Requirements for
Reliable Exposure Assessment of ENM in Air

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Scope & Content

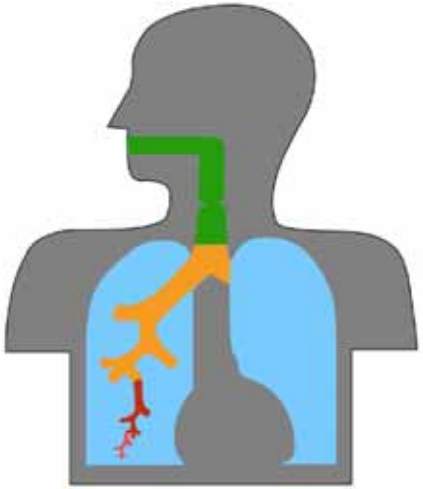
- Type of particle related data required for reliable assessment
- NP characteristics (“metrics”) responsible for effects on/in biological systems
- Metrics which are accessible today - and which are not
- Correlation between aerosol metrics and toxicity data

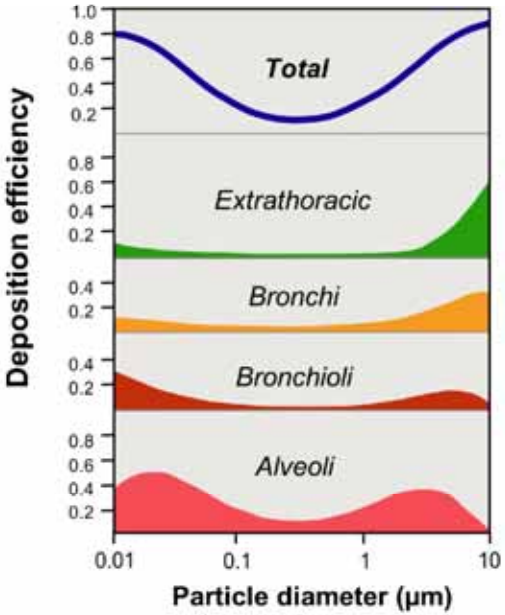
The issue: reliable exposure assessment

Dose = concentration x time x lung deposition efficiency

- *Respiratory deposition efficiency as a function of particle size generally well understood*

  ICRP 66 (1994)





- **What about concentration?**
  - *Most simple case: material dissolves rapidly in tissue fluids*
  - *Then particle concentration + chemical composition => toxic effect (not a "nano" issue)*
  - *The metrics conundrum: number - surface area - mass concentration?*
- ***Particle "functionality" with regard to specific biological effects***
  - *Particle morphology, catalytic activity, ROS activity etc.*
  - *The paradigm of "toxicity ~ particle concentration" is inoperable and outdated*

NP „functionality“ in biological systems and mechanistic pathways of noxious action

- **Multidemensional space of effects and mechanisms**
  - *“Chemical” toxicity (on the molecular level - simple case)*
  - *“Morphological” toxicity*
  - *Oxidative stress*
  - *Genotoxicity*
  - *Cytotoxicity*
- **Mechanistic pathways undoubtedly material specific**
  - *Multitude of nanostructured materials*
  - *For a given material, dose is of course concentration dependent*
- **In addition: particle size specific (“N - S - M”)**
  - *Deposition in the respiratory system*
  - *After deposition: translocation, penetration of biological barriers*
  - *(Particle morphology relevant for a limited number of species)*
- **Need material specific concentration and size distribution**

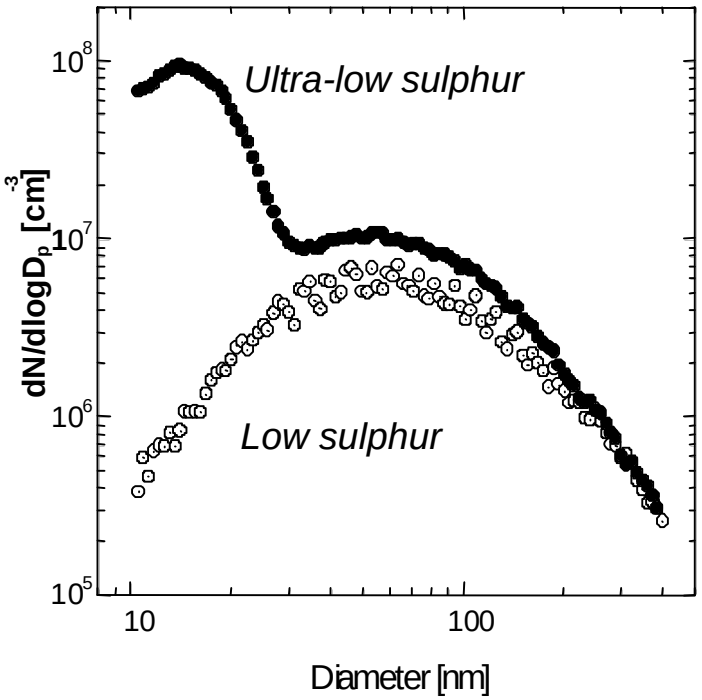
Aerosol related metrics accessible today

- **Particle size & concentration readily and accurately measured on line**
  - *Concentration in terms of number, surface area*
  - *Concentration size resolved or within certain (e.g. “respirable”) range*
  - *Question of cost*
  - *Part of NANODEVICE project: cost reduction for existing techniques*
- **Differentiation against ambient background aerosol on basis of size alone remains problematic**
  - *Possible technically to get around it by differential diagnostic tricks*
  - *Not a solution for monitoring*
  - *Part of NANODEVICE project: material or function specific techniques*
- ***Particle chemical composition: sampling & off-line analysis***
- ***Particle morphology: sampling & off-line analysis (TEM, SEM)***

Ambient background aerosols

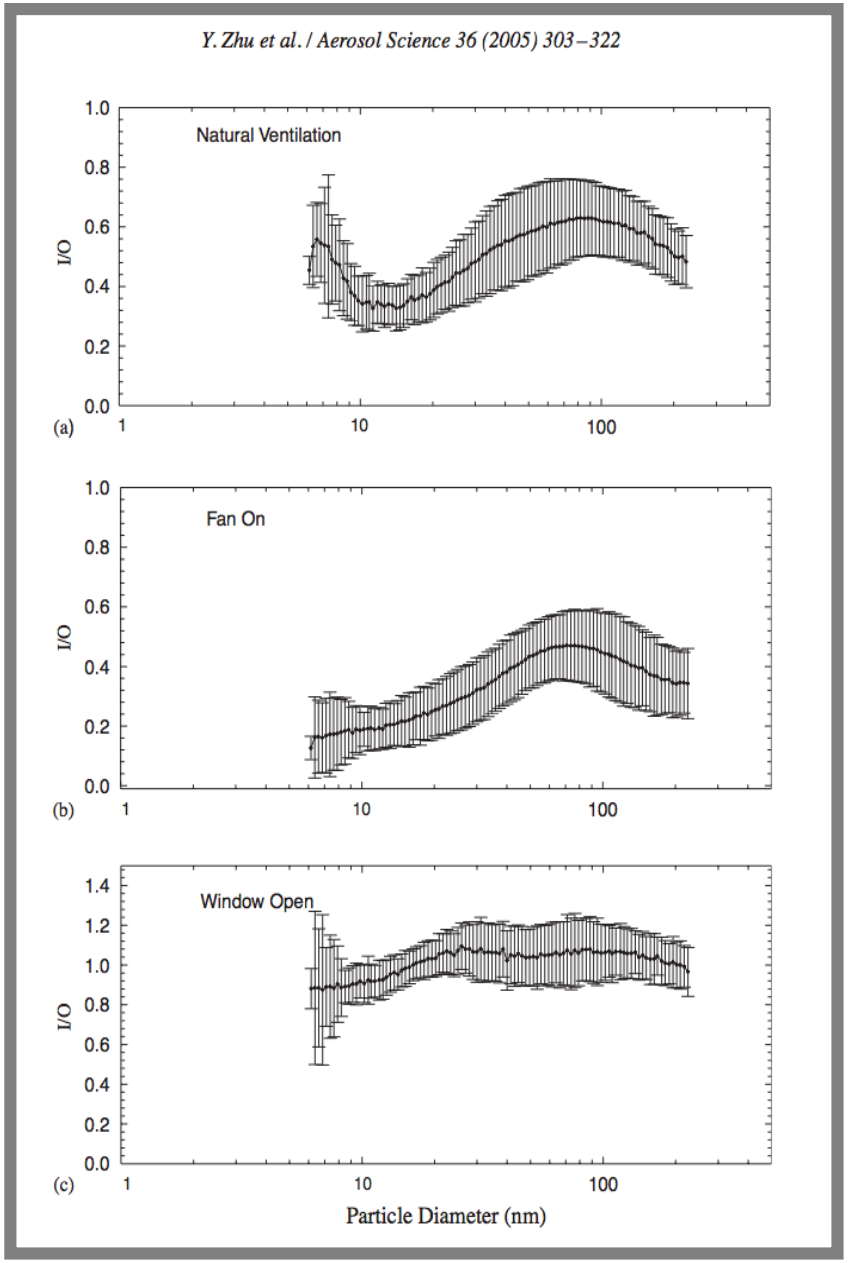
Indoor/outdoor concentration ratios vs. Size

(here: for a residential environment)



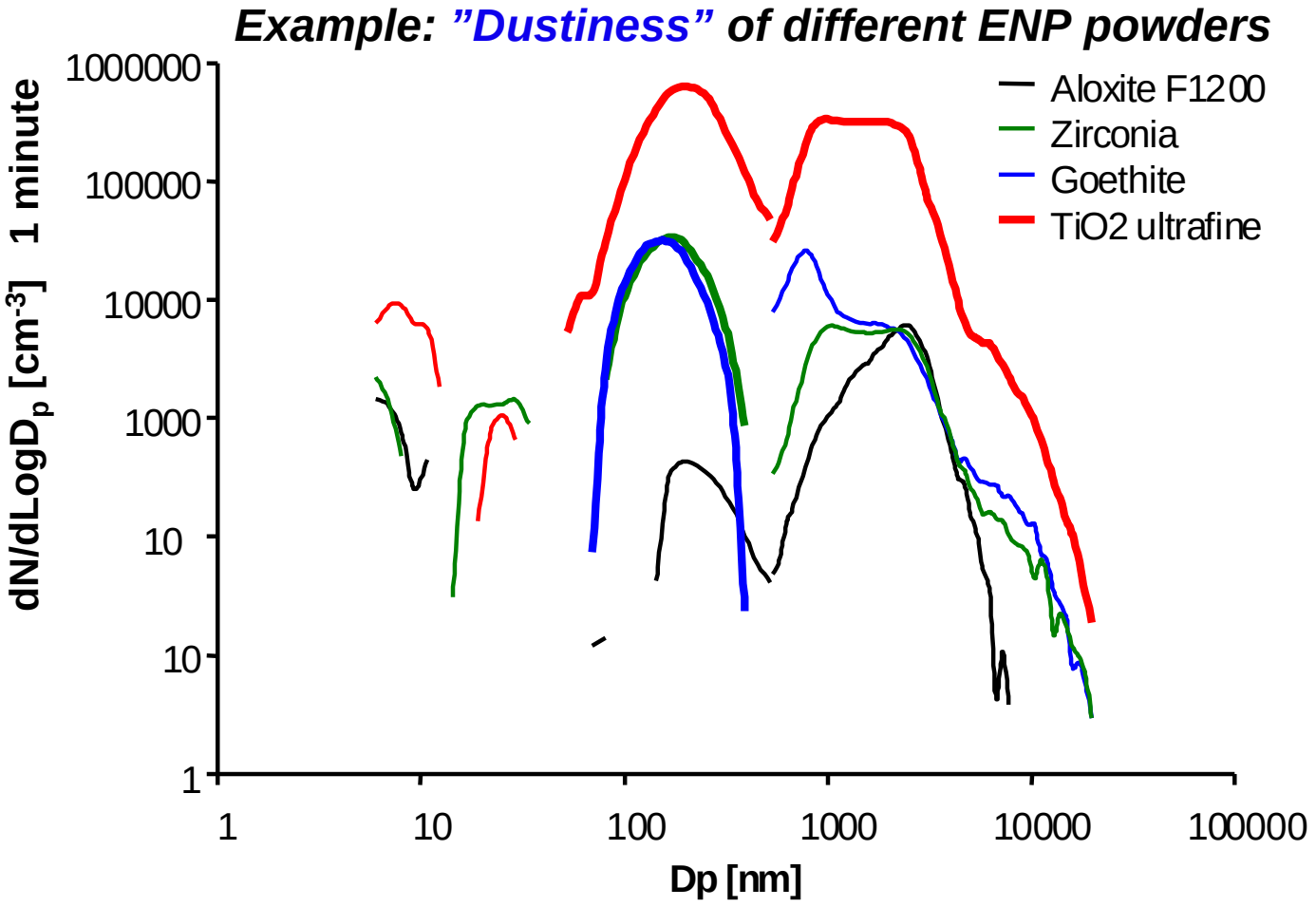
Typical size distribution of diesel aerosol

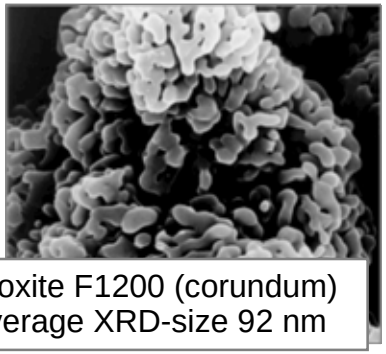
(an important constituent of environmental aerosols)



Courtesy L. Morawska

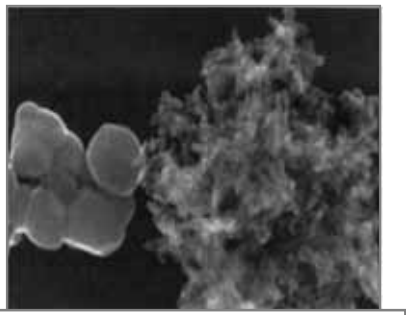
Large variability also of industrial NP sources





Aloxite F1200 (corundum)
average XRD-size 92 nm

granulated zirconia
averg. XRD-size 27 nm



Highly aggregated "free" TiO_2
average XRD-size = 19 nm

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FOR THE WORKING ENVIRONMENT

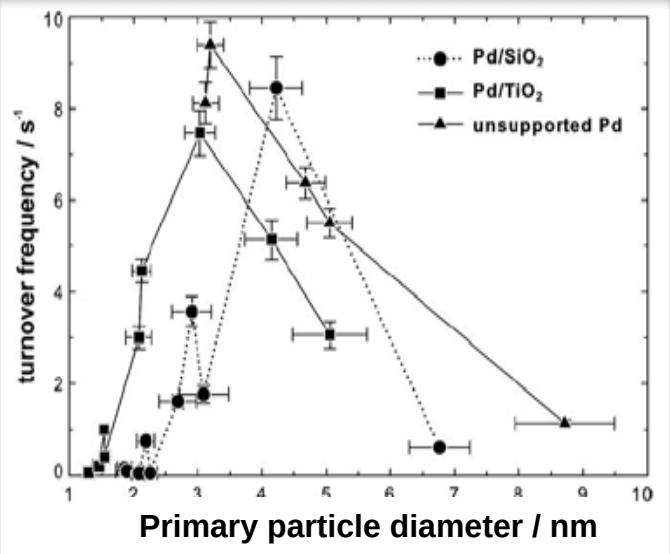
Schneider and Jensen, Ann. Occ. Hyg. 52 (2008)
Jensen et al. J. Nanopart. Res. 11 (2009)

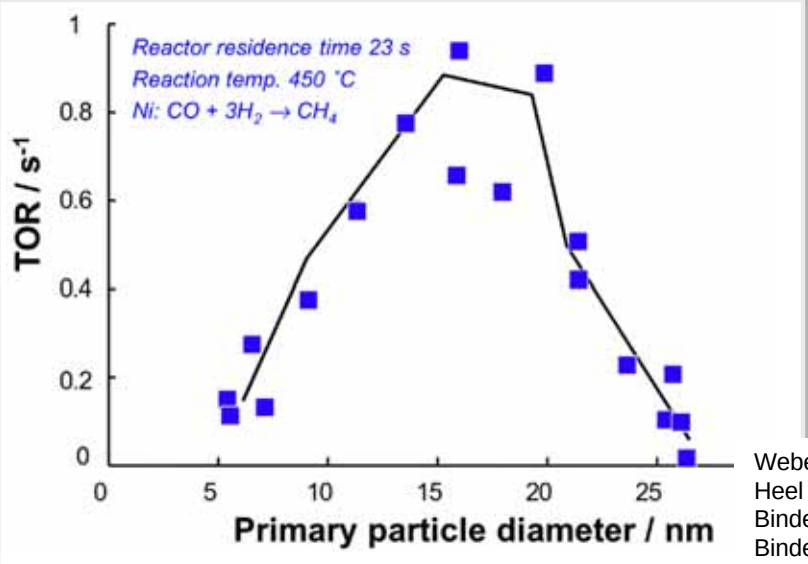
Need for exposure information specific to material, function and morphology

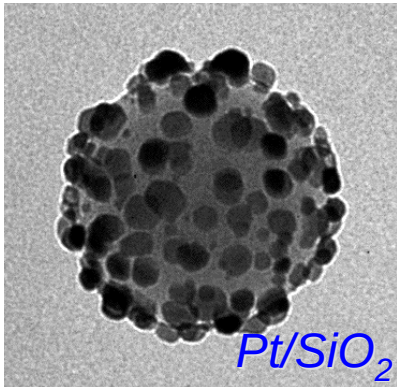
- **Direct measurement of nanoaerosol size and concentration masked by background**
- **Chemical composition/concentration not rapidly accessible (off-line sampling and analysis)**
- **Chemical composition/concentration not sufficient for assessment**
  - ***Particle "functionality" ≠ particle concentration***
  - *Examples on following slides*
  - ***Particle functionality with regard to specific biological effects*** *??*

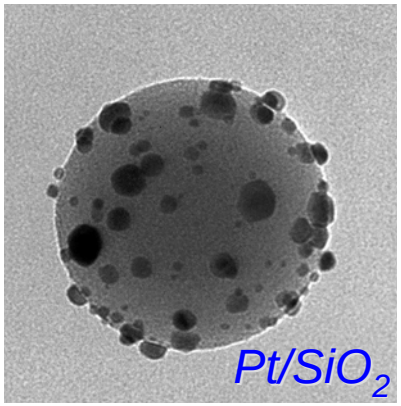
Structure vs. (catalytic) function of ENP

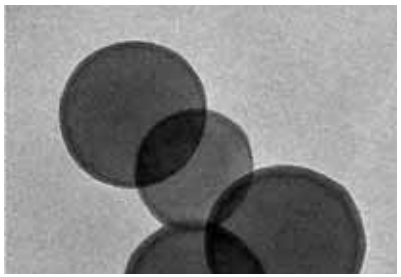
Catalyst function (turn-over frequency)

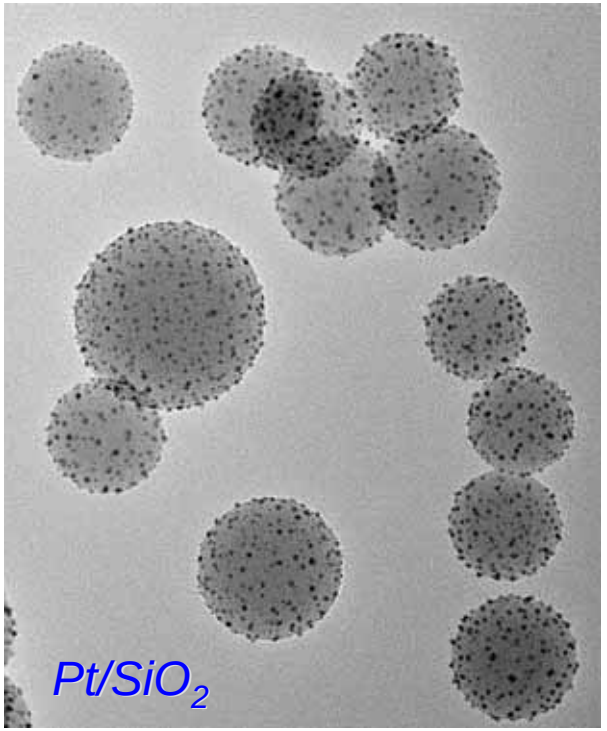


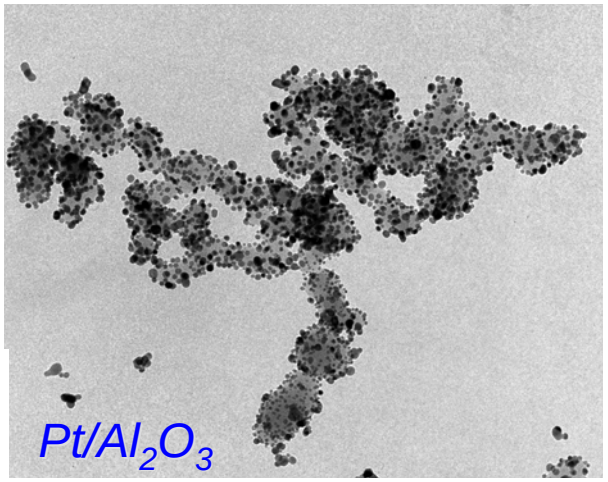








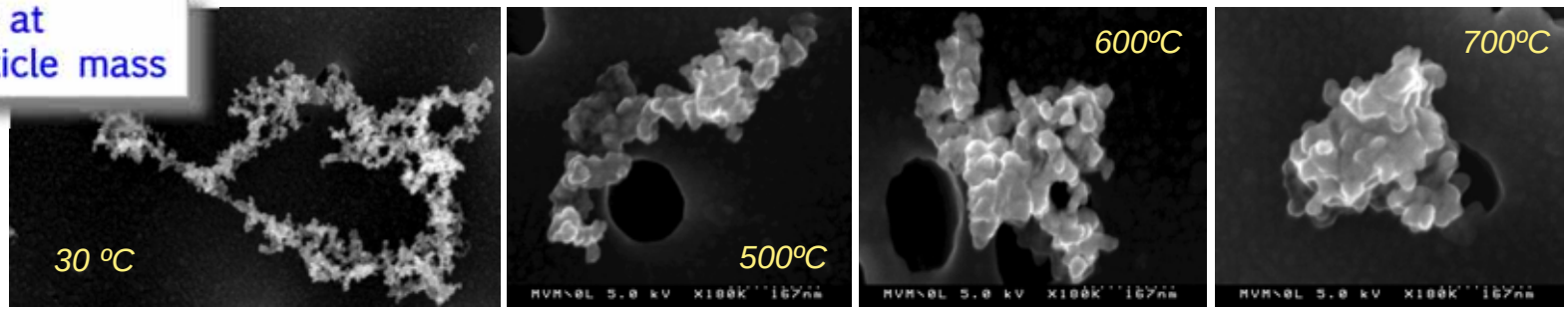




Weber et al. (2003, 2006) J. Nanoparticle Res.
Heel & Kasper (2005) Aerosol Sci. & Technol.
Binder et al. (2007) Chem. Vapor Deposition
Binder et al. (2009) J. Catalysis

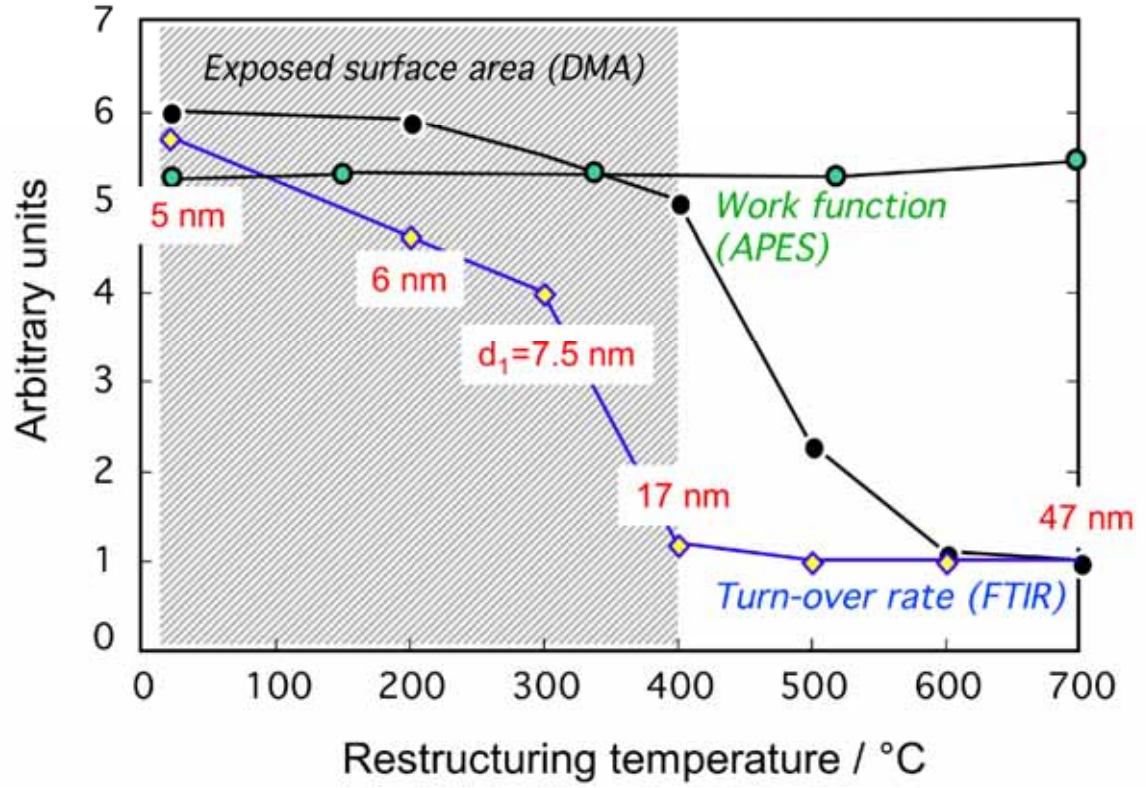
Structural change vs. catalytic activity

Restructuring at constant particle mass



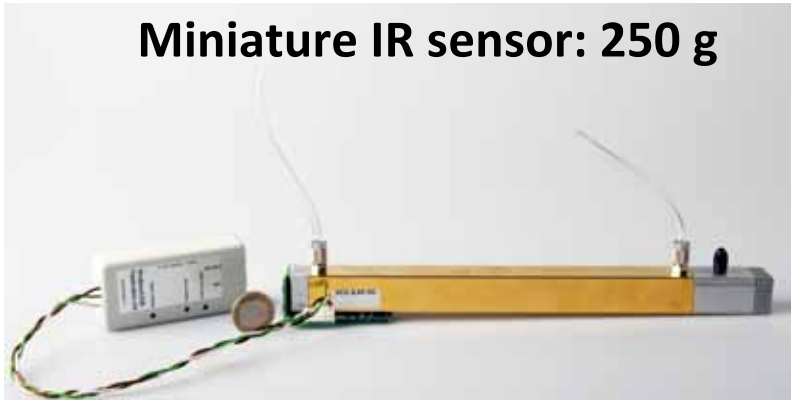
Activity vs. structure for constant aerosol mass

H_2 oxidation on unsupported Pt



Weber et al. (2003) J. Nanoparticle Res.

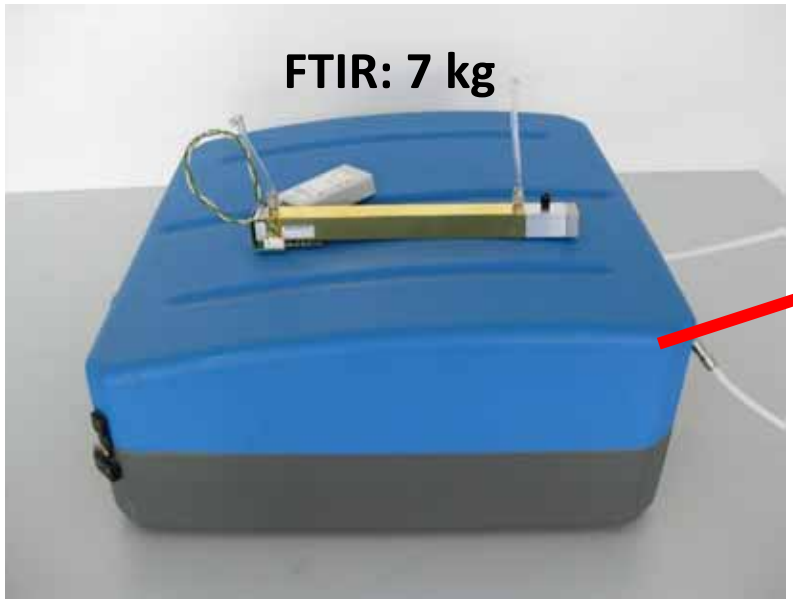
Catalytic Activity Aerosol Monitor (CAAM)

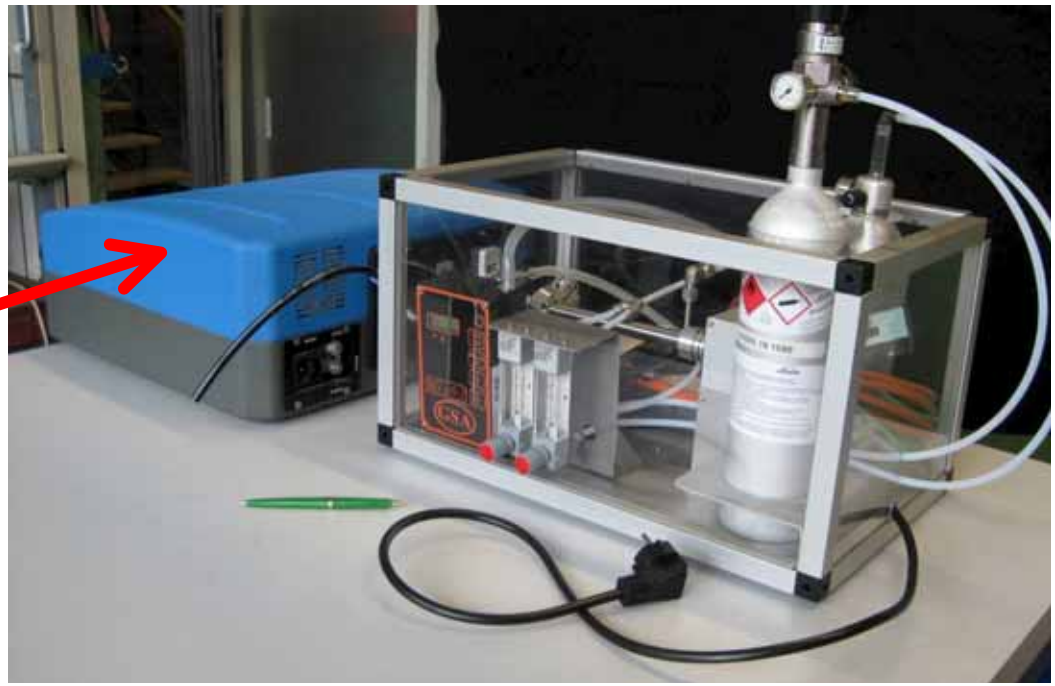


		Detection Limit [1)]	Sampling time [2)]
Pd	C_2H_4 hydration	2 ng	< 1 s
Ni	CO methanisation	1.6 µg	< 10 s
Pt	H_2 oxidation	2.2 µg	< 14 s
Fe_2O_3	CO oxidation	28 µg	< 3 min

[1)] assuming 10 ppm detection limit for FTIR

[2)] assuming 1 mg/m^3 concentration and 10 L/min sampling rate





Neubauer et al. (2011) Journal of Physics
Neubauer et al. (2012) J. Occup. Hyghiene

A suitable metric for “catalytic activity” in the context of risk assessment

- ***Instead of activity per mass or surface area of catalyst***
  Turn-Over Frequency [s^{-1}] ***CAAM measures activity per m^3 of air***

- ***Another challenge:***
  Connect reactivity of NP in aerosol phase with in-vitro biological reactivity

Conclusions

- **What we can measure today, we can measure very accurately, but the information is insufficient for assessment**
- **Critical NP properties not accessible in real time, at best with laborious off-line techniques**
- **Need for more material/function specific information (Also need more biological effects related info !) Major effort from both toxicology and aerosol science**
- **As we are designing more and more intelligent nanomaterials, our measurement and assessment techniques should be at least as intelligent as the particles !**