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# Magnetophoresis behaviour at low gradient magnetic field and size control of nickel single core nanobeads

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#### ABSTRACT

Magnetic separation of organic compounds, proteins, nucleic acids and other biomolecules, and cells from complex reaction mixtures is becoming the most suitable solution for large production in bioindustrial purification and extraction processes. Optimal magnetic properties can be achieved by the use of metals. However, they are extremely sensitive to oxidation and degradation under atmospheric conditions. In this work Ni nanoparticles are synthesised by conventional solution reduction processs with the addition of a non-ionic surfactant as a surface agent. The nanoparticles were surfacted in citric acid and then coated with silica to form single core Ni nanobeads. A magnetophoresis study at different magnetic field gradients and at the different steps of synthesis route was performed using Horizontal Low Gradient Magnetic Field (HLGMF) systems. The reversible aggregation times are reduced to a few seconds, allowing a very fast separation process.

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### 1. Introduction

In recent years, substantial progress has been made in developing technologies in the field of magnetic microspheres, magnetic nanospheres and ferrofluids. Nanospheres and microspheres containing a magnetic core in a nonmagnetic matrix are used in numerous biological applications [1]. They are used, for example, as carriers, which can be targeted to a particular site using an external magnetic field.

Magnetic separation of organic compounds, proteins, nucleic acids and other biomolecules, and cells from complex reaction mixtures is becoming the most suitable solution for large scale production in bioindustrial purification and extraction processes. For in-vivo applications, it is important that well-defined biocompatible coatings surround the magnetic particles to prevent any aggregation, and also enable efficient protection of the body from toxicity. However, for in-vitro applications, biocompatible coatings are not indispensable; particles could be coated with non-toxic materials inert to chemical and biological mediums. The current commercial nanoparticles for in-vitro application are coated with polystyrene, different copolymers or silica [2–4].

Due to the low surface/volume ratio of the microspheres, and the unclear magnetic behaviour of the particles, commercial

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magnetic micro- and nanobeads have low efficiency for large volume production and potential industrial application. These limitations make their use as efficient and low cost carriers for bioindustrial purification and extraction processes difficult [5].

Scientific bibliography shows the important labours for the improvement and understanding of the magnetic behaviour of magnetic nanoparticles and magnetic micro- and nanospheres. Most of the scientific studies converge on liquid-phase synthesis of the magnetite particles. Despite their lower magnetic susceptibility, magnetite and maghemite are particularly desirable to be synthesised by liquid phase due to their great potential as oxidatively stable nanomagnetic particles with diverse applications [6]. The liquid-phase process of magnetic nanoparticles synthesis is very laborious and comprises different stages, normally developed under atmospheric conditions: precipitation, stabilisation, coating and suspension.

The essential steps in the synthesis and different applications are the manipulation, recovery and removal of the magnetic particles using external magnetic fields (magnetophoresis) [7]. In the simplest form, magnetic separation can be achieved by placing a permanent magnet in the proximity of the suspension containing the magnetic particles conjugated with the captured targets. This approach is limited to separate micron scale magnetic beads. More sophisticated magnetic separation devices were developed to capture magnetic particles during continuous flow. These flow-trough devices generally fall into columnar flow devices, planar flow devices or devices that combine columnar and planar flow systems [8]. Columnar flow systems consist

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of a large flow column ranging from millimetres to tens of centimeters in size, accompanied with an assembly of large external permanent magnet or electromagnets, which generate a non-uniform field to capture the magnetic particles [9]. These devices suffer from low field gradients and require conjugate beads to be highly magnetic. Planar flow devices consist of flow channels with dimensions on the order of 10  $\mu$ m. Magnetic material or electromagnets are patterned directly next to or inside the flow channel. These devices offer high magnetic gradient, but the small cross-sectional area and the limited number of flow channels restrict the throughput [10].

In this work, we report the synthesis and characterisation of single core Ni nanobeads. Ni nanoparticles with diameter ranging from 80 to 120 nm were synthesised by conventional solution reduction process. With the addition of a non-ionic surfactant as a surface agent, the diameter was reduced and controlled to 50–55 nm. To avoid magnetic aggregation, and assure monodispersed nickel nanospheres, the Ni nanoparticles were surfacted in citric acid. At the end of the process the surfacted nanoparticles were coated with silica to form single-core Ni nanobeads. HRTEM and SQUID characterisation was performed on the samples to define their structural and magnetic properties.

An extensive magnetophoresis study was performed using Horizontal Low Gradient Magnetic Field (HLGMF) [11]. These systems provide high magnetic forces, implying fast separation and low magnetic nanoparticle losses and the developed processes are easily scalable for industrial application. As reported by De la Cuevas et al. [12], the magnetophoresis process at HLGMF is driven by a cooperative phenomenon consisting of reversible aggregation of the particles, followed by moving of the aggregates to the walls of the bottle. Different reversible aggregation times were observed at different HLGMFs, at each step of the synthesis route. The obtained results prove that in the case of Ni–silica core–shell aqueous suspensions on applying a low gradient magnetic field, magnetic interaction overcomes the electrostatic repulsion, allowing very fast separation processes.

#### 2. Materials and methods

## 2.1. Synthesis of single core nickel nanobeads

Single core nickel nanobeads were prepared by mixing hydrazine monohydrate ( $N_2H_4$ – $H_2O$ ) 2 M, nickel (II) chloride hexahydrate (NiCl<sub>2</sub> · 6 H<sub>2</sub>O) 0.2 M and sodium hydroxide (NaOH) 8 M in the molar proportion 5:1:32. The pH value was about 11. The resulting solution was kept at 60 °C for 1 h until black powder precipitated completely. Finally, the product was washed with distilled water and ethanol several times, and then dried in a vacuum drying oven at room temperature. In order to control the size distribution of the nickel nanoparticles, the non-ionic surfactant Triton Tx-100, was introduced in the reaction mixture at a molar concentration below its critical micelles concentration (CMC) and at a [Ni]/[Tx-100] molar ratio of 5 [13].

Citric acid (CA) was used to stabilise the magnetic nanoparticles, according to the method proposed by Campelj et al. [14]. Approximately 3 g of nanoparticles were mixed with 65 mL of aqueous solution of 2% CA (0.02 mg mL<sup>-1</sup>). The pH value of the mixture was adjusted to pH=5 and then raised to pH=10 using concentrated ammonia. The adsorption step of the CA was maintained at 80 °C and rigorously stirred for 60 min. The prepared suspension was washed with distilled water and magnetically separated several times to remove the excess of CA.

The CA-modified nanoparticles were coated with silica using tetraethyl orthosilicate (TEOS). 10 mL of CA-modified nanoparticles aqueous solution was mixed in a 20 mL ethanol solution (35%)

v/v) containing 3% (v/v) TEOS. The pH value of the solution was maintained at 11 for 90 min.

#### 2.2. Characterisation methods

A JEOL JEM-1210 electron microscope operating at 200 keV was used for transmission electron microscopy characterisation. The samples were prepared by deposition of a droplet of particles solution on a copper grid coated with carbon and allowed to dry. SEM imaging was performed with a FEI Nova 200 (FEG/SEM). Dynamic light scattering (DLS) and  $\zeta$  potential were determined with a Malvern Zetasizer, NANO ZS (Malvern Instruments Limited, UK), using a He-Ne laser (wavelength of 633 nm) and a detector angle of 173°. Nanoparticles dispersion was analysed in a polystyrene cell or in a folded capillary cell, for size distribution or zeta potential measurements, respectively. The zeta potential values were calculated using the Smoluchowski equation. Hysteresis loops were measured with a superconducting quantum interference device (SQUID) magnetometer (Quantum Design MPMS5XL). The experimental results were corrected for the holder contribution.

#### 2.3. Magnetophoresis experiments

The magnetophoresis setups employed in our experiment are the SEPMAG LAB  $1 \times 25$  mL 1042 and 2042 systems [11]. The system consists of a cylindrical cavity containing a high permanent magnetic field with a uniform horizontal gradient pointing toward the walls of the cylindrical vessel. The magnetophoresis experiments are performed in low gradient magnetic field (LGMF) (< 100 T/m), by placing a bottle of radius 1.5 cm containing 25 mL of nanoparticles aqueous solution inside the SEPMAG cylindrical cavity. The initial grey-black dispersion becomes transparent progressively, reaching a transparent final state with all particles close to the walls of the bottle. Opacity measurements were performed using the external light source SEPMAG CBL Q250 mL [11]. Due to the magnetic field gradient values in the three sepmag systems used in this study, 15, 30 and 60 T/m, the absolute values of the magnetic field vary radially from 0 to 0.225, 0 to 0.45, and 0 to 0.9 T, respectively, being zero at the centre and maximal at the cylindrical walls. At the instant zero (when the bottle is inserted on the device) only the nanoparticles nearer the axis are not saturated. Once the process starts, the beads move radially and in a few seconds all the beads are in the region where the magnetic field is high enough to saturate them. The amount of the volume not saturated at the starting time is below 20% for the 15 T/m system, less than 5% for 30 T/m and less than 2% for 60 T/m. Typical magnetophoresis curves consist of a plateau corresponding to the reversible aggregation time followed by a progressive decay of the suspension opacity until 100% transparency is reached.

#### 3. Results and discussion

## 3.1. Influence of synthesis parameters on the size of nickel nanoparticles

Following the protocol described in Section 2.1 monodisperse nickel nanoparticles of a size below 120 nm were obtained. As reported by Liu et al. [15], these monodispersed nickel nanospheres are characterised by magnetic single domain structure. Other work refers to Ni single domain structure when the diameter of the nanoparticles is below 100 nm, reaching the superparamagnetic properties when the diameter is below 30 nm [16]. The results of the room temperature hysteresis loop measured by SQUID are depicted in Fig. 1. Typical ferromagnetic properties of the Ni nanospheres are observed. The Ni nanoparticles reach the regime of saturation at about 1 kOe (0.1 T). This result demonstrates that the Ni nanoparticles are working at saturation regime inside the sepmag system.

The Ni particles were coated with silica to obtain core-shell structure, chemically inert toward air and acids and suitable for the formation of covalent bonds and the binding of functional groups [16]. The CA-modified nanoparticles were coated under the conditions described in Section 2.1. The size and morphology of the silica coated nanoparticles were examined by using high resolution transmission electron microscopy (HRTEM). As shown in Fig. 2, the nanoparticles were successfully coated and monodispersed single core Ni nanobeads were obtained. The thickness of the silica coating is about 2 nm.

In the classical model of LaMer and Dinegar, the process of synthesising monodispersed particles occurs in two steps: (1) nucleation and (2) growth [3]. These two steps depend on the reactants and the parameters controlling the reaction. When nickel is added to hydrazine a complex is formed. This complex is irreversibly reduced to metal by the addition of sodium hydroxide, which catalyses the reduction action of hydrazine [13].

The reaction mechanism includes the formation of nickel hydroxide nanoparticles, which upon dissolution, reduction, nucleation and growth result in nickel nanoparticles. The size of the formed nanoparticles depends strongly on collision and coalescence rates of nickel nucleus during nucleation step. To achieve a better control of the size of the nanoparticles, the non-ionic surfactant Tx-100 (Triton) was chosen to prepare Ni nanoparticles. The polar heads of X-100 (Triton) adsorbed on Ni nanoparticles can form a protective layer (Fig. 3) and act as an inhibitor, which is in favour of the formation of the spherical nanoparticles with homogeneous size.

As shown in Fig. 3, the size of Ni was successfully controlled and a homogeneous distribution of about 55 nm diameter size of the nanoparticles was obtained, allowing single core nanobeads of about 57 nm (55 nm core and 2 nm silica shell). In Fig. 4, we can observe that the hysteresis loop at 20 K is asymmetric around H=0( $\Delta H=75$  Oe). This behaviour could be explained by the exchange bias phenomena, associated with the exchange anisotropy created at the interface between the NiO and Ni [15,17]. The HRTEM images of these nanoparticles (not shown in this report) demonstrate the formation of a discontinuous NiO layer on the surface of the Ni nanoparticles has been reported in another work [18]. Hysteresis loop at 300 K shows that the nanoparticles reach the saturation regime at about 1 kOe (0.1 T), confirming that inside the sepmag systems the nanoparticles are working in the regime of saturation.

# 3.2. Magnetophoresis behaviour of the obtained nanoparticles and core-shell structure

Magnetophoresis measurements were performed on the obtained Ni nanobeads at different magnetic field gradients: 60, 30 and 15 T/m. The concentration of the suspensions was fixed to 5 g/L. Fig. 5 depicts the magnetophoresis behaviour of nanobeads obtained without using Tx-100 (Triton) as surface inhibitor. As previously mentioned, a typical magnetophoresis curve presents a plateau corresponding to the reversible aggregation time, followed by a progressive decrease of the suspension opacity [12]. The curves depicted in Fig. 5 indicate that the separation time is



Fig. 1. SEM images of citric acid modified Ni nanoparticles and hysteresis loop of Ni nanoparticles at room temperature.



Fig. 2. HRTEM images of the obtained Ni-silica core-shell structures showing silica coating of about 2 nm.



Fig. 3. Description of synthesis route of the controlled size Ni-silica core-shell structures. Ni nanoparticles havean homogeneous size of about 55 nm.

significantly reduced by increasing the magnetic field gradient. At 60 T/m (not shown), the separation process is completed within a few seconds, making it difficult to monitor the process and distinguish the different expected steps of the magnetophoresis process. On applying 30 T/m, no plateau corresponding to reversible aggregation time was observed and complete separation was achieved within 10 s. At 15 T/m. the separation process is significantly slower; however, the curve still shows a very short plateau corresponding to the reversible aggregation time of the Ni–silica core–shell structure. These results indicate that, as expected, the obtained metallic single core nanobeads allow a very fast separation process.



**Fig. 4.** Hysteresis loop measured at 20 and 300 K. Inset shows the asymmetry around H=0 at 20 K.

The results obtained when Ni nanoparticles were precipitated in the presence of Tx-100 (Triton) surfactant are shown in Fig. 6. By applying 15 T/m magnetic field gradient, at pH $\sim$  10.5, the aggregation time increases from less than 2 s for non-modified Ni nanoparticles to 4 s for CA-modified nanoparticles. The CA-modified nanoparticles were prepared as described in Section 2.1. CA has three dissociable protons associated with its three carboxylate groups. It has been claimed that CA acts as an adsorbate tribasic acid on metal oxides (adsorbent) [19]. The deprotonation of CA depends on the pH of the suspension. At  $pH \sim 5.5$  CA appears mainly with two deprotonated species (AH<sup>2-</sup>), and is then adsorbed onto the nanoparticles surface positively charged [20]. At pH~10, CA appears at their fully deprotonated state  $(A^{3-})$ . The CA may be adsorbed on the surface of the nanoparticles by coordinating via one or two of the carboxylate functionalities depending on the steric necessity and the curvature of the surface. When the CA affinity limit is reached, the CA adsorption increases further and a rearrangement of CA binding towards a tighter packed surface structure can occur. Only one carboxylate



**Fig. 5.** Magnetophoresis curves of synthesised Ni–silica core–shell structures at 15 and 30 T/m magnetic field gradient. Nucleation of Ni nanoparticles was performed without Tx-100 (Triton) as surface inhibitor.



**Fig. 6.** Reversible aggregation times of Ni nanoparticles at each step of synthesis route: as synthesised nanoparticles (square), CA-modified nanoparticles (circle) and obtained core-shell structure (triangle). Nucleation of Ni nanoparticles was controlled using Tx-100as a surface inhibitor.

group of CA will be bound to the nanoparticles surface. In these conditions, there will be at least one carboxylic acid group exposed to the solvent that should be responsible for the surface charge. Furthermore, the presence of a terminal carboxylic group provides a possible way of extending the bond formation [21]. The chemisorption process provides the electrostatic stability of the suspension.

The reversible aggregation strongly depends on the total interaction potential between the particles, magnetisation and size of the nanobeads, as well as on the concentration of the suspension [12,22,23]. The measured  $\zeta$  potentials of the non-modified Ni nanoparticles and the CA-modified Ni nanoparticles are -16 and -43 mV, respectively. Considering this important differences between the surface charge of the non-modified and CA-modified Ni nanoparticles, and the contribution of the high electrostatic stabilisation to obtain a stable suspension, we expected a larger reversible aggregation time of the CA-modified nanoparticles with respect to the non-modified nanoparticles [23]. However a difference of 2 s was observed. This result suggests that in the case of metallic single core nanobeads, the attractive magnetic interactions overcome the electrostatic repulsion, allowing a very short separation time.

In the case of Ni–silica core–shell structure, the aggregation time takes about 3 s (Fig. 6) and the measured  $\zeta$  potential is -30 mV.

#### 4. Conclusions

Monodispersed single core Ni-silica core-shell structures were successfully prepared using a wet chemical solution method. The control of the Ni nanoparticles size through controlling the nickel nucleation step was persued using a non-ionic surfactant. Ni core was coated with a thin film of silica to improve its chemical resistance. Magnetophoresis behaviour at different magnetic field gradients and at different steps of synthesis route was monitored. The results demonstrate that in the case of single core Ni-silica core-shell structures, the attractive magnetic interactions overcome the electrostatic repulsion, allowing a very short separation time. These results may have a very high impact in bioindustrial purification and extraction processes in terms of efficiency and quality separation.

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