Magneto-optical FeGa$_2$O$_4$ nanoparticles as dual-modality high contrast efficacy $T_2$ imaging and cathodoluminescent agents†

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The magneto-optical FeGa$_2$O$_4$ nanoparticles with high Fe mass magnetization exhibited a high-performance $T_2$-lowering effect and displayed cathodoluminescence.

Magnetic resonance imaging (MRI) is one of the most powerful techniques in medical diagnosis because of its noninvasiveness, excellent spatial resolution, and real-time monitoring ability. After loading paramagnetic and superparamagnetic materials, the spin–lattice relaxation ($T_1$) and spin–spin relaxation ($T_2$) times can be efficiently shortened, which causes the contrast in the marker and targeting areas to change. MR contrast agents are categorized into paramagnetic $T_1$-positive agents and $T_2$-negative agents of superparamagnetic particles. Much effort has been devoted to fabricating nanoparticle-based MR contrast agents to improve local contrast enhancement and to combine therapeutic effects. Recently, we have developed hollow/porous Ga$_2$O$_3$ nanospheres and Ga$_2$O(CO$_3$)$_2$-H$_2$O particles for $T_1$-positive agents, Au$_x$Cu$_y$ nanoshells with bimodal MR contrast agents for $T_1$ and $T_2$ contrast enhancement, and Gd silicate nanoshells and superparamagnetic Fe$_2$O$_3$ nanoparticles for $T_2$-negative agents. MRI nanoprobes, e.g., Gd$_2$(CO$_3$)$_3$-H$_2$O/silica/Au hybrid particles and Gd$_2$O$_3$/C nanoshells, were developed for photothermal killing cancer cells.

Current researches on Fe$_3$O$_4$ nanoparticles primarily involve their use in cell separation, drug delivery, hyperthermia, and $T_2$ contrast enhancement MRI agents because of their high level of magnetization and biocompatibility. Fe$_3$O$_4$ is recognized as an inverse spinel structure, with a general formula [AB$_2$O$_4$]. In this present synthesis, the amorphous GaOOH particle was used as a Ga source. Laser ablation of the Ga plate in a 5 mL H$_2$O–2-propanol solution, which contained cetyltrimethylammonium bromide (CTAB) and polyvinyl alcohol (PVA) stabilizers, was used to prepare amorphous GaOOH particles. For a later reaction, FeCl$_2$ (2 mg) and urea (0.1 g) were added to 5 mL of amorphous GaOOH solution and then transferred to a reflux condenser at 120 °C for 2.5 h (see ESI†). When amorphous GaOOH, FeCl$_3$, and urea were mixed, the solution first turned light yellow and then gradually to black as reflux occurred. This color change implied the generation of FeGa$_2$O$_4$ nanoparticles. Fig. 1a shows the X-ray diffraction (XRD) pattern of the collected powder. All of the reflection peaks were well matched to a series of FeGa$_2$O$_4$ (JPCDS No. 74–2229). The lattice constant was calculated as 0.8379 nm. No trace of other impurities could be found. The crystallite size, deduced to be $\sim$23 nm, was derived, using Scherrer’s equation, from the XRD reflection peaks. Energy dispersive spectroscopy (EDS) measurements (inset in Fig. 1a) were also obtained to determine Fe, Ga, and O elements from a single nanoparticle.
at 300 K displayed a superparamagnetic property with a reversible hysteresis loop, which gave a saturation magnetization value of ~43.1 emu per g of FeGa2O4 nanoparticles. Because the composite of FeGa2O4 nanoparticles involved diamagnetic Ga3+ and PVA/CTAB capping, the magnetization contribution of FeGa2O4 nanoparticles is considered only from its magnetic iron content. Taking into account the Fe fraction determined using inductively coupled plasma atomic emission spectrometer (ICP-AES) analysis, the high mass magnetization of FeGa2O4 nanoparticles was estimated as ca. 104 emu per mass of Fe. At 5 K, however, the M–H plot of FeGa2O4 nanoparticles clearly turned to irreversible, ferromagnetic behavior with the remanence magnetization \( M_r \) of ~15 emu g\(^{-1}\) and coercivity \( H_c \) of ~400 Oe. The saturation magnetization value of FeGa2O4 nanoparticles at 5 K was ~55.5 emu g\(^{-1}\) corresponding to a 110 emu per mass of Fe.

Fig. 2b, which shows the temperature dependence of zero-field-cool (ZFC) and field-cool (FC) magnetization plots in a temperature range between 5 K and 300 K in a 500 Oe field, provides insight into the superparamagnetic properties of FeGa2O4 nanoparticles. ZFC magnetization increases as the temperature rises from 5 K and reaches a maximum at the blocking temperature \( T_b = \sim 247 \) K. Above ~247 K, the magnetization decreases due to the increase in thermal fluctuation. Superparamagnetic nanoparticles develop ferromagnetic properties when the temperature is below \( T_b \). The FC and ZFC curves are irreversible below the irreversible temperature \( T_{irr} = \sim 292 \) K, which is defined as the blocking temperature of particles with the highest energy barrier. The FC curve shows that magnetization is not significantly higher at lower temperatures. This behavior may be ascribed to the existence of dipole–dipole interactions between nanoparticles against spins aligning under the applied field as the temperature decreases.

The FeGa2O4 nanoparticles were prepared with PVA and CTAB, added as protection agents. Thermogravimetric analysis (TGA) of the resulting FeGa2O4 nanoparticles indicated two-step weight loss: an initial weight loss of ~2.4% (25–175 °C) (adsorbed water) and a second weight loss of ~15.8% (175–450 °C) (organic capping molecules) (see Fig. S1a). Interestingly, Fourier transform infrared (FTIR) measurements of FeGa2O4, pure PVA, and pure CTAB assignment showed that FeGa2O4 and PVA spectra of similar appearance with close peaks [the hydroxyl group (–OH) group] and acetate group (–OCOCH\(_3\)), which indicated PVA coverage on the FeGa2O4 surface (see Fig. S1b). On the other hand, the characteristic peaks of CTAB appeared ambiguous on the spectra of FeGa2O4. X-Ray photoelectron spectra (XPS) analysis was then used to characterize the FeGa2O4 nanoparticle surface. Binding energy peaked at 398 eV for determinate N(ls) signal, which was the result of the \( \text{CH}_3\text{N}^+ \) in the CTAB head group (see Fig. S1c). Therefore, we speculated the sequential deposition of CTAB and PVA on the FeGa2O4 nanoparticle surface. We hypothesized that the capping of positively charged CTA+ to FeGa2O4 particles occurs as the seeds are generated in the basic reaction and subsequently co-assemble with the polar hydroxyl group and carbonyl group (C=O) of PVA onto the CTA+ layer of FeGa2O4 particles. The weakly negative
charged surface (−6.8) of resulting FeGa₂O₄ nanoparticles was determined at pH = 6 using ζ-potentials, which implied the negative charged end of the C=O bond on the oxygen (δ−) outward from layer-by-layer configuration of shielding the positively charged CTA⁺ surface of FeGa₂O₄ nanoparticles by PVA.

Because of the high Fe mass magnetization for FeGa₂O₄ nanoparticles, the longitudinal relaxation (1/T₁) and transverse relaxation (1/T₂) rates as a function of Fe ion concentrations of FeGa₂O₄ nanoparticles (0.012 to 0.200 mM) in 0.5% agarose gel were measured using the 3T MR imaging system. Fig. 3 shows the MR assays of a T₁- and T₂-weighted imaging phantom. The MR signals in the T₁-weighted contrast change are ambiguous. However, a sequence of T₂-weighted images was substantially darkened as the Fe ion concentration increased. Measuring longitudinal (T₁⁻¹) and transverse (T₂⁻¹) proton relaxation rates at various concentrations of iron ion showed the following proton relaxivities of FeGa₂O₄ nanoparticles: r₁ = 146.9 s⁻¹ mM⁻¹ and r₂ = 1.24 s⁻¹ mM⁻¹ (see Fig. S2†). The ratio of r₂/r₁ is the reference value for MR contrast agent enhancement. When the ratio of r₂/r₁ is larger than 10, the contrast agent is considered a negative contrast agent. Based on the relaxivities of FeGa₂O₄, the ratio of r₂/r₁ was estimated as ~119. The resulting r₂ value is larger than the currently reported magnetic nanoparticles measured using a 3T system: Fe₃O₄ nanoparticles (r₂ = 121.13 s⁻¹ mM⁻¹)⁴⁻⁸ and commercial AMI-227 Fe₃O₄ nanoparticles (r₂ = 127.8 s⁻¹ mM⁻¹).⁶,b A high-performance T₂-lowering ability has given FeGa₂O₄ as an effective nano-MRI contrast agent.

To examine the biocompatibility of the FeGa₂O₄ nanoparticles, we used a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay for cell viability experiments on a Vero (monkey kidney) cell line (see Fig. S3†). The cytotoxicity of FeGa₂O₄ nanoparticles was estimated by incubating nanoparticles with Vero cells for 24 h. The nanoparticles were tested at a range (0–100 μg mL⁻¹) of doses.

Based on these sample doses, FeGa₂O₄ nanoparticles exhibited good cell viability: at least 92% at 100 μg mL⁻¹.

FeGa₂O₄ nanoparticles are also considered a potential cathodoluminescent phosphor. Fig. 4a shows the room-temperature cathodoluminescence spectrum of FeGa₂O₄ nanoparticles operated at 10 kV. The cathodoluminescence spectrum covered the spectrum from UV to red emission with peaks at 360 nm (2.99 eV), 452 nm (2.74 eV), 505 nm (2.45 eV), 571 nm (2.17 eV), and 686 nm (1.8 eV). Fig. 4b shows that the broadband emission of FeGa₂O₄ nanoparticles yielded a white light with the CIE (International Commission on Illumination) chromaticity coordinates x = 0.335 and y = 0.326. White-light emission is most suitable for illuminating light sources and is appropriate for various displays.

The well-studied ZnGa₂O₄ blue phosphor displays cathodoluminescence emission ranging from UV to visible wavelength;¹⁷,¹⁸,²⁸–³¹ these colors are related to the existence of oxygen vacancies.¹⁸,²⁸ self-activated optical centers of Ga³⁺ at octahedral and tetrahedral sites,²⁸ a ratio of Ga³⁺/Zn²⁺, and impurity dopants.³¹ The UV luminescence (360 nm) of ZnGa₂O₄ is thought to originate from Ga³⁺ at the A sites of the spinel structure²⁸ or to increase the ionicity of O²⁻ to metal leading to oxygen vacancies.¹⁸,²⁸ The blue emission band is generally attributed to the self-activated optical centers of octahedral Ga-O groups in the spinel lattices.¹⁸,²⁸–³¹ The appearance of 680 nm in ZnGa₂O₄ is attributed to oxygen vacancies.¹⁸,²⁸–³¹ Accordingly, the generation of self-activation centers from the octahedral Ga-O transitions may provide a reason for the blue emission in FeGa₂O₄ nanoparticles. However, the UV emission band may be from the Ga³⁺ ions in the tetrahedral site of FeGa₂O₄ or oxygen vacancies. In fact, the Fe ions within the FeGa₂O₄ structure may also influence its luminescence. Detailed studies of the cathodoluminescence mechanisms of FeGa₂O₄ nanoparticles are required.

In conclusion, we synthesized magneto-optical FeGa₂O₄ nanoparticles ~25 nm in size. The hysteresis and ZFC-FC measurements showed the superparamagnetic behavior of FeGa₂O₄ nanoparticles with high magnetization: 104 emu per mass of Fe. Because of their high Fe mass magnetization, FeGa₂O₄ nanoparticles apparently darkened T₂-weighted imaging contrast with a large relaxivity r₂ of 146.9 s⁻¹ mM⁻¹, which suggested that they are an effective negative MRI agent. FeGa₂O₄ nanoparticles also showed cathodoluminescence emission from UV to visible, which means that they are a potential cathodoluminescence phosphor for fluorescent display and biosensor devices.

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References


