International Journal on Magnetic Particle Imaging
Vol 8, No 1, Suppl 1, Article ID 2203072, 3 Pages

Infinite Science Publishing

Proceedings Article

A synthesis apparatus for the continuous flow synthesis of Magnetic Nanoparticles

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Abstract

In magnetic particle imaging, superparamagnetic iron oxide nanoparticles are used as a tracer material. By utilizing the non-linear magnetization of the particles, their concentration in the body can be determined with high spatial and temporal resolution. Some of the important properties of the particles are their core diameter, hydrodynamic diameter, size distribution, and magnetic properties. In order to be able to produce particles with adequate quality and high reproducibility, a prototype of a continuous-flow synthesis apparatus is designed and tested. This research deals with the design and construction of a device that can use the co-precipitation synthesis method to synthesis particles in continuous flow.

I. Introduction

Depending on size and composition of the magnetic nanoparticle, they have different physical and magnetic properties. This gives them a high degree of versatility, enabling them to be used in the most diverse areas of science such as in high-frequency circuits in radio technology, as well as in the field of data storage. In biomedical engineering their potential applications are also being intensively investigated. Current research includes suitability for the targeted transport of drugs, as well as their use in cancer therapy by means of hyperthermia [1,2].

In 2005, Bernhard Gleich and Jürgen Weizenecker presented a new imaging modality called Magnetic Particle Imaging (MPI). For creating a 3D image in a specific volume, MPI relies on time-varying magnetic fields and the nonlinear magnetization behavior of the magnetic nanoparticles (MNPs). The concentration of the MNPs play a vital role in the signal intensity as well as in the spatial and temporal resolution. Therefore, there is an immense need to synthesis MNPs specifically intended for MPI for both diagnostic and therapeutic applications [3].

A variety of methods exist to synthesize MNPs. The alkaline precipitation is the most preferred method so far. It is suitable because of its low synthesis time, low cost, and high yield. In addition, it allows the MNPs to be produced in an aqueous solution, which makes it highly suitable for in-vivo applications due to biocompatibility. However, the MNPs produced by this synthesis method suffer from wide size distributions making them inhomogeneous and needs some extra filtration steps to achieve some homogeneity [3]. The aim of the research is to develop a prototype of a continuous-flow synthesis apparatus (CFSA) to ensure continuous synthesis of the MNPs in sufficient quantity and quality with desired physical and magnetic properties with alkaline precipitation at 60 °C.

II. Material and methods

The CFSA consists of several different modules as shown in Figure 1. First and foremost important module is the 3D printed synthesis module (A). Followed by its heat-

10.18416/ijmpi.2022.2203072

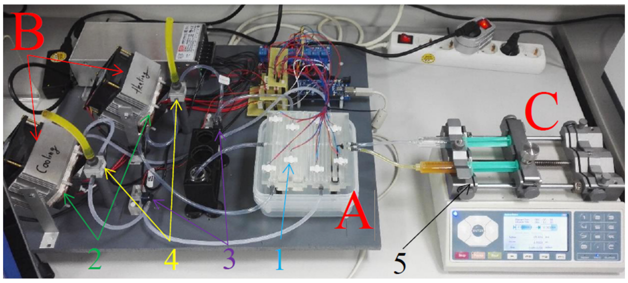

Figure 1: Setup of the CFSA with: Synthesis module (A), heating and cooling module (B), and syringe (5) loaded in syringe pump Nexus 3000 (C).

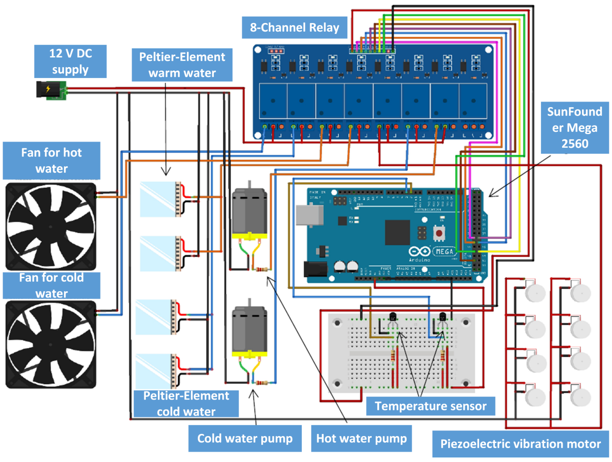

Figure 2: Electrical Setup of the CFSA with power supply, relays, pumps, piezoelectric vibration motors etc. controlled via SunFound Mega 2560.

ing and cooling module for providing specific synthesis environment for nucleation and growth (B). The system incorporates electric vibration motors (1) attached to the synthesis module (A) to provide a continuous mixing to prevent agglomeration of iron(II)-and iron(III)chloride salts with ammonia. The temperatures needed for the synthesis of MNPs is achieved by cooling and heating of water with the help of Peltier elements (2). This cooled and heated water is pumped underneath the reaction path in the synthesis module (A) via separate chambers. This circulates continuously in the synthesis chamber with the aid of two micro-pumps (3) and a water reservoir (4) to maintain a constant temperature for nucleation and growth of MNPs. From the micro-pumps, the water flows through copper tubes attached with copper plates to the respective Peltier element. Thermal paste is used to achieve maximum transfer of heat energy between the flowing water and the Peltier element.

Furthermore, Peltier elements and copper tube plates are mounted to a heat sink by means of screws, which is intended to dissipate excess heat produced by the Peltier element itself. Fans are attached to the heat sinks, which

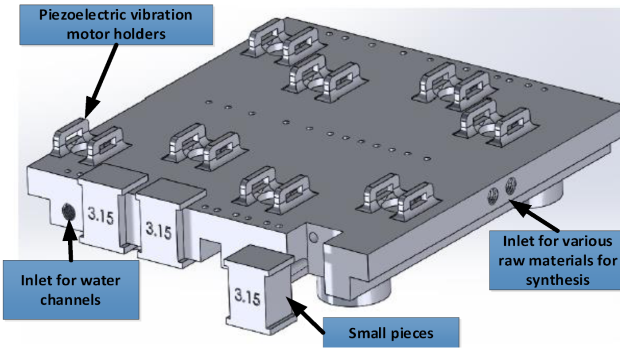

Figure 3: The synthesis module designed in Solidworks and printed using Formlabs Form 3.

helps in keeping a small temperature difference between the cold and warm sides of the Peltier elements. Two temperature sensors are embedded in sockets of the copper tube plates (not shown in Figure), which allows simultaneous temperature measurement as well as a feedback loop to control the temperature of hot and cold water throughout the duration of the synthesis process.

Figure 2 shows the schematic layout of the electrical components used in the CFSA. The system is supplied with power from a mounted power supply unit which is connected to relay unit containing eight channels. This is controlled via a SunFounder Mega 2560. The switching of the various modules depends on the synthesis steps and is controlled with the help of Arduino via a software.

The synthesis module was designed in Solidworks is shown in Figure 3 and was printed using Formlabs Form 3 using Clear Resin, which can be easily tolerate temperatures of up to 60° C without causing structural deformation. The synthesis module basically consists of two parts the main body housing the channels for synthesis as well as chambers for hot and cold water. Furthermore, small pieces are used for completing the channels as shown in Fig 3.

The small pieces will be used in future experiments as a structure for holding transmit and receive coil to analyze the magnetic properties of MNPs at different stages of the synthesis process.

III. Experiment and results

Before carrying out the synthesis, the solutions containing raw materials as well as the CFSA were to be prepared. The first solution consisted of Fe^{2+} (0.30 g) and Fe^{2+} (0.79 g), and dextran T70 (1.5 g) in a 15 ml water suspension. The second solution contained only 15 ml of ammonia. Both the solutions were delivered with the help of a syringe pump at a flow rate of 0.08 ml/min for Sample 1 and 0.10 ml/min for Sample 2. Before CFSA could be used, the water chambers and water reservoirs were completely filled with distilled water. On the software side the

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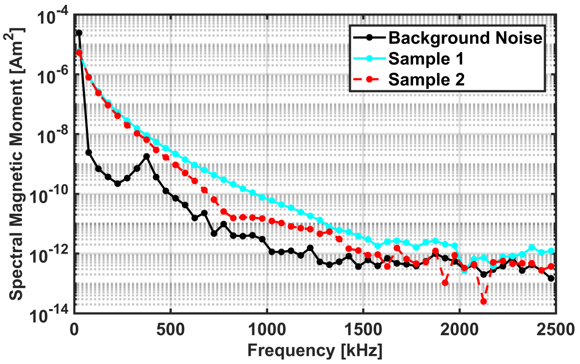

Figure 4: The spectral magnetic moment of the particles: Sample 1 (Blue), Sample 2 (Red) and the background noise (black) of the MPS device.

parameters like total duration of the synthesis (60 min), temperature of the cooling water (0 °C), and temperature of the warm water (60 °C) were set. After the completion of the synthesis, a 10 µl sample of the synthesized particles were measured in MPS [4]. The spectral magnetic moment of the particles are shown in the Figure 4.

As it can be seen in Figure 4 there is a formation of nanoparticles. The amplitude of spectral magnetic moment for both the samples are above the background noise of the MPS device. But the samples are weakly magnetic as compared to commercially available magnetic nanoparticles.

IV. Conclusions

With the designed apparatus, it is possible to synthesis magnetic nanoparticles in continuous flow but there is need to find out the right parameters. Sometimes agglomeration of the magnetic nanoparticles were observed in the synthesis module due to high concentration of the iron salts. Therefore, further experimentation is needed to synthesis magnetic nanoparticles suitable for MPI.

Author's statement

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

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