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Article

Continuous High-Flow System to Trap and Separate Magnetic Particles from Liquid Mixtures

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Abstract: Bio-separation of natural molecules as well as clinical compounds has been constantly developed in last decades. Several techniques are available but the majority of them presents drawbacks such us impossibility to be applied for industrial purposes. The main limitations for the scaling up are high costs and the fact that the devices work with microfluid dynamics. Nevertheless, magnetic bio-separation is considered the most prone to be used for large scale applications. Herein, we propose a simple magnetic separation method that is not based on microfluid dynamics, can work in a continuous- and high-flow rate and can be easily automated in order to be used for standard separation purposes. It is based on the use of an anisotropic flexible ferric magnetic stripe, Teflon hoses and a pumping device. We show the modelling of the separation process along with an experimental test on iron oxide magnetic particles. The results showed that it is possible to remove, and separately collect, more than 92% of magnetic particles from a liquid solution of 100 ml in roughly 15 minutes.

Key words: Bio-separation, magnetic separation, magnetic particles, continuous-flow

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1. Introduction

In recent decades, the application of magnetic iron oxide micro- and nano-particles has been established in various technological fields, such as magnetic separation of biomolecules and ions, biosensors, biofuel production and others [1] [2] [3] [4]. Working with iron oxide particles is becoming main stream subject thanks to the facility that such kind of materials can be modified by a variety of chemical groups which confer them specific selective or catalytic properties [5]. Furthermore, iron oxide nano-particles present magnetic properties, and in particular superparamagnetism, which allows to remotely control them making their manipulation easy and cost-effective [6]. In addition, a new method of synthesis has been recently proposed, which can guarantee a cost-effective production of magnetic particles which may further reduce the running cost of separation methods based on magnetism [7]. Nevertheless, biotechnological applications of iron oxide particles are still confined to the research level (lab scale devices) or for low-throughput clinical applications [8] [9]. Indeed, most systems based on the use of magnetic elements are design to work with microfluid dynamic or are able to process samples in bath-based fashion, therefore discontinuously. The need of robust and high-productivity methods is demanded especially in bioscience where, independently from the reaction or process involving magnetic particles, once such composite materials are mixed or added to a given solution, inevitably at the end of workflow they must be separated/harvested from the reaction vessel. Therefore, it is vital for a good productivity and processivity of reactions involving magnetic particles to ensure that large volumes of solution can be treated and magnetic particles withdrew in the most fast and accurate way. To address this issue, in this paper it is investigated whether it is possible to operate a magnetic particle trapping and separation system using a flexible magnetic surface and a spiral-arranged hose to separate particles from a liquid solution, whose volume is in the order of 100 ml. It is presented herein, the experimental test of the magnetic separation system, together with a modelling of the separation process. The system proposed has the potential to be fully automated and could be further exploited to concentrate magnetic particles dispersed in large volume of solvent with a rate in the order of ml per second.

2. Materials and Methods

A Teflon hose 100mm length with a 4mm external diameter and 3mm internal diameter was used for the experiment. 80mm of the teflon hose were coiled into 8 turns around a 50 ml tube. The magnetic field was generated by alternating North – South magnetic lines Figure 1a. The anisotropic flexible ferric magnetic stripe was 40mm wide with adhesive surface and has been purchase from Magnitech, Greece. The magnetic core figure 1b can easily be inserted into the tube with the coiled Teflon hose. A peristaltic pump PLP 380 Dullabo was used together with a pump head of 10 rolling cylinders and a specific hose with a diameter of 4mm, and a 3way splitter with a manually adjustable valve. For the liquid solution we used ethanol ≥98 (Honeywell, Germany), oleic acid 90% (Alfa Aesar, Germany), Iron oxide (Fe_3O_4) magnetic particles with a purity of 99% have been purchased from ChemicalStore, USA.

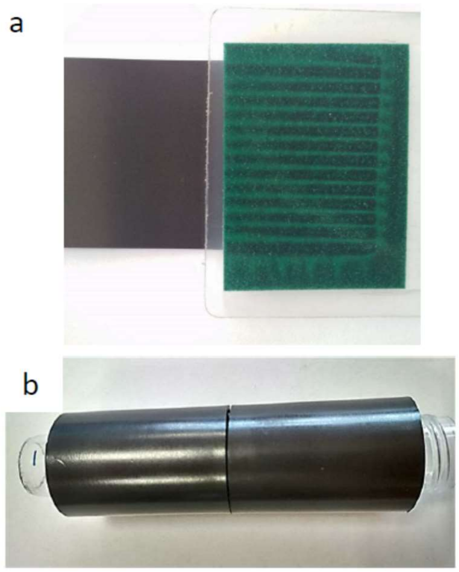

Figure 1. a) anisotropic ferric magnetic stripe with a magnetic field viewer b) magnetic core assembled with the magnetic stripe

3. Results

Design of a spiral magnetic separator

ANSYS fluent was used in order to simulate the fluid flow inside the spiral hose. As seen in figure 2, there is laminar flow all over the tube with no turbulences in the fluid flow.

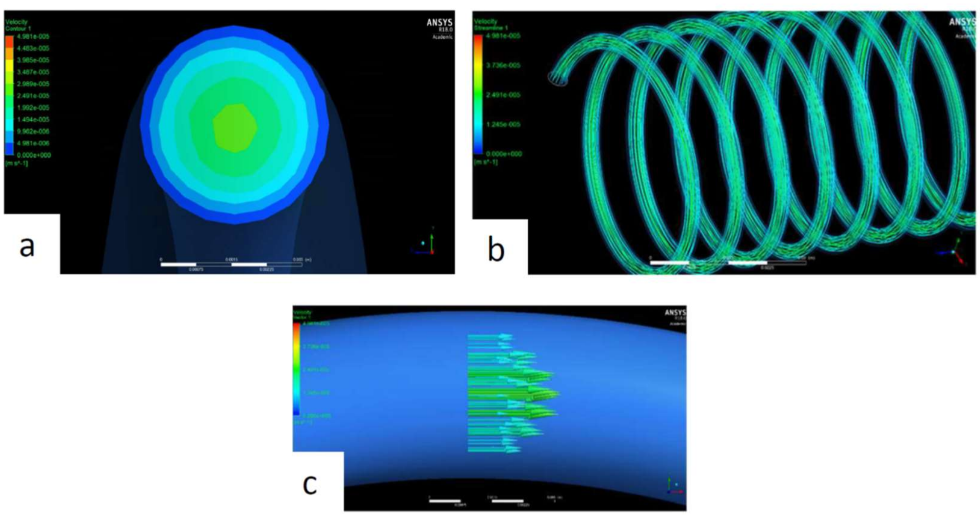

Figure 2. a) cross section view – velocity contours b) laminar flow distribution in the spiral hose c) lateral view – velocity vectors

Based on this simulation, the magnetic particles that are close to the hose walls move slower than those in the center and thus, they can be retained easier by the magnetic field. However, due to the fact that a spiral geometry was used, the mixing of the particles was allowed and statistically, the majority of the particles could be trapped. Thus, it can be assessed that the purity of the solution depends not only on the velocity of the fluid, but also on the number of the turns of the helical coil and the concentration of the particles in the solution. By defining the velocity of the fluid, it is also possible to define the fluid force applied on the magnetic particles by using Stoke's law:

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$$\overrightarrow{F_d} = 6\pi\mu R\vec{u} \qquad (1)$$

where:
μ: is the viscosity of the solution
R: is the radius of the particle
u: is the velocity of the fluid
Thus, having determined the fluid force applied on magnetic particles, it is possible to define the magnetic force needed in order to retain the magnetic particles in the spiral hose. The alternating polarity magnetic sheet (figure 3) propagates a high gradient magnetic field only from one side close to its surface that allows to retain particles evenly at the inner part of the spiral hose.

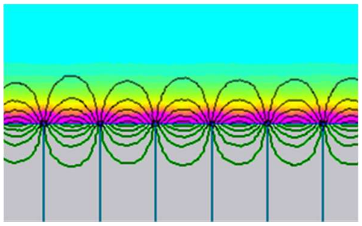

Figure 3. Schematic representation of magnetic field generated by the anisotropic ferric magnetic stripe. Only one side of the stripe is highly magnetized

The equation of the force applied on a sphere is given:

$$\overrightarrow{F_M} = \frac{4\pi\alpha^3}{3}\frac{\mu_0\chi}{(1+{\chi}/{3})}\vec{H}\frac{d\vec{H}}{d\vec{x}} = \frac{2\pi\alpha^3}{3}\frac{\mu_0\chi}{(1+{\chi}/{3})}\nabla\left(\left|\vec{H}\right|^2\right) \qquad (2)$$

where:
α is the radius of the particle
μ_o is the vacuum's magnetic permeability
$\vec{H}$ is the magnetic field intensity
$\frac{d\vec{H}}{d\vec{x}}$ is the magnetic field gradient

Thus, by asserting the equilibrium between the magnetic and the fluidic forces, it is possible to define the highest velocity over which the particles are not able to be retained in the spiral hose laid over the magnetic core.

Trapping, separation and concentration of magnetic particles by a spiral magnetic separator.

To test the system, we used magnetic particles dissolved in ethanol containing 5% of oleic acid. 0.1 gram of magnetite has been dissolved in 100 ml of alcoholic solvent by thoroughly shaking the flask (figure 4a and supplemental figure 1). The resulting solution was homogenous, with magnetite particles well dispersed and showed an intense dark color. The peristaltic pump was set to a pumping rate of roughly 0.1 ml/sec and one side of the propelling hose was immerse in alcoholic solution containing particles, whereas the other side connected to the inlet pipe of the spiral separator (figure 4b and supplemental figure 2). The system was turned on and as the solution started to reach the pipe wrapped around the magnetic surface the magnetic particles initiated to be trapped by means of magnetic force along the entire spiral (Figure 4c). As it can be seen from figure 4c, magnetic particles accumulate gradually, with the majority at the inlet side, as the solution was moving from the inlet towards the outlet side. Eventually, at the end of the process, the majority of the magnetic particles were trapped near the inlet side (Figure 4d). This was due to the progressive impoverishment of magnetic particles inside the solution since they were gradually attracted as they were travelling along the spiral system. Once all

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alcoholic mixture was pumped through the spiral hose the peristaltic pump was let to run for a few seconds more in order to empty all the piping system.

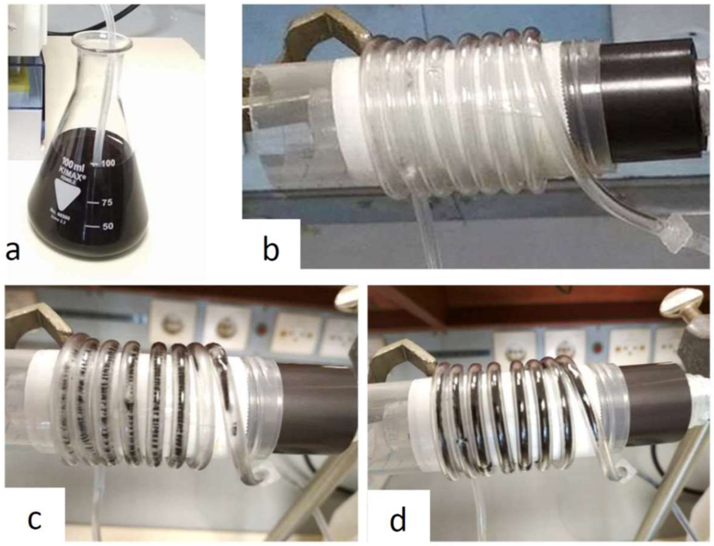

Figure 4. a) alcoholic solution with magnetic particles, b) spiral teflon hose coiled over the magnet core, c) gradual accumulation of magnetic particles, d) final accumulation of magnetic particles.

The solution deprived of magnetic particles was collect in a clean flask, and as it can be seen from its color almost all magnetic particles have been trapped by the spiral hose (Figure 5).

Figure 5. Complete apparatus after magnetic separation. Magnetic particles are trapped on the spiral hose without liquid covering them

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It is important to mention that even without any liquid phase covering magnetic particles, they remained firmly attached to the spiral hose. To assess the trapping capacity of our method, we used a spectrophotometer assay. We arbitrarily chosen to measure the alcoholic solution's absorbance at 600 nm before and after passing it through the spiral system. The result showed that more the 90% of magnetite was retained in the hose facing the magnetic band (Figure 6).

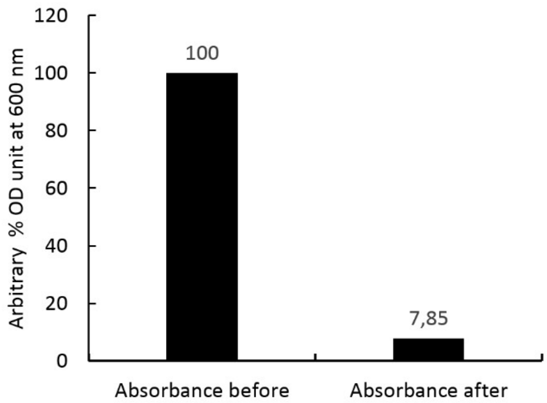

Figure 6 Spectrophotometer analysis of the optical density (OD) of alcoholic solutions before and after magnetic separation measured at 600nm

Finally, to elute magnetic particles from the system, we first separated the magnetic core from the spiral hose (figure 7a) and subsequently used 20 ml of alcoholic solution (Figure 7b and supplemental figure 2) to remove and collect magnetic particles in a separate flask (figure 7c). After passing the 20 ml of fresh alcoholic solution, the magnetic particles were completely removed from the spiral hose (Figure 7d).

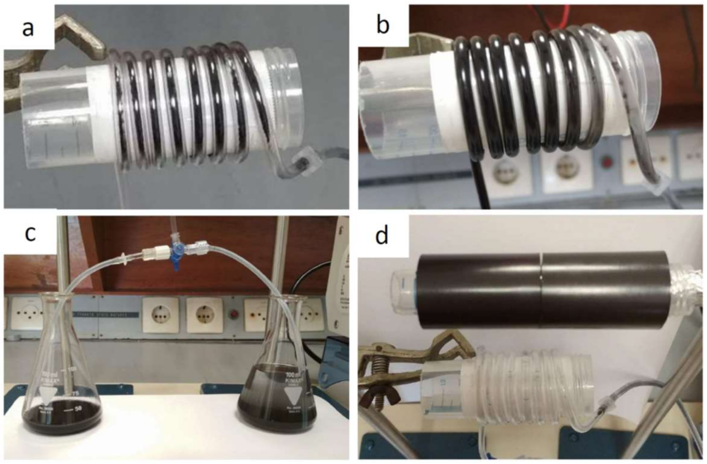

Figure 7 a) magnetic core removal, b) harvesting of magnetic particles form spiral hose c) magnetic particles collection into separate flasks d) spiral hose completely clean after magnetic particles harvesting

4. Discussion

Our group has recently demonstrated that by using properly configurated magnetic nanoparticles it possible to remove many ions from seawater [2]. The state-of-the-art of magnetic separators available today in the market, though, does not offer solutions to separate magnetic materials from large amount of liquid mixture. Indeed, all systems are based on microfluid devices as well as on the use of permanent magnet or electromagnet able to attract magnetic materials towards a specific side of the reaction vessel. We proposed in this work a

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simple and reliable solution to remove magnetic particles from a given liquid mixture at a rate of ml *per* minute and in a continuous-flow fashion. The method is based on the use of an anisotropic flexible ferric magnet folded over a cylindric shape (magnetic core) around which a Teflon hose is wrapped in order to form a spiral structure that surrounds the magnetic cone itself. These two main components are in closed contact, nonetheless they can be easily separated apart from each other since the magnetic core can be ejected from spiral hose. This arrangement guaranties a big trapping surface in small volume. Such a method can be fully automated and by implementing its design it could be possible not only to trap and elute magnetic particles in a small volume, but also perform washing septs, routinely used when biomolecules are isolated by means of a magnetic procedure. Indeed, by adding automated multiway valves it could be possible to pass through the spiral hose trapping magnetic particles additional solvents or buffers, which may remove impurities and not bound molecules. It is also important to mention that the trapping ability could be increased to virtually 100%, by few technical implementations. As it has been showed by the fluid flow simulations, the velocity of the solution inside the hose cross-section is not constant. Indeed, it increases moving from the hose walls towards the center. This phenomenon limits the trapping potential of the magnetic surface. Indeed, particles that are running in the center experience a different fluid force than those near the wall hose. To overcame this phenomenon, it could be enough to alter the constant fluid flow in order to increase solution mixing. This could be achieved, e.g., by just introducing in the spiral hose air that creates bubbles, which in turn will alter the fluid flow.

5. Conclusion

We reported in this work a simple method to separate magnetic particles from a liquid solution in a continuous- and high-flow manner. The apparatus is simple and can be easily automated in order to establish a system that can perform isolation and/or purification activities based on magnetic particles.

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Author Contributions: G. Banis executed all simulations using dedicated software. G. Banis and M. Kouli performed experiments and draft the paper. E. Hristoforou and A. Ferraro design the work and substantively revised data and manuscript.

Conflicts of Interest: All authors declare no conflicts.

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