Uncertainty of reconstructions of spatially distributed magnetic nanoparticles under realistic noise conditions

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Magnetorelaxometry (MRX) is a measurement technique able to sense the magnetic field originating from magnetic nanoparticles (MNPs). The concentration distribution of MNPs can be recovered by interpreting the MRX measurement data with a numerical model, i.e., by solving an inverse problem. We investigate the actual impact of noise on the MNP reconstruction quality when using distributed excitation coil configurations and how the excitation setup needs to be adapted when prior information on the MRX noise is known. Results show that an approximately 4 times larger sensitivity can be attained when adapting the excitation setup to the known realistic noise. The proposed methodology is able to assess the sensitivity limits of the MRX measurement setup more accurately compared to convenient noise models. © 2014 AIP Publishing LLC.

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I. INTRODUCTION

Magnetic nanoparticles (MNPs) are able to reach areas in the body which are difficult to access due to their small diameter. Moreover, they possess a high saturation magnetization which enables them to be measured non-invasively using sensitive magnetic sensors including superconducting quantum interference devices (SQUIDs)1 or Fluxgates.2 These and other properties3 make MNP suitable for biomedical applications such as hyperthermia4 or immunoassays labeling.5 These modalities require accurate knowledge on the spatial MNP distribution for optimal operation. It has been shown that magnetorelaxometry (MRX) has the ability to recover quantitatively both the absolute concentration of magnetic nanoparticles as well as their spatial distribution.6 An MRX experiment consists of a magnetizing field (in the order of mT) applied by an external coil setup, traditionally a Helmholtz coil,1 large enough to guarantee a homogeneous field within the volume containing the MNPs. Distributed coil configurations and their heterogeneous magnetic fields increase the accuracy of reconstruction compared to the traditional coil setup.7 The MNPs align their magnetic moment along the direction of the magnetizing field. Typically, after 1 s this field is switched off and the decaying magnetic field originating from the MNPs (in the order of pT) is measured using sensitive magnetic sensors. The quantitative spatial MNP distribution can be obtained by correctly interpreting the MRX data using a numerical model. A so-called inverse problem needs to be solved which comprises comparing the computed magnetic fields at sensor locations with the measured data. Uncertainties are introduced in the reconstruction due to modeling errors, measurement noise and ill-posedness (large number of unknowns compared to the number of sensors). We study the actual impact of noise on the MNP reconstruction quality when using distributed excitation coil configurations and how the excitation setup needs to be adapted when prior information on the MRX noise is known. So to have correct assessment of the impact of noise, actual noise MRX measurements are performed on the 304 SQUID vector magnetometer at the Physikalisch-Technische Bundesanstalt, Berlin.6

II. METHODS

A. MRX under realistic noise conditions

A volume of 6.6 cm×3.3 cm×3.3 cm is considered, wherein a certain MNP distribution is contained. The volume is tessellated into \(N_v\) cubical voxels with voxel size \(s_v\). Two discretization levels are studied in this paper, i.e., \(s_v = 1.1\) cm and \(s_v = 3\) mm. The excitation coil setup is a distributed coil configuration that consists of 48 planar coils of about 1 cm diameter, positioned at different locations.8 24 coils are located in a plane parallel to the SQUID sensors with 12 coils between the sensors and the volume (i.e., the upper coils) and 12 coils below the volume. The other 2×12 coils are equally distributed in two planes perpendicular to the measurement plane with the volume under study positioned between them (see Figs. 1 and 3(a)). By activating the coils in the latter two planes (with same electric current flowing in the coils), a homogeneous activation of the MNP distribution is achieved. Activating a single coil, results in a heterogeneous activation, i.e., the MNPs are magnetically excited with voxel-dependent orientation and magnitude. The coils are placed at a distance of 6 mm from the volume.

The measurements in the SQUIDs \(V_{\text{meas}} \in \mathbb{R}^{N_v}\) can be related to the MNP concentration distribution \(c \in \mathbb{R}^{N_v}\) and include a noise term \(n : V_{\text{meas}} = L \cdot c + n\). \(L\) is the lead field matrix whose elements can be calculated using Biot-Savart’s
law and depends on the excitation coil setup. \( c \) can be estimated by solving an inverse problem which consists in calculating the Moore-Penrose pseudo-inverse of \( L : c^* = L^\dagger \cdot N_{s} \) using truncated singular value decomposition (tSVD). The reconstruction quality of \( c \) is measured in this paper using 3 parameters: correlation coefficient (maximum score is 1, meaning correct reconstruction both in absolute values as in distribution), mean \( \mu \), and standard deviation \( \sigma \). So to investigate thoroughly the impact of \( n \) on the reconstruction quality and on how to adapt the sequential activations to the specific noise in the measurement setup, MRX measurements are performed in the absence of magnetic nanoparticles. Sensor values are registered for a time period of 1.08 s at a sample rate of 250 Hz. The time window and sampling rate are chosen so to match the magnetic properties of the MNPs. For each of the \( N_s \) sensors, the root mean square (RMS) is acquired over the time period. About 8200 RMS values of the sensors were measured (271 sensors and 48 measurements). Fig. 1 shows the period. About 8200 RMS values of the sensors were measured (271 sensors and 48 measurements). Fig. 1 shows the period. 

FIG. 1. The measured RMS noise values show two characteristic peaks resulting from the SQUID orientation. Inset: studied MRX setup.

B. Noise adapted sequential activations

Distributed coil configurations enable acquisition of different measurements since the MNPs are differently activated. Depending on the electric currents flowing through each coil, a lead field matrix can be generated. In case \( N_{sa}\) sequential activations are carried out, the measurement vector extends to \( N_{sa}N_s \) dimensions and the overall lead field matrix to a \( N_{sa}N_s \times N_c \) dimensional matrix.

We propose the following methodology for determining the necessary sequential activations that enable accurate reconstruction of MNP distributions. We place a low Fe concentration (typically 1 mg) in the center of the volume and simulate, for each of the \( N_c \) coils separately activated, the sensor values. The center of the volume is chosen because it has the lowest measurement sensitivity. By adding the measured MRX noise data, we can inversely calculate the MNP distribution and calculate the correlation score. The reconstructions associated having a correlation score \( > \rho \) are selected. Random groups of \( N \) coils containing at least 1 coil with a correlation score \( > \rho \) are formed. \( N \) is increased until a similar or larger correlation score is obtained with respect to the correlation score of the \( N_c \) coils used together and activated sequentially. For each \( N \) the random group formation is repeated \( \frac{N_c}{N} \) factorial times so to determine the optimal sequential activation group.

III. RESULTS AND DISCUSSION

In this section, we first investigate the impact of noise on the reconstruction quality and then adapt the sequential coil activation to improve the reconstruction quality under realistic noise conditions. \( c_{\text{noise}} \) is reconstructed using a homogeneous and heterogeneous \( (N_c = 48) \) coil activation. When subtracting the two \( c_{\text{noise}} \) reconstructions of the white Gaussian noise and measured noise model, a large discrepancy is observed: a relative error of 34% \( \pm \) 5% is obtained for the homogeneous activation and an even increased error of 38% \( \pm \) 3% is seen for the heterogeneous sequential activation. As noted in Fig. 1, the measurement setup has a characteristic noise depending on the sensors’ locations which has an influence on the reconstruction. The spatial differences do not depend on grid size.

Table I shows the reconstruction quality for a simulated MRX experiment without noise (sMRX), a simulated MRX experiment with Gaussian white noise (sMRX + wgn) with an assumed SNR of 20 dB, a simulated MRX experiment with added measured noise (sMRX + mn) and an experiment with actual MRX measurement data (xMRX). Simulations with measured noise achieve reconstruction scores equal to actual experiments, which allows an improved analysis of the performance of the setup compared to the other noise model. Note that the measurements are here performed in a magnetically shielded room yielding low noise levels and indicate that other MRX setups with higher noise levels exhibit a larger discrepancy when using traditional noise models compared to measured noise, because the correlation score of the xMRX will decrease and the sMRX + wgn will still result in similar scores (98%–95%, for their typical SNRs). The results demonstrate that actual noise measurements indeed yield a better assessment of the setup’s performance. We investigated the impact of increasing the number of activated coils on the reconstruction quality including realistic noise for varying Fe concentrations (0.001 mg–5 mg) placed in the middle of the volume under study (with \( s_e = 1.1 \) cm). Fig. 2 (left) shows the increase in accuracy of reconstruction when increasing the

<table>
<thead>
<tr>
<th>Type</th>
<th>Correlation (%)</th>
<th>( \mu ) (mg Fe)</th>
<th>( \sigma ) (mg Fe)</th>
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<tbody>
<tr>
<td>sMRX + wgn (20 dB)</td>
<td>98.7</td>
<td>0.018</td>
<td>0.03</td>
</tr>
<tr>
<td>sMRX + mn</td>
<td>96.1</td>
<td>0.233</td>
<td>0.54</td>
</tr>
<tr>
<td>xMRX</td>
<td>96.2</td>
<td>0.358</td>
<td>0.58</td>
</tr>
</tbody>
</table>

TABLE I Reconstruction quality when using Gaussian white noise (sMRX + wgn), noise data (sMRX + mn), and actual MRX measurement (xMRX).
number of activation coils. The correlation coefficients are here averaged in the case of 200 noise samples. This figure also shows the sensitivity limits of the setup with respect to determining the concentration of a single volume due to the noise in the measurements: below 0.05 mg Fe the correlation score decreases dramatically from a general score of 90%–100% for 48 coils to a score of only 20%–45%. Note that an increased number of coils does not necessarily increase the reconstruction quality. The correlation scores can decrease due to the possible inconsistency of the overdetermined linear system of equations. We applied the methodology described in Sec. II B for an Fe concentration of 1 mg, \(q = 0.6\), and \(N\) initialized on 6. Only 18 coils need to be employed for accurate reconstruction. Fig. 3(a) illustrates the coils that need to be activated. Exploiting the noise distribution (Fig. 1) clearly demonstrates the asymmetry in the optimal coils for activation. Using the subset of 18 coils, we study the impact of increasing the number of coils on the reconstruction quality, see Fig. 2 (right). We observe that lower Fe concentrations can be reconstructed more accurately (sensitivity limit of 0.25 mg instead of 1 mg) because of the use of the adapted activation coils. While for the non-adapted coils, 1 mg is better reconstructed starting from 25 coils (correlation score of 85% for 25 coils and 65% for 24 coils); the adapted coils manage this starting from only 10 coils (correlation score of 91% for 10 coils and 65% for 9 coils).

The noise adapted coil sequence was finally used for recovering spatially distributed MNP distributions so to validate the methodology. These distributions are randomly generated using fractal Brownian motion. In 90% of the distributions, the best result was achieved with (sMRX + mn) simulations. Fig. 3 shows an example. Fig. 3(b) is the actual distribution, Fig. 3(c) is the reconstruction for sMRX + mn (correlation of 98%), and Fig. 3(d) is the reconstruction (correlation of 45%) using sMRX + wgn (20 dB). These results clearly show that exploiting the realistic noise distribution of the setup and adapting the activation coils to that noise distribution, can improve the reconstruction quality.

IV. CONCLUSION

The impact of measured noise on MRX reconstruction is studied. Results show that solving the inverse problem with realistic noise, more closely approximates actual experiments than when assuming Gaussian white noise. In a distributed coil configuration setup, the noise is even more reflected in the reconstructions and an adequate quantification in the simulations is necessary as to improve setup performance analysis.