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High gradient nested Halbach system for steering magnetic particles

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Abstract

To transport drugs within the brain to their desired application site it is necessary to overcome the blood brain barrier (BBB). To protect the brain from the penetration of harmful substances, the BBB forms an endogenous protection. Different approaches exist to overcome the BBB. One possible approach are magnetic nanoparticles which can be used to move drugs through the blood-brain barrier using magnetic guidance. The system described here consists of three rings of permanent magnets in Halbach configuration with an inner diameter of 5.5 cm, which generate a high gradient of 5.8 T/m at the center. The system is used as a demonstrator for future BBB experiments and to study the effect of application time and gradient strength on the transport mechanism.

I. Introduction

The blood-brain barrier (BBB) is part of the neurovascular unit (NVU) that, among other things, protects the human brain from potentially harmful substances [1]. The BBB consists of a tightly interconnected layer of endothelial cells. In some cases, for example tumor treatment, it is necessary to penetrate the BBB in order to deliver drugs to the intended site [2]. *In vitro* models exist and are useful to mimic the BBB and test experiments on penetration, even if they cannot perfectly represent the BBB [3]. *In vivo* experiments on penetration of the BBB with magnetic nanoparticles (MNPs) of size 770 nm at a gradient strength of 1.39 T/m and pulsed magnetic field have been successfully performed [4].

In this work, a system of permanent magnets in Halbach arrangement is presented, which can generate a gradient of up to 5.8 T/m. It offers the possibility to vary the gradient strength and thus to evaluate suitable field strengths for different MNPs. Halbach arrangements have a wide range of applications, for example, it is possible to realize MPI and also MRI with Halbach permanent magnet arrangements, as well as experiments to control MNPs, as also presented in this work [5, 6]. Cell models, for example for BBB cell experiments, can be placed in the center of the setup in a Petri dish and different gradient strengths can be adjusted by rotating the independent Halbach rings.

II. Methods and materials

The Halbach alignment of the permanent magnets makes it possible to maximize the magnetic field on one side of the array while nearly canceling it on the other side. This results in no stray field outside the rings in the ideal case [7].

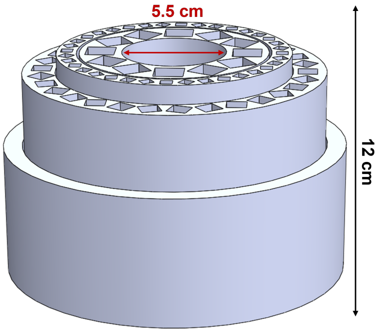

Figure 1: CAD model of the Halbach setup, which consists of three rings filled with permanent magnets in Halbach configuration with the specified dimensions.

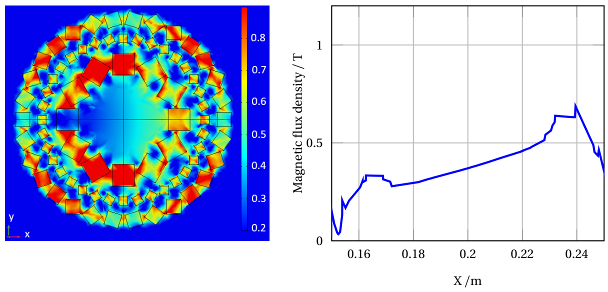

Figure 2: Simulation of the Halbach structure of three rings. On the left the superposition of the magnetic fields is shown, on the right the plot describing the increase of the magnetic flux density in x-direction in the center of the setup. The quadrupoles are not rotated, so that the gradient is maximal.

The system presented here is a Halbach setup consisting of three rings. The innermost ring is fixed, while the two outer ones can be rotated independently. The inner ring generates a dipole field that produces a homogeneous magnetic field in the center. This ensures that particles in the field are magnetized in the direction of the magnetic field. The quadrupoles generate a gradient field, which has a field-free point in the center. Both quadrupole rings generate a field of equal strength, so that the superimposed field of both can be varied by rotating the rings relative to each other. This allows the gradient to be adjusted and even cancelled. To ensure that the magnetic field of both quadrupoles is the same, 36 holes of the size 0.6 cm x 10 cm and 30 holes of the size 0.1 cm x 8 cm were filled with suitable NdFeB permanent magnets in the inner and outer ring respectively.
By superimposing the fields of the dipole and the quadrupoles, the FFP is shifted outside the bore resulting in a linear increasing field of uniform direction. The force acting on a single MNP is dependent on the gradient of the magnetic field and the magnetic moment of the particle [8]. The movement of the particles due to the force is in the direction of the increasing magnetic field [5, 9]. If the quadrupoles are rotated in relation to the dipole, the direction of the gradient and thus the direction of the force acting on the particles can be changed. The aim is to study the relationship between gradient strength and application time on the concentration within the brain tissue for different particle systems and surface coatings.

II.I. Simulation

COMSOL Multiphysics and MATLAB (The MathWorks, Inc) were used to simulate this setup. The two qudrupoles should each generate the same field, so that the variation of the magnetic field is possible. By adding the homogeneous magnetic field generated by the dipole to the field of the two quadrupoles, the field free point (FFP) generated at the center gets shifted out of the setup, so that a gradient field of uniform direction is generated in the center.

III. Results

The simulation shows that a gradient with a maximum strength of approximately 5.8 T/m forms in the center of the structure (see Figure 2). By rotating the quadrupoles against each other, their field can be cancelled so that only the homogeneous magnetic field generated by the dipole can be seen (see Figure 3). In between, the gradient can be increased linearly.
The rings were designed to take in commercially available permanent magnets. A petri dish can be placed in the center of the setup for in vitro experiments.The finished setup can be seen in Figure 4. The setup was made with by additive manufactureing and the permanent magnets were inserted afterwards. The magnets are held in their device with the help of lids, also 3D printed, fixed with brass and plastic screws. In total there are 444 NdFeB magnets in the setup and the total weight is 6.4 kg. For easier rotation of the two quadrupoles, handles were designed on the rings. The whole assembly is mounted on a plexiglass plate so that the dipole ring is fixed.

IV. Discussion

The ability to vary the gradient at the center of the setup allows simulations and in vitro experiments to evaluate the magnetic field strength necessary to penetrate the BBB with different particles. The setup is compactly designed and built so that experiments can be carried out flexibly. Although the system was primarily designed for in vitro experiments, upscaling for in vivo experiments is theoretically conceivable. However, the magnetic fields would decrease with increasing radius, which can not be easily compensated. The system presented here offers

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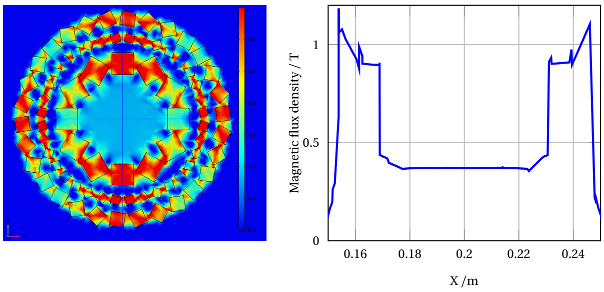

Figure 3: Simulation of the Halbach structure of three rings. On the left the superposition of the magnetic fields, on the right the representation of the strength of the homogeneous magnetic field generated by the dipole in x-direction. The quadrupoles are rotated by 45 degrees to each other, so that their fields cancel each other out and only the field of the dipole can be measured.

Figure 4: Assembled Halbach system consisting of two quadrupoles and one dipole with a 5.5 cm hole in the center and handles for easy rotation of the outer rings.

the possibility to investigate which field strengths are required for a specific particle system .

V. Conclusion

A three-ring Halbach setup was simulated for the manipulation of magnetic nanoparticles, which can generate a gradient that can be varied between 0 T/m and 5.8 T/m by rotating the individual rings. The rings were designed and then printed so that commercially available NdFeB permanent magnets could be used to generate the magnetic field. The simulated setup has already been built and is now ready for in vitro experiments. For this purpose, a holder has been installed in the center of the setup in order to place Petri dishes in it.

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Author’s statement

Conflict of interest: Authors state no conflict of interest.

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