NanoMag Survey 4 Applications

Summary of Results - 19th October, 2016

The fourth, and final, NanoMag survey looked at applications of MNPs and whether available particles limit performance of these applications. It also included questions on the importance of MNPs' characteristics (such as single or multiple magnetic cores, hydrodynamic size and colloidal stability) to their purpose.

NOTE: In each question "application(s)" refers to the current use or intended use of MNPs.

- Questions written by Leo J. Van Ijzendoorn, Tech. Univ. Eindhoven
- Created July 2016; Closed October 9th, 2016
- 220 mailing list
- 38 responses (40 responses but two were duplicates)
- 10 incomplete
- 28 complete = **12.7% response rate**

Spain had the most responses with 11

Followed by:

- USA & Germany 4 each
- UK & Sweden 2 each
- Five other countries 1 each

Q1: asked for personal details (omitted in this summary)

Q2: What is the role of your company/institution when you work with magnetic nanoparticles (choose as many as you like)

- Developing applications for magnetic particles **27%**
- Developing/producing equipment to characterise magnetic particles **20%**
- Particle manufacturing **17%**
- Applying MNPs for *in vitro* diagnostics **14%**
- Applying MNPs for *in vivo* therapy or treatment **14%**

Other

- Characterisation of particles **3%**
- Theoretical studies of MNP particles **3%**
- Standardisation and metrology of MNPs **2%**

Q3: In which application areas do you work with MNPs (choose as many as you like)?

- Hyperthermia **31%**
- Magnetic targeting therapy/drug delivery **19%**
- Biosensing techniques for in vitro diagnostics (surface or volume based) **15%**
- Imaging with MRI **15%**
- Magnetic separation techniques for cells & immunoassays **12%**
- Imaging with MPI **2%**

Other:

- Reference methods & materials **3%**
- Imaging techniques **3%**

Q4: Is the performance of your application(s) limited by the available particles?

- Yes 62%
- No 38%

In what way?

Range of problems:

- Magnetic properties
- Shape
- Heating generation
- Sensitivity
- Specificity
- Reproducibility
- Wide size distribution
- Uncontrollable aggregation
- No free choice of structural or magnetic parameters
- Surface functionalisation
- Stability
- Bioavailability

Comments:

- "*Anisotropy, size, size distribution and defects influence the AC response of the MNP.*"
- *"Some applications need specific particles in terms of size and coating."*
- *"Colloidal stability is required and not always achieved after nanoparticle functionalization."*
- *"Below some threshold, beads start to move individually instead of collectively, reducing the performance of biomagnetic separation systems."*
- *"In the case of magnetic hyperthermia, nanoparticles ideally need to have high heating efficiency, be able to target the tumour area and disperse homogeneously and be biocompatible."*
- *"In the case of MNPs for imaging, finding a suitable interplay between T1 and T2 relaxation times (for dual contrasts)."*
- *"In the case of NPs for hyperthermia, keeping their performance, as tested in vitro, when they go in vivo."*
- *"Detection of the nanoparticles themselves which are labelling the analyte is so absolutely dependent on the kind and quality of the particles.*

Q5: Please rate the importance of each of the following properties for your application(s) of magnetic particles (1=low, 6=high). (Participants chose values from 1 – 6 for each of these factors; results show the total number of marks given.)

- Magnetic susceptibility and saturation magnetic moment of the particles **94 points**
- Particle size distribution **84 points**
- Chemical particle functionalisation **83 points**
- Chemical composition of particles (e.g. which iron oxide) **75 points**
- Remanance/coercivity **66 points**
- Magnetic relaxation behaviour **63 points**

Q6: Is it important for your application(s) to know whether MNPs contain a single magnetic core (magnetic crystallite i.e. single core particles) or may contain several cores (i.e. multi-core particles)

Yes **79%**

No **21%**

Q7: Is it important for your application(s) to know the hydrodynamic size distribution and/or the core size distribution of magnetic nanoparticles?

- Both hydrodynamic & core size distribution **64%**
- Hydrodynamic size distribution **18%**
- Core size distribution **18%**

Question 8 overpage…

Q8: Of the techniques that you employ to characterise magnetic particles, which are the most important, and why?

Technique:	**Used for:**
SQUID magnetometer	Provides blocking temperature and saturation magnetization at room temperature
AC magnetometer	Shows hysteresis losses and determining the magnetic saturation
DC magnetometry	Study the magnetic response as a function of field and temperature, exchange bias, etc
AC susceptometer	Hints on relaxation mechanisms and for obtaining the saturation magnetization
SAR characterization	For assessing heating capabilities
TEM	To analyse the shape & size distribution
DLS	Shows quality of the colloidal state and the real size of the MNPs in the studied medium
B/H curves	Measurement of the magnetic moment versus magnetic field. The measurement gives information about saturation magnetization, magnetic susceptibility and remanence in one measurement.
XRD	Checks the phase and crystallinity
AF4-MALS	Gives good accuracy and relatively high resolution in the size distribution
MPS spectroscopy, MRX.	Information on static and dynamic magnetic properties. MPS and MRX are very fast for a large number of samples
TGA	To determine the concentration of the nanoparticles solution

Q9: Is the chemical function of the magnetic nanoparticles important for your application(s)?

Yes **86%** No **14%**

If yes, can you manufacture MNPs with different surface chemistries?

19 answers shows **13 (68%) can** & **6 (32%) can't** (although one organisation says that this capability is in progress)

- *"Preferred strategy is the "convergent grafting" with well characterized molecules terminated by a phosphonate anchoring end-group"*
- *"The final properties are concentration dependent, i.e. the solvent plays also an important role, not only the particle."*
- *"Manufacture the particles with the surface "a la carte"*
- *"Manufacture the magnetic nanoparticles with different surface modifications according to the need of the special application."*

Q10: Which origin of colloidal stability and/or particle aggregation plays a role in your applications?

- Both magnetic and chemical origins **70%**
- Magnetic **15%**
- Chemical **15%**

Q11: How do you measure the degree of colloidal stability and/or particle aggregation of the MNPs in your application(s)?

- Of the 28 complete responses; 9 skipped the question; and 8 preferred **Dynamic Light Scattering (DLS)**

The remaining answers included:

- TEM
- AF4-MALS
- MPS
- MRX
- Zeta potential
- Turbiscan
- PCS
- Scattering
- Precise polymer synthesis
- Magnetophoretical velocity
- Imaging by flow methods
- Sedimentation by visual inspection
- Magnetisation versus frequency
- AC susceptibility measurements

Q12: Are the applications that you investigate or commercially exploit done with MNPs from different manufacturers?

Yes **57%**

No **43%**

Does performance depend on the origin of the particles?

- *"We see a lot of variety."*
- *"For biodiagnostics we stick to Micromod particles."*
- *"Frequently even the same manufacturer sends different particles with each order."*

Q13: Have you experienced issues with the reproducibility of the performance of your applications(s) for different batches of MNPs?

- No **23%**
- Yes, performance is dependent on batch-to-batch variations in the chemical properties **12%**
- Yes, performance is dependent on batch-to-batch variations in the magnetic properties **19%**
- The performance depends on both chemical and magnetic properties **46%**

Which methods do you employ to verify consistency of MNP batches?

TEM, DLS, VSM, Squid, Relaxometry, Heating rates

Q14: Which bio-application areas will benefit most, in terms of technology, from the standardisation of the magnetic properties of MNPs (choose as many as you like)?

- Hyperthermia **23%**
- Imaging with MRI **17%**
- Imaging with MPI **16%**
- Biosensing techniques for in vitro diagnostics (surface or volume based) **16%**
- Magnetic separation techniques for cells and immunoassays **14%**
- Magnetic targeting therapy/drug delivery **14%**

Other: Cell labelling for tissue regeneration

Q15: Are there other applications that will benefit, in terms of technology, from the standardisation of the magnetic properties of MNPs (e.g. food & agriculture, water remediation, instrumentation etc.)?

- Analytical instrumentation
- Water remediation
- Environmental transport
- Protein purification
- DNA extraction
- Cell separation
- Magnetic refrigeration

  - *"Every application can benefit from standardisation….it is not the magnetic properties that are important, but rather the high oxygen content with the large surface of iron oxide MNP."*

Q16: Which bio-application areas of MNPs has in your opinion the highest commercial potential (1=low, 6=high)? (Participants chose values from 1 – 6 for each of these factors; results show the total number of marks given.)

- Biosensing techniques for in vitro diagnostics (surface or volume based) **102 points**
- Imaging with MRI **89 points**
- Magnetic separation techniques for cells and immunoassays **85 points**
- Imaging with MPI **76 points**
- Hyperthermia **69 points**
- Magnetic targeting therapy/drug delivery **64 points**

Q17: Are there other applications that will benefit, in terms of commercialisation, from the standardisation of the magnetic properties of MNPs (e.g. food & agriculture, water remediation, instrumentation etc.)?

- Analytical instrumentation
- Water remediation
- Magnetic inks
- Magnetic refrigeration

  - *"A general climate of trust & reasonable control is a prerequisite for commercial success of the relatively new MNP technologies."*