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Focusing of Fe₃O₄ nanoparticles using a rotating magnetic field in various environments

Ryszard Krzyminiewski^a, Bernadeta Dobosz^a, Grzegorz Schroeder^b, Joanna Kurczewska^{b,*}
^a Medical Physics Division, Faculty of Physics, Adam Mickiewicz University in Poznań, Umultowska 85, 61-614 Poznań, Poland

^b Faculty of Chemistry, Adam Mickiewicz University in Poznań, Umultowska 89B, 61-614 Poznań, Poland

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ABSTRACT

The paper shows the application of a new method – Magnetic Nanoparticles Focusing 3D, MNF-3D – for focusing of magnetic nanoparticles at any point in a three-dimensional space between the rotating magnet system. The results of focusing process of nanoparticles in water, human blood, human serum and polyurethane sponge are presented. Additionally, blood flow was also considered. The effectiveness of nanoparticle focusing was monitored optically and quantitatively by electron spin resonance method. The method enabled focusing of magnetic nanoparticles within a few minutes in different environments. A good efficiency of focusing process was observed for all the samples.

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1. Introduction

Nanomaterials, including nanoparticles, are extensively studied by many research groups due to their potential application in various areas of life [1–4]. Many authors focus on medical use of magnetic nanoparticles as drug carriers in targeted therapies [5–8]. The surface of magnetic nanoparticles is often functionalized in order to adapt their properties to the intended purpose, while their transport can be controlled by an external magnetic field [9–11]. Specific properties of magnetic nanoparticles are especially important for their application in medical therapy, i.e. chemotherapy and radiotherapy.

There are several techniques described in literature for controlling of magnetic nanoparticles [12–15]. Attraction of magnetic nanoparticles is relatively simple in case of skin lesions and it requires only one magnet [16,17]. However, most tumors are localized away from skin surface. Therefore the concentration of such nanoparticles in the treatment site, where a drug should be released from the magnetic carrier (targeted therapy), still remains unresolved issue. Targeted therapy assumes that magnetic nanoparticles with the drug attached are administered into bloodstream, and subsequently transported to cancer tissue by the magnetic field of required configuration. It is very important to investigate the influence of magnetic nanoparticles on living organ-

isms, including their interactions with blood, during their transport to targeted site. The interaction of nanoparticles with proteins in blood (a formation of nanoparticle protein corona) has been already described [18,19], but the influence of magnetic field on these interactions has not been studied yet. Also the flow of nanoparticles and their behavior in tissue in the presence of magnetic field have not been examined yet. This mechanism is particularly important for intravenous administration of nanodrugs.

Electron spin resonance (ESR) belongs to methods applicable to investigate physical properties of various types of nanomaterials, including magnetic [9,10,20–23] and polymer nanoparticles [24]. Quality, size of nanoparticles and the influence of external conditions (environment, temperature, magnetic field) on physical properties of the particles can be controlled with ESR method. It provides valuable information on the evolution of magnetism of magnetic nanoparticles with different coatings and suspended liquids [10]. Moreover it allows to determine a number of parameters (anisotropy field, effective anisotropy coefficient, etc.), giving detailed information about magnetic properties of the material studied [21,25].

Our research group has already designed and described the principles of a new method, Magnetic Nanoparticles Focusing 3D (MNF-3D), for focusing of magnetic particles at any point in a three dimensional space in aqueous solution [11]. Based on our knowledge, it was the first report of the method for concentration of magnetic particles in three dimensions. The aim of this study was to show the effectiveness of the system designed, based on four

* Corresponding author.

E-mail address: asiaw@amu.edu.pl (J. Kurczewska).

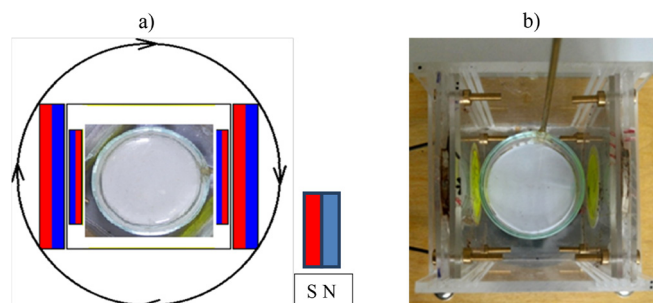


Fig. 1. Schematic representation of arrangement of the magnets in the MNF-3D system, a magnetic field configuration and a beaker between the magnets: a) top view, b) photo of the system.

magnets in an appropriate configuration, rotating around the sample containing magnetic nanoparticles, for focusing them in 3D space in different media. In this paper, we present the results of iron(II,III) oxide nanoparticles focusing in water, human blood and human serum as well as in polyurethane sponge – a model of tissue. Additionally, a peristaltic pump was used in order to observe focusing of nanoparticles in a flowing blood. Furthermore, electron spin resonance method was applied in order to determine any changes in concentration of nanoparticles in the samples during their focusing.

2. Experimental

2.1. Materials

Model magnetic nanoparticles ($\text{Fe}_3\text{O}_4@\text{SiO}_2$) were composed of the commercial magnetite core covered with silica layer according to the Stöber method [26]. The nanoparticles were prepared according to the procedure previously described [11]. In brief, the commercial iron(II,III) oxide nanopowder (Fe_3O_4 ; Aldrich; particle size < 50 nm) was initially coated with citric acid and then with silica layer in the presence of tetraethyl orthosilicate (TEOS; Aldrich). The magnetic silica nanoparticles (particle size 20–50 nm) were suspended in different media and applied in the system designed.

The samples of human blood and human serum were obtained from patients from Greater Poland Cancer Centre (Poznań, Poland) with the consent of the Bioethical Commission at Karol Marcinkowski Medical University in Poznań, Poland, Agreement No. 937/16. A commercially available polyurethane sponge was used as a model tissue.

2.2. Methods

2.2.1. MNF-3D system

The magnetic nanoparticles studied were concentrated using Magnetic Nanoparticles Focusing 3D (MNF-3D) system, rotating with a frequency of 0 to 5 Hz. The system designed consists of four neodymium permanent magnets arranged as shown in Fig. 1. A laboratory beaker (diameter 34 mm) was placed inside the system. The sample with nanoparticles (8 ml) was poured into the beaker.

The magnetite nanoparticles $\text{Fe}_3\text{O}_4@\text{SiO}_2$ were dispersed in water (0.8 mg/ml). The samples with human blood and human serum were prepared by diluting the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ aqueous solutions in a 1 : 1 volume ratio. In order to describe the focusing process in the model tissue, a polyurethane sponge was soaked in the $\text{Fe}_3\text{O}_4@\text{SiO}_2$ solution and placed in the magnetic system.

The neodymium magnets rotate around a laboratory glassware containing the sample studied. Two magnets (magnetic induction

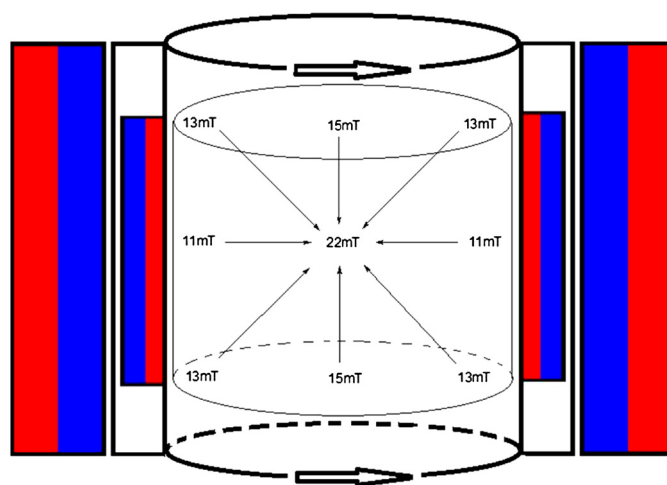


Fig. 2. Distribution of magnetic field in a beaker during rotation of the magnets.

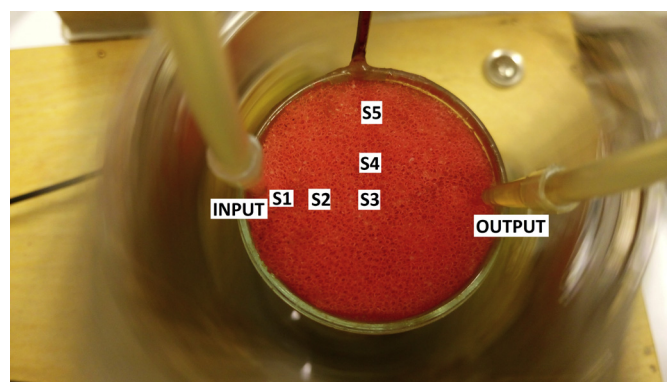


Fig. 3. The scheme of magnetic nanoparticles flowing through the polyurethane sponge.

60 mT; diameter 70 mm) produce strong homogeneous magnetic field of N–S at the location of the sample. Two others (magnetic induction 30 mT, diameter 35 mm) produce magnetic field of opposite orientation to the bigger ones (Fig. 1). Therefore maximum values of magnetic field in the intersection point of symmetry axis with rotation axis of four magnets are achieved (Fig. 2). The center of focusing is the intersection of the axis of magnets system rotation and the axis of symmetry passing through the center of the magnets. The distribution of magnetic field along the axis of system rotation is shown in Fig. 2. Maximum value is achieved at the central point and it decreases with distance from it. Therefore, the magnetic nanoparticles are directed to the central point, and such field configuration allows focusing of nanoparticles in 3D area.

The values of magnetic field in the experiments performed were about 22 mT and 12 mT in the rotation center and on the edge of the glassware respectively. Therefore, the average gradient of the magnetic field was 10 mT/17 mm (0.59 mT/mm).

In order to investigate a focusing process of nanoparticles in flowing liquids the miniature peristaltic pump BQ50-1J model (flow rates 0.0002–20.0000 ml/min) was applied. Polyurethane sponge, placed in MNF-3D system, was soaked with water and then $\text{Fe}_3\text{O}_4@\text{SiO}_2$ solution (50 ml) flowed through the sponge for 1 hour. The schematic representation of this experiment is presented in Fig. 3. After certain time intervals (2.5–60 minutes), the samples were taken from the selected points (S1–S5) and the concentration of nanoparticles was studied by ESR measurements.

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