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Superparamagnetic silica-iron oxide nanocomposites

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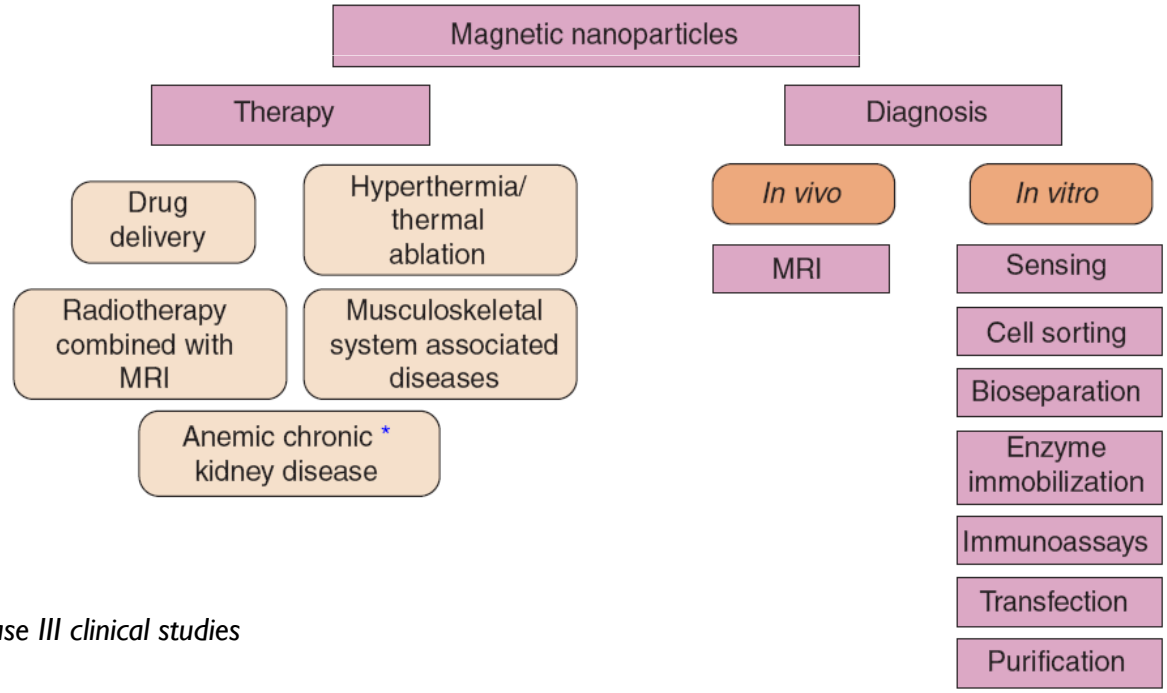
Biomedical applications of magnetic NPs

Major advantages of magnetic NPs :

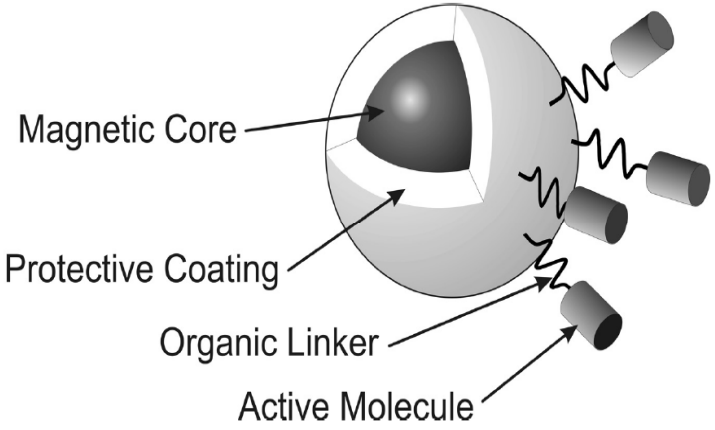
- Can be visualized (magnetic resonance imaging, MRI: FDA-approved contrast agents)
- Can be guided or held in place by means of a magnetic field
- Can be heated in a magnetic field to trigger drug release or to produce hyperthermia/thermal ablation of tissue (also for other NPs capable of absorbing NIR, μ-wave, ultrasound radiation)



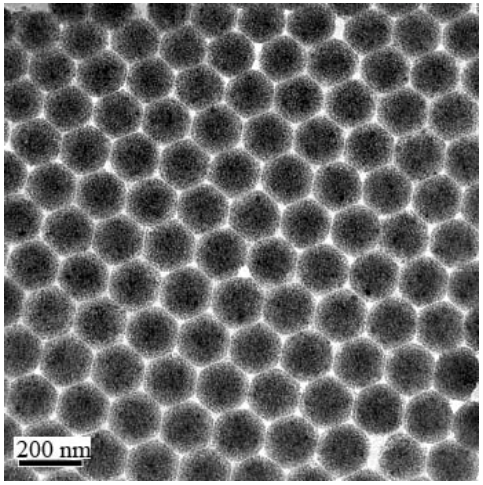
* *Ferumoxytol in Phase III clinical studies*

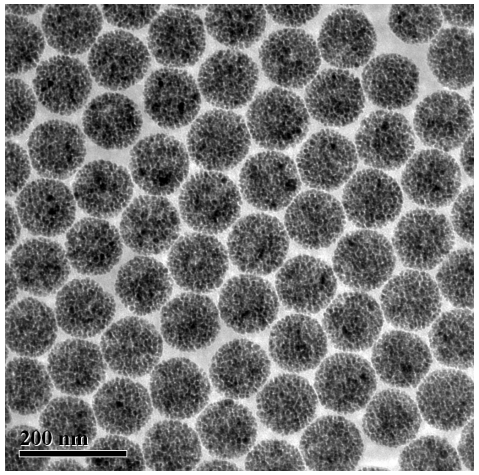
Biomedical applications of magnetic NPs: Drug & Gene Delivery

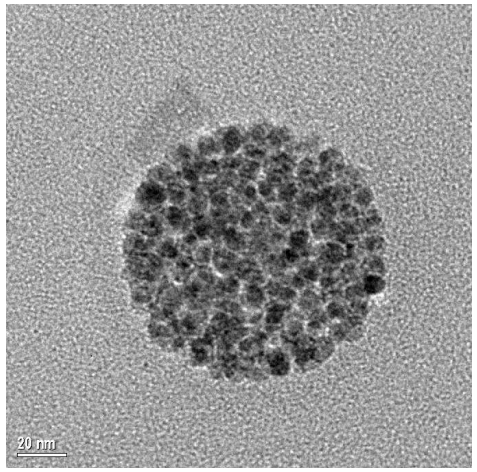
- Basic idea: therapeutic agents are attached to or encapsulated within a magnetic micro- or NP
- Usually consist of a magnetic core with a polymer or metal (oxide) coating which can be functionalized
- For (usually) microparticles also porous particles with precipitated magnetic NPs in the pores
- Cytotoxic drugs, genes, targeting ligands (antibodies) attached to the functionalized shell
- After injection, by applying a magnetic field over the target site the particle/therapeutic agent complex is captured and extravasated at the target → **magnetic targeting**
- For *in vitro* gene transfection high-field, high-gradient magnetic fields can be used to increase sedimentation rates, particle internalization and gene expression → **magnetofection**



Superparamagnetic iron oxide nanoparticles (SPION)







- The NBC group is a world leader in the synthesis of monodispersed magnetite particles for biomedical use (commercialized through the Allrun company in Shanghai)
- The magnetite particles can be synthesized in different sizes, and consist of aggregates of smaller magnetite crystals → high magnetization
- The small magnetite crystallite size makes the particles superparamegnetic, which is ideal for **high-throughput *in vitro* diagnostics** (immunoassays) and as **magnetic contrast agents** in MRI applications *in vivo*
- Also potential **hyperthermia agents**, where the magnetic particles are heated selectively by application of an high frequency magnetic field (e.g. hyperthermia of tumors)

Core – shell magnetic nanoparticles

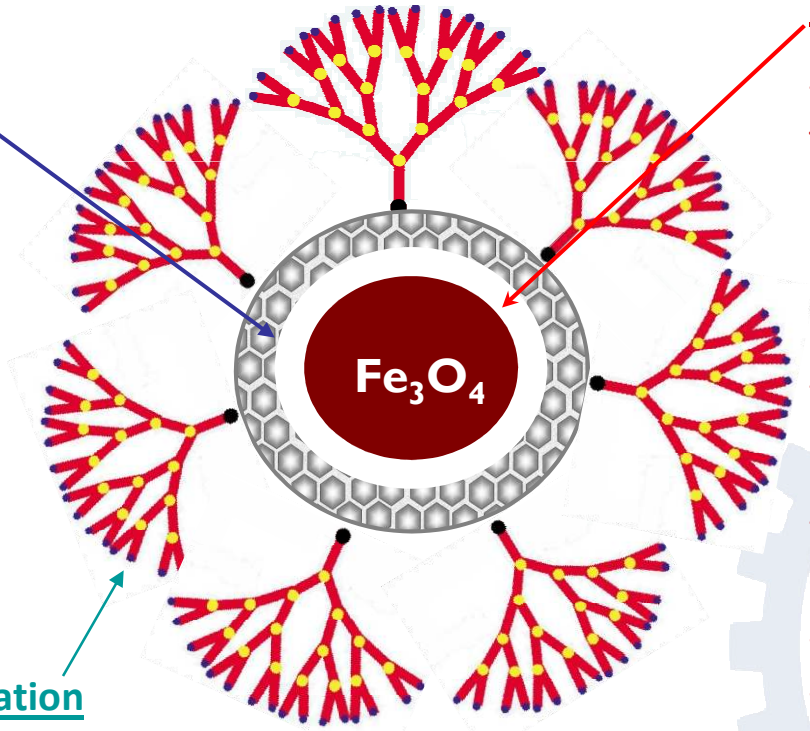
- Some biomedical applications require **core-shell magnetic NPs** consisting of a metal or metallic oxide core, encapsulated in an inorganic or a polymeric coating that renders the particles *biocompatible, stable, and may serve as a support for biomolecules* as well as *protect the core from leaching*

Mesoporous layer

-for carrying large amounts of payloads (drugs/ proteins)

- drastic increase in effective surface area

- efficient further functionalization



Middle silica layer

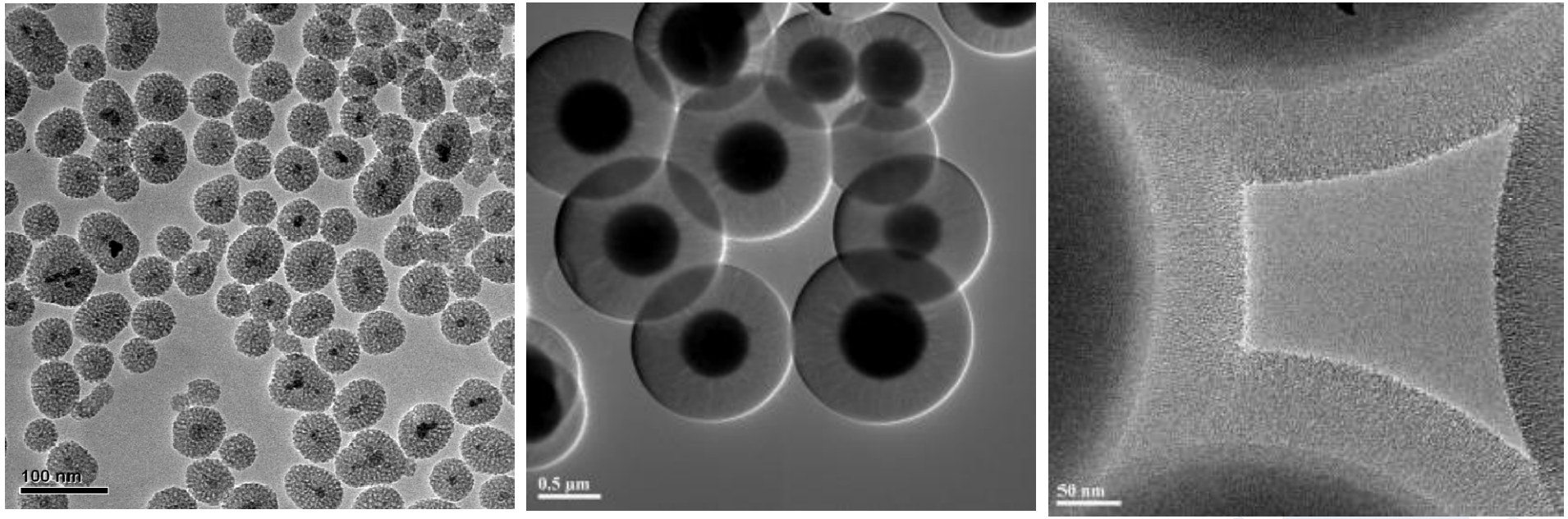
- provides for easy further functionalization by all methods known for silica (including deposition of a mesoporous layer)

- Enhanced biocompatibility

- facilitates stabilization in an environment with slightly alkaline pH or high salinity (IEP 2-3 instead of almost neutral)

Further functionalization of the particle surface + surface charge tuning

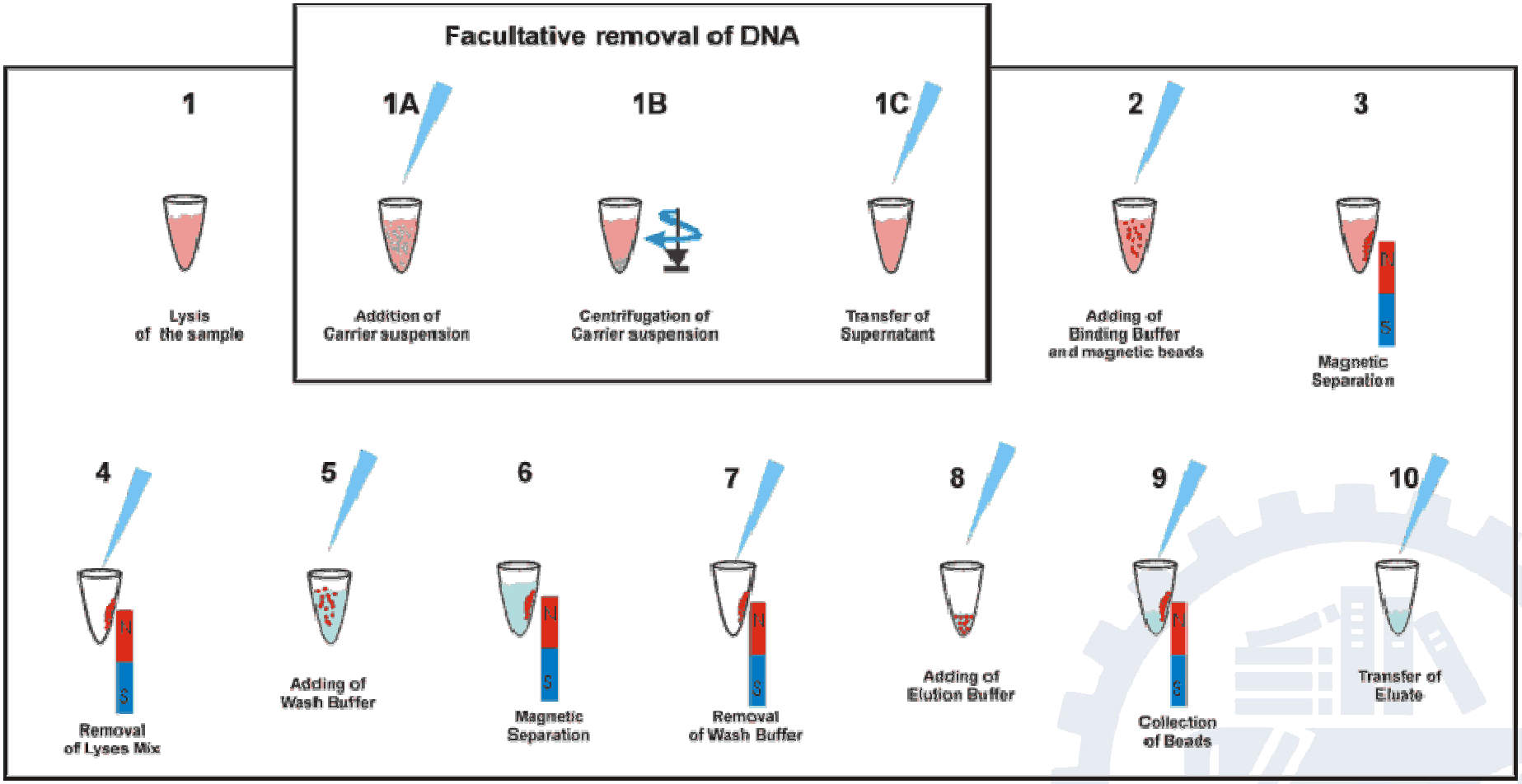
Magnetic SiO_2-SPION composites



TEM images & samples by Jixi Zhang, Nano Biomedical Research Center, Med-X Institute, STJU

- SPIONs of different sizes (including single crystals) can be coated with non-porous and/or mesoporous layers forming versatile nanocomposites
- **High magnetic moment** coupled with a mesoporous silica layer used for separation of (short) DNA & *in vitro* diagnostics (mag. aggregates i.e. beads)
- Single magnetite crystals for efficient vascular magnetic resonance imaging

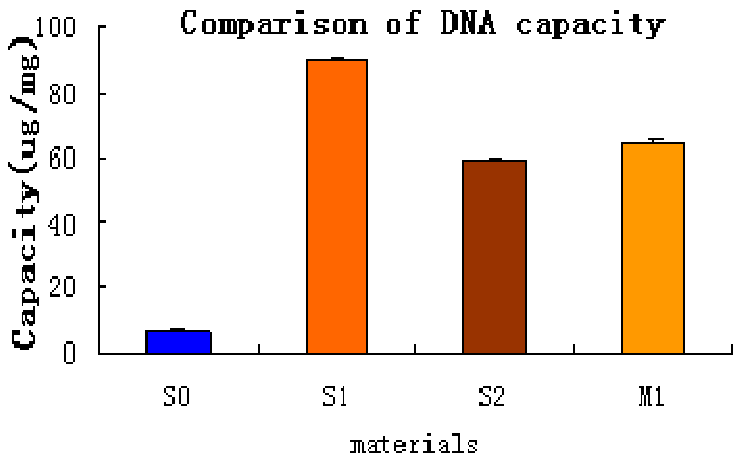
SiO_2-Fe_3O_4 core-shell structures for DNA separation

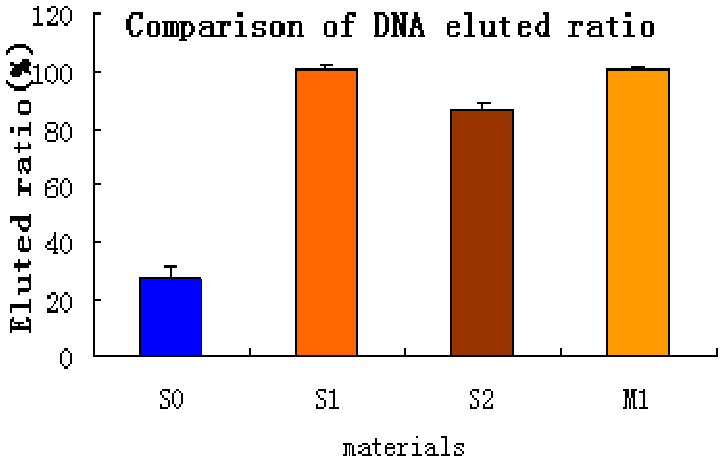


- High-throughput magnetic DNA separation process

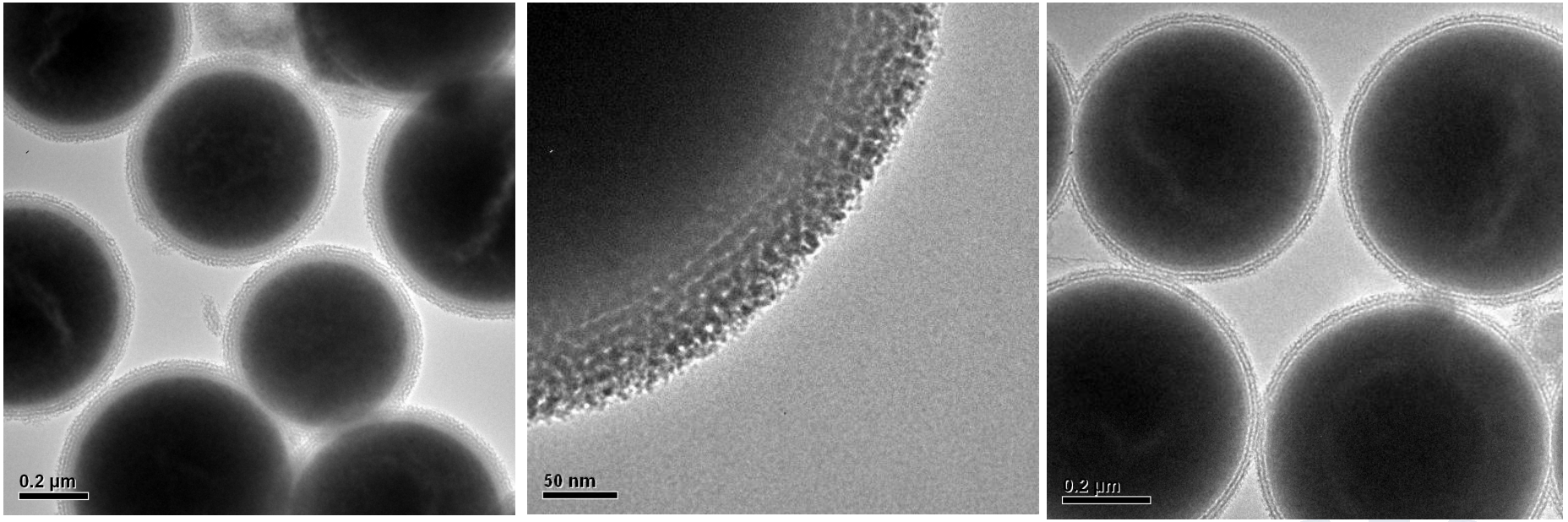
SiO_2-Fe_3O_4 core-shell structures for DNA separation

- Nanostructured probes for biomolecule sensing (DNA, proteins)
- Automated *in vitro* assays based on magnetic separation
- Mesoporous coated materials showed huge capacity of DNA compared with standard silica beads, nearly ten times more than beads with a smooth surface.
- Adsorbed DNA is easily re-released from the surface of the beads - the eluted ratio reaches nearly 100%.
- Salmon sperm DNA (ave. 250 bp)





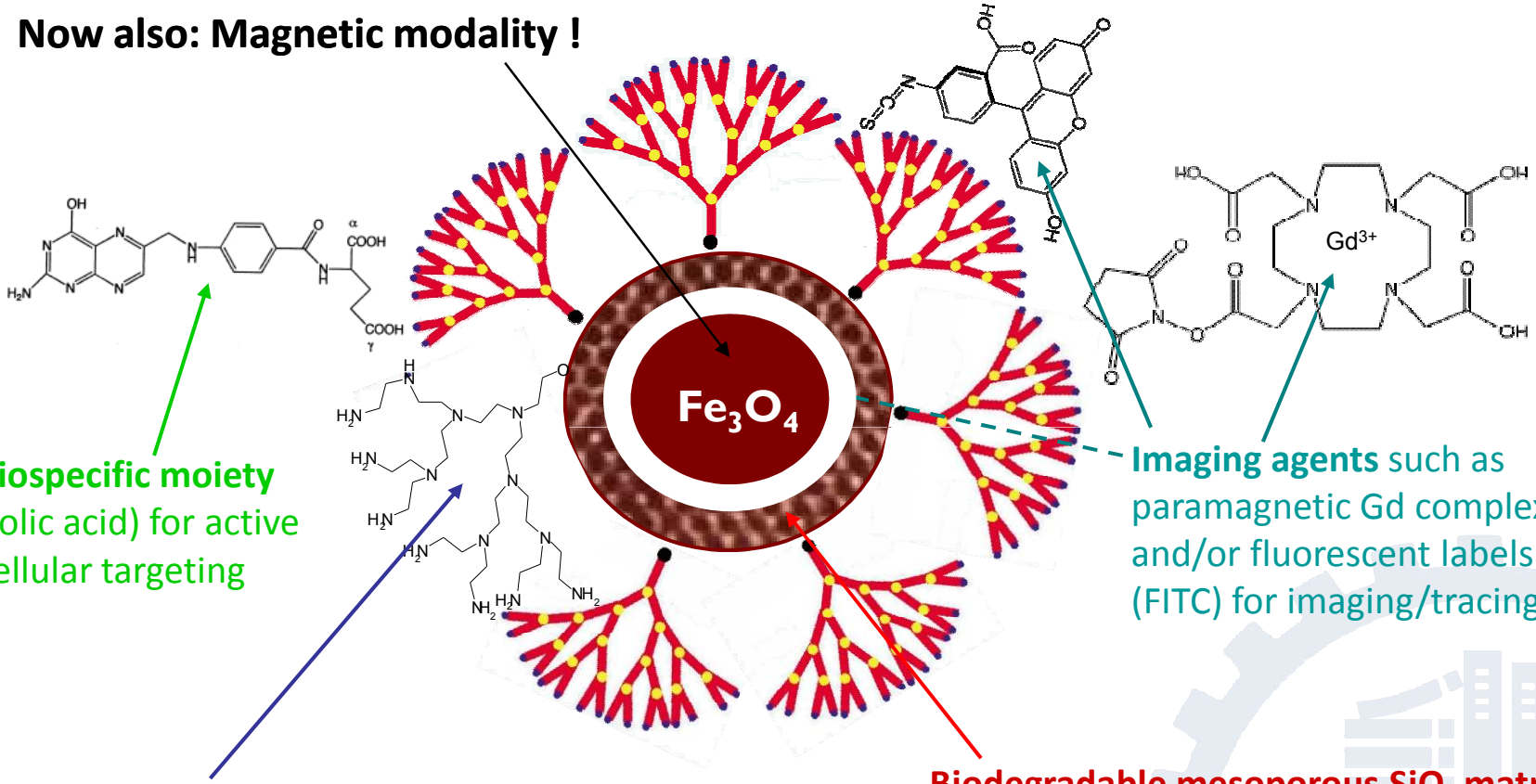
Pore-expanded core-shell SPIONs (”Nanowheels”)



- The standard pore size of mesoporous shells is limited to ~3 nm → OK for small-molecular drugs (drug delivery) and short-stranded DNA (diagnostics/separation)
- For macromolecular substances such as proteins (drug delivery/separation/diagnostics) or longer DNA strands larger pores would be needed
- Pore expansion protocols used for swelling of regular mesoporous silica generally unsuccessful
- Successful creation of pore sizes of 7 – 8 nm within uniform shells and thick pore walls

And the quest continues...

Now also: Magnetic modality !



Biospecific moiety (folic acid) for active cellular targeting

Imaging agents such as paramagnetic Gd complexes and/or fluorescent labels (FITC) for imaging/tracing

PEI-layer for a) providing reactive "hooks" for attachment, b) particle suspension stabilization, c) surface charge tuning → promoting RES evasion d) promoting endosomal escape, and possibly also: e) molecular gate properties (pH)

Biodegradable mesoporous SiO_2 matrix

for loading of large amounts of **drugs** for therapeutic delivery

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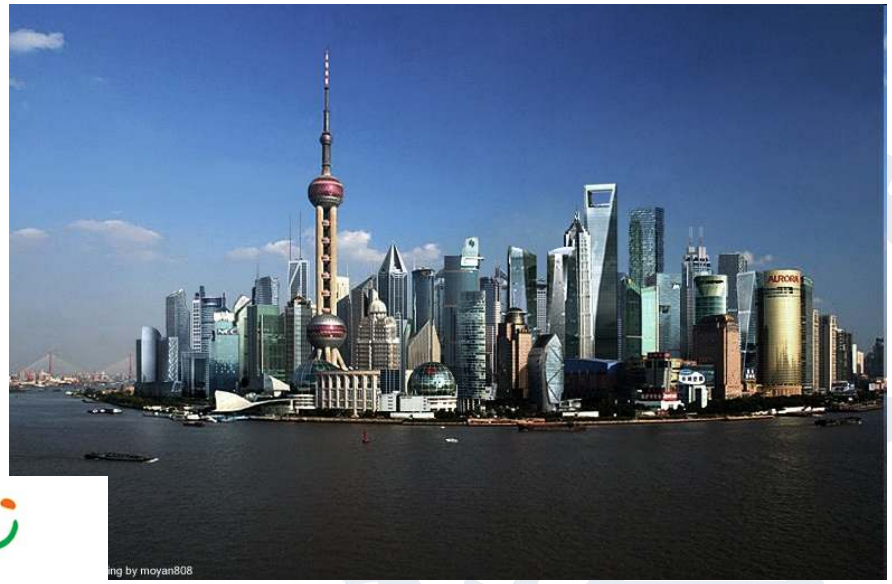
- The audience for listening !!!



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