ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

UNIVERSITÉ DE GENÈVE

NanoDiaRA

Particles, Molecules & Cells · Diagnosis in-vitro & in-vivo · Rheumatoid Arthritis & Osteoarthritis

EFFECTS OF DIFFERENT SURFACE CHARGE BASED SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES (SPION) ON BIODISTRIBUTION IN RAT AND EX VIVO PROTEIN FISHING

Usawadee Sakulkhu[1], Lionel Maurizi[1], Azza Gramoun[2], Marie-Gabrielle Beuzelin[1], Géraldine Coullerez[1], Jean-Paul Vallée[2], Heinrich Hofmann[1]

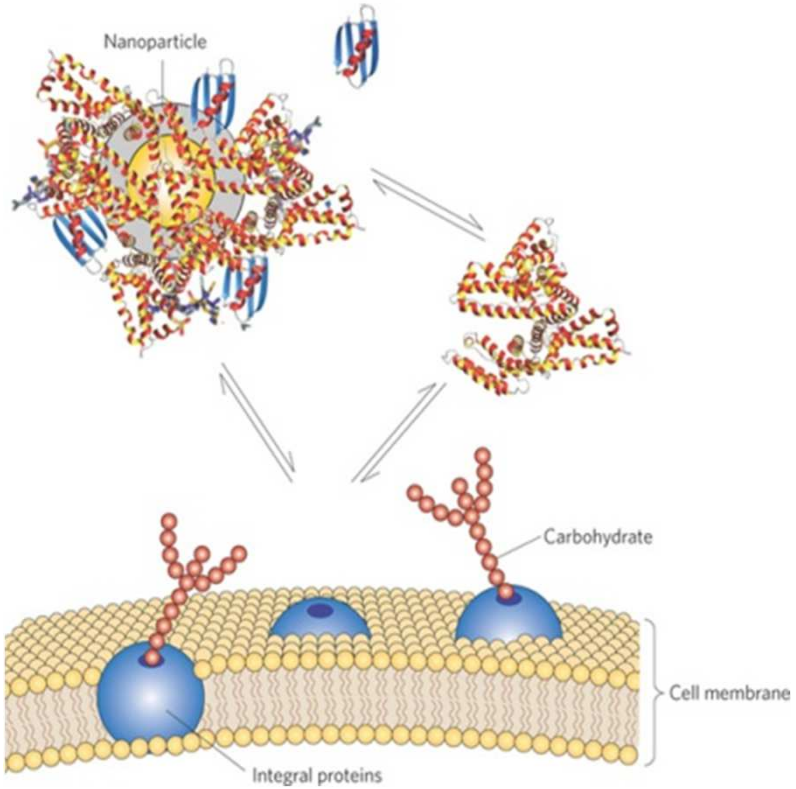
[1]Powder Technology Laboratory, École Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland

[2] Departement of Radiology, University of Geneva and Geneva University Hospital, 1211 Geneva 14, Switzerland

Nanosafe 2012, 13th to 15th November 2012
Minatec, Grenoble, France

Outline

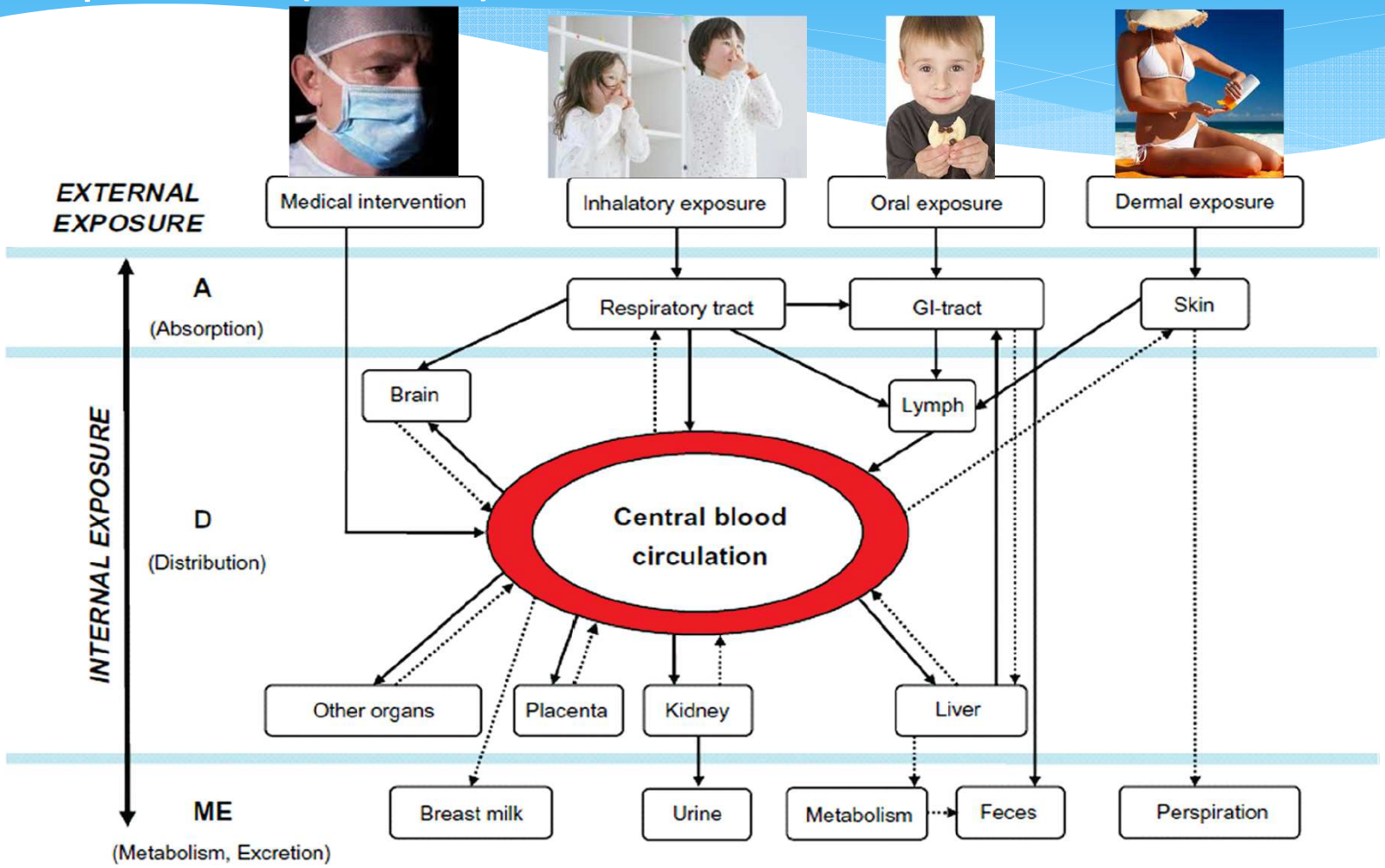
* Introduction
* Materials and Methods
* Results and Discussion
* Summary



Nanomedicine: Sizing up targets with nanoparticles, Rod Minchin, Nature Nanotechnology 3, 12 - 13 (2008)

Introduction:

Absorption, distribution, metabolism and excretion of Nanoparticle (ADME)

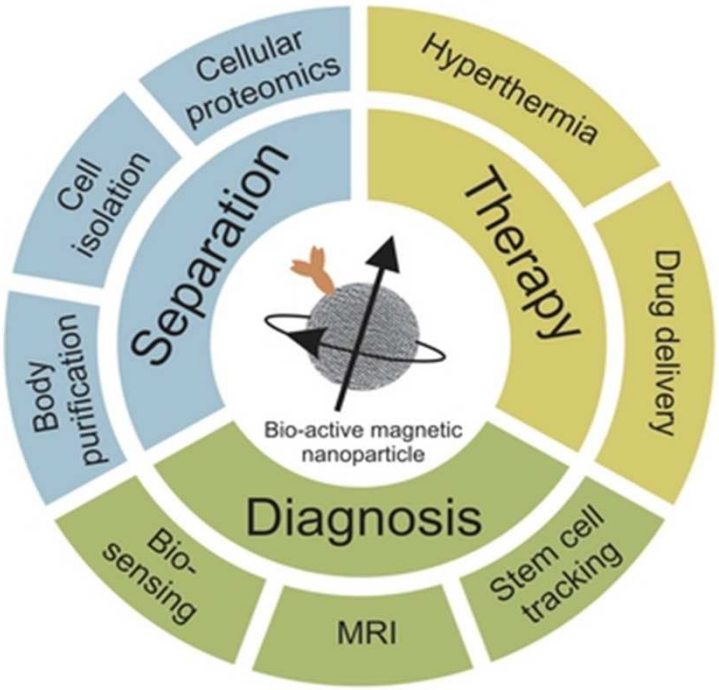


Physiologically Based Pharmacokinetic Modeling of Nanoparticles, Mingguang Li et al., VOL. 4 · NO. 11, 6303–6317 (2010)

Introduction:

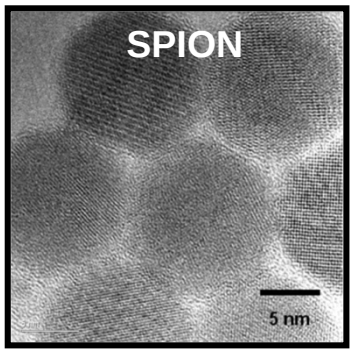
SuperParamagnetic Iron Oxide Nanoparticles (SPION)

SPION Applications



Particle characteristics:

- Primary crystalline iron oxide particles (γ–Fe_2O_3, maghemite)
- Mean diameter of 8±1nm (TEM)
- Superparamagnetic behaviour at room temperature
- Single particles, beads
- Characterization *in vitro*
- Application *in vivo*

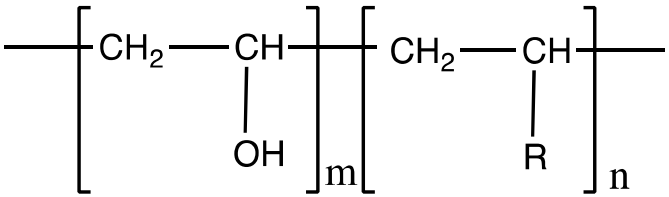


A. Petri-Fink, H. Hofmann ,NanoBioscience, IEEE Transactions on, 6/4 ,2007; 289.
D. Hellstern, et al, J. Nanoscience and Nanotechnology, 6/9-10, 2006; 2829.

Aim

* To investigate the effects of different surface charge SPION on biodistribution in Rat and adsorbed protein fishing.

Polyvinyl alcohol (PVA):



PVA
AminoPVA
CarboxyPVA

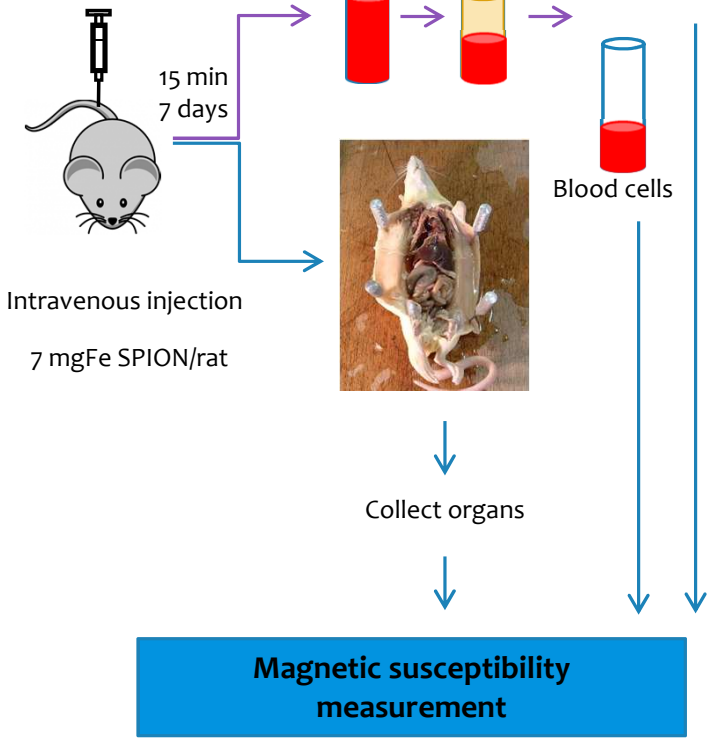
R= OH
R= NH2
R= COOH

Nanoparticle characteristics (at pH7.4)

Functional group	Hydrodynamic size (nm)	Zeta potential (mV)	Charge
-NH2	90±31	+13±3	Positive
-OH	95±18	+6±1	Neutral
-COOH	91±22	-15±1	Negative

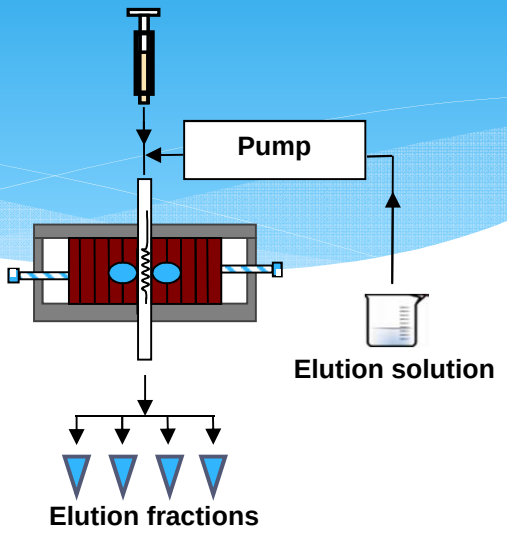
Interaction of Functionalized Superparamagnetic Iron Oxide Nanoparticles with Brain Structures
Feride Cengelli, et al, JPET July 2006 vol. 318 no. 1 108-116

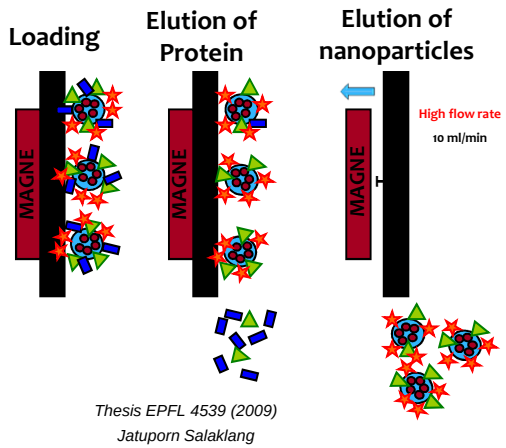
Methods



A magnetic reactor for protein separation

- Nanoparticle-protein complex
- Nanoparticles loading to a magnetic reactor
- Washing & Elution of particle bound proteins
- Elution of nanoparticles
- Elution of tightly bound proteins from particles with a sample buffer
- Protein separation by SDS-PAGE





Thesis EPFL 4539 (2009)
Jatuporn Salaklang

Elution fractions: FT, PBS1, PBS2, PBS(0.5MNaCl), PBS(1.0MNaCl),PBS (2.0MNaCl), NP

Results

* Biodistribution (Magnetic susceptibility)
  * Biodistributions: Positively charged , Neutral, Negatively charged Nanoparticles at 15 min
  * Biodistributions: Positively charged Nanoparticles at 15 min and 7 days
* Protein fishing (SDS-PAGE)

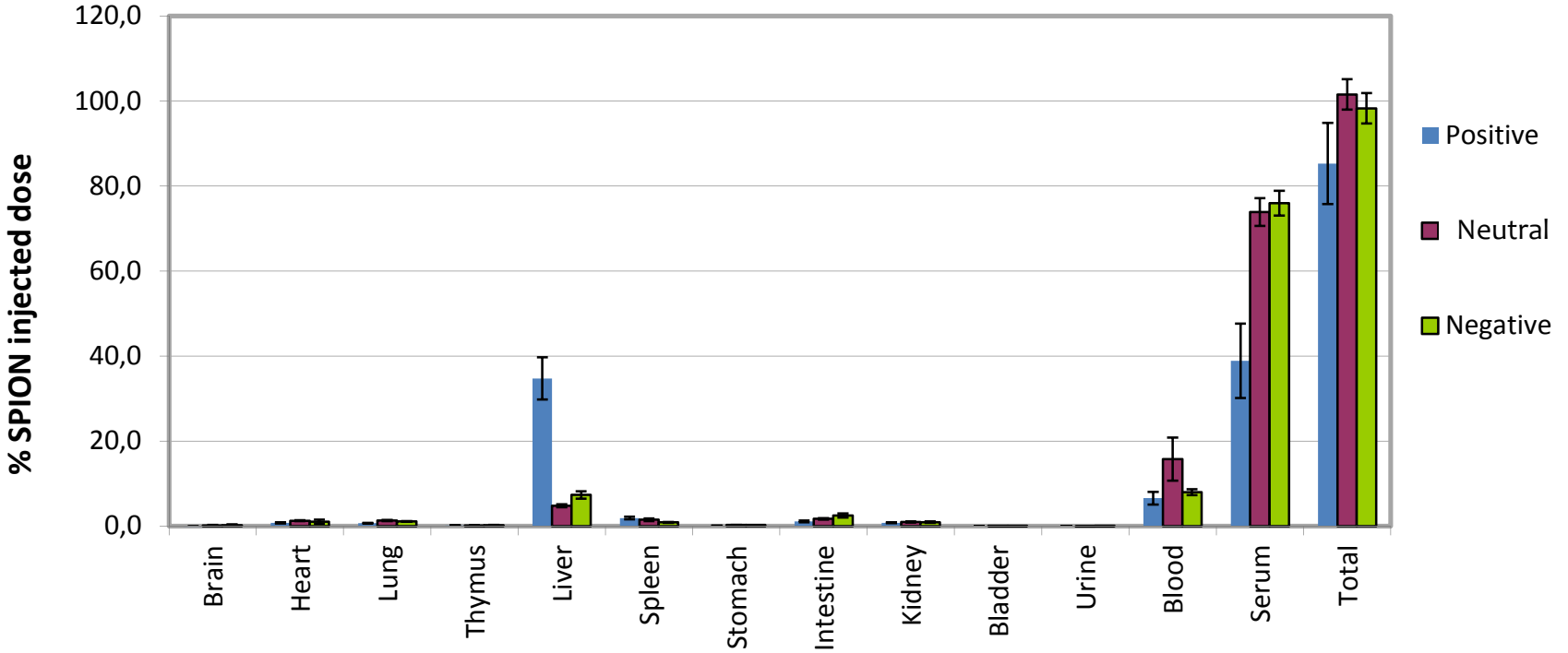
Results:

Organ list for Biodistribution by Magnetic susceptibility

Sample	Information
Whole blood cells	Blood
Serum	
Heart	Circulation
Brain	Evidence of NP across Blood brain barrier
Thymus	Immune system (T-Lymphocyte)
Lung	Respiratory system
Liver	Reticuloendothelial system (RES)
Spleen	
Stomach	Digestive system
Intestine (small+large)	
Kidney	Renal Clearance
Bladder	
Bladder content (Urine)	

Result:

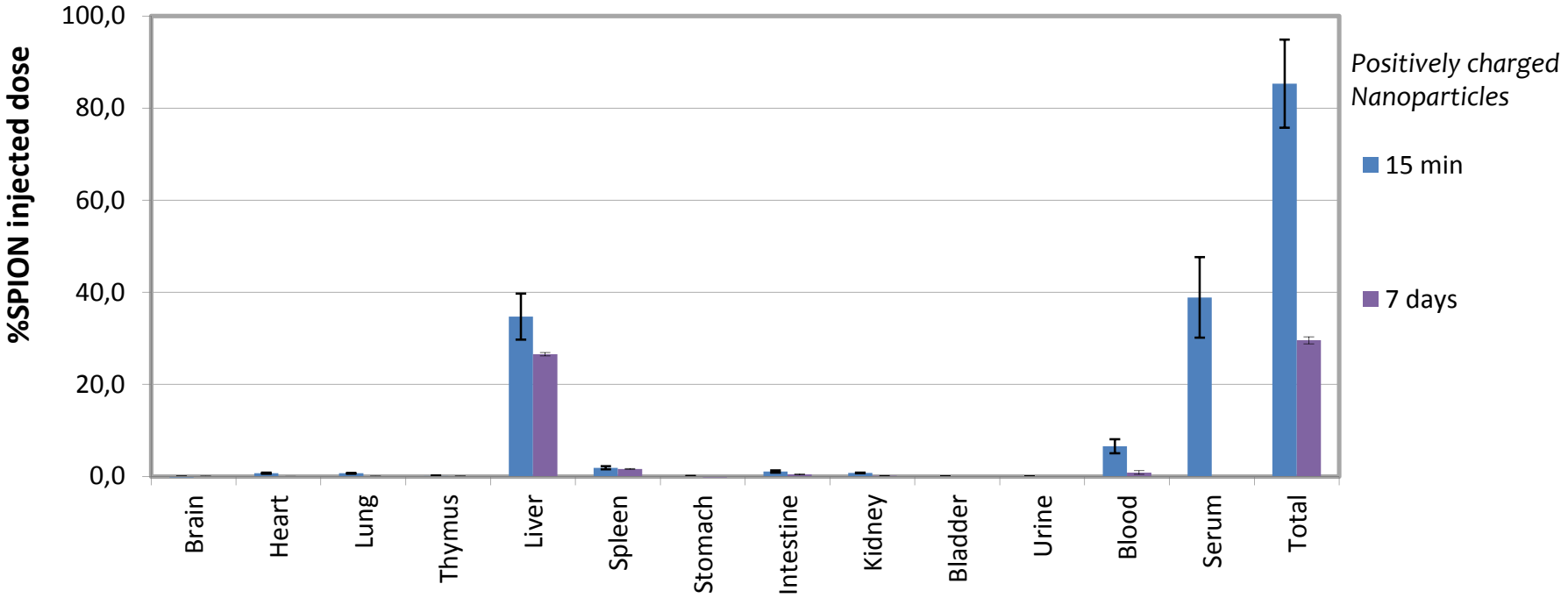
Biodistribution of 3 different charged nanoparticles at 15 min post-injection



- Almost 100% of SPION injected dose were recovered.
- Nanoparticles are mainly found in Liver and Serum.
- Slightly positive and negative have similar behaviour.

Result:

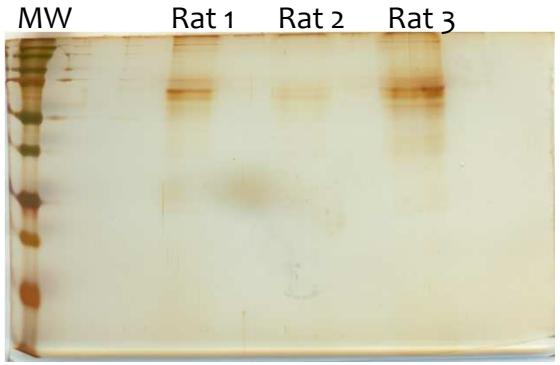
Biodistribution of ***Positively*** charged nanoparticle at 15 min and 7 days post-injection



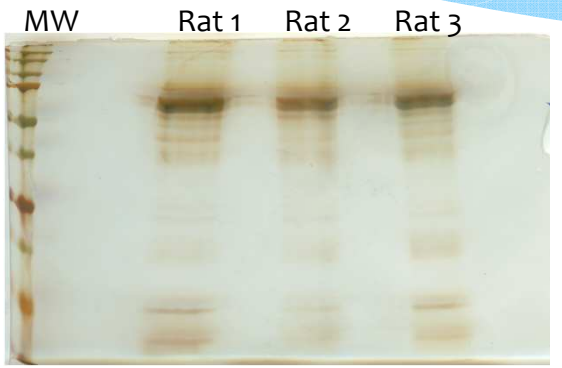
- At 7 days post-injection
  - 30% of SPION injected dose was detected
  - 90% of detected SPION located in Liver and No SPION was detected in blood.

Results:
SDS-PAGE (silver staining)

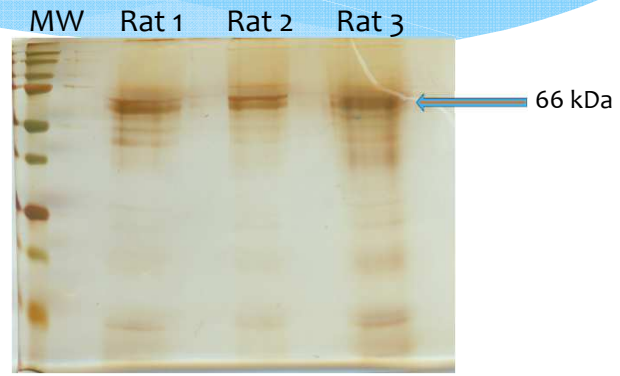
Positively charge NP at 15 min



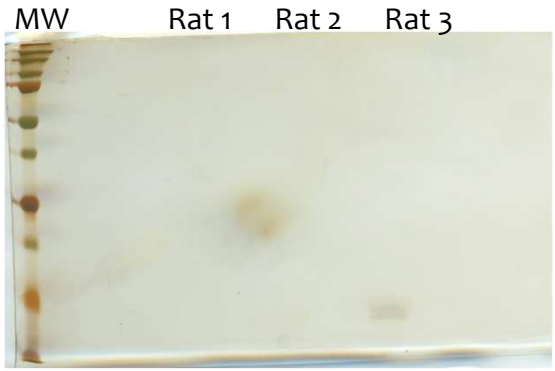
Neutral NP at 15 min



Negatively charged NP at 15 min



Positively charged NP at 7 days



- Common protein at 66 kDa
- Neutral and Negatively charged nanoparticles share the similar pattern of protein adsorption.
- From the intensity of the bands, detected proteins are correlated to SPION amount in serum.

Summary
Different surface charged PVA coated SPION

* Neutral and Negatively charged Nanoparticles have a similar behaviour on Biodistribution and Protein adsorption.
* Neutral and Negatively charged Nanoparticles seems to stay longer in blood stream compare to Positively charged nanoparticles.
* 60% of Positively charged nanoparticle decreased after 7 days post-injection.
* Protein fishing can be correlated to the biodistribution .

Acknowledgements

* Swiss National Science Foundation (SNSF: 205321-120161)
* European Project FP7 (NanoDiaRA)

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

UNIVERSITÉ DE GENÈVE

NanoDiaRA

Particles, Molecules & Cells · Diagnosis in-vitro & in-vivo · Rheumatoid Arthritis & Osteoarthritis

Thank you very much for your attention