FROM PARTICLES TO ORIENTED ASSEMBLIES: EFFECTS ON MAGNETISM AND APPLICABILITY

M. Angelakeris, Associate Professor
School of Physics, Aristotle University
Thessaloniki-Greece
INTRODUCTION
BIOMEDICAL NANOMAGNETICS

Spheres with diameter < 100 nm, < 100,000 atoms

Magnetic Nano Particles

Reproducibility
Uniformness
Stability
Morphology
Arrangement
Co-ordination

Spin configuration
Dipolar Interactions
Exchange Interactions

From particles to oriented assemblies: Effects on magnetism and applicability
INTRODUCTION

MNPS + BIOMEDICINE?

Specific Loss Power

\[ SLP = \frac{\mu_0H_M^2I(M,I)}{2\rho} (1+(\omega T)^2) \]

\[ \frac{1}{\tau} = \frac{1}{\tau_0} e^{\frac{kT}{3nV}} + kT \]

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INTRODUCTION
MNPS + BIOMEDICINE?

- 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
Chemistry
Crystal Structure
Surface Cover
Functionalization

Nanoparticles due to their multivalency and multifunctionality, pose challenge for understanding their pharmacokinetics because different components will have different features that affect their toxicity, distribution, clearance and catabolism.

M. Angelakeris, Physics-AUTH, agelaker@auth.gr
INTRODUCTION

MAGNETIC FIELDS + BIOMEDICINE?

A restriction limits the range of frequency that can be employed, considering the safety and patient tolerance limits below which the eddy current effects are affordable.

Originally, a maximum field - frequency product

\[ H \times f \leq 4.85 \times 10^8 \text{ A m}^{-1} \text{s}^{-1} \] called the Atkinson-Brezovich limit was proposed in 1984, based on micron-sized magnetic implants.

However, up to date practice, has shown that such a limitation is rather stringent and should be reconsidered by including both the nanoscale character of the particles and the treatment itself.

<table>
<thead>
<tr>
<th>H (kA m(^{-1}))</th>
<th>f (kHz)</th>
<th>H(\times f) ((\times 10^9 \text{ A m}^{-1} \text{s}^{-1}))</th>
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</thead>
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<tr>
<td>18</td>
<td>100</td>
<td>1.8(^1)</td>
</tr>
<tr>
<td>10</td>
<td>410</td>
<td>4.1(^2)</td>
</tr>
<tr>
<td>32</td>
<td>183</td>
<td>5.9(^3)</td>
</tr>
<tr>
<td>19</td>
<td>435</td>
<td>8.3(^4)</td>
</tr>
<tr>
<td>37.3</td>
<td>500</td>
<td>18.7(^5)</td>
</tr>
</tbody>
</table>

1. B. Thiesen & A. Jordan (1\(^{\text{st}}\) clinical magnetic hyperthermia application) Int. J. Hyperthermia, September 2008; 24(6): 467–474
5. H. Mamiya, Journal of Nanomaterials 2013, Article ID 752973

Magnetic nanoparticles: A multifunctional vehicle for modern theranostics
M. Angelakeris Biochimica et Biophysica Acta 1861 (2017) 1642–1651
INTRODUCTION
WHICH MNPS TO CHOOSE?

From particles to oriented assemblies: Effects on magnetism and applicability

Assemblies
Magnetism
Application

Assemblies

M anyone

H

SPM

SD

MD

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INTRODUCTION
WHICH MNPS TO CHOOSE?

Phases
MnFe₂O₄: Dalton Trans. 44, 5396 (2015)

Shapes
Scientific Reports, 3:1652 (2013)

Mix & Match

Core-Shell
RSC Adv. 6, 72918 (2016)

Multi-core

Arrays
Scientific Reports 6, 37934 (2016)
Scientific Reports 6, 38382 (2016)
TUNING THE MAGNETISM

From particles to oriented assemblies: Effects on magnetism and applicability

Metallic Fe
hard/soft interface
Fe₃O₄ or γ-Fe₂O₃

<table>
<thead>
<tr>
<th>Core/Shell(s) (nm)</th>
<th>Scheme</th>
</tr>
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<tbody>
<tr>
<td>F01 44/3</td>
<td></td>
</tr>
<tr>
<td>F02 42/2/3</td>
<td></td>
</tr>
<tr>
<td>F03 25/1/3</td>
<td></td>
</tr>
<tr>
<td>F04 24/4/8</td>
<td></td>
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<tr>
<td>F05 30/24</td>
<td></td>
</tr>
<tr>
<td>F06 43/-</td>
<td></td>
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</tbody>
</table>
TUNING THE MAGNETISM

MFe$_2$O$_4$, $M=$Mn, Co

hard/soft interface

MFe$_2$O$_4$, $M=$Co, Mn or Fe

RSC Adv. 6, 72918 (2016).

M. Angelakeris, Physics-AUTH, agelaker@auth.gr
TUNING THE MAGNETISM

- Cluster size dependent magnetic properties

Magnetite nanoparticles were prepared by the aqueous co-precipitation of ferric and ferrous salts at alkaline conditions at high temperature.

RSC Adv. 6, 53107 (2016).
LINEAR CHAINS-SYNTHESIS

SEM images for 40 nm MNPs with 2 mg/mL concentration and 1 mg/mL agarose content at lower and higher magnification.
LINEAR CHAINS-FORMATION MECHANISM

Molecular Dynamics simulations based on on-the-fly coarse-grain (CG) model of chain formation of 40 nm MNPs.

Time evolution of the average length of the chains: as the simulation evolves, chains with increasing length appear. The length and density of chains increases with the particle concentration and is stabilized after 400 s.

Projection in z-x plane of the chain formation of MNPs in an external field of 40 mT.

The dimensions of 3D computational space were $x = y = z = L(d_0) = (80d_0)$ where $d_0$ is the MNPs diameter of 40 nm.

The number of MNPs was set to 380, 760, 1520 for the concentrations of 1, 2 and 4 mg/mL, respectively.
Major magnetic hysteresis loops at 1 T of 40 nm MNPs at 100 and 300 K with the magnetic field applied parallel to the alignment direction of random (blue lines) and the chain (red lines) samples at 100 and 300 K.

MNPs’ alignment influence on magnetic hyperthermia efficiency as expressed by SLP values by varying MNPs’ concentrations for two different configurations (random and chain) at 765 kHz frequency and 30 mT field with MNPs sizes of 40 nm (solid symbol) and 10 nm (open symbol). For chain samples, SLP values refer to measurements performed with the AC hyperthermia field applied parallel to the alignment direction of the chain samples.
M. Angelakeris, Physics-AUTH, agelaker@auth.gr

From particles to oriented assemblies: Effects on magnetism and applicability

**MAGNETIC HYPERTHERMIA + MRI**

- Spherical iron nanoparticles of 75 nm.
- Biocompatible MgO shell and bcc Fe core.
- Significant uptake for the different cell lines (42 -126 pg Fe/cell).
- Concentration-dependent cytotoxicity profile
- SLP was estimated to be in the region of 100-500 W/g Fe.
- Fast thermal response (15 °C/ 10 min)

T2-weigthed MR images of mouse body before (left) and after injection of NPs. Because of the negative contrast properties of the solution, the liver appears hypointense in images after contrast injection (see arrow). (B) Color-coded T2 maps, from yellow (high T2) to green (low T2). (C) Comparison of magnetic signal from targeted liver at the same time points as imaged by MRI. Maximum concentrations (~ 90% of the injected dose) were observed 24 hours after injection.

MAGNETIC HYPERTHERMIA + DRUG RELEASE SYSTEM

- Highly faceted Iron Oxide MNPs
- Encapsulation in biodegradable block copolymers
- Hyperthermia & Taxol drug release

CONCLUSIONS

✓ MNPs, in general, may appear either as isolated nano-entities such as nano-spheres, -cubes, hexagonal polyhedrons, or form larger aggregates such as rings, or nanowires due to dipolar interactions between the particles.

✓ The configuration of MNPs in 2D or even 3D assemblies, is proposed as an alternative way to control their macroscopic magnetic response on demand.

✓ Mobility of the MNPs within the colloidal dispersion affects the assembly formation success rate, since diverse effects, such as magnetic, electrostatic, viscous, gravitational and molecular interactions are involved.

✓ Such assemblies directly affect the hysteresis losses, the effective anisotropy and susceptibility.

✓ Depending on conditions, MNPs may arrange randomly or in order, according to the complex three-dimensional magnetic dipolar coupling between them in conjunction with external field interaction.

✓ A facile formation is chain arrays which can be routinevely realized through the dispersion of MNPs in a gel matrix and application of an external magnetic field.

✓ Consequently, the controlled assembly of MNPs into chains inducing shape anisotropy along the alignment axis may open an alternative way to optimized heating efficiencies.
ACKNOWLEDGEMENTS

Group members

- K. Simeonidis, Dr.
- D. Sakellari, Dr.
- A. Makridis, PhD student
- E. Mirovali, PhD student
- N. Maniotis, PhD student
- O. Kalogirou, Professor
- T. Samaras, Professor

Colleagues

- M. Farle, M. Spasova, U. Wiedwald, Germany
- M. Morales, Ll. Balcels, C. Boubeta, D. Serantes, Spain
- K. Chliclia, K. Spriridopoulou, Greece

Thank you for your attention