

# **Nanoparticles and their behaviour in biological fluid**

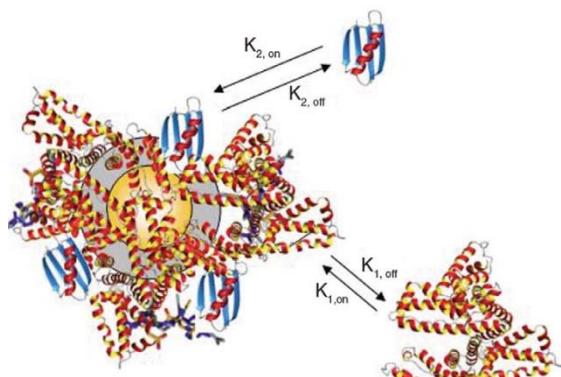
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Isabelle Geissbuehler, Géraldine Coullerez,  
Heinrich Hofman, Alke Fink

## I. Why does nanoparticles and their behaviour in biological fluid become interesting?

- Nanomedicine (cytotoxicity, drug delivery, Imaging)
- Nanosafety
- Bionanoscience (formation of the corona)

### Extracellular nanoparticles

- Nanoparticle
- Suspending media
- Solid-liquid interface
- Nano-bio interface



### Inter-Intracellular nanoparticles

- Nanoparticle-cell interaction
- Intracellular signaling (e.g. Kinases, phosphates, adaptors)
- Cytoskeleton rearrangement for particle uptake
- Gene expression
- Inflammatory cytokine production
- Cell death

Iseult Lynch and Kenneth A.Dawson. *Nanotoday* VOL 3, 2008;40.

Andre E.Nel, *Nature materials*. VOL8, 2009; 543.

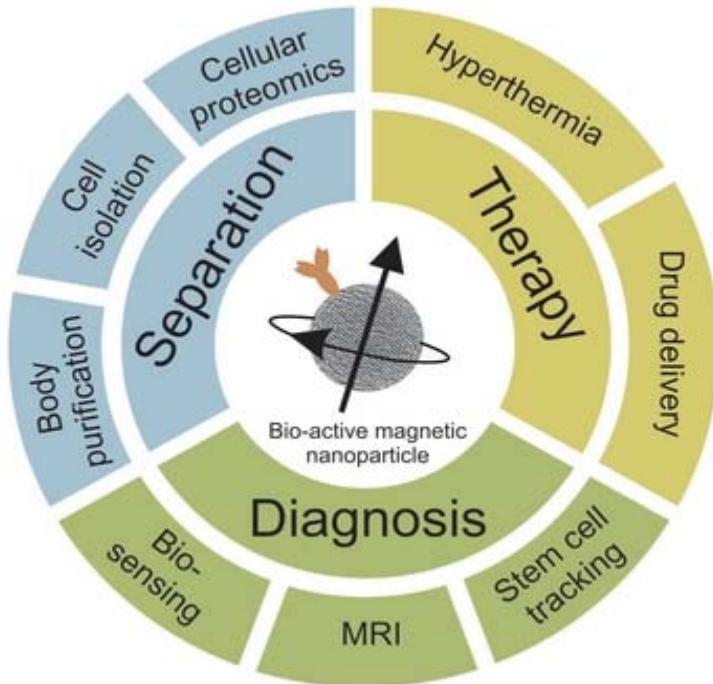
Marina A. Dobrovolskaia & Scott E. McNeil. *Nature Nanotechnology* VOL 2, 2007; 469

# Aims

1. The preparation of a **particle library** on the basis of SPIONs.
2. The systematic investigation of the **colloidal behaviour** of such nanoparticles in **different environments**.
3. **Protein adsorption**

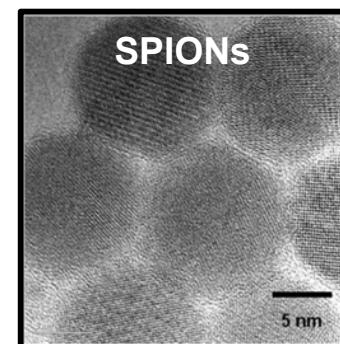
# Introduction

## II. What and Why: SPIONs (SuperParamagnetic Iron Oxide Nanoparticles)?



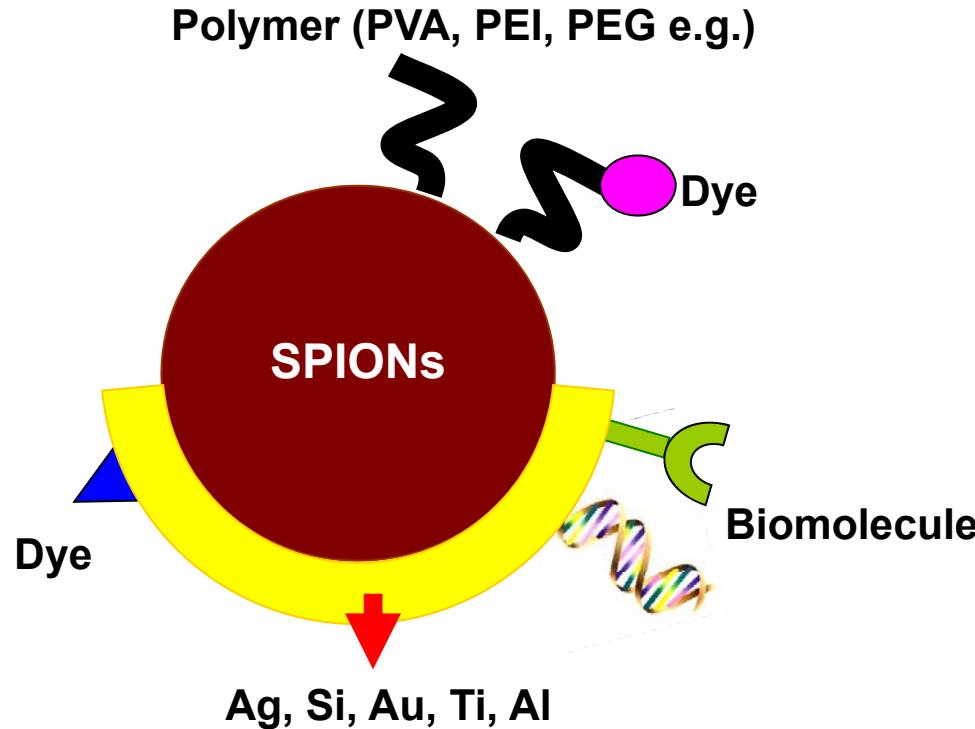
### Particle characteristics:

- Primary crystalline iron oxide particles ( $\gamma\text{-Fe}_2\text{O}_3$ , maghemite)
- Mean diameter of  $9 \pm 1\text{ nm}$  (TEM)
- Superparamagnetic behaviour at room temperature
- Single particles, beads
- Characterization *in vitro*
- Application *in vivo*



A. Petri-Fink, H. Hofmann ,*NanoBioscience, IEEE Transactions on*, 6/4 ,2007; 289.  
D. Hellstern, et al, *J. Nanoscience and Nanotechnology*, 6/9-10, 2006; 2829.

## III. Why surface coating of SPIONs?

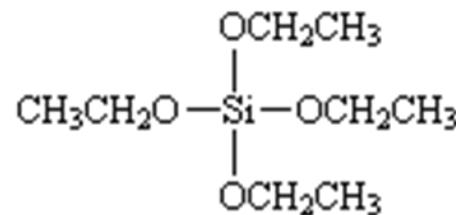
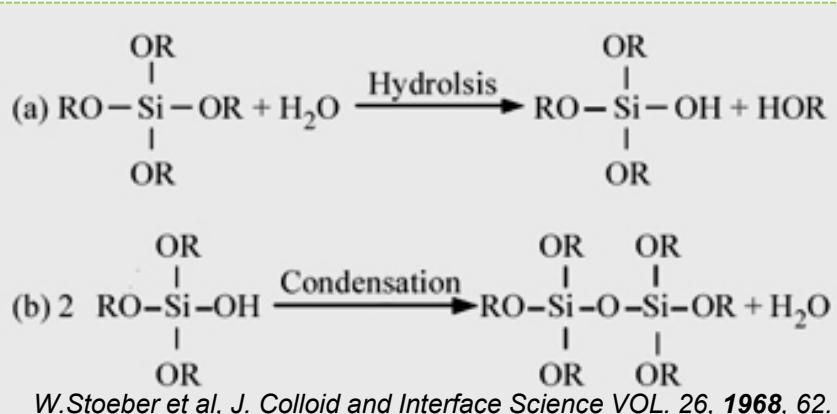


**Bi or Multifunctional nanoparticle based on magnetic core**

(imaging, diagnosis, drug delivery, photocatalysis, solar energy conversion)

# •Silica coated SPIONS

results



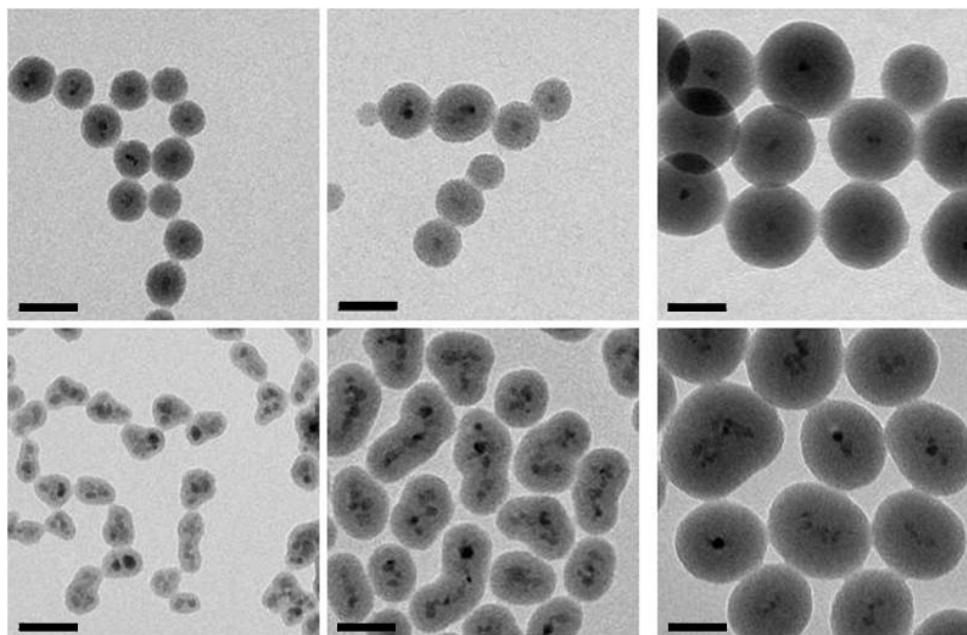
TEOS: Tetraethylorthosilicate

Single core-silica coated SPIONS  
(MRI)

Multi core silica coated SPIONS  
(Cell and protein separation, dianostic)

- TEOS/SPIONS
- Ammonia
- SPIONS/Total volume

TEM image of  $\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$

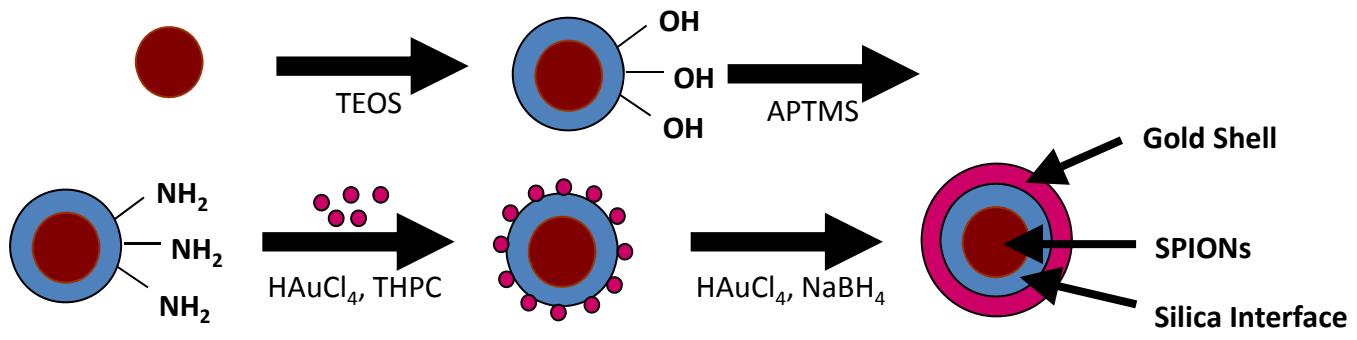


Scale bar = 50 nm

# •Gold coated SPIONs

results

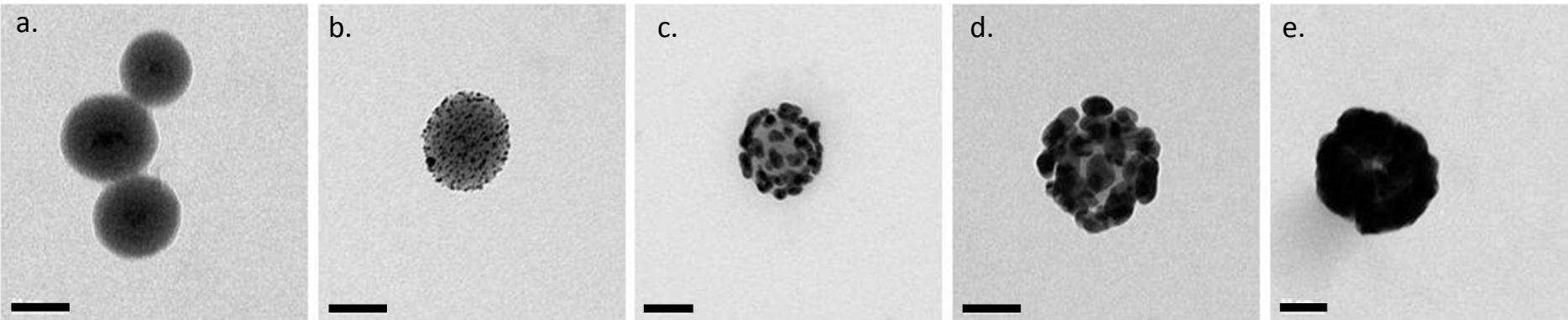
Xiaojun Ji et al, J.Phys.Chem.C VOL 111, 2007;6245, James C.Y.Kah et al, Gold Bulletin, VOL41/1, 2008;23.  
Michael R.Rasch et al, Langmuir VOL 25, 2009;11777.



THPC:Tetrakis(hydroxymethyl)phosphonium chloride

APTMS: 3-aminopropyltriethoxysilane

TEM image of  $\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2/\text{Au}$



increasing of gold precursor concentration

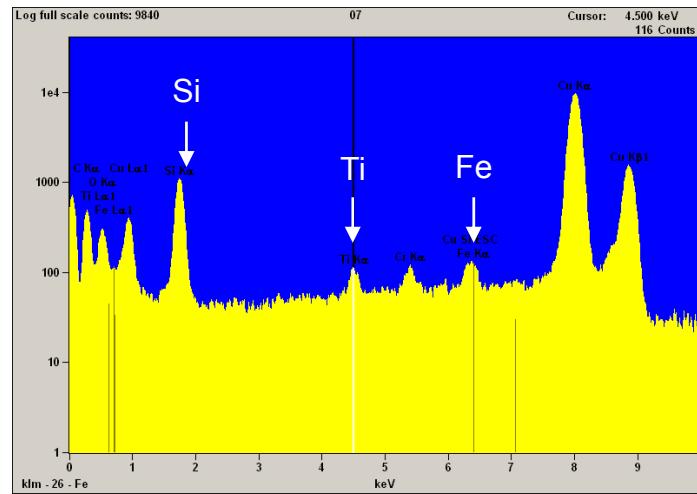
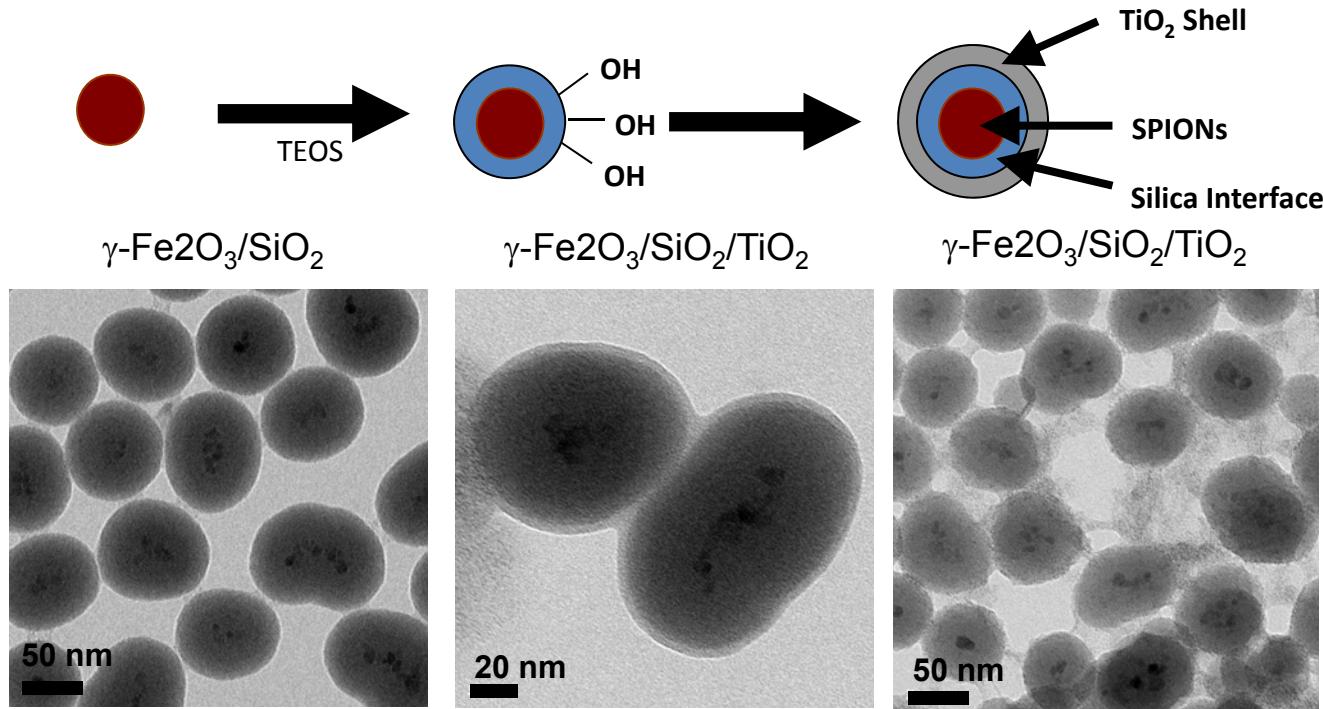
$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$

$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$   
+  
Gold seeds

# •**Titania coated SPIONS**

results

Sébastien Abramson, J Nanopart Res, VOL 11, 2009; 459

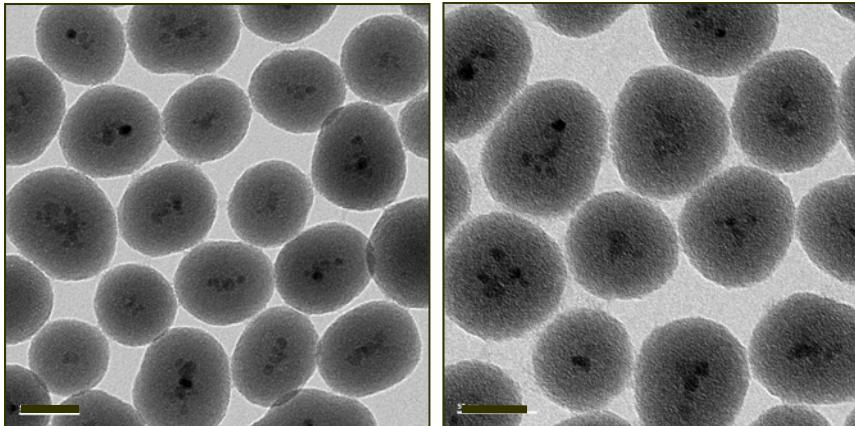


**Energy-dispersive X-ray spectroscopy  
(EDS or EDX)**

# TEM

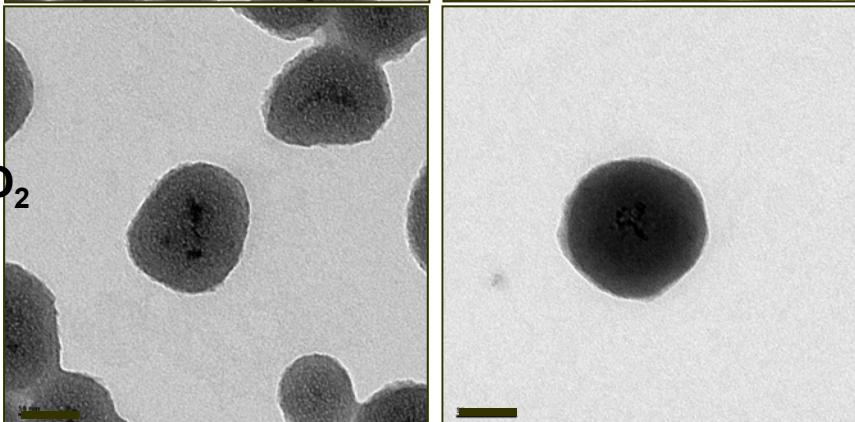
# results

$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$



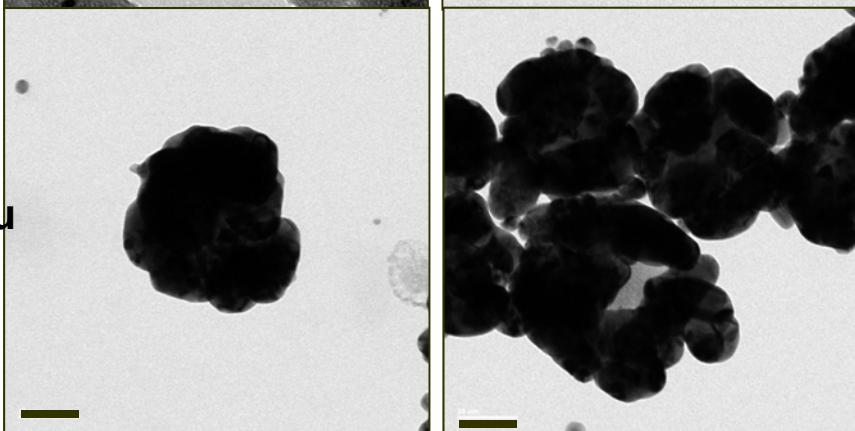
Size (nm) : 84 nm  
Zeta potential (mV):  $-35.76 \pm 0.54$

$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2/\text{TiO}_2$



Size (nm) : 86 nm  
Zeta potential (mV):  $-30.89 \pm 0.55$

$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2/\text{Au}$



Size (nm) : 144 nm  
Zeta potential (mV):  $-16.19 \pm 0.91$

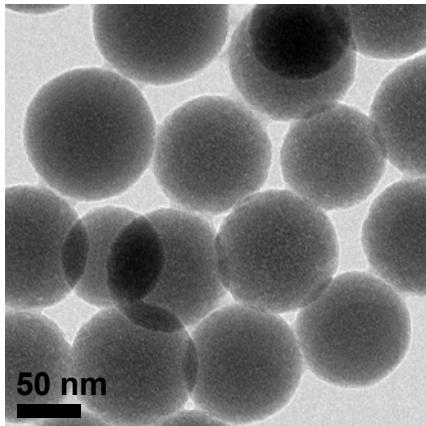
Scale bar = 50 nm

# Protein adsorption of $\text{SiO}_2$ and $\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$ at 0 and 24 h

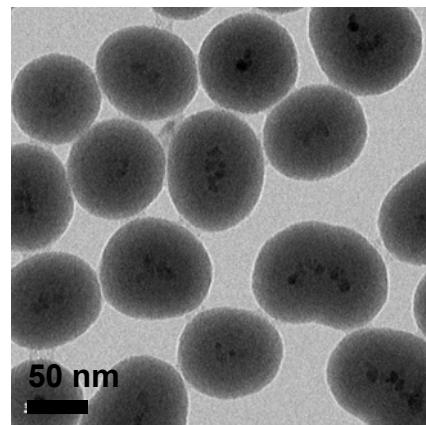
results

Same material surface nanoparticles

$\text{SiO}_2$



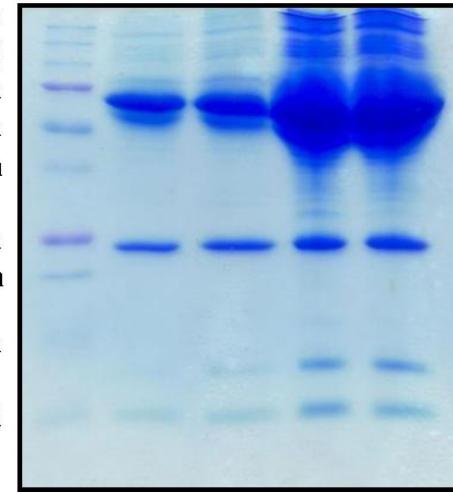
$\gamma\text{-Fe}_2\text{O}_3/\text{SiO}_2$



## 1D SDS-PAGE

Lane:

250 kDa  
150 kDa  
100 kDa  
75 kDa  
50 kDa  
37 kDa  
25 kDa  
20 kDa  
15 kDa  
10 kDa



0 h    24 h

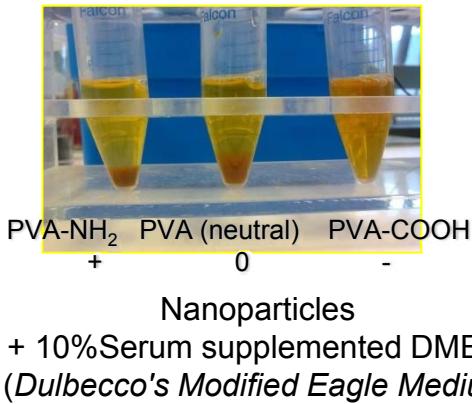


Nanoparticles with the same surface share the same pattern of adsorbed proteins.

# Magnetic reactor for protein separation

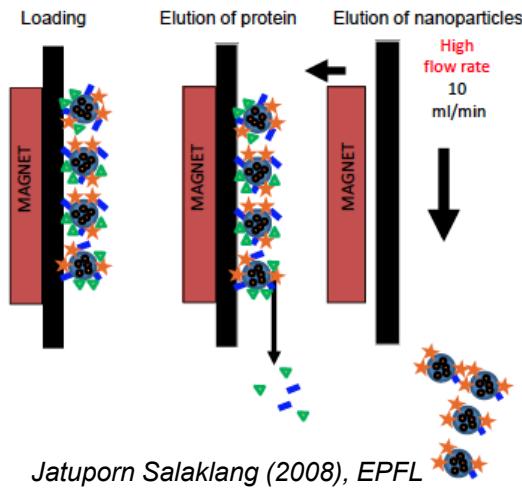
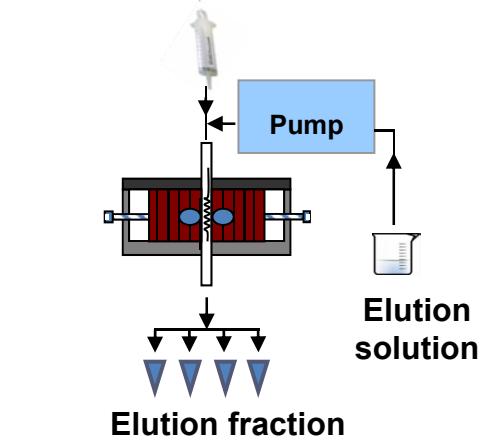
## results

### 1. Particle incubation



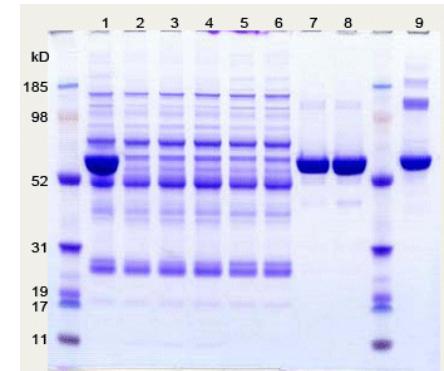
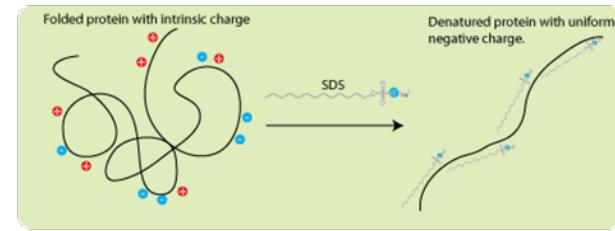
- Control volume and flow rate of elution step
- Reduce solution contamination during the process

### 2. Magnetic separation



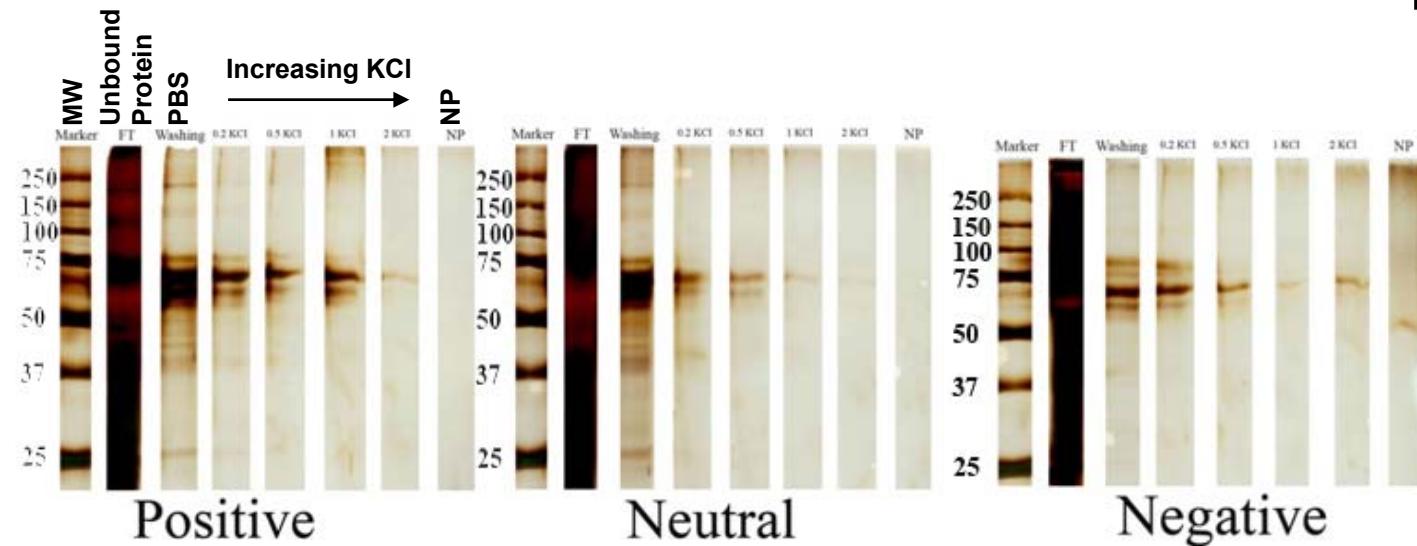
### 3. SDS-PAGE

(Sodium Dodecyl Sulfate Polyacrylamide Gel Electrophoresis)

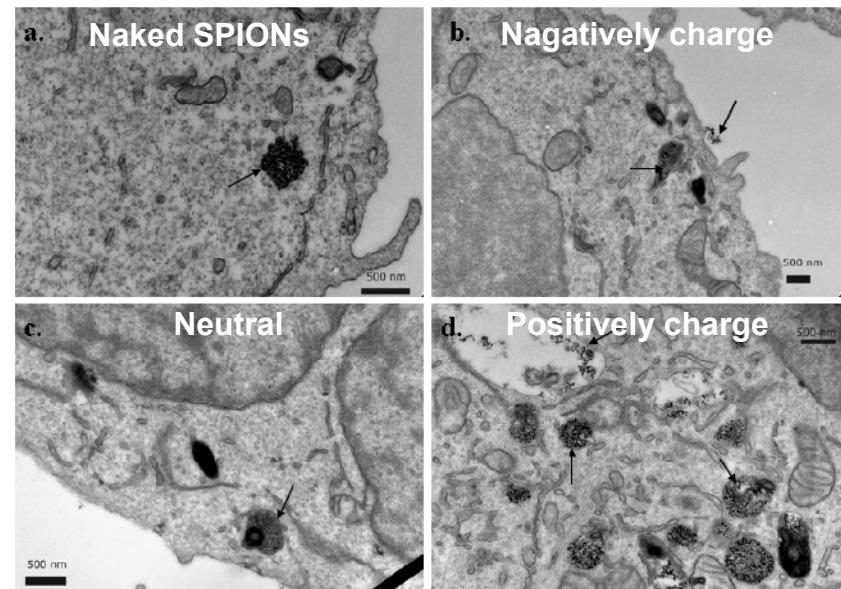


# Protein adsorption of different charge surface (Polyvinylalcohol) at 1 h

results

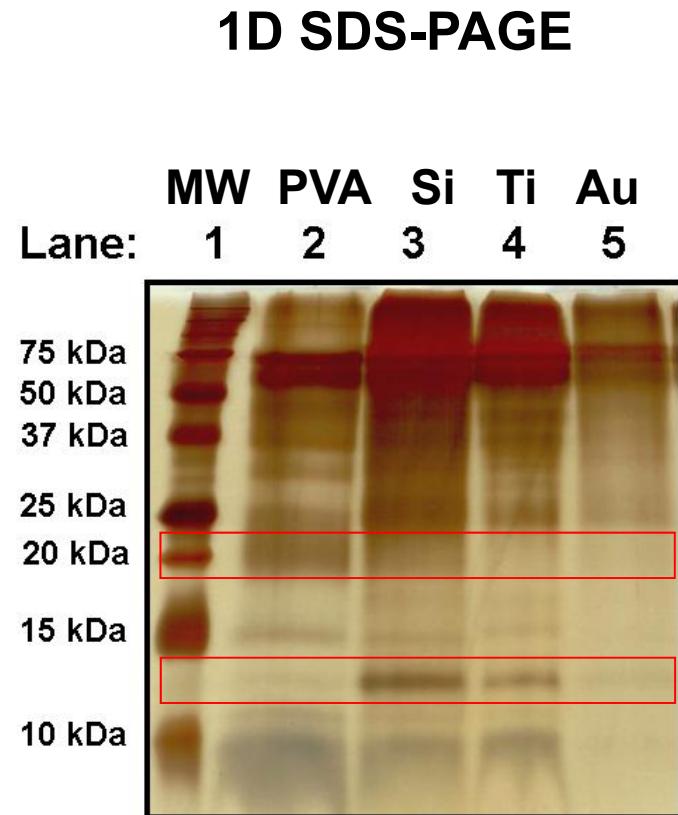
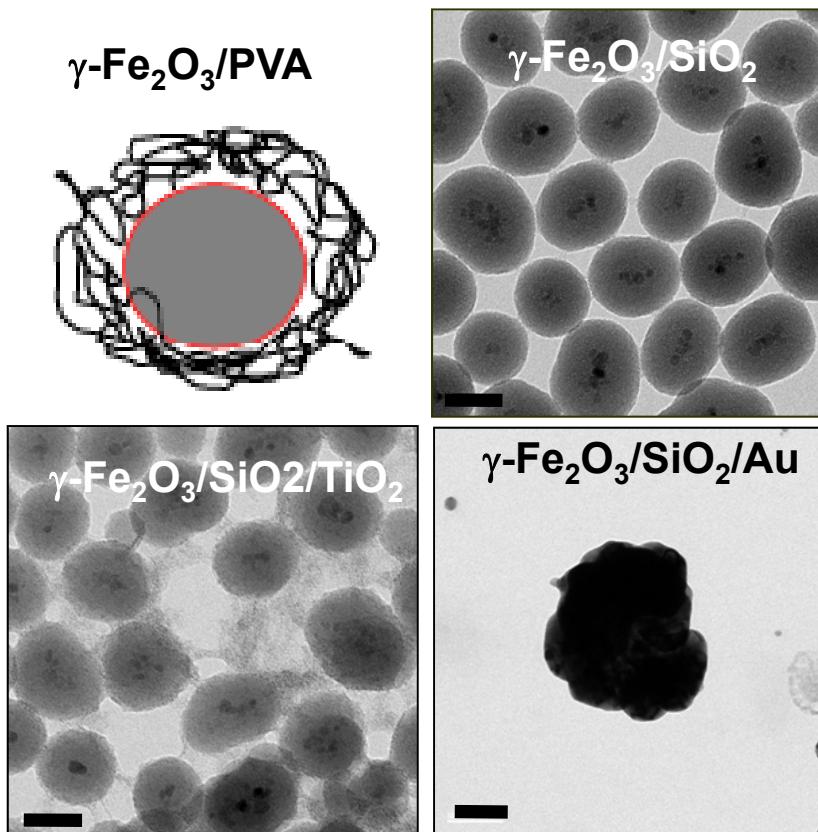


PVA-SPIONs	Charge	Zeta potential (mV)
PVA-NH <sub>2</sub>	positive	43.34 ± 0.91
PVA (neutral)	neutral	9.28 ± 0.75
PVA-COOH	negative	-15.92 ± 0.56



# Protein adsorption of different material surface at 24 h

results



## **Conclusion**

- Nanoparticle library based on SPIONs was successfully produced.
- Core material has no affect on protein adsorption.
- Different of surface properties facilitate for a specific proteins fishing.
- Define adsorbed protein will be performed by MS

## **Out look**

- Combination of methods for data interpretation is necessary for understanding particles behavior and particle-cell interaction.

# Acknowledgement

- SNF and European project FP7 (NanoDiaRA)
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- Dr. Morteza Mahmoudi

**Thank you very much for  
your attention**