Review

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Colloidal magnetic nanocrystal clusters: variable length-scale interaction mechanisms, synergetic functionalities and technological advantages

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Abstract: Magnetic particles of optimized nanoscale dimensions can be utilized as building blocks to generate colloidal nanocrystal assemblies with controlled size, well-defined morphology, and tailored properties. Recent advances in the state-of-the-art surfactant-assisted approaches for the directed aggregation of inorganic nanocrystals into cluster-like entities are discussed, and the synthesis parameters that determine their geometrical arrangement are highlighted. This review pays attention to the enhanced physical properties of iron oxide nanoclusters, while it also points to their emerging collective magnetic response. The current progress in experiment and theory for evaluating the strength and the role of intra- and inter-cluster interactions is analyzed in view of the spatial arrangement of the component nanocrystals. Numerous approaches have been proposed for the critical role of dipole-dipole and exchange interactions in establishing the nature of the nanoclusters’ cooperative magnetic behavior (be it ferromagnetic or spin-glass like). Finally, we point out why the purposeful engineering of the nanoclusters’ magnetic characteristics, including their surface functionality, may facilitate their use in diverse technological sectors ranging from nanomedicine and photonics to catalysis.

Keywords: assembly; colloidal nanocrystal clusters; iron oxides; magnetic interactions; theranostics.

1 Introduction

Single-crystal inorganic magnetic nanoparticles (henceforth, nanocrystals) have attracted increasing attention in the recent years due to their unique applications in various fields, including magnetic storage [1], electronics [2], solar energy conversion [3, 4], plasmonics [5], medical diagnosis [6], and therapy [7]. The magnetic nanocrystals are an appealing subject of study because they exhibit a vastly different physical behavior from that in their bulk counterparts [8]. Magnetism is a quantum mechanical property, and as such, nanoscale size and shape particle modifications can lead to its evolution in an unexpected way [9, 10]. For these reasons, a variety of methodologies have been utilized, but among them, the surfactant-assisted chemical approaches hold a prominent place. The latter have been extensively used because they can allow developing finely size- and shape-tailored magnetic nanocrystals by careful regulation of thermodynamically and kinetically driven growth processes in liquid media. In the general case, an organometallic precursor and a surfactant are dissolved in a high boiling point solvent, and the solution is heated at elevated temperatures (~200–300°C). Each nanocrystal consists of an inorganic monocrystalline core of desired chemical composition and is capped with a layer of tightly bound capping molecules. The type of the organic molecules determines the colloidal stability and solubility of the nanocrystals in aqueous or organic solvents. The chemical nature of such capping molecules, the reaction time, and the concentration of the reactants can be chosen in order to control the dimensions of the nanoscale particles [11], as well as to determine the appropriate morphology of either centrosymmetric (e.g. spheres, cubes) or more anisotropic (e.g. rods, tetrapods) shape characteristics [12].

As the controlled synthesis of individual nanocrystals advances, the need for protocols to develop complex materials with enhanced or new properties rises. In this
direction, improved or collective physical properties can be obtained by bringing magnetic nanocrystals next to one another at distances where they can interact. If preformed, they can be encapsulated in an organic [13–17] or inorganic [18–20] matrix in order to form an aggregate or can grow and assemble together at high temperature via a single-step process. Colloidal assemblies of either type have been stabilized by the balance between the electrostatic, entailing the capping molecules and the magnetic interactions involving the incorporated inorganic subunits. Different morphologies, compact or loose structures with diameters ranging from 30 to a few hundred nm have been obtained with the previous synthesis strategies. Colloidal assemblies of inorganic nanocrystals are commonly called nanoclusters [15, 21–29], but in the literature, they can also be found as nanoflowers [30], nanoroses [17], multi-core particles [31, 32], nanoassemblies [13, 14, 33, 34], porous particles [35], flower-like mesocrystals [36], nanobeads [37, 38], and pomegranate-like particles [34]. Furthermore, it is worth noting that these can be delivered with diverse chemical origin, including nanoclusters of ZnO [39, 40], CoO, CuO, In2O3 [40], CoO [40], MnO [40], ZnSe [40], CuCr2S4 [43], PbS [44], and TiO2 [45]. In addition, function-driven requirements led to the growth of bi-modal clusters, consisting of two chemically different material sections, namely, a magnetic particle assembly combined with a metallic (Au and Ag nanocrystals or Au shell) [17, 37, 46, 47] or instead a fluorescent (Zn-doped AgInS2 quantum dots) [27] part. The combination in the same structure of distinct inorganic material sections, encompassing different physical properties, is appealing due to the potential for achieving simultaneously diverse functionality, as for example bio-separation and sensing [38] or diagnosis and therapy [17, 27].

Recently, the effects of particle assembly, as these evolve because of the spatial arrangement of the component units and the emergence of magnetic coupling mechanisms across the strongly correlated building blocks, have been a source of revived research interest. To put this in perspective, we first need to consider the case of an individual spherical nanocrystal. This nanoscale particle, when it is below a characteristic size and depending on the material phase, behaves as a single magnetic domain. Then, it may exhibit a novel magnetic response, entailing sizeable magnetization but no coercivity, thus, offering unique advantages for modern magnetically driven applications. Such individual nanoparticle systems are called superparamagnets; their magnetic moments are not interacting and can fluctuate at random when the thermal energy, k_B T, is larger than the anisotropy energy (KV; where K is the magnetic anisotropy constant, V is the volume of the nanocrystal) [48]. In the case, though, where these nanocrystals assemble in a nanocluster-like structure, a collective magnetic behavior is likely to emerge. In terms of the inter-particle dipole-dipole interactions involved, the new larger entity may entail [49–51]: (i) a superparamagnetic character for non- or weakly-interacting particles (low dipolar interaction strength, g) [52], and (ii) a superspin glass for strongly interacting particles (high g) [53–56], which is a behavior analogous to a canonical spin glass. When the inter-particle interactions are very strong, the superspin moments are coupled ferromagnetically, and the assemblies are called superferromagnetic [57]. Therefore, these secondary structures can retain the magnetic behavior of the individual nanocrystals (superparamagnetic, no coercivity) [31] or can develop a new response (ferromagnetic, open hysteresis loop) [21] depending on the way their building blocks are arranged. The magnetic behavior of these complex structures is not affected exclusively by the inter-particle dipolar interactions [58], and also, the magnetic exchange [59] or other anisotropy-related terms (size, morphology, crystalline phase, or surface spin disorder) [60, 61] have also been found to play a significant role (Figure 1). Interestingly,
recent literature reports, where the materials’ magnetic-related parameters (saturation magnetization, $M_s$; coercive field, $H_C$) are compared, highlight the effect of the anisotropy on the magnetic properties of a nanoscale system. For example, when cubic and spherical ferrite nanocrystals of the same volume are considered, an enhanced saturation magnetization [60, 62] and a lower coercivity ($H_C$) [63, 64] are found for the cubic system. For example, when cubic and spherical ferrite anisotropy on the magnetic properties of a nanoscale system. For example, when cubic and spherical ferrite nanoscale anisotropy is compared, highlight the effect of the anisotropy on the magnetic properties of a nanoscale system. For example, when cubic and spherical ferrite nanocrystals of the same volume are considered, an enhanced saturation magnetization [60, 62] and a lower coercivity ($H_C$) [63, 64] are found for the cubic system. 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2.1 Single-step synthesis protocols

2.1.1 Organometallic and solvothermal routes

A metallic precursor, such as metal chlorides \([14–16, 25, 26, 28, 31, 33, 35, 77–87]\) or acetylacetonates \([36, 88–90]\) are dissolved in a solvent like ether \([36, 88–90]\), or glycol \([14, 15, 25, 26, 31, 33, 35, 77, 79–87]\), or water \([16]\), or THF-ethanol \([28]\) in a glass flask equipped with a heating mantle or in an autoclave (Figure 2A–E). A capping agent is also added in the reaction mixture at room temperature (Table 1) to control the size and the shape of the system. The type of the capping ligand determines the nanoparticle dispersibility in an organic solvent or in water. The reaction solution is heated at a high temperature of 200–300°C, usually with a rate of 1–10 K/min. After reacting for a given time, the process is stopped by decreasing the temperature and the as-formed nanoclusters are purified (i.e. centrifuged to remove the excess of the unreacted species). Ferrite nanoclusters of different chemical composition, such as \(\text{Fe}_3\text{O}_4\), \(\gamma\text{-Fe}_2\text{O}_3\), \(\alpha\text{-Fe}_2\text{O}_3\), \(M\text{Fe}_2\text{O}_4\) (\(M=\text{Zn, Mn, Co, Ni, Mg}\)) (Table 1), have been prepared with single-step routes.

The formation of the nanoclusters in a polyol-based protocol relies on a two-stage growth model \([15, 16, 28, 82]\). Primary nanocrystals first nucleate in a supersaturated solution resulting from the solvent-mediated hydrolysis of \(\text{Fe}^{3+}\). The molecules of the capping agent “bind” on the surface of the nanocrystals introducing electrostatic repulsion between them (Figure 3). The newly formed nanocrystals tend to aggregate by oriented attachment in order to reduce their high surface energy \([14, 16, 21, 28, 35, 79, 81, 83–85, 87]\). The balance between the opposing forces determines the size and the morphology of the secondary structures (Figure 3). Either a perfect crystallographic orientation or a small misalignment among the incorporated particles has been found in these sorts.

Figure 2: Transmission electron microscopy (TEM) images of iron oxide colloidal nanoclusters prepared by single-step solvothermal (A, B) \([16, 79]\), organometallic (C–E) \([36, 84, 88]\) and biomineralization (F) \([29]\) routes.

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Table 1: Possible surfactant-assisted methods for the development of iron oxide colloidal magnetic nanoclusters.

<table>
<thead>
<tr>
<th>Chemical nature</th>
<th>Number of steps</th>
<th>Type of synthesis</th>
<th>Capping ligand</th>
<th>Magnetic state</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe₃O₄, γ-Fe₂O₃</td>
<td>1</td>
<td>High-T organometallic route</td>
<td>Amine, polymer, citrate</td>
<td>SPM</td>
<td>[13, 14, 31, 77, 91–93]</td>
</tr>
<tr>
<td>MFe₂O₄ (M=Zn, Mn, Co, Ni)</td>
<td></td>
<td>High-T organometallic route</td>
<td>PEG, oleic acid/amine, PEG-diacid</td>
<td>SPM</td>
<td>[33, 88]</td>
</tr>
<tr>
<td>FeO₃, γ-Fe₂O₃</td>
<td>High-T organometallic route</td>
<td>Dendron, dendrimers, polymer</td>
<td>Ferri/ferro</td>
<td>[21, 36, 89, 90]</td>
<td></td>
</tr>
<tr>
<td>Fe₃O₄, γ-Fe₂O₃</td>
<td>Solvothermal</td>
<td>Dendron, dendrimers, polymer</td>
<td>Ferri/ferro</td>
<td>[15, 23, 25, 26, 35, 78, 79, 82, 84–86, 94]</td>
<td></td>
</tr>
<tr>
<td>Fe₃O₄, γ-Fe₂O₃</td>
<td>Encapsulation</td>
<td>Hydrogel, polymer, SiO₂</td>
<td>SPM</td>
<td>[38, 95, 96]</td>
<td></td>
</tr>
<tr>
<td>Fe₃O₄</td>
<td>Encapsulation</td>
<td>Polysaccharides polymer</td>
<td>SPM</td>
<td>[22, 34, 97]</td>
<td></td>
</tr>
<tr>
<td>Fe₃O₄</td>
<td>Encapsulation</td>
<td>Micelles, block copolymer</td>
<td>–</td>
<td>[24, 99, 100]</td>
<td></td>
</tr>
<tr>
<td>Fe₃O₄</td>
<td>Encapsulation</td>
<td>Copolymer</td>
<td>SPM</td>
<td>[103]</td>
<td></td>
</tr>
</tbody>
</table>

PEG, polyethylene glycol; SDS, sodium dodecyl sulfate.

Figure 3: Formation process of the colloidal nanocrystal clusters and possible interactions among neighboring nanocrystals at different growth stages. Sodium citrate molecules adsorbed on the surface of the inorganic magnetic nuclei result in electrostatic repulsive forces between them. Simultaneously, the surface tension (attractive force) of nanocrystals favors oriented attachment in order to reduce their surface energy during the aggregation process. The latter depends on the balance of the two opposing forces [15]. Reproduced by permission of The Royal Society of Chemistry.

of reactions. Utilizing a glycol of high reductive ability, such as the 1,2-propylene glycol, a small misalignment between the incorporated units in the nanoclusters has been obtained (Figure 4A), while a perfect alignment is achieved with a glycol of lower reductive ability, such as the ethylene glycol (Figure 4B) [84]. The reductive ability of the solvent is the key parameter that determines the nucleation and growth rates of the primary nanocrystals. In ethylene glycol, the growth rate of the primary nanocrystals is relatively slow, and they have enough time to self-assemble along the same crystallographic orientation within the nanocluster (Figure 2D). In 1,2-propylene glycol, the higher nucleation and growth rates of the primary nanocrystals cause quicker aggregation and produce misalignment. In some cases, the oriented attachment is followed by a fusion and Ostwald ripening processes, with the results that the incorporated units become more elongated (Figure 2B) [79].

In addition to the solvent reductive ability in the polyol process, the orientation of the particles in the nanoclusters is sensitive to the type of the surfactant molecules. A polycrystalline assembly has been obtained by utilizing poly(γ-glutamic acid) (PGA) as the stabilizing agent [26]. The nanoclusters’ formation in this case is different from that using polyelectrolytes described earlier, and the role
of the PGA-surfactant in this process is unique. PGA-stabilized \( \text{NH}_3 \) bubbles were formed through a Pickering emulsion process, and these bubbles were entrapped within the inter-particle spacing of the nanoclusters. Following the reaction, the trapped \( \text{NH}_3 \) bubbles were forced out and gave rise to empty channels among the petals formed by the component nanocrystals.

It is worth pointing the possible alignment of the particles in non-polyol processes. Polycrystalline nanoclusters are obtained when the solvothermal reaction occurs in water, and the nanoclusters are stabilized with polyacrylamide [16]. However, efficient crystallographic alignment is observed by utilizing large poly(phenylenepyridyl) dendron/dendrimer as capping molecules and ether as a solvent (Figure 2E) [36, 89, 90]. The dendron/dendrimer surfactants self-assemble in the reaction mixture and “embrace” the nanocrystal surface by means of both interior and exterior pyridine groups of the molecules. The self-assembly of the capping agent allows for the oriented aggregation of the primary nanocrystals. Then, these seeds grow further due to a fusion process and become elongated larger units (petals).

The nanocluster size is determined mainly from the relative strength of the electrostatic forces between the preformed, charged nanocrystals [21]. Weaker Coulombic repulsion among the nanoclusters leads to their decreased separation in the reactant liquid, with effect in the formation of nanoclusters of larger diameter. A way to attenuate the electrostatic repulsion among the particles is to reduce the population of surfactant molecules on the primary nanocrystals. This decrease can be achieved by lowering the concentration of the surfactant [15, 35] or introducing water molecules [21, 83, 85] in the reaction mixture. The influence of the water in the growth is justified by considering the higher affinity of the water molecules to coordinate stronger to the surface metal cations than that of the capping molecules, thus, rendering the inorganic particles less charged. In the absence of surfactant in the reaction medium, a non-spherical morphology has been observed indicating the role of electrostatic interactions in the morphology and the shape of the nanoclusters [28].

Moreover, the nanocluster size can be effectively controlled by varying the reaction time [79, 86], the precursor concentration [86, 87], and the quantity of the reductive agent of the organometallic precursor [104]. Yin et al. succeeded in synthesizing nanoclusters with diameters ranging from 30 to 180 nm. These were capped with polyacrylic acid, through a thermolysis process in diethylene glycol by simply varying the volume of the NaOH solution injected in the precursor solution [104]. Later, Xuan et al. utilized a solvothermal process, with sodium acrylate as surfactant in a mixture of diethylene glycol and ethylene glycol and succeeded to obtain nanoclusters of a variable diameter [82]. Interestingly, the size of the component nanoparticles could be tuned from 7.5 to 21.5 nm by simply increasing the NaOAc/Na acrylate ratio while that of the whole structure, by tuning the ethylene glycol/diethylene glycol ratio (Figure 5) [82].

### 2.1.2 Soft biomineralization route

Recently, a different single-step approach, mimicking the process that so far has been achieved only by nature in iron-oxidizing bacteria, has been explored to synthesize magnetic nanoclusters [29]. In this way, magnetite nanoclusters of 45 nm in diameter have been obtained through biomineralization and epitaxial aggregation in the presence of alginate at ambient conditions (Figure 2F). It is the first time
that magnetic nanoclusters of crystallographically oriented primary nanocrystals (~6 nm) are developed through a soft mineralization route at ambient temperature and pressure conditions while utilizing a biopolymer. The polymer (sodium alginate) solution of the precursor was heated at 50°C for 1 h and 30 min. These dense nanoclusters exhibited a very high magnetophoretic response, which together with the utilization of the biogenic and biodegradable polymer validate their use as a potential theranostic agent.

### 2.2 Multi-step synthesis protocols

#### 2.2.1 Encapsulation of pre-formed nanocrystals

Magnetic nanoclusters (nanobeads) have been synthesized by entrapping surfactant coated maghemite nanocrystals within an amphiphilic polymer [P$_{18}$-poly(maleic anhydride-alt-1-octadecene] (Figure 6A) [38]. The pre-formed nanocrystals were dissolved in THF, and a second solvent was added in which the nanocrystals were not soluble. The solubility of the polymer was altered, and effectively aggregated particles were obtained and wrapped by the polymer chains. The size of the nanoclusters was mainly dictated by the solubility of the polymer in the solvent and by the concentration of the polymer. Adding a solvent in which the polymer was insoluble yielded small secondary structures, while adding a solvent in which the polymer is soluble allowed for larger structures embedding a large number of primary nanocrystals to be formed.

Different types of molecules, as encapsulating agents of iron oxide nanoparticles, have been used, including polymers/block copolymers (Figure 6A, B) [24, 99, 98, 101, 94], micelles (Figure 6C) [100], polysaccharides [22, 32], or hydrogels [95]. For example, aggregated iron oxide particles with controlled size have been prepared by utilizing methods based on acid/base interactions involving pre-formed nanocrystals in an organic solvent (Figure 6C) [100]. By increasing the acidity of the organic solution, the pre-formed nanocrystals start to aggregate, and the aggregation process continues until the desired size is obtained. Following this step, the aggregated particles are encapsulated in a phospholipid monolayer to yield stable micelles of nanoclusters [100].
2.2.2 Evaporation-induced nanoclusters

In this process, the pre-formed nanocrystal building blocks were dispersed in a non-polar organic solvent (e.g. cyclohexane, dodecane) to form an oil phase (Figure 7) [18]. At the same time, an aqueous solution was prepared with a surfactant such as sodium dodecyl sulfate (SDS). Under sonication or stirring, these two phases are mixed to form a mini-emulsion. The mini-emulsion is heated, and the organic solvent is left to evaporate. The nanocrystals aggregate in the secondary structures and are stabilized by the surfactant in the water phase. The nanoclusters were removed from the solution and added to a solution of polyoxyethylene sorbitan monooleate (Tween-80). The Tween-80-modified nanoclusters are further added to a Stöber system (water, ethanol, ammonium hydroxide, ethanol, TEOS) after hydrolysis and are then capped with the SiO₂ layer (Figure 6D). The size of the nanoclusters can be tuned by changing the concentration of the nanocrystals and the surfactant in the oil phase. Polystyrene [94] or copolymer [103] can also be introduced instead of the SDS as surfactant in the oil phase.

3 Variable length-scale microscopic mechanisms and collective magnetic behavior in iron oxide nanoclusters

Controlled clustering of inorganic nanocrystals in three-dimensional, homogeneous secondary structures opens new prospects in materials science and engineering because of their challenging magnetically-mediated applications, ranging from photonics to biomedicine. However, despite the numerous examples of currently developed magnetic nanoclusters (Table 1), there is only limited work on the systematic explanation of the emerging cooperative physical mechanisms that arise because of various types of interactions in these nanostructures.

In order to comprehend some of the aspects of their complex behavior, let us now consider some of the fundamental physical quantities that govern nanoscale magnetic systems. In the general case, one may assume that each magnetic nanocrystal may possess a uniaxial anisotropy axis, and as such, its magnetic anisotropy energy is given by $E = KV \sin^2 \theta$, where $\theta$ is the angle between the direction of the magnetization ($M$) and the easy-axis, $V$ is the volume of the particle, and $K$ is the effective magnetic anisotropy constant [58, 105, 106]. Effectively, there are two energy minima at $\theta = 0$ and $\theta = \pi$, which correspond to the parallel or antiparallel magnetization directions ($\parallel$) with respect to the easy-axis, while they are separated by an energy barrier $\Delta E_B = KV$ (Figure 8). For small-enough nanocrystals, the thermal energy may be sufficient to reverse the magnetization when $k_B T > KV$. For all temperatures above the so-called blocking temperature, $T_B$, the nanocrystals are non-interacting, and no-coercivity ($H_C$) is observed in the magnetization curves ($M$ vs. $H$). For these superparamagnetic systems, the fluctuation of the magnetization is described by the characteristic relaxation time ($\tau$) given by the Néel-Brown model:

$$\tau = \tau_0 \exp \left( \frac{KV}{k_B T} \right)$$

where $\tau_0$ is the attempt time [107].
However, the dynamics of the magnetization reversal process are sensitive to the internal spin structure of the nanocrystals. Vacancies, broken bonds, and lattice strain at the surface produce various canted spin structures and alter its surface spin configuration [106]. Anomalous magnetic properties at low temperatures, such as time-dependent moment, open hysteresis loops at high magnetic field, and shifted hysteresis loops after field-cooling protocols have been observed in ferrite nanocrystals [108]. In order to explain this sort of magnetic behavior, a theoretical model has been proposed by Kodama et al. in which the magnetic structure of a nanocrystal can be simulated with a core attaining ferrimagnetically aligned spins and a surface layer adopting a spin glass-like structure (Figure 9) [108]. The canted spins on the surface of the nanocrystal have multiple stable configurations. Owing to the exchange interactions between the core and the surface spins, the cooling field may select a surface spin configuration, which favors the particle being magnetized in the direction of the field. The open hysteresis loops and time-dependent moment are due to surface spin disorder, rather than magnetization reversal of the whole particle. In view of such surface and interface effects, Monte Carlo simulations have been instrumental in order to explore the effect of the disordered shell thickness on the emerging exchange-bias phenomena [109].

More recently, theoretical approaches have pointed out that when maghemite ($\gamma$-Fe$_2$O$_3$) nanocrystals assemble in colloidal nanocluster form, the collective magnetic behavior is strongly dependent on factors affecting the nanocrystals’ magnetic anisotropy or surface spin structure ($J_{ij}$), as well as the possible interactions among neighboring nanocrystals, such as of dipole-dipole (g) or exchange type (J) (Figure 10) [21, 58]. Assuming that the constituent nanocrystals attain a core/surface-type topology, the model introduces a classical uniaxial spin vector for the core ($S_c$), while two surface spins for the shell ($S_s$, $S_b$; assuming ferrimagnetic-like interaction). The total energy of the system can then be written as follows:
The first three energy terms describe the nearest neighbor Heisenberg exchange interactions between the core spin and the two surface spins, the fourth and the fifth terms give the anisotropy energy for the core and the surface, while the sixth term is the Zeeman energy. The last term describes the important role of dipolar interactions among the spins at various topologically different regions [21].

In the following sections, we will elaborate on the above-mentioned competing mechanisms in the total energy, highlight how these could be experimentally probed, while selected literature claims will be utilized to exemplify their impact on the physical response of nanoscale assemblies.

3.1 The role of dipole-dipole interactions

Enhanced saturation magnetization (Figure 11A), reduced coercive field at low temperature, higher blocking temperature (Figure 11B), and an obvious flatness of the field-cooled curves (Figure 11B) compared to those of individual nanocrystals are worth to be noted in the case of ferrite nanoclusters [21, 31]. Similarly, a shift toward a higher temperature for the maximum of the zero field-cooled magnetization curve and a reduced coercivity at low temperature have been observed for systems that adopt a raised volume fraction ($\phi$) for the inorganic magnetic phase [110] or even when the morphology [111, 112] allows for very short distances between particles; all such postulate to the presence of dipole-dipole interactions. The nanocrystals were found to be non-interacting when the distance between them exceeds 47 nm [112]. Literature results on various types of nanocrystal assemblies in which their magnetic behavior is governed by dipole-dipole interactions, motivate us to explore further such inter-particle interactions so that technologically useful nanomaterials can be realized.

Unique information about the strength of the dipolar interactions among the component nanocrystals in such systems can be obtained by means of ac magnetic measurements and the associated analysis of the frequency ($f$) dispersion of the ac susceptibility, $\chi' = \chi'' + \chi''''$. When particles assemble in a secondary structure, inter-particle dipolar interaction strength ($g$) increases, and the relaxation times deviate from the common Arrhenius law (equation 1). Depending on the magnitude of $g$, the relaxation time, $\tau$, follows either a Vogel-Fulcher law or power law descriptions. When the nanocrystals interact with intermediate strength dipolar interactions, the phenomenological Vogel-Fulcher law approximation may hold:

$$\tau = \tau_0 \exp \left( \frac{E_a / k_B}{T - T_0} \right)$$

where $T_0$ represents a qualitative estimate of the inter-particle interaction energy, and $E_a / k_B$ is the activation energy to overcome the barrier of the magnetization reversal [113]. When the $g$ becomes stronger, the magnetic moments (superspins) of the nanoparticles freeze collectively into a spin glass state (superspin glass) below a
characteristic critical temperature, and a power law may provide an adequate description of the dynamics:

$$\tau = \tau_0 \left( \frac{T^*}{T - T^*} \right)^z$$

where $T^*$ is the glass transition temperature for $f \to 0$, and $z$ is the critical exponent, which takes values from 4 to 12 for a typical spin glass system [51, 114].

In order to evaluate the strength of dipolar interactions, Peddis et al. studied the magnetic behavior of ensembles made of multiple cobalt-ferrite nanocrystals arranged in different topological manners [115]. The nanocrystals assumed to be organized in 2D superlattices (of two different nanocrystal concentrations) (Figure 12A, B, D, E) or self-assembled in 3D nanoclusters (Figure 12C, F). The inter-particle interactions can be tuned in these arrangements by varying the nanocrystal concentration. Coupled properties have been observed only in the randomly packed 2D particle assembly (Figure 12B, E) and in the 3D nanocluster sample (Figure 12C, F). The blocking temperatures were found almost equal for the two samples and larger than that for the more organized superparamagnetic 2D assembly (Figure 12A, D), indicating the existence of dipolar interactions in the former two cases. Furthermore, a reduced magnetic anisotropy has been claimed in the case of the 3D nanoclusters in which the incorporated nanocrystals were crystallographically oriented (Figure 12C, F) compared to those of randomly oriented nanocrystals in the randomly packed 2D particle assembly (Figure 12B, E) [115].

On the other hand, the phenomenological power law (equation 4) has been utilized to fit the frequency dependence of the real part of the susceptibility, $\chi'(T)$. The resultant value of the attempt time, $\tau_0$, for the two denser samples (Figure 12B, C, E, F) was found to be one order of magnitude longer than that of the corresponding superparamagnetic particle assembly (Figure 12A, D). Such an increase in the attempt time, when dipolar interactions become stronger, is in agreement with earlier reports concerned with individual nanoparticles. In one such case, the dipolar interaction strength was tuned by modifying the shell thickness of $\gamma$-Fe$_2$O$_3$@SiO$_2$ core-shell nanocrystals [112] while in another example by increasing the inorganic particle volume fraction within a frozen ferrofluid of Fe-C nanocrystals [116].

The similar value of the attempt time for the randomly packed 2D particle assembly (Figure 12B, E) and the 3D nanocluster sample (Figure 12C, F) implies that the dipolar

---

**Figure 12:** Different topological arrangements of nanocrystals in 2D superlattices of low nanocrystal concentration (A, D), randomly packed 2D particle assembly of high nanocrystal concentration (B, E) and 3D nanoclusters (C, F). Reprinted (adapted) with permission from Ref. [115]. Copyright (2013), American Chemical Society.
interactions among the nanocrystals in these two systems are of comparable strength. The reduced anisotropy in the case of the 3D nanoclusters indicates the role of the crystallographic orientation of the incorporated nanocrystals in the magnetic response of the system.

### 3.2 In the quest for exchange coupling among surface spins

Colloidal nanoclusters have been found to be ferromagnetic/ferrimagnetic [21, 32, 36, 80, 81, 83, 89, 98] or superparamagnetic [13–16, 22, 24, 31, 33, 35, 77, 79, 82, 84, 85] at ambient conditions. The ferrimagnetic/ferromagnetic behavior of nanoclusters may be attributed either to ferromagnetic incorporated nanoparticles of sufficient large diameter (>20 nm) [80, 81] or to strong intra-cluster interactions [21]. Lartigue et al. showed that maghemite nanoclusters of 30 nm in diameter, which are illustrated in Figure 13A, were superparamagnetic (lack of hysteresis) at room temperature [31]. Their collective magnetic behavior was illustrated in complex ferromagnetic resonance spectra (FMR), which are consisted of several absorption lines at different resonance fields and, in particular, lower than that observed for individual particles (Figure 13C). The highly asymmetrical FMR spectra were explained by assuming exchange interactions among surface spins, as well as reduced magnetic anisotropy. In these systems, the nanocrystals were assembled in sufficient close contact within the clusters. As a result, the crystallographic orientation of the cores could continue across the interfaces, thus, facilitating exchange interactions among the neighboring surface spins [29, 31]. On another account though, for nanoclusters of a similar chemical phase (Figure 13B) that were studied by a combination of SQUID magnetometry and local probe Mössbauer spectroscopy (Figure 13E, F), the differing ferrimagnetic character has been identified. In these nanostructures, their collective properties are governed by strong intra-cluster dipole-dipole interactions, as well as exchange interactions, which are established within each nanocrystal incorporated in the cluster entities. However, no evidence for exchange interactions between the spins of neighboring nanoclusters in clusters could be found [21]. Mössbauer spectra of these nanoclusters have displayed magnetically split absorption lines, without any hyperfine magnetic field collapse, thus, supporting the collective ferrimagnetic behavior of the nanoclusters (Figure 13E, F). Additionally, these spectra showed narrower lines with higher hyperfine magnetic fields compared to the corresponding values measured for their individual superparamagnetic counterparts (~13 nm) (Figure 13D).

The possible emergence of exchange interactions among the surface spins of neighboring nanoclusters in CoFe2O4 clusters have been investigated by the analysis of the remanent magnetization curves, measured by isothermal remanent magnetization (IRM) and direct current demagnetization (DCD) protocols [115]. The two types of magnetization are related according to the Wohlfarth equation:

\[
\delta m = m_{\text{DCD}} - (1-2m_{\text{IRM}})
\]  

When \(\delta m\) is plotted for the aforementioned magnetic nanoclusters (Figure 14A – sample SACoFeDM), a negative deviation is indicative of prevailing dipolar interactions, with no operative exchange coupling. Even in the case of a close-packed system of bare (no capping molecules) maghemite nanocrystals and a volume fraction of 67% for the inorganic magnetic phase, exchange interactions seem to play a minor role [117]. In support comes the evolution of the supertwin glass freezing temperature \(T_f\) (\(T_f\approx T_{\text{peak}}\)) (symbols; Figure 14B), which hardly deviates from the value expected exclusively from dipolar interactions (red line; Figure 14B).

### 3.3 Spin glass behavior and cooperative microscopic mechanisms

Further insight to the origin of the microscopic mechanisms emerges from the analysis of the frequency

---

**Figure 13:** TEM images of superparamagnetic [31] (A) and ferrimagnetic [21] (B) maghemite nanoclusters. FMR (MC0 – 2) [31] (C) and Mössbauer spectra for superparamagnetic and ferrimagnetic (50 and 86 nm) nanoclusters, respectively (E, F) [21]. For comparison, the FMR spectra (Sample SC) [31] (C) and Mössbauer spectra for the individual nanocrystals are also shown [21] (D).

(A, C) Reprinted (adapted) with permission from Ref. [31]. Copyright (2012), American Chemical Society.

(B, D–F) Reproduced from Ref. [21] with permission of The Royal Society of Chemistry.
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upon heating in a weak probing field [51]. The glassy state reflects in the decrease of the magnetization in the aging curve (curve after waiting) compared to the reference one (without waiting).

It is, however, a common practice to study the frequency dispersion of the ac susceptibility in order to extract information on the underlined spin dynamics, which influence the macroscopic magnetic response of the system. In view of this, recent studies on nanoclusters, capped with polyacrylic acid and carrying a raised volume fraction for the inorganic phase 60–70%, have pointed out that the imaginary part of the susceptibility, $\chi''(T)$, can be very informative (Figure 15A).

The identified two maxima in the $\chi''(T)$ were evaluated on the basis of a phenomenological power law (equation 4), which pointed out the presence of two different spin dynamical regimes (Figure 15B, C) [21]. The high-temperature broader peak could be attributed to the blocking of the superspins while the lower-temperature one to a surface spin glass freezing. Memory effects that were identified in both magnetic regimes spoke in favor of the spin glass behavior from both dispersion of the dynamical (ac) susceptibility and the investigation of possible memory effects. The latter have been observed in systems capable of developing strong dipole-dipole interactions (superspin glass systems) [118, 119] or when surface spin disorder is available [120]. In order to study their impact, a specialized thermal cycling protocol is employed. Namely, the sample is cooled to a temperature below the glass transition by obeying a zero field protocol and is kept at this temperature for a given time. After waiting, it is further cooled to some lower temperature, and then, the magnetization is measured

![Figure 14: (A) Field dependence of $\delta_m$ calculated from the Wohlfarth equation (5) for ferrite nanoclusters [115]. (B) Superspin glass freezing temperature ($T_f = T_{\text{peak}}$, where the $T_{\text{peak}}$ is the temperature at which the zero field-cooled magnetization curve measured upon heating, after stopping for 3 h during the cooling stage, has a maximum) as a function of the concentration of magnetic component in compacted samples of maghemite nanocrystals [117] (B). The dashed red line represents the behavior for when the exchange interactions are ignored. (A) Reprinted (adapted) with permission from Ref. [115]. Copyright (2013), American Chemical Society. (B) Reprinted (adapted) with permission from Ref. [117]. Copyright (2013), American Chemical Society.](image1)

![Figure 15: Frequency dependence of the imaginary part, $\chi''(T)$, of the ac susceptibility for maghemite nanoclusters of 50 nm in diameter (A). Power law analysis of the frequency dispersion of the low (B) and high (C) temperature $\chi''(T)$ maxima. Temperature dependence of the difference, $\Delta \chi = \chi_{\text{wait}}(T) - \chi_{\text{ref}}(T)$, of the zero field-cooled dc susceptibility curves before and after waiting for $10^4$ s at 35 K (filled squares) and at 110 K (crossed squares) (D) [21]. Reproduced with permission of The Royal Society of Chemistry.](image2)
types of contributions (Figure 15D). The memory effects in the zero field-cooled dc susceptibility at high temperature together with the flatness of the associated field-cooled curve below a characteristic temperature are indentifying features of the peculiar properties of a superspin glass system [118, 119]. Similar characteristics have been also observed for nanocrystal assemblies with 35% [54] and 44% [56] magnetic material volume fractions. The memory effects at low temperature are accompanied by a spin glass freezing due to the surface defect environment of the incorporated nanocrystals [52, 121–123]. A canted surface spin structure has been found previously in antiferromagnetic NiO nanocrystals (Figure 16A) [122, 124] and also in ferrimagnetic ferrite nanocrystals (Figure 16B) [123]. In addition, a minimal exchange bias field has been measured in maghemite nanoclusters stabilized with polyacrylic acid [21]. Contrary to that, an exchange bias associated with a possible surface spin structure of clusters where amine [31] or oleic acid [115] were the capping agents could not be resolved.

Similar features in the imaginary part of the ac susceptibility, \( \chi''(T) \), have been found in magnetite nanoclusters capped with dendrons (Figure 16C) [90]. In this system though, the maximum \( \chi''(T) \) at low temperature is attributed to superparamagnetism [90] and not to surface spin disorder like that established in polyacrylic acid-capped maghemite nanoclusters [21]. In such dendron-capped magnetite nanoclusters, the Vogel-Fulcher law has been utilized to fit the ac susceptibility data, and the resultant value of the attempt time was found to be comparable to that reported for nanoparticulate systems with intermediate-strength dipolar interactions [123]. The strength of the dipolar interactions among the particles and the absence of a spin glass freezing in the low temperature regime were also supported by the estimation of the relative variation of the \( \chi'' \) peak temperature position per frequency decade, known as the Mydosh parameter, which is given from the equation:

\[
\text{Mydosh parameter} = 10 \times \log_{10} \left( \frac{T_{\text{peak}}}{f} \right) = \text{constant}
\]

where \( T_{\text{peak}} \) is the peak temperature and \( f \) is the frequency. This parameter provides a measure of the temperature dependence of the magnetic response and is useful in identifying the magnetic behavior of the material.

**Figure 16:** Temperature dependence of the real, \( \chi'(T) \) (solid symbols) and imaginary, \( \chi''(T) \) (open symbols) parts of the ac susceptibility for frequencies \( 10 \leq f \leq 10^4 \) Hz and \( H=10 \) Oe for NiO nanocrystals of 6 nm diameter. Inset: High temperature region [124] (A). Temperature dependence of real part, \( \chi' \), of the ac susceptibility of NiFe\(_2\)O\(_4\) nanoparticles, \( \chi' \), at \( f=300 \) Hz and \( H=3 \) Oe [123] (B). Temperature dependence of the imaginary part, \( \chi'' \), of the ac susceptibility for magnetic nanoclusters capped with dendrons [90] (C).

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(B) © IOP Publishing. Reproduced from Ref. [123] with permission. All rights reserved.

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The estimation of the latter, in the case of dendron-capped clusters, falls in the range that predicts a blocking process associated with intermediate strength dipolar interactions \((0.05 < \psi < 0.13)\) and not to a spin glass state that would have been expected for values in the range \(0.005 < \psi < 0.05\) \([125]\). In the dendron-based system, the superparamagnetic behavior likely originates from nano-clusters incorporating a larger average distance among their constituent nanocrystals. The extra potential of such nanoclusters arises from our ability to tune the interparticle separation by changing the generation of the dendron capping ligand \([90]\).

### 3.4 On the origin of various mechanisms by Monte Carlo simulations

Identifying the origin of spin glass effects such as those discussed above for various magnetic nanoclusters can be somewhat troublesome especially when a number of microscopic physical processes are simultaneously active (equation 2). Therefore, theoretical investigations, which are based on quantum Monte Carlo simulations, utilizing the Metropolis algorithm, can be instrumental in that respect \([21]\). These, for example, can entail calculations of the isothermal magnetization curves at low temperature as well as the temperature dependence of the magnetization under zero and field-cooled protocols.

In one such recent study of maghemite nanoclusters, the utilized model corroborated that each nanocrystal in the assembly could assume a core/surface-like morphology \([21]\). Consequently, the model introduced a core spin anisotropy axis parallel from particle to particle within each cluster entity, but the surface spins assumed to be at a random direction with respect to the core (Figure 10). Guided by the experimental evidence, the theory proved that the rational identification of the operative interaction mechanisms could be possible \([8]\). Owing to the presence of the capping ligand and literature claims (see Section 3.2), no contribution from direct exchange interactions among surface spins \((J)\) was incorporated in the model, but instead, their magnetic behavior was mainly found to be governed by the established dipolar forces (Figure 10). To identify the factors dictating the spin glass behavior, either the dipolar interactions \((g=0)\) or the intra-particle spin exchange interactions \((J_{12}=J_{23}=0)\) were selectively switched off. The Monte Carlo simulations suggested that the spin glass dynamics are driven by strong dipolar interactions among the incorporated nanocrystals, while an additional spin disorder due to the defected nanocrystal coordination environment was essential. Such theoretical insight was proven to be in accord with arguments provided by ac susceptibility experiments (see Section 3.3).

### 4 Synergetic functionalities for magnetically mediated applications

The intense magnetic responsiveness of the colloidal nanoclusters and our capability to engineer it so that it operates together with other physicochemical properties (photonic, electronic, catalytic, mechanical, etc.) presents us with nanosized objects of remarkable technological horizons. For example, this may pertain to highly sought nanoprobe that can be exploited in biomedical applications, including magnetic resonance imaging (MRI), magnetic particle hyperthermia, and even for targeted drug delivery. The capability of the nanoclusters to assemble into large-area periodically arranged arrays when driven by an external magnetic field opens additional prospects in the field of magnetically responsive photonic crystals. Furthermore, with the modular armory of colloidal chemistry tools, multi-component nanoclusters (such as those composed of metallic/catalytic sections, assembled on a magnetic carrier) can show the way for diverse bi-modal functions, such as the magnetically recoverable catalysts. The following sections elaborate a bit further on those attributes of magnetic nanoclusters, which render them efficient nanoscale functional components for different applications with important socioeconomic value.

#### 4.1 Biomedical applications

##### 4.1.1 Nanoclusters as contrast agents in magnetic resonance imaging (MRI)

Magnetic ferrite nanomaterials are emerging as promising probes in the diagnosis of various diseases, especially in the area of magnetic resonance imaging (MRI). These materials can be delivered in the regions of interest via intravenous injection and cause the shortening of the longitudinal \((T_1)\) and transverse \((T_2)\) nuclear relaxation times of protons thus attaining improved tissue contrast. Among the various contrast agents, paramagnetic
compounds (gadolinium based) mainly increase the spin lattice relaxation rate (by loss of energy to the surrounding lattice), $r_1 (1/T_1)$, of the water protons and improve the bright contrast in the regions where they are delivered. On the other hand, superparamagnetic nanoscale compounds raise the spin-spin relaxation rate (by loss of the phase coherence of the precessing nuclear spins due to spin-spin interactions), $r_2 (1/T_2)$, and enhance the dark contrast in the tissue where they are localized [126]. Individual nanocrystals of this nature (in the presence of an external magnetic field) may generate a strong perturbation of the local dipolar field in their vicinity, which in turn accelerates the water proton relaxation and results in darker contrast in the MR images.

When magnetic nanocrystals assemble in secondary structures, their magnetic moments not only interact through dipole-dipole interactions, but an enhanced saturation magnetization ($M_s$) (Figure 11A) is attained compared to that of individual nanocrystals. As a result, a stronger perturbing local magnetic field in their vicinity can be expected. The water protons straddling around nanocluster entities are expected to relax even faster than when superparamagnetic individual nanocrystals are present in the surrounding media. Recent studies have shown that the transverse relaxivity, $r_2$, necessary for improved “dark contrast” in such systems, is considerably enhanced (approximately three to four times) compared to individual nanocrystals and commercial products, such as the Endorem® (Figure 17) [25, 31, 100, 127]. In the case of cluster-like systems of volume $V$, under an external magnetic field $B_0$, $r_2$ can be estimated by the equation:

$$r_2 = \frac{1}{T_2} \left( \frac{64 \pi}{135} \right) \left[ \mu_0 \gamma H L(x) \pi^{1/2} \right] N_c C_{av} R_D$$

(7)

where $\mu_0$ is the vacuum magnetic permeability, $\gamma$ is the proton gyromagnetic ratio, $\mu$ the magnetic moment of the constituent nanocrystals, $N$ is the number of nanocrystals in the nanocluster, $L(x)$ is the Langevin function $[-\coth(x) - 1/x$, where $x=M_s V B_0/k_B T]$, $N_A$ is the Avogadro number, $C_{av}$ is the concentration of the nanoclusters, $R$ is the radius of the nanoclusters, and $D$ is the water diffusion coefficient [126, 128]. This quantitative description tells us that in terms of materials-design strategies, one has to consider a number of magneto-structural parameters. The latter, when optimized, benefit the transverse relaxivity generated by complex structures of increased magnetic material volume fraction ($\varphi$).

According to equation 7, the transverse relaxivity is proportional to the square of the magnetic moment ($\mu$) and the number of the constituent nanocrystals ($N$) in the nanoclusters. The magnetic moment of the individual nanocrystals can be tailored by tuning their size and their chemical composition. The $r_2$ has been found that increases with the diameter of the incorporated units in the nanoclusters [82]. Among the magnetic nanoclusters of different chemical compositions, including Fe$_3$O$_4$ [13, 14, 24, 25, 29, 82, 83, 94, 95], $\gamma$-Fe$_2$O$_3$ [31, 127, 129], MnFe$_2$O$_4$ [22, 34], ZnFe$_2$O$_4$ [83], the polymer capped magnetite nanoclusters of diameter 64 nm [25] and the Mn-doped ferrite nanoclusters encapsulated in silica layer [34], have shown the highest $r_2$ values. The first system showed an $r_2$ of 650 mm$^{-1}$s$^{-1}$ and the latter of 695 mm$^{-1}$s$^{-1}$, which are among the highest values reported for magnetic iron oxide materials, to date. Importantly, variations in composition and doping have a significant impact on the saturation magnetization ($M_s$) and the value of the $r_2$.

Such parameters have been considered before for the case of $(Zn,M_{1-x})Fe_2O_4$ ($M=Mn^{2+}$, Fe$^{3+}$) individual nanocrystals,
and their evolution upon doping is shown schematically in Figure 18A [130, 131]. When Fe$^{2+}$ at the tetrahedral (Td) holes is substituted by non-magnetic Zn$^{2+}$, the antiparallel spin interactions between the magnetic cations in the octahedral (Oh) holes and Td holes are reduced. In effect, this leads to an increase in the $M_s$ and eventually a rise in the $r_2$ (Figure 18B, C).

An alternative way to increase the $M_s$ and eventually the $r_2$ is to increase the number of the constituent inorganic subunits in the nanoclusters. Increased number of particles can be incorporated by tuning the volume fraction of the magnetic material ($\varphi$) in the nanoclusters. Recently, the synthesis of maghemite nanoclusters with tunable $\varphi$ has been successfully demonstrated [21, 127]. Nanoclusters of variable volume fraction can evolve to display superparamagnetism or ferrimagnetism. Although the majority of them have been reported to be superparamagnetic at ambient conditions, two ferrimagnetic systems, with high transverse relaxivity and a very good stability in aqueous media, have lately emerged as promising probes for MR imaging. These systems consisted of nanoclusters of $\varphi=60$ and 72% capped with a polyacrylate [127] (Figure 19C) or encapsulated in liposomes [132]. Despite their ferrimagnetic response at ambient conditions, the rational choice of their surfactant molecules prevented their agglomeration and raised their potential for applicability.

In order to study the role of the nanocluster size and the local magnetic field on the $r_2$, each nanocluster can be considered as a large magnetized sphere, with its magnetization assumed to be aligned with the external magnetic field [128, 133]. In this case, the magnitude of transverse relaxation rate will be determined by the product of the angular frequency shift $\Delta \omega = \mu_0 M_s \gamma / 3$ and the translational diffusion time of the water protons around the nanocluster, $\tau_D = R^2 / 4D$. According to the outer-sphere diffusion theory, the spin-spin relaxation occurs in the motional averaging regime (MAR) when $\Delta \omega \tau_D < 1$; however, when the motional averaging

Figure 18: Schematics depicting the evolution of the spin alignment involving the tetrahedral (Td) and octahedral (Oh) interstices in the spinel structure of the undoped ($x=0$) and Zn$^{2+}$-doped ($x=0.2$ and 0.4) ferrite nanocrystals under an applied magnetic field (A). Saturation magnetization, $M_s$ (B) and transverse relaxation rate, $r_2$ (C) for different levels of Zn$^{2+}$ doping. Reprinted with permission from Ref. [130]. Copyright (2009), John Wiley and Sons.
conditions break, the $T_2$ is given by the static dephasing regime (SDR) (Figure 19A) [128, 133, 134]. The $r_2$ increases with the nanocluster diameter in the so-called motional average regime (MAR); then, a plateau with a maximum value is attained in the static dephasing regime (SDR) and finally decreases in the echo-limiting regime (ELR) (Figure 19A).

In view of the above, an elaborate model proposed by Vuong et al. for the prediction of the evolution of $r_2$, in addition to the size (hydrodynamic diameter) and the $M_s$ of the nanoclusters, has successfully introduced the magnetic material volume fraction ($\phi$) inside the nanoclusters as a third, significant mediating parameter [135]. The model utilizes the classical MAR and SDR assumptions and takes into account the structural and magnetic parameters of the cluster-like ensembles. Importantly, it can account for the experimental data when the relaxivities are appropriately normalized by means of the intracluster magnetic material volume fraction.

The validity of the proposed models have been verified experimentally by superparamagnetic magnetite nanoclusters (of 13 nm–180 nm diameter) capped with a polyacrylate polymer (Figure 19B) [25] and by ferrimagnetic maghemite nanoclusters of 50 and 86 nm diameter (red and black symbols, respectively) [127]. MAR, motional averaging regime; SDR, static dephasing regime; ELR, echo-limiting regime.

Figure 19: (A) Computer-generated variation of the transverse relaxivity ($r_2 = 1/T_2$) on the translational diffusion time $\tau_D$ ($\tau_D \sim R^2$; $R$ the radius of the nanoclusters), for different echo times ranging from 0.1 to 20 ms, as predicted by the outer-sphere relaxation theory [128]. Experimental data for (B) superparamagnetic polyacrylate capped magnetite nanoclusters [25] and (C) for ferrimagnetic maghemite nanoclusters of 50 and 86 nm diameter (red and black symbols, respectively) [127]. MAR, motional averaging regime; SDR, static dephasing regime; ELR, echo-limiting regime.

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of the infected tissues [97, 139–141]. The heat-generation mechanisms can be attributed to two different phenomena: magnetic moment relaxation and hysteresis loss. The relaxation is of two types: Néel (spin rotation) and Brown (whole particle rotation), which take place simultaneously [141]. The relaxation time, $\tau$, of spins within a nanocrystal with hydrodynamic volume $V$ is given by the equation:

$$
\frac{1}{\tau} = \frac{1}{\tau_N} + \frac{1}{\tau_B} + \frac{k_B T}{3nV}
$$

where $\tau_N$ is the Néel relaxation time, $\tau_B$ is the Brownian relaxation time, $\tau_0$ is the attempt time, $K$ is the magnetic anisotropy constant, $T$ is the absolute temperature, $k_B$ is the Boltzmann constant, and $n$ is the viscosity constant of the surrounding medium [142]. A calculation based on the possible relaxation times leads to the determination of the heat dissipation in the surroundings. This is represented by the specific loss power (SLP) [131] according to the equation:

$$
\text{SLP} = \mu_0 H M \times L(x) \omega^2 \tau
$$

where $M_s$ is the saturation magnetization, $\mu_0$ is the vacuum permeability, $H$ is the ac magnetic field strength, $\rho$ is the density of the magnetic material, $L(x)$ is the Langevin function, and $\omega$ is the angular frequency.

As the SLP increases with the frequency and the strength of the external magnetic field, someone would expect that we could increase indefinitely the field control parameters to gain more efficient heat release. However, humans cannot tolerate alternating magnetic field with a large $H$-$f$ product, due to unwanted side effects. An alternative way to attain a better efficiency, with a lower dose and milder magnetic field conditions, is to optimize the size of the magnetic particle mediators [143, 144], as well as to improve their magnetic characteristics ($M_s$, $H_c$, $K$) by tuning the composition [97, 130], shape [66], and morphology [30, 145]. Broadly speaking, the SLP values go through a maximum at a certain particle size and magnetic anisotropy constant. Therefore, magnetic nanoparticles with high $M_s$ values, an optimal $K$, and high size monodispersity (SLP$^{-1}/\sigma$, where $\sigma$ the size distribution) are desirable for effective hyperthermia [131].

In view of these, it is clear that different mechanisms may be responsible for the heat release at the surrounding regions when magnetic nanocrystals are exposed at an ac magnetic field. These mechanisms are strongly related to the characteristics of the nanocrystals, as these are reflected in their magnetic state and the microscopic mechanisms establishing it. For example, ferromagnetic nanocrystals release heat by the hysteresis loss mechanism ($P_{FM} = \mu_0 f \dot{\Phi} H \, dM$), with the amount of generated
heat being proportional to the applied frequency ($f$) and the area of the hysteresis loop ($-2\mu_0 M_s H_c$) [139]. Qualitatively, the evolution of SLP in this case may follow the variation of $H_c$ with the physical dimensions (Figure 20). Superparamagnetic nanocrystals, on the other hand, produce heat through Néel and Brown relaxation mechanisms ($P_{\text{SPM}} = \mu_0 \pi f \chi'' H^2$). The Néel relaxation scales with the magnetic anisotropy energy barrier ($-K_V$) that must be overcome for the magnetization reversal of a particle (equation 9) (Figure 8). At the same time, the Brownian relaxation time increases with the viscosity of the surrounding medium, $n$ [146], as well as with the global diameter of the nanocrystal, $D$ (equation 9). Theoretical models proposed for a suspension of non-interacting particles in the blood have indicated the dominant role of the Néel relaxation for nanoparticles in the size range of 6–10 nm, while pointed to the efficiency of the Brownian relaxation for larger particles [147]. Even though the magnetic anisotropy and the microscopic mechanisms involved among strongly correlated particles are known to play an important role in their magnetic state, understanding the physical processes responsible for the heat response in nanoscale cluster-like systems is still limited.

Their unique magnetic properties together with the ability to synthesize size and composition-tunable nanocrystals proved a strong motivation for their study as potential heat mediators in magnetic hyperthermia [13, 30–32, 88, 93, 97, 140, 148]. An enhanced SLP value of 1175 W/g has been found for maghemite nanoclusters under an alternating magnetic field of 21.5 kAm$^{-1}$ (at a frequency of 700 kHz) [30]. This value is similar to that observed for nanocrystals of enhanced magnetic anisotropy (nanocubes of 20 nm) [60]. Interestingly, the superparamagnetic multibranched Mn-Zn ferrite nanoclusters (Figure 2C) have the higher SLP value compared to spherical, cubic, or star-like individual nanocrystals of the same chemical phase [88]. In addition, nanoclusters of stoichiometric spinel ferrites (i.e. MnFe$_2$O$_4$ and ZnFe$_2$O$_4$) have shown an enhanced heating efficiency compared to those of non-stoichiometric (Mn$\text{$_{1-x}$}$Zn$_{x}$Fe$_2$O$_4$) character, therefore, indicating the influence of the composition on the heating efficiency of a nanoscale system [97]. Preliminary in vitro magnetic hyperthermia experiments of amine-capped magnetite nanoclusters or polymer-capped Mn-Zn ferrite nanoclusters are highly promising. These nanomaterials have displayed a successful ability to kill cancer cells (74–90% dead cells) [93] even in a very short time (within 15 min) [97]. Furthermore, in vivo studies of hyperthermia treatment with PEGylated nanoclusters modified by folic acid have shown that with the application of a moderate ac magnetic field of 8 kA/m (at $f$=230 kHz) to a mouse, 1 day after the intravenous injection of the nanoclusters, significantly inhibited tumor growth (Figure 21) [140].

In a fashion analogous to the evolution of MRI relaxivities, a range of morphologies (Figure 20), associated with different magnetic material volume fractions, variable strength dipolar interactions, and emerging microscopic mechanisms (see Section 3.2) were shown to impact heat release. The SLP has been found enhanced compared to that of individual nanocrystals when superparamagnetic nanoclusters were capped with amine [30], while the opposite effect was observed for superparamagnetic nanocrystals embedded in polystyrene (PS) nanospheres [145]. Calculation of Néel and Brown relaxation times in the latter unveiled that the Néel relaxation is faster than the Brownian and shorter than the measurement time [145]. These calculations indicated that the Néel relaxation is the leading mechanism together with the hysteresis losses for hyperthermia heating [145, 148]. The dissimilar variation of the SLP upon the applied magnetic field strength, namely, being proportional to $H$ for the amine-capped clusters [30] and to $H^2$ for the PS-encapsulated nanoclusters [145] reveal that the interactions among nanocrystals are mainly present in the first case. The existence of dipole-dipole interactions in this type of clusters has also been proven from the decrease in the SLP with the particle concentration. In view of the above, the SLP of the aforementioned amine-capped nanocluster system has been found enhanced (1175 W/g, under a field of 21.5 kAm$^{-1}$, at 700 kHz) [18] compared to the superparamagnetic commercial product Endorem® (115 W/g, under a field of 37.3 kA/m, at 500 kHz) [149]. Interestingly, the heating efficiency of the latter is shown to be much reduced compared
to superparamagnetic iron oxide nanocrystals, a consequence of its broad size distribution and poorer crystallinity, both originating from its synthesis protocol [150, 151].

A large effort has been placed in order to develop theoretical frameworks that could explain the dipole-dipole effect on the heat release and its consequence for improved hyperthermia. The discrepancy between the theoretical model for the prediction of the SLP, as derived on the basis of the Stoner-Wohlfarth model and numerical simulations based only on magneto-structural intrinsic parameters (i.e. volume of nanocrystals, magnetic anisotropy, and saturation magnetization), as well as experimental data have all revealed the necessity of models where the dipolar interactions must be taken into account [143]. Along these lines, a theoretical model proposed by Singh et al. attempted to explain the emergence of ferromagnetism when nanocrystals are assembled together [147]. When the number of the particles increases in a blood suspension, the particles interact via dipole-dipole coupling to produce a dipolar field \( H_d \) and subsequently a permanent dipole moment. A clear transition from the paramagnetic Langevin behavior at a lower concentration \( H_d=0 \) to the emergence of hysteresis loop contributions at higher concentration \( H_d=0 \) has been observed. The heat dissipation in the latter case is several orders of magnitude greater than in the case of non-interacting particles.

In addition to the SLP enhancement because of dipolar interaction effects, the exact way in which this type of mechanism affects the dynamics of a system, and as a result, the heat dissipation in hyperthermia experiments has been the aim of models developed by Haase et al. [152] and Landi et al. [153]. The former group of authors followed an approach based on the Landau-Lifschitz-Gilbert equation of motion; having included Langevin dynamics for the thermal response, a decreased hysteresis area and a reduced heating effect have been found for the systems of high concentration [152]. The second team of authors, having included dipolar interactions in the Fokker-Planck equation, which describes the time evolution of the system, indicated that even moderate changes in the particle concentration may have significant effect on the heat dissipation [153]. The thermal response first increases up to a point where the dipolar interactions become comparable with the anisotropy field, after which it starts to decrease with the concentration in this second model [153].

In view of such observations, there is increasing theoretical interest to find the optimum particle concentration (in terms of the magnetic material volume fraction) that can be of great value for the development of efficient magnetic hyperthermia applications [148]. Materials-design criteria can then be developed so that we can employ the dipolar interactions as an avenue that operates for the benefit of raised heating response with nanocluster systems.

### 4.1.3 Nanoclusters as drug carriers in site-specific drug delivery

The utilization of magnetic nanocrystals especially ferrite nanocrystals as carriers for site-specific drug delivery has been the subject of extended interest in late years. Usually, a magnetic drug nanocarrier consisted of a magnetic core capped with an organic shell in which the therapeutic drugs are integrated [131, 139, 154–156]. In principle, the drug nanocarriers should possess a high surface area to maximize drug loading and attain strong magnetic response for easy manipulation and separation from the blood by utilizing an external magnetic field. The small nanocrystals in the range of a few nm exhibit weak magnetic response, thus, making difficult their manipulation in a physiological fluid. This technological requirement can be addressed by introducing nanoclusters, with enhanced magnetic properties. Additionally, the carrier’s porous structure may offer an extended surface accessible for drug loading, effectively leading to a more efficient drug delivery. It must be pointed out that except the magnetic nature of the carrier, there is a number of issues requiring optimization when dealing with this type of biomedical applications. Among them, toxicity, stability, and site-specific binding are factors that should be taken into account by means of rational choice of the capping shell during the carrier developing stages.

Ferrite nanoclusters, well-dispersed and stable in a physiological media have been studied for their potential use as nanocarriers in magnetically controlled drug delivery by encapsulating chemically diverse drug agents; some of them include ibuprofen (typical antiinflammatory drug) [35], tamoxifen citrate (anti-estrogen drug for the treatment of breast cancer) [95], doxorubicin (anticancer drug) [29, 33, 95], multicationic drug gentamicin (aminoglycoside antibiotic) [24], and paclitaxel (anticancer drug) [26]. Bearing in mind the porous-like structure of the nanoscale clusters, their ability to enhance the drug-loading efficacy (up to ~40% wt) has also been demonstrated [24, 26].

Such systems have been found to present enhanced relaxivity, thus, having the great advantage to enable us monitoring the drug biodistribution via magnetic resonance imaging, while at the same time, they do not undermine their capacity to be employed for medical diagnostic purposes and ultimately for treatment of patients [24, 29, 95].
4.2 Magnetically mediated photonic crystals

On another account, the utilization of magnetic nanocrystals as building blocks to develop magnetically mediated photonic crystals has been shown. Such a diverse technological perspective has been explored over the last 15 years on the basis of superparamagnetic iron oxide (~10 nm) [157, 158] or ferromagnetic cobalt ferrite (~20 nm) [159] nanocrystals encapsulated in polystyrene spheres (~120–150 nm). These particles were shown to arrange in chain-like structures when guided by an external magnetic field, therefore, operating as functional components for the construction of photonic crystals. In effect, the spacing between the particle chains in liquid media could be tuned by the strength of the applied field. As a result, tunable light-diffraction conditions could be attained that, in turn, allow for the modifying the photonic response of the system in the visible part of the spectrum.

More recently, superparamagnetic colloidal ferrite nanoclusters have been employed in photonic applications [16, 77, 92]. These size-tunable nanoclusters retain their superparamagnetism, while possessing a much higher saturation magnetization than individual nanocrystals. Their advantageous capping molecule (polyacrylic acid) renders them highly dispersed in aqueous media where they can form a photonic crystal directly. Their strikingly colorful optical response (Figure 22A) is the outcome of their directed assembly in chain-like structures stabilized by the balance of attractive magnetic \( F_{at} = 6(\mu^2/d^6) \), where \( \mu \) is the magnetic moment of the nanoclusters, and \( d \) is the distance between the clusters in the chains) and repulsive electrostatic \( F_{el} = \pi \varepsilon \zeta^2 \kappa D e^{-\kappa h} \), where \( \varepsilon \) is the dielectric constant of the medium, \( \zeta \) is the \( \zeta \) potential of the cluster, \( \kappa \) is the Debye-Hückel length, \( h \) is the distance between the nanoclusters chains, and \( D \) is the diameter of the nanoclusters) forces under an application of an external magnetic field [160].

These nanoclusters, when dispersed in aqueous media, diffract the visible light (Figure 22A), while the optical reflectivity of the system blue shifts (730–450 nm) by controlling the field strength (85–350 G) at the solution position (Figure 22B) [77]. In terms of their potential implementation in photonics, it is worth noting that the material can achieve a widely tunable diffraction wavelength range, which depends critically on the size of the nanoclusters. Clusters of large size (>160 nm) preferentially diffract the red light at relatively weak magnetic fields, while the smaller nanoclusters (<100 nm) diffract the blue part of the spectrum at stronger magnetic fields [77]. Similar optical behavior has been observed in aqueous solution of Zn-based ferrite nanoclusters [16]. Furthermore, a layer of SiO\(_2\) around the magnetic nanoclusters has been grown with the purpose to improve their long-term colloidal stability [20, 161]. In effect, a solvation

Figure 22: (A) Photographs taken under an increasing external magnetic field strength (85–350 G, from left to the right) for magnetite nanocluster aqueous solutions contained in a vial [77]. (B) UV-reflectance spectra from the same solution [77]. Films of nanoclusters embedded in a resin [91] (C) and in PDMS after photopolymerization [76] (D) under an applied magnetic field. (A) Reprinted with permission from Ref. [77]. Copyright (2007), John Wiley and Sons. (B) Reprinted with permission from Ref. [77]. Copyright (2007), John Wiley and Sons. (C) Reprinted (adapted) with permission from Ref. [91]. Copyright (2009), American Chemical Society. (D) Reprinted (adapted) with permission from Ref. [76]. Copyright (2012), American Chemical Society.
layer around the silica-covered particle is formed through hydrogen bonding, and the modified nanoclusters can now be directed to assemble to non-aqueous solutions, such as alkanols [161]. The electrostatic interactions in this case are weak, and a strong repulsive solvation force develops to balance the magnetic forces. Although the direct manipulation of such photonic crystals, entailing colloidal particle dispersions, may prove somewhat challenging, this difficulty can be overcome by embedding the nanoclusters in appropriate matrices, such as a resin [91] or PDMS [20, 76] (Figure 22C, D). The subsequent photopolymerization process of the matrix polymer can be utilized in order to “freeze” the nanocluster chain-like structure and enhance their capability for photonic technologies.

4.3 Magnetically recoverable catalysts

Although numerous active and selective homogeneous catalysts are described in literature, <20% of such processes are used in industry, while heterogeneous catalysis is clearly prevailing [90, 162]. This should be ascribed to the difficulty of the separation of homogeneous catalysts from reaction solutions. The separation can be performed, but it is time and energy consuming [163], often with environmental implications. In view of this complication, magnetically recoverable catalysts have attracted considerable attention due to their potential to combine catalytic properties and efficient materials’ recovery, thus, minimizing the total cost [164–171] and help preserve the environment. Generally, the magnetically recoverable catalysts consisted of a magnetic part and a noble metal. In the bulk noble metal catalysts, the metal particles tend to aggregate during the reaction process leading to the reduction of the catalytic activity. However, multifunctional, Fe₃O₄-noble metal hybrid nanoclusters present ideal nanomaterials to overcome this limitation. High density of well-separated metallic nanoparticles could be formed and supported at specific sites on the porous surface of the nanoclusters [89, 90]. These hybrid nanostructures could then exhibit high catalytic performance and fast recovery in the presence of an external magnetic field.

In one such promising recent example, a magnetically recoverable catalyst was obtained via encapsulation of Pd nanocrystals in dendron/dendrimer shells of ferrimagnetic magnetite nanoclusters, which subsequently was tested for its functionality in the selective hydrogenation of dimethylethynylcarbinol to dimethylvinylcarbinol [89]. The catalytic activity in these systems depends on the dendrimer generation, which determines the specific sites for the growth of the Pd nanocrystals as well as their size. The highest turnover frequency in the hydrogenation was found for an optimum Pd nanocrystal size around ~1.5 nm [89, 90]. The catalytic activity was also examined for larger (~3 nm) and smaller (~0.9 nm) Pd nanocrystals, but the catalytic performance was proven weaker [89]. Importantly, the stability of this system has been demonstrated by its repeated use in up to three catalytic cycles.

Building upon the complexity of the nanostructure and its impact on the catalytic functionality, Ge et al. studied magnetite nanoclusters covered with silica, which was also decorated with many satellite silica-Au hybrid spheres for the efficient reduction of 4-nitrophenol [19]. The magnetic core was grafted with a thick layer of poly(N-isopropylacrylamide) in which the silica particles were incorporated. Au nanoparticles were grown on the surface of the silica particles, thus, forming the catalytic sectors. These nanoclusters, with the strong magnetic response, could produce efficient magnetic separation, while on the other hand, the multiple silica spheres provided the surface for high loading of catalytically active species (Au).

5 Perspectives

The recent progress on complex colloidal systems of individual nanocrystals arranged in tailored cluster-like structures has been reviewed. Nanoclusters of this type are a unique model system for fundamental studies when compared to nanocrystals that are either packed in powders or organized in two-dimensional superlattices. It is characterized by higher dimensionality of interactions, which, however, are still mediated by nanoscale features. With their varying packing density, the individual nanocrystals in the clusters experience interactions which affect the collective macroscopic behavior, postulating to a hierarchy of length-scale-dependent mechanisms. The co-existence of these within the same particle ensemble is shown to require a combination of commonly accessible probing methods for their characterization. Based upon these, it has been clearly revealed that the bulk magnetic state of the nanoclusters is strongly mediated by the underlined dynamical processes. Several groups have shown that the latter are critically dependent on the component particle magnetic anisotropy (including size, shape, crystalline phase, and surface spin disorder), as well as the possible inter-particle interactions. In view of these, there are a number of issues to be explored before the full potential of magnetic nanoclusters is realized in practical applications.
One such challenge pertains to the systematic study of the evaluation of spin dynamics in nanoclusters designed to carry a different type of magnetic anisotropy and varying inter-particle interactions. The former could be modified by tuning the size and shape of the incorporated nanocrystal units or importantly by choosing the chemical composition and its associated structural polytype. On the other hand, the inter-particle interactions may be altered by raising the magnetic phase volume fraction or by selecting the capping molecules, which would determine the inter-particle spacing. Such tunable nanostructures can be obtained upon careful modification of the chemical synthesis parameters, with the single-step avenues likely offering a quick and wide (against multi-step protocols) phase-space exploration.

On another account, the magnetic anisotropy of the nanoclusters could be also effectively modified in favor of applications by means of magnetic exchange coupling imposed by appropriately engineered surfaces and interfaces carried by the incorporated particle subunits. The morphological evolution of the latter (not only in terms of shape) from single- to multi-material systems of core@shell-type would further promote the enhanced magnetic properties of the nanoclusters, in terms of saturation magnetization and coercivity.

Rationalization of experimental results would require synergy with theory. Such a prerequisite would be indispensable, as spin-dynamical processes are difficult to disentangle when surface spin disorder, exchange, or dipole-dipole interactions appear to be simultaneously active in colloidal nanoassemblies. The fundamental understanding of their origin is expected to help in optimizing those magneto-structural attributes, which are set out by the application-specific requirements (for example, high MRI contrast quality or enhanced heat response in magnetic hyperthermia). Moreover, the dimension of the system as a modular surface chemistry carrier could offer economical alternatives for studies with antibodies or molecules for efficient targeted drug delivery or bio-marking.

The synthetic pathways for the development of such functional nanoclusters require that we follow and understand the evolution of their properties upon the assembly of their subunits. This may also require that we move beyond traditional lab-based techniques with insufficient spatial resolution and utilize unique sets of state-of-the-art characterization tools that can cover multiple length scales ranging from the nanometer dimensions of the individual constituent nanoparticles to the <100 nm mesoscopic scale relevant to the clusters themselves. A few of such high-resolution tools that can strengthen our armory include (i) STEM mode capabilities of electron microscopy to analyze the surface spin-canting effects. (ii) 3D high-resolution electron tomography, combined with micromagnetic calculations to unveil the intracommune interactions. (iii) Soft X-ray spectromicroscopy at synchrotron sources to quantify element-specific magnetic moments. (iv) Atomic pair distribution function (PDF) data with high-Q resolution (in synchrotron or neutron science labs) to complement traditional crystallographic approaches in order to uncover the role of intermediate (∼1 nm, at surfaces and interfaces) and longer length-scale (>10 nm, particle-particle order) structural modifications on properties.

In this review, we have summarized the recent progress in the field of colloidal magnetic nanocrystal clusters. Such nanomaterials could be mostly challenging from a fundamental point of view, as well as because of their technological advantages especially in view of their exploitation in biomedical applications. Theranostic agents could emerge with significant socioeconomic impact to current procedures in diagnosis and therapy, in addition to the potential for the development of novel products in the multibillion dollar pharmaceutical and healthcare markets.

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Out of the list of other references, the following ones can be retrieved:


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