Université de Paris

Effects of inhaled nanoparticles on a lung surfactant fluid

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Deposition profiles with respect to NP size

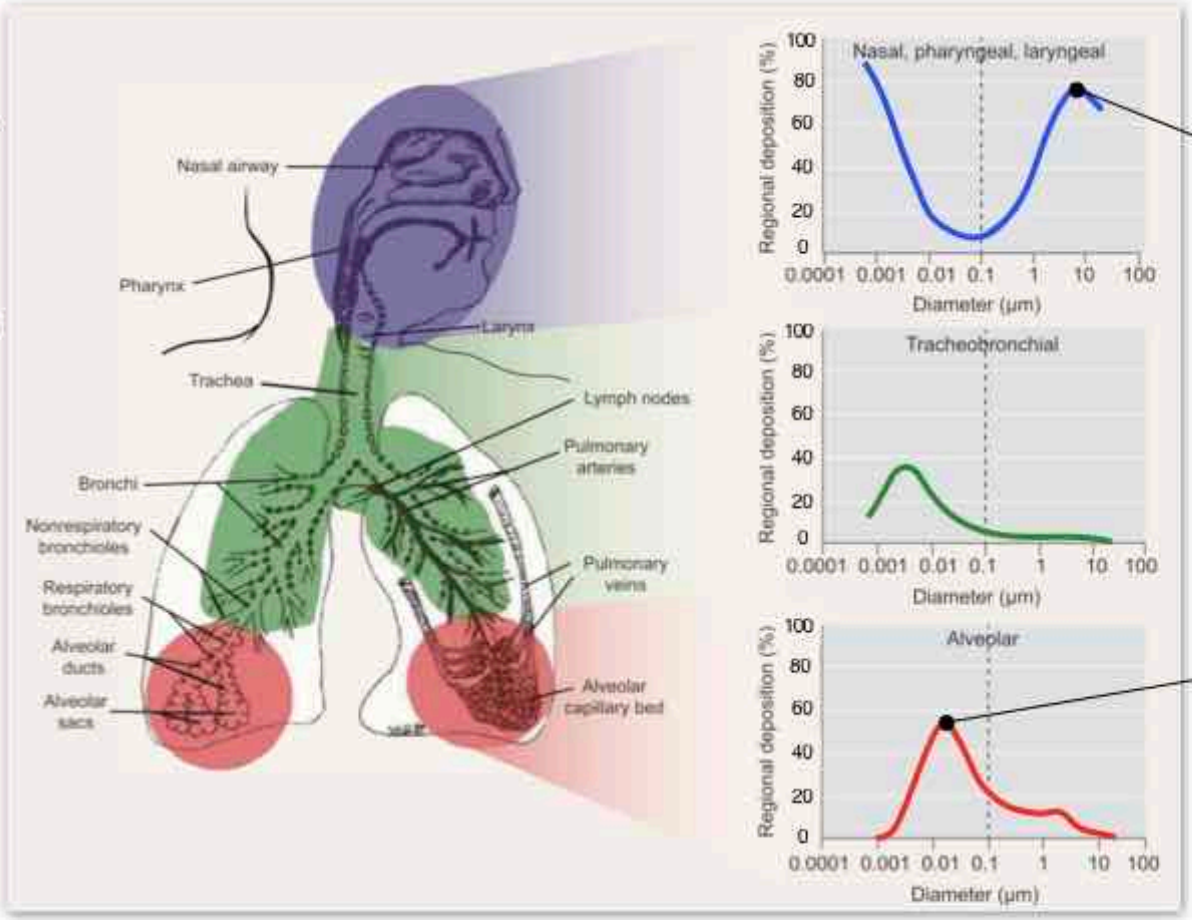
$PM_{2.5}$ are Particulate Matter < 2.5 µm

Mechanisms • Impaction • Sedimentation • Diffusion

Upper airways

Bronchial region

Alveolar region



5 µm particles have a probability of 75% to deposit in the upper airways

20 nm particles have a probability of 55% to deposit in the alveolar region

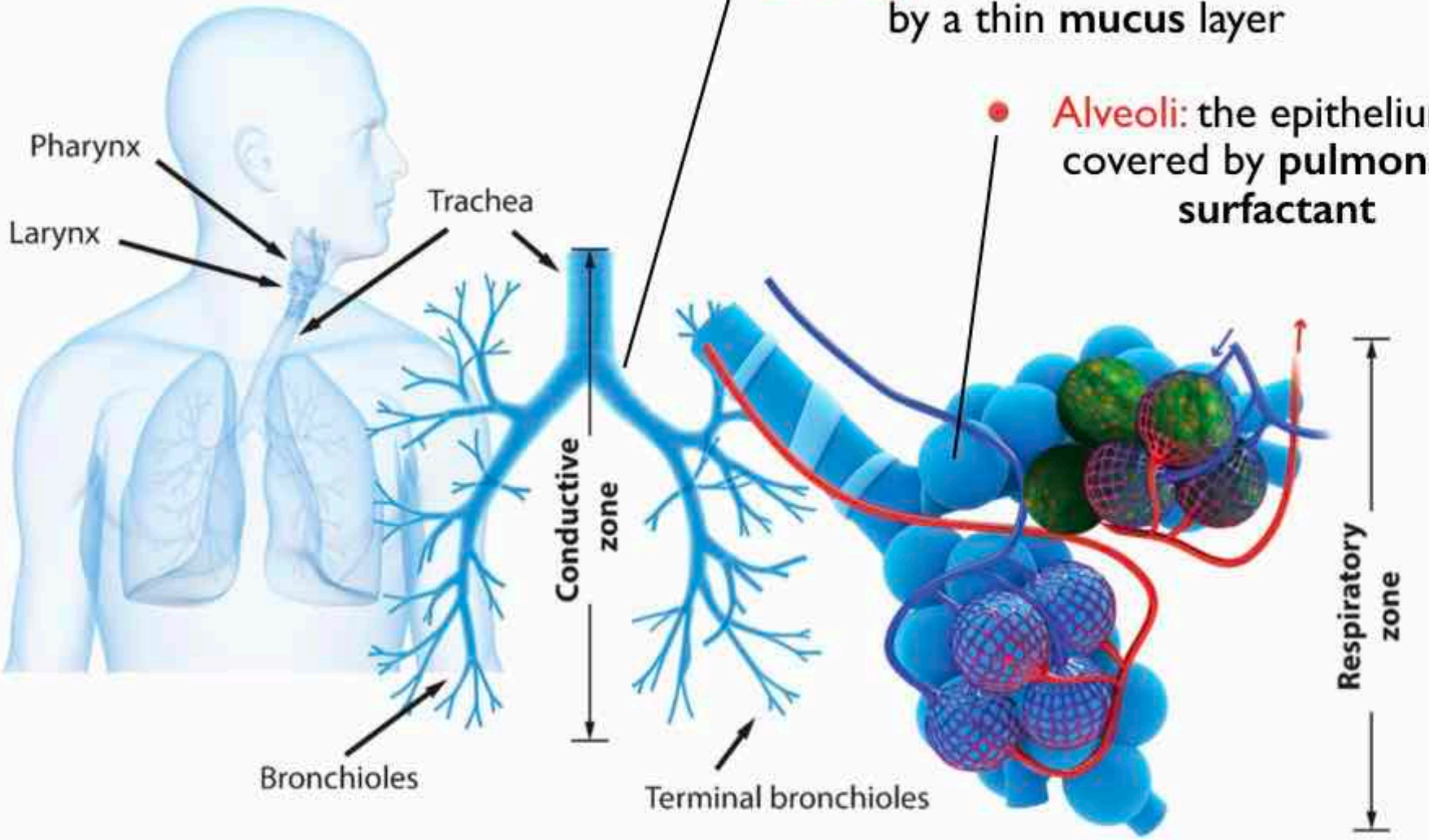
Deposition probability

NPs particles (< 100 nm) penetrate deeper into the alveolar region and deposit at high percentages

Lung fluids

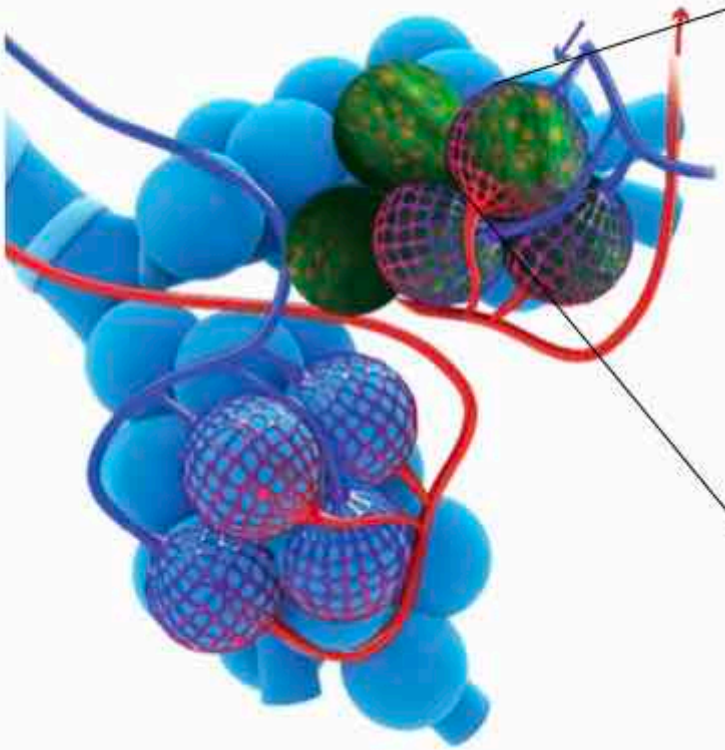
Respiratory track

- Bronchi: the epithelium is covered by a thin **mucus** layer
- Alveoli: the epithelium is covered by **pulmonary surfactant**

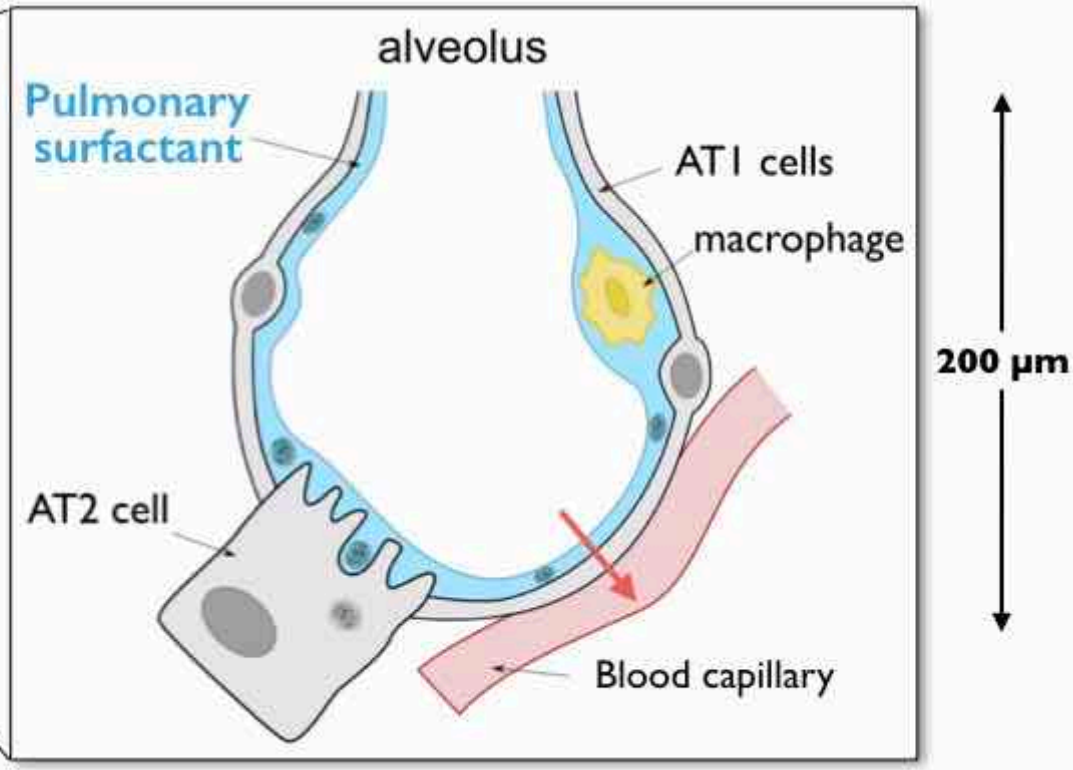


Inhaled particles in the lungs

Respiratory track



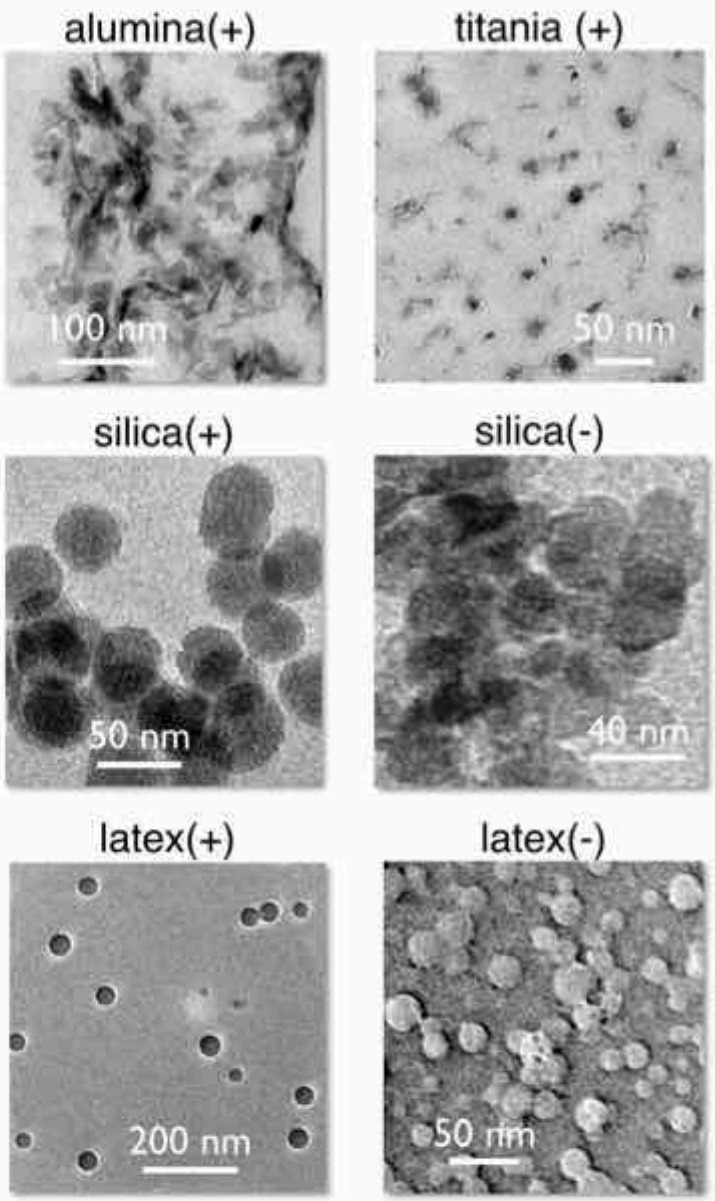
Alveolus schematics



Question

How do nanoparticles interact with pulmonary surfactant?

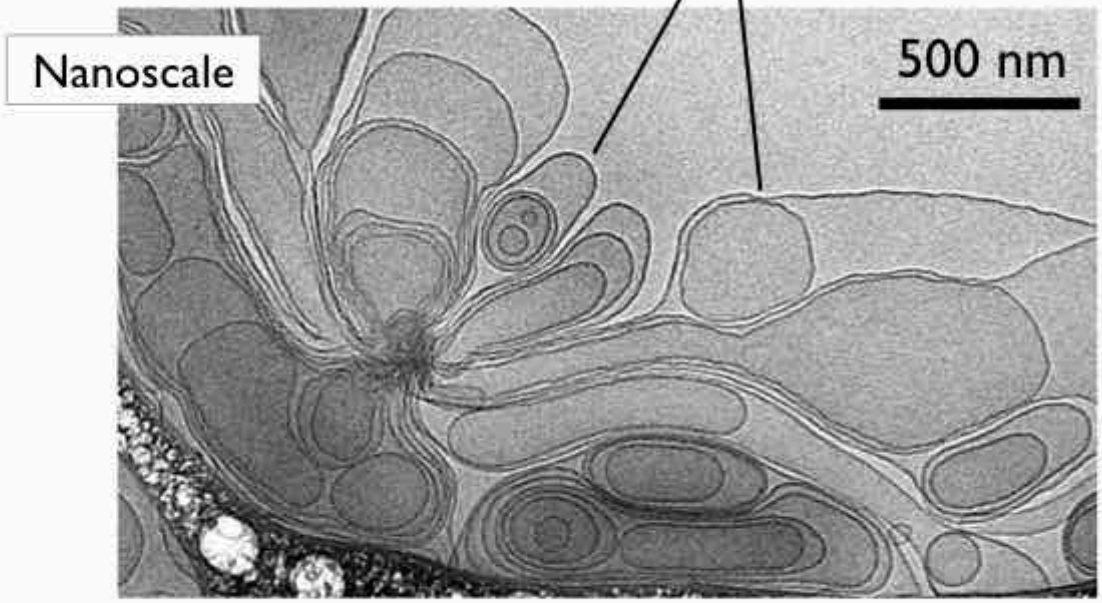
Nanoparticles



Pulmonary surfactant

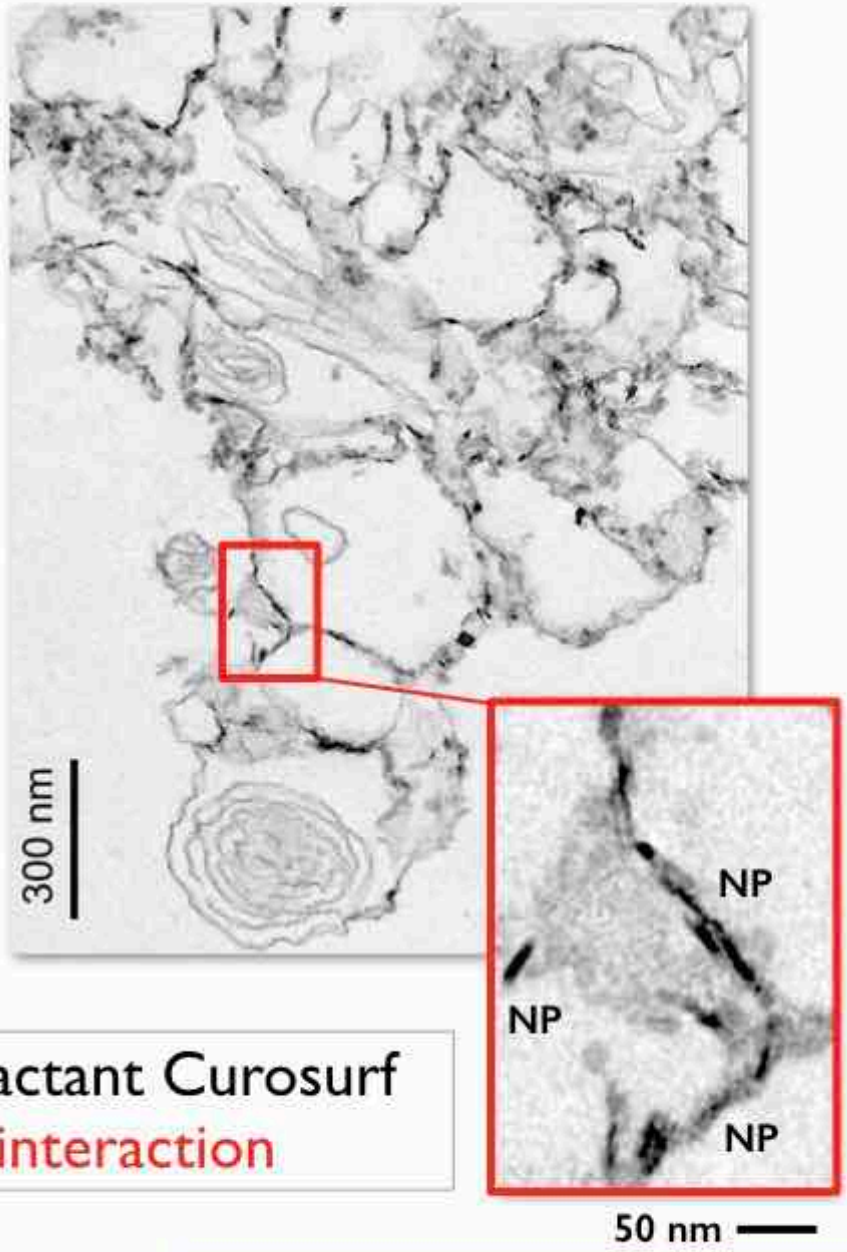
Curosurf

- From Chiesi (Italy)
- Porcine origin
- Administered to premature infants (< 32 weeks)
- Multivesicular **vesicles** (negatively charged)



NP-vesicle interactions

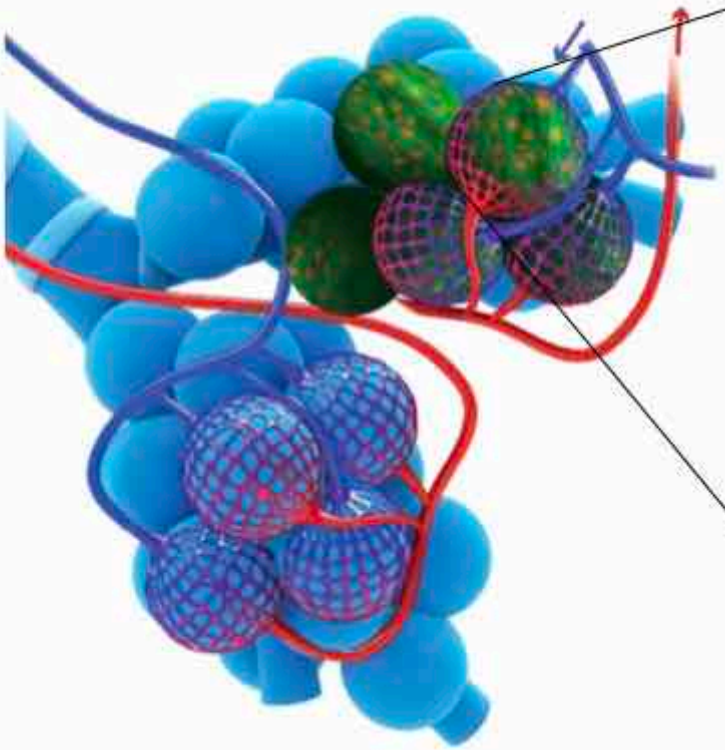
	Nanoparticle	Size nm	Charge density nm^{-2}
Positive	Alumina (+)	40	+ 7.3*e*
	Titania (+)	15	n.d.
	Silica (+)	42	+ 0.62*e*
	Latex (+)	34	+ 0.33*e*
negative	Silica (-)	20	- 0.31*e*
	Latex (-)	30	- 0.05*e*



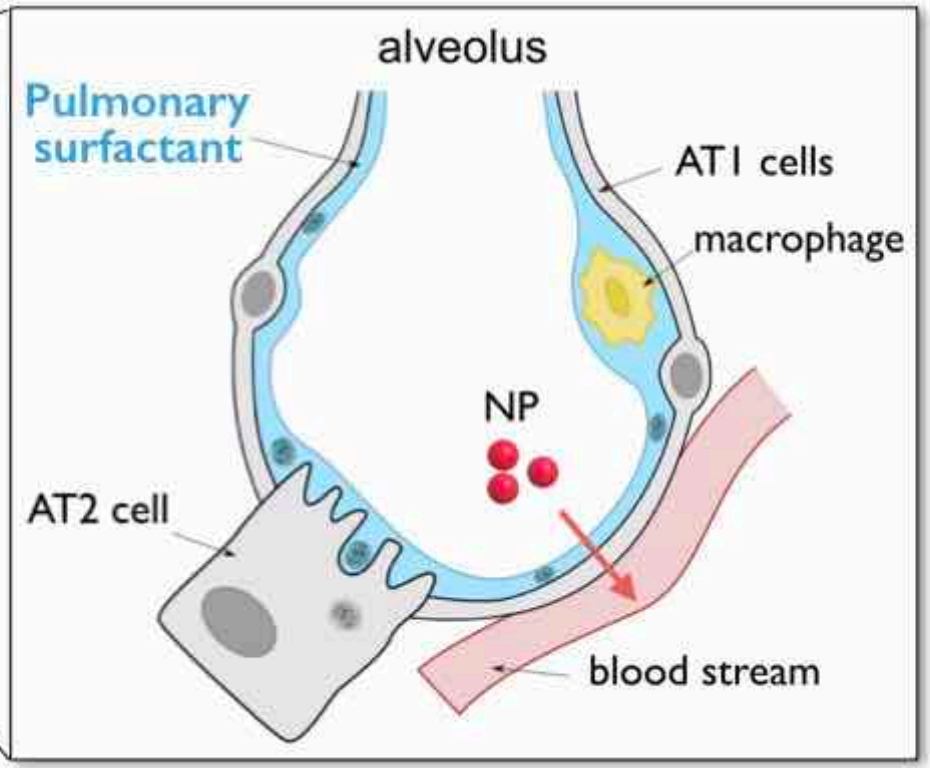
Nanoparticles and the biomimetic surfactant Curosurf interact primarily *via* electrostatic interaction

NP-cell interactions

Respiratory track



Alveolus schematics



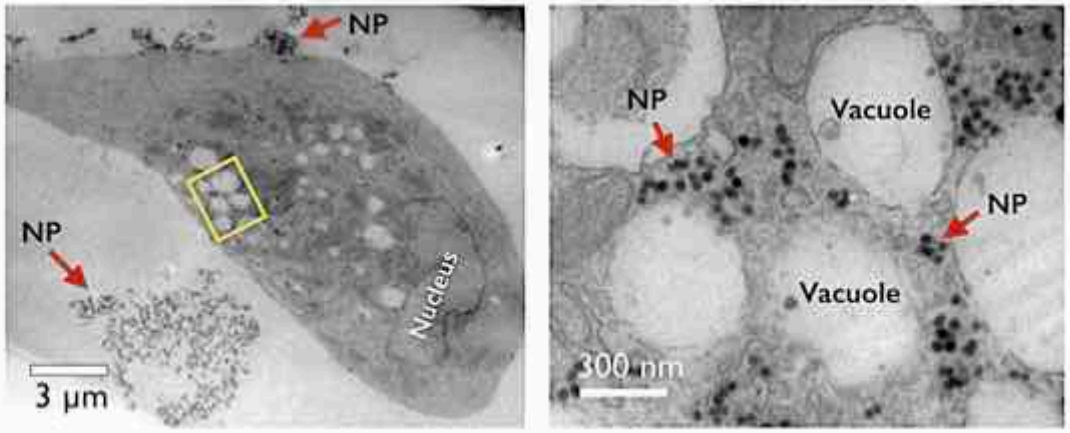
Question

Does the surfactant favor or prevent cellular internalization?

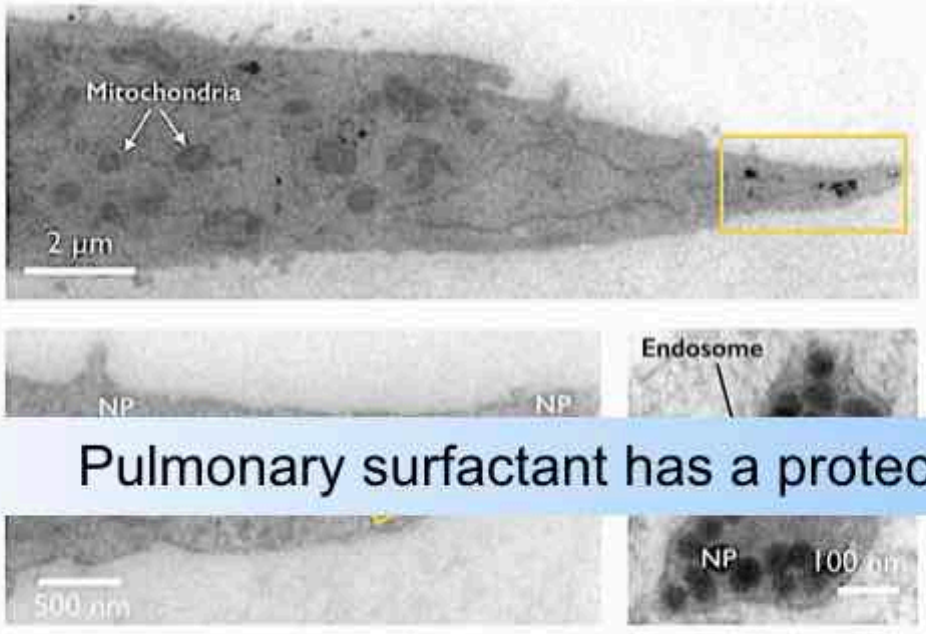
NP-cell interactions

A549 epithelial cells / positive silica

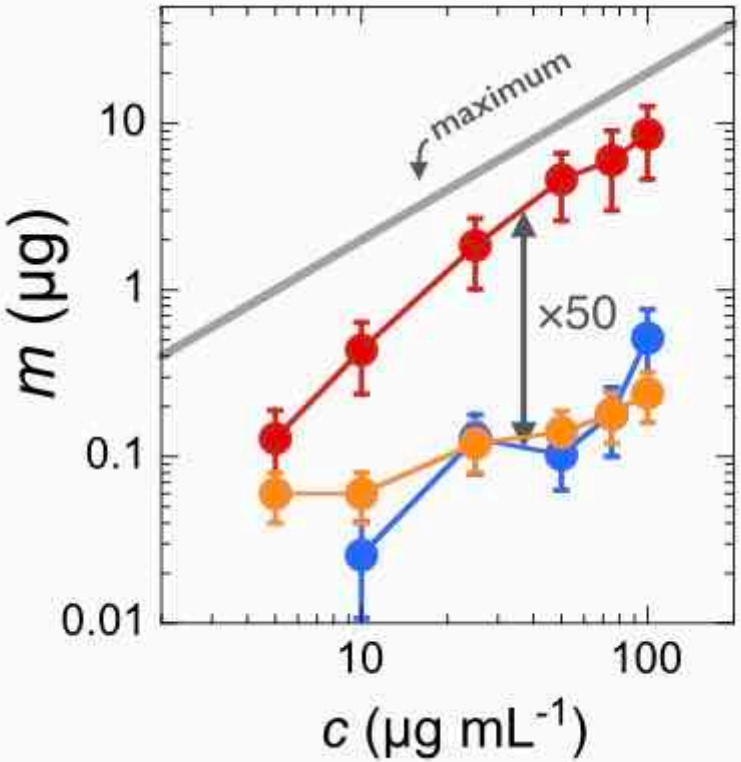
without surfactant



with surfactant



Quantification assay

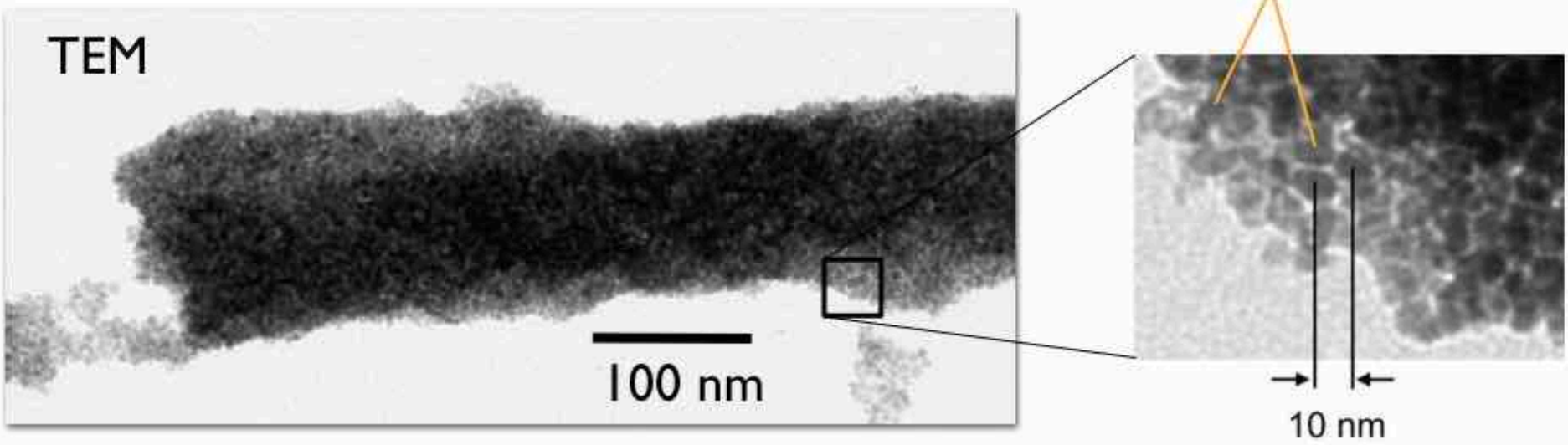


endocytosis

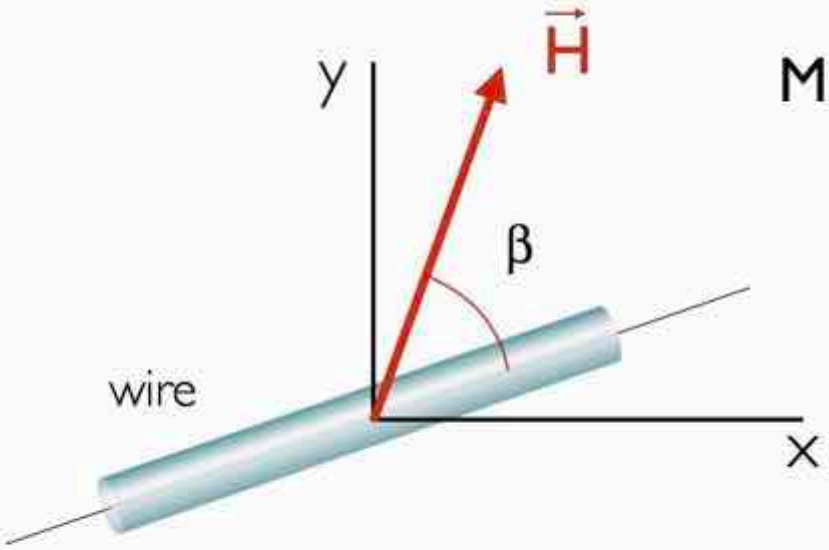
Pulmonary surfactant has a protective role and prevents cellular entry

Active microrheology

Active microrheology



Volume fraction of particles
30 vol. %



Magnetic torque

$$\Gamma_{Mag} = \frac{1}{2}\mu_0 V \Delta\chi H^2 sin\,(2\beta)$$

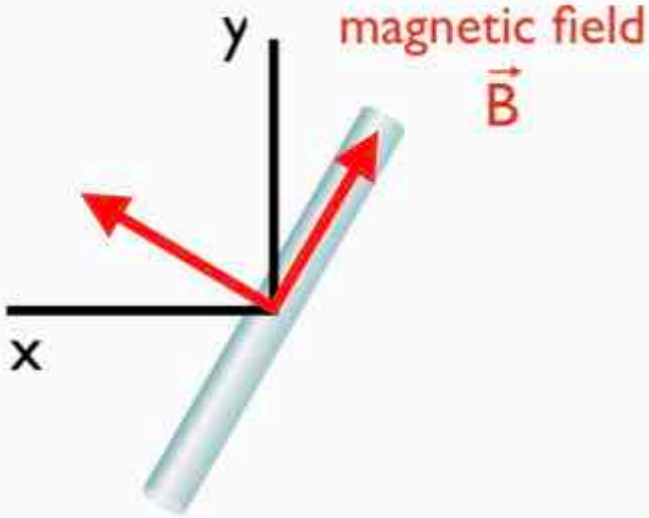
wire volume

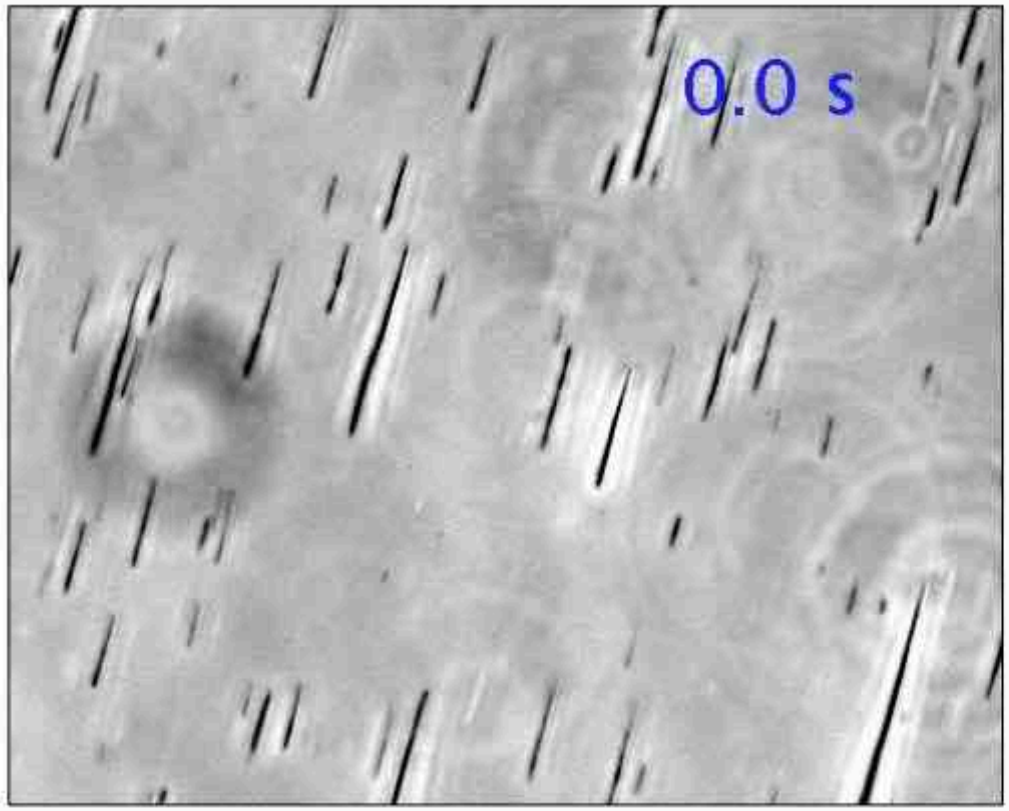
susceptibility anisotropy

magnetic excitation

Response to a magnetic field

90°-flip of the magnetic field





- The wires are superparamagnetic
- Their response to a field depends on the length and diameter

Curosurf viscosity

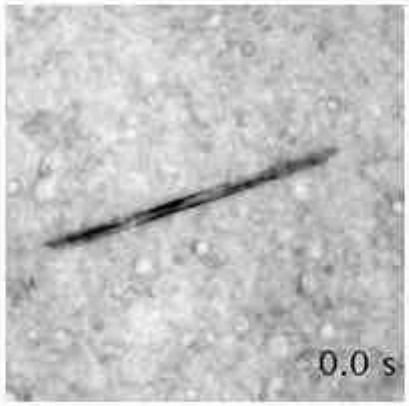
Curosurf

Krieger-Do

$\eta_{K-D}(c) = \eta$

Le-Phuong-Anh Thai
M2 Internship 2019

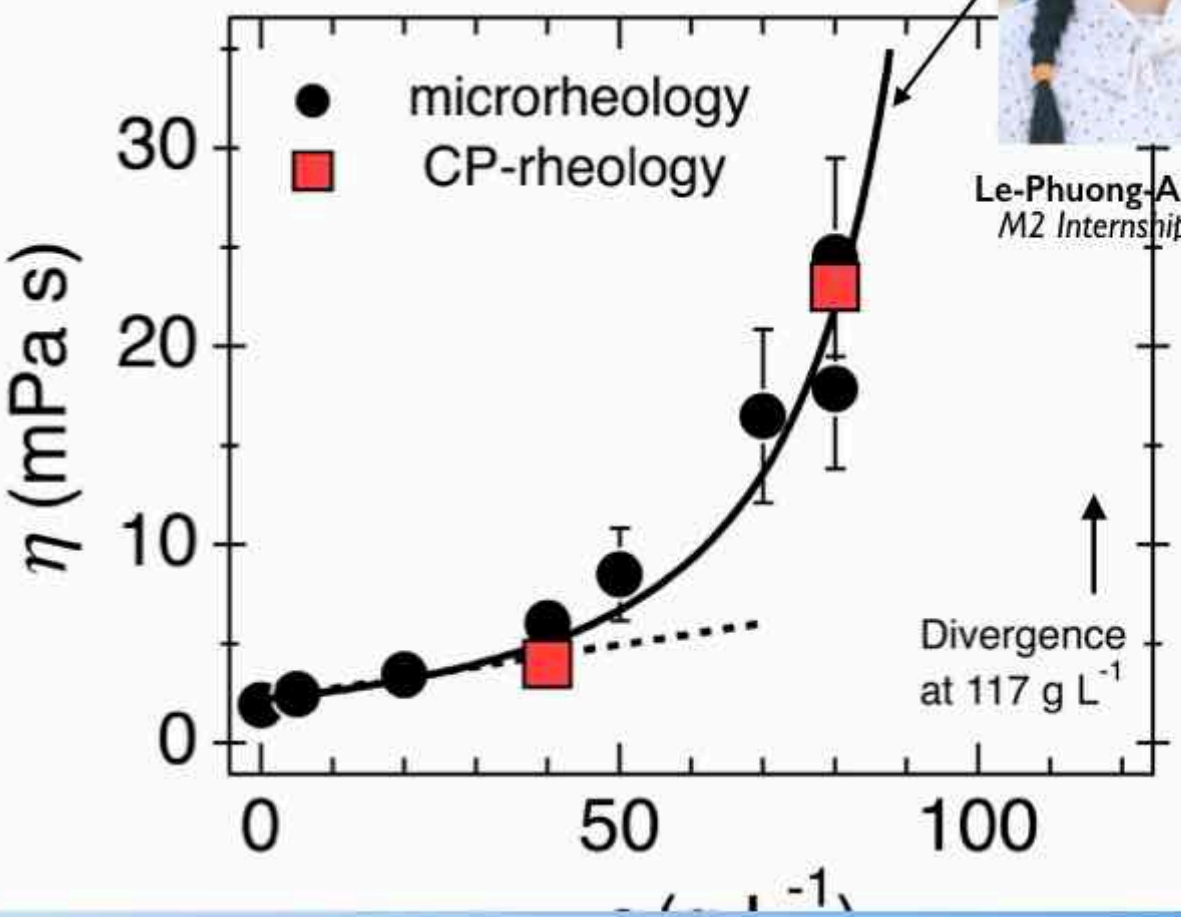
Synchronous rotation



20 µm

ω_C

Hindered rotation



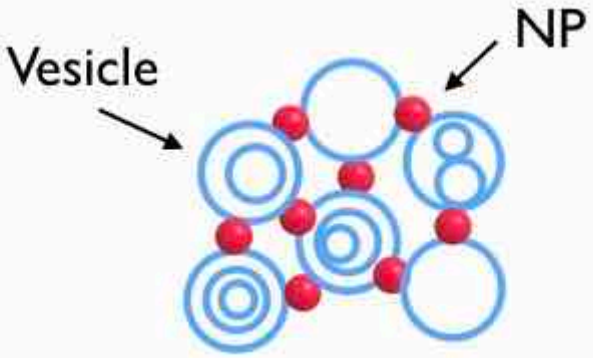
Curosurf displays a sol-to-gel transition at 117 g L^{-1} (ϕ ~ 65%)
At physiological concentration, Curosurf is a highly crowded dispersion

$8 \quad \eta \quad L^2$

η static viscosity

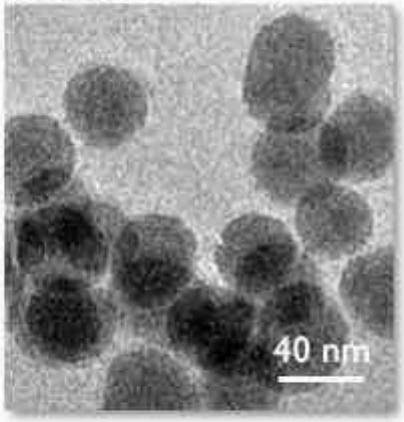
$\Delta\chi$ susceptibility anisotropy

Effects of nanoparticles



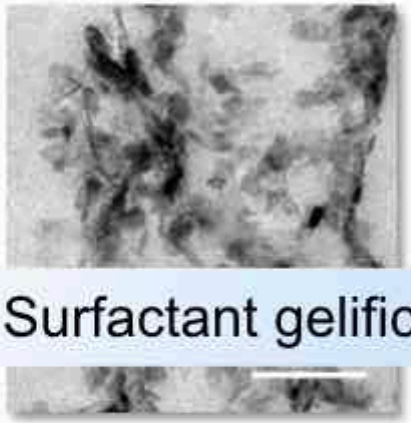
- Curosurf (40 g L^{-1})
  Physiological concentration

- Silica

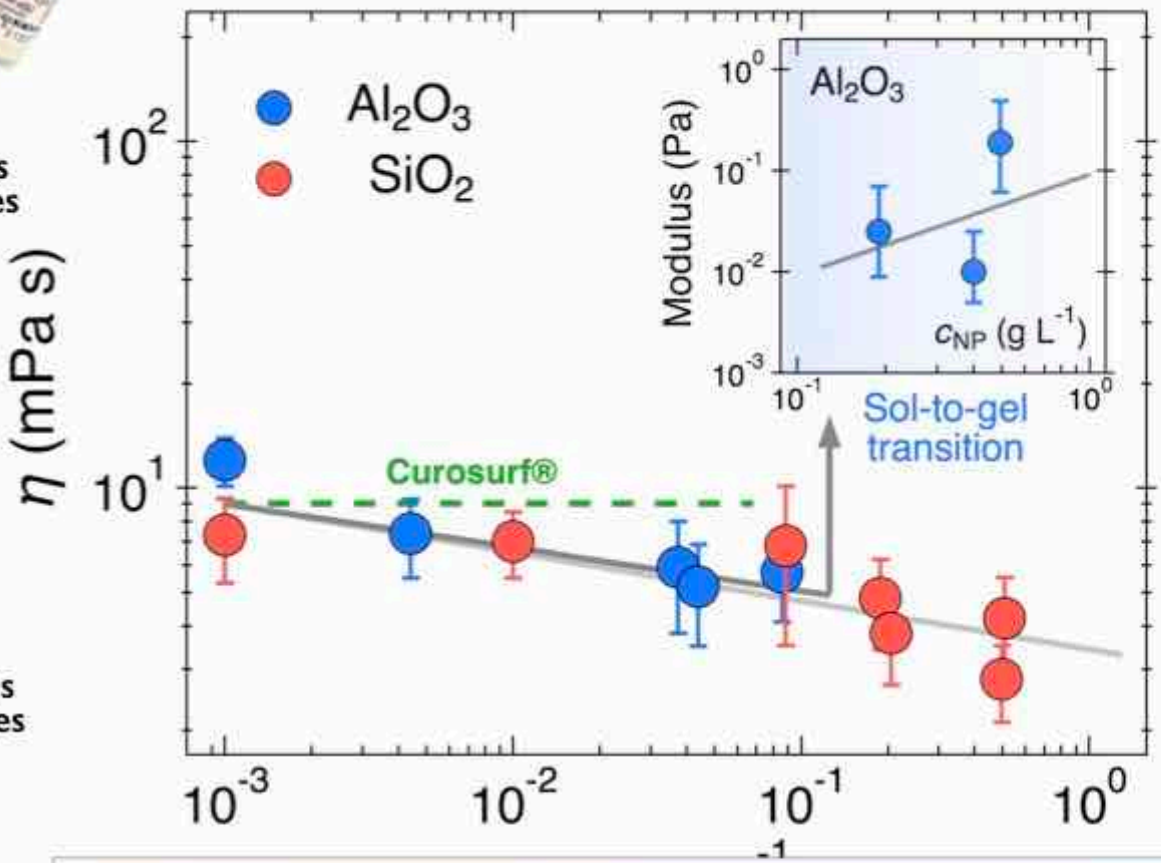


Mild interactions with vesicles

- Alumina



Strong interactions with vesicles



Surfactant gelification may impair the fluid recirculation during beathing

Conclusion

I - Pulmonary surfactant and nanoparticles

- Pulmonary surfactant has a protective effect towards inhaled particles
- Cell entry is lowered by a factor 50 with respect to bare particles

II - Pulmonary surfactant rheology

- At physiological concentration, pulmonary surfactant is a low viscosity Newton fluid (8 times that of water)
- Interaction with nanoparticles cause a fluidification or a gelification of the dispersion at nanoparticle concentrations compatible to inhaled doses

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Thank you for your attention

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