682. Capturing of FePt nanoparticles in a stream of a liquid

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Abstract. This study considers capturing of FePt nanoparticle in a magnetic field when the particles are injected into a stream of flowing liquid. A roller pump is used to induce a flow of water at several flow rates to assess the growth of FePt aggregation near magnetic field source. The particles are injected into the system using a micro syringe pump at different flow rates. The aggregations are observed with a microscope. Subsequently some estimation is performed with respect to a magnetic hyperthermia, which is a part of a method for treating undesirable biological entities in blood vessels.

Keywords: FePt paramagnetic nanoparticles, magnetic capturing, treatment of atherosclerosis.

Introduction

Research on medical application of paramagnetic nanoparticles is increasing in such fields as magnetic drug targeting, magnetic hyperthermia, use of contrast agents, controlled cell growth etc. However, so far there have been no claims for proposing a system that would include magnetic hyperthermia system as a subsystem for eliminating biological entities in human blood vessels. Combined with magnetic capturing subsystem for capturing of magnetic or/and paramagnetic nanoparticles one could efficiently address problem of eliminating biological substance comprising atherosclerosis in a certain stage of development of said disease. So far only theoretical estimations were done for working principles of such a system. The working material in such a system is colloidal solution of magnetic or/and paramagnetic nanoparticles, which is compatible with human vascular system. Two main requirements for such a working material can be derived: chemical stability in working environment, magnetic properties that allow efficient capturing of the magnetic/paramagnetic nanoparticles within a safe-to-use magnetic field, and subsequent heating of developed aggregation. Here we address controllability of FePt paramagnetic nanoparticles, to be more precise - their clusters. The working environment requires particles to have magnetization large enough to be able to withstand the forces induced on nanoparticles or their clusters by a stream of a liquid having flow rate of 20 ml/min – 60 ml/min. The diameter of lumen of said flow path is ~2 mm. These are parameters of *arteria radialis* located in an arm [1]. Thus particles are subjected to velocity of a liquid from 1,59 m/min to 4,78 m/min at the centre region of liquid flowing environment.

FePt nanoparticles

According to research [2], iron-platinum nanoparticles are a promising material for use in magnetic hyperthermia. The reasons are that in presents of high Curie temperature, high saturation magnetization and high chemical stability is achieved. But it is hard to synthesize them with average diameter larger than 5 nm with uniform size. This represents a problem, because such small particles are hard to control using magnetic field because of insufficient magnetic susceptibility, subsequently insufficient magnetic driving force acted on particles. The holding force is directly proportional to particles magnetization and their size. Although particle size is limited to ~ 9 nm, average diameter of clusters of FePt nanoparticles can be ~50 nm. Magnetization graph of colloidal solution of FePt nanoparticle used in our experiment is given in Fig. 1. Average size range of: particles ~ 6 nm, their clusters ~ 50 nm. Density of particles in a colloidal solution was $2.9 \cdot 10^{-5}$ g/µl. The sample was produced in Prof. Y. Kitamoto Laboratory in Department of Innovative and Engineered Materials, Tokyo Institute of Technology.

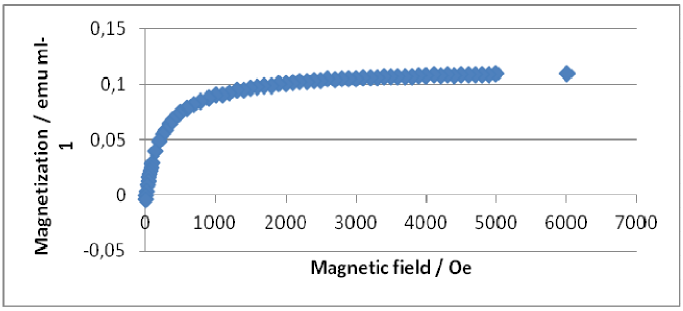

Fig. 1. Magnetization curve of solution of FePt nanoparticles

Experimental setup

Primary objective of the experiment was to evaluate the aggregation of the FePt nanoparticles of a colloidal solution near a source zone of a magnetic field. To create an efficient trapping zone for paramagnetic nanoparticles two square (20 mm x 20 mm x 20 mm) neodymium permanent magnets (grade – 35, attractive suction force - 16,704 kgf) were used at two sides of a glass tube. At the middle zone, ~ 4 mm from each magnet, of the glass tube a magnetic field of ~6000 Oe was generated.

Distilled water (viscosity $\sim\eta = 1 \times 10^{-3}$ Pa s) was used as the stream fluid, which was pumped using *Masterflex L/S* digital drive pump at several different flow rates. In this case, as this experiment is intended to get some insight in the interaction of magnetic field captured nanoparticles and a liquid flow in a nearly cylindrical body, to be more precise - like in *arteria radialis*, the minimum desirable flow rate in experiment is 20 ml/min. The diameter of *lumen* of *a. radialis* is > 1.6 mm; the glass tube, in which the aggregation of particles is monitored, inner diameter is 2 mm (length 100 mm). Tubing of the same diameter as the glass tube was used to supply water into the glass tube. The FePt nanoparticles were injected into the system using a micro syringe drive *AS ONE* with a 500 µl syringe. FePt based colloidal fluid was supplied into the water stream at the beginning of glass tube via tubing with inner diameter of 1 mm. Sedimentation observations were done using microscope Olimpus SZX7 with attached digital camera.

Experiment using a FePt sample

The starting fluid flow rate in glass tube was 10 ml/min. Because it is unknown at what flow rates particles can aggregate near the magnet, the flow rate was chosen randomly. The sample colloidal solution was injected into the water flow at a 10 µl/min rate. Each time after dispensing 50 µl of paramagnetic solution a picture was taken of the area of particle aggregation near the wall of glass tube besides a magnet. As it is inefficient to use only one magnet, when using two magnets (facing each other with different poles) the glass tube is put closer to one of two magnets to ensure the aggregation of particles at desired location. Distance from the centre of the glass tube to the *L* magnet is about 3 mm and to the *R* magnet is about 6 mm. In Fig. 2a one can see particle aggregation after injected ~10 µl of colloidal suspension.

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From Fig. 2 it can be clearly seen that aggregation does not “grow” after initial clumping of nanoparticles. In this case the limit of “growth” height is limited by the stream velocity, which is different at different regions going from wall of the glass tube to its centre. At flow rate of 10 ml/min, the height (direction from the wall of tube to the centre) of the aggregation is ~0.7 mm. And the aggregation is formed ~5 mm downstream from the centre axis of the magnets. Afterwards the flow rate of water was increased to 15 ml/min, leaving the colloidal suspension injection rate at 10 µl/min. In Fig. 3 one can observe, that the amount of aggregated particles is significantly diminished. Analogously to the previous case, the particle aggregation amount does not change in time after it reaches certain amount (after about ~20 µl).

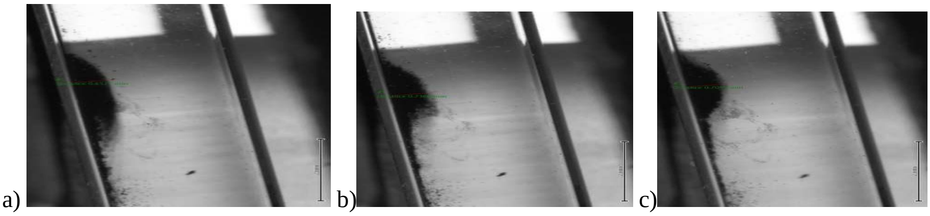


Fig. 2. Aggregation of FePt nanoparticles at the fluid flow rate of 10 ml/min, colloidal solution injection rate – 10 µl/min: a) after dispensing ~10 µl of FePt based c.s.; b) after disp. 50 µl of c.s.; c) after disp. 200 µl of c.s.

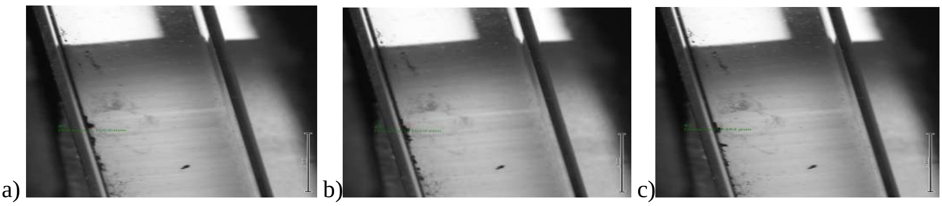
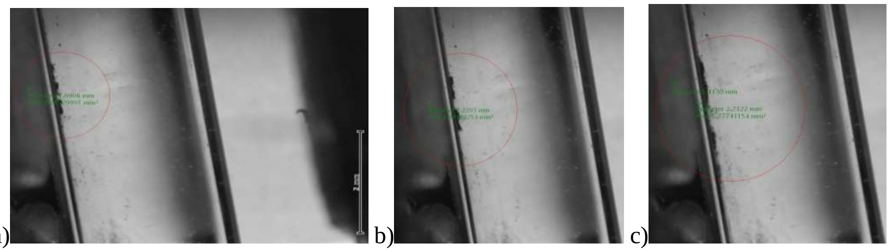


Fig. 3. Aggregation of FePt nanoparticles at the fluid flow rate of 15 ml/min, colloidal solution injection rate – 10 µl/min: a) after dispensing 50 µl of FePt based c.s.; b) after disp. 150 µl of c.s.; c) after disp. 250 µl of c.s.

In the last trial (Fig. 4) the water flow rate was set to 20 ml/min, leaving the colloidal suspension injection rate at 10 µl/min. An aggregation was formed at about 7 mm from the centre of magnets centre line. It is worth noticing that the sedimentation forms further and further from the centre of magnet centre line with increase of the flow rate. Formed clusters tend to migrate (total length of path is ~5mm) to the centre line and backwards. It happens due to working principle of roller pump (three rollers subsequently are squeezing the tubing thus producing pulsating flow).

Fig. 4. Aggregation of FePt nanoparticles at the fluid flow rate of 20 ml/min, colloidal solution injection rate – 10 µl/min: a) after dispensing 50 µl of FePt based c.s.; b) after disp. 100 µl of c.s.; c) after disp. 150 µl of c.s.

When it was established, that any further increase in flow rate is unnecessary, because the aggregation size cannot be increased/decreased efficiently to desired amount (if necessary), like at the flow rate of 10 ml/min, the flow rate was not increased anymore. Lastly injection rate was increased to 50 µl/min, leaving the flow rate at 20 ml/min. The effect – increase of amount of aggregated particles (Fig. 5).



a) b) c)

Fig. 5. Aggregation of FePt nanoparticles at the fluid flow rate of 20 ml/min, colloidal solution injection rate – 50 µl/min: a) after dispensing 50 µl of FePt based c.s.; b) after disp. 100 µl of c.s.; c) after disp. 150 µl of c.s.

Results and discussion

Major drawback of the experiment is that the liquid used in experiment to induce flow was 3-4 times less viscous than target viscosity of a real system, as blood viscosity is ~$3\cdot10^{-3}$ – $4\cdot10^{-3}$ Pa·s (at 37 ºC) while viscosity of the distilled water is ~$1\cdot10^{-3}$ Pa·s. Nevertheless, the goal of the experiment was to investigate the way particles undergo aggregation, magnitude of the magnetic field needed for the particles to aggregate and what flow rates of the main stream, in a cylindrical-shaped body, the particles can hold up their build-up. At the flow rate of water of 10 ml/min and colloidal solution of FePt particles injection rate – 10 µl/min the in a 2 mm inner diameter glass tube the build-up is formed downstream in the third part at the magnet face area. Increasing the flow rate of the water to 15 µl/min and subsequently to 20 µl/min it becomes clear that particles cannot withstand the drag force induced by flowing liquid which becomes grater then the force on a volume of a magnetic liquid which is given by [3]:

$$F=F_g+F_m \tag{1}$$

where F_g is gravitational force and F_m is magnetic traction force. The sum can be further written as:

$$F=\rho Vg+\mu_0\cdot MV\cdot \partial H/\partial z\ g/g \tag{2}$$

where V is given volume of magnetic fluid, ρ is the density of the magnetic fluid, μ_0 is the magnetic permeability of a vacuum, M is the magnetization of the fluid, H is the magnetic field strength, $\partial H/\partial z$ is the vertical magnetic field gradient and g is gravitational acceleration.

According to formula increase in volume of magnetic particles will produce larger magnetic traction force, which is magnetic capturing force. This might also be applied taking volume as volume of individual clusters of nanoparticles. It is self-evident, that the greater volume of particles is grouped the grater magnetization thus magnetic response to the applied field. The experiment demonstrated that in the case of FePt paramagnetic nanoparticles the size of clusters (average size ~50 nm) is not sufficient. Experiment revealed that increasing the input volume of colloidal solution, thus nanoparticles, into the stream also increases aggregation of particles at the said area in the glass tube. As one might reach sufficient magnetic response of paramagnetic nanoparticles in a stream of water at ≥20 ml/min flow rate it will be impossible to reach same effect in a stream of a liquid with 3-4 times greater viscosity. Presumably, a successful application of paramagnetic FePt nanoparticles in the case of a liquid with higher viscosity depends whether it is possible or not to produce FePt particles of size 100 nm or grater. Also, considering magnetic hyperthermia, a crucial factor is the power P absorbed (dissipated) by nanoparticles of volume V given by [4]:

$$P = \frac{M_S^2 H_l^2 V}{2kT\tau} \frac{\omega^2\tau^2}{1+\omega^2\tau^2} \quad (3)$$

where H_l is an ac magnetic field amplitude, ω angular frequency, M_s is saturation magnetization, τ is Neel relaxation time and T is temperature.

Nevertheless, according to research [2], [4], [5], ~10nm to ~40 nm diameter of nanoparticles (FePt ~10 nm, γ-Fe_2O_3 and Fe_3O_4 ~15-25 nm, FeCo ~30-40 nm) is optimum for achieving maximum heating rate. Thus further research is necessary to establish a ratio between the size of nanoparticles, their concentration and input rate into the stream to achieve capturing of required amount, yet to be determined, of nanoparticles for efficient heating rate.

Conclusions

From experimental results it is evident that FePt particles of bigger size are necessary. In this experiment particles of ~5 nm to ~10 nm, which formed clusters of ~50 nm, were used. It was necessary to determine the flow rate of water at which the particles can be stopped at a considerably large amount: even at water viscosity ($\sim 1\cdot 10^{-3}$ Pa·s at 25 ºC), flow rate ~10 ml/min is limit for considerable aggregation of said FePt nanoparticles. Considering that blood viscosity is $\sim 3\cdot 10^{-3} - 4\cdot 10^{-3}$ Pa·s (at 37 ºC) it should significantly decrease the amount of aggregated particles event at this rate of fluid flow or prevent from forming at all. Next step is to use larger particles and their clusters, also include using Fe_2O_3 and Fe_3O_4 for capturing in a stream of liquid with near-to-blood viscosity.

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