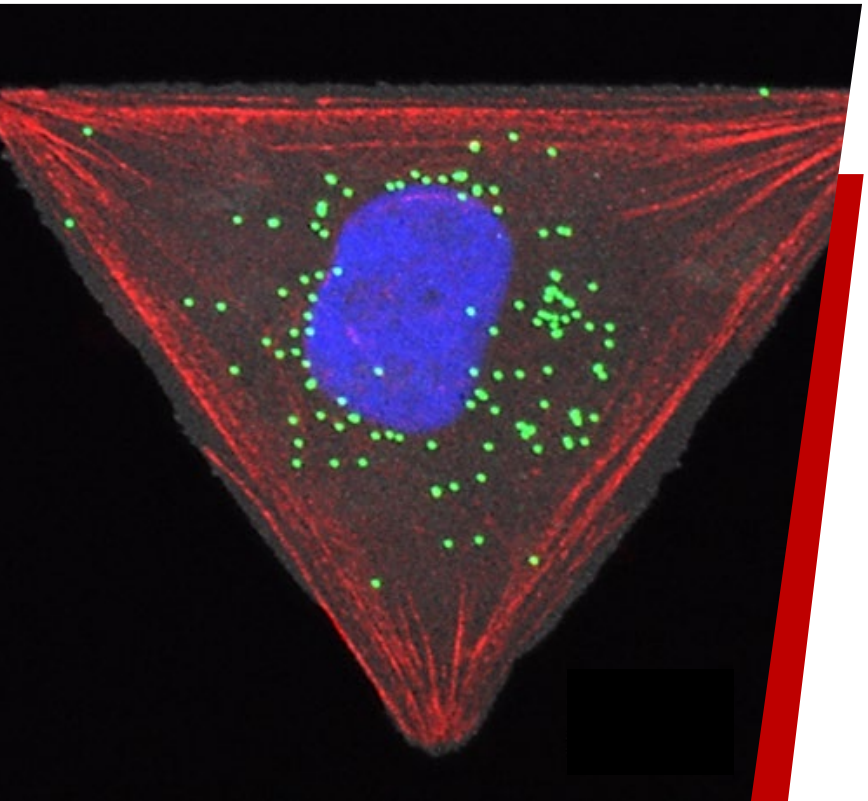
Empa
Materials Science and Technology

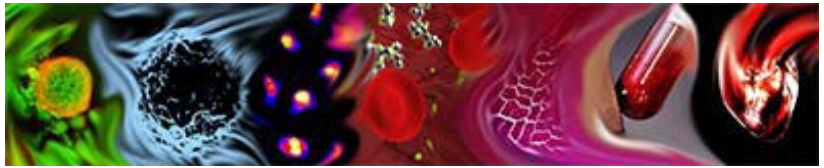


Principals in Nanosafety research

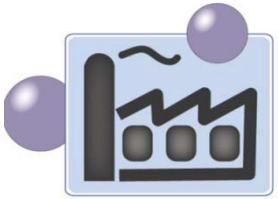
Prof. Dr. Peter Wick
Head Particles-Biology Interactions, Empa
Summerschool, August 19-23 2024, Visp, CH

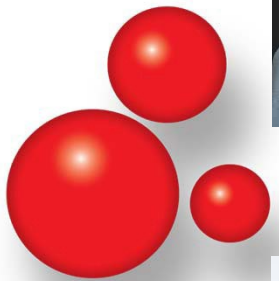
Particles-Biology Interactions research topics and group structure

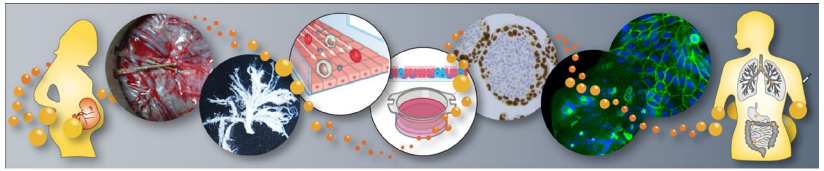
We develop transformative (nano)material designs and concepts for precision health solutions addressing the unmet needs of our society.



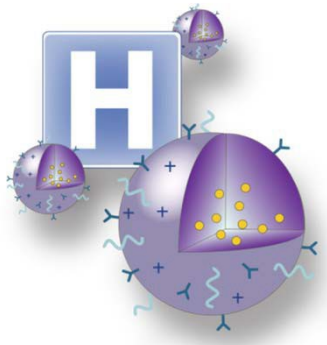
Rational design of functionalized (nano)materials for precision health solutions







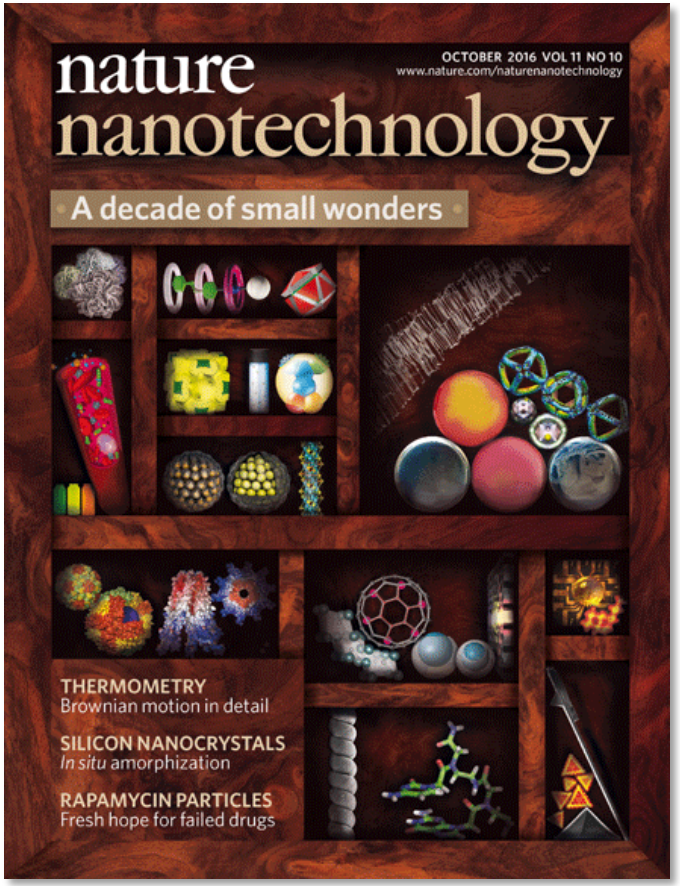
Understanding (nano)material biotransformation, transport and effects at biological barriers and tissues

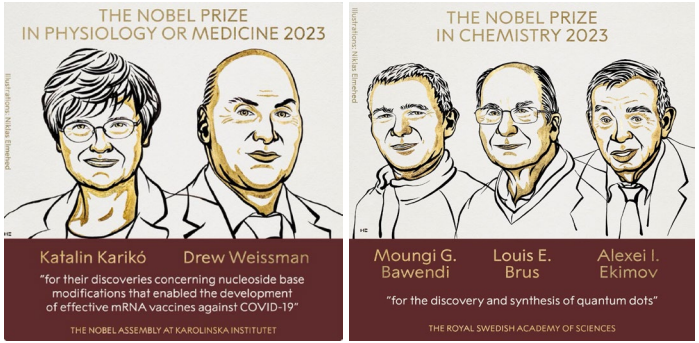


My teaching vision

- Research shapes the world and our society along the global challenges
- Privileged position: do research and be interlinked with students
- Proud to transfer my knowledge into an interdisciplinary field and stimulate the next generation of scientist / engineers
- Stimulating time together with intensive exchanges – also beyond this course (e.g. bachelor or master or PhD student)
- Questions and discussions welcome

Nanomaterials are small wonders





Experiment

Size Definition of Nanomaterials

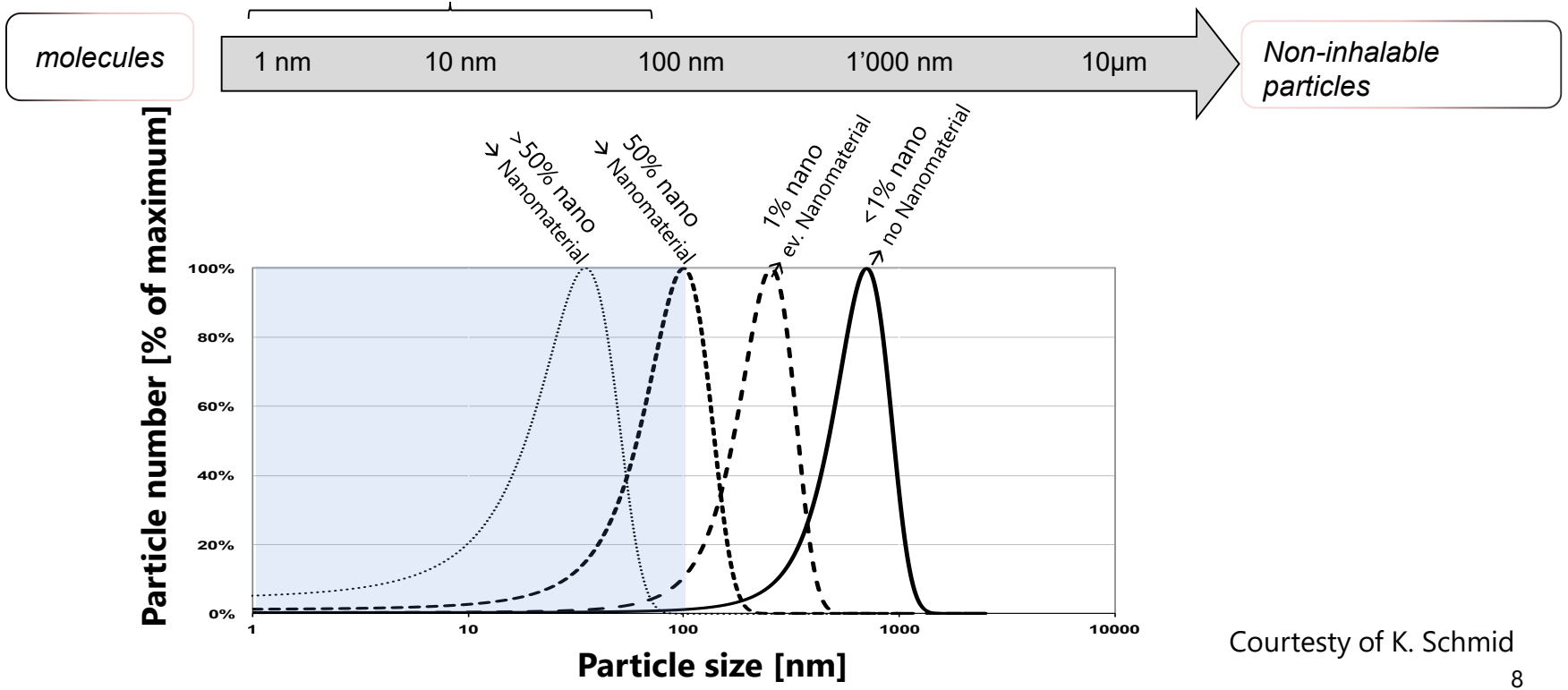
- ‘Nanomaterial’ means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm. (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011H0696)

- Swiss Precautionary Matrix extended the ‘critical’ size to < 500 nm primary particles size or agglomerates

Consequences of the size definition

500 nm – „precautionary safety approach“ avoid unexpected side effects

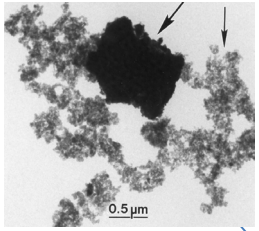
100 nm – size definition of nanoparticles after ISO



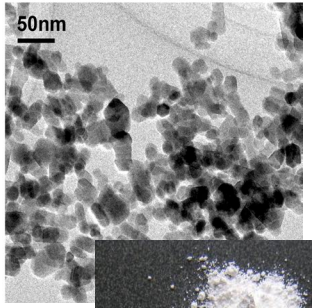
Courtesy of K. Schmid

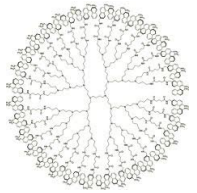
Nanoparticles are a ‘new’ class of materials

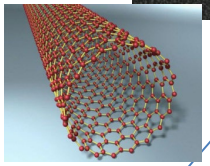
anthropogenic NP

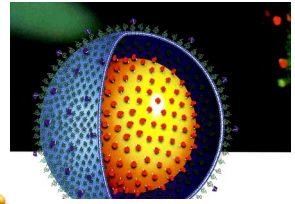


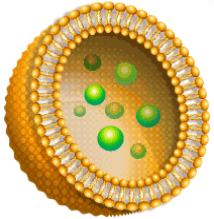
(bio)persistente NP

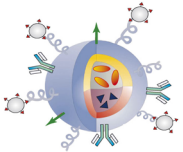






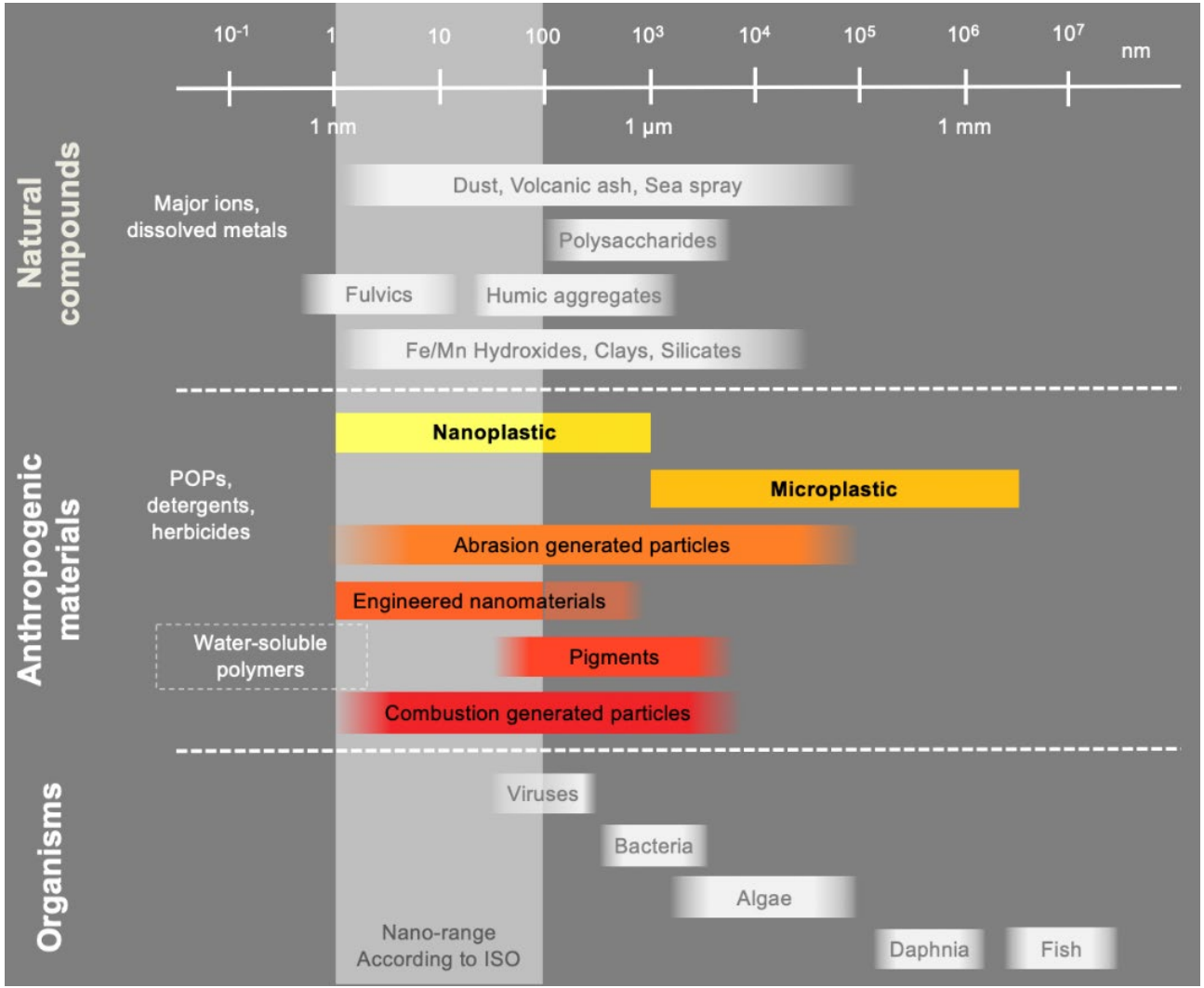






natural occurring NP

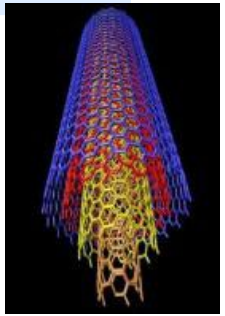
resorbable NP



Mitrano, Wick, Nowack Nat Nanotech 2021

What are the most important nanomaterials?

	tons / year
Cupper carbonate	70‘000
SiO_2	*~ 50‘000*
TiO_2	17‘000
ZnO	2400
CNT	350
Ag	250
Fullerene	5



Adapted from Gottschalk et al 2009

Courtesy of B. Nowack

Which (nano)material is the most toxic?

Salt grains

Asbestos

TiO_2

Quartz

Graphene

Gold

Silver

SiO_2

Soot

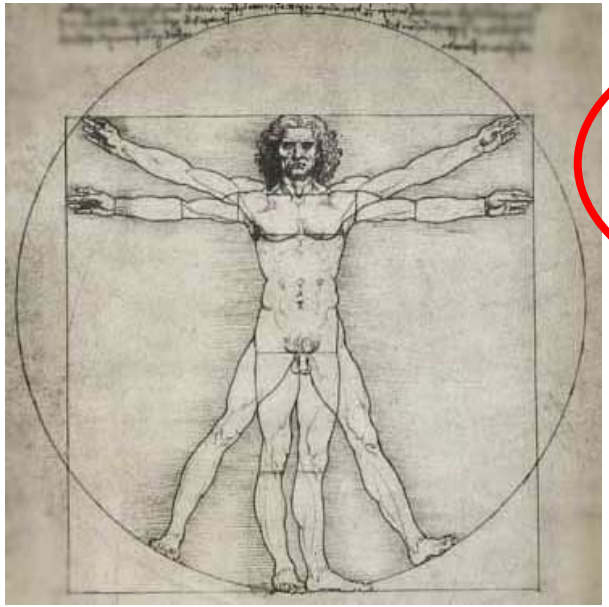
CNTs

Exposure scenario and biological effects of nanoparticles

nose:
olfactoric nerve
bypass BBB

injection:
efficient distribution in the body (4 - 5l cardiac output per minute)

gastrointestinal tract:
surface: 2000m^2 incl Microvilli
pH 2, intestinal mucosa thick;
distance to blood vessels **big**

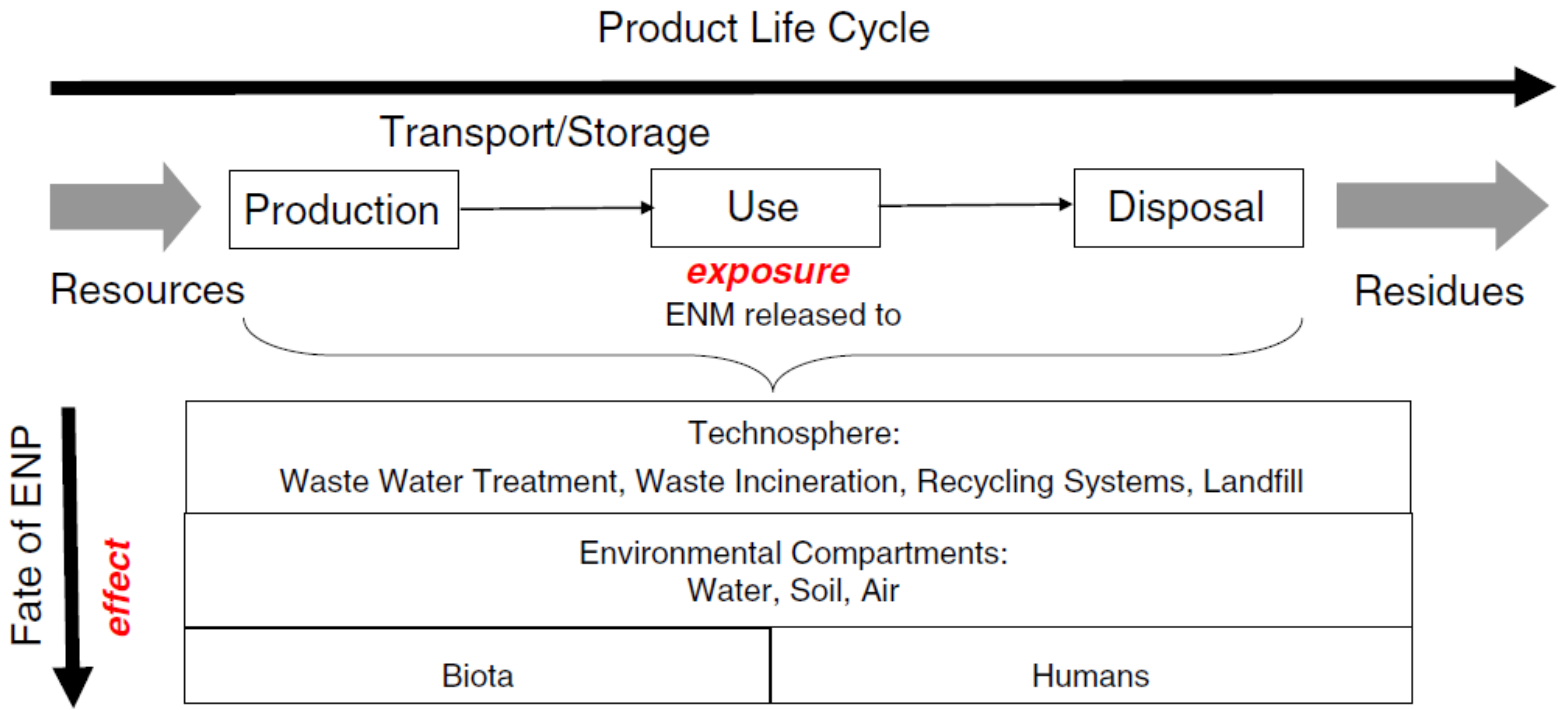


lung:
140 m^2
air / blood barrier
very thin < 2 µm

skin:
1.8 m^2
barrier **very thick**,
epidermis, horny skin

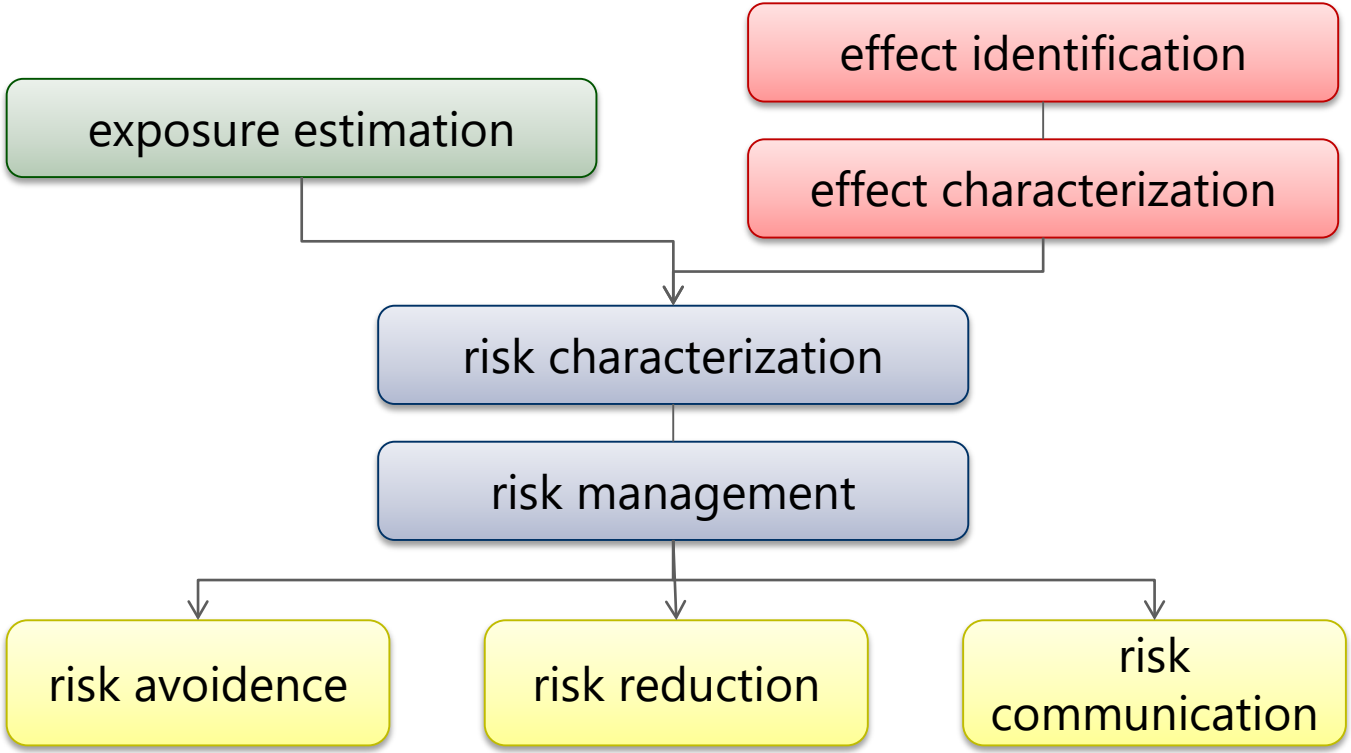
hair follicle	20/cm^2
respiratory glands	150/cm^2
sebaceous glands	15/cm^2

The life cycle of nano-enabled products determines dose, exposure, fate and risk scenarios



Som, Wick et al 2011 Environ Intern

How to determine a risk?



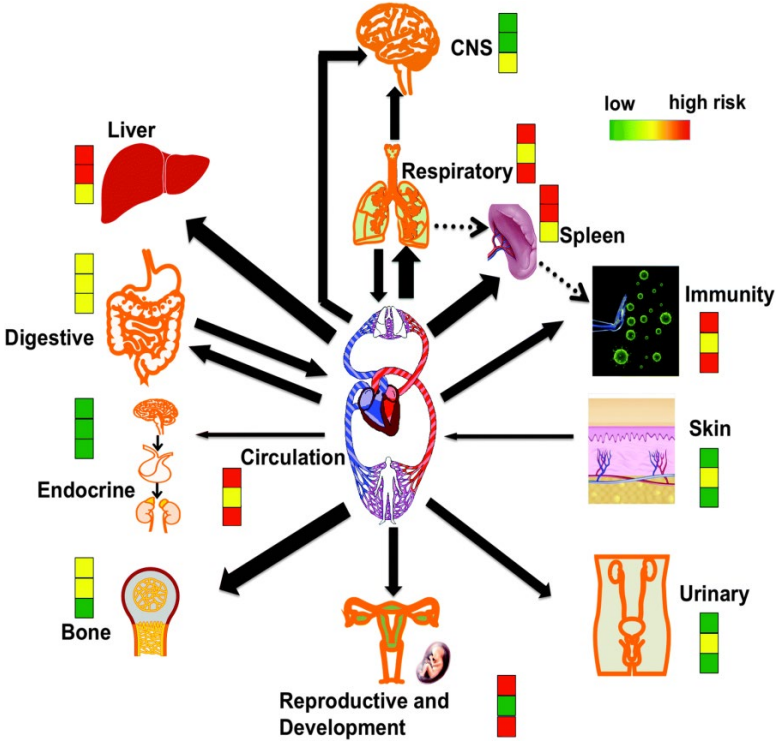
$$R = f_P \{E, H\}$$

Krug and Wick Angew Chem 2011; Som et al ACR 2013

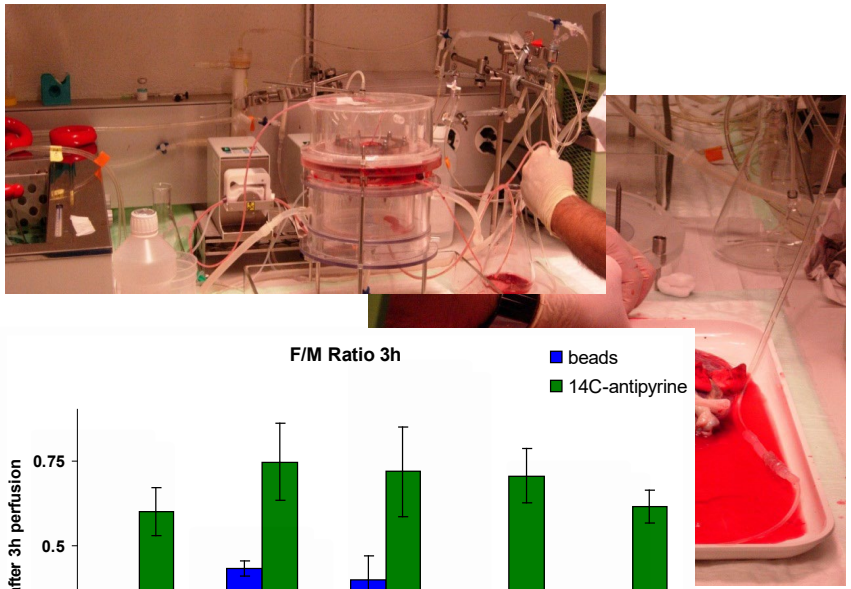
Questions so far - Break?

What do you think makes ‘Nanotoxicology’ different from classical Toxicology

1. Uptake / translocation: size matters!

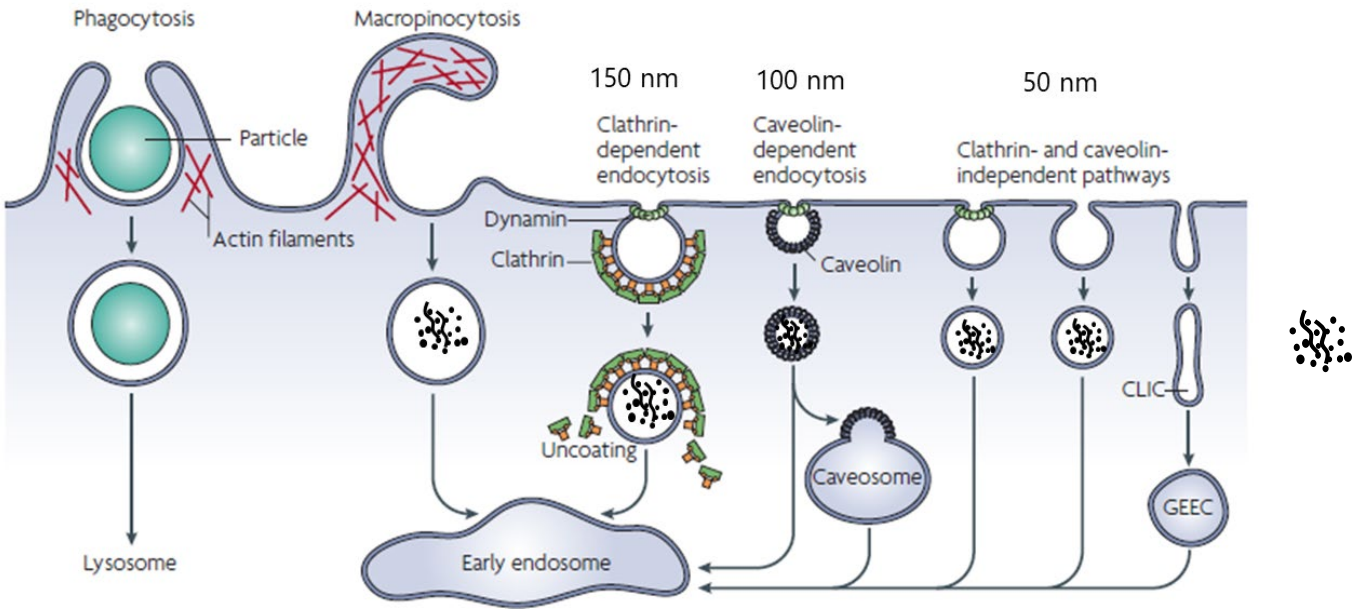


Zhang et al 2014 Chem Soc Rev



Wick et al 2010; Grafmüller et al 2015

Cellular uptake



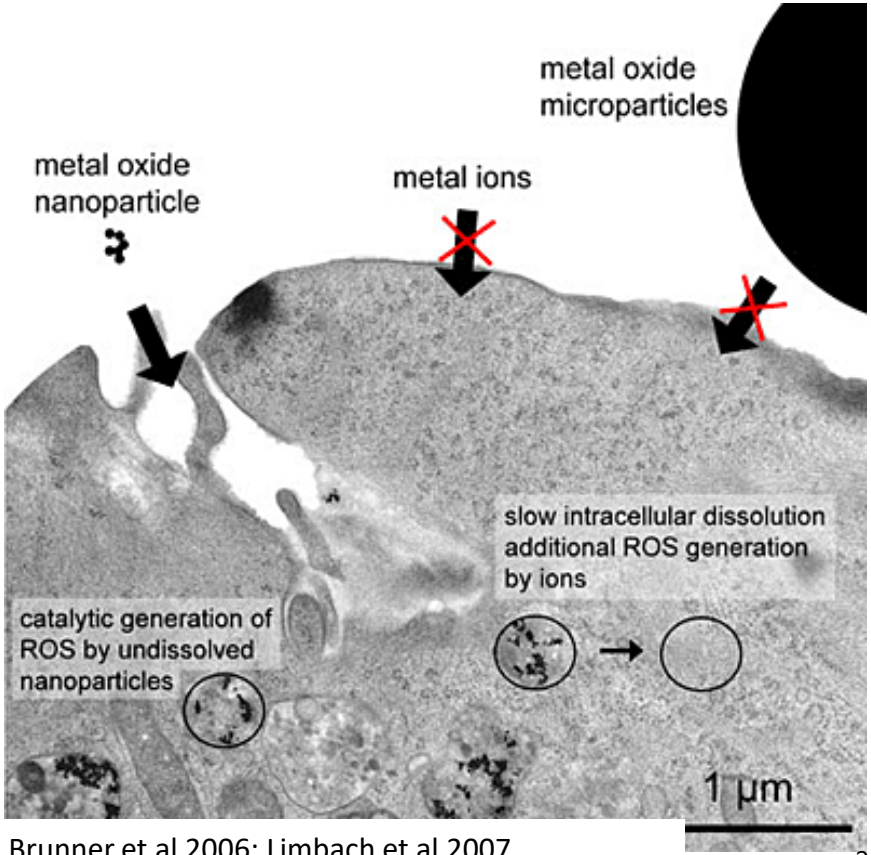
Macrophages are dedicated to clean up foreign particles (viruses and bacteria) or NMs

Natural detoxifying pathway may not work with NPs especially with soluble ones

Mayor and Pagano 2007 Nature Reviews Molecular Cell Biology

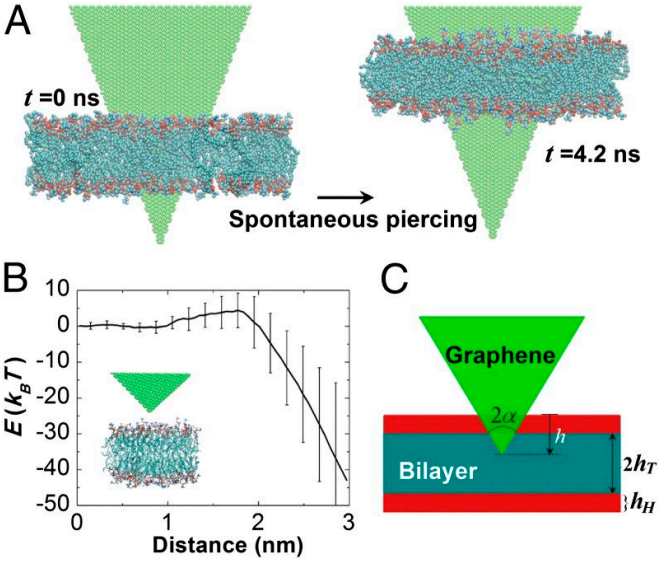
Trojan Horse mechanism

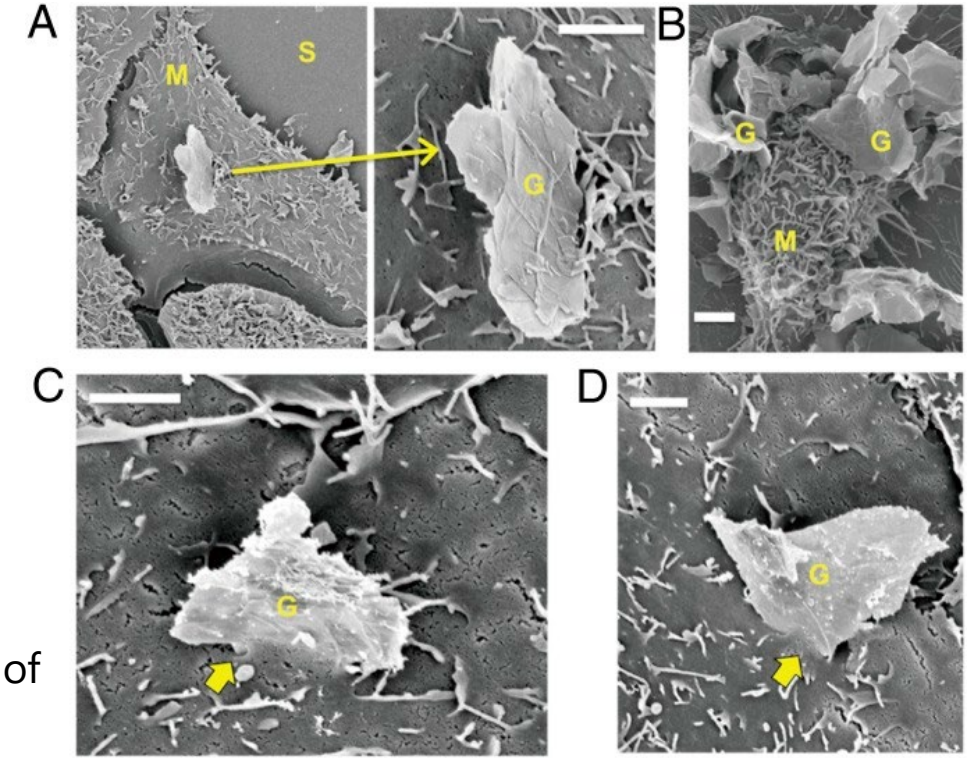
- Nanomaterials were taken up and may reach cells or tissues which were not affected when exposed to ist bulk or ionic form
- Promising opportunity for pharmaceutical engineering
- Modulate the bioavailability of xenobiotic
- Understanding the underlying mechanism necesary for both the pharmaceuttical as well as toxicological science



Brunner et al 2006; Limbach et al 2007

Cellular uptake of 2D material – a different pathway?

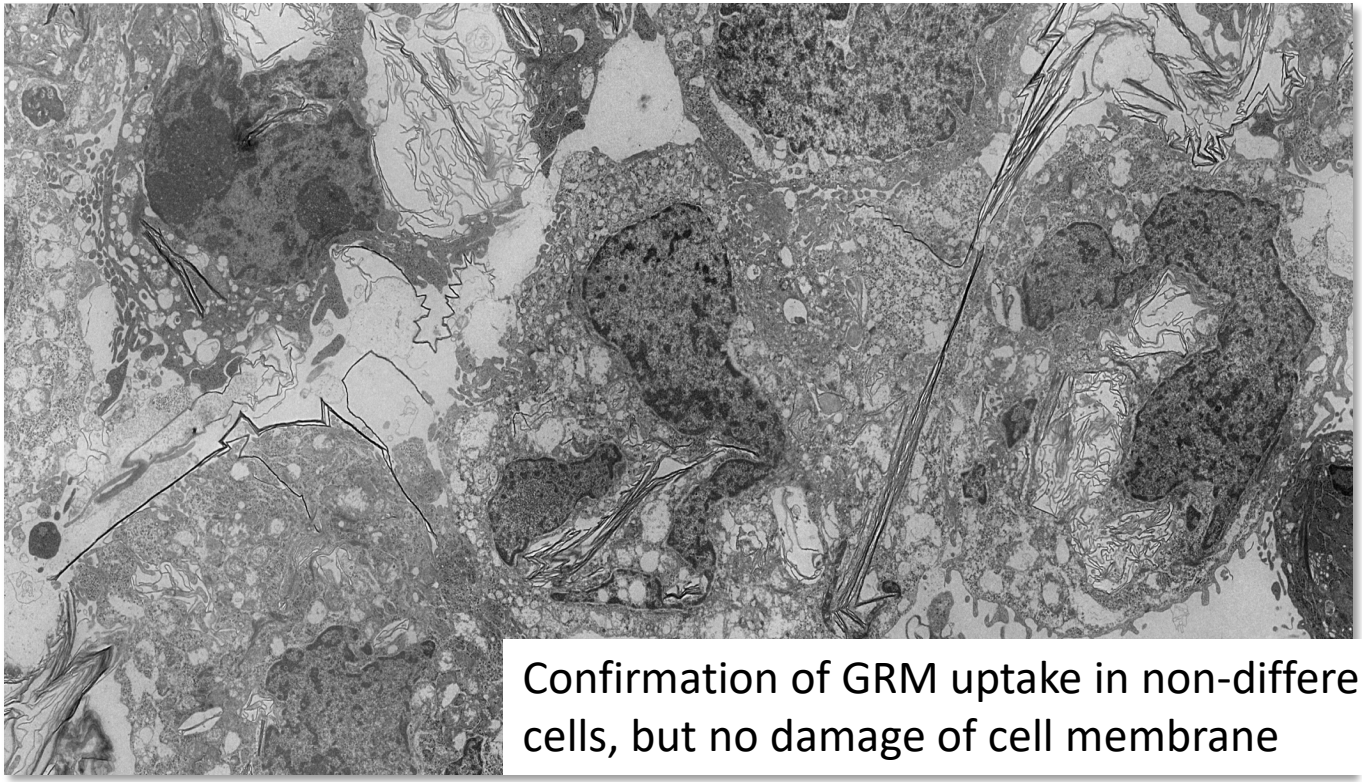




edge-first uptake and complete internalization for a range of FLG samples of 0.5- to 10-μm lateral dimension

Li Y et al 2013 PNAS

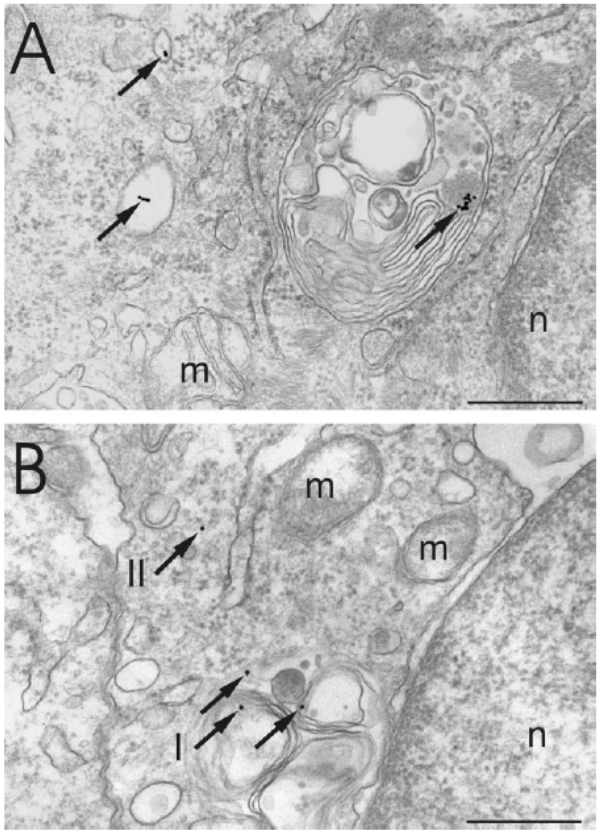
Cell state specific uptake: an example with entherocytes and graphene related material

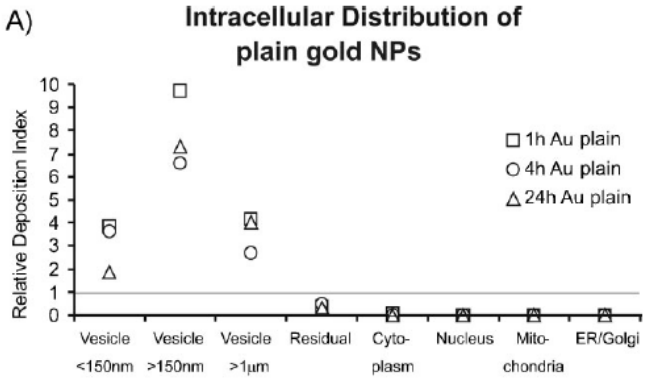


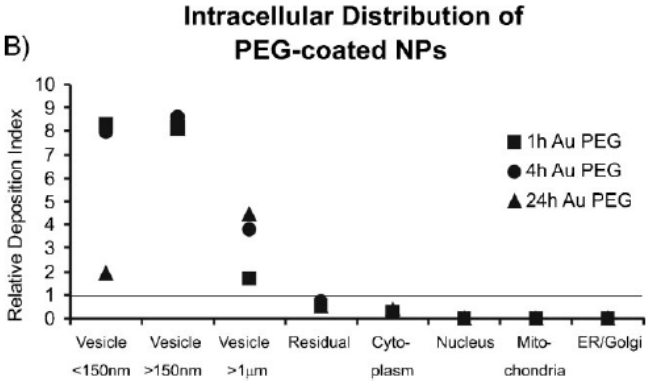
Confirmation of GRM uptake in non-differentiated Caco-2 cells, but no damage of cell membrane

Kucki et al 2017

Quantitative analysis of NP cellular fate





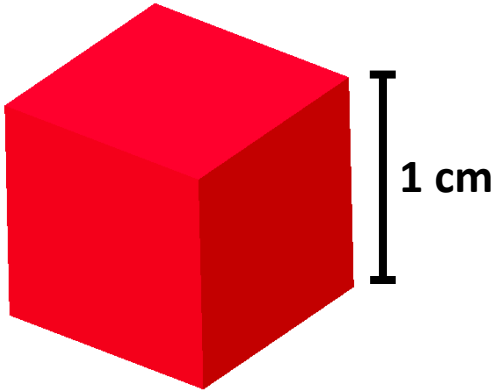


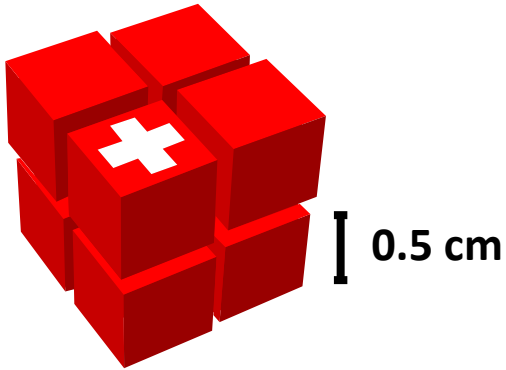
Brandenberger et al 2010 Small

2. Surface / Volume ratio of Nanomaterials

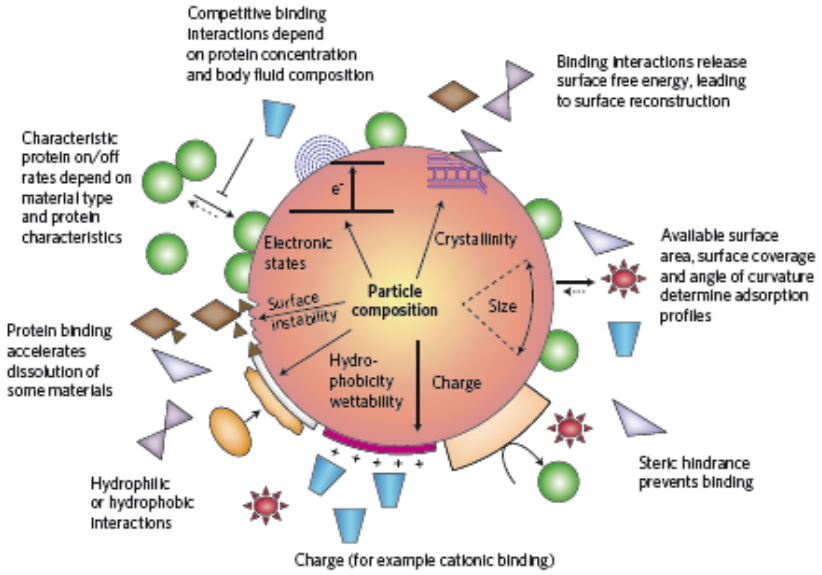
- Exercise: estimate of the total surface by cutting down a cube of 1 cm edge length into 1nm cubes

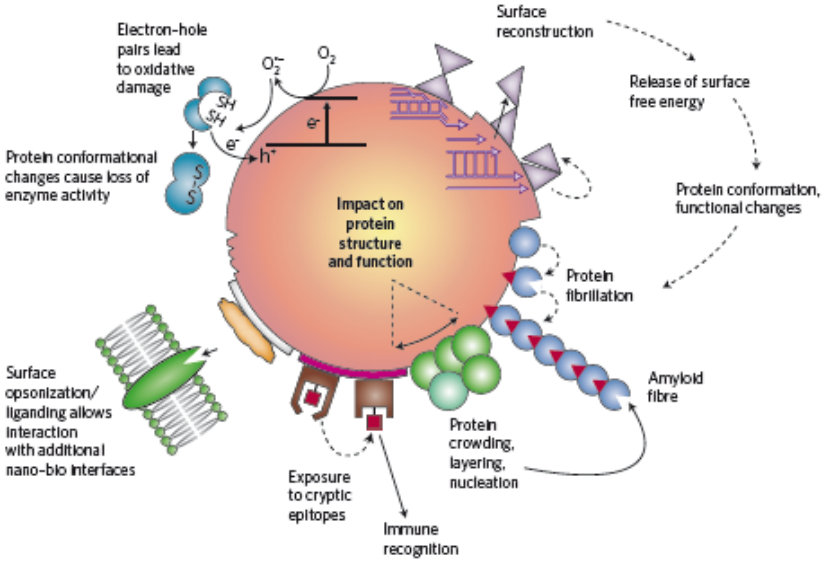
Down sizing material generate larger surface with the same total mass





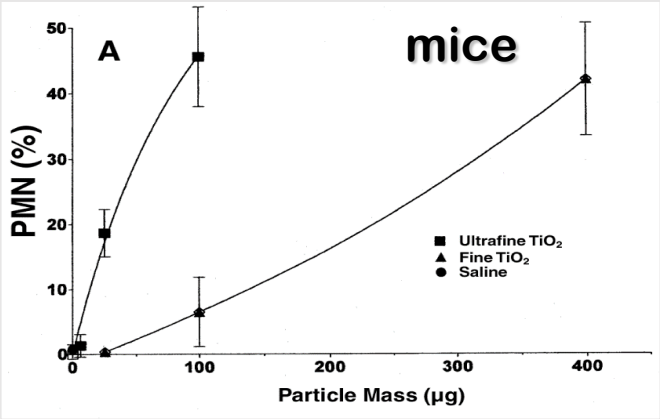
Surface effects: key element for nanomaterial – cell interactions

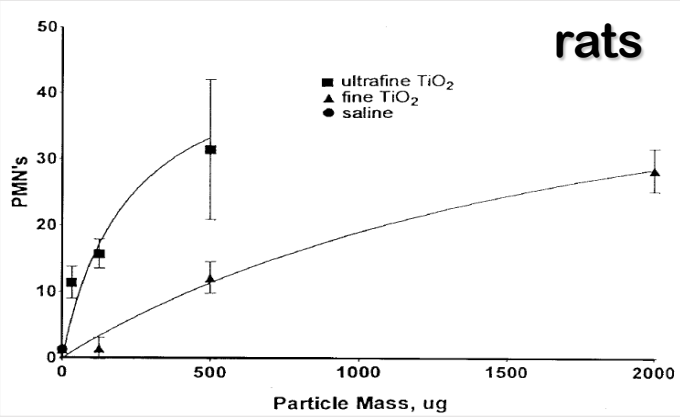




Nel et al 2009 Nat Mat

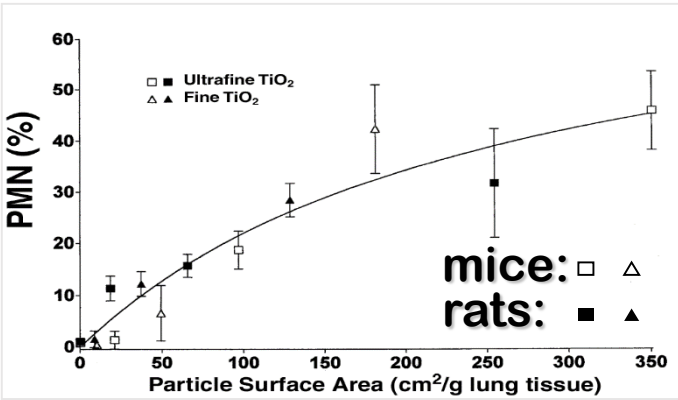
Acute effects of nanomaterials in the lung



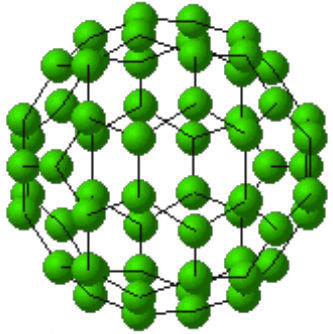


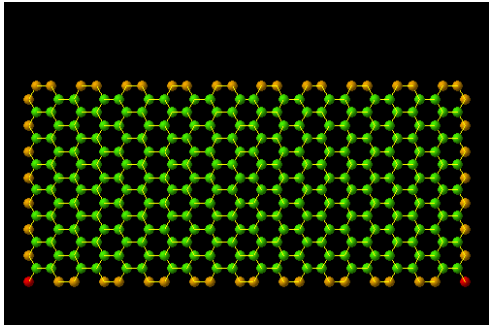
Inflammatory cell response in lung lavage (procent of Neutrophils) 24hr after intratracheal instillation of fine (~250 nm) or ultrafine (~20 nm) TiO_2 particles in rats and mice.

Oberdörster et al., 2000: HEI-Report 96
Oberdörster 2001: Int. Arch. Occup. Environ. Health, 74, 1-8

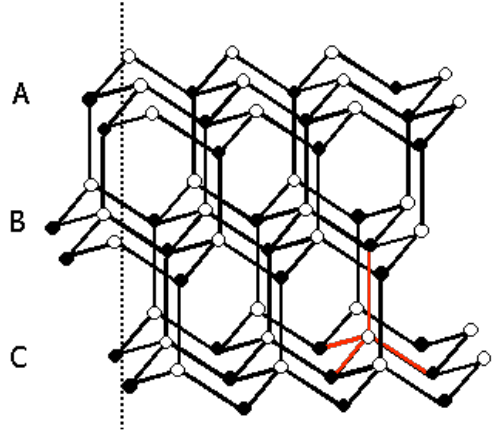


3. One material – different appearance

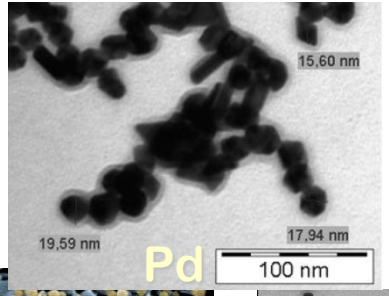


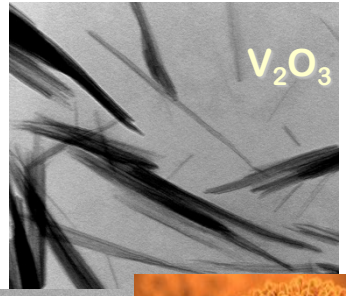


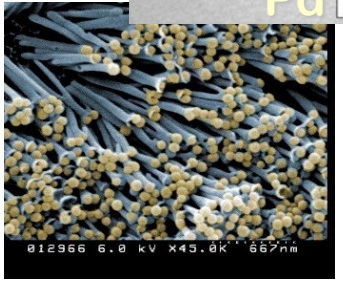
and others…

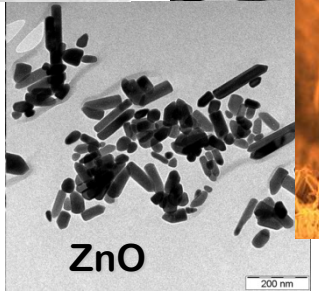


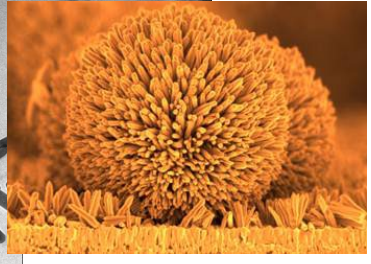
carbon





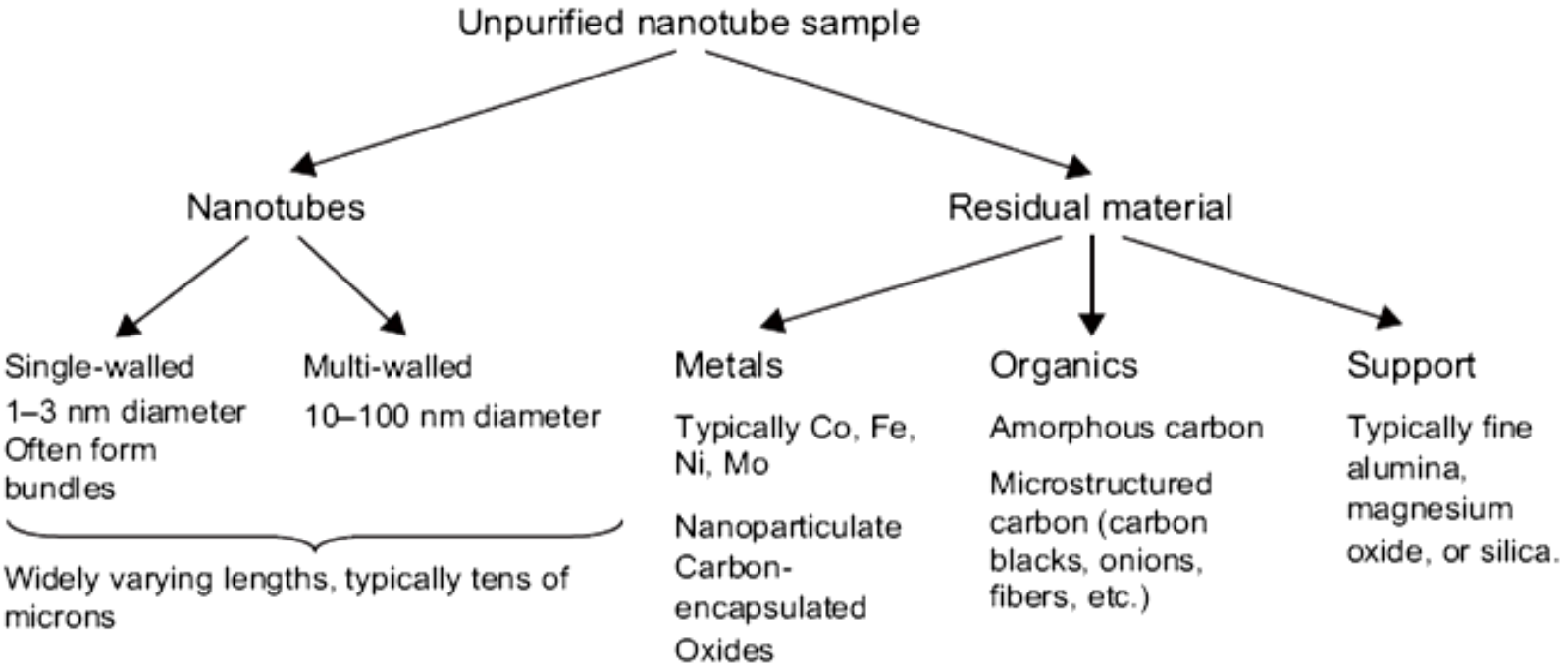




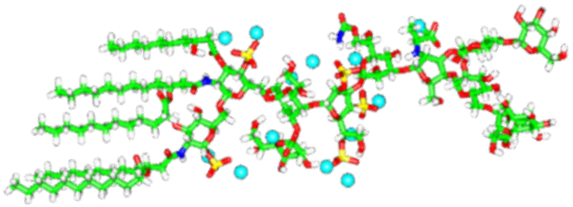


Possible components in a sample of unpurified carbon nanotubes

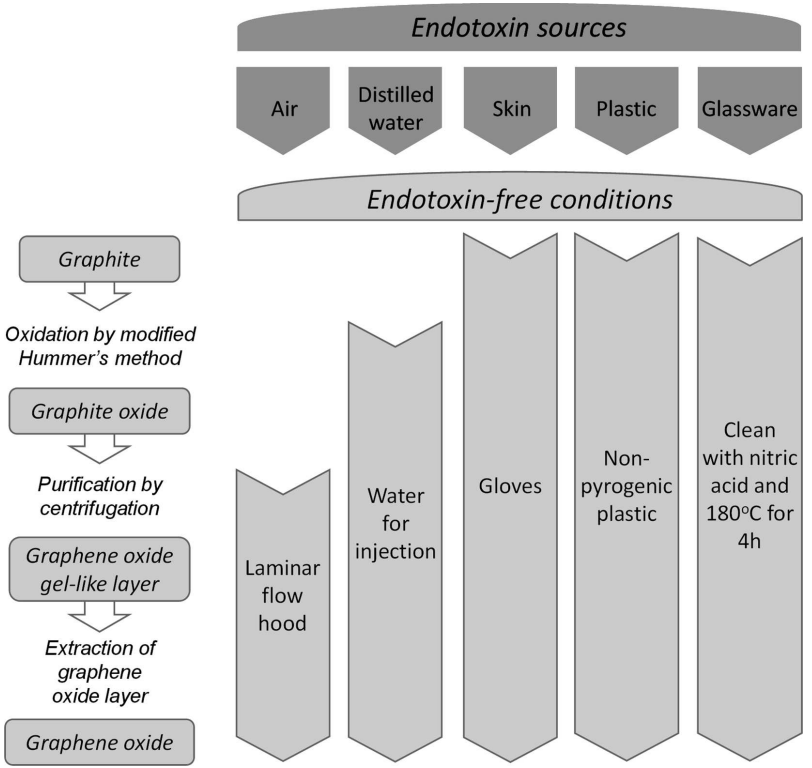
DONALDSON ET AL. TOXICOLOGICAL SCIENCES **92(1)**, 5–22 (2006)



Contaminations disguise the toxicological assessment

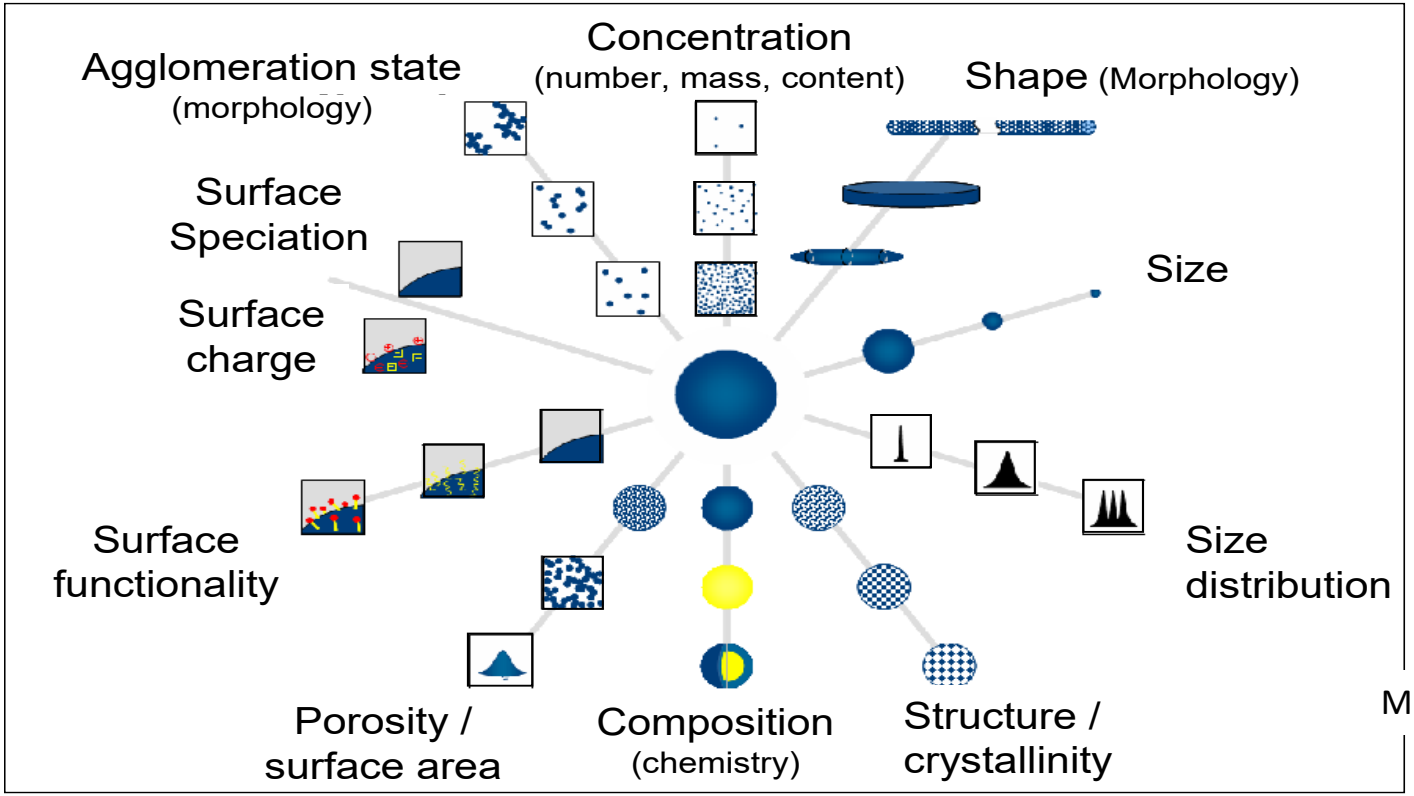


Lipopolysaccharides (LPS) residues form bacterial cell wall trigger immune reactions
NPs potential to interfere with common *Limulus amebocyte* lysate (LAL) assay



Mukherjee, Wick et al 2016 PLOS One

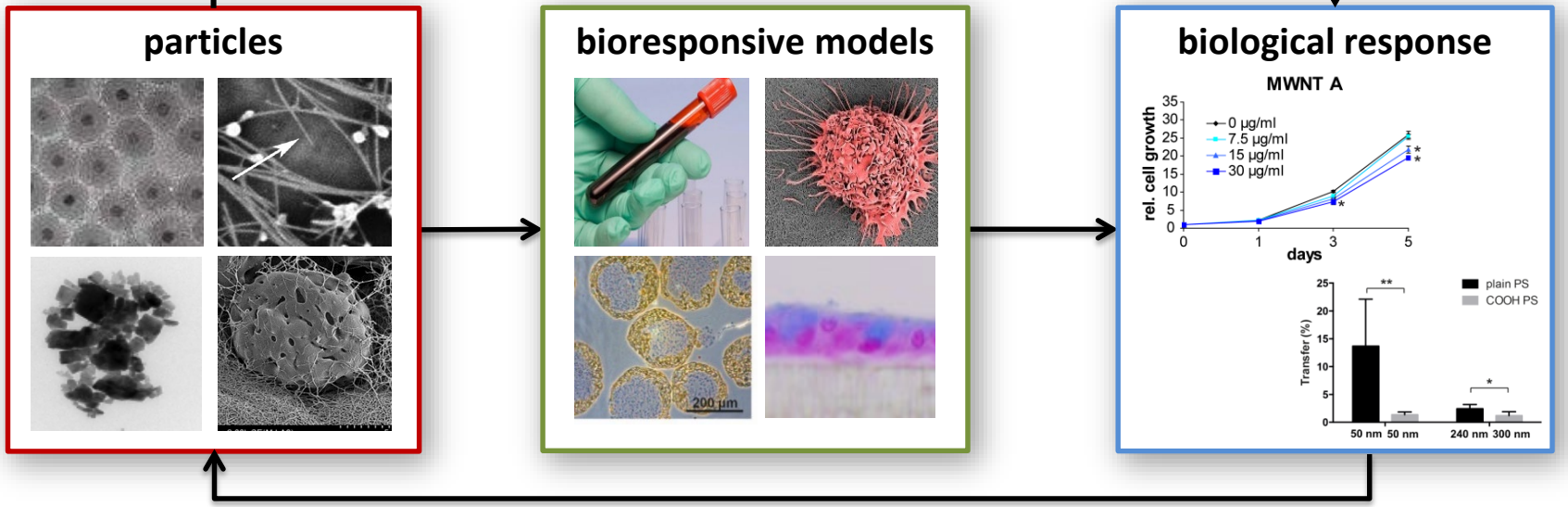
Comprehensive material characterization is necessary prior to any biological work



M. Hassellov, et al 2008

Correlation of particles properties with biological responses towards prediction

‘modelling and simulations’



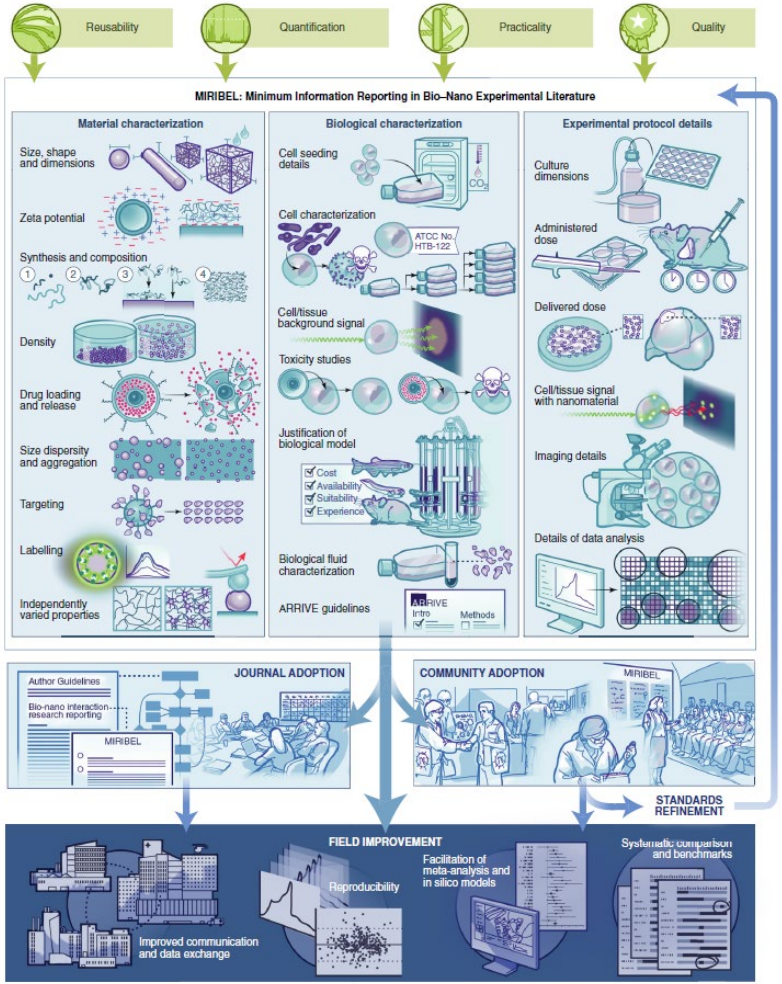
‘safe-by-design’

ITS Nano

Prioritizing nanosafety research to develop a stakeholder driven intelligent testing strategy

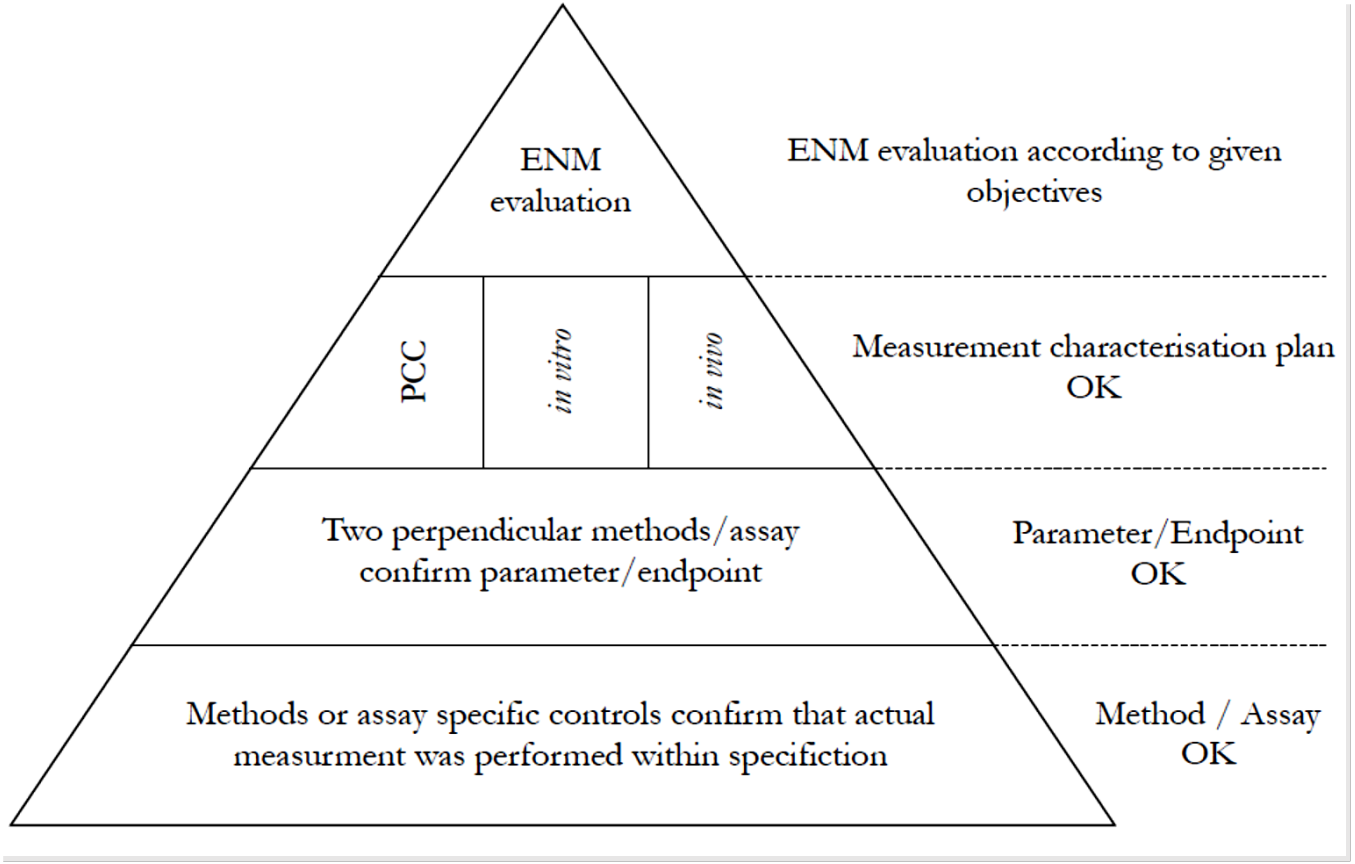
Stone V. et al 2014 P&FT

Minimum information reporting in bio-nano experimental literature



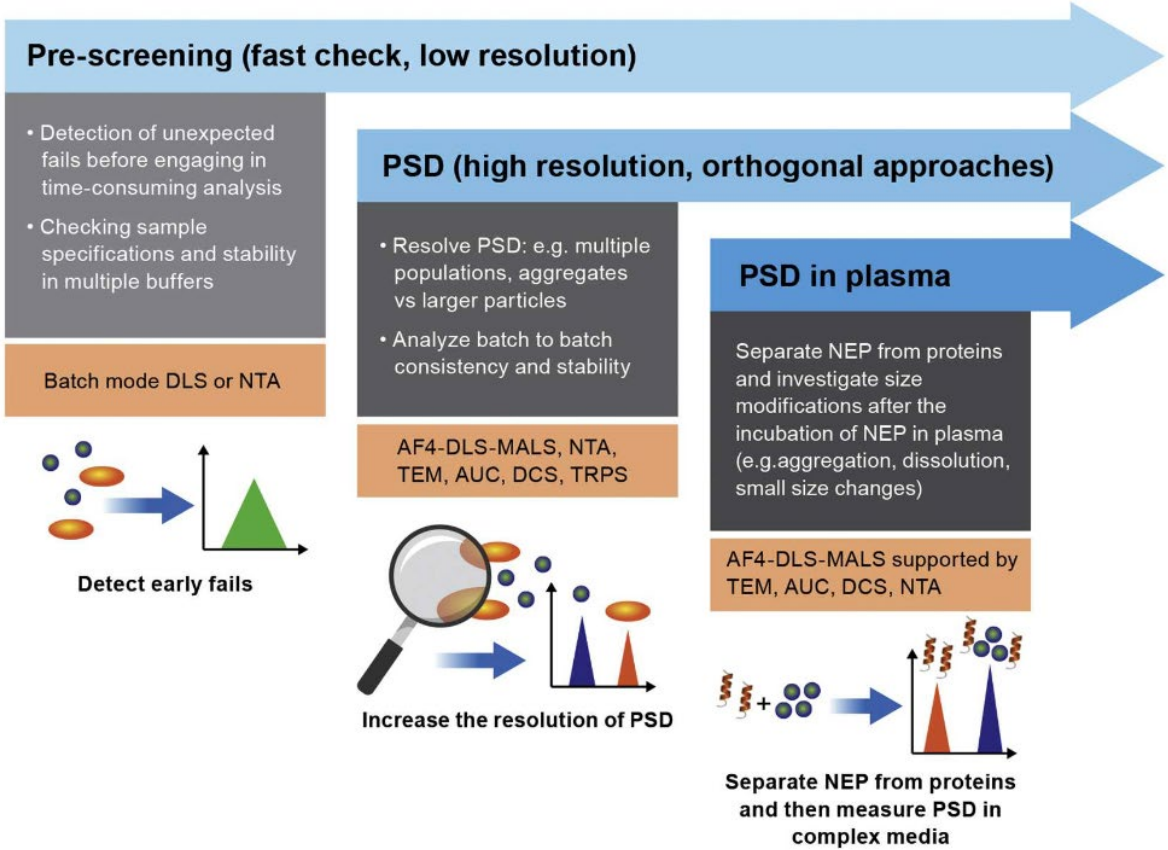
Faria M et al Nat Nanotech 13 (2018), 77-785

The pyramid of measurement science-based nanomaterial evaluation: the 'orthogonal' approach



Rösslein M. et al 2011 Nanomedicine

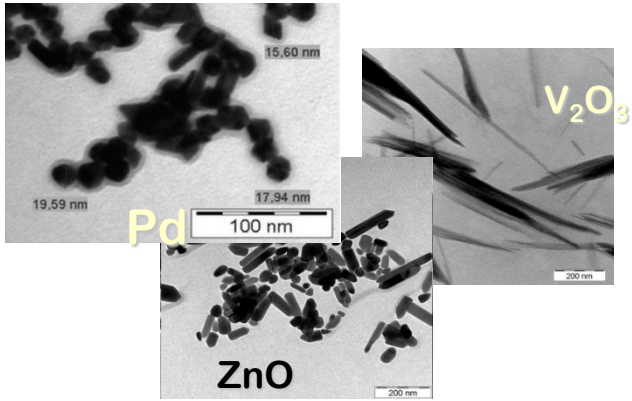
Step by step approach to measure particles size distribution



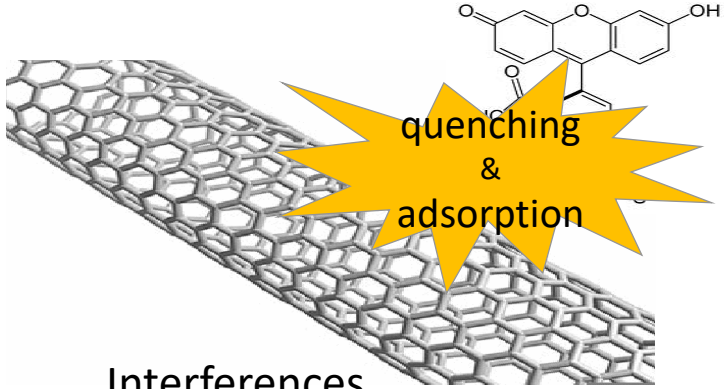
Larger or more?

Caputo, Rösslein et al 2019 JCR
Maguire, Rösslein et al 2018 STAM
Maguire, Rösslein et al 2017 J Micro-and Nanofacturing
Mehn, Caputo, Rösslein et al 2017 RSC Advances
Toman, Rösslein et al 2016 Methrologia
Hole, Rösslein et al 2013 J Nanopart Res
Hirsch, Rösslein et al 2011 Nanomedicine
Roebben, Rösslein et al 2011 J Nanopart Res

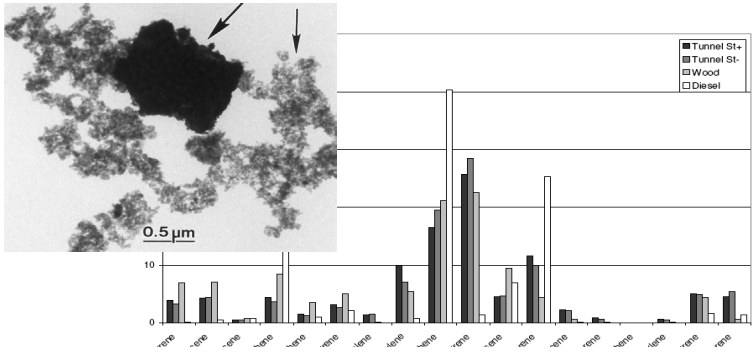
Consequences for the effect assessment of NPs



Material characterization

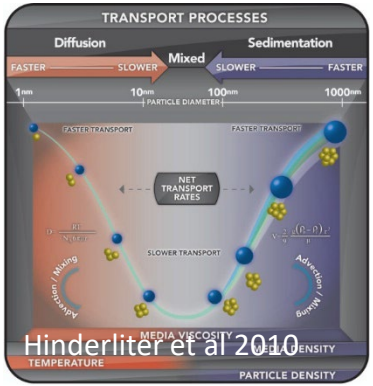


Interferences



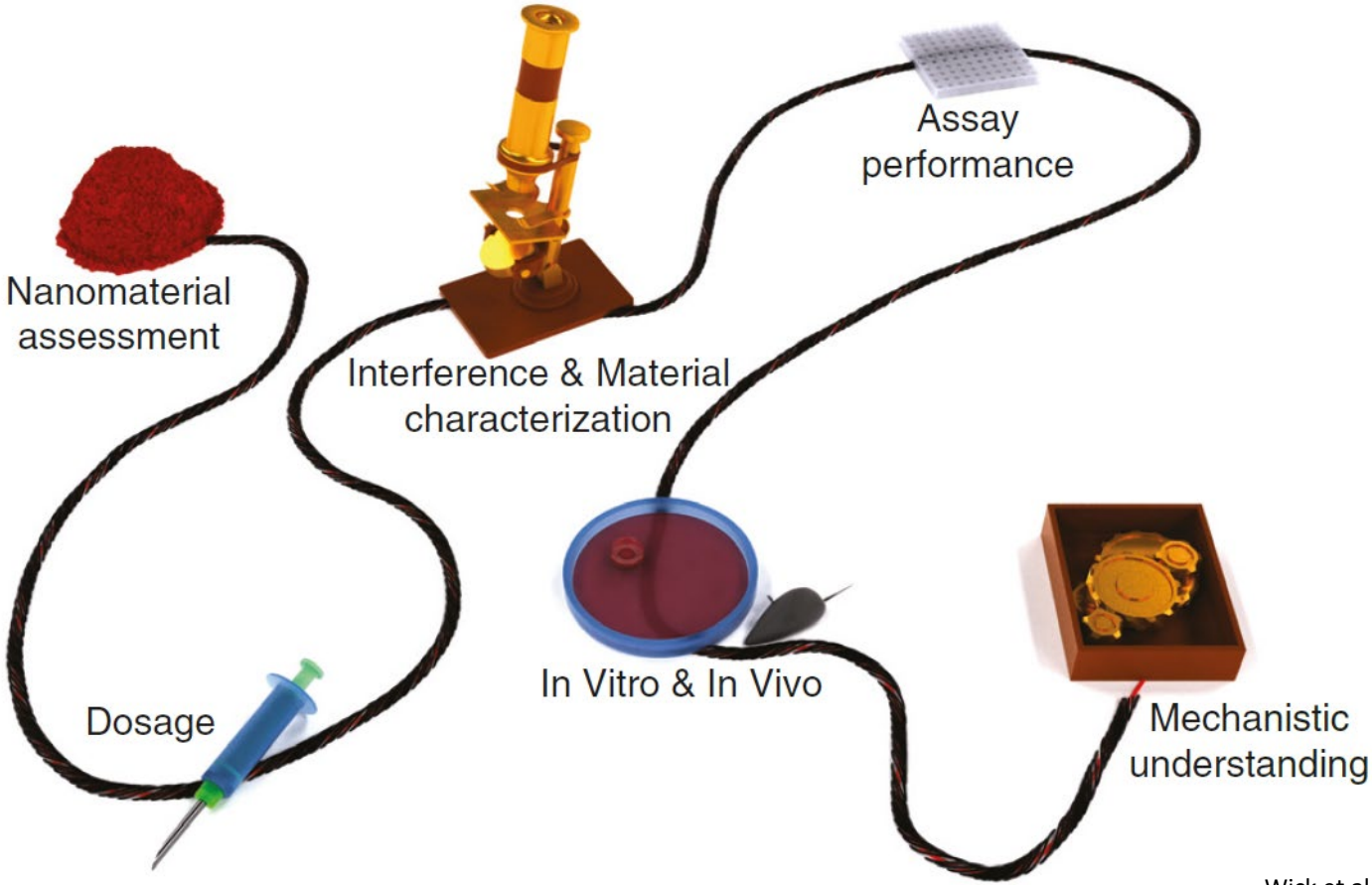
PAH – polycyclic aromatic hydrocarbon

Dose



Hinderliter et al 2010

Conclusion



Wick et al 2015 Eur J Nanomed