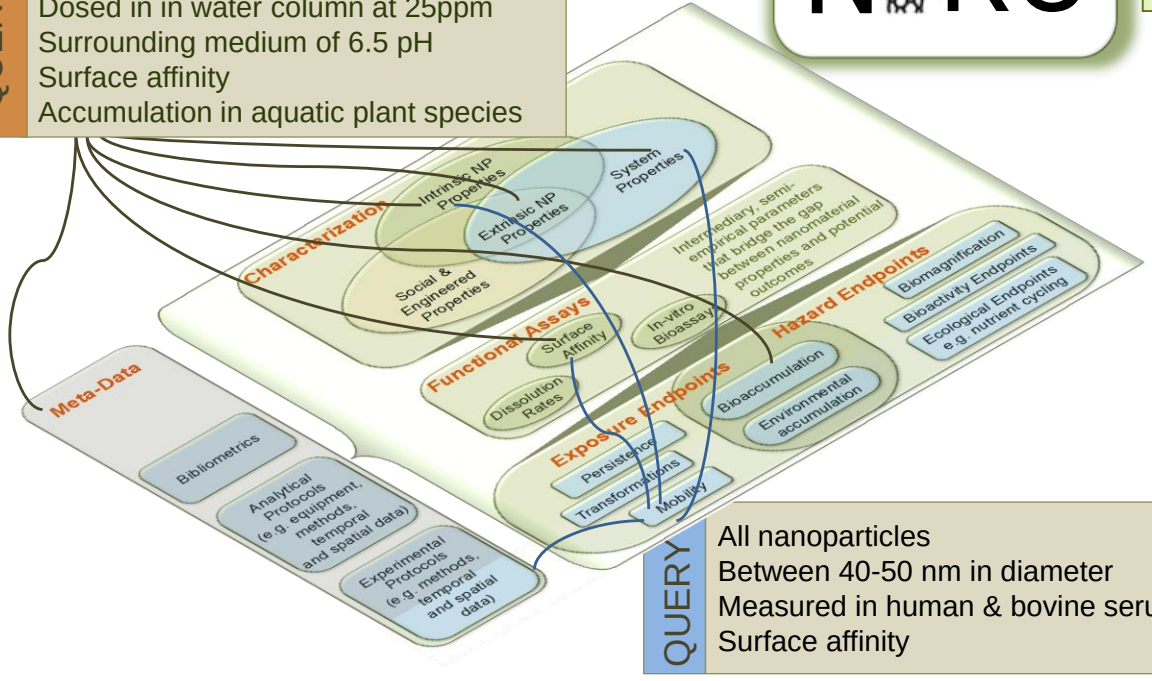
We can collect and share data for nanoEHS

- Important for read across

QUERY 1

Citrate coated nanoAg particles
Between 40-50 nm in diameter
Dosed in in water column at 25ppm
Surrounding medium of 6.5 pH
Surface affinity
Accumulation in aquatic plant species



QUERY

All nanoparticles
Between 40-50 nm in diameter
Measured in human & bovine serum
Surface affinity

NIKC

Active projects throughout US & EU

NBI KNOWLEDGEBASE

NANOMATERIALREGISTRY

rivm National Institute for Public Health and the Environment

NANOREG

ProSafe

NanoFASE

Serenade

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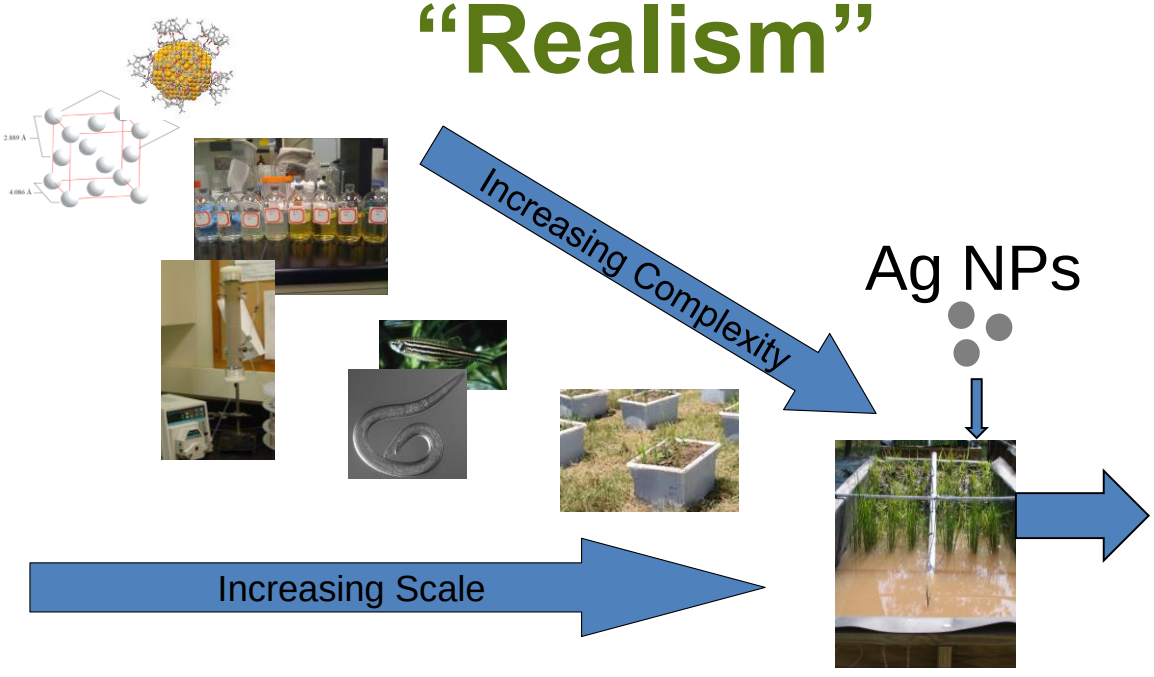
Regulation of Nanomaterials is Advancing

- Adapting existing regulatory programs to include nanomaterials
  - TSCA New chemical review
  - REACH Registration
  - EU Cosmetics directive
- Labeling and Information Disclosure
  - Proposed TSCA reporting and recordkeeping rule
  - European registries
- International Cooperation
  - Canada-U.S. regulatory cooperation council
  - OECD Working party on manufactured nanomaterials

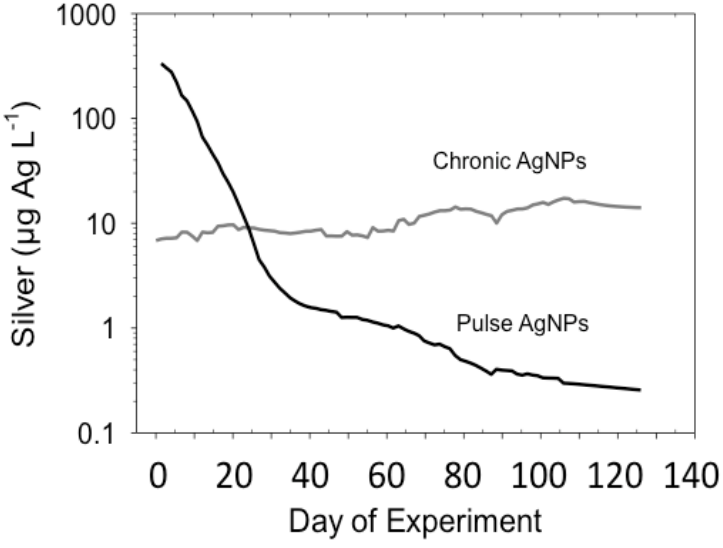
Where is nanoEHS Heading?

- "Realism"
  - Relevant exposure scenarios (functional assays)
  - Chronic low dose studies
  - Use of "transformed" materials in testing
- Optimizing Benefit-Risk Ratio ("Safe by design")
  - Leveraging nanoEHS knowledge for effective and safe applications of nanomaterials
  - Environmental applications (water treatment, remediation)
- Categorization (groupings) of nanomaterials

“Realism”



Dosing Strategy



- Incorporating “realism”
- Using relevant exposure scenarios/routes
- Chronic vs. acute exposures

Selck et al 2016.

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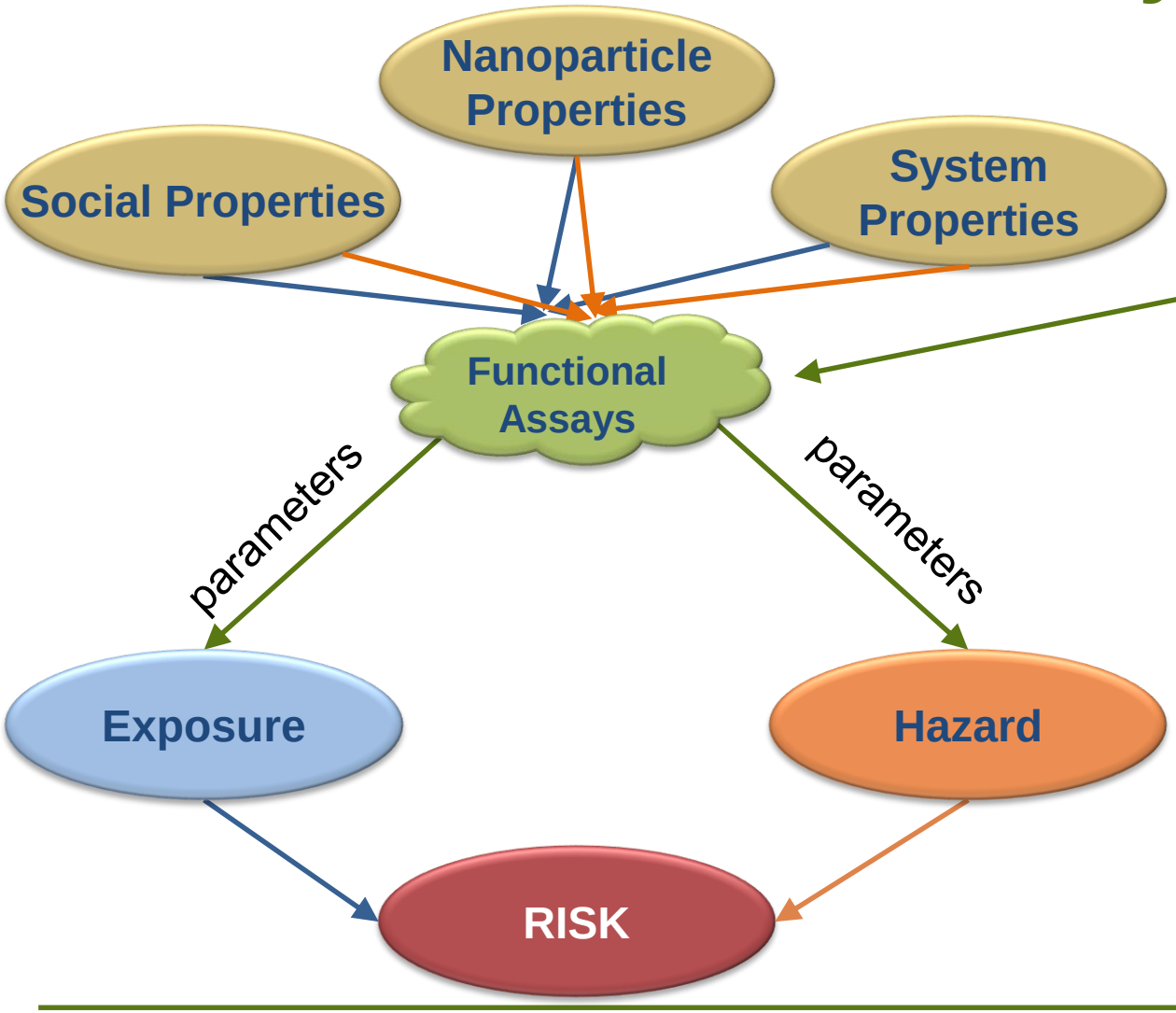
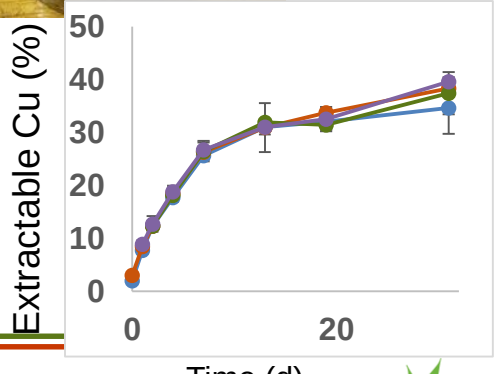
Functional Assays

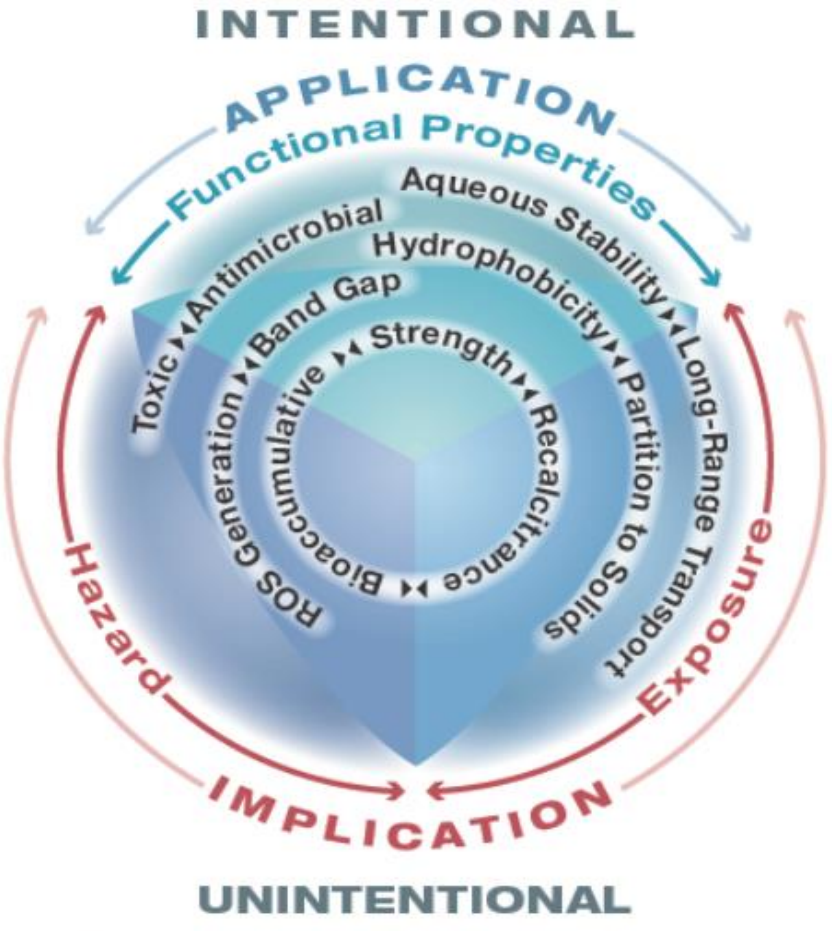


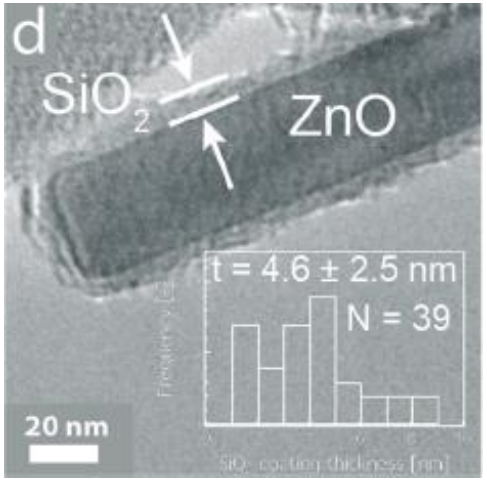
- Measurement in **prescribed system**
- Quantifies a meaningful process for exposure, hazard or both
- Provides *rate constants* for exposure and hazard models

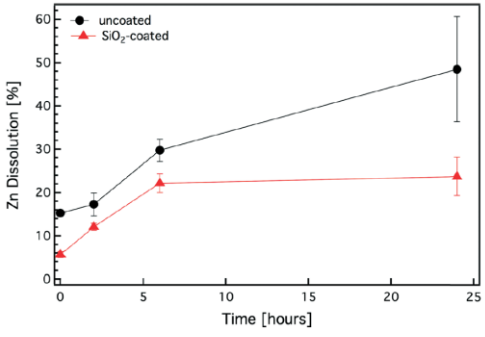


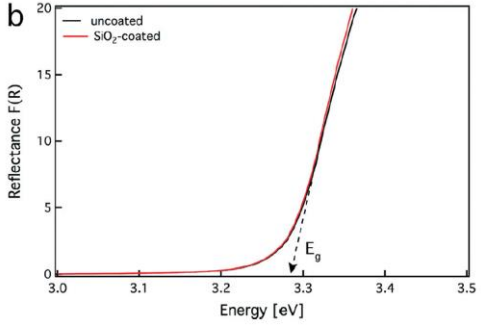
Hendren et al., 2015 *Sci. Tot. Env*. 536 p 1029

Optimizing Benefit-Risk Ratio ("Safe by Design")







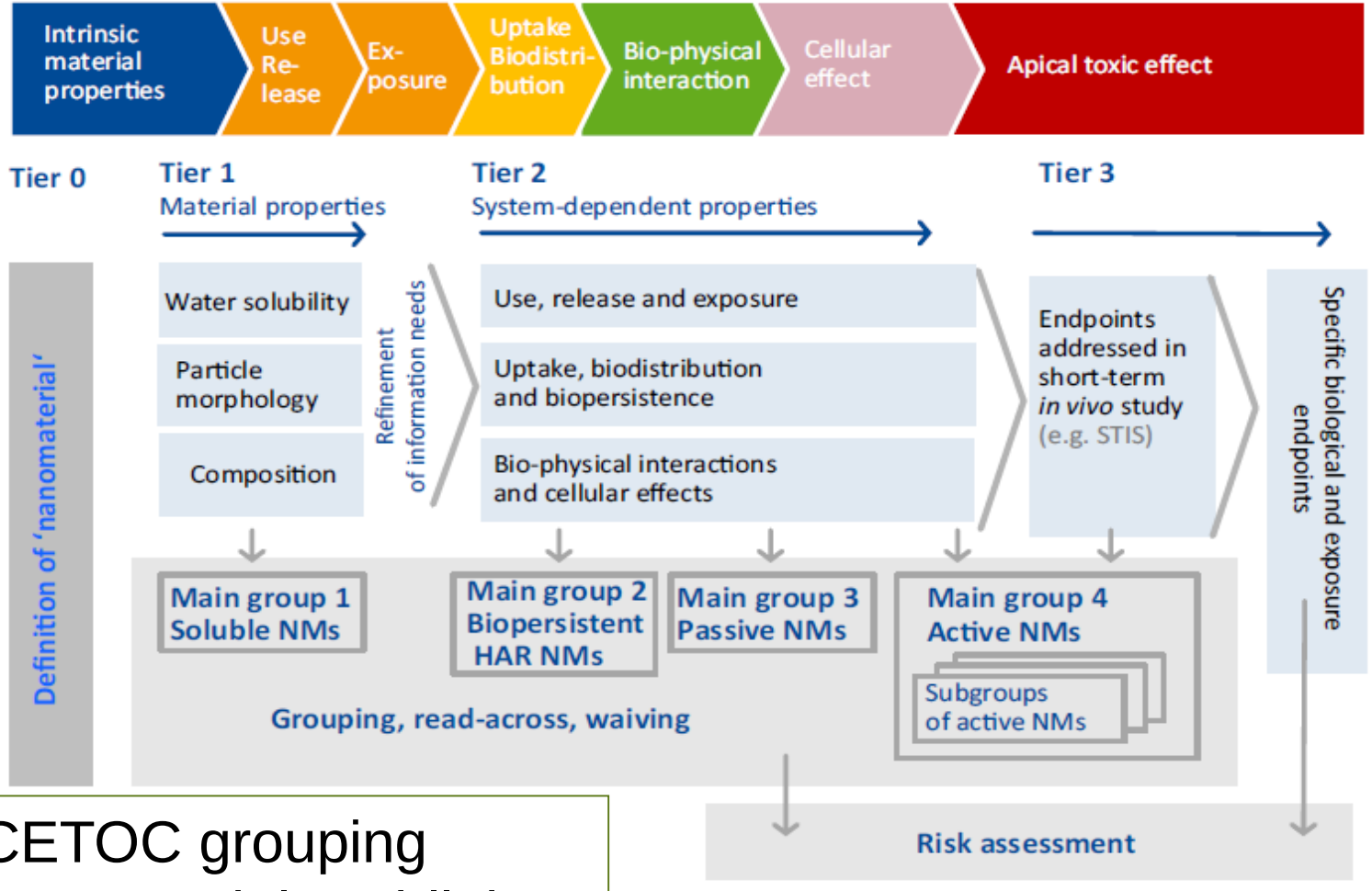


Dissolution

Same band gap

Sotiriou et al 2014 *ES Nano* 1 144

Nanomaterial Categorization and Read-Across



ECETOC grouping
From Wendel Wohlleben

Carnegie Mellon

Arts et al 2015 *Res. Tox. Pharm*. 71 S1-S27

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Some Important Gaps in Understanding

- No “accepted” testing protocols for nanoEHS
  - “translational roadmap” for exposure assessment
  - Validated bioassays for hazard and dosimetry metrics needed
- Models require further evolution
  - Lack of *rate* data to parameterize and validate models
  - Improve measurements in biological/environments media
  - Need sources of emissions
- Chronic low dose exposures not well studied
- Data and metadata standards needed for nanoinformatics
- Exposures during “use phase” are unknown
- Methods to quantify benefits of nanotechnology are lacking
- Effectiveness of public and private governance mechanisms
- “Next-generation” materials are not being addressed

Exposures along the Lifecycle

Manufacturing

Workplace exposure

Use Phase

Exposure Potential??

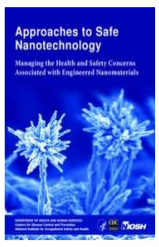
End of Life

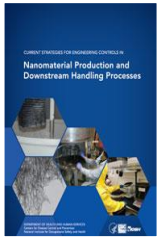
Nanotechnology Research Center at NIOSH
Moving safely and responsibly into the future

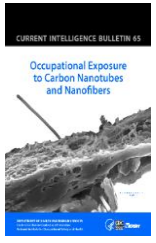
Research is prioritized

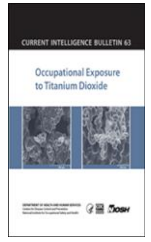
NIOSH Nanotechnology Strategic Plan for 2013-2016

Guidance Documents









NIOSH work produces results:

Safe practices protect workers and result in business success and public trust.

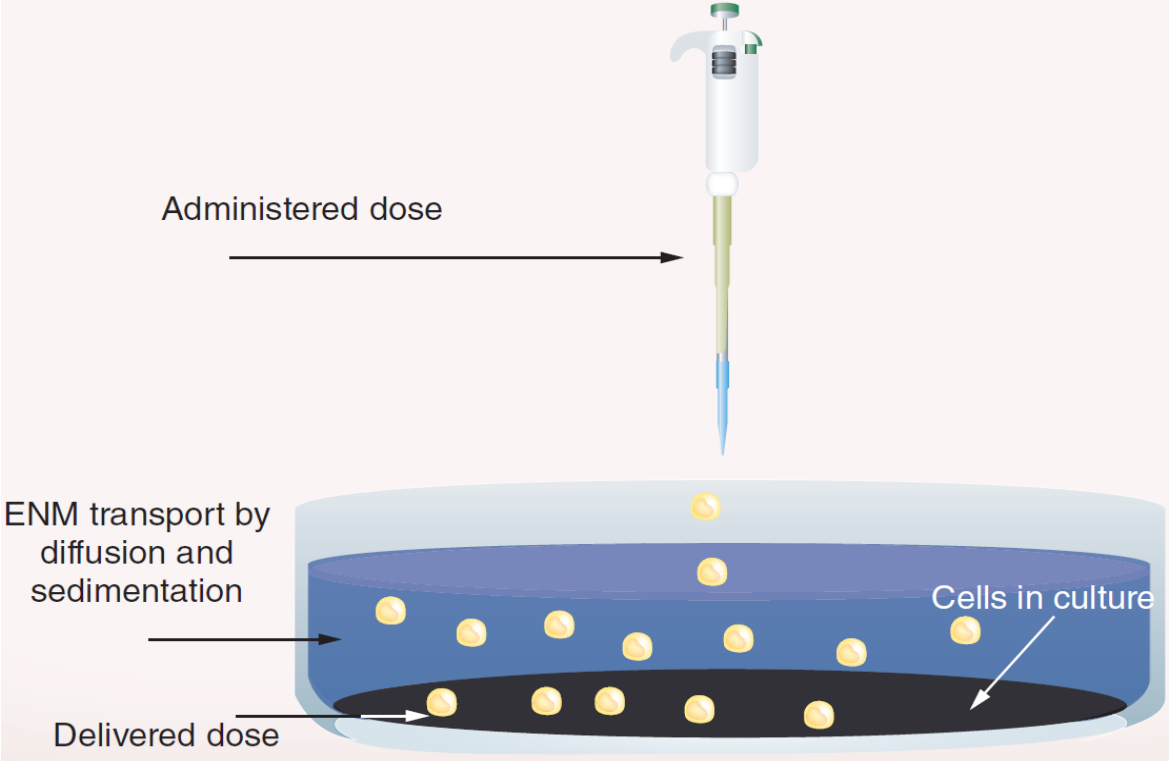
Economic growth will come from responsible advancements in manufacturing.

Partnerships with the private sector are key to the NIOSH success story. NIOSH is recognized by stakeholders as the "**most trusted and collaborative**" agency.

Research is reported

NIOSH Nanotechnology Progress Report for 2007-2011

Dosimetry is Challenging



Dosimetry models

Cohen et al 2015, Nanomedicine 129

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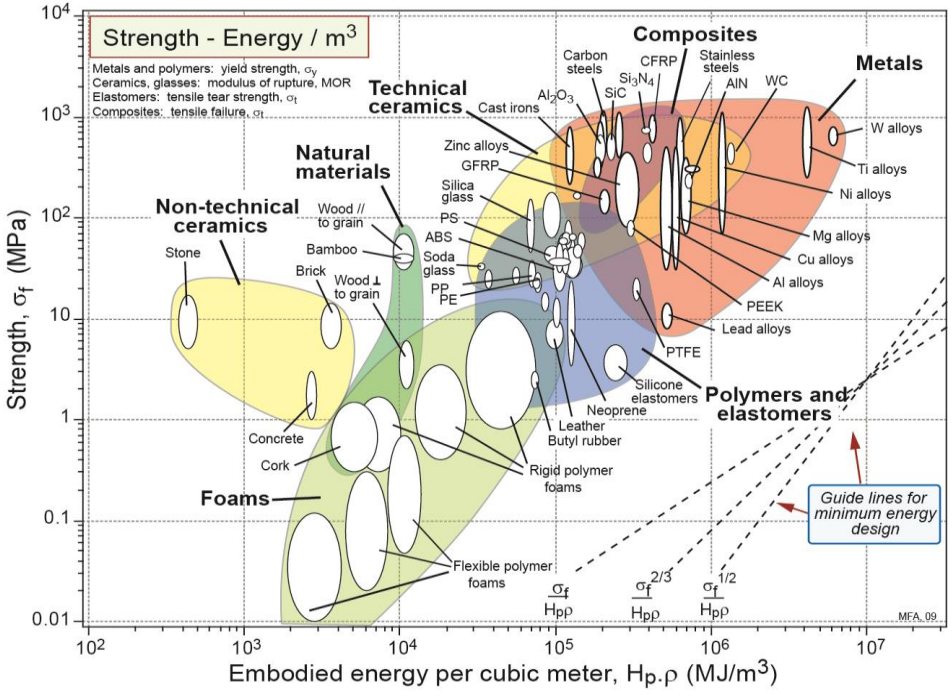
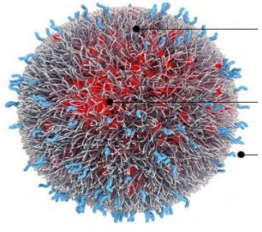
Harnessing and Quantifying the Benefits of Nanotechnology

Ashby Diagrams for Nano?





- Energy
- Carbon sequestration
- **Sustainable agriculture**
- Clean water
- Restore/improve urban infrastructure
- Better medicines

From Nanomaterials to Nanomachines!

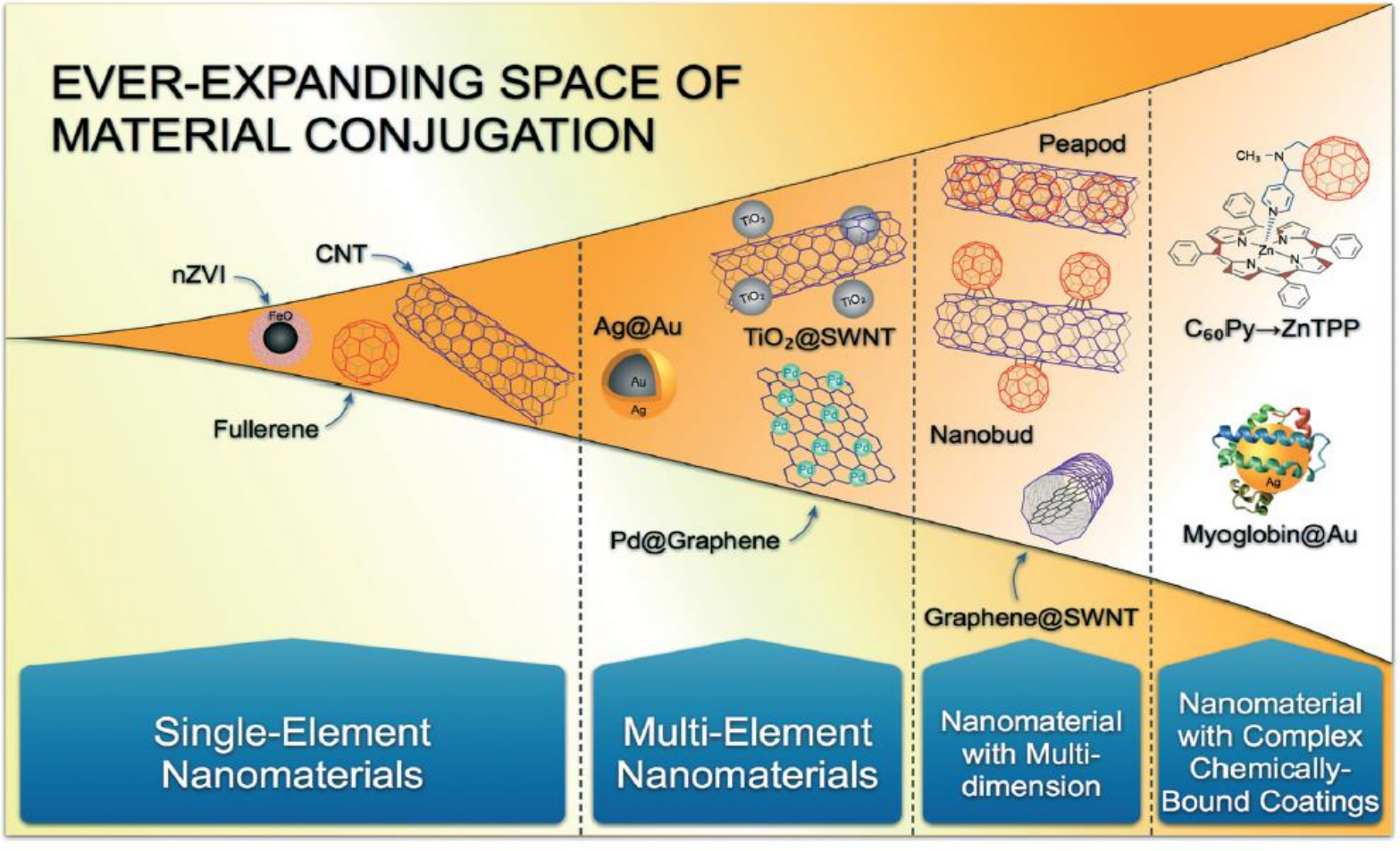


Fig. 3 Schematic showing the ever-expanding space of nanomaterial conjugation and the resulting permutations of nanomaterials.

Saleh et al., 2015 *ES Nano* 2 11-18

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Questions to Consider in Breakouts

- Are there gaps in the draft goals and objectives? Are there objectives no longer needed?
- What will be the new/hot areas of research or challenges in the next 5-10 years?
- Outside of additional funding, what can the Federal Government do to support activities or address challenges in the areas above?
- How will we know when the nanotechnology enterprise is successful for NanoEHS? How do we measure this?
- What progress has been made in understanding the ethical, legal, and societal implications of nanotechnology? How has that progress been communicated?

NanoEHS Panel

- Brian Thrall
  - Pacific Northwest National Laboratory
  - nanomaterial cellular interactions

- Matt Hull
  - Virginia Tech (ICTAS, VTSuN, NanoSafe Inc.)
  - nanomaterial environmental fate/effects and nanoinformatics

- Debbie Kaiser
  - NIST
  - materials science, measurement and standards

- Timothy Malloy
  - UCLA
  - Environmental regulation and policy