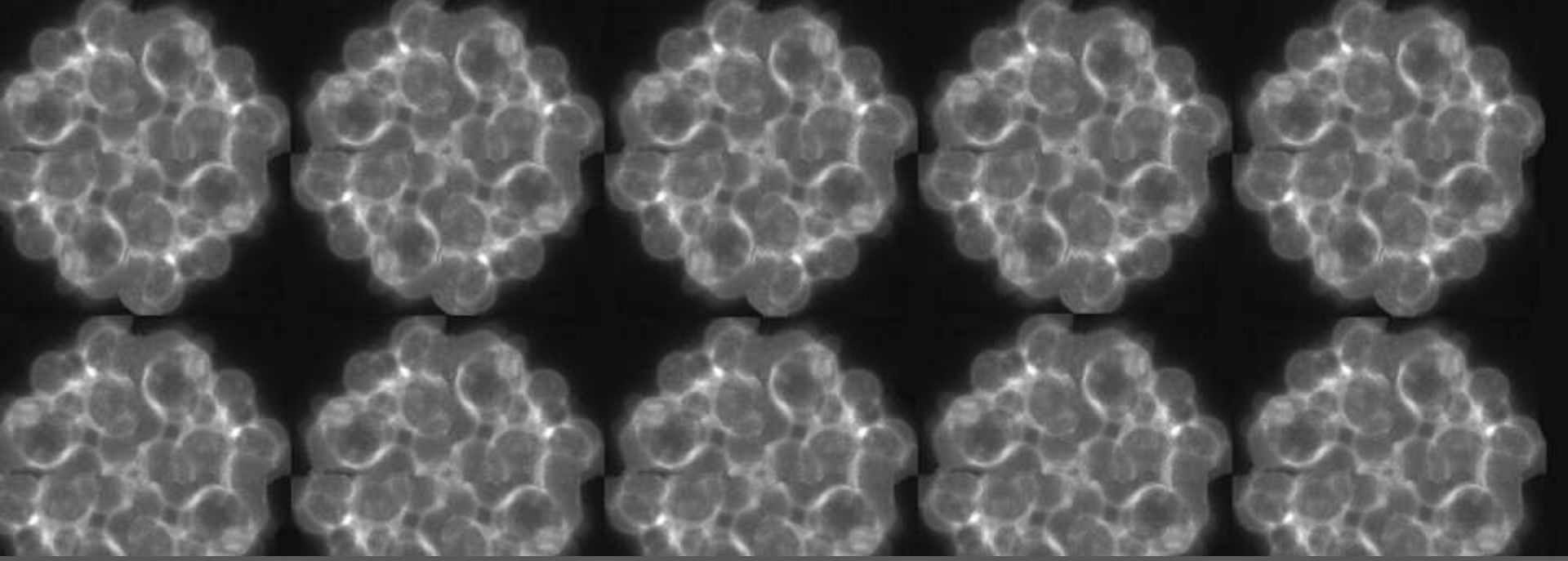


Magnetic nanoparticles for drug delivery

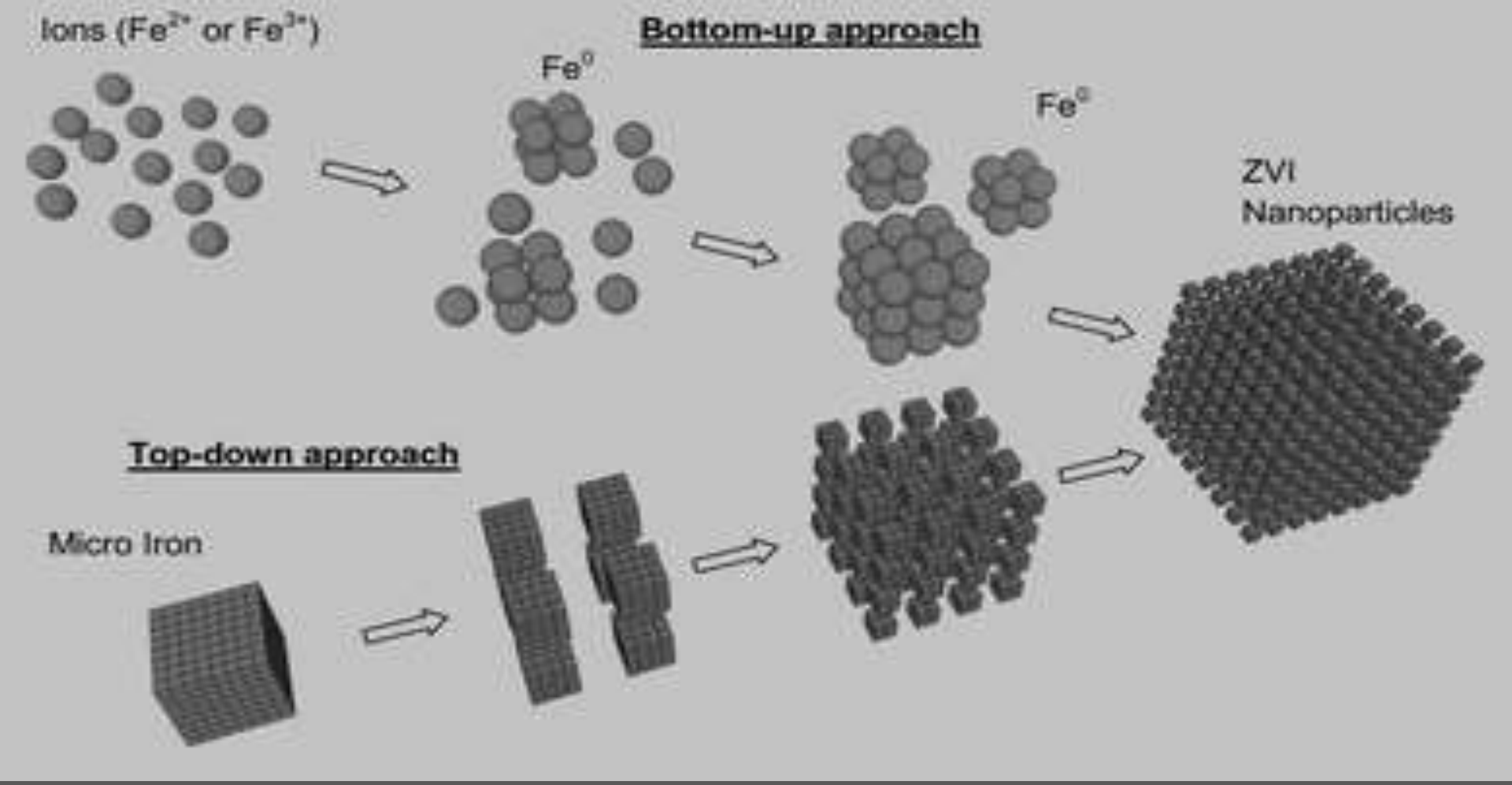
JUYOUNG KWON

I. Introduction : nanoparticles(NPs) & magnetic nanoparticles(MNPs)

II. Current status in clinical trials

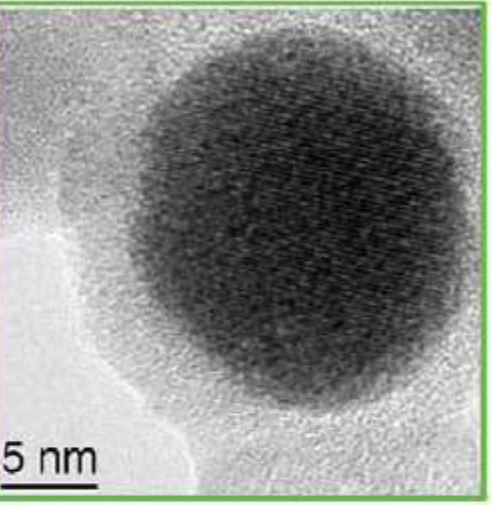
III. Essential requirements for fabrication of MNPs

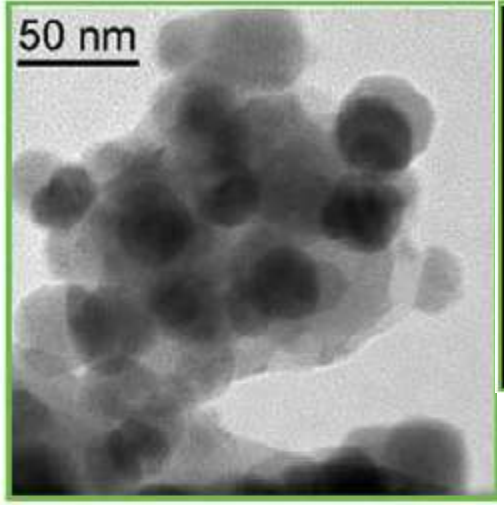
IV. Example of application

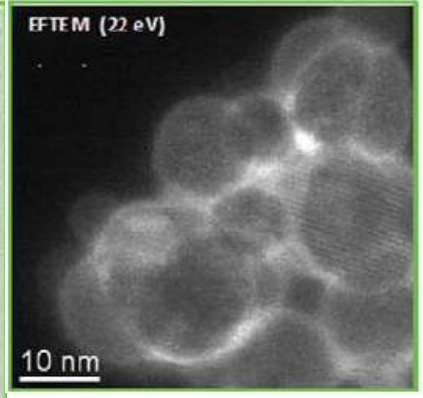


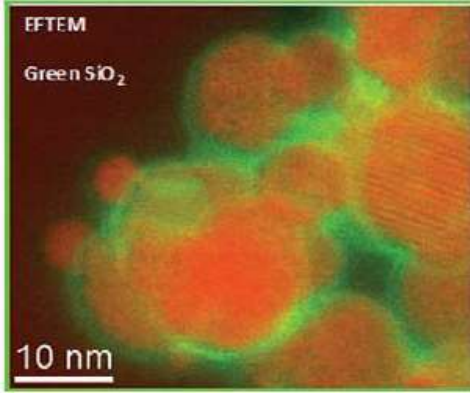
Nanoparticles (NPs)

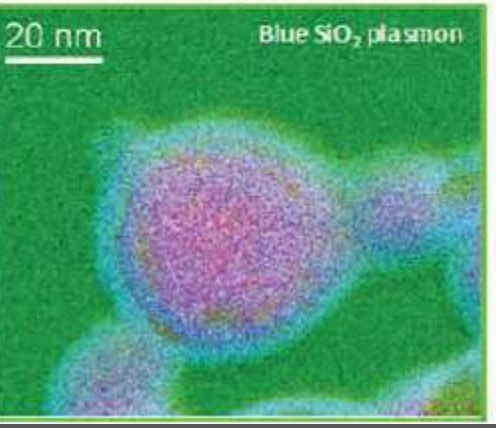
- ✓ Made of inorganic or organic(polymeric) materials
- ✓ Characteristics different from those of bulk materials of the same composition
  ∵ Size effects
- ✓ Mainly bottom-up methods : Self-assembly

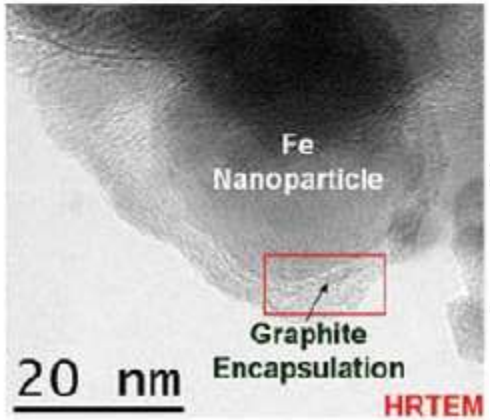






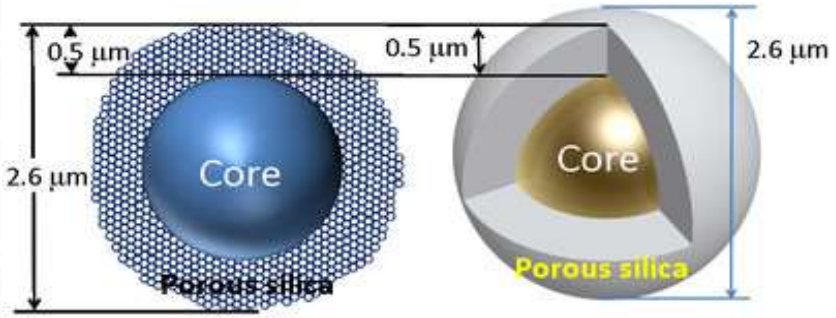






THE SOLUTION...

Schematic Diagram of Core Shell silica

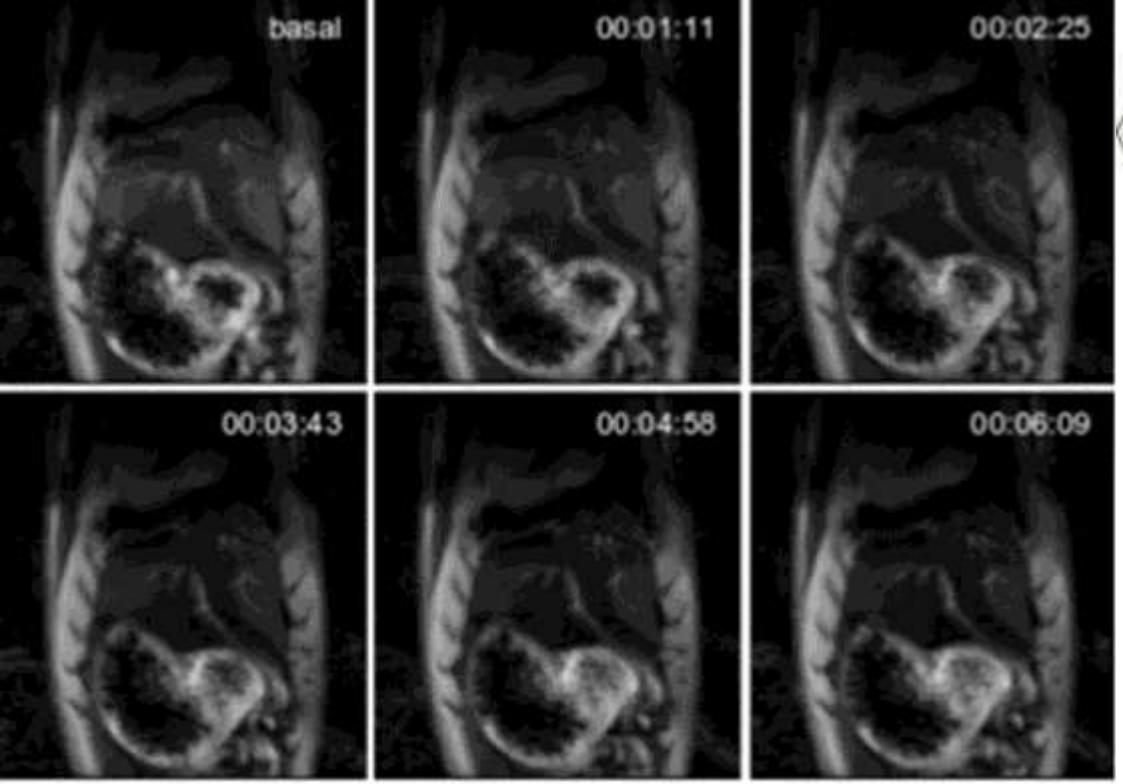


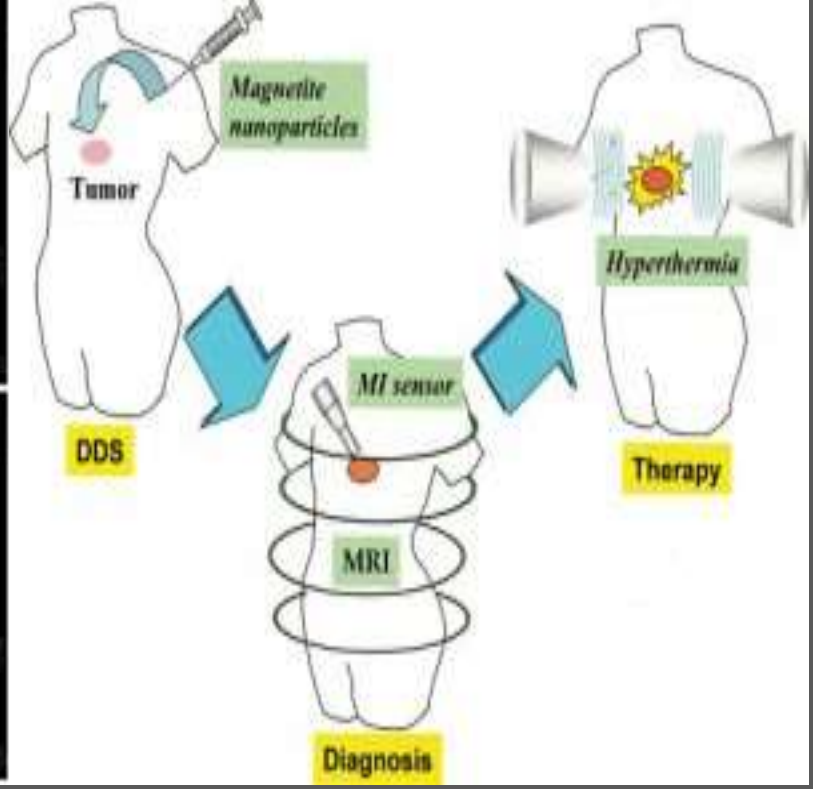
Particle diameter: 2.6 μm, Core diameter: 1.6 μm, Thickness of porous silica: 0.5 μm
Pore volume: 0.30mL/g, Specific surface area: 150 m^2/g, Pore diameter: 9 nm
The ratio of porous silica volume: 77%

Magnetic nanoparticles (MNPs)

- ✓ Require for biomedical application
- ✓ Core-shell structure
  - Core : metal or metallic oxide
  - Coating : inorganic or polymeric materials

→ renders particles biocompatible, stable, serve as a support for biomolecules

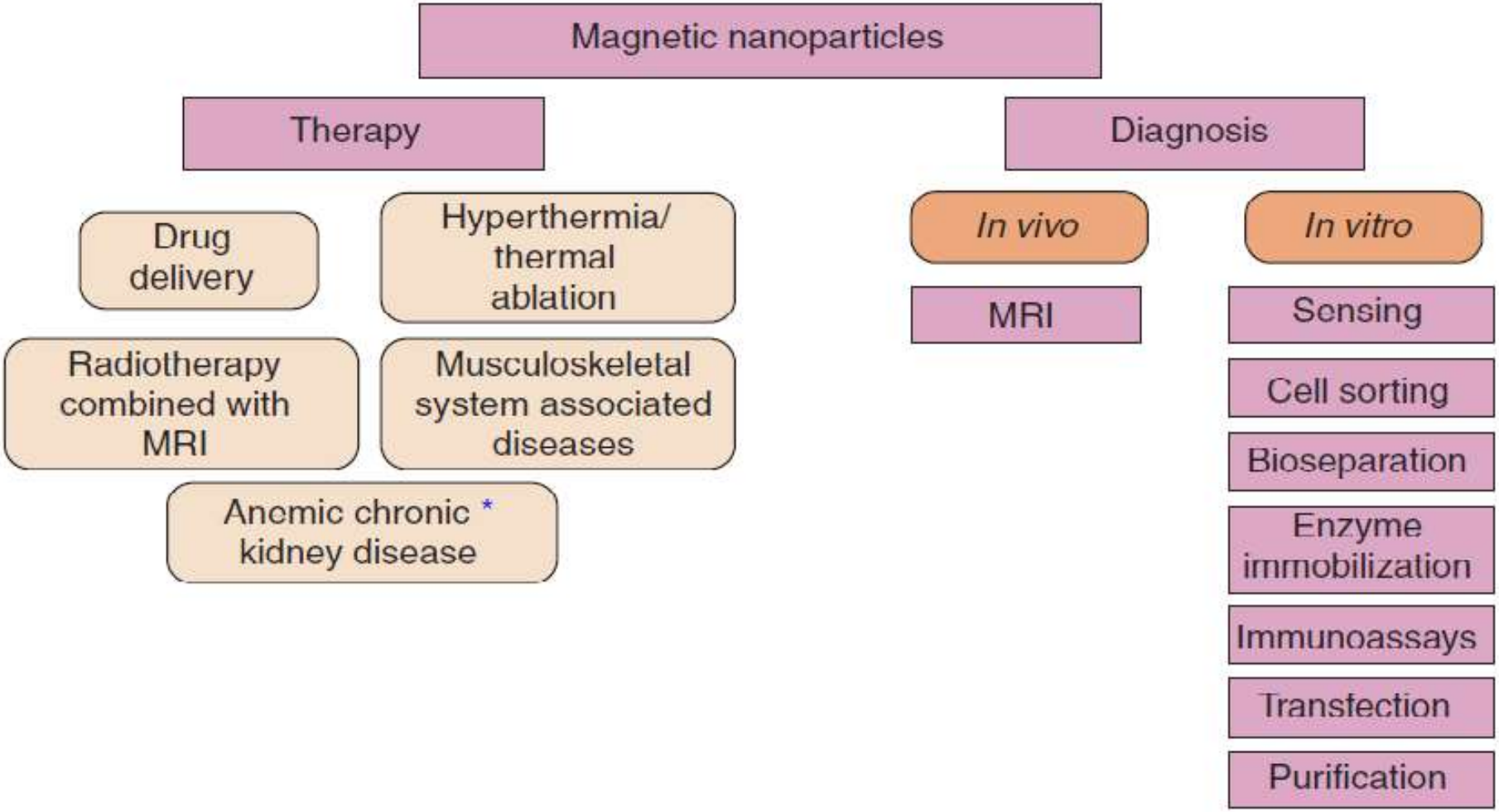




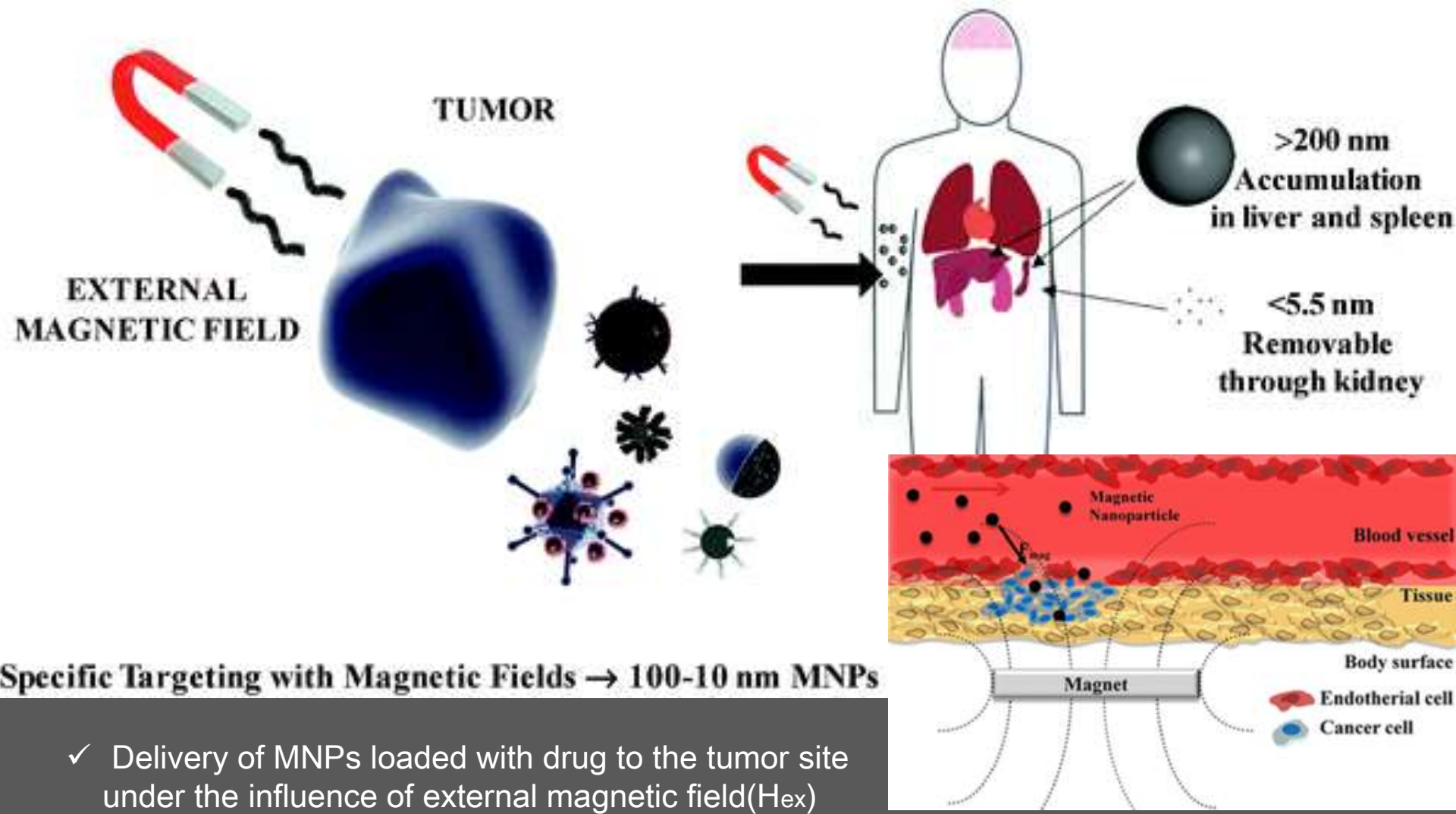
General applications of MNPs

- ✓ Magnetic contrast agents in MRI
- ✓ Hyperthermia agents
- ✓ **Magnetic vectors**

  : directed by means of a magnetic field gradient towards a certain location, such as in the case of the targeted drug delivery



- ✓ Exploit intrinsic properties of MNPs (Biocompatability & Selective targeting) to obtain medical breakthroughs in diagnosis and drug delivery
- ✓ Most promising applications : diagnosis and treatment of cancer

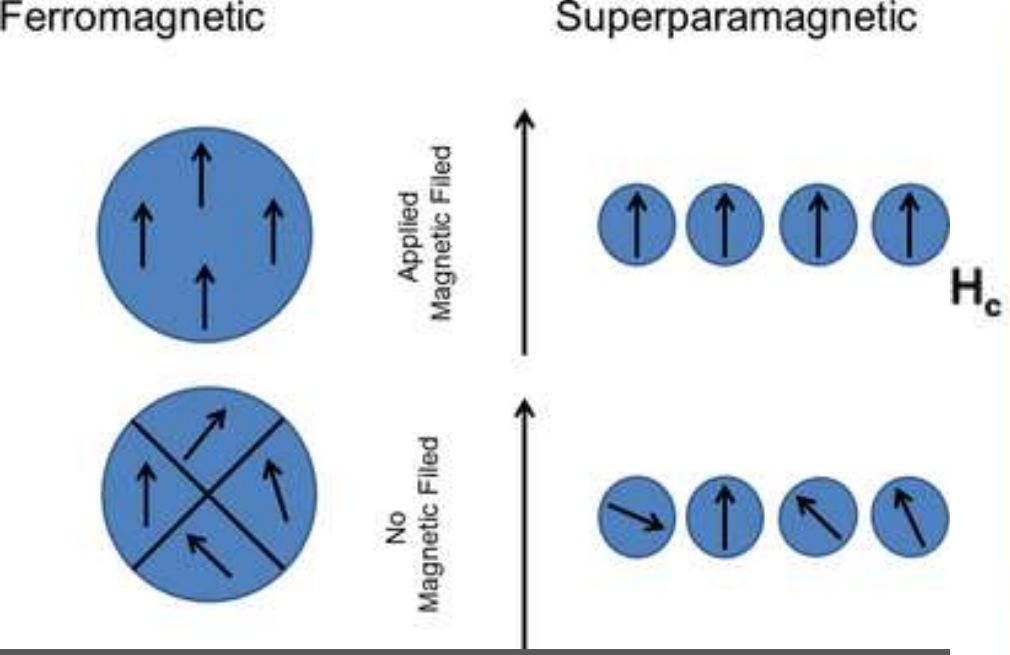


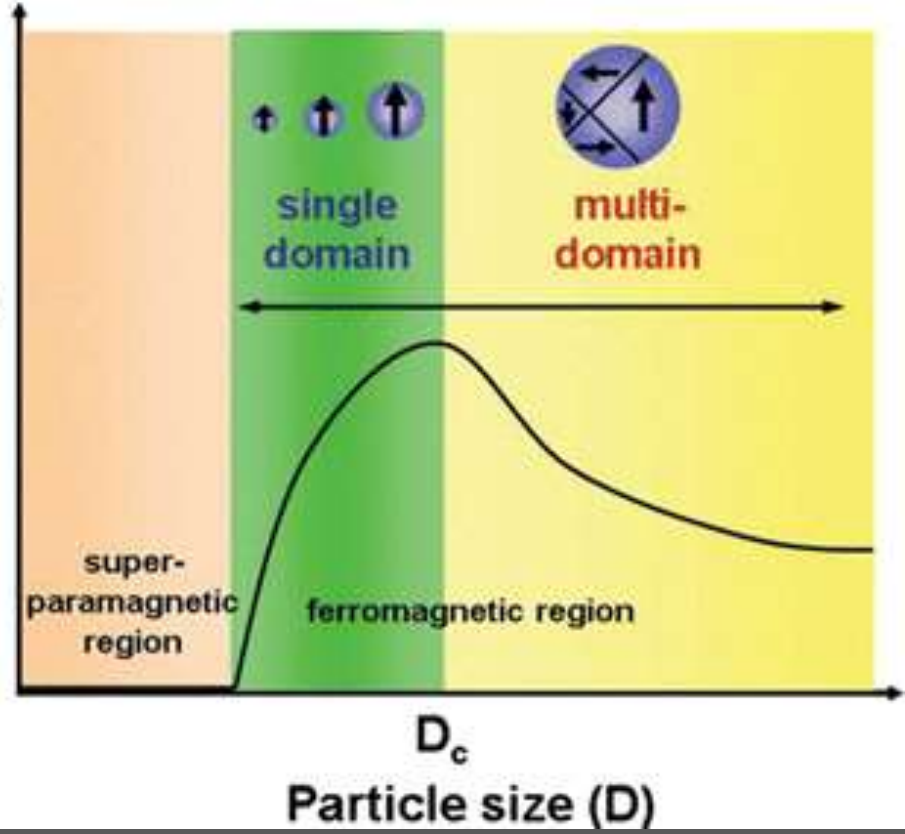
Specific Targeting with Magnetic Fields → 100-10 nm MNPs

- ✓ Delivery of MNPs loaded with drug to the tumor site under the influence of external magnetic field(H_{ex})

- ✓ Only magnetic(active) : under the influence of H_{ex}
- ✓ Rendered nonmagnetic(inactive) : once H_{ex} is removed

→ Such magnetic properties acquired by very small nanoparticles (<10nm)

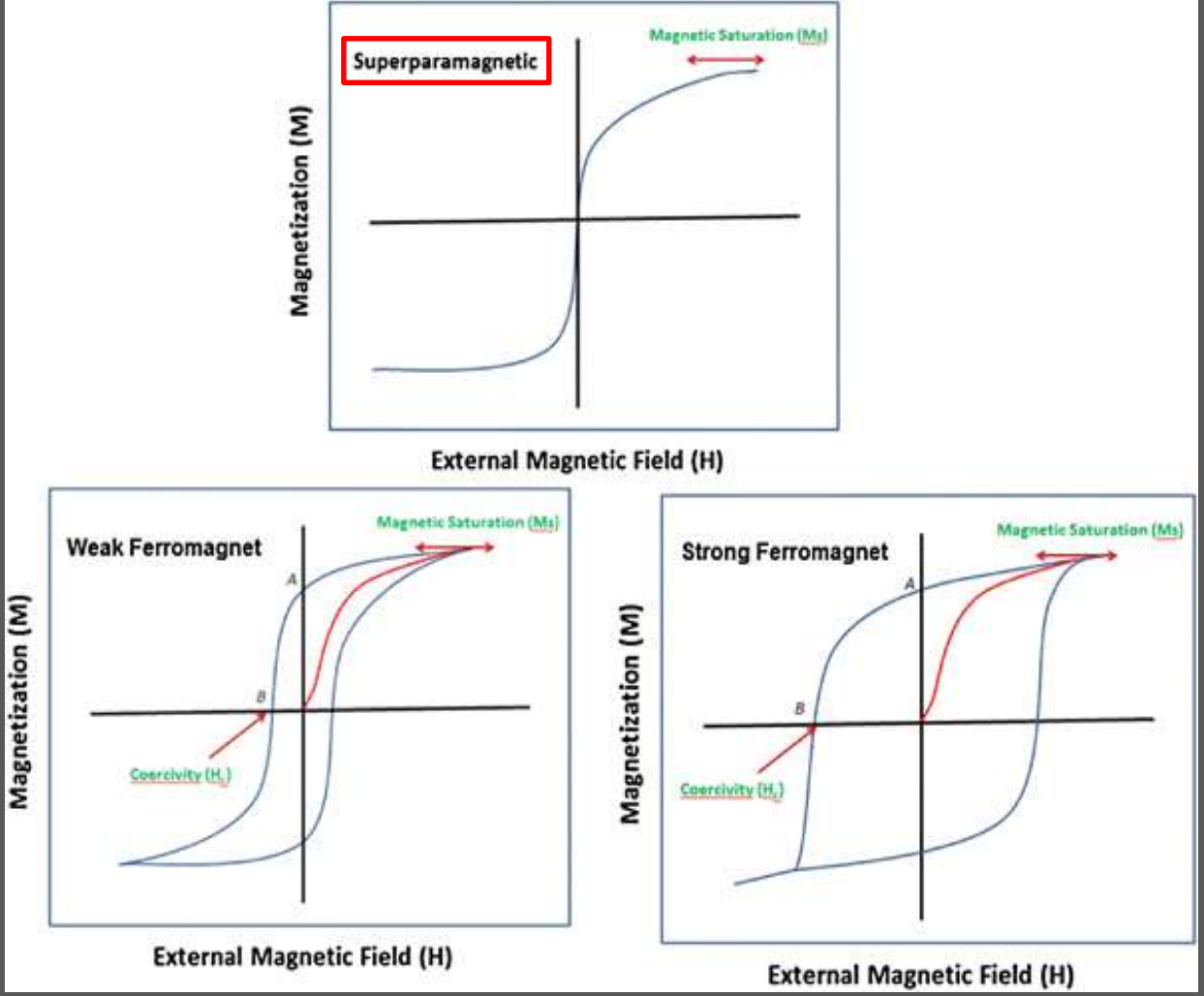




- ✓ Dimension of MNPs reduced
  : E(creating domain wall) > E(supporting single-domain state)

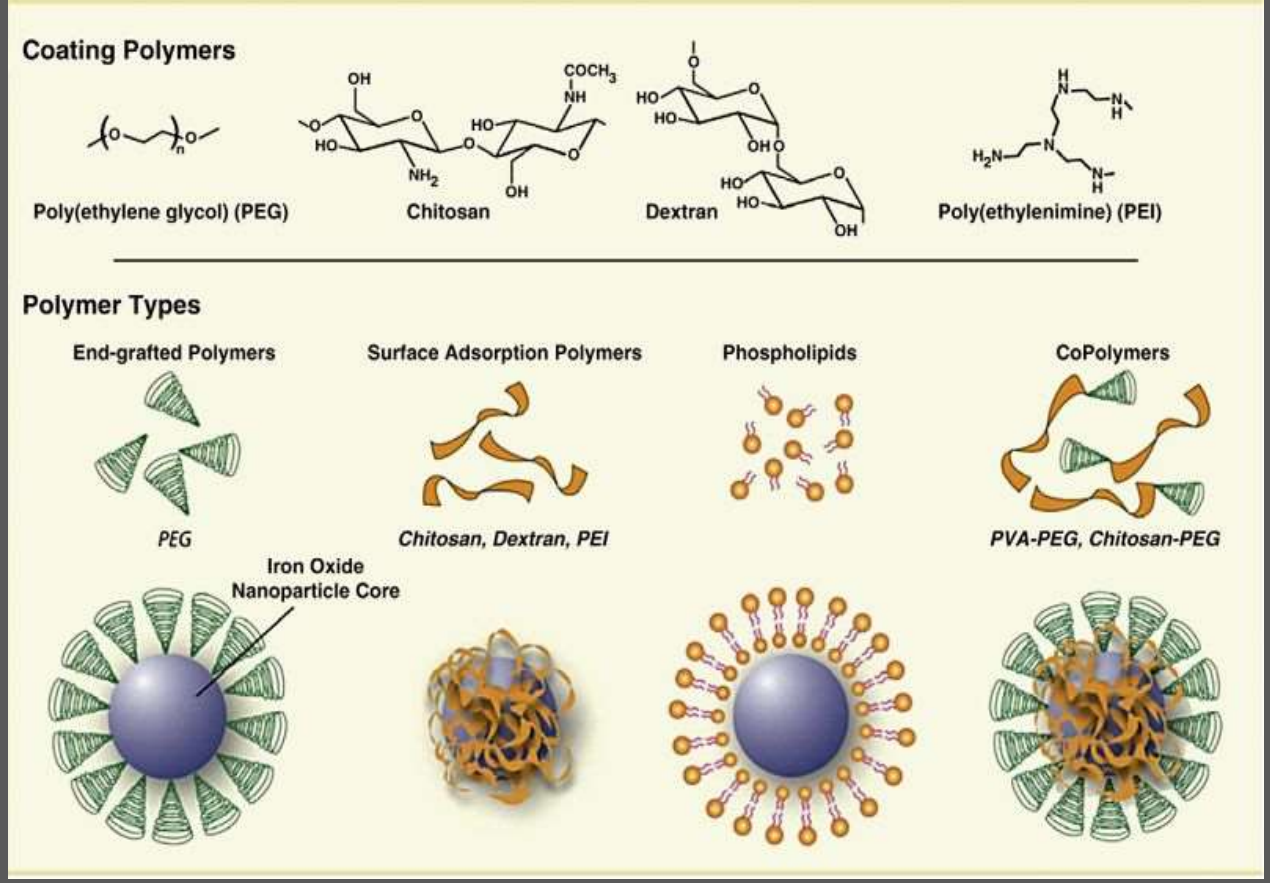
- ✓ Below a critical size
  - All domain walls washed away : Single-domain state
  - Hc = 0

"Superparamagnetic"



Superparamagnetic NPs

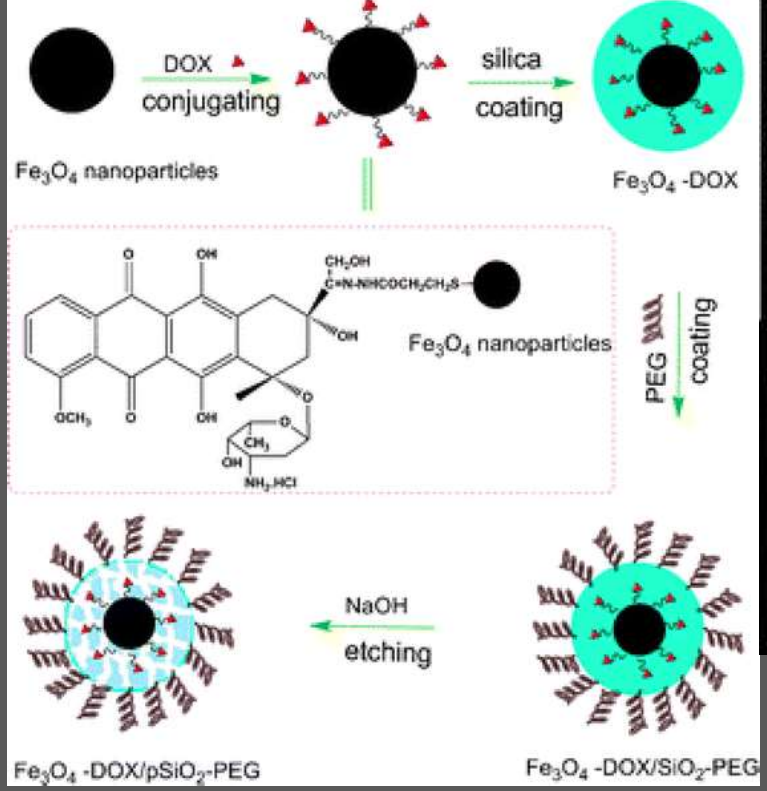
- ✓ Magnetic (in the presence of external magnet) , Nonmagnetic (removed external magnet)
- ✓ Avoid an 'active' behavior of the particles when there is no applied field
- ✓ Reverted to nonmagnetic states by removing Hex to allow them to be excreted

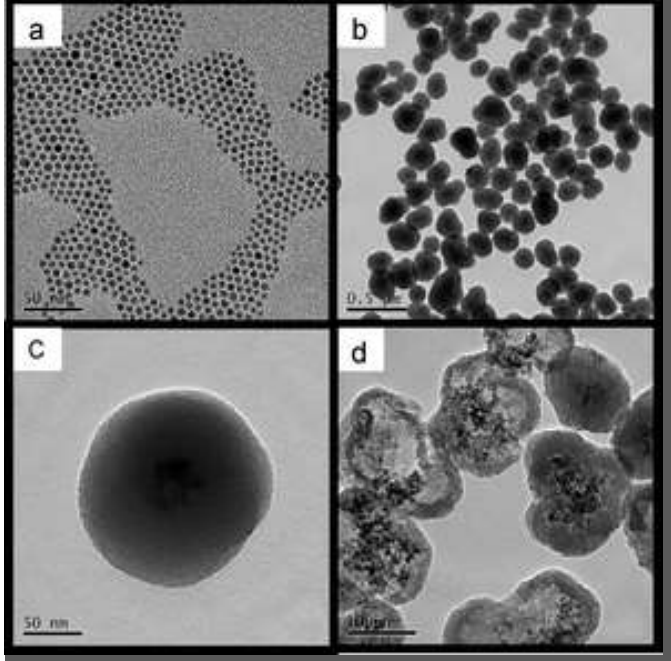


Surface modification

- ✓ Use of MNPs **in vivo** needs surface modification
- ✓ **To protect** from reticuloendothelial system and **increase the stability** of molecule in vivo
- ✓ Commonly used : **organic ligands** (polyethylene glycol, dextran, aminosilanes)

- ✓ Modulate the magnetic properties
  - by modifying the anisotropy
  - by decreasing the surface magnetic moment of the metal atoms located at the surface of the particles



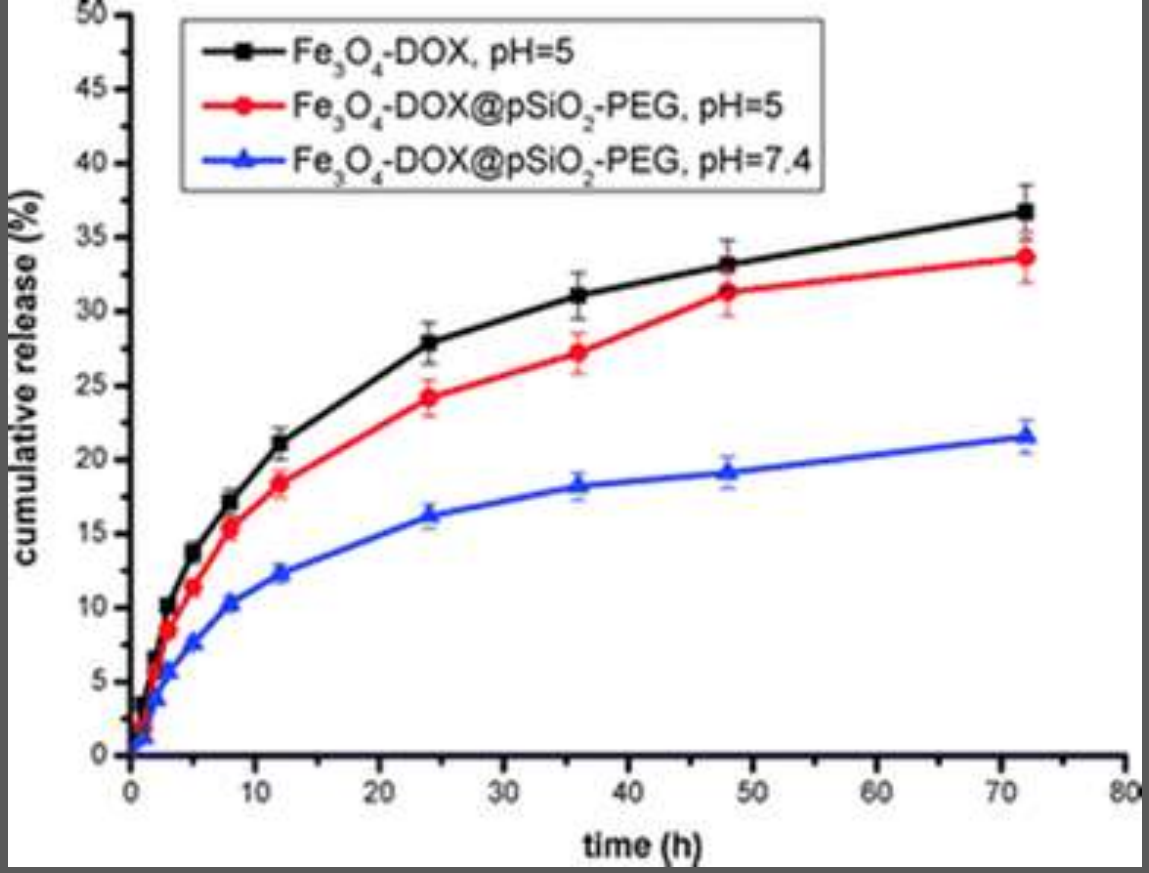


TEM images of (a) as-prepared Fe_3O_4 nanoparticles
(b, c) Fe_3O_4-DOX/SiO_2 core/shell nanoparticles
(d) Fe_3O_4-DOX /pSiO_2-PEG core/shell nanoparticles

- ✓ Existing structural model
  1) drugs conjugated to surface of polymer coated MNPs
  2) Mixture of drugs & MNPs embedded in polymer

  → However, simple direct attachment of drug molecules to the surface of particles, can cause serious problems since the drug can be dissociated from the system and released in non-target areas.

- ✓ **Doxorubicin(DOX)** chemically bonded to Fe3O4 nanoparticles
- ✓ **Polyethylene glycol(PEG)** functionalized porous silica shell.
- ✓ **Porous silica shell**
  - Protective layer for drug molecules and magnetite nanoparticles
  - Thin barrier for the DOX release from the carrier.



- ✓ **Slower of DOX** than seen in DOX-conjugated ferrite NPs alone (because of the presence of the porous silica shell)
  → Decrease the amount of DOX dissociated from the carrier prior to release in non-target spots during transportation

- ✓ **Biocompatible polymer PEG** allowed to escape reticuloendothelial system, thus allowing drugs to be administered prolonged periods of time.

- Drug delivery system using MNPs provides a number of advantages in view of the carrier's therapeutic functionality
  - ✓ Good biocompatibility
  - ✓ Ease of functionalization with targeting ligands
  - ✓ High sensitivity to Hex
  - ✓ Barrier on the drug release (diffusion-control)

- Resolve primary concerns in conventional cancer therapies
  - ✓ Minimize invasive procedure
  - ✓ Reduce side effects to healthy tissues

THANK YOU