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Magnetic nanoparticle imaging by random and maximum length sequences of inhomogeneous activation fields

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***Abstract*— Biomedical applications of magnetic nanoparticles require a precise knowledge of their biodistribution. From multi-channel magnetorelaxometry measurements, this distribution can be determined by means of inverse methods. It was recently shown that the combination of sequential inhomogeneous excitation fields in these measurements is favorable regarding the reconstruction accuracy when compared to homogeneous activation . In this paper, approaches for the determination of activation sequences for these measurements are investigated. Therefor, consecutive activation of single coils, random activation patterns and families of m-sequences are examined in computer simulations involving a sample measurement setup and compared with respect to the relative condition number of the system matrix. We obtain that the values of this condition number decrease with larger number of measurement samples for all approaches. Random sequences and m-sequences reveal similar results with a significant reduction of the required number of samples. We conclude that the application of pseudo-random sequences for sequential activation in the magnetorelaxometry imaging of magnetic nanoparticles considerably reduces the number of required sequences while preserving the relevant measurement information.**

I. INTRODUCTION

Magnetic nanoparticles offer a large variety of promising biomedical applications, among them magnetic drug targeting, magnetic hyperthermia. All these applications share the need for a quantitative and precise detection of the particles with respect to monitoring their safety and efficiency. We presented a method for the spatially resolved quantification of magnetic nanoparticles in tissue based on magnetic relaxation measurements [1]. From multichannel measurements of the decay of the particles' magnetization after being exposed to a homogeneous magnetic excitation field, their distribution can be reconstructed using a minimum norm estimation technique [2]. It could be shown that combining the reconstruction results of sequential inhomogeneous magnetization fields considerably improves the spatial resolution of this technique [3] and is favorable when compared to homogeneous activation regarding the reconstruction accuracy [4]. However, a consecutive activation of one single coil per measurement sample is too time consuming and not practicable in experimental measurements. In this paper, we address the problem of defining activation patterns for sequential inhomogeneous stimulations. It aims at finding suitable and effective excitation sequences. For this purpose, random and pseudo-random sequences are employed and compared to the sequential activation of single coils. The evaluation is based on the condition of the system matrix.

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II. METHODS

A. Setup

The setup employed for the simulations in this paper comprises 45 excitation coils (diameter $40\,\mathrm{mm}$) arranged in regular arrays positioned around the region of interest. As figure 1 illustrates, 9 coils were placed in the X-, X+, Y-, Y+ and Z- plane, respectively.

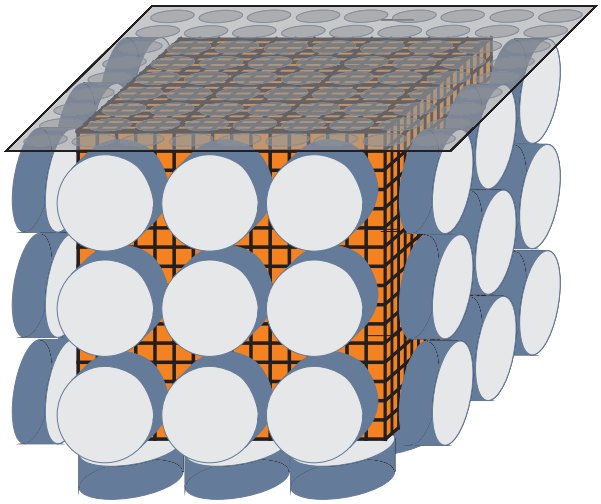

Fig. 1. Schematic representation of the simulation setup with the excitation coils positioned in 5 planes around the source region containing 16 by 16 by 16 voxels and one plane of sensors above the sources.

A total of 97 magnetic sensors are modeled to sit on regular grids in two planes above the source space. 81 sensors are oriented normal to the z-direction (see figure 1). 16 sensors are positioned in a second plane above, 8 oriented in x and 8 oriented in y direction (these sensors are not shown in figure 1 for clarity). The source space consists of 4096 cubic voxels with an edge length of $6\,\mathrm{mm}$.

B. Forward / Inverse Model

The contribution of the volume elements at location $\vec{r_i}$ containing magnetic nanoparticles with a concentration n_i to the magnetic field $\vec{B}$ in the sensor point $\vec{r_s}$ can be expressed by

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$$\vec{B}(\vec{r_s}) = \frac{\mu_0}{4\pi}\vec{d_s}\sum_i \left(\frac{3\vec{r}}{|\vec{r}|^5}\vec{r} - \frac{1}{|\vec{r}|^3}\right)\cdot\vec{H}(\vec{r_i})\cdot n_i. \quad (1)$$

with $\vec{r} = \vec{r_s} - \vec{r_i}$ and $\vec{d_s}$ being the normal vector of the SQUID's flux pickup loop. Combining the relations above for all sensor positions leads to

$$\vec{b} = \mathbf{L}\cdot\vec{n} \quad (2)$$

Here, $\vec{b}$ contains the magnetic field amplitudes in the sensor positions and $\mathbf{L}$ is the system matrix with the dimensions q by m (q - number of sensors, m - number of voxels). Combining multiple measurement samples with different excitation geometries results in a system matrix with the dimensions cq by m where c is the number of samples.

The system matrix incorporates information on sensors, sources and excitation properties. In the process of solving the inverse problem, the condition of $\mathbf{L}$ has crucial importance for the stability of the inverse solution $\vec{n}$ regarding numerical errors and noise contained in the measurement $\vec{b}$ and therewith influences the reconstruction quality.

C. Sequential Excitation

The simplest possible sequence of switching the excitation coils is a consecutive activation of one single coil per sample. However, this is ineffective and requires a large number of measurement cycles.

On the other hand, switching on randomly selected coils in each sample reduces the number of required samples to reach a certain imaging result. As these sequences are not deterministic and reproducible, this method is not suitable for most biomedical measurements. For the simulations in this paper, each coil has an activation probability of $p = 0.5$ in every sample.

Pseudo-random sequences offer similar properties, but they are generated deterministically, thus ensuring reproducibility and comparability of imaging results. In this paper, families of binary maximum-length sequences (m-sequences) are employed for the definition of the excitation sequences. These sequences are created by linear feedback shift registers. In our simulations, the members of a family of m-sequences, each defining the activation pattern of one measurement sample, are generated by shifting the initial sequence.

D. Condition analysis

To analyze the condition of a system matrix $\mathbf{L}$, the condition number κ with respect to the L2-norm is typically applied:

$$\kappa(\mathbf{L}) = \|\mathbf{L}\|\|\mathbf{L}^+\| = \sigma_1(\mathbf{L})\sigma_n(\mathbf{L})^{-1} \quad (3)$$

in which σ_i is the i-th of n singular values (SVs) of $\mathbf{L}$, with $\sigma_i \geq \sigma_{i+1}$. In order to compare different sensor and excitation setups resulting in a varying number of elements in the system matrix, a relative condition number is computed (see for example [5]):

$$\kappa_r(\mathbf{L}) = \sigma_1(\mathbf{L})\sigma_r(\mathbf{L})^{-1} \quad (4)$$

where σ_r is a singular value predefined with respect to the underlying source space. For the simulations in this paper, a value of $r = 291$ was selected according to typical similar inverse problems, which is equal to three times the number of sensors.

III. RESULTS

In order to evaluate the performance of the proposed sequences, the values of the relative condition number $\kappa_{291}(\mathbf{L})$ with respect to the described simulation setup were determined. Figure 2 compares these values for sequential, random and pseudo-random activation patterns for different sequence lengths. To ensure the comparability of the results, the current values in the excitation coils were normalized in the single coil activation to compensate the higher number of activated coils in each sample for random sequences and m-sequences.

For singular consecutive activations, $\kappa_{291}(\mathbf{L})$ clearly decreases with the length of the sequence, resulting in an improved condition of the underlying inverse problem. On the other hand, random sequences and m-sequences show similar behavior: After an initial decay, the values of the relative condition number approach a lower bound which indicates that no more information is added to the inverse problem in sequences with more than 10 samples. For the maximum length of 45 samples, the consecutive excitation performs better than random and pseudo-random sequences.

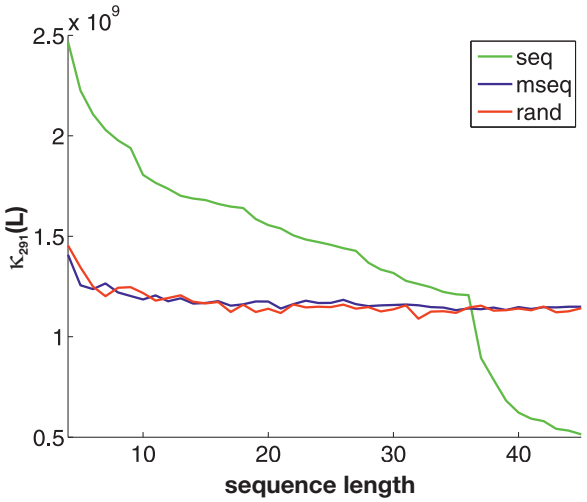

Fig. 2. Comparison of relative condition number values between consecutive (green), random sequences (red) and families of m-sequences (blue) for different sequence lengths.

Figure 3 displays the singular values of L for families of m-sequences with the number of samples varying from 1 to 45. All curves show similar values for the largest SVs, suggesting that most of the relevant information is contained

in these values. A high number of sequences results in a large amount of very small singular values that do not add much measurement information but lead to instable inverse solutions. It can be concluded that a number of 10 sequences will practically be sufficient to obtain the relevant information for a stable solution of the inverse problem, which is in accordance with the findings from figure 2.

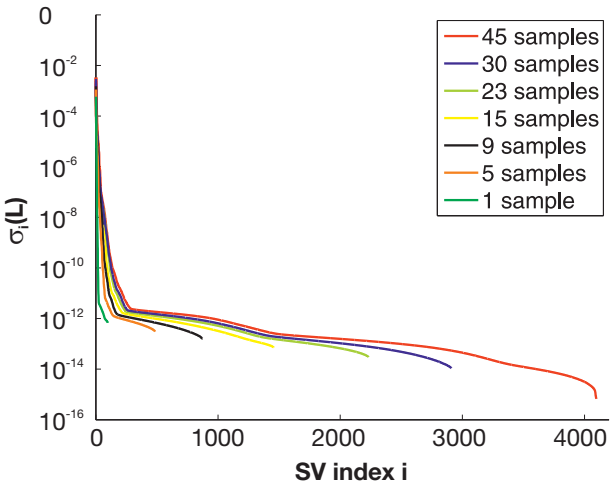

Fig. 3. Singular values of the system matrices for families of m-sequences with different number of measurement samples.

IV. CONCLUSION & OUTLOOK

This paper introduces novel excitation schemes for the imaging of magnetic nanoparticles by magnetorelaxometry with sequential inhomogeneous excitation fields. By analyzing the system matrix of the underlying inverse problem it could be shown that using random sequences and families of m-sequences considerably reduces the number of required measurement cycles compared to the consecutive activation of single coils while preserving the relevant information. For the investigated simulation setup, a number of 10 samples is suggested compared to 45 in single coil activation.

In future work, we will extend the simulations to other simulation setups. In this respect, also reconstruction results for realistic sources will be investigated. To further improve the performance of the excitation schemes, random sequences and m-sequences with different probabilities will be considered. Finally, different pseudo-random sequences, e.g. Kasami sequences, will be employed and examined.

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