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Experimental and Simulative Analysis of Magnetic Nanoparticle Accumulation Using Various Halbach Arrays

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Abstract: One of the major challenges in using magnetic nanoparticles in biomedical applications is still the accurate steering and trapping of these particles at a desired location, like at a tumor. Halbach arrays are well-established here as they generate the strongest magnetic force. However, these arrays are mechanically unstable, and thus, their potential to attract magnetic particles is often investigated fully numerically. Hence, this paper provides instructions on how to easily produce Halbach arrays using permanent magnets and metal glue. In total, three Halbach arrays of five, seven, and nine magnets were produced and analyzed regarding their potential for capturing magnetic particles in a background flow, numerically using COMSOL Multiphysics and in measurements. Furthermore, the Halbach arrays are compared with two other array configurations with all magnetizations in the same directions and alternating once. Overall, the simulation results were in good agreement with the measurement results. The amount of captured particles was significantly higher in measurements for the Halbach arrays with 8.2 %, compared to the array with alternating magnetization direction with 6.6 % captured particles. Therefore, using Halbach arrays to capture or steer magnetic nanoparticles in a background flow is strongly recommended.

Keywords: cancer treatment, Halbach array, magnetic array, magnetic drug targeting, MDT, magnetic nanoparticles, particle steering, SPIONs.

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1 Introduction

Magnetic nanoparticles are well-established in various research directions and widely used in different medical applications [1], e. g. as contrast agents in magnetic resonance imaging [2] or ultrasound [3], magnetic particle imaging [4], or in cancer therapy [5]. For treating cancer, these particles can be used as carriers for the cancer drug, which is often named as magnetic drug targeting (MDT) [1]. An MDT treatment is very promising [1] as it provides high effectiveness and low side effects, which have already been proven in animal studies [6]. Nevertheless, in most of the aforementioned applications, it is crucial to transport the magnetic nanoparticles to the region of interest (e. g. the tumor) and, especially in cancer therapy, to capture the particles. However, this particle steering is still an open research topic [5]. The biggest challenge in particle steering is that the particles are tiny but move nearly as fast as the background flow [7]. Hence, strong magnetic forces are necessary.

In the literature, so-called Halbach arrays have proven to be particularly suitable for particle steering, as they generate the strongest magnetic force over a large distance [7–9]. However, Halbach arrays are mechanically unstable due to the magnetic torque [10, 11]. Therefore, many publications on particle deflection or steering with Halbach arrays are purely numerical [5]. This paper explains a simple and low-cost realization of Halbach arrays using permanent magnets (PMs) and commercially available low-cost metal glue. Finally, the capturing performance of Halbach arrays with different lengths on magnetic nanoparticles in a background flow is analyzed in measurements and compared with numerical results from COMSOL Multiphysics® 5.4.

2 Fundamentals

2.1 Linear Halbach Arrays

A Halbach array is an arrangement of magnets where the single magnets are arranged so that the magnetic field is superimposed constructively and destructively on opposite sides of the array [10, 12]. This structure maximizes the magnetic force on the nanoparticles, which is crucial for effective particle steering or capturing [5, 7, 9, 12]. The strongest magnetic force can be realized by rotating the magnetization direction of the indi-

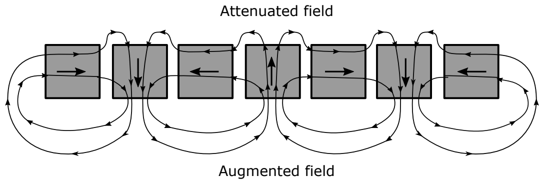

Fig. 1: Magnetization pattern and indicated magnetic field lines of a linear Halbach array. The magnetic field is superimposed on each side of the array, resulting in a strong and weak side.

vidual magnets by 90° (see [5]), as shown in Figure 1. However, due to the magnetic torque, Halbach arrays are mechanically unstable [11].

2.2 Magnetic Nanoparticles

The favored particles for MDT are superparamagnetic iron-oxide nanoparticles (SPIONs) as they have a high susceptibility χ with no remanence [13]. Therefore, SPIONs strongly interact with magnetic fields while agglomeration is prevented, which is essential for clinical applications as it would clog the vessels. Moreover, SPIONs are biocompatible [2, 6]. The SPIONs used in this work were synthesized by the Section for Experimental Oncology and Nanomedicine (SEON) of the University Hospital in Erlangen. They consist of magnetite (Fe_3O_4), are arranged in clusters with approx. 66 SPIONs per cluster and approx. $6.77 \cdot 10^{13}$ clusters per milliliter. An overview of the SPIONs' parameters is given in Table 1.

3 Methods

3.1 Simulation Model and its Evaluation

In this paper, the number of SPIONs captured by different magnetic arrays made of PMs is investigated numerically and with measurements. The numerical studies were conducted using COMSOL Multiphysics® 5.4. Here, a 3D model consisting of the magnetic arrays touching a straight tube and surrounded by an air-field sphere with a perfectly matched layer was built up. The geometry for a Halbach array with five PMs and captured SPIONs in a tube is depicted in Figure 2. The setup parameters are summarized in Table 2. The tube has a length of 80 mm, is filled with deionized (DI) water and a no-slip boundary condition (velocity equals zero) was applied. For the PMs, NdFeB magnets were used. In every simulation, one SPION pulse was released at the time $t = 0$ s, and the propagation of the SPIONs in the vessel was analyzed in a time-dependent study for 100 s with a time step of 0.1 s. The number of captured SPIONs $N_{\text{c,sim}}$ at the vessel wall was extracted. For simplification, particle-particle interactions were neglected.

Tab. 1: Parameters of the utilized SPIONs and clusters.

Parameter	Value	Unit
Hydrodynamic cluster diameter	50	nm
Iron-oxide particle diameter	9.5	nm
Fe concentration	7.5	mg/ml
Density of magnetite	5.2	g/ml

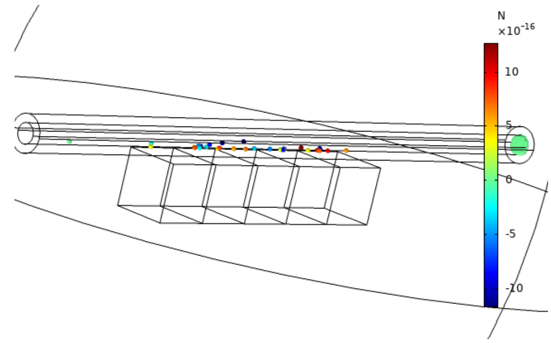

Fig. 2: Captured SPIONs by the Halbach array with the strong side towards the vessel. The color of the particles corresponds to the magnetic force in the propagation direction of the particles.

In total six simulation scenarios with five different magnetic arrays were conducted. Figure 3 summarizes all investigated PM structures. Firstly, an array consisting of five PMs was examined in which the magnetization direction of all PMs points in the direction of the tube. In the next step, the magnetization direction was alternated towards and away from the tube. Moreover, three different Halbach array configurations with five, seven, and nine PMs were analyzed, all with the strong side facing the tube. In the reference simulation, no magnetic field was applied. All PM configurations were produced to compare simulations and measurements.

3.2 Production of Linear Halbach Arrays

In this paper, three Halbach arrays with five, seven, and nine cube-shaped PMs were produced. For the production, opposing sides of the individual PMs were covered with a commercially available low-cost metal glue and then alternately placed between two metal objects in the correct order. Next, the single PMs were fixed together by pushing the PMs sideways in a line. Once the applied glue has hardened, the arrays can be carefully removed from the magnetic objects. For additional stabilization, the arrays can be encapsulated in epoxy resin. In this paper, the epoxy resin had approx. a thickness of 2 mm and

Tab. 2: Overview of the parameters for the simulation and measurement setup.

Category	Value	Label
PM	$5 \times 5 \times 5$ mm	Size of single PM
	10^6 A/m	Magnetization
Vessel	0.76 mm	Inner radius of the tube
	0.86 mm	Wall thickness of the tube
	1 ml/min	Average background velocity
Particles	2200 kg/m^3	Mass density
	500	Number of simulated particles
	25 nm	Radius of one particle
	10	Permeability

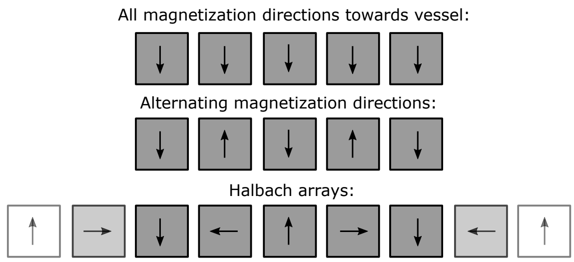

Fig. 3: Overview of the investigated magnetic array structures.

in order to keep the distance between the tube and the magnets as small as possible, the epoxy resin was not applied to the strong side of the array. Figure 4 shows an exemplary photo of the array with nine magnets.

3.3 Measurement Setup and its Evaluation

For analyzing the relative amount of captured SPIONs in measurements $N_{\mathrm{c,meas}}$, for all six simulation scenarios described in section 3.1, comparative measurements were conducted. For every scenario, in total five measurements were conducted, and the mean value and standard deviation was derived. A photo of the measurement setup is depicted in Figure 5. The velocity flow in a tube from Ismatec® Tygon ST with an inner radius of 0.76 mm and a wall thickness of 0.86 mm (see Table 2) is generated using a peristaltic pump. The tube was filled with DI water. Then, SPIONs are injected continuously like in a typical MDT treatment [5, 6]. During the measurement process, the tube was ensured not to sag. For measuring the amount of captured SPIONs, the particles were detected using a Barington® MS3 susceptometer. Here, the maximum value of the peak was extracted, and for deriving $N_{\mathrm{c,meas}}$, these maximum susceptibilities χ_{max} were normalized on the reference value without an applied magnetic field.

4 Results and Discussion

In the following section, the results of the simulation and measurements are discussed and compared. The resulting relative amount of captured SPIONs for the simulations and measurements are summarized in Table 3.

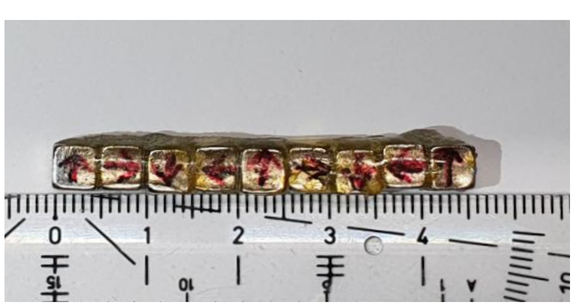

Fig. 4: Photo of the produced Halbach array with nine magnets.

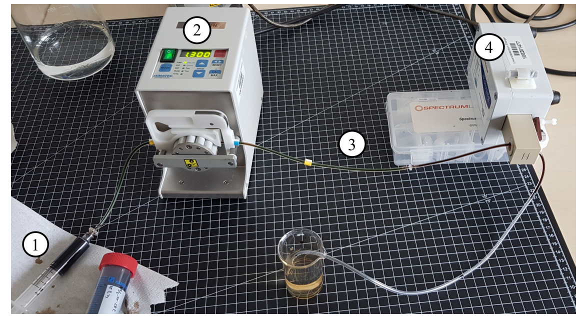

Fig. 5: Setup of the SPIONs deflection experiment, (1) syringe with SPIONs, (2) peristaltic pump for providing the velocity flow, (3) positioning of the magnetic arrays, (4) susceptometer for evaluating the amount of passed SPIONs.

4.1 Simulation Results

Figure 2 shows that the SPION pulse is washed with the velocity flow along the vessel, and the magnetic array captures some particles at the vessel wall. As expected, in the case where no magnetic field is applied, no SPIONs are trapped at the vessel wall (compare Table 3). For the array with all magnets pointing in the direction of the tube $N_{\mathrm{c,sim}}$ is the smallest. For the alternating magnetization directions, 6 % of the SPIONs get captured, and for the Halbach array with the same length $N_{\mathrm{c,sim}} = 6.2\,\%$. For longer Halbach arrays, more SPIONs get captured because, as already shown in the literature [5], the impact time of the magnetic field on the SPIONs is longer.

4.2 Measurement Results

In the measurements, the χ_{max} of the SPIONs was evaluated, which in turn was used to calculate $N_{\mathrm{c,meas}}$ by a normalization on the reference. As expected, χ_{max} is the highest without magnets and decreases with a stronger magnetic field as more particles are captured at the tube's wall (see Table 3). Similar to the simulation results, $N_{\mathrm{c,meas}}$ is the smallest for the array with all magnetization directions towards the tube followed by the alternating magnetizations with 6.6 % and the Halbach array with 8.2 %. Moreover, with 11.5 %, the most SPIONs were captured for the longest Halbach array with nine PMs.

4.3 Comparison of Simulation and Measurement Results

By comparing the simulation and measurement results in Table 3, overall, a good agreement was achieved. However, for the array with all magnetization directions towards the tube $N_{\mathrm{c,meas}} < N_{\mathrm{c,sim}}$. In contrast, for all other arrays $N_{\mathrm{c,meas}}$ was greater than $N_{\mathrm{c,sim}}$. The deviation is caused, on the one hand, by the simulation model, in which many effects, such as the particle-particle interaction or retroaction of the particles on the magnetic field, were not taken into account. In our previous research [14], we have shown that especially the retroaction has a significant impact on the magnetic force, which

Tab. 3: Summary of the simulation and measurement results. The maximum susceptibility χ_{max} and standard deviation was extracted in the measurements. N_{c} corresponds to the amount of captured SPIONs, and in the case of the measurements, is calculated by normalizing χ_{max} on the reference measurement.

Magnetic Array	Simulations: $N_{\text{c,sim}}$	Measurements: χ_{max}	$N_{\text{c,meas}}$
Reference (no magnets)	0 %	$3.05 \cdot 10^{-3}$ $\pm 1.05 \cdot 10^{-5}$	0 %
5 magnets towards tube	3.8 %	$3.02 \cdot 10^{-3}$ $\pm 4.88 \cdot 10^{-6}$	1.0 %
5 magnets alternating	6.0 %	$2.85 \cdot 10^{-3}$ $\pm 4.64 \cdot 10^{-6}$	6.6 %
Halbach (5 magnets)	6.2 %	$2.80 \cdot 10^{-3}$ $\pm 1.30 \cdot 10^{-5}$	8.2 %
Halbach (7 magnets)	9.0 %	$2.73 \cdot 10^{-3}$ $\pm 7.55 \cdot 10^{-6}$	10.5 %
Halbach (9 magnets)	10.8 %	$2.70 \cdot 10^{-3}$ $\pm 1.07 \cdot 10^{-5}$	11.5 %

could explain the larger number of captured particles. In addition, only a limited number of 500 particles are considered in the simulations, whereas in the measurements, there are approx. $6.77 \cdot 10^{13}$ particle clusters per milliliter. On the other hand, the measurement setup and its evaluation were rather simple: The SPIONs were injected continuously, and only the decrease in the maximum susceptibility was evaluated. Thus, for simplification, the amount of SPIONs that remain in the tube (e. g. due to gravitation) is neglected as this number has to be determined in a complicated way via the mass [15]. In addition, the reproducibility of the results needs to be confirmed.

5 Conclusion

In this paper, different PM arrays were investigated numerically and in measurements regarding their performance in capturing SPIONs. As Halbach arrays are known from the literature [5, 7, 9, 12] to provide the strongest magnetic force, three Halbach arrays of five, seven, and nine magnets were produced. Moreover, this paper provided an instruction on how to produce linear Halbach arrays out of PMs and glue. Overall, the simulation and measurement results were in good accordance with the same trends. The Halbach array captured more particles than the arrays, with all magnetization directions pointing toward the vessel and alternating magnetization directions. Moreover, as expected, the longer the Halbach array, the more particles were captured by the magnets. Nevertheless, as the measurement evaluation of the captured SPIONs was quite simple, it will be improved by sending multiple pulses and considering the width of the pulses. Furthermore, the simulation model will be further developed, moving away from considering individual particles to an inhomogeneous medium with magnetic properties.

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