Using Nanoparticle Imaging Probes

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Nanoscience and Nanotechnology

•The essence of Nanoscience and Nanotechnology is the ability to fabricate and engineer materials, structures and systems where the manipulation of the properties and functionalities is a result of the control of the material's **building blocks** whose dimension is in the nanometer regime.

•Nanotechnology is an enabling technology by which existing materials, virtually all man-made materials, can acquire novel properties and functionalities making them suitable for numerous novel applications varying from structural and functional to advanced biomedical in-vivo and in-vitro applications.

OBJECTIVES

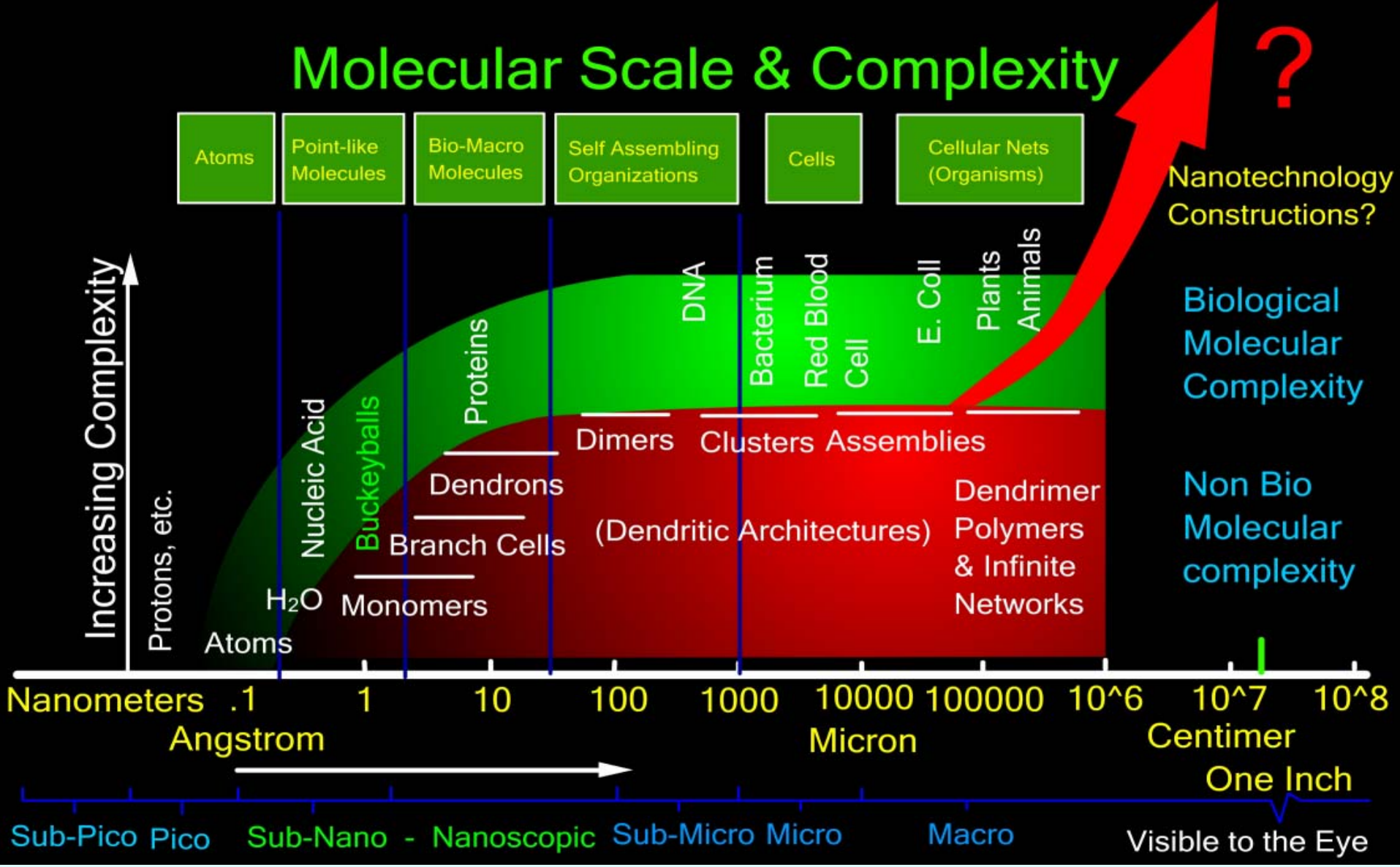
A) Design and Preparation of Nanoparticles

B) Multifunctional Biocompatible and Biodegradable Nanoparticles

C) Fabrication of Template-Assisted Synthesis Core-Shell Structure

D) Modeling of the Controlled Release of Drug

E) Applications of gold-coated and dextran-coated SPION as contrast enhancers in experimental MRI Imaging: Labeling of neural stem cells



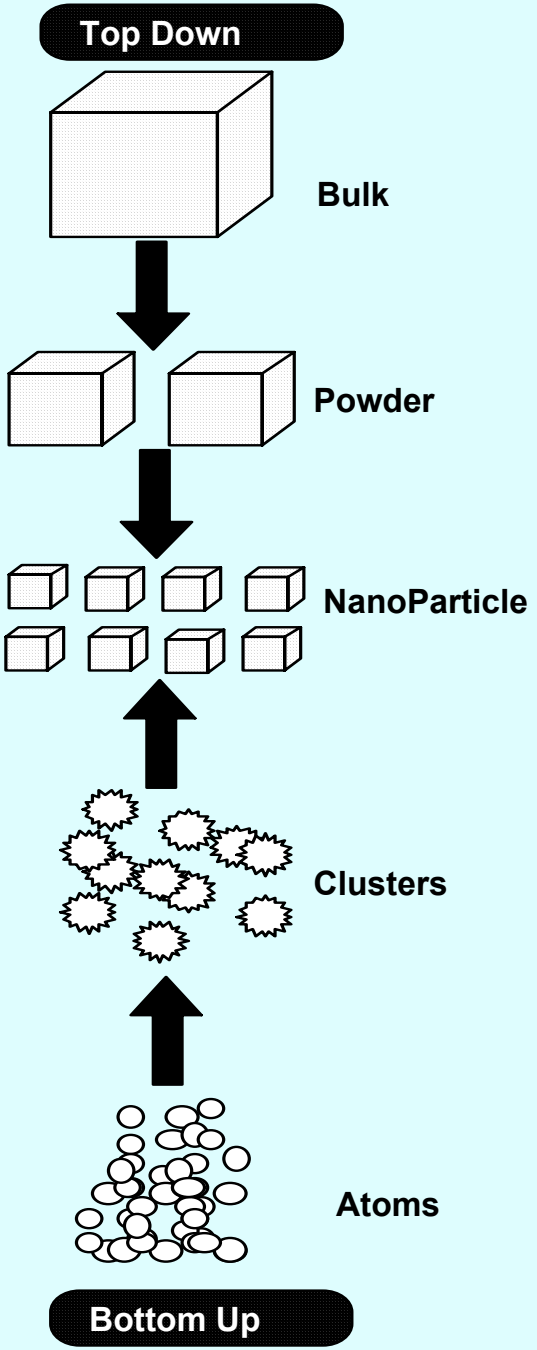
"Bottom-up"

Self-assembly
Molecular Materials

"Top-down"

E-beam Lithography
Microcontact printing

NANOMATERIAL SYNTHESIS AND PROCESSING

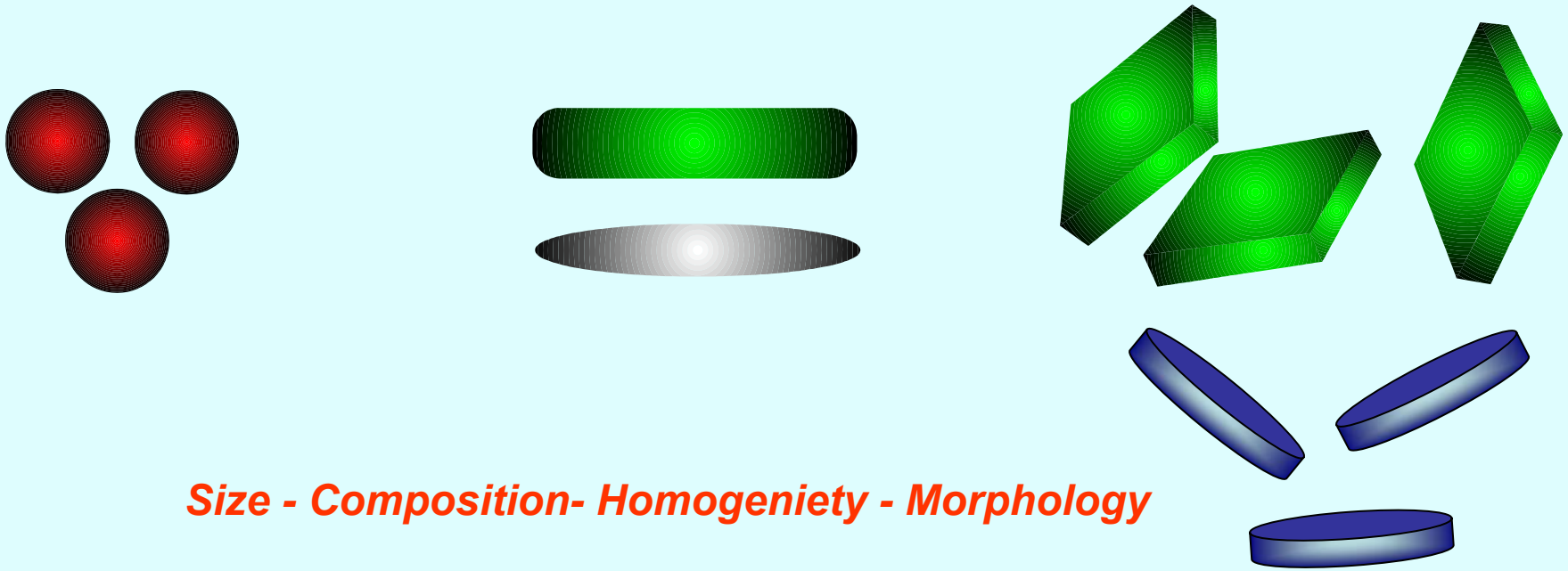


Schematic representation of the building up of Nanostructures.

Nano Building Blocks

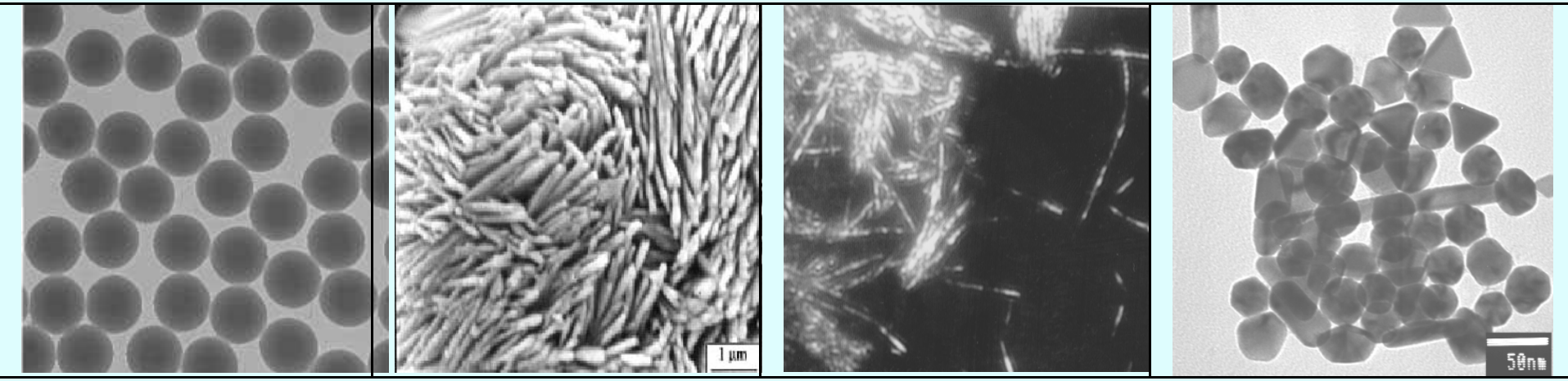
“ Nano Objects - Lego Fabrications”

1st generation nanoparticles



Size - Composition- Homogeniety - Morphology

EXAMPLES OF FIRST GENERATION NANOPARTICLES



(a) (b) (c) (d)

(a) TEM image of perfectly spherical polystyrene nanospheres,

(b) SEM image of ZnO precursor,

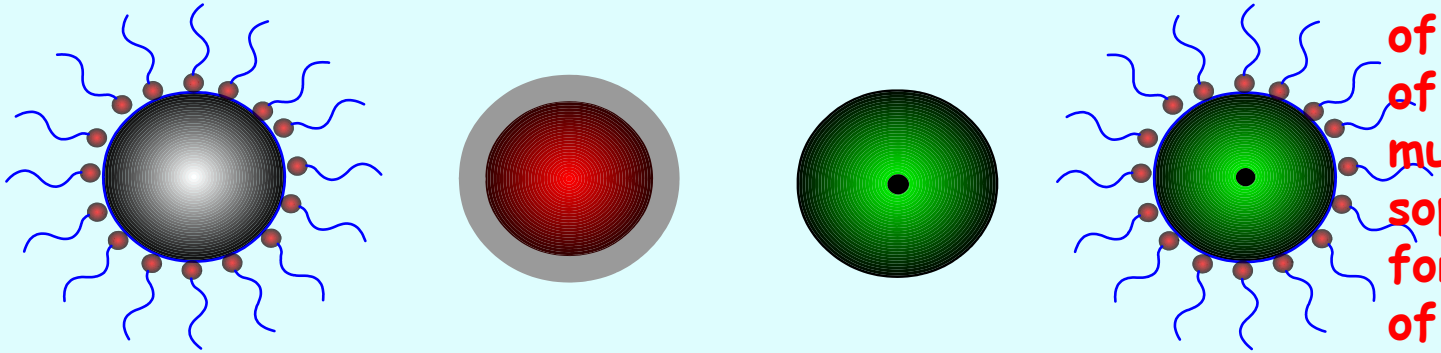
(c) Optical microscope image of Au nanowire with high aspect ratio and

(d) TEM image of Au nanoparticles with different morphologies.

The "First Generation Nanoparticles" can be considered to be those particles obtained at the early stage of the development of nanostructured materials

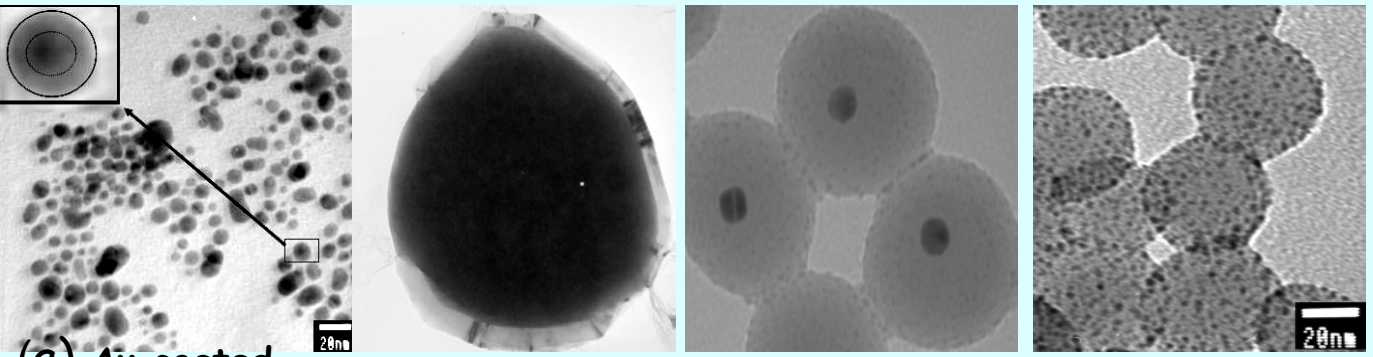
EXAMPLES OF SECOND GENERATION NANOPARTICLES

Second generation nanoparticles have emerged as a result of increasing degree of complexity, multifunctionality and sophistication needed for the engineering of nanostructures for advanced applications



(a) (b) (c) (d)

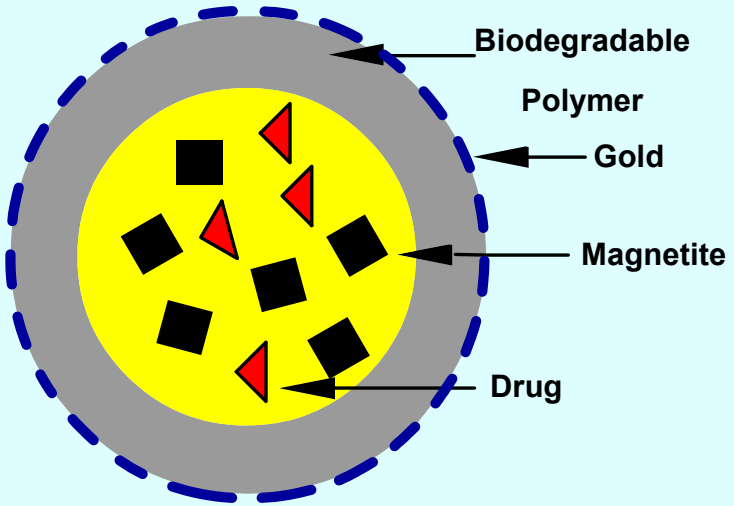
Evolution of second-generation nanoparticles. (a) Nanoparticles coated with surfactant for forming stable suspension, (b) Nanoparticle coated with thin metallic layer, (c) Small nanoparticle coated with porous ceramic layer and (d) dispersion of core-shell combination of (a) and (c) for stable suspension.

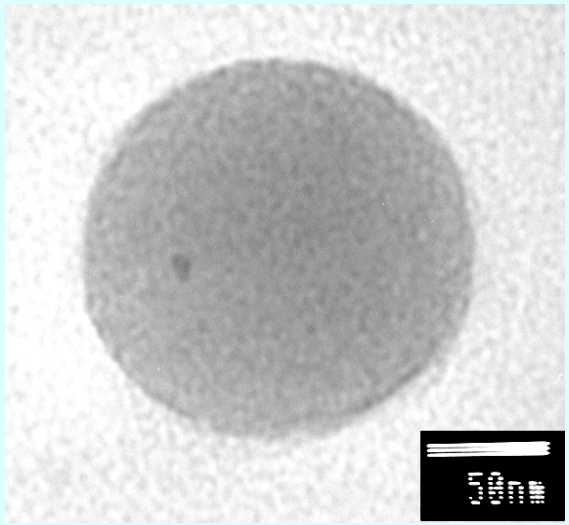


TEM images of second-generation nanoparticles.

(a) Au coated magnetite nanoparticles prepared by sequential microemulsion processing (b) Au coated SiO2, (c) SiO2 coated Au nanospheres prepared by sol-gel method, (d) self-assembled Au nanoparticles on SiO2 nanospheres

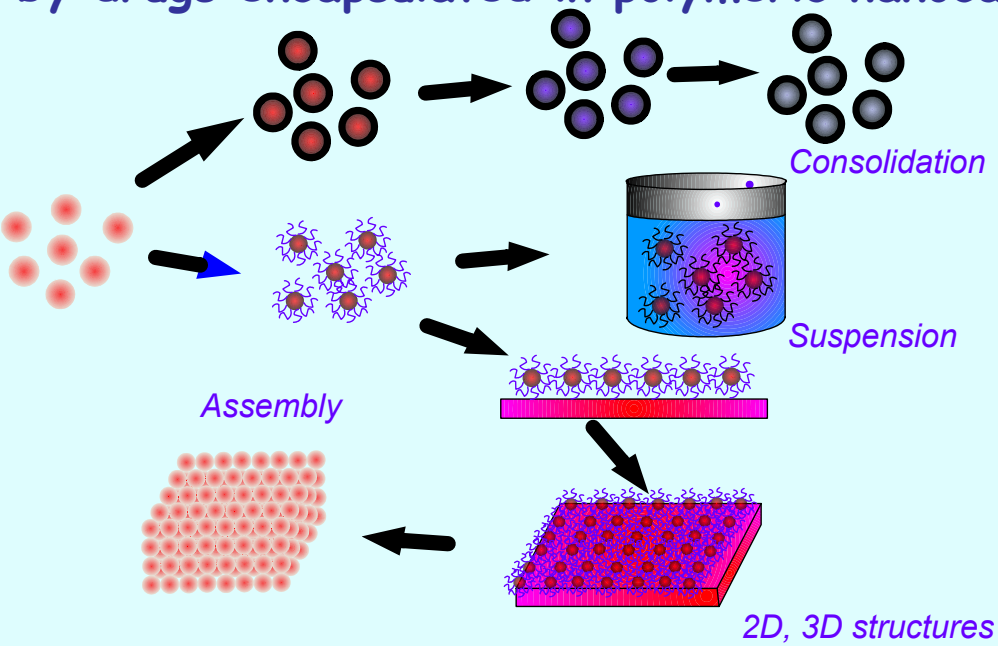
EXAMPLES OF ADVANCED GENERATION NANOPARTICLES



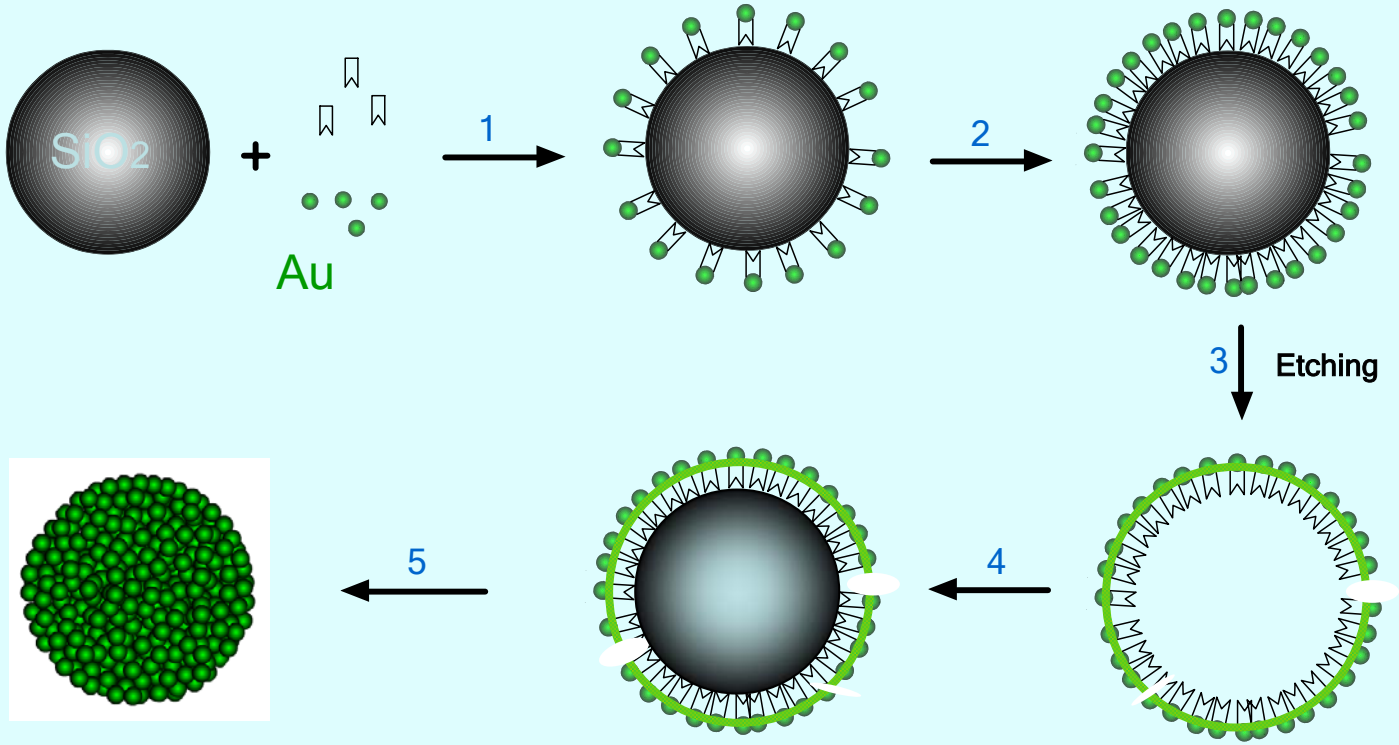


Advanced generation nanoparticles engineering and use in nanotechnology has recently emerged as the need for the fabrication of nanoparticles with highest degree of complexity.

Schematic representation and TEM image of target-oriented drug release by drugs encapsulated in polymeric nanocapsule.



A general overview of the construction of 2D and 3D nanostructures with nanoparticles as building blocks.



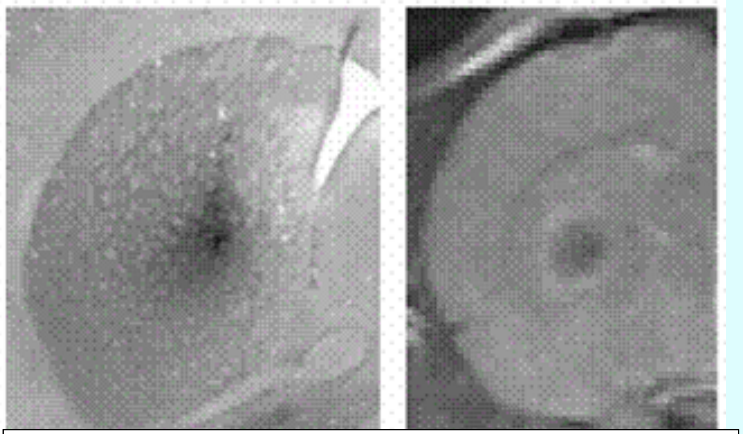
Fabrication of Complex structures via Self assembly and Templating

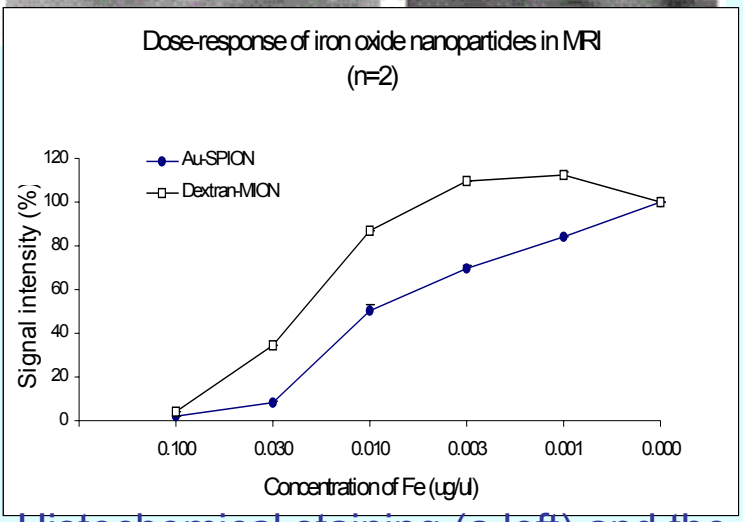
Uncoated Superparamagnetic Ion Oxide Nanoparticles (SPION) have been tested in-vitro with human dermal fibroblast cells

Conclusions

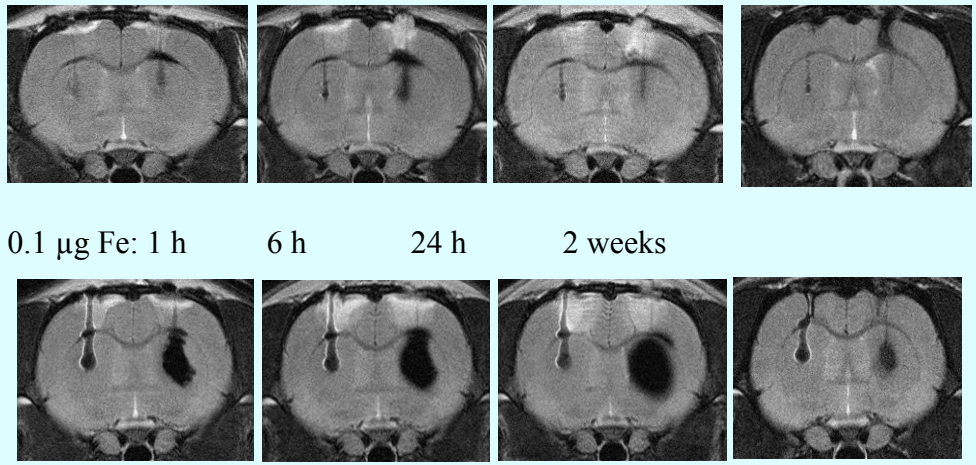
- All cells appear well spread with defined cytoskeletal features at both the 6 and 24 hrs time points.
- Cells incubated with the nanoparticles exhibit prominent stress fibre formation and tubulin clearly radiating out from the tubulin organizing centre by the nucleus, exactly as the control cells.).
- The cells incubated with BSA-APTMS-coated SPION appeared to show similar background levels of clathrin to the control cells at both time points.
- A cell response similar to control cells is demonstrated with no adverse cell damage and no endocytosis.
- However, the cells incubated with the LAA-coated SPION is demonstrated an increase in clathrin production, particularly at the cell filopodia. This suggests that the particles are partially being up-taken into the cell body via endocytosis.

Applications of gold-coated and dextran-coated SPION as contrast enhancers in experimental MRI: Labeling of neural stem cells. In-vivo (rat

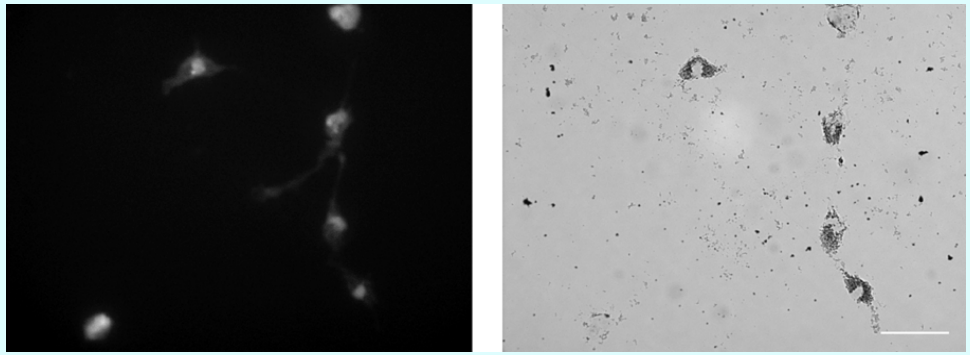




Histochemical staining (a left) and the MRI image (b right) of the MIONs (0.1 µg Fe/0.5 µl/min) 3 h after the infusion into the rat striatum. The effect of Dextran-MION and Au-SPION at different concentrations on suppression of T2 relaxation signals.



MR images showing the diffusion of Dextran-MION (right tracks) and Au-SPION (left tracks) particles in the striatum of the rat. The nanoparticles were infused at concentrations of 0.1 µg Fe (top panels) and 1 µg Fe (bottom panels) in 0.5 µl, the infusion speed was 0.5 µl/min.

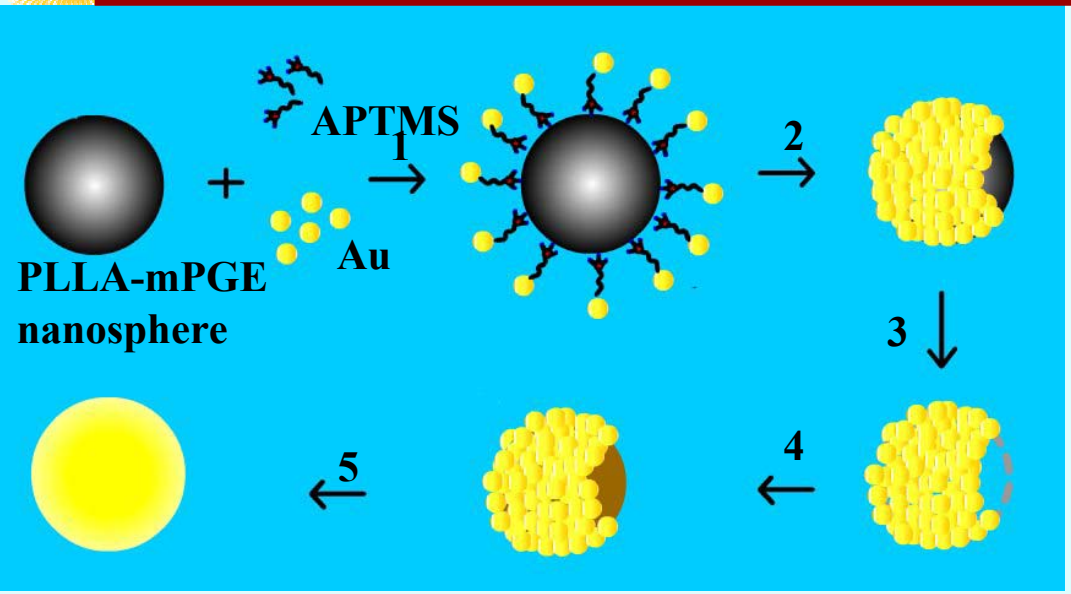


Labeling stem cells from adult rat spinal cord with Au-SPIONs. Left - GFP fluorescence, Right - Ag-enhanced staining of Au-SPIONs. (bar 10 µm)

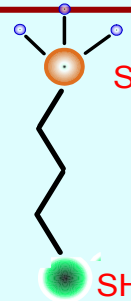
Welcome to Rutgers The State University of New Jersey

Fabrication of complex structures by self-assembly

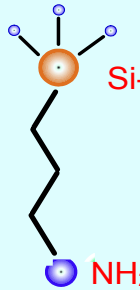
Colloidal Templating



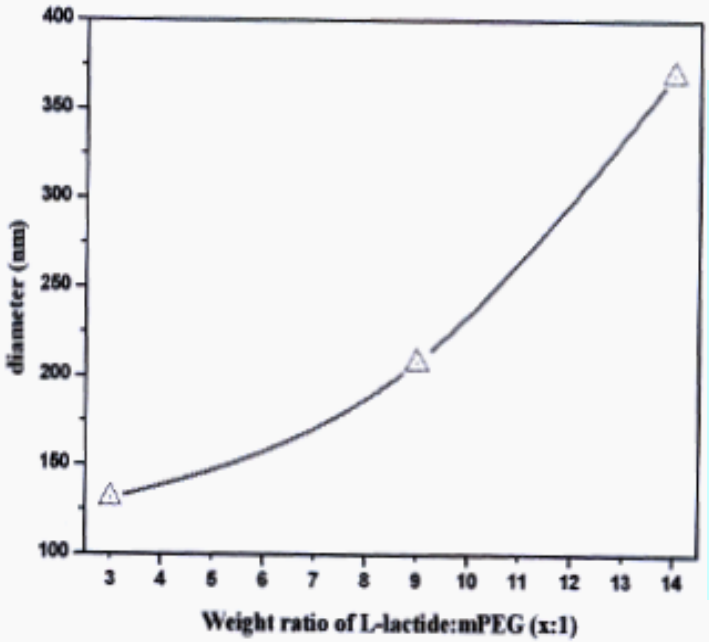
Functional Molecules



MPTMS : Mercapto propyl trimethoxy silane



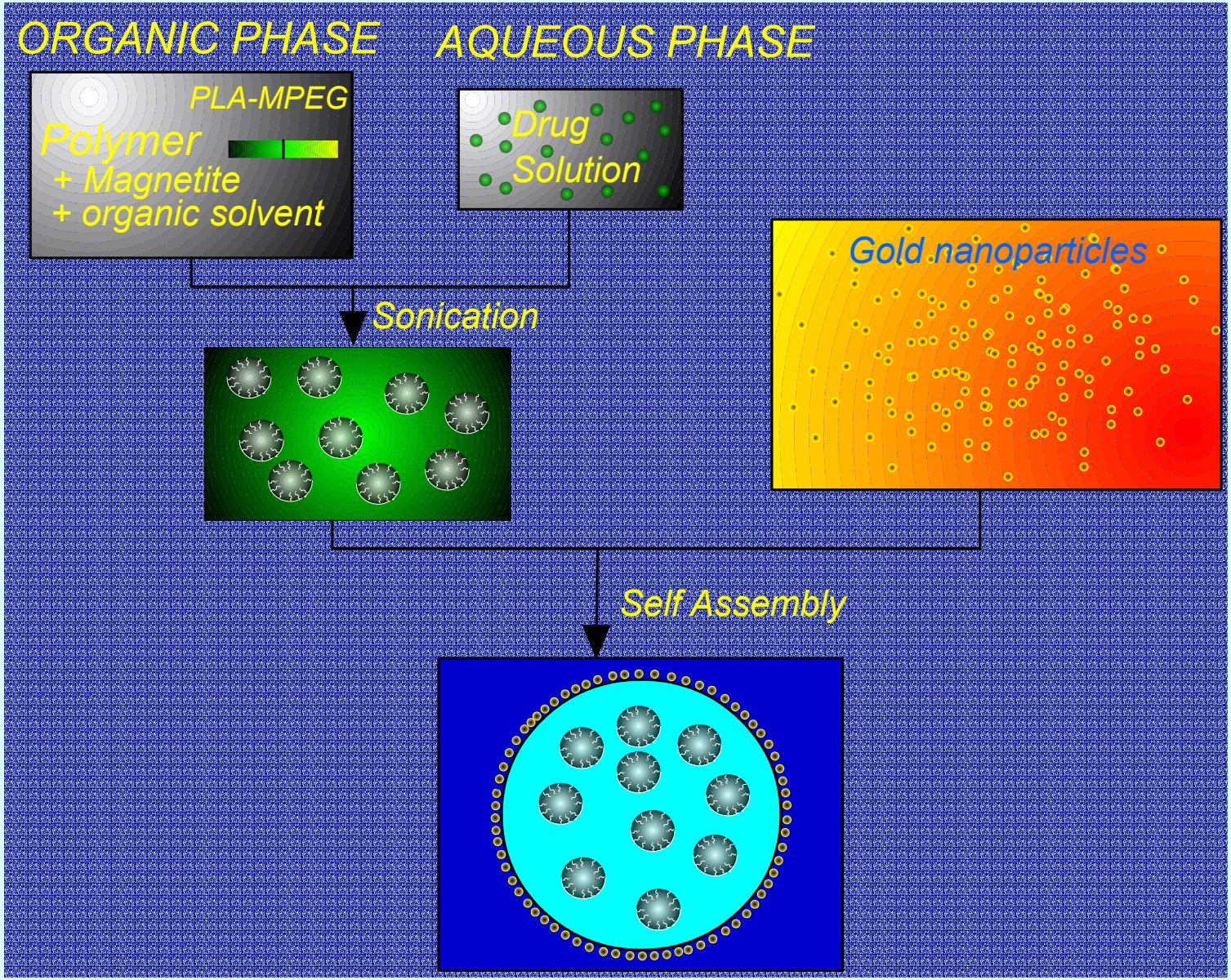
APTMS : Amino propyl trimethoxy silane



Ring Polymerization (ROP)

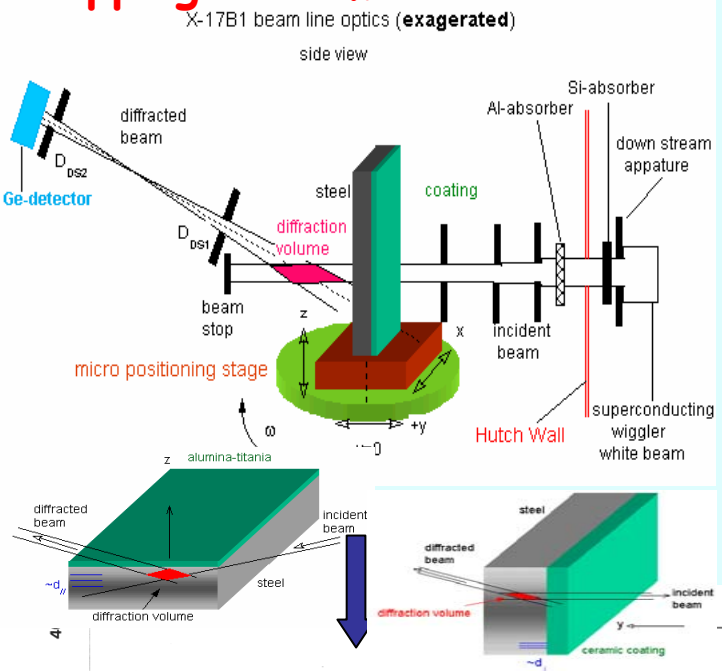
- PLLA-mPEG Magnetic Amphiphilic diblock Copolymer biodegradable nanospheres for drug delivery
- Poly(L-lactic acid) and methoxy-poly (ethylene glycol) by water-in- emulsion-solvent diffusion method.
- Entrapment of Fe_3O_4 superparamagnetic nanoparticles
- Au nanoparticle coating on the nanospheres for better stabilization and drug release rate.
- Nanosphere size controlled by PLLA concentration

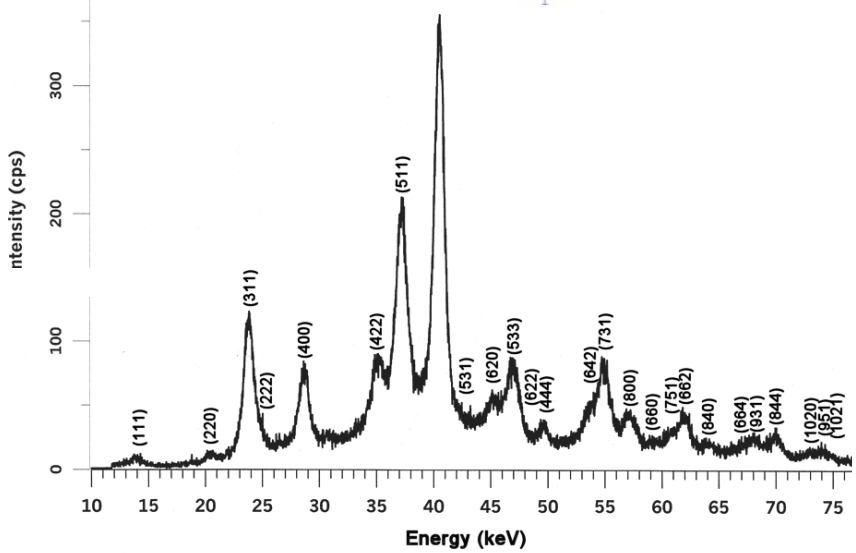
Magnetic nanospheres for drug delivery



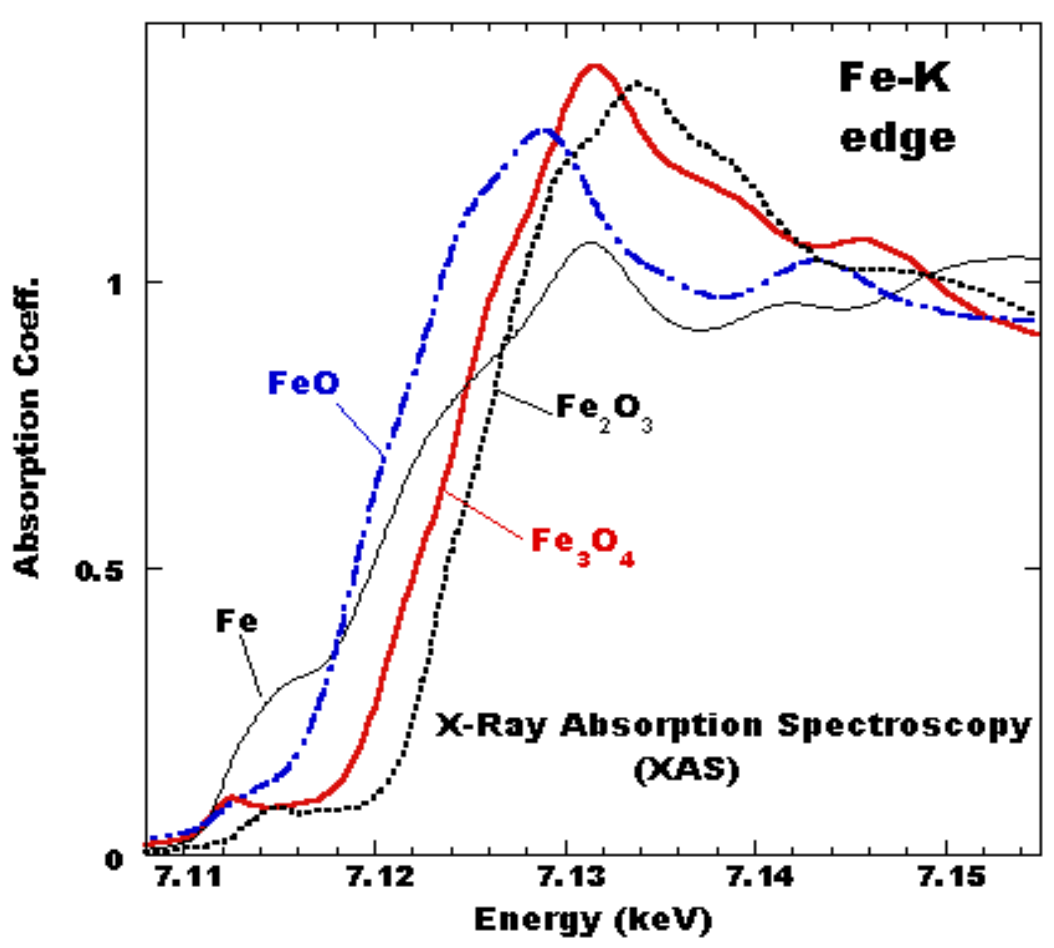
Advanced Characterization of Magnetite nanoparticles

Energy Dispersive X-Ray Diffraction Strain Mapping Schematic X17-B1 NSLS BNL

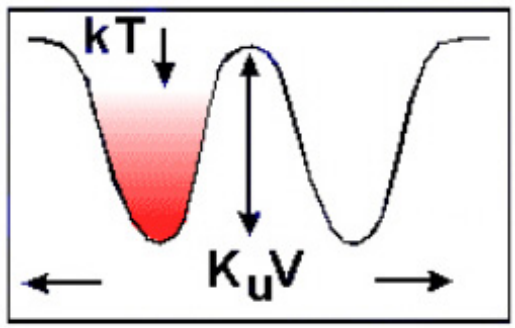




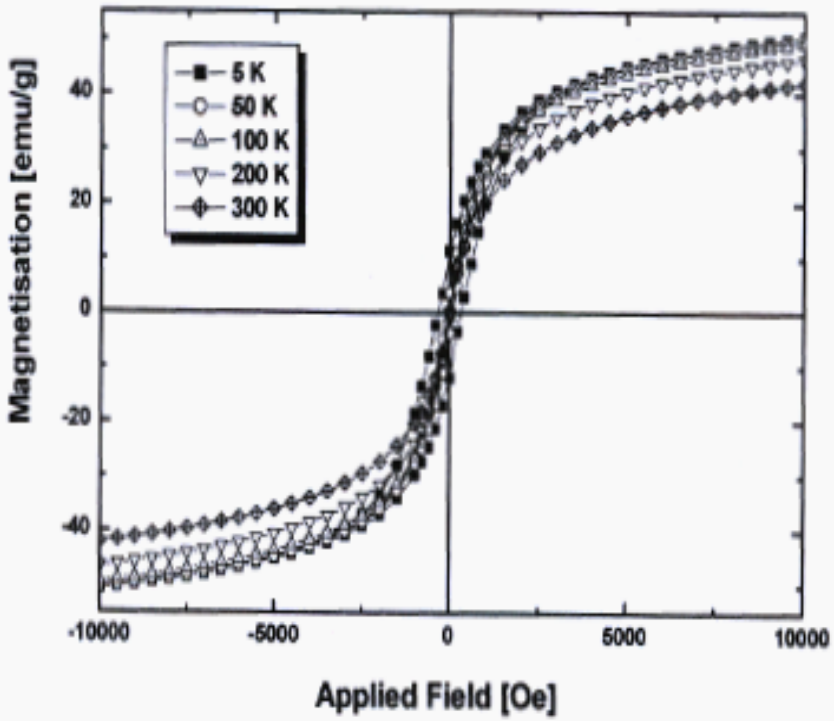
X-ray absorption Spectroscopy (XAS) Synchrotron Light Source Brookhaven Nat Lab



Superparamagnetic behavior of 6-10 nm size Fe_3O_4 nanoparticles

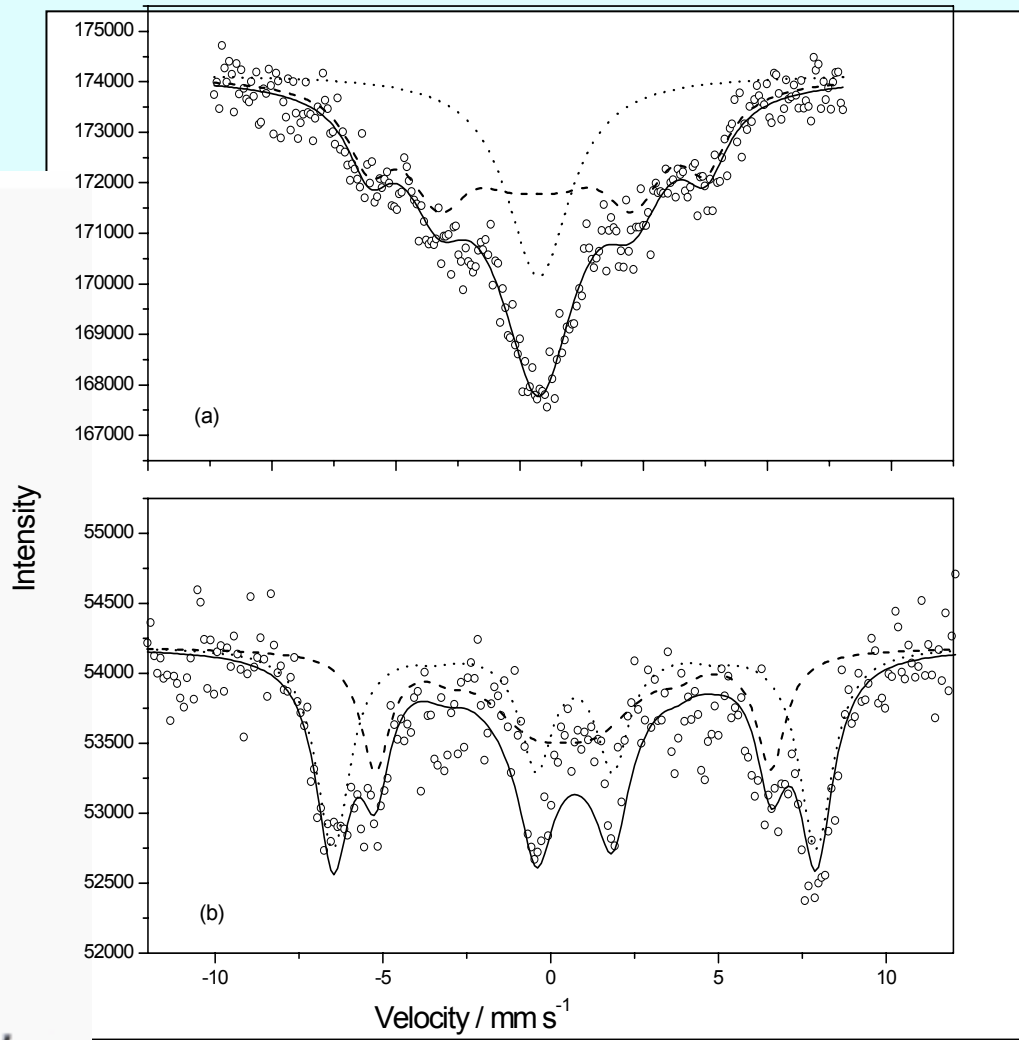


$$\tau = \tau_0 e^{K_u V / kT}$$

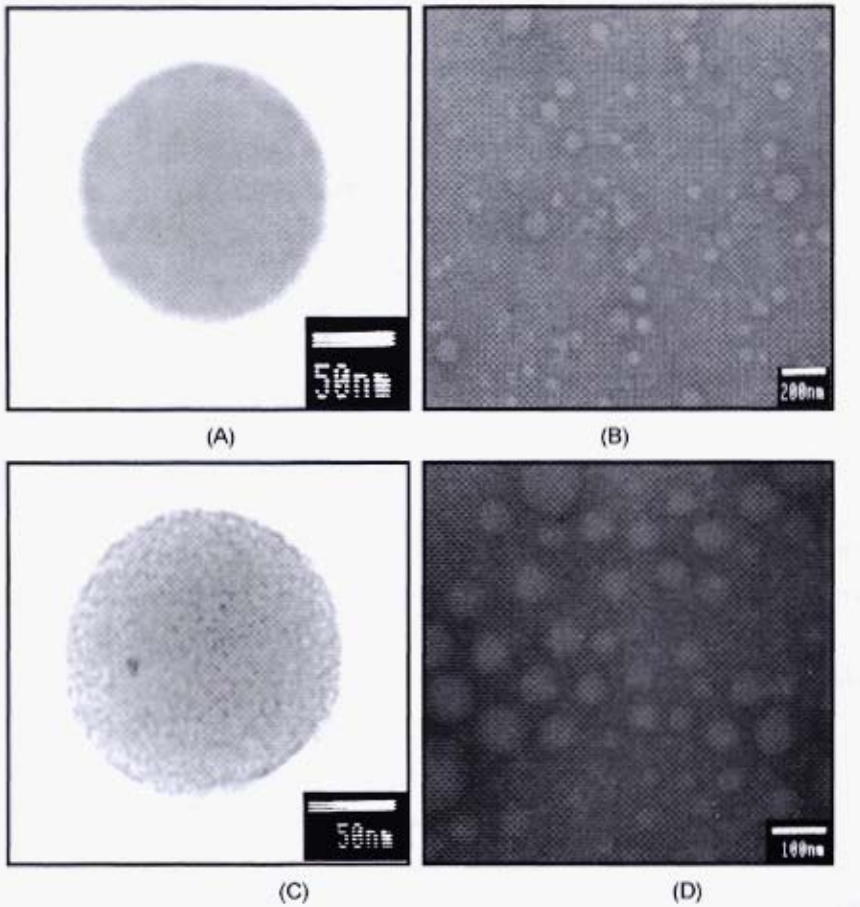


5. Magnetization versus applied magnetic field for Fe_3O_4 nanoparticles.

Mössbauer spectra of MPEG-coated SPION in the absence (a) and presence (b) of external magnetic field (Hext = 1.7 kOe).

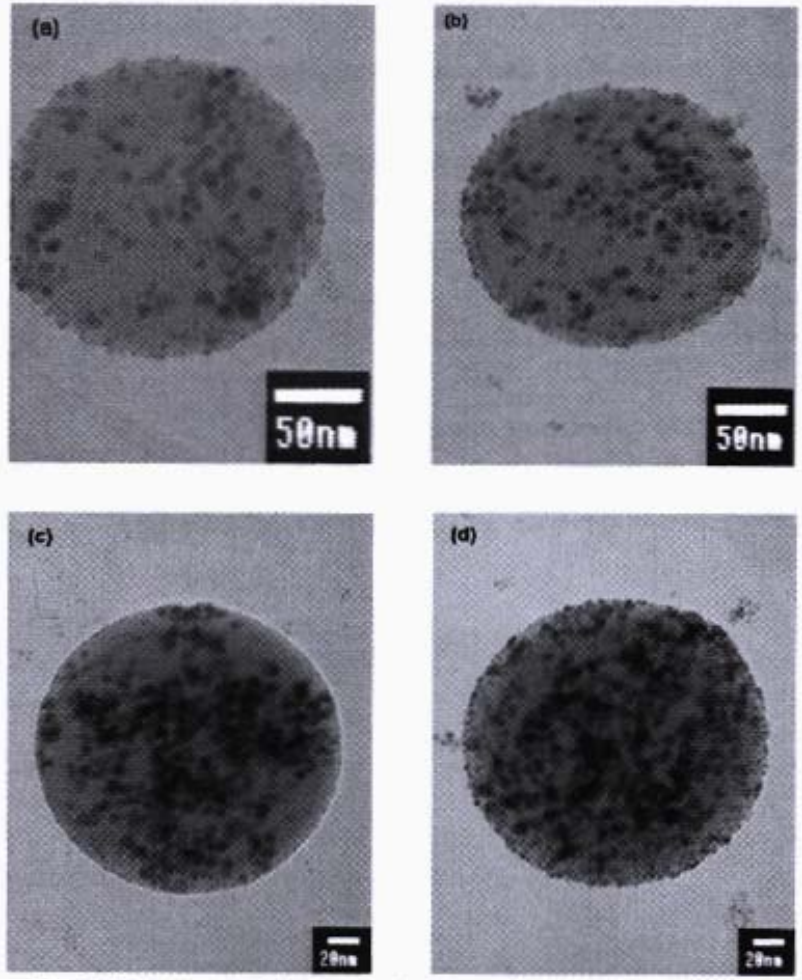


TEM PLLA-mPEG nanoparticles with Protein & Magnetite



Transmission electron micrographs (TEM) of the developed protein loaded PLLA-mPEG nanoparticles (A and B). (C) and (D) show magnetite and protein loaded PLLA-mPEG nanoparticles.

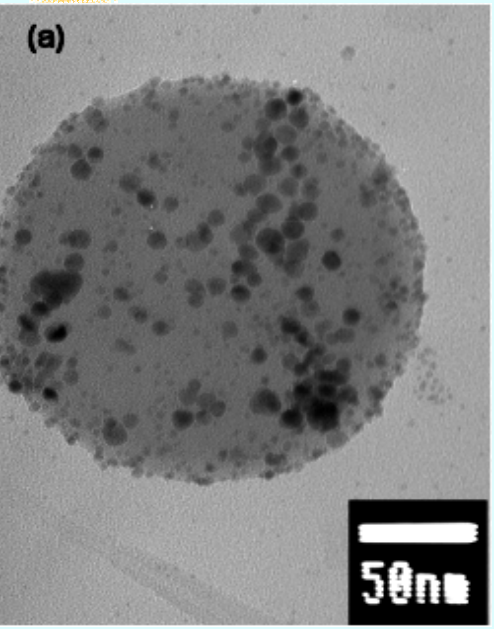
TEM PLLA-mPEG copolymer nanosheres with Au nanoshell

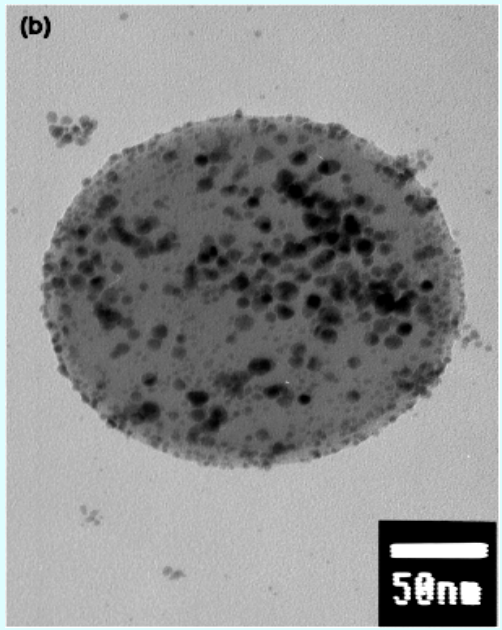


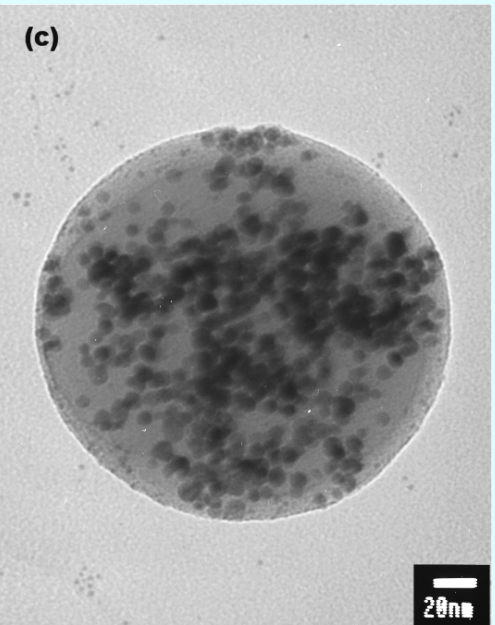
TEM images of Au nanoshell growth on diblock copolymer PLLA-PEG nanospheres.

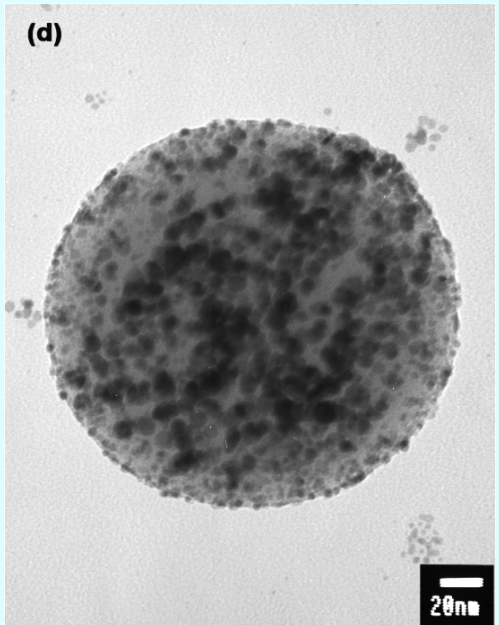
Retain the micelles in the emulsion after sonication.

Gold coating of the copolymer nanospheres



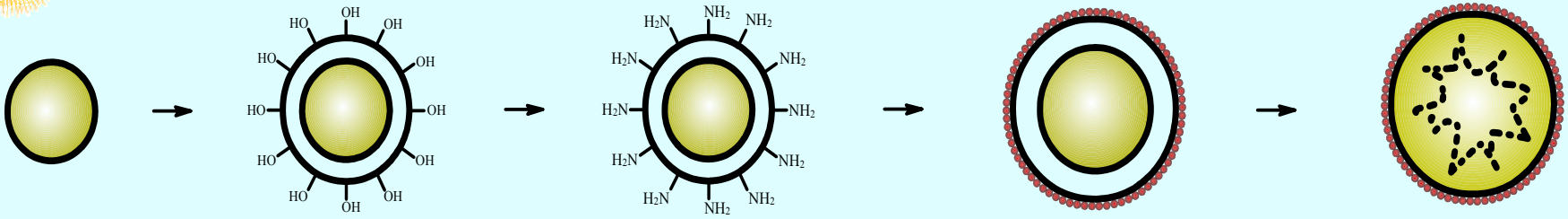






The self-assembly of gold nanoparticles on the polymeric micelles improved the heat absorbance of the 'smart' drug carriers followed by the fabrication of 'shell-in-shell' structures.

I II III IV V



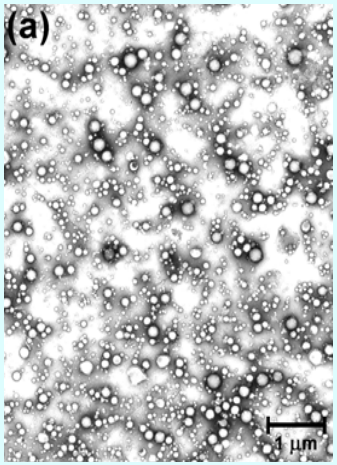
Hydrophilic drug loaded PNIPAAm-PDLA sphere

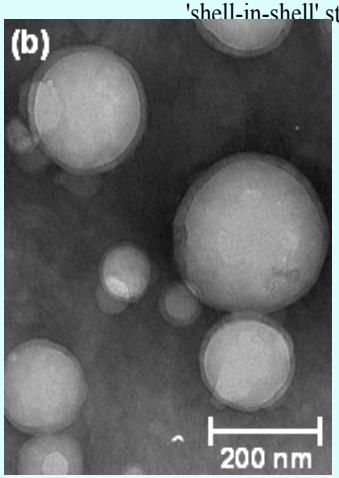
PNIPAAm-PDLA@PLLA-PEG 'shell-in-shell' structure

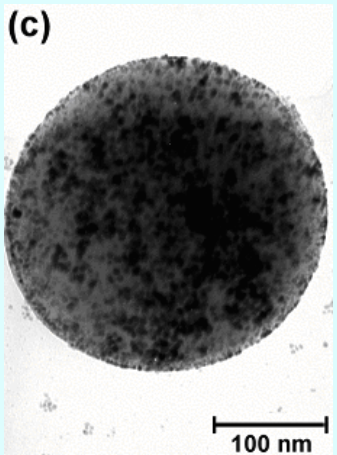
Functionalization of PNIPAAm-PDLA@PLLA-PEG 'shell-in-shell' structure with APTMS

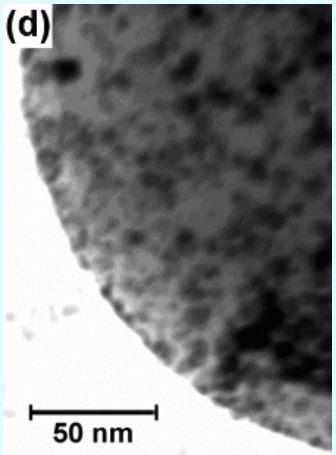
In-situ reduction and self-assembly of Au nanoparticles on the surface of PNIPAAm-PDLA@PLLA-PEG 'shell-in-shell' structure

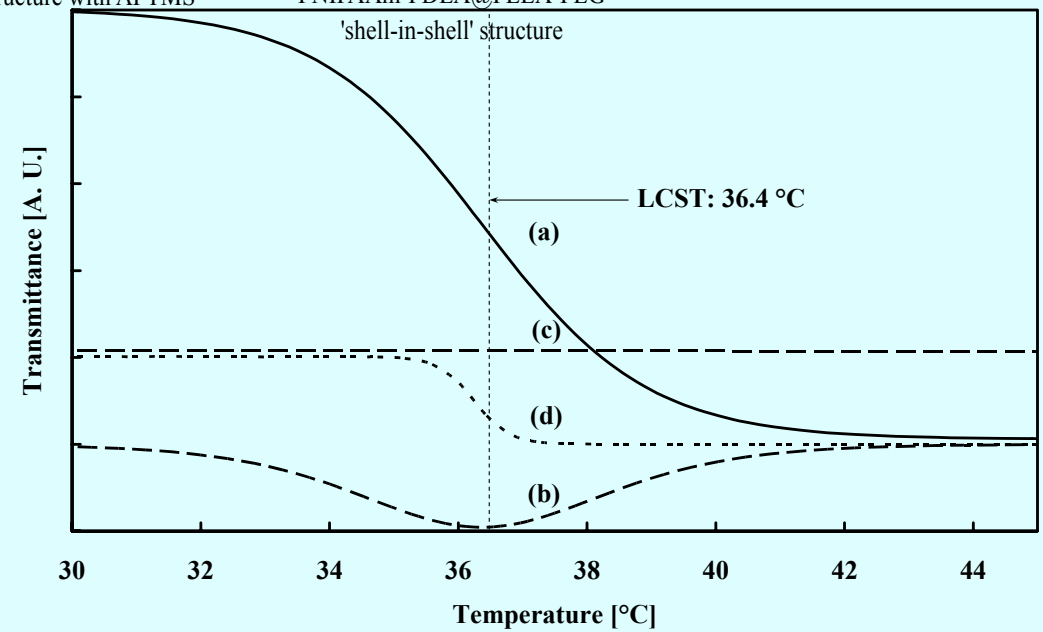
Collapse of the inner shell by heating up to the LCST around 37 ¡ŒC







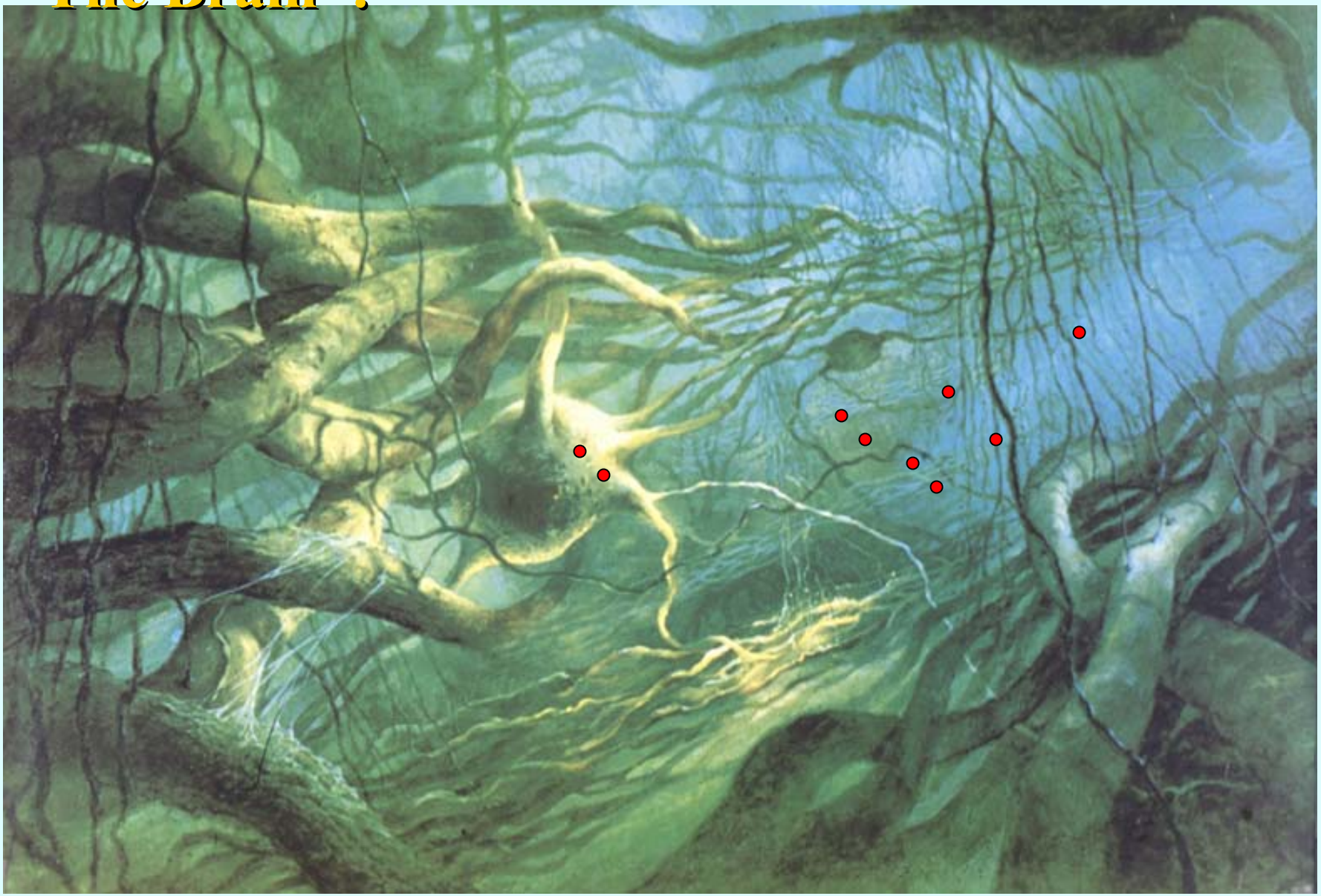




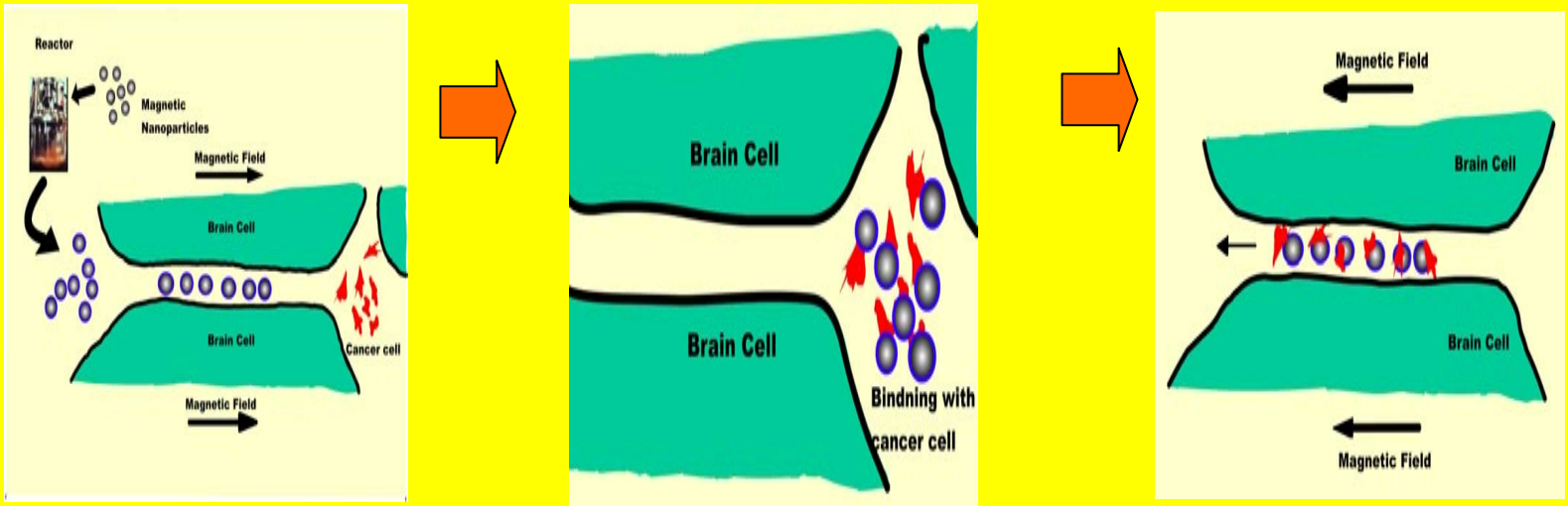
UV-VIS spectra at 500 nm for the measurement of turbidity of: a) PNIPAAm-PDLA dissolved in chloroform. b) derivative curve of a). c) PLLA-PEG spheres in 'Oil-in-Water' emulsion. d) PNIPAAm-PDLA@PLLA-PEG 'shell-in-shell' structures in 'Wate in-Oil-in-Water' emulsion

Magnetic Nanoparticles in Biomedical Applicat

The Brain !



Magnetic Targeting



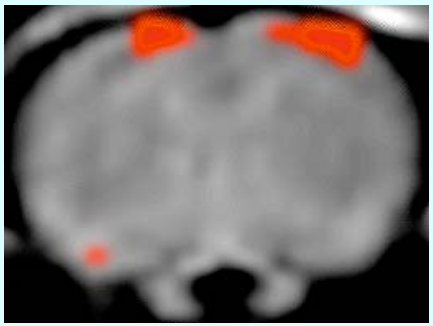
Insertion of functionalized magnetic particles in brain

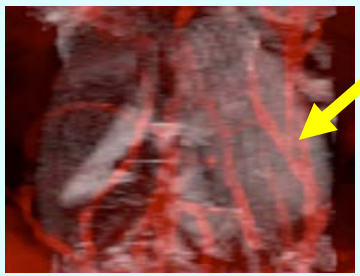
Reaction of functionalized nanoparticles with target

Removal of target-loaded magnetic particles

Magnetic Nanoparticles in Biomedical Applications

fMRI



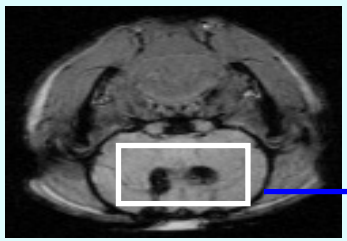


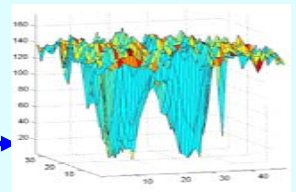
Neuron

Magnetic Core

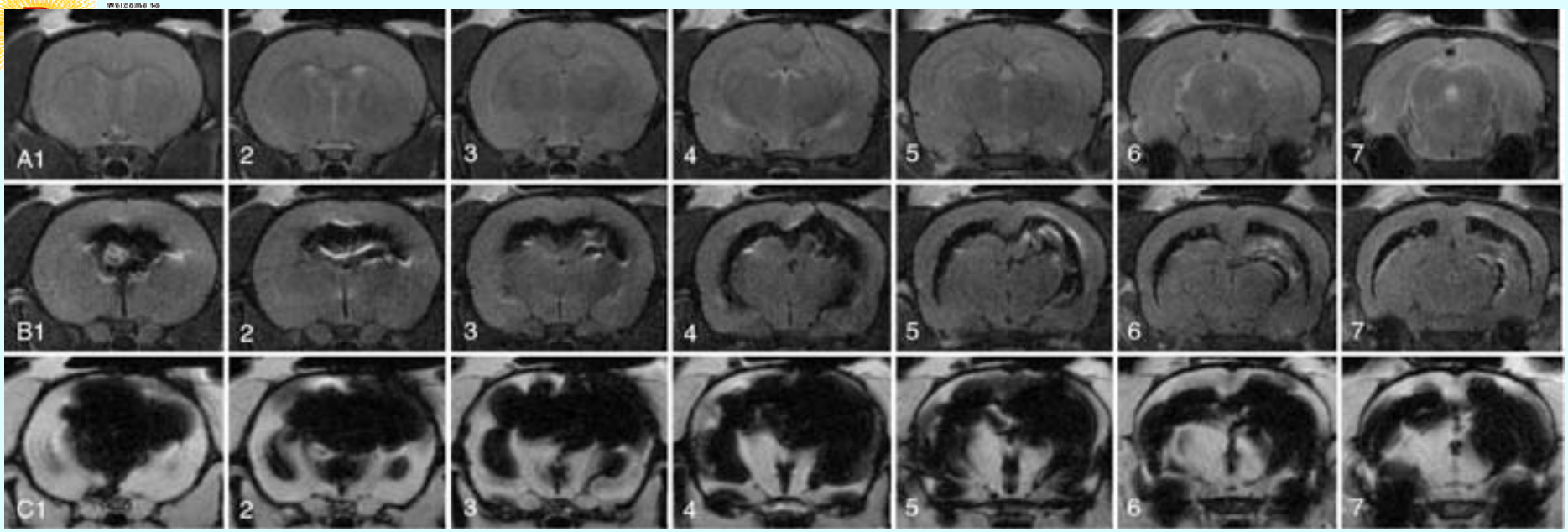
Dextrane

Magnetic Targeting Nanoparticles





B. Bjelke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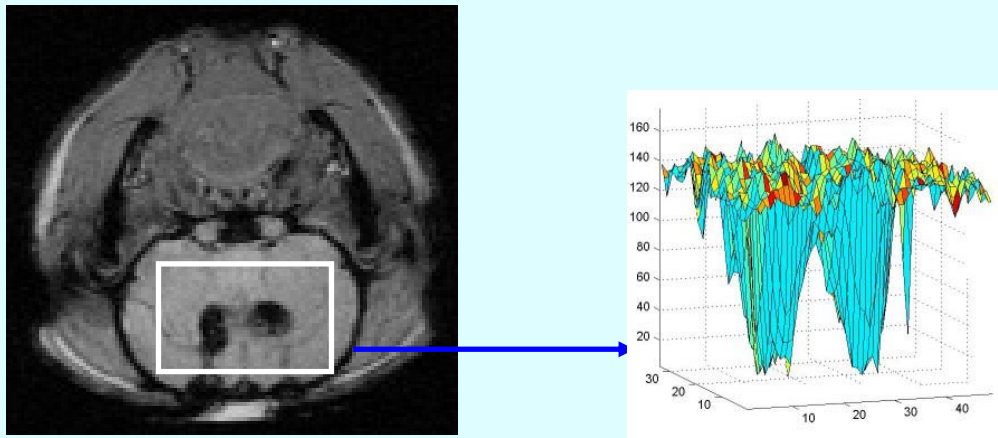
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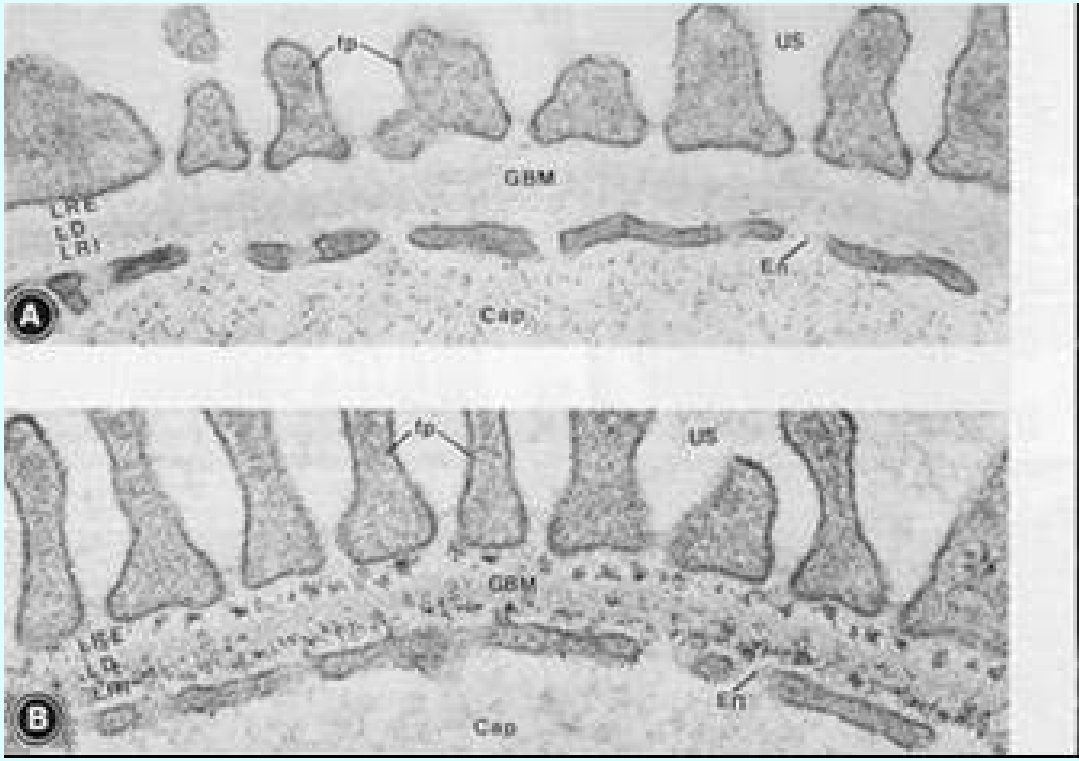
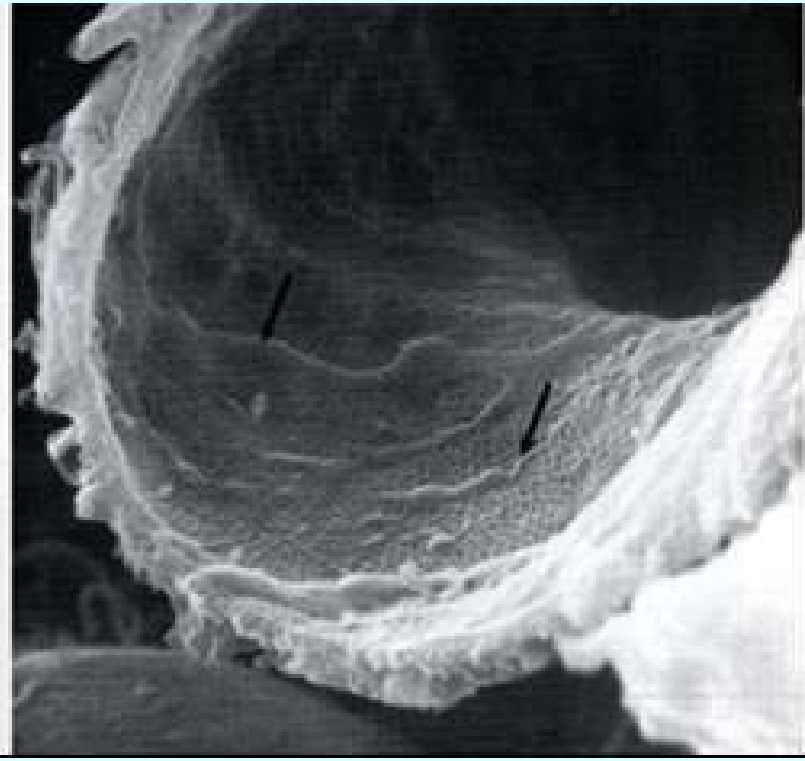
Applications of Magnetic Nanoparticles in Renal Diseases





Early experiments performed in rats have shown the remarkable capability of magnetic nanoparticles to infiltrate into the basement membrane (thickness of the order of 30 nm) for kidney functional restoration .The experiment indicates that it is feasible to access key sites of the glomerular capillary wall using iron-based nanoparticles for drug or gene delivery.

Conclusions

•Stable surface modified magnetite nanoparticles have been prepared with controlled chemical coprecipitation that form stable dispersions.

•Gold coated nanoparticles are assembled on the surface of spheres using self -assembly method with APTMS (aminopropyltrimethoxysilane)

•The concentration of gold nanoparticle on the silica surface is artificially controlled the rate of drug release besides the biodegradable polymer.

•Size and shape controlled superparamagnetic nanoparticle have been introduced into the polymeric matrix to deliver the drug-loaded polymeric nanosphere through biological fluid.

•BSA as an example of protein has been successfully encapsulated inside the magnetite modified polymeric nanosphere.

•The present study illustrates that the superparamagnetic Au-coated nanoparticles exert powerful contrast-enhancing properties in MRI and have a profound endocytotic properties both in vivo and in vitro.

• It is suggested that the Au-SPIONs may represent superior MRI labels for tracking the transplanted neural stem cells in vivo.

•NSLS-II Biomedical Imaging at nanoscale is of great advantage

The Challenges?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