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A short overview of the research capacity of National Centre for Micro and Nanomaterials, University POLITEHNICA of Bucharest

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EuroNanoForum, 12-14 June 2019

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15 Faculties covering the main Engineering Fields;
~35 000 students enrolled in BSc-MSc-PhD programs:

- BSc: 16 fields and 81 BSc programs
- MSc: 19 fields and 158 MSc programs
- PhD: 19 fields;

53 departments and 38 R&D centres;
~1400 teaching and research staff

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CNMN Centrul național de micro și nanomateriale

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26 permanent research staff + 9 full positions for 2+2 years + 10 part time positions;
~40 docs and postdocs and many MSc and BSc;
Over 2000m^2 research, technical and administrative spaces;
The R&D infrastructure worth over 15 mil Eur;
Research outcome:
Over 100 ISI papers/year; 15 ongoing research projects; 15 patent applications and issued patents in the last 5 years.

Zhevlwh= www.foodsafety.upb.ro
www.micronanotech.ro

Hpdlo= cnmn@upb.ro
cnpsa@upb.ro

Z kdw#zh#fdq#grB

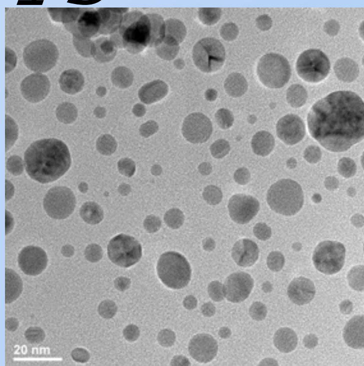
Materials Design

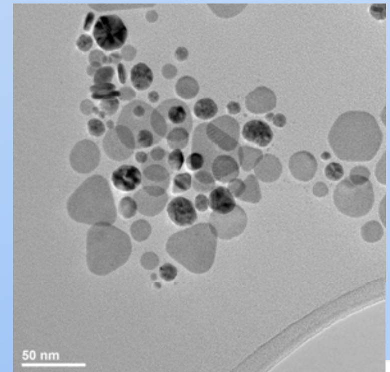
Materials Synthesis

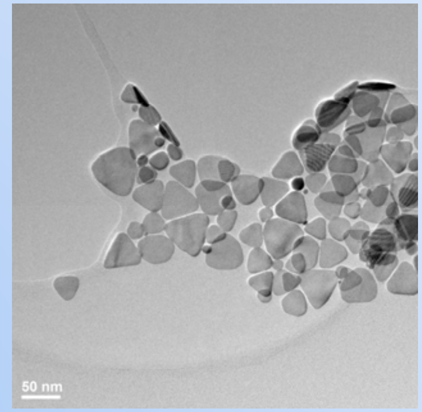
Materials Processing

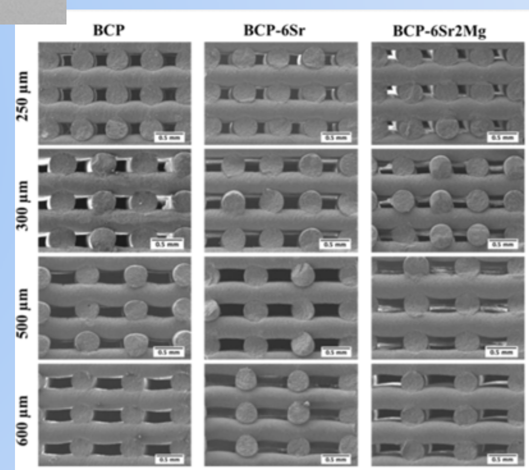
Materials Characterization

Materials Evaluation









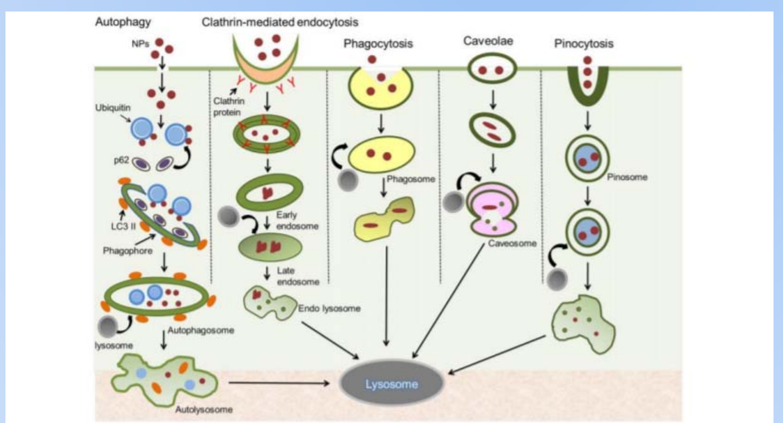


Figure 2. Schematic representation of plausible methods of cellular uptake of AgNPs [243]. Reprinted with permission from [243]. Elsevier, 2015.

Nanostructured materials

Nanomaterials for diagnosis and treatment;
Tissue regeneration (bone and skin);
Coatings for cardiovascular devices;
Drug delivery systems:
- **Antimicrobial;**
- **Antitumoral;**
- **Anti-inflammatory activity;**
- **Etc.**

Materials for environmental applications;
- **Heavy metals removal;**
- **Organic pollutants removal by sorption/degradation;**
- **Antimicrobial activity;**
- **Etc.;**

Energy Applications;

Pure phases

0D
1D
2D
3D

Core@shell structure:

Fe_3O_4@SA;
Ag@SA

Composites and nanocomposites:

COLL/HA
CS/HA
CS/ZnO
GO/ZnO; rGO/ZnO

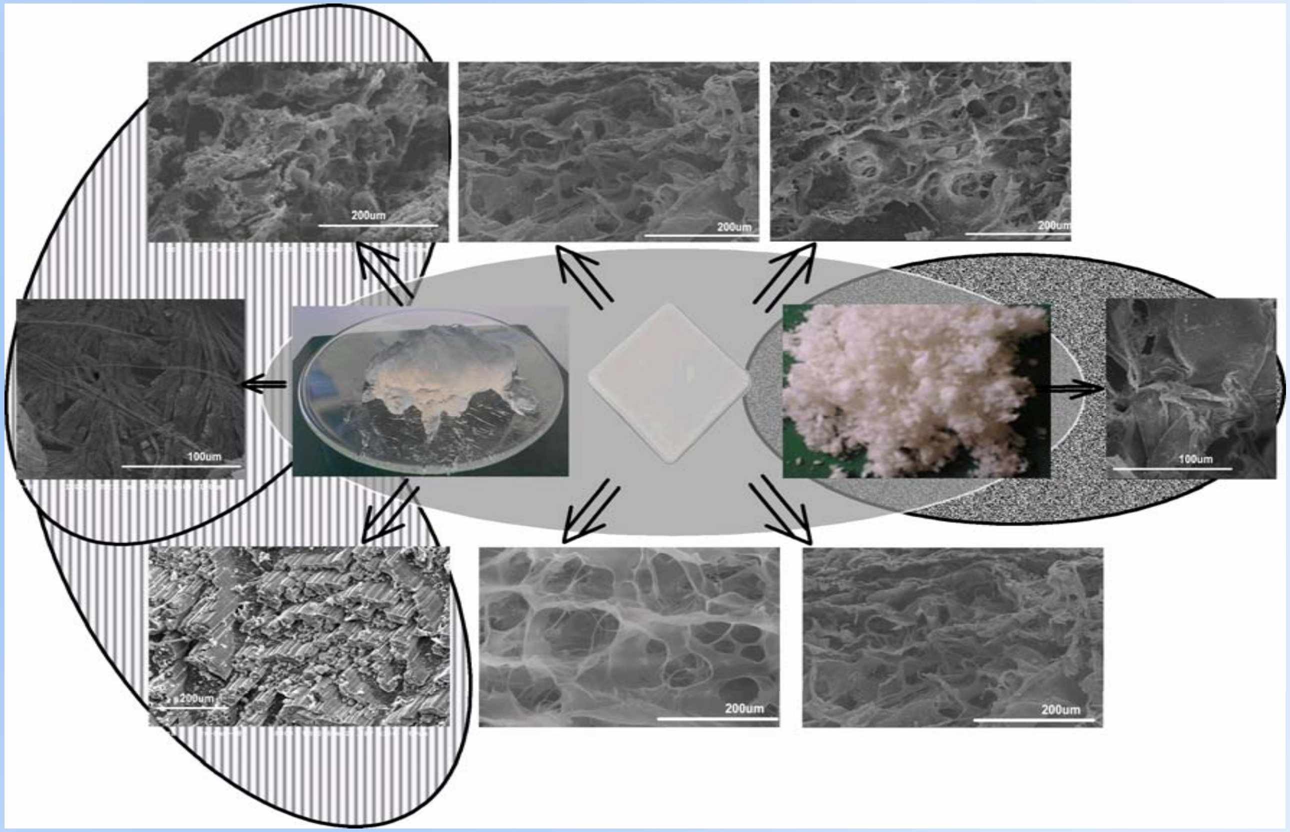
Fe_3O_4 $CuFe_2O_4$ Fe_2O_3 $CoFe_2O_4$ $NiFe_2O_4$ Ag Au ZnO Graphene CuO TiO_2 Al_2O_3 ZrO_2

MSH MCM41 MCM48 SiO_2 MCM50 SBA 15 SiC Graphene oxide

$Ca_5(PO_4)_3$ $CaHPO_4$ $CaSiO_3$ $Ca_5(PO_4)_3OH$ $CaHPO_4$ x $2H_2O$ $CaCO_3$

COLL/HA composite nanomaterials for bone regeneration/grafting

- Precursors and general conditions:
  - Collagen gel (1,54 - 3,21 %); collagen matrices or collagen fibers
  - $Ca(OH)_2$ suspension
  - NaH_2PO_4 solution
  - Temperature 33–35 ^{0}C
  - pH of the Precipitation step 8,5 – 9,5
- Specific conditions
  - Drying conditions
  - Electric fields;
  - Layer by layer mineralization;
  - Addition of ternary components



A. FICAI, E. ANDRONESCU, et al., Chem Eng J, 2010;160(2):794-800
A. FICAI, E. ANDRONESCU, et. al., Materials Letters 2010;64(4);541-544
A. FICAI, E. ANDRONESCU, et al., Rev. Mat. Plastice; 2009:46(1):11-15

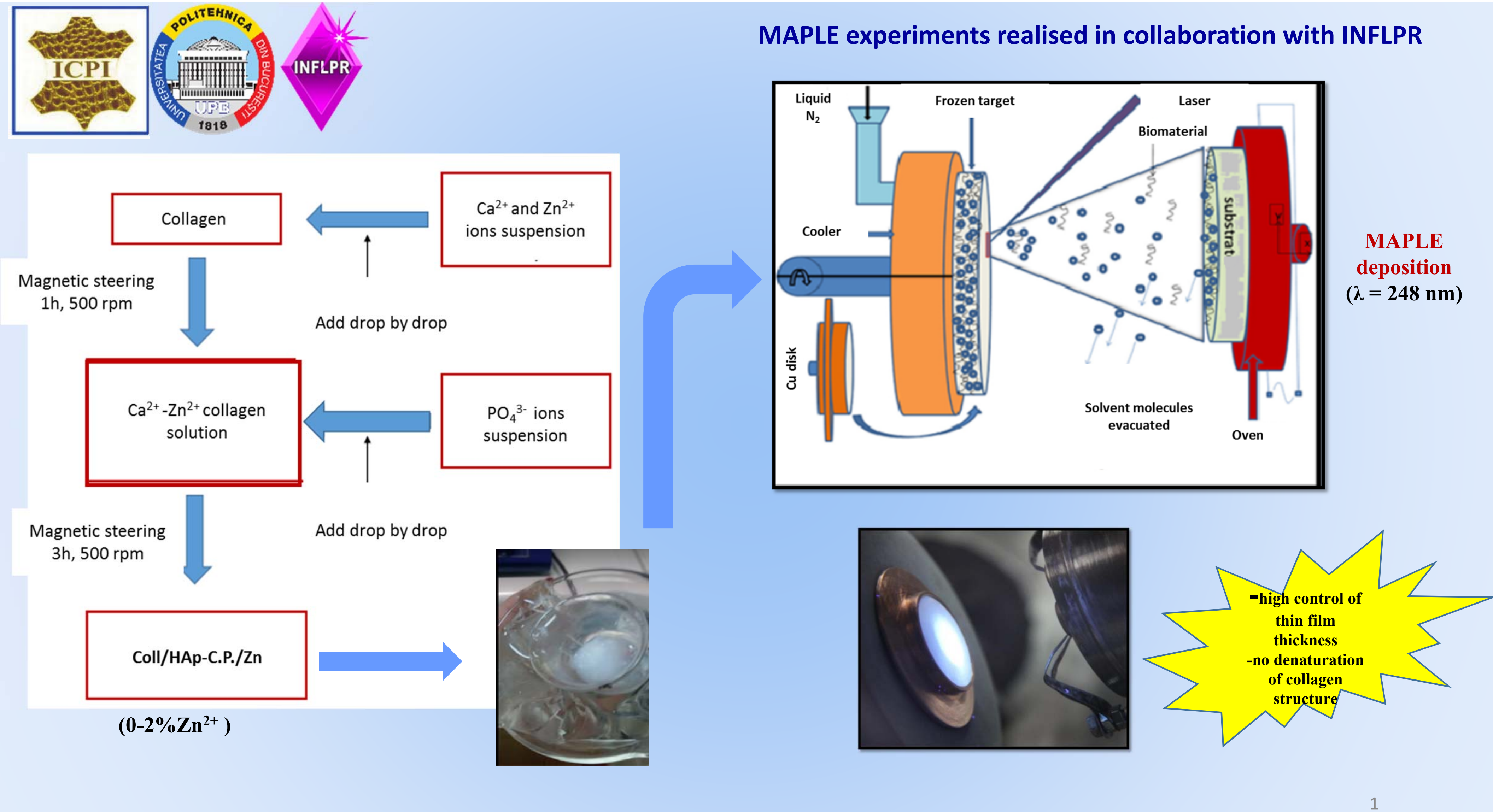
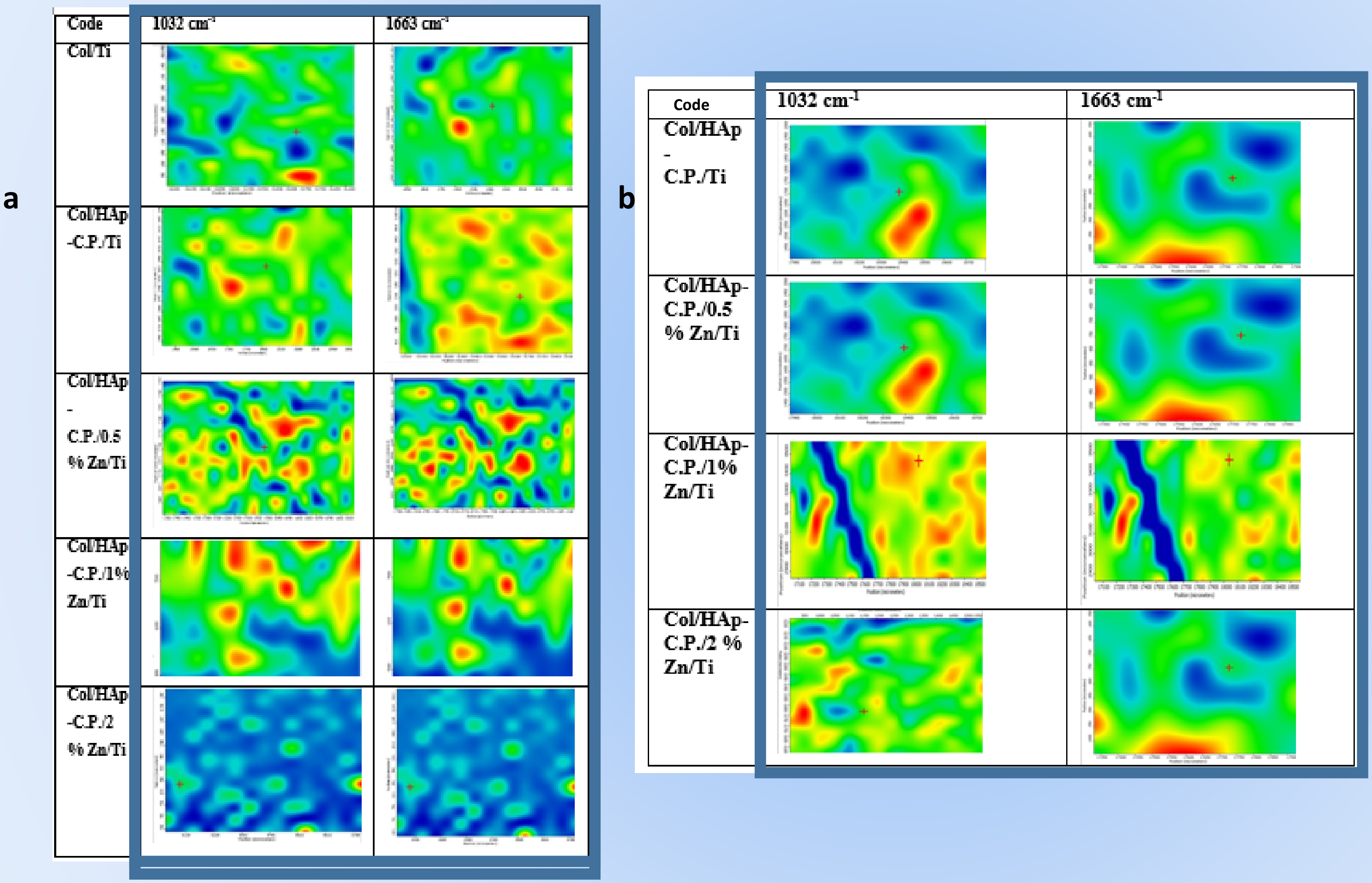


Fig. 1. Experimental principle of Coll/HAp-C.P./Zn thin films deposited by MAPLE on Ti substrate

2. Results

a. IR Mapping



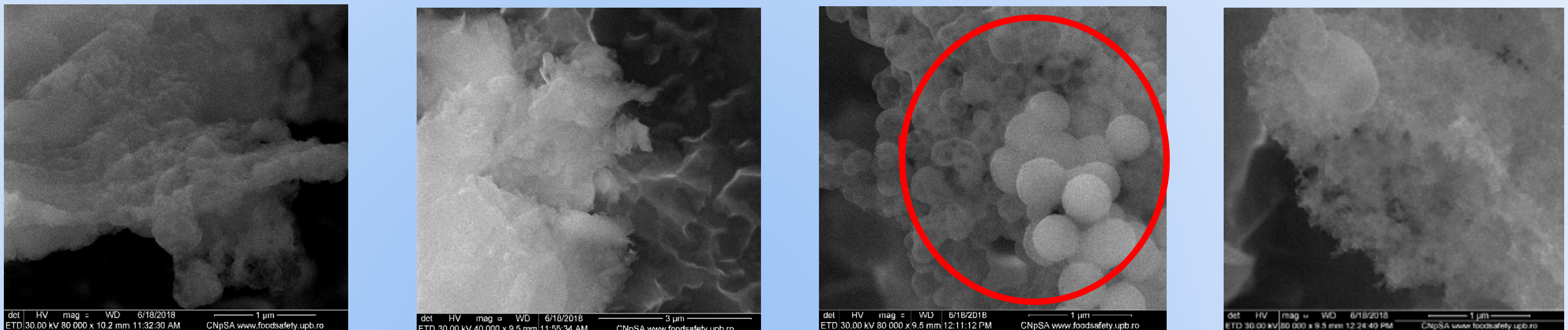
- improved film homogeneity even at increased % of Zn ion substituent
- after immersion in SBF, the formation of apatite was confirmed by an accentuated density area, especially for higher % of Zn

Fig. 2. IR Mapping of Coll/HAp-C.P./Zn^{2}/Ti deposited by MAPLE (a) simple and (b) after 2 weeks in SBF

b.SEM analysis

0% Zn^{2+} **0.5 % Zn^{2+}** **1 % Zn^{2+}** **2 % Zn^{2+}**

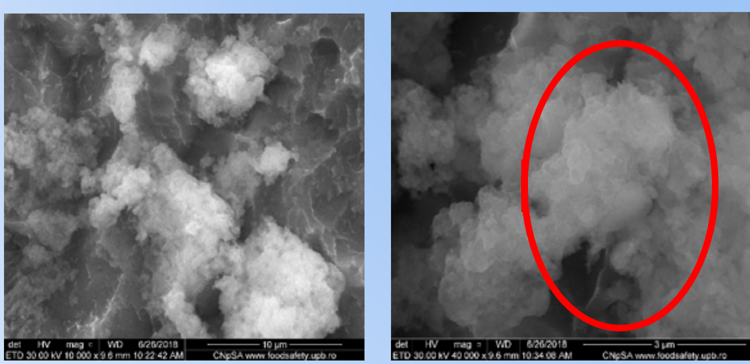
Before SBF immersion

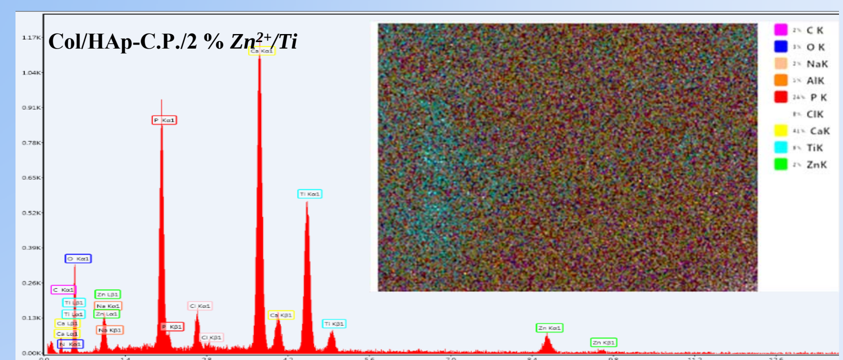


By increasing the Zn % it was observed the formation of spherical morphologies which may denote a supplementary crystallization process during cationic apatite substitution

0% Zn^{2+} **2 % Zn^{2+}**

After SBF immersion





During the ionic exchanges specific to SBF immersion, at higher Zn% it was noted the formation of different clusters that are correlated with the growth of an apatite layer simulating a biological process; in the same time, the film homogeneity was not affected (see EDAX map) due to an improved synergism between collagen and inorganic material, but also by preserving the collagen structure during deposition.

Fig. 3. SEM analysis of Coll/HAp-C.P./Zn^{2+}/Ti thin films deposited by MAPLE

c. Cellular biocompatibility assays

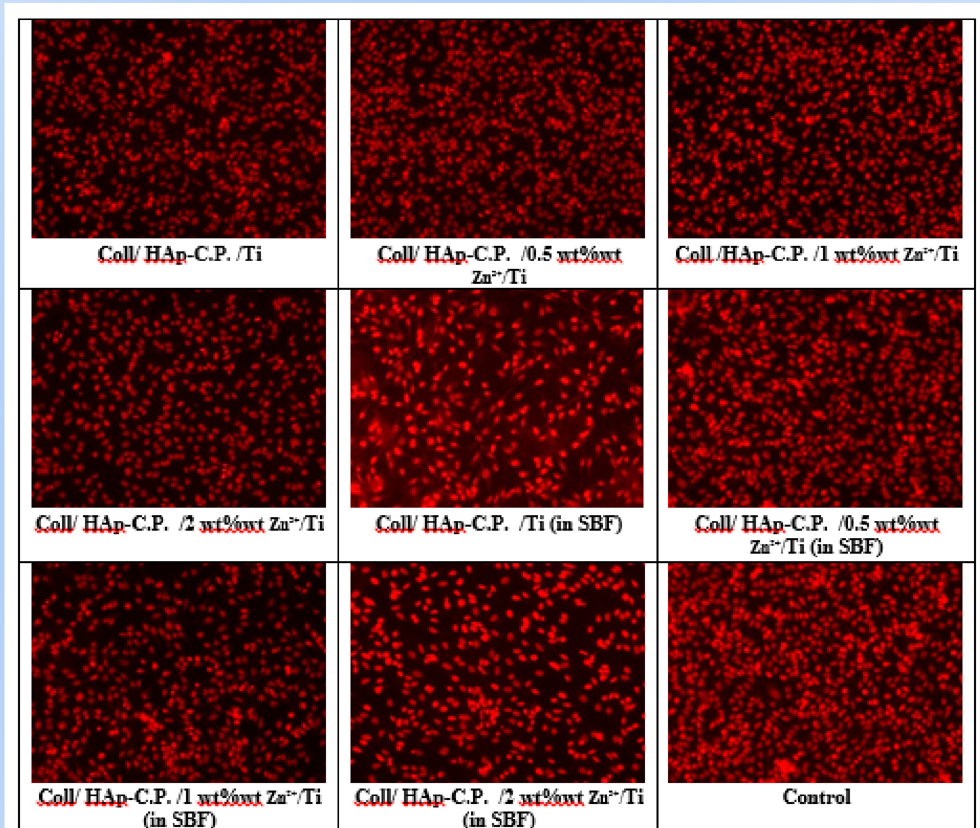
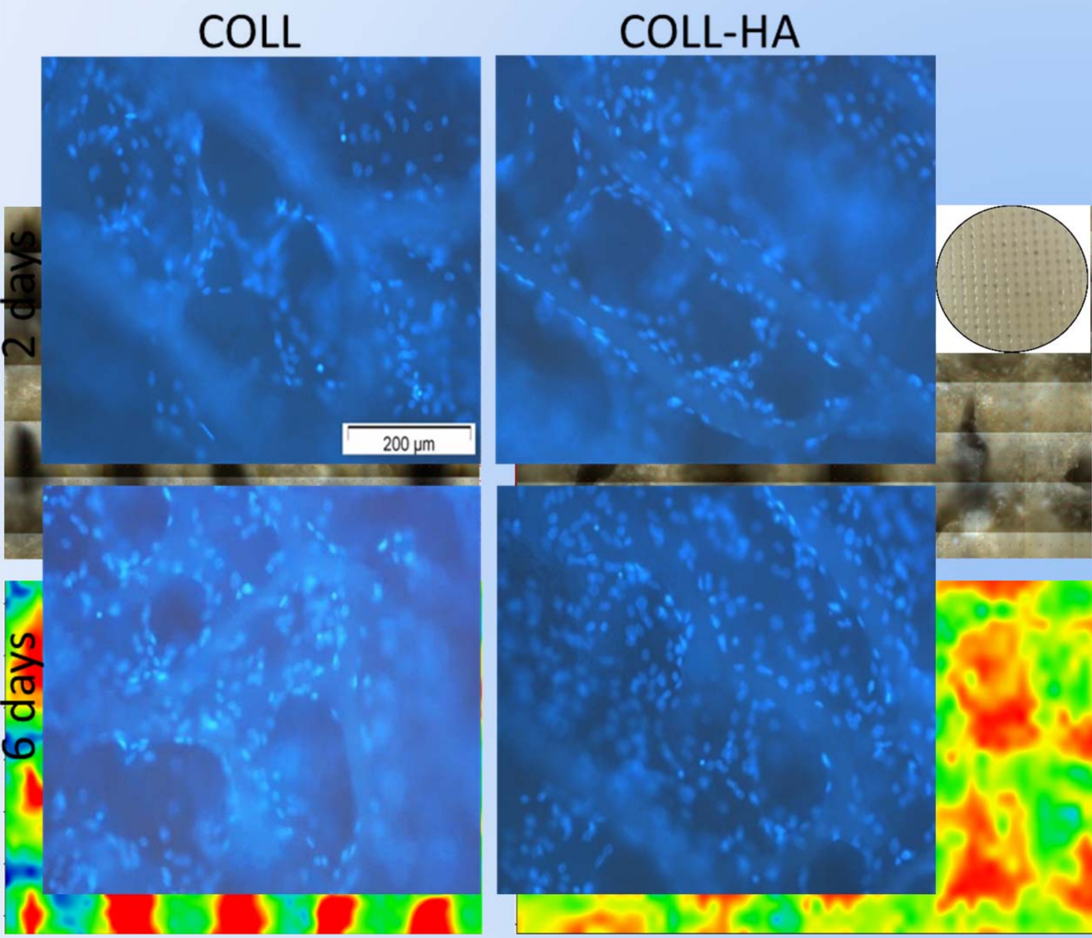


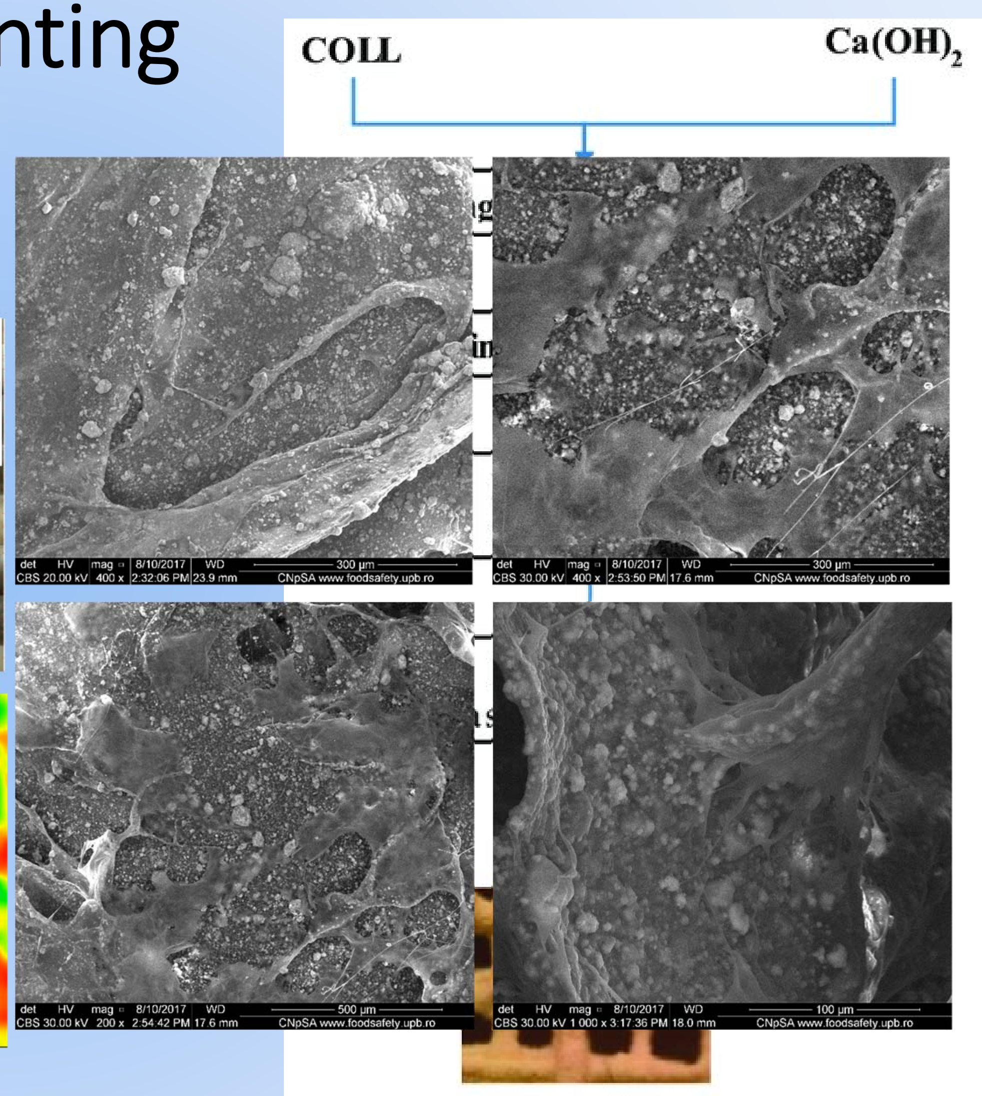
Fig. 4. Fluorescent microscopy images of cells grown on Coll/Zn^{2+}-CaPs thin films deposited on Ti by MAPLE

I.A.Neacsu, L.V.Arsenie, R. Trusca, I. L. Ardelean, N. Mihailescu, I. N.Mihailescu, C. Ristoscu, C. Bleotu, A. Ficai, E. Andronescu, Nanomaterials, **2019**, 9(5), 692-706

3D printing



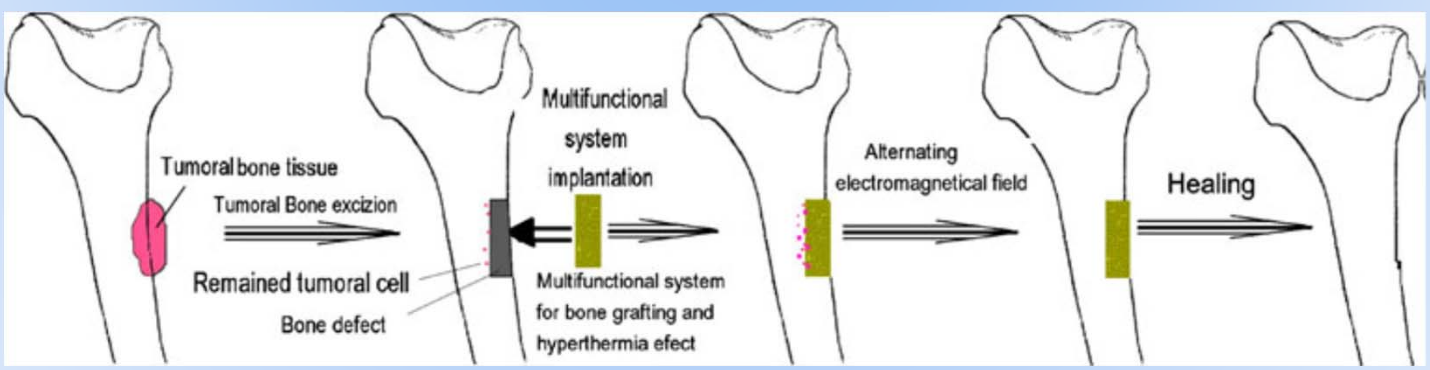
COLL
COLL-HA
2 days
6 days
200 µm



COLL
Ca(OH)$_2$
300 µm
300 µm
500 µm
100 µm
CNpSA www.foodsafety.upb.ro

Overview – bone cancer

- **Bone cancer treatment is mainly based on surgery and radio- and chemo-therapy;**
- Unconventional therapies are a challenge of the future: hyperthermia, phototherapy, the use of nanoparticles and natural extracts, stem cell transplants, or many other less used therapies.



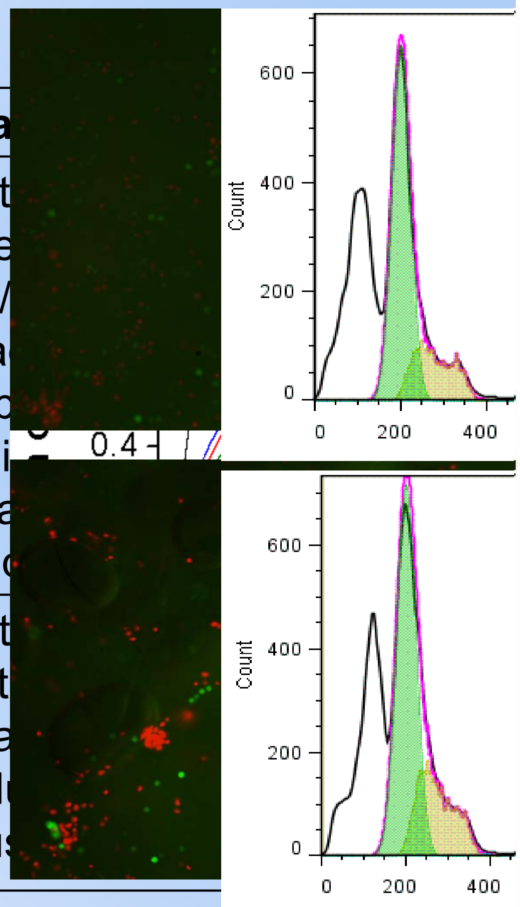
E. ANDRONESCU, M. FICAI, G. VOICU, D. MANZU, A. FICAI; Journal of Materials Sciences-Materials in Medicine; 2010:21(7): 2237–2242

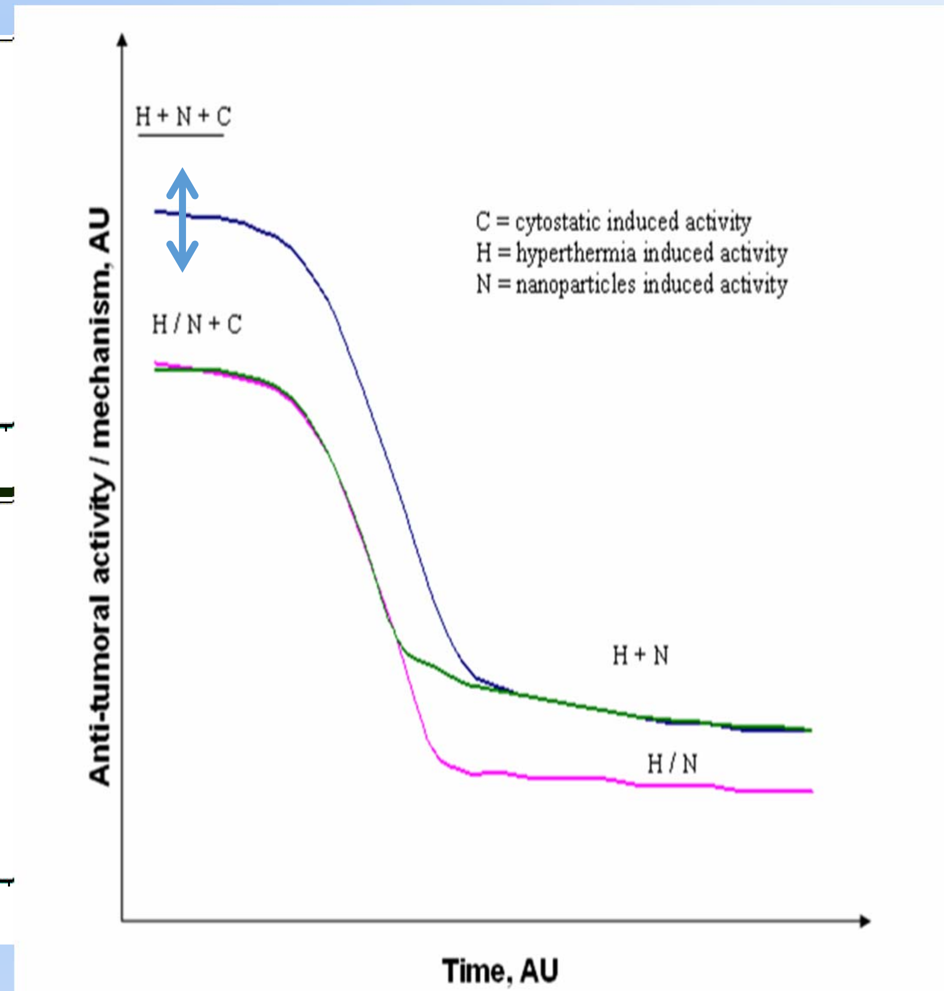
Multifunctional materials for bone cancer treatment

Sample	Main characteristics
COLL/ HA-CisPt	Composite material based on collagen, hydroxyapatite and cisplatin with regenerative and antitumoral role. The main goal of this system is the low level of systemic toxicity because of the loco-regional delivery of the cisplatin and reduced interaction with healthy tissue. Due to the "targeted delivery" the amount of cisplatin could be reduced.
COLL/ HA-Fe_3O_4	Composite material based on collagen, hydroxyapatite and magnetite nanoparticles with regenerative and antitumoral role. The antitumoral activity is induced by the hysteresis loop of the magnetite. The main advantages of the use of magnetite are: its good biocompatibility (lack of cytotoxicity) and good antitumoral activity when exposed to an external, proper electromagnetic field.
COLL/ HA-Fe_3O_4-Ag	Composite material based on collagen, hydroxyapatite, magnetite and silver nanoparticles with regenerative and antiseptic/antitumoral role. This system joins the advantages of the COLL/HA-CisPt and COLL/HA-Fe_3O_4 multifunctional systems.

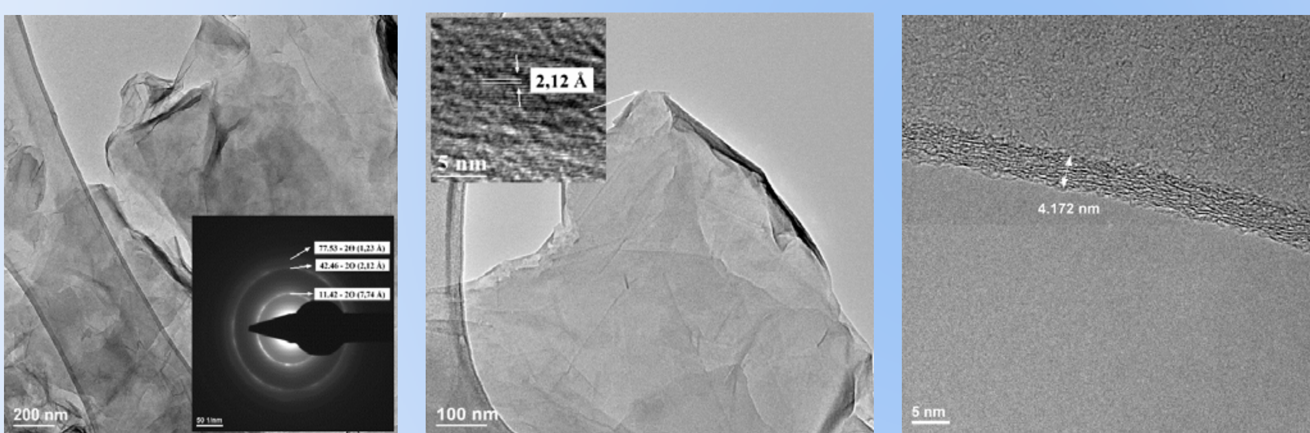
Multifunctional materials for bone cancer treatment

Sample	Main cha
COLL/HA-Fe_3O_4-CisPt (LbL)	Composit with re COLL/ new a rate (b intensi the ma consec
COLL/HA-Fe_3O_4-Ag-CisPt	Composit cisplat mainta but, d becaus

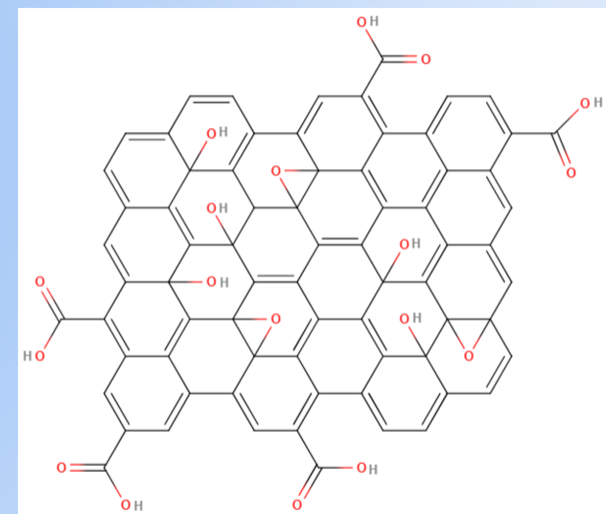




Multifunctional Platforms Based on Graphene Oxide and Natural Products



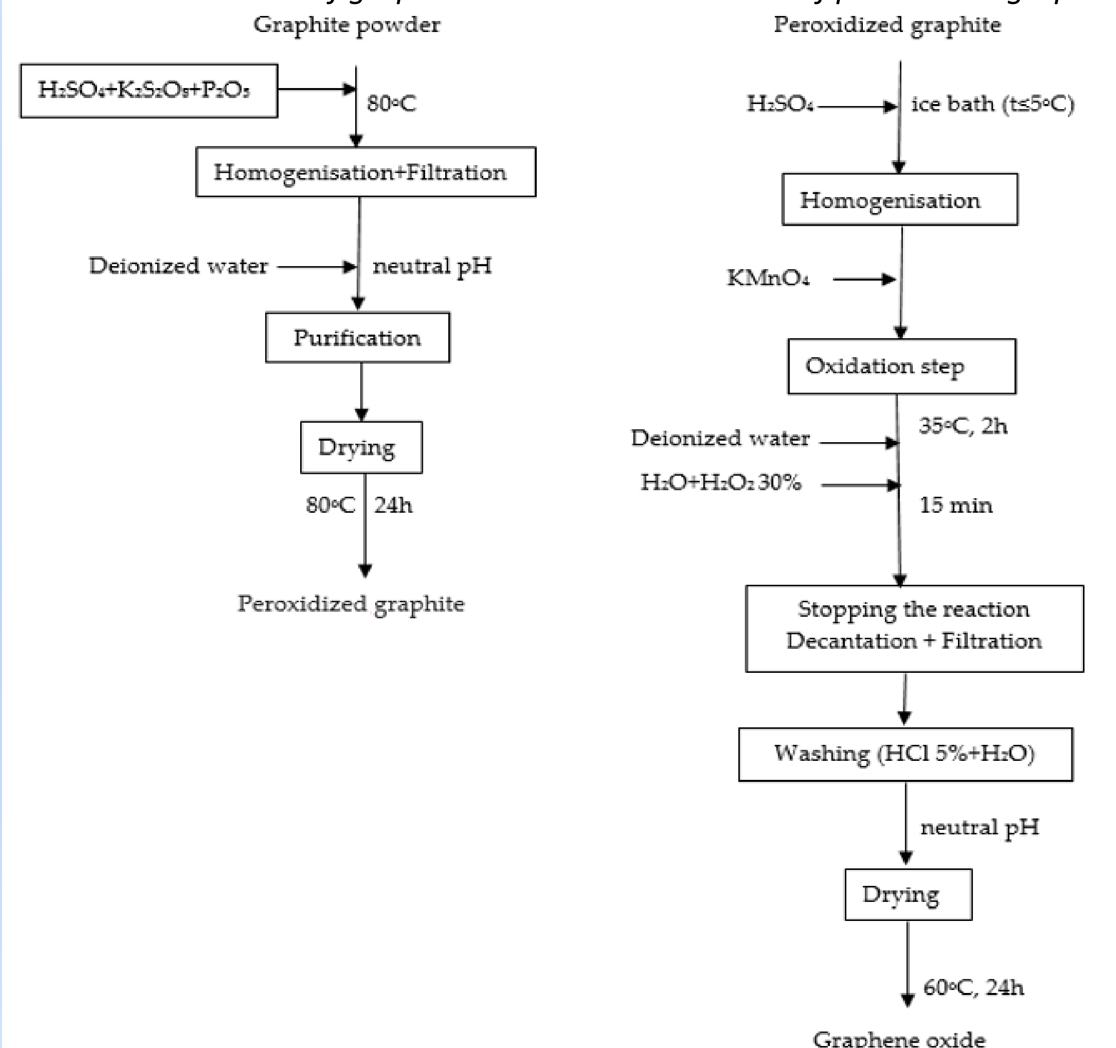
TEM image and SAED pattern—insert (**a**), TEM image with an HRTEM image—insert (**b**) and lateral view of the graphene layer indicating the thickness (**c**) of GO sheets.



Graphene oxide structure

Synthesis of Graphene Oxide

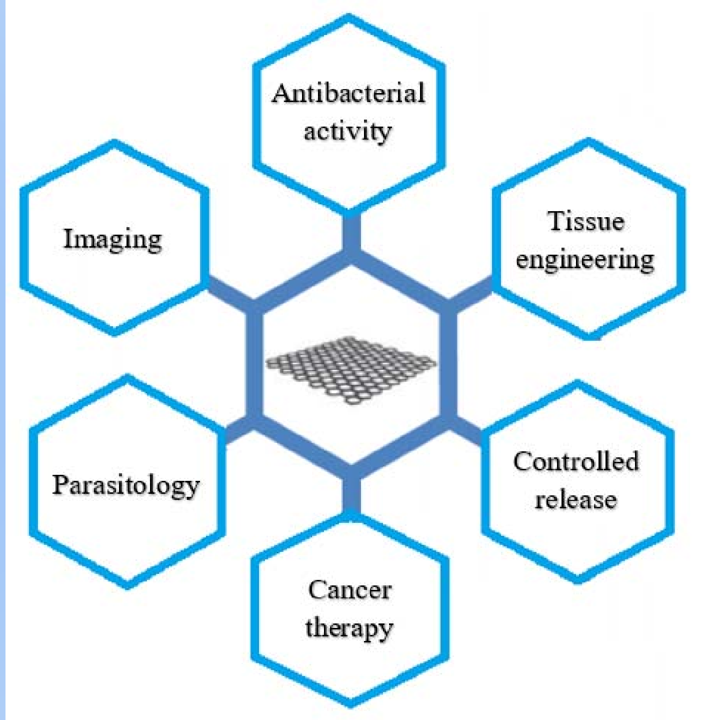
Phase I: *Peroxidation of graphite* **Phase II**: *Oxidation of peroxidized graphite*



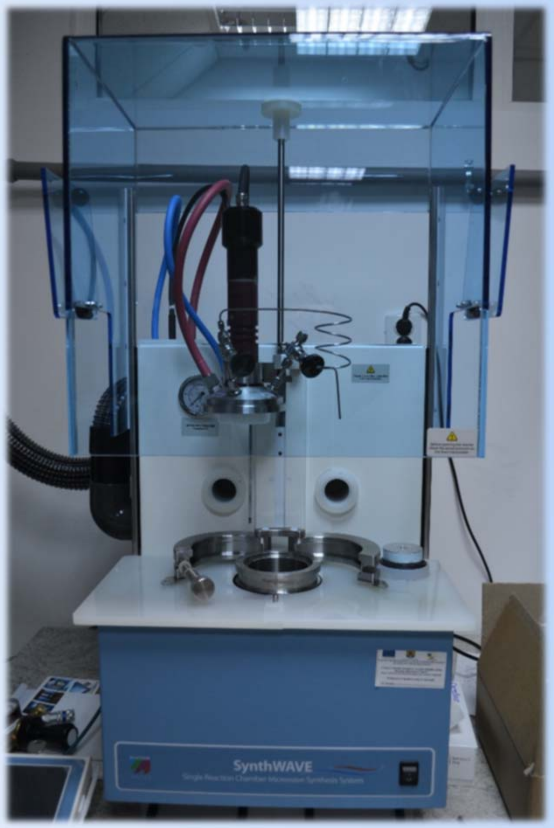
Jianchang, L., et al., *The Preparation of Graphene Oxide and Its Derivatives and Their Application in Bio-Tribological Systems*. Lubricants, 2014. **2**: p. 137-161.

Applications of GO

- the systems which are not able to release the biologically active agents are suitable for certain applications (such as preventing infections, cancer spreading inside the grafts containing graphene oxide, etc.)
- the systems releasing biologically active agents can be exploited in a classical way, as a platform for delivery of biologically active agents (especially in the treatment of cancer and severe infections).
- in vitro and in vivo studies are necessary to demonstrate the ability of these platforms in the treatment of cancer and severe infections and in development of drug delivery systems and optical biosensing.



Research infrastructure
Microwave assisted hydrothermal synthesis unit (Milestone)

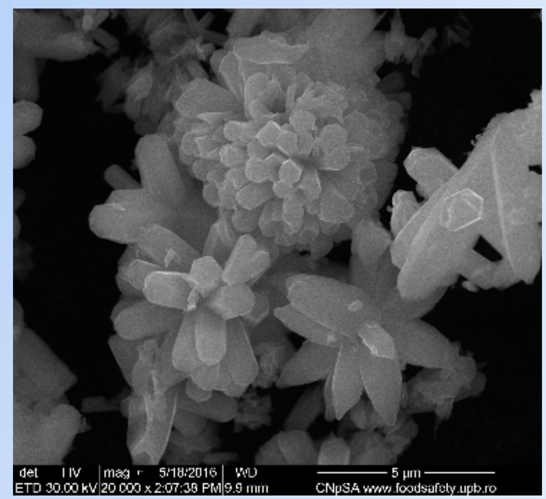


The system handles single or multiple reactions at temperatures up to 300°C and pressures up to 199 bar;

Possibility to scale up reactions from grams to kilograms range;

Synthesis of micro/nanostructured materials;

Possibility to make 5 sample simultaneous.



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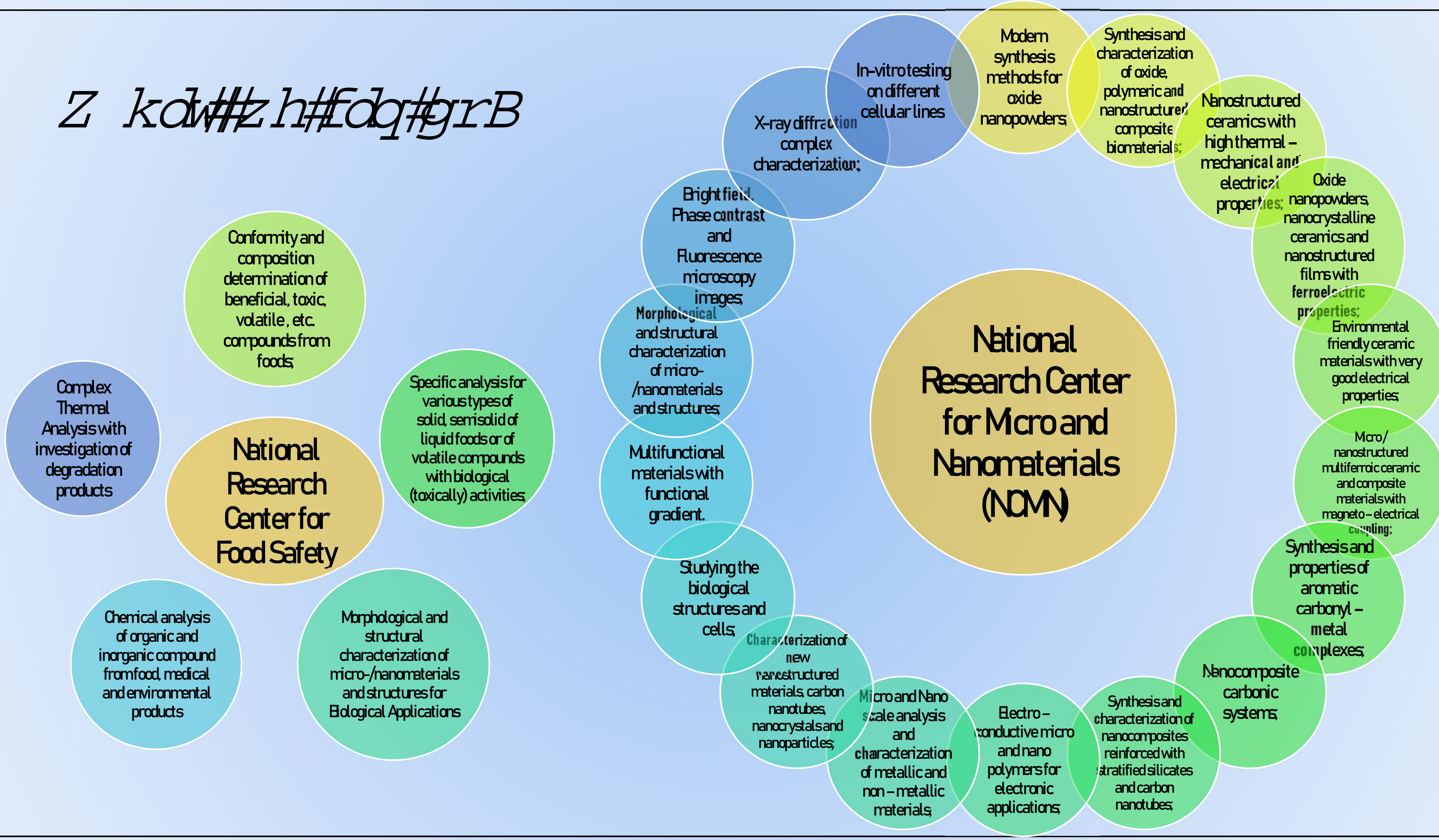
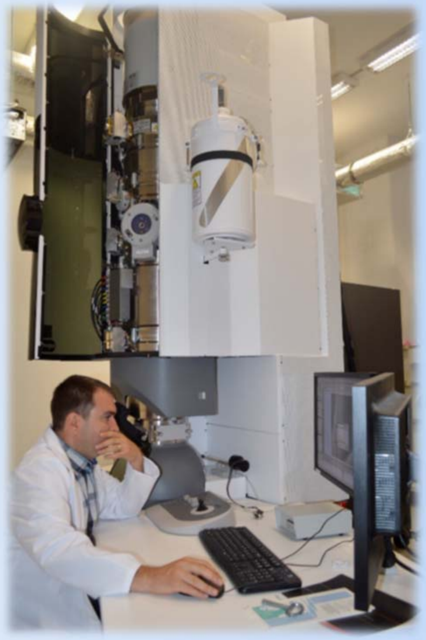


Research infrastructure
High Resolution Scanning Transmission Electron Microscope (Crio-TEM) Titan Themis



Bright Field TEM Analysis (BF-TEM);

Selected Area Electron Diffraction (SAED);

High Resolution Scanning TEM analysis (HR-STEM);

Crio TEM/STEM with Low Dose Capabilities;

High Resolution TEM analysis (HR-TEM);

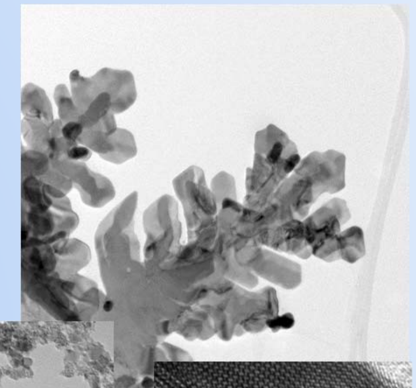
Nanodiffraction;

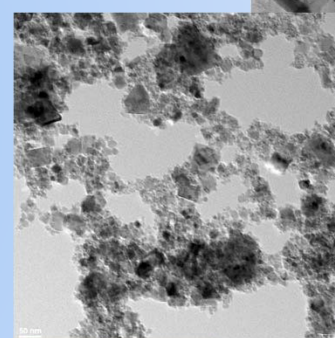
EELS analysis/mapping;

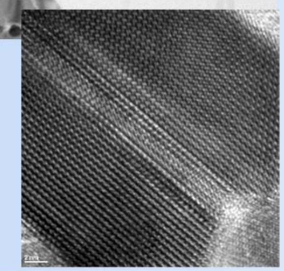
Point EDX and EDX mapping;

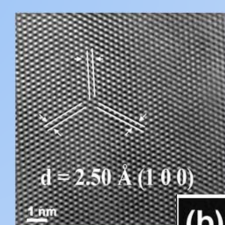
TEM/STEM Tomography;

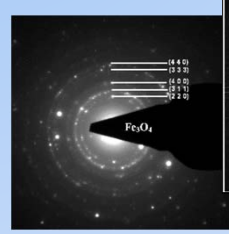
Atomic resolution mapping;

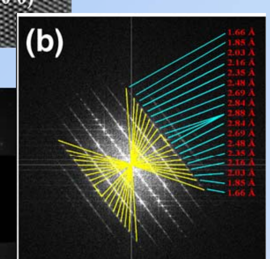


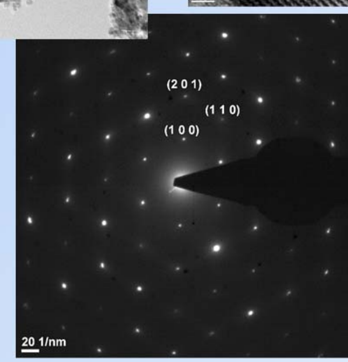












Research infrastructure
High Resolution Scanning Transmission Electron Microscope
Tecnai G2 F30 S-TWIN

Bright Field TEM Analysis (BF-TEM);

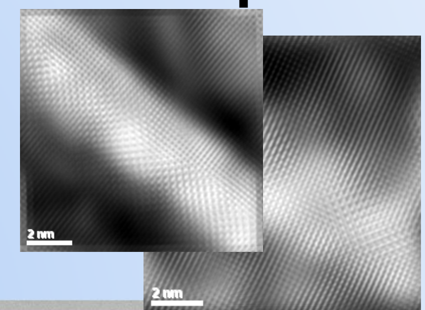
Selected Area Electron Diffraction (SAED);

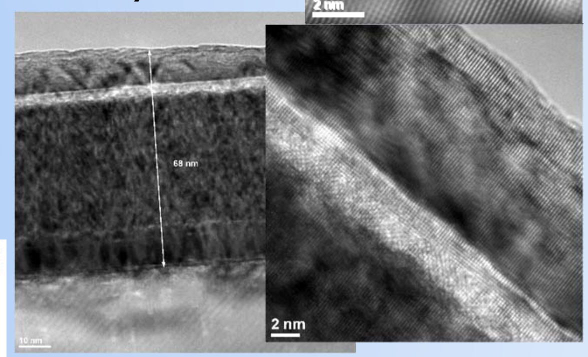
High Resolution Scanning TEM analysis (HR-STEM);

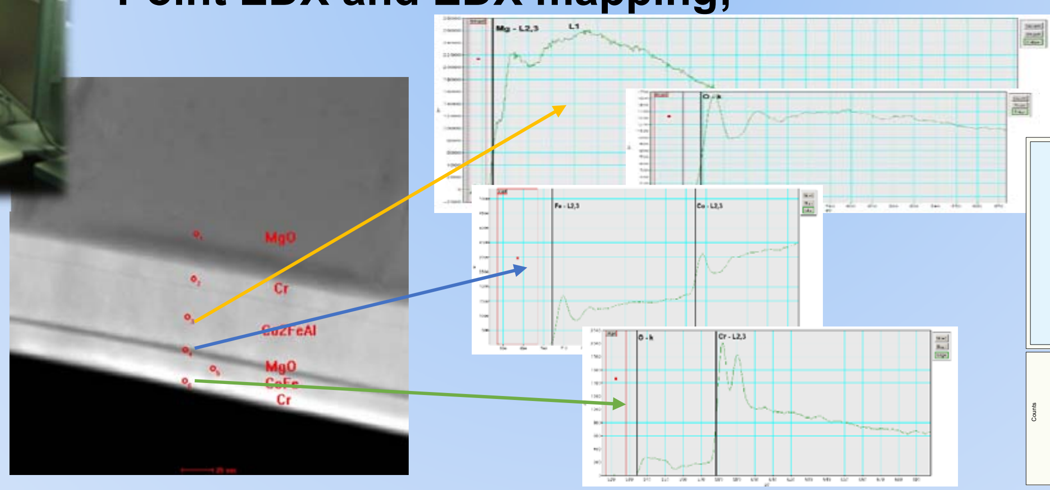
High Resolution TEM analysis (HR-TEM);

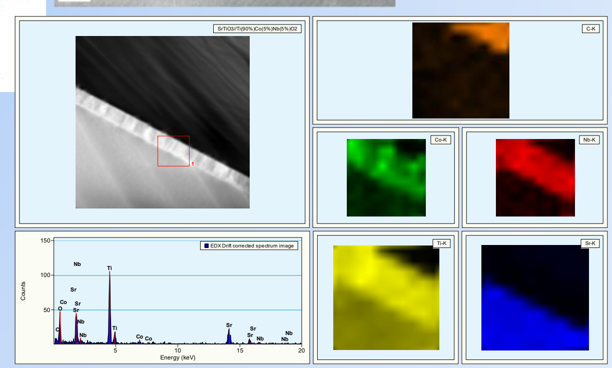
EELS analysis/mapping;

Point EDX and EDX mapping;

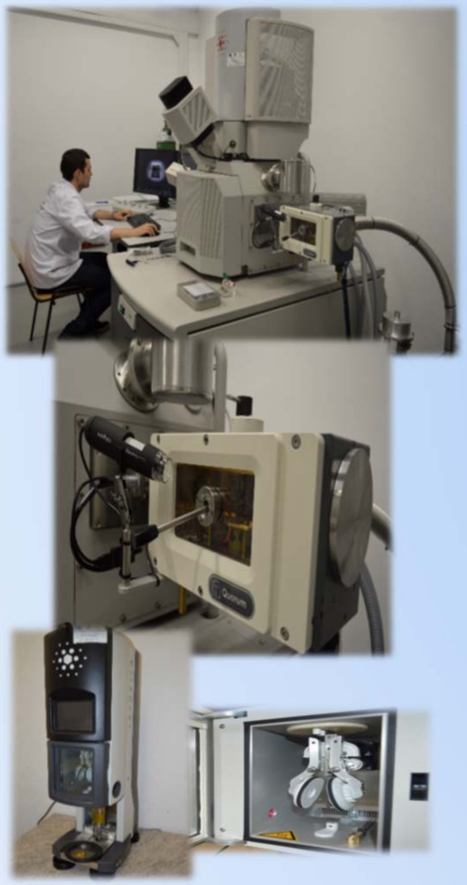








Research infrastructure
High Resolution Scanning Dual Beam Electron Microscope (Crio-SEM) Versa 3D



High Resolution SEM imaging;

FIB TEM sample preparation and Nanostructuring;

Directional BSE (Back scattering electron);

Pt deposition/Carbon Milling;

Wet STEM;

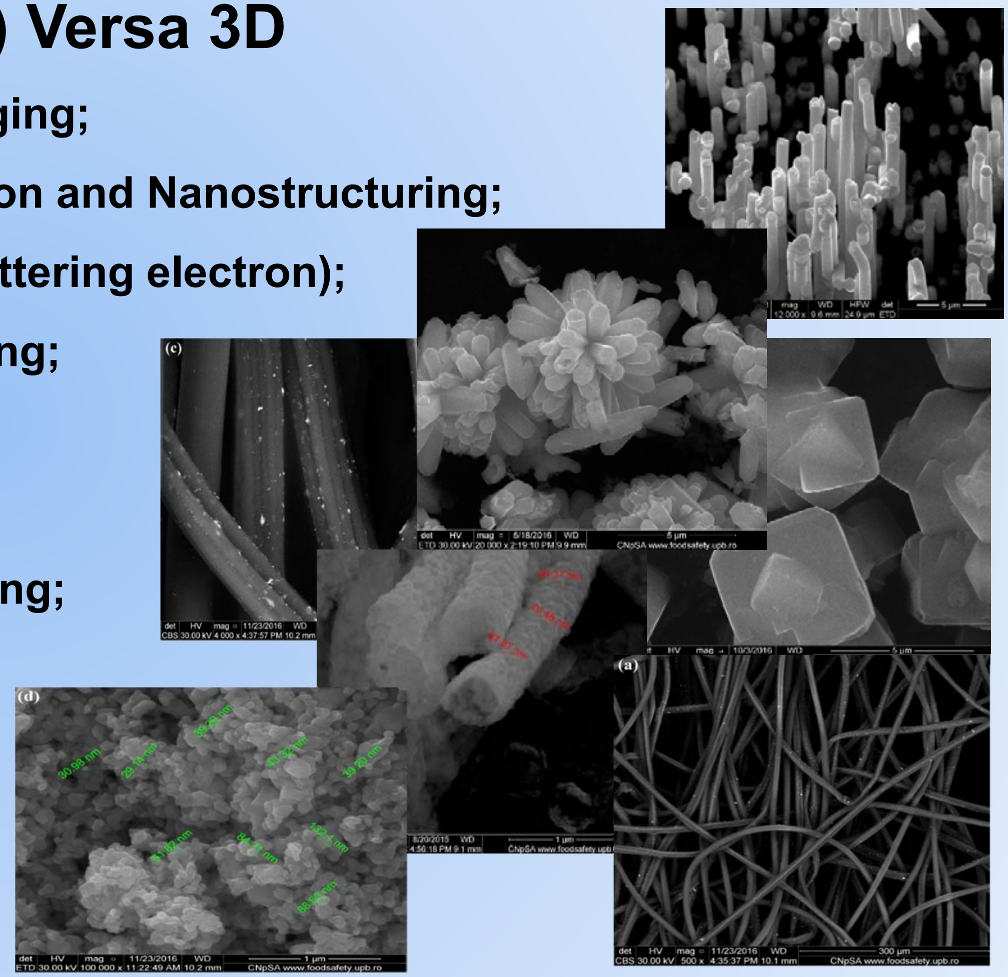
Nanomanipulation;

Point EDX and EDX mapping;

Low vacuum SEM;

ESEM;

Crio SEM.

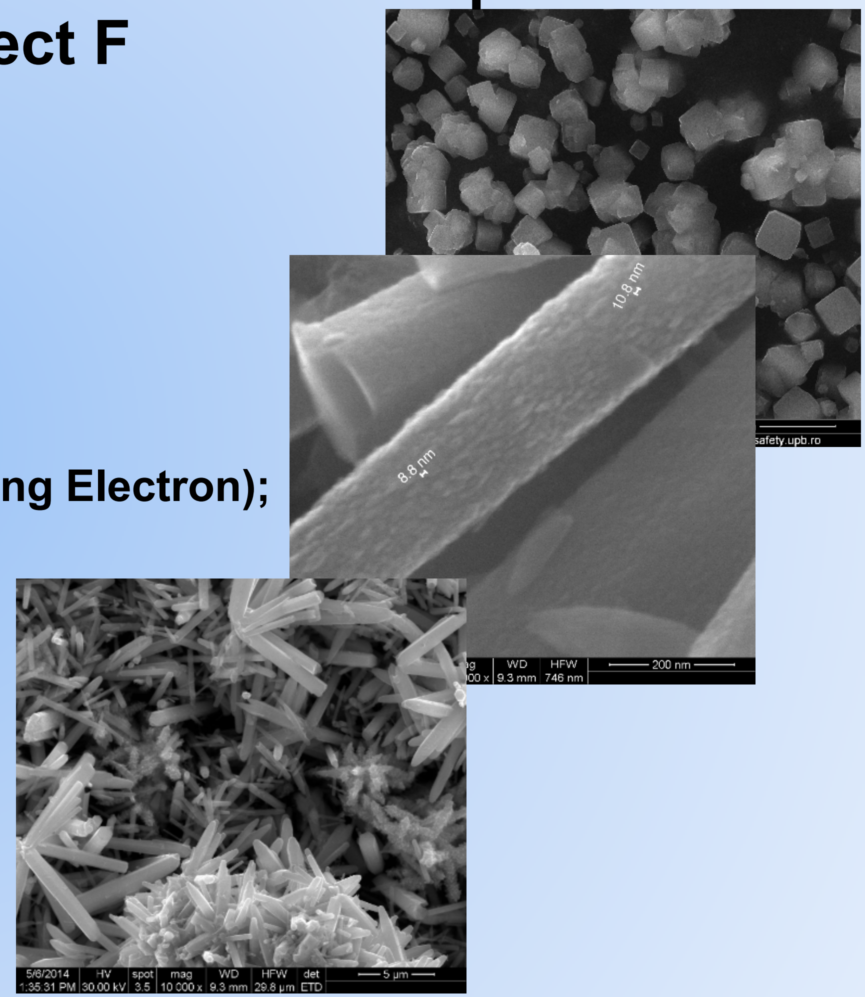


Research infrastructure
High Resolution Scanning Electron Microscope (HR-SEM) Inspect F

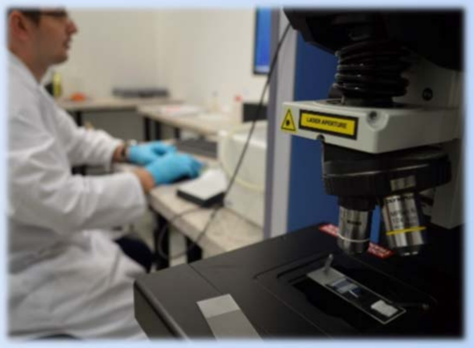
High Resolution SEM imaging;

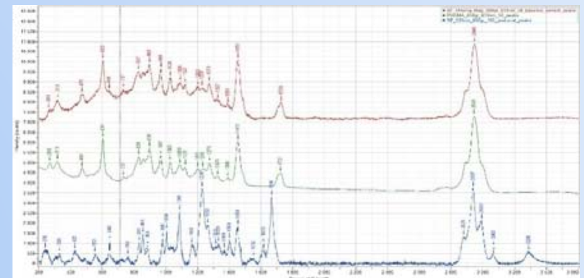
Directional BSED (Back Scattering Electron);

Point EDX and EDX mapping;

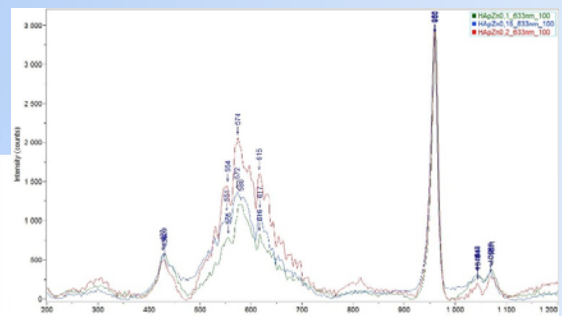


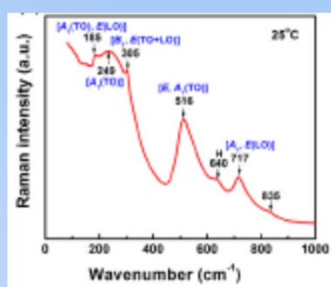
Research infrastructure
RAMAN Microcopy/Spectrometry Horiba

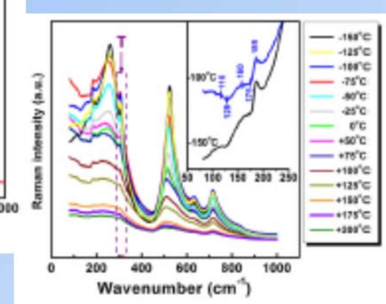




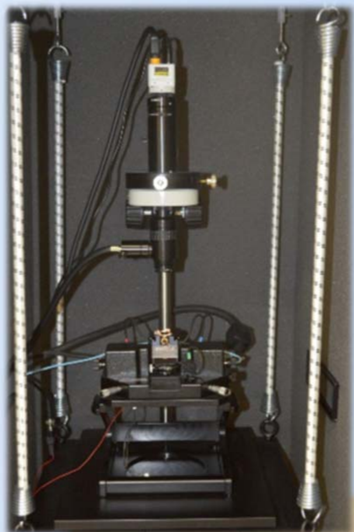
- Non-destructive spectral analyses;
- UV-VIS and NIR options;
- Accessory (MACRO-CH) for liquids;
- Thermostated cell (software controlled, - 196°C to 600°C);
- Single point analysis and multi-point analysis;
- Mapping possibilities.

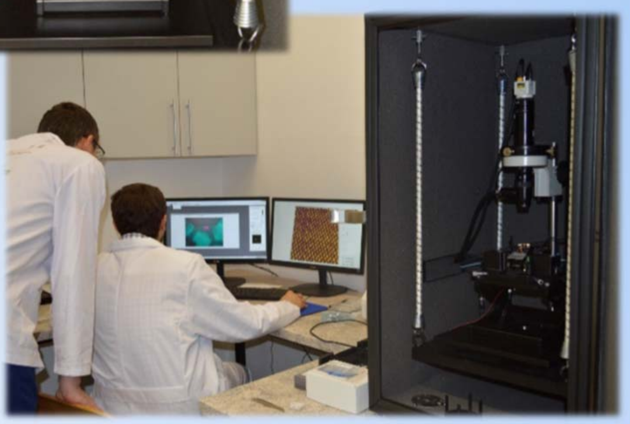






Research infrastructure
AFM Microscopy Keysight (Former Agilent)
Agilent 5500



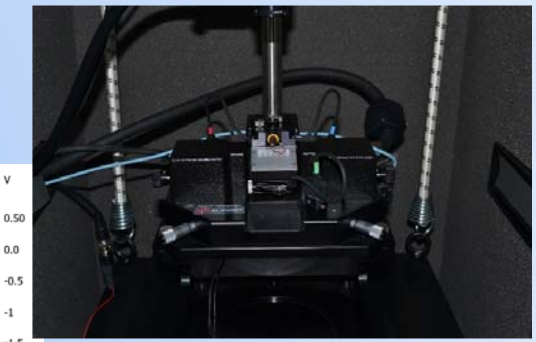


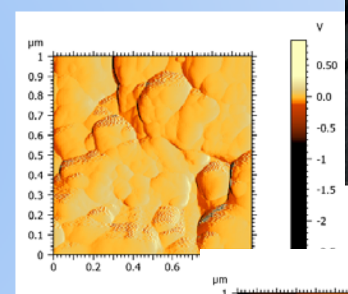
Surface analysis (topography) – tapping mode;

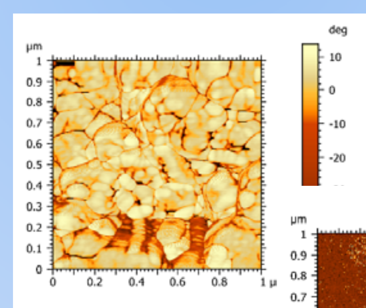
STM, MFM, KFM, PFM, ESEM, Environmental AFM;

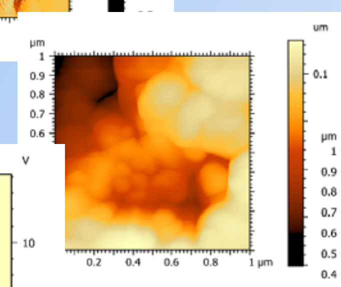
Heating and cooling experiments;

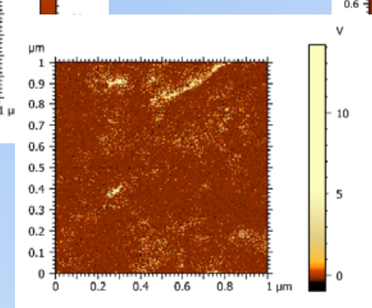
Liquid cell imaging.

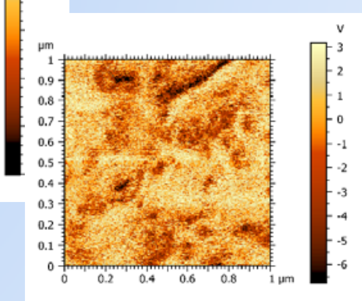










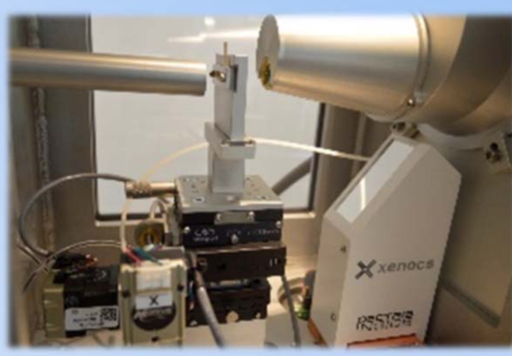


Research infrastructure
Small Angle X-Ray Scattering Diffractometer
XEUSS

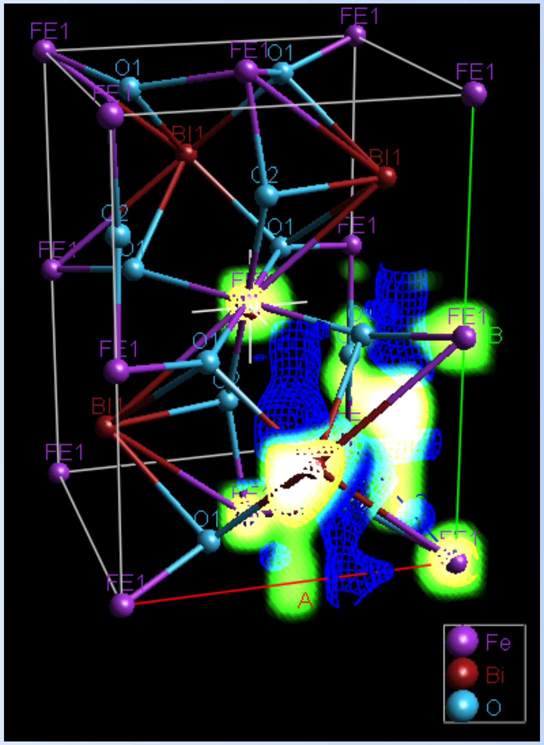
Suspension SAXS & WAXS (with solvent reference);

Powder SAXS & WAXS (oxides, nitrides, polymers etc.) ;

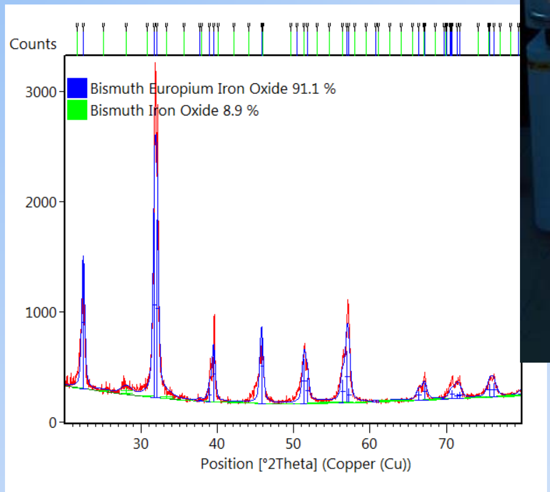
Thin film GISAXS.



Research infrastructure
X-Ray Diffractometer PANalytical EMPIREAN



- Semi quantitative phase analysis;
- High resolution thin film analysis;
- XRR (X-Ray reflectometry);
- Grazing Incidence;
- Pole figures;
- Epitaxy;
- Texture;
- Rietveld refinement.



Research infrastructure
Gas Chromatograph coupled with Mass Spectrometer Agilent
and
Liquid Chromatograph coupled with Hybrid Mass Spectrometer Agilent

Quantification and identifications of biological active agents, pollutants, pesticides, antibiotics, metabolites, dying agents, aromatic compounds, etc. from water, foods, or other matrices;

In both cases (GC or LC), due to the high performances of the hybrid mass spectrometers the quantification of the trace elements can be assured, including selected ion monitoring mode can be used.

Research infrastructure
Inductive Coupled Plasma Mass Spectrometer QQQ COUPLED with LASER ablation and Liquid Chromatography capability

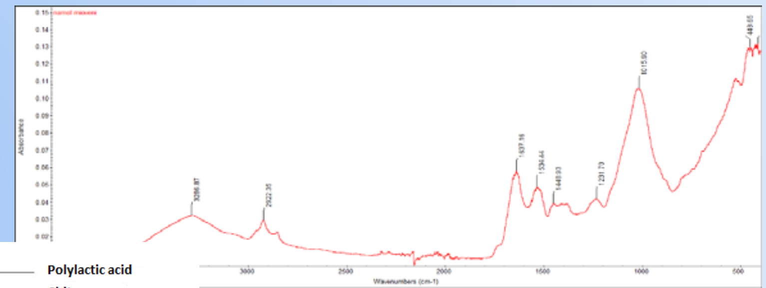
Quantitative and semi quantitative analysis for a wide range of samples including liquids and solids. For liquids, direct injection of the (mineralized) samples can be done but also direct semi-quantitative assessments can be done for insoluble samples (glasses, for instance) by laser ablation.

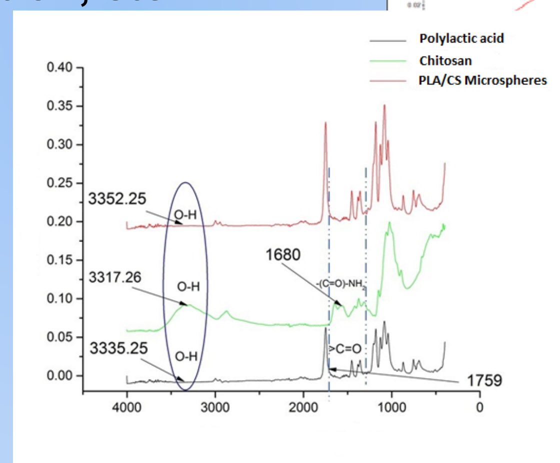
The quantification limit is low enough to the most of the elements and therefore the method can be used in many applications (medical, environmental, etc.), the coupling of the LC unit allowing also speciation capabilities.

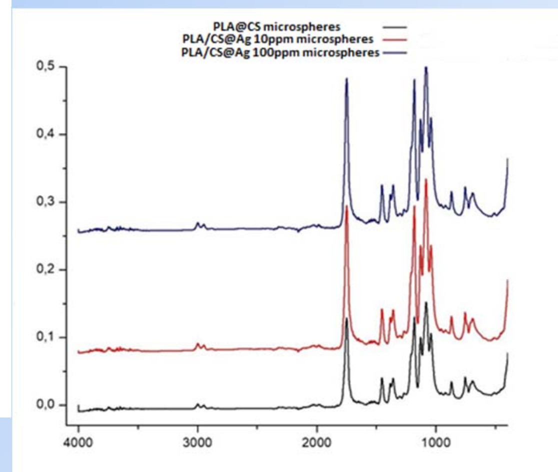
Research infrastructure
FTIR Spectrometry and microscopy Thermo Fisher

FT Raman module, NIR capabilities, room temperature and heated (300°C) ATR unit; Series capabilities to monitor thermal changes during heating;

FTIR microscopy for evaluation of the homogeneity of the samples; surface evaluation and degradation, etc.





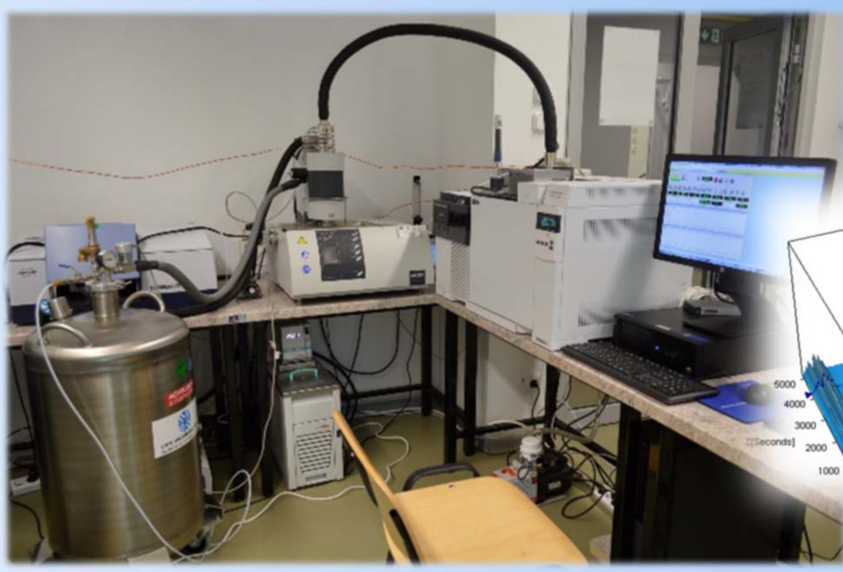


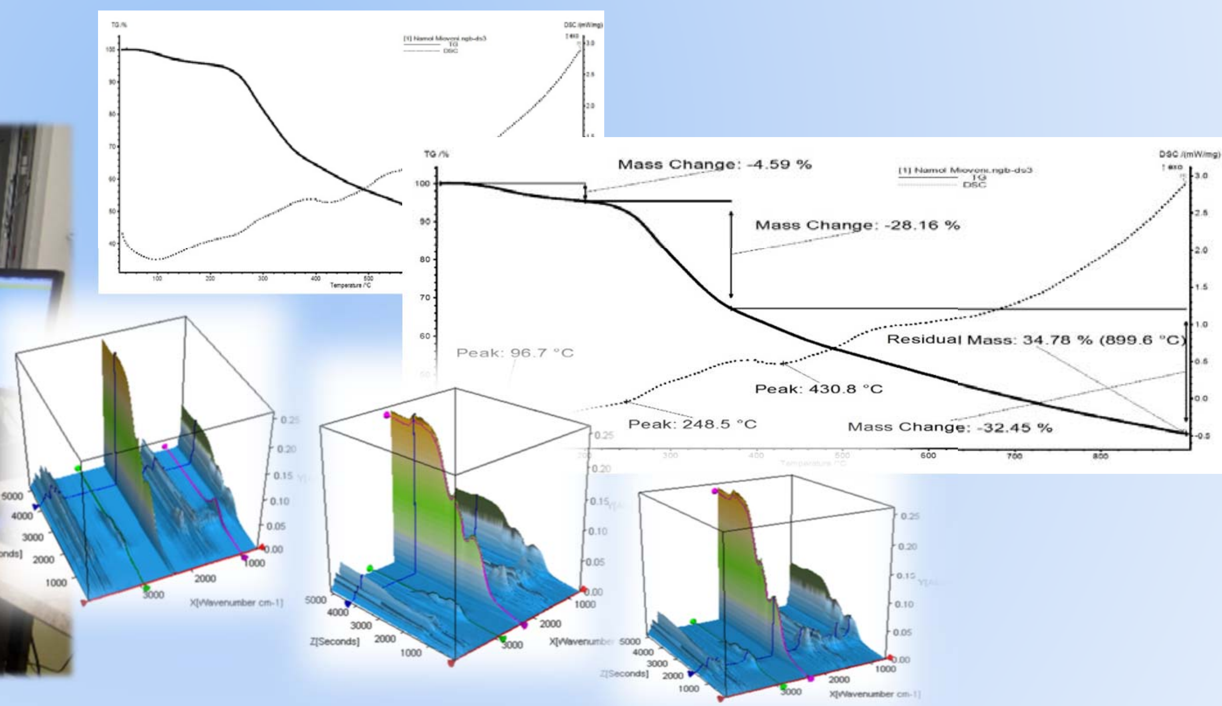
Research infrastructure
Simultaneous thermal analyzer coupled with GCMS and gaseous FTIR NETZSCH – Agilent - Bruker

Simultaneous TG-DSC analysis from L_{N2} to 1000°C;

GC-MS analysis of evolved gases;

FTIR analysis of evolved gases.



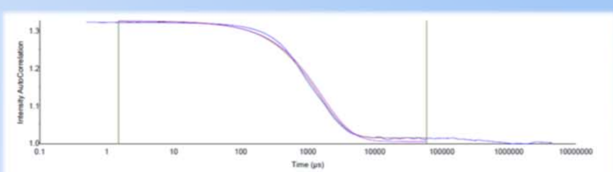


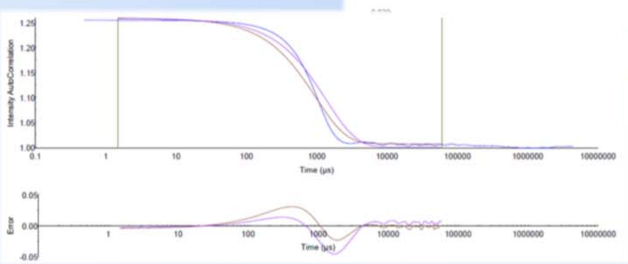
Research infrastructure
Zeta particle analyzer Beckman Coulter

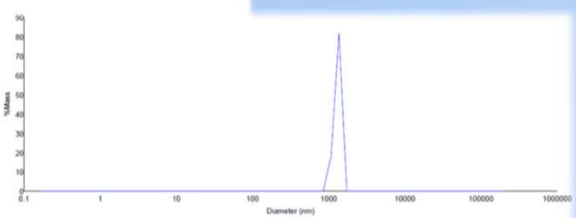
Fast measurements of nanoparticle electrophoretic mobilities (molecular charge and interfacial potential - zeta potential);

Non-destructive measurements of the diameter of nanoparticles and protein samples;

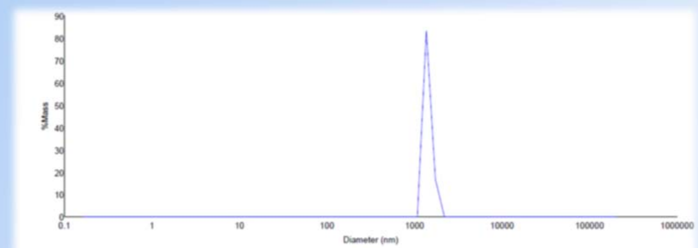
Measurements of traditionally very challenging protein samples (antibody formulations, bovine serum albumin, lysozyme).







	Radius (nm)	Diffusion Coefficient (cm²/s)	Mw-R (kDa)	%Pd	%Intensity	%Mass	Diameter (nm)	Pd (nm)	Pd Index
eak 1	657.2	3.7e-009	13185221.3	8.5	100.0	100.0	1314.5	55.70	0.01



	Radius (nm)	Diffusion Coefficient (cm²/s)	Mw-R (kDa)	%Pd	%Intensity	%Mass	Diameter (nm)	Pd (nm)	Pd Index
eak 1	714.1	3.4e-009	16008486.3	9.6	100.0	100.0	1428.1	68.41	0.01

Research infrastructure
Sample preparation laboratory

climatic chamber

working chamber with controlled atmosphere

freeze

furnace for thermal calcination treatments

equipment for the preparation of biological samples

ultramicrotome

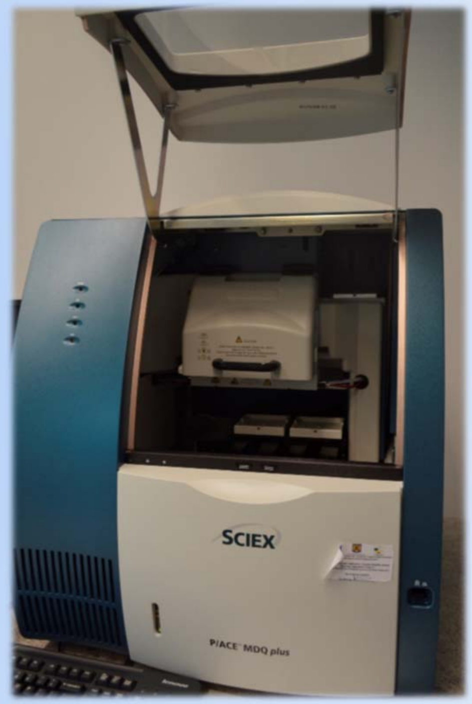
Automatic extractor for AND and ARN/ tissue homogenizer

furnace for thermal treatments with connection to 3 inert gases

Research infrastructure
"*in vitro*" cell culture laboratory

Flow Cytometer

Optical microscopy



Capillary Electrophoresis

ELISA

Current and Recent Research Projects

COST Action 029/18 (CA17118) *Identifying Biomarkers Through Translational Research for Prevention and Stratification of Colorectal Cancer (TRANSCOLONCAN)*

COST Action CA18132; Functional Glyconanomaterials for the Development of Diagnostics and Targeted Therapeutic Probes, 2018-2022

PN-III-P4-ID-PCCF-2016-0114; Selection and dissemination of antibiotic resistance genes from wastewater treatment plants into the aquatic environment and clinical reservoirs, 2018-2022 (Partner);

PN-III-P1-1.2-PCCDI-2017-0697; Intelligent therapies for non-communicable diseases based on controlled release of pharmacological compounds from encapsulated engineered cells and targeted bionanoparticles, 2018-2020

PN-III-P1-1.2-PCCDI-2017-0629; Innovative Bionanomaterials for treatment and diagnosis, 2018-2020

PN-III-P1-1.2-PCCDI-2017-0749; Bioactive nanostructures for innovative therapeutical strategies, 2018-2020

PN-III-P1-1.2-PCCDI-2017-0689; Lib2Life - Revitalizing libraries and cultural heritage through advanced technologies, 2018-2020

Grants JINR·RO 2018; Complementary characterization and SANS modelling of magnetic multi-layered suprastructures for targeted cancer therapy; Topic #04-4-1121 2015/2020, 2018;

Project JINR-RO 2018; Development and characterisation of magnetic nanostructures for targeted cancer therapy;

Project JINR-RO 2018; Mesoporous silica doped with magnetite nanoparticles for controlled release rate of biologically active substances, 2018;

PN-III-P2-2. 1-PED-2016-0952 “Biomimetic porous structures developed by 3D-printing for bone tissue engineering”, 2017-2018

PN-III-P2-2. 1-PTE-2016-0146; Novel nanostructured polymeric composite designed for pallet lining, connecting plate and other components for the railway industry, 2016-2018

Recent Research Articles

Radulescu M, Popescu S, Ficai D, Sonmez M, Oprea O, Spoiala A, et al. Advances in Drug Delivery Systems, from 0 to 3D Superstructures. Current drug targets. 2018;19:393-405.

Negut I, Grumezescu V, Ficai A, Grumezescu AM, Holban AM, Popescu RC, et al. MAPLE deposition of Nigella sativa functionalized Fe3O4 nanoparticles for antimicrobial coatings. Appl Surf Sci. 2018;455:513-21.

Teodor ED, Gatea F, Ficai A, Radu GL. Functionalized Magnetic Nanostructures for Anticancer Therapy. Current drug targets. 2018;19:239-47.

Sonmez M, Ficai D, Ficai A, Alexandrescu L, Georgescu M, Trusca R, et al. Applications of mesoporous silica in biosensing and controlled release of insulin. Int J Pharmaceut. 2018;549:179-200.

Mutlu EC, Ficai A, Ficai D, Yildirim AB, Yildirim M, Oktar FN, et al. Chitosan/poly(ethylene glycol)/hyaluronic acid biocompatible patches obtained by electrospraying. Biomed Mater. 2018;13.

Marin MM, Kaya MGA, Ficai A, Ghica MV, Popa L, Tutuianu R. Collagen Hydrolysate-Based Ingestible Bioproducts for the Treatment of Gastric Disorders. Rev Rom Mater. 2018;48:121-6.

Grumezescu V, Negut I, Grumezescu AM, Ficai A, Dorcioman G, Socol G, et al. MAPLE fabricated coatings based on magnetite nanoparticles embedded into biopolymeric spheres resistant to microbial colonization. Appl Surf Sci. 2018;448:230-6.

Ficai D, Grumezescu V, Fufa OM, Popescu RC, Holban AM, Ficai A, et al. Antibiofilm Coatings Based on PLGA and Nanostructured Cefepime-Functionalized Magnetite. Nanomaterials-Basel. 2018;8.

Ficai D, Ardelean IL, Holban AM, Ditu LM, Gudovan D, Sonmez M, et al. Manufacturing nanostructured chitosan-based 2D sheets with prolonged antimicrobial activity. Rom J Morphol Embryo. 2018;59:517-25.

Burdusel AC, Gherasim O, Grumezescu AM, Mogoanta L, Ficai A, Andronescu E. Biomedical Applications of Silver Nanoparticles: An Up-to-Date Overview. Nanomaterials-Basel. 2018;8.

Ardelean IL, Gudovan D, Ficai D, Ficai A, Andronescu E, Albu-Kaya MG, et al. Collagen/hydroxyapatite bone grafts manufactured by homogeneous/heterogeneous 3D printing. Mater Lett. 2018;231:179-82.

Concluding remarks

- The high performance R&D facilities existing in our laboratories is currently exploited in high quality researches generating new knowledge, PhD thesis, papers and patents;
- Most of the results are possible due to the collaboration with complementary research groups;
- We are looking to extend our collaboration with the existing partners and looking for new partners for ongoing projects;
- We are inviting all of you to be in contact with us and to visit our R&D infrastructure today, between 14:00 and 16:00!

Thank you!
Let’s collaborate!

On behalf of CNMN team,

Prof. habil. Anton FICAI
anton.ficai@upb.ro

www.foodsafety.upb.ro
www.micronanotech.ro