

TEMPERATURE DEPENDENCE OF THE MAGNETIZATION OF PREPARATIONS FOR MAGNETIC HYPERTHERMIA

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The temperature dependence of the magnetization in weak magnetic fields is investigated with a squid magnetometer for magnetic liquids based on dextran ferrite, dextran-ferrite powders, cefasorbent, and manganite, that is, for materials that are intensively investigated in laboratories engaged in the development of magnetic hyperthermia agents. The temperature was changed in the range from 4 to 330 K, and the magnetizing fields were 1–3 mT.

INTRODUCTION

The magnetic hyperthermia of malignant tumors is a perspective method of treatment of oncological diseases [1–4]. However, introduction of this method in clinical practice faces many physicochemical and technological problems. First of all, it is necessary to produce ferrites with particle diameters of about 10 nm having a Curie point of $\sim 45^\circ\text{C}$ [5], high magnetization levels in weak fields, wide hysteresis loops, and low toxicity [6] and capable of long-term storage that can be completely assimilated by mammals in the process of metabolism [7, 8]. The number of works devoted to these problems is progressively growing; however, physical investigations on this subject are not coordinated and hence the data on the magnetic properties of preparations for magnetic hyperthermia are incomplete. In the present study, we investigate some ferrites used in experimental magnetic hyperthermia of tumors based on a unified procedure of measuring the temperature dependence of the magnetization of materials in fields close to those of magnetic inductors [1, 3, 4] at temperatures in the range from helium ones to the temperature of a human body [2–4].

The procedure consists in cooling of samples in the zero magnetic field down to the boiling temperature of liquid helium with subsequent switching on of the magnetizing magnetic field (zero-field cooling (ZFC) mode) and measuring the magnetization in a constant field as a function of the temperature which raises to room temperature in the same field. After that the sample temperature is reduced, and the temperature dependence of the magnetization is measured down to helium temperature (FC mode) in the same field. These dependences immediately show a character of the examined substance. A standard ferromagnet gives a reversible dependence. If superparamagnetism or blocking is realized in the material, the curves strongly diverge. In addition, the temperature dependence of the magnetization in the ZFC mode allows the temperature to be estimated at which separate domains in cross-linked particles are unblocked.

1. EXPERIMENTAL PROCEDURE

The magnetic moment of a magnetized sample was measured with a squid-magnetometer setup [9]. The examined sample with a mass of ~ 1 mg was put in a special quartz ampoule of specified purity grade 5 mm in diameter placed on the axis of the anti-Dewar vessel in a chamber the temperature in which was changed from 2.2 to ~ 350 K. A uniform magnetic field was created using a niobium-titanic tube put in the main helium bath.

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Two astatically wound reception loops formed a uniform superconducting circuit with an alarm coil placed in one of the holes of the symmetric niobium squid. The magnetic flux created by the magnetized sample was proportional to the magnetic moment of the sample. It was measured when the ampoule moved from one loop to another. The magnetic field was measured by the Hall probe to within 1%, and the temperature was measured with a Cu-CuFe thermocouple with accuracy, on average, up to 0.01 K.

The main sources of errors (spread of points) were radio noise, vibrations of the setup, and sharp changes of the atmospheric pressure.

A magnetic liquid sample formed a liquid droplet in a microtest tube from fused quartz 2 mm in diameter and 4 mm in length put at the bottom of a measuring quartz ampoule. The probe mass was about 10–20 mg. Powdered samples were put at the bottom of the measuring quartz ampoule and were pressed from above with a piece of cotton wool giving very small readings of the magnetometer. The magnetite sample distributed over a plastic was shaped as a sheet fragment rolled into a tube 3 mm in diameter and 3 mm in length and put at the bottom of the measuring ampoule. A sample of metal nickel shaped as a cylinder 0.12 mm in diameter and 1.5 mm in length was glued to the side wall of the ampoule with its straight side.

Before the sample was put in the measuring chamber of the magnetometer, the residual magnetic field was carefully removed from the superconducting magnetizing niobium-titanic tube so that it did not exceed 0.02 mT. After that the ampoule with the sample was held at the top of the anti-Dewar vessel for a few minutes in a helium flow to reduce the amount of air in the ampoule. Then the rod was lowered down the chamber.

Despite careful shielding of the cryostat, the sample inevitably passed through uncontrollable magnetic fields on its way down; therefore, cooling in the zero magnetic field (ZFC mode) can be considered only as a rough approximation; however, uncontrollable magnetic fields did not exceed 0.02 mT.

Once the sample temperature had decreased to that of liquid helium (4.2 K), a magnetic field of ~1 mT was switched on, and measurements began. The sample moved from one reception loop to another in the constant magnetic field, and the magnetometer response was measured. The temperature was increased in steps. Each new temperature step was stabilized to within 0.01 K at low temperatures and to within 0.1 K at high temperatures. The criterion for the temperature stability was the same readings of the device taken when the sample moved from the top down and from the bottom upwards. Usually, the temperature increment was ~5 K at low temperatures and ~10 K at high temperatures.

Once the temperature of the sample had reached its maximum, cooling of the sample began in the same field (mode FC) approximately with the same temperature decrements and temperature stabilization at each reading point down to helium temperature.

The magnetic moment of the sample was determined as

$$p_m = 4.419 \cdot 10^{-9} \cdot N_q [\text{A} \cdot \text{m}^2],$$

where N_q is a reading of the quantum magnetometer.

The specific magnetization was determined by division of p_m into the sample mass, in kg. The specific magnetic susceptibility was determined as

$$\chi_{sp} = \mu_0 J_{sp} / B [\text{m}^3/\text{kg}]$$

or

$$\chi_{sp} = \chi_{sp} / 4\pi \cdot 10^{-3} [\text{emu/g}],$$

where B is the magnetic field [T], J_{sp} is the specific magnetization [$\text{A} \cdot \text{m}^2/\text{kg}$ or emu/g], and μ_0 is the magnetic constant ($4\pi \cdot 10^{-7} \text{ H/m}$). The sample mass is nothing but the mass of dextran-ferrite or another dry magnet. We neglected the diamagnetic reading of water, amorphous carbon, or plastic matrix as well as the demagnetization factor of nanoferroparticles assuming that it was close to unity.

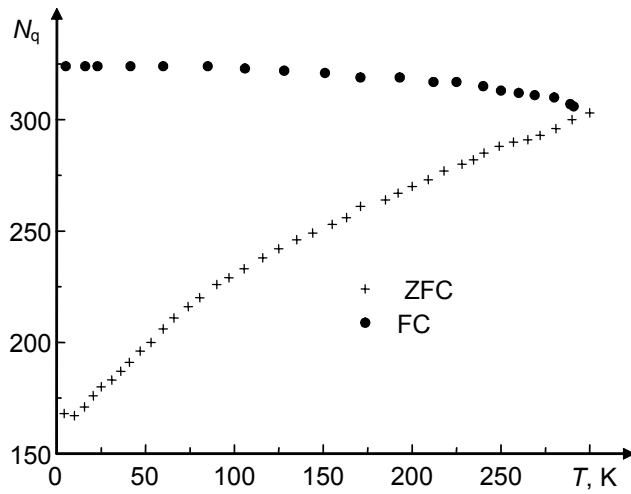


Fig. 1

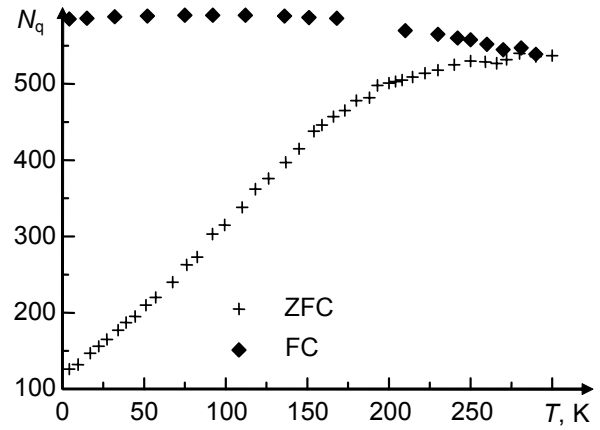


Fig. 2

Fig. 1. Temperature dependence of the magnetization of a magnetic liquid formed by a dextran-ferrite colloid solution in water. The sample mass was 15.7 mg, and the dextran-ferrite mass was 5.57 mg. The magnetizing field was 4.75 mT. Here N_q denotes magnetometer readings.

Fig. 2. Temperature dependence of the magnetization of the magnetite dry powder without dextran coating with the surface activated by chlorine ions. The sample mass was 0.9 mg. The magnetizing field was 2.93 mT. Here N_q denotes magnetometer readings.

2. RESULTS AND DISCUSSION

Figure 1 shows the temperature dependence of the magnetic moment of the dextran-ferrite colloid solution. The magnetization curve in the ZFC mode has a flat maximum at a temperature of about 160 K. At room temperature, the specific magnetization makes up $0.722 \text{ A} \cdot \text{m}^2/\text{kg}$. At helium temperature, the magnetization in the FC mode is greater than in the ZFC mode by a factor of 4.24, that is, the fraction of the classical ferromagnet makes up 23.6%. Attention is drawn to the fact that the maximum of the magnetization curve in the ZFC mode does not correspond to the Néel temperature equal to 190 K for FeO. In addition, irreversibility of magnetization curves in the FC and ZFC modes demonstrates that the usual antiferromagnetic mechanism for which both curves coincide does not work in this case. As a criterion of the unusual material, the ratio of magnetization readings ZFC/FC at helium temperature can be used with other conditions remaining the same.

Unlike the colloid suspension, powdered dextran-ferrites have no maximum in the temperature dependence of magnetization (Figs. 2 and 3). The ratio of magnetizations in ZFC/FC modes for dextran-ferrite deposited in the presence of chlorine ions makes up 21.5%, and that for the standard powder makes up 31.4%. The absence of maxima in magnetization curves below room temperature unambiguously demonstrates that ferromagnetic particles in a dry powder represent large clusters of many nanoblocks.

Commercially available magnetite incorporated as crystal nanoblocks into the polymeric matrix [10] is manifested as a flat maximum at a temperature of 170 K in the ZFC magnetization curve (Fig. 4), which is very similar to the ZFC curve for the magnetic liquid (Fig. 1). However, this temperature also differs by 20 K from the Néel temperature for FeO, and this difference is much greater than the error in measuring the temperature.

If we compare the specific magnetite magnetizations in the form of the magnetic liquid, polymeric matrix filler, and dry powder, attention is drawn to low magnetization of the magnetic liquid agent in comparison with waterless materials (Table 1).

TABLE 1

Material	Mode of measurements	T , K	$\chi_{sp} \cdot 10^3$, m ³ /kg	ZFC/FC ratio at 4.2 K, %
Magnetic liquid	ZFC	4.2	0.062	23.7
	FC	4.2	0.262	
		300	0.191	
Magnetite in the polymeric matrix	ZFC	4.2	0.32	14.9
	FC	4.2	2.15	
		300	1.08	
Dextran-ferrite deposited in the presence of chlorine ions	ZFC	4.2	0.24	21.6
	FC	4.2	1.11	
		300	1.02	
Standard dextran-ferrite	ZFC	4.2	0.446	31.4
	FC	4.2	1.42	
		300	1.45	

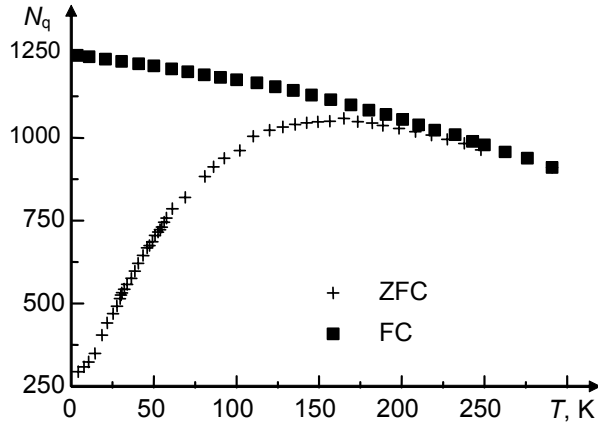


Fig. 3

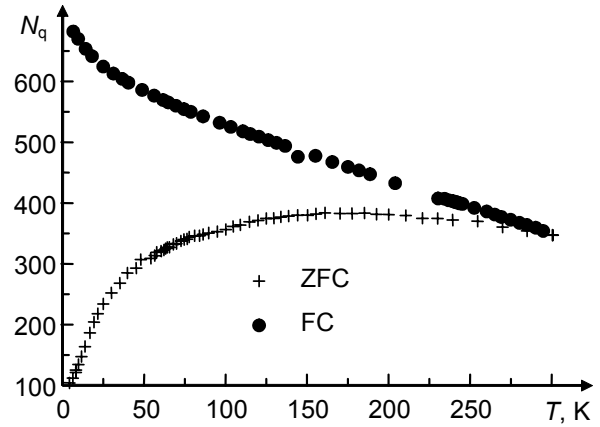


Fig. 4

Fig. 3. Magnetization as a function of temperature of the dextran-ferrite dry powder after standard synthesis [1]. The magnetite mass was 1.5 mg. The magnetizing field was 2.91 mT. Here N_q denotes magnetometer readings.

Fig. 4. Magnetization curves in the ZFC and FC modes for commercially available magnetite and magnetite incorporated into the polymeric matrix. The Fe_3O_4 mass was 0.4 mg, and the magnetizing field was 4.45 mT. Here N_q denotes magnetometer readings.

It should be noted that x-ray phase analysis of the examined dextran-ferrite sample shows the presence of only one phase – noble spinel. Nevertheless, the magnetite susceptibilities of the magnetic liquid, solid matrix, and powder differ by almost an order of magnitude. We explain this by the fact that separate Fe_3O_4 monodomain blocks in the magnetic liquid and dry dextran-ferrite can efficiently interact like in a spin glass. In the case of water solution, these blocks are separated by water molecules. In the case of dry materials, clusters are formed from a large number of blocks. As a result, the exchange interaction energy of blocks turns out to be much greater than in the case of their separation.

If we assume that the magnetic energy of the block has the order of kT at the temperature of maximum in the magnetization curve, the average block size can be estimated as follows:

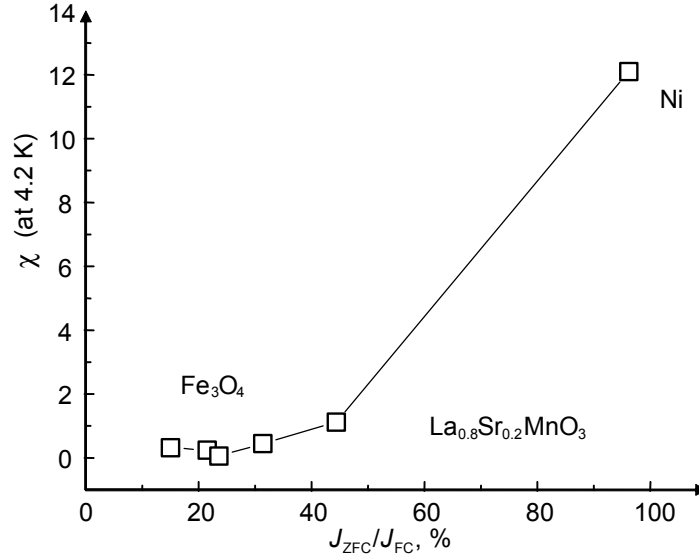


Fig. 5. Dependence of the magnetic susceptibility χ in the ZFC mode at 4.2 K on the criterion $\eta = J_{spZFC}/J_{spFC}$ at 4.2 K.

$$a = (MkT_{max}/p_m B \rho)^{1/3},$$

where M is the Fe_3O_4 molecular mass, p_m is the magnetic moment of a single magnetite molecule equal to 4.1 Bohr magneton, B is the magnetizing field [T], and ρ is the density of the material (5 g/cm^3). According to this estimate, the average block size is about 10 nm both for the magnetic liquid and Fe_3O_4 in the solid matrix. It is difficult to assume that the block sizes in dry powders will differ significantly; therefore, in dry dextran-ferrites we deal most likely with large clusters of monodomain blocks having significant positive energy of exchange interaction similar to the spin glass. The irreversible magnetization curves, that is, a significant excess of magnetization in the FC mode at 4.2 K in comparison with the magnetization in the ZFC mode also counts in favor of the spin-glass interaction. The ratio J_{spZFC}/J_{spFC} at 4.2 K can be considered as a criterion for classical ferromagnet or a criterion for ensemble deviation from the spin-glass system. Then the closer the material to the classical ferromagnet, the higher the magnetization in the ZFC mode at 4.2 K. Figure 5 shows this dependence for magnetite, manganite, and pure nickel.

Based on the foregoing, of great interest are measurements of Kim *et al.* [11]. For the magnetic liquid based on dextran-ferrite, Kim *et al.* obtained $T_{max} = 65 \text{ K}$; moreover, the FC curve had its maximum at the same temperature. The estimated average block size was about 7 nm. The behavior of the magnetization curve in the FC mode with a clearly defined maximum at 65 K still remains obscure, but the magnetization curves in the ZFC and FC modes differ strongly, and the ratio of magnetizations in ZFC/FC modes makes up 17% at helium temperature, which is in agreement with our measurements.

Thus, the dependence of the magnetization of nanoparticle ensembles obtained in the present study is well within the framework of the advanced theory of cobalt-based nanoparticle systems [10]. If we consider the so-called blocking temperature which is roughly equal to the temperature of the maximum in the ZFC curve, the magnetic anisotropy energy will be

$$\Delta E_a \sim 25kT_b$$

or

$$\Delta E_a \sim 0.35 \text{ eV}$$

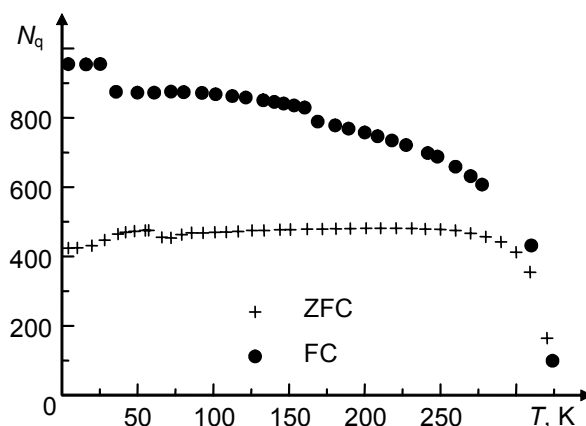


Fig. 6. Temperature dependence of the $\text{La}_{0.8}\text{Sr}_{0.2}\text{MnO}_3$ powder magnetization. The magnetizing field was 2.99 mT, and the sample mass was 0.7 mg. Here N_q denotes magnetometer readings.

for a single monodomain block. This quantity is extremely important for estimation of the efficiency of magnetic hyperthermia agents.

In the modern theory of magnetic nanoparticle ensembles, each monodomain block containing a few thousand magnet molecules is considered as a separate magnetic moment of a certain macrospin. Since the temperature dependence of the magnetization is very similar to that of spin glasses, the term cluster glass is used for such systems: separate blocks and even groups of one-domain blocks interact in these clusters, and each block can be considered as a magnetic needle. In view of this notion, the absence of maxima in the temperature dependence of the powdered ferrite magnetization becomes clear. After sedimentation and drying, very large clusters of monodomain blocks with high blocking temperatures yet inaccessible to us are formed in powdered ferrites.

The most perspective materials for magnetic hyperthermia are ferromagnets with a Curie temperature of $\sim 44\text{--}45^\circ\text{C}$. Their search is intensively conducted, but creation of magnetic liquids on their basis is connected with many technological and purely biological difficulties.

Manganite is one of the materials with a low Curie temperature. We investigated $\text{La}_{0.8}\text{Sr}_{0.2}\text{MnO}_3$ in the form of well-crystallized powder with particle sizes of about 10 μm . Figure 6 shows the temperature dependence of the magnetization of this material. A very flat maximum in the magnetization curve in the ZFC mode corresponds to a temperature of 200 K. Ferromagnetism vanishes at temperatures of about 50°C . The behavior of the magnetization curves in ZFC and FC modes has some special features of unknown nature. At helium temperature, the ratio of magnetizations ZFC/FC modes makes up 44.4%, which is within the framework of the cluster glass singularity (Fig. 5). The estimated one-domain block size is 11.5 nm. Moreover, huge agglomerates comprising a few tens of blocks are formed.

The so-called cefasorbents are also intensively investigated as potential magnetic hyperthermia agents. They represent materials prepared by joint recondensation of iron and carbon in a high-temperature plasma. Figure 7 shows the temperature dependence of the magnetization of this material. It can be easily seen that the dependences of the magnetization in the ZFC and FC modes differ strongly from the above-discussed curves for ferrite. The ratio of magnetizations in ZFC/FC modes at 4.2 K makes up 52%, which demonstrates that the mechanisms of interaction of magnetic blocks discussed above are hardly applicable here. Indeed, x-ray functional analysis shows the presence of $\alpha\text{-Fe}$, $\gamma\text{-Fe}_2\text{O}_3$, several percent of Fe_3C , and amorphous carbon in this material. This very complex multiphase system comprising a mixture of particles of classical ferromagnets, ferrites, and amorphous phases yields the result shown in Fig. 7.

Finally, the temperature dependence of the magnetization of pure annealed nickel was taken as a reference one for a comparison (Fig. 8). As expected, magnetizations in the ZFC and FC modes virtually coincided. It seems likely that a small divergence of curves at 4.2 K is caused by partial metal oxidation during annealing.

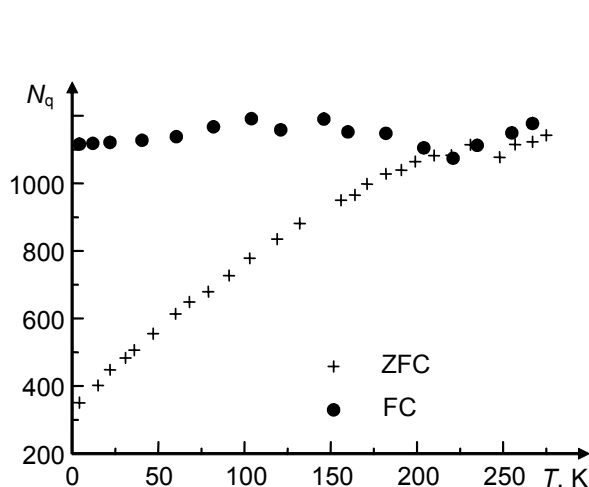


Fig. 7

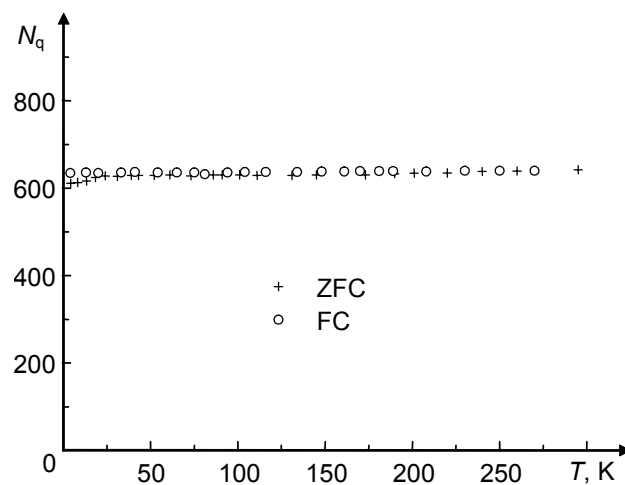


Fig. 8

Fig. 7. Fe-C powder magnetization versus the temperature. The magnetizing field was 4.9 mT. The sample mass was 1 mg. Here N_q denotes magnetometer readings.

Fig. 8. Temperature dependence of the magnetization of a pure annealed nickel sample in the form of a wire 0.12 mm in diameter and 1.5 mm in length with the axis along the magnetizing field direction. The magnetizing field was 1.84 mT. Here N_q denotes magnetometer readings.

CONCLUSIONS

From the results presented above it is clear that these studies are of interest both for fundamental and applied sciences. Apparently, in the examined systems we deal with ensembles of magnetic moments with interacting single-domain magnet blocks. We believe that the behavior of particle ensembles is best described by the term cluster glass.

Attention is drawn to the important role of the matrix and solvent in the case of the magnetic liquid. This directly indicates the interaction of particle blocks in the ensemble.

Further investigations in this direction are urgent, because a better understanding of the magnetization processes in these systems will help us to find materials best suitable for magnetic hyperthermia.

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