Department for Nanostructured Materials

Head: Prof. Spomenka Kobe

14 Ph. D
16 Young researchers
1 Technician
1 Business secretary

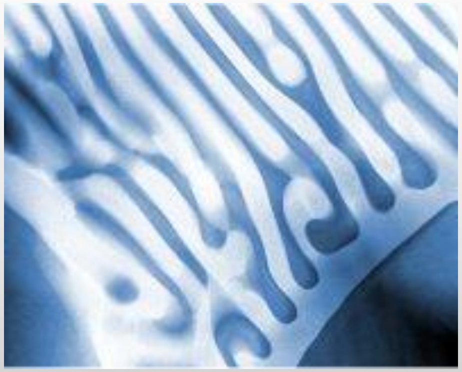
Mission..

- The basic and applied research in the Department for Nanostructured Materials includes ceramic materials, metals, intermetallic alloys and minerals. Our research encompasses conventional processing as well as the development of new technologies and methods for preparing new materials with novel properties.

- It includes experimental and theoretical investigations of structures, analyses of chemical compositions at the atomic level, and measurements and calculations of physical properties, all of which help us to improve the properties of micro- and nanostructured materials.

Activities…

- **Basic research**
  - National research program
  - Projects for ARRS
  - European projects

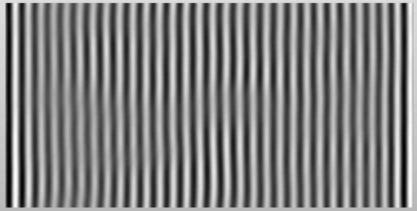


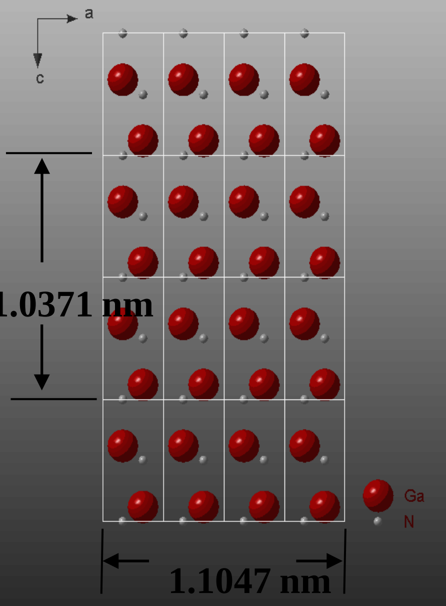
- **Applied research**
  - Industry
  - European projects

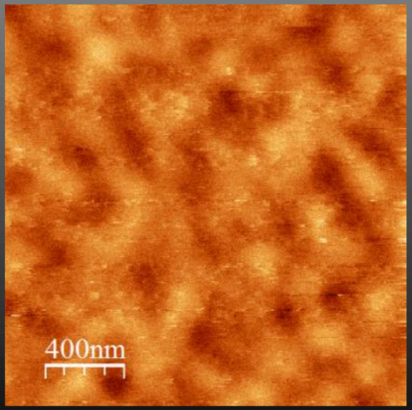
- **Education**
  - International postgraduate school “Jožef Stefan”
  - FKKT, NTF, FMF

Center for Electron Microscopy

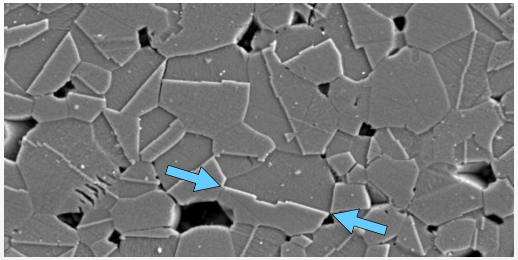
- Atomic scale structure and chemistry determination of planar faults and grain boundaries in inorganic materials
- Exaggerated and anisotropic grain-growth phenomena studies in inorganic materials
- Development and implementation of new analytical methods in electron microscopy
- Expertise in the field of materials characterization by electron microscopy methods
- AFM/MFM analyses





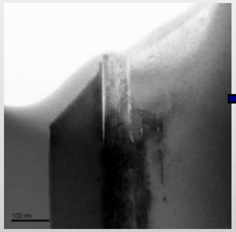


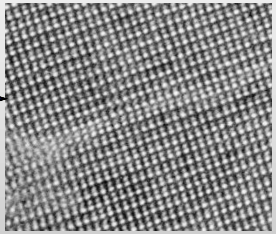
Content..



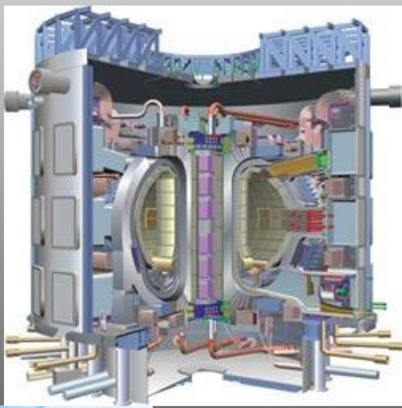
Ceramics

- ZnO
- Perovskites ($SrTiO_3$, $BaTiO_3$)
- SiC, ZnS, TiO_2….
- ….other natural and synthetic minerals



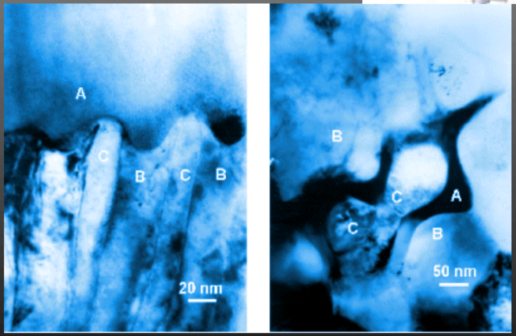


Materials for biomedical application, multifunctional electronic components, materials for extreme conditions



Intermetallic compounds

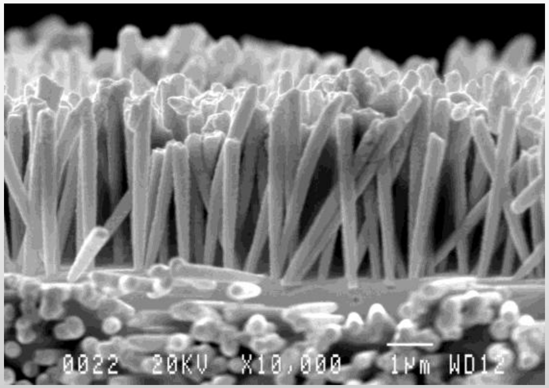
- Sm-Co, Nd-Fe-B, Sm-Fe-N magnet
- CoPt, FePd thin films, nano structures
- Quasi crystals for Hydrogen storage
- Magnetocaloric materials

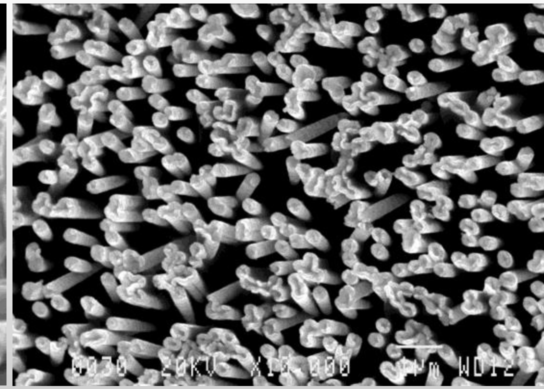


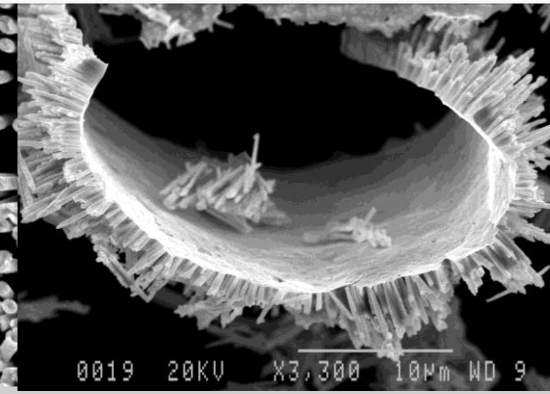
Nano-dimension materials

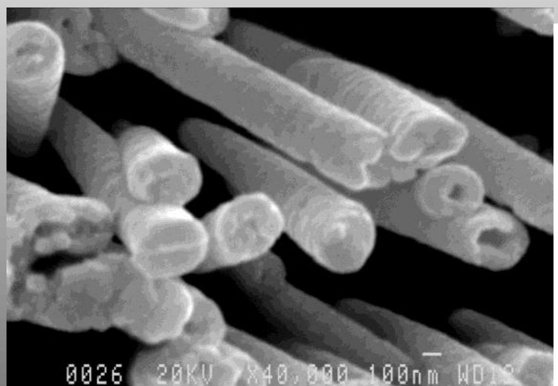
- 1D and 2D Fe-Pd-based nanostructures for drug delivery and magnetic storage.
- Perovskite $BaTiO_3$ nanorods and $SrTiO_3$ nanotubes for micro-nano humidity sensors.
- $SrTiO_3$ single nanotubes exhibite a photo-effect under UV radiation.
- Nano-sized TiO_2 powders in either rutile or anatase. Anatase was used and tested in DSSC (dye-sensitized solar cell) solar cells.
- Spherical ZnO nano-powders. Transparent and conductive ZnO thin films for optoelectronics.

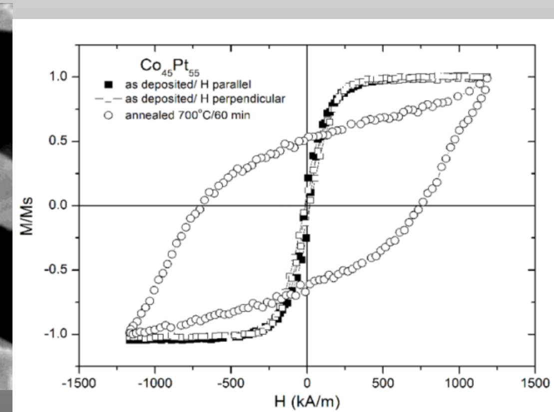
Ferromagnetic nanostructures

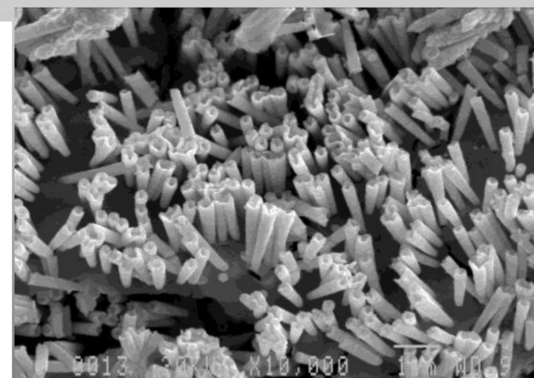












Ferromagnetic nanotubes with high coercivity based on $Fe_{50}Pd_{50}$ synthesized by electro deposition (for magnetic nano systems, catalysis, in medicine, for magnetic recording etc.)

Magnetic nanoparticles for drug delivery?

[1]K. Žužek-Rožman, [1]S. Kobe, [2]M. Bele, [2]U. Maver, [3]P. Kloucek

[1]Jožef Stefan Institute, SI
[2]National Institute of Chemistry, SI
[3]University of Neuchatel, CH

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Outline:

- Introduction
- Experimental
- Results
- Conclusions

Introduction

Aim..

- The significant advances of past years in nano-scale materials science, intelligent drug delivery systems, mathematical modeling and computational techniques give us an opportunity to design and optimize functional materials for desired applications.

- Simultaneously, a variety of potent cancer and/or healing drugs were found. They are very effective in cancer treatment, but have intolerable side effects on the healthy tissues or are rapidly degraded by the enzymes present in the human body.

- The only way to use these drugs is by using Targeted Drug Delivery systems, which encapsulate them until released on demand. An interdisciplinary approach of the mentioned fields provides the pathway.

European dimension..

Magnetic Composite Nano-Capsules
for Targeted Drug Delivery and Imaging

- Our interdisciplinary research focuses on the design, micro-fabrication and a subsequent evaluation of functionalized polymeric nano-composite capsules with imbedded magnetostrictive nano-rods.
- The polymeric nano-composite matrix is synthesized to be able to carry pharmaceuticals that can be released upon activation by a moderate magnetic field generated by MRI.
- This novel nanotechnology forms an active drug delivery vehicle. The activation mechanism is based on a phase transition associated with a hysteresis.
- We will develop a system that can change magnetic energy into mechanical work. This unique physical phenomenon allows for a truly programmable, drug independent, open loop, targeted delivery nanotechnology.

Goal..

- The goal is to achieve a significant taming of the undesirable side-affects of chemotherapy; it will improve both gene-therapy and tumor's imaging.
- In the case of cancer treatment, recent advances brought variety of novel therapeutic molecules but these advances outpaced the development of delivery technologies.
- Even the new carriers based on golden nano-shells, quantum dots or magnetic particles (magnetite) cannot be used with these new therapeutics.
- Our research focuses on removing this gap.

- A special case will be represented by magnetic shape memory nanotubes, which will be incorporated into functionalized nano-composite capsules.
- The capsules based on brittle xerogel act as a delivery system with drug molecules incorporated into the capsule’s fractal-like structure.
- The surface of the nano-capsules is functionalized for a spot delivery to desired targets in the body (such as into the tumor cells).
- The nano-composite xerogel matrix will be able to carry potent drugs that can be released upon remote activation by a moderate magnetic field generated by the magnetic resonance imaging (MRI).

Team..

- Research team consists of materials scientists, chemists, researchers in materials characterization, mathematics, and oncologists while relying on a substantial industrial participation.

- The final goal is to deliver a novel bio-nano-mechanical system to tame the side effects of chemotherapy.

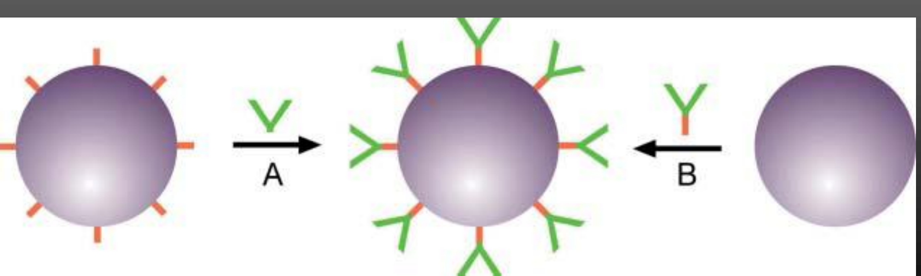
Our research addresses:

- nano-fabrication, synthesis, and subsequent evaluation of magnetic nanotubes with different characteristics and
- assessing their biomedical potential as carrier systems for targeted drug delivery.
- Such intelligent drug delivery systems possess a huge potential to lower the dosages of administered drugs and with this the costs and patient suffering during treatment.

- Nano-particles are comprised of a ferromagnetic shape memory alloy.
- The amount of the force excerpted on the polymeric encapsulation and enclosure during the actuation is proportional to the area of the hysteresis curve.
- This “device” provides an efficient nano-technology suitable for targeted delivery of potent, otherwise undeliverable, drugs to even deeply embedded tumors.
- We can achieve the sought-after targeted chemotherapy because of the reduced amount of therapeutics required, the localization, non-invasive actuation, and because of the capsules critical size.
- The capsule's size, one or below one micron; its composition will guarantee rapid clearance of the remnants from the body after drug delivery through passive extravasations'.

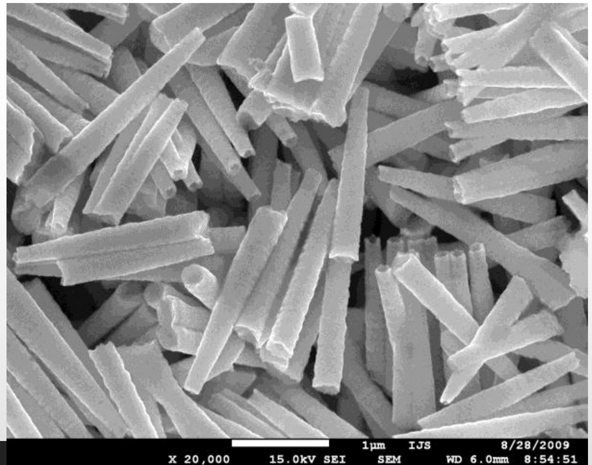
BREAKTHROUGHS

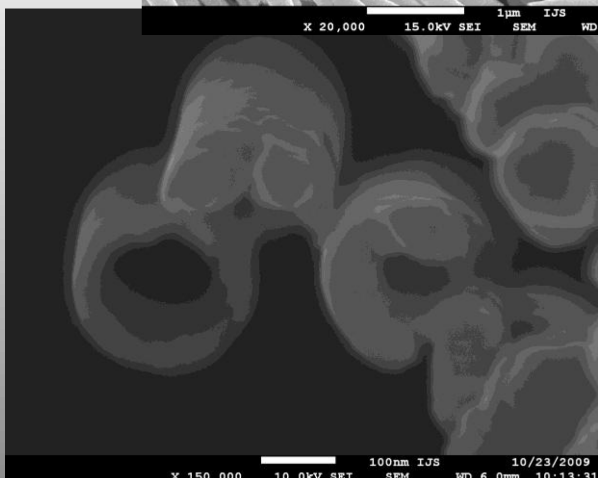
- The ultimate breakthrough contribution of the project will be the development and characterization of the magnetostrictive degradable xerogels forming an open loop drug delivery capsules (Jožef Stefan Institute).
- Second breakthrough in the synthesis of magnetostrictive nano-rods will be sub-micron micro-fluidic encapsulation (National Institute of Chemistry).
- Mathematical modeling and simulations of the transport of nano-particles in the interstitial tissue matrices (University of Neuchatel, CH).

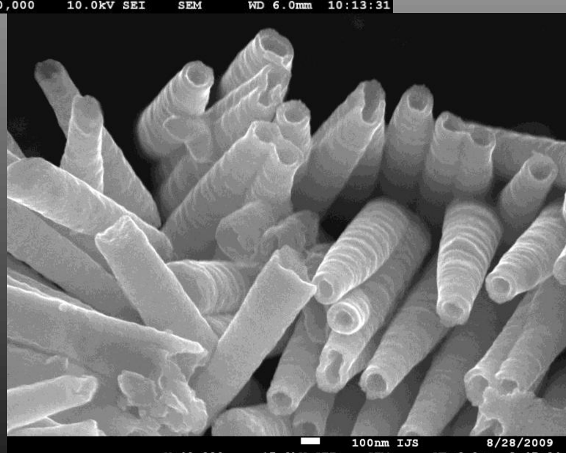


Nano Capsules

Experimental







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Electrodeposited Fe-Pd-based magnetic nanostructures

<u>Kristina Žužek Rožman</u>

Darja Pečko, Zoran Samardžija
Paul McGuiness, Spomenka Kobe, Nina Kostevšek

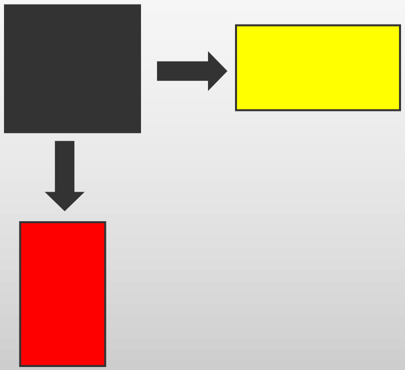
Department for nanostructured materials, Jozef Stefan Institute

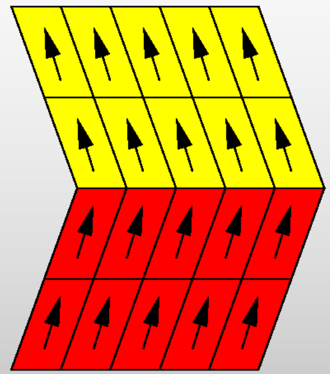
Uroš Maver, Peter Nadrah, Marjan Bele

National Institute of Chemistry

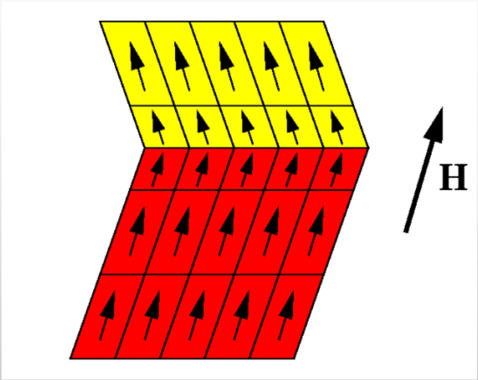
Magnetic shape memory alloys-MSM

$Fe_{70}Pd_{30}$





H=0



H≠0

Key properties for the MSM effect:

1. Martensitic transformation (twinned microstructure)

2. High magnetic anisotropy energy (MAE) in the martensitic phase

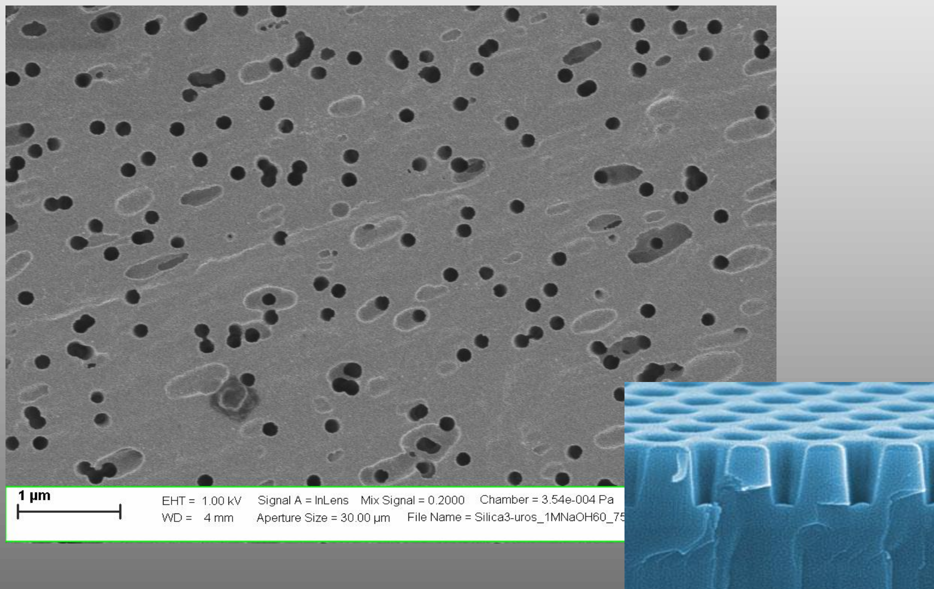
Magnetic field induced redistribution of twin variants

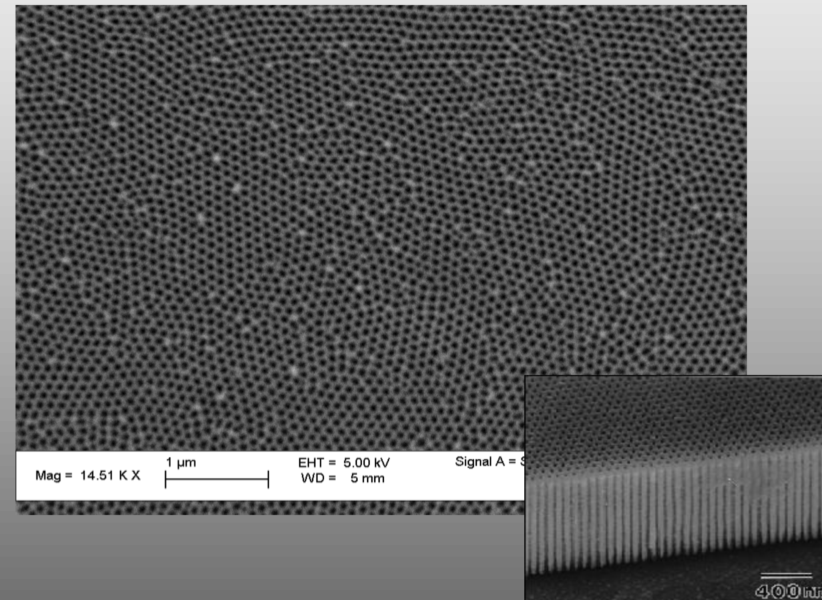
Shape changes up to 10 %

http://www.fyslab.hut.fi/epm/heusler/

(Template assisted) Electrodeposition

- **bottom up approach**
- **low cost deposition method (no vacuum equipment)**
- **low material loss**
- **flexible 1D nanostructures (nanowires, nanotubes) can be synthesised into templates**





Track-etched polycarbonate membrane

- Available in wide variety of pore sizes
- Low porosity 10^9 and <u>randomly</u> distributed pores
- pore diameter 200 nm
- pore width 10 µm

Porous alumina

- High porosity 10^{11}
- Pores are arranged in hexagonal array
- Commercially available only in limited number of pore diameters

Plating of nanotubes and nanowires

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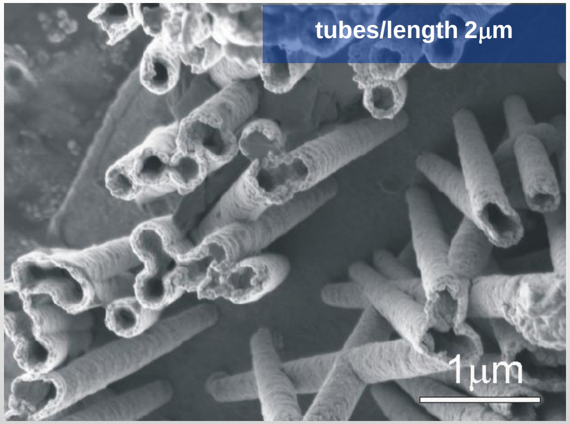
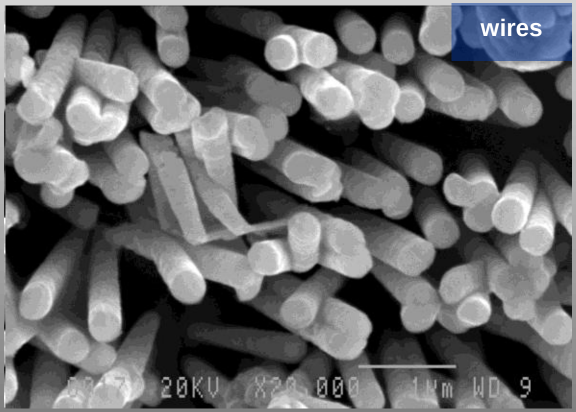
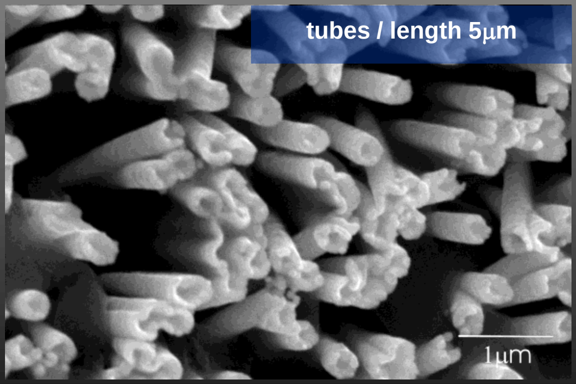
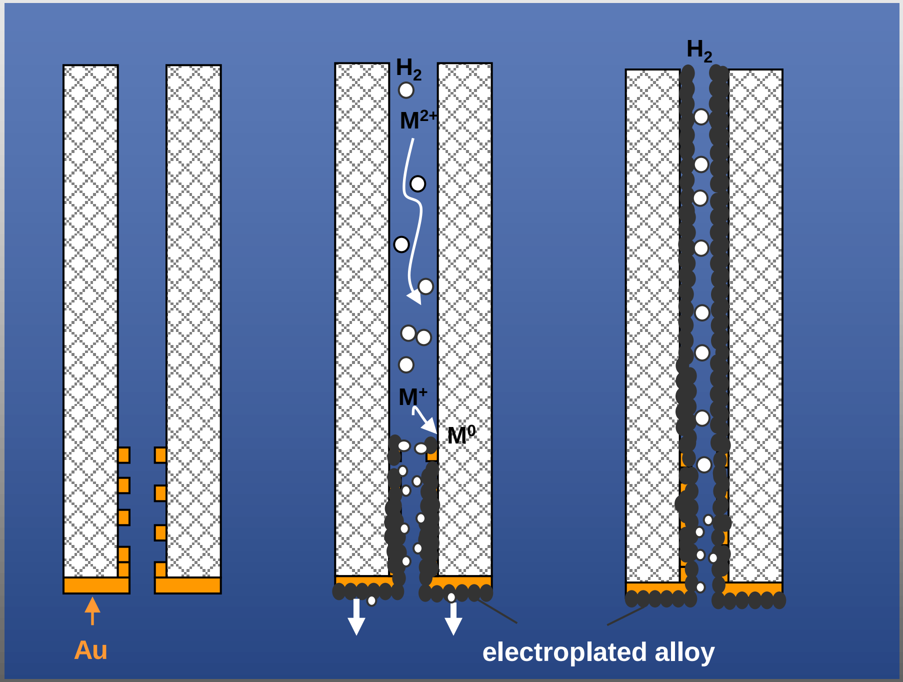






Mechanism of the nanotubes/nanowires DIRECT formation with no template pre-treatment



Necessary conditions

1. Partially blocked membranes
2. Appropriate deposition rates (kinetics) and diffusion
3. Hydrogen evolution

K. Žužek Rožman et al., Mater. Chem. Phys. 2009

Electrodeposition of Fe-Pd-based nanotubes

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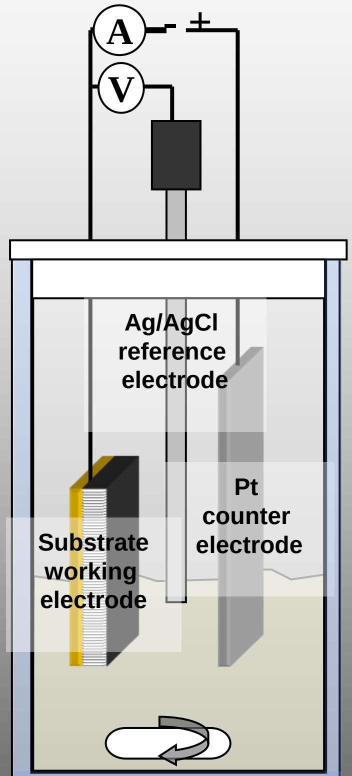
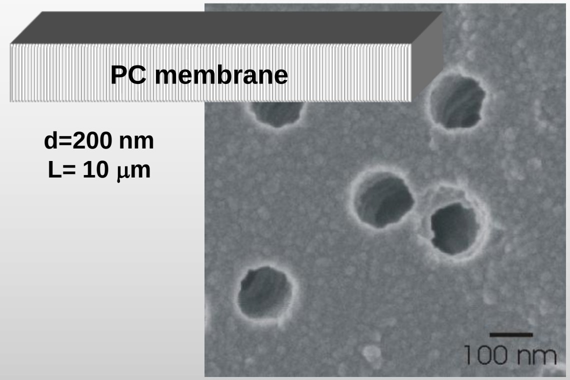
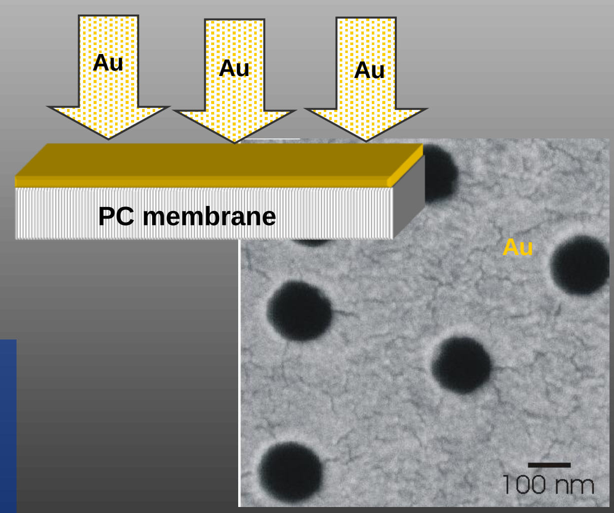
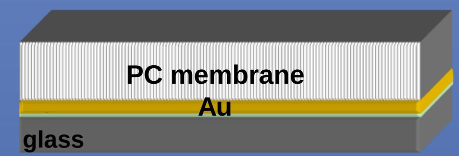






Experimental
Ammonium citrate: $c((NH_4)_2C_6H_6O_7)$ = 0.2 M
$PdCl_2$: 2-6 mM
$FeCl_2$: 14-18 mM
pH=9
T= room T
time= 300s-1200s
E vs. EAg/AgCl =-1.5 V and lower

Potentiostatic depositions (-1.5 V and lower)



As-deposited FePd + (CH_2Cl_2)
SEM/EDS/XRD/VSM(θ)

Heat treatment
(forming gas Ar+7% H_2)
400-600ºC/1h

Heat treated samples
Magnetic properties
XRD/VSM

Results..

$Fe_{70}Pd_{30}$ nanotubes prepared by electro deposition were successfully functionalized with a model drug, i.e., paracetamol.

The proposed type of release:

with an initial burst and a slower release of the remaining drug could be suitable for applications where a fast action is required, which then has to be maintained for a certain time period

Functionalization..

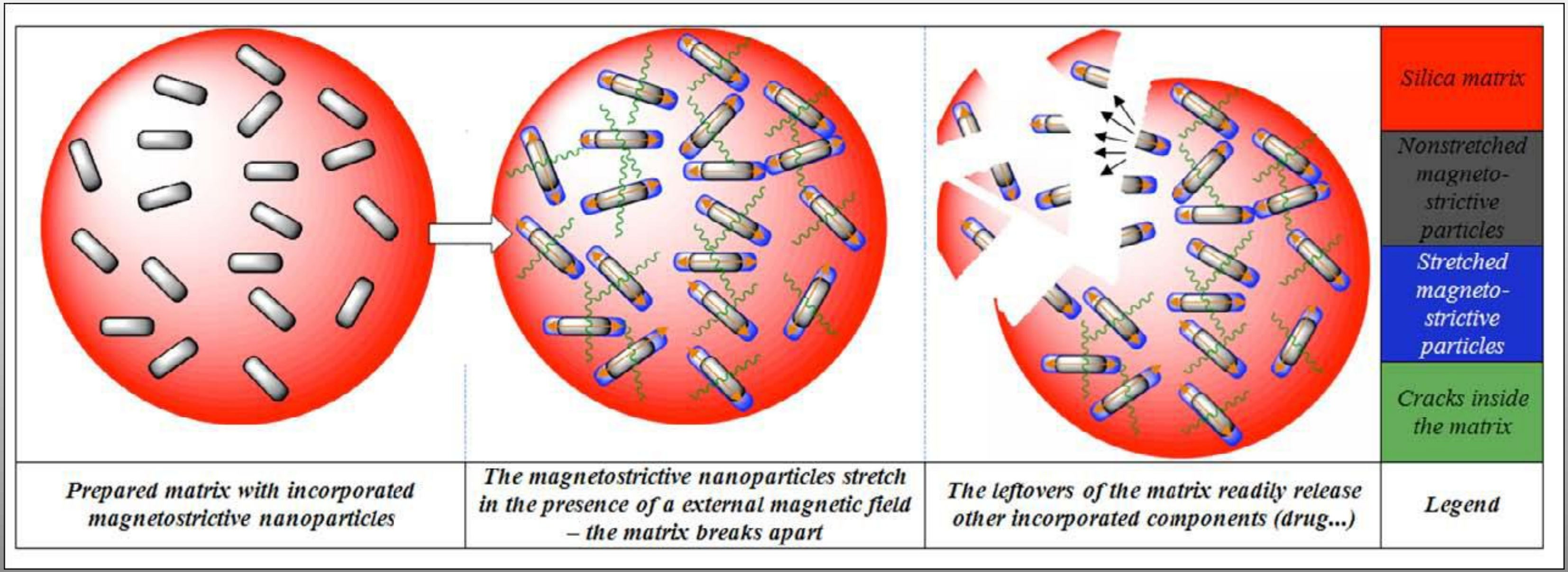
- Examples of successfully prepared materials using the sol–gel technique are silica xerogels intended for sustained and controlled release of ibuprofene, dexmedetomidine or indomethacine.

- The drug substance incorporated into the sol is distributed within the porous silica xerogel network. It has been shown that basic drugs release in a sustained manner whereas neutral drugs are released very quickly from silica.

- Silica causes no adverse tissue reactions and degrades in the body to $Si(OH)_4$, which is eliminated through the kidneys.

- Addition of organic modifiers is widely used for modifying the morphology and surface characteristics of silica xerogels prepared with the precursor TEOS (tetra-ethyl-ortho-silicate).

Schematics of the drug delivery



Schematics of the drug delivery based on the external actuation by a magnetic field acting on the magnetostrictive nano-rods.

Imbedding of magnetostrictive nanoparticles in a tunable brittle xerogel matrix that can be loaded with large therapeutical molecules.

$Fe_{70}Pd_{30}$ nanotubes/ Drug release mechanism

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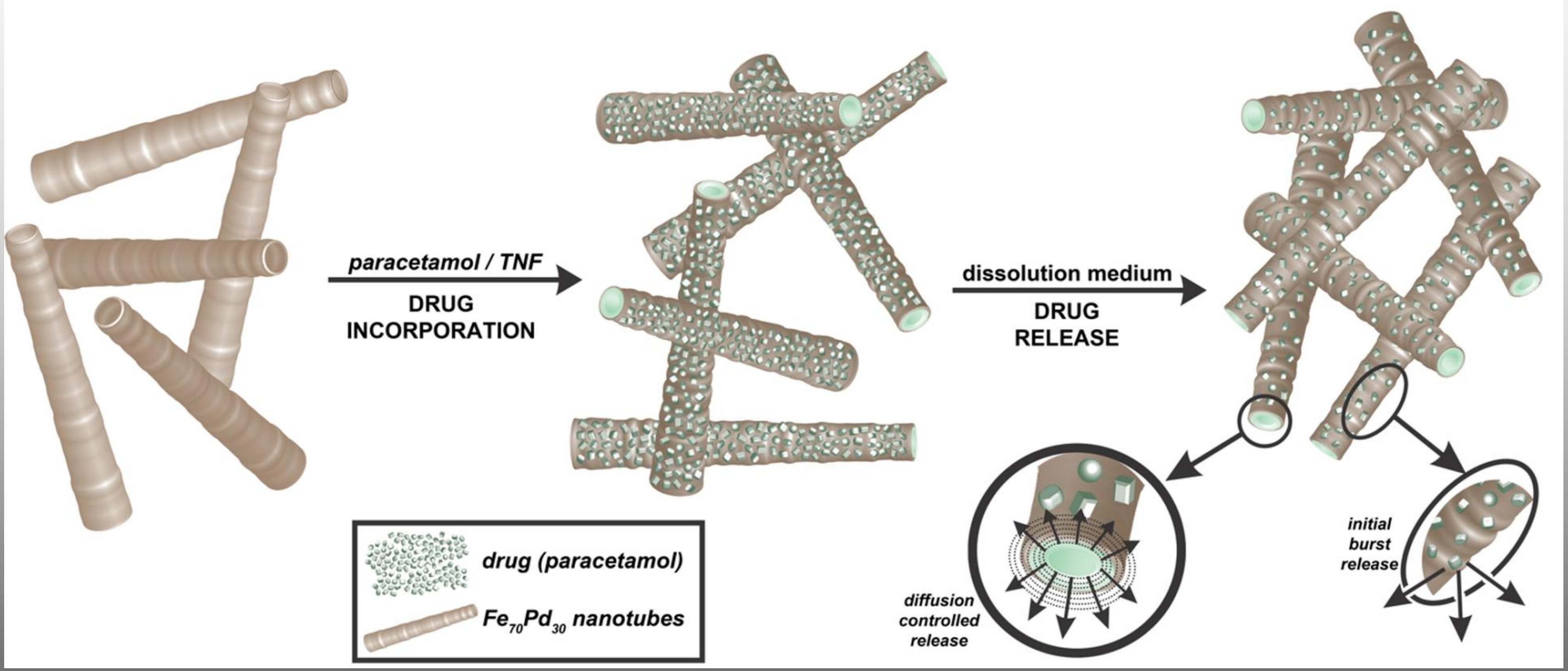
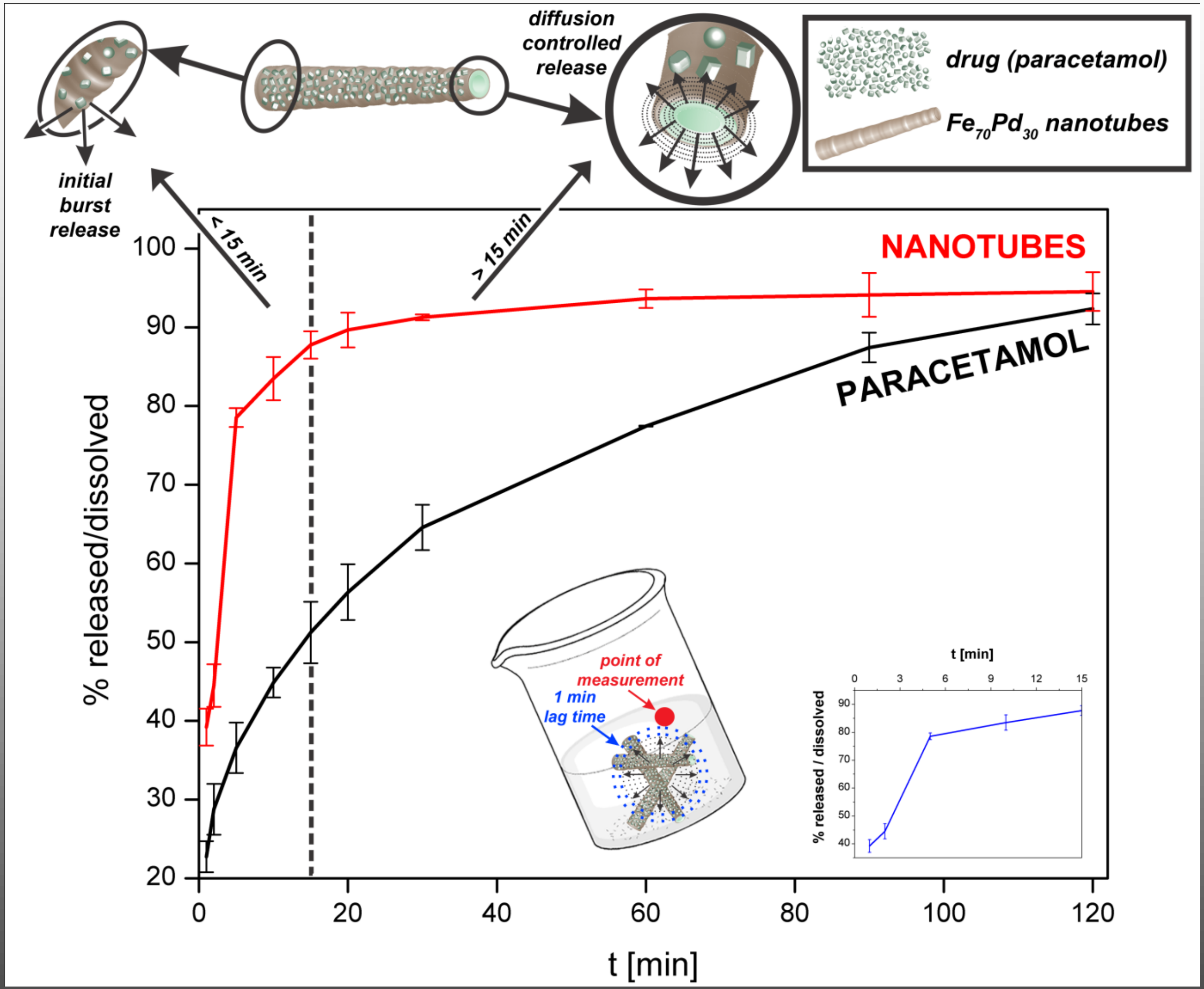


Experimental release profile suggests the application where it is important to reduce pain quickly and then maintain this condition for an extended period of time.

$Fe_{70}Pd_{30}$ nanotubes/ Drug release experiments



Initial burst followed by a diffusion controlled release

$Fe_{70}Pd_{30}$ nanotubes/ FUNCTIONALIZATION

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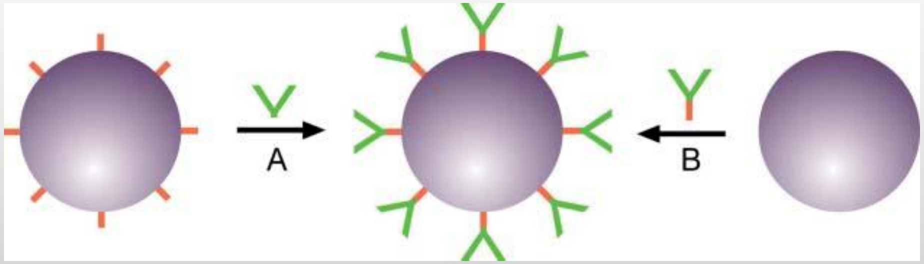
Attaching biofunctional molecules to a nano-object

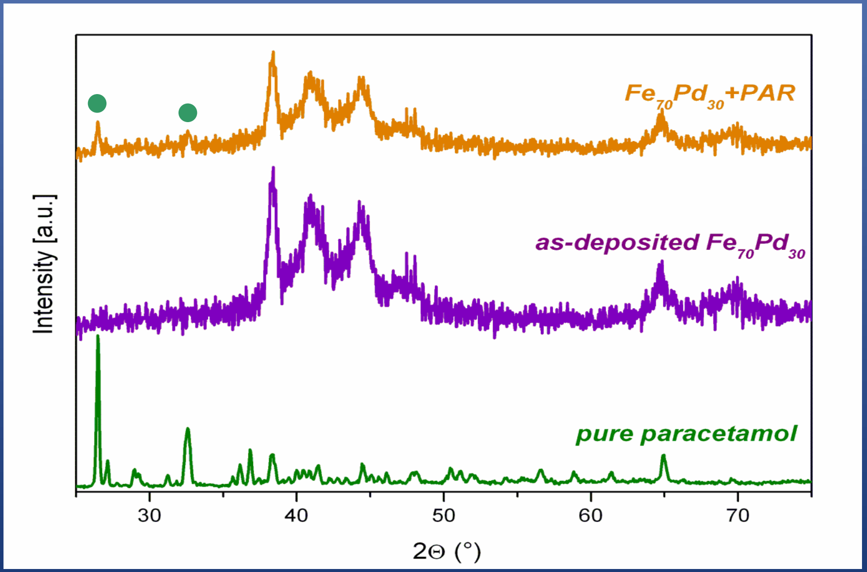


Paracetamol attachement

Zeta potential measurements

Water+Fe-Pd nanotubes aglomeration

Water+Fe-Pd nanotubes+ammonia stable suspension



Large constant zeta potential region → functionalization in different environments

$Fe_{70}Pd_{30}$ nanotubes for possible drug delivery applications

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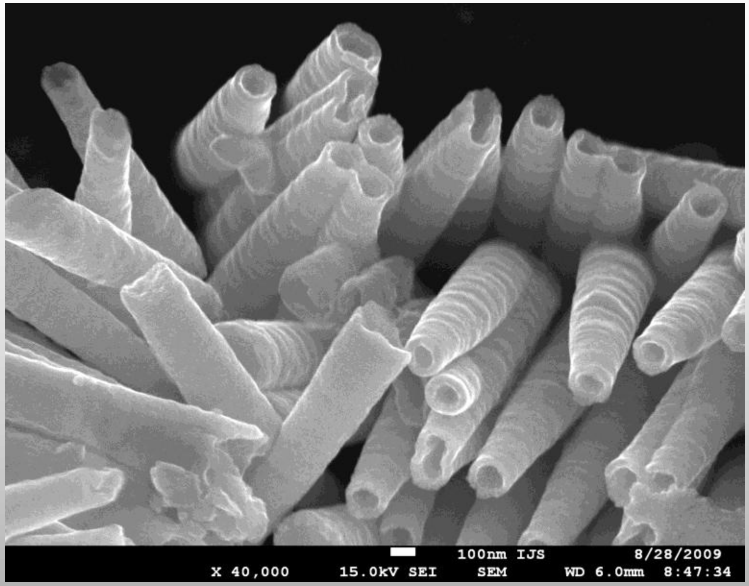

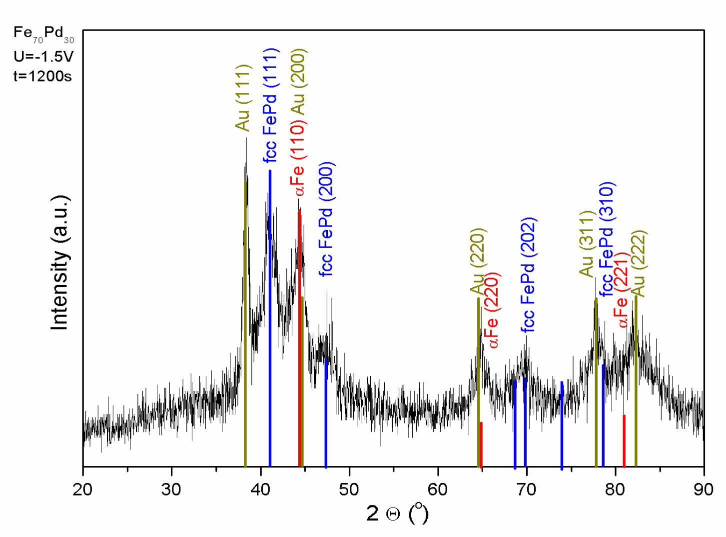

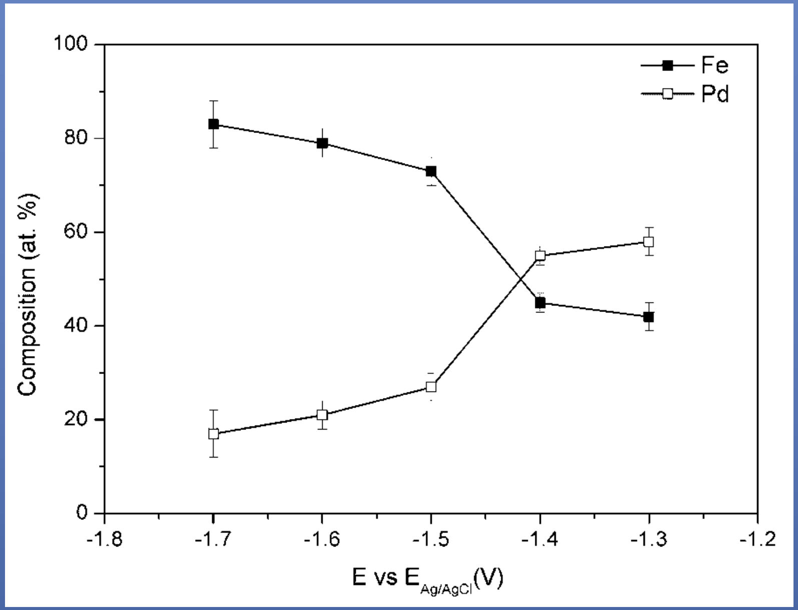

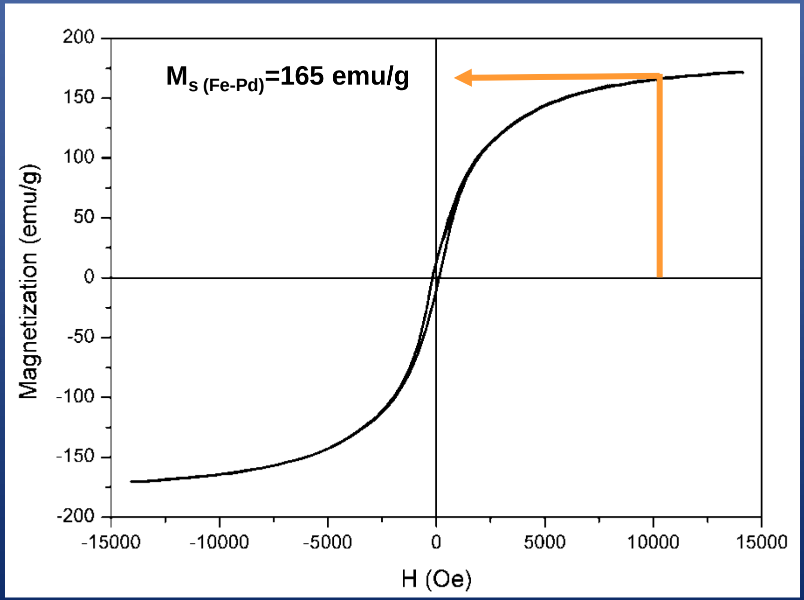

K. Žužek Rožman et al., Mater. Chem. Phys. submitted

Conclusions...

- Electrodeposition represents feasible and efficient means of producing nanostructured materials with tailorable properties.
- Tubular structures of Fe-Pd can be prepared directly.
- After appropriate heat treatment magnetic properties can be significantly improved in $L1_0$-based alloys.
- Fe-Pd nanotubes of MSM composition with potential in medical application were successfully synthesized and functionalized.
- Further investigations of the hard magnetic properties will proceed via the deposition into thermally resistant AAO templates

- Nano-device, based on a novel random heterogeneous elasto-ferromagnetic composite, forms an active drug delivery vehicle.
- The activation mechanism is based on a phase transition induced by the strain – external magnetic field hysteresis of the nano-rods.
- We are proposing a nanodynamic system that can change magnetic energy into mechanical work. The phase transition leads to a strain in the nano-rods that breaks the xerogel matrix in a controlled manner leading to a subsequent release of the incorporated drug.
- This novel application of a unique physical phenomenon allows for a truly programmable, drug independent, open loop, targeted delivery system exploiting the convergence of nano-scale material science, chemistry, biology, pharmacology, and physics.

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The successful completion of the research will have an enormous impact on the field of nano-medicine by opening the possibilities to use custom tailored active nanodevices capable to deliver potent drugs.

Drugs will be encapsulated in generic (non-drug specific) containers, sheltering the patient’s healthy tissues and release them upon noninvasive (as in non-surgical) external actuation.

Thank you for your attention!

This video shows a cancer cell with gold nanoparticles inside. The cell tries to divide, but the nanoparticles prevent it from reproducing.

Credit: Mostafa El-Sayed/Georgia Tech