Journal of Magnetism and Magnetic Materials 427 (2017) 139–143

Contents lists available at ScienceDirect

Journal of Magnetism and Magnetic Materials

journal homepage: www.elsevier.com/locate/jmmm

3D imaging of magnetic particles using the 7-channel magnetoencephalography device without pre-magnetization or displacement of the sample

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ARTICLE INFO

Keywords:
Magnetic nanoparticles
Ferrofluids
Magnetoencephalography
Spectral analysis
Functional tomography

ABSTRACT

SQUID-based magnetoencephalography device was used for the measurement of a magnetic noise generated by ferrofluid in the stationary standing vial. It was found that a free surface of the ferrofluid generates spontaneous magnetic field sufficient to detect the presence of nanoparticles in the experimental setup. The spatial distribution of elementary magnetic sources was reconstructed by the frequency-pattern analysis of multichannel time series. The localization of ferrofluids was performed based on the analysis of quasirandom time series in two cases of oscillation source. One of them was infrasound from outer noise, and another one was the human heartbeat. These results are prospective for 3D imaging of magnetic particles without pre-magnetization.

1. Introduction

The transparency of biological tissue to low-frequency magnetic fields permits the magnetic particles imaging (MPI) within the body. Usually the MPI method requires a sample containing the superparamagnetic particles, an oscillating magnetic field and/or a static magnetic field, and a magnetic field detector, which can be based on receive coils [1] or superconducting quantum interference devices (SQUID) [2]. The high sensitivity of SQUIDs allows the detection of magnetic nanoparticles in the samples subjected to the motion in the geomagnetic field instead of the pre-magnetization [3]. The possibility of the detection of magnetic nanoparticles in the ferrofluid using 151-channel SQUIDs based magneto-encephalography (MEG) device without pre-magnetization and mechanical movement of the sample was first demonstrated in [4]. The authors of the last paper installed a glass vial of magnetite nanoparticles based ferrofluid at stationary location within the MEG helmet region. They found that the frequency spectrum of the MEG data with the sample present was greater than the baseline sensor noise. Furthermore, the comparison between spatial contour maps of the frequency data measured without the sample and with the sample showed a distinct increase in frequency power just at the location of the sample. These results pointed to the possibility of MEG imaging of magnetic nanoparticles within living organisms.

The purposes of our work were to clarify the physical mechanism of the magnetic signal generation by the stationary vial of ferrofluid inside the MEG device and to verify the possibility of using the effect for the 3D imaging of ferrofluids.

2. Materials and methods

2.1. Synthesis of ferrofluids

Magnetite nanoparticles were prepared by sol-gel method. Aqueous solutions of iron chloride (1 g. $FeCl_2 \times 4H_2O$ + 2,72 g. $FeCl_3 \times 6H_2O$) were added to the 125 ml of 0.7 M ammonia solution and stirred vigorously for 30 min. Then the resulting suspension was precipitated on the magnet and the supernatant was poured. Then, the resulting precipitate was washed 4 times with aqueous solution of citrate (20 mg/ml), each time the suspension was precipitated on a magnet and the supernatant was poured. Water was then added to the precipitate. The mean size of the resulting nanoparticles 10–12 nm was evaluated by the Mossbauer spectroscopy method.

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http://dx.doi.org/10.1016/j.jmmm.2016.10.055
Received 26 June 2016; Received in revised form 8 October 2016; Accepted 11 October 2016

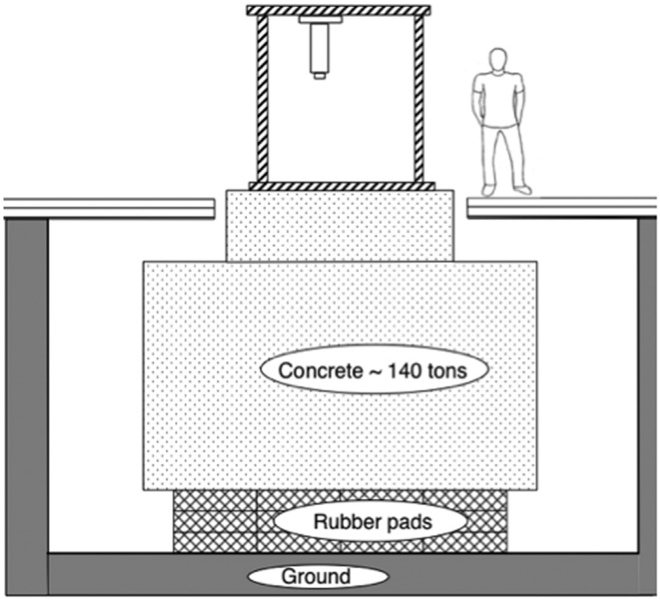

Fig. 1. The structure of the vibration-isolated foundation under the camera with the 7-channel MEG device situated in National Research Center "Kurchatov institute", Moscow.

2.2. Multichannel magnetic measurements

The measurements were carried out at 7-channel MEG device, designed for non-contact recording of a magnetic encephalogram of a human brain [5,6]. The planar set of sensors has a hexagonal structure and includes 7 second-order SQUID gradiometers. One gradiometer is located in the center of the hexagon. The distances between the gradiometers are 30 mm. The sensors demonstrate an intrinsic noise level lower than 5 fT/√Hz.

The MEG device is placed inside a thick-walled aluminum camera, designed for shielding from an alternating electromagnetic field. No shielding from static magnetic field is used. The camera is placed on the vibration-isolated foundation, shown in the Fig. 1. The total noise level of about 20–40 fT/√Hz was measured at urban conditions of Moscow city.

2.3. Data analysis

Quasirandom time series were recorded by the MEG device and then processed with recently developed method [7–9], based on the Fourier transform and coherence analysis. The method was developed in [7] to study various complex systems, and was applied to investigate the human brain spontaneous activity [8–10].

At the first step of this method, the set of discrete experimental vectors $\{\mathbf{b}_k\}$ is transformed into the set of continuous functions $\{\widetilde{B}_k(t)\}$:

$$\widetilde{B}_k(t)=F(\mathbf{b}_k,\ t),\ t\in[0,T],\ k=1,\dots,K. \tag{1}$$

where T is the time of measurement, k is the channel number, F is a function corresponding to the particular interpolation methodology [11]. The multichannel Fourier transform calculates a set of spectra for interpolated experimental functions:

$$a_{nk}=\frac{2}{T}\int_0^T\widetilde{B}_k(t)\cos(2\pi\nu_n t)dt,\ b_{nk}=\frac{2}{T}\int_0^T\widetilde{B}_k(t)\sin(2\pi\nu_n t)dt, \tag{2}$$

where a_{nk}, b_{nk} are Fourier coefficients for the frequency ν_n in the channel number k, and $n = 1, \dots N$, $N = \nu_{max}T$, where ν_{max} is the highest desirable frequency. The coefficient for n=0 is not considered, because the constant field component has no meaning in SQUID measurements.

To reveal the detailed frequency structure of the system, all spectra are calculated for the whole time of registration. The step in frequency is equal to $\Delta\nu=\nu_n-\nu_{n-1}=1/T$, thus frequency resolution is determined by the recording time. Gaussian quadrature formulas are used to calculate integrals for any interval [0, T]. In this study, all time series were measured for 20 min, thus providing frequency resolution 0,000833 Hz. In order to study the system in frequency space, we restore multichannel signal at every frequency ν_n in all channels and analyze the functions obtained:

$$B_{nk}(t)=\rho_{nk}\sin(2\pi\nu_n t+\varphi_{nk}), \tag{3}$$

where $\rho_{nk}=\sqrt{a_{nk}^2+b_{nk}^2}$, φ_{nk}=atan2$(a_{nk},\ b_{nk})$, a_{nk}, b_{nk} are Fourier coefficients, found in (2), $t\in[0,T_{\nu_n}]$, $T_{\nu_n}=1/\nu_n$ is the period of this frequency.

If $\varphi_{nk}=\varphi_n$, then formula (3) describes a coherent multichannel oscillation and can be written as

$$B_{nk}(t)=\rho_n\hat{\rho}_{nk}\sin(2\pi\nu_n t+\varphi_n), \tag{4}$$

where $\rho_n=\sqrt{\sum_{k=1}^{K}\rho_{nk}^2}$ is the amplitude, and $\hat{\rho}_{nk}=\rho_{nk}/\rho_n$ is the normalized pattern of oscillation. The normalized pattern $\hat{\rho}_{nk}$ makes it possible to determine the spatial structure of the source from the inverse problem solution, and this structure is constant throughout the entire period of the oscillation. The time course of the field is determined by the function $\rho_n\sin(2\pi\nu_n t+\varphi_n)$ which is common for all channels, i.e. this source is oscillating as a whole at the frequency ν_n.

The theoretical foundations for the reconstruction of static functional entities, or sources, have been developed in [7–9]. This reconstruction is based on detailed frequency analysis and extraction of the frequencies, having high coherence and similar patterns.

The algorithm of massive frequency-pattern analysis was formulated as:

1. Fourier Transform of the multichannel signal.
2. Inverse Fourier Transform – restoration of the signal at each frequency.
3. If the coherence at the particular frequency is close to 1, then use the pattern and frequency as elementary coherent oscillation.
4. If the restored signal consists of several phase-shifted coherent oscillations, then extract those oscillations.

After the fourth step of this analysis, the initial multichannel signal is represented as a sum of elementary coherent oscillations:

$$B_k(t)\cong\sum_{n=1}^{N}\sum_{m=1}^{M}D_{mn}\hat{\rho}_{mnk}\sin(2\pi\nu_n t+\varphi_{mn}),\nu_n=n/T,\ N=\nu_{max}T, \tag{5}$$

where M is maximal number of coherent oscillations, extracted at the frequency ν_n.

Each elementary oscillation is characterized by frequency ν_n, phase φ_{mn}, amplitude D_{mn}, normalized pattern $\hat{\boldsymbol{\rho}}_{mn}$ and is produced by the functional entity having a constant spatial structure.

The method of functional tomography reconstructs the structure of the system from the analysis of the set of normalized patterns $\{\hat{\boldsymbol{\rho}}_{mn}\}$. The functional tomogram displays a 3-dimensional map of the energy produced by all the sources located at a given point. In order to build a functional tomogram, the space under study is divided into $N_x\times N_y\times N_z$ elementary cubicles with centers in $\mathbf{r}_{ijs}$. The edge of the cubicle (spatial resolution) in this study is 1 mm. To calculate the energy produced by all the sources located in the center of the cubicle, the set of L trial magnetic dipoles $\mathbf{Q}_{ijsl}$ is build. The magnetic induction from the trial source can be derived from [12] for the coil with current I, radius a and direction $\mathbf{Q}_{ijsl}$, located in $\mathbf{r}_{ijs}$. For the sensor with location $\mathbf{r}_k$ and direction $\mathbf{n}_k$, the element of the trial pattern will be: