Characterizing and imaging magnetic nanoparticles by optical magnetometry

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Abstract. We review our ongoing work on deploying optical (atomic) magnetometry for measuring the magnetic response of magnetic nanoparticle (MNP) samples, yielding MNP size distributions, and other sample parameters like Néel relaxation time $\tau$, saturation magnetisation $M_s$, anisotropy constant $K$ and magnetic susceptibility $\chi$. We address magnetorelaxation (MRX) signals, in which the decaying magnetisation $M(t)$ following a magnetising pulse is recorded by a single atomic magnetometer or by a novel magnetic source imaging camera (MSIC) allowing spatially resolved MRX studies of distributed MNP samples. We further show that optical magnetometers can be used for a direct measurement of the $M(H)$ and $dM/dH(H)$ dependencies of MNP samples, the latter forming the basis for an optical magnetometer implementation of the MPI (Magnetic Particle Imaging) method. All experiments are in view of developing biomedical imaging modalities.

1. Introduction

The deployment of magnetic nanoparticles (MNPs) for biomedical applications has steadily increased in the past decade [1]. The use of MNPs as MRI contrast agents and for hyperthermia is well investigated. More importantly, functionalised MNPs injected into the blood stream have a high potential for targeted drug delivery to biological entities, such as tumors or organs. In view of clinical applications, most MNP-based methods require quantitative imaging methods for monitoring the spatial MNP distribution in the biological tissue. Magnetorelaxation (MRX, [2]) imaging and Magnetic Particle Imaging (MPI, [3]) are two imaging modalities that are actively being developed towards this goal. On the other hand, there is also an evident need for measuring and optimising the MNP properties, in particular their size distribution. The average size and the size dispersion as well as specific magnetisation and magnetisation relaxation rates of MNPs in sample are important parameters in view of obtaining the highest possible MNP detection sensitivity with the lowest possible quantity of injected MNPs.

The imaging and characterisation of MNP samples both rely on the particles superparamagnetic character, related to the fact that MNPs of sufficiently small size are single ferromagnetic domains. As such, the magnetisation versus magnetic field dependence, $M(H)$, of an MNP ensemble is described by the Langevin function

$$L \left( x = \frac{H}{H_K} \right) = \frac{M(x)}{M_s} = \coth x - \frac{1}{x},$$

(1)
where the saturation field
\[ H_k = \frac{k_B T}{\mu_0 M_s V} , \] (2)
is a function of the (particle size and material dependent) saturation magnetisation, \( M_s \), and the MNPs core volume, \( V \). The characteristic features of this magnetisation behaviour are (a) the absence of hysteresis and (b) the relatively modest value (few mT) of the saturation field \( B_k = \mu_0 H_k \).

All applications mentioned above rely on magnetising the MNP located, say at \( \vec{r} = 0 \), by a magnetic excitation field \( \vec{H}(\vec{r}=0) \), and detecting the magnetic flux density \( \vec{B}(\vec{r}) \propto M(0) \) produced by the sample magnetisation \( M(0) \) with a magnetometer located at \( \vec{r} \). In most conventional magnetic MNP experiments one deploys excitation fields \( \vec{H}(\vec{r}=0,t) \) that harmonically oscillate at \( \omega_{\text{exc}} \), in combination with detection of \( \vec{B}(\vec{r},t) \), or rather \( d\vec{B}(\vec{r},t)/dt \) by a pick-up loop based on Faraday’s induction law. Because of the time-derivative, the pick-up signal grows like \( \omega_{\text{exc}} \), thus favouring high-frequency excitation.

We strongly believe that atomic magnetometers (AM) present an interesting alternative to the pick-up loop detection of MNP signals, since their performance does not degrade with decreasing frequency, thus allowing efficient low-frequency, and even DC detection. Here we review several proof-of-principle experiments that we have performed along these lines.

2. Magneto-relaxation (MRX)

Magnetised MNPs, when immobilised (e.g., when attached to a cell surface, or embedded in a matrix/tissue) have Néel relaxation times in the range of seconds to minutes, depending on the particles’ size. This property is used in MRX to discriminate signals from blocked MNPs against signals produced by MNPs in body fluids, whose magnetisation relaxes on the sub-ms time-scale. MRX consists in magnetising the particles by a static field \( \vec{H}_{\text{exc}} \) of several mT for a given amount of time, and then monitoring the decaying magnetic flux density’s magnitude \( B(t) \), after \( \vec{H}_{\text{exc}} \) has been switched off. In [4] we have shown that two AMs (operated as a gradiometer) can be used to monitor \( B(t) \) decaying from a few nT down to a few pT over two minutes. In that paper we have also revised the functional time-dependence of the MRX-decay, and discussed under which simplifying assumptions the signal reduces to
\[ B(t) \propto \ln \left( 1 + \frac{\tau}{t} \right) . \] (3)

We have compared relaxation curves from various samples having average MNP particle radii ranging from 14 to 21 nm. Fits of the results have further allowed us extracting the saturation magnetisation \( M_s \) and the so-called magnetic anisotropy constant \( K \), defining the Néel relaxation time
\[ \tau = \tau_0 \exp \frac{KV}{k_B T} \quad \text{with} \quad \tau_0 \approx 10^{-9} \text{s}, \] (4)
and to study the dependence of \( M_s \) and \( K \) on particle size.

3. Magnetic source imaging camera (MSIC)
The conventional MRX recording using a single magnetometer does not yield direct information about the MNPs’ spatial distribution. The latter can be assessed by simultaneously recording MRX signals with an AM array. Based on the methods described by Fescenko and Weis [5], we have developed a magnetic source imaging camera (MSIC), i.e., a device yielding a direct visualisation of the two-dimensional spatial distribution of a specific component \( B_i \) of the flux density vector produced by a magnetised MNP sample. The MSIC principle is sketched in figure 1a. A sheet of circularly-polarised resonant laser light prepares a layer of spin-polarised
Cs atoms contained with a buffer gas in a cubic vapour cell. A CCD camera records fluorescence from that layer.

Figure 1. a): MSIC principle: The fluorescence emitted by each point \( \vec{r} \) of the spin-polarised atomic layer depends on the projection \( \delta B_H \) of \( \delta \vec{B}_{\text{MNP}}(\vec{r}) \) on \( \vec{B}_0 \); b) CCD frames representing fluorescence produced by dried MNP sample and the (time-logarithmic) MRX decay of the integrated fluorescence signal, fitted by equation 3.

A weak magnetic field \( \vec{B}_0 \) defines – by virtue of the Hanle effect [6] – the detected component of the flux density \( \delta \vec{B}_{\text{MNP}}(\vec{r}) \parallel \vec{B}_0 \) produced by the object of interest, here a magnetised MNP sample. \( \delta \vec{B}_{\text{MNP}}(\vec{r}) \) changes the total field, and hence the atomic spin polarisation at each position \( \vec{r} \) in the sheet. Since the fluorescence yield depends on the degree and orientation of the local spin polarisation, the fluorescence from each point thus changes in a specific manner as discussed in [5, 6]. Figure 1.b shows CCD frames that represent the fluorescence changes (proportional to \( \delta B_H \)) induced by magnetised MNPs [6] and the samples magnetisation decay (MRX signal).

4. AC susceptometry (ACS) and Magnetic Particle Imaging (MPI)

In contrast to blocked MNPs, the magnetisation of MNPs suspended in a fluid undergoes a very fast (sub-ms) Brown relaxation through rotational diffusion. This fact prevents their detection by MRX, but allows the particles to react quasi-instantaneously to oscillating drive fields \( \vec{H}(t) \) producing a related response \( \vec{B}_{\text{MNP}}(t) \). Because of the nonlinear \( B_{\text{MNP}}(H) \propto M_{\text{MNP}}(H) \) relation given by equation 2, a monochromatic drive oscillating at \( \omega_{\text{drive}} \) produces odd overtones at \((2n+1)\omega_{\text{drive}}\) in the Fourier spectrum of the \( B_{\text{MNP}}(t) \) response. We have developed AM-based methods [7] allowing the direct recording (figure 2) of the \( B_{\text{MNP}}(H) \) dependence and its derivative \( dB_{\text{MNP}}/dH(H) \). The method can be applied to MNP samples containing down to 1 \( \mu \text{g} \) of iron and can be used to extract MNP size distribution [8].

The fact that the \( dB_{\text{MNP}}/dH \) signal peaks at \( H=0 \) can be used for measuring spatial MNP distributions. Suppose that a bulk sample containing an inhomogeneous MNP distribution is exposed to an inhomogeneous drive field, such that \( H=0 \) at one specific point (zero field point, ZFP) in the sample. Suppose further that the \( H \) field in other parts of the sample is sufficiently strong to saturate the MNP magnetisation at those points. The magnetometer will then detect \( dB_{\text{MNP}}/dH \) signals only from MNPs located at or near the ZFP. A record of the magnetometer signal while scanning the ZFP position through the bulk will thus yield information of the spatial MNP distribution.

The method of Magnetic Particle Imaging (MPI) was invented a decade ago by researchers at Philips [3]. It relies, in its originally proposed an realised variant, on the analysis of the MNP response in the frequency-domain. The method deployed by us is related to a variant of MPI known as X-space MPI that was demonstrated so far only with pick-up coil detection [9].

Currently, both frequency-space and X-space implementations of MPI deploy drive fields oscillating at 25 kHz, together with pick-up coil detection. The high frequency at which the high
Figure 2. Magnetisation curve and its derivative of a water-suspended MNP (Ferrotec EMG707) sample containing 3 mg of iron. Details of the experimental methods are given in Ref. [7].

Power drive field oscillates leads to concerns regarding heating and peripheral nerve stimulation of patients. We believe that AM-detection offers a promising perspective for developing a low-frequency MPI-scanner that may circumvent those issues.

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