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An Innovative Application of Super-Paramagnetic Iron Oxide Nanoparticles for Magnetic Separation

George Banis[a], Maria E. Kouli[a], Angelo Ferraro[a,b], Antonio Molino[c], Despina Karatza[d], Simeone Chianese[d], Dino Musmarra[d], Evangelos Hristoforou[a]*

[a] School of Electrical and Computer Engineering, National Technical University of Athens, Zografou Campus, 9, Iroon Polytechniou str, 15780 Athens, Greece
[b] Institute of Physics, Laboratory of Functional Programmable Materials of Quantum Electronics for Biomedicine, Kazan Federal University, 18 Kremlyovskaya Street, Kazan 420008, Russia
[c] ENEA, Italian National Agency for New Technologies, Energy and Sustainable Economic Development, Research Centre of Portici. P. Enrico Fermi, 1, 80055 Portici (NA), Italy
[d] Department of Civil and Building Engineering, Design and Environment, Università degli Studi della Campania “L. Vanvitelli”, Real Casa dell’Annunziata, Via Roma 9, 81031 Aversa (CE), Italy
*hristoforou@ece.ntua.gr

In the last decades, iron oxide nanoparticle application has taken root in several technological fields, such as magnetic separation of biomolecules, biosensors, bio-fuel production, nano-devices and nano-adsorption. Various approaches can be found for the magnetic nanoparticle manufacturing. Among them a new technology to manufacture core-cell super-paramagnetic iron oxide nanoparticles (SPIONs), based on a vapour composition using single ion precursors, like cyclodextrines, has been recently developed.

In this paper, we present the synthesis of functionalized SPIONs as well as the modelling for an innovative application of this magnetic nanotechnology. It consists on the use of SPIONs to trap target organic or inorganic molecules in a continuous-flow apparatus. SPIONs with proper ligands are immobilized on a magnetic surface. On that surface, the solution containing target molecules is circulated. We modelled the magnetic properties of the magnetic surface and SPIONs as well as the velocity of liquid needed in order to avoid removal of nanoparticles by the solution flow.

1. Introduction

Nanostructured materials with size between 1 and 100 nm are classified as nanoparticles. Such kind of nanomaterials may hold exclusive electrical, chemical, structural, and magnetic properties which are suitable for biotechnological applications. Among them, nanoparticles possessing magnetic properties offer great advantages due to a characteristic, named superparamagnetism, that makes magnetic nanoparticles attractive for biomedical applications because the risk of forming agglomerates is very low in the absence of magnetic fields. Indeed, single magnetic domains manifest magnetization only in response to applied magnetic fields. In particular, superparamagnetic nanoparticles are suitable for imaging and drug delivery (Sun et al., 2008), gene therapy and gene delivery (Majidi et al., 2015); isolation and purification of DNA and RNA (Berensmeier, 2006); isolation and purification of proteins (Safarik et al., 2004), hyperthermia and magnetomechanical cell disruption for cancer therapies (Liu et al., 2012; Kim et al., 2010), cell immobilization for bioscience research (Tseng et al., 2012); stem cell therapies for tissue regeneration (Cromer et al., 2011). Moreover, superparamagnetic nanoparticles can be used in several techniques for pollutant removal (Chiavola et al., 2016), such as adsorption, which is one of the main techniques for air emission and wastewater treatment (Karatza et al., 2013; Molino et al., 2013).

The superparamagnetic iron oxide nanoparticles (SPIONs) synthesis is simple, inexpensive and depending on the protocol used sufficiently fast. Magnetic nanoparticles are synthesized from a variety of metallic atoms combined eventually with oxygen including iron oxides, such as Fe_3O_4 and γ-Fe_2O_3 (Adamaki et al., 2016; Metaxa et al., 2016), spinel-type ferromagnets such as $MgFe_2O_4$, $MnFe_2O_4$, and $CoFe_2O_4$, alloys such as $CoPt_3$ and FePt as well as pure metals such as Fe and Co.

In this paper, we propose the use of SPIONs made of iron oxides as tools for bio-magnetic separation/purification of organic and inorganic molecules in a given liquid solution. The method proposed aims to tackle the drawbacks connected with scalability of the actual purification protocols (e.g. affinity chromatography) and other methods based on magnetic separation (e.g. no possibility to operate in continuous-flow).

2. Synthesis of magnetic nanoparticles by microwave assisted co-precipitation

Referring to the synthesis of the particle magnetic core (paramagnetic in micro-scale: 0.1 to 1000 microns or superparamagnetic in nano-scale: 1 to 100 nanometers) which is the backbone of the process, we used the hybrid microwave assisted co-precipitation – thermal decomposition method. Microwaves are region of the electromagnetic waves with a wavelength between 0.1 and 100 cm, corresponding to frequencies between 0.3 - 300 GHz. The operating principle of this method is based on the high power of microwave and the heating from the inside of the solution, which leads to oscillation of the bonds of the molecules. The bonds which vibrate are those of the solvent and those inherent in the solid bodies, the outcome is the heat of the entire solution. The nano- and micro-particles designed are strictly magnetic and their core might be either a metal, or a metal oxide with either ferromagnetic, paramagnetic or superparamagnetic (in case of nanoparticles of specific diameter). Such materials can be ferrous oxides, iron, nickel, gold and others.

2.1. Magnetic nanoparticles preparation

40 ml of deionized water have been added in a beaker with 1gr of polyvinyl alcohol (PVA) powder and 7 ml of NH_4OH (solution A). PVA was used as surfactant agent to create suitable chemical groups for subsequent nanoparticles functionalization. The solution A was stirred at 90ºC for 10 minutes. In a second beaker, 40 ml of deionized water have been mixed with 2.36 gr $FeCl_3$ and 0.86 $FeCl_2$ gr (solution B). Solution A has been combined with solution A and the resulting mixture (C) was put in a microwave furnace. The solution C has been heated at the lowest power for 2.5 minute. After microwave treatment, a liquid mixture containing magnetic nanoparticles was obtained. The nanoparticles have been removed from the solution via magnetic decantation and then washed five times with deionized water and ethanol. Finally, magnetic nanoparticles have been dried for 12 hours at 70ºC under vacuum atmosphere. A representative TEM image of magnetic nanoparticles is showed in figure 1.

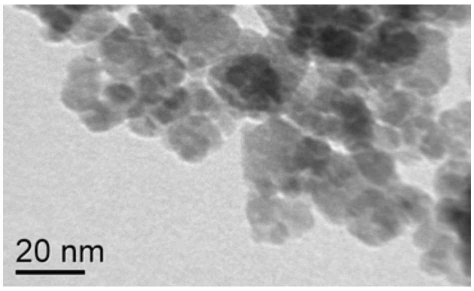

Figure. 1: TEM image of iron oxide magnetic nanoparticles produced by microwave assisted co-precipitation

3. Modelling of magnetic nanoparticles and magnetic surface

Simulations in ANSYS were realized aiming to design, study and optimize the appropriate magnetic surface. An experimental setup was designed in order to verify the simulations. The setup is formed by an array of permanent magnets, a plastic surface, a peristaltic pump and silicon tube (Figure 2 and Figure 5).

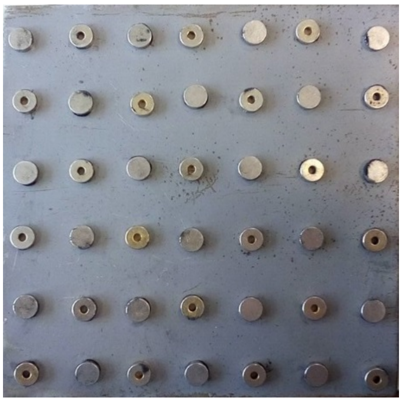

Figure. 2: Neodymium magnets array

Figure 2 shows a 10x10 cm foil of soft steel that was used together with 42 small neodymium magnets to realize the magnetic surface. The magnetic field created by the magnetic array was simulated and is depicted in Figure 3.

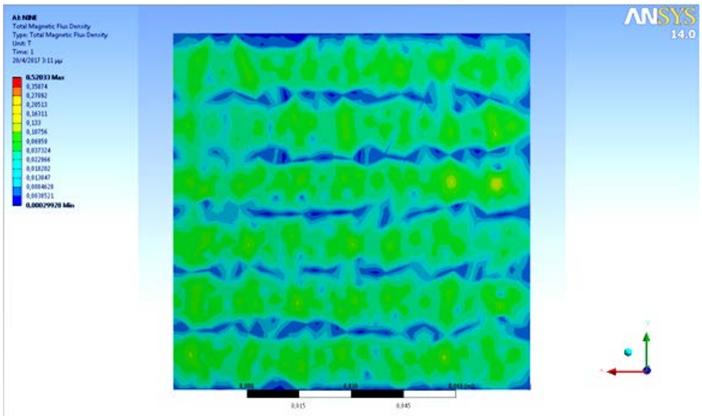

Figure.3: Total magnetic flux density on plastic surface

As can be seen from the simulation, the magnetic flux density on the surface has a minimum value of 1mT (blue areas) between the vertical columns formed by the neodymium array, whereas above each magnet the value of the magnetic flux density is around 80mT. This way, in a few millimetres, a high gradient magnetic field is created which causes SPIONs to preferably move towards higher magnetic field areas (yellow-red areas).

Above each neodymium magnet, the shape of the created magnetic field has an intense spatial gradient in 3 dimensions (Figure 4) which provides enough magnetic force to retain SPIONs against a water (or other liquid) stream. We then calculated the force applied by a magnetic field (magnetic field intensity *H*) on magnetic particle of radius *α(m)* and magnetic susceptibility χ by using the following equation:

$$\overrightarrow{F_M} = \frac{4\pi\alpha^3}{3}\frac{\mu_o\chi}{(1+{}^{\chi}\!/_{3})}\vec{H}\frac{d\vec{H}}{d\vec{x}} = \frac{2\pi\alpha^3}{3}\frac{\mu_o}{(1+{}^{\chi}\!/_{3})}\nabla\left(\left|\vec{H}\right|^2\right) \tag{1}$$

The magnetic susceptibility of the SPIONs is χ~20 (Zhao et al., 2013). The magnetic force depends strongly on the size of the nanoparticles. Furthermore, it can be concluded that the magnetic force is being increased accordingly to the increase of the magnetic field gradient. The steeper is the gradient, the bigger is the force applied on a nanoparticle.

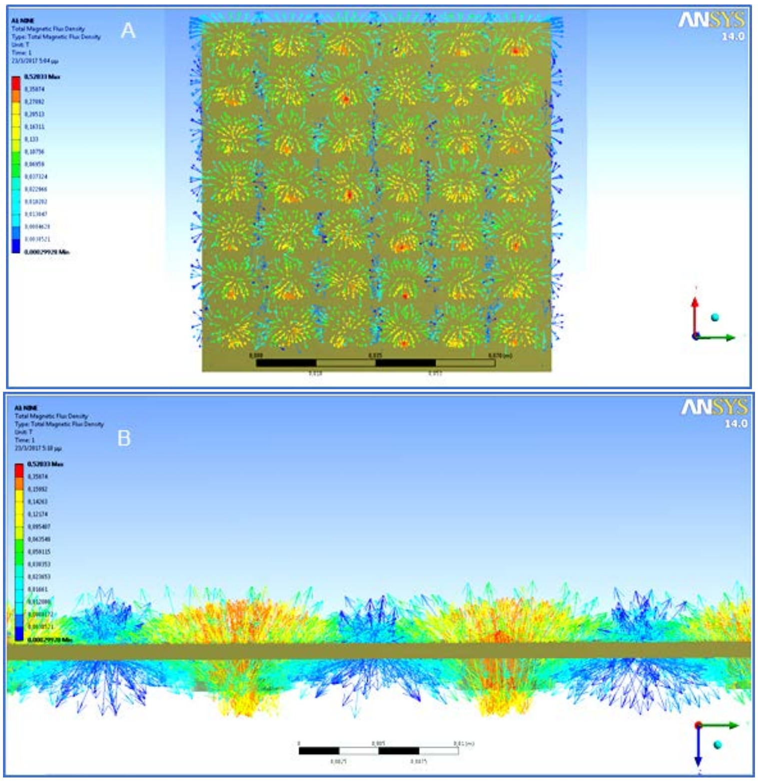

Figure. 4: Magnetic flux density vectors. A) on x, y axis and B) on y, z axis

Knowing the magnetic field at each point, a mean value of the magnetic field gradient can be calculated. On y axis where the grid of magnets is denser, the gradient is 15 T/m, on x axis 9,5 T/m and on z axis 3,3T/m.
To establish the velocity of water or other fluids that can be circulated on the SPIONs immobilized on top of the magnetic surface we used the following Stoke's law:

$$F_d = 6\pi\mu R u \qquad (2)$$

where μ is the viscosity of the medium, R is the radius of the SPION and u is the velocity of the fluid.
The condition that defines the effectiveness of the SPIONs' retaining is that the magnetic force must be bigger than the fluid force at least at one section of the x axis. That way, it is ensured that there is a "magnetic barrier" able to immobilize the SPIONs on the plastic surface and inhibit them from escaping with the fluid flow.
The SPIONs under the influence of the magnetic field create clusters of a few μm and thus the force applied on them is much bigger than that applied on one nanoparticle since the magnetic force depends on the third power of the radius of the particle (α^3, equation 1).
Assuming that the SPIONs aggregate in clusters of 100μm, the magnetic force on these clusters is being calculated from a minimum of 36 nN (blue areas) to 840 nN (yellow-red areas). The max velocity of the fluid for the two values corresponds to 0.019 m/s to 0.44 m/s. Above these values, the SPIONs' clusters are not able to be retained on the magnetic surface.
The experimental procedure was realized to compare the results of the simulations. The setup was consisted of a plastic surface (ABS) (120x100x1mm), the array of 42 neodymium magnets (N52) (2x5mm) located underneath the plastic surface, a peristaltic pump, two tanks and a silicon tube (d=5mm).

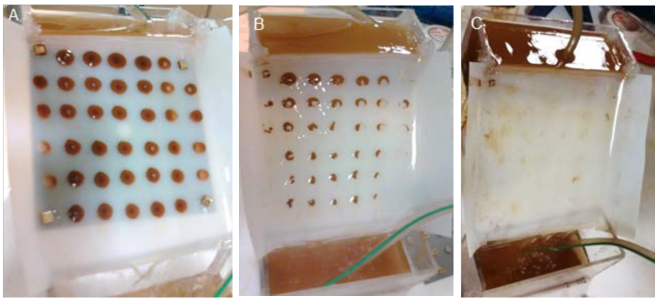

Fig. 5 Experimental setup A) the SPIONs are retained at the areas above the magnets B) after the magnets are removed, the flow gradually washes away the SPIONs C) after a few seconds the SPIONs are completely removed.

The SPIONs were suspended in an ethanol-oleic acid mix in order to avert agglomeration and they were being circulated via the pump through the magnetic surface. From the first pass, the SPIONs were retained on the surface. After removing the magnetic array, the SPIONs started washing away with the flow. The same experiment was repeated several times at different velocities in order to assert the max velocity allowing the SPIONs to be retained on the surface and they were in accordance with the simulations.

4. Discussion

The use of magnetic nanoparticles for bio-separation/extraction of valuable compounds from natural crops or their by-products (Sarno et al., 2016; Manaenkov et al., 2016), as well as for adsorption of dangerous materials (Chiavola et al., 2016; Petralito et al., 2016; Zuorro et al. 2013), has been successfully demonstrated in recent years. However, yet the vast majority of magnetic separations are executed in a non-continuous fashion and still these techniques remain at lab-scale. Making magnetic separation a continuous-flow process and at the same time scaling it up requires well-defined knowledge of the magnetic forces as well as the gradient of the magnetic field on the magnetic particles and how the circulating fluid affects those properties.

Concerning bio-separation, chromatography is the elective technique currently used world-wide, which is based on the use of two phases, one stationary and one mobile, packed on a column. This approach, however, presents high cost, difficulty in scaling-up and low throughput that, especially for biomedical purposes, poses many issues. For example, at industrial scale the purification of monoclonal antibodies via chromatographic approaches may require a column's volume of about 2,000-litres and more than 50,000-litres of buffer solutions (Thömmes and Etzel, 2007). Furthermore, chromatographic columns can be used only at the final stage of purification since they cannot be loaded with raw mixtures because of the presence of minute suspended solids (Fields et al., 2015). Removal of hazardous elements from wastewater also struggles with issues associated to scalability, even though the most important problem is related to the continuous-flow operation. At the present the most popular method consists in the addition of functionalized magnetic particles (adsorbent) to the waste liquid in a closed container. Subsequently, magnetic particles that have trapped the hazardous material are recovered by means of potent magnets. While this method offers the possibility to treat relatively high amount of wastewater, it remains inefficient because the mixture needs to be stirred continuously and is quite time-consuming.

To solve issues connected with bio-separation and adsorption by means of magnetic particles, we have studied the possibility to immobilize magnetic particles, which can be functionalized with a variety of ligands, over a magnetic surface on which a fluid can be continuously circulated. Indeed, with this approach, bio-separation as well as adsorption can be easily scaled-up since the active surface can be enlarged by using arrays of magnetic surfaces which can be organized vertically. Furthermore, high volumes of liquid can be treated without supplemental agitation and, most import, the process can work in a continuous fashion without interruption until all magnetic particles are saturated. Finally, depending on the ultimate purpose, magnetic particles can be harvested and either regenerated to be re-used or further processed to separate the target compound from the magnetic material.

5. Conclusion

In this paper, the synthesis of SPIONs as well as the modelling for an innovative application of this magnetic nanotechnology were proposed. The hybrid microwave assisted co-precipitation – thermal decomposition method to synthetize the particles magnetic core was used. Bio-magnetic separation of organic and inorganic molecules from a liquid solution by using SPIONs was investigated by modelling the magnetic properties of the magnetic surface and SPIONs as well as the velocity of liquid needed in order to avoid removal of nanoparticles by the solution flow. The feasibility of the immobilization of SPIONs onto a magnetic surface while a liquid solution flows on them continuously was highlighted. The key parameters to avoid loss of SPIONs due to dynamic forces associated with the fluid movement can be easily calculated and relate to the nanoparticles size as well as the magnetic gradient.

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