Model colloids to study surface - ligand interactions in nanosized Fe$_3$O$_4$

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Abstract. Using electrodispersion of metallic iron in an aqueous environment without additional reagents we create a chemically clean model system based on nanosized synthetic magnetite where the details of magnetic metal oxide - surfactant chemisorption can be studied by high fidelity magnetometry with nanometric precision. A comparative analysis of model colloidal solutions based on oleic acid and iron Fe$^{2+}$ oleate indicates a significant influence of the mode of surfactant adsorption on the magnetic diameter of the particles.

1. Introduction
Solubilized magnetic nanoparticles sized in the low nano-range (below 10 nm) are prospective vehicles for guided drug transport (magnetic drug targeting) [1], potential therapeutic means enabling magnetic hyperthermia [2] and candidates for next generation T2*/T2 contrast agents achieving negative contrast enhancement in magnetic resonance imaging, several of which were approved for clinical use (Ferumoxsil, Ferumoxide, Ferucarbotran etc.) and some in different phases of clinical trials [3][4]. Relative chemical inertness and biocompatibility [5] are required for these purposes and superparamagnetic iron oxide based nanoparticles (SPIONs), which are predominantly produced by chemical condensation of the ferromagnetic phase (co-precipitation, hydrothermal synthesis, thermolysis), best fulfil this role [1][6][7]. However, the colloids obtained from chemical synthesis are always polluted with residual by-products requiring many purification steps before they could be used in biomedical applications.

In turn, surfactants play a vital role to enable solubilisation and solution processing of nanoparticles via a simple, easily scalable and highly versatile colloidal route. Among those, carboxylic acids (e.g. oleic acid) are used extensively in the chemical synthesis and stabilization of nanomaterials based on metal oxides. However, the difficulty of exercising precise compositional control over the solutions produced by a chemical route obscures many aspects of the surface - ligand interactions. The oleic acid (OA), which is by far the most employed surfactant to effectuate colloidal systems based on magnetic iron oxide (magnetite), binds tightly to the surface of nanoparticles with its carboxylate group forming an adsorption layer that prevents the coagulation of the particles. Meanwhile, this surfactant acting as an acid may chemically interact with the metal forming non-ferromagnetic salts – oleates. This behaviour may eventually affect the disperse composition of the formed colloidal system and is undesirable.

Herein, we present a comparative analysis of two model colloidal systems, produced by an alternative non-chemical route, one stabilized by oleic acid [8][9] and the other by iron Fe$^{2+}$ oleate salt.
(Fe$^{2+}$-OL), which acts as a surfactant, but where carboxylate groups are passivated by bidentate coordination to a Fe$^{2+}$ ion [10]. We prepare a clean reference system by physical condensation that is based on electric ablation of metallic granules immersed in a dielectric fluid by high frequency-pulsed spark discharges forming a luminous network of conductive channels between the granules in the particle bed and the electrodes [11]. The vaporized material is ejected at high temperature and rapidly quenched in situ condensing in the form of nanoparticles with well-defined spherical morphology. Electric dispersion uses no chemicals except the original substance from which the nanoparticles are produced, utilizes only electric power and does not require chemical precursors or produce waste, hence, avoiding the ambiguity of chemical composition characteristic for commonly used synthetic methods.

2. Experimental section

**Synthesis of nanoparticles.** A 10 g portion of biocompatible coarse-grained metallic iron powder (pharmaceutical iron *Ferrum reductum*, intended for therapeutic oral administration) with particles sized 0.3–1.5 mm (mesh -14+50) of no particular shape was added to 200 ml of distilled water. Flat steel electrodes connected to a spectrometric discharge generator operating at 100 Hz were pressed onto the particle bed. After turning on the generator a luminous network of sparks forms within the particle bed. Reactive dispersion of iron using distilled water as the working dielectric is accompanied by rapid oxidation of ejected iron and the formation of magnetite [11]. After 15 min of operation the initially transparent liquid turns completely black evidencing the condensation of nanodispersed phase. Then the supernatant is decanted and centrifuged, after that the precipitate is washed several times with acetone and dried. The distinct advantage of producing magnetite nanoparticles by electrodispersion of iron in distilled water is that the absence of chemical by-products, such as salts, acids or bases, which accompany chemical synthesis, in the obtained materials is assured.

**Synthesis of iron Fe$^{2+}$ oleate.** The salt is prepared by a reaction of metal chloride and sodium oleate [12]. For this purpose 3.6 g portion of iron(II) chloride tetrahydrate (FeCl$_2$·4H$_2$O, Sigma-Aldrich, 99%) was dissolved in 12 ml of distilled water and 14 g of sodium oleate (Sigma-Aldrich, 82%) was dissolved in a mixture comprising 6 ml of distilled water, 24 ml of ethanol and 42 ml of n-hexane. The resulting solutions were transferred to a reactor heated to 70 °C and mixed for 4 h under argon flow. The mixture was transferred to a separation funnel and the upper organic layer containing hexane solution of iron Fe$^{2+}$ oleate was decanted and washed several times with distilled water.

**Synthesis of model colloids (Fe$_3$O$_4$)@OA and (Fe$_3$O$_4$)@Fe$^{2+}$-OL.** To establish a reliable reference the protocol for the synthesis of model colloidal systems is the same, only changing the type of used surfactant: for model system (Fe$_3$O$_4$)@OA the oleic acid (Sigma-Aldrich, 90%) was used, whereas for model system (Fe$_3$O$_4$)@Fe$^{2+}$-OL the iron Fe$^{2+}$ oleate synthesized in the previous step was employed. Initially, series of surfactant solutions were prepared at various concentrations of employed surfactant in undecane – an alkane hydrocarbon solvent, which has a convenient temperature range and well dissolves OA. A portion of 0.3 g of dried powder of nanoparticles produced by electrodispersion was added to 10 ml of surfactant solution and redispersed by treating with ultrasound for 30 min at nominal output power of 30 W. Subsequently the suspension was centrifuged for 10 min at 4000 g. The supernatant containing a stable colloidal solution was decanted and retained for further characterization.

**Characterization of materials.** The model colloidal solutions (Fe$_3$O$_4$)@OA and (Fe$_3$O$_4$)@Fe$^{2+}$-OL produced at various concentrations of surfactant solutions were studied by vibrating sample magnetometry (vibrating sample magnetometer Lake Shore Cryotronics, Inc., model 7404 VSM) - a non-invasive and non-destructive investigative technique for probing the susceptibility, magnetization or hysteresis of magnetic materials that can provide information on the nanoscopic scale. Briefly, a small sample (~40 mg) of liquid material is magnetized within a region of uniform magnetic-flux density with variable strength (-10 kOe…+10 kOe) and subjected to vibrational excitation at low frequency, and the magnetic moment of the sample is deduced.
3. Results and Discussion

A characteristic magnetization curve measured for a sample based on \((\text{Fe}_3\text{O}_4)@\text{Fe}^{2+}\text{OL}\) model system (Figure 1, left) shows a superparamagnetic response with no hysteresis, which is modulated by a paramagnetic contribution due to the presence of a paramagnetic salt – iron oleate – in the solution. The correction of the magnetization against parasitic processes in the first order of magnetic field \(H\) is straightforward and can be achieved without difficulty

\[ \sigma^*(H) = \sigma(H) - \gamma H \]

where \(\gamma\) is the effective paramagnetic susceptibility.

![Figure 1](image.png)

**Figure 1** Results of magnetometric measurements of a model colloid based on \((\text{Fe}_3\text{O}_4)@\text{Fe}^{2+}\text{OL}\): left – measured magnetization curve, inset shows detailed view of the initial region; right – saturation magnetization as a function of surfactant content in the solution.

The saturation magnetization \(\sigma_s = \sigma^*(H \to \infty)\) shows a dependence on the surfactant content in the solution (Figure 1, right), which is initially a power law at low iron \(\text{Fe}^{2+}\) oleate concentration and gradually reaches saturation. The method of determining the size distribution of magnetic nanoparticles from the magnetization curve is based on representing the corrected curve \(\sigma^*(H)\) in the form of a functional, whose kernel is the Langevin function \(L(x) = \coth x - \frac{1}{x}\). In CGS system:

\[ \sigma^*(H) = I_s \int_{m_1}^{m_2} f(m) L\left(\frac{mH}{kT}\right) dm \]

where \(f(m)\) is the volume density of the distribution function of magnetic moments \(m\) of the particles and \(I_s\) is the spontaneous magnetization of the particle material. The reconstruction is quite accurate as evidenced by the solid line in Figure 1, left.

![Figure 2](image.png)

**Figure 2** Results of magnetometric analysis: left - particle size distribution of model colloidal system (a) \((\text{Fe}_3\text{O}_4)@\text{Fe}^{2+}\text{OL}\) based on iron \(\text{Fe}^{2+}\) oleate, (b) \((\text{Fe}_3\text{O}_4)@\text{OA}\) based on oleic acid; right – corresponding dependence of average magnetometric size on surfactant concentration.
In the magnetogranulometric procedure the obtained distribution of magnetic moments unambiguously corresponds to the particle size distribution, because the magnetic moment of a superparamagnetic particle is proportional to its volume [13]. Our results indicate that the surfactant content does not appreciably affect the reconstructed size distribution. A typical example for both model systems is shown in Figure 2, left and has a slightly bidisperse structure. However, the average magnetic size ($d$) in the case of oleic acid based colloid (Fe$_3$O$_4$)@OA is noticeably larger than the system based on iron Fe$^{2+}$ oleate (Fe$_3$O$_4$)@Fe$^{3+}$OL. This discrepancy is robustly observed independently of the surfactant loading in the solution (Figure 2, right).

4. Conclusions
Here we have systematically studied two model colloids based on a well defined reference system produced by a non-chemical route – physical condensation via electrodispersion, which uses no chemicals except the original substance from which the nanoparticles are produced, without any additional precursors – one stabilized by a covalently bound surfactant and the other with non-covalent binding. It appears that due to their high surface energy the OA either completely dissolves the ultrasmall particles (below approx. 4-4.5 nm) and converts the contained material into an oleate salt or somehow affects the magnetically “dead” layer on the surface of these particles making them invisible to our analysis. The prepared model systems present a unique opportunity to study size focusing regimes [14] in thermolytic processing of oxide nanocrystals with nanometric precision.

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