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HEATING EFFECT IN BIOCOMPATIBLE MAGNETIC FLUIDS WITH THE BSA SURFACTANT LAYER

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To be able to use magnetic fluids (MF) in medical applications, the magnetic nanoparticles suspended in the fluid must be coated with a substance, which would ensure their stability, biodegradability and nontoxicity in a physiological medium. An important application in biomedicine is magnetic fluid hyperthermia, offering a possibility to increase the tumour temperature to 41–46°C to kill tumour cells. In the work, the influence of the surfactant on the heat effect has been studied.

Introduction. Ionic magnetic fluids are usually toxic materials, therefore, the magnetic nanoparticles suspended in them must be coated with a substance, which would ensure their stability, biodegradability and nontoxicity in a physiological medium [1]. The coating layer of a biological molecule such as dextran, polyethylene glycol, BSA would provide some protection against toxicity. When the biocompatible molecule is coated with a second surfactant, the toxicity of magnetic particles in a living organism can be inhibited [2].

The study reported in this work was performed for two magnetic fluids. In one MF, the magnetic particles were coated with a single biological layer, while in the other, with two layers of two different surfactants. The structures of these fluids, essential from the point of view of their medical applications, were studied by the method based on absorption of ultrasound waves propagating in them. The magnetic fluid most often is injected into veins and by the circulating blood transported to a target spot [3]. Therefore, the samples cannot aggregate as it would block their flow and render the treatment ineffective.

1. Materials and methods. The magnetic fluids used in this work were produced by chemical precipitation of Fe^{2+} and Fe^{3+} salts in an alkaline aqueous medium [4, 5]. The subjects of the study were two water-based biocompatible fluids: sample A, whose magnetite particles (Fe_3O_4) were coated with BSA (bovine serum albumin), and sample B, which was coated with natrium oleate and BSA. The colloidal particles have a quasi-spherical shape [6] with a mean diameter ($d \approx 10\,\mathrm{nm}$). Table 1 presents the properties of the samples of the biocompatible magnetic fluids. The particles' radius was accurately measured by a

Table 1. Biocompatible magnetic fluid characteristics.

name	particles	carrier liquid	surfactant	conc., mg/ml	density, g/cm^3
Sample A	Fe_3O_4	water	BSA (bovine serum albumin)	8	1.004
Sample B	Fe_3O_4	water	natrium oleate +BSA	11	1.009

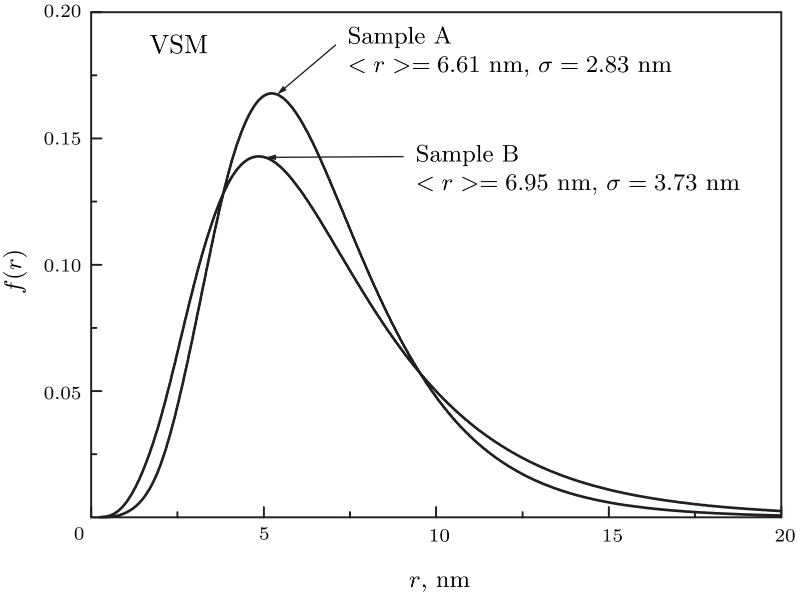

Fig. 1. Particle-size distribution function obtained from VSM measurements.

vibrating sample magnetometer (VSM). Fig. 1 shows the distribution of magnetic particles obtained from VSM measurements described by the lognormal distribution function. The magnetic fluid hyperthermia method was previously described in details [7].

2. Results. Magnetic fluid hyperthermia offers a possibility to increase the tumour temperature to 41–46°C to kill tumour cells [8], therefore, in the work the influence of the surfactant on the heat effect was studied. In the experiment performed, over a sufficiently longer time of heating when the heat loss released from the sample to its environment begins to play a role, the process can be described by the following equation [7]:

$$T(t) = T_{\text{initial}} + \Delta T_{\max}\left(1 - \mathrm{e}^{-t/\tau}\right), \tag{1}$$

where $\Delta T_{\max}$ is the temperature change in the steady state (when $t \to \infty$), τ is the time constant of heating).

Figs. 2*a* (sample A) and 2*b* (sample B) show the temperature changes in time for the samples subjected to an alternating field of selected amplitudes at the frequency $f = 1500\,\text{kHz}$. When the magnetic fluid contains only superparamagnetic particles, the thermal power density, according to the Rosensweig relation [9] is proportional to the square of the amplitude of the magnetic field intensity:

$$P[\mathrm{W/m^3}] = \mu_0 \pi \chi_0 f H^2 \frac{2\pi f \tau}{1 + (2\pi f \tau)^2} = c_p \rho (\Delta T/\Delta t)_{t=0}, \tag{2}$$

where f is the frequency of the alternating magnetic field, χ_0 is the initial magnetic susceptibility, $\mu_0 = 4\pi \cdot 10^{-7}\,\mathrm{H/m}$.

Fig. 3*a* and 3*b* illustrate the relationships between the values of $(\Delta T/\Delta t)_{t=0}$ and the square of the magnetic field intensity H^2 for both magnetic fluid samples. On the basis of the square function fit to the experimental values, the following relations between $(\Delta T/\Delta t)_{t=0}$ and the magnetic field intensity were obtained; for sample A:

$$\left(\frac{\mathrm{d}T}{\mathrm{d}t}\right)_{t=0} = \left(\frac{H}{25911}\right)^2, \tag{3}$$

and for sample B:

$$\left(\frac{\mathrm{d}T}{\mathrm{d}t}\right)_{t=0} = \left(\frac{H}{22596}\right)^2. \tag{4}$$

To conclude which of the two samples is more suitable for magnetic fluid hyperthermia, their specific absorption rate values (SAR) should be compared.

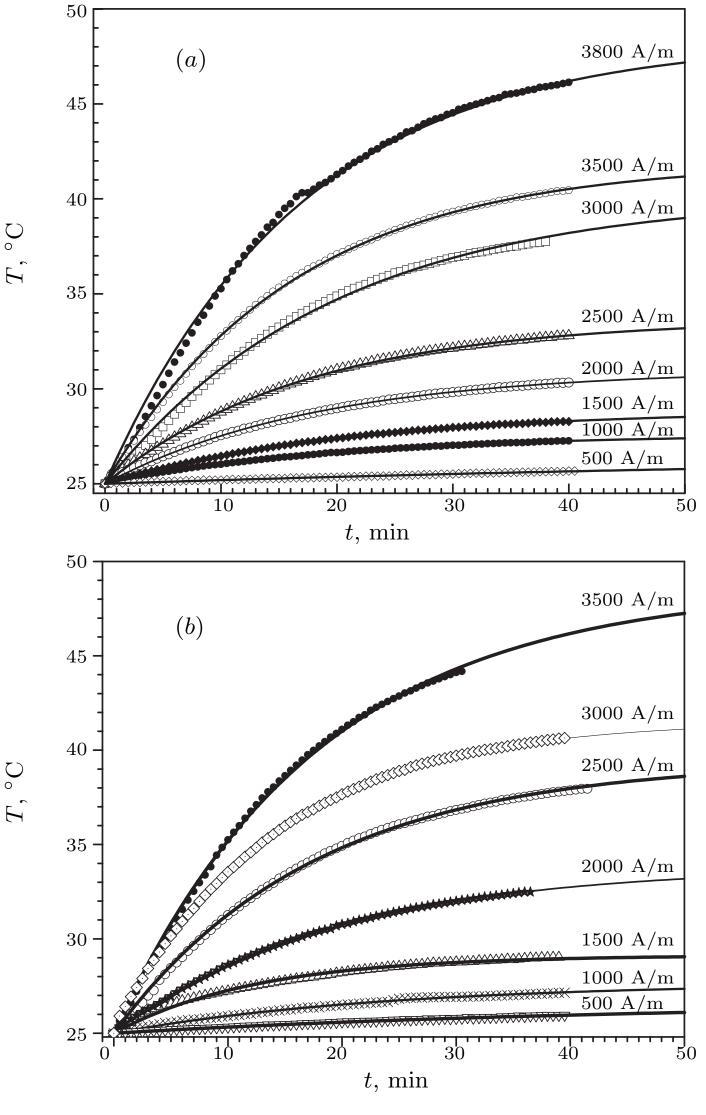

Fig. 2. Temperature changes in time for the sample subjected to various amplitude values of an alternating magnetic field, at constant frequency $f = 1500\,\mathrm{kHz}$. (a) Sample A, (b) sample B.

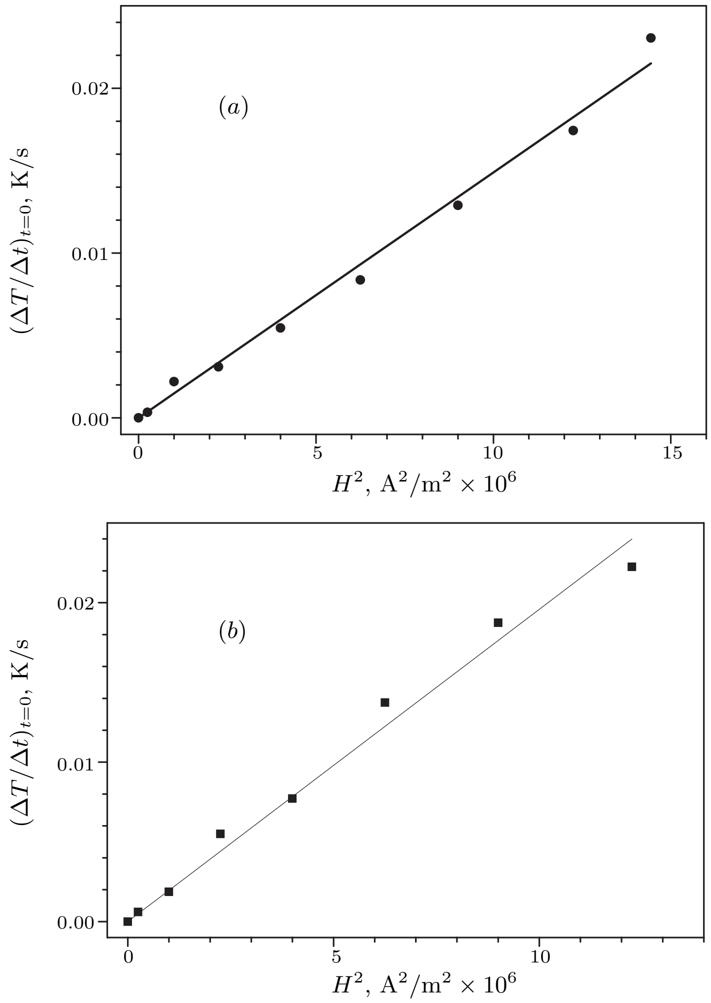

Fig. 3. The dependence of $(\Delta T/\Delta t)_{t=0}$ on the square of the magnetic field amplitude H^2 for the magnetic fluids (A and B samples) at the selected frequency 1500 kHz and the parabolic function of the fit according to Eqs. (3) and (4). (*a*) Sample A: $(\Delta T/\Delta t)_{t=0} = (H/25911)^2$, (*b*) sample B: $(\Delta T/\Delta t)_{t=0} = (H/22596)^2$.

These values are calculated from the following equation:

$$\mathrm{SAR} = \frac{C\rho}{m_{\mathrm{ferrite}}} \left(\frac{\Delta T}{\Delta t} \right)_{t=0}, \tag{5}$$

where C is the sample specific heat capacity, $(\Delta T/\Delta t)_{t=0}$ is the initial slope of the time-dependent temperature curve. The specific heat of a highly diluted magnetic fluid is close to that of water $C \cong C_{\mathrm{water}} = 4180\ \mathrm{J \cdot kg^{-1} \cdot K^{-1}}$ and the density of the fluid is given in Table 1. m_{Ferrite} is the total content in the fluid. In our experiment, the ferrofluids used had a ferrite concentration of 8 and 11 mg/ml. As follows from the values calculated from Eqs. (3)–(4), sample B shows a higher initial slope of the time-dependent temperature curve $(\mathrm{d}T/\mathrm{d}t)_{t=0}$, which means that, using this sample, more thermal energy is released, so this sample is more suitable for hyperthermia. It is also a result of higher magnetic particle volume concentration of sample B. On the other hand, the difference in the type of coating should not essentially change the value of SAR, which is a consequence of the fact that the relaxation loss according to the Néel mechanism is dominant, taking into account the average size of the magnetite grains of about 10 nm [9]. Despite this fact, regarding the polydispersity of the two samples determined by the VSM method, a possible small content of magnetic grains of greater size ($r \gg 10$ nm) may be responsible for the released thermal power being proportional to H^n, so:

$$P \propto \left(\frac{\mathrm{d}T}{\mathrm{d}t}\right)_{t=0} \propto H^n. \tag{6}$$

In an extreme case, results of the hyperthermia experiments [10] performed in magnetic fluids with particles of diameters $\cong 100$ nm brought the exponent value $n \cong 3$. When both super-paramagnetic (SPM) and ferromagnetic (FM) particles are polydispersed, there is an additional heat loss related to the magnetic hysteresis

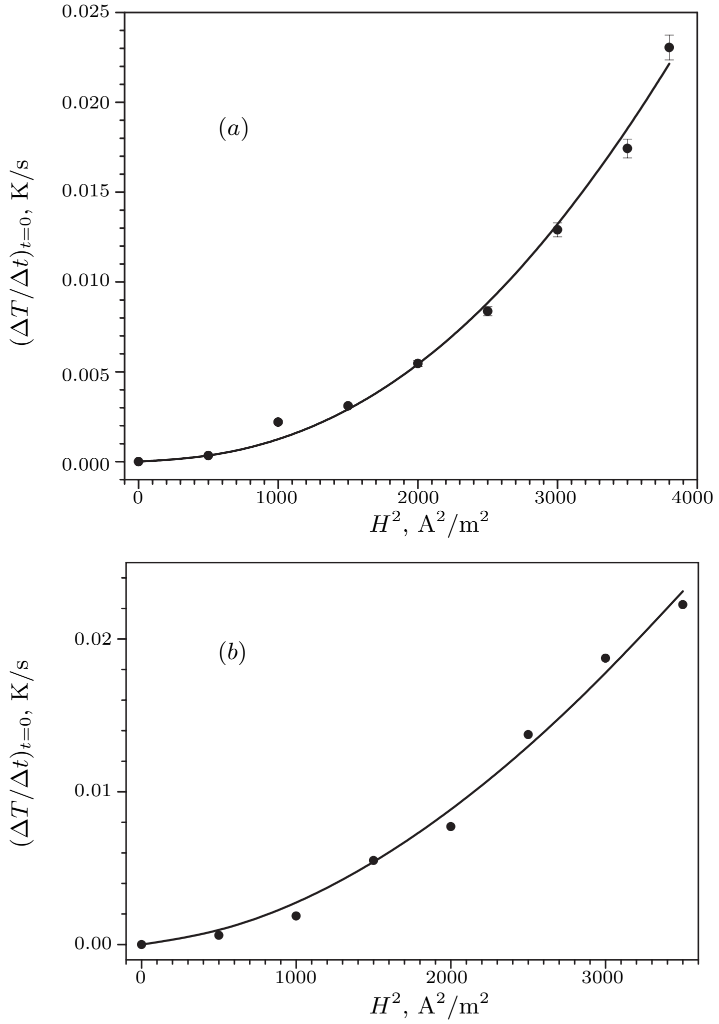

Fig. 4. The dependence of $(\Delta T/\Delta t)_{t=0}$ on the magnetic field amplitude H for the magnetic fluids (A and B samples) at the selected frequency 1500 kHz and function (7) of the fit. (*a*) Sample A: $(\Delta T/\Delta t)_{t=0} = (H/20892)^{2.235}$, (*b*) sample B: $(\Delta T/\Delta t)_{t=0} = (H/33083)^{1.94}$.

loop. Therefore, when the experimental data are fitted with a function type,

$$\left(\frac{\mathrm{d}T}{\mathrm{d}t}\right)_{t=0} = \left(\frac{H}{b}\right)^n, \tag{7}$$

where b and n are the fit parameters, the result $n > 2$ suggests the presence of greater size particles in the sample, being the reason for the heat loss following from the hysteresis loop. It is known that the size of magnetic particles influences the coercive field intensity [11]. FM particles have hysteretic properties, and the amount of heat generated per unit volume is given by the frequency multiplied by the area of the hysteresis loop [3]:

$$P_{\mathrm{FM}} = \mu_0 f \oint H \mathrm{d}M. \tag{8}$$

On the basis of the experimental values of $(\Delta T/\Delta t)_{t=0}$ as a function of H presented in Figs. 4*a* and 4*b* and functions (7) fitted to these data, the values of $n_{\mathrm{A}} = 2.235 \pm 0.125$ and $n_{\mathrm{B}} = 1.94 \pm 0.06$ for sample A and B have been brough respectively. The values of n obtained from the fit and the error of the fit imply that sample A ($n_{\mathrm{A}} = 2.11 \div 2.36$) contains some ferromagnetic grains responsible for the thermal loss because of hysteresis. The results for sample B indicate that it contains super-paramagnetic particles ($n_{\mathrm{B}} \cong 2$).

The SAR values presented in Fig. 5, obtained for both samples using formulae (5) and (7), indicate that in the considered magnetic field intensity range both samples release a similar amount of the heat energy. The numerically expressions for SAR can be written as:

$$\mathrm{SAR}_{\mathrm{A}} = 383.4 \left(\frac{H}{20892}\right)^{2.235}, \mathrm{W/g_{ferrite}}, \tag{9}$$

and

$$\mathrm{SAR}_{\mathrm{B}} = 524.6 \left(\frac{H}{33083}\right)^{1.94}, \mathrm{W/g_{ferrite}}, \tag{10}$$

for samples A and B, respectively.

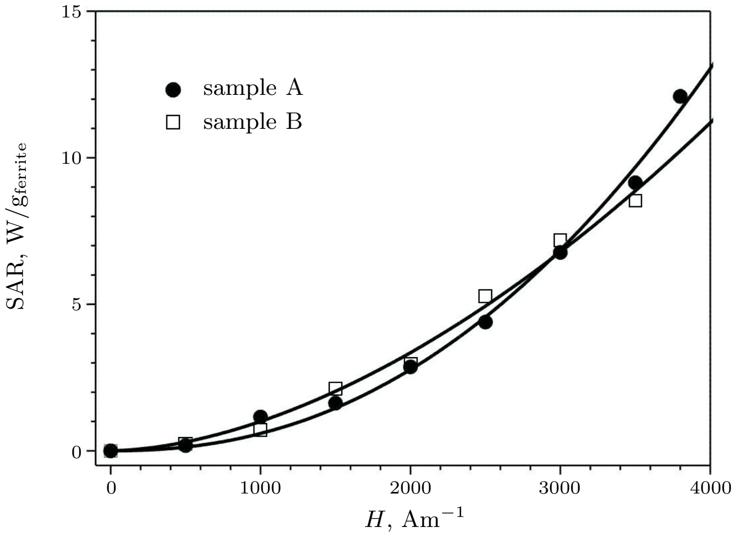

Fig. 5. Experimental SAR values for samples A and B at f =1500 kHz defined from relation (5) and the fit by functions (5) and (7).

3. Conclusions. The hyperthermic tests performed have shown that sample A contains super- and partly ferromagnetic grains ($n_{\mathrm{A}} > 2$), while sample B behaves like a typical super-paramagnetic ($n_{\mathrm{B}} \cong 2$). As follows from the SAR values obtained, both samples are suitable for application in hyperthermia. From the function course presented in Fig. 5 results that SAR for both samples is comparable despite different concentration ϕ_V values. The reason probably is the surfactant structure difference.

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