Direct and indirect toxic mechanism of nanoparticles. Evidence and models.

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Introduction

Environmental emissions and exposure remain largely unknown!

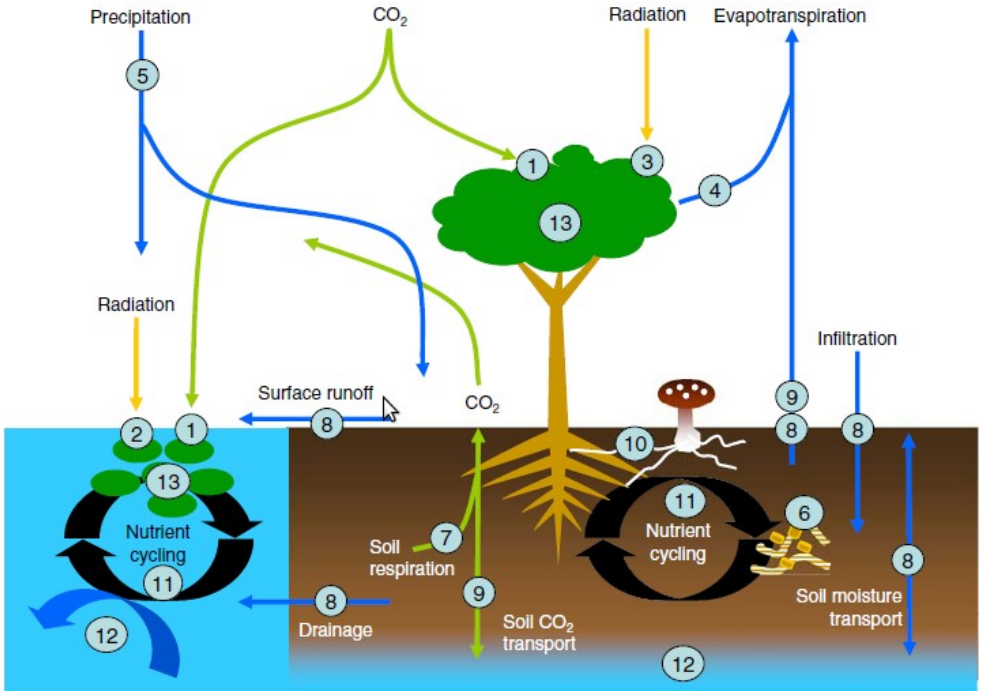
* Mueller and Nowack, ES&T (2008)
(models) in Switzerland surface water.
CNT : 6 Kg/year,
Nano-Ag : 620 kg/year,
NanoTiO2 : 47300 Kg/year gives PEC of 0.016 mg/l.

* Park et al. (2008) gives for CeO_2 (exp. And models) 0.2 g/year (0.07 % of the PM exposure)

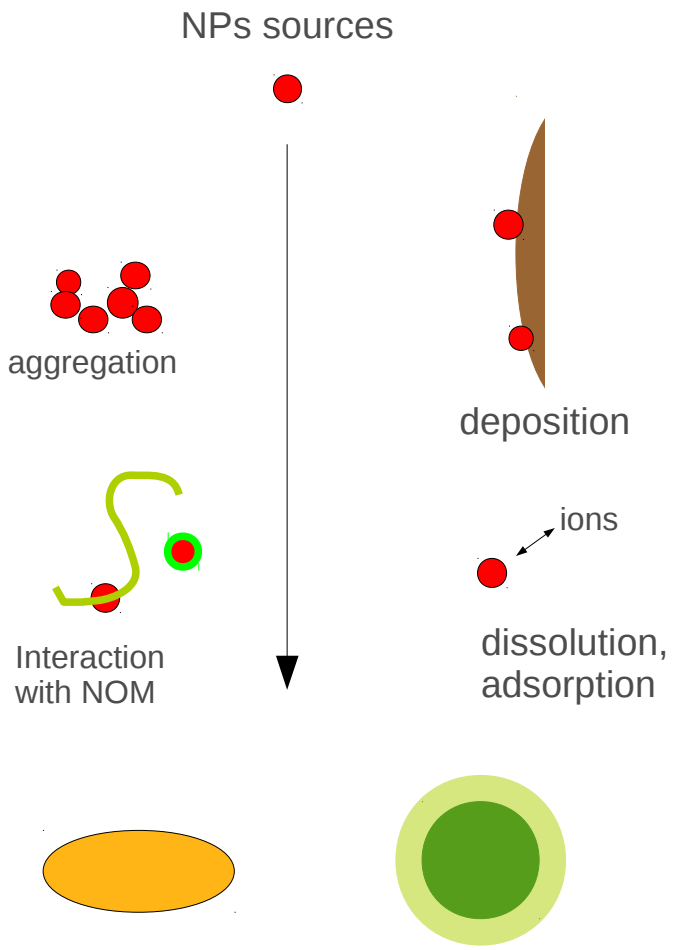
Environmental accumulation in sediments can be significant.
Koelmans, Nowack and Wiesner, Environ. Pollut. (2009) factors of 1000-10000 are realistic. Calculated up to 4.10^6 for carbonaceous ENP.

Introduction

Simplified scheme of some terrestrial and aquatic ecosystem processes (Navarro et al., Ecotoxicology **2008**).



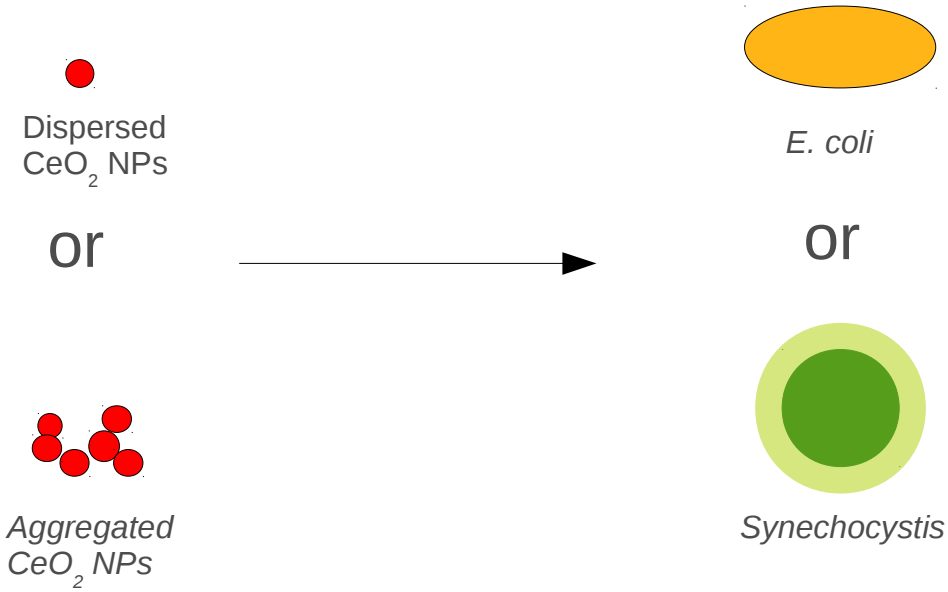
NPs interact with a complex ecosystem containing multiple and diverse organisms (bacteria, algae, fungi, plants...).



Modified NPs interacts with organisms

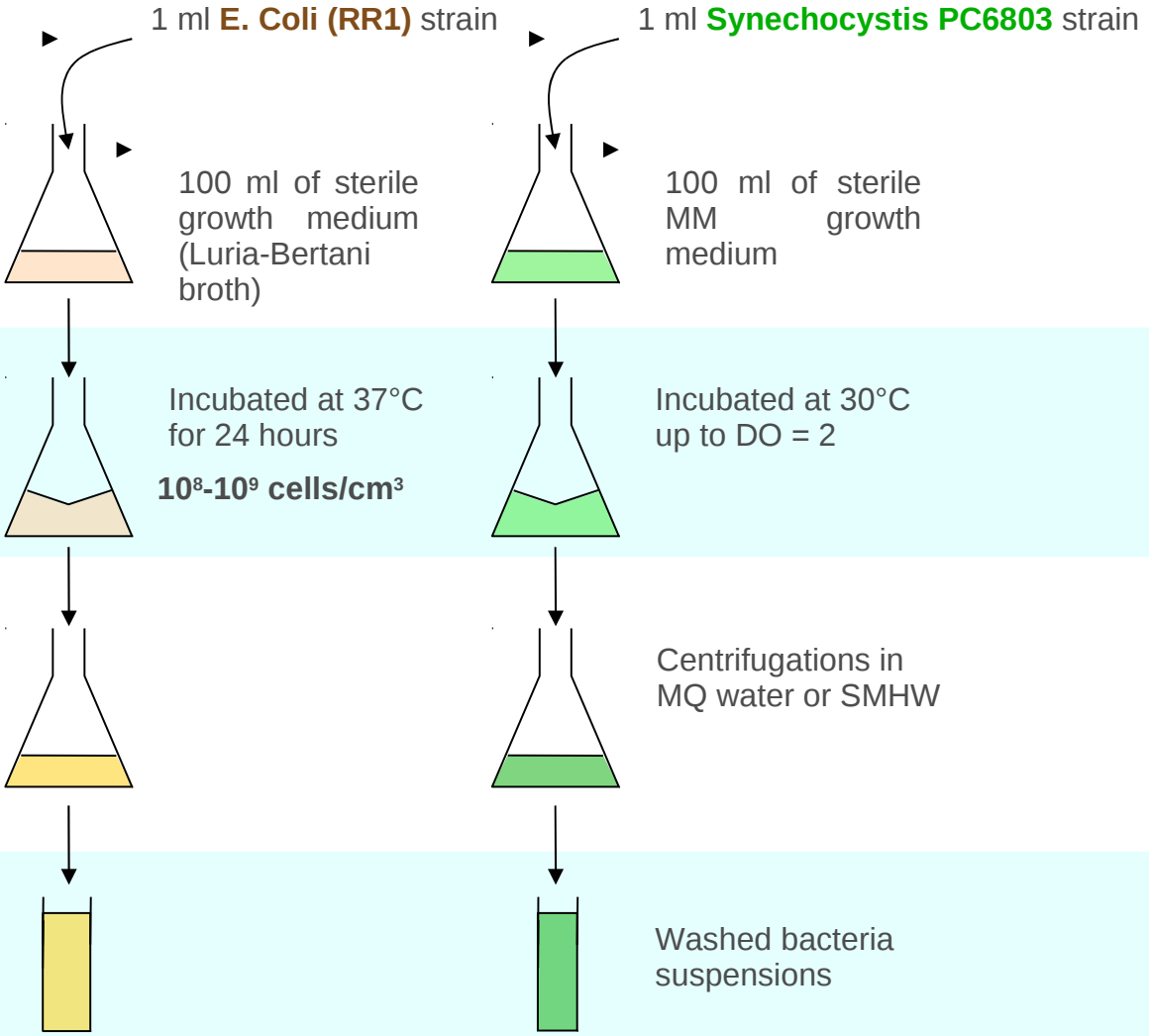
Introduction

Interaction of aggregated and dispersed CeO_2 NPs on *E. coli* or *Synechocystis.*



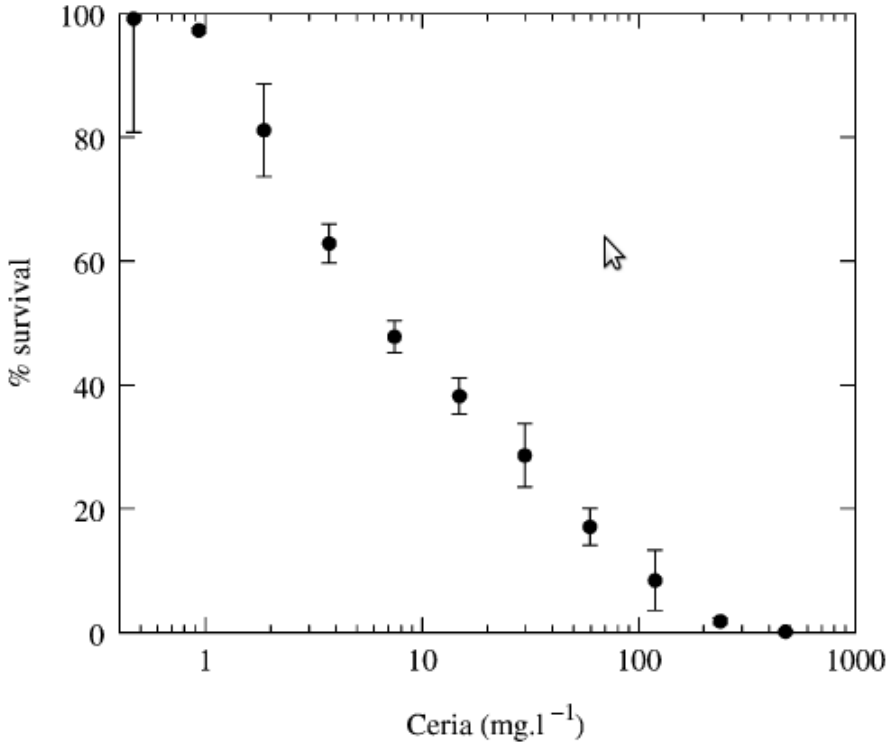
What is the toxicity and the mechanisms?

Contact protocols



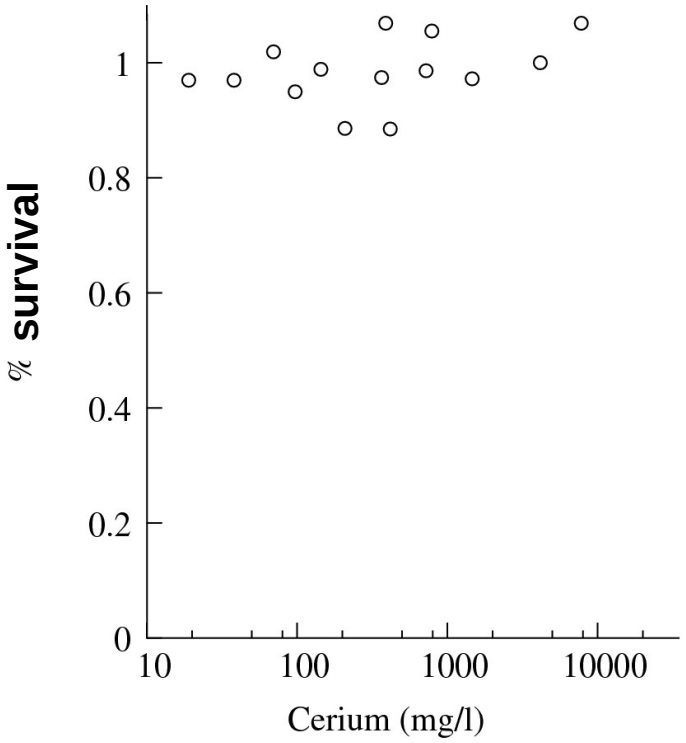
Interaction between CeO_2 NPs and *E. coli*

CeO_2 dispersed



Strong adsorption at the bacteria cell wall.
Clear dose response
LD50 < 10mg/l.

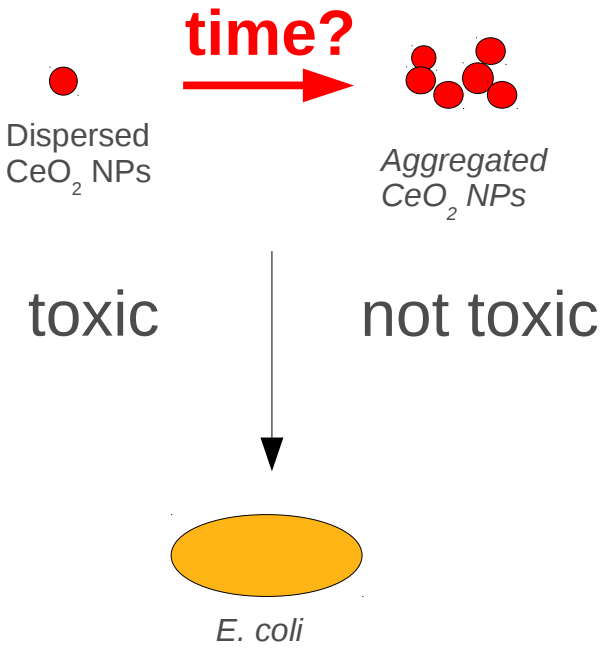
CeO_2 agregated



Strong reduction of the CeO_2 NP. No toxicity.

Thill et al., ES&T **2006,** Zeyons et al. Nanotoxicology accepted

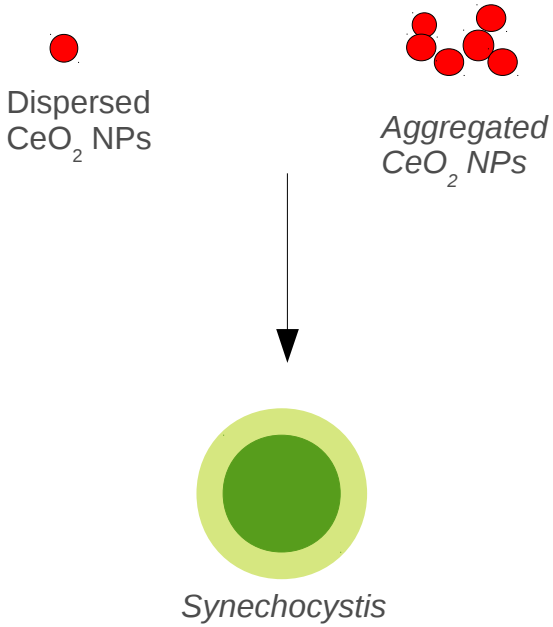
Two mechanisms



Close contact between NPs and cells required.
Only dispersed NPs are toxic

Thill et al. ES&T (2006), CeO_2
Lyon et Alvarez (2008), nC60
Battin et al. ES&T (2009), TiO_2

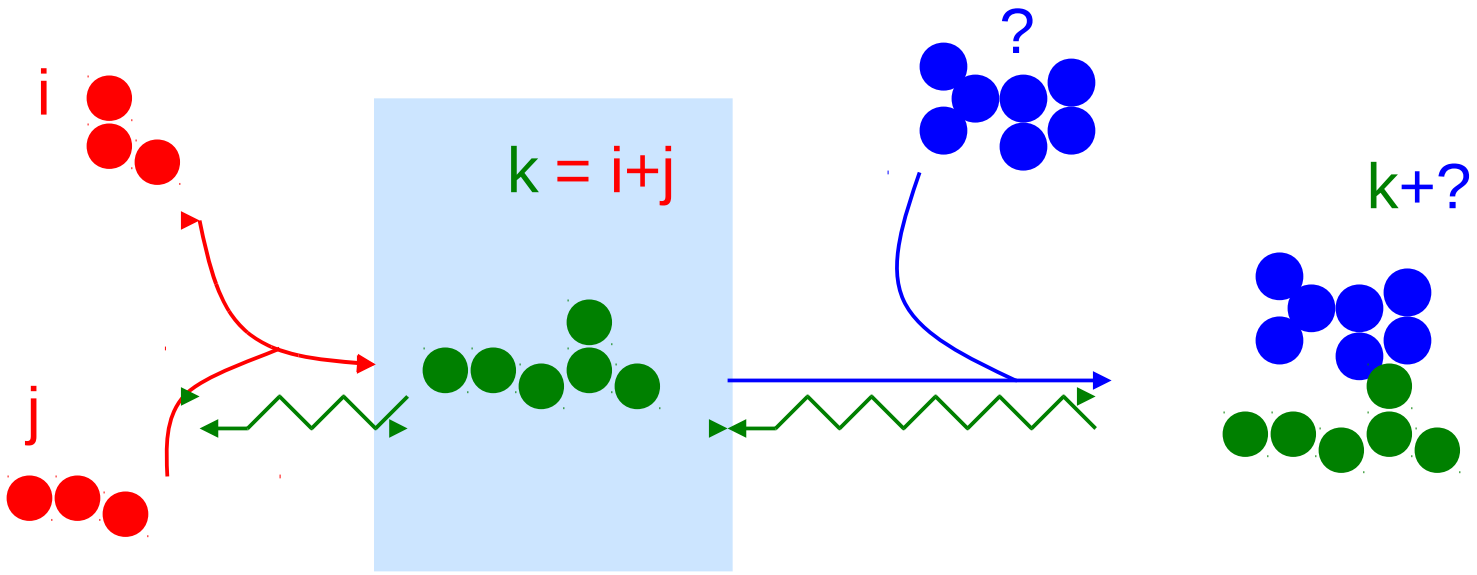
"Direct" mechanism



Aggregation state is not important pH shift when not in buffered media controls the toxicity.
Same category as : release of soluble toxic ions (Ag^+, Zn^{2+}, Cd^{2+}), release of adsorbed toxic molecules etc...

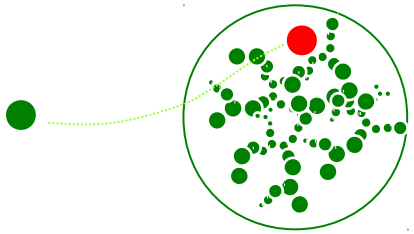
"Indirect" mechanism

Adsorption / aggregation kinetic model



$$\frac{dn_k(t)}{dt} = \sum_{i+j=k}^{\infty} \beta(i,j) n_i(t) n_j(t) - \sum_{i}^{\infty} \beta(i,k) n_i(t) n_k(t) + \sum_{i}^{\infty} F(i,k) n_{(i+k)}(t) - \sum_{i+j=k}^{\infty} F(i,j) n_{(i+j)}(t)$$

β computed using collision kernels adapted
for fractal aggregates. (Veerapaneni et Wiesner 1996)
Possibility of varying fractal dimensions during aggregation.
(Thill, Wiesner et al. JCIS, 2001)



Adapted for nano-micro mixtures (work in progress CEINT, iCEINT)

Time scale for NP aggregation ?

If only one nanoparticle type of size r_{NP} and concentration C.

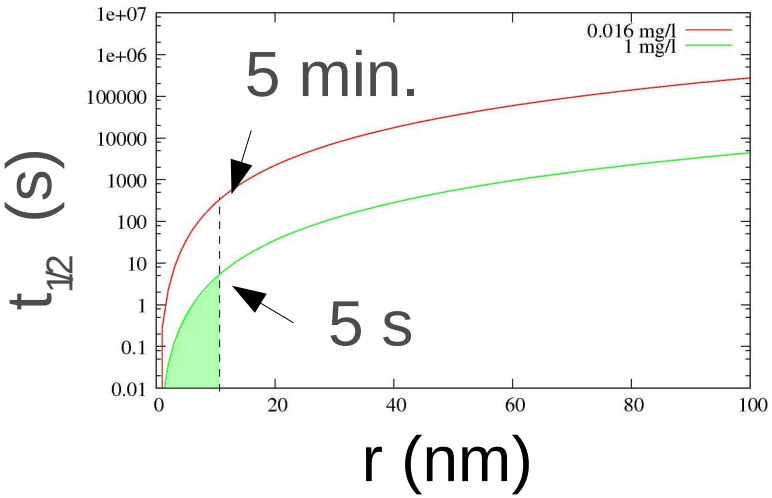
Then at t=0 : $n_1(0) = C/v_{NP}\,\rho$ and $n_i(0)=0 \quad \forall\, i \neq 1$

$$\frac{dn_k(t)}{dt} = \sum_{i+j=k}^{\infty} \beta(i,j)\, n_i(t)\, n_j(t) - \sum_{i}^{\infty} \beta(i,k)\, n_i(t)\, n_k(t) + \sum_{i}^{\infty} F(i,k)\, n_{(i+k)}(t) - \sum_{i+j=k}^{\infty} F(i,j)\, n_{(i+j)}(t)$$

Equation reduces to : $\dfrac{dn_1(t)}{dt} = -\beta(1,1)\, n_1(t)^2 \longrightarrow \dfrac{1}{n_1(0)} - \dfrac{1}{n_1(t)} = -\beta(1,1)\, t$

If $t_{1/2}$ is the time when $n_1(t_{1/2}) = n_1(0)/2$

$$t_{1/2} = \frac{\pi\, \rho\, \nu}{kT}\, \frac{r_{NP}^3}{C}$$



$t_{1/2}$ < 5s for 10 nm NP at 1 mg/l

with ν= 0.00089 kg/(m.s)

T = 298 K

ρ = 6500 kg/m³

C=0.016 or 1 mg/l

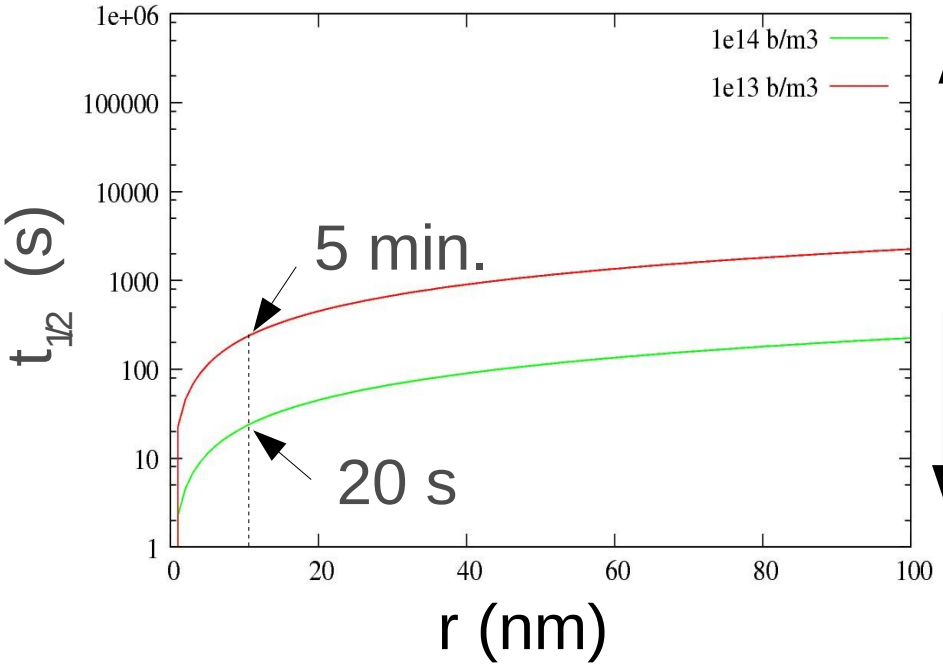
Time scale for NP/bacteria adsorption ?

A mixture of NP at concentration n_s radius r_s and bacteria at a concentration n_b of radius r_b. At initial time, if only adsorption on bacteria is possible :

$$\frac{dn_s(t)}{dt} = -\beta(s,b)\,n_s(t)\,n_b(t) \approx \frac{2kT}{3\nu}\frac{r_b}{r_s}\,n_b(t)\,n_s(t) \qquad \ln\left(\frac{n_s(t)}{n_s(0)}\right) = \frac{-2kT}{3\nu}\frac{r_b}{r_s}\,n_b\,t$$

If $t_{1/2}$ is the time when $n_1(t_{1/2}) = n_1(0)/2$

$$t_{1/2} = \frac{3\nu\ln(2)}{2kT}\frac{r_s}{r_b}\frac{1}{n_b}$$



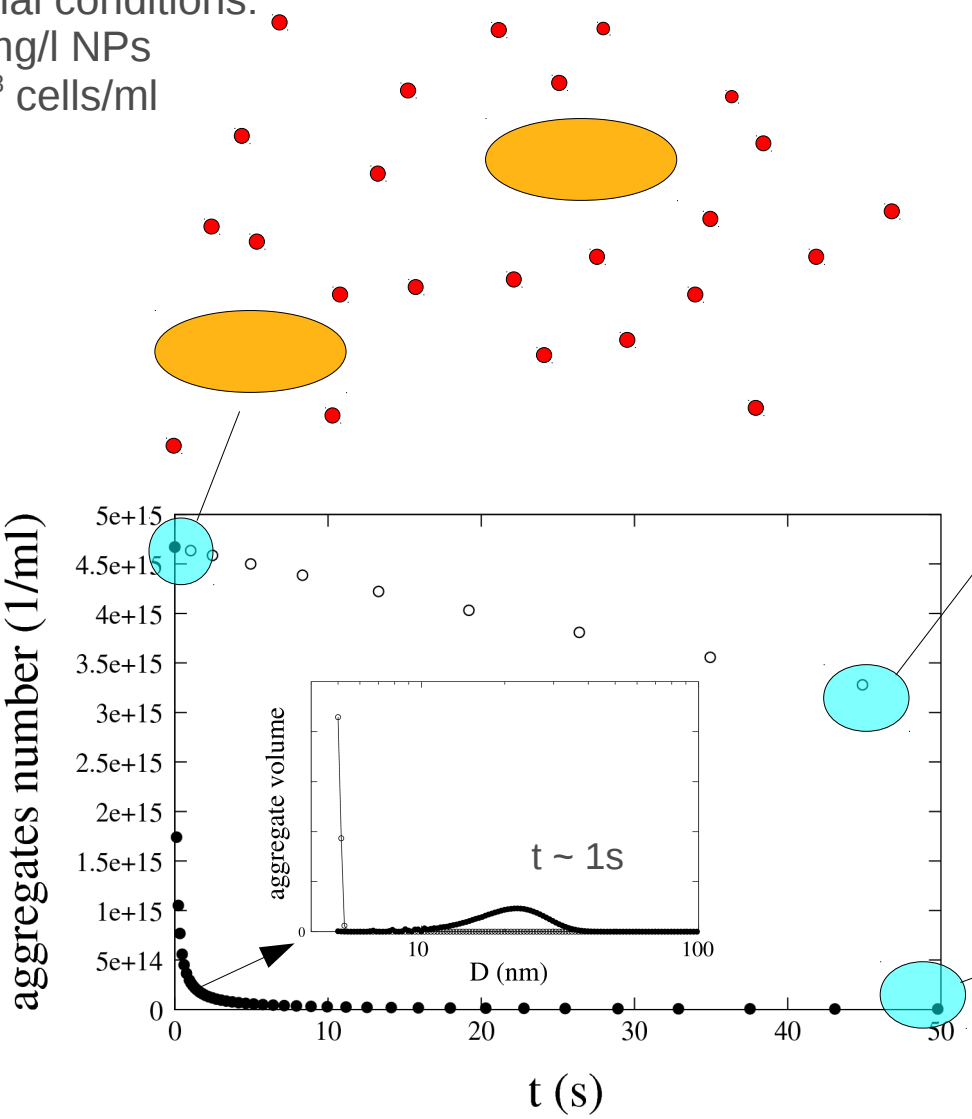
Environmental concentrations

Concentrated culture, biofilm

Adsorption / aggregation kinetic model

Initial conditions:
3 mg/l NPs
10^8 cells/ml

In water : stable NPs
only adsorption



In medium : unstable NPs
adsorption +
aggregation

Conclusions and perspectives

- Toxicity of NPs can be induced by **"direct"** (requiring physical contact) or **"indirect"** mechanism.

- NPs aggregation state may not be a critical parameter for **"indirect" toxicity**.

- Competition between aggregation/deposition and adsorption has to be considered to assess potential **"direct" toxicity** especially in environmental relevant scenario.

- Are environmentally relevant exposure scenario in favor of **"direct"** toxic mechanism? (bio-accumulation? and genotoxicity!)

Safe production and use of nanomaterials

See further announcements on www.nanosafe.org