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Drive-field Frequency Dependent MPI Performance of Single-Core Magnetite Nanoparticle Tracers

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Abstract

The drive-field frequency of Magnetic Particle Imaging (MPI) systems plays an important role for system design, safety requirements and tracer selection. Because the commonly utilized MPI drive-field frequency of 25 kHz might be increased in future system generations to avoid peripheral nerve stimulation, a performance evaluation of tracers at higher frequencies is desirable. We have studied single-core magnetite nanoparticles that were optimized for MPI applications, utilizing Magnetic Particle Spectrometers (MPS) with drive-field frequencies in the range from 1 kHz up to 100 kHz. The particles have core diameters of 25 nm and a hydrodynamic size of 77 nm. Measurements in the frequency range above 5 kHz were carried out with a newly designed MPS system. In addition, to exclude possible particle interaction, samples of different concentrations were characterized and compared.

Keywords

Magnetic particle imaging; magnetic particle spectroscopy; magnetic particles; tracer performance

I. Introduction

The drive-field frequency of Magnetic Particle Imaging (MPI) systems plays an important role for system design, safety requirements and tracer selection. Current MPI systems widely use a drive frequency of 25 kHz, which has the potential to cause peripheral nerve stimulation at higher field strengths [1], [2]. Increasing the drive frequency can avoid this effect, provided the tracer performance remains optimal in spite of any changes in particle dynamics. Measurements using a Magnetic Particle Spectrometer (MPS) are well suited to evaluate whether a particle tracer achieves satisfactory performance [3] and can be used for optimizing them at drive frequencies above 25 kHz.

In addition, the investigation of the drive-field-frequency dependent particle behavior helps develop proper physical models of magnetic relaxation and thus better understanding of particle properties. A possible application is the determination of particle mobility from the magnetic response.

II. Materials and Methods

A. Single core magnetite nanoparticle tracers

We examined suspensions of single core magnetite nanoparticle tracers, denoted as UW-A, with emphasis on their MPI performance. The average core diameter was determined to be 25.3 nm with geometric standard deviation of 0.23, by fitting $M(H)$ data, assuming a single log-normal distribution. These results agree well with TEM measurements that showed 25 nm core size with geometric standard deviation of 0.21. Dynamic light scattering was used to obtain the mean hydrodynamic diameter of 77 nm, with a polydispersity index of 0.065 indicating a monodisperse size distribution. These particle tracers, having a wide range of applications in biomedicine [4], were specifically tailored for MPI applications and showed superior performance in previous experiments [5], [6].

B. Magnetic particle spectrometers

Magnetic particle spectrometers can be regarded as 0-dimensional MPI scanners, generating a pure sinusoidal drive-field of high amplitude to explore the dynamic nonlinearity of the nanoparticle's magnetization curve. As the mode of operation lies in the nonlinear regime of the particles, the observed dynamics can be different from those determined by methods with smaller amplitudes, such as AC susceptibility. For the same reason, static measurements may also lead to different results.

We have built a modular MPS system that was specifically designed to explore particle behavior at higher drive frequencies. A solenoid coil is used to generate a homogenous drive-field. The maximum field inhomogeneity within the sample volume of up to 200 μl is less than 1% according to simulations. A gradiometric detection system is used to measure the response of the sample while suppressing direct feed-through from the drive-field. In contrast to a single detection coil followed by bandstop filters, this method retains acceptable dynamic range at the drive frequency and allows dynamic $M(H)$ measurements. Fig. 1 shows the coil system with the excitation coil visible at the center.

Our novel MPS allows drive-field frequencies of 10 kHz, 25 kHz, 50 kHz and 100 kHz with amplitudes up to 35mT.

A second MPS system [7] is used for the evaluation at lower drive frequencies ranging from 1 kHz to 10 kHz. As we have shown before, this range is especially suited to examine particle mobility [8].

C. MPI performance of magnetic nanoparticle tracers

MPI scanners rely on the nonlinearity of the magnetization response of magnetic nanoparticle tracers when subjected to magnetic fields of sufficient amplitude. Most scanners use a field free point or a field free line that is shifted through the sample via a

drive-field. The resulting nonlinear response of the particles in conjunction with a static gradient is used to reconstruct image information from the detected signal. This can be achieved in the frequency domain by first acquiring a system function and solving the inverse problem of the spectral image data [9]. Another method is to utilize the known dependence of the field-free-point position and the acquisition time, allowing x-space reconstruction in the time domain [10].

Both approaches benefit from particle tracers with a high magnetic moment and a narrow and steep dynamic $M(H)$ response. In the frequency domain, this results in a spectrum with high amplitude and a flat slope of harmonic decay. In time domain this corresponds to a high and narrow point spread function (PSF), which can be characterized by the FWHM value. Therefore, the harmonic amplitudes as well as the FWHM of the PSF are key parameters for the determination of tracer behavior.

In order to assess the MPI performance of the aforementioned particle tracers, we evaluate the change of these key parameters as the drive frequency is increased. The point spread function is calculated according to [11] by

$$\frac{d}{dH}m(H) = \frac{dm(H(t))}{dt} \frac{dt}{dH}. \quad (1)$$

It is possible to obtain dm/dt using the voltage $v(t)$ which is induced in the detection coil. According to Faraday's law

$$v(t) = -\mu_0 S \left(\frac{d}{dt}m(t) \right), \quad (2)$$

where S is the sensitivity of the coil. Substituting (2) and the known dependence $H(t) = H_{pk} \sin \omega t$ into (1) we obtain an expression that calculates dm/dH from the measured signal

$$\frac{d}{dH}m(H) = \frac{-v(t)}{\mu_0 S} \cdot \frac{1}{H_{pk} \omega \cos \omega t}. \quad (3)$$

The parametric plot of $H(t)$ and $dm(t)/dH(t)$ is referred to as PSF. The aforementioned FWHM value is calculated using this plot.

In order to obtain the magnetic excitation field, the current through the excitation coil is acquired synchronously with the detection signal. The corresponding magnetic field is known through simulations and has been verified experimentally using a Gauss meter.

As the utilized MPS has a gradiometric detection system, it is possible to obtain $m(H)$ by integrating (2) to calculate $m(t)$ and plotting $H(t)$ and $m(t)$ as a parametric curve.

III. Results

Fig. 2 shows the odd harmonic amplitudes of the magnetic moment of UW-A particles. Frequencies below 10 kHz were measured using the low frequency MPS setup. The rate of

decrease in harmonic amplitude became steeper as the drive frequency was increased. Due to the acquisition bandwidth, the number of acquired harmonics at higher drive frequencies is reduced. The frequency dependence due to Faraday's law has been removed from the data.

The examined particles exhibited a rich spectrum of harmonics at all drive frequencies. However, the steeper harmonic decay at higher frequencies has the tendency to reduce the number of observable harmonics.

Changes due to particle dynamics were also observed in the time domain in the form of a widened dynamic $M(H)$ response (Fig. 3). As the particles are superparamagnetic, the observed hysteresis, which increased with the drive frequency, is a dynamic effect and was absent in static $M(H)$ measurements.

Another parameter that reflects the dynamic behavior in the time domain is the FWHM of the particle PSF. Table I shows the results of PSF FWHM measurements at the examined drive frequencies. Clearly, the PSF monotonically widened as the drive frequency was increased.

All currently available MPI systems use coils to detect the particle signal. Due to Faraday's law, the detection amplitude increases proportional to the frequency for a given amplitude of particle magnetization. Fig. 4 shows the raw spectral signal acquired by the MPS setups. As expected, the amplitude of the harmonics rises with the drive frequency. However, this is offset by the steeper harmonic decay.

For all drive frequencies above 5 kHz we observed an intercept point at which the detected signal dropped below the one at lower drive frequencies. The harmonic number at which this intercept point occurs can vary across system setups, as transfer characteristics are part of the data and remain uncorrected at this point. Coil impedances in conjunction with the input impedance of the preamplifier can lead to a deviation from a pure frequency proportional transfer function, especially at higher harmonics.

In order to check particle stability and to exclude effects due to particle interaction, all measurements were carried out at different concentrations. After normalization to the iron concentration (ranging from 2.5 mmol/l to 25 mmol/l), all samples showed the same response.

For comparison with other commercial particle systems, Fig. 5 shows the results of UW-A particles and Resovist®, which is the commonly used MPI tracer. The hydrodynamic diameter of Resovist was reported to be 45 nm [12]. The core consists of (5-7) nm crystallites that form effective "magnetic particles" with sizes up to 20 nm [12]. Due to the wide distribution of magnetic properties, only a fraction of Resovist particles contribute significantly to the MPS response [13].

The observed performance of UW-A exceeded that of Resovist over the entire drive frequency range consistently by at least 12dB harmonic amplitude for the same amount of iron in the sample. For drive frequencies up to 50 kHz and spectral amplitudes beyond the

13th harmonic, UW-A achieved ten times the amplitude of Resovist. Interestingly, the increase in harmonic decay was similar for both particle systems at higher harmonics.

IV. Discussion

The examined particle tracers show a rich spectrum of harmonics at all applied drive frequencies up to 100 kHz, making them a suitable tracer for MPI applications. However, particle dynamics reduce the performance as the drive frequency is increased. Faraday's law does not fully compensate this effect so that a net decrease in resolution for MPI applications can be expected if the excitation amplitude is held constant. This can be deduced from the reduced number of observable harmonics and the widened PSF.

On the other hand, SAR limits require the excitation amplitude to be decreased at higher frequencies [14], reducing the slew rate of the magnetic field. As particle dynamics are related to the sweep rate of the field, it can be expected that the observed performance loss will be mitigated at reduced excitation amplitudes [15]. However, a reduced field of view and therefore a potentially increased scanning time would result.

Overall, the UW-A particle tracers retain superior performance compared to commercial Resovist® over the entire frequency range, even at high sweep rates. There was no observable particle interaction as measurements scaled linearly with particle concentration.

Measurements in biological media at excitation field strengths related to SAR limits seem to be the next step for a complete performance evaluation at increased drive frequencies.

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Fig. 1.
MPS system for drive frequencies ranging from 10 kHz to 100 kHz

Fig. 2.

Odd harmonic amplitudes of the particle moment at 25 mT drive field amplitude and drive frequencies between 1 kHz and 100 kHz. As the drive frequency is increased, the slope of the harmonics becomes steeper.

Fig. 3.

Dynamic magnetization curves for different excitation frequencies and 25 mT field amplitude. The $M(H)$ response becomes wider as the frequency is increased. This increase, as well as the hysteresis result from particle dynamics.

Fig. 4.

Amplitudes of odd harmonics in the detection signal. Due to Faraday's law the amplitude increases with the drive-field frequency and counters the steeper harmonic decay up to an intercept point.

Fig. 5.

Comparison between the odd harmonic amplitudes of Resovist and UW-A particles at different drive frequencies. The amplitude of the excitation field was 25 mT. The signals have been normalized to the amount of iron in the sample.

TABLE I

FWHM of the PSF for different drive frequencies and 25 mT field amplitude

drive frequency (kHz)	FWHM (mT)
1	1.008
5	3.371
10	5.440
25	7.761
50	11.049
100	16.509