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Araştırma Makalesi / ResearchArticle

Taşınabilir Manyetik Nanoparçacık Spektrometresi

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Anahtar kelimeler
Manyetik parçacık spektrometresi; Manyetik nanoparçacık parametreleri, Doğrusal olmayan mıknatıslanma; FFT; Veri analizi

Özet

Manyetik parçacık spektrometresi (MPS), belirli manyetik alan değerlerinde süper paramanyetik demir oksit nanoparçacıklarının doğrusal olmayan tepkisini ve manyetik doygunluğunu kullanır. Zamanla değişen bir manyetik uyarıcı bobinlerin alanı parçacıkların mıknatıslanmasının maksimum ve minimum değer arasında değişmesine neden olur. Genel olarak, uygulanan alan geçici olarak değiştirildiğinde manyetik bir nanoparçacığın yönünü değiştirmenin iki yolu vardır. Parçacığın kendisi Brownian dönüşü adı verilen fiziksel bir dönüş gerçekleştirir veya parçacık içindeki manyetik moment Néel dönüşü adı verilen sabit bir yapıda dönebilir. Viskoz bir ortamda, uygulanan frekansa bağlı olan ve baskın bir işlem olan her iki dönme tipinin kombinasyonu gerçekleşir. Relaksometre olarak da bilinen bu sistem, MPS çalışmalarındaki manyetik nanoparçacıkların yoğunluğunu ve ilgili hesaplamaları yaparak nanoparçacıklarındurulma sürelerinin ölçümünü dikkate alır. Brownian veya Néeldurulma süreleri, kimyasal olarak bağlı veya bağlı olmayan manyetik nanoparçacıkların dış değişken manyetik alana verdiği tepkiye göre hesaplanabilir. Bu çalışmada, nanoparçacıkların durulma zamanları gibi özelliklerinin analiz edilmesini sağlayan bir spektrometre öncelikle tasarlanmış ve yapımı gerçekleştirilmiştir Spektrometreden elde edilen MPS sinyalleri veri toplama kartı ile bilgisayara aktarılabilir ve Python programlama dilinde yazılmış bir yazılımla veri analizi yapılabilir.

Portable Magnetic Nanoparticle Spectrometer

Keywords
Magnetic particle spectrometer;Magnetic nanoparticles Parameters;Nonlinear magnetization; FFT;Data analysis

Abstract

The magnetic particle spectrometer (MPS) uses the nonlinear response of super-paramagnetic iron oxide nanoparticles and magnetic saturation at certain magnetic field values. A time-varying magnetic field of excitation coils causes the magnetization of the particles to vary between the maximum and the minimum value. Generally, there are two ways in which a magnetic nanoparticle can change the direction when the applied area is temporarily changed. The particle itself performs a physical rotation called the Brown return, or the magnetic moment in the particle can rotate in a fixed structure called the Néel return. In a viscous environment, the combination of both types of rotation takes place, which depends on the frequency applied and is a dominant process. This system, also known as the relaxometer, takes into account the density of the magnetic nanoparticles in the MPS studies and the measurement of the relaxation times of the nanoparticles by making the corresponding calculations. Brownian or Néelrelaxation times can be calculated according to the reaction of chemically bound or unbound magnetic nanoparticles to the external variable magnetic field. In this study, a spectrometer was first designed and constructed to analyze the properties of nanoparticles such as relaxation times. MPS signals obtained from the spectrometer can be transferred to the computer with data acquisition card and data analysis can be done with a software written in python programming language.

1. Introduction

Magnetic particle imaging (MPI), which displays the spatial distribution of super paramagnetic iron oxide nanoparticles, is a new tomographic imaging technique. In this technique, the signal is taken from the iron oxide nanoparticles, which are characterized as tracers. Monitoring the quality of these tracers is important for tissue health, and studies in this area are not yet enough. Based on nonlinear magnetization of magnetic nanoparticles, MPS can accurately measure the high-level harmonic components of the signals it detects with the spectral analysis method. In general, these signals are analyzed using the Langevin function model, which is expanded by a Debye front factor that defines the dynamic magnetic properties of the particles [1]-[2]-[3]. However, this model is a coarse approach that has not only correctly defined the phase of the harmonics [8]. In this study, a magnetic particle spectrometer can be interpreted as a zero-sized MPI scanner containing a drive field coil and a receiver coil. The following sections describe the current setup that can perform MPS measurements with a freely adjustable excitation frequency in the range of 1 kHz to 10 kHz. This setup demonstrates the possibility of identifying the different properties of nanoparticles, such as the effect of Brownian and Néel rotation on signal quality.

2. Methods

MPI relies on the non-linear magnetization curve of magnetic nanoparticles. When a time varying magnetic field $H(t) = H_0 \, sin(2\pi f_0 t)$is applied to the nano-particles, a magnetization *M(H(t))* is observed. Due to the non-linearity of M, the frequency spectrum of the magnetization response does not only consist of the frequency f_0, but also of higher harmonics. Figure 1 shows this process, response of magnetic particles to an external magnetic field theory of nonlinear magnetization [5].

According to the Langevin theory of paramagnetism [6], the magnetization curve of the particles can be described by

$$M(t) = m_s c \left(coth\left(\frac{m_s \mu_0 \, H(t)}{k_B T}\right) - \frac{k_B T}{m_s \mu_0 \, H(t)} \right) \qquad (1)$$

where $\mu_0$denotes the permeability of vacuum, $k_B$the Boltzmann constant, *T* the temperature as Kelvin, *c* the sample concentration, and $m_s = \frac{1}{6} D^3 M_s$the magnetic moment of the particles at saturation [7]. The particles are characterized by their diameter *D* and the saturation magnetization M_s [8]. In eq. (1) it is assumed that the concentration *c* of the nanoparticles is homogeneous within the probe. Furthermore, the magnetic field *H*(*t*) is nearly homogeneous in the probe chamber and has only one spatial component. This can be achieved by using a solenoid coil to generate the magnetic field, where the probe chamber lays inside the coil.

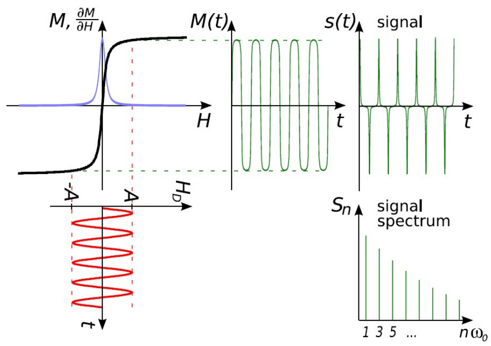

Figure 1. BasicMPIprinciple.ThedrivefieldH(t)generatesaparticle responseM(t)thatinducesavoltagein thereceivecoils.Thetime-dependentvoltageismeasuredandconstitutestherawsignals(t)αdM(t)/dt.Duetothenon-linear magnetizationcurve,thesignalspectrum$S_n$containshigherharmonicsofthedrivefrequencyf_0,whichareusedforparticle detectionandimaging.Forreference,thederivativeofthe magnetizationcurve∂M/∂Hisalsoshown(bluecurve).

3. MaterialsandEquipment

Magnetic nanoparticle detector assembly consists of the following components; function signal generator, power amplifier, band-pass filter, coil system, band stop filter, signal amplifier, data acquisition card and PC, Figure 2.

3.1 Function signal generator

Signal generator must be generate a desired frequency sinusoidal signal with constant amplitude and does not contain any harmoniccomponent. Figure 3 shows the complete schematic of the sinus generator performed. The XR-2206 is a function generator that produces high quality sinus, square, triangle, ramp and pulse waves with high stability and accuracy. The amplitude and frequency of the output waveforms can also be modified by an external voltage to be applied. The operating frequency can be selected externally in a range of 0.01 Hz to 1 MHz [9]. The frequency is given as follows:

$$f_0 = \frac{1}{2\pi RC} \quad (Hz) \qquad (2)$$

The sinusoidal generator produces the sinusoidal signal so perfectly that the bandpass filter shown in figure 1 is not used in this study.

3.2Power amplifier

Since the function generator’s output signal is not powerful enough to make excitation coil produce oscillation magnetic field with a certain amplitude, power amplifier is necessary for the detection. The output of the power amplifier must be linear and bandwidth wide enough. Figure 4 shows a power amplifier with TDA2050 integrated circuit in this study. The TDA2050 heats up excessively at high currents and is mounted on a fan cooler. According to the manufacturer's data of the TDA2050 integrated circuit, the maximum permissible current value of this unit is limited to 5 A, which can deliver 50 W of output power [10]. The 35 VDC supply source of the cooling fan must be independent of the supply source, otherwise unwanted harmonics may leak into the output of this power amplifier

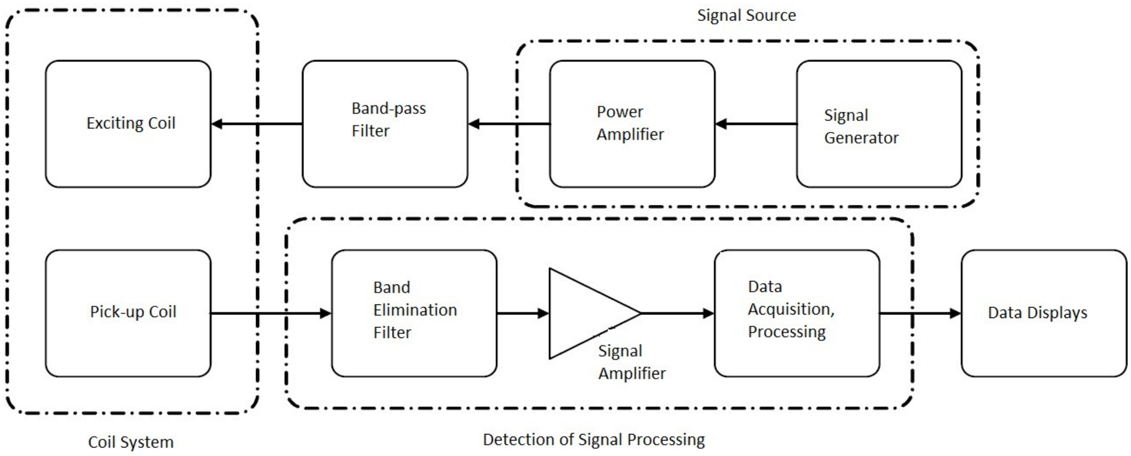

Figure 2. The system schematic of magnetic nanoparticles detection.

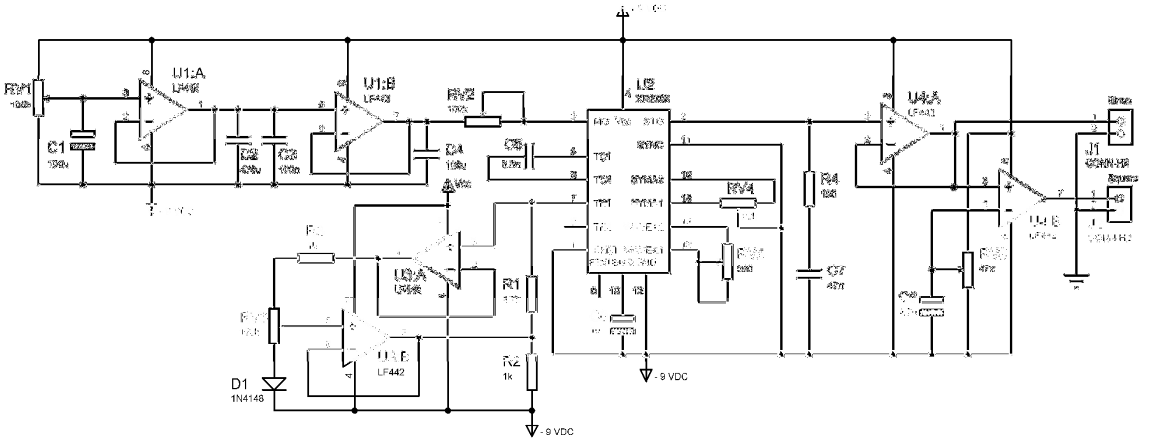

Figure 3. Sinus signal generator with XR2206

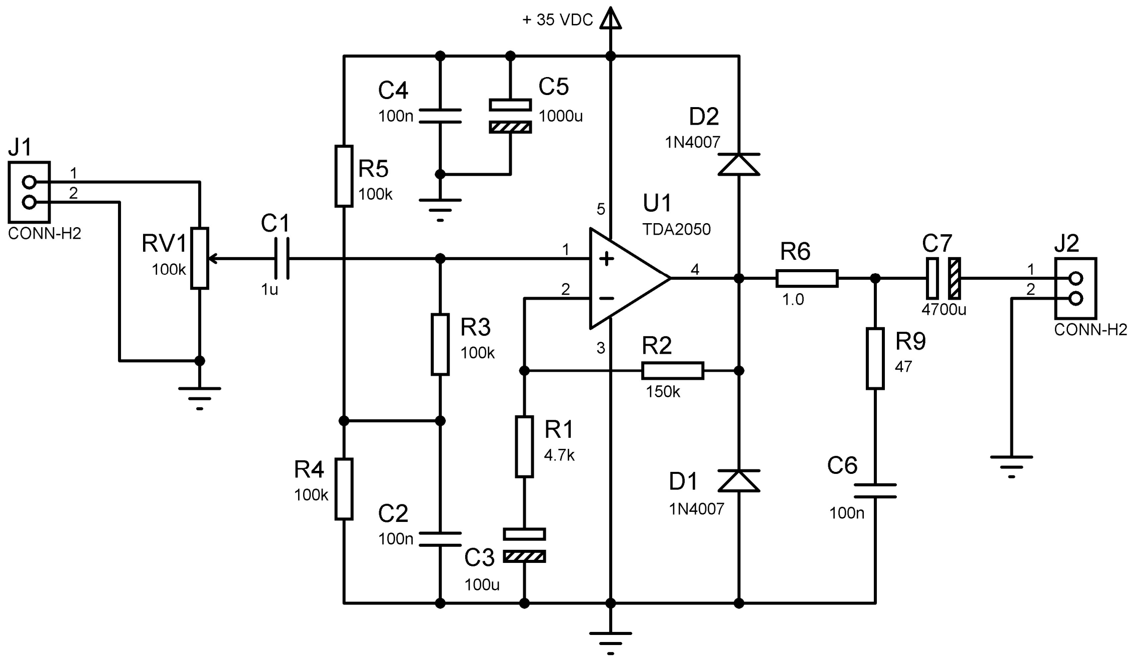

Figure 4. Current drive power amplifier with TDA2050

3.3Band-pass filter

To ensure that the output signal from the detection coil contains only harmonics, a band stop filter should be connected to the output of the detection coil in series. Since the main purpose is to prevent the base band signals, it can be accomplished using high-pass filter or twin t notch filter. Figure 5 shows a twin notch filter made in this study. A notch filter,also known as band limiting circuits, can be used to remove a particular frequency. It is usually fixedfrequency, but some of the notch frequency can be adjusted. Due to the high Q value, the bandwidth

of these filters is very small. An ideal notch filter should give a smooth frequency response on all other frequencies, except for the notch frequency.

In reality, perfection cannot be achieved, but when used with operational amplifier cores, high attenuation and narrow notches can be achieved [11].

3.4 Lownoiseamplifier

It is not possible to perceive because of the amplitude of the MPS signal containing the harmonic frequencies is too small. The output impedance of the gradiometer receiver coil must match the input impedance of the data acquisition board.It is an important solution to improve signal/noise ratio by selecting appropriate electronic design and its components. Figure 6 shows the preamplifier circuit consisting of integrated two operational amplifiers.

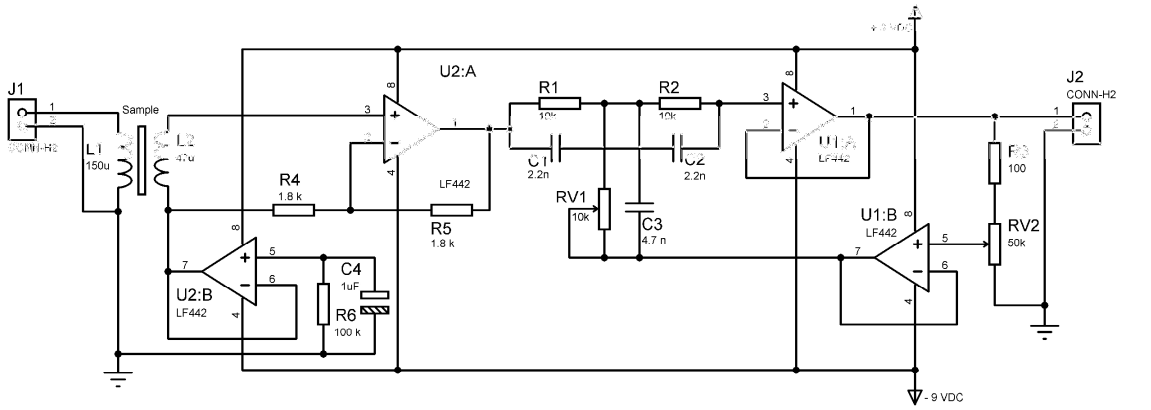

Figure 5. Twin t notch filter with buffers. L1 and L2 are the transmitting and gradiometer receiving coils, respectively

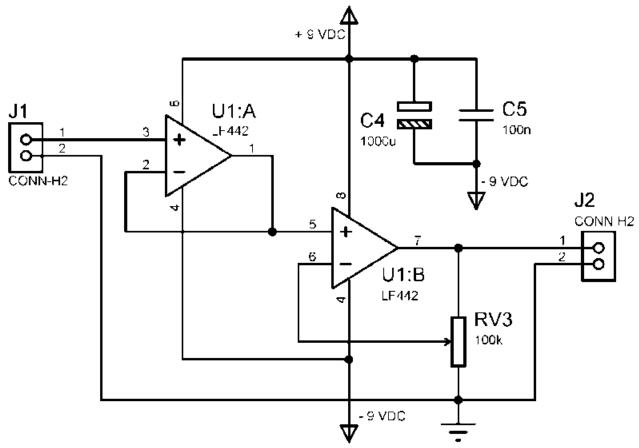

Figure 6. Operational trans conductance amplifier.

In the first, the unit gain is the monitor, in a sense the impedance converter and the output signal monitors the input signal. The second one is the unit that performs the actual amplification of the input signal and is known in the terminology as “operational trans conductance amplifier, (OTA)" [12].The notch filter and the preamplifier together form a signal conditioner. The conditioner amplifies the very small MPS signals sufficiently enough to transmit the signal to the data acquisition card with an improved signal to noise ratio.

3.5 Data acquisitionandprocessing

MPS signals are analog signals and must be converted to digital data encoded in a binary number system in order to process these signals. For this purpose, the sound card embedded in the motherboard of a laptop and the Pythonprogramming language were used to access this sound card. The numerical data obtained from the sound card can be stored and converted into a database with a software written in this language.

3.6 Coilsystem

As mentioned earlier, MPS uses the nonlinear response of super paramagnetic nanoparticles and magnetic saturation in certain magnetic fields, which is why the coil system is required to stimulate nanoparticles and detect their response. Figure 7 shows the coil system consisting of transmitter/driver and gradiometer receiver coil. The upper coil is the driver coil. This coil causes the nanoparticles to be excited by turning the high frequency currents having the known frequency and sufficiently large amplitude into the magneticfield. The inductance of thiscoil made by winding a thin wire on a carcass can be calculated from the following relation:

$$L = \frac{0.8\,\mathcal{N}^2 r^2}{6r + 9.\ell + c} \quad (\mu H) \qquad (3)$$

Here, N is the number of turns, r is the radius of the coil, ℓ is the length of the coil, and c is the thickness of the coil. Units must be taken in mm. The Biot-Savart law can calculate the magnitude of the magnetic field generated by the high frequency current passing through these two solenoid coils along the axis of the coil as

$$H(t) = \frac{N}{2\sqrt{(l/2)^2 + r^2}}\, i(t) \quad A/m \qquad (4)$$

The last expression is the rearranged version of the same law and $i(t)$is the value of the current flowing through the coil [1]. In Figure 7, the left-most coil is the gradiometer receiver coil.The windings on both ends of the coil have the same number of turns and winding the same direction.

The total number of windings of both ends is equal to the number of windings of the middle coilbut wound in the opposite direction. Coils with these properties are known as gradiometer or differential coils. This is very important in the MPS study because the amplitude of the excitation signal induced in the receiver coil is much larger than the signal of the nanoparticles,suppressing the signal of the particles and therefore the gradient coil is used to remove thesignal that is caused by the excitation [16].The number of turns of the gradiometer coil made in the study was wrapped around 47 turns for the windings at both ends, 94 for the middle windings but in the reverse direction. In addition, the receiver coil should be placed concentrically inside the exciter coil, and the capsule containing the nanoparticles to be measured should be placed in the middle of this receiver coil. In addition, the drive coil was wound with aluminum foil and grounded. In the thumbnail, there is a superparamagnetic iron oxide Fe_3O_4 solution in the capsule (nanomag® - MIP, surface: NH_2, Size: 100 nm, c(Fe) = 5.0 g/ml).

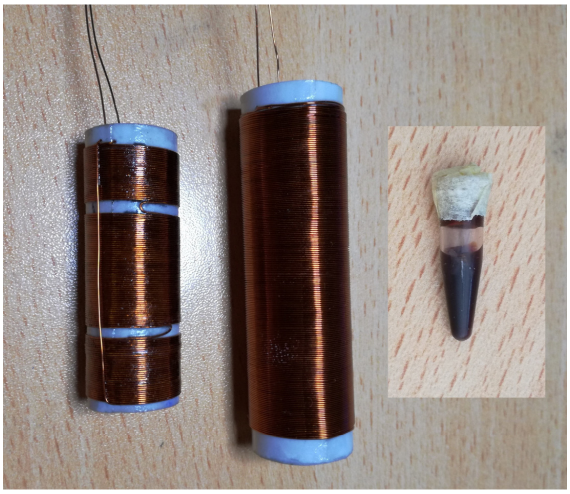

Figure 7. The coil system consisting of transmitter / driver and gradiometer receiver coil.

The accuracy of the signals of super paramagnetic nanoparticles detected in this system as described above for each component was obtained after calibration of the whole system. After ensuring correctness, the obtained signals can be displayed as a spectrum on the screen by performing Fourier transform. The signal flow of the system is shown in Figure 8.

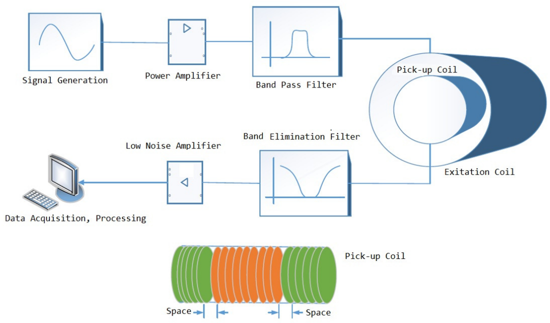

Figure 8. The signal flow of the system.

4.Measurements andResults

Figure 9 shows the finished state of the spectrometer; the operating frequency is 1.556 kHz and this value can be changed according to the expression (2). Figure 10 is a view of the MPS signal received in this spectrometer.

According to the signal processing theory, the sampling frequency must be at least twice as large as the frequency of the signal to be digitized. The sampling frequencies of the sound card we use can be changed via software. In this study, MPS signals obtained with 16 kHz and 38 kHz sampling frequencies and their FFT transformations are given in Figure 11 and Figure 12. The codes used for the FFT conversion of the MPS signal were written in Python version 3.6.8.

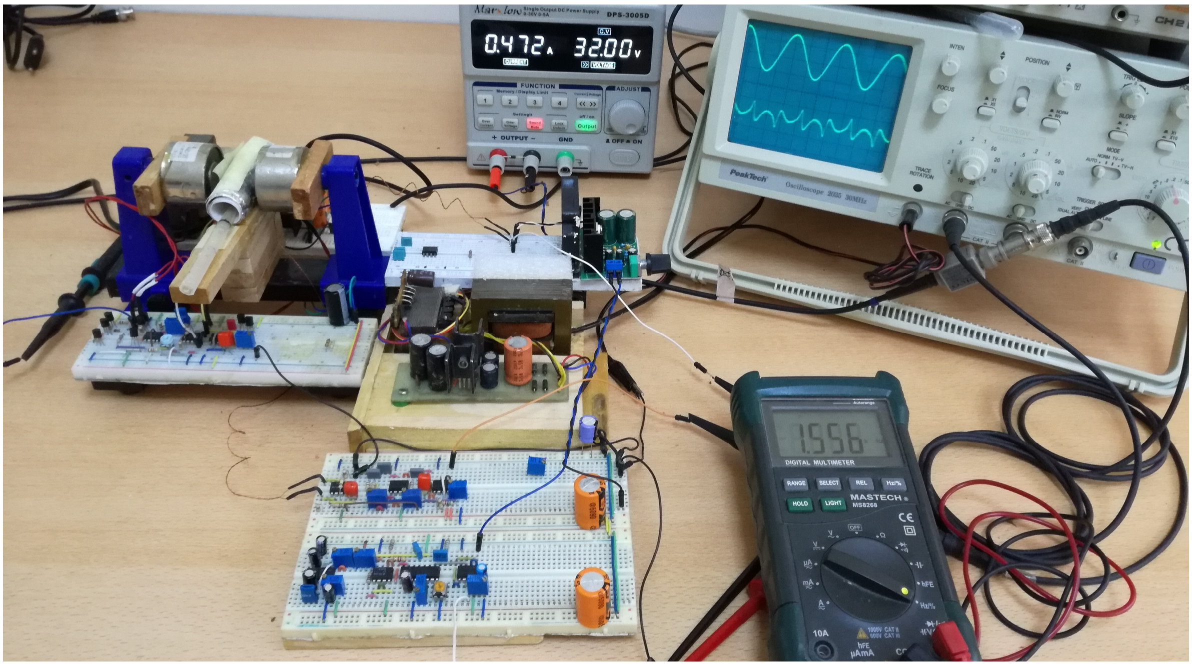

Figure 9. Magnetic nanoparticle detection system based on a sound card embedded on a laptop.

The values of the FFT peaks obtained from both sampling frequencies are the same and these peak values are the monovalent harmonic components of the fundamental frequency matching the nanoparticles. Table 1 summarizes these values and the graph is given in Figure 13.

In Figure 13, the upper end of the exponential curve obtained because of the graphical adaptation of the FFT peak points is cut off since the first harmonic in the particle spectrum cannot be used because the band stop filter suppresses the basic frequency.

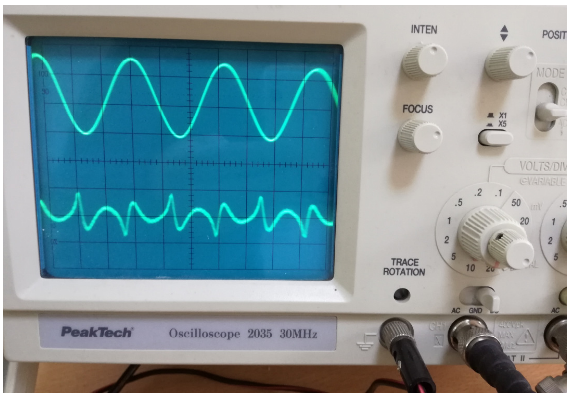

Figure 10. Observed MPS signal

Table 1. FFT peak values.

Odd frequency harmonics		
2n-1	**Frequencies (kHz)**	**Peaks (dB)**
1f	1.556	4.1856
3f	4.668	2.0750
5f	7.780	1.3899
7f	10.892	0.6984
9f	14.004	0.4199
11f	17.116	0.2264

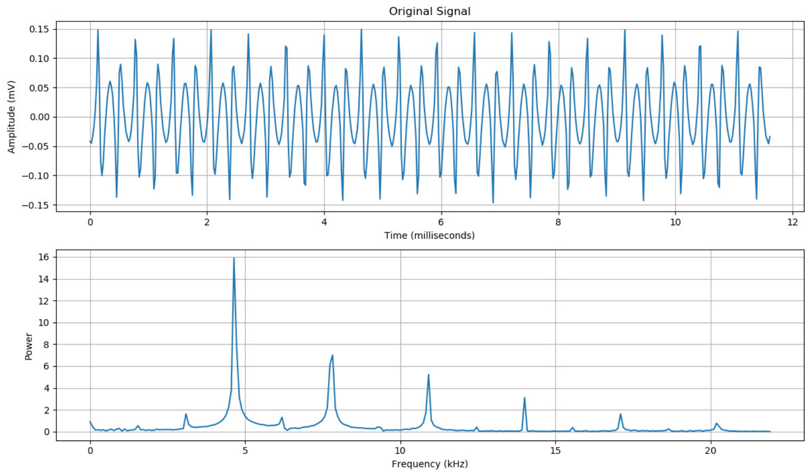

Figure 11. 16 KHz sampled MPS signal and FFT

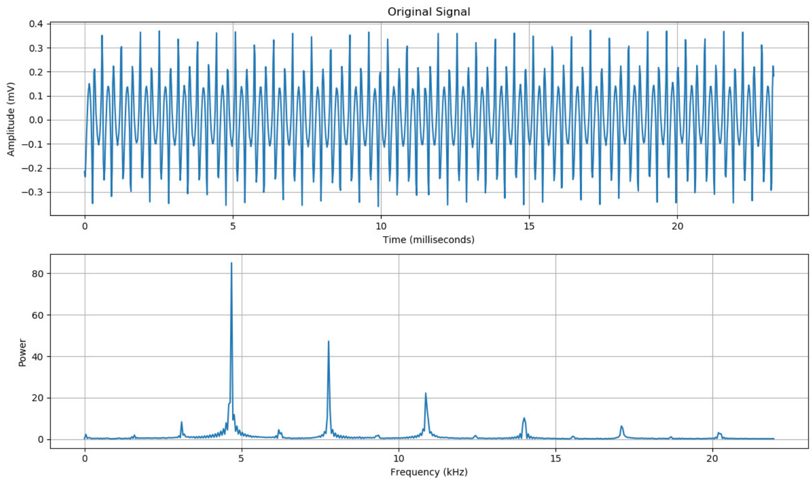

Figure 12. 38 KHz sampled MPS signal and FFT

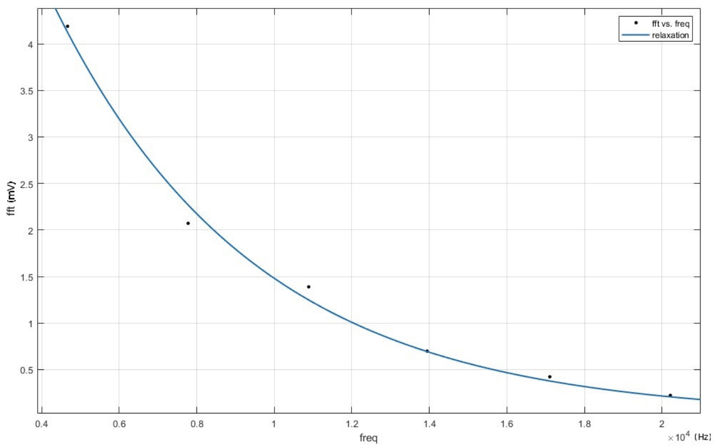

Figure 13. Frequency spectrum decays exponentially with increasing frequency.

5. Conclusions

In this study, the MPS system which is designed and experimentally performed can be interpreted as a zero-dimensional MPI scanner. This system needs to be developed to detect small diameter and low magnetic nanoparticle concentrations. This requires software algorithms with high quality hardware circuits. It also allows the creation of a database in the following stages. As a result, this experimental magnetic particle spectrometer (MPS) is a useful tool for real-time monitoring of its suitability during particle synthesis and for monitoring the imaging quality of the particle.

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