Effect of core size distribution on magnetic nanoparticle harmonics for thermometry

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We investigated the effect of core size distribution on the performance of a magnetic nanoparticle thermometer (MNPT) in circumstances when Néel relaxation dominates the dynamic behavior of particles. Numerical simulations revealed the effects of excitation field strength and core size distribution on the temperature dependence of the amplitude and phase of harmonics. In MNPT, the field dependences of sensitivity deviated significantly from those calculated when the core size distribution was neglected. These simulation results were compared with those from experiments for which reasonable agreement was obtained. These findings must be carefully considered when designing an optimal MNPT system.

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Magnetic nanoparticles (MNPs) have been widely studied for biomedical applications such as magnetic particle hyperthermia (MPH)1–3 and magnetic particle imaging (MPI).4–6 MPH involves locally heating up cancer/tumor tissue above 43 °C to kill cancer/tumor cells.7 In MPH, temperatures around the MNPs must be controlled so that the normal surrounding tissue is not damaged. Therefore, accurate temperature monitoring is crucial in realizing this non-/low-invasive cancer treatment.8,9 MPI is a new modality for imaging the spatial distribution of MNPs. Temperature monitoring is also important in realizing high quality MPI because the magnetization of the MNPs is affected by the physical state of the surroundings such as temperature and viscosity.9–11

The magnetic nanoparticle thermometer (MNPT) is a novel tool using MNPs for non-invasive temperature measurements.12–16 Weaver et al. proposed a method for measuring temperatures using the ratio of the intensities of the 5th (M5) and 3rd (M3) harmonic magnetizations of MNPs.12 A MNPT using the phase lag of the fundamental (ϕ1) or 3rd (ϕ3) harmonic magnetization of MNPs was proposed in Refs. 17 and 15, respectively. Accurate temperature measurements were achieved in these previous studies. Nonetheless, little study has been done on how the amplitude of the excitation field and the core size distribution affect harmonic magnetizations and the sensitivity of temperature measurement. Pi et al. investigated the influence of the core size distribution on the magnetization signals for MNPT.3 Because the Langevin model used in Ref. 18 ignores the relaxation time of MNPs, this approach is restricted to a low-frequency excitation field.

In this study, we investigated the effect of core size distribution on the performance of the MNPT when the frequency and amplitude of the excitation field are relatively high. Numerical simulations based on the Fokker–Planck equation were performed to reveal the effects of excitation field strength and core size distribution on the temperature dependence of the amplitude and phase of the harmonics. The field dependences of the sensitivity in temperature measurement diverged from those calculated when the core size distribution was neglected. The results were compared with those of experiments, and a reasonable agreement was obtained between the two.

In the present study, we used a sample called MS1 (Meito Sangyo, Japan). MS1 is magnetically fractionated MNPs from a Ferucarbotran sample,20–22 and one of the promising candidates for both MNHT and MPI applications because it has a large number of MNPs, that become the source of heat generated and MPI signals.20,21 Figure 1(a) represents the distribution of the core size dc of the MS1 sample, which was estimated from the static M–H curve.23–25 The distribution is represented as nVc versus dc curve, where n is the number density (in unit of m–3), Vc is the core volume. As shown, dc distributes from 5 to 40 nm, and nVc has a peak value at dc_typ = 22.3 nm. We calculated the field-dependent Brownian relaxation time τB(H) and Néel relaxation time τN(H). The analytical expression [Eq. (16) in Ref. 25] was applied to calculate τB(H), and we used the saturation magnetization Msat = 388 kA m–1 measured from the M–H curve, a typical hydrodynamic diameter dh = 68 nm measured with dynamic light scattering setup (Malvern Instruments Zetasizer Nano ZS), and the viscosity of water η = 0.917 mPa s at 297 K.26 The expression [Eq. (3.132) in Ref. 27] was used to calculate τN(H), and we used the anisotropy constant K = 4 kJ m–3, which was obtained in a previous study.20 In Fig. 1(b), τN1, τN2 and τN3 were calculated for dh = 22, 30 and 35 nm, respectively.

As shown in Fig. 1(b), condition that τB ≫ τN is satisfied for all dc values when μBH > 6 mT. This means that the dynamic behavior of MNPs is dominated by the Néel relaxation when μBH > 6 mT. The horizontal broken line in Fig. 1(b) represents the time Tm = 1/(2πf) when f = 20 kHz. As shown, τB is much longer than Tm, i.e., f = 20 kHz is well above the Brownian frequency 1/(2πτB). This result indicates that the effect of the Brownian relaxation can be almost neglected when MS1 is magnetized with high amplitude and high frequency.28 Figure 1(c) represents the M–H curve

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measured at 20 kHz when the viscosity of the solution was changed. The measurements were performed using a measurement system developed at Kyushu University.29) Symbols and lines represent the results obtained for \( \eta = 0.917 \text{ mPa} \cdot \text{s} \) and \( \eta = 13.4 \text{ mPa} \cdot \text{s} \), respectively. The results for \( \mu_0 H_{ac} = 6 \) and 20 mT are shown.

Fig. 1. (Color online) (a) Core size distribution of the MS1 sample estimated from the static \( M-H \) curve. Here, \( n \) and \( V_c \) represent the number density of the MNP having the core size \( d_c \) and the core volume, respectively. (b) Field dependent Brownian and Néel relaxation times, where \( \tau_{N1}, \tau_{N2} \) and \( \tau_{M} \) were calculated for \( d_c = 22, 30 \) and 35 nm, respectively, and \( T_{m} = 1/2(2\pi f) \) at \( f = 20 \text{ kHz} \). (c) \( M-H \) curves measured at 20 kHz for the cases of \( \eta = 0.917 \text{ mPa} \cdot \text{s} \) and \( \eta = 13.4 \text{ mPa} \cdot \text{s} \). The results for \( \mu_0 H_{ac} = 6 \) and 20 mT are shown.

Figures 2(a) and 2(b) show the simulation results of the magnitudes of the fundamental, 3rd, and 5th harmonic magnetizations (\( M_1, M_3, M_5 \)) and the phase lags (\( \phi_1, \phi_3, \phi_5 \)) when \( \mu_0 H_{ac} \) was changed from 6 to 20 mT and \( f = 20 \text{ kHz} \). Note that the values of \( 3M_1 \) and \( 5M_5 \) are shown because \( M_5 \) becomes very small compared to \( M_1 \). The phase lag \( \phi_i \) is defined so that the time evolution of the \( i \)th harmonic magnetization becomes \( M_i(t) = M_i \sin(2\pi f t - \phi_i) \) for excitation field \( H_{ac} \sin(2\pi f t) \). As shown in Fig. 2(a), \( M_1, M_3, \) and \( M_5 \) increase with increasing \( H_{ac} \). We observed interesting behavior in the field dependences of the phase lags (\( \phi_1, \phi_3, \phi_5 \)) as shown in Fig. 2(b). For example, \( \phi_3 \) increased with \( H_{ac} \) for \( H_{ac} < 10 \text{ mT} \) \( \mu_0 \) and then decreased with \( H_{ac} > 10 \text{ mT} \) \( \mu_0 \). A similar behavior for \( \phi_5 \) was found as shown in Fig. 2(b). We note that, for an ensemble of identical MNP, the phase lag monotonically decreases with increasing \( H_{ac} \) due to the field-dependent relaxation time shown in Fig. 1(b). Therefore, Fig. 2(b) indicates that the field dependences of the phase lags are considerably affected by the core size distribution.

Figures 2(c) and 2(d) represent the experimental results of \( M_1 \) and \( \phi_i \) (\( i = 1, 3, 5 \)). In the experiment, the frequency was fixed at \( f = 20 \text{ kHz} \), and \( \mu_0 H_{ac} \) was changed from 2 to 20 mT. As shown, measured field dependences of \( M_i \) and \( \phi_i \) are similar to those obtained with the numerical simulation. Especially, the interesting behavior of \( \phi_3 \) and \( \phi_5 \) was confirmed in the experiment. We also note that similar values of \( M_1 \) and \( \phi_1 \) were obtained in both the experiment and simulation.

We next studied the temperature dependences of \( M_i/M_1 \) and \( \phi_i \) to explore the sensitivity of the temperature measurements when they are used in the MNPT. Figures 3(a) and 3(b) represent the simulation results of the \( M_i/M_1 \) versus \( T \) and \( \phi_i \) versus \( T \) curves, respectively. In the simulation, we assumed, for simplicity, that \( M_1 \) and \( K \) were independent of the temperature. We also set \( f = 25 \text{ kHz} \) to compare the experimental results (to be shown later). As shown in Fig. 3(a), the values of \( M_i/M_1 \) were almost independent of \( T \) for \( \mu_0 H_{ac} = 10 \text{ mT} \). This means that the sensitivity of the temperature measurement in MNPT is very low in this case. In contrast, \( M_3/M_1 \) increased linearly with \( T \) for \( \mu_0 H_{ac} = 15 \) and 20 mT. This indicates that these excitation field amplitudes can be used for MNPT.
To investigate the sensitivity when using $M_A/M_3$, we determine the value $S_{M53}$ using the slope of the $M_A/M_3$ versus $T$ curve [Fig. 3(a)]. The solid line in Fig. 4(a) represents the dependence of $S_{M53}$ on $H_{ac}$. The sensitivity $S_{M53}$ is evidently very small and becomes negative for $\mu_0H_{ac} < 10$ mT. We obtain large $S_{M53}$ values for $\mu_0H_{ac} > 10$ mT, having a maximum value of $6.8 \times 10^{-4}$ K$^{-1}$ at $\mu_0H_{ac} = 13.3$ mT.

The solid line in Fig. 4(b) represents the simulation result on the $H_{ac}$ dependence of the sensitivity $S_{\phi3}$; its value was obtained from the slope of $\phi_3$ versus $T$ curve [Fig. 3(b)]. As shown, $|S_{\phi3}|$ first increases with $H_{ac}$ for $\mu_0H_{ac} \approx 11.8$ mT, has a maximum value of 0.135 deg K$^{-1}$ at $\mu_0H_{ac} = 11.8$ mT, and then decreases with $H_{ac}$.

To clarify the effect of the core size distribution on the MNPT performance, we calculated $S_{M53}$ and $S_{\phi3}$ for mono-disperse MNP. We considered a particle diameter $d_c$, which is a typical core diameter of MS1, and $f$ [Fig. 1(a)]. The dashed lines in Fig. 4 show the numerical simulation results for $d_c$, $f = 22.3$ nm. As can be seen, the field dependences of $S_{M53}$ and $S_{\phi3}$ are completely different from those calculated when the core size distribution was taken into account. The optimal value of $H_{ac}$, at which $|S_{M53}|$ becomes maximum, differs between the two cases. The polarity of $S_{M53}$ is also opposite between the two cases. For $S_{\phi3}$, there is no clear optimal value of $H_{ac}$ for the case of the monodisperse particle. These differences indicate that the properties of $S_{M53}$ and $S_{\phi3}$ are considerably affected by the core size distribution.

To validate the simulation results, we measured the $M_A/M_3$ versus $T$ and $\phi_3$ versus $T$ curves of MS1, and obtained the values of $S_{M53}$ and $S_{\phi3}$ from the slope of the curves. The measurements were performed at $f = 25$ kHz from 296 to 326 K (23 to 53 $^\circ$C) using the magnetic particle spectroscopy equipment developed at TU Braunschweig. The circles in Fig. 4 represent the experimental results. As shown, $S_{M53}$ and $S_{\phi3}$ first increase with $H_{ac}$ for $H_{ac} < 12$ mT/$\mu_0$, become maximum at around 12 mT/$\mu_0$, and finally decrease with $H_{ac}$. These behaviors are similar to those of the simulation ones. In particular, the optimum value of $H_{ac} \approx 12$ mT/$\mu_0$ agrees with that obtained from the numerical simulation. The polarity of the measured $S_{M53}$ also agrees with those of the simulations. This agreement indicates that the core size distribution significantly affects the performance of the MNPT.

We note, however, that there are obvious deviations between experimental and simulated data. For example, the measured $S_{\phi3}$ is about two times larger than the simulated one [Fig. 4(b)]. We note that the temperature dependences of $M_1$ and $K$ were neglected in the simulation. These dependences need to be included for a quantitative evaluation of $S_{M53}$ and $S_{\phi3}$. We also note that $S_{M53}$ smoothly changed with $H_{ac}$ in the experiment, while $S_{M53}$ rapidly decreased when $H_{ac} < 10$ mT/$\mu_0$ in the simulation [Fig. 4(a)]. In the present simulations, we assumed that all of the easy axes are aligned in the field direction for simplicity. This assumption will become inaccurate at low $H_{ac}$ values because the alignment of the easy axes due to the AC field considerably depends on $H_{ac}$. Therefore, it is also necessary to clarify the effect of $H_{ac}$ on the degree of alignment of the easy axes.

In conclusion, we investigated the effect of core size distribution on the performance of MNPT when MS1 was magnetized with relatively large amplitude ($>6$ mT) and high frequency ($>20$ kHz). In this case, dynamic behavior of particles is dominated by the Néel relaxation. It was shown...
that the sensitivities $S_{M52}$ and $S_{A3}$ in temperature measurement depend on the amplitude of the excitation field, and the field dependences are affected by the core size distribution. Therefore, it is important to take into account the core size distribution for appropriately designing a MNPT system.

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