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Research Article

Temperature-dependent MPS measurements

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Abstract

The non-linear signal generation in Magnetic Particle Imaging (MPI) using magnetic nanoparticles as tracer materials is still not fully explained and a far-reaching research area. Magnetic Particle Spectroscopy (MPS) was developed to investigate the particle behavior at high externally applied magnetic field strengths and to derive mathematical models which describe the physical processes in MPI in detail. A new MPS setup was built which allows measurements between −13° C and +114° C in order to investigate the temperature dependence of the harmonics spectra. Temperature-dependent MPS measurements of diluted FeraSpin^{TM} XL, either as suspension or freeze-dried in a mannitol matrix, using the new setup are shown and exemplarily discussed.

I. Introduction

Magnetic Particle Spectroscopy (MPS) is an increasingly important measurement system for the quantification of magnetic nanoparticles (MNP) in biomedical applications. Due to its close relationship to Magnetic Particle Imaging (MPI) [1, 2], MPS measurements provide an aptitude examination of their suitability for the diagnostic imaging modality [3]. Compared to MNP characterization methods like magnetorelaxometry (MRX) and AC susceptometry (ACS), MPS is characterized by very short measurement times and high magnetic field strengths and it provides information on both static and dynamic MNP properties. The higher harmonics emitted by the MNP in MPS measurements contain information about very small changes of the particle's behavior. Therefore, MPS is very sensitive to the particle's non-linear relaxation characteristics [4].

In a first approximation, the integral magnetization of the sample volume can be described by the adiabatic Langevin function, including the magnetic energy $E_M = m\mu_0 H(t)$ and the thermal energy $E_T = k_B T$, weighted with the magnetic moment m of a single MNP and the molar particle concentration c:

$$M(H) = mc\left(\coth\left(\frac{E_M}{E_T}\right) - \frac{E_T}{E_M}\right). \tag{1}$$

A differential pickup coil is used to suppress the applied magnetic field and to be able to measure the fundamental frequency. An ideally compensated voltage signal induced by the magnetization changes of the MNP accumulation only includes the derivative of the magnetic flux density emitted by the MNP. The sensitivity of the differential pickup coil depends on the number of windings N and its geometry:

$$U_{ind}(t) = -N\frac{d}{dt}\iint \mu_0 M(H(t))\,dA. \tag{2}$$

The Fourier transform of the induced voltage signal which corresponds to the derivative of the particle's magnetization results in a typical MPS magnitude spectrum. Under the assumption of a static or quasi-static magnetization, i.e. neglecting the particle dynamics, the magnetization curve exhibits a reduced slope with increasing temperatures (Fig. 1, left). Hence, a significant decrease of the higher harmonics is expected (Fig. 1, right).

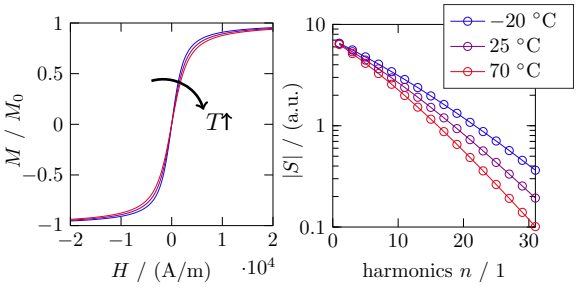

Figure 1: Exemplary simulation results of the Langevin functions for different temperatures normalized to $M_0 = mc$ (left) and corresponding simulated MPS magnitude spectra of odd harmonics (right) using a common MPI particle set (spherical, $d_c = 25\,\text{nm}$, $M_s = 300\,\text{kA/m}$).

Generally, MPS measurements also include information about the MNP dynamics. The reorientation of the magnetic moment of MNP in response to an externally applied magnetic field is governed by two coupled relaxation mechanisms: the Néel relaxation and the Brownian rotation. As a further approximation, both relaxation processes can be examined as decoupled and field-independent processes. The Néel relaxation depends on the crystal, surface and shape anisotropy of the core material expressed by an effective anisotropy constant K. Under specification of the core volume V_c, the Boltzmann constant k_B, the ambient temperature T and an empirically evaluated time constant $\tau_0 \approx 1\,\text{ns}$, the specific zero-field relaxation time is given by:

$$\tau_{N,0} = \tau_0 \exp\left(\frac{K V_c}{k_B T}\right). \tag{3}$$

For magnetic nanoparticles, the effective anisotropy is generally dominated by surface and/or shape anisotropy and can thus be assumed as temperature independent. The Brownian relaxation is the spatial rotation process triggered by the applied magnetic field. The Brownian relaxation is often characterized by its specific zero-field relaxation time

$$\tau_{B,0} = \frac{3\eta V_h}{k_B T} \tag{4}$$

including the dynamic viscosity η, the hydrodynamic volume V_h and the thermal energy $E_T = k_B T$. The dynamic viscosity of the surrounding media is temperature-dependent itself. This relationship is given by the Arrhenius-Andrade equation [5] and applicable for most Newtonian fluids:

$$\eta = \eta_0 \exp\left(\frac{E_A}{E_T}\right). \tag{5}$$

It depends on a typical zero-viscosity η_0 for a certain temperature, the activation energy E_A and the thermal energy E_T. The effective relaxation time can be modeled as a parallel arrangement of both relaxation times:

$$\tau_{eff,0} = \frac{\tau_{N,0}\tau_{B,0}}{\tau_{N,0} + \tau_{B,0}}. \tag{6}$$

It should be noted that for the magnetic field amplitudes typically applied in a MPS measurement, field-dependent Néel and Brownian relaxation times should be included, both being dependent on the dimensionless parameter $\xi = \frac{mB}{k_B T}$ [6] which provides an additional influence of temperature.

II. Experimental

The Néel relaxation, the Brownian relaxation including the dynamic viscosity of the surrounding media and the static magnetization curve represent the obvious influencing factors of temperature-dependent MPS measurements. To investigate the temperature dependence, a new MPS setup was designed.

II.I. Setup

The new MPS setup (see Fig. 2) allows temperature-dependent measurements in a sample temperature control range of at least −13° C to +114° C. The sample is housed in a Shapal™ ceramic rod serving as pickup coil bobbin as well. The ceramic temperature is maintained by a Peltier element providing both cooling and heating capability.

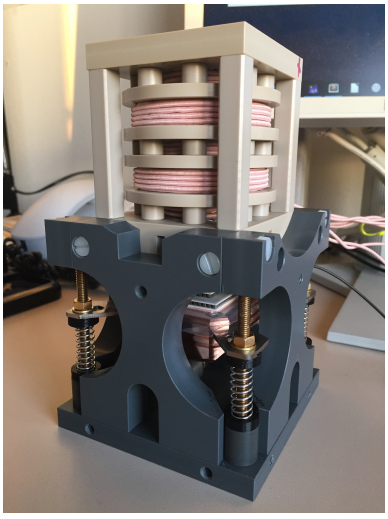

Figure 2: New MPS system offering cooling and heating capability by using a Peltier element to control the sample temperature.

Different electrical powers of the Peltier element lead to corresponding terminal temperatures of the sample which are measured with a Pt-100 temperature sensor placed in deionized water and mounted in a sample bin

made of glass (see Fig. 3). Colored lines represent measured data while the gray lines represent extrapolated data to estimate end values of the step responses. Measurements of the heating process have been stopped for high temperatures since the sample tube would have been damaged. Measurement times for low temperatures have been extended to cover the phase transition of the medium. The jump of the step response at $R_{Pt100} = 97.6\,\Omega$ ($T \approx -6.14°$ C) indicates the phase transition of the subcooled deionized water to ice.

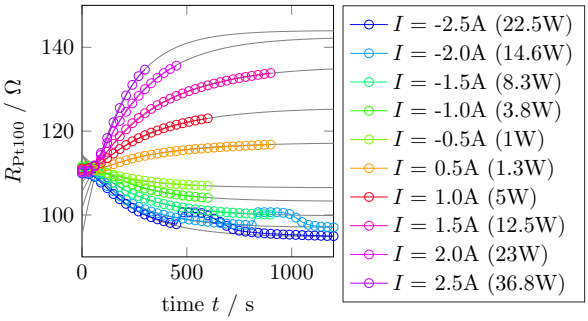

Figure 3: MPS temperature control path step responses for different electrical powers driving the Peltier element.

In addition to an AC excitation by a vertically placed solenoid coil, a DC offset field can be superimposed by using an outer mounted Helmholtz coil pair.

II.II. Materials

MPS measurements were performed on FeraSpin^{TM} XL suspensions from nanoPET Pharma GmbH (Berlin, Germany). FeraSpin^{TM} XL is a fraction of FeraSpin^{TM} R with a hydrodynamic size of around 60 nm. A comprehensive magnetic characterization of FeraSpin^{TM} XL applying static M(H), ACS and MRX measurements indicated that roughly 34 % of MNP follow the (small-amplitude) sinusoidal excitation field via the Brownian mechanism [7].

Measurements were performed on suspensions and immobilized particles. Immobilization was done by freeze-drying the particles in a mannitol matrix. The sample volume amounts to 150 μl each.

III. Results

Fig. 4 shows odd harmonics of temperature-dependent MPS measurement data recorded on a diluted suspension (10 %) of FeraSpin^{TM} XL and on a freeze-dried Brownian-blocked sample. The excitation frequency was chosen to be $f_0 = 5$ kHz to emphasize the Brownian influences since the particles would not be able to follow the field at high frequencies in this way. The excitation field peak amplitude was regulated to $\mu_0\hat{H} = 25$ mT since the corresponding field strength ensures the magnetic saturation of the particle sample and therefore improves the signal strength in MPS measurements. The temperature-dependent spectral changes of the higher harmonics are color-coded plotted from blue ($T \approx 0°$ C) to red ($T \approx 70°$ C).

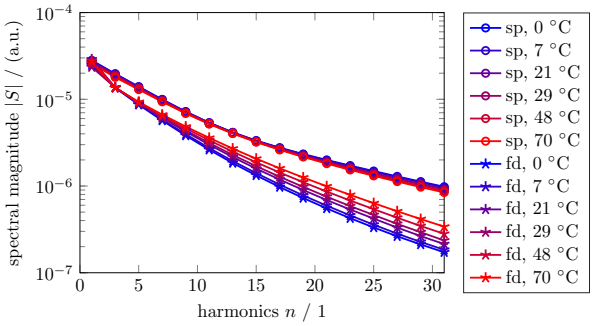

Figure 4: Temperature-dependent MPS measurement data ($f_0 = 5$ kHz, $\mu_0\hat{H} = 25$ mT) of nanoPET FeraSpin^{TM} XL prepared as diluted (10 %) suspension (sp) and freeze-dried (fd) sample.

Note that the suspension sample is not in a frozen state at $T \approx 0°$ C since the freezing temperature of the medium is even lower (compare with Fig. 3).

The higher harmonics of the spectrum measured on the suspension show a slight decrease with rising temperature whereas the spectra recorded on the immobilized sample exhibit a clear reduction of the decay.

Fig. 5 and Fig. 6 visualize the corresponding temperature-dependent reconstructed point spread functions (PSF) of the suspension and the freeze-dried sample.

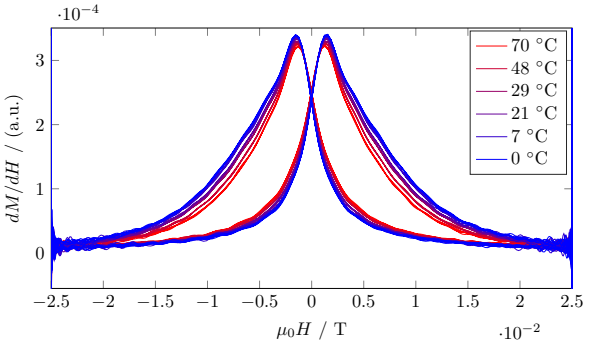

Figure 5: Temperature-dependent reconstructed point spread function of a diluted (10 %) nanoPET FeraSpin^{TM} XL suspension sample.

IV. Discussion and Outlook

Diluted FeraSpin^{TM} XL suspensions were investigated in MPS measurements with respect to the influence of tem-

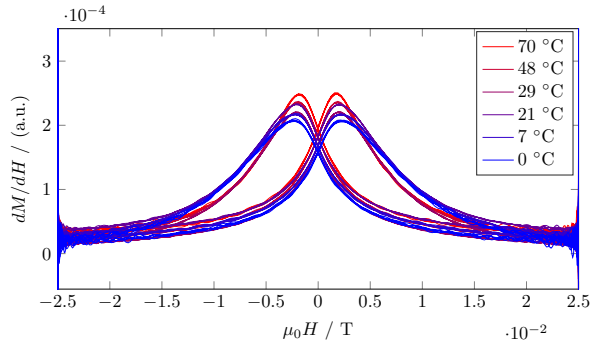

Figure 6: Temperature-dependent reconstructed point spread function of a diluted (10 %) freeze-dried (mannitol) nanoPET FeraSpin^{TM} XL sample.

perature. Although having a smaller signal compared to the original suspensions, diluted samples were chosen to better emulate the concentration of injected suspensions in *in vivo* experiments and to minimize particle interactions. First temperature-dependent MPS measurements show a non-linear relation of the measured harmonics spectra with the sample temperature. It should be noted that the temperature dependence of the suspensions is small compared to the temperature dependence of the spectra obtained for the freeze-dried sample. An explanation for these observations is still pending but could be justified by opposing temperature-dependent influences (e.g. slope of the quasi-static magnetization curve vs. viscosity of the medium and relaxation time of the particles). For nanoparticles relaxing via the Brownian mechanism, the temperature dependency can be attributed to the magnetization curve, described by the Langevin function for quasi-static scenarios, the Brownian relaxation time and the viscosity of the medium. The temperature dependence of the nanoparticle contribution dominated by the Néel-relaxation is caused by the temperature dependencies of the magnetization curve and the Néel relaxation time. Apart from this, there may be other factors that influence the MPS measurements, e.g. temperature dependence of shape or crystal anisotropy. The scaling of the higher harmonics of the freeze-dried sample behaves inversely to the scaling described by the quasi-static Langevin function modeling approach. The observations suggest the importance of particle magnetization dynamics when developing models describing MPS or MPI measurements. The Brownian motion of the particles in the freeze-dried sample is inhibited. Therefore, the spectral changes of the freeze-dried samples can be attributed to the Néel relaxation mechanism which becomes significantly faster with increasing temperature. As can be seen in Fig. 5 and Fig. 6, even in the time domain and the reconstructed PSF – relevant for MPI – a significant change with temperature is evident. To clarify the temperature-dependent observations, a mathematical model including dynamics is required. A dynamic particle model must also include field-dependent relaxation times since the impact is not negligible at all. Currently, we are working on a MNP model implementation considering the relevant physical influencing factors, based on the Landau-Lifshitz-Gilbert equation to model the Néel relaxation and the Newtonian rotation equation covering Brownian rotation. From such simulations, we hope to derive simplified model expressions, which can be utilized for parameter identification in experimental data.

Furthermore, setup improvements regarding the signal-to-noise ratio and further measurements of different particle systems are planned. In addition, system characterization and calibration are in progress and will help to provide reliable magnitude and phase (or real and imaginary part) data.

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Financial support by the German Research Foundation DFG via SPP1681 under grant no. SCHI383/2-1 and LU800/4-2, under grant no. LU800/5-1 as well as by the European Commission Framework Programme 7 under the NanoMag project (grant agreement no: 604448) is acknowledged.

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