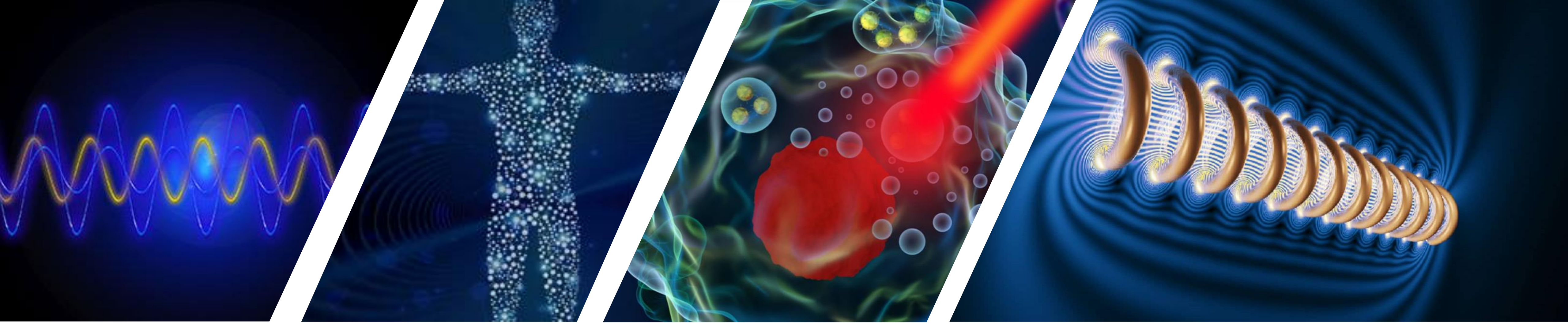

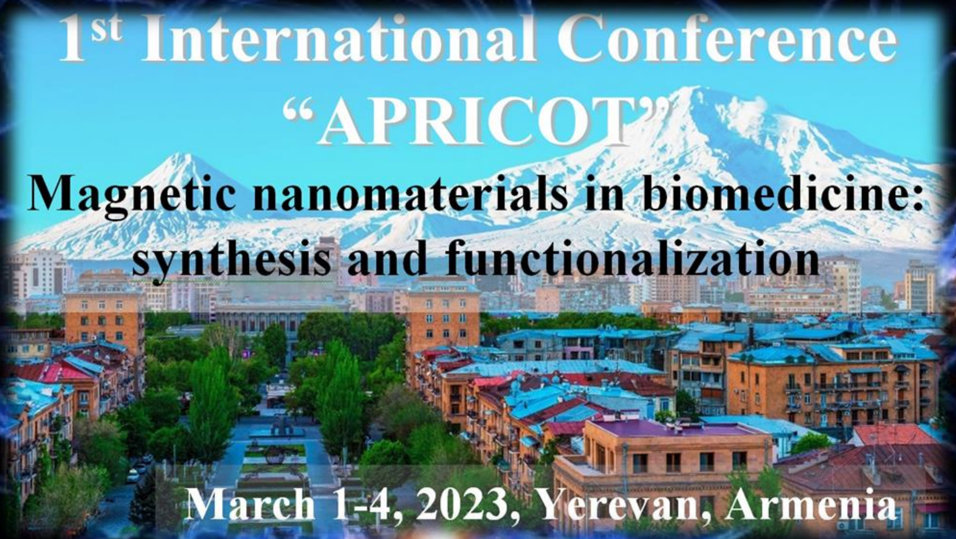

Magna Charta

Magnetic Nanostructure Characterization

Technology & Applications

http://magnacharta.physics.auth.gr

Tuning nanomagnetism for biomedical applications

M. Angelakeris, professor,

MagnaCharta, School of Physics

Aristotle University, Thessaloniki Greece


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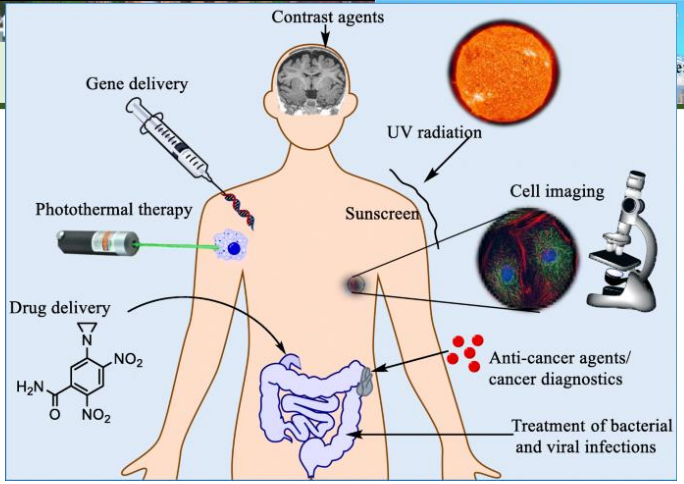
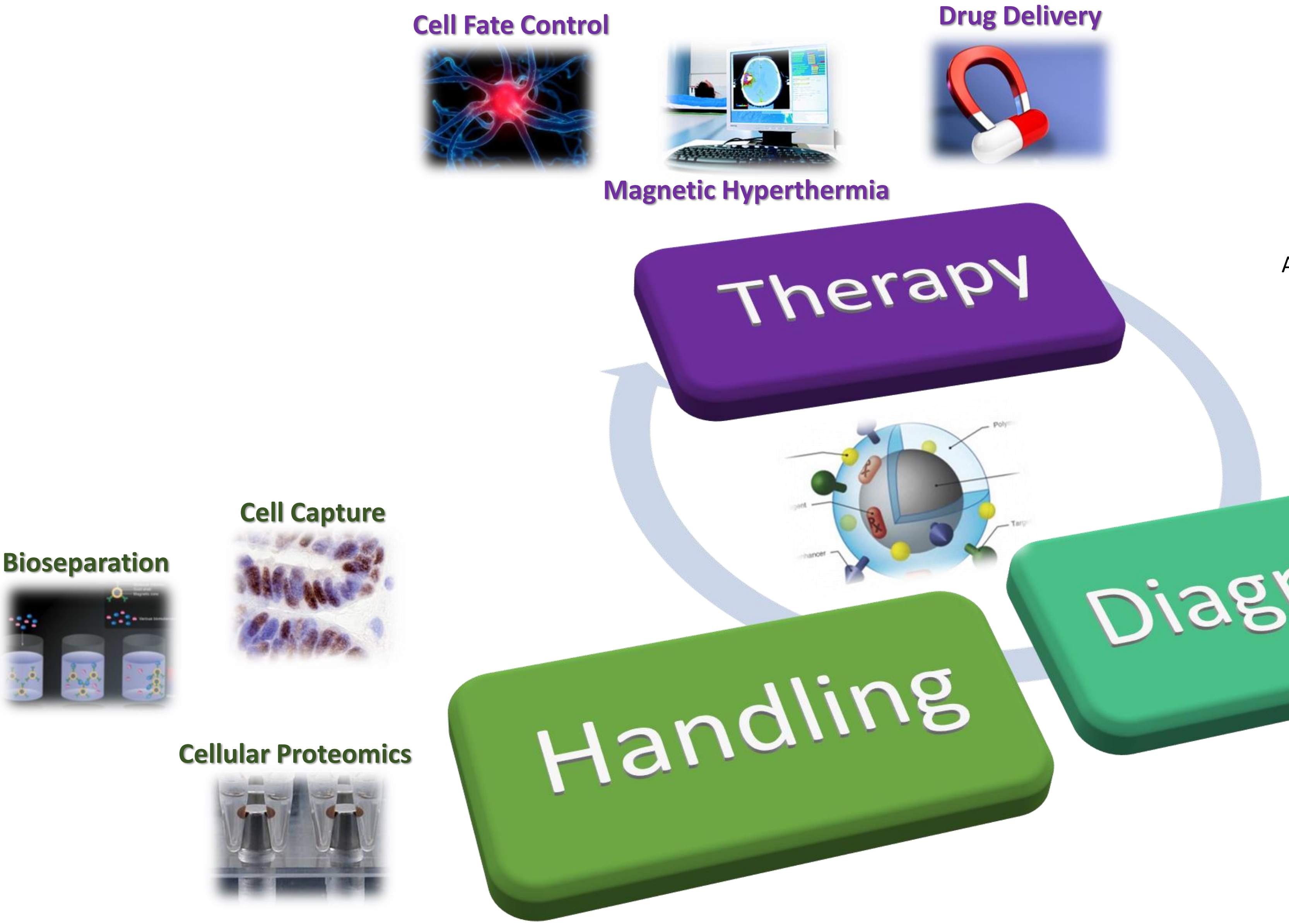
Charta
Magnetic Nanostructure Characterization
Technology & Applications
http://magnacharta.physics.auth.gr

Biomedical Nanomagnetism

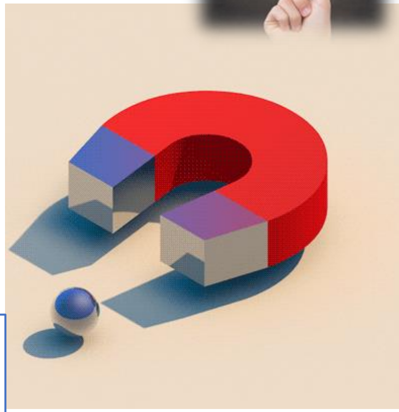


Anderson et al. Nanoscale Research Letters (2019) 14:188



Key idea

Magnetism is a class of physical phenomena that are mediated by magnetic fields. The most familiar effects occur in ferromagnetic materials, which are strongly attracted by magnetic fields.



Maximize Particle - Field Interaction

Magnetic Field

Magnetic Nanoparticle

Maximum Effect

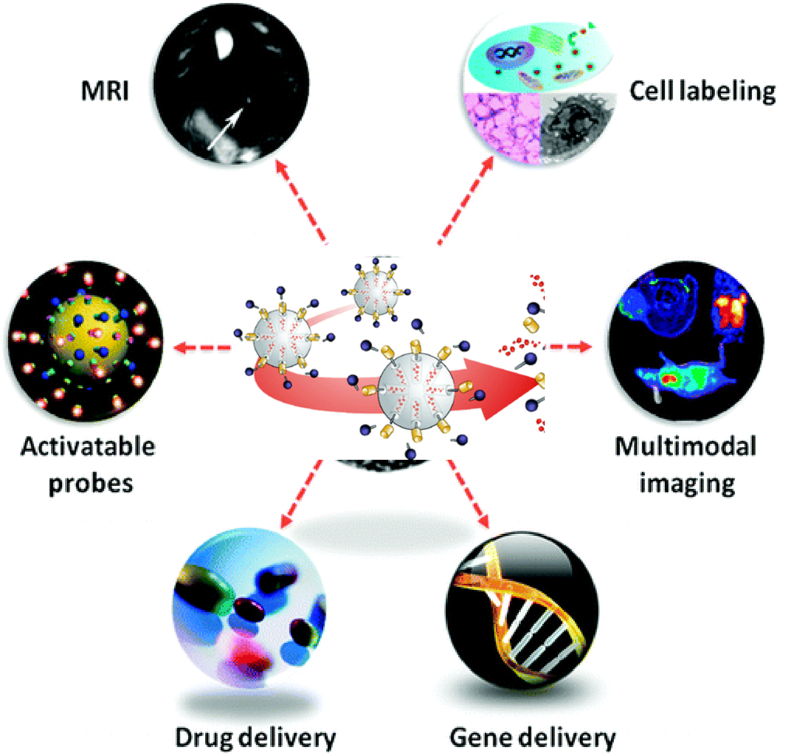
Issues to consider

Tuning nanomagnetism for biomedical applications

Magnetically Driven Treatments

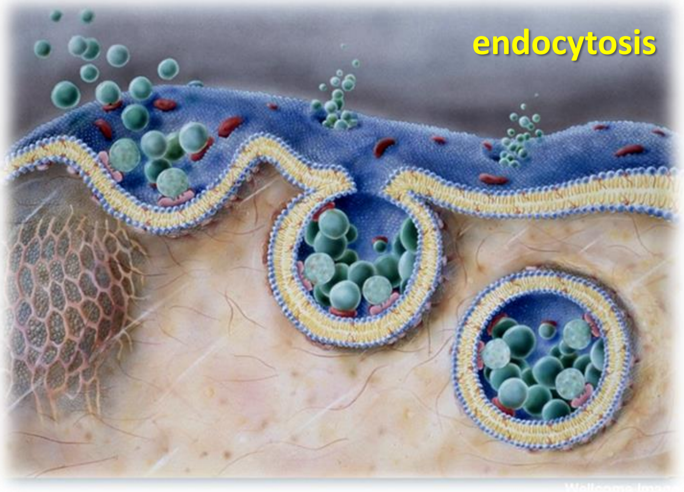
Magnetic field driven treatments involve the delivery of an energy form to tissues, resulting in a physiological change or stimulation, which can in turn be used to generate specific effects.

Magnetic nanoparticles (MNPs) entered also in the play of magnetically driven treatments, particularly, in modern theranostics, as multifunctional carriers delivering specific 'cargo' under the guidance of an external magnetic field.



On the other side…

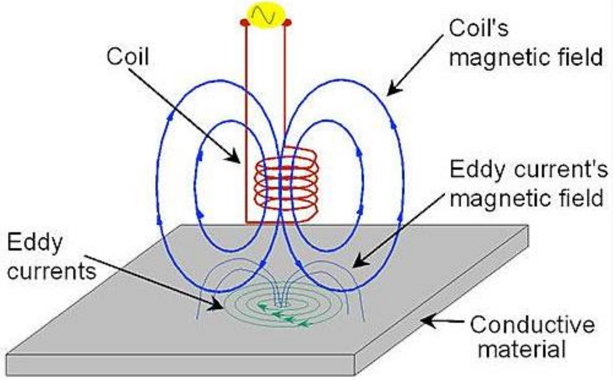
- Nanoparticle formulations should be able to overcome major biological barriers to reach their targets.
- Intravenous injection of nanomaterials introduces new concerns such as dosage, distribution and circulation times as in pharmaceuticals.
- Possible changes in magnetic behavior upon injection and interactions with cells such as specific binding and endocytosis.
- Nanoparticle agglomerations or regions of high concentration with inter-particle interactions lead to altered magnetic properties.



- Do the specific magnetic fields with respect to amplitude & frequency pass harmlessly within human body?

Risks from magnetic fields

AMF generator system produces not only a magnetic field, but also an electric field. The electric field penetrates normal tissue and induces eddy currents, which result in unwanted heating of normal tissues.

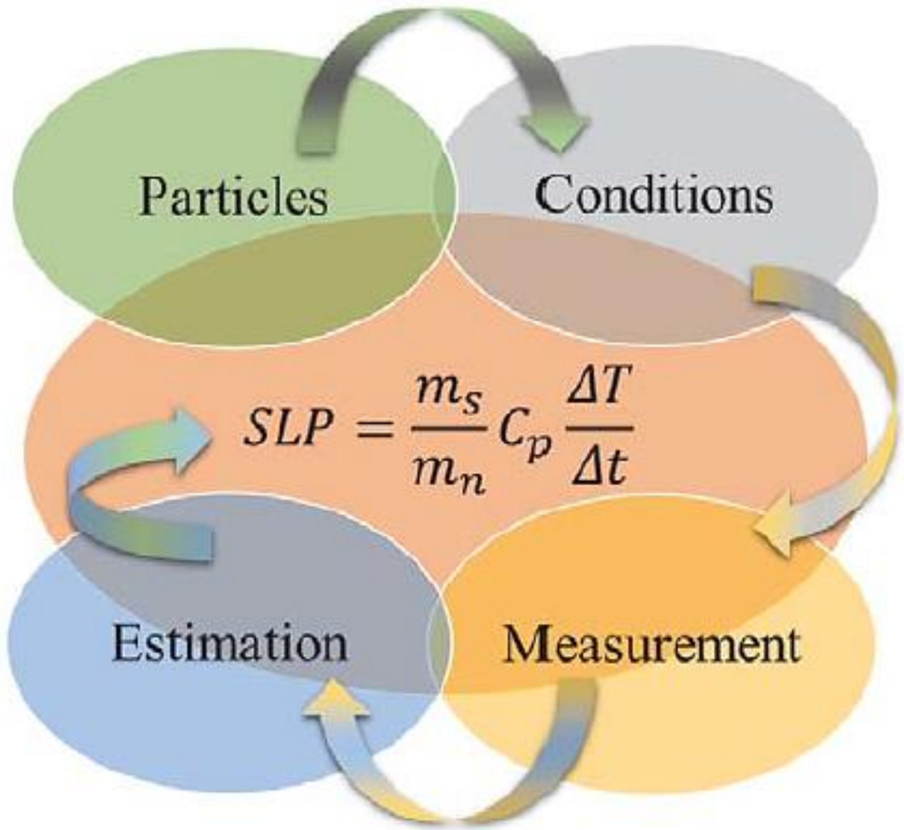


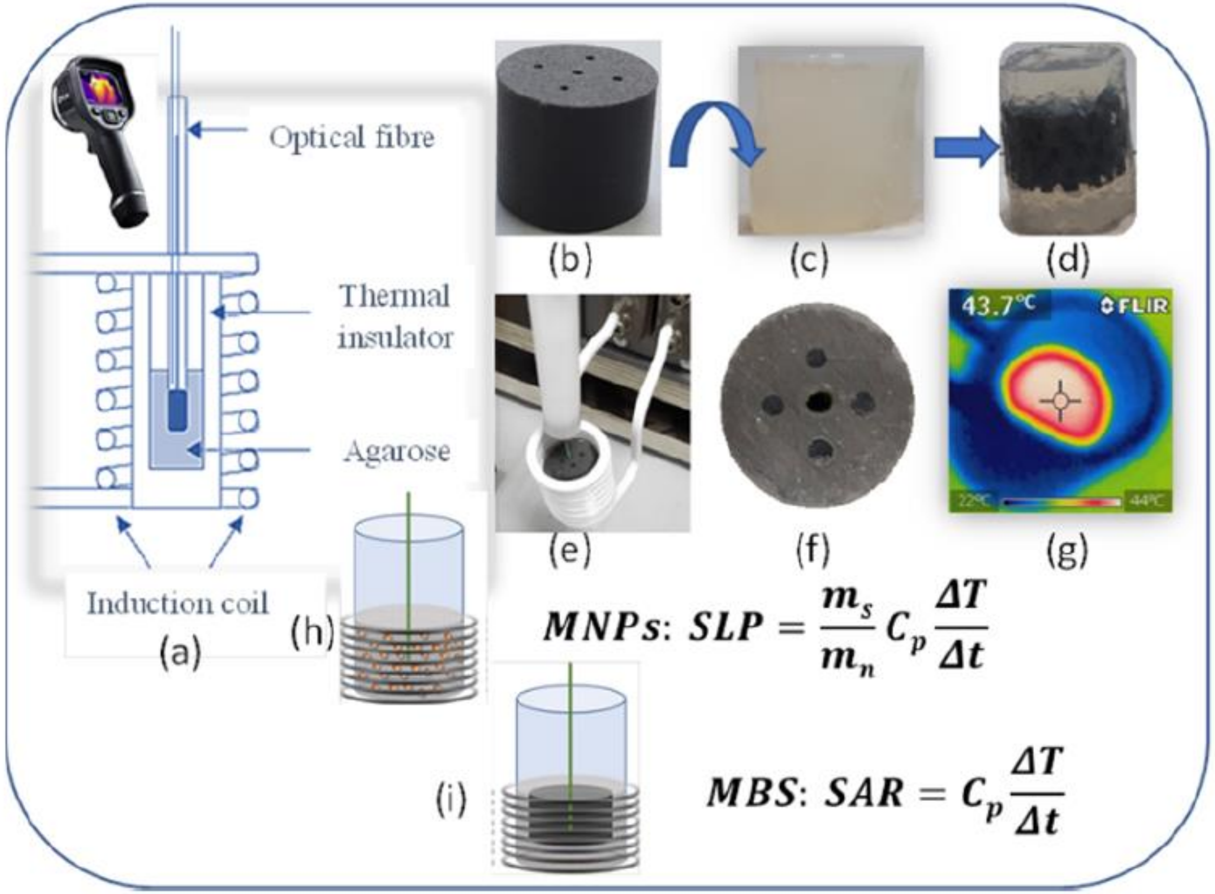
Problems due AMF application

1. Unwanted increase in temperature in healthy tissues
2. magnetic stimulation
3. muscle contraction
4. nervous stimulation
5. magnetophosphines
6. cardiac arrhythmias
7. patient discomfort

Measuring protocols

A standardisation protocol for accurate evaluation of specific loss power in magnetic hyperthermia
J. Phys. D: Appl. Phys. 52 (2019) 255001





An accurate standardization protocol for heating efficiency determination of 3D printed magnetic bone scaffolds
J. Phys. D: Appl. Phys. 55 (2022) 435002

Questions to answer

18:46

What Particles?

Which Conditions?

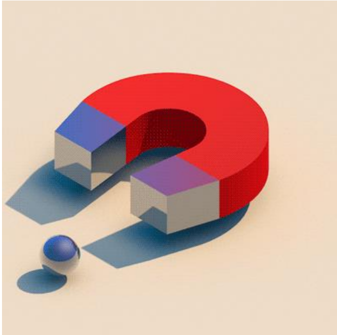
How will it perform in bio?

Question 1: What particles?

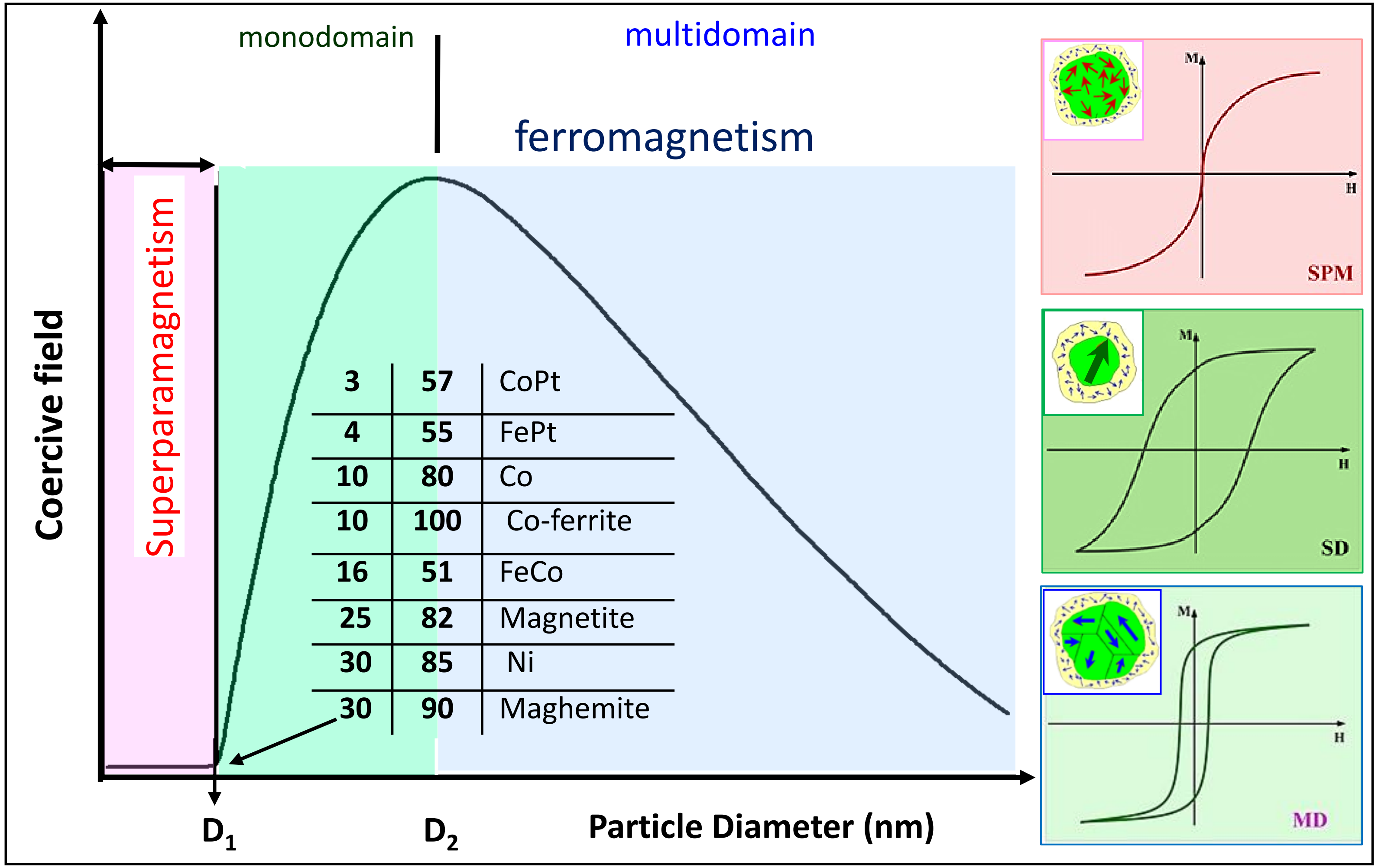
Tuning nanomagnetism for biomedical applications

Which size?

Magnetism is a phenomenon mediated by magnetic fields. The most familiar effects occur in ferromagnetic materials, which are strongly attracted by magnetic fields.



Maximize Particle - Field Interaction



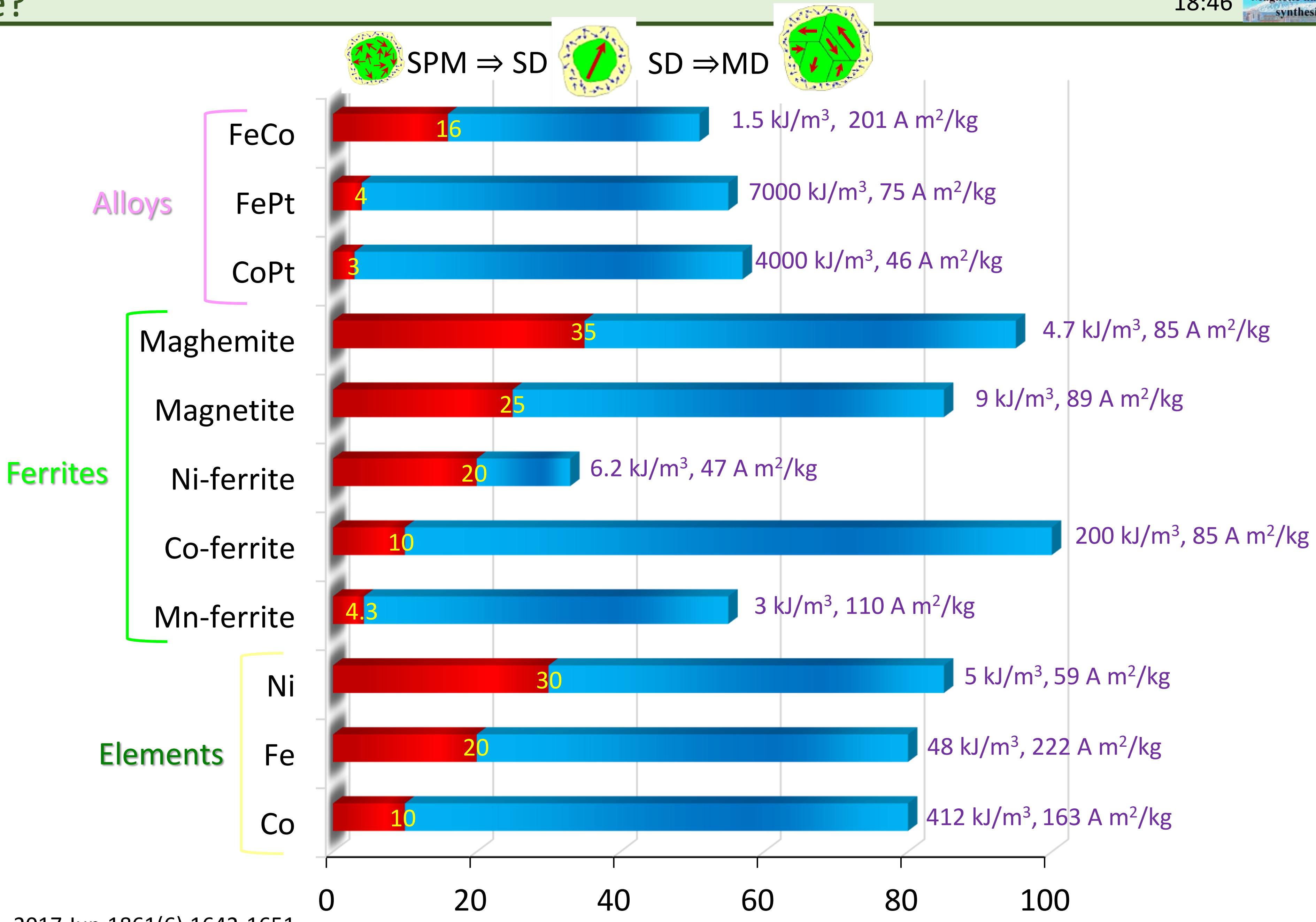
3	57	CoPt
4	55	FePt
10	80	Co
10	100	Co-ferrite
16	51	FeCo
25	82	Magnetite
30	85	Ni
30	90	Maghemite

$$P_{SPM} = \mu_0 \pi f \chi'' H^2$$

$$P_{FM} = \mu_0 f \oint H dM$$

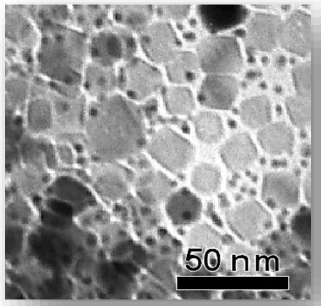
Biochimica et Biophysica Acta 1861 (2017) 1642–1651,

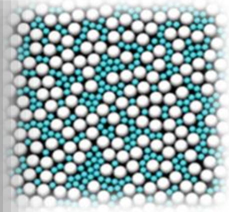
Which size?



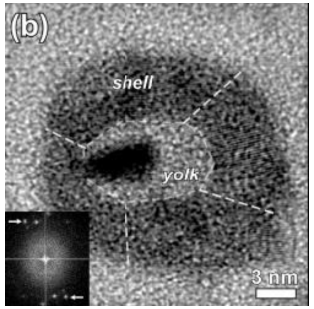
Biochim Biophys Acta Gen Subj. 2017 Jun;1861(6):1642-1651

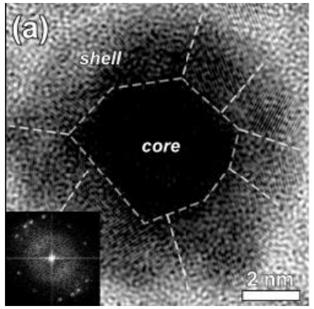
Which morphology?



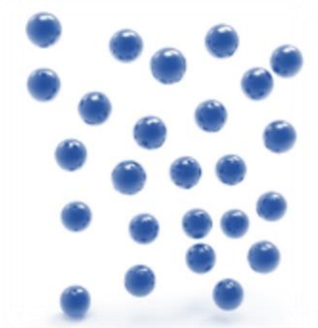


mix & match



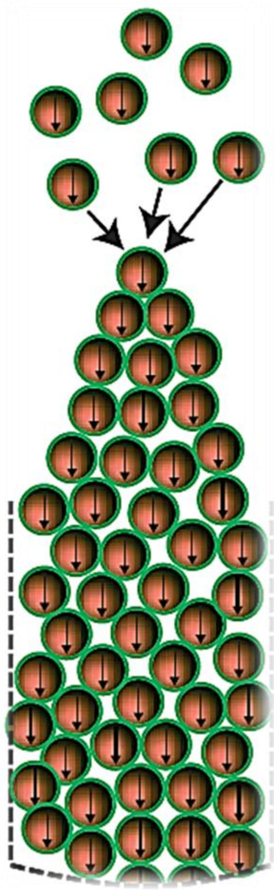


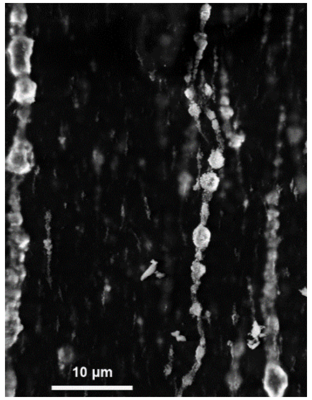
core-shell

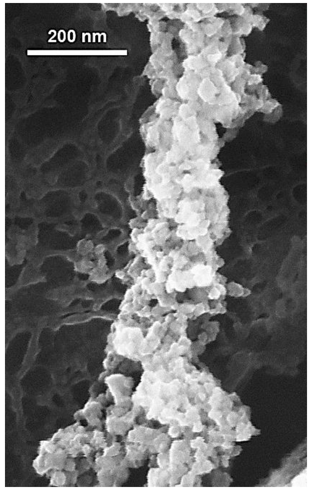


single-core

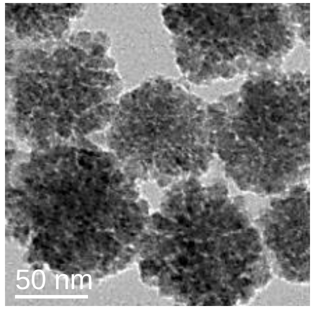
arrays

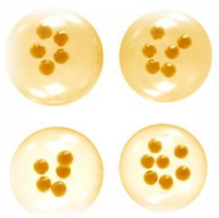






multi-core





Which morphology?

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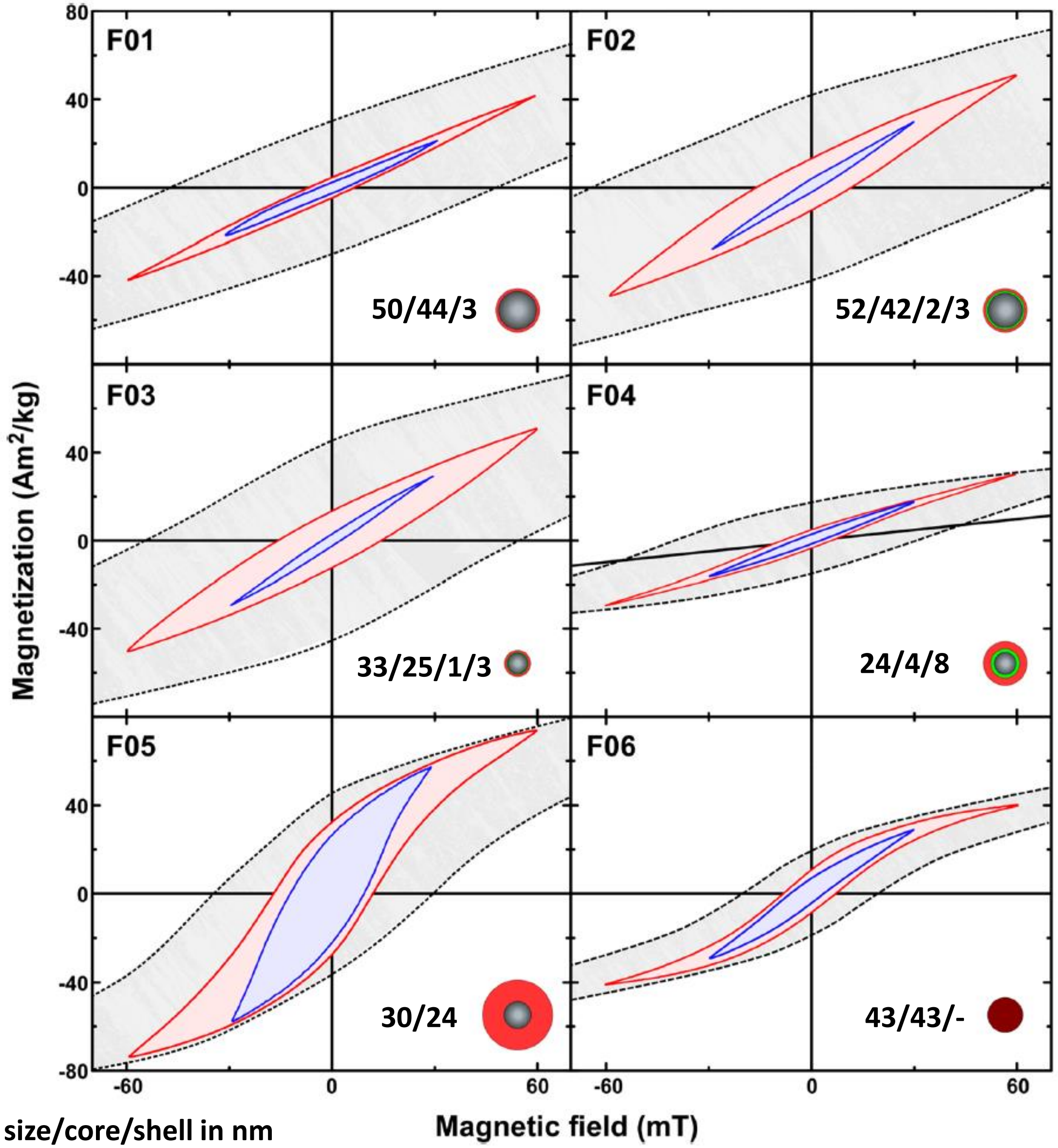
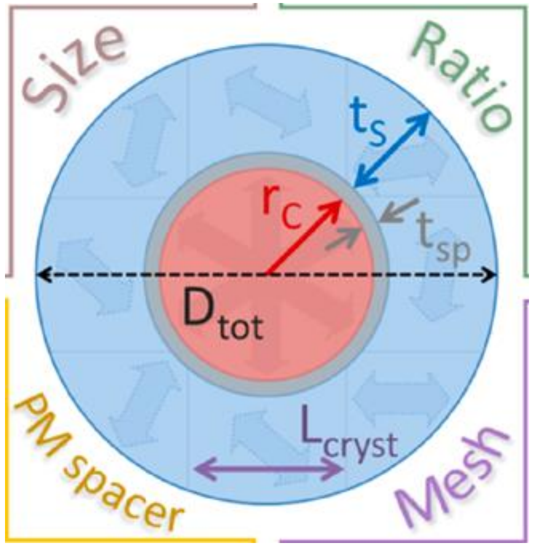
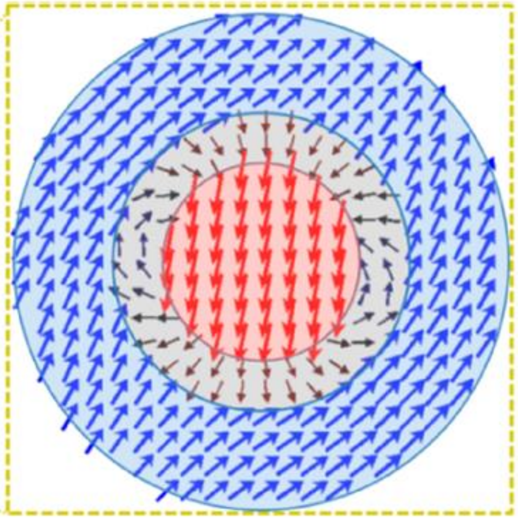
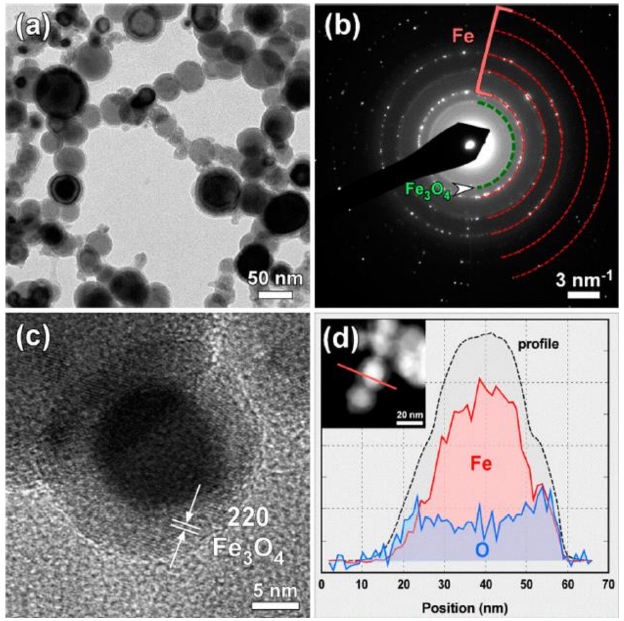
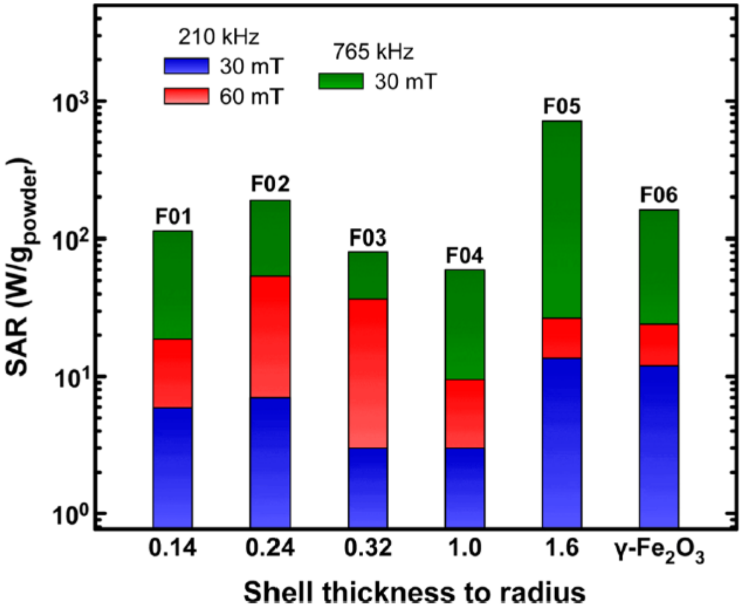


size/core/shell in nm



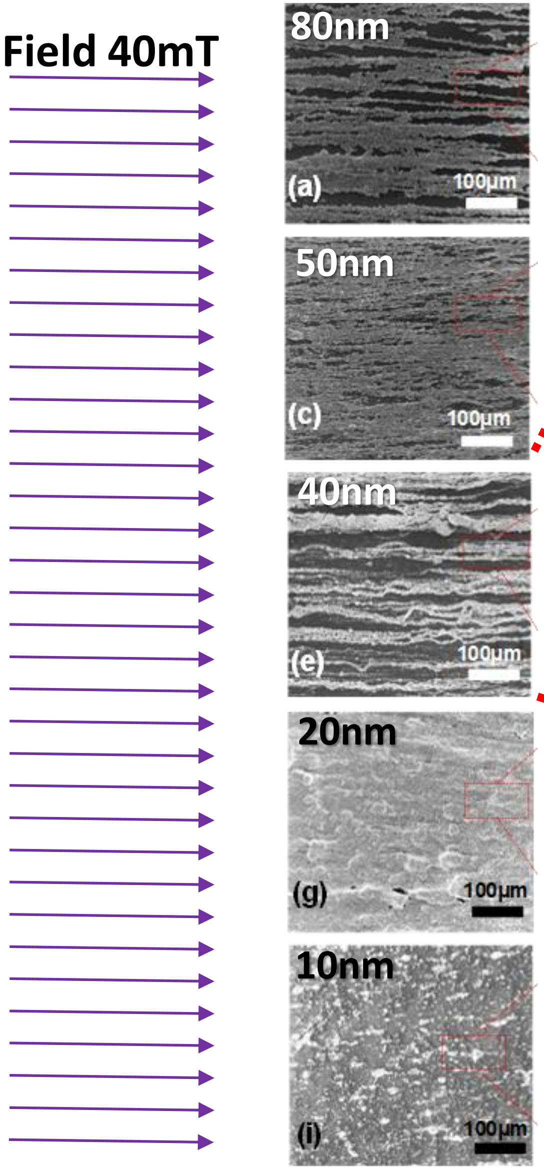


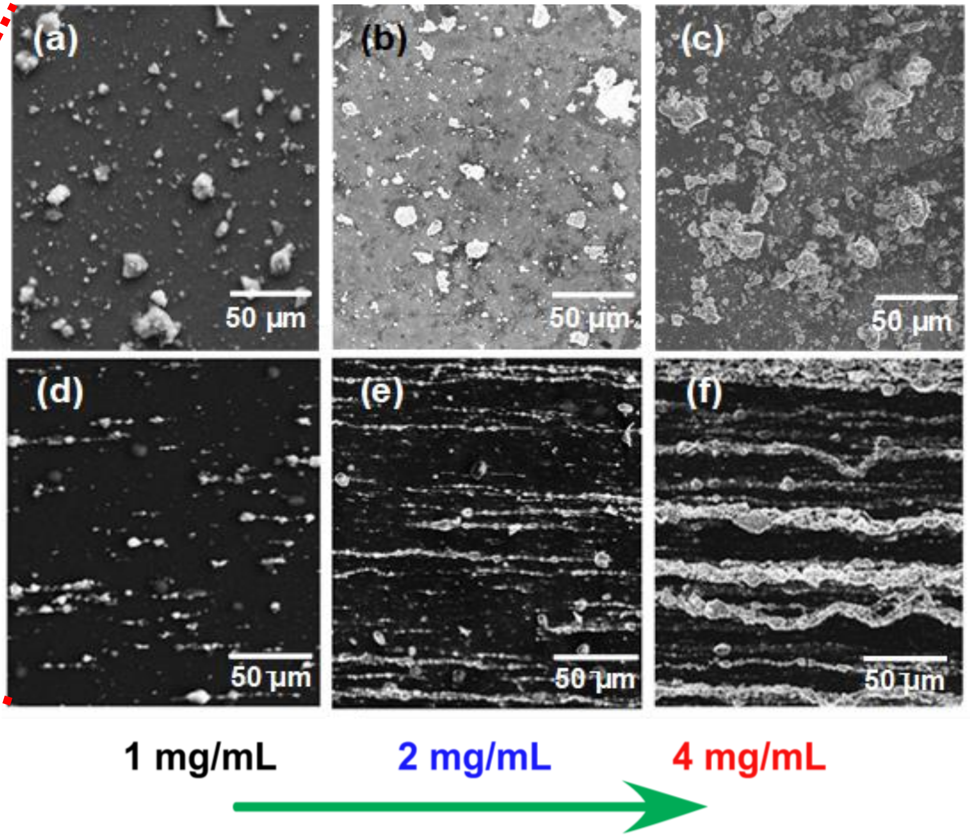


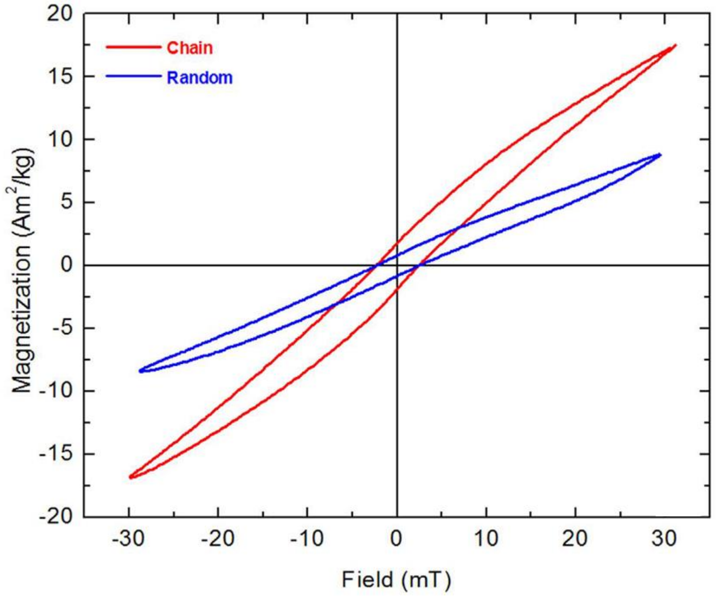


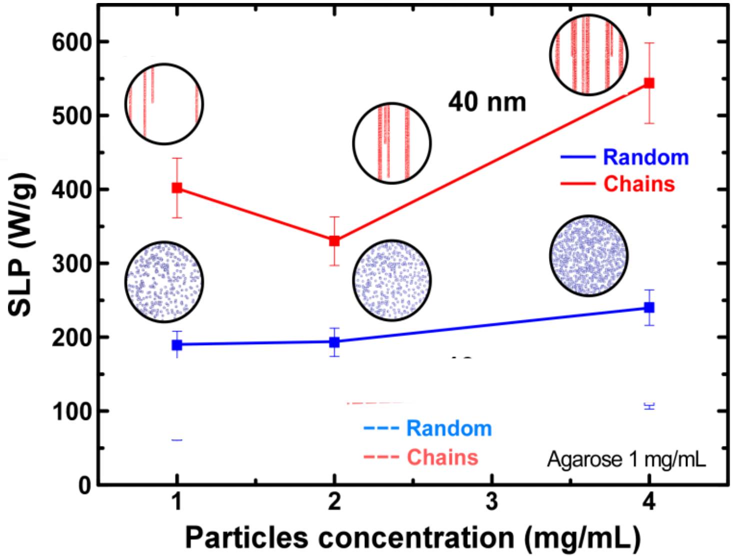
ACS Appl. Nano Mater. 2020, 3, 5, 4465–4476

Which morphology?







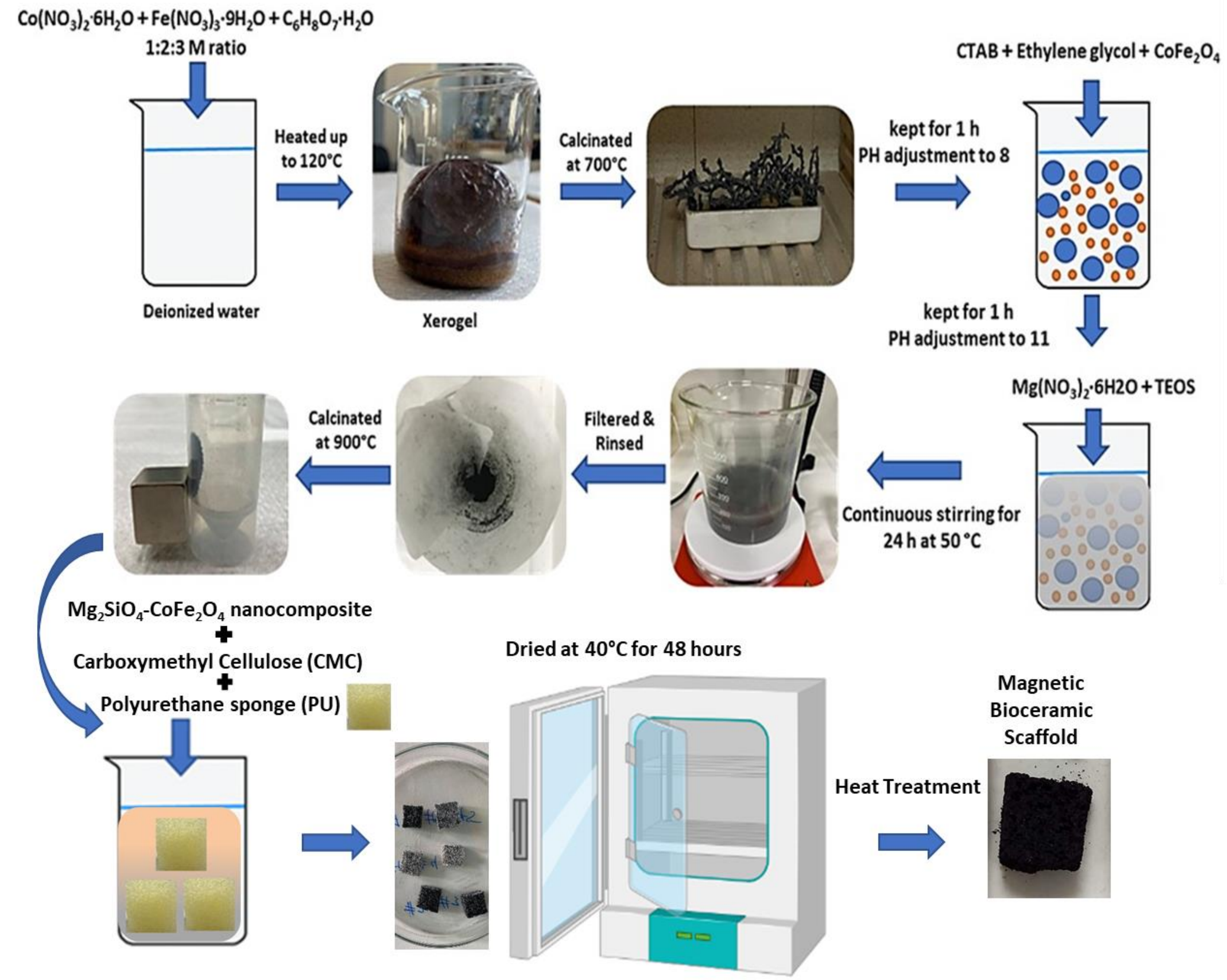


- The hysteresis loop area of the chain is higher than the one of the random case.
- Magnetization rises faster in chains, indicating that the susceptibility is larger.

Scientific Reports, E. Myrovali et al. 6:37934, 2016

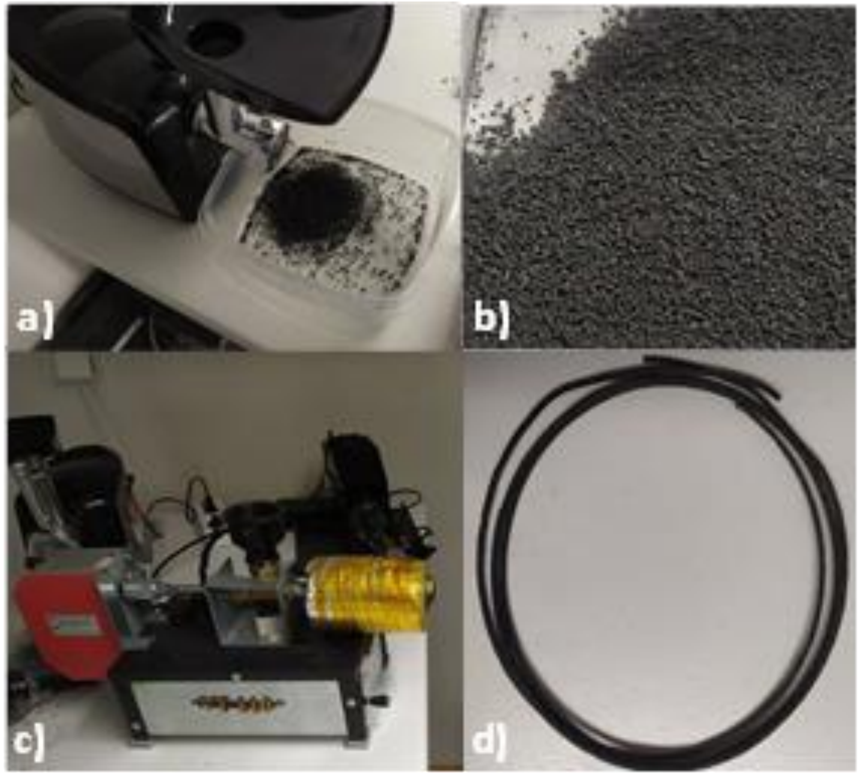
From MNPs to Magnetic Scaffolds

18:46



Synthesis and characterization of a novel multifunctional magnetic bioceramic nanocomposite,
K. Kazeli poster

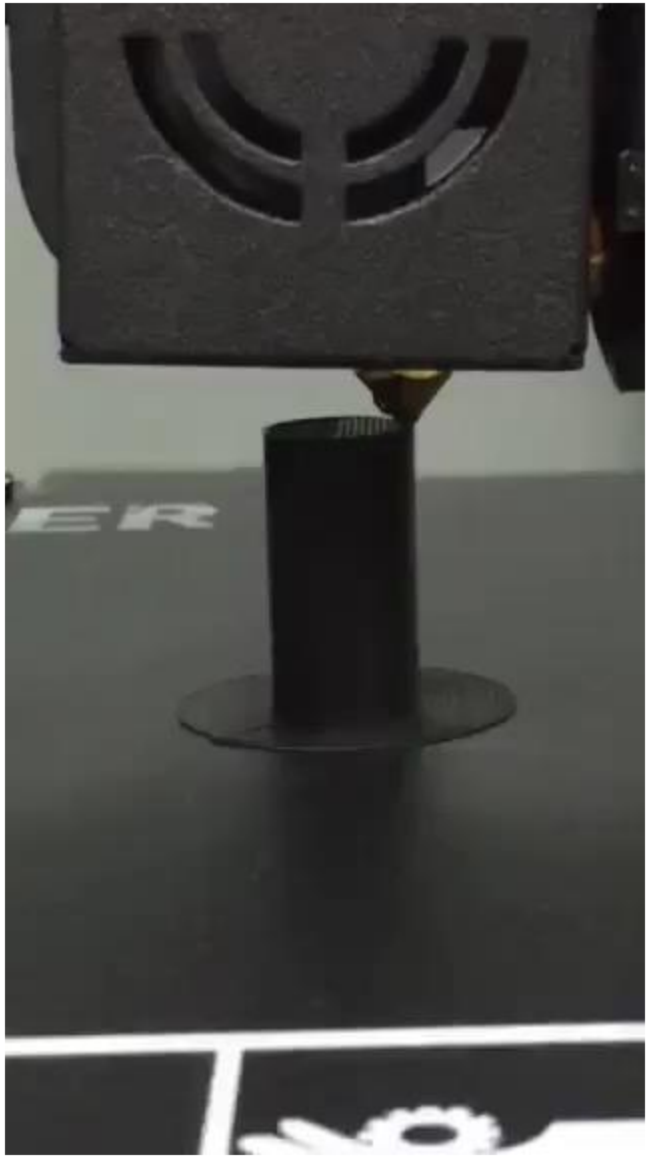
Novel Designs

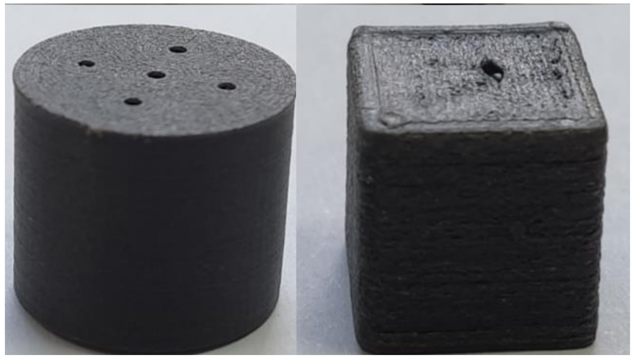


Commercial 3D printing filaments

Homogenous dispersion of MNPs

Tunable magnetic features





3D magnetic printing: From filament fabrication to hyperthermia scaffolds, A. Makridis, oral presentation

Question 2: Which conditions?

Tuning nanomagnetism for biomedical applications

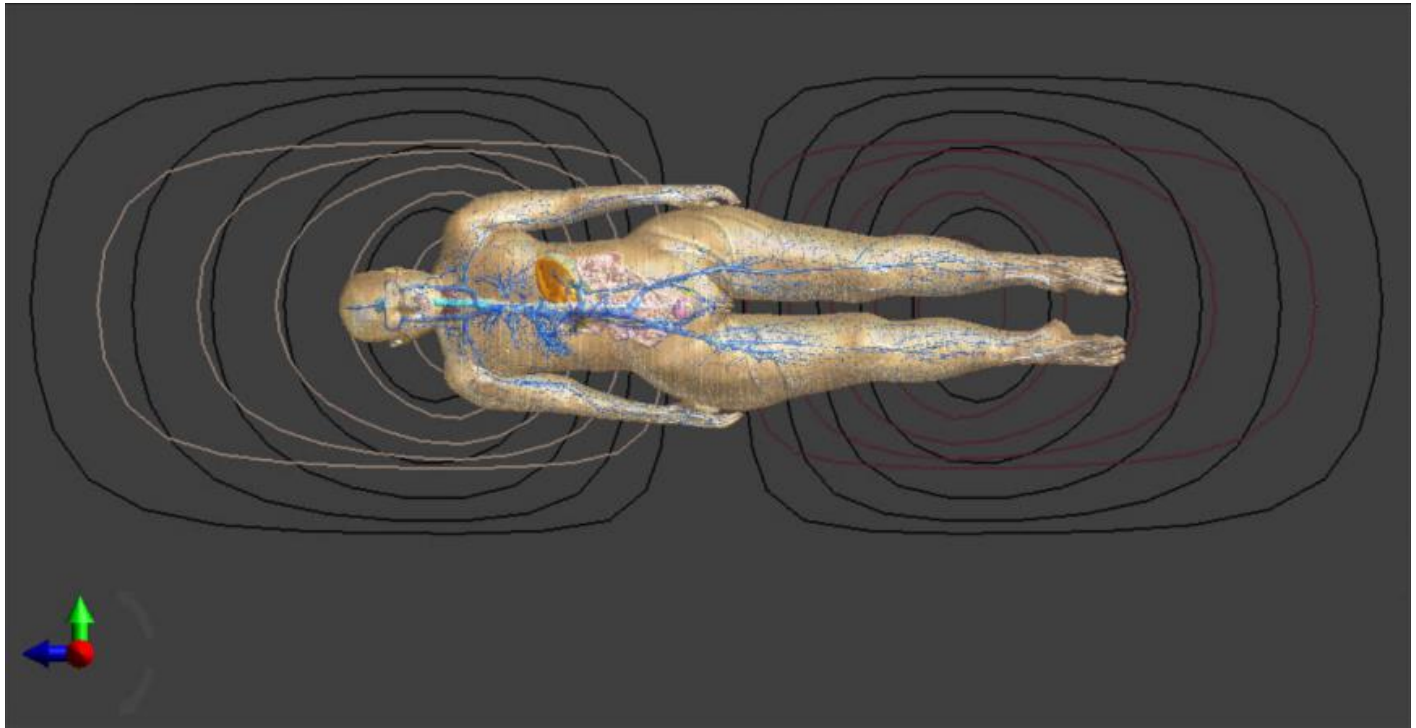
MRI Setup

Typically, magnetic fields in clinical MRI range between 1.5 and 3.0 T, while research MRI scanners beyond 10 T have also been reported.

A typical clinical MRI device consists of a magnetic field setup (major magnet, shim coils and gradient coils) and a signal processing section (radiofrequency [RF] transmitter and receiver, computer to acquire data).

Side effects

- Sim4LifeC software is used for MRI simulation components & conditions
- import the model of a human body (Yoon Sun 26 years old, 1.52 m height, 54.6 kg weight and 23.6 kg/m^2 BMI).
- model contains each tissue, bone, muscle, vain and other organs with realistic values on properties such as thermal and dielectric ones.



Continuous lines around the human body represent the gradient field lines

Nanomedicine, 2021, 16: 11

Side effects of magnetic fields

18:46

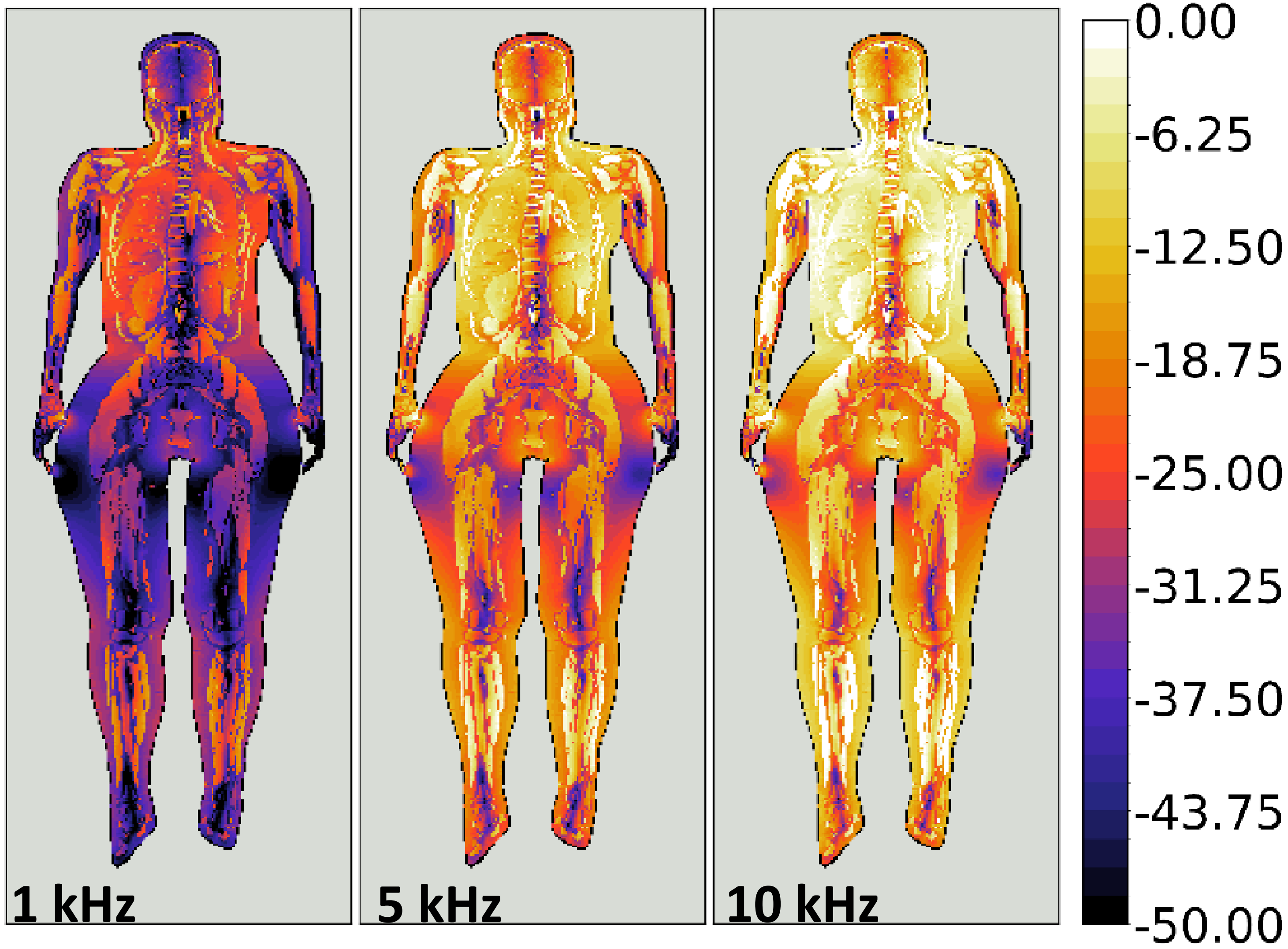


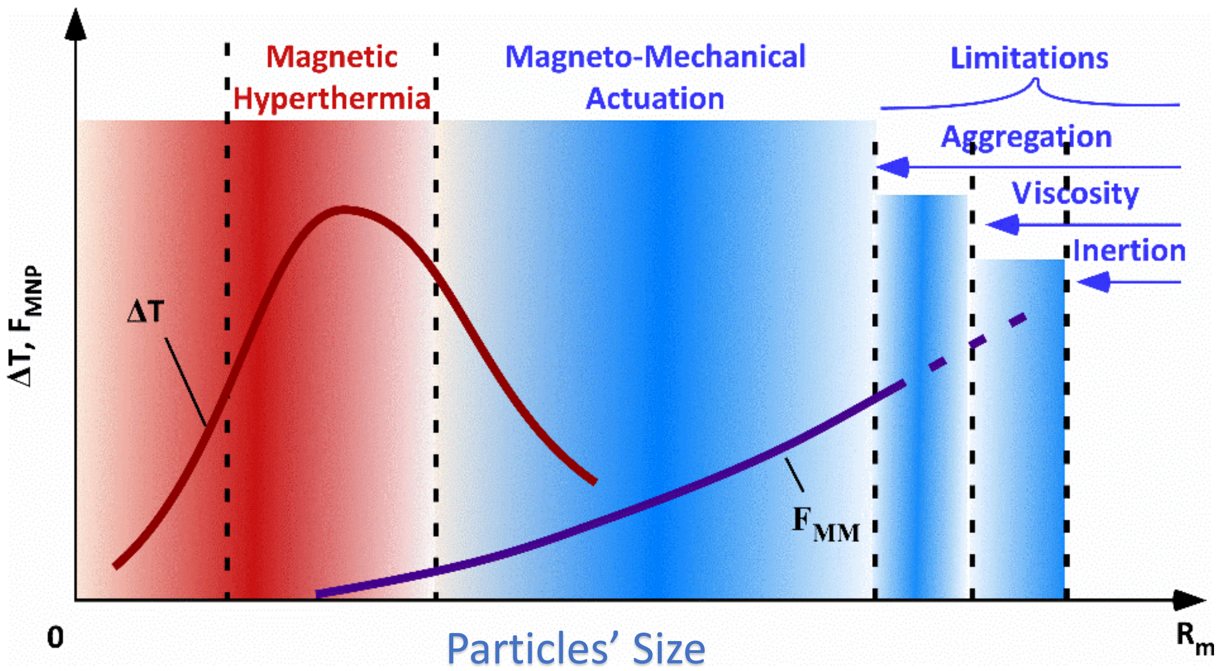
Illustration of the intensity of eddy currents in human body

Color bar in a logarithmic scale corresponds to the intensity of eddy currents measured in A/m^2

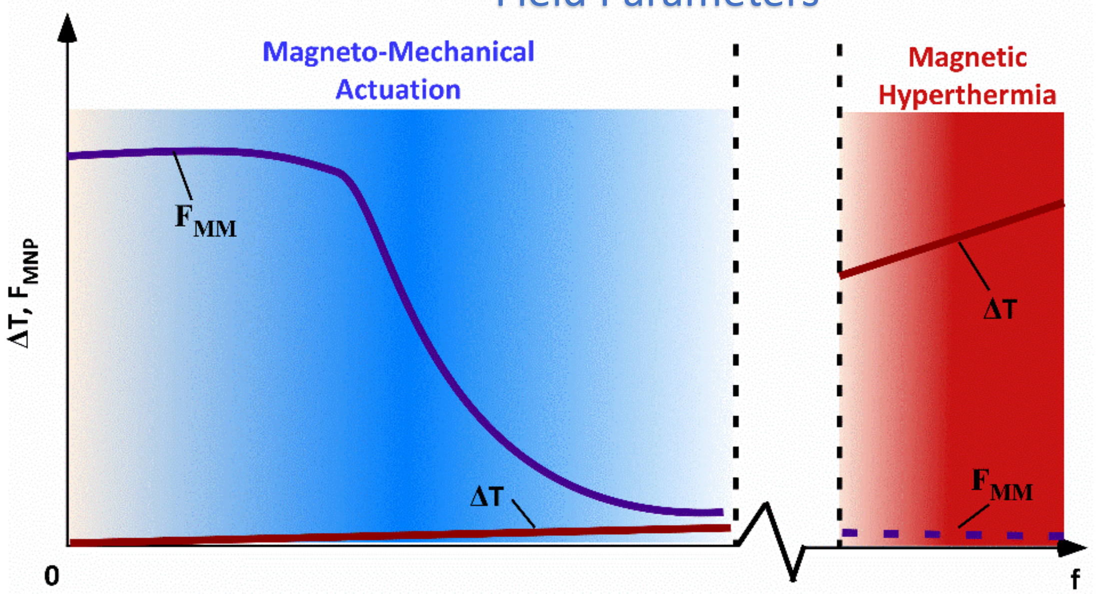
Nanomedicine, 2021, 16: 11

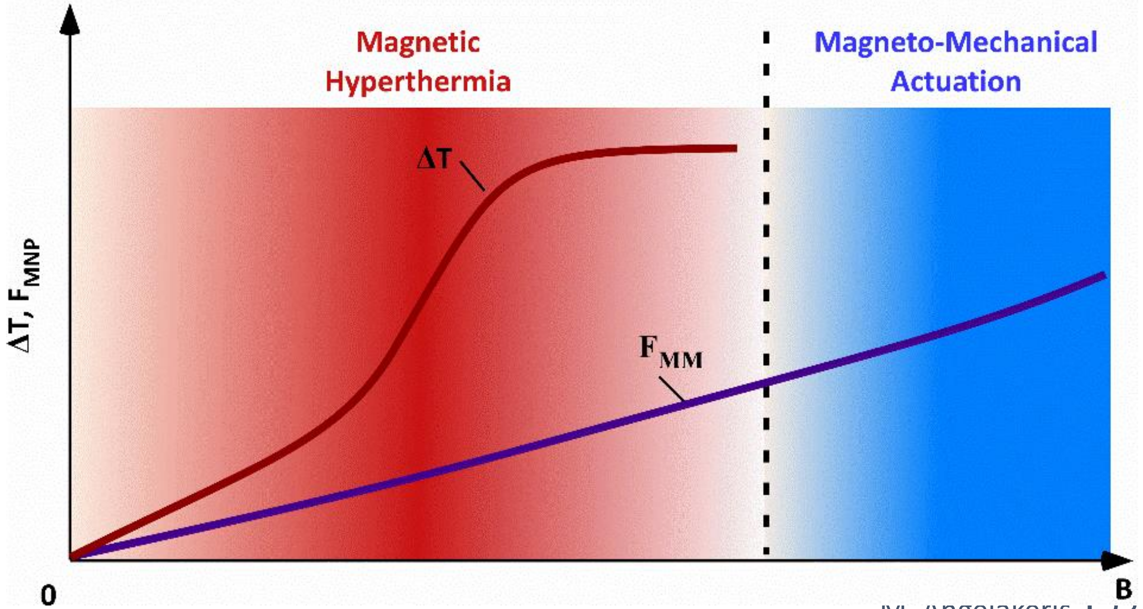
Particles & Fields

Optimal Conditions
for magnetic hyperthermia (ΔT)
and magneto-mechanical (F_{MM}) application



Field Parameters





A. Makridis, PhD Thesis, April 2019, School of Physics-AUTh

Criterion for safe use of magnetic fields

According to the induction law, the induced heating power is proportional to $\mathbf{(H \cdot f \cdot D)^2}$

Atkinson et al developed a treatment system, based on eddy current heating of implantable metal thermoseeds.

Brezovich found for a loop diameter of ~ 30 cm that a 'test person has a sensation of warmth, but withstands the treatment for more than one hour without major discomfort

Exposure to fields where the product $\mathbf{H \cdot f < 4.85 \times 10^8 Am^{-1} s^{-1}}$ is safe and tolerable

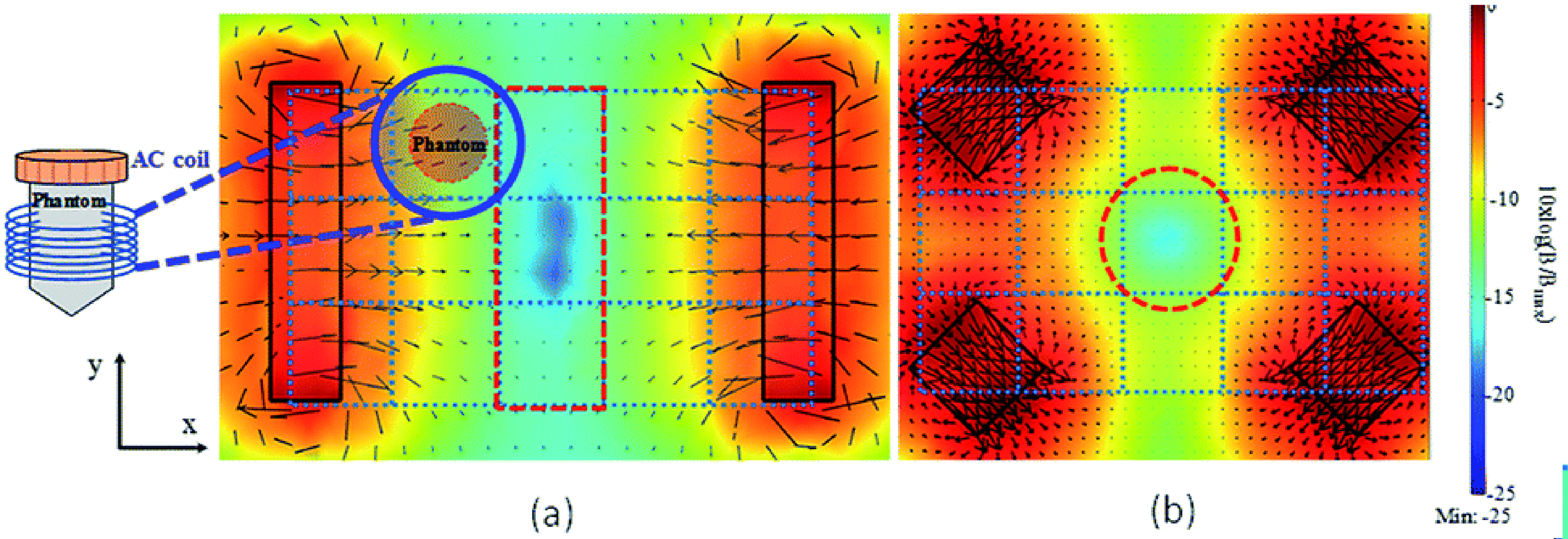
First commercially developed equipment (Gneveckow et al 2004)

reached a product of $1.8 \cdot 10^9 Am^{-1} s^{-1}$

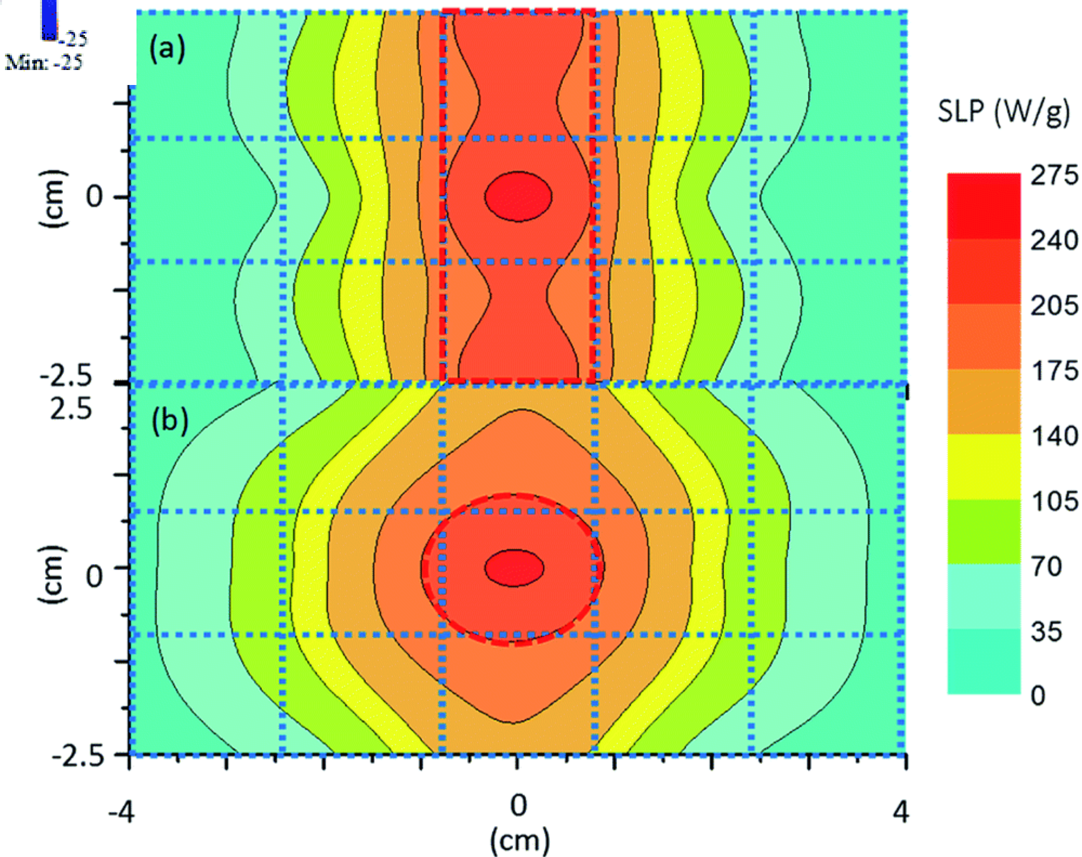
but for smaller diameter of the body region and smaller time scale

Particle type dependent magnetic losses: SPM particles ~ H^2, FM particles ~ H^3

Field Focus



minimization of heat side-impact on surrounding healthy tissues



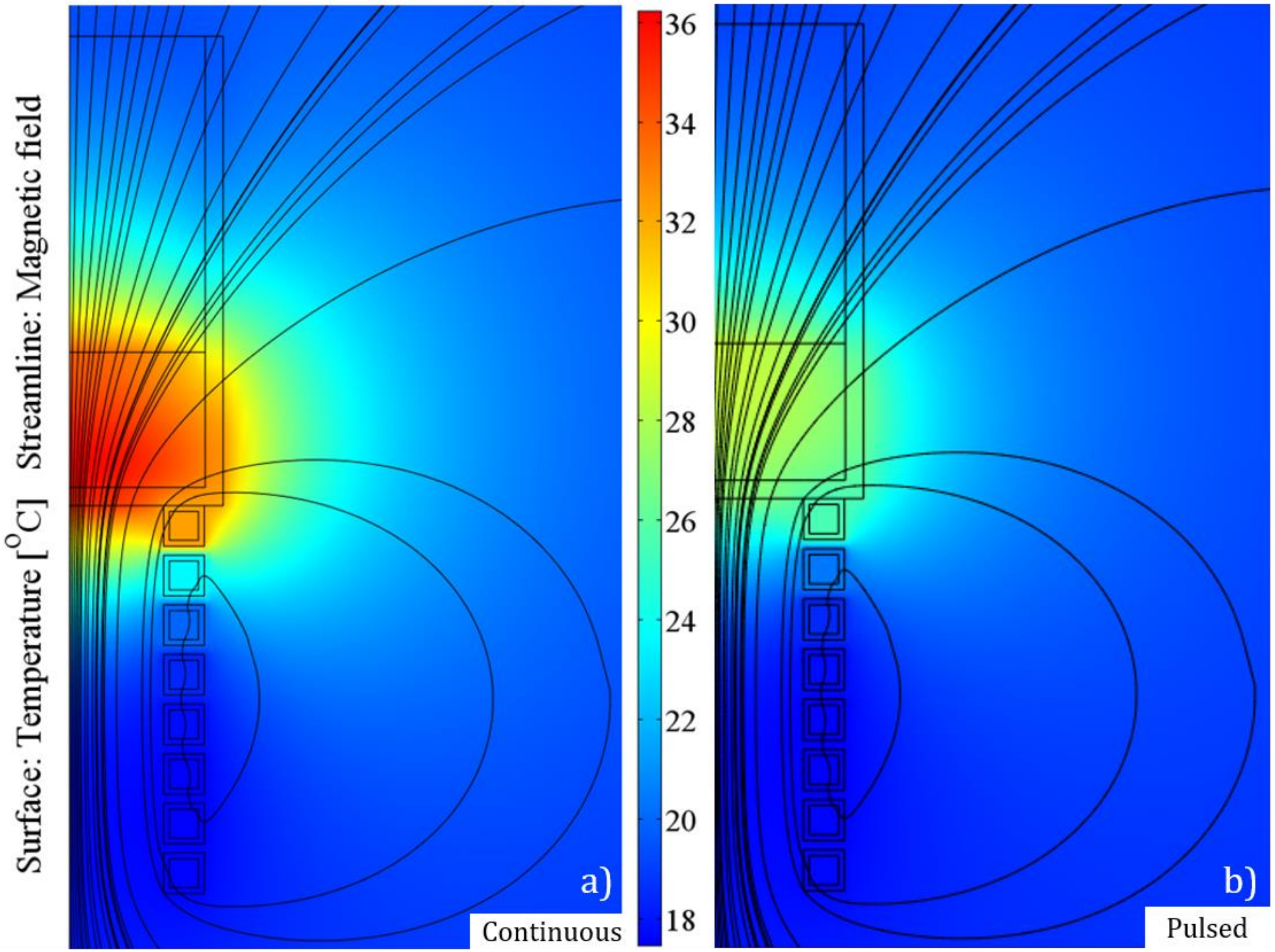
MPH much more effective

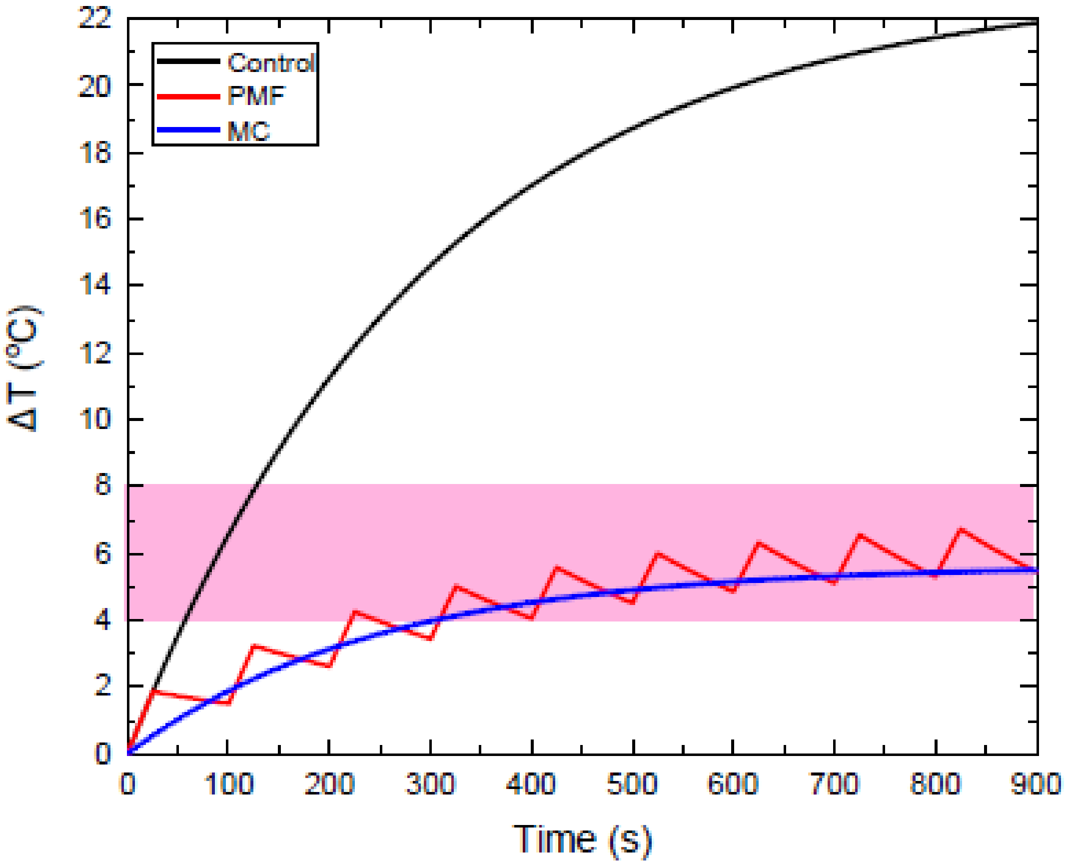
- better focusing capabilities
- tunable heat localization

Nanoscale Adv., 2020,2, 408-416

Field ON/OFFs

18:46

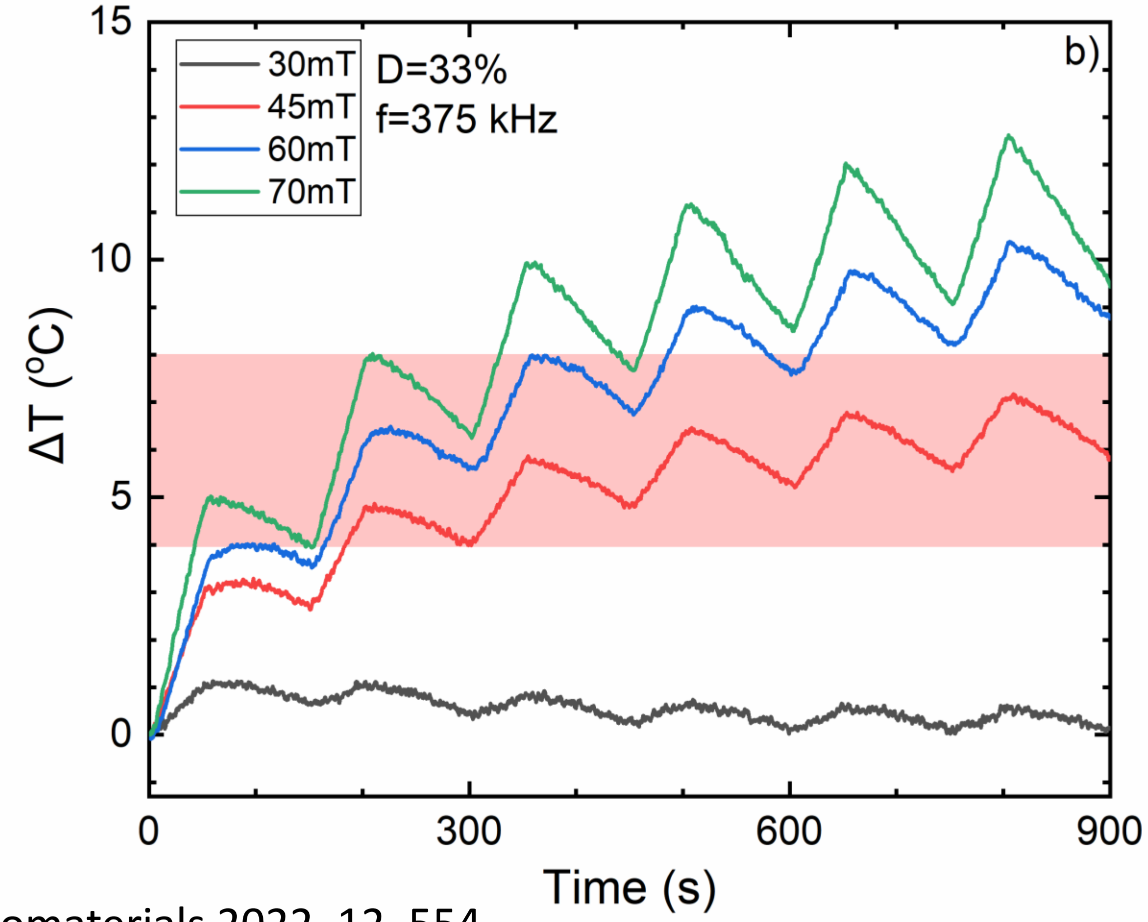


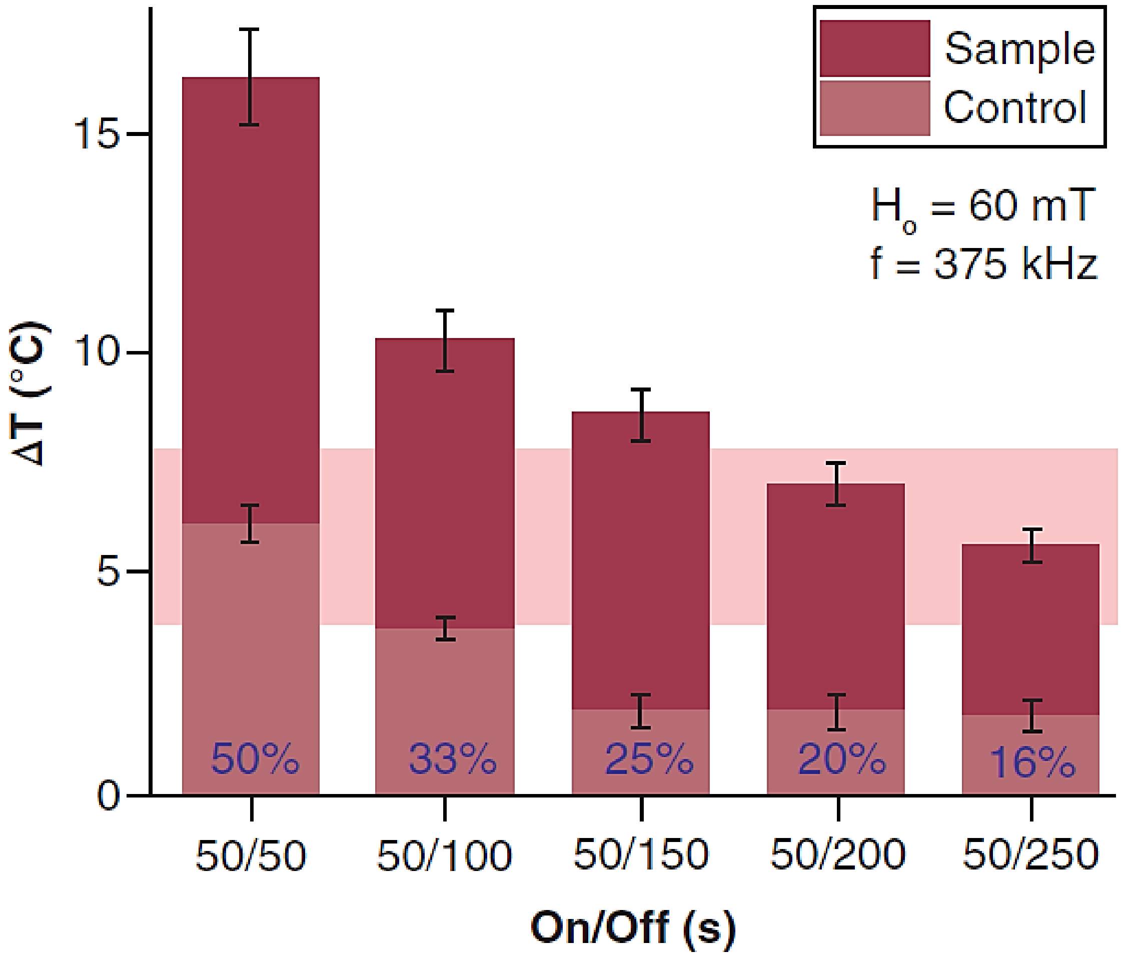


Nanomaterials 2022, 12, 554
Int J Hyperthermia 2021;38(1):511-522
Nanomedicine, 2021, 16: 11

Field ON/OFFs

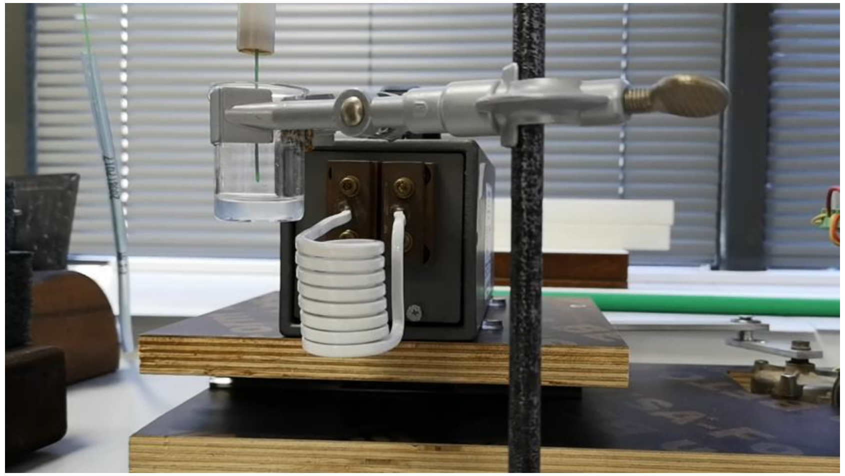
$$\text{Duty Cycle} = \frac{\text{Field ON time (s)}}{\text{Field ON time (s)} + \text{Field OFF time (s)}} \text{ x } 100\%$$

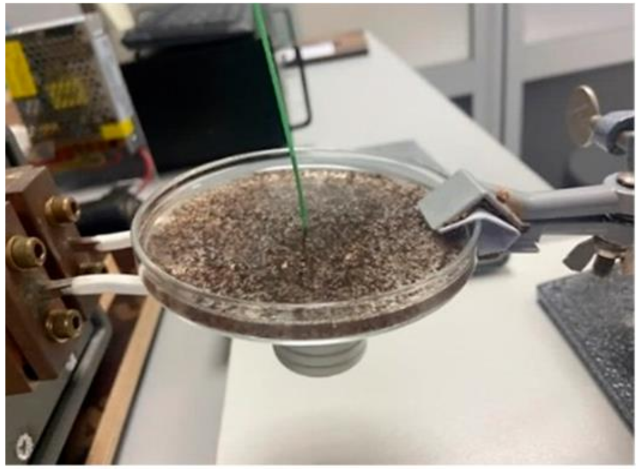


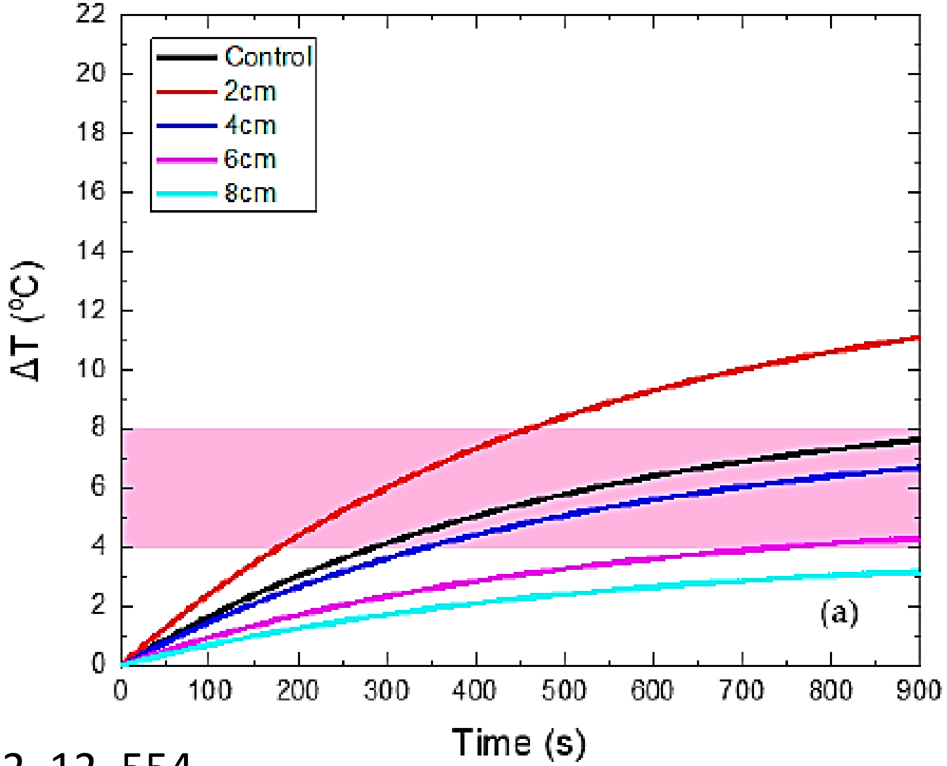


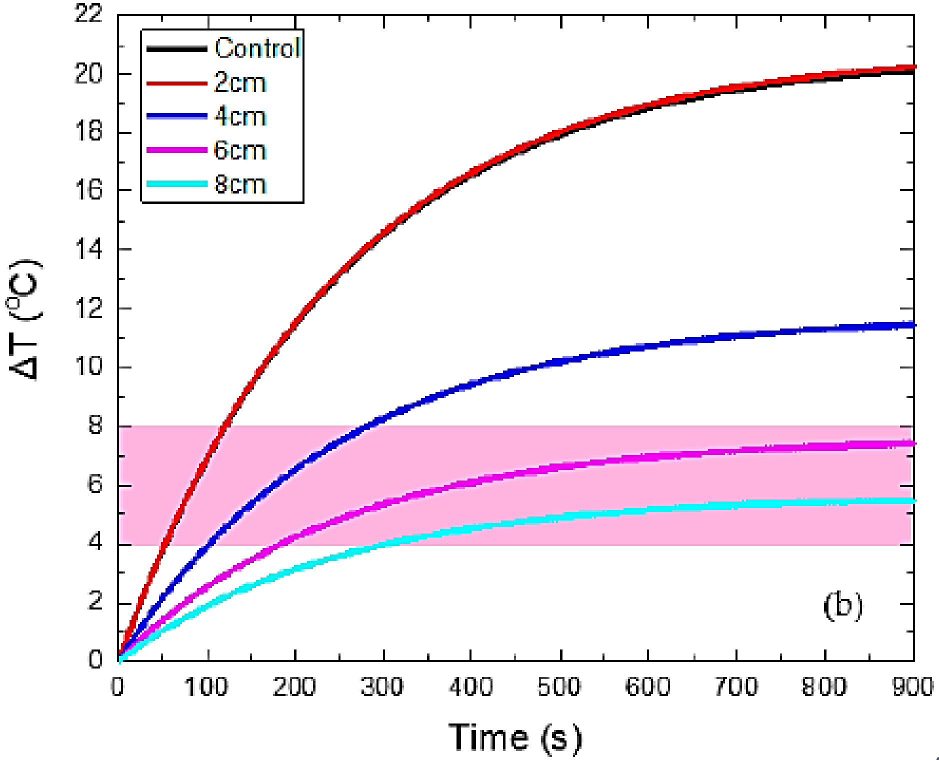
Nanomaterials 2022, 12, 554
Int J Hyperthermia 2021;38(1):511-522
Nanomedicine, 2021, 16: 11

Field IN/OUTs



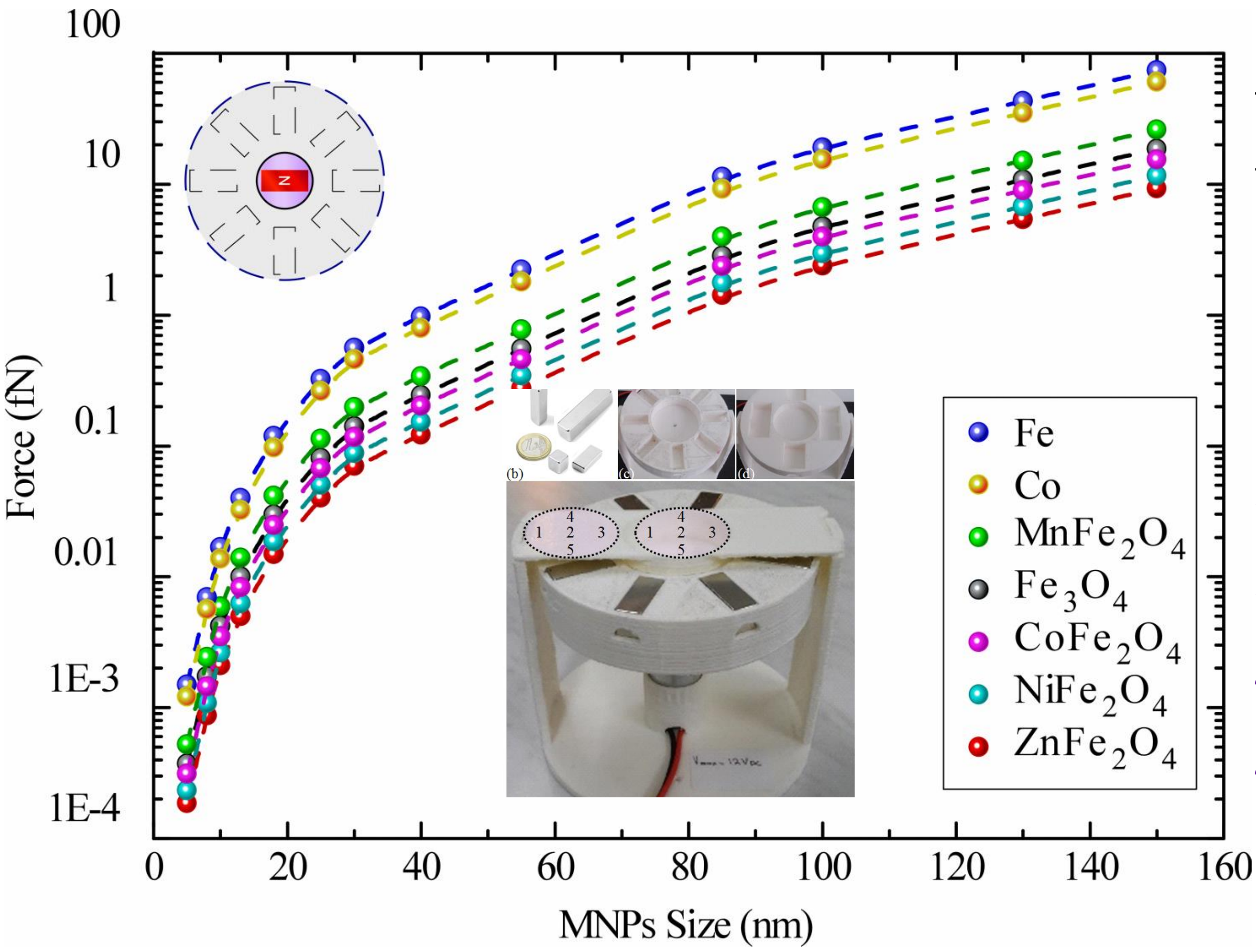






Nanomaterials 2022, 12, 554

Field modes



Collective forces (/cell) range from 10 to 750 pN, when the corresponding nanoparticle concentration varies from 10 to 250 pg/cell, respectively.

Forces of such strength (tens to hundreds of pN) acting on different cell types can reprogram and cause an effect on cell's differentiation.

1-10 pN: *internal cytoskeleton stress*

10-100 pN: *stretch a DNA molecule*

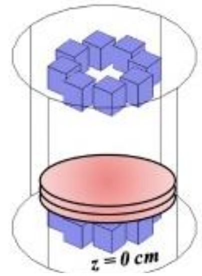
5-70 pN: *neuron cells, mechanical sensitivity*

50-460 pN: *intracellular transport of the macrophages in the cytoplasm*

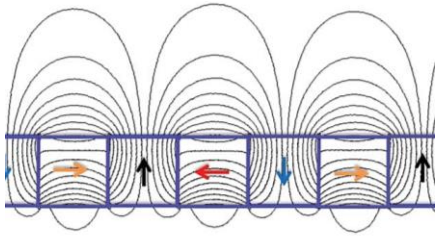
N. Maniotis et al. JMMM 2017

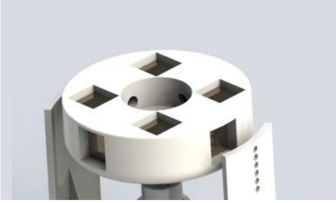
Field modes

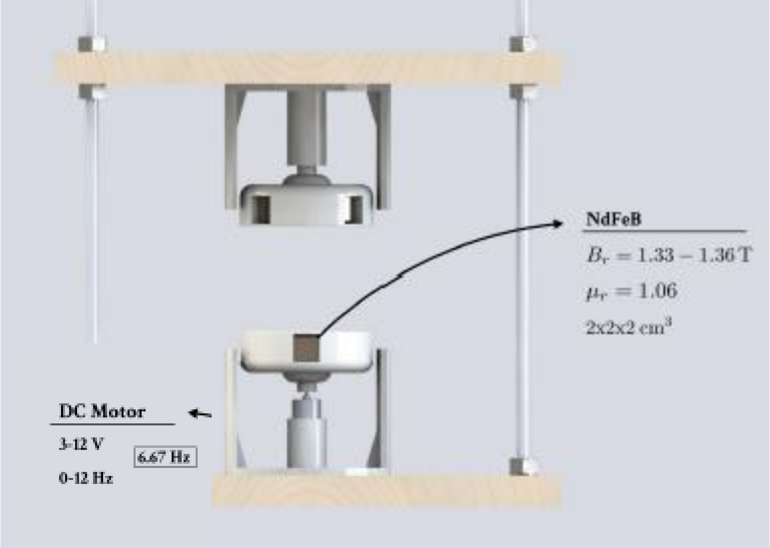
A Halbach array is an arrangement of permanent magnets that makes the magnetic field on one side of the array stronger, while cancelling the field to near zero on the other side.



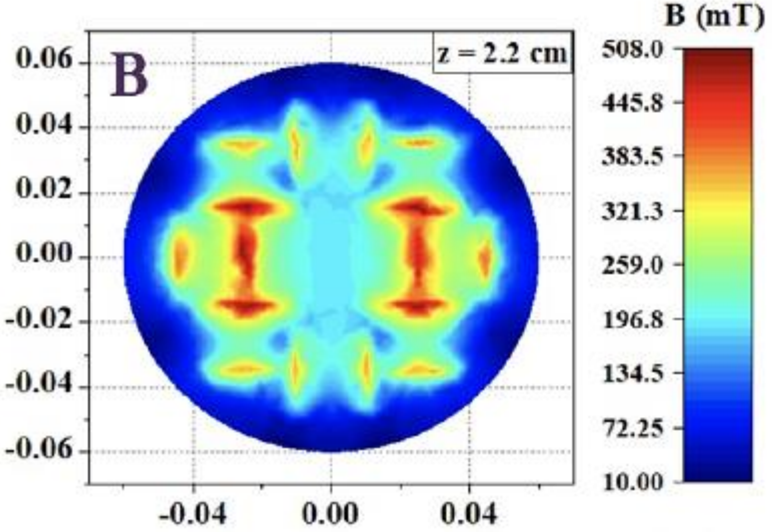
z = 2.2 cm

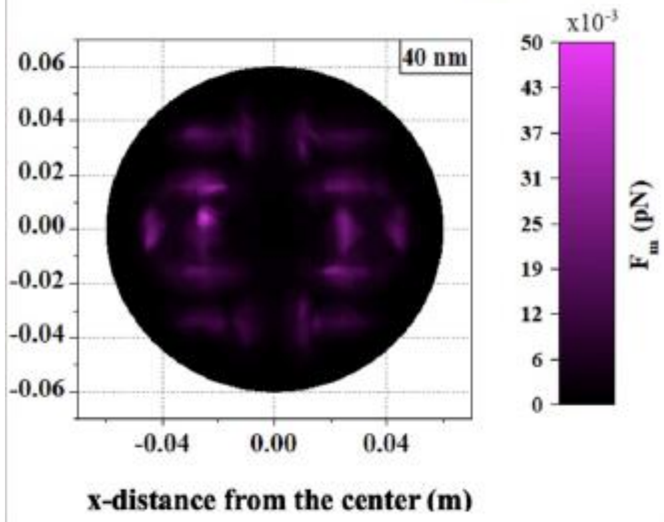






∇B





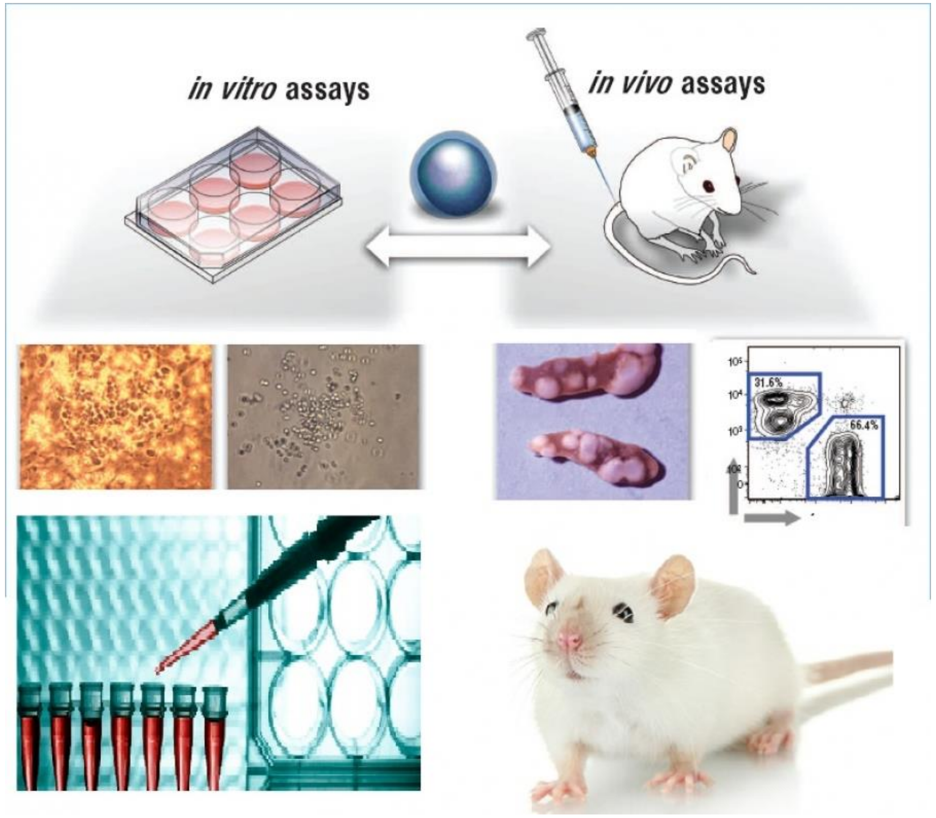
F_m

Question 3: How will it perform in bio?

Tuning nanomagnetism for biomedical applications

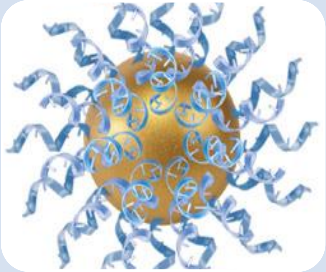
Biomedical Constraints

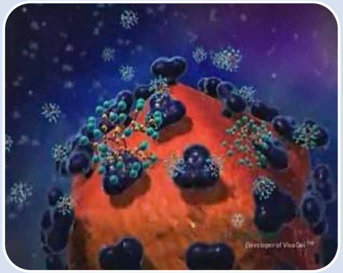
In silico → *In vitro* → *Ex vivo* → *In vivo*



- **Biocompatible surface**
- **Long blood half-life**
- **Minimal toxicity**
- **Colloidal stability over a wide pH range**
- **Evade or Allow uptake by RES**
- **Specific biomolecule Interactions**

The 3Ds





Dose

Concentration

Dosology

Dimensions

Size

Surface Area

Aspect Ratio

Durability

Chemictry

Crystal Structure

Surface Cover

Functionalization

Biomedical Constraints

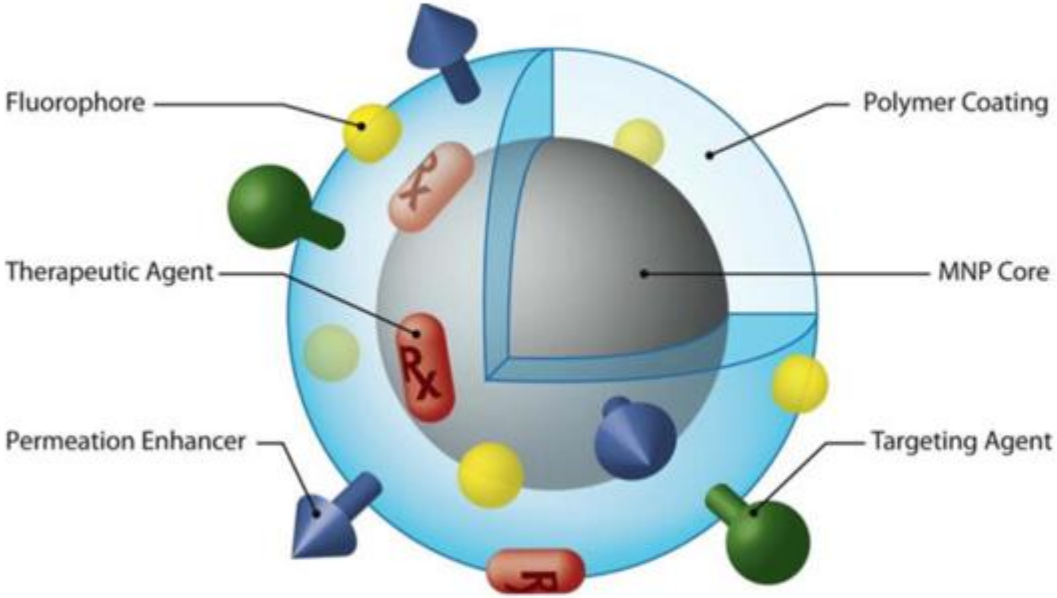
Stronger magnetic response to minimize size & dosage

Direct instead of intravenous injection

Functionalization to

selectively target malignant sites and

sustain hostile environment



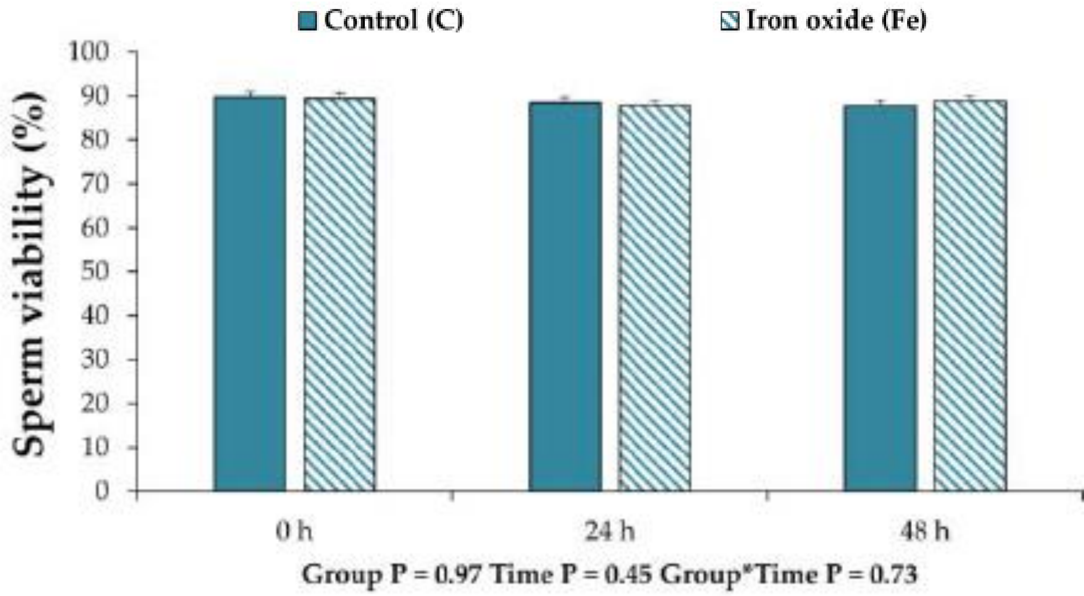
MNPs as Antibiotics

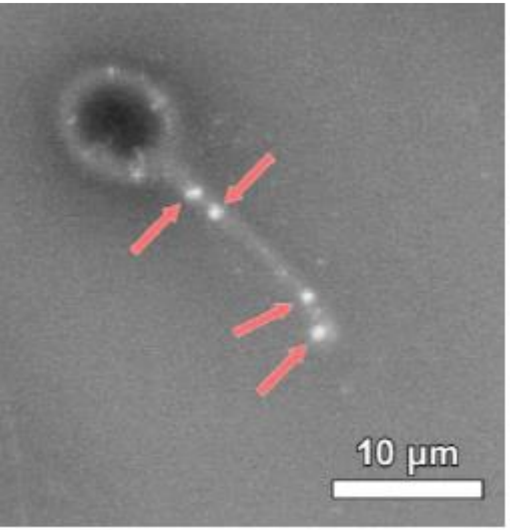
nanomaterials

Nanomaterials **2020**, 10, 1568

Article

Iron Oxide Nanoparticles as an Alternative to Antibiotics Additive on Extended Boar Semen





- ✓ Semen samples of control group (C) and group Fe with Fe_3O_4 (Fe; 0.192 mg/mL semen)
- ✓ The samples after treatment were stored (17 C) for 48 h
- ✓ and sperm parameters (computer-assisted sperm analyzer (CASA) variables; morphology; viability, hypo-osmotic swelling test (HOST); DNA integrity) were evaluated at storage times 0, 24, 48 h.
- ✓ The microbiological results revealed a significant reduction of the bacterial load in group Fe compared to control at both 24 and 48 h.

animals

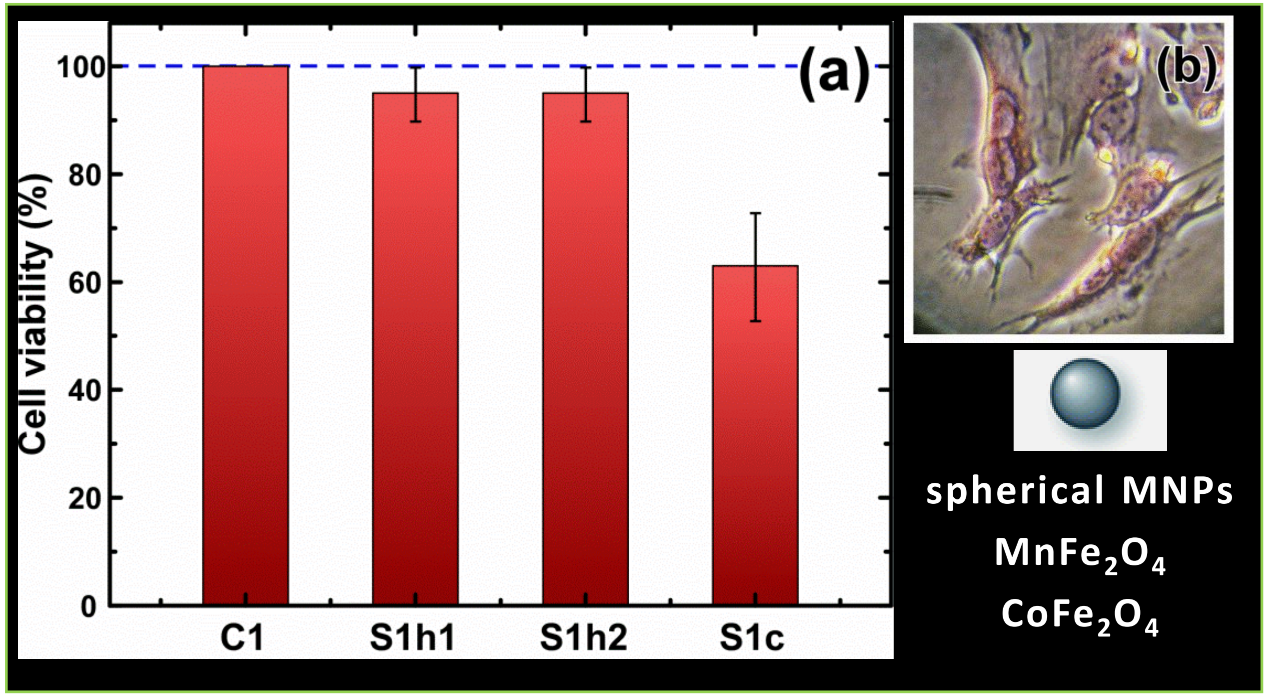
Animals **2021**, 11, 1011.

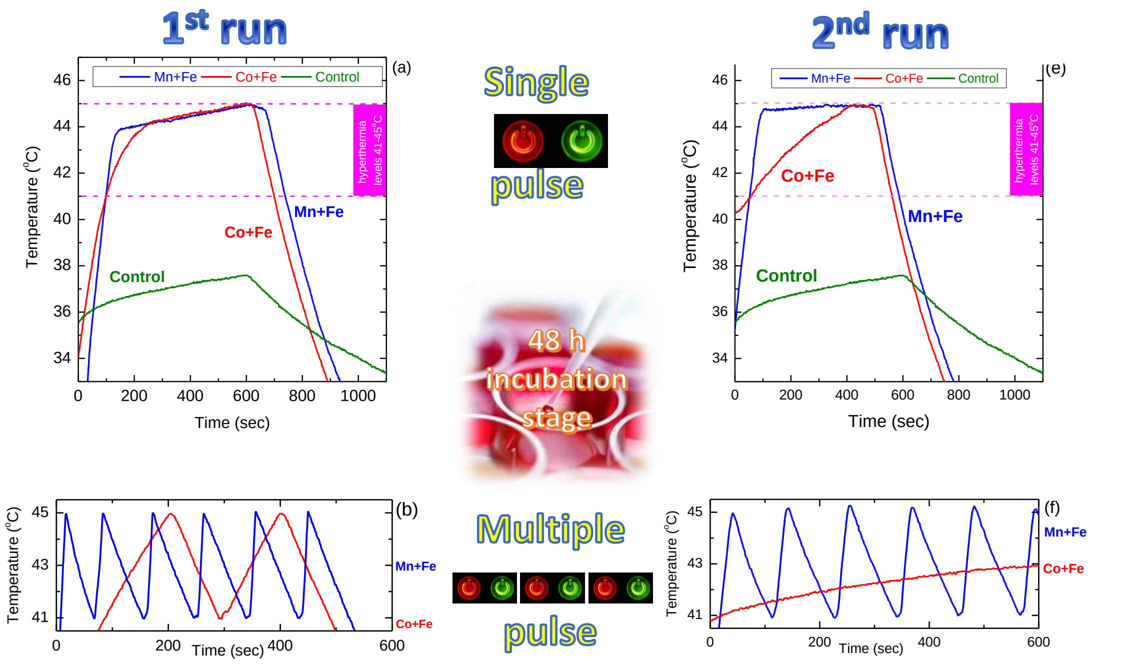
MDPI

Article

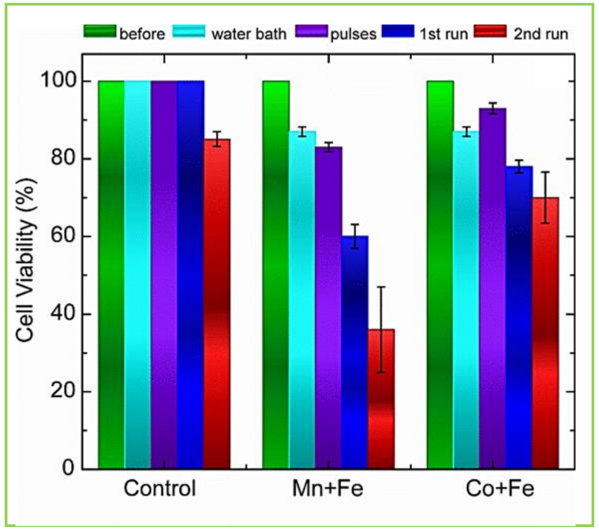
Toxic and Microbiological Effects of Iron Oxide and Silver Nanoparticles as Additives on Extended Ram Semen

Field ON/OFFs





Comparative viability for the three cell lines : S1h1: primary bone marrow-derived osteoblasts, S1h2: 3T3-L1 fibroblast-like preadipocytes, C1 and S1c: Saos-2 osteoblasts control and sample (b), (c) Optical microscope images (36x) of Saos-2 osteoblast cell line control sample and MNPs after Prussian blue staining.

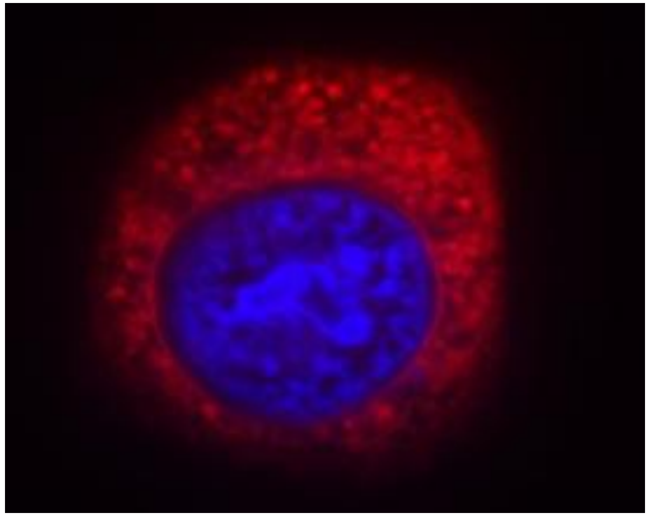


J. Mater. Chem. B, 2014, 2, 8390.
Int J Hyperthermia, 2017, 32(7):778-85.

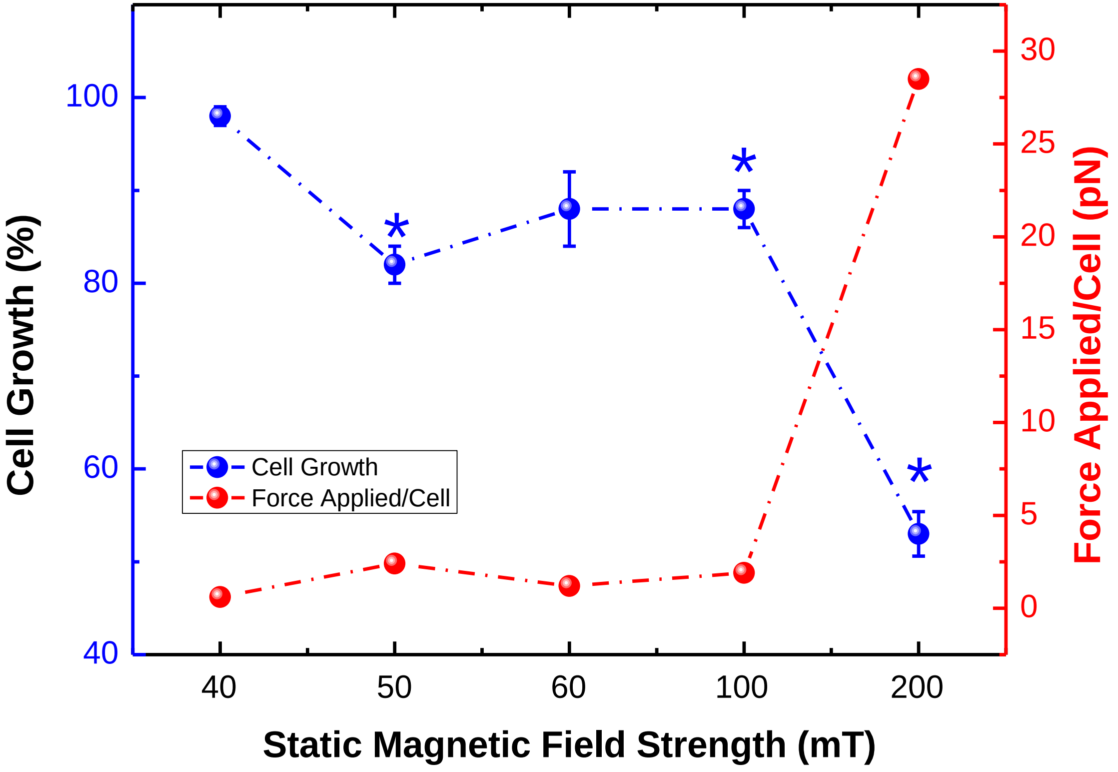
Field modes

Non-cytotoxic concentration of nano-screenMAG/R and fluidMAG-D (100 nm) nanoparticles for HT29 cells, after a co-incubation period for up to 48 hours, with the SRB assay).

100 µg/mL of MNPs do not inhibit proliferation of HT29 cells, compared to control, untreated cells.



Internalization of nano-screenMAG/R (100 nm) by HT29 cells after 48 h of incubation (100 µg/mL).



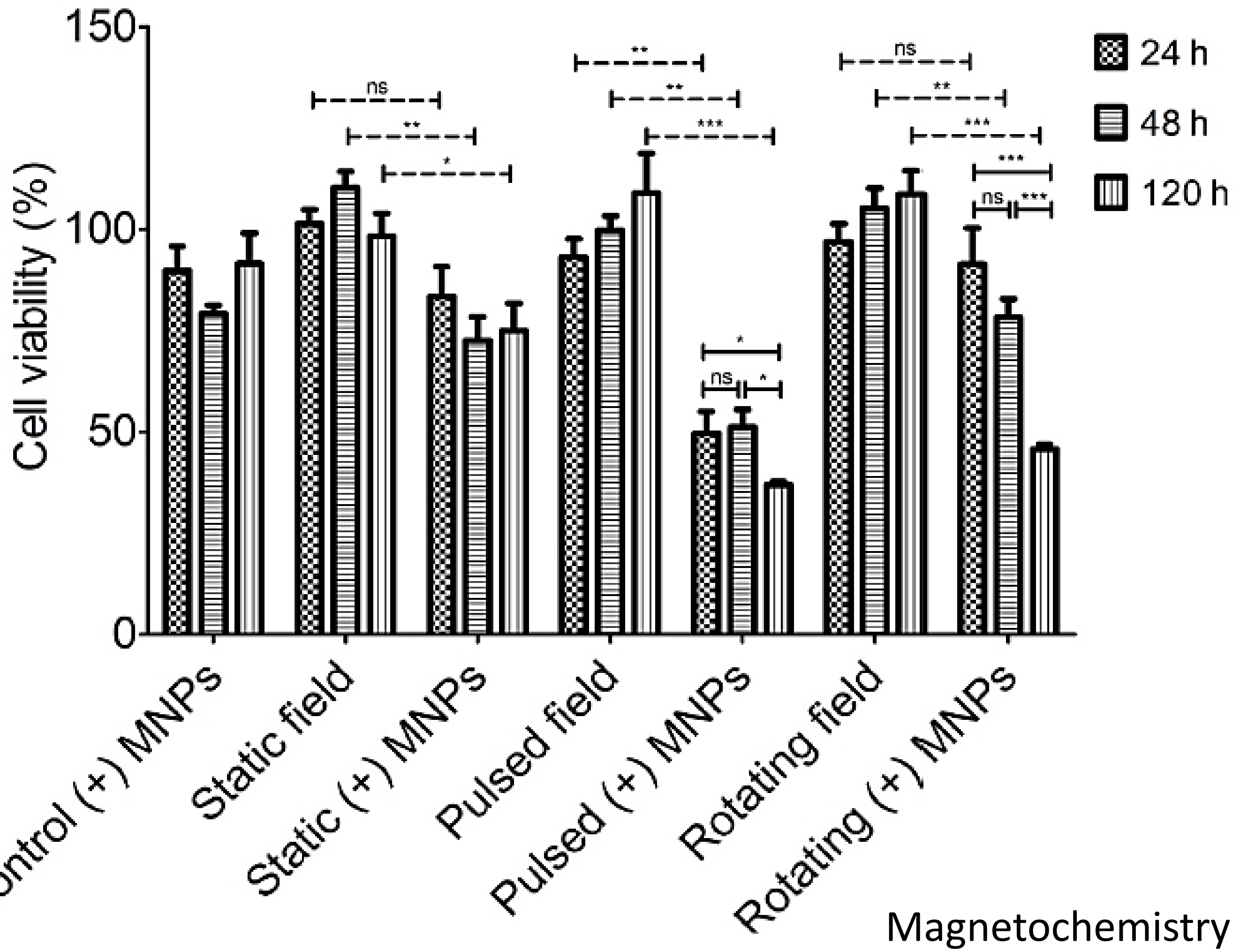
Cell growth dependence on magnetic flux density magnitudes and subsequent applied forces, exerted from external static magnetic fields of various strengths on endocytosed magnetic nanoparticles.

Journal of Magnetism and Magnetic Materials 470, 6-11, 2019
Nanotechnology ***29****, 17, 175101 (2018).*

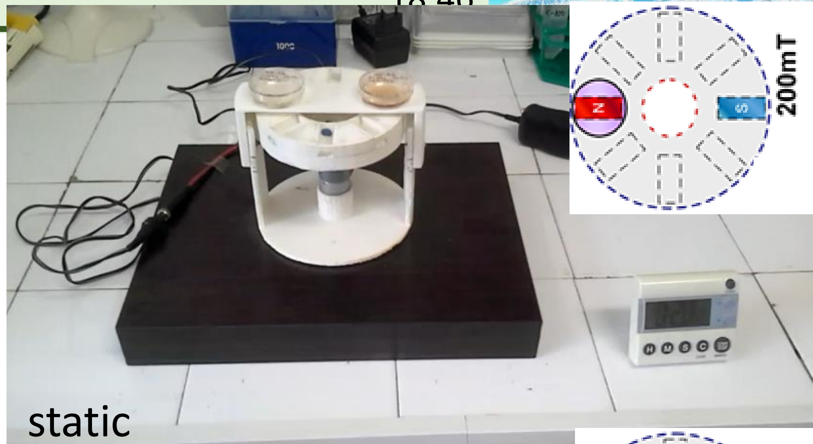
Field modes

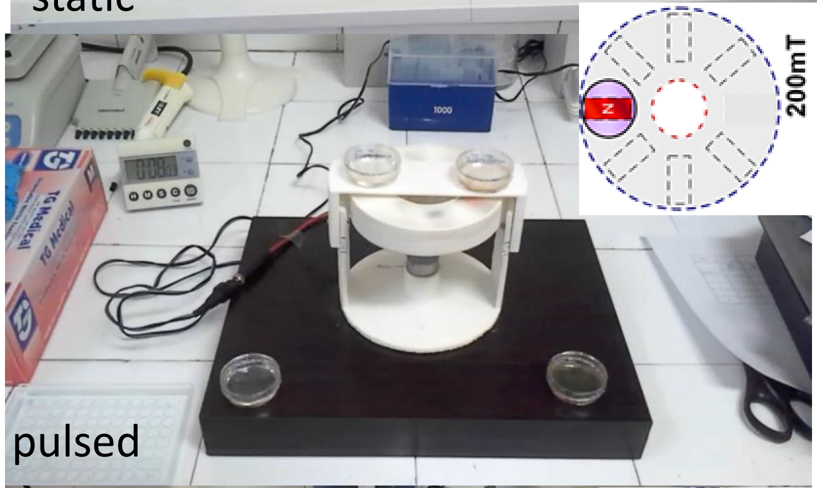
Cell Behavioral Changes after the Application of Magneto-Mechanical Activation to Normal and Cancer Cells

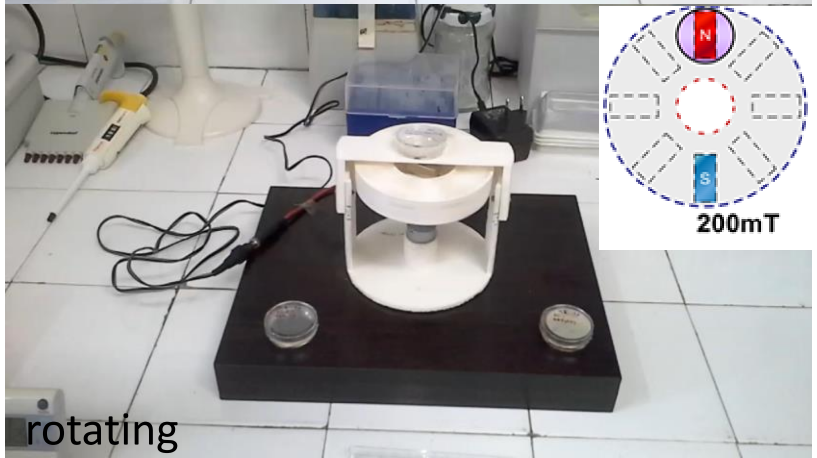
Cancer:MCF-7, MDA-MB-231 and normal: MCF-10A



Magnetochemistry **2022**, 8, 21

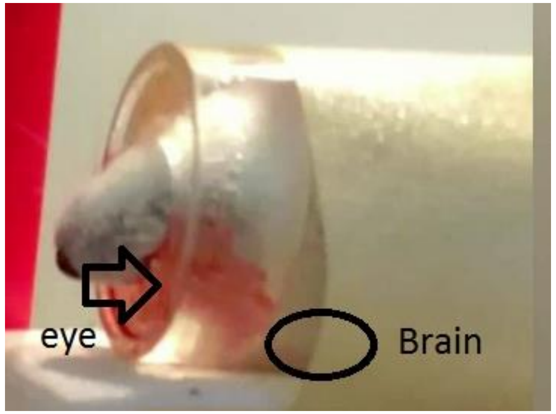






Field modes in-vivo

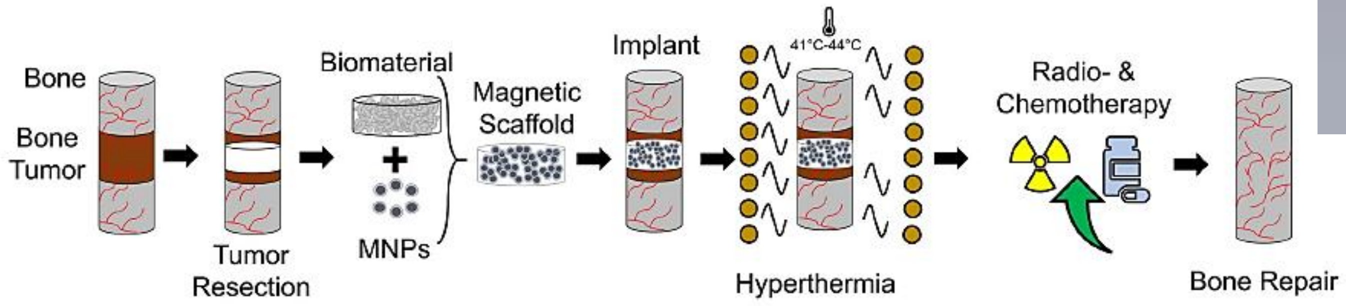
18:46

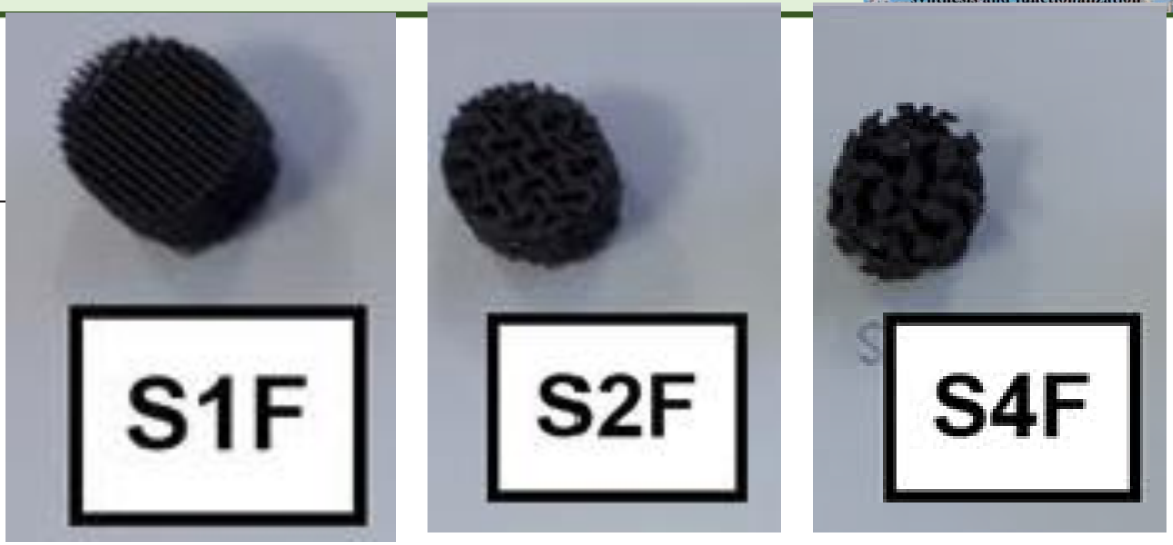


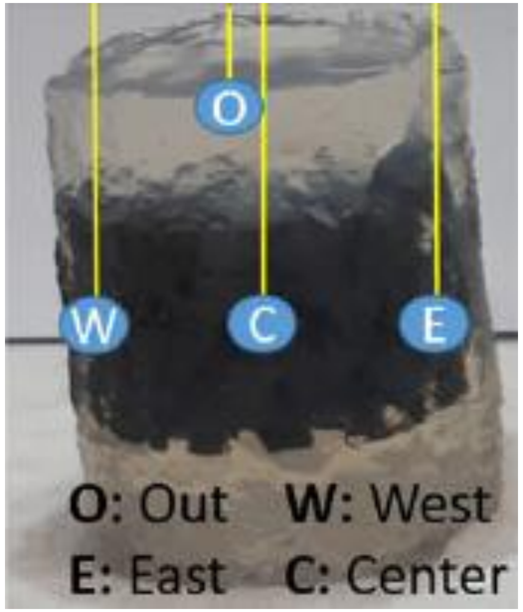
IEEE Access
Multidisciplinary ⁝ Rapid Review ⁝ Open Access Journal

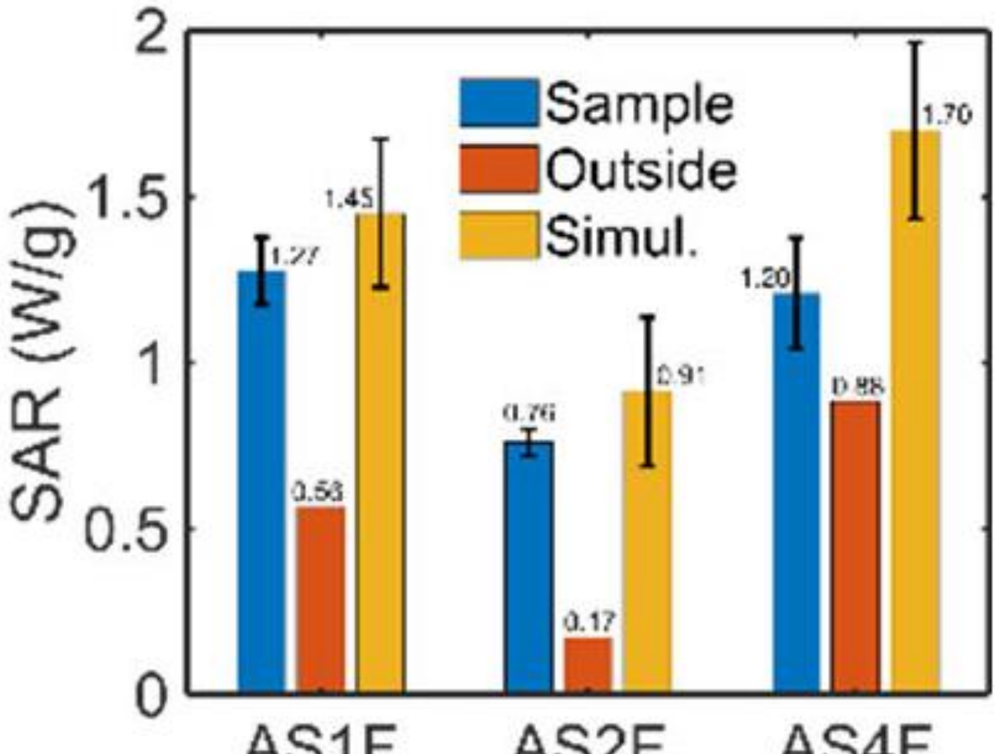
IEEE Access, vol. 10, pp. 19768-19779, 2022

Design and Characterization of Magnetic Scaffolds for Bone Tumor Hyperthermia









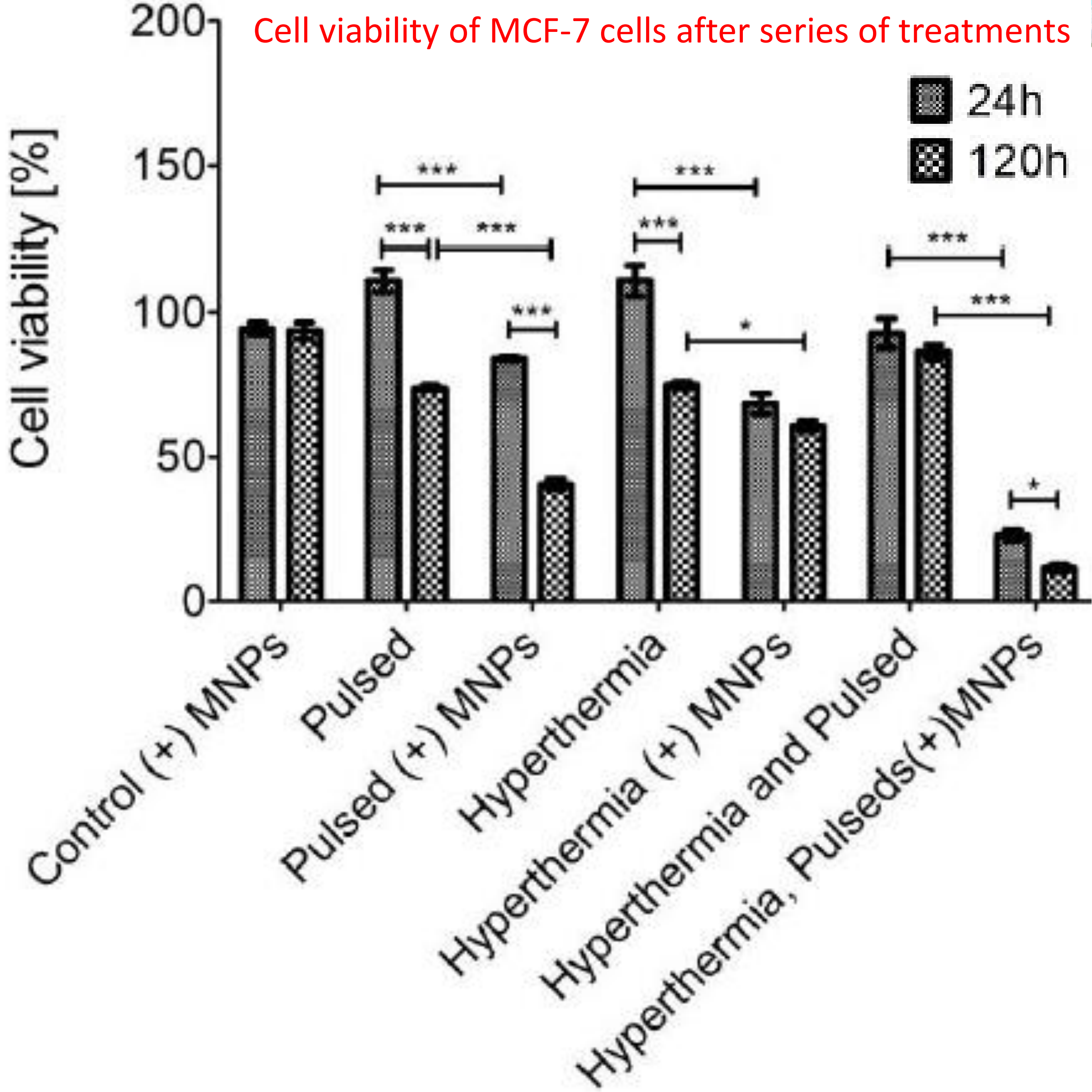
Synergies

breast cancer (MCF-7) and non-cancerous (MCF-10A) cells with and without MNPs were treated

(a) for 15 min with magnetic hyperthermia,

(b) for 30 min with magneto-mechanical activation,

(c) by a successive treatment consisting of a 15-min magnetic hyperthermia cycle and 30 min of magneto-mechanical activation.



magnetochemistry
MDPI

Article

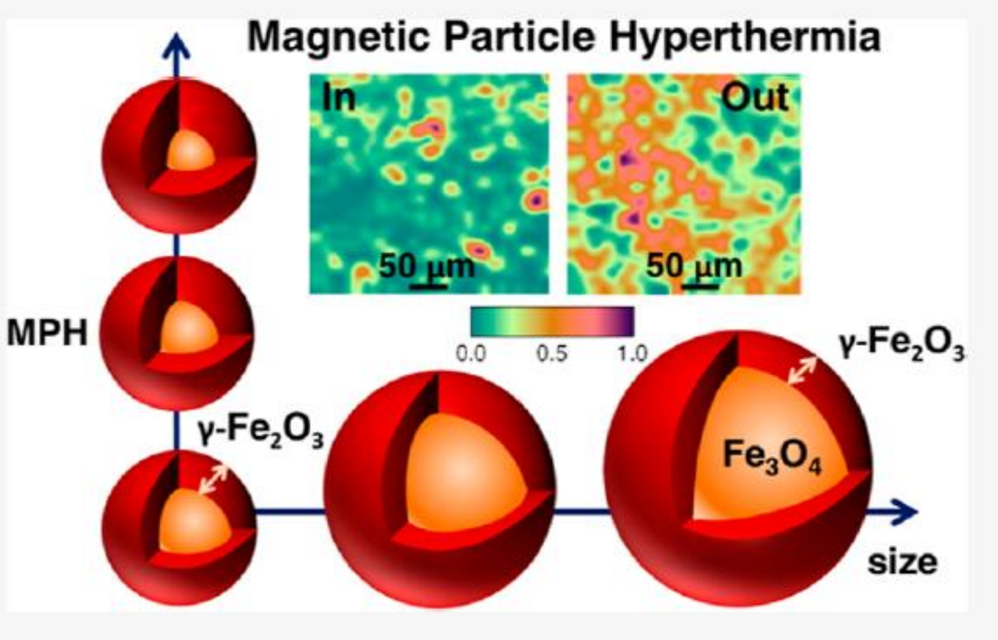
Synergistic Effect of Combined Treatment with Magnetic Hyperthermia and Magneto-Mechanical Stress of Breast Cancer Cells

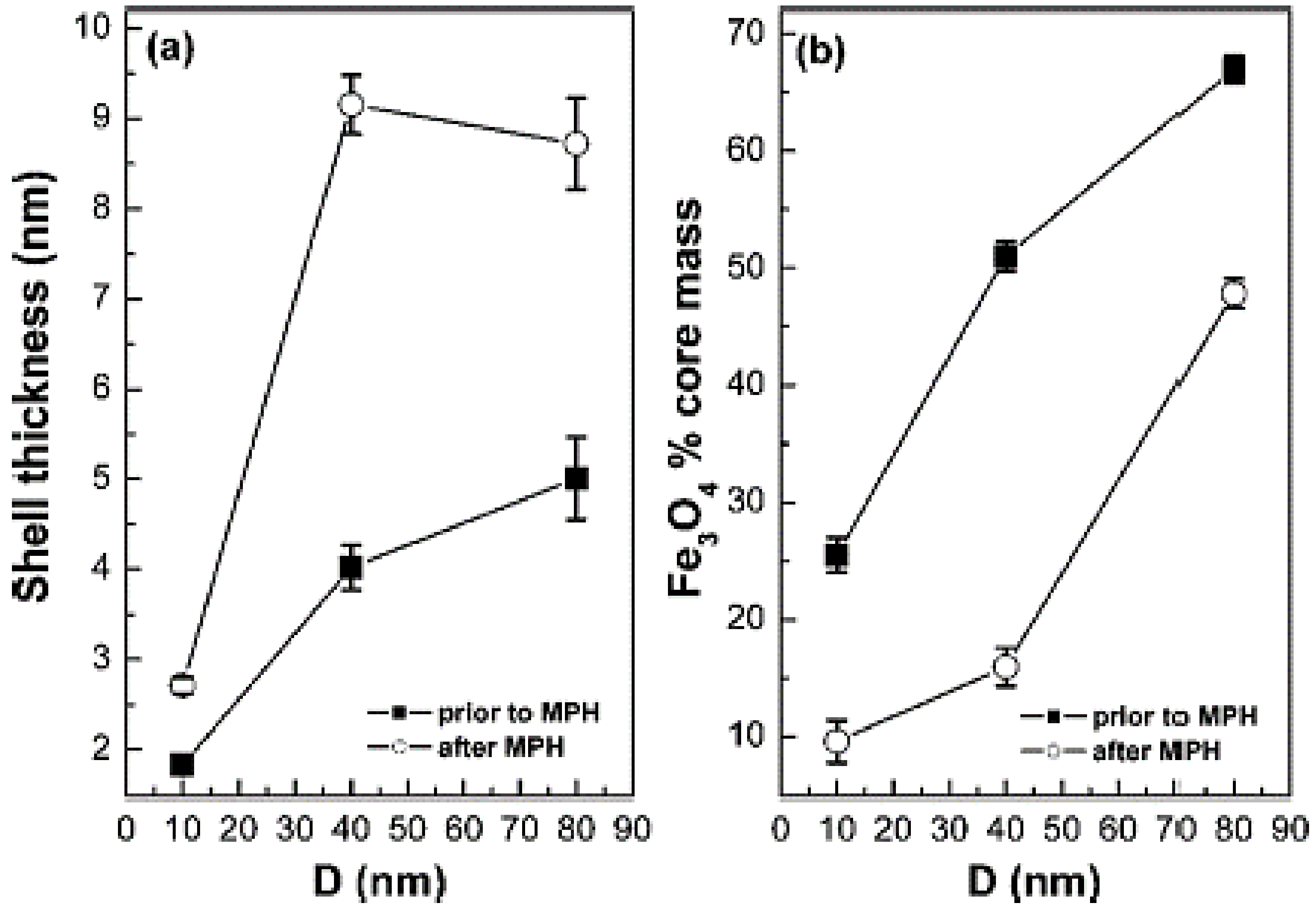
Magnetochemistry **2022**, 8, 117

After treatment

Addressing the Effect of Magnetic Particle Hyperthermia Application on the Composition and Spatial Distribution of Iron Oxide Nanoparticles Using X-ray Spectroscopic Techniques

J. Phys. Chem. C 2022, 126, 10101–10109





(a) Effect of MNP diameter and MPH treatment on the thickness of the oxidized layer in the core/shell Fe_3O_4/γ-Fe_2O_3 MNPs.
(b) Reduction in the fraction of the magnetite core due to the formation of an oxidized maghemite shell as a function of the MNP diameter, prior to and after MPH treatment.

Answers to Questions

What Particles?

Which Conditions?

How will it perform in bio?

Particles

- Material Choice
- Size
- Shape

Ensemble

- Water Transfer
- Interactions

Conditions

- Frequency
- Field intensity
- Magnetic Profile

Add-ons

- Drugs
- MRI
- Thermal Dose

Bio-practice

- biocompatibilty
- toxicity
- In-vivo efficiency

Take home message

Localization of

MNPs & magnetic field

to minimize

toxicity, risks & side effects

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Magnetic Nanostructure Characterization Technology & Applications

http://magnacharta.physics.auth.gr

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