Effect of Poly(Ethylene Glycol) Coating on the Acoustic Properties of Biocompatible Magnetic Fluid

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Abstract   The aim of this study was to investigate the influence of a poly(ethylene glycol) surface-active coating on the mechanical properties of biocompatible magnetic fluids. The coating of long-chain polymer molecules on ferrite particles serves as a protective layer that prevents agglomeration of the particles and minimizes the direct exposure of the ferrite surface to the biological environment. A useful method of studying mechanical properties of magnetic fluids is based on using ultrasound.

Keywords   Adiabatic compressibility · Biocompatibility · Magnetic fluid · Ultrasonic velocity and absorption

1 Introduction

A magnetic fluid is a suspension of monodomain magnetic nanoparticles covered with a surfactant layer in an organic or inorganic liquid carrier. The high stability of a ferrofluid is achieved through a combination of particle thermal motion and steric repulsion, both working against Van der Waals and magnetic dipole interactions that tend to stick the particles together. In recent years, the design and synthesis of biocompatible magnetic fluids have gained special interest with emphasis on their application in medicine in areas such as drug targeting and magnetic hyperthermia. The use of the materials in clinical practice demands the solving of the problems of their toxicity and biocompatibility. Biocompatibility is a property of a biomaterial which, besides its basic function in the body, does not cause the worsening of the patient's state or new complications [1]. The biological properties of biomaterials depend on the state

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of their surface, and many methods used to change this surface permit one to keep these favorable properties. One of the methods relies on the covering of the biomaterial with a beneficial coating [1], e.g., poly(ethylene glycol) (PEG). Nanoparticles covered with PEG are biocompatible, i.e., nonimmunogenic, nonantigenic, and protein-resistant. This is because PEG has uncharged hydrophilic residues, and very high surface mobility leading to high steric exclusion [2–4]. The aim of this study was to investigate the influence of a PEG surface-active coating on the mechanical properties of biocompatible magnetic fluids using ultrasonic spectroscopy.

2 Materials and Methods

The synthesis of our aqueous magnetic fluid was based on co-precipitation of Fe^{2+} and Fe^{3+} salts by NH_4OH at $60\,°C$. In a typical synthesis to obtain 1 g of Fe_3O_4 precipitate, 0.86 g of $FeCl_2 \cdot 4H_2O$ and 2.35 g of $FeCl_3 \cdot 6H_2O$ were dissolved in 40 ml of deionized water by vigorous stirring, such that $Fe^{3+}/Fe^{2+} = 2$. As the solution was heated to $80\,°C$, 5.6 ml of 25 % NH_4OH were added. The precipitate was washed out by magnetic decantation with distilled water. Sodium oleate ($C_{17}H_{33}COONa$) as a first surfactant (10 mass% with respect to Fe_3O_4) was used for the modification of prepared magnetic particles to prevent their agglomeration. To improve stability and increase the circulation half-time of the particles, the PEG as a second surfactant was added to the system magnetite–oleate and stirred over 3 h. The samples denoted as MF-oleate/PEG_1, MF-oleate/PEG_2, and MF-oleate/PEG_3 were prepared using PEG from Sigma-Aldrich Corp. ($1,000\,g \cdot mol^{-1}$) and contained different ratios of PEG to magnetite (Fe_3O_4), i.e., 2.5 mg/100 mg, 25 mg/100 mg, and 250 mg/100 mg, respectively. The magnetic liquid (designated as MF-oleate) with only an oleate surfactant layer was also studied for comparison. The values of the magnetic parameters obtained from VSM measurements for all samples studied are listed in Table 1 [5].

In our ultrasonic measurements, a broadband transducer (Optel) with a center frequency of 5 MHz ($\lambda \approx 300\,\mu m$) was used. A block diagram of the experimental setup is shown in Fig. 1. The transducer was driven by a Matec pulser/receiver SR-9000 card which provides a unipolar spike pulse with an amplitude of 400 V and a rise time of 8 ns. The received signal was sampled and recorded in a digital oscilloscope (LeCroy 9310AM). The power spectrum of the echo signal was determined by using a fast Fourier transform algorithm with the aid of a MatLab 9.0 software package.

Table 1 Values of saturation magnetization, M_s, volume fraction of magnetite phase, ϕ_V, mean magnetic diameter, $\langle x \rangle$, and standard deviation of particle sizes, σ, of the samples obtained by means of the VSM method

Sample	PEG/Fe_3O_4	M_s ($A \cdot m^{-1}$)	ϕ_V (%)	$\langle x \rangle$ (nm)	σ (nm)
MF-oleate/PEG_1	2.5 mg/100 mg	1,266	0.27	9.81	5.09
MF-oleate/PEG_2	25 mg/100 mg	1,165	0.25	9.87	5.41
MF-oleate/PEG_3	250 mg/100 mg	1,213	0.26	9.88	5.26
MF-oleate		2,331	0.52	9.58	3.72

Fig. 1 A block diagram
of experimental setup
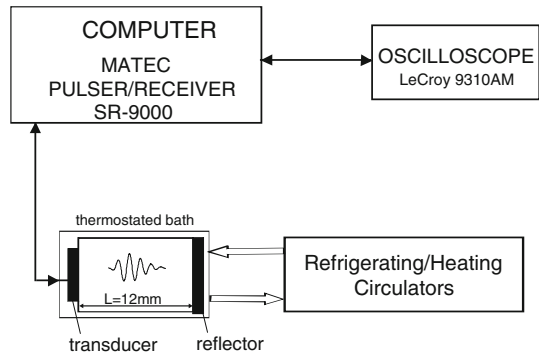
A measuring cell (made of brass) with a fixed distance between the transducer and reflector was used. The path length (back and forth) traversed by the ultrasonic pulse inside the medium was $2L = (24.0 \pm 0.1)$ mm. The temperature of the sample in the measurement cell was kept constant ($\pm 0.1\,^{\circ}$C) by a thermostated bath.

The velocity of the ultrasonic wave was determined from the relation,

$$c(f) = \frac{2\pi f L}{2\pi n - \varphi_{\mathrm{m}} - \varphi_{\mathrm{w}}}, \tag{1}$$

where n is an integer associated with the ambiguity of the phase shift; φ_{m} and φ_{w} denote the phases of the signals traveled through the sample and water used as a reference medium, respectively. The attenuation coefficient measured in excess of that of water can be expressed as

$$\alpha(f) = -\frac{1}{2L} \ln\left(\frac{P_{\mathrm{m}}(f)}{P_{\mathrm{w}}(f)}\right) + \frac{1}{2L} \ln\left(\frac{R_{\mathrm{mb}}}{R_{\mathrm{wb}}}\right), \tag{2}$$

where $P_{\mathrm{m}}(f)$, $P_{\mathrm{w}}(f)$ are the power spectra of the echo signal reflected from the wall of the measuring cell filled with magnetic liquid and water, respectively, $R_{\mathrm{mb}} = 0.833$ is the acoustic power reflection coefficient at the inner side of the measuring cell containing the magnetic liquid, and $R_{\mathrm{wb}} = 0.831$ is the acoustic power reflection coefficient at the inner side of the measuring cell containing water. The uncertainty of the ultrasonic measurements described above is estimated to be about 2 % to 5 %.

Additionally, we carried out viscosity and density measurements. The shear viscosity coefficient of the studied magnetic liquids was measured using a Digital Brookfield Rheometer DV II+ in the cone-plate geometry. The temperature of the sample in the measurement cell was kept constant ($\pm 0.1\,^{\circ}$C) by a thermostated bath. The measurements were performed in the temperature range from 15 °C to 50 °C, and the results were well represented by a power law form which is characteristic of glass-like polymeric systems and can be used to fit the results of viscosity measurements in surfactant-rich solutions [6];

$$\eta = A\left(\frac{T}{T^*} - 1\right)^{-m}, \tag{3}$$

where A and m are empirical constants and T^* represents the glass transition temperature and can be treated as a reference temperature.

The density was measured using a "DMA-38" microprocessor densimeter from Anton Paar that operates by the method proposed by Kratky et al. [7].

3 Results and Discussion

A useful method of studying mechanical properties of magnetic liquids is based on ultrasound. Figure 2 shows the measured velocity of the ultrasonic wave. The measured ultrasound velocity in the MF-oleate sample, $1473\,\text{m} \cdot \text{s}^{-1}$, was close to that in pure water [8]. The velocity of ultrasonic waves is determined mainly by the chemical composition of the magnetic fluid, so the addition of PEG leads to significantly greater values of the speed of sound in MF-PEG samples in comparison with the MF-oleate sample. The velocity increases at a given temperature with increasing content of PEG in samples MF-oleate/PEG_1, MF-oleate/PEG_2, and MF-oleate/PEG_3. No dispersion of sound was observed in the studied frequency range. The speed-of-sound values allow the determination of the adiabatic compressibility, β_s, from the well-known Laplace formula [9]:

$$\beta_s = \frac{1}{c^2 \rho}, \tag{4}$$

where c is the speed of sound and ρ is the density of the fluid. The measured density of the studied magnetic fluids is shown in Fig. 3. The values of the adiabatic
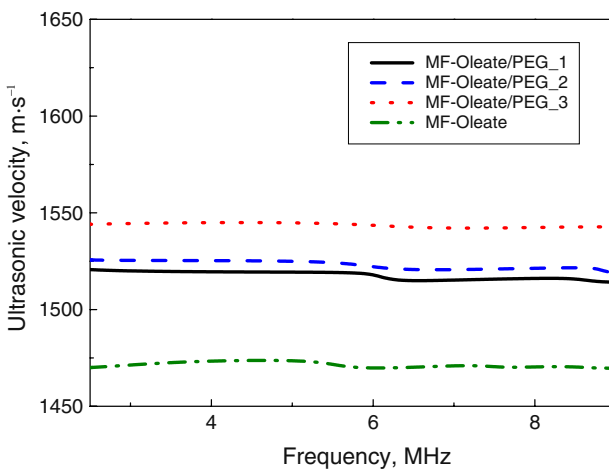
Fig. 2 Measured spectra from MF-oleate and MF-oleate/PEG samples showing the effect of a PEG layer on ultrasonic velocity
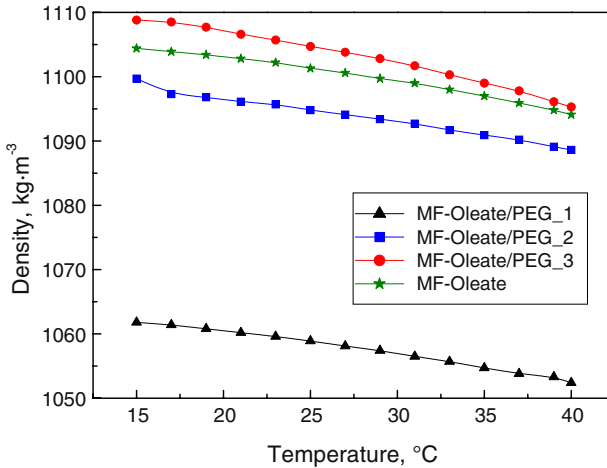
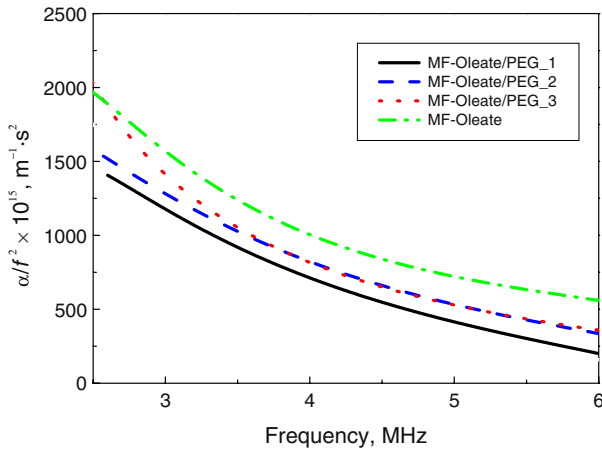**Fig. 3** Temperature dependence of the density of studied magnetic fluids

Table 2 Values of adiabatic compressibility, β_s, for MF-oleate/PEG and MF-oleate samples determined from ultrasonic measurements for temperature $T = 25\,°C$

| Sample	PEG/Fe$_3$O$_4$	$c\,(\mathrm{m \cdot s^{-1}})$	$\rho\,(\mathrm{kg \cdot m^{-3}})$	$\beta_s \times 10^{-10}\,(\mathrm{m^2 \cdot N^{-1}})$
MF-oleate/PEG_1	2.5 mg/100 mg	1,518	1058.9	4.10
MF-oleate/PEG_2	25 mg/100 mg	1,525	1094.8	3.93
MF-oleate/PEG_3	250 mg/100 mg	1,544	1104.7	3.80
MF-oleate		1,473	1101.3	4.19

compressibility calculated from Eq. 4 are listed in Table 2. The results show the change in the compressibility coefficient with changes in the PEG content.

Figure 4 shows the experimental results of the attenuation of the ultrasonic wave per frequency squared over the frequency range from 2.5 MHz to 6 MHz at 25 °C for the magnetic liquids studied in the absence of an external magnetic field. As seen from the figure, α/f^2 decreases monotonically, and the attenuation can be attributed to the friction and heat exchange between the particles and the surrounding medium as well as to the decay of the acoustic wave in the forward direction due to scattering by the particles [10]. The observed ultrasonic attenuation in the MF-oleate sample without the PEG layer is higher than attenuation in the MF-oleate/PEG samples due to twice as large concentration of magnetite particles.

The attenuation of the ultrasonic wave in magnetic liquids is determined mainly by the size, shape, and distribution of magnetite particles dispersed in the carrier liquids. Figure 4 shows that the addition of PEG has some effect on the measured ultrasonic properties of MF-oleate/PEG samples. The ultrasonic attenuation appears to increase with increasing content of PEG. This is perhaps due to the changes in the particle size distribution function rather than the increase in the shear viscosity since the latter does not account for the increase in the coefficient of ultrasonic absorption as calculated from the Stokes formula. It is known that the addition of the PEG layer leads

Fig. 4 Measured spectra from MF-oleate and MF-PEG samples showing the effects of a PEG layer on ultrasonic attenuation
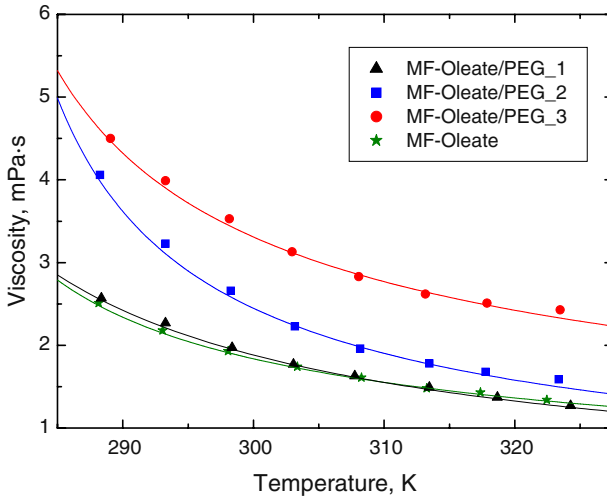
Fig. 5 Temperature dependence of the shear viscosity of magnetic fluids. *Solid lines* represent fit of Eq. 3 to the experimental data

to an increase of the hydrodynamic radius of the particles [11]. The stronger increase of ultrasonic absorption in an MF-oleate/PEG_3 sample (highest content of PEG) in the low frequency region seems to indicate the presence of a relaxation process related to the monomer exchange between micelles formed by PEG molecules and the suspending liquid [12].

All studied magnetic liquids with the additional PEG layer had the same volume fraction of the magnetite phase (Table 1); they differed only in the amount of PEG which was greater than necessary to cover the magnetic particles. As a result, the rest of the PEG remained as free molecules in the carrier liquid (water). There they could

form long-lived supramolecular structures such as micelles or bilayer membranes with molecular components that were in rapid dynamic equilibrium with the surrounding solution and with each other [12]. The acoustic properties of biocompatible magnetic liquids containing free surfactant molecules depend on the distribution of PEG between discrete (particles) and continuous (liquid) phases. This is supported by the results of our density (Fig. 3) and viscosity (Fig. 5) measurements. Their dependence on concentration of PEG is similar to that of aqueous solutions of PEG: density, ρ, and viscosity, η, increase in a nonlinear manner with PEG concentration and decrease with temperature [13,14]. The ultrasonic measurements of water solutions of PEG also showed that the velocity of ultrasonic waves increased with concentration at a given temperature [15,16]. The interaction of PEGs (flowing freely in the carrier liquid) with water play an important role in the physicochemical properties of the magnetic liquids.

4 Conclusions

The velocity of ultrasonic waves is determined mainly by the chemical composition of the magnetic fluid, so the addition of PEG leads to significantly greater values of the speed of sound. The velocity increases with increasing content of PEG in the samples. By contrast, the attenuation of the ultrasonic wave in magnetic fluids is determined mainly by the size, shape, and distribution of magnetite particles dispersed in carrier liquids. Results show that the addition of the PEG shell has some effect on the measured ultrasonic properties. This is perhaps due to the changes in the particle size distribution function. The attenuation also appears to increase with increasing content of PEG.

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