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Synthesis and processing of magnetic nanoparticles

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Inorganic nanomaterials and their unique physical properties are the center of modern material science due to their potential technological importance. Among the existing structures, magnetic iron oxide nanoparticles (MNPs), including magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3), exhibit remarkable magnetic properties, called 'superparamagnetism', making these nanostructures suitable for a wide range of applications. Because their physico-chemical properties play an important role in major applications, our review focuses on the synthesis approaches giving rise to the best control of size and shape.

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Introduction

In the last decades, the synthesis of inorganic nanoparticles has been intensively pursued because of their many technological possibilities. Indeed, the reduction of the size to the nanometer scale has led to the discovery of novel and extraordinary properties which found many applications in various technological fields.

Among existing inorganic nano-systems, magnetic iron oxide nanoparticles (i.e., magnetite and maghemite) have emerged as a very promising tool. When reducing the size from bulk to the nanometer size (<20 nm), iron oxide material (ferrimagnetic) acquires novel magnetic properties called 'superparamagnetism'. When superparamagnetic objects are submitted to a magnetic field, their global magnetic moment aligns in the direction of the field, but when the field decreases to zero, the magnetic moment of the sample immediately returns to zero. This non-remanence is due to the return to equilibrium of the magnetic moments through Néel relaxation, when the particles are small enough, or through the diffusive rotation of the particle in the solvent in the case of larger particles [1].

Among exploited applications of superparamagnetic nano-systems, we can quote catalysis [2•,3–6], high density magnetic data storage [7], gas sensors [8,9], inks and toners for xenography [10] or polluting agent removal [11,12]. Thanks to their magnetic properties and poorly toxic character [13], magnetic iron oxide nanoparticles (NPs) have also extensively been used for a large panel of biomedical applications, especially for magnetic resonance imaging (MRI) [14,15••,16]. Some iron oxide-based systems have already been used clinically [13] for the detection of hepatic or spleen anomalies, and the development of emerging areas such as magnetic hyperthermia [17,18•,19,20], cell tracking [21–23], drug delivery [24], molecular imaging [25–27] or, more recently, magnetic particle imaging [28,29] have encouraged researchers to continue their effort in the development of reliable procedures to afford nanoparticles exhibiting desired properties. As an example, to be conveniently used in bio-related applications, the ideal magnetic supports should have high magnetic properties, small size and narrow size distribution, high surface functionality, well-defined morphology, in addition to nontoxicity and biocompatibility. These characteristics can be achieved by the optimization of the preparation process.

Iron oxide nanoparticles synthesis

Because of their great potential in a wide range of applications, numerous synthetic methods were developed to produce iron oxide nanoparticles, with good control of shape, composition, size and size distribution [13,16,27,30]. The manufacturing of nanoparticles can be roughly categorized as either 'top-down' (reduction of the size from the bulk material) or 'bottom-up' (from molecular reagents to the nanosized structure). Typically, the bottom-up methods are preferred due to the possibility to obtain smaller particles, with good control over their size, shape and size distribution.

Upon all existing methods, iron salts co-precipitation in aqueous solution probably represents the simplest and most efficient way to produce magnetic nanoparticles at the gram-scale. The particles obtained by this method generally exhibit a mean diameter inferior to 50 nm. In a typical procedure, an alkaline source (NaOH or NH_4OH) is added to a mixture of ferrous and ferric salts. Stable suspensions are obtained by washing the flocculate with acid or basic solutions. Following the experimental conditions (stoichiometry, pH, ionic strength, temperature, nature of the salts, etc.), the size and the shape of the particles can be adjusted as previously studied by Jolivet [31] and Hui [32]. Even if the method is fast, easy to implement and inexpensive (high yield and low cost of the precursors), it affords poorly crystalline particles, characterized by a quite broad size distribution which consequently requires size sorting procedures to reduce the polydispersity index of the batches.

Stable magnetite colloids can be produced by performing the reaction in the presence of polymers, such as dextran [33], or polyacrylic acid [19]. The use of such process often leads to the formation of particle clusters embedded in a polymeric matrix, which can be undesirable for the desired application. The method is also efficient for the preparation of nanocomposites. In this way, Kalantari [34] has recently prepared Fe_3O_4/talc for environmental applications by the alkaline co-precipitation of iron(II)/iron(III) chlorides in a suspension of talc. Similarly, cellulose/Fe_3O_4 nanocomposites have been synthesized for arsenic removal applications [34].

A better control of the size distribution and magnetic properties can be obtained in the presence of surfactants. Small sized ferrites (including Fe_3O_4, $CoFe_2O_4$ and $MnFe_2O_4$) [35] were prepared by using alkanolamines (isopropanolamine and diisopropanolamine) as the alkaline source and as complexing agents. This allows to control the particle size during the synthesis process and to improve the spin rearrangement at the surface (thinner magnetic 'dead' layers) conferring better magnetic properties when compared to the classical method. In a recent report, Van Tendeloo [36] studied the influence of surfactants (cetyl trimethylammonium bromide (CTAB), polyvinyl pyrrolidone (PVP) and sodium cholate) on the structural and magnetic properties of NPs. Even if TEM measurements on the various iron oxide nanoparticle batches did not reveal any surfactant effect on the morphological properties of NPs, the estimated average particle and crystallite size distributions appear to depend on the choice of the surfactant.

Alternatively, leading the reaction in a solvent which can play a role of surfactant revealed to be highly efficient for the control of the physico-chemical parameters. Diethyleneglycol (DEG) was used as a solvent by Qu and co-workers [37] for the preparation of small-sized spherical NPs. More than the chelating properties of DEG which give a good control of the size distribution, the possibility to work at high temperature allows to improve the crystallinity and the magnetic properties of the particles. A similar protocol has been proposed by the team of Muller for the preparation of bimodal particles MRI/optical imaging [23,38].

Toward the fine tuning of the IONPs properties

Even if such particles exhibit a quite good control of the size distribution when comparing with particles obtained with the classical route, it can be necessary, following the intended application, to achieve an optimal control of the shape, size and size distribution. It is reported that the production of highly monodispersed NPs (in size and morphology) can be achieved by the decomposition of iron organic complexes performed at high temperature. Because of the high temperature, the nanoparticles are well crystallized and present high saturation moments. Generally, the reaction occurs in the presence of surfactants (long hydrocarbon chains), which guarantee the growth control and a good particle dispersibility in apolar solvent (n-heptan, chloroform or tetrahydrofuran). The reaction can be performed either by progressively warming a mixture of the iron precursor and surfactant(s) in a high boiling point solvent, or alternatively by injecting a solution of the iron complex in a hot solution containing the surfactants (this method is referred as the 'hot injection'). Both methods are reported to provide well-defined NPs.

Historically, Rockenberger and collaborators [39] were the first to report a non-hydrolytic method for the preparation of transition metal oxides. To proceed, Fe(III) *N*-nitrosophenylhydroxylamine was injected in octylamine at high temperature to produce 4–10 nm particles. Since that work, many authors have reported the synthesis of well-controlled magnetic nanoparticles from different iron precursors, the most studied being iron(0) pentacarbonyl, iron(III) acetylacetonate and iron(III) oleate. The last one represents an interesting option since it can be easily obtained after reaction between cheap and innocuous reagents, that is iron(III) chloride and sodium oleate.

Typically, two main strategies are used to vary the size of the NPs. The first one is referred the 'seed mediated growth' and implies the addition of iron precursor to pre-existing nuclei. This strategy has been used by Sun for the synthesis of various-sized NPs (4 nm, 8 nm, 12 nm and 16 nm) starting from 4 nm seeds.

Alternatively, the nanoparticle size could be controlled by varying experimental parameters such as reaction time, temperature, ligand/precursor ratio [40] as well as the solvents with different boiling points [41,42]. This method is also referred as the 'heating-up' process. Demortière *et al.* [41] employed that strategy for the synthesis of spherical NPs with average size ranging from 4 to 28 nm. That study confirmed the solvent-dependent size-control of this procedure, suggesting that its nature influences the decomposition rate of the iron(III) precursor, influencing thus the monomer concentration and consequently the formation of nuclei.