Zn- and (Mn, Zn)-substituted versus unsubstituted magnetite nanoparticles: structural, magnetic and hyperthermic properties

N Jović Orsini1, M M Milić1 and T E Torres2

1 Institute of Nuclear Sciences ‘Vinča’, Laboratory of Theoretical Physics and Condensed Matter Physics (020), University of Belgrade, PO Box 522, RS-11001 Belgrade, Serbia
2 Instituto de Nanociencia de Aragón and Departamento de Física de la Materia Condensada, Universidad de Zaragoza, Mariano Esquillor s/n, E-500018, Zaragoza, Spain

E-mail: natasaj@vin.bg.ac.rs

Received 11 July 2019, revised 19 December 2019
Accepted for publication 17 February 2020
Published 13 March 2020

Abstract

In this work, we studied structural and magnetic properties of 18 nm sized Zn-substituted magnetite, 28 nm sized unsubstituted and 17 nm sized (Mn, Zn)-substituted iron oxide nanoparticles, synthesized by thermal decomposition method. Their features were examined by analyzing the x-ray diffraction data, $^{57}$Fe Mössbauer spectra and magnetization measurements by SQUID interferometer. The microstructure was inspected comparing the different size and strain broadening models incorporated into Fullprof software. In terms of crystallinity and size dispersion, applied synthesis protocol shows superiority over decomposition of iron oleate and the co-precipitation synthesis route. The saturation magnetization at $T = 5$ K was found to be within the $M_S = 91.2$–98.6 A m$^2$ kg$^{-1}$ range, while at 300 K $M_S$ of pure and Zn-substituted Fe$_3$O$_4$ nanoparticles is 83.6 and 86.2 A m$^2$ kg$^{-1}$, respectively. Effective magnetic anisotropy constant $K_{eff}$, estimated under slow measurements by SQUID, is below 20 kJ m$^{-3}$ in all three samples. Some preliminary measurements of the magnetic hyperthermia performance, expressed via specific absorption rate value showed that the best heating performances were displayed by 18 nm sized oleic acid-coated Zn$_{0.13}$Fe$_{2.87}$O$_4$ cubo-octahedrons with SAR $\cong$ 425 W/gFe at $H_0 = 20$ kA m$^{-1}$ and $f = 228$ kHz.

Supplementary material for this article is available online

Keywords: magnetite-based nanoparticles, Mössbauer spectroscopy, magnetic hyperthermia, microstructure

(Some figures may appear in colour only in the online journal)

1. Introduction

Magnetite (Fe$_3$O$_4$) and a series of mixed spinel ferrites (MOFe$_2$O$_3$, M being the divalent transition metal cations) have been of a technological and scientific interest for a long time. Their nanoparticulate forms have been exploited in medicine and new technologies in the last decades [1–4]. Due to the satisfied biocompatibility and biodegradability, ferrofluids based on superparamagnetic iron oxide-based nanoparticles (IONPs) have high potential for applications in medical diagnostic and curing procedures, particularly as contrast media for biomedical imaging (magnetic particle (MPI) or resonance (MRI) imaging) [5, 6] as magnetically-driven drug/gene delivery systems [7] or magnetic thermo-seeds for magnetic particle hyperthermia (MPH) treatment of ill tissues [7–12]. Other iron oxide-based nanostructures, such
as dumbbell, porous, core/shell, hollow or hybrid ones, have been also investigated for biomedical applications [13].

The applicability of the magnetic nanoparticles in biomedicine is closely related to their own characteristics such as magnetic and microstructural features (e.g. size and shape, surface chemistry, composition, degree of crystallinity). Another important item, which should be considered regarding their bio-applicability is the way how MNPs interact with cells. The magnetic properties of nanoparticles are usually altered in in vivo conditions due to the unavoidable nanoparticle’s clustering and movement restriction after interaction with cells [14]. Consequently, their biomedical performances are changed.

One of the promising application of superparamagnetic IONPs is their use for magnetic hyperthermia therapy [7–12]. Under exposure to an alternating magnetic field, superparamagnetic IONPs suspended in a fluid can absorb energy from the applied AC magnetic field and release it as heat. If they are properly functionalized and located in ill tissues, they will be able to inhibit activity of cancer cells by locally increasing temperature [7, 12]. To improve the heating efficiency, IONPs should possess the optimal size and shape, narrow size distribution and enhanced magnetic performances (e.g. high $M_s$ and $K_{eff}$ value). In recent years, remarkable achievements in tailoring the optimal size and shape of nanoparticles have been accomplished [9, 10, 15, 16]. Once that the particle size close to the critical value (related to the transition from superparamagnetic to ferrimagnetic regime) is reached, further increase of the heating efficiency can be achieved by changing the composition of IONPs from pure $(\text{Fe}_3\text{O}_4)$ toward substituted-magnetite $(\text{Fe}_{3-x}\text{M}_x\text{O}_4)$ nanoparticles [1, 5, 17]. It was shown that Zn-substituted $\text{Fe}_3\text{O}_4$ nanoparticles represent one of the best choices, due to the low toxicity of Zn ions and the positive impact of Zn-ion substitution on the magnetic saturation value. Magnetite is a typical inverse spinel with one half of $\text{Fe}^{3+}$ ions in tetrahedral (A) sites, and the second half of $\text{Fe}^{3+}$ and all $\text{Fe}^{2+}$ ions in octahedral (B) sites. The effect of magnetic $\text{Fe}^{3+}$ ions substitution by diamagnetic $\text{Zn}^{2+}$ ones at the tetrahedral, A-sites of the spinel lattice (represented by the formula $\text{AB}_2\text{O}_4$ (S.G. Fd\text{3m})), is well known and visible by increases of the saturation magnetization, $M_s$, for doping level up to $x\approx0.4$ [18]. Relating to hyperthermia or magnetic sensing potential, superiority of cubic over spherical nanoparticles has been revealed, as well as of Zn-doped over pure $\text{Fe}_3\text{O}_4$ nanoparticles [6, 19, 20]. Recently, it has been revealed that silica-coated nonstoichiometric Gd–Zn ferrite exhibits the most promising therapeutic capability at relatively low particle concentrations [8]. Further improvement in the heating performance has been observed when $\text{Fe}_3\text{O}_4$ nanoparticles change shape and move from three-dim objects (spherical and cubic) to one-dim objects (nanorods) [15]. In terms of inter-particle interactions, Tong et al. reported that well dispersed 33 nm sized ferromagnetic iron oxide nanocrystals heat much better than their aggregates [9].

Along with magnetic properties, the microstructure of nanoparticles is important item in defining the nanoparticle’s biomedical performances [21–25]. For that reason, a closer relation between the degrees of the nanoparticles crystallinity, phase composition and the magnetic response should be established. It could give better insight into understanding of hyperthermia efficiency of magnetic nanoparticles.

In this paper, we report on the structural, magnetic and hyperthermic characteristics of three samples, composed of unsubstituted, Zn- and (Mn, Zn)-substituted $\text{Fe}_3\text{O}_4$ nanoparticles, synthesized by thermal decomposition method. We discuss the main advantages of this method (e.g. production of well crystallized nanoparticles with narrow size distribution) keeping in mind all shortcomings (use of expensive and environmentally harmful substances, need of a post-synthesis treatment to transfer nanoparticles into water, etc). The degree of crystallinity and microstrains in the samples were evaluated from refinement of the XRD data using the Fullprof program. Different combinations of the size and strain broadening models were tested (isotropic versus anisotropic), and the comparative analysis was done. Magnetic characterization of the powdered samples was performed using the Mössbauer spectroscopy and measurements by SQUID. Some preliminary measurements of the magnetic hyperthermia performance (expressed via the SAR value), were carried out on ferrofluids made of oleic acid-coated $\text{Fe}_3\text{O}_4$ nanoparticles (pure and substituted), dispersed in hexane, under physiologically tolerable AC magnetic field conditions.

2. Materials and methods

2.1. Chemicals

Iron(III) acetylacetonate $(\text{Fe(acac})_3)$, $\geqslant99.9\%$ p.a. Sigma Aldrich), zinc(II) acetylacetonate hydrate $(\text{Zn(acac})_2\text{-hydrate, Aldrich})$, zinc(II) chloride $(\text{ZnCl}_2, \geqslant97\%, \text{Sigma Aldrich})$, iron(II) chloride tetrahydrate $(\text{FeCl}_2\cdot4\text{H}_2\text{O}, \geqslant99.0\%$ p.a. Sigma Aldrich), benzyl ether (98%, Aldrich), oleic acid (technical grade, $>90\%$, Aldrich), oleylamine (technical grade, $>70\%$, Aldrich).

2.2. Synthesis of magnetite-based cuboctahedral nanoparticles

Unsubstituted and Zn- and (Mn, Zn)-substituted magnetite nanoparticles were synthesized by thermal decomposition of metal precursors (acetylacetanate and chloride salts), in benzyl ether, under bubbling of nitrogen, in the presence of oleic acid and oleylamine as surfactants. Not any reducing agent was used. The concentration of metal cations was kept constant at 0.1 mol per dm$^3$ of solvent. The molar ratios of the used reactants, given in the table 1, were set up according to the desired compositions of the products: $\text{Zn}_0.4\text{Fe}_{2.6}\text{O}_4$, in samples 1 and 2, and $\text{Mn}_0.2\text{Zn}_0.8\text{Fe}_2\text{O}_4$ in sample 3. Due to the fact that incorporation of $\text{Zn}^{2+}$ ions into a spinel structure is difficult to achieve when this synthesis route is chosen, two different sources of $\text{Zn}^{2+}$ ions were used, $\text{Zn(acac})_2$ (sample 1) or $\text{ZnCl}_2$ salt (samples 2 and 3). In the sample 2, the $\text{FeCl}_2\cdot4\text{H}_2\text{O}$ precursor was used as a source of $\text{Fe}^{2+}$ ions.
In a typical procedure, the Zn-containing sample 1 (i.e. Z18) was synthesized starting from a mixture of Zn(acac)\_2 hydrate (0.8 mmol), Fe(acac)\_3 (5.2 mmol), oleic acid (24 mmol), and 60 ml of benzyl ether (the cations-to-OA molar ratio was kept at 1:4). The mixture was poured in a three neck flask (250 ml volume) and mechanically stirred at room temperature for 30 min under nitrogen flow. The heating started, first up to 200 °C, followed by aging for \( \sim 2 \) h at that temperature, and then up to the boiling temperature of the mixture (\( \sim 290 °C \)) under refluxing conditions (see figure S1, available online at stacks.iop.org/NANO/31/225707/mmmedia). A heating rate to reflux was around 8 °C min\(^{-1}\), and the reaction time was about one hour. Afterwards, the flask was removed from a heating mantle and the product of reaction was left to cool down to room temperature. The black precipitate was magnetically collected, washed two or three times in an excess of ethanol and hexane, and re-dispersed in an organic phase. The precipitation was left to cool down to room temperature. The nanoparticles morphology, average size and size distribution were obtained after precipitation of nano-powdered specimens of the prepared samples, used for characterization, were obtained using a scanning electron microscope connected with an EDX analysis unit.

XRD patterns of all three samples were collected using Rigaku SmartLab diffractometer and Cu K\( \alpha \) and K\( \beta \) radiation. The XRD data were collected in a 2\( \theta \) range between 10° and 90° or 100°, with the step-size of 0.02°, and a speed counting rate of 0.2° s. The collected data were fitted using the program Fullprof based on the Rietveld method. Both, structural and microstructural parameters were refined for all samples in the space group Fd\( \bar{3} \)m (No.227), assuming a spinel structure. XRD peak profiles were modeled by the Thomson–Cox–Hasting modified pseudo-Voigt (TCH-pV) function. A correction for instrumental broadening was done considering the experimental profile as a convolution of the instrumental profile and the specimen profile. The instrumental resolution function (IRF) was obtained upon refinement of the standard, lanthanum hexaboride (LaB\(_6\)). Following structural parameters: lattice constant,\( a \), fractional coordinates for oxygen in 32e site and isotropic displacement parameters,\( B \), as well as microstructural parameters: the average crystallite size,\( d_{\text{XRD}} \), and microstrain, were fitted. The background was refined using linear interpolation between selected points.

Magnetic properties of the samples were studied using the Mössbauer spectroscopy and measurements of the magnetization by MPMS XL-5 SQUID magnetometer. The Mössbauer spectra of samples were collected at room temperature, in transmission geometry using a \( ^{57}\text{Fe} \) source. Field-cooled (FC) and zero-field-cooled (ZFC) DC magnetization measurements were performed in a magnetic field of 7.96 kA m\(^{-1} \) (100 Oe), in the 5–300 K temperature range, following standard protocol. Hysteresis loops,\( M(H) \), were recorded at 5 and 300 K at magnetic field up to 3978.88 kA m\(^{-1} \) (50 kOe). To calculate the mass magnetization accurately, the thermogravimetric analysis (TGA) and the differential thermal analysis (DTA) were employed using a TA SDT 2960 instrument. TGA/DTA analysis was performed in air, at a heating rate of 10 °C min\(^{-1} \), up to 700 °C. The weight loss due to evaporation of organic phase (in wt%), obtained by the TGA/DTA analysis, was re-calculated taking into account that during heating the partial oxidation takes place, bringing in a mixture of hematite and magnetite phases (proved by the XRD analysis of thermally treated samples; not shown).

**Table 1.** Molar ratios of metal precursors, oleic acid (OA) and oleylamine (OM), dissolved in 60 ml of benzyl ether.

| Sample | Zn(acac)\(_2 \) hydrate (mmol) | Fe(acac)\(_3 \) (mmol) | MnCl\(_2\)-4H\(_2\)O (mmol) | ZnCl\(_2\) (mmol) | FeCl\(_3\)·3H\(_2\)O (mmol) | OA (mmol) | OM (mmol) | Actual stoichiometry (EDX) |
|--------|-------------------------------|------------------------|-----------------|-----------------|------------------------|---------|---------|--------------------------|
| 1-Z18  | 0.8                           | 5.2                    | —               | —               | —                      | 24      | —       | Zn\(_{0.18}\)Fe\(_{2.85}\)O\(_4\) |
| 2-F28  | —                             | 4                      | —               | —               | 0.8                    | 1.2     | 18      | Fe\(_3\)O\(_4\)            |
| 3-MZ17 | —                             | 4                      | 1               | 1               | —                      | 18      | 18      | Mn\(_{0.98}\)Zn\(_{0.02}\)Fe\(_{2.9}\)O\(_4\) |

2.3. Characterization

Morphology, structure, microstructure and composition of the samples were analyzed by transmission electron microscopy (TEM), x-ray diffraction (XRD) and energy-dispersion x-ray (EDX) spectroscopy. Magnetic properties were studied from \( ^{57}\text{Fe} \) Mössbauer spectra analysis and the temperature and field dependence of magnetization (measured by SQUID). The powdered specimens of the prepared samples, used for characterization, were obtained after precipitation of nanocrystals from hexane upon adding ethanol and drying under nitrogen flow.

TEM (FEI TECNAI T20, 200 kV) and HRTEM (FEI TECNAI T30, 300 kV) microscopes were used to examine the nanoparticles morphology, average size and size distribution. Nanoparticle specimens for TEM were prepared by placing a drop of a diluted solution (in hexane) onto a carbon-coated copper grid. Images were analyzed using the Digital Micrograph program. To estimate the average particle size from TEM, between 200 and 400 nanoparticles were counted.
nanoparticles (1, 2, and 3) dispersed in hexane, were done using a calorimetric analyzer (DM 100 Series, by nBunaNanoScale Biomagnetics, Spain). The specific absorption rate (SAR) of all samples was determined from the measurement of the temperature rise in time, \( T(t) \), when the ferrofluids (previously placed in a 2 ml glass holder) were exposed to an alternating magnetic field, \( H = H_0 \sin(\omega t) \) (\( H_0 \)—is the magnetic field amplitude, and \( \omega \)—is an angular velocity) [7].

The \( T(t) \) curves were recorded using an optical fiber temperature probe immersed inside the ferrofluids. During the measurements, a glass holder with ferrofluids 1 and 2 was placed in a high-vacuum environment allowing us to consider almost adiabatic conditions of SAR measurements. The \( T(t) \) curves for ferrofluid 3 were recorded five months later under slightly different conditions (frequency was 252 kHz instead of 228 kHz and without vacuum isolation). The following expression was used to estimate SAR value:

\[
\text{SAR}(W/g_e) \cong \rho_{\text{hexane}} \times c_{\text{hexane}} \times (\Delta T/\Delta t)_{\text{max}} \times [x_{\text{Fe}}]^{-1},
\]

where \( \rho_{\text{hexane}} = 654.8 \text{ kg m}^{-3} \) is the density and \( c_{\text{hexane}} = 2.26 \text{ J g}^{-1} \text{ °C} \) is the specific heat capacity of hexane, \( (\Delta T/\Delta t)_{\text{max}} \) is the initial slope of the heating curve \( T(t) \) and \([x_{\text{Fe}}] \) is the average concentration of Fe\(^{3+}\) ions in ferrofluids. The \( [x_{\text{Fe}}] \) was determined comparing the UV–vis absorbance of Fe\(^{3+}\) ions from sample solutions (after oxidation) with the calibration curve measured using the UV- absorbance of patron solutions of known, but different Fe\(^{3+}\) concentrations [26].

Patron solutions were prepared from iron standard solution (in a mixture of 6M H\(_2\)SO\(_4\) and 65% HNO\(_3\)). The absorbance was measured by UV–visible spectrometer when solution was exposed to irradiation (\( \lambda = 480 \text{ nm} \)).

### 2.4. Rietveld refinement

The structural and microstructural parameters of Zn-doped (sample 1), unsubstituted (sample 2), and (Mn, Zn)-containing (sample 3) magnetite, were refined in a model in which the stoichiometry of the samples was adjusted according to the results obtained by EDX analysis (see figure S2). The cations distribution was modeled in accordance with the preferred cations occupancy and not refined. Such an assumption is reliable since, for x-rays, ions with low electron density difference do not distinguish significantly. In the Zn- and (Mn, Zn)-containing magnetite all zinc cations occupy tetrahedrally coordinated, 8r sites (A-sites). Although in nanostructured Zn-doped magnetite (Zn\(_{x}\)Fe\(_{3-x}\)O\(_4\)), the Zn\(^{2+}\) ions can occupy both A and B sites, for \( x<0.4 \), the Zn\(^{2+}\) ions follow their high preference for tetrahedral A-sites, valid for bulk materials [5, 18]. In addition, cations distribution in the (Mn, Zn)-doped sample was previously set up in the way so that all manganese ions were considered to be +2 valence and in A-sites, even though it is known that the manganese ions can easily vary the valence state (between +2/+3), and that Mn\(^{3+}\) ions preferably occupy octahedral, B-sites (16d) [27].

After refinement of the Mössbauer spectra, the presence of Mn\(^{3+}\) ions in B-sites was allowed. The attempt to refine occupation parameters of cations and to determined the cations distribution failed due to the fact that the zinc (3d\(^{10}\)4s\(^{2}\)) and iron (3d\(^{6}\)4s\(^{2}\)) are the fourth, while manganese (3d\(^{5}\)4s\(^{2}\)) and iron are the nearest neighbors in the periodic system. As such, they are hardly distinguished for x-rays. In addition, refinement of the crystal structure solely, when pseudo-Voigt function was used to delineate diffraction profiles and the instrumental broadening was disregarded, gave very good agreement between experimental and refined XRD patterns, regardless the cations distribution over the 8a and 16d sites.

When the microstructural analysis was applied, the XRD peak profiles were modeled by the TCH-pV function and the IRF function was included (see section 2.3). Different combinations of the isotropic/anisotropic size and strain broadening were considered during refinement. An anisotropic size broadening was considered as a linear combination of spherical harmonics [28]. In the case of an anisotropic strain broadening, the Stephens parameters, \( S_{420} \) and \( S_{220} \), for m3m symmetry, were refined [28, 29].

### 3. Results and discussion

#### 3.1. Composition, morphology and size

The experimental XRD patterns of all three samples, 1, 2 and 3, are shown in the figure S3 (see supplementary Info). All reflections were indexed in a spinel structure with cubic symmetry (space group Fd-3m, No. 227). The reflection at 2θ ~32° with very low intensity (observed in all three XRD patterns), is a satellite of the major (311) spinel reflection caused by Cu Kβ radiation of wavelength 1.392 17 Å. It might be accidentally ascribed to the (100) reflection of ZnO phase. Since, no improvement in the crystal structure refinement was observed in a two phases model, ZnO phase presence was ruled out. The presence of hematite or FeO as an impurity was excluded in all three samples due to the results of Mössbauer spectra analysis (see forthcoming results).

The EDX analysis on selected surfaces of the studied samples showed that the amount of incorporated Zn and Mn ions into the spinel structure is notably lower than it was set up by the initial stoichiometry of precursors (table 1). According to it, the sample 1 is Zn-doped, the sample 2 is unsubstituted, while the sample 3 is (Mn, Zn)-containing magnetite, with the stoichiometry Zn\(_{0.13}\)Fe\(_{2.87}\)O\(_4\), Fe\(_3\)O\(_4\) and Mn\(_{0.06}\)Zn\(_{0.04}\)Fe\(_{2.8}\)O\(_4\), respectively.

TEM images of the samples 1, 2 and 3, and their size distributions are shown in figure 1. The highest uniformity of particles size and shape is achieved in the sample 1. It is evident that most of the nanoparticles are cubo-octahedra-like in shape. Nanoparticles with shapes different than those are observed in the samples 2 and 3, but significantly less in number. Average edge dimensions of the nanoparticles, obtained by fitting the size distribution with Gauss function, were found to be 18.3, 28.1 and 17.2 nm for 1, 2 and 3, respectively. According to the results of EDX and TEM analysis we re-label the samples as: 1 is Z18, 2 is F28 and 3 is MZ17, where the capital latter indicate composition, while the number indicates the average particle size.
For the sake of comparison, Zn-substituted Fe₃O₄ nanoparticles were synthesized following the classical thermal decomposition synthesis (when 1,2-hexadecanediol was used as a reducing agent). Thus obtained nanoparticles are quasi-spherical with an average diameter \( \sim 10 \text{ nm} \) (figure S4). Based on the literature data, the polyalcohol, when acting as a reducing agent, can produce polyaldehydes and polyorganic acids, whose presence during the synthesis can suppress formation of bigger nanoparticles \[30\]. Thus, partial reducing or avoiding adding of polyalcohol in the synthesis seems to be the easiest way to obtain bigger nanoparticles. In addition, by fine tuning of the cations/capping ligands molar ratio and the heating rate to reflux, it is possible to further manipulate the size and shape of nanoparticles \[16\]. Such an approach in the thermal decomposition of metal precursors becomes competitive to the co-precipitation synthesis route \[22, 23\], the two steps synthesis via decomposition of iron oleate complexes \[31, 32\], or polyol method \[33\], in the sense of designing bigger nanoparticles with high degree of crystallinity and low density of defects.

Following the above mentioned modification in the synthesis procedure, it seems that Zn²⁺ ions are built in into the spinel structure more efficiently when Zn(acac)₂ salt is used (sample 1), instead of ZnCl₂ precursor (samples 2 and 3). Generally, building-in Zn ions into the spinel structure is difficult and dependent on the used precursors for Zn ions \[5, 17, 34, 35\]. The large difference in the decomposition temperature between Zn(acac)₂ \( (T_{\text{dec}} \approx 248 \, ^\circ\text{C}) \) and Fe(acac)₃ \( (T_{\text{dec}} \approx 180 \, ^\circ\text{C}) \) salts of almost 70 \(^\circ\text{C}\), obviously impedes the incorporation of zinc ions into the spinel crystal structure \[34, 35\]. It might be also that presence of water, introduced as bounded molecules to chloride salts (in samples 2-F27 and 3-MZ17), has negative impact on this process.

3.2. Crystal structure and microstructure analysis

Rietveld analysis. The experimental XRD patterns of all three samples, Z18, F28 and MZ17, were fitted using FullProf program based on the Rietveld method. Different combinations of the isotropic/anisotropic size and strain broadening were considered during refinement of the microstructural parameters. A rather good agreement between the experimental and modeled XRD pattern was obtained when an anisotropic size broadening was considered, regardless whether the isotropic or anisotropic strain broadening was applied. For these two models, the obtained values for all refined parameters overlapped within
the standard deviations (table S1). Further improvement in the refinement (lower goodness-of-fit, GoF) was achieved when, in addition to the anisotropic size broadening (which contribute to the Lorentzian component of the profile function), we introduced a contribution of an isotropic size broadening via a Gaussian function, and kept the isotropic strain broadening model [36]. Following this model, we observed decrease of the average apparent size (App-Size) values for about 11% (in Z18 and MZ17) and 16% (in F28), and the average maximum strain values for more than 50% (Max-Strain = 1/4 apparent strain Stokes-Wilson), compared to the values obtained following previous models. The comparative analysis of the refined structural and microstructural parameters for each applied model, as well as the refined and calculated cation-oxygen bond distances and the reliability factors are given for the sample Z18 in the supplementary (table S1).

Although the best agreement between the experimental and refined XRD data (the lowest GoF) gave the model: (isotropic + anisotropic) size and isotropic strain broadening, the results presented here are obtained in the frame of the model which considers an anisotropic size broadening and an anisotropic strain broadening. One of the reasons for this is that we were able to refine all parameters simultaneously, what is not quite common situation for nanocrystals (therefore, is interesting to show). The second reason is that the shape of Z18 nanocrystallites obtained upon refinement the XRD data in this model fits in the best way the real shape of nanoparticles observed by HRTEM (figures 2(b) and (d)). The experimental and refined XRD data of the samples Z18, F28 and MZ17 applying a model which consider an anisotropic size broadening and an anisotropic strain broadening contribution, as well as the projection on xy-plane of the average crystallite size and the average maximum strain in the reciprocal space, are shown in figure 3, while the main results of the Rietveld refinement are summarized in table 2.

Lattice parameters show typical values of bulk magnetite and vary slightly by changing the composition, \( a = (8.391-8.396) \) Å. Slight increase of the lattice parameter, \( a \), in Zn-doped sample, Z18, compared to the unsubstituted magnetite, F28, indicates that the Zn\(^{2+}\) ions are incorporated into the tetrahedrally coordinated, A-sites in the spinel lattice. Oppositely, slight decrease of the lattice parameter in (Mn, Zn)-containing sample, MZ17, compared to F28, could be an indication that some Mn\(^{2+}\) ions are oxidized into Mn\(^{3+}\) and sited at octahedrally coordinated, B-sites, replacing Fe\(^{3+}\) ions.

Microstructural analysis showed that the size of coherent domains, \( \delta_{\text{XRD}} \), for applied model matches the average particle size estimated using TEM, \( \langle d\rangle_{\text{TEM}} \) (see table 2). In addition, the shape of Z18 nanocrystallites obtained upon refinement the XRD data fits the shape observed by HRTEM (figures 2(b) and (d)). A low value of the applied maximum strain (i.e., the microstrain) is obtained in all three samples indicating the low density of crystal imperfections. The low density of crystal imperfections is also confirmed in the sample Z18 by HRTEM observation (figure 2(b)). In substituted Fe\(_3\)O\(_4\) cuboctahedral nanoparticles, Z18 and MZ17, with similar particle size and substitution level, x (\( x = 0.13 \) and \( x = 0.10 \), respectively), microstrain is almost of the same order, while in the unsubstituted magnetite F28, microstrain decreases (table 2). Presumably, the density of crystal imperfections in nanocrystals synthesized by thermal decomposition method can be inversely related with a particle size and/or substitution level.

3.3. Mössbauer spectra analysis

To observe changes in the local environment of Fe ions caused by substituting Fe\(^{3+}\) ions with Zn\(^{2+}\) or (Zn\(^{2+}\)/Mn\(^{3/3+}\)) in the spinel lattice, we used the Mössbauer spectroscopy. The experimental and fitted zero-field transmission Mössbauer spectra of Z18, F28 and MZ17 samples, collected at ambient conditions, are shown in figure 4. All three spectra are composed of two magnetic components typical for magnetite, representing two inequivalent A (tetrahedral) and B (octahedral) Fe ion positions in the spinel AB\(_2\)O\(_4\) structure [37]. No characteristic paramagnetic components appear despite the nanoparticulate nature of the samples indicating that all particles are blocked at room temperature (\( T_{M}^{\text{Moss}} > RT \)) for the experimental time window of measurements defined by the Mössbauer spectroscopy (\( T_{M}^{\text{Moss}} = \gamma_{\text{Larmor}} \approx 10^{-8} - 10^{-9} \) s for \( ^{57}\text{Fe} \)). The RT spectra of samples F28, Z18 and MZ17 were fitted with two, three and four magnetic sextets, respectively, giving the best results. The fitted hyperfine parameters values are summarized in table 3.

Mössbauer spectrum of unsubstituted Fe\(_3\)O\(_4\) (F28). Mössbauer spectrum of the sample F28, which is by EDX measurements identified as unsubstituted magnetite, was fitted with two magnetic components belonging to Fe ions.
on sites with different local surrounding. The magnetic sextet \( A_1 \) with lower isomer shift, \( \delta \) and a higher hyperfine field, \( B_{hf} \) was attributed to the \( Fe^{3+} \) ions residing on the A sites. The second component, \( B_1 \) was assigned to the mixture of \( Fe^{3+} \) and \( Fe^{2+} \) ions at the B sites. The quadrupole shift, \( \varepsilon \) was find to be close to zero for both sites indicating symmetric charge distribution around iron nucleus. The values of the fit parameters are in good agreement with values reported in the literature for pure magnetite (even though the hyperfine fields are somewhat lower than the ones obtained for bulk magnetite) [38, 39]. However, the obtained ratio of spectral areas of A and B sextets, of \( R_{A/B} = 0.97 \), for \( F28 \) sample is
The results of Rietveld refinement of XRPD patterns of samples 1-Z18, 2-F28 and 3-MZ17 in the model which consider a combination of an anisotropic size broadening and an anisotropic strain broadening.

| Sample     | 1-Z18          | 2-F28          | 3-MZ17         |
|------------|----------------|----------------|----------------|
| Composition| Zn$_{0.13}$Fe$_{2.87}$O$_4$ | Fe$_3$O$_4$ | Mn$_{0.06}$Zn$_{0.02}$Fe$_{2.9}$O$_4$ |
| Occupancy set up at: | (Zn$_{0.13}$Fe$_{2.87}$)$_{2/3}$[Fe$_{0.87}$Fe$_{1.13}$]O$_4$ | [Fe$^{2+}$Fe$^{6+}$]$^4$ | (Mn$_{0.03}$Fe$_{0.06}$)$_{2/3}$[Fe$_{0.97}$Mn$_{0.03}$]$_{1/3}$ |
| Average particle size, $\langle d \rangle_{TEM}$ (nm) | 18.3 ± 4.0 | 28 ± 10 | 17.2 ± 4.8 |
| Average App-Size, $d_{XRD}$ (nm) | 19.7(2.0)$^1$ | 25.9(1.6)$^1$ | 16.1(1.1)$^1$ |
| Along [111] | 17.7 | 23.6 | 14.2 |
| Along [110] | 20.7 | 28.0 | 17.5 |
| Along [100] | 24.7 | 27.6 | 17.0 |
| Applied Max-Strain($\times 10^{-4}$) | 21(8) | 13(2) | 21(8) |
| Density, $\rho$ (g cm$^{-3}$) | 5.224 | 5.202 | 5.212 |
| Lattice constant, $a$ (Å) | 8.3965(1) | 8.3934(2) | 8.3917(1) |
| Oxygen parameter, $u$ | 0.2528(2) | 0.2518(2) | 0.2532(2) |

$^1$ Measure of anisotropy, no standard deviation.

The room temperature Mössbauer spectra of sample Z18, F28 and MZ17. In substituted samples, Z18 and MZ17, the background was adjusted with an addition of a broad singlet line (with zero quadrupole splitting). The presence of larger amount of Fe$^{3+}$ ions in the sample, indicating that the sample contains a certain amount of maghemitized magnetite [23, 42]. The broadening of the inner sextet compared to the outer one additionally indicates that our sample can be consisted of partially oxidized magnetite. Since the oxidation of magnetite is followed by the vacancy formation, the nonstoichiometric magnetite can be represented in the following form: (Fe$^{3+}$)$_{x}$(Fe$^{3+}$)$_{1-x}$O$_4$, where $x$ stand for a vacancy (it is assumed that vacancy are formed exclusively on the octahedral sites of the spinel structure) [43].

Following procedure from the paper of Costa et al [43] we were able to estimate the amount of vacancies in the sample. It was found that the chemical formula of the sample F28 can be Fe$_{2.92}$O$_4$. The estimated number of vacancies are in concordance with the previous Mössbauer studies on nonstoichiometric partially oxidized magnetite [43, 44].

Mössbauer spectrum of Zn-substituted Fe$_3$O$_4$ (Z18). It can be readily seen that, compared to unsubstituted Fe$_3$O$_4$, F28, the spectrum of Zn-doped Fe$_3$O$_4$, Z18, displays less resolved sextets which is the result of incorporation of the nonmagnetic Zn$^{2+}$ ions at A sites of the magnetite spinel structure. It was reported that for low values of Zn doping ($x < 0.4$) [18] or $x < 1/3$ [48], the Zn ions preferentially occupy A sites which leads to broadening of the B absorption lines. Namely, incorporation of nonmagnetic Zn$^{2+}$ ion at the A sites cause the break of four magnetic A–B connections [22], thus leading to the weakening of A–O–B superexchange interactions and, consequently to the lowering of hyperfine fields values. Random distribution of Zn ions on A sites produces nonuniform hyperfine fields on B-sites, thus causing significantly higher than the theoretical value 0.5 predicted for stoichiometric magnetite (this value is valid if the same recoil fraction is assumed for both A and B sites, and it can be slightly larger if the recoil fraction is assumed to be larger for A sites [37]). The literature results revealed that for Fe$_3$O$_4$, $R_{A/B} = 1.09 \pm 0.04$ at room temperature [40]. Accordingly, we could expect a possible nonstoichiometry of the sample (the intensity of B line relative to the A line reduces in nonstoichiometric magnetite [41]). This points out to the
the line broadening of inner sextets. Therefore, the Mössbauer spectrum of Zn-substituted magnetite (figure 4), with composition Zn0.13Fe2.87O4 predicted by EDX analysis, was fitted with three sextets. The sextet A1 was assigned to the Fe3+ ions at A sites, while the two sextets, B1 and B2, with higher values of the isomer shift, δ and lower hyperfine field values, \( B_{hf} \) were attributed to the Fe2+ ions residing on B sites (see table 3). Due to the decreased magnetic coupling strength between Fe3+ in A and B sites (invoked by nonmagnetic substitution on A-sites), hyperfine fields values are slightly lower for the sample Z18 compared to the sample F28. A smaller \( B_{hf} \) value of component B2 can be associated with a part of iron ions on B sites which are coupled with lower number of Fe3+ ions on A-sites. In addition, the lower isomer shift value of the components assigned to the octahedral B-sites, \( \delta_B \) (isomer shift of A sites remains almost unchanged) is due to the increased number of Fe3+ ions on the B sites. This excess of Fe3+ ions appears as a consequence of the fact that the neutral charge balance requires one Fe2+ ion on B site to be oxidized to Fe3+, for each Fe3+ on A site replaced by Zn2+ ion, or some vacancies to be generated at B sites [48]. The relative spectral area between A and B components is significantly reduced (\( R_{A/B} = 0.61 \)) in Z18, due to Fe3+ ions replacement. Here it is worth to remember that for low density of vacancies and low degree of iron substitution, the rapid electron hopping process between Fe2+ and Fe3+ ions on B-sites will not be suppressed at room temperature [49].

Mössbauer spectrum of (Mn, Zn)-substituted Fe3O4 (MF17).

The Mössbauer spectrum of the Mn and Mn ions substituted Fe3O4 sample, MF17, having stoichiometry Mn0.06Zn0.3Fe2.6O4, is drastically altered compared to the other two samples. For thus low doping, Zn2+ ions enter only A sites replacing Fe3+ ions, while the XRD analysis indicates that Mn ions probably replace Fe ions on both A- and B-sites. Nevertheless, even a small amount of Mn-substituted sample strongly affects the shape and the intensity of the spectrum [50, 51]. Replacement of iron by manganese ions is evidenced by the high broadening and decreased intensity of both, and especially inner band associated with octahedral (B) sites. A more pronounced decrease of the B component intensity can be an indication that manganese ions occupies B-sites [50], The best fit of the Mössbauer spectrum was obtained when it was fitted with four components (two for tetrahedral and two for octahedral Fe sites). Two sextets, A1 and A2, having the same value of isomer shifts (\( \delta = 0.28 \text{ mm s}^{-1} \)), but different values of hyperfine fields, are assigned to the Fe3+ ions on the A-sites with nonequivalent environments. Accordingly, part of the Fe3+ ions (A2) are subjected to hyperfine field with lower \( B_{hf} \) values, but larger quadrupole shift, \( \varepsilon \), implying slight distortion of charge symmetry around Fe3+ ions on the tetrahedral sites. It is probably due to the presence of manganese ions on B sites which introduce the Jahn–Teller distortion of crystal field symmetry [41, 51, 52]. Based on this result, in the final refinement of the XRD data of sample MZ17, the cation occupancy was set up so that some Mn ions occupy the B sites. Another set of two magnetic components, B1 and B2, with larger isomer shifts, \( \delta \) and smaller hyperfine fields, \( B_{hf} \) (table 3), were assigned to the Fe2+ and Fe3+ ions on the B-sites. The component B2 originates from parts of the lattice where iron ions have larger number of nonmagnetic ions as neighbors on A sites (therefore reduced hyperfine field), and where larger number of iron ions are oxidized to Fe3+ (therefore smaller isomer shift) [37, 53]. The other component, B1, having hyperfine parameters similar to those of pure magnetite sample, can be again ascribed to the Fe2+/Fe3+ ions on octahedral sites with electron hopping occurring in a “regular” environment, i.e. not having zinc and manganese ions as neighbors. Somewhat reduced hyperfine field values of the components assigned to the B sites is in concordance with previous findings on Mn doping decreasing the hyperfine fields for these sites [54].

In conclusion, the isomer shift values for A1, A2 and B1 components (\( \delta_{A1} \) and \( \delta_{A2(B1)} \)) were found to be almost the same in all three samples, indicating that the 57Fe ions on the tetrahedral (A) and partially on the octahedral (B1) sites of spinel lattice see no changes in the electron density with the variation in particle size and the composition. Upon substitution with Zn or (Mn, Zn) ions, broadening of the magnetic sextets was observed, inferring the introduction of additional component(s) (one for Zn- and two for (Mn, Zn)-substituted sample). The additional component, delineated to the 57Fe ions on octahedral B2 sites, has the lower \( \delta_{A2} \) value and weaken hyperfine magnetic fields, and can be explained as being due to the distortion in the B-sites invoked by

---

**Table 3.** Fitted room temperature Mössbauer parameters: \( \delta \)—isomer shift, \( B_{hf} \)—magnetic hyperfine field, \( \varepsilon \)—quadrupole shift and \( F_{exp} \)—line width, for Z18, F28 and MZ17 samples.

| Sample | Assignment | \( \delta \) (mm s\(^{-1}\)) | \( B_{hf} \) (T) | \( \varepsilon \) (mm s\(^{-1}\)) | Ratio (%) |
|--------|------------|-----------------------------|-----------------|-----------------------------|-----------|
| F28    | A1: (Fe\(^{3+}\))<sub>oct</sub> | 0.29 | 47.7 | −0.008 | 45.6 |
|        | B1: (Fe\(^{2+}\)/Fe\(^{3+}\))<sub>ext</sub> | 0.65 | 45.3 | −0.008 | 48.9 |
| Z18    | A1: (Fe\(^{3+}\))<sub>oct</sub> | 0.29 | 47.2 | −0.006 | 36.3 |
|        | B1: (Fe\(^{2+}\)/Fe\(^{3+}\))<sub>ext</sub> | 0.65 | 44.1 | −0.007 | 44.3 |
|        | B2: (Fe\(^{3+}\))<sub>ext</sub> | 0.49 | 41.3 | −0.054 | 15.5 |
| MZ17   | A1: (Fe\(^{3+}\))<sub>oct</sub> | 0.28 | 47.9 | −0.007 | 31.4 |
|        | A2: (Fe\(^{3+}\))<sub>oct</sub> | 0.28 | 45.7 | −0.050 | 16.51 |
|        | B1: (Fe\(^{2+}\)/Fe\(^{3+}\))<sub>ext</sub> | 0.65 | 44.7 | −0.009 | 24.27 |
|        | B2: (Fe\(^{2+}\)/Fe\(^{3+}\))<sub>ext</sub> | 0.55 | 42.5 | −0.020 | 20.80 |
nonmagnetic substitution in the A-sublattice. At the same time, the partial oxidation of Fe$^{2+}$ ions at B-sites takes place. The second component A$_2$ introduced to delineate the Mössbauer spectrum of sample MZ17 was assigned to the $^{57}$Fe ions on tetrahedral A-sites which feel distortion invoked by substitution on the B-sites, probably with manganese ions. Manganese ions have high ability to change valence state, and as Mn$^{2+}$ it has high preference for B-sites, where can it have high distortion by substitution on the B-sites, probably with manganese ions.

4. Magnetic characterization

Magnetic responses of unsubstituted, Zn- and (Mn, Zn)-substituted Fe$_3$O$_4$ powdered nanoparticles in a static (DC) magnetic field were studied from measurements of the field and temperature dependence of DC magnetization, $M(H)$ and $M(T)$. To calculate mass magnetization of samples, we performed TGA/DTA analysis. The weight loss due to evaporation of organic phase, gave the residue corresponding to 94.7, 96.5 and 92.2 wt% of the original weight of samples Z18, F28 and MZ17, respectively (see figure S5). Thus obtained weight loss was re-calculated taking into account that during TGA/DTA experiment the partial oxidation takes place bringing in a mixture of hematite and magnetite phases (proved by the XRD analysis).

The zero-field-cooled magnetization curves ($M_{ZFC}$, figure 5(a)) do not rich the maximum in a field of 7.96 kA m$^{-1}$ (100 Oe) up to 300 K, suggesting the existence of strong interparticle interactions. The magnetic dipole-dipole interactions modify the energy barrier $\Delta E_A = K_{eff}V$, $K_{eff}$ is an effective anisotropy constant, and shift the average blocking temperature, $<T_B>$, to higher temperature range [14]. The drop of $M_{ZFC}$ value observed in the sample F28 at $T_B \approx 117$ K is assigned to the Verwey transition, which should involves slight distortion of the crystal structure and change in the symmetry of crystal lattice from face centered cubic to rhombohedral [58]. Consequently, it should bring about the transformation of the magnetocrystalline anisotropy symmetry from cubic to uniaxial when passing from $T > T_V$ to $T < T_V$ [42]. Since, in high-purity magnetite, the Verwey temperature $T_V$ range between 110 and 125 K [59], we can assume that the core of F28 nanoparticles has stoichiometry very close to pure Fe$_3$O$_4$ [41]. On the contrary, in doped Z18 and MZ17 nanoparticles, the Verwey transition has not been experimentally observed owing to the stoichiometry deviations in samples caused by the presence of chemical dopants [60, 61]. A sudden slope change in the ZFC magnetization curve, which occurs at $T_S \sim 40$ K in all three samples (figure 5(a)), could come from the relaxation processes occurring in particles with smaller size or the freezing associated with the frustrated interactions among surface spins [23, 62].

The hysteresis loops of all three samples, recorded at 300 and 5 K, are shown in figures 5(b), (c). The $M_S$, $H_C$ and $M_R$ values are extracted and given in the table 4. At 5 K, the samples show a ferromagnetic behavior, with the $H_C$ value similar in the substituted samples Z18 and MZ17, and somewhat higher coercivity, $H_C$, in the pure F28 magnetite. At 300 K, only unsubstituted 28 nm sized Fe$_3$O$_4$ nanoparticles show the remanence and coercivity, while in the samples, Z18 and MZ17, $H_C$ and $M_R$ are zero at 300 K. It means that the ensemble of 28 nm sized unsubstituted Fe$_3$O$_4$ nanoparticles exhibit weak ferrimagnetic features at 300 K coming from the part of nanoparticles which size exceeds the critical value for superparamagnetic behavior and, therefore, the thermal energy is not enough to overcome the energy barrier, $\Delta E_A$. The saturation magnetization values, $M_S$ at 5 K range from 91.2 A m$^2$ kg$^{-1}$ (sample MZ17) to 98.6 A m$^2$ kg$^{-1}$Fe$_3$O$_4$ (sample Z18), overcoming the $M_S$ value of bulk magnetite ($\sim 95$ A m$^2$ kg$^{-1}$) in Zn-substituted sample (table 4). With increasing temperature up to 300 K, $M_S$ value remains high in Z18 and F28 (see table 4), indicating the good crystallinity and low density of the structural defects in
magnetite particles with size below 30 nm [63]. The maghemitized surface layer, predicted by Mössbauer spectra analysis in F28, as well as the surface spin disorder, have a minor (decreasing) effect on the $M_s$ value.

In order to estimate the effective magnetic anisotropy constant $K_{\text{eff}}$, we have used a simple analytical approach based on the relation between the coercivity of magnetic nanoparticles, $H_C$, and the magnetic anisotropy energy of single domain nanoparticles, $\Delta E_A$, with uniaxial symmetry, represented by the equation: $\mu_0 H_C = 0.48 \left( K_{\text{eff}}/M_s \right)$ [1 $− (T/T_B)$] [33, 64]. The fact that $K_{\text{eff}}$ of the ensemble of magnetic nanoparticles depends on the distribution of the easy axes of magnetization in space is partially delineated with the parameter $\gamma$, which takes value 0.77 for an ensemble of randomly oriented particles and 0.5 for an ensemble of aligned particles [65]. In our case the term $(T/T_B)$ can be neglected, since the ZFC-FC magnetization measurements point out that the blocking temperature of samples is high. Thus, using the simplified formula, $K_{\text{eff}} = \mu_0 H_C M_s / 0.96$, the experimental $H_C$ and $M_s$ values obtained from the hysteresis loops at 5 K (table 4), as well as the density of material, $\rho$ given as the output of XRD refinements, we estimated $K_{\text{eff}}$ values of 12.9, 17.4 and 12.1 kJ m$^{-3}$ for Z18, F28 and MZ17, respectively. These values are rather consistent with those found in the literature [66]. Just to note that the $K_{\text{eff}}$ value will be increased for approximately 6% in Z18 and MZ17, e.g. ~4% in F28, considering the random distribution of nanoparticles, and maximum ~15% for an assembly of aligned nanocrystallites ($\gamma = 0.5$) (we suppose the $T_B$ lies between 200 and 300 K in the substituted, and ~300 K in unsubstituted Fe$_3$O$_4$). Even with such increments, $K_{\text{eff}}$ would be below 20 kJ m$^{-3}$.

Such estimated $K_{\text{eff}}$ value (from DC magnetic measurements at $T \ll T_B$) usually is related to the single-particle anisotropy properties at room temperature [67, 68]. According to it, the $K_{\text{eff}}$ value in the substituted samples, Z18 and MZ17, is very close to the first order magnetocrystalline anisotropy constant, $K_1$ of bulk magnetite regarding the cubic symmetry (intermediate literature value for $K_1$(Fe$_3$O$_4$) is between 11 and 14 kJ m$^{-3}$) [23, 42, 69]. In unsubstituted F28 sample, the resulting anisotropy constant $K_{\text{eff}}$ is higher than $K_1$ probably due to the contribution of the shape anisotropy (should be considered for elongated NPs with the aspect ratio >1.1 [67]), and/or the anisotropy coming from the magnetodipole interaction of the particles. It is well known that with increasing particle size, the interparticle interactions increases and tend to form aggregates of nanocrystals [70]. Additionally, it seems that the surface anisotropy can be neglected in all three samples due to the diminishing effect of surface spin disordered in cubic-like nanoparticles at low temperatures [20, 70]. Following the simple analytical approach, the anisotropy properties of Z18 and MZ17 samples seem to be dominated by crystal-field effect [69, 71].

It is worth mentioning that the problem with estimation of $K_{\text{eff}}$ still remain opened for nanoparticulate systems. For an ensemble of the magnetic nanoparticles it is difficult to evaluate $K_{\text{eff}}$ due to the fact that apart from the magnetocrystalline, the shape and the surface anisotropies, the anisotropy comes from interparticle interactions and is dependent on the configuration of the particles inside ensembles (i.e. orientation of their easy axis of magnetization relative to the applied magnetic field). When an ensemble of magnetic nanoparticles is subject to an alternating current (AC) magnetic field (as in magnetic hyperthermia application), then the effective anisotropy $K_{\text{eff}}$ can be changed (the magnetization process, as well as the topology of the particles can be changed). Thus, $K_{\text{eff}}$ may obey particular dependence upon the frequency, $f$ and AC field amplitude, $H_0$ variations [70, 72, 73]. This fact can significantly change the hyperthermia efficiency of magnetic nanoparticles. Comparing some literature results based on ferromagnetic resonance experiments, we may expect decrease of the $K_{\text{eff}}$ with increasing frequency $f$ [70], as well as with a field amplitude $H_0$ increase [72]. Additionally, a significant reduce of the $K_{\text{eff}}$ can be found in in vivo conditions, when IONPs are taken by live cells [14]. With decreasing the $K_{\text{eff}}$ value, a metastable regime of heating can be established in AC magnetic fields.

More realistic description of the $K_{\text{eff}}$ can be obtained from the numerical calculations for multi-particle systems. Another alternative approach is an atomistic spin model [74]. These methods should involve the consideration of the surface spin disorder, the shape anisotropy, the topology of the nanoparticles in an ensemble, the diamagnetic contribution, the Zeeman’s splitting of atomic energy levels in the magnetic field. A complexity of determining the $K_{\text{eff}}$ values (especially under AC magnetic conditions) are reflected on a heating efficiency study.

**Table 4.** Saturation magnetization ($M_s$), coercive field ($H_C$), ratio $M_d/M_s$ and the magnetic moment per formula unit ($\mu_0\gamma$), estimated from the hysteresis loops measured at 300 and 5 K; an effective anisotropy constant ($K_{\text{eff}}$) at 5 K estimated from DC magnetic measurements; the heating efficiency of ferrofluids expressed by the specific absorption rate (SAR), measured in the AC magnetic field ($H_0 = 23.87$ kA m$^{-1}$ and $f = 228$ kHz (for Z18 and F28) or 252 kHz (for MZ17)); the intrinsic loss parameter (ILP).

| Sample | $M_s$ (A m$^{-2}$ kg$^{-1}$) | $H_C$ (kA m$^{-1}$) | $\mu_0\gamma$ (\mu$_B$) | $M_d/M_s$ | $H_C$ (kA m$^{-1}$) | $\mu_0\gamma$ (\mu$_B$) | $K_{\text{eff}}$ (kJ m$^{-1}$) | SAR (W/g$_{Fe}$) | ILP (nHm$^{-2}$ kg$^{-1}$) |
|--------|-----------------|-----------------|-----------------|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 1-Z18  | 86.2            | ~0.0            | 3.6             |           | 98.6           | 0.17            | 19.1            | 4.1             | 12.9            | 525             | 4.04            |
| 2-F28  | 83.6            | 2.23            | 3.5             |           | 93.3           | 0.18            | 27.45           | 3.9             | 17.4            | 285             | 2.19            |
| 3-MZ17 | 77.6            | ~0.0            | 3.2             |           | 91.2           | 0.18            | 19.5            | 3.8             | 12.1            | 426             | 2.97            |
3.5. Heating abilities of pure, Zn- and (Mn, Zn)-doped samples

In figure 6 are shown the heating ability of oleic acid (OA)-coated magnetic Z18, F28 and MZ17 nanoseeds dispersed in hexane, when the nanoparticle were exposed to AC magnetic field of amplitudes, $H_0$ in the range between 7 and 23.87 kA m and frequency $f = 228$ or 252 kHz. Some characteristic hyperthermia curves of the samples are given in figure S6. The values of the intensity of magnetic field $H_0$ and frequency $f$ are in the range commonly used in the literature [6, 20, 21, 65], even though their product, $H_0 \times f$ (between $1.6 \times 10^9$ and $6.0 \times 10^9$ A m$^{-1}$s$^{-1}$), exceeds the value limited by the Atkinson–Brezovich criterion ($4.85 \times 10^8$ A m$^{-1}$s$^{-1}$) [75], for one order of magnitude. If we assume that the magnetic hyperthermia treatment will be applied locally (for tissue heating), the use of larger field-frequency product may be considered tolerable for the human body [76].

As we can see from figure 6, the increase of SAR value upon field amplitude is observed for higher $H_0$ values in all three samples, with the difference in the offset of the heating for substituted and unsubstituted samples. Substituted samples, Z18 and MZ17, start to release heat before the F28 ferrofluid (i.e. F28 nanoseeds needs higher amplitude of the applied field, $H_0$, to start to generate heat). The estimated SAR values of three samples seems to be correlated with the FC magnetization value, $M_{FC}$, measured in a low field of 7.96 kA m$^{-1}$ (100 Oe), as well as the saturation magnetization to coercivity ratio, $M_S/H_C$, at 5 K. The unsubstituted magnetite nanoparticles, F28, have the lowest $M_{FC}$ and $M_S/H_C$ values and consequently lower heating potential under the same experimental conditions ($H_0, f$), in comparison with Z18 and MZ17. This can be partially due to the broader particle size distribution in F28 (bigger NPs, which stay blocked and do not participate in the transformation of magnetic to thermal energy), as well as to the formation of nanoclusters. The relaxation time for nanoclusters and single nanoparticles can differ [77], consequently bringing the changes in the heating abilities (i.e. SAR values). In addition, the lower intrinsic loss parameters value, ILP (ILP = SAR/($H_0^2 f$)), could also indicate on the formation of nanoclusters in the sample F28 (see table 4). Zinc-substituted Fe$_3$O$_4$ cubo-octahedrons, Z18, show the best heating performances. This sample has a good potential for using in the hyperthermia therapy. On inspection of literature, we just mention some SAR and ILP values of nanoparticles similar in size, composition and shape with here studied ones. Thus, 18 nm sized Zn$_{0.4}$Fe$_{2.6}$O$_4$ cubes have shown SAR = 1860 W g$^{-1}$ at $H_0 = 37.4$ kA m$^{-1}$ and $f = 500$ kHz (ILP = 2.66 nH m$^2$ kg$^{-1}$) [20], while 15.4 nm sized Zn$_{0.3}$Fe$_{2.7}$O$_4$ cubes possess higher heating potential, i.e. SAR = 1019.2 W g$^{-1}$ at $H_0 = 16$ kA m$^{-1}$ and $f = 380$ kHz, and ILP = 10.5 nH m$^2$ kg$^{-1}$ [6]. On the other hand, 17 nm and 26 nm sized octopods of composition FeO–Fe$_3$O$_4$ have SAR and ILP values of ~190 and 150 W g$^{-1}$ and 1 and 0.8 nH m$^2$ kg$^{-1}$, respectively, when are exposed to AC field of $H_0 = 24.67$ kA m$^{-1}$ and $f = 310$ kHz [65]. Bigger iron oxide nanocubes, with an average size ~23 nm have SAR = 375 W g$^{-1}$ at $H_0 = 24$ kA m$^{-1}$ and $f = 301$ kHz [21], and very similar ILP value (2.16 nH m$^2$ kg$^{-1}$), as our F28 nanoparticles. To what extent the heating ability of our nanoparticles will be influenced by the media viscosity, clustering and interparticle interactions will be a task for our future investigations.

4. Conclusion

The single crystalline Fe$_3$O$_4$-based nanoparticles, pure or substituted by zinc or (zinc, manganese) of size above 15 nm were fabricated by a thermal decomposition of metal precursors. The incorporation of Zn$^{2+}$ ions into a spinel structure was found to be difficult, even though two different sources of Zn$^{2+}$ ions were used, Zn(acac)$_2$ and ZnCl$_2$ salt. The XRD analysis revealed presence of the pure magnetite-based phase in all three samples. In terms of crystallinity and size dispersion, this synthesis protocol shows superiority over decomposition of iron oleate and the co-precipitation synthesis route. High saturation magnetization and single magnetic phase were detected in all three samples. Slightly cation-deficient maghemite phase could only be presented at the nanoparticle’s surface, but is negligible for magnetization diminution. 18 nm sized Zn$_{0.4}$Fe$_{2.6}$O$_4$ cuboctahedrons, with
the specific absorption rate, SAR \( \approx 425 \text{ W/g}_{\text{Fe}} \) at \( H_0 = 20 \text{ kA m}^{-1} \) and \( f = 228 \text{ kHz} \), show the best heating performance.

**Acknowledgments**

The article is based upon work from COST Action RADIO-MAG (TD1402), supported by COST (European Cooperation in Science and Technology). NJO gives special thanks to Professor Gerardo Goya of University of Zaragoza for his support to get STSM grant and for providing work facilities at the Institute of Nanoscience of Aragón. NJO and MMM acknowledge the Ministry of Education, Science and Technological Development of the Serbian Republic for financial support through the projects No. 45015 and 171027. TET. acknowledge financial support from the Spanish Ministerio de Economia y Competitividad (MINECO) through project MAT2016-78201-P and by the Aragón Regional Government through the Research Groups grants (E-26 and E28-17R) co-financed by the FEDER Operational Program Aragón 2014–2020 ‘Building Europe from Aragon’. We are grateful to the Advanced Microscopy Laboratory (LMA) and the SAI-UZ for technical assistance. We thank Dr V Spasojević for the magnetometer measurements, Dr V Ivanovski and Dr A Umičević for the Mössbauer spectra collecting, Professor N Cvetičanin for TGA/DTA data collecting and Professor A Kremenović for critical reading of the text.

**ORCID iDs**

N Jović Orsini @ https://orcid.org/0000-0003-1613-3361
M M Milić @ https://orcid.org/0000-0002-0285-2819
T E Torres @ https://orcid.org/0000-0002-6116-9331

**References**

[1] Xu C and Sun S 2013 New forms of superparamagnetic nanoparticles for biomedical applications *Adv. Drug Deliv. Rev.* 65 732–43

[2] Torres-Lugo M and Rinaldi C 2013 Thermal potentiation of chemotherapy by magnetic nanoparticles *Nanomedicine* 8 1689–707

[3] Zhu Y-F, Ni Q-Q, Fu Y-Q and Natsuki T 2013 Synthesis and microwave absorption properties of electromagnetic functionalized Fe3O4-polyaniline hollow sphere nanocomposites produced by electrostatic self-assembly *J. Nanopart. Res.* 15 1988

[4] Zhang J and Yu A 2015 Nanostructured transition metal oxides as advanced anodes for lithium-ion batteries *Sci. Bull.* 60 823–38

[5] Jang J-t, Nah H, Lee J-H, Moon S H, Kim M G and Cheon J 2009 Critical enhancements of MRI contrast and hyperthermic effects by dopant-controlled magnetic nanoparticles *Angew. Chem., Int. Ed.* 48 1234–8

[6] Bauer I M, Situ S F, Griswold M A and Samia A C S 2016 High-performance iron oxide nanoparticles for magnetic particle imaging—guided hyperthermia (hMPI) *Nanoscale* 8 12162

[7] Goya G F, Grazu V and Ibarra M R 2008 Magnetic nanoparticles for cancer therapy *Curr. Nanosci.* 4 1–16

[8] Starch S F H L, Eberhardt C, Boss A, Hirt A M and Pratsinis S E 2018 Coercivity determines magnetic particle heating *Adv. Hel. Magn.* 7 1800287

[9] Tong S, Quinto C A, Zhang L, Mohindra P and Bao G 2017 Size-dependent heating of magnetic iron oxide nanoparticles *ACS Nano* 11 6808–16

[10] Iacovita C, Florea A, Dudric R, Pall E, Iulian Moldovan A, Tetean R, Stiuluic R and Lucaciu C 2016 Small versus large iron oxide magnetic nanoparticles: hyperthermia and cell uptake properties *Molecules* 21 1357

[11] Xie W, Guo Z, Gao F, Gao Q, Wang D, Liaw B-s, Cai Q, Sun X, Wang X and Zhao L 2018 Shape-, size- and structure-controlled synthesis and biocompatibility of iron oxide nanoparticles for magnetic theranostics *Theranostics* 8 3284–307

[12] Noh S-H, Ho Moon S, Shin T-H, Lim Y and Cheon J 2017 Recent advances of magneto-thermal capabilities of nanoparticles: from design principles to biomedical applications *Nano Today* 13 6178

[13] Hao R, Xing R, Xu Z, Hou Y, Gao S and Sun S 2010 Synthesis, functionalization, and biomedical applications of multifunctional magnetic nanoparticles *Adv. Mater.* 22 2729–42

[14] Cabrera D, Coene A, Leliaert J, Artés-Ibáñez E J, Dupré L, Telling N D and Teran F J 2018 Dynamical magnetic response of iron oxide nanoparticles inside live cells *ACS Nano* 12 2741–52

[15] Das R, Alonso J, Nemati Porskhokh Z, Kalappattil V, Torres D, Phan M-H, Gariao E, Angel Garcia J, Sanchez Llamazares J and Land Srikanta H 2016 Tunable high aspect ratio Iron Oxide nanorods for enhanced hyperthermia *J. Phys. Chem. C* 120 10086–93

[16] Moya C, Battie X and Labarta A 2015 The effect of oleic acid on the synthesis of Fe3-O4 nanoparticles over a wide size range *Phys. Chem. Chem. Phys.* 17 27373–9

[17] Bárcena C, Sra A K, Chauhey G S, Khemtong C, Ping Liu J and Gao J 2008 Zinc ferrite nanoparticles as MRI contrast agents *Chem. Commun.* 2224–6

[18] Yang Y, Liu X, Yang Y, Xiao W, Li Z, Xue D, Li F and Ding J 2013 Synthesis of nonstoichiometric zinc ferrite nanoparticles with extraordinary room temperature magnetism and their diverse applications *J. Mater. Chem. C* 1 2875–85

[19] Kolhatkar A G et al 2017 Magnetic sensing potential of Fe3O4 nanocubes exceeds that of Fe3O4 nanospheres *ACS Omega* 2 8010–9

[20] Noh S-H, Na W, Jang J-T, Lee J-H, Jung Lee E, Ho Moon S, Lim Y, Shin J-S and Cheon J 2012 Nanoscale magnetism control via surface and exchange anisotropy for optimized ferrimagnetic hysteresis *Nano Lett.* 12 3716–21

[21] Lak A et al 2018 Fe2+ deficiencies, FeO subdomains, and structural defects favor magnetic hyperthermia performance of Iron Oxide nanocubes inside intracelular environment *Nano Lett.* 18 6856–66

[22] Mendoza Zélie P, Pasquevich G A, Stewart S J, Fernández van Raap M B, Aphsteguy J, Bruvera I J, Laborde C, Pianciola B, Jacobo S and Sánchez F H 2013 Structural and magnetic study of zinc-doped magnetite nanoparticles and ferrofluids for hyperthermia applications *J. Phys. D: Appl. Phys.* 46 125006

[23] Andrés Vergés M, Costa R, Roca A G, Marco J F, Goza G F, Serna C J and Morales M P 2008 Uniform and water stable functionalized Fe3O4-polyaniline hollow sphere nanocubes exceeds that of Fe3O4 nanospheres *Adv. Mater.* 20 12080–9

[24] Pacakova B, Kubíčková S, Salas G, Mantlíková A, Marcielio M, Morales M P, Nizansky D and Veijpravova J...
2017 Internal structure of magnetic nanoparticle determines magnetic response. Nanoscale 9 5129–40

[25] Ichikawa R U, Roca A G, López-Ortega A, Estrader M, Peral I, Turullas X and Nogués J 2018 Combining x-ray whole powder pattern modeling, rietveld and pair distribution function analyses as a novel bulk approach to study interfaces in heterostructures: oxidation front in FeO/Fe3O4 core/shell nanoparticles as a case study. Small 14 e1800804

[26] Jović Orsini N, Babić-Stojić B, Spasojević V, Calataluy M P, Cvjetičanin N and Goya G F 2018 Magnetic and power absorption measurements on iron oxide nanoparticles synthesized by thermal decomposition of Fe(acac)3. J. Magn. Magn. Mater. 449 286–96

[27] Bonsdorf G, Denecke M A, Schäfer K, Christen S, Langhein H and Gun'ner W 1997 x-ray absorption spectroscopic and Mössbauer studies of redox and cation-ordering processes in manganese ferrite. Solid State Ion. 101–103 351–7

[28] Rodríguez-Carvajal J 2001 Recent developments of the program FULLPROF. J UCUC Commission on Powder Diffraction Newsletter vol 26, pp. 12–9

[29] Stephens P W 1999 Phenomenological model of anisotropic peak broadening in powder diffraction. J. Appl. Phys. 89 281–9

[30] Cheon J-W, Seo J-W and Lee J-H 2006 Preparation method of magnetic and metal oxide nanoparticles. Korean PATENT PCT WO 2006/052042 A1 https://google.com/patents/WO2006052042A1

[31] Lak A, Kraken M, Ludwig F, Kornowski A, Eberbeck D, Sievers S, Litterst F J, Weller H and Schilling M 2013 Size dependent structural and magnetic properties of FeO–Fe3O4 nanoparticles. Nanoscale 5 12286–95

[32] Shavel A, Rodríguez-González B, Pacifico J, Spasova M, Farle M and Liz-Marzán L M 2009 Shape control in iron oxide nanocrystal synthesis, induced by triacyltrimmonium ions. Chem. Mater. 21 1326–32

[33] Yang H, Ogawa T, Hasegawa D and Takahashi K 2008 Synthesis and magnetic properties of monodisperse maghemite nanocubes. J. Appl. Phys. 103 07D526

[34] Liang W-I, Zhang X, Bustillo K, Chiu C-H, Wu W-W, Xu J, Chu Y-H and Zheng H 2015 In situ study of spinel ferrite nanocrystal growth using liquid cell transmission electron microscopy. Chem. Micro. 27 8146–52

[35] Baird N et al 2016 Zinc-containing magnetic oxides stabilized by a polymer: one phase or two? ACS Appl. Mater. Interfaces 8 891–9

[36] Rodríguez-Carvajal J 1993 Recent advances in magnetic structure determination by neutron powder diffraction. Physica B 192 55–69

[37] Gorski C A and Scherer M M 2010 Determination of nanoparticle magnetite stoichiometry by Mössbauer spectroscopy, acidic dissolution, and powder x-ray diffraction: a critical review. Am. Mineral. 95 1017–26

[38] Wen K, Hong J, Choi S, Lee H-W, Ahn J-P, Kim C S and Lee S W 2004 Easy synthesis and magnetic properties of iron oxide nanoparticles. Chem. Mater. 16 2814–8

[39] Dézsi I, Cs F, Gombkőtő Á, Szűcs I, Gubicza J and Ungár T 2008 Phase transition in nanomagnetite. J. Appl. Phys. 103 104312

[40] Aunersten H and Hafner S S 1973 Vacancy distribution in synthetic spinels of the series Fe2O3–γ–Fe2O3. Z. Kristallogr. 137 321–40

[41] Schmidbauer E and Keller M 2006 Magnetic hysteresis properties, Mössbauer spectra and structural data of spherical 250 nm particles of solid solutions Fe3O4–γ–Fe2O3. J. Magn. Magn. Mater. 297 107–17

[42] Lima E J, Brandl A L, Arêlario A D and Goya G F 2006 Spin disorder and magnetic anisotropy in Fe2O3 nanoparticles. J. Appl. Phys. 99 083908

[43] da Costa G M, Blanco-Andújar C, De Grave E and Pankhurst Q A 2014 Magnetic nanoparticles for in vivo use: a critical assessment of their composition. J. Phys. Chem. B 118 11738–46

[44] Ramdani A, Steinmetz J, Gleitzer C, Coey J M D and Friedt J M 1987 Perturbation de l’échange électronique rapide par les lacunes cationiques dans Fe3−xO4 (x ≤ 0, 09). J. Phys. Chem. Solids 48 217–28

[45] Yang J B, Zhou X D, Yelon W B, James W J, Cai Q, Gopalakrishnan K V, Malik S K, Sun X C and Nikles D E 2004 Magnetic and structural studies of the verwey transition in Fe3−xO4 nanoparticles. J. Appl. Phys. 95 7540–2

[46] Santoyo Salazar J, Perez L, de Abril O, Truong Phuoc L, Ihiawakrim D, Vazquez M, Greneche J M, Begin-Colin S and Pourry G 2011 Magnetic iron oxide nanoparticles in 10–40 nm range: composition in terms of magnetite/maghemite ratio and effect on the magnetic properties. Nanoscale 3 2591–6

[47] Dauo T J, Pourry G, Bégin-Colin S, Greneche J M, Ulhão-Bouillet C, Legare P, Bernhardt P, Leuvrey C and Rogez G 2006 Hydrothermal synthesis of monodisperse maghemite nanoparticles. Chem. Mater. 18 4399–404

[48] Wen M, Li Q and Li Y 2006 Magnetic, electronic and structural properties of ZnFe2−xO4. J. Electron Spectrosc. Relat. Phenom. 153 65–70

[49] Handke B, Haber J, Slezak T, Kubik M and Korecki J 2001 Magnesium interdiffusion and surface oxidation in magnetite epitaxial films grown on MgO (100). Vacuum 63 331–6

[50] Olivier L C A, Fabris J D, Rios R R V A, Mussel W N and Lago R M 2004 Fe3−xMn4−xO4 catalysts: phase transformations and carbon monoxide oxidation. Appl. Catal. B 259 253–9

[51] Antic B, Kremenovic A, Jovic N, Pavlovic M B, Jovalekic C, Nikolic A S, Goya G F and Weidenthaler C 2012 Magnetization enhancement and cation valences in nonstoichiometric (Mn, Fe)2O3 nanoparticles. J. Appl. Phys. 111 074309

[52] Logtering F K and Van Diepen A M 1973 Valencies of manganese and iron ions in cubic ferrites as observed in paramagnetic Mössbauer spectra. J. Phys. Chem. Solids 34 1369–77

[53] Di Corato R, Alici A, Rela S, Grenèche J-M, Pugliese G, Pellegrino T, Slager T, Kubik M and Korecki J 2001 Magnesium interdiffusion and surface oxidation in magneteite epitaxial films grown on MgO (100). Vacuum 63 331–6

[54] Sorensu M, Diamandescu L, Brand R A and Tarabanasu-Mihală D 2004 Mössbauer study of manganese-doped magnetite below the verwey transition. Mater. Lett. 58 885–8

[55] Greenwood N N and Gibb T C 1971 Mössbauer Spectroscopy (London: Chapman and Hall) p 241

[56] Martínez B, Roig A, obradors X, Molins E, Rouanet A and Monty C 1996 J. Appl. Phys. 79 2580–6

[57] Fock J, Bogart L K, González-Alonso D, Espeso J I, Martinez B, Roig A, Obrados X, Molins E, Rouanet A and Pankhurst Q A J. Phys. D: Appl. Phys. 30 265005

[58] Palmer W 1963 Magnetocrystalline anisotropy of magnetite at low temperature. Phys. Rev. 131 1057–62

[59] Kołodziej T, Kozłowski A, Piekarcz P, Tabiś W, Kąkol Z, Zając M, Tarnawski Z, Honig J M, Oleś A M and Parlinis K 2012 Nuclear inelastic scattering studies of lattice dynamics in magnetite with a first- and second-order verwey transition. Phys. Rev. B 85 104301
Aragón R, Buttrey D J, Shepherd J P and Honig J M 1985 Influence of nonstoichiometry on the verwey transition Phys. Rev. B 31 430–6

Özdemir O, Dunlop D J and Moskowitz B M 1993 The effect of oxidation on the verwey transition in magnetite Geophys. Res. Lett. 20 1671–4

Daou T J, Grenèche J M, Pourroy G, Buathong S, Derory A, Ulhaq-Bouillet C, Donnio B, Guillon D and Begin-Colin S 2008 Coupling agent effect on magnetic properties of functionalized magnetite-based nanoparticles Chem. Mater. 20 5869–75

Özdemir O, Dunlop D J and Moskowitz B M 1993 The effect of oxidation on the verwey transition in magnetite Geophys. Res. Lett. 20 1671–4

Daou T J, Grenèche J M, Pourroy G, Buathong S, Derory A, Ulhaq-Bouillet C, Donnio B, Guillon D and Begin-Colin S 2008 Coupling agent effect on magnetic properties of functionalized magnetite-based nanoparticles Chem. Mater. 20 5869–75

Nedelkoski Z et al 2017 Origin of reduced magnetization and domain formation in small magnetite nanoparticles Sci. Rep. 7 45997

Stoner E C and Wohlfarth E P 1948 A mechanism of magnetic hysteresis in heterogeneous alloys Phil. Trans. R. Soc. A240 599–642

Usov N A and Barandiaran J M 2012 Magnetic nanoparticles with combined anisotropy J. Appl. Phys. 112 053915

Schmitz D, Schmitz-Antoniak C, Warland A, Darbandi M, Haldar S, Bhandary S, Eriksson O, Sanyal B and Wende H 2014 The dipole moment of the spin density as a local indicator for phase transitions Sci. Rep. 4 5760

Mechanical properties of magnetic nanoparticles in hyperthermia applications and medical applications Nanotechnology 31 (2020) 225707 N Jovič Orsini et al