Leveraging nanoparticle environmental health and safety research in the study of micro- and nano-plastics

Mark R. Wiesner,

Duke University, University of Rennes

(Mélanie Auffan, Greg Lowry, Jaleesia Amos, Nathan Bossa, Jerome Rose, Emilie Bernhardt, Jean-Yves Bottero, Jason Unrine, Kim Jones, Christine Hendren, and many others!)

INFRAMES

Serenade

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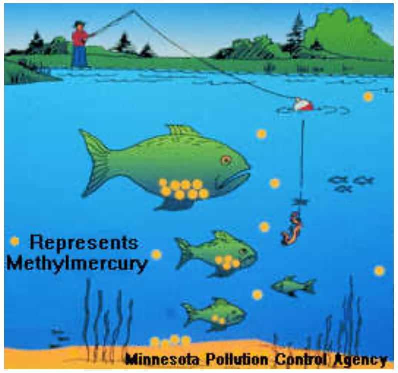
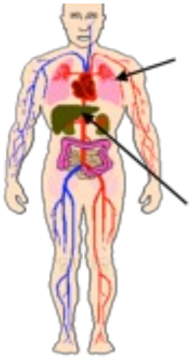
1999: Speculation on environmental & health impacts

"Imaginons une fuite dans l'environnement de ces molécules, dûe à un accident dans l'usine de production, ou simplement quand le produit manufacturé finira en déchet. Représenteront-elles une menace pour la santé, comme l'amiante ? Quel sera leur impact sur les écosystèmes?"
***Libération (French Daily)*, 2 December 2000.**





Is it [carbon nanotubes] the next best thing to sliced bread, or the next asbestos?- **Small Times, March 8, 2002.**

Possible nanomaterial impacts
- bioconcentration
- interference with cell division
- interference with proteins
- Trojan horse effect for other materials
- facilitated transport
- oxidative damage

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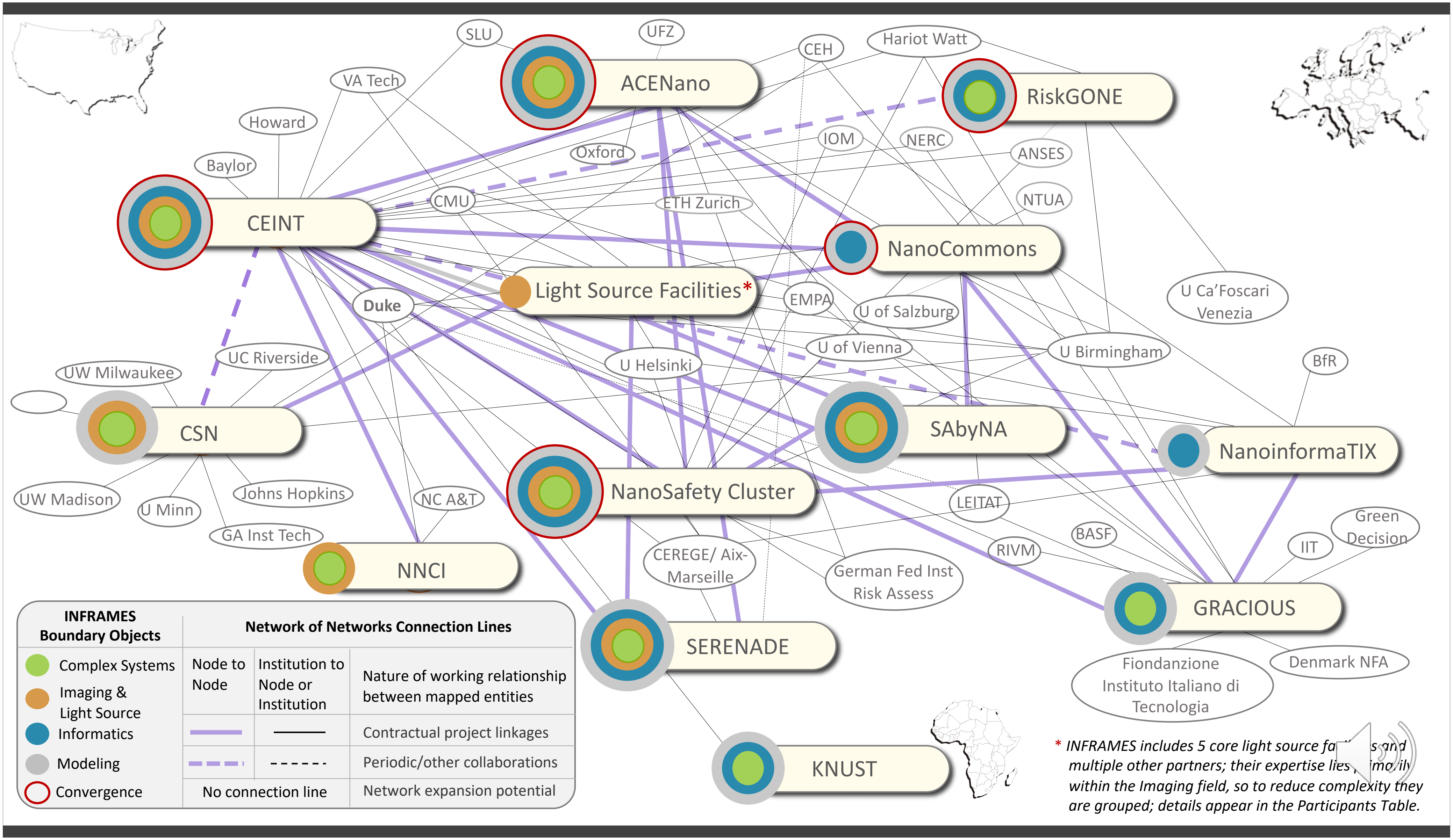

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Lesson 1:
The toxicity of small (nano) particles can be largely predicted from:

- Composition
- Redox properties
- Solubility
- Persistence (for inhalation)

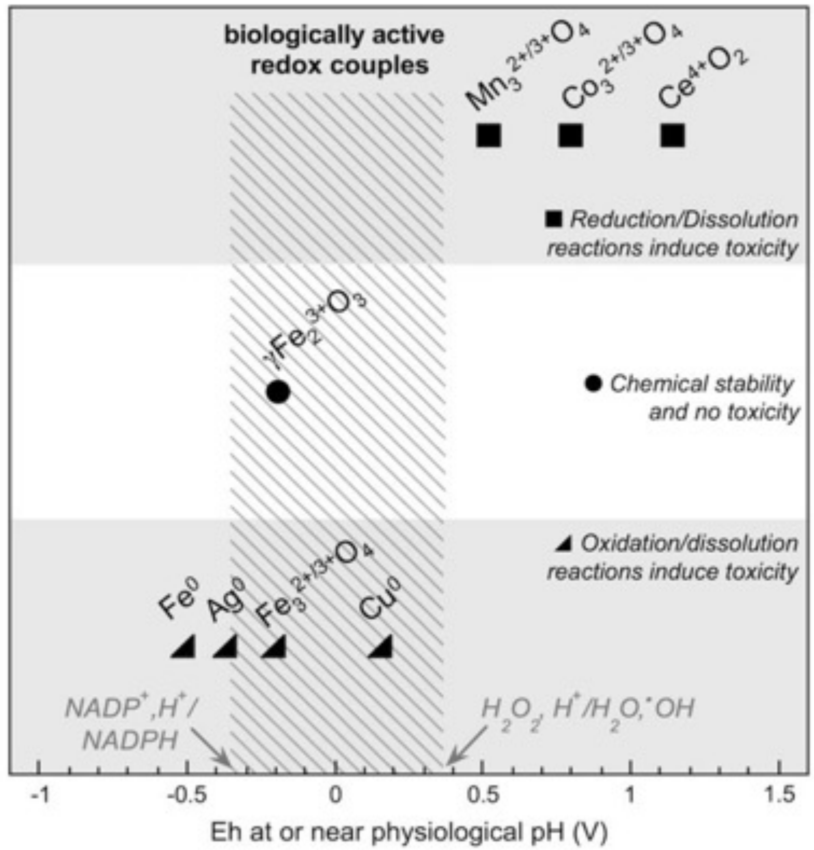
Chemical stability of metallic nanoparticles: A parameter controlling their potential cellular toxicity in vitro

Mélanie Auffan [a,*], Jérôme Rose [b,c], Mark R. Wiesner [a], Jean-Yves Bottero [b,c]

[a] Duke University, Civil and Environmental Engineering Department, 121 Hudson Hall, Durham, NC 27708, USA
[b] CEREGE, UMR 6635 CNRS/Aix-Marseille Université, Europôle de l'Arbois, 13545 Aix en Provence, France
[c] ECOREV, FR n° 3098, Europôle de l'Arbois, 13545 Aix-en-Provence, France

The ability of metallic nanoparticles to be oxidized, reduced or dissolved in biological media can be used to predict their toxicity in vitro.

Environmental Pollution 157 (2009) 1127–1133



Inhalation toxicity brings in additional factors

Well-know rules of particle inhalation apply- nothing particularly “nano” shown to date.

Europe may call TiO2 a carcinogen | June 19, 2017 Issue - Vol. 95 Issue 25 | Chemical & Engineering News

Inhalation studies in rats spark push for classification

ELSEVIER

Toxicology and Applied Pharmacology

Volume 79, Issue 2, 30 June 1985, Pages 179-192

Pulmonary response of rats exposed to titanium dioxide (TiO_2) by inhalation for two years

K.P. Lee, H.J. Trochimowicz, C.F. Reinhardt

Research Article

Carcinogenic Hazards from Inhaled Carbon Black, Titanium Dioxide, and Talc not Containing Asbestos or Asbestiform Fibers: Recent Evaluations by an *IARC Monographs* Working Group

Robert A. Baan

Pages 213-228 | Received 25 Sep 2006, Accepted 04 Jan 2007, Published online: 20 Oct 2008

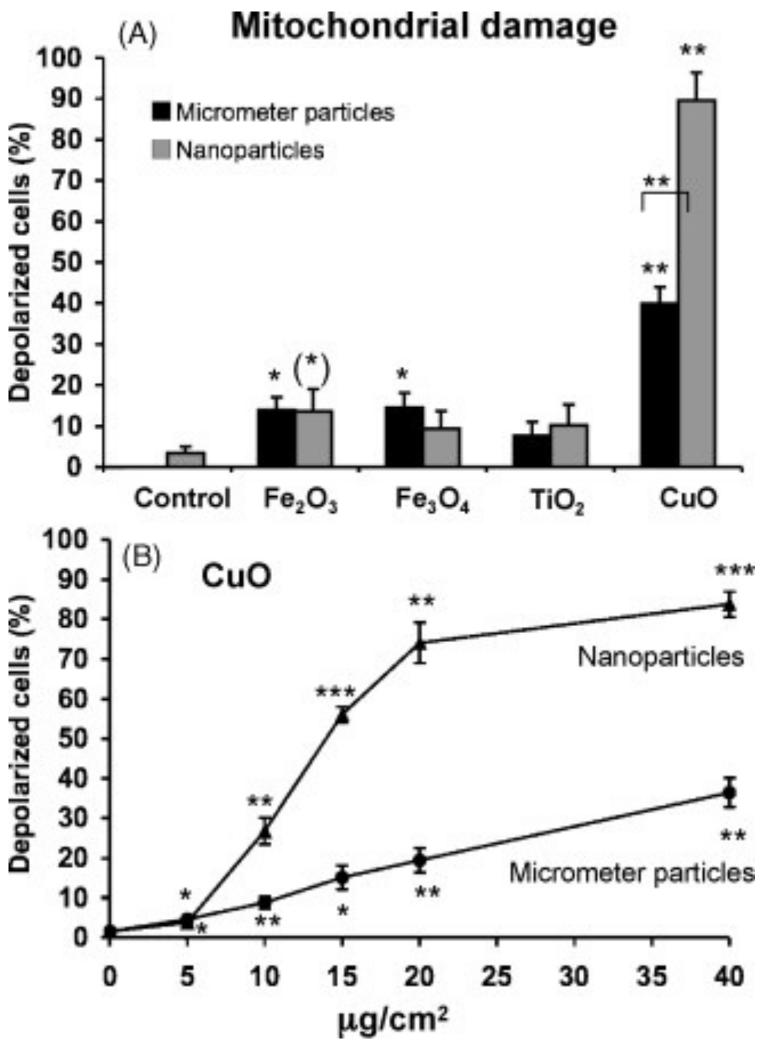
Journal

Inhalation Toxicology ›

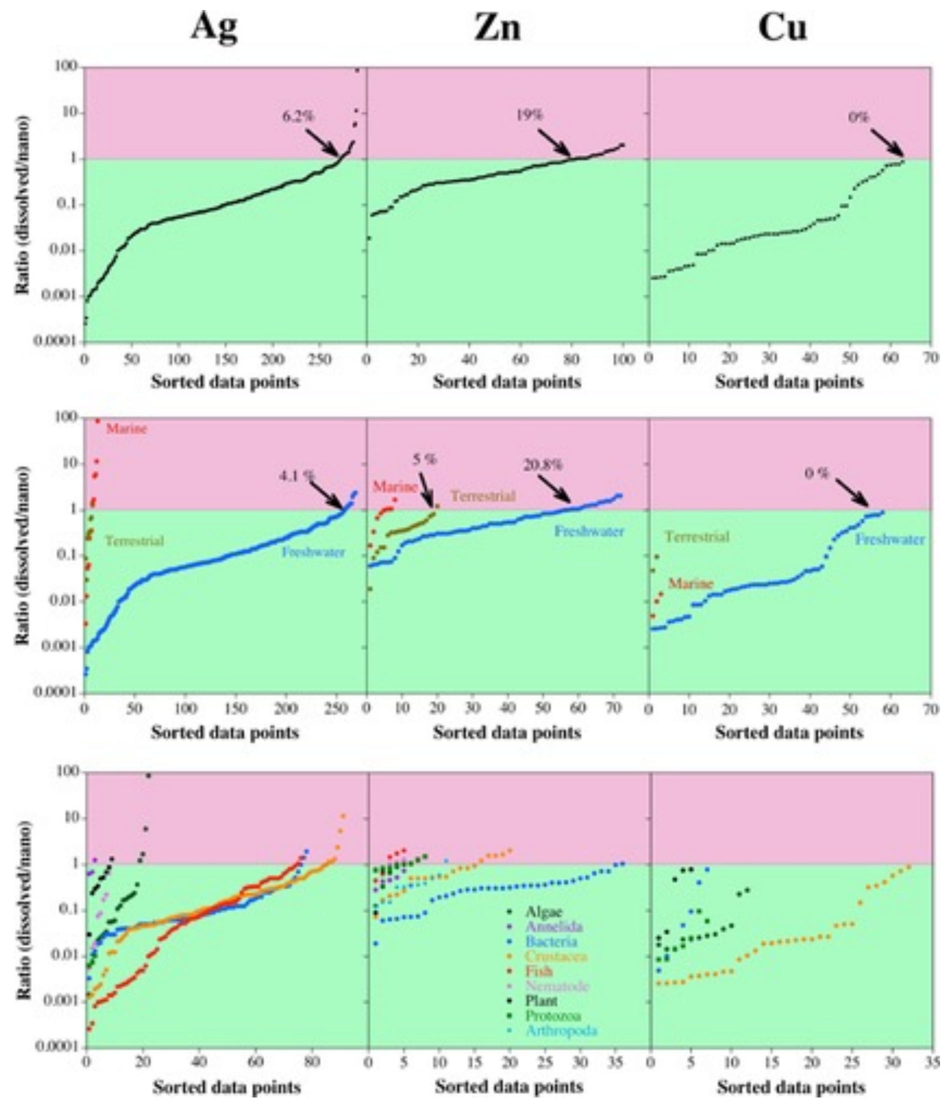
International Forum for Respiratory Research

Volume 19, 2007 - Issue sup1

Lesson 2:
Exposure, dose, and ADME behavior of a material in a nanoscale format can differ from that of the bulk material, resulting in altered dose-response curves.

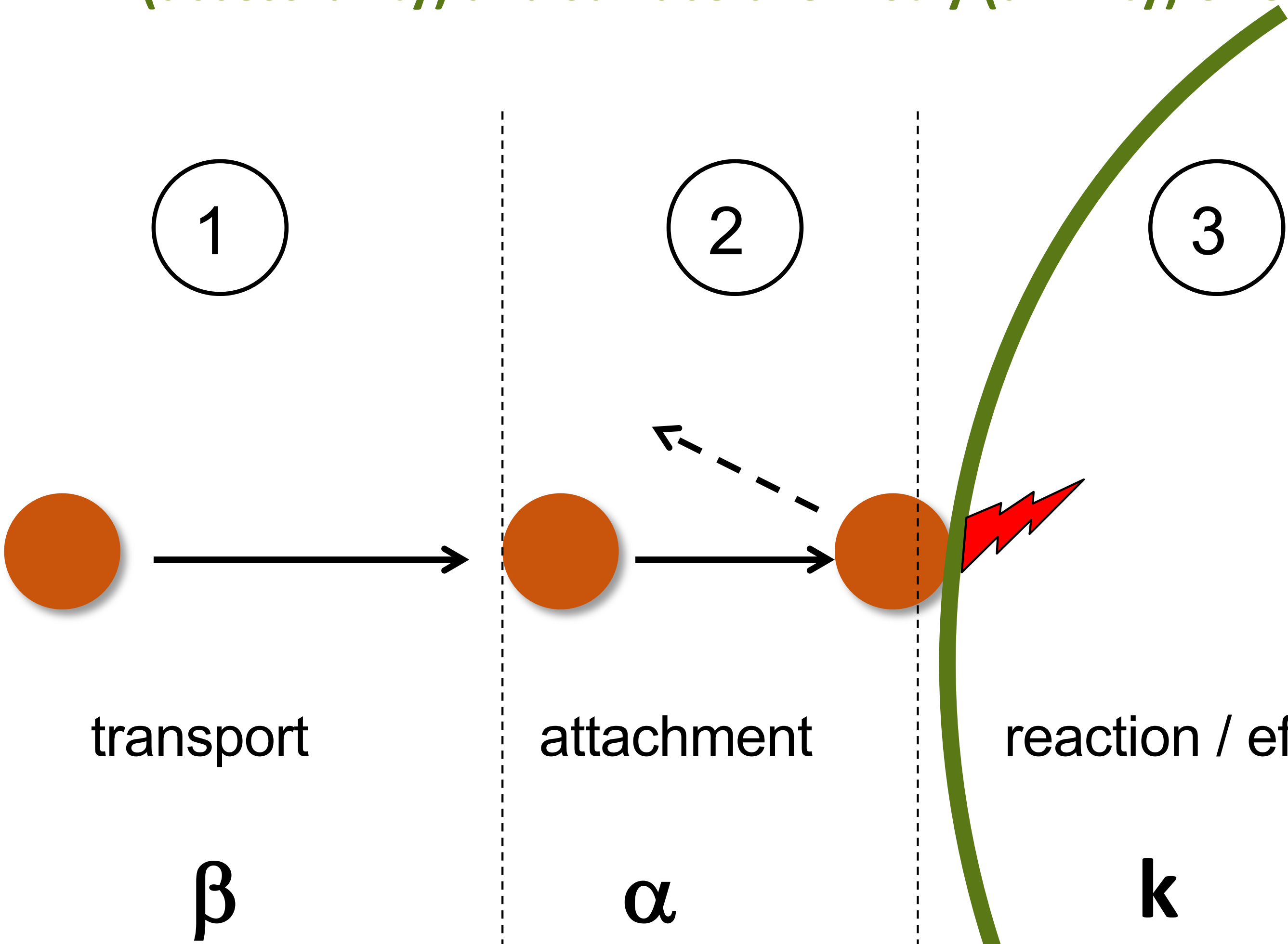


Karlsson et al, 2009, https://doi.org/10.1016/j.toxlet.2009.03.014



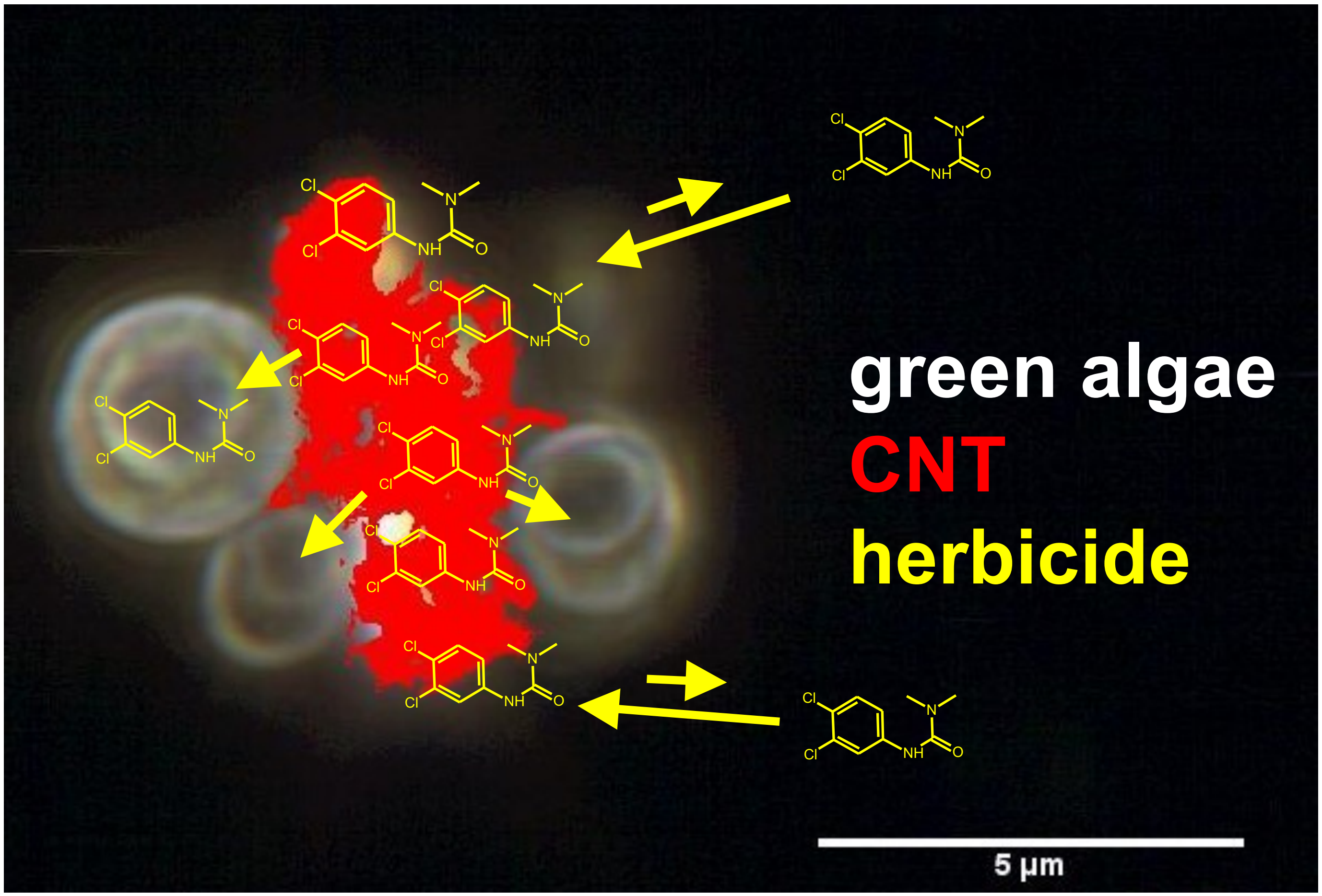
Notter et al, 2014, **https://doi-org.proxy.lib.duke.edu/10.1002/etc.2732**

Nano-scale differences in exposure, dose, and ADME are due to both size (accessibility) and surface chemistry (affinity) effects.



$$k_T = \frac{k_{red}\alpha_{NB}\beta n B}{k_{red} + \alpha_{NB}\beta n B}$$

Nanoparticle delivery of pesticide



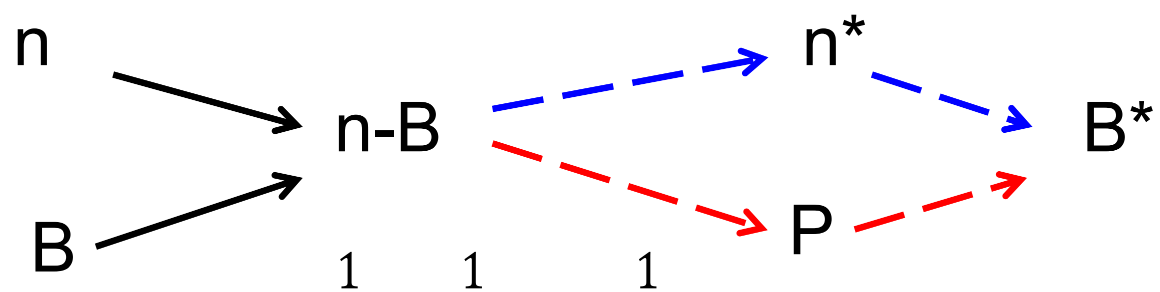
Schwab *et al.* *Env Poll*, 2014

Examples of nanoparticle reactivity

Effect	Underlying reaction
Toxicity to plants and fish by nano Ag	Nano silver dissolution
Viral inactivation by fullerol	Singlet oxygen generation
Bacterial inactivation by CeO2	Ce reduction
Toxicity of herbicide on NP	Herbicide desorption

heteroäggregation

reaction



$$\frac{1}{k_T} = \frac{1}{k_{red}} + \frac{1}{\alpha_{NB}\beta nB}$$

$$k_T = \frac{k_{red}\alpha_{NB}\beta nB}{k_{red} + \alpha_{NB}\beta nB}$$

Lesson 3:
A generalizable nano-based mechanism of toxicity has not been observed

and

“no unique human diseases or environmental impacts have been reported that are specific to NMs”

Grassian et al., 2016, Env. Sci Nano

Approximate acute toxicities of several materials

Chemical/Material	LD50 (mg/kg) oral dose to rats or mice
Sugar	29 700
Ethyl alchohol	14 000
Vinegar	3 310
NaCl	3 000
Nanomaterials (CNTs, nanoAg, NanoTiO2)	>2000
Atrazine	1 870
Malathion	1 200
Asprin	1 000
Caffeine	130
DDT	100
Arsenic	48
Parathion	3.6
Strychnine	2
Nicotine	1
Aflatoxin - B	0.009
Dioxin (TCDD)	0.001
Botulin toxin	0.00001

Hodge and Sterner Scale (1943)
Materials with LD50 50-500 moderately toxic,
less than 50 highly or extremely (<1) toxic

Modified from P. Buell and J. Gerard (1994) Chemistry in Environmental Perspective (Upper Saddle River, NJ, Prentice Hall)

Endocrine disruption, other chronic effects

Nanomaterial	Effects? (+=beneficial, -= detrimental)
Thyroid function	
Ag-NPs	- tadpoles
ZnO NP	0 tadpoles
CdTe QDs	- tadpoles
Cr NPs	0 rats
Insulin and metabolism	
TiO2 NP	- Fao rat hepatoma cells
CeO2 NP	+ Pancreatic islets
CrCl3-NPs	- pigs
Cr-NPs (40–50 nm)	- rats decreased insulin and cortisol and increased sera levels of IGF-I
DWCNT	- mice Increased serum levels of IGF-1
CeO2-NPs	+ rat biomarkers for diabetes
neuroendocrine	
C60	+ rat adrenal cell line – increased survival
MnO NPs	- rat PC-12 culture DA, Dopamine; DOPAC, dihydroxyphenylacetic acid
Ag NPs	- rat PC-12 culture lower DA DOPAC
Cu NPs	- rat PC-12 culture lower DA DOPAC
Au NP	- rat adrenal culture - lower and slower secretion of epinephrine molecules.
Ag NP	- rat adrenal culture - lower and slower secretion of epinephrine molecules.
SiO2 NP (15 nm)	rat PC-12 culture lower DA DOPAC
Pituitary gland	
CrCl3-NPs (40–70 nm)	0 –pigs - differences in GH level
Estrogenic effects	
CdTe-QDs (~3 nm)	- Human MCF-7 breast cancer cell line
CdS-QDs (4.2 ± 1 nm)	0 *Gasterosteus aculeatus*
Nano-rich exhaust	-/+ rats (progesterone higher or lower)
(CdS)/CdTe capped-QDs	- trout up regulation of VTG
C60	- zebrafish – reduced bioavailability of synth estrogen
Ag NPs (20 nm)	- trout decrease in liver expression of VTG-like proteins
Reproductive system	
TiO2 NP (30 nm)	- reduced viability of CH0-K1 cell cuture
Various TiO2 NPs (rutile/anatse)	0 Chinese Hamster Ovaries (CHO) no chromosomal aberrations
TiO2	0 ovary cells of hamsters
MWCNTs (diameter ~10 nm)	0 CHO

Summarized from

Int J Mol Sci. 2013 Aug; 14(8): 16732–16801.
Published online 2013 Aug 14.
doi: 10.3390/ijms140816732
PMCID: PMC3759935

The Effects of Nanomaterials as Endocrine Disruptors

Ivo Iavicoli,* Luca Fontana, Veruscka Leso, and Antonio Bergamaschi

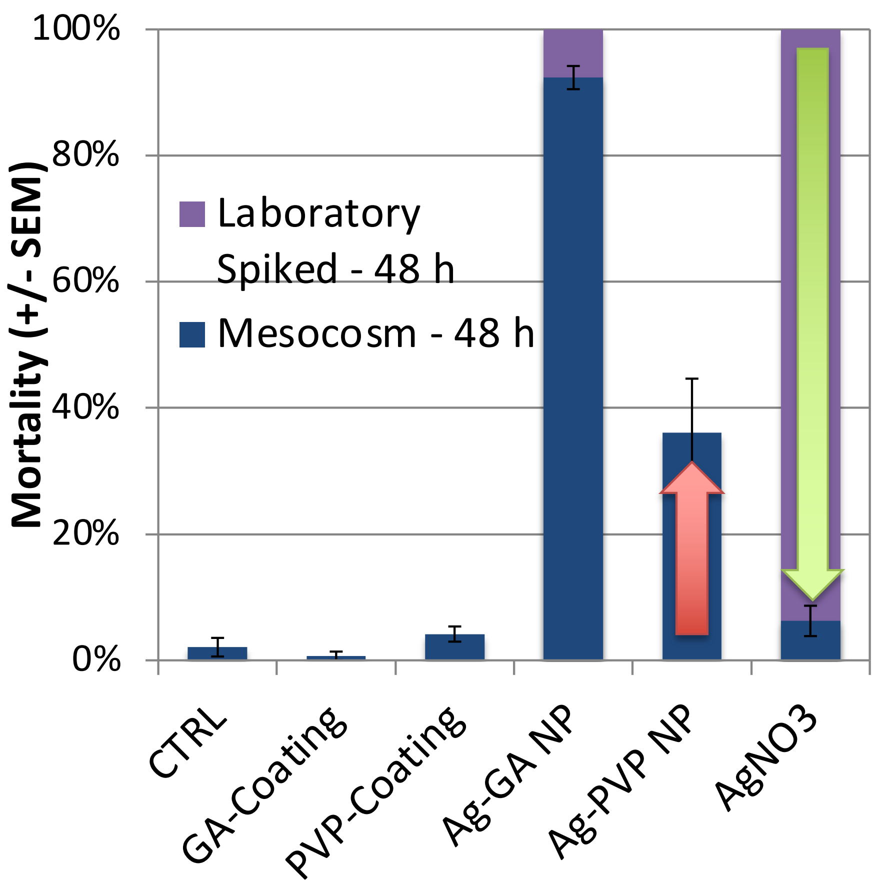
Chronic effects found when at least of the following occurs:

1) **high doses**
2) **in vitro**
3) **NPs made from known toxic material**

Lesson 4:
Transformations in complex environmental and physiological systems change everything

Mesocosm Results

Mesocosm Toxicity - 24 h post dosing
***Fundulus* Larval Mortality**



NSF EF-0830093

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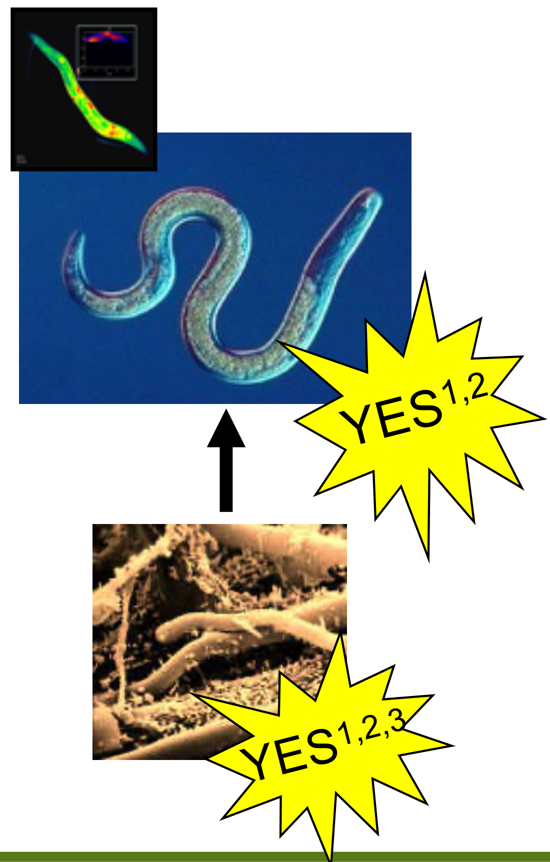
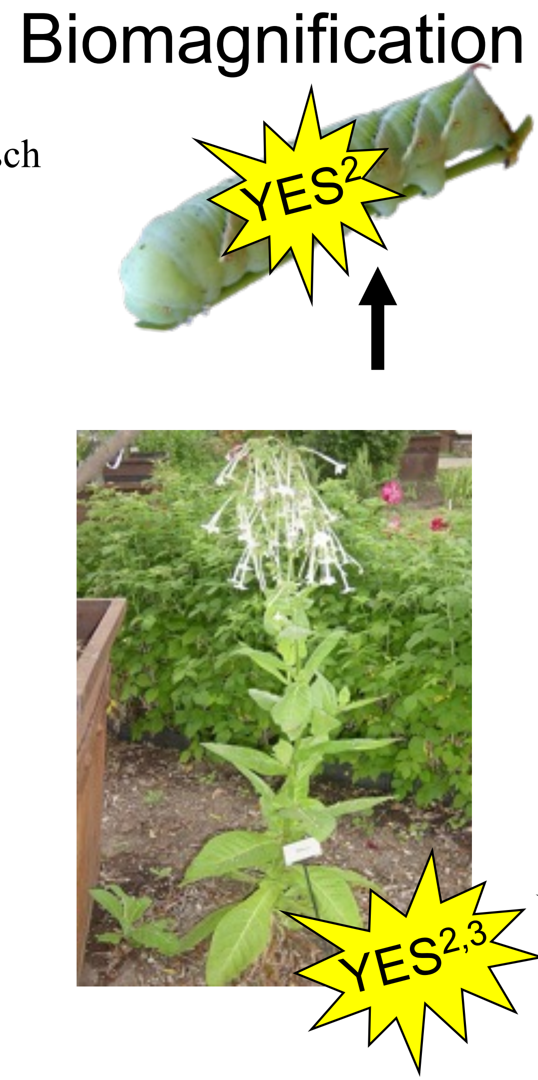
Lesson 5:
Nano-scale materials readily interact with organisms and ecosystems, often exhibiting:

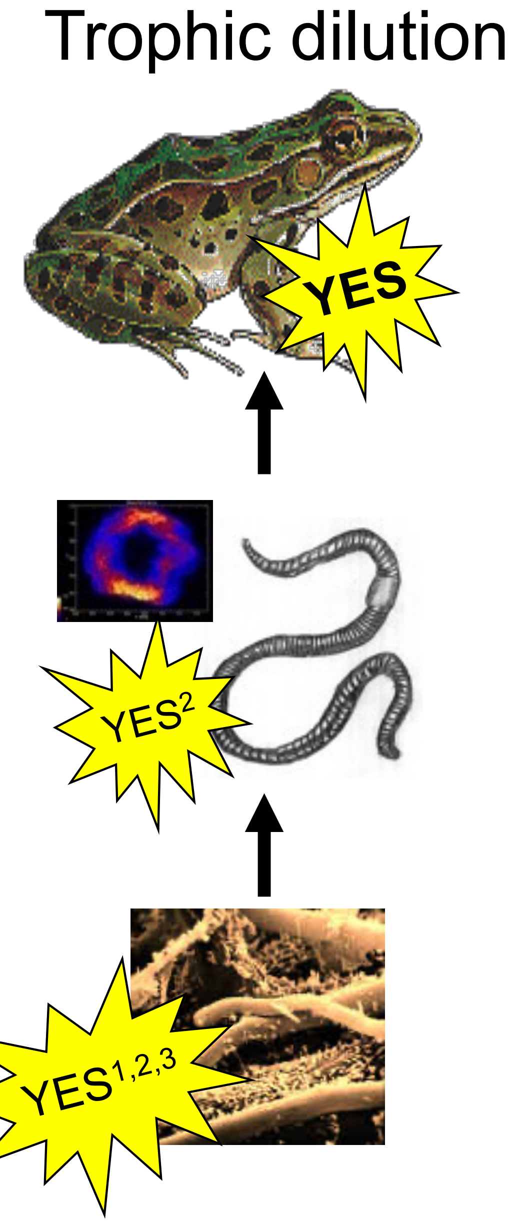
- bioaccumulation
- trophic transfer and,
- inter-generational effects

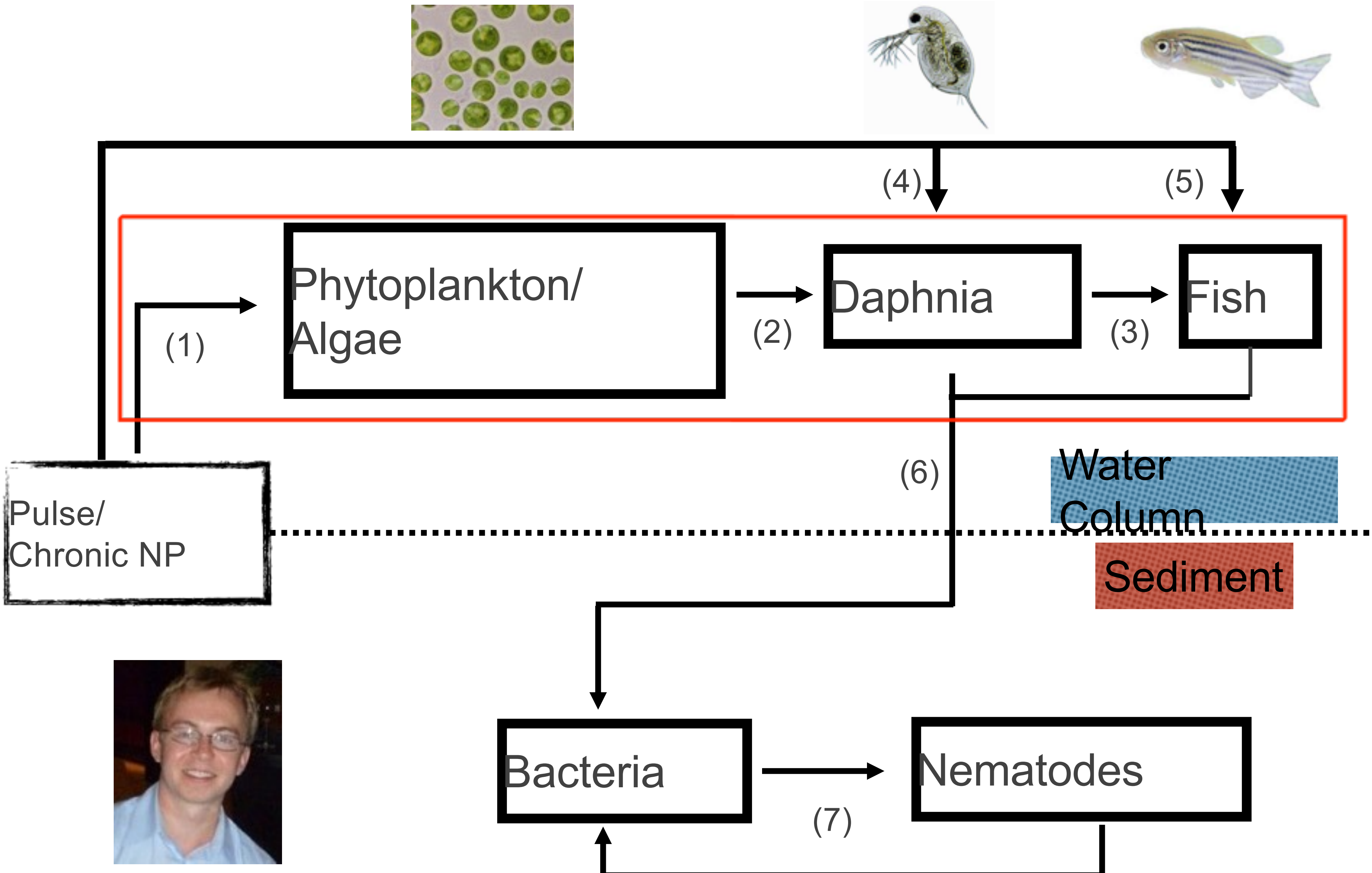
Observations of trophic transfer

[1]Joel Meyer
[2]Paul Bertsch and Jason Unrine
[3]Emily Bernhardt, Curt Richardson & Claudia Gunsch
[4]Dana Hunt









Nick Geitner

Duke University

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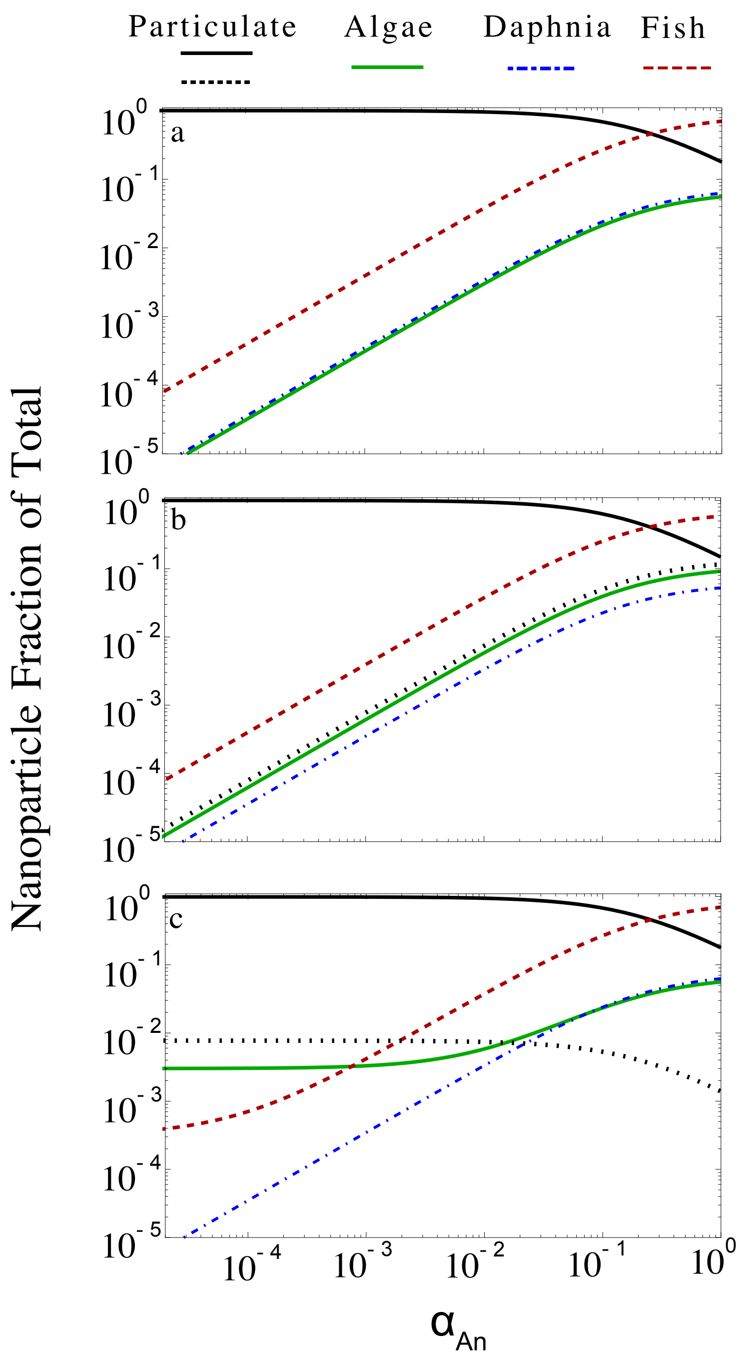
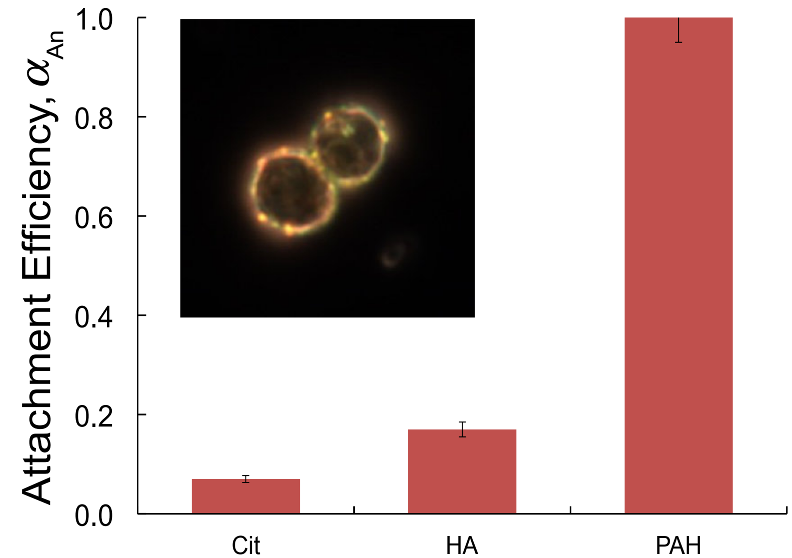
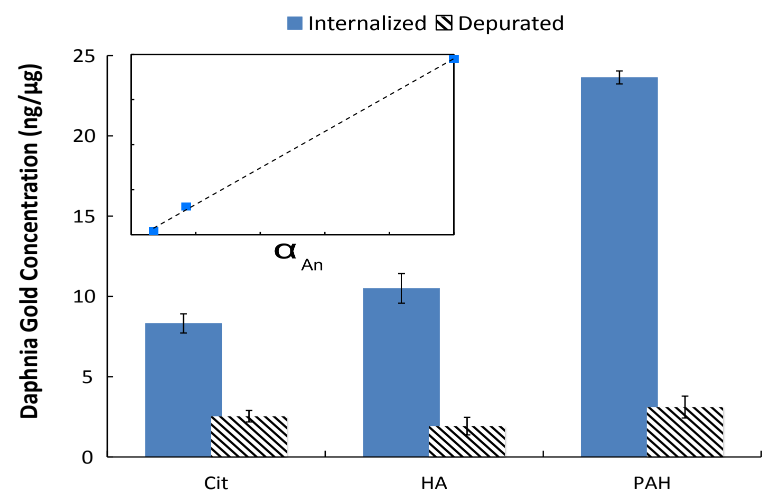
Surface affinity predicts bioäccumulation



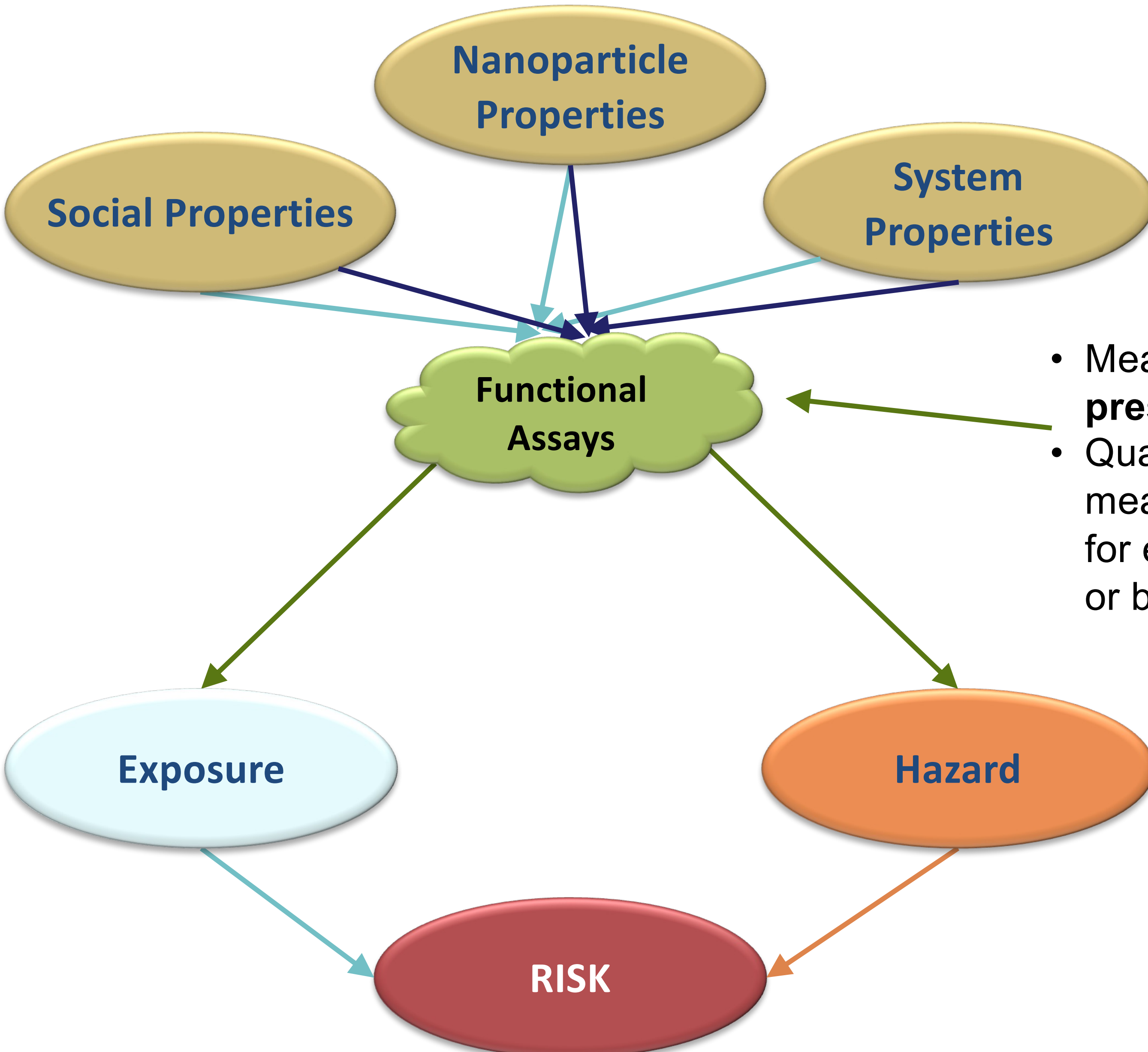




Lesson 6:
no unique mapping of nanoparticle risk from the intrinsic properties of the nanomaterial

BUT

Nanomaterial behavior can be largely predicted from a small number of Functional Assays



- Measurement in **prescribed system**
- Quantifies a meaningful process for exposure, hazard or both

Long list of parameters suggested to predict nanoparticle behavior

Composition

Density

Zeta potential

Organic coatings

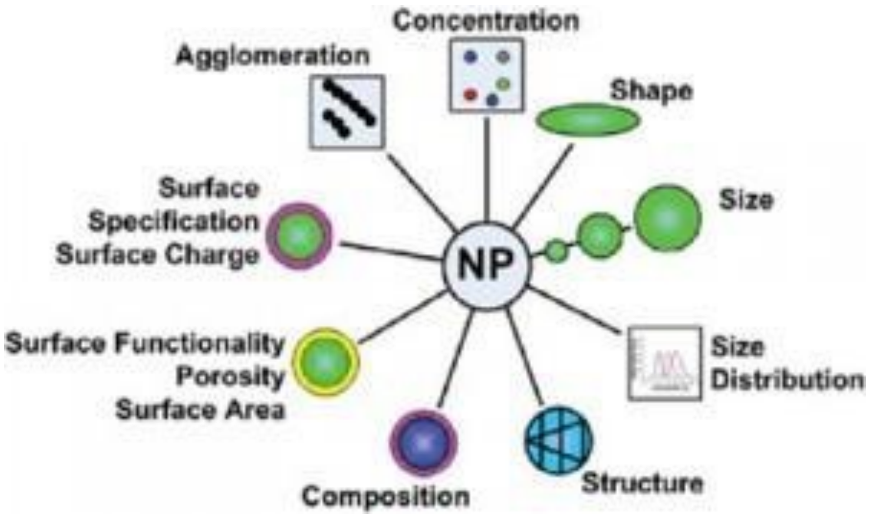
Size

Size distribution

Shape

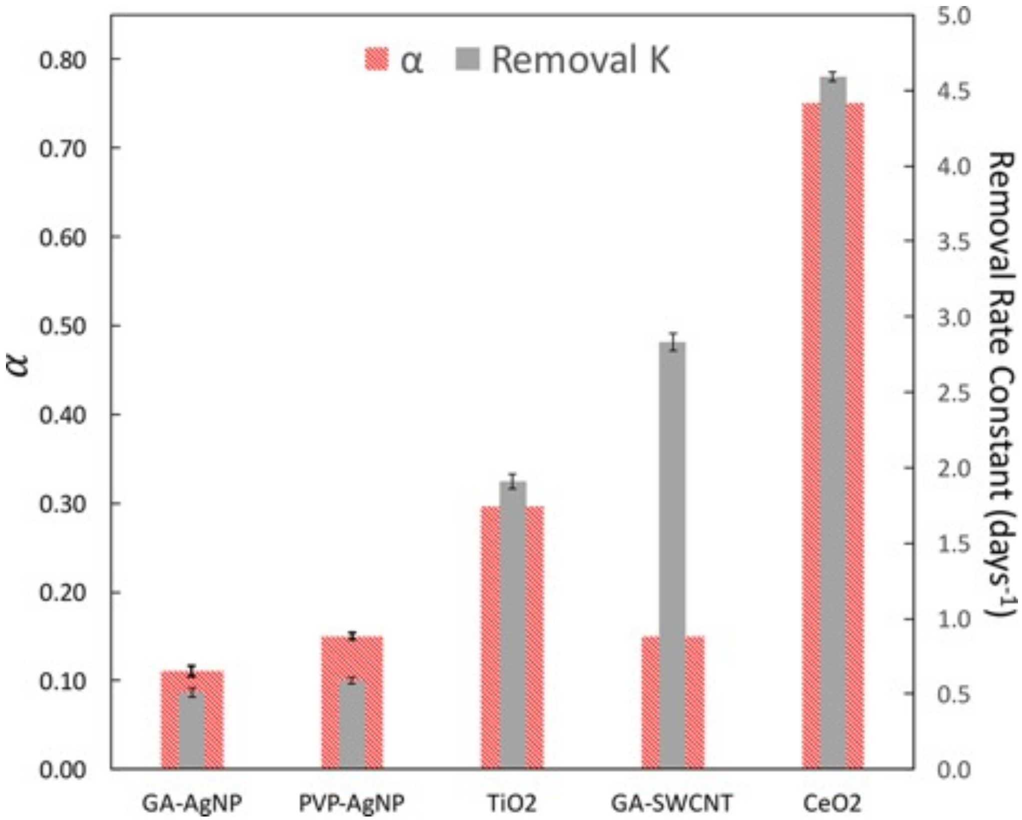
Settling rate

Aggregation rate…

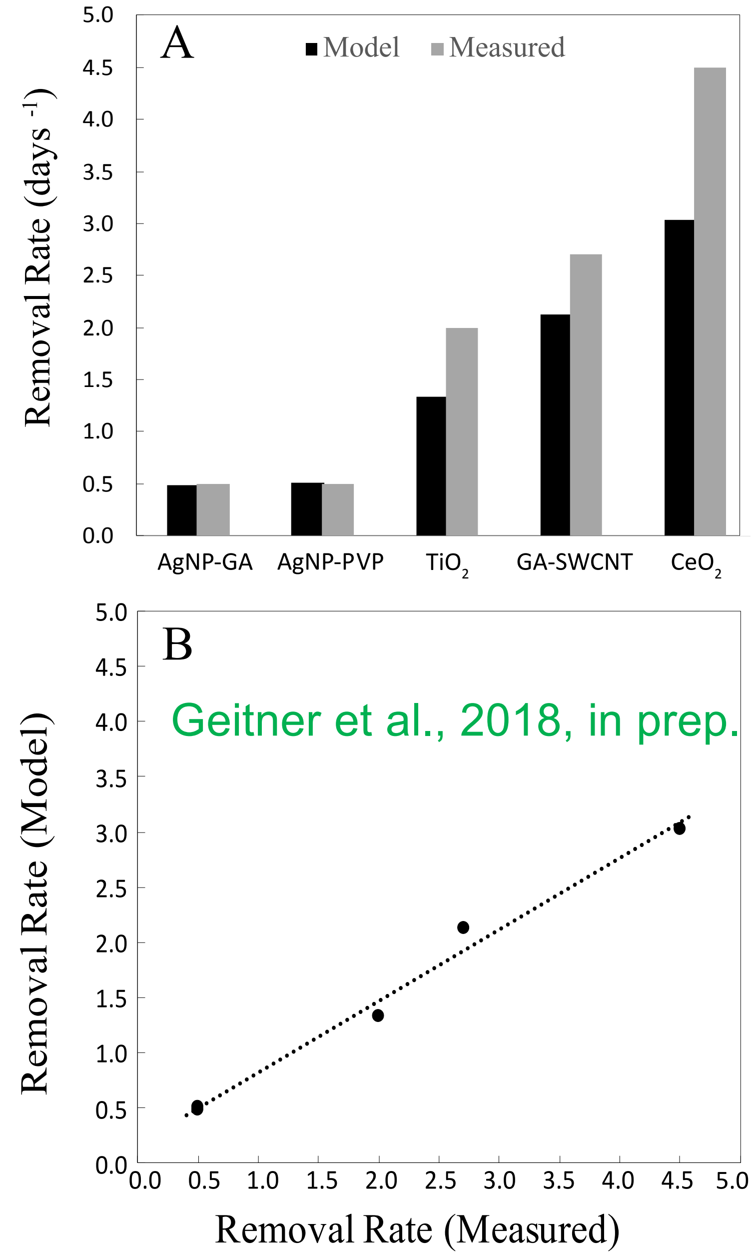


https://nanocomposix.com/pages/nanotoxicology-particle-selection

Functional assay for attachment coefficient predicts NP fate in complex system



Espinasse et al., 2018, ES&T



Geitner et al., 2018, in prep.

What happens to plastics in the environment

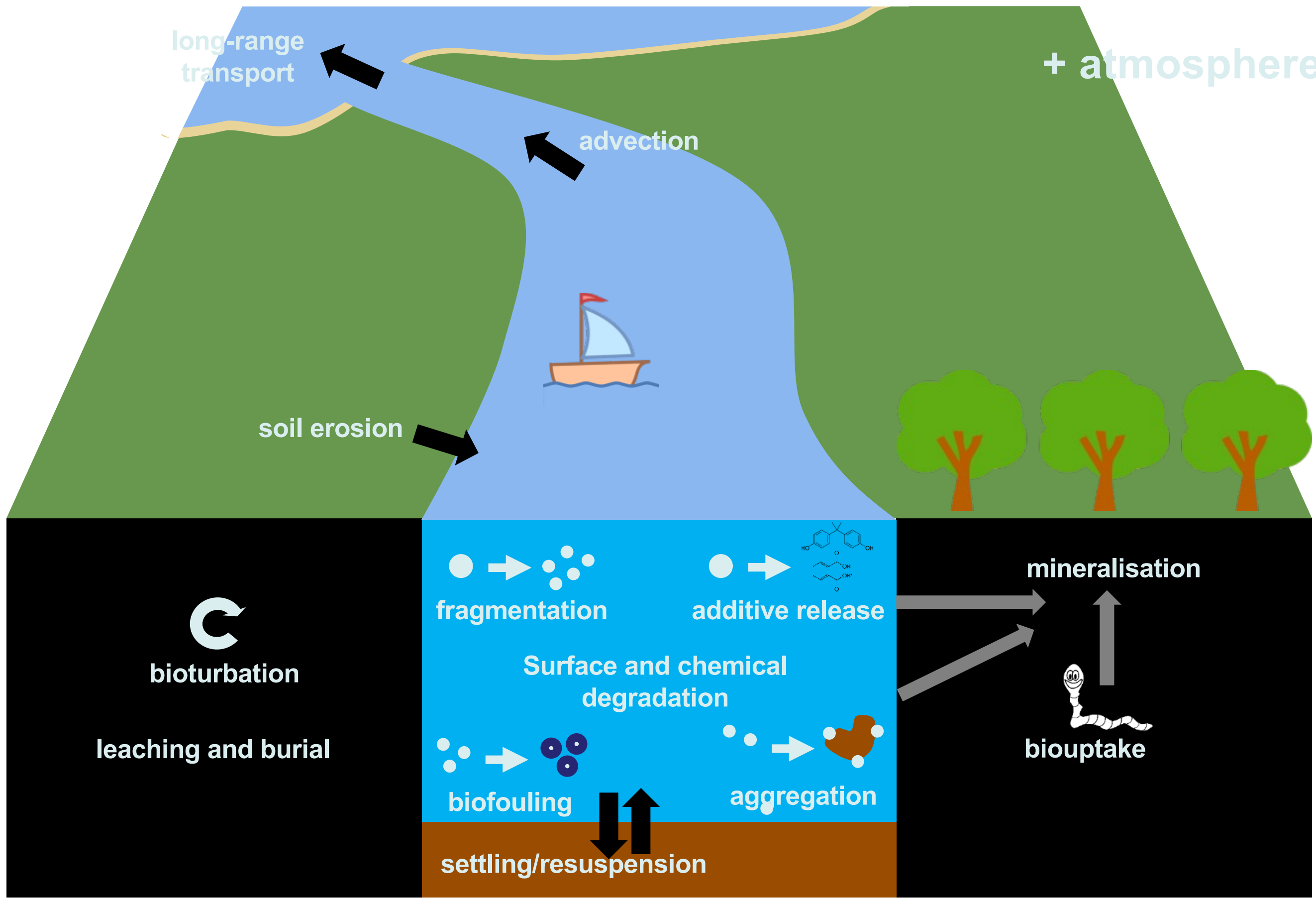
UK Centre for Ecology and Hydrology

BASF We create chemistry

Duke

UNIVERSITY OF AMSTERDAM

Cefic-LRI Programme
European Chemical Industry Council - Cefic aisbl



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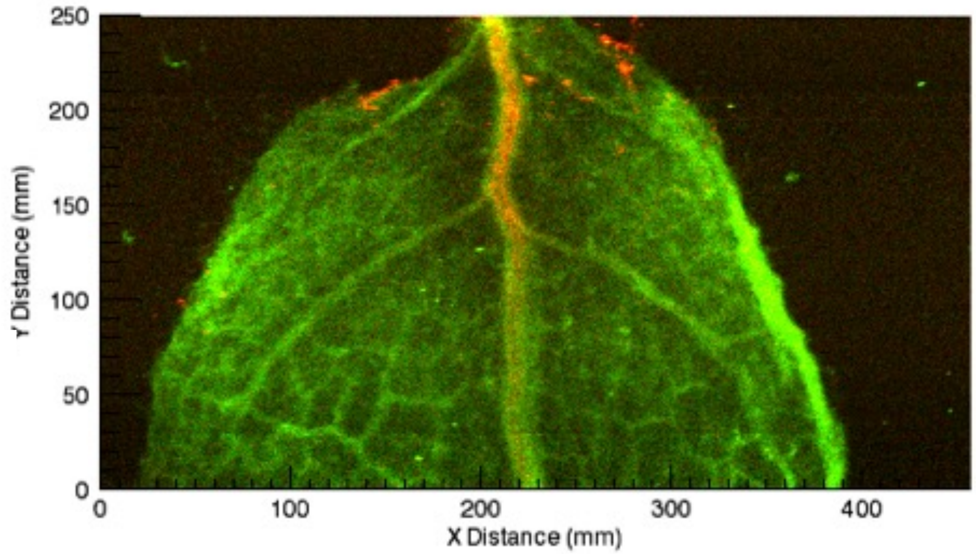
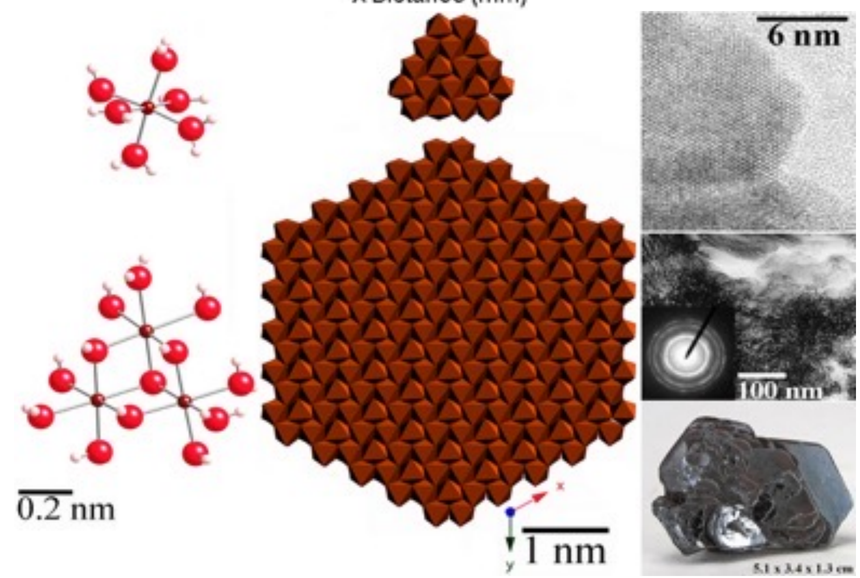
Lesson 7:
Exposure to natural and incidental nano-scale particles is many orders of magnitude greater than that to engineered nanomaterials

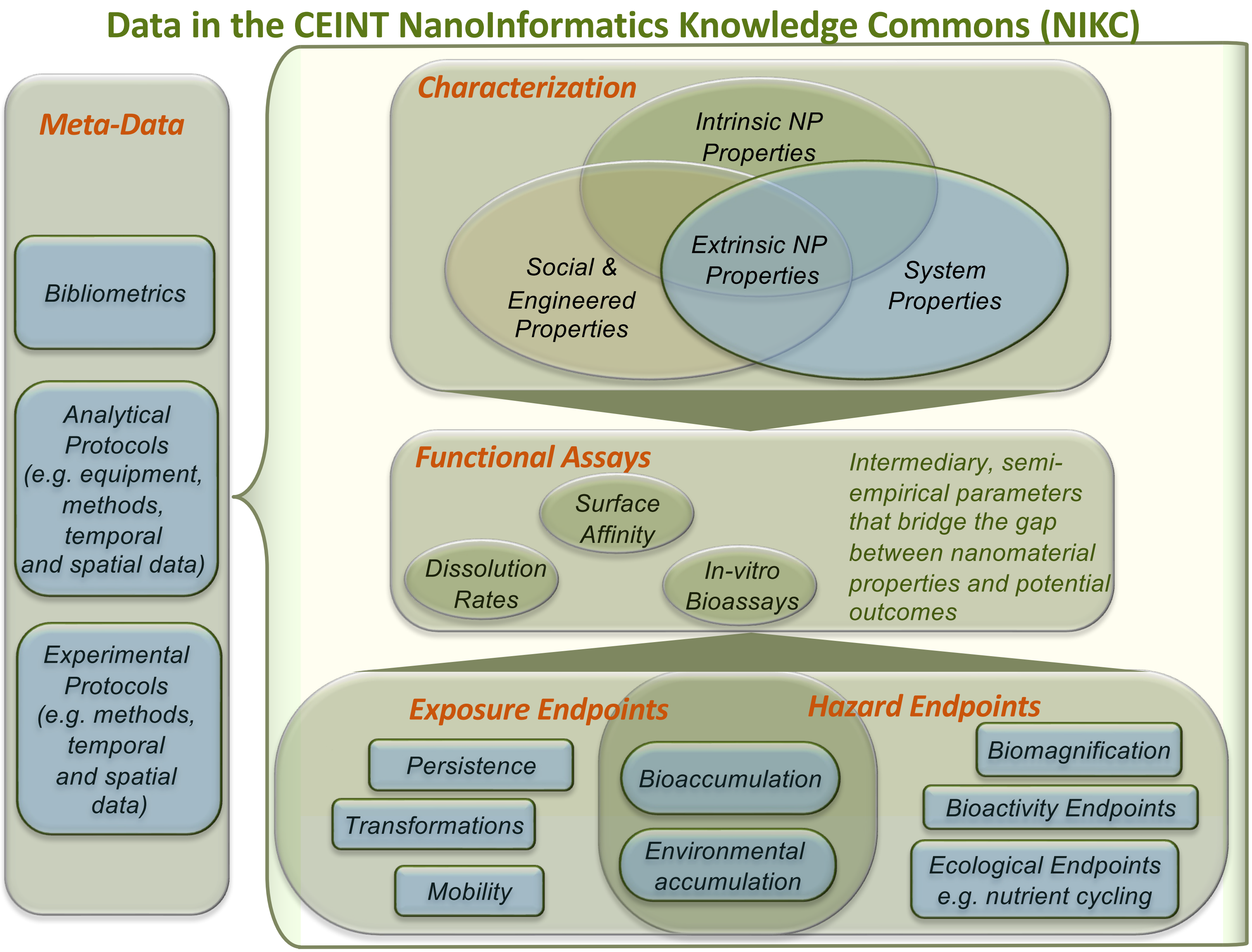
Relative amounts of natural, incidental, and manufactured nanomaterials

Soils worldwide produce 10^5 times more NP's annually than industry





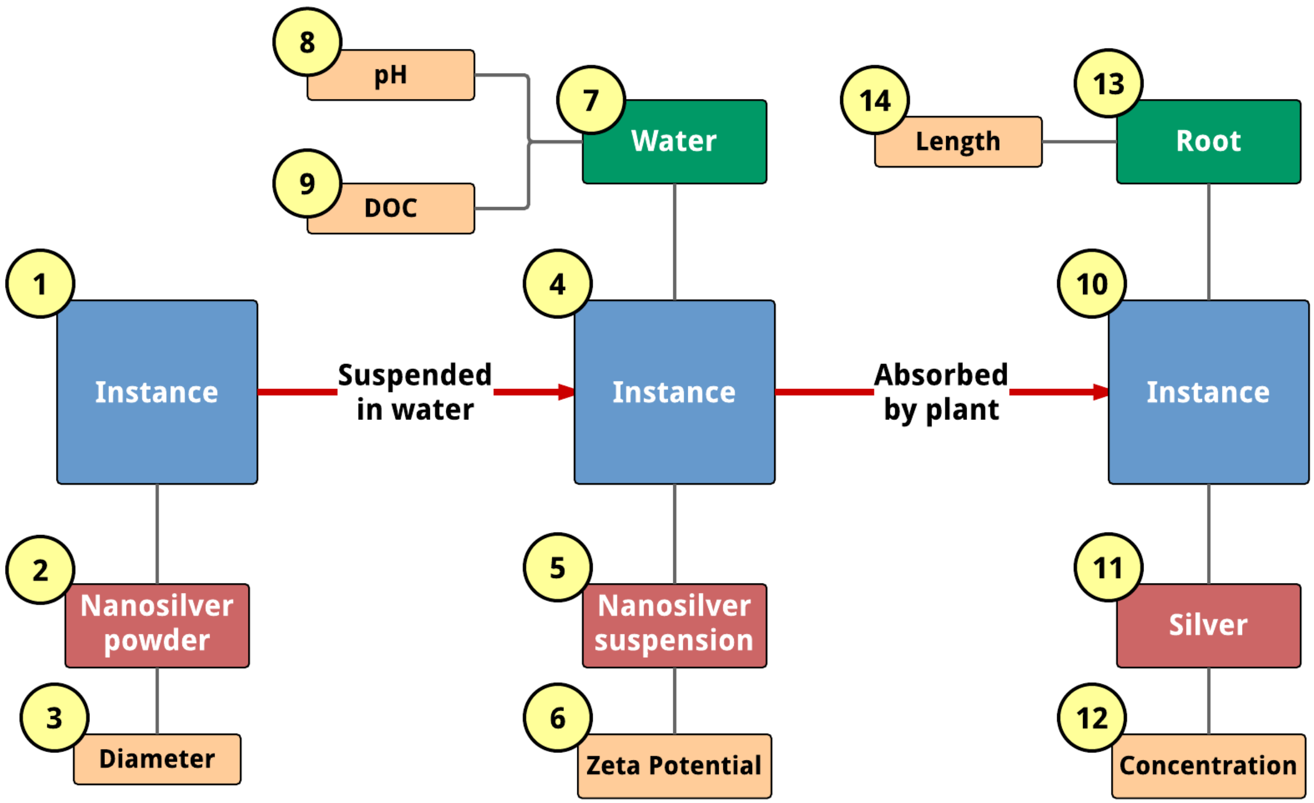
Lesson 7: Data platforms are needed to track changes in materials over time: Instance Mapping


Data in the CEINT NanoInformatics Knowledge Commons (NIKC)
Meta-Data
Bibliometrics
Analytical Protocols (e.g. equipment, methods, temporal and spatial data)
Experimental Protocols (e.g. methods, temporal and spatial data)
Characterization
Intrinsic NP Properties
Social & Engineered Properties
Extrinsic NP Properties
System Properties
Functional Assays
Surface Affinity
Dissolution Rates
In-vitro Bioassays
Intermediary, semi-empirical parameters that bridge the gap between nanomaterial properties and potential outcomes
Exposure Endpoints
Hazard Endpoints
Persistence
Transformations
Mobility
Bioaccumulation
Environmental accumulation
Biomagnification
Bioactivity Endpoints
Ecological Endpoints e.g. nutrient cycling

Instance Mapping

Populating Measurement Table

Accumulation of Nanosilver by Plant



The NanoInformatics Knowledge Commons

Conclusions

1. Approximately 25 years of Nano EHS research has yielded methods, models and protocols that can benefit research on micro/nanoplastics

2. Particle toxicity appears to be primarily predictable based on composition and, for inhalation, persistence and shape.

3. To date a uniquely "nano" mechanisms for toxicity has not been established

4. Natural and incidental nanomaterials predominate from an exposure perspective- Nanoplastics are one such example