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STUDY OF STRUCTURAL CHANGES IN BIOCOMPATIBLE FLUID BY THE ACOUSTIC SPECTROSCOPY

Š. HARDOŇ[1a], J. KÚDELČÍK[1b], M. RAJŇÁK[2a, 3], M. KUBOVČÍKOVÁ[2b]

[1] Department of Physics, Faculty of Electrical Engineering and Information Technology, University of Zilina, Univerzitná 12, Žilina, Slovakia
Email: [a] *stefan.hardon@feit.uniza.sk*, [b] *jozef.kudelcik@feit.uniza.sk*
[2] Department of Magnetism, Institute of Experimental Physics SAS, Watsonova 47 Košice, Slovakia
Email: [a] *rajnak@saske.sk*, [b] *kubovcikova@saske.sk*
[3] Faculty of Electrical Engineering and Informatics, Technical University of Košice, Letná 9, Košice, Slovakia

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Abstract. Magnetic fluids with nanoparticles offer some attractive applications in biomedicine. Biocompatible magnetic fluids are used for diagnostics and therapy in medical applications, in pharmacy, and biosensors. These fluids are used as a delivery system for anticancer agents in a locoregional tumor therapy-magnetic drug targeting and hyperthermia. For the study of the influence of an external magnetic field on the aggregation processes of magnetic nanoparticles in biocompatible magnetic fluids, acoustic spectroscopy was used. The jump changes of the magnetic flux density to the values 100, 200 and 300 mT at various temperatures were applied to the investigated fluid. The measured changes of the acoustic attenuation by the presence of the magnetic fields were the results of nanoparticle aggregations into new structures.

Keywords: biocompatible magnetic fluid, nanoparticle aggregation, acoustic attenuation, acoustic spectroscopy.

1. INTRODUCTION

Nowadays the magnetic nanoparticles offer various attractive possibilities and applications in biomedicine, as magnetic drug targeting, magnetic resonance imaging, hyperthermia effect and so on [1–8]. They have controllable sizes ranging from a few nanometers up to tens of nanometers, with dimensions smaller or comparable to those of a protein (5–50 nm), a gene (2 nm wide and 10–100 nm long), a virus (20–450 nm), or a cell (10–100 μm). In biomedicine, magnetic nanoparticles are mixed into a suitable biological solution to form the biocompatible magnetic fluids with a wide range of uses in living organisms. Biocompatible fluids are also used in ophthalmologic surgery procedures and as a contrasting agent in magnetic resonance imaging [2, 4]. The main important attribute is that these nanoparticles are magnetic, and can be manipulated by a magnetic field gradient. The intrinsic penetrability of a magnetic field into human tissue allows up many applications involving a transport or immobilization of magnetic nanoparticles, or a magnetically tagged biological entity. In this way,

they can deliver a drug, (for example an anticancer drug) to a targeted region of the body, such as a tumor [9]. The magnetic nanoparticles also react resonantly to a time-varying magnetic field. Application of these type of fields can heat the magnetic nanoparticles, which leads to their use as hyperthermia agents (delivering toxic amounts of thermal energy to targeted bodies), and radiotherapy (moderate degree of tissue warming results in more effective malignant cell destruction) [1, 4, 5, 9, 10]. These and other potential applications are available in biomedicine as a result of the special physical properties of magnetic nanoparticles [10–12].

The study of structural changes and properties of biocompatible magnetic fluids in the presence of the magnetic field is very interesting and important for their biomedical application. The water-based magnetic fluids can be used for diagnostics and therapy in medical applications, in pharmacy, and in biosensors. For application in biomedical purposes [13], the magnetic particles must be pre-coated with substances that ensure their stability, biodegradability, and non-toxicity in a physiological medium [14–17]. The properties of a water-based biocompatible magnetic fluid in the magnetic field have been studied by several authors [1, 2, 18, 19]. The acoustic spectroscopy can be used to investigate magnetic fluid under the application of the magnetic field because of the changes in the magnetic fluid-structure influence on the acoustic properties of the fluid such as the ultrasound wave velocity c and the absorption coefficient (α) of ultrasonic wave [19]. In this paper, the acoustic spectroscopy to study the influence of external magnetic flux density on α in a biocompatible magnetic fluid is presented.

2. ACOUSTIC SPECTROSCOPY OF INVESTIGATED BIOCOMPATIBLE MAGNETIC FLUID

The studied substance was the magnetic biocompatible fluid based on the water. The basic properties of Fe_3O_4 nanoparticles are as follows: purity 97%, form nanopowder, spherical nanoparticle, diameters 50–100 nm (SEM) [20], surface area 60 m^2/g, and bulk density 0.84 g/mL. A surfactant, oleic acid, was used to stabilize the nanoparticles and prevent them from coalescing.

The mean diameter of nanoparticles was determined by two methods: by the ultrasound spectrometer DT-100 (Fig. 1) and from the magnetization curve with the magnetization of saturation was 3.93 Am^2/kg (Fig. 2). 64 nm was obtained from both methods. Taking into account the saturation magnetization value of the bulk magnetite, the magnetic volume fraction has been determined to be 4%.

The techniques of acoustic spectroscopy in our department are long used to study properties and changes in the structural arrangement of nanoparticles in magnetic fluid, investigation of structural changes of doped liquid crystals by the external electric and magnetic field, to the study of properties of the phosphate glasses and a few years back to the study of MOS structures [21–24]. The investigated biocompatible fluid was placed in the thermostatted closed measuring cell and the temperature was stabilized with an accuracy of ± 0.1°C by water thermostat Julabo model F25.

The distance between two parallel to each other piezoelectric transducers was 9 mm. The frequency of the acoustic wave was 11.7 MHz with a pulse length of 0.24 μs. The experimental arrangement of the acoustic spectroscopy and its more detailed description can be found in the work [25].

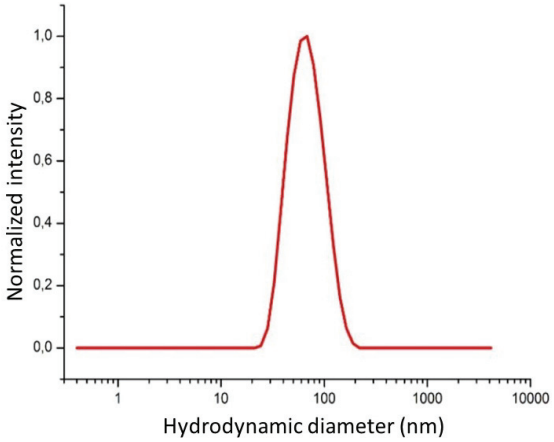

Fig. 1 – Distribution curve for the hydrodynamic diameter of Fe_3O_4 nanoparticles measured by the ultrasound spectrometer DT-100.

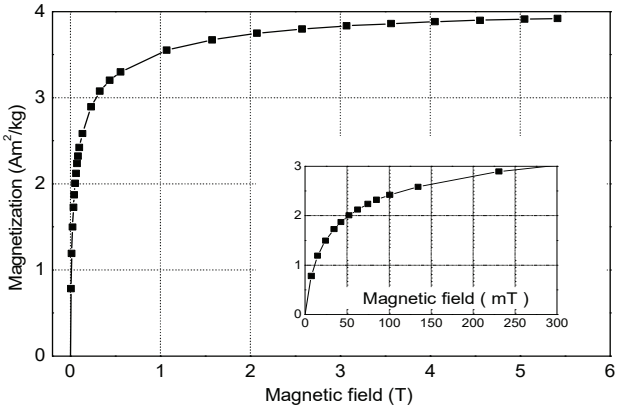

Fig. 2 – Magnetization curve of studied biocompatible magnetic fluid.

3. INFLUENCE OF THE MAGNETIC FIELD

As with all materials, the parameters of the biocompatible fluid depend also on the temperature [26]. This dependence is evident from a decrease of viscosity term and an increase of velocity of the acoustic wave with temperature (Fig. 3). The velocity of an ultrasonic wave in the absence of a magnetic field was measured

using a time of propagation. The ultrasonic velocity was determined from the difference of time of amplitude peaks measured at multiple reflections in the cell.

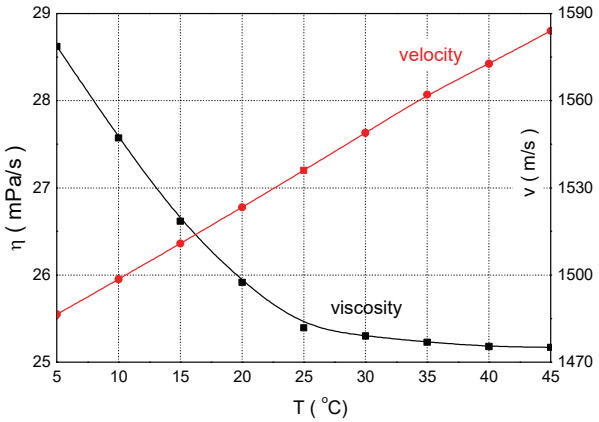

Fig. 3 – The temperature dependence of the viscosity and the acoustic velocity in the studied biocompatible fluid.

Figure 4 shows the changes in acoustic attenuation for jump changes of the magnetic flux density from to 200 mT at three temperatures 25°C, 35°C and 45°C. The magnetic flux density had a parallel orientation to the wave vector of the acoustic wave. At the beginning of the measurement, the magnetic flux density was set to the value of 0 mT and after 5 minutes its jump change was applied. During the next 30 minutes, the value of magnetic flux density was constant (200 mT) and after this time it was switched off.

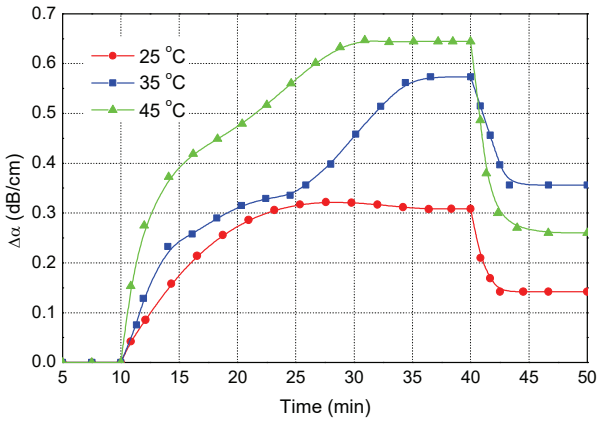

Fig. 4 – Experimental data of the changes of acoustic attenuation for three temperatures (● 25°C, ■ 35°C, ▼ 45°C) at the value of magnetic flux density 200 mT.

Immediately after jump change of the magnetic flux density, various changes of the acoustic attenuation ($\Delta\alpha$) were observed and their developments depended on the temperature. At the temperature of 25°C, the acoustic attenuation increased 15 minutes and then achieving a stable value. The increase of $\Delta\alpha$ was due to the rotation of magnetic nanoparticles in direction of the magnetic flux density and their sequential connection to new structures [27, 28]. When the investigated fluid has 35 °C the increase to sable value was almost 25 minutes. At 45°C the acoustic attenuation increased faster than at 35°C and the stable value was achieved after 20 minutes. After switch off the magnetic flux density, the acoustic attenuation decreased around 3 minutes to almost half the value of the stable acoustic attenuation at given temperatures. This value was constant for more than tens of minutes. For this reason, we can conclude that a lifetime of a part of nanoparticle structures was relatively long.

The influence of three different step changes of the magnetic flux density at 35°C on the changes in the acoustic attenuation is illustrated in Fig. 5. The process of measurement was the same as in the previous measurement. After jump change of the magnetic flux density to a given value, various changes of the acoustic attenuation were observed again and their developments depended on this value. At jump change to the value 100 mT, the acoustic attenuation only slowly increased during a whole time without achieving a stable value. In this field, the process of structural changes was more than half an hour. The development of acoustic attenuation at 200 mT at 35°C is the same as in Fig. 3. At 300 mT the acoustic attenuation increased faster than as at lower fields and the stable value was achieved after about 12 minutes, but its value was slightly smaller than at 200 mT. After switch off the magnetic field, $\Delta\alpha$ decreased during a few minutes, but it also did not reach the initial value of the acoustic attenuation.

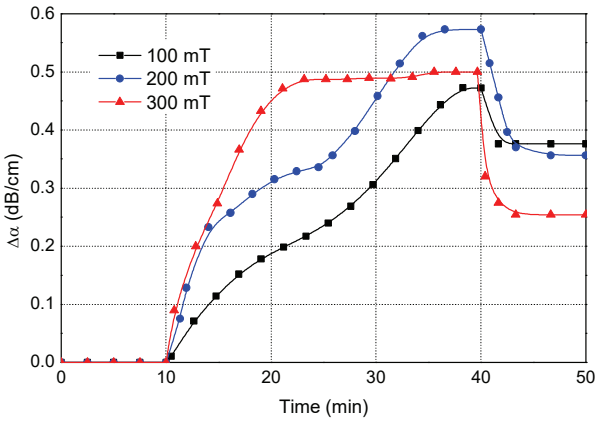

Fig. 5 – The development of acoustic attenuation at the different jumps changes of magnetic flux density (■ – 100 mT, ● – 200 mT, ▲ – 300 mT) at temperature 35°C.

Figure 6 showed the hysteresis effect of the acoustic attenuation at the linear change of magnetic flux density at 35°C. At this type of measurement, the magnetic flux density linear increased to 200 mT during 30 minutes and then it decreased to 0 mT same time. At first, the acoustic attenuation is monotonous, then it increased from the value of 60 mT, and from 170 mT the attenuation was almost stable. At the linear decrease of magnetic flux density, the acoustic attenuation slowly changes to 160 mT, and then it decreased faster. From 50 mT it can observe a slow monotonic return to almost the initial value of acoustic attenuation.

4. DISCUSSION

The interaction between the magnetic moments of the nanoparticles in water-based biocompatible fluid and the external magnetic field leads to their aggregation into new structures [9, 27–30]. These rearrangements in the investigated fluid cause the changes of the acoustic attenuation because the interaction between the structures of magnetic nanoparticles and the propagated acoustic wave leads to the additional attenuation of the acoustic wave.

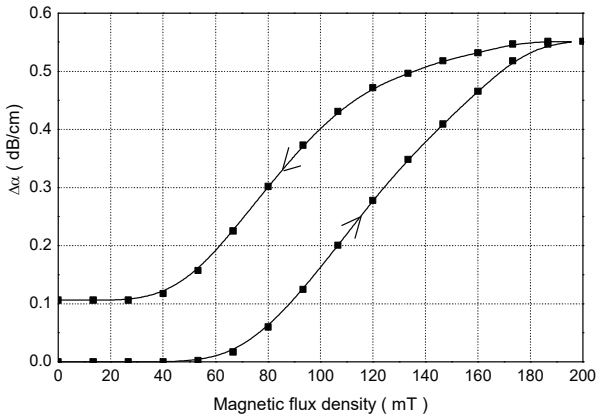

Fig. 6 – The hysteresis effect of acoustic attenuation at the linear change (6.6 mT/min) of the magnetic flux density at 35°C.

The application of the jumped magnetic flux density of constant value clearly showed that processes leading to the creation of structures were time-dependent and step-by-step (Figs. 4, 5). The acoustic spectroscopy at various temperatures confirmed, that the application of the magnetic flux density had an influence on the rearrangement of magnetic nanoparticles into structures like dimers, trimers, thin and thick chains, or clusters [27]. At the temperature of 25°C and 200 mT, the processes of rearrangement of nanoparticles took the shortest time (Fig. 4). Since the change of $\Delta\alpha$ was small, we suppose, that the final structures were small,

dimers, trimers, or thin chains. This effect could be caused by a double layer of surfactant on magnetic nanoparticles. At very low temperatures longer chains cannot be created because Brown motion is very small. In the case of higher temperatures, the process of nanoparticle restructuring reached its equilibrium after 25 minutes at 35°C and 20 minutes at 45°C, respectively. At these temperatures $\Delta\alpha$ was higher, so the structures could be bigger thick chains or clusters.

The measurement at different jumps changes of the magnetic flux density at temperature 35°C (Fig. 5) showed that the fastest achievement of a stable value of acoustic attenuation was for the highest value, 300 mT. This field ensures sufficient stability of the resulting structures, so we expect thick chains or clusters with good stability. At lower fields, the time stabilization of time took longer, so could be only short or thin chains. The development of the acoustic attenuation after switch off the magnetic flux density clearly showed that longer chains were decayed in a shorter time and the lifetime of smaller structures was relatively long. This conclusion results from that the acoustic attenuation did not return to its initial value in 10 minutes. The return of acoustic attenuation to almost initial value was observed at the linear change of magnetic flux density (Fig. 6).

The value of acoustic attenuation also influences on other parameters characterizing a biocompatible fluid. Important parameters are its density and viscosity (Fig. 3), which decrease with temperature [31, 32]. The temperature dependence of these parameters influence on the time constant of creation, as well as the decay of aggregations of nanoparticles.

Nanoparticles move mainly due to Brownian thermal motion and their velocity increases with temperature. This means that in the case of larger nanoparticles (our case), more structures could be created with increasing temperature. At higher speeds, the nanoparticles get closer faster because their kinetic energy is insufficient to overcome the barriers double layer of surfactant around magnetic nanoparticles [33]. When they are close enough bond together due to a stronger magnetic force than at smaller nanoparticles. This is the reason why we observe bigger structures (thick chains or clusters) at the studied higher temperatures than at lower temperatures (Fig. 4). On the other hand, smaller nanoparticles approach too fast with increasing temperatures, so their weaker magnetic forces cannot connect them, which then causes a decrease in attenuation with temperature [29–36]. This statement is supported by the article [33], where we observed a decrease in the acoustic attenuation with temperature for the biocompatible liquid with magnetic nanoparticles of the diameter of 9.47 nm.

5. CONCLUSION

The presented results for the biocompatible magnetic fluid based on the water showed the creation of structures in presence magnetic field, which was confirmed by the change of the acoustic attenuation. Due to the larger diameter of the

nanoparticles with increasing temperature, bigger nanoparticle structures could be formed. Investigated biocompatible magnetic fluid appears as a perspective tool for application in clinical trials and can also be used for magnetic hyperthermia.

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