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Variation of Magnetic Particle Imaging Tracer Performance With Amplitude and Frequency of the Applied Magnetic Field

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Abstract

The magnetic response of magnetic particle imaging (MPI) tracers varies with the slew rate of the applied magnetic field, as well as with the tracer's average magnetic core size. Currently, 25 kHz and 20 mT/ μ_0 drive fields are common in MPI, but lower field amplitudes may be necessary for patient safety in future designs. We studied how several different sizes of monodisperse MPI tracers behaved under different drive field amplitude and frequency, using magnetic particle spectrometry and ac hysteresis for drive field conditions at 16, 26, and 40 kHz, with field amplitudes from 5 to 40 mT/ μ_0 . We observed that both field amplitude and frequency can influence the tracer behavior, but that the magnetic behavior is consistent when the slew rate (the product of field amplitude and frequency) is consistent. However, smaller amplitudes provide a correspondingly smaller field of view, sometimes resulting in excitation of a minor hysteresis loop.

Index Terms

AC hysteresis; iron oxide nanoparticles; magnetic particle imaging (MPI); magnetic particle spectrometry (MPS); MPI tracers

I. Introduction

Magnetic particle spectrometry (MPS) [1]–[3] is a powerful technique for analyzing the magnetic behavior of nanoparticle tracers under conditions relevant for magnetic particle imaging (MPI). MPS has enabled fundamental investigations of complex MPI tracer

behavior [3], [4] and proved to be a useful *in vitro* analytical tool to support animal studies, for example, studies to evaluate the blood circulation time of magnetic nanoparticles [5].

During MPS measurements, nanoparticle magnetization is excited by an alternating magnetic field to induce a signal in a receiver coil. Subsequently, the signal is processed to generate a characteristic harmonic spectrum and/or the tracer response, defined to be the derivative of particle magnetic moment with respect to field, $m'(H(t))$. These datasets provide information about how magnetic particles respond to an applied field under a variety of conditions.

While the harmonic spectrum and tracer response are often used when presenting MPS data, the hysteresis loop is a complementary presentation that is commonly used to understand magnetic materials. In particular, ac hysteresis loops, acquired with an ac field, such as in an MPS, are relevant for understanding the dynamic magnetization of materials used in MPI or magnetic fluid hyperthermia [6].

In this paper, we measured the response of MPI tracers to several excitation field amplitudes and frequencies, using an MPS at the University of Washington in Seattle and an ac hysteresis device at Yokohama National University in Japan. Our goal was to investigate whether tracers optimized for MPI at the current-standard drive field frequency of ~ 25 kHz and amplitude of ~ 20 mT/ μ_0 will be effective under different drive field conditions, including those that comply with newly determined MPI safety limits [7].

II. Methods

A. Particle Preparation

Magnetite (Fe_3O_4) nanoparticles were synthesized by the pyrolysis of the Fe(III) oleate precursor with excess oleic acid surfactant in 1-octadecene. After synthesis, oleic acid coated magnetite nanoparticles were transferred from organic to aqueous phase using a PEGylated amphiphilic polymer [poly(maleic anhydride-alt-1 octadecene)-poly(-ethylene glycol); PEG $M_n = 20$ kDa]. Detailed synthesis and phase transfer methods have been reported [8].

In this paper, three nanoparticle samples with median core diameters of 14, 22, and 26 nm and narrow size distributions were studied. Median core diameter, d_c , was measured by TEM and by fitting room temperature vibrating sample magnetometer (VSM) data to the Langevin function and assuming a log-normal size distribution with geometric standard deviation $\exp(\sigma)$ [9], [10]. Hydrodynamic size was measured by dynamic light scattering using a Malvern Zetasizer. Properties of the nanoparticle tracers are provided in Table I.

B. MPS Measurements at University of Washington

MPI signal was measured using a custom-built MPS that excites tracer magnetization and measures the signal induced in a receive coil by the MPI tracer response, $m'(H(t))$. The University of Washington MPS first described in [3] was recently modified to operate at additional excitation field frequencies of 15.5 and 40.2 kHz. For all MPS measurements, 10 μl of nanoparticle solution at concentrations of 22.1 mgFe/ml (14 nm core), 35.6 mgFe/ml

(22 nm core), and 29.6 mgFe/ml (26 nm core) was transferred to 0.6 ml microcentrifuge tubes and inserted into the system. The MPI signal was measured with the exciting field of 5, 10, 20, and 40 mT/ μ_0 at 15.5, 26.0, and 40.2 kHz. MPI signal testing was always performed in triplicate.

MPS data was analyzed using standard procedures discussed in [11]–[13]. The magnetic field applied by the MPS can be described mathematically by

$$H(t) = H_0 \sin(\omega t) \quad (1)$$

in which H_0 is the peak excitation amplitude [A/m] and ω the angular frequency ($2\pi f_0$). The received voltage, V , is

$$V(t) = -\mu_0 \cdot S \cdot m'(t) = -\mu_0 \cdot S \cdot m'(H(t)) \cdot H'(t) \quad (2)$$

in which μ_0 is the vacuum permeability [$4\pi \times 10^{-7}$ V · s/A · m] and S is the coil sensitivity [1/m]. Rearranging (2) yields the MPI tracer response

$$m'(H(t)) = \frac{-1}{\mu_0 \cdot S \cdot \omega \cdot H_0 \cos(\omega t)} V(t) \quad (3)$$

which has units of [m^3]. The tracer response is visualized as a parametric plot {H, dm/dH} since the field, $H(t)$, is known for all times t . Though not discussed here, harmonic spectra were also generated by Fourier transform of received signal, $V(t)$.

To complement MPS results, ac hysteresis measurements were performed independently on the same set of three samples at identical sample concentrations. All ac hysteresis loops presented here were measured at Yokohama National University using a custom-built circuit [6]. A 250-turn, water-cooled solenoid coil with a 55 mm diameter was used to excite tracer magnetization that generated the signal in a gradiometer receive coil. A glass tube ($\phi = 1.5$ mm) was used as the sample holder. Hysteresis loops were determined by numerical integration of (3).

III. Results

In Fig. 1(a)–(c), we have plotted $m'(H(t))$ for three different tracers after excitation with 26 kHz, 20 mT/ μ_0 applied field. The response, $m'(H(t))$, was calculated using (2) and normalized to iron content. Only the half of the tracer response that corresponds to the increasing magnetic field sweep is displayed. The maximum intensity of the tracer response increases with nanoparticle size. The corresponding ac hysteresis loops, acquired under the same applied field conditions, are shown in Fig 1(d) and show a trend toward increased susceptibility and coercivity as the tracer magnetic core size increases. These results confirm that the particle response depends strongly on magnetic particle size, as previously reported [3], [4], [10].

In Fig. 1(b) and (e), tracer responses and ac hysteresis loops are plotted for the 26 nm tracer under three different excitation field frequencies: 15.5, 26.0, and 40.2 kHz. In each case, the

field amplitude was $20 \text{ mT}/\mu_0$. We reiterate that the influence of slew rate, $\mu_0 H_0 \omega$, on received voltage due to Faraday's law has been removed from all data in Fig. 1, according to (3). We observe in Fig. 1(b) and (e) that the change in tracer magnetism is minor with frequency for the measured frequency range. A slight difference in tracer response was observed between the 15.5 kHz excitation and the two higher frequencies; in Fig. 1(b), the response curves for higher frequencies are shifted to the right, i.e., toward higher fields. The ac hysteresis loops measured at each frequency were very nearly the same. Though not shown here, the same trends were observed with increasing frequency for the 14 and 22 nm samples when the field amplitude was constant.

In Fig. 1(c) and (f), tracer responses and ac hysteresis loops are plotted for the 26 nm sample after excitation by a constant frequency (26 kHz) field when the field amplitude was varied from 5 to $40 \text{ mT}/\mu_0$. For small field excitations ($20 \text{ mT}/\mu_0$), the tracer magnetization remained in the quasi-linear regime and did not fully saturate. As a result, the tracer response did not fall to zero. This behavior corresponds to a minor hysteresis loop. In contrast, tracer magnetization saturated when the excitation field amplitude was greater or equal to about $20 \text{ mT}/\mu_0$, resulting in a major hysteresis loop and in the tracer response decaying fully to zero at the edges of the field of view.

When different combinations of amplitude and frequency produced a similar magnetic slew rate ($\mu_0 H_0 \omega$), the tracer response was similar. An example is provided in Fig. 2. Two different sets of conditions produced slew rates that differed by about 20%: $40 \text{ mT}/\mu_0$ amplitude at 15.5 kHz and $20 \text{ mT}/\mu_0$ at 26 kHz produced slew rates of 3900 and 3270 $\text{T}/\mu_0/\text{s}$, respectively. There is an obvious difference in the field of view, but where the curves overlap they are similar. In Fig. 2(a), differences due to Faraday's law have been removed according to (3), showing that the tracer response was indeed the same for both sets of conditions. In contrast, when the measured voltage was not scaled by the slew rate, as shown in Fig. 2(b), a 20% difference resulted that matched the 20% difference in slew rates.

Each of the three samples displayed superparamagnetic behavior, with no coercivity, in dc measurements of magnetization versus field (Fig. 3).

IV. Discussion

In our experiments, 22 and 26 nm tracers showed ferromagnetic behavior under the given experimental conditions, since they featured an open hysteresis loop, but 14 nm tracer showed a mostly superparamagnetic character, with a very slight open loop.

The MPI tracer response is expected to vary with the slew rate, $\mu_0 H_0 \omega$, of the applied field due to finite magnetic relaxation rates. We observed slight changes in the tracer response when we varied the slew rate by holding the field amplitude constant and changing the frequency from 15.5 to 40 kHz. We would expect to see a greater change in response if the frequency range were further increased and a logical next step would be to further extend the excitation field frequency by one or more orders of magnitude.

Changing slew rate by holding frequency constant and varying the field amplitude did impact the magnetization response in our experiments. Most significantly, changing the field

amplitude changed the effective field of view: for small amplitudes the tracer magnetization did not fully saturate and thus only a portion of the full response was observed, resulting in minor hysteresis loops. In addition, the width of the tracer response, $m'(H(t))$, narrowed slightly with decreasing amplitude and slew rate, possibly due to greater impact of thermal energy at lower slew rates. As $H'(t)$ decreased, the likelihood of magnetic reversal at lower field strengths increased, due to thermal excitations. Though we observed the response to vary with field amplitude, the magnitude of change was relatively small for the range of measured conditions.

To avoid peripheral nerve stimulation and specific absorption [7], it may require MPI drive field amplitudes to be lower than the current standard, 20–25 mT/ μ_0 . Since the received signal, $V(t)$, scales with slew rate according to Faraday's law, concomitantly increasing excitation frequency may provide some signal gain to offset what is lost by reducing amplitude. However, gains would be partially offset by increases in receive coil resistance and receive chain bandwidth at higher frequencies. Furthermore, while the field of view will vary with the drive field amplitude, it should be possible to combine many small fields of view into an MPI image without a loss to image quality. A variable field of view and frame rate would allow a user to optimize image quality for a given application. Our results indicate that well-optimized MPI tracers can be expected to show a similar magnetic response over a range of excitation field frequencies and amplitudes and the same response if the magnetic slew rate is held constant.

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Fig. 1.

MPS ($m(H(t))$) and ac hysteresis results for varying particle size, drive field frequency, and amplitude. (a) MPS and (d) ac hysteresis for all sizes at 26 kHz, 20 mT/ μ_0 . (b) MPS and (e) ac hysteresis for 26 nm at 20 mT/ μ_0 , all frequencies. (c) MPS and (f) ac hysteresis for 26 nm diameter sample at 26 kHz and amplitude varied from 5 to 40 mT/ μ_0 .

Fig. 2.

(a) Tracer response of 26 nm tracer under two different conditions that generated similar magnetic slew rates: 40 mT/μ_0 field amplitude at 15.5 kHz and 20 mT/μ_0 field amplitude at 26 kHz. The angular slew rates ($\mu_0 H_0 \omega$) were 3900 and 3270 T/s, respectively. (b) Received voltage was scaled with the slew rate, according to (2).

Fig. 3.
All three tracers showed superparamagnetic behavior in dc hysteresis loops measured by VSM.

TABLE I

Physical Properties of Nanoparticle Tracers

Sample	d_c nm (σ)		d_H nm(PDI)
	TEM	VSM	
14 nm	*	14.4 (0.17)	75 (0.17)
22 nm	22.0 (0.13)	21.5 (0.24)	71 (0.15)
26 nm	25.8 (0.16)	22.5 (0.30)	63 (0.15)