

Proceedings of the 17th Czech and Slovak Conference on Magnetism, Košice, Slovakia, June 3–7, 2019

Nanoparticles Coated by Porous SiO₂: Core@Shell Nanosystems for Biomedical Applications

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Magnetic based nanosystems can be used for diagnostic and imaging techniques or can help in the treatment process by acting as a drug carrier in intelligent drug delivery systems. For such applications, these systems must be stable, biocompatible, with reasonable magnetic properties and non-invasive in relation to living organisms. Among others, core@shell platforms are widely used for these purposes. Therefore, we have prepared composites consisting of Fe₃O₄ magnetic core and SiO₂ biocompatible shell through a combination of self-assembly and co-precipitation techniques. The systems with three different core sizes were prepared and subsequently coated with porous SiO₂. Afterwards, the magnetic properties of prepared samples were investigated in the temperature range 2–350 K using a SQUID-based magnetometer. Structure, size, and morphology were characterized by X-ray diffraction and transmission electron microscopy methods. Our experimental study confirms that the magnetic properties of studied systems are affected by the size of particles. It has been shown that smaller particles exhibit lower values of magnetic moment. We have confirmed the dominance of the ferromagnetic phase in uncoated Fe₃O₄ magnetic core, while on the other hand, the superparamagnetic phase increases and became substantial in coated Fe₃O₄mSiO₂ composites.

DOI: [10.12693/APhysPolA.137.733](https://doi.org/10.12693/APhysPolA.137.733)

PACS/topics: magnetic nanoparticles, mesoporous silica, core@shell, drug delivery

1. Introduction

Magnetic nanoparticles are one of the most utilized nanosystems in terms of applications to living organisms for diagnostics and therapy in medicine. These nanoparticles can be easily functionalized for different purposes so that they can serve as contrast agents in *in vivo* diagnostics or as transport vesicles in drug delivery systems. Magnetic core itself, in this study Fe₃O₄ (magnetite), is susceptible to corrosion and very reactive due to the high surface energy caused by the high surface-volume ratio. Functionalization can be obtained by coating the magnetic cores with suitable biocompatible compounds. Biocompatible surface coating is commonly realized by organic layers like poly-ethylene glycol (PEG) or inorganic materials like mesoporous silica (SiO₂) [1]. Surface coating can stabilize the surface layer of nanoparticles and prevents the reactivity and toxicity of nanosystem, as well as agglomeration caused by attractive electrostatic forces. The surface layer can also be used for the incorporation of different ligands or antibodies, which are necessary for drug delivery because they aim for desired cells and serve as targeting molecules for active transport systems [2, 3].

In our study, we focused on preparing Fe₃O₄ magnetite cores that are coated with a porous SiO₂ shell with a regular porous structure. The drug (e.g., Naproxen, Indomethacin, 5-Fluorouracil) is planned to be incorporated into the pores. The preparation of such multicomposite systems is based on chemical “bottom-up” techniques. Magnetic nanoparticles with controlled properties and sizes can be prepared via chemical synthesis. Size is a very important parameter because it directly affects the transport mechanism of particles through the cell membrane [4]. By adjusting the size, it is also possible to control magnetic properties and particularly the magnetic moment of the particles. In our study, we worked with Fe₃O₄, which is typically ferromagnetic. However, the decomposition of ferromagnet to magnetic domains is not energy efficient below the critical size of the object. The fine particle becomes a single domain, also leading to change of its magnetic state to superparamagnetic [3]. Such nanoparticles randomly flip the direction of their magnetization when thermally excited. Therefore, with the absence of external magnetic field applied, net magnetization is to zero. The coating of the nanoparticles by silica affects their magnetic properties, and the shell itself introduces its diamagnetic contribution to the system [5]. The application of the Langevin theory to the monodisperse nanoparticle system above the superparamagnetic blocking temperature (T_B) enables to describe its magnetization as follows [6]:

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$$M = M_S \left[\coth \left(\frac{m_P H}{k_B T} \right) - \frac{k_B T}{m_P H} \right], \quad (1)$$

where M_S is saturation magnetization, m_P is the magnetic moment of nanoparticle, k_B is the Boltzmann constant, T is temperature, and H represents the external magnetic field. However, this relation is valid only for uniformly sized nanoparticles. Usually, distribution of particle sizes occurs in fabricated nanoparticle assemblies, hence the systems also exhibit a distribution of magnetic moments. Magnetization (M) in the applied magnetic field (H) is therefore described as a distribution of the Langevin functions [6]:

$$M = \int_0^{\infty} L \left(\frac{m_P H}{k_B T} \right) f(m_P) dm_P, \quad (2)$$

where L is the Langevin function and $f(m_P)$ is the size distribution of magnetic moments.

2. Experimental

Samples containing three different concentrations of Fe^{3+} ions: 0.005, 0.01, and 0.05 M were prepared similarly, as is mentioned in [7]. The first step was the chemical synthesis of magnetite cores employing the coprecipitation method. The coating of these cores proceeded as follows. Three solutions consisting of CTAB and NaOH were prepared and mixed with Fe_3O_4 magnetic nanoparticles, separately for each molar ratio. Solutions were sonicated and mechanically stirred at 60 °C. Then TEOS was slowly added dropwise. Resulting products were separated from the solution with a magnet and washed several times with water and ethanol. The last step involved calcination of the product at 500 °C for 7 h, which resulted in a porous structure shell.

Characterization of nanoparticles size and structure was performed on a JEOL JEM-2100F transmission electron microscope (TEM). X-ray diffraction (XRD) experiments were performed in reflection mode with the Bragg–Brentano parafocusing geometry using a Rigaku Ultima IV multipurpose diffractometer. X-ray lamp with $\text{Cu } K_{\alpha 1,2}$ radiation ($\lambda = 0.154 \text{ nm}$) was used. Powder samples were put on a glass sample holder. Diffracted photons were collected using a D/teX ultra-high-speed position-sensitive detector system by scanning 2θ range from 10° up to 90° with the step size of 0.02°. In order to obtain instrument resolution function, a standard sample of silica was measured under identical conditions. Magnetic properties were investigated by the SQUID-based magnetometer (Quantum Design MPMS 5 XL) in zero field cooling/field cooling modes (ZFC/FC) in the temperature range 2–350 K under DC field up to 5 T. The Langevin fits were calculated using (1) and (2), in which the particle size distribution is included.

3. Results and discussion

In order to investigate the magnetic properties of the presented samples, we measured field and temperature

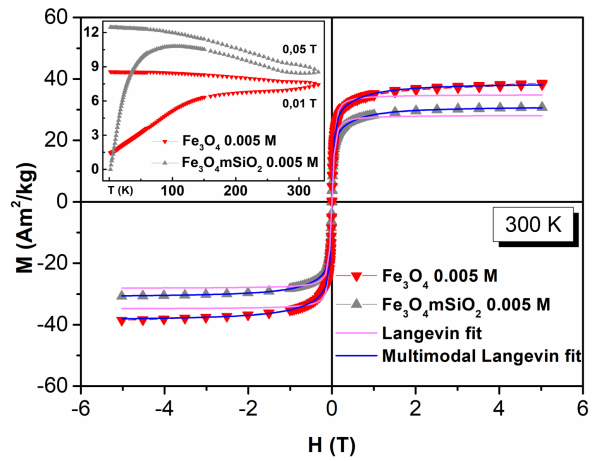


Fig. 1. $M(H)$ and $M(T)$ dependences of samples (1): Fe_3O_4 0.005 M and $\text{Fe}_3\text{O}_4\text{mSiO}_2$ 0.005 M.

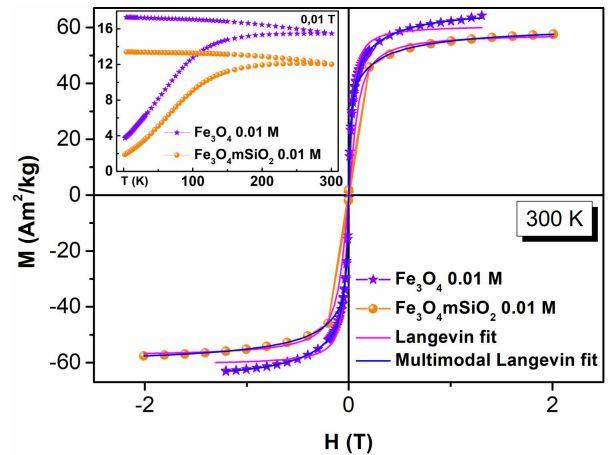


Fig. 2. $M(H)$ and $M(T)$ dependences of samples (2): Fe_3O_4 0.01 M and $\text{Fe}_3\text{O}_4\text{mSiO}_2$ 0.01 M.

dependences of magnetization. We have compared magnetization of pure magnetic cores with the coated ones so that we can validate the effect of the coating process on magnetization value. As it was expected and afterwards experimentally confirmed, coated samples showed lower values of magnetization.

In Figs. 1–3, the experimental data for $M(H)$ and $M(T)$ are displayed. Temperature dependence was measured in ZFC/FC regimes, and it reveals the presence of wide ZFC maximum. This indicates the existence of superparamagnetic blocking temperature distribution in the studied nanosystems. It can be seen in Fig. 1 and Fig. 3 that the continuance of ZFC/FC curves is much more undulated than that in Fig. 2, where the course is rather regular. These features are characteristics for the multiphase system, in which the phases with different values of magnetization (magnetic arrangement) are presented. As it is obvious from the literature [2, 4], in the case when the ferromagnetic phase is doped by the antiferromagnetic system, the decrease of magnetization

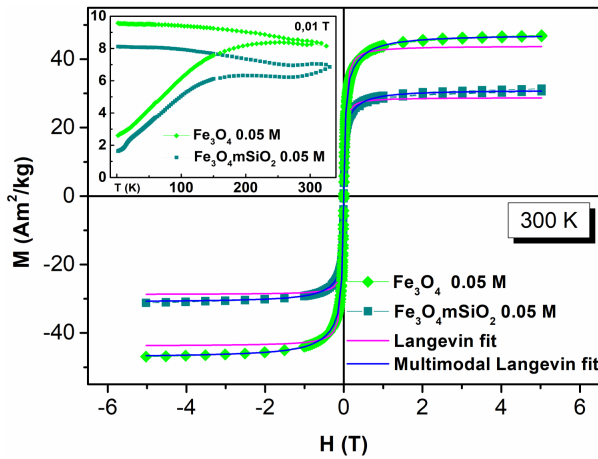


Fig. 3. $M(H)$ and $M(T)$ dependences of samples (3): Fe_3O_4 0.05 M and $\text{Fe}_3\text{O}_4\text{mSiO}_2$ 0.05 M.

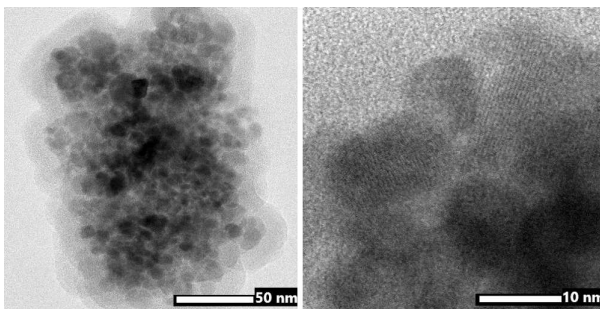


Fig. 4. TEM micrographs of sample $\text{Fe}_3\text{O}_4\text{mSiO}_2$ 0.01 M.

(magnetic moment) was observed. The highest value of magnetization saturation $M_S \approx 60 \text{ A m}^2/\text{kg}$ shows the sample (2), which retains its high magnetization value even after SiO_2 coating, indicating the presence of the Fe_3O_4 phase. On the other hand, in the sample (1), the decreasing magnetization suggests the formation of the antiferromagnetic hematite phase, similar to the sample (3). In order to determine the magnetic moment distribution of nanoparticle systems, we fitted (1) and (2) to the experimental data. Note however that Eq. (1) considers the uniform size of all the particles in the systems, which is not likely to be achieved. Commonly a variety of sizes, and obviously magnetic moments, is present in prepared samples. The size distribution of magnetic moments is included in (2), and as can be seen in Figs. 1–3, multimodal Langevin function fitted the data better than classic Langevin fit, which considers only one size of particles.

Among all studied nanosystems, sample $\text{Fe}_3\text{O}_4\text{mSiO}_2$ 0.01 M shows the best correlation with multimodal Langevin fit, hence it was examined more profoundly by transmission electron microscope. In Fig. 4 the structure and size of the investigated system are showed. As it is apparent from the picture, particles are aggregated and covered by silica shells.

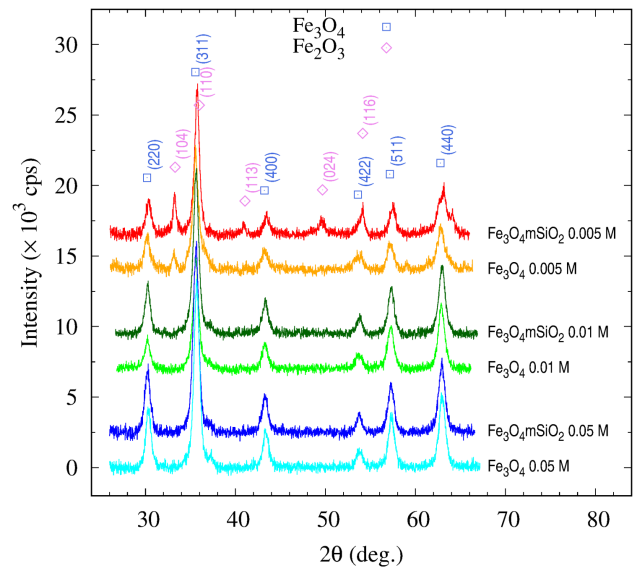


Fig. 5. Comparison of XRD patterns of powder samples.

The phase composition of the samples was also investigated. As can be seen from Fig. 5, XRD patterns suggest that the phase composition of all the samples is similar and consists of the Fe_3O_4 phase. The only exception is the sample (1), where the presence of minor hematite phase was observed. During the sample preparation process, the concentration of Fe^{3+} ions is the lowest, therefore the particles are smaller in comparison to the other two samples. Due to significantly higher surface to volume ratio, the oxidation process in smaller nanoparticles started earlier. This oxidation process was also confirmed from XRD analysis by the presence of the Fe_2O_3 (hematite) phase. Observed Bragg reflections are much broader when compared to the reference material and indicate the presence of nanometer sized crystallites.

4. Conclusions

The present study is focused on the examination of the properties of core@shell (magnetite@silica, $\text{Fe}_3\text{O}_4@\text{SiO}_2$) nanosystems with porous shell and dependence of the magnetic moment on the core size. We have studied three Fe_3O_4 based nanosystems (6 samples), each of which was prepared under the conditions with different concentrations of Fe^{3+} ions. All these samples showed superparamagnetic behavior. It is commonly known that the magnetic moment changes with the size of particles. We have confirmed the size dependence of magnetic moment from behaviors of $M(T)$ and $M(H)$. It has been found that in all samples, the wide size distribution of magnetic moments is present, and sample (2) was picked for better observation because, among all samples, it retains the highest magnetization even after the coating process. XRD analysis confirmed that in all samples, the magnetite phase was present, but in the case of the sample (1), hematite phase was also created because

the oxidation process occurred earlier. Although these magnetite@silica composites are suitable candidates for a wide spectrum of biomedical applications, prepared nanosystems will be functionalized and doped with anti-cancer or inflammatory drugs, so they can be used as drug delivery systems in theragnostic, cancer diagnostics, and therapy.

Acknowledgments

This work was supported by the Development Operational Programme Research and Innovation for the project “New unconventional magnetic materials for applications”, ITMS: 313011T544, co-funded by the European Regional Development Fund (ERDF).

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