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Colorize magnetic nanoparticles using a search coil based testing method

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ABSTRACT

Different magnetic nanoparticles (MNPs) possess unique spectral responses to AC magnetic field and we can use this specific magnetic property of MNPs as "colors" in the detection. In this paper, a detection scheme for magnetic nanoparticle size distribution is demonstrated by using an MNPs and search-coils integrated detection system. A low frequency (50 Hz) sinusoidal magnetic field is applied to drive MNPs into saturated region. Then a high frequency sinusoidal field sweeping from 5 kHz to 35 kHz is applied in order to generate mixing frequency signals, which are collected by a pair of balanced search coils. These harmonics are highly specific to the nonlinearity of magnetization curve of the MNPs. Previous work focused on using the amplitude and phase of the 3rd harmonic or the amplitude ratio of the 5th harmonic over 3rd harmonic. Here we demonstrate to use the amplitude and phase information of both 3rd and 5th harmonics as magnetic "colors" of MNPs. It is found that this method effectively reduces the magnetic colorization error.

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1. Introduction

Magnetic nanoparticles (MNPs) are good candidate for biomedical detection because of their comparable size to biomolecules. Biochemically modified MNPs are able to bind with specific kind of antibodies, which is called specific binding process. Many research groups have succeed in detecting the molecular binding process in real-time [1] and distinguishing different concentrations of antibodies by using a MNPs and search-coils integrated detection system [2]. But the detection scheme in the field is limited by detecting only one kind of antibody in each test. In this paper we investigate the possibility of detecting different kinds of MNPs in one test. Our experiment is based on a mixing frequency method [3,4]. Two sinusoidal magnetic fields are applied to the MNP solution sample simultaneously. One low frequency field with amplitude of 100 Oe (A_L) and frequency of 50 Hz (f_L), expressed as $A_L \cos\left(2\pi f_L t\right)$ is applied to drive MNPs into nonlinear region [5]. Magnetization curve of nanoparticles in our experiment is measured using a vibrating sample magnetometer (VSM) at room temperature shown in Fig. 1. A high frequency magnetic field with amplitude of 10 Oe (A_H) and an adjustable sweeping frequency (f_H), written as $A_H \cos\left(2\pi f_H t\right)$, is applied to generate mixing frequency signals which work as "colors" of different MNPs. By sweeping high frequency field from 5 kHz to 35 kHz, we can obtain many properties specific to MNPs. The response harmonic signals are linear combination of f_H and f_L, expressed as $mf_H \pm nf_L$. Some researchers used amplitude and phase of the 3rd ($f_H \pm 2f_L$) harmonic to characterize MNPs [6,7] or the parameters of MNP solution [8], and others used the amplitude ratio of the 5th ($f_H \pm 4f_L$) over 3rd harmonic to characterize MNPs [1,9]. In this paper, we analyze both amplitudes and phases of the 3rd and 5th harmonics in order to reduce the magnetic colorization error. We show experimentally that as we sweep the high frequency field, the trend of amplitudes and phases of harmonics are specific to MNPs. In principle, each kind of MNPs can be modified to react with one kind of antibody. This implies that using search coil based immunoassay, we may be able to detect more than one kind of antibody in one test.

2. Theory

2.1. Brownian and Néel relaxation

The total relaxation time τ is a combined mechanism of both the Brownian and Néel relaxation, which reflects the MNPs' ability to follow the change of applied sinusoidal magnetic field. Brownian relaxation is the physical rotation of hydrodynamic volume of

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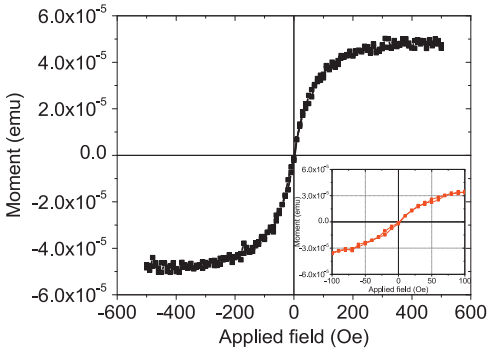

Fig. 1. Magnetization curve of iron oxide nanoparticles (SHP-25, Ocean NanoTech) in water solution at room temperature measured by VSM.

nanoparticles, relaxation time τ_B is expressed as

$$\tau_B = \frac{3\eta V_H}{k_B T} \tag{1}$$

where η is viscosity of the MNP solution, V_H is hydrodynamic volume of each nanoparticle, $k_B$is Boltzmann constant, and T is absolute temperature in Kelvin.

Néel relaxation is the internal reorientation of magnetic moment inside the core of nanoparticles, relaxation time τ_N is written as

$$\tau_N = \tau_0 \exp\left(\frac{KV_m}{k_B T}\right) \tag{2}$$

where the time constant $\tau_0 = 10^{-9}$ s, K is anisotropy constant of MNP, V_m is volume of the magnetic core of each nanoparticle.

Total relaxation time τ is a linear combination of τ_B and τ_N:

$$\tau = \frac{\tau_N \tau_B}{\tau_N + \tau_B} \tag{3}$$

2.2. Magnetization theory

Total field applied to the sample is the sum of the high frequency sinusoidal field and low frequency sinusoidal field, expressed as

$$H = A_L \cos(2\pi f_L t) + A_H \cos(2\pi f_H t) \tag{4}$$

Magnetization of MNPs can be approximated by the static Langevin function [10]:

$$\frac{M}{M_s} = L\left(\frac{m_0\mu_0 H}{k_B T}\right) \tag{5}$$

where M_s is the saturation magnetization of the MNP, M is the magnetization of the MNP under an applied field of H, m_0 is the magnetic moment of one nanoparticle, and H is the total applied field expressed in formula (4). Taylor expansion near zero magnetization shows the 3rd $(f_H \pm 2f_L)$ and 5th $(f_H \pm 4f_L)$ harmonic components as following:

$$\begin{aligned}\frac{M}{M_s} = L\left(\frac{m_0\mu_0 H}{k_B T}\right) &= \frac{1}{3}\left(\frac{m_0\mu_0}{k_B T}\right)H - \frac{1}{45}\left(\frac{m_0\mu_0}{k_B T}\right)^3 H^3 + \frac{2}{945}\left(\frac{m_0\mu_0}{k_B T}\right)^5 H^5 + \ldots = \ldots \\ &+ \left[-\frac{1}{60}A_H A_L^2\left(\frac{m_0\mu_0}{k_B T}\right)^3 + \frac{1}{252}A_H^3 A_L^2\left(\frac{m_0\mu_0}{k_B T}\right)^5\right. \\ &\left.+\frac{1}{378}A_H A_L^4\left(\frac{m_0\mu_0}{k_B T}\right)^5 + \ldots\right]\cos\left[2\pi(f_H \pm 2f_L)t\right] \\ &+ \left[\frac{1}{1512}A_H A_L^4\left(\frac{m_0\mu_0}{k_B T}\right)^5 + \ldots\right]\cos\left[2\pi(f_H \pm 4f_L)t\right] + \ldots\end{aligned} \tag{6}$$

Assuming a constant phase lag ϕ and there is no rotational motion of the carrier medium, we can obtain the actual phase lag ϕ and the magnetization amplitude M_0shown as follows [11]:

$$\phi = \arctan(\omega\tau) \tag{7}$$

$$M_0 = M\cos(\phi) \tag{8}$$

where ω is angular frequency and $\tau$is total relaxation time.

According to Lenz law, the induced voltage sensed by detection coil (also called search coil) is expressed as following:

$$V \propto \frac{dM_0}{dt}\nu_{volume\ of\ particle} \tag{9}$$

Hence, the collected signals in detection coil is specific to the characteristics of MNPs, such as relaxation time. The 3rd and 5th harmonics are among the best candidates to intuitively show the specific characteristics MNPs.

2.3. Experimental system setup

The schematic setup of our search-coil based detection system is shown in Fig. 2. In our experiment, digital acquisition card (DAQ, NI USB-6289, 18-Bit, 625 kS/s), LabVIEW and Matlab are used for instrumental control and signal processing, respectively. DAQ generates the high frequency sinusoidal voltage and the low frequency sinusoidal voltage, both signals are amplified by instrument amplifiers (IA) and then go through the high frequency excitation coil and the low frequency excitation coil, respectively. One pair of pick up coils with differentially wounded 1000 rounds of fine copper wire are installed in the middle of excitation coils. According to Lenz law, the induced voltage from MNP sample is

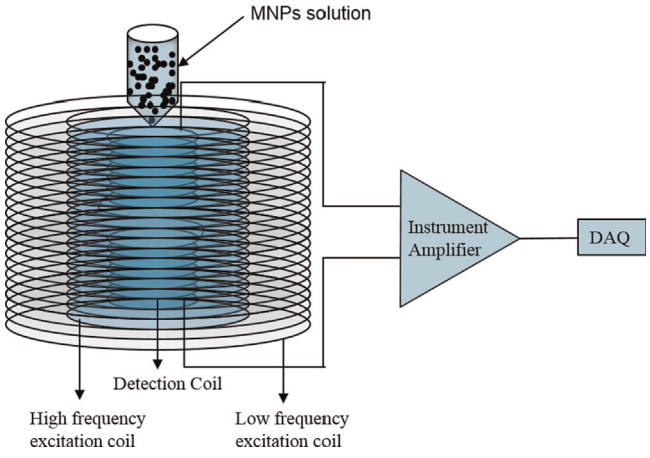

Fig. 2. Search-coil based MNPs detection system experimental setup.

Table 1
Experimental samples.

Sample	1	2	3	4	5
25 nm Particles (1 μg/μL)	20 μL	40 μL	60 μL	80 μL	100 μL
10 nm Particles (1 μg/μL)	80 μL	60 μL	40 μL	20 μL	0 μL

collected by the detection coils and transferred back to DAQ for further analysis. During the whole process, LabVIEW controls the excitation field and analyses the feedback signals from DAQ. We recorded the feedback signals before and after inserting MNP samples into the detection coils so as to cancel out the unbalanced field and noise. Changes in amplitudes and phases from 3rd and 5th harmonics are what we mainly concerned in our experiment.

3. Samples and experimental details

In this experiment, we used 1 μg/μL SHP-25 nanoparticles (purchased from Ocean NanoTech, iron oxide core MNPs of 25 nm diameter coated with 2 nm carboxylic acid) and 1 μg/μL SHP-10 (purchased from Ocean NanoTech, iron oxide core MNPs of 10 nm diameter coated with 2 nm carboxylic acid) nanoparticles. Then mixed them in different proportions listed in Table 1.

Signals were collected before and after we put the MNPs solution into the detection coil. Then we extracted amplitudes and phases from 3rd and 5th harmonics and compared the differences before and after we inserted the samples into the detection coil.

4. Results and discussion

For iron oxide nanoparticles with diameter larger than 20 nm, Brownian relaxation dominates, and Neel relaxation becomes the dominant factor when particle's diameter is less than 20 nm [4]. In this experiment, we used SHP-10 MNPs for which Neel relaxation dominates, and Brownian relaxation dominates for SHP-25.

Sample 5 has the largest average particle size, then sample 4, sample 3, sample 2, and sample 1 has the smallest average particle size. Amplitudes and phases of 3rd and 5th harmonics were collected and compared between each other, shown in Fig. 3.

As shown above, with the same concentration, larger particles produce higher amplitude in both the 3rd and 5th harmonics. And their amplitudes decrease greatly as we sweep the high frequency field from 5 kHz to 35 kHz. For MNP samples with smaller average size, they produce smaller amplitudes and change little as we sweep the high frequency.

As can be noticed, all the 5 samples have almost the same phase lag when the sweeping field has a frequency of 5 kHz. As we increase the sweeping frequency, larger particles have larger phase lag compared to smaller particles.

5. Conclusions

In this paper, we first introduced the limitation of current magnetic nanoparticles and search-coils integrated detection research. We investigated the possibility of detecting two kinds of nanoparticles in one test. We mixed SHP-25 and SHP-10 nanoparticles in different portions, and collected the signals induced by the MNP samples from the detection coils. Furthermore, instead of analyzing the 3rd harmonics, we chose to analyze the amplitudes

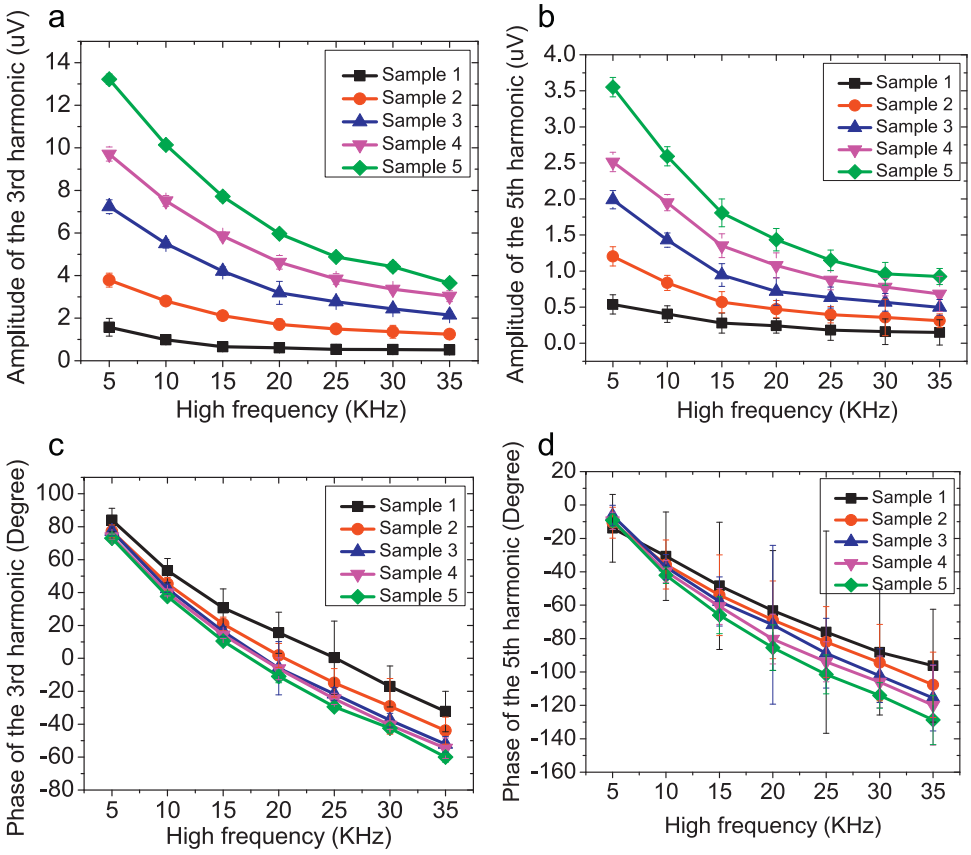

Fig. 3. (a) Amplitude of the 3rd harmonic; (b) amplitude of the 5th harmonic; (c) phase of the 3rd harmonic; and (d) phase of the 5th harmonic.

and phases of both 3rd and 5th harmonics to effectively reduce the colorization error.

By comparing the collected data of 5 samples, we found that, with the same concentration, magnetic nanoparticle solution with a larger average particle size could induce higher amplitude, and its amplitude changes greatly with sweeping high frequency. At lower sweeping frequency, the 5 samples have almost the same phase lag. As the sweeping frequency goes higher, phase of large particles drop faster.

This paper demonstrated an easier and simpler way to calibrate amounts of MNPs. The results showed the importance of harmonic phases in determining amounts of each MNP. In Nikitin′s paper [5], the amplitudes of harmonics are utilized while the phase information is omitted. For high frequency magnetic field, amplitude signal has higher SNR from 5 KHz to 15 KHz, phase signal has higher SNR from 25 KHz to 35 KHz. In future applications, we can prepare a comparison chart first, and test an unknown amount of MNP solution. Then we insert the collected curve into comparison chart and estimate the range of amount using the data of two nearest curves.

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Appendix A. Supplementary information

Supplementary data associated with this article can be found in the online version at. http://dx.doi.org/10.1016/j.jmmm.2014.10.034

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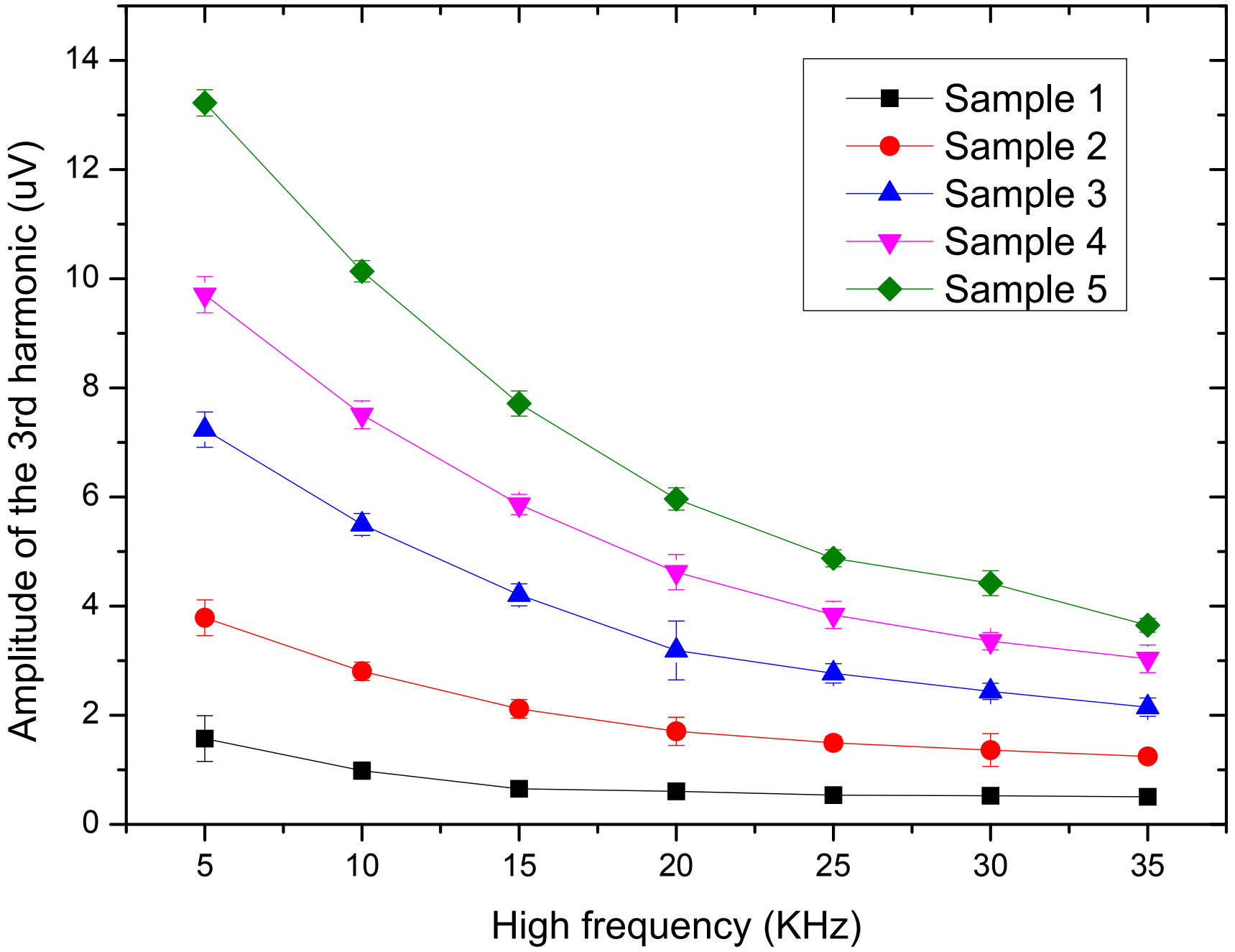
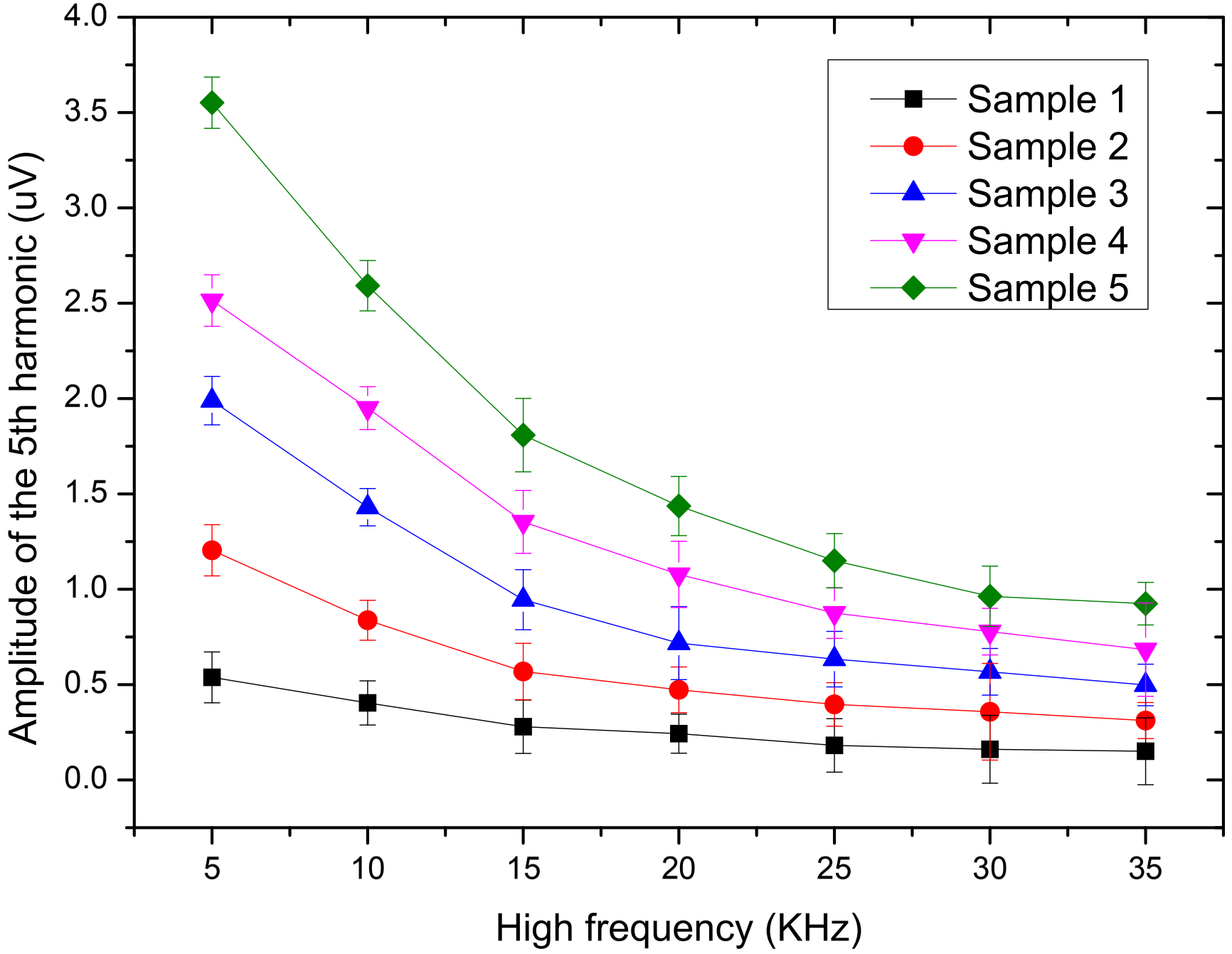
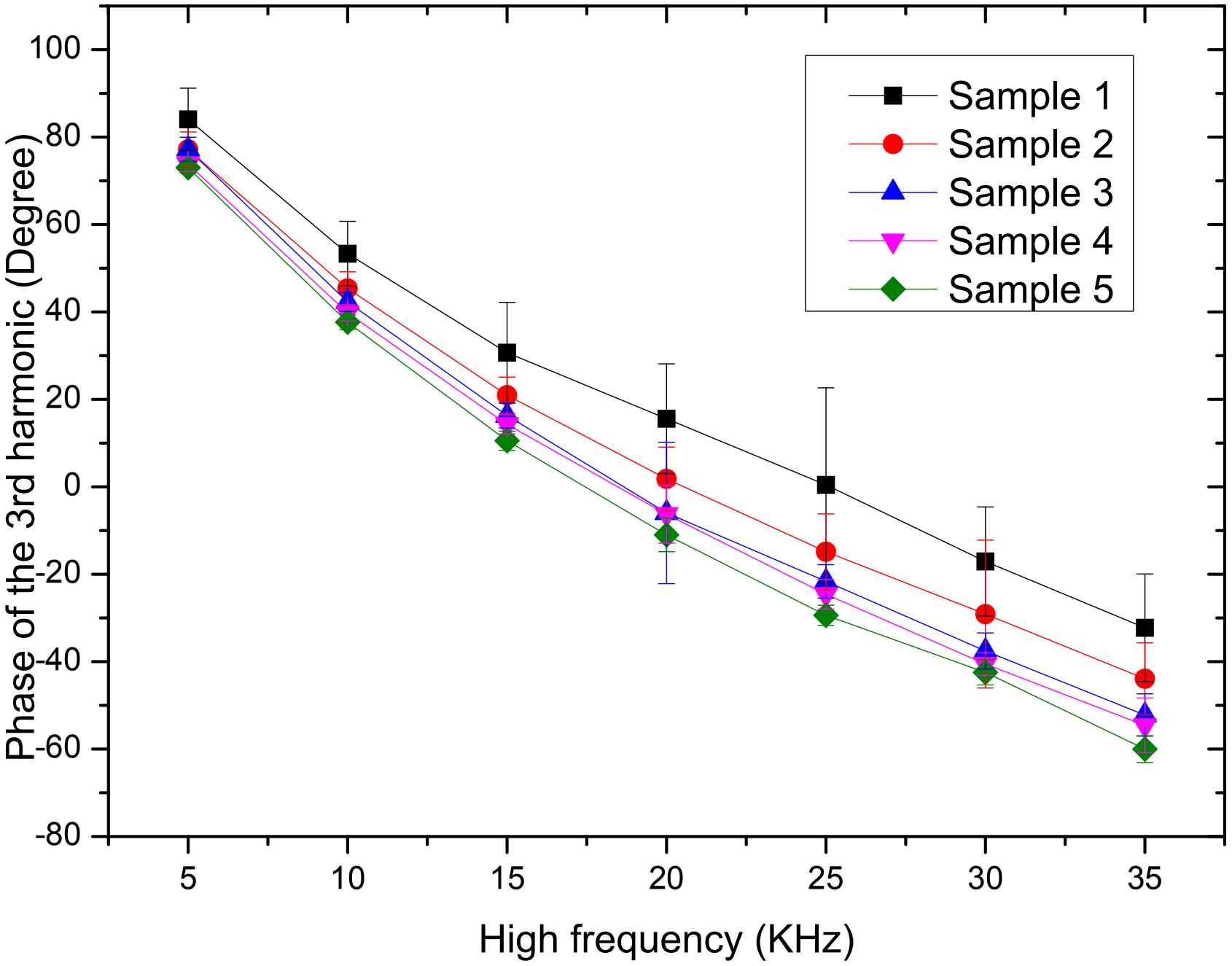
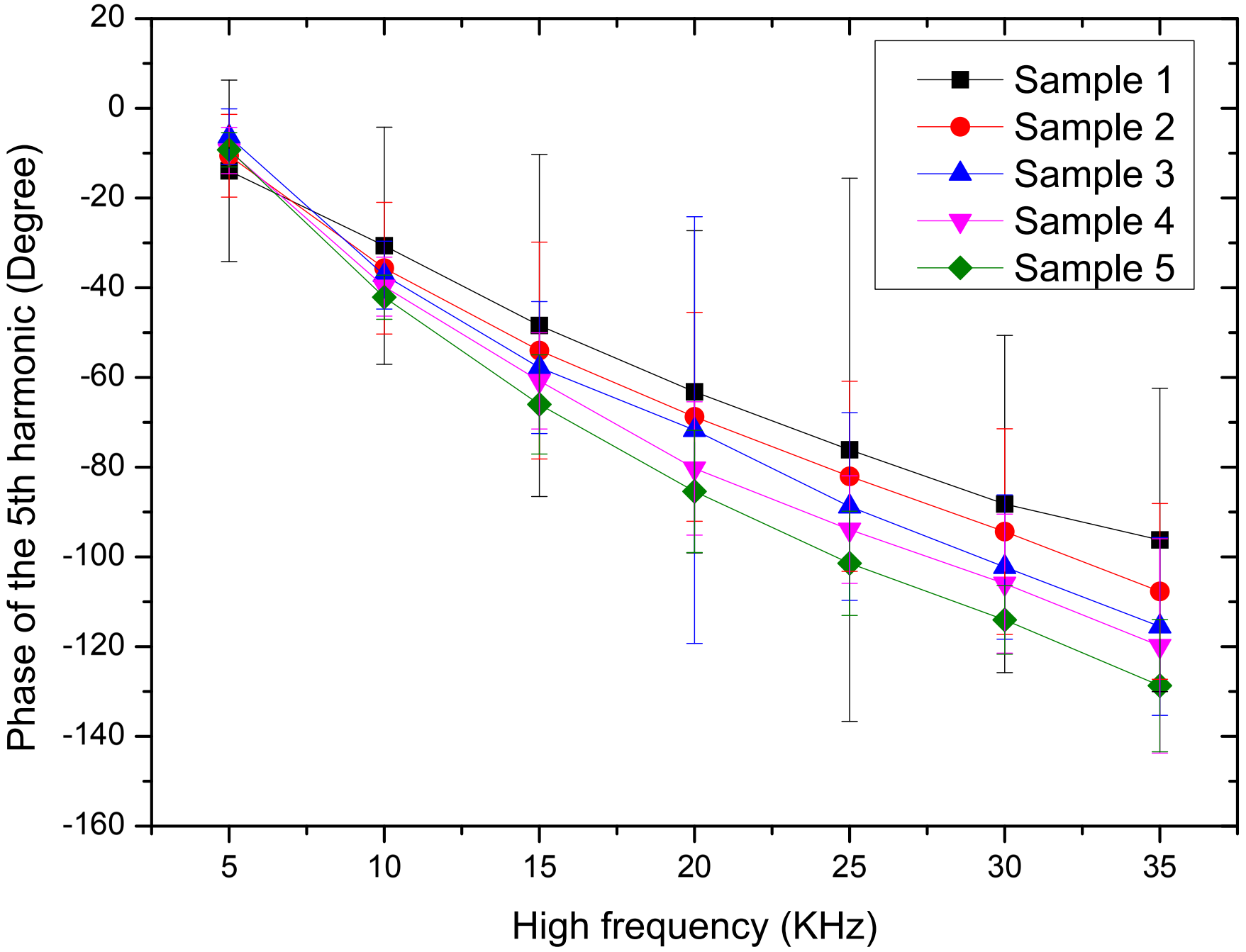
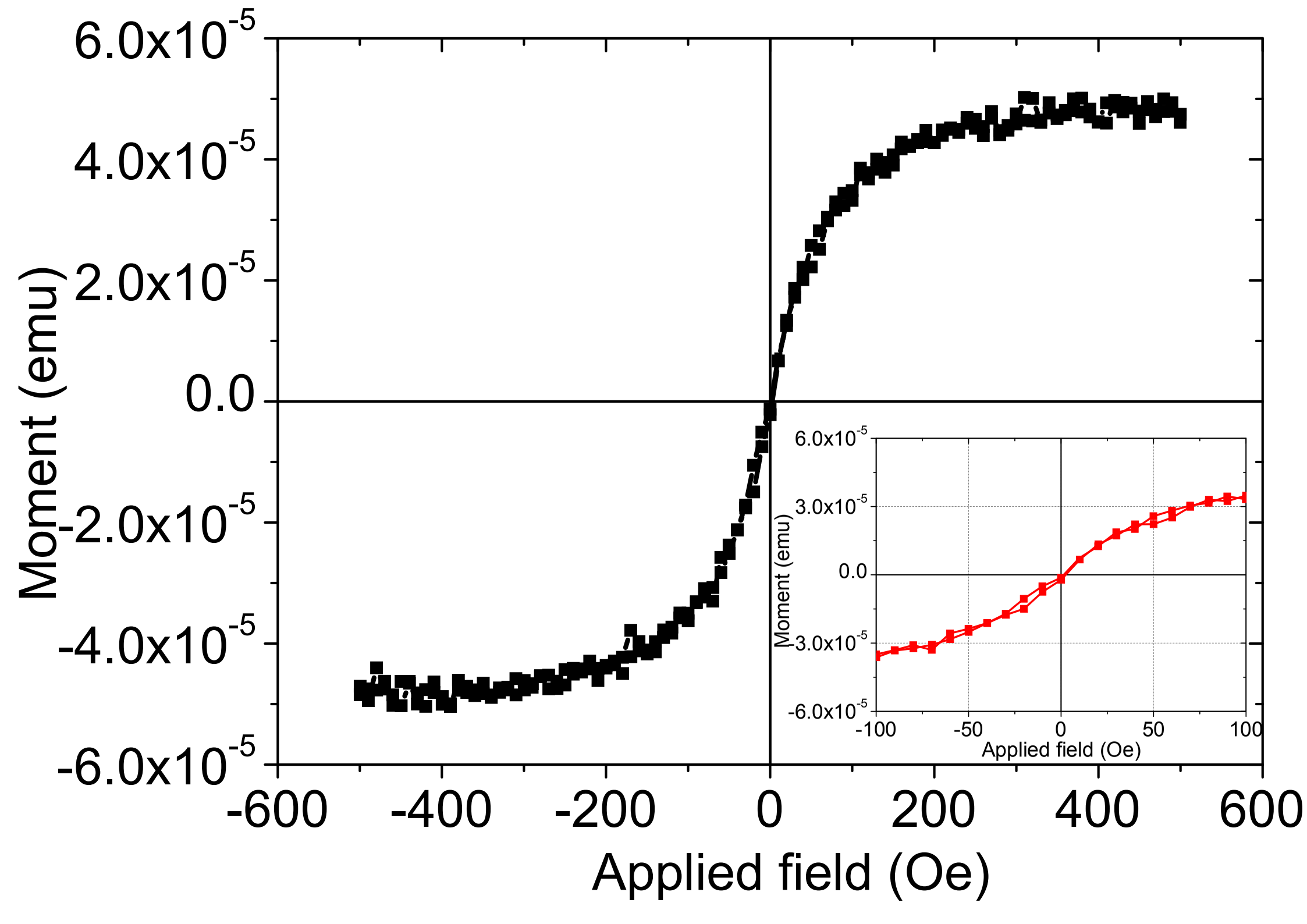

Amplitude of the 3rd harmonic (uV)
High frequency (KHz)
0
2
4
6
8
10
12
14
5
10
15
20
25
30
35
Sample 1
Sample 2
Sample 3
Sample 4
Sample 5


Amplitude of the 5th harmonic (uV)
High frequency (KHz)
Sample 1
Sample 2
Sample 3
Sample 4
Sample 5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5
10
15
20
25
30
35


Phase of the 3rd harmonic (Degree)
High frequency (KHz)
Sample 1
Sample 2
Sample 3
Sample 4
Sample 5
100
80
60
40
20
0
-20
-40
-60
-80
5
10
15
20
25
30
35


Phase of the 5th harmonic (Degree)
20
0
-20
-40
-60
-80
-100
-120
-140
-160
5
10
15
20
25
30
35
High frequency (KHz)
Sample 1
Sample 2
Sample 3
Sample 4
Sample 5


6.0x10-5
4.0x10-5
2.0x10-5
0.0
-2.0x10-5
-4.0x10-5
-6.0x10-5
Moment (emu)
-600
-400
-200
0
200
400
600
Applied field (Oe)
6.0x10-5
3.0x10-5
0.0
-3.0x10-5
-6.0x10-5
Moment (emu)
-100
-50
0
50
100
Applied field (Oe)