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Construction of a device for magnetic separation of superparamagnetic iron oxide nanoparticles

Abstract: Suspensions of iron oxide particles, so called ferrofluids, are successfully used in various technical, biochemical and medical applications. For example they find use in the area of sensor engineering, magnetic resonance imaging (MRI) and especially magnetic particle imaging (MPI). MPI is a new tomographic imaging technique that determines the spatial distribution of superparamagnetic iron oxide nanoparticles (SPIONs). Besides a very high spatial and temporal resolution MPI provides quantitative realtime imaging. The nanoparticles cause a magnetization change that can be measured. As the particle size distribution has a huge impact on the magnetization behavior an important parameter for optimization. While synthesizing, SPIONs particles with various dimensions are formed what necessitates a systematic separation by size. For this purpose a construction of a simple device for magnetic separation of SPIONs has been developed. First attempts of separation show the potential of this method.

Keywords: Magnetic Separation; Magnetic Nanoparticles; Magnetic Particle Imaging

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1 Introduction

Today in the area of medical engineering there are various techniques for medical imaging. These techniques differ in costs available bore sizes or resolution, as well as quantitativeness and sensitivity. MPI provides high resolution images without radiation like in CT, has a faster acquisition than magnetic resonance imaging and works with non-harmful iron oxide based tracer [1]. Therefore it combines the advantages of the imaging methods. It quantitatively measures the spatial distribution of superparamagnetic iron oxide nanoparticles (SPIONs) and is able to capture even fast distribution changes of those particles. Hence it is possible to create realistic high-resolution images without using radioactive tracers or ionizing radiation. To reach this, MPI exploits the nonlinear magnetization behaviour of SPIONs to determine their spatial distribution and concentration in the field of view. To measure a particle response, they have to be excited by a sinusoidal oscillating magnetic field. This leads to a change of the particle magnetization, which is recorded by a receive coil. Since Resovist is the only tracer approved for human use, which is not optimised for MPI, the synthesis and characterization of suitable tracers is required for further research. Simulations have shown that mono-modal suspensions of particles with a magnetic core size of approximately 30 nm are most suitable for MPI[2]. During the wet-chemical synthesis particles of various sizes are produced, what makes systematically separation necessary. This work presents a technical realization of a separation apparatus that uses the magnetic properties of the particles. Particles with a larger core diameter are supposed to be held by magnetic attracting force in the separator by an oscillating magnetic field whereas particles having a smaller core diameter will be rinsed out. The separation results are then evaluated by means of the Magnetic Particle Spectroscopy (MPS).

2 Material and methods

The basic idea of the separation relies on the theory that particles with a larger core size will experience a larger magnetic attracting force and will be held in the measurement chamber by the magnetic field. Small particles however will be washed out. Therefore, a separation device has to provide a sufficient large magnetic field inside the separation chamber.

2.1 Magnetic field configuration

As providing large magnetic fields with air coils is very power consuming one can increase the magnetic field enormously by winding the coil around a magnetically soft iron core. The relative permeabilities $\mu$ of those cores is greater than the permeability of free space $\mu_0$ which is most often expressed by a relative permeability $\mu_r = \frac{\mu}{\mu_0}$ [3]. Since the separation chamber has to be placed within the magnetic field, an iron core with an air gap is the basis
of the construction. If the air gap is sufficiently small, one can assume, that the magnetic flux density \( B \) in both the iron core and the air is constant (see Fig. 1). However the magnetic field strength is given by

\[
H_{\text{air}} = \frac{B}{\mu_0} \quad \text{and} \quad H_{\text{iron}} = \frac{B}{\mu_0 \cdot \mu_r}.
\]  

(1)

Since the magnetic field strength is just the flux per average field line length \( l \) the magnetic flux \( \Theta \) is

\[
H = \frac{\Theta}{l} \quad \Leftrightarrow \quad \Theta = H \cdot l.
\]

(2)

Moreover the magnetic flux is defined by

\[
\Theta = N \cdot I \quad \Leftrightarrow \quad I = \frac{\Theta}{N}
\]

(3)

where \( N \) is the amount of windings and \( I \) the current. According to the mesh rule the current that is required to generate a specific magnetic flux density is [4]

\[
I = \frac{B}{N \cdot \mu_0} \cdot \left( l_{\text{iron}} \cdot \frac{1}{\mu_r} + l_{\text{air}} \right).
\]

(4)

\[\text{Figure 1: An iron core with the average field line length } l_{\text{iron}}. \text{ The magnetic field lines run right throught an air gap } l_{\text{air}}. \text{ The current } I \text{ through the windings } N \text{ generates the magnetic flux } \Theta[4].]\]

\[\text{2.2 Magnetic separation chamber}\]

Magnetic columns made by Miltenyi Biotec are filled with small iron spheres and are often used in the particle size separation. Those iron spheres increase the local field gradient by a factor of 10.000 and produce an inhomogeneous field inside the column. This is the reason why magnetic particles stay in the column whereas non magnetic particles rinse out. After the small fraction of the particles are washed out, the big particles can be extracted by switching off the external magnetic field.

A similar behavior can be reached by reconstructing the columns. In order to avoid eddy current loss the casing of the column is preferably made from an electrically non-conductive material like plastic. To amplify the magnetic field in the separation chamber soft magnetic matrices are used. Materials that are suitable for this purpose are metallic spheres, needles, frits, pinhole apertures and wires in the form of grids or steel wool. Fig. 2a shows a self build separation column that is made from a plastic syringe and untreated steel wool.

\[\text{2.3 Assembly of the construction}\]

The coil for the construction is made from a toroidal iron powder core by Micromentals and braid wire by Elektrisola (Cross-section: 1.9635 mm\(^2\), 1000 single wires à 0.5 \( \mu \) m). Powder cores have the advantage, that there is much lower eddy current loss since the iron powder is mixed with an insulator before it is pressed. As the isolation gives no contribution to the magnetic flux, those cores provide lower permeabilities. The iron powder core that is used for the construction has a permeability of \( \mu_r = 10 \) and suitable for applications up to 500 MHz[5].

To place the separation column in the magnetic core, a two centimeter gap has been cutted. Before the chamber is integrated, the cut surfaces are coated with stainless lacquer so that no metal powder will be removed from the interior.
of the core.
The implemented coil has 200 windings with a mean field line length 39.9 cm. From the equations mentioned above, a needed current of 4.6 A is needed to generate a 20 mT strong magnetic field within the air gap. This value is checked with a gaussmeter and the result is that a current of 12.7 A is needed to generate the desired magnetic field. This difference could result from the fact that the air gap is too wide so that the magnetic field lines will not go straight through the gap.

In order to generate the desired current of 12.7 A a Signal Generator Rigol DG1022 is connected to a power amplifier AE Techron 7724. For an optimal output the resistance of source and load have to be matched. At a frequency of 500 Hz, the inductance of the coil is measured to be $L_{TX} = 1.95$ mH with an equivalent serial resistance of 340 mΩ. The desired load resistance of the amplifier is given to be 8 Ohm [6]. The adjustment is made by an impedance converter, which is realized by parallel and series circuits of capacities. Fig. 3 shows the circuit of the impedance converter.

In order to adapt the source and load resistance to each other, the values of the capacities must be calculated. The result of the calculation for the parallel capacity $C_p$ and the series capacity $C_s$ is then

$$C_s = 71.18 \mu F \quad \text{and} \quad C_p = 192.45 \mu F. \quad (5)$$

Since one can buy capacitors only in terms of the E-series, a standardized sequence of characteristic values of electrical components, the impedance matching is realized with the following capacitors

$$C_s = 68 \mu F \quad \text{and} \quad C_p = 220 \mu F. \quad (6)$$

These capacitance difference shifts both the resonance frequency and load. As the amplifier can handle these small differences the chosen capacitors were used for the implementation.

### 2.4 Separation process

Once the column is placed in the air gap a sinusoidal signal of 500 Hz with a field strength of 20 mT is applied. To avoid changes of the field strength current and voltage of the system can be controlled on an oscilloscope. When the field amplitude is stably reached, one pours 8 mL of a nanoparticle suspension into the column. Subsequently, 8 mL of distilled water are added to the column and the washout is collected in a sample bottle. This rinsing procedure is repeated four to six times. After that the field is switched off, before the remaining devices can be turned off. In the last step the column is rinsed out a final time and the eluate is collected again.

### 3 Results

For the quality of imaging with MPI, the core diameter is crucial, which should be as consistent as possible. This parameter is measured with the Magnetic Particle Spectrometer (MPS), which is described below. Furthermore the finished construction is provided with a safety enclosure and is shown in Fig. 5.

#### 3.1 Magnetic particle spectrometer

Magnetic Particle Spectroscopy has been developed as a supporting method for evaluating the properties of magnetic nanoparticle tracers for MPI. It was demonstrated that one is able to reconstruct the core size distribution from the measured MPS spectrum [8]. MPS is basically a zero-dimensional MPI scanner. It consists of one drive field coil and one receive coil. In contrast to a MPI scanner, no gradient field is applied. Thus, all particles are subjected to the same oscillation field. The magnetization response is then picked up by an receive coil and transformed into frequency space to get the harmonic spectrum. By using a mathematical model, that describes the signal chain and the magnetization behaviour of the particles, it is possible to estimate the particle core size distribution by means of curve fitting the model to the measured signal spectrum [7]. Fig. 4 shows the core size distribution after a separation process.
Figure 4: Particle size distribution after separation with a recreated separation column measured with MPS.

Figure 5: Constructed device for magnetic separation with a safety enclosure.

4 Discussion

In this work we discussed the construction of a simple device for magnetic separation of SPIONs. Considering the particle size distribution in Fig. 4 it can be seen that the particles of the first rinsing have the largest average core diameter (19 nm) and the particles of the residue the smallest one (11 nm). Considering the remaining curves, it is noticeable that the maximum of the particle size distribution moves with each additional rinsing a little further to lower diameters. This result contraindicate the original separation theory.

One reason that the particles are not separated in a particular order might be that the pressure exerted by the distilled water in the column on the particles is too high and no particles are held by the magnetic field so that they are consequently pressed out of the column. Further results with other nanoparticle suspensions have shown that the particles are separated, but there is no particular separation order. Summing up it can be said that the separation with the recreated column is a promising approach for magnetic separation. Other column types and field strength as well as frequencies can easily be tested to gain more detailed information about the exact mechanism behind the separation.

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Author’s Statement
Conflict of interest: Authors state no conflict of interest. Material and Methods: Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

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