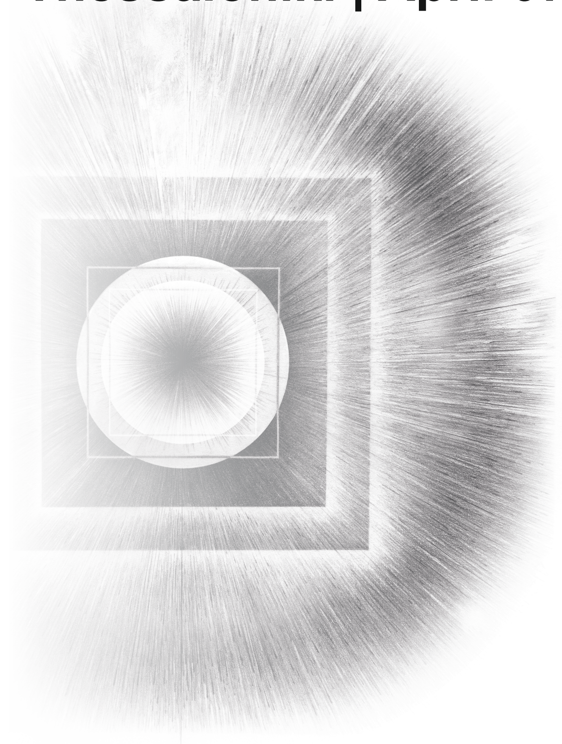
Training Workshop

Magnetic Nanohybrids for Cancer Therapy

MaNaCa

Magna Charta

Thessaloniki | April 07-09, 2022



Book of Abstracts

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CIRI-AUTh

MaNaCa Twinning | Horizon2020 project
Grant agreement No 857502 (2019-2023)

SCOPE

This is the 4th training workshop combined with a summer school within the framework of the MaNaCa Twinning|Horizon2020 project (2019-2023). This workshop will focus on structural and magnetic characterization of magnetic nanohybrids and their application for cancer therapy. Aiming to establish a tradition, this workshop will provide training in the basic principles of nanomagnetism and its biomedical applicability thorough a broad series of fundamental lectures, while offering the latest insights into up-to-date aspects of magnetically driven cancer therapies. To explain the general properties of magnetic materials and magnetic nanoparticles as well as magnetic scaffolds.

WORKSHOP PROGRAM

This workshop, held in English, is addressed to Greek and foreigner graduate and PhD students, as well as to post-doc and young researchers working on the field of magnetic nanomaterials exploring their biomedical applicability. Program consists of one morning and two early afternoon lecture sessions. Students may hang their posters, present them by flash presentations in specific sessions and discuss their results throughout the workshop. In the last day, Lab courses will take place where students will receive guidelines how to present their work, apply for proposal and how to follow a rigorous protocol for sample preparation and experimental/theoretical evaluation of magnetic particle hyperthermia.

ABOUT MaNaCa Project

The MaNaCa project (Magnetic Nanohybrids For Cancer Therapy) intends to develop the scientific and technological capacity as well as raising the research profile of the Institute for Physical Research of the National Academy of Sciences (IPR-NAS) in Armenia.

From a scientific standpoint, MaNaCa will focus on the structural and magnetic characterization of magnetic nanohybrids and their application for cancer therapy. The project's aim will be accomplished by networking IPR-NAS with two internationally-leading research organizations: the Aristotle University of Thessaloniki (AUTH) in Greece and the University of Duisburg – Essen (UDE) in Germany.

Throughout the project, the research partners will be supported for management ad dissemination by Intelligentsia Consultants Sàrl (INT), a consultancy company based in Luxembourg which has already collaborated on several occasions with the Widening partner.

During the project, which will have a total duration of three years, the partners will carry out a research and innovation strategy with these objectives:

1. Stimulating scientific excellence and innovation capacity of IPR-NAS regarding magnetic nanohybrids for cancer therapy.
2. Improve the career prospects of early stage researchers of IPR-NAS and the Twinning partners
3. Raise the research profile of IPR-NAS and the Twinning Partners In order to accomplish this task, the consortium partners will implement several actions through the project's work packages: (WP1) exchange of senior researchers; (WP2) exchange of early stage researchers; and (WP3) dissemination and outreach.

Project management (WP4) will be coordinated by IPR-NAS with the support of INT. In addition to staff exchanges, project's activities will include technical training, joint publications, joint participation to conferences, organization of summer schools, workshops and an international conference. MaNaCa operates under the grant agreement No 857502 (2019-2022) Projects-Twinning | Horizon 2020.

VENUE

The workshop takes place at CIRI-AUTH: Center of Interdisciplinary Research and Innovation of Aristotle University of Thessaloniki. The Center for Interdisciplinary Research and Innovation started its operation in 2014, signaling the AUTH's pursuit to redefine the role of research for the development of the country and to form new more effective interdisciplinary cooperation structures. Since 2015, and after three calls for proposals, 22 research teams have joined.

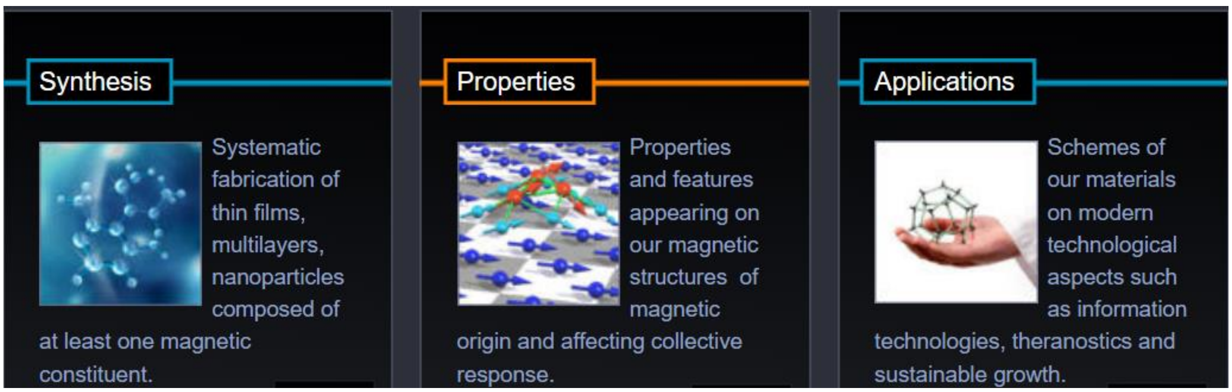
CIRI's main mission is to promote and develop interdisciplinarity in an open and collaborative environment of excellence, utilizing AUTH's research infrastructures at local, national and European level, expanding the University's synergy with society and contributing to economic and social development of the country.

Address	CIRI-AUTH ΑΠΘ, Balkan Center, Builidings A & B 10th km Thessalonikis-Thermis, PO BOX 8318 Post Code 57001

MagnaCharta GROUP

MagnaCharta group works on modern magnetic nanomaterials such as magnetic nanoparticles, multilayers and thin films. Our interests start from systematic synthesis and robust investigation of physical properties and conclude to technological applicability of nanomagnetism on diverse aspects such as information storage, biomedicine and sustainable growth.

For more information visit http://magnacharta.physics.auth.gr



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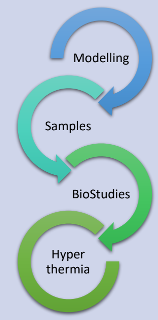
WORKSHOP PROGRAM

ORAL PRESENTATIONS

	Thursday 07.04	Friday 08.04	Saturday 09.04
09^{00}-11^{00}		**Properties** **H. Sarafidis, Greece** *Mossbauer Spectroscopy in Fe oxides* **A. Semisalova, Germany** *Ferromagnetic resonance study of magnetic nanoparticles for biomedical applications* **D. Karfaridis, Greece** *X-ray Photoelectron Spectroscopy: Principles and application on magnetic nanomaterials* **J. Kioseoglou, Greece** *Tailoring magnetic exchange bias and Curie temperature in Ni-based nanoclusters*	**Lab courses** 
	11^{00}-11^{30} ***Coffee Break***		12^{00}-13^{00} ***Lunch***
11^{30}-13^{30}	***Arrivals*** ***Registration opens at 13^{00}***	**Magnetic nanohybrids** **F. Pinakidou, Greece** *Probing the nanostructure of magnetic cementite nanoparticles using X-Ray Absorption Spectroscopic techniques* **N. Sisakyan, Armenia** *Iron-Cementite nanoparticles in carbon matrix: Synthesis, structure and magnetic properties* **N. Tetos, Germany** *Magnetically-actuated cell manipulation with "nanoflower"-shaped magnetic nanoparticles* **N. Maniotis, Greece** *Micromagnetic analysis tools for revaluation of magnetic nanoparticle physical properties in magnetic hyperthermia* **H. Gyulasaryan, Armenia** *Synthesis, structure, and magnetic properties of (Fe-Fe_3O_4)/C core-shell nanoparticles*	***Excursion to Lake Kerkini*** ***13^{00}-21^{00}***
	13^{30}-15^{00} ***Lunch Break***		
15^{00}-17^{00}	**Materials** **M. Angelakeris , Greece** *Workshop Opening* **U. Wiedwald, Germany** *From physical design to medical applications of magnetic nanoparticles for cancer therapy* **S. Mourdikoudis, Czech Republic** *Colloidal chemical routes for the synthesis of magnetic nanostructures destined for biomedical applications. What to choose?* **A. Elsukova, Sweden** *More than an image: advanced electron microscopy methods for material characterization* ***Poster flash presentations (5 min/Poster)***	**Perspectives** **K. Giannousi, Greece** *Bio-applications of metal-based nanoparticles* **M. Efremova, Germany** *A new approach to magnetic sensing and actuation of mammalian cells based on genetically encoded encapsulin protein* **K. Spyridopoulou, Greece** *Preclinical study design considerations in cancer nanomedicine* **A. Assimopoulou, Greece** *Magnetic nanostructures as drug delivery systems for natural products* **M. Angelakeris, Greece** *Closing Remarks*	*Lunches and coffee breaks take place at Poster Session Room* *In parallel, students may hang their posters, present and discuss their results*
	17^{00}-17^{30} ***Coffee Break***		
17^{30}	***Visit at Noesis, Workshop Dinner***	***MaNaCa Project Meeting***	

POSTER PRESENTATIONS (Onsite & 5 min flash presentations)

P01	**Synthesis and characterization of a novel multifunctional magnetic bioceramic nanocomposites** *K. Kazeli, Greece*
P02	**Single-step solid state-pyrolysis of carbon-Fe_3C submicron spheres** *E. Papadopoulou, Germany*
P03	**Alternative protocols to optimize magnetic hyperthermia efficiency** *A. R. Tsiapla, Greece*
P04	**Synthesis of Fe-based magnetic nanoparticles by pyrolysis method** *G. Chilingaryan and V. Avagyan, Armenia*
P05	**Tuning synthesis of Fe_3O_4 nanoparticles: the role of surface charge on Cr(VI) uptake** *K. Kalaitzidou, P. Asimakidou, Greece*
P06	***Structural properties of Fe/Fe3C cementite nanoparticles using spectroscopic techniques*** *K. Kontou, Greece (web)*
P07	**Investigation of the heating properties of Fe_3O_4 magnetite nanoparticles dispersed in agarose** *I. N. Sahin, Germany*
P08	**4D Printing: Synthesis, characterization and mechanical evaluation of ferromagnetic hybrid scaffolds for magnetic hyperthermia** *A. Alexandridis, Germany*

LAB COURSES-HANDS ON (Saturday 09/04/2022, 09^{00}-12^{00})

Samples	**Magnetic Nanoparticles**. Synthetic routes using the aqueous chemical coprecipitation method, highlighted as a cost-effective and fast process, easily expandable on an industrial level.
	3D Printed Scaffolds. Elaboration of 3D printing technology to fabricate magnetic scaffolds using a Fused Deposition Modeling printer, either with a commercial magnetic filament or with a handmade polymer bonded magnetic filament.
	3D printed Magnetic Devices. Design and manufacture of devices that can produce high spatial gradients of the magnetic flux density (120 T/m) strong mechanical forces and torques that can be applied on cells when incubated with MNPs.
BioStudies	This Lab is focusing to provide briefly state-of-the-art of nanomaterial application for cancer therapy, on a theoretical level, and a real-time demonstration on experimental design and synthesis routes of magnetic materials focused on biomedical applications, utilizing the Magna Charta Lab equipment, and provided devices.
Hyperthermia	After a brief introduction on the magnetic hyperthermia origin following a short presentation on the Magna Charta lab devices and equipment, the experimental process will be analyzed and presented in a real-time demonstration.
Modelling	In the first part of this course, we will find out how we can easily set up a hysteresis loop in OOMMF software. In the second part, we will present how to build numerical models with finite element method and more specifically with the COMSOL software for the description of the phenomena that take place in a magnetic hyperthermia experiment.

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ABSTRACTS

Oral Presentations
Thursday 07/04/2022
Afternoon Session

From Physical Design to Medical Applications of Magnetic Nanoparticles for Cancer Therapy

Ulf Wiedwald[1*]

[1]Faculty of Physics and Center for Nanointegration Duisburg-Essen, University of Duisburg-Essen, Germany
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The application of magnetic nanoparticles (MNPs) in biomedicine and theranostics is one of the most dynamic fields of nanoparticles research. In this work, examples for the use of multifunctional hybrid MNPs are presented. We designed, synthesized and tested various MNPs like ferrites [1-3], core-shell architectures [4], and magnetite-gold (Fe_3O_4-Au) hybrids [5-7] for optimized performance, e.g. in magnetic resonance imaging (MRI) and magnetic particle hyperthermia (MPH) for the localized treatment of cancer. For MPH, the specific loss power (SLP) should be optimized for minimized side effects in patients. This is usually achieved by the choice of diameters [6], particle shape [7] or materials [4]. Another approach is the optimization of dipolar interactions between MNPs for maximized heating capabilities [3,8].
By *in vitro* and *in vivo* investigations, we have shown that controlled MPH provided by cobalt ferrite nanoparticles has different effects on tumor cells depending on temperature [9]. The cell death can be triggered by MPH. Interestingly, heating at 42-43°C (mild MPH) varies in different cell lines. *In vivo* data further shows that mild MPH is not effective for metastatic 4T1 tumor therapy, while it is efficient for curing non-metastatic CT26-bearing mice. MPH at 46-48°C and 58-60°C increases the long-term survival of 4T1-bearing mice providing primary tumor clearance and metastasis inhibition. We further studied the toxicity of cobalt ferrite MNPs [10]. Although such MNPs are often excluded for biomedical applications due to their (assumed) toxicity, *in vivo* studies reveal cobalt ferrite MNPs do not have toxic effects at concentrations close to those used previously for efficient MHT [10].
The results were obtained in collaboration with colleagues from the Aristotle University of Thessaloniki, Greece, the National University of Science and Technology MISIS, Moscow, Russian Federation, and the University of Duisburg-Essen, Germany.

[1] S. Liébana Viñas et al., J. Magn. Magn. Mater. 415, 20 (2016).
[2] K. Simeonidis et al., RSC Advances 6, 53107 (2016).
[3] E. Myrovali et al., Sci. Rep. 6, 37934 (2016).
[4] S. Liébana-Viñas et al., RSC Advances 6, 72918 (2016).
[5] M. V. Efremova et al., Sci. Rep. 8, 11295 (2018).
[6] M. V. Efremova et al., Beilstein J. Nanotechnol. 9, 2684 (2018).
[7] Y. Nalench et al., Journal of Materials Chemistry B 8, 3886 (2020).
[8] E. Myrovali et al., ACS Applied Materials & Interfaces 13, 21602-21612 (2021).
[9] A. S. Garanina et al., Nanomedicine: Nanotechnol., Biol. and Med. 25, 102171 (2020).
[10] A. S. Garanina et al., Nanomaterials 12, 38 (2022).

Colloidal chemical routes for the synthesis of magnetic nanostructures destined for biomedical applications. What to choose?

Stefanos Mourdikoudis[1*]

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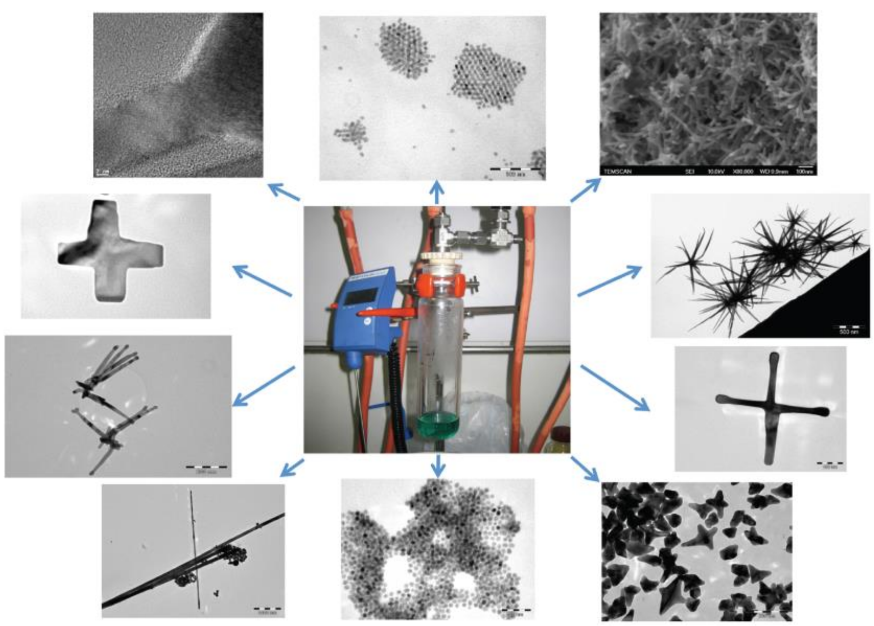
** corresponding author: mourdikt@vscht.cz*

The synthesis of magnetic nanoparticles is a research field which showed a tremendous progress during the last decades. Applications in environment, magnetic recording and biology/biomedicine are strongly responsible for such exponential increase in the interest to fabricate high quality magnetic nanoparticles. However, concerns regarding the environmental hazards, the cost, and the degree of biocompability for the resulting nanoparticles have been raised. Top-down production methods are often able to produce large amounts of nanoparticles which, nevertheless, may contain an alarming degree of structural defects, in certain cases. Colloidal chemical bottom-up routes are beneficial approaches for the acquisition of high-quality, cost-effective, 'green' and sufficiently biocompatible magnetic nanostructures which can be of use for applications such as magnetic hyperthermia and magnetic resonance imaging. We present different branches of the above-mentioned chemical routes in an attempt to understand the criteria behind the choice of the each time most suitable synthetic method.



Magnetic nanostructures with diverse morphologies prepared by different colloidal chemical pathways

More than an image: advanced transmission electron microscopy methods for material characterization

Anna Elsukova[1*]

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Transmission electron microscopy (TEM) occupies a special place in material characterization. Electron wavelength, far shorter than that of light, allows imaging of extremely small structure down to atomic resolution. In addition to that, one can access the information about local elemental composition and chemical state with the help of energy dispersive X-ray (EDX) and electron energy-loss (EELS) spectroscopies. These techniques already became a staple in material characterization. The latest developments in TEM probe even deeper into the properties of organic and inorganic matter. In my talk I will give a general introduction into the principles of "classic" TEM methods and present some of the advanced ones: vibrational EELS, electron holography, imaging with segmented detectors and in-situ TEM microscopy in gases and liquids.

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ABSTRACTS

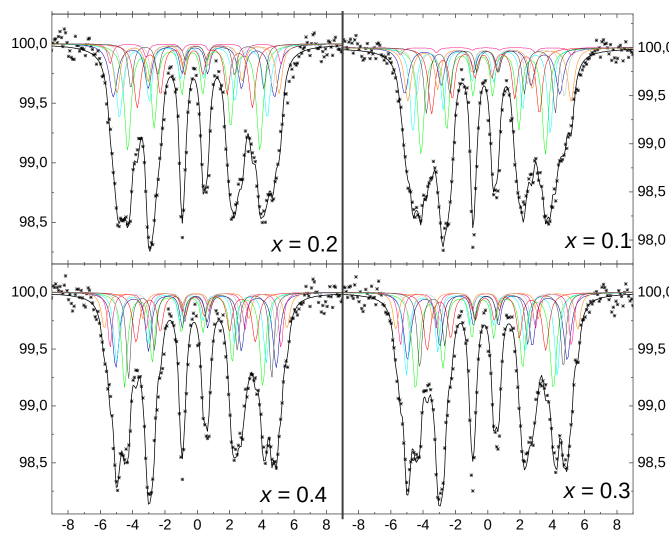
Oral Presentations
Friday 08/04/2022
Morning Session

Mössbauer Spectroscopy in Fe oxides

C. Sarafidis[1,2*]

[1]School of Physics, Aristotle University of Thessaloniki, 54124, Greece
[2]MagnaCharta, CIRI-AUTH, Thessaloniki, 57001 Greece
** corresponding author: hsara@auth.gr*

Nuclear gamma-ray resonance or Mössbauer Spectroscopy as it is widely known has been proven a valuable tool in materials science. It focuses on the effect of the chemical environment of a solid in the hyperfine structure of the energy levels within the atomic nuclei of the solid. Although it is an experimental technique with enormous energy resolution its implementation has a rather good benefit over cost benchmark and while it may not provide by itself a complete answer about magnetic, chemical, and structural properties it often provides unique information. Mössbauer Spectroscopy detects a specific nucleus depending on the experimental setup and one of the most suitable is ^{57}Fe, an isotope with rather large abundance in natural Fe, 2.71%. The existence of Fe in a plentiful of magnetic materials with different oxidation and spin states and its crucial role in a wide variety of magnetic properties make nuclear gamma-ray resonance important in studies of magnetic materials, especially when combined with the sensitivity of the relevant spectra on magnetic properties. The main scope of the presentation is to demonstrate when a Mössbauer Spectrum would be useful and what kind of information may be retrieved. After a brief introduction in Mössbauer Spectroscopy, case studies and applications in various magnetic materials with emphasis in Fe oxides will be presented.



Ferromagnetic resonance study of magnetic nanoparticles for biomedical applications

Anna S. Semisalova

AG Farle, Faculty of Physics & CENIDE, University of Duisburg-Essen
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Ferromagnetic resonance (FMR) is a powerful spectroscopy method for characterization of magnetic properties of material such as magnetic anisotropy, relaxation rate (magnetic damping), g-factor [1]. When applied to an ensemble of nanoparticles, FMR allows to investigate their distribution and orientation. The phenomenon of FMR represents an absorption of microwave radiation due to precession of magnetization in an external DC magnetic field, it is usually detected in GHz range by sweeping the DC magnetic field/frequency to reach the resonance conditions. In this tutorial talk, the application of FMR spectroscopy to study the magnetic anisotropy [2], superparamagnetic behavior of nanoparticles [3], dipole-dipole interactions and their role in chain formation and hyperthermia efficiency [4] will be discussed. In addition, resonant spin-excitation offers an alternative approach to hyperthermia via the magnetothermal heat generation using microwave excitation [5].

1. Michael Farle, *Rep. Prog. Phys.* 61, 755 (1998)
2. Bo Tian et al., *ACS Sens.* 6, 1093 (2018)
3. Carolin Antoniak et al., *Mod. Phys. Lett.* B 21, 1111 (2007)
4. Eirini Myrovali et al., *Sci. Rep.* 6, 37934 (2016)
5. Jae-Hyeok Lee et al., *Sci. Rep.* 11, 4969 (2021)

X-ray Photoelectron Spectroscopy: Principles and Application on Magnetic Nanomaterials

Dimitrios Karfaridis[1] and George Vourlias[1]

[1]AMDe lab, Department of Physics, Aristotle University of Thessaloniki, 54124, Greece
** corresponding author: dkarfari@physics.auth.gr*

X-ray photoelectron spectroscopy (XPS) is an analytical method for material identification, structural and chemical state analysis. The analysis is performed when the sample's surface is irradiated with soft X-rays to ionize atoms and release photoelectrons from the nucleus. The kinetic energy of the escaped photoelectrons is limited by the depth that can be obtained, giving the technique a high surface sensitivity by limiting up the sampling depth to a few nanometers (~ 5 nm). Photoelectrons are collected and analyzed by the instrument giving spectra of the emitted intensity as a function of the kinetic or beam energy of the electrons. Since each element has a unique set of binding energies, this technique can be used to determine the quality of elements. Also, the peak regions in the nominal bond energy can quantify the concentration of the respective components. Small changes in the binding energy (chemical shifts) provide vital data on the chemical state of the sample, enabling chemical analysis of the surface (short-range) without destroying the sample. The XPS can be used in various materials, revealing some substantial results. The conclusions from the XPS analysis can be compared with the physical properties of the mater resolving their origin, associating the effects with the chemical and physical states of the structures. Here, XPS is compared with the magnetic properties of the matter. With the high sensitivity, XPS has the capability to detect magnetic nanomaterials and magnetic heterostructures even in low concentrations and in ultra-thin geometries (films). Magnetic materials in different chemical states act differently depending on the free spins and the magnetic moments that the atomic states release on an atomic grid. Therefore, it is perceived that XPS could serve as a useful "tool" for a deeper comprehension of the origin of the magnetic properties in nanoscale and the potential induced from the low dimensions phenomena in magnetism.

Tailoring magnetic exchange bias and Curie temperature in Ni-based nanoclusters

M. Bohra[1,2], S. Giaremis[3], V. Singh[1], S. Steinhauer[1], J. Kioseoglou[3*], P. Grammatikopoulos[1]

[1]Nanoparticles by Design Unit, Okinawa Institute of Science and Technology Graduate University, 1919-1 Tancha Onna-Son, Okinawa 904-0495, Japan
[2]Mahindra University École Centrale School of Engineering (MEC), Survey Number 62/1A, Bahadurpally Jeedimetla, Hyderabad 500043, Telangana, India
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** corresponding author: sifisl@auth.gr*

Ni-based nanoparticles have attracted scientific interest lately due to their interesting magnetic properties. Structural and compositional modifications are demonstrated to be able to act as means for the tuning of their critical temperature. Moreover, the exchange bias effect is observed in such systems, but its origins are not yet fully uncovered. The potential technological impact is discussed, as exchange bias can also be used for eliminating the superparamagnetic limit, which hinders the magnetic properties of nanoparticles.

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ABSTRACTS

Oral Presentations
Friday 08/04/2022
Midday Session

Probing the nanostructure of magnetic cementite nanoparticles using X-Ray Absorption Spectroscopic techniques

Fani Pinakidou[1*], Maria Katsikini[1], Mavroeidis Angelakeris[1], Eleni C. Paloura[1] and Aram Manukyan[2]

[1]Aristotle University of Thessaloniki, School of Physics, Section of Solid State Physics, 54124, Thessaloniki, Greece

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The nanostructure of carbon-encapsulated iron-cementite (Fe-Fe_3C) nanoparticles (NPs) is addressed using X-Ray Absorption Near Edge (XANES) and X-Ray Absorption Fine Structure (EXAFS) spectroscopies. The nanoparticles were synthesized by single-step solid-state pyrolysis of iron phthalocyanine at temperatures (T_{pyr}) ranging from 800 to 1000°C. It is revealed that, irrespective of the T_{pyr}, none of the studied NPs displayed the characteristic Fe-*K*-XANES profile either of bulk Fe or Fe_3C; however, the experimental spectra can be accounted for as a linear combination (LC) of reference samples. Indeed, it was possible to reproduce simultaneously both the edge position and the white line (shape and position) of the XANES spectra of the studied NPs, using a LC of the spectra of synthesized Fe_3C NPs (d = 21,3 nm) and of an Fe-foil; this successful reproduction is a strong indication of a core/shell scheme. The LC fitting analysis results illustrate that when the NPs are obtained upon pyrolysis in the temperature range 800-870 °C, the dominant phase is Fe_3C, i.e. the Fe_3C:Fe ratio lies between 93.2 to 86.3 wt% (±7). On the other hand, when the synthesis of the NPs is achieved at higher pyrolysis temperatures, 900 to 1000 °C, the contribution of α-Fe becomes also important, i.e. the Fe_3C:Fe ratio is now found equal to 59.8-45.4 wt%. The argument that the local environment of the iron atoms in the (Fe-Fe_3C)/C NPs is a combination of those in α-iron and in Fe_3C is further supported by the Fe-*K*-EXAFS analysis results. Previous studies on similar (Fe-Fe_3C)/C nanoparticles supported that the most probable architecture is that of a core/shell, where the core is comprised of iron while cementite is the shell (Fe@Fe_3C) [1]. Thus, assuming that the studied NPs also adopt a core/shell structure, it is possible to calculate the thickness of the Fe_3C shell by merely using the relative volume fractions of the individual Fe-phases, as determined from the EXAFS analysis results. It is demonstrated that in the core/shell model of the Fe@Fe_3C NPs, increasing the pyrolysis temperature by 200 °C yields almost a two-fold decrease in the shell thickness (from 6.32 nm (±0.32) to 3.71 nm (±0.18)). Consequently, a proper control of the synthesis conditions that in turn govern the characteristics of the Fe@Fe_3C core/shell structure may benefit towards the production of highly efficient NPs with improved magnetic characteristics required for implementation in Magnetic Hyperthermia applications.

[1] L. Avakyan, A. Manukyan, A. Bogdan, H. Gyulasaryan, J. Coutinho, E. Paramonova, G. Sukharina, V. Srabionyan, E. Sharoyan, L. Bugaev, Journal of Nanoparticle Research, 22 (2020) 30

Iron-Cementite Nanoparticles in Carbon Matrix: Synthesis, Structure and Magnetic Properties

Narek Sisakyan[1]*, Harutyun Gyulasaryan[1], Elisavet Papadopoulou[2], Nicolaos Tetos[2], Gayane Chilingaryan[1], Eirini Myrovali[3], Antonis Makridis[3], Makis Angelakeris[3], Michael Farle[2], Marina Spasova[2], Aram Manukyan[1]

[1]Institute for Physical Research of National Academy of Sciences, Armenia
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[3]Physics Department, Aristotle University of Thessaloniki, Greece
** corresponding author: sisakyan@gmail.com*

Magnetic nanoparticles (MNPs) are promising for a variety of biomedical applications, including magnetic hyperthermia, magnetic resonance imaging (MRI) data, tissue engineering, and the delivery of drugs. A particularly important topic is the study of bi-magnetic nanoparticles with core-shell architecture, where both the core and the shell exhibit magnetic properties. Such architecture causes a magnetic interaction with core and shell allowing to tune the magnetic characteristics, in particular, to increase the magnetic anisotropy, which will lead to an increase of coercive field H_c.

In this work, iron-cementite (Fe-Fe_3C) nanoparticles in a carbon matrix were synthesized by a solid-phase pyrolysis of iron phthalocyanine ($FeC_{32}H_{16}N_8$) at 850 °C and 5 min. The structure, morphology and sizes of the fabricated composite has been investigated using X-ray diffraction spectrometer, high resolution transmission and scanning transmission electron microscope (HRTEM, STEM). The magnetic properties at various temperatures were studied using physical property measurement system (PPMS). Although Fe_3C decomposes to iron (Fe) and carbon (C) at 750°C, the temperature dependence of magnetization after three cycle shows incomplete decomposition of Fe_3C and stabilization up to 1000 K (see figure).

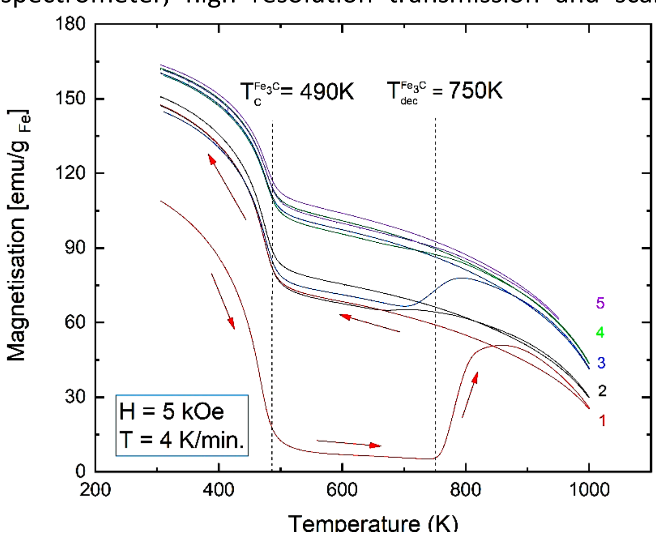

Figure 1. Five cycles of temperature dependence of magnetization at 300-1000 K.

This work was supported by European Union's Horizon 2020 research and innovation programme under grant agreement No 857502 (MaNaCa).

Magnetically-Actuated Cell Manipulation with "Nanoflower"-Shaped Magnetic Nanoparticles

Nikolaos Tetos[1*], Iuliia P. Novoselova[2], Cornelia Monzel[2] and Ulf Wiedwald[1]

[1]Faculty of Physics, University of Duisburg-Essen, 47057 Duisburg, Germany
[2]Experimental Medical Physics, Heinrich-Heine University Düsseldorf, 40225 Düsseldorf, Germany
** corresponding author: nikolaos.tetos@uni-due.de*

Owing to their magnetic properties and biocompatibility, iron-oxide nanoparticles are frequently considered for a variety of biomedical applications such as magnetic resonance imaging (MRI), drug delivery and magnetic particle hyperthermia (MPH) [1,2]. Recent studies have proposed magneto-mechanical force-induced cell apoptosis by magnetic nanoparticles (MNPs) in low-frequency alternating magnetic fields as a promising and simple tool for cancer treatment [3].
In this work we investigate the cytotoxic effect of dextran-coated Fe_3O_4-"nanoflower"-shaped MNPs (micromod Partikeltechnologie GmbH, Rostock, Germany) (c = 1 mg/mL) on HeLa wild type cells in a unidirectional low-frequency (f = 1 – 20 Hz) alternating magnetic field (B = 80 mT) for 30 and 60 min. For this, we use a novel configuration of a magnetic setup for simultaneous or sequential magneto-mechanical and MPH treatment. Cellular uptake was quantified by means of vibrating sample magnetometry (VSM) with an average number of 750 NPs/cell, which is comparable to previous studies [4]. The apoptotic effect of magneto-actuated iron-oxide MNPs with hydrodynamic diameter of 70 nm was investigated qualitatively and quantitatively via optical microscopy and fluorescence spectroscopy. Interestingly, HeLa cells incubated with MNPs showed no apoptotic behavior or any morphological changes after magneto-mechanical actuation. Further, control measurements of cells in absence of MNPs revealed that cell viability was not affected even for the 60 min magnetic excitation. Additionally, the superparamagnetic MNPs have a saturation magnetization of 69 Am2/kg and exhibit good magnetic properties for MPH [5,6]. So, we aim for the enhancement of cell apoptosis by a chain arrangement of MNPs through a static magnetic field [2] and a subsequent MPH treatment feasible in our setup.

[1] Q. A. Pankhurst et al., J. Phys. D: Appl. Phys. 36, R167-R181 (2003).
[2] E. Myrovali et al., Sci. Rep. 6, 37934 (2016).
[3] C. Naud et al., Nanoscale Adv. 2, 3632-3655 (2020).
[4] B. D. Chithrani and W. C. W. Chan, Nano Lett. 7, 1542-1550 (2007).
[5] P. Bender et al., J. Phys. Chem. C 122, 3068–3077 (2018)
[6] I. P. Novoselova et al., Nanomaterials 11, 2267 (2021)

Micromagnetic analysis tools for revaluation of magnetic nanoparticle physical properties in magnetic hyperthermia

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Magnetic nanoparticle hyperthermia (MNH) is a novel, minimally invasive, therapeutic modality, which is used as a cancer treatment. The key measure used for characterizing the heating efficiency of magnetic nanoparticles (MNPs) in MNH is the specific loss power (SLP), which may be derived from the magnetic hysteresis loop area. In this work, the issue on whether dynamic magnetic properties of a poly-dispersed ferrofluid, modelled using micromagnetic simulations, can be extrapolated to analyze SLP values acquired at high frequencies of excitation fields is addressed. Micromagnetic finite difference simulations were performed by using OOMMF software package to obtain the dynamic hysteresis loops under a 24 kA/m field amplitude and for various frequencies (50-765 kHz). In OOMMF, finite difference method was used to find the solution of nonlinear Landau-Lifshitz Gilbert (LLG) equation which describes the precessional motion of nanoparticles magnetization when applying an effective magnetic field. To create a system of randomly oriented nanoparticles having a certain volume fraction, 0.04%, that corresponds to a ferrofluid concentration of 2 mg/mL, we start with a perfect simple cubic lattice with a large lattice spacing so that the particle-particle distance is large enough to neglect dipolar interactions (non-interacting MNPs). System under study is a set of spherical magnetite nanoparticles of 30 nm with a lognormal size distribution. When the frequency of the applied magnetic field, f, was below ~300 kHz, SLP(f) followed an exponential increase trend. At this regime, the hysteresis area increases with f due to the increase of the phase delay in the magnetization response. After a critical f, MNPs magnetization reaches the maximum phase delay (maximum relaxation time of spins) and so any increase in f leaves unaffected the hysteresis area. To validate our approach, we employed a coupled electromagnetic-thermal model, based on COMSOL Multiphysics simulations that provides an accurate estimation of magnetic field and temperature distribution within the ferrofluid. The time-dependent temperature curves are obtained after 30 min. of MPH treatment for the same magnetic field amplitude used in OOMMF simulations (24 kA/m) and for two representative f values. One at low (375 kHz) and one at high (765 kHz) frequency regime. In each case, the MNPs volumetric power dissipation, imported in heat transfer model to find the temperature curves, is taken equal to the corresponding SLP(f) value. The numerical MPH curves were found in excellent agreement with the experimental data that observed under the same conditions. The research project was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the "2nd Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers" (Project Number: 00046 MagnoSorb).

Synthesis, Structure and Magnetic Properties of $(Fe\text{-}Fe_3O_4)/C$ Core-Shell Nanoparticles

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Iron based magnetic nanoparticles are valuable in biomedical applications due to their low toxicity and high magnetization at room temperature. Nanoparticles based on Fe and Fe_3O_4 with a core-shell architecture are efficient mediators for heat transfer in an alternating magnetic field. For the application of hyperthermia, surface modification of nanoparticles using biocompatible metals is important, since nanoparticles must be non-toxic in nature. To use nanoparticles for advanced biomedical applications, they need to be further modified with functional ligands.
In this work, carbon coated iron-magnetite ($Fe\text{-}Fe_3O_4$) nanoparticles were synthesized by a solid-phase pyrolysis of iron phthalocyanine ($FeC_{32}H_{16}N_8$) followed by annealing in an oxygen media at 250°C and 1h to form a (Fe_3O_4) shell on fcc Fe nanoparticles. The quantitative composition of the "core-shell" architecture was controlled by changing the concentration of oxygen. The structure, chemical composition and morphology of these materials was investigated using HRTEM, STEM, X-ray diffraction (XRD) and Raman spectroscopy. The magnetic properties at various temperatures were studied by SQUID magnetometry. The HRTEM and HAADF-STEM images with corresponding elemental data mapping are shown in Fig.1.

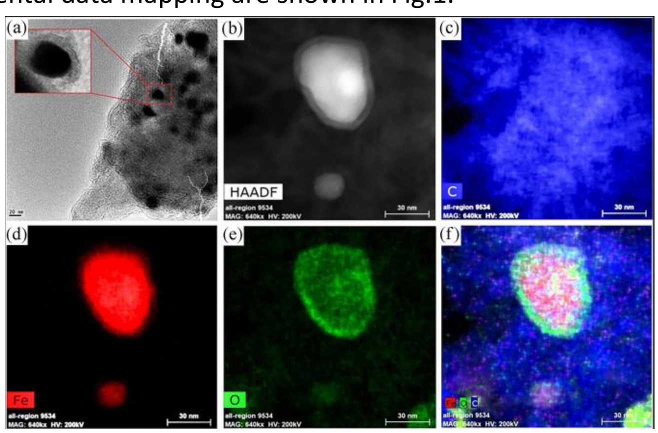

Fig. 1. TEM image of the $(Fe\text{-}Fe_3O_4)/C$ nanocomposite (a), HAADF-STEM image of $Fe\text{-}Fe_3O_4$ nanoparticles (b) with elemental mapping (c–f).

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Training Workshop

Magnetic Nanohybrids for Cancer Therapy

MaNaCa

MaNaCa Twinning | Horizon2020 project
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Thessaloniki | April 07-09, 2022

ABSTRACTS

Oral Presentations
Friday 08/04/2022
Afternoon Session

Bio-applications of Metal-based Nanoparticles

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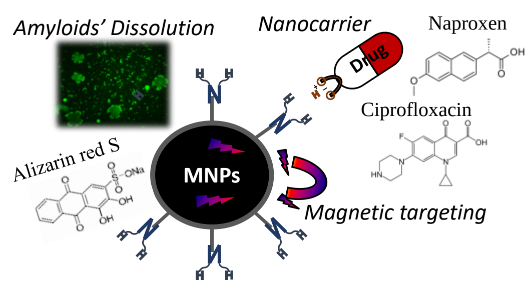
Metal-based nanoparticles possess unique physical and chemical properties that make them appropriate for various bio-applications, while structural alterations lead in different potential related to biological functions. Herein, we present various metal oxides and their ability to act as nano-theranostics; i) Ferrites (MFe_2O_4, M:Zn,Mn) have been solvothermally prepared with/or without microwave irradiation and functionalized further into nanocarriers of nonsteroidal anti-inflammatory drugs (NSAIDs) and/or antibiotics, offering simultaneously the ability for magnetic resonance imaging and magnetic targeting; ii) In the terrain of central nervous system diseases, zinc-doped ferrite NPs have been tested for their ability to dissolve amyloid plaque formations through magnetomechanical forces that can be induced under a low-frequency magnetic field; iii) Naked ZnO NPs were immobilized by alizarin, a natural anthraquinone compound to boost their anti-amyloidogenic and antioxidant activity. Meanwhile, alizarin molecules have pronounced imaging properties as proved by the optical microscopy, and in so they could be implemented as biomarkers for the diagnosis of aggregated protein forms; iv) Coated ZnO NPs, CuO NPs and bimetallic copper-zinc (CuZn) NPs could serve as innovative tools to face the ongoing crisis of antimicrobial resistance. Those NPs have been tested against pathogenic bacteria, while their co-administration with commercial antibiotics was applied as a modern strategy to kill resistant bacterial species.



References: 1) I. Eleftheriadou, **K. Giannousi,*** E. Protonotariou, L. Skoura, M. Arsenakis, C. Dendrinou-Samara, & A. Sivropoulou, *ACS Applied Nano Materials* 2021, 4, 9, 9799–9810. **2)** O. Antonoglou, **K. Giannousi**, S. Mourdikoudis, C. Dendrinou-Samara, *Nanotechnology* 2020*,* 31(46)**. 3) K. Giannousi**, O. Antonoglou, C. Dendrinou-Samara, *ACS Chem. Neurosci.* 2019, 10:3796-3804. **4) K. Giannousi**, E. Koutroumpis, V. Georgiadou, V. Karagkounis, C. Dendrinou-Samara, *Eur. J. Inorg. Chem.* 2019, 1895-1903.

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A new approach to magnetic sensing and actuation of mammalian cells based on genetically encoded encapsulin proteins

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Spherical proteinaceous nanoreactors called encapsulins naturally occurring in bacteria such as *Quasibacillus thermotolerans* can be expressed in mammalian HEK293T and HepG2 cells. These encapsulins (QtEnc) represent a two-component system consisting of a nanoshell and a ferroxidase cargo, enabling import and sequestration of up to 60000 iron atoms inside the nanocompartment. Genetic constructs and experimental details are given in Sigmund et al, ACS Nano 2019 and Efremova et al, Pharmaceutics 2021.
A small fraction of HEK293T cells grown in a Fe-containing medium and expressing QtEnc can be isolated via magnet-assisted cell sorting. Transmission electron microscopy and Energy Dispersive X-Ray Spectroscopy revealed that each sorted cell contains thousands of electron-dense, Fe-containing nanoparticles with an average diameter of 30±3 nm. Vibrating sample magnetometry proved the ferrimagnetic response of the sorted cells at 5-250K, which suggests the presence of magnetic phases different from antiferromagnetic ferrihydrite. In agreement with this, QtEnc expression and Fe loading increased the T2-weighted contrast in magnetic resonance imaging of HEK293T and HepG2 cells.
Finally, we performed a proof-of-principle experiment showing the potential of QtEnc expression for cell manipulation when HEK293T cells were plated in the presence of a permanent magnet. According to the optical microscopy results, the sorted cells were predominantly attracted to the edges of a magnetic cube immersed into the cell medium.

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Preclinical study design considerations in cancer nanomedicine

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Nanomaterials have been proven to be an excellent platform for the design of novel biomedical applications in cancer research. New nano-based strategies are being proposed in drug delivery, tumor targeting, gene silencing, cancer radiotherapy, phototherapy, and for the development of novel diagnostic assays.

However, clinical translation of these promising technologies has been challenging. The complex interactions between nano-objects and biological systems make the prediction of nano-objects' behaviour very difficult, even in highly controlled experimental settings. Moreover, the in vitro biological assays commonly employed have been developed and optimized mainly for the investigation of chemicals. Nanoparticles, due to their unique physicochemical properties, tend to interfere with these assays in various ways such as by affecting the processes of signal generation and detection.

Beyond in vitro cell-based assays, the in vivo preclinical studies should also be designed carefully. Different preclinical tumor models result in the detection of inconsistent biological responses against the same nanoformulations. Moreover, physicochemical, pharmacokinetic and pharmacodynamic properties of individual nanoformulations as well as their safety and efficacy profiles greatly vary among different experimental settings with even minor adjustments.

The lack of adaptation of the different methodologies in the context of nanotechnology, leads to misinterpretation of the observed effects which is reflected in the lack of comparability of the results between laboratories. Moreover, lack of proper positive and negative controls and poorly reported complicacies and inconsistencies, further hamper the generation of accurate and reproducible data. Therefore, standardized protocols should be developed by defining and reporting the specific interference-causing experimental parameters. Study design must be outlined in extensive detail, alternative assays examining the same effects should be selected, in vitro and in vivo model systems should be carefully chosen and bioactivities should be investigated over extended time periods. Moreover, biologically realistic nanoparticle concentrations should be used and nanomaterial formulations should be characterized over time, not only in their solid state but after exposure in biological environments as well.

High quality study design could raise the clinical translation rate in cancer nanomedicine. By employing various different methodologies and optimizing existing protocols while openly and thoroughly reporting study design and troubleshooting, researchers will be able to understand, identify, monitor and control the factors that affect biological responses to nanomaterials, accelerating the potential clinical translation of their findings.

Magnetic nanostructures as drug delivery systems for natural products

A. Assimopoulou

Training Workshop

Magnetic Nanohybrids for Cancer Therapy

MaNaCa

MaNaCa Twinning | Horizon2020 project
Grant agreement No 857502 (2019-2023)

Thessaloniki | April 07-09, 2022

ABSTRACTS

Poster Session

Synthesis and characterization of a novel multifunctional magnetic bioceramic nanocomposites

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Developing bioactive three-dimensional (3D) scaffolds to support bone regeneration has recently become a key area of focus within bone tissue engineering. A promising strategy in tissue engineering, is the use of bone augmenting bioceramic scaffolds occasionally with magnetic properties, to enhance bone regeneration through a synergistic action of in situ apatite formation derived from bioceramics, stem cell stimulation and differentiation towards the osteogenic lineage from targeted magnetic field application. The main aim of this study is to design a new magnetic bioceramic nanocomposite and subsequently fabricate a multifunctional 3D scaffold, via polymer sponge method, able to address different challenging issues like physico-chemical and biological features, bioactivity, biocompatibility together with bone malignant tissues through hyperthermia, bone infection through antibiotic release. The synthetic approach goes along with the synthesis of $CoFe_2O_4$ nanoparticles, followed by the fabrication of Mg_2SiO_4-$CoFe_2O_4$ nanocomposite, implementing a two-pot sol-gel synthesis strategy to coat the magnetic nanoparticles. Finally, 3D scaffolds are fabricated through polymer sponge technique. The as synthesized materials were characterized with X-Ray Diffraction and FTIR analysis, at all stages, for the accurate definition of their structure and morphology. Magnetic characterization of the non-coated $CoFe_2O_4$ nanoparticles and the coated nanocomposite is carried out to determine the magnetic response of all samples, using a vibrating sample magnetometer (VSM) and the results exhibited that room temperature saturation magnetization is decreasing for the nanocomposite-coated materials, indirect evidence for the successful coating with a non-magnetic shell. Also, TGA performed, in order to analyze their thermal profile in conjunction with Magnetic Particle Hyperthermia to investigate the hyperthermia capabilities experimental details about the heat induction properties of different specimens containing magnetic particles are assessed. Finally, the specific loss power (SLP) of the studied specimens is calculated.

Single-step solid state-pyrolysis of carbon-Fe_3C submicron spheres

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Magnetic carbon submicron spheres have received considerable attention because of their ability to be steered by a magnetic field and generate heat when exposed to an alternating magnetic field. They were widely used to purify water by absorbing pollutants providing also good recyclability [1-3]. The carbon spheres with a diameter of 500-800 nm were successfully synthesized by a single-step solid-state pyrolysis of iron (III) phthalocyanine as metal precursor at temperatures of 800°C and 900°C. The influence of different pyrolysis parameters such as temperature, pressure and duration, on the morphology, structure and magnetic properties was investigated. Transmission Electron Microscopy (TEM) and X-Ray Diffraction (XRD) studies reveal that cementite (Fe_3C) nanoparticles (NPs) with a diameter of 14 nm to 80 nm are embedded in amorphous carbon spheres. Fe_3C NPs have a crystallite size of 13.8 ± 0.7 nm and 9.5 ± 1.3 nm for the samples fabricated at T = 800 °C for 5 min. and T = 900°C for 1020 min., respectively. The decreasing crystallite size is justified by the appearance of new iron-containing phases caused by partial thermal disintegration of the Fe_3C. The magnetic properties confirm the presence of randomly oriented single-domain and non-interacting particles for the sample fabricated at 800°C. The temperature dependence of coercivity for single-domain NPs is described by the modified Kneller's law due to the broad size distribution. A transition to multi-domain state is observed with increasing the pyrolysis temperature up to 900°C.

[1] Y. Long et al., RSC Adv. 6 103910 (2016)
[2] H. Sun et al., ACS Appl. Mater. Interfaces 4 6235–6241 (2012)
[3] X. Hu et al., J. Mater. Chem 22 15947 (2012)

Alternative protocols to optimize magnetic hyperthermia efficiency

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Magnetic particle hyperthermia is an adjunct cancer treatment based mainly on the heat production of MNPs under an alternating magnetic field. As the cancer regions are subjected to thermal stress, at the same time the healthy surrounding tissues may undergo similar heat shocks from the induced eddy currents, due to the developed electric fields. Eddy currents have been shown to be one of the main causes limiting the effectiveness of magnetic particle hyperthermia therapy in clinical trials. More specifically, eddy currents result to potentially harmful unnecessary heating in regions surrounding the malignant ones and for this reason alternative hyperthermia protocols are being developed to limit them as much as possible. The mitigation of eddy currents is accomplished by applying two different alternative hyperthermia protocols. In the first one, pulsed field mode application with ON/OFF cycles instead of the standard continuous one, is applied. The goal in this case is to allow the heat to disperse and dissipate during the OFF-time interval, thus reducing its power and eventually the heating in the surroundings. The second one, concerns the relative coil's movement through a motion device, which was developed for this purpose. Again, heat is dispersed and dissipated this time, during the movement. Experiments in agarose phantom models showed that eddy currents in the healthy tissues (phantom without magnetic nanoparticles) are reduced by 75 %, when a pulsed field mode is applied and by 57%, when the magnetic field source is moving. At the same time, the corresponding effects on the cancer tissues (phantom with magnetic nanoparticles) were 57 % and 70 % in the pulsed field mode and the movement, respectively. To conclude, the results of those two alternative protocols were quite promising, as it was shown that we successfully attenuate undesirable heating on surrounding healthy tissues, without sparing beneficial effect within the malignant region, thus treatment remains reliable yet with milder side-effects. Finally, comparing the two protocols, pulsed mode showed better results, as the greatest reduction was observed in the healthy tissues and not in cancer ones, a phenomenon that was obviously occurred in the second proposed movement - protocol.

Synthesis of Fe-based Magnetic Nanoparticles by Pyrolysis Method

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Nanoparticles of $Fe_x(Fe_3O_4)_{1-x}$ and $Fe_x(Fe_3C)_{1-x}$ (where $0 \leq x \leq 1$) coated with a graphite-like carbon shell can be conveniently synthesized using solid-phase pyrolysis of the corresponding metal-organic compound, like iron phthalocyanine or ferrocene. The pyrolysis was conducted in a closed quartz ampoule according to the following reaction:

$$Fe(C_{32}N_8H_{16}) \xrightarrow[-8H_2,-4N_2]{T_{pyr},t_{pyr},p} Fe + 32C,$$

where T_{pyr} is the pyrolysis temperature (600–1100 °C), t_{pyr} - pyrolysis time (3–2000 min), p – self-generated pressure in the reaction ampoule. The first stage of the pyrolysis leads to the formation of iron clusters in the carbon matrix with high degree of graphitization. Then, during the growth of iron nanoparticles, the surface iron atoms interact with carbon atoms and form iron carbide Fe_3C. By changing the temperature and the time of pyrolysis, it is possible to synthesize the both nanoparticles of Fe@C and Fe_3C@C as well as nanoalloys (Fe-Fe_3C)@C.
To synthesize (Fe_3O_4)@C nanocomposite material, the Fe@C nanoparticles additionally annealed at 250 °C under the oxygen media. By varying the oxygen pressure in the range of 10^{-3} – 1 bar, it is possible to control the composition of $Fe_x(Fe_3O_4)_{1-x}$ ($0 \leq x \leq 1$).
By changing the pyrolysis parameters (pressure, temperature, time) it is possible to synthesize Fe-based nanoparticles in a carbon matrix with mean size of 5-20 nm. After the synthesis of nanocomposites, the ultrasonic treatment and the size separation of the nanoparticles will be implemented to obtain nanoparticles with a narrow size distribution.

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Tuning synthesis of Fe_3O_4 nanoparticles: the role of surface charge on Cr(VI) uptake

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Water treatment research has justified the potential of Fe_3O_4 nanoparticles to operate as a promising Cr(VI) removal adsorbent. Here, the possibility to optimize Cr(VI) uptake capacity by tuning iron oxide nanoparticles synthesis parameters of the oxidative precipitation methodology is discussed. Results show that hydroxyl excess, as defined by the balance of acidic and alkaline compounds in the reaction mixture, may determine the observed efficiency according to the impact in the reducing activity and the surface charge. Adjusting the hydroxyl excess above +0.02 multiplied the Cr(VI) uptake by a factor of 9 reaching a value of 2.5 mg/g. Such increase is attributed to the high specific surface area of the isolated nanoparticles and the improved stabilization of Fe^{2+} species in the structure of Fe_3O_4. A similar increase of efficiency was found when hydroxyl deficiency (<-0.05) was applied during synthesis. In this case, despite the high degree of aggregation and lower Fe^{2+} presence, the activation of an exchange mechanism between adsorbed sulfates and chromate oxyanions seems to assist the capture process.
Considering the high magnetic response of Fe_3O_4 nanoparticles as another significant advantage for their facile removal toward implementation in drinking water purification, a successful step beyond was the development of nanocomposites based on their combination with Sn^{2+} oxy-hydroxides which are known as the best performing materials in Cr(VI) capture introducing a reduction/adsorption mechanism. Indeed, embedding Fe_3O_4 nanoparticles (5-20 %wt.) onto the spherical assemblies of the tin oxy-hydroxide ($Sn_{21}O_6(OH)_{14}Cl_{16}$), maintained a significant Cr(VI) capacity above 6 mg/g while succeeding a residual concentration below the drinking water limit of 25 μg/L.

The research project was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the “2nd Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers” (Project Number: 00046 MagnoSorb).

Structural properties of Fe/Fe_3C cementite nanoparticles using spectroscopic techniques

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This work is focused on the structural properties of cementite (Fe-Fe_3C) magnetic nanoparticles dedicated to cancer treatment applications, namely hyperthermia, with the use of alternating magnetic fields. Magnetic nanoparticles are already implemented in biomedical applications, but cementite nanoparticles showed some prospect due to their bio-compatibility and their exceptional magnetic properties. The studied nanoparticles were synthesized by solid state pyrolysis at different temperatures and different time durations. The samples were fabricated under no-air conditions in the range of 700-1100°C and with time durations of 5, 15 and 30 minutes. The nanoparticles were characterized with the following techniques, XRD (X-Ray Diffraction), XPS (X-Ray Photoelectron Spectroscopy) and XANES (X-Ray Absorption Near Edge Fine Structure) Spectroscopy. The combined results demonstrate a dependence between the pyrolysis temperature and the Fe elemental concentration in the samples and similarly that both the crystallinity and atom arrangement into the lattice are modified due to the different pyrolysis temperatures. XRD analysis of the patterns show that the nanoparticles synthesized in temperatures 800-1000 °C have sizes between 15-10nm with Fe peaks being more intense for higher temperatures. XPS spectra reveal the bonding between the elements of cementite nanoparticles, showing the expected cementite formation. XANES results, agreeing with XRD speculations, indicate that Fe becomes dominant for higher temperatures as it is observed by sample and reference spectra and the quantitative results extracted from the fitting. The aforementioned characteristics are closely related to the magnetic properties of the nanoparticles and in turn to their high performance as candidates in hyperthermia applications.

Investigation of the heating properties of Fe_3O_4 magnetite nanoparticles dispersed in agarose

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Magnetic hyperthermia has emerged as a promising method for the local treatment of cancer cells. The main goal is to heat biocompatible magnetic iron oxide nanoparticles in an external alternating magnetic field in such a way that lethal temperatures for the tumor cell of at least 43°C are reached. Within the scope of this research, Fe_3O_4 nanoparticles with an average diameter of 114nm dispersed in agarose, have been analysed. The particles are mainly in the multidomain state, and the hysteresis losses contribute to particle heating instead of the well-known Neel and Brown relaxation in super paramagnets. To determine the heating properties called specific loss power (SLP) magnetic flux densities of 20mT to 55mT were used with frequencies ranging from 103kHz to 247kHz, which are in the human tolerable range. From the literature it is known that the SLP behaves directly proportional to the frequency and has a constant exponent of $\alpha \leq 3$ for the magnetic field strength. In fact, the measured values show a linear dependence to the frequency, but a constant exponent was not determined. Moreover, the specific loss power does not show any dependence on the viscosity of the agarose. Overall, temperature increases of up to 40°C were successfully achieved and an average SLP value of 139 W/g was obtained.

4D Printing: Synthesis, Characterization and Mechanical Evaluation of Ferromagnetic Hybrid Scaffolds for Magnetic Hyperthermia

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Four-dimensional (4D) printing is an additive manufacturing process that combines three-dimensional (3D) printing with stimuli-responsive materials, allowing time dependent controlled modification of properties on printed structures, by applying an external stimulus such as temperature, UV light and magnetic field. In addition, polymers invariably attracting scientific interest as they can be easily modified by adding various nanoparticles, while some of them are biocompatible with low toxicity. Furthermore, magnetic nanoparticles also attract scientific interest in the field of biomedicine, due to their biocompatibility and their unique properties, when an external magnetic field applied, promoting their use for Magnetic Hyperthermia (MH) cancer treatment techniques. According to this approach:

- A specific protocol for the formation of ferromagnetic filaments was designed.
- Polylactic acid (PLA) as a prime material and magnetite nanoparticles (MNP) as dispersed phase used, in proportions of 10% and 20% by weight.
- Cylindrical and dog-bone shaped samples created by a Fused Deposition Modeling (FDM) 3D printer, according to specific protocols and bibliographic references.

For the characterization of the nanocomposite filaments and printed structures, a series of techniques were followed. The results suggested:

- The success of the filament formation protocol due to the high dispersion of the magnetite phase as electron microscopy shown.
- The morphology of hysteresis loops is directly dependent on the weight percentage of nanoparticles and is affected by the presence of other microparticles.
- The application of alternating magnetic field to the structures and the simultaneous monitoring of their temperature showed that MH can be achieved and controlled.

Future research investigates the contribution of nanoparticles to mechanical properties. Hence, it will be possible to determine that the use of MNP's promotes the optimization of two parameters such as durability and hyperthermia for real applications in biomedicine.

Training Workshop

Magnetic Nanohybrids for Cancer Therapy

MaNaCa

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Thessaloniki | April 07-09, 2022

LABORATORY COURSES

Saturday 09/04/2022

INTRODUCTION

Optimization of the magnetic nanoparticle hyperthermia requires the application of concepts across multiple disciplines, including chemistry, physics and materials science. Therefore, this technology presents an opportunity to teach students foundational concepts in science and engineering. In the following MaNaCa hands-on, students will be divided into 4 working groups with general topics: Samples, BioStudies, Hyperthermia and Modelling. The learning objectives of this laboratory module are:

- To explain the general properties of magnetic materials and magnetic nanoparticles as well as magnetic scaffolds.
- To describe some of the synthetic methods used to fabricate magnetic systems for hyperthermia cancer therapy.
- To outline the mechanisms of heating of single- and multi-domain magnetic materials.
- To examine the magnetic hyperthermia application from a biological point of view.
- To quantify the effect of applied current, suspension viscosity, and nanoparticle concentration on the SLP and explain the phenomenon within the context of Brownian and Néel relaxation time.

SAMPLES

Magnetic Nanoparticles

Iron oxide nanoparticles have emerged as one of the primary nanomaterials for biomedical applications, due to their long blood retention time, their biodegradability and their low toxicity. They can be used in technological applications, including clinical needs such as magnetic hyperthermia. Among the widely used synthesis routes used for synthesizing iron oxide MNPs are coprecipitation, thermal decomposition, microemulsion, and sol-gel methods. However, compared to other synthesis routes, the coprecipitation method is generally preferred, due to its high yield and facile controls. More specifically, for the coprecipitation reaction, the concentration of precursors and the reaction temperature significantly affect the size, size distribution, phase and surface chemistry of resultant MNPs. First, we present the synthetic route using the aqueous chemical coprecipitation method. It has been highlighted as a cost-effective and fast process, easily expandable on an industrial level. Using the aqueous version of this method, we may avoid the use of hazardous solvents and reagents and high reaction temperatures or pressures. In that sense, aqueous coprecipitation can be eco-friendly. It is the simplest method to prepare MNPs from aqueous iron salt (Fe^{2+}, Fe^{+3}) solution. Next, we present the fabrication processes used to produce phantom with agarose solution. Gels and especially those from agarose, are routinely used as phantom models, while they comprise the only transparent porous materials, which successfully simulate animal tissues.

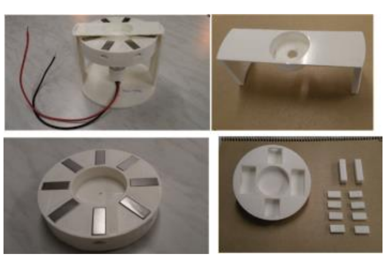
SAMPLES

3D Printed Scaffolds

Three-dimensional printing technology has emerged as a promising tool for meticulously fabricated scaffolds with a high precision and accuracy, resulting to intricately detailed biomimetic 3D structures. To this end, magnetic scaffolds (MS) are becoming increasingly attractive in tissue engineering, due to their ability to enhance bone tissue formation and in combination with MNPs they can, not only promote bone repair and regeneration, but drug delivery, as well. At the same time, like MNPs, MS can play the role of thermal seeds as alternative agents in magnetic hyperthermia converting their magnetic energy into heat under the application of external magnetic field. In this lab, we elaborate 3D printing technology to fabricate MS. 3D-printed MS of several cylindrical shape structures and different densities are 3D-printed using a Zmorph 2.0 S FDM (Fused Deposition Modeling) printer, either with a commercial magnetic filament, provided by Proto-Pasta (PP), composed by PolyLactic Acid (PLA) and iron or with a handmade polymer bonded magnetic filament. Scaffolds' designs are created using Inventor Autodesk (modeling software) whereby a unit cell structure can be transposed at a fixed geometry through a wider 3D model. Conventional heating evaluation experimental approaches used on MNPs are not applicable for large-scale magnets. For this reason, a reliable estimation sequence of the heating efficiency, i.e., the specific absorption rate of the magnetic scaffolds, is introduced, analyzed and discussed in conjunction with the specific loss power, which is the respective quantitative index for evaluating the MNPs' heating efficacy. The final case is studied and discussed in the Hyperthermia Session of the Hands-on MaNaCa workshop.

SAMPLES

3D Printed Magnetic Devices

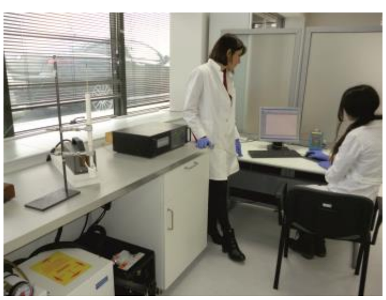


The generation of mechanical forces via magnetic fields, the so-called magneto-mechanical effect (MME), is a promising method for the manipulation of MNPs inside varying environments. The combination of static, alternating, or rotating magnetic fields with MNPs allows the transformation of electromagnetic to mechanical energy. Such an aspect may be exploited for biomedical purposes provided nanoparticles successfully bind to the cancer cell membrane and eventually affect cells by exerting magneto-mechanical stress. Unlike hyperthermia, which requires high frequencies to induce heating (above 100 kHz to several MHz), MME can be achieved at frequencies below 100 Hz. To produce these fields and to quantify the corresponding forces, tunable magnetic field applicators have been constructed, typically with moderate field intensity and field inhomogeneity. To overcome this, novel 3D printed magneto-mechanical systems, designed to produce stronger homogeneous magnetic fields, can be manufactured by 3D printing. In this hands-on, we look through the design and the manufacture of these devices that can produce high spatial gradients of the magnetic flux density (120 T/m) strong mechanical forces and torques that can be applied on cells when incubated with MNPs. The 3D polymer rotating turntable printouts operate with DC motors at variable voltage amplitude (3–12 V) resulting in a tunable physical rotation frequency (0–16 Hz).

BIO STUDIES

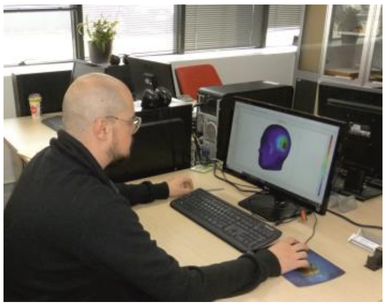
The constant development of medicine has rendered early diagnosis and precise treatment of its development direction. Nanotechnology has provided a new platform for medicine development. As a result of unique features, nanomaterials have been extensively studied and applied in the medical field. As one kind of the nanomaterials, MNPs possess not only the general characteristics of nanoparticles, but also the magnetic properties. After being surface-modified, MNPs can possess excellent biocompatibility, which is suitable for medical application. For example, surface-modified MNPs can be used as vectors, allowing for drug or gene directional transportation under the action of the magnetic field to realize targeted therapy. Moreover, under the action of applied magnetic field, MNPs have unique magnetic sensitivity, which can thus be applied in MRI. Furthermore, the magnetocaloric effect of MNPs has also provided a new means for tumor treatment. All in all, the application of MNPs will further promote the development of the medical field. This Lab is focusing firstly, to provide briefly state-of-the-art of nanomaterial application for cancer therapy, on a theoretical level, and secondly in a real-time demonstration on experimental design and synthesis routes of magnetic materials focused on biomedical applications, utilizing the Magna Charta Lab equipment, and provided devices. More specifically, the attendees will be familiarized with a bottom-up, two-pot approach synthesis of bioceramic MNPs, intended for scaffolds fabrication. Next, a demonstration on two different routes/approaches of scaffolds fabrication (3d printed, pu replica foams) will take place, in which, we will analyze the pros n cons of each approach and the recommended strategy/approach suitable for different biomedical applications. The attendees will have the chance to get acquainted/familiar with a compound Optical Microscope (OM) equipped with a CCD camera, observe and calculate a variety of parameters on different given samples.

HYPERTHERMIA



This Lab Course is focusing on the experiment as well as on the evaluation of Magnetic Particle Hyperthermia. After a brief introduction on the magnetic hyperthermia origin following a short presentation on the Magna Charta lab devices and equipment, the experimental process will be analyzed and presented in a real-time demonstration. Adjusted protocols and experimental strategies will be presented, targeting to the best heating results under harmless routes. In magnetic particle hyperthermia, a promising least-invasive cancer treatment, malignant regions in proximity with MNPs undergo heat stress, while unavoidably surrounding healthy tissues may also suffer from heat, either directly or indirectly by the induced eddy currents, due to the developed electric fields as well. Here, we propose a facile upgrade of a typical magnetic particle hyperthermia protocol, to selectively mitigate eddy currents' heating without compromising the beneficial role of heating in malignant regions. Hence, two different alternative protocols will be applied concerning 1) a pulsed field mode with ON/OFF cycles and 2) a relative motion of the magnetic field source toward the under study sample. The goal is to allow the heat to disperse and dissipate during the OFF-time interval in the first protocol and during the motion of magnetic field source in the second one, thus reducing its power and eventually the heating in the surroundings. Experimental part ends with the heating evaluation of the examined nanoparticle system.

MODELLING



MNPs have attracted much attention, due to their wide range of applications. For biomedical purposes, magnetic hyperthermia is a developing method that uses nanoparticles for cancer treatment by taking advantage of their heating upon exposure to an alternating external magnetic field. Along with pre-clinical experiments, computer simulations of MNPs are used to better understand the details of the heating process, which guides further experiments and more efficient cancer treatment. Magnetic properties and heating of nanoparticles are quantified by their magnetization-field hysteresis loop area. In the first part of this course, we will find out how we can easily set up a hysteresis loop in OOMMF software - the Object Oriented Micromagnetic Framework. This software utilizes the technique of micromagnetic simulation, which is a numerical method that uses the Landau-Lifshitz-Gilbert (LLG) equation for describing the magnetization dynamics of nanoparticles. MNPs of varying size, shape and material will be used as the system under study in order to extract their fundamental magnetic properties such as their saturation magnetization, remanence magnetization and coercive field for different alternating magnetic field amplitudes and frequencies that are typically used in magnetic hyperthermia application. Moreover, in the second part of this course, we will present how to build numerical models with finite element method and more specifically with the COMSOL software for the description of the phenomena that take place in a magnetic hyperthermia experiment. In particular, we aim at the estimation of the spatial distribution of the magnetic field and the spatiotemporal temperature distribution by taking into account, all the appropriate field and heat transfer boundary conditions. Thus, we will be able to calculate the magnetic hyperthermia curve (temperature increase) in an aqueous dispersion of MNPs.