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Three-dimensional magnetic nanoparticle imaging using small field gradient and multiple pickup coils

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ABSTRACT

We propose a magnetic particle imaging (MPI) method based on third harmonic signal detection using a small field gradient and multiple pickup coils. First, we developed a system using two pickup coils and performed three-dimensional detection of two magnetic nanoparticle (MNP) samples, which were spaced 15 mm apart. In the experiments, an excitation field strength of 1.6 mT was used at an operating frequency of 3 kHz. A DC gradient field with a typical value of 0.2 T/m was also used to produce the so-called field-free line. A third harmonic signal generated by the MNP samples was detected using the two pickup coils, and the samples were then mechanically scanned to obtain field maps. The field maps were subsequently analyzed using the nonnegative least squares method to obtain three-dimensional position information for the MNP samples. The results show that the positions of the two MNP samples were estimated with good accuracy, despite the small field gradient used. Further improvement in MPI performance will be achieved by increasing the number of pickup coils used.

1. Introduction

Magnetic nanoparticles (MNPs) have been widely studied for use in biomedical applications. One of these applications is the so-called magnetic particle imaging (MPI), which is used to detect the positions and numbers of MNPs that are accumulated in a human (or animal) body for in vivo medical diagnosis purposes [1–12]. In this application, the MNPs are magnetized using an excitation field, and the resulting signal from the MNPs is detected using one or multiple pickup coil(s). The positions and numbers of the MNPs can then be reconstructed from the measured data through solution of an inverse problem.

The signal that is detected using the pickup coil, B_s, is known to be determined by two terms. The first term is the response of the MNPs to the excitation field, i.e., the magnetization signal B_{MNP}. The other term is the relative distance between the MNPs and the pickup coil. Based on these characteristics, three typical MPI methods have been developed.

The first method involves application of a homogeneous AC excitation field and measurement of the contour map of the signal field generated by the MNP sample [1–3]. In this case, the relative distance between the MNPs and the pickup coil varies at each measurement point. This means that the contour map includes the required information about the spatial distribution of the MNPs. The MNP distribution can therefore be reconstructed from the contour map by solving the inverse problem. While this method requires a relatively simple measurement system, the spatial resolution of MNP detection is reduced when the MNPs are located far away from the pickup coil. This is because the signal field broadening increases in this case.

The second method involves use of an inhomogeneous AC excitation field [4,5]. In this case, the excitation field strength is spatially distributed, and B_{MNP} for the MNPs is determined by the excitation field at the MNP positions. Therefore, if the distribution of the excitation field is known beforehand, additional information about the spatial distribution of the MNPs can be obtained based on B_{MNP}. As a result, the contour map of the signal field obtained using the inhomogeneous excitation field contains much more information about the MNP spatial distribution than that in the homogeneous excitation field case. While the spatial resolution of MNP detection can be improved using this method, this spatial resolution is significantly dependent on the excitation field distribution profile. Therefore, optimum inhomogeneous excitation field design is a crucial factor.

The third method involves the use of an additional DC gradient field to produce the so-called field-free point (FFP) [6–12]. Because of the properties of the MNPs, the magnetization signal B_{MNP}, which is composed of harmonic signals, is generated selectively from the MNPs that are located at the FFP. This means that the information with regard to the MNP spatial distribution can be acquired using the

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FFP. The signal field from the MNPs located at the FFP can be detected using a large pickup coil. By three-dimensional scanning of the FFP, we can obtain the spatial distribution of the MNPs. While high spatial resolution can be achieved in MNP detection, we need to develop a gradient coil that can generate a strong field gradient (typically 1–2 T/m). This is because MPI spatial resolution is proportional to the field gradient. Additionally, we also need to develop a method to perform three-dimensional scanning of the FFP.

In our previous work, we developed a two-dimensional MPI system that used third-harmonic signal detection and the FFP [12]. In this system, we used a relatively low AC excitation field (1.6 mT) and small field gradient (0.3 T/m). We demonstrated spatial resolution of 10 mm with this system, despite the low field gradient. This was achieved using the properties of the MNPs. Specifically, the field gradient, which is necessary to maintain the spatial resolution of the process, can be reduced by reducing the excitation field, as shown in Ref. [13]. As a result, we were able to use a compact power supply for the coil systems.

In this work, we extend the previous system to develop three-dimensional MPI. For this system, we use a gradient field that produces a field-free line (FFL). We also use multiple pickup coils for signal detection. This combination of the FFL with multiple pickup coils allows us to obtain three-dimensional information about the spatial distribution of the MNPs. We first developed an MPI system that used two pickup coils and a field gradient of approximately 0.2 T/m. Using the resulting system, we then performed three-dimensional detection of two MNP samples. The signal field contour maps were measured using the two pickup coils when the MNP samples were mechanically scanned. Then, we reconstructed the three-dimensional distribution of the MNPs from the measurement contour maps by solving the inverse problem using the nonnegative least squares (NNLS) method.

2. Method

2.1. Measurement system

Fig. 1 shows a schematic depiction of the MPI system using third-harmonic signal detection. The system was previously described in detail in Refs. [12] and [14]. The measurement system consists of three coils, which are the excitation, pickup, and gradient coils. The excitation coils are 300 mm in diameter and are spaced 300 mm apart. An excitation field B_{ac} with a root mean square value of 1.6 mT and an operating frequency of f =2.93 kHz was applied along the y direction via the excitation coils. An MNP sample was magnetized by the excitation field and generated a third harmonic signal B_s at f =8.79 kHz as a result because of the nonlinear magnetization of the MNP sample. The z-component of the signal field was then detected using the two pickup coils.

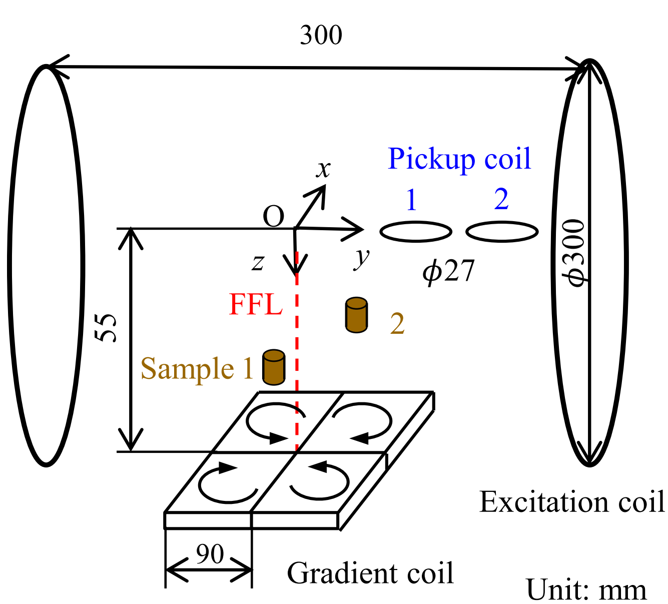

Fig. 1. Schematic diagram of measurement system.

Pickup coils 1 and 2 were set at positions (x_p, y_p, z_p) =(0, 15 mm, 0) and (0, 60 mm, 0) in xyz coordinates, respectively, as shown in Fig. 1. The pickup coils were made from Cu Litz wire, and the average diameter and number of turns of these coils were D =27 mm and N =200, respectively. The coils were cooled to 77 K using liquid nitrogen to reduce thermal noise. The inductances of pickup coils 1 and 2 were L_1 =0.927 mH and L_2 =0.937 mH, respectively, and the corresponding resistances were R_1 =0.43 Ω and R_2 =0.41 Ω at T=77 K, respectively. Pickup coils 1 and 2 were connected to resonant capacitances of C_1 =0.3581 μF and C_2 =0.3351 μF, respectively, to enhance the third harmonic signal that is generated in the pickup coils. The resulting voltage was amplified using a low-noise preamplifier (SA-421F5, NF Corp.), and the third harmonic signal was then measured using a lock-in amplifier (LI5640, NF Corp.). The magnetic field noise of the detection system reached a minimum at the resonant frequency. We obtained the magnetic field noise of the pickup coil $S_B^{1/2}$ =9 fT/Hz$^{1/2}$ at a signal frequency of f =8.79 kHz.

The gradient field was generated using a planar coil that consisted of four square coils, as shown in Fig. 1 [12]. Each of these square coils had an average side length of 90 mm and comprised 200 turns. A DC current of 3.5 A was supplied to the gradient coil in the direction shown in Fig. 1.

Fig. 2 shows the calculated distribution of the magnetic field generated by the gradient coil. Fig. 2(a) shows the distribution of $|\boldsymbol{B}_{dc}|$ in the yz plane at x=0, where $|\boldsymbol{B}_{dc}|$ is the absolute value of the DC gradient field. As shown, $|\boldsymbol{B}_{dc}|$ becomes zero along the z axis, i.e., along the line that passes through the center of the gradient coil. The FFL was therefore generated along this line.

Fig. 2(b) shows the distribution of $|\boldsymbol{B}_{dc}|$ in the xy plane at z=50 mm. It can be shown that the gradient field mainly has x and y components near the FFL, and the field distribution can then be expressed approximately as

$$\boldsymbol{B}_{dc}=(Gy,\ \ Gx,0), \tag{1}$$

where G is the field gradient. The value of G varied from 0.15 to 0.25 T/m as the z position changed from 30 to 50 mm.

As shown in Fig. 1, the combination of the FFL and the two pickup coils was used in the method presented here to obtain the required information about the three-dimensional positioning of the MNP sample. When the sample is scanned in the xy plane around the FFL, a high third-harmonic signal is generated by the sample. Therefore, the MNP distribution in the xy plane can be acquired using the FFL. We note that the FFL is essential for improved spatial resolution, although the field gradient is small. The spatial resolution deteriorates dramatically if we do not use the FFL.

However, we cannot obtain sufficient information about the MNP distribution along the z axis using a single pickup coil. Two pickup coils were therefore used to increase the information that is acquired. Because pickup coils 1 and 2 have different distances r for the same sample, we can obtain the required information on r from a comparison of the signal fields measured using pickup coils 1 and 2. In particular, the information required about the z-position of the sample can be obtained. In this manner, we can acquire the three-dimensional position information for the MNP sample using the combination of the FFL with multiple pickup coils.

2.2. Imaging procedure

In this experiment, three-dimensional detection of two MNP samples was performed using the following procedure. First, the two MNP samples were set at different sample positions, denoted by (x_s, y_s,

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