

“Toxicological and Environmental Issues of Engineered Inorganic Nanoparticles”

Isaac Ojea Jiménez

Outline

- *Introduction*
- *Fate of NPs*
- *Common Interferences*
- *Aggregation*
- *Protein Corona*
- *Biodegradation*
- *Conclusions*

ICN: <http://www.nanocat.org>

NANOWIKI: www.nanowiki.info

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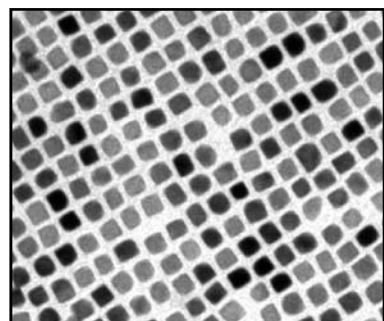
Lorena García

Zoë Megson

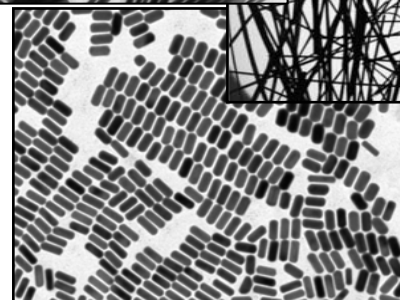
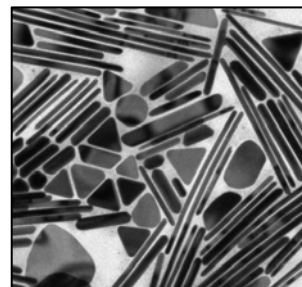
Edgar Gonzalez



Size, Shape, Composition and Surface Coating Control by design



Au spheres (4 – 40 nm), rods,
cubic boxes, tubes
Ag spheres, rods, cubes
Pt spheres, multipods, cubes
Pd cubic boxes

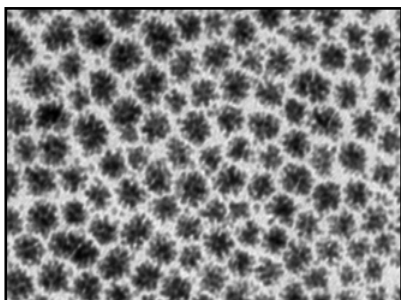
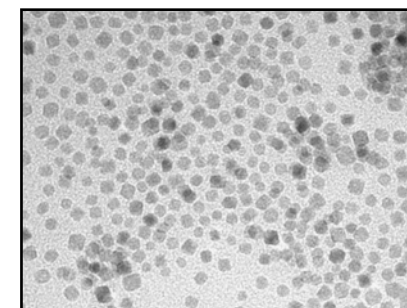
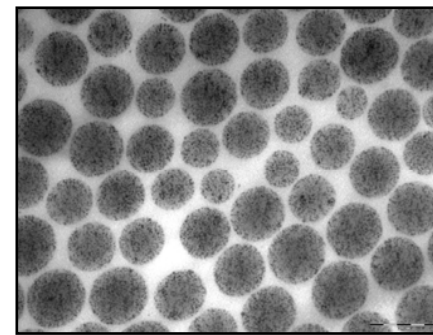
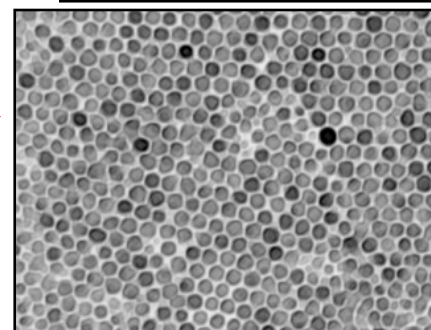


Fe spheres
 Fe_3O_4 spheres
 Fe_2O_3 spheres, hollow spheres

Co spheres, disks
CoO spheres, hollow spheres

CeO_2 spheres, belts
 TiO_2 spheres
ZnO spheres

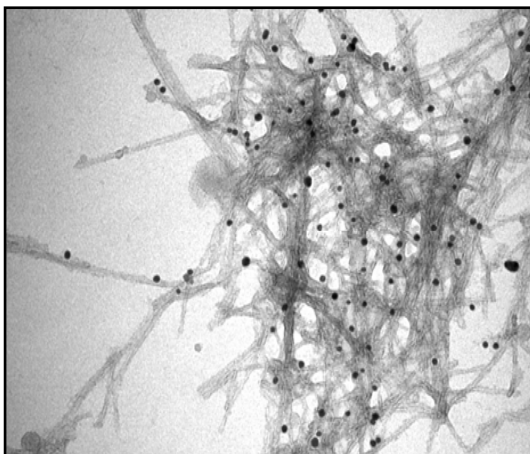
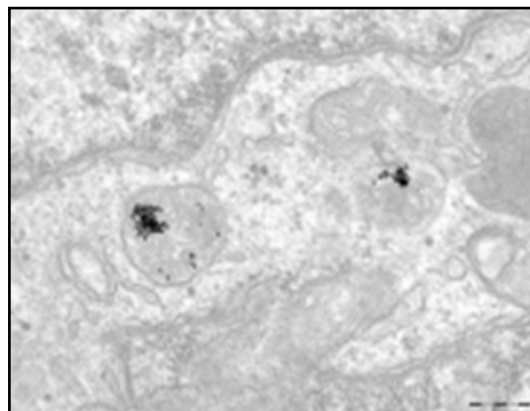
CoPt
Co-organic-Au



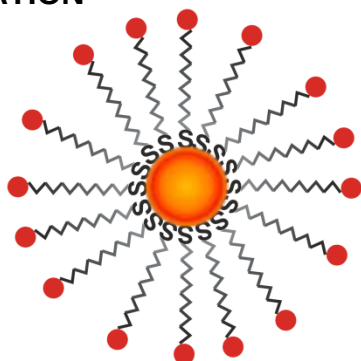
1 SYNTHESIS



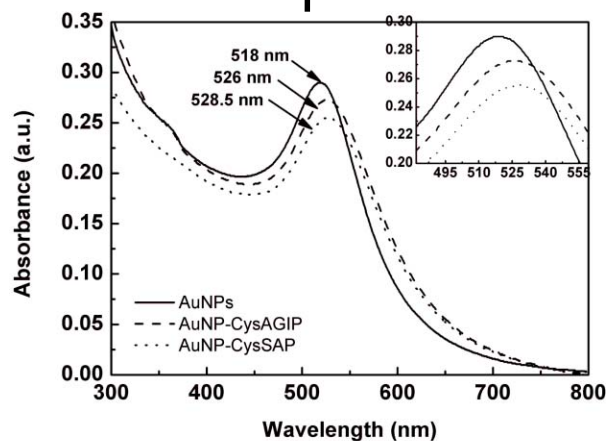
Characterization



2 CONJUGATION



Purification



CHARACTERIZATION

APPLICATIONS

4

Activation of Immune System

Photoablation of Protein Deposits

Drug Delivery (*cis platin*)

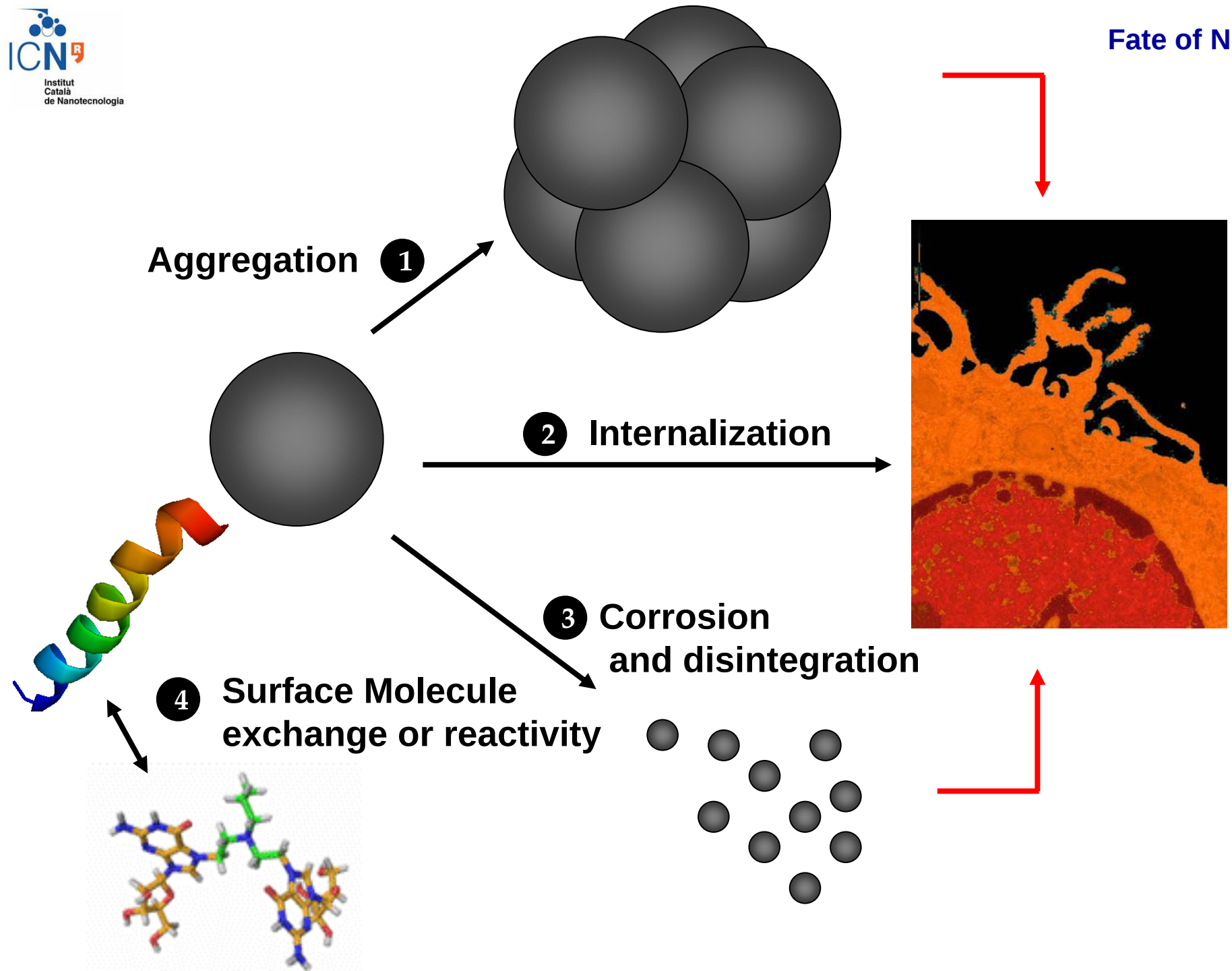
Vaccination

Environmental Remediation

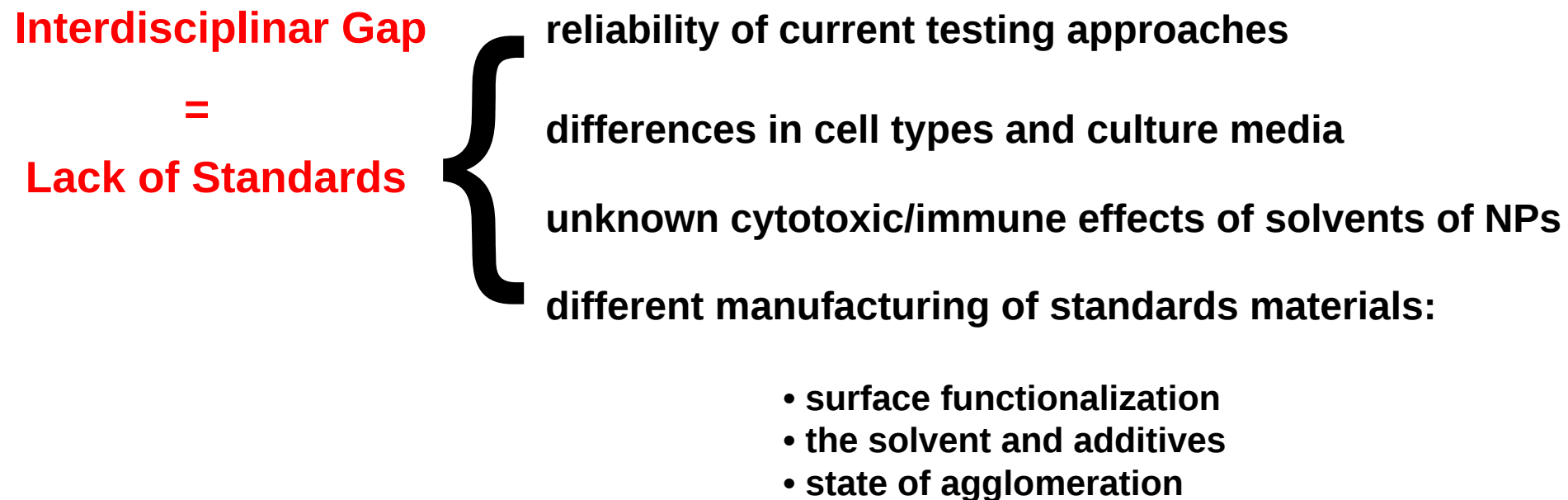
Textile

Cosmetics (TiO₂)

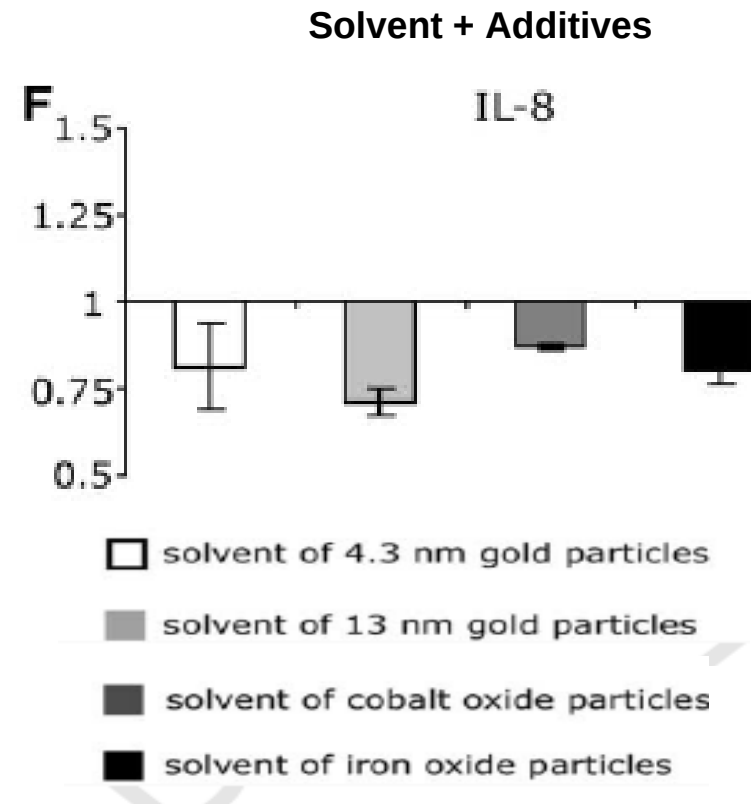
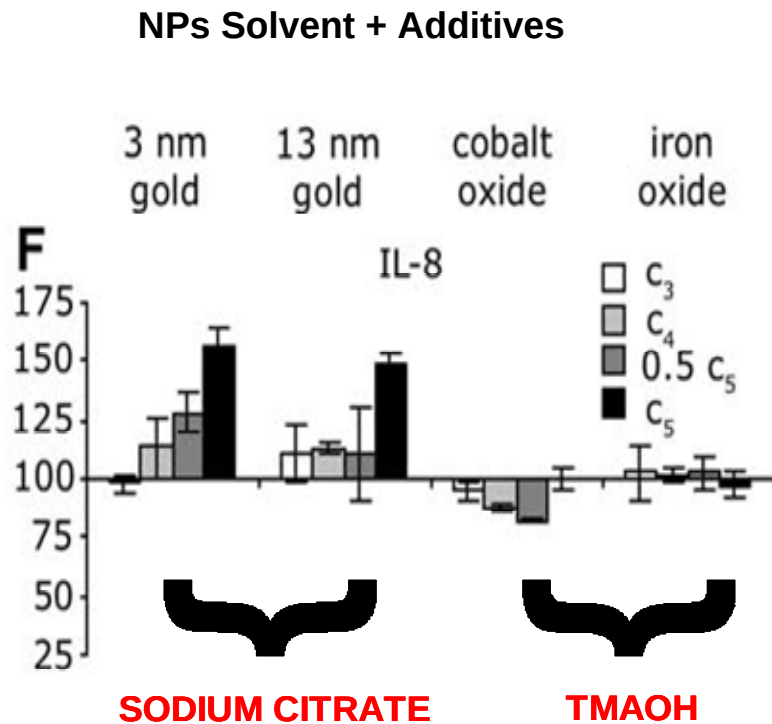
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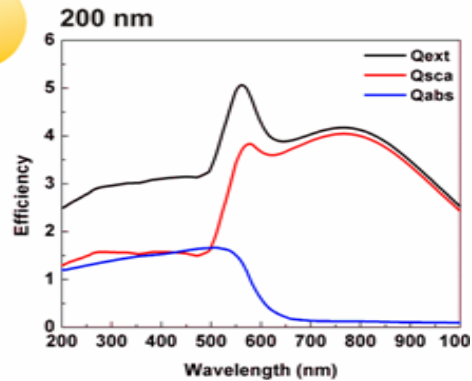
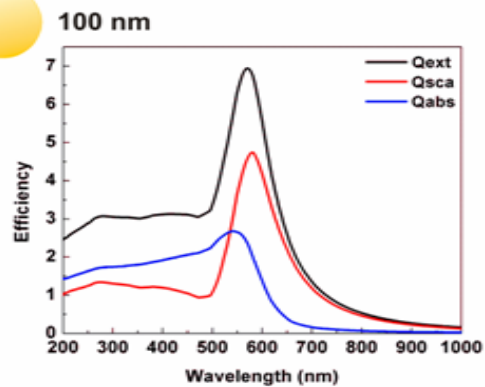
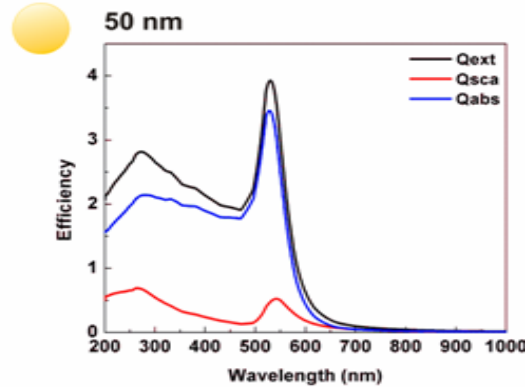
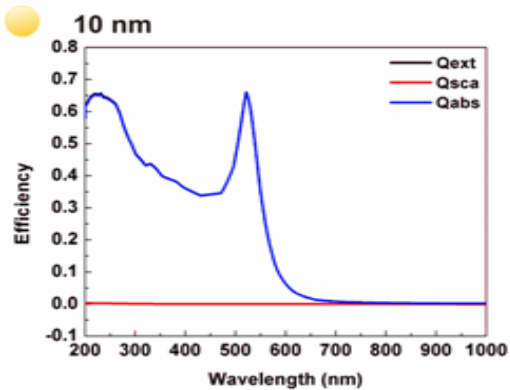
It is well known that colloidal particles are systems out of chemical equilibrium, in a metastable phase. Their final fate is the **desintegration** or **agglomeration** towards more stable phases. Thus, characterization of NPs **1) once produced**, **2) as used** (administered or other mechanisms of human exposure) and **3) after using** is required since physico-chemical changes occur while in solution, what may have a significant impact on observed toxicological responses that go far from the classical paradigms of toxicology.



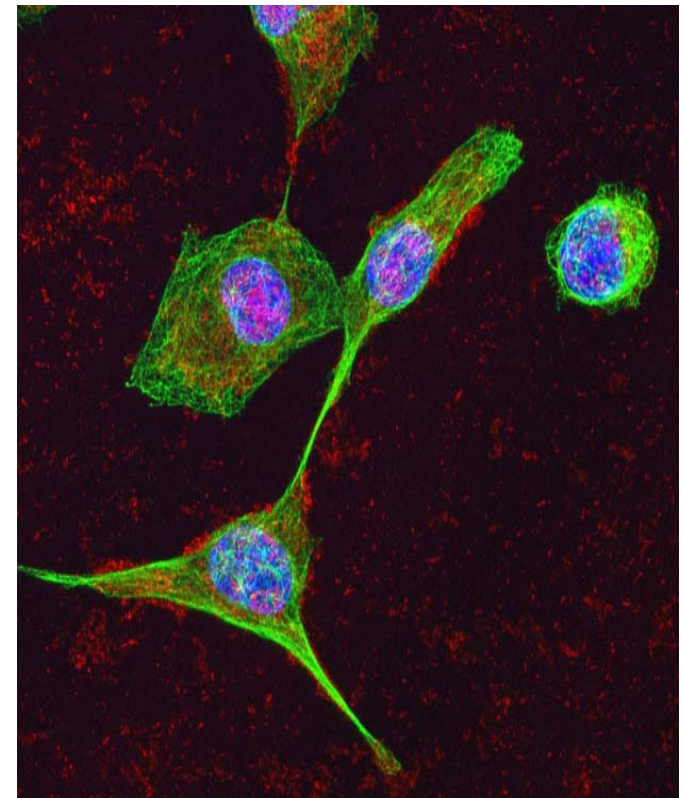
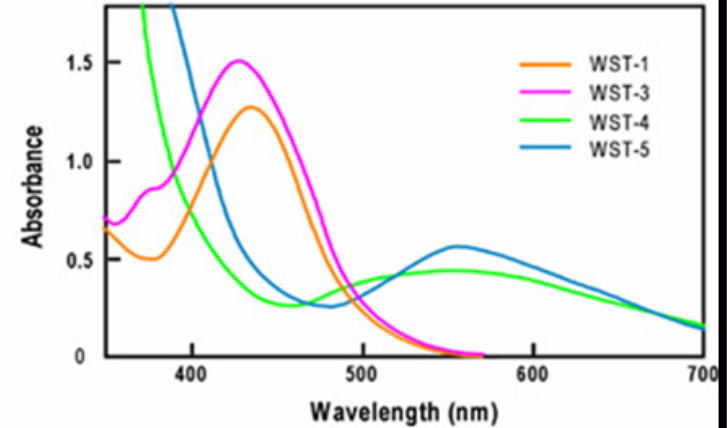
Study of immunomodulatory effects: Cytokine secretion by NHBE cells



SPR peak of Au NPs of different sizes

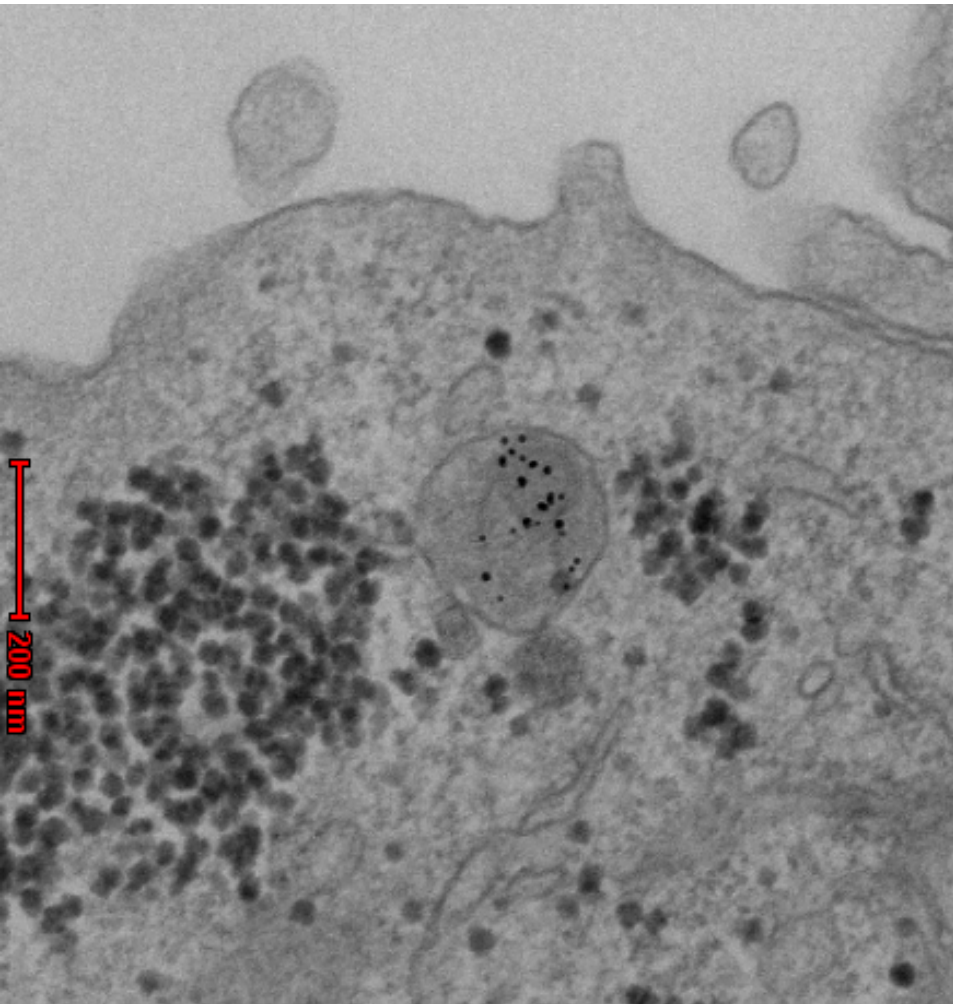


Absorption Spectra of WST Formazan Dyes

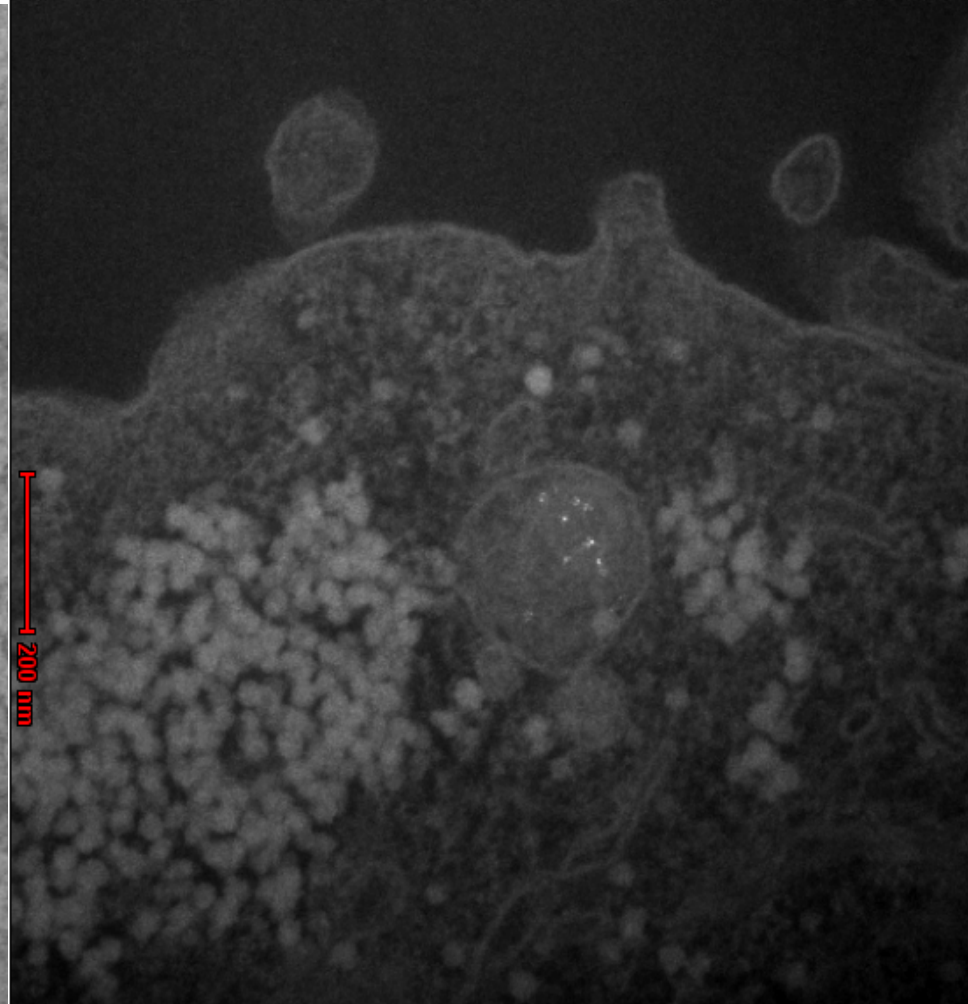


AuNP INTERNALIZATION IN HeLa

Bright Field

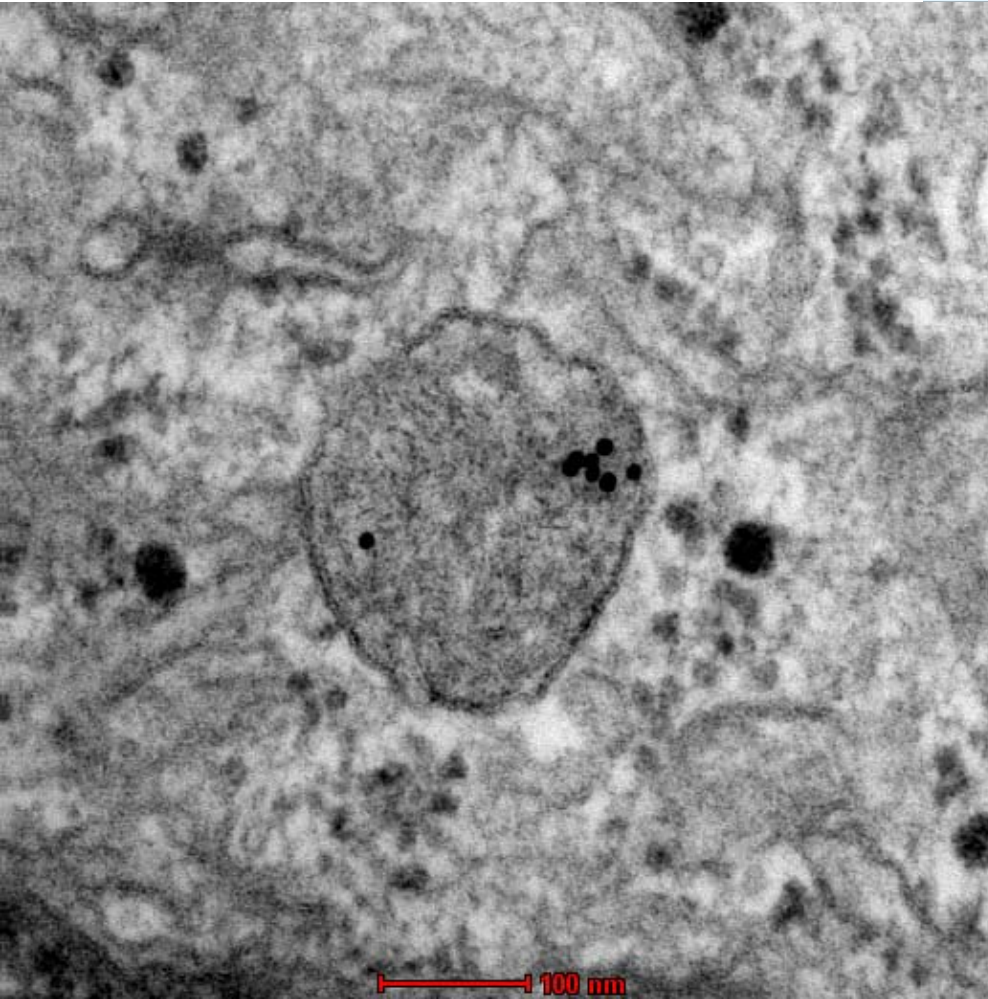


Dark Field

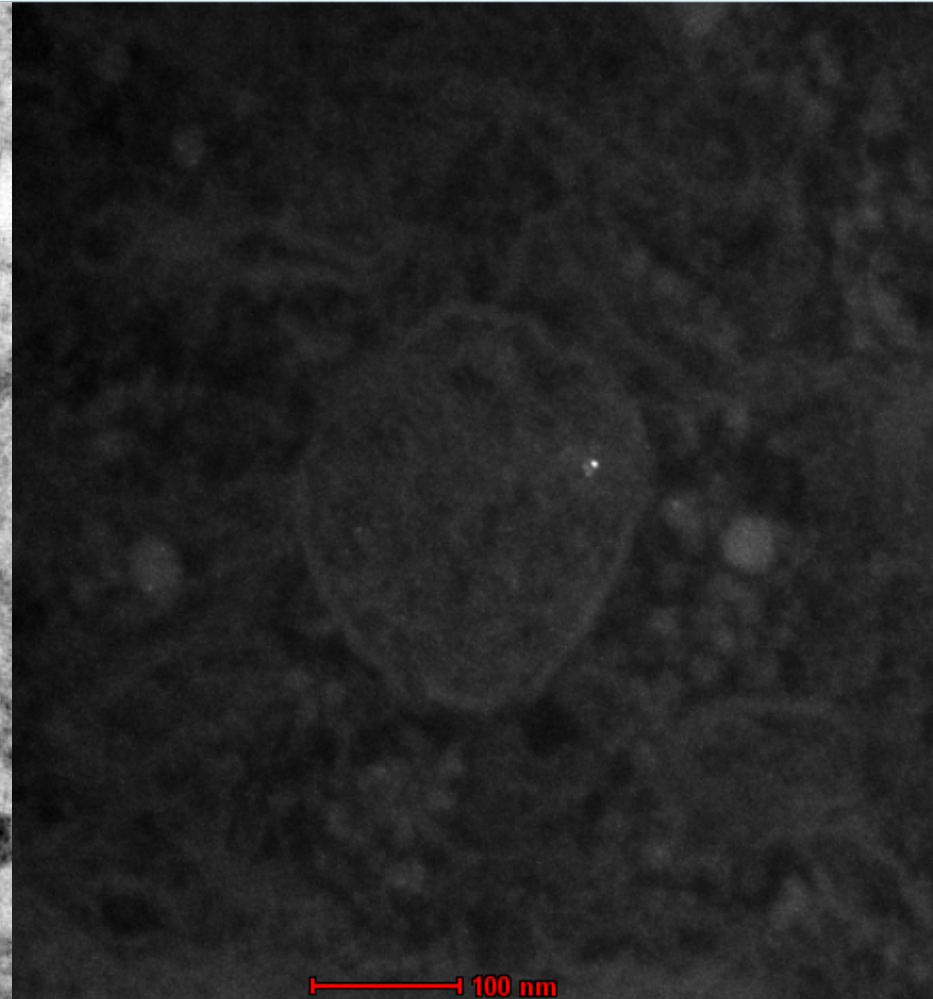


AuNP INTERNALIZATION IN HeLa

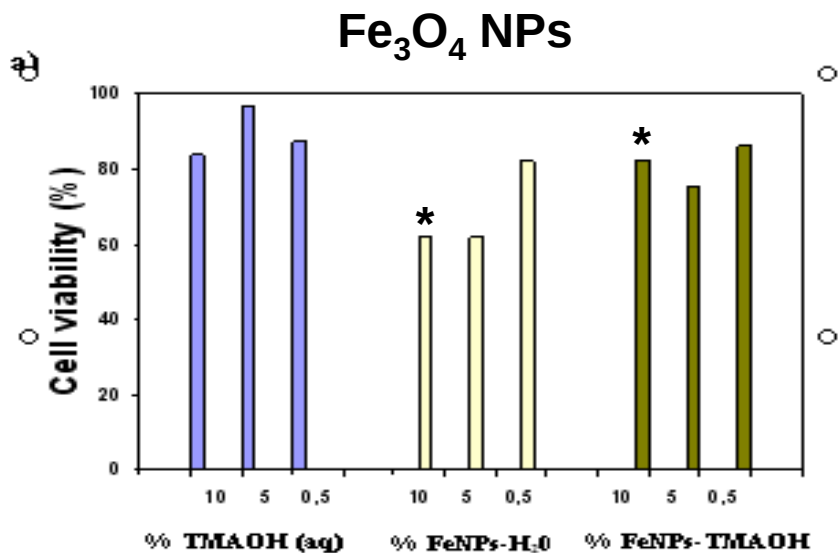
Bright Field



Dark Field

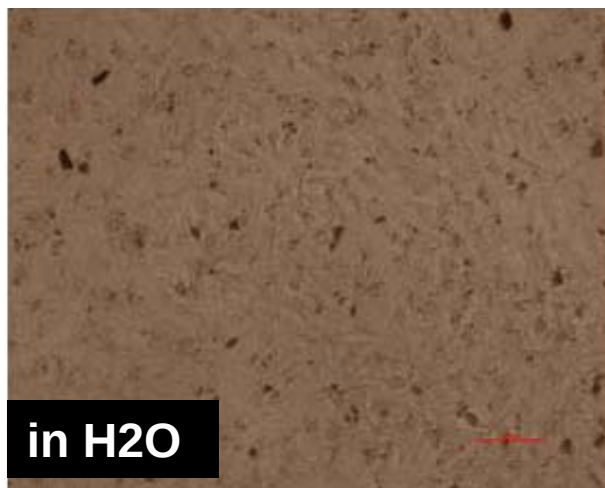


Viability tests in HeLa cells (MTT assay)



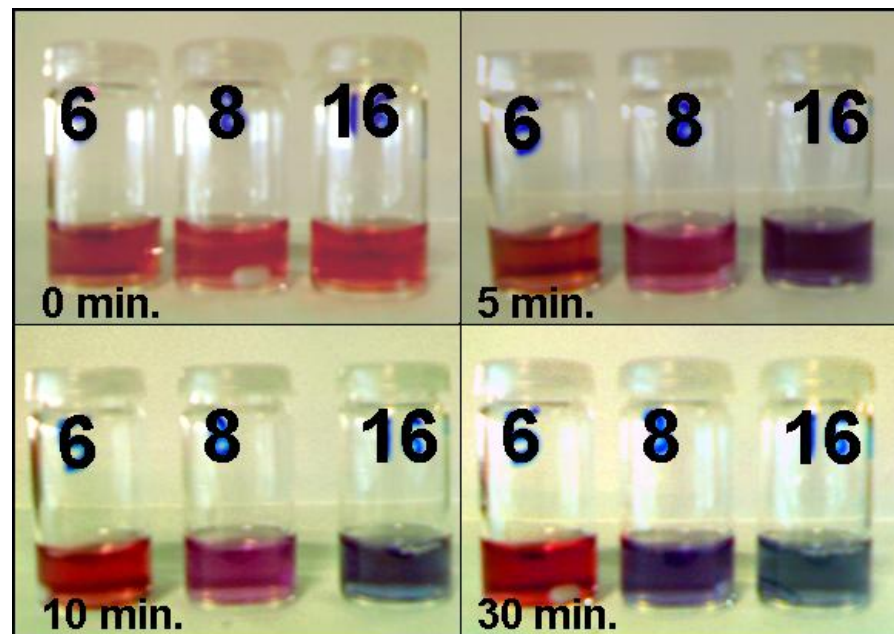
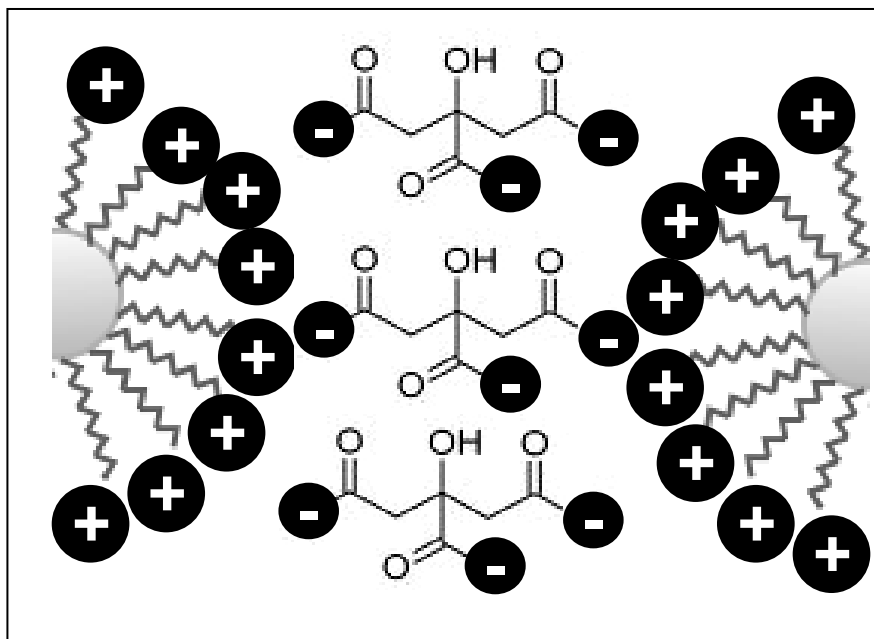
- stability of the nanoparticles suspension, beyond the chemical nature of the sample, has a strong effect on cell viability

- very small NPs can penetrate and travel without causing effects but **aggregates** can accumulate in some structures and **alter their environment and biodistribution**



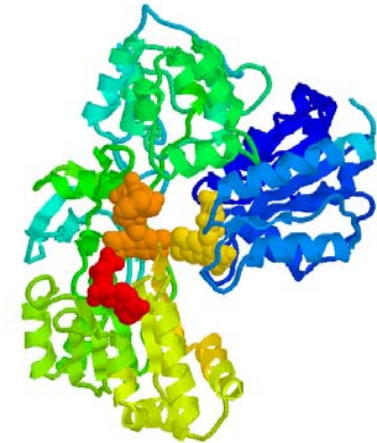
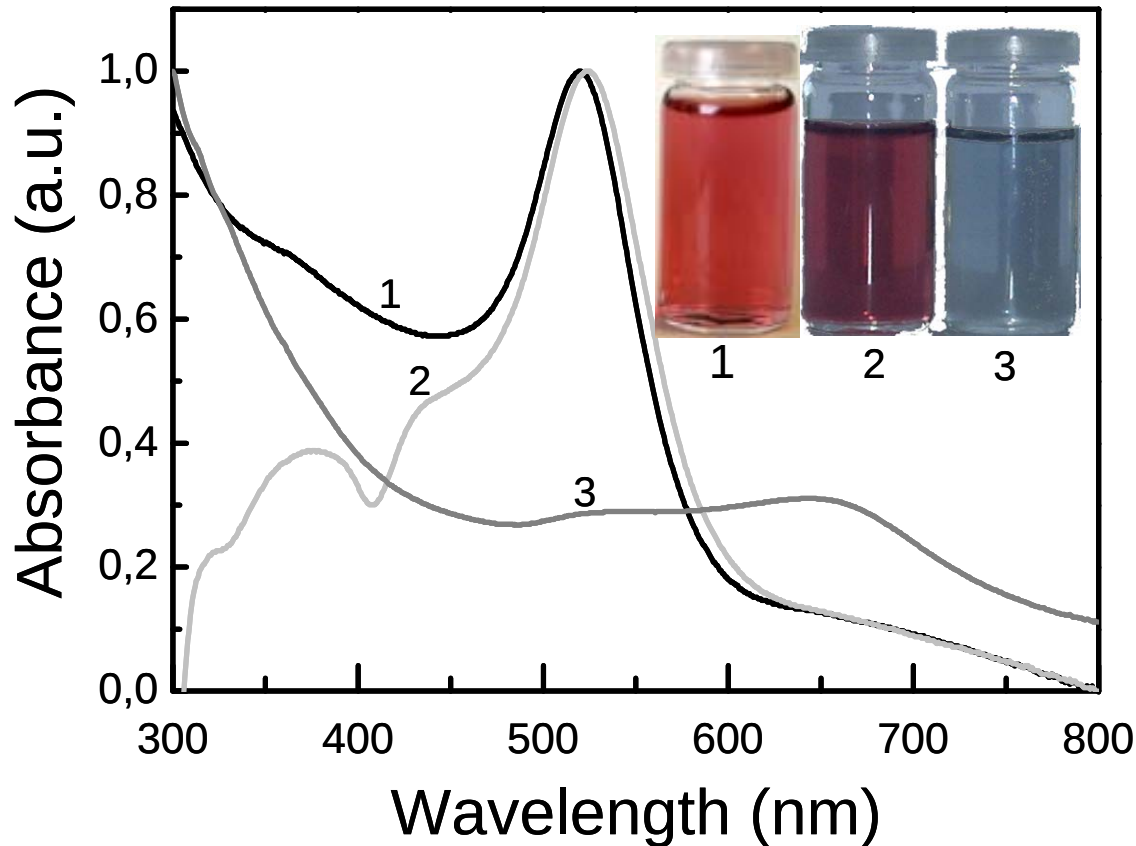
Au NP – **citrate** (stable)
 +
 CIPGNVG-PEG-NH₃⁺ (stable)

} unstable NPs



Σ WEAK INTERACTIONS = SIZE DEPENDING STRONG BONDS

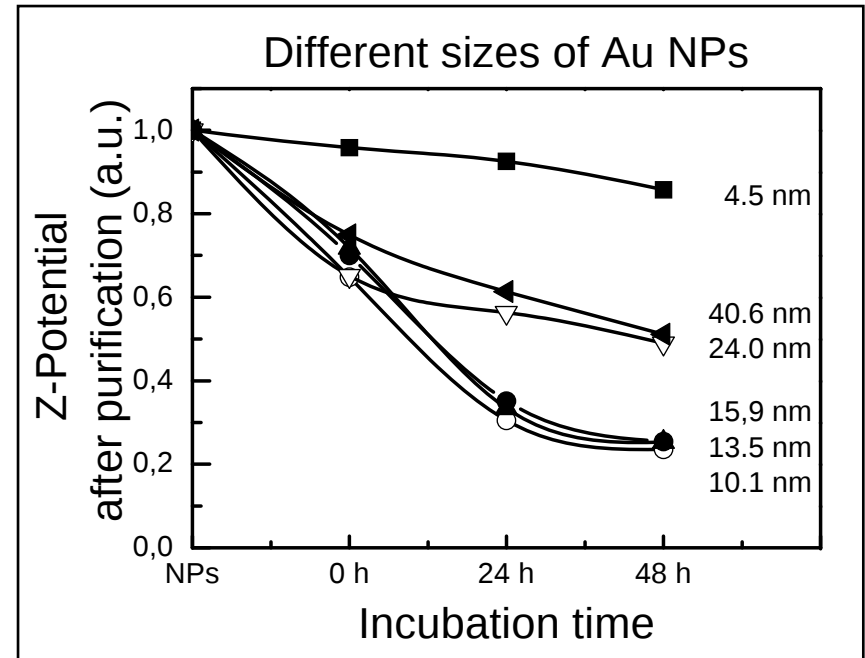
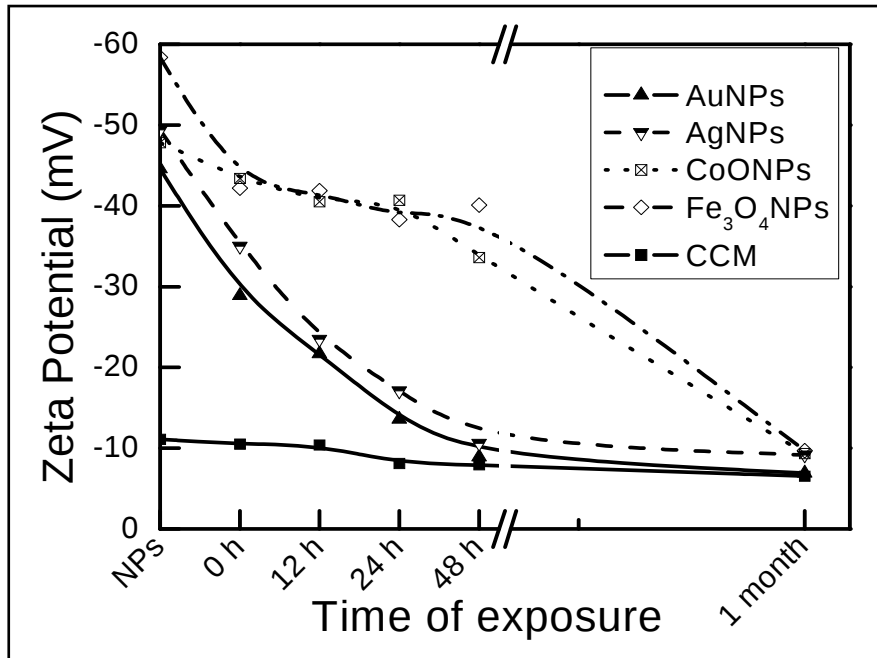
AuNPs before and after exposure to DMEM and (DMEM + serum)



- Available inorganic NP surfaces are immediately coated with biomolecules in a non-specific way when they are in contact with biological media.

1) AuNPs in sodium citrate, 2) AuNPs in DMEM + serum, 3) AuNPs in DMEM

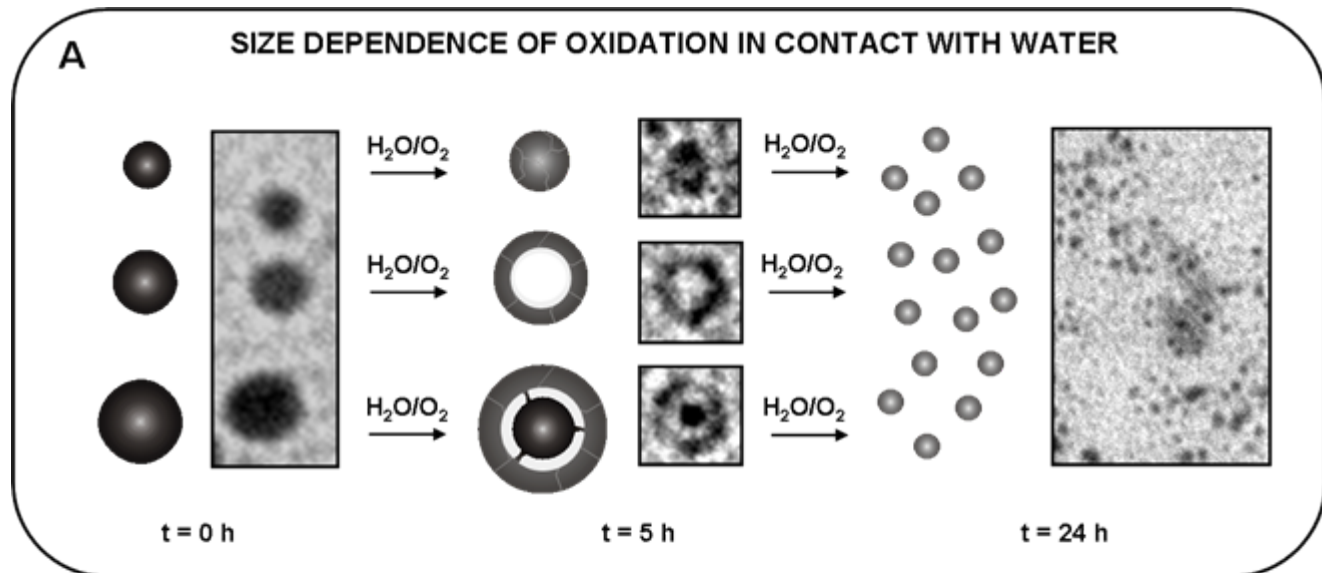
THE NANOPARTICLE PROTEIN CORONA: TIME DEPENDENCE



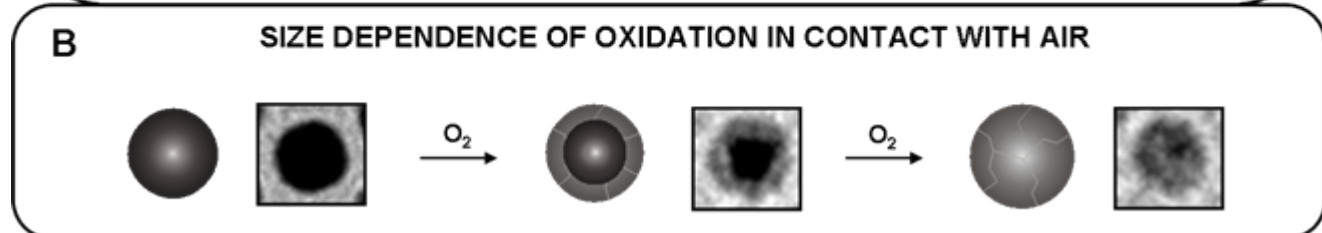
Vroman Effect At The Nanoparticle Surface

Co NP 8 nm in different environments

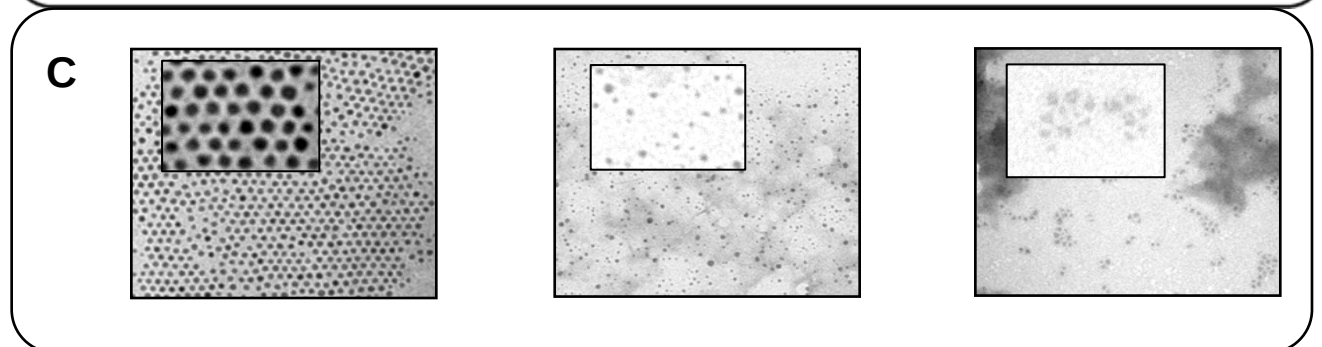
aqueous
media



air

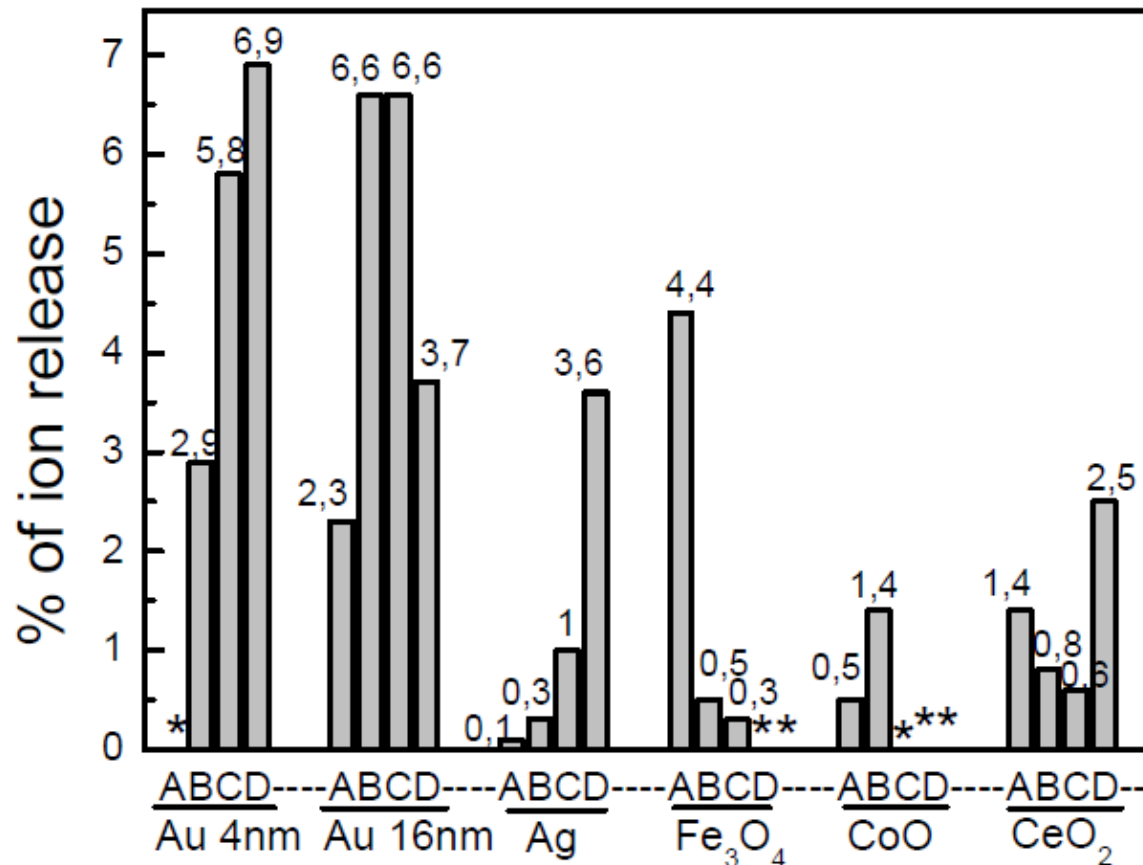


CCM



Biodegradation often is more aggressive than degradation

Biodegradation often is more aggressive than chemical degradation



A = NPs in their solvent

B = NPs in CCM

C = NPs in CCM + dialysis

D = NPs incubated with cells

Concluding Remarks

- NPs are very unstable and sticky, and tend to aggregate very easy with all types of surfaces or disintegrate in other minor entities
- Aggregation is not only a change of the effective size but also results in non-comparable dosis and mechanisms of exposure
- Analytical characterization of nanoparticles in the biological context is yet not fully understood, since there is a crucial need of standards (NPs and methodologies)
- Although the present studies in general rule out short-term effects of NPs in health, further studies are needed for longer terms.

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Series on the Safety of Manufactured Nanomaterials

**WORKING PARTY ON MANUFACTURED NANOMATERIALS:
LIST OF MANUFACTURED NANOMATERIALS AND LIST OF
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Environment Directorate
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
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