

MAGNETIC RESONANCE OF DEXTRAN- AND DMSA-COATED MAGNETITE-BASED MAGNETIC FLUIDS: PARTICLE INTERACTION INVESTIGATION

J.G. Santos¹, N. Buske², C. Gansau², & P.C. Morais¹

¹ Universidade de Brasília, Instituto de Física, Núcleo de Física Aplicada, 70919-970 Brasília-DF, Brazil

² Berlin Heart AG, Wiesenweg 10, D-12247 Berlin, Germany

INTRODUCTION: Magnetic resonance (MR) has been successfully used to investigate different aspects of ionic and surfacted magnetic fluids (MFs). Most of the experimental data refer to the MR from the core nanoparticle instead of from doping species intentionally introduced in the MF sample. The effects of the particle concentration, nanoparticle size, coating agents, ionic strength, and temperature upon the resonance linewidth or/and resonance field have been investigated in the last ten years. Very recently, however, investigation of the kinetic disposition of biocompatible magnetic fluids (BMFs) endovenously administered in mice has been performed using MR experiments [1]. However, to be used as an analytical technique while probing nanosized magnets in living beings and biological materials, the analysis of the resonance spectra has to be previously performed in a wide range of nanoparticle concentration, say from 10^{12} to 10^{17} cm⁻³. This is particularly important because specific tissues and cells may, under certain conditions, concentrate nanosized particles either internally in the cell or externally attached to the cell membrane. Aggregation of magnetic nanoparticles in a small cluster or in a chain-like structure is expected to change the MR lineshape or even to cause MR line splitting. In the present study a systematic investigation of the resonance spectra of BMFs is carried out at room temperature and in the concentration range of 2×10^{13} to 5×10^{16} particle/cm³.

METHODS: The two biocompatible magnetic fluids used in this study are based on magnetite nanoparticles (9.4 nm in average diameter) coated with dextran and DMSA (dimercaptosuccinic acid). After precipitation, magnetite nanoparticles were surface-coated to produce stable BMF samples at physiological pH and salinity. Typical sample preparation routine can be found in Ref. [2]. Room temperature resonance measurements were performed using a commercial spectrometer (Bruker ESP-300) tuned around 9.421 GHz.

RESULTS & DISCUSSION: Figure 1 shows the room-temperature resonance spectra (first

derivative of the absorption curve) of dextran-coated (sample BMF1) and DMSA-coated (sample BMF2). Magnetic resonance spectra of the samples containing high, intermediate, and low particle concentrations are reasonably well described by one single resonance line, differently of typical resonance spectra observed in ionic MFs.

Open and full circles in Fig. 2 represent the room-temperature resonance field (H_R) versus resonance linewidth (ΔH_R) of samples BMF1 and BMF2, respectively. Dashed and solid lines in Fig. 2 represent the best numerical fit of H_R versus ΔH_R according to [3]:

$$H_R = A(\Delta H_R)^2 \quad , \quad (1)$$

where A is a fitting parameter. Note the stronger resonance field deviation between the two sets of data at higher values of the resonance field, i.e. at lower nanoparticle concentration.

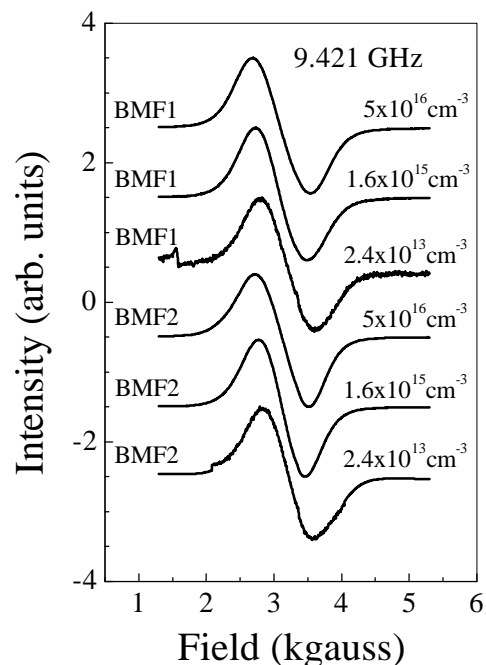


Fig. 1: Typical room-temperature magnetic resonance spectra taken from samples BMF1 and BMF2, at different particle concentrations.

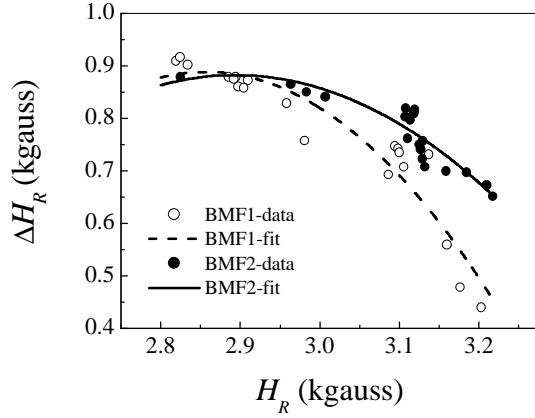


Fig. 2: Resonance field versus resonance linewidth for samples BMF1 and BMF2. Dashed and solid lines represent the best fit of the data according to Eq. (1).

Figure 3 shows the resonance field (H_R) versus the inverse of particle concentration ($1/C$) for the two samples investigated. Solid lines in Fig. 3 represent the best fit of H_R versus $1/C$, according to the model described in Ref. [1]. The description of H_R versus $1/C$ starts with the basic resonance equation, i.e. $H_{EFF} = \omega_R/g$, where H_{EFF} is the effective field at the resonance center, ω_R is the microwave frequency, and g is the gyromagnetic ratio. At low particle concentration the effective field is mainly a combination of the external field (H_E), the anisotropy field (H_K), and the demagnetizing field (H_D) [4]. Only the demagnetizing field depends upon C . At the resonance condition, $H_E = H_R$, the basic resonance equation is rewritten as $H_R = \omega_R/g - H_K - H_D$. The demagnetizing field of an assembly of isolated spherical nanoparticles in a magnetically inert matrix, however, is given by $H_D = (4\pi/3)[(1/p) - 1]M$, where M is the magnetization associated to the magnetic nanoparticle and p is the volumetric packing fraction of the nanoparticle in the matrix [5]. Note that the relationship between p and C is $p = \pi DC/6$, where D is the nanoparticle diameter. Therefore, at the low-concentration end the relationship between H_R and C would be written as $H_R = H_0 + K_1/C$, where H_0 and K_1 are fitting parameters. The data in Fig. 3, however, shows a linear relationship between H_R and $1/C$ only at nanoparticle concentrations below about 10^{14} cm^{-3} . Above 10^{14} cm^{-3} particle-particle (dipole) interaction plays a key role in the H_R versus $1/C$ curve, as revealed by the abrupt change of the H_R versus $1/C$ slope.

Inclusion of the particle-particle interaction in the description of the H_R versus $1/C$ curve is

realized via the relationship between the shift of the resonance field and the shift in the resonance linewidth, as described in Eq. (1) [3]. However, the linewidth shift has been successfully described by $\Delta H_R = BC \tanh(K_2 + K_3 C^2)$ [6]. The $K_3 C^2$ term describes the dipole-dipole interaction at the higher end of nanoparticle concentration, as discussed in Ref. [6]. The resonance field now reads:

$$H_R = H_0 + K_1/C - B^2 C^2 \tanh^2(K_2 + K_3 C^2) \quad , \quad (2)$$

where H_0 , B , and K_j ($j = 1, 2, 3$) are fitting parameters. In Fig. 3 the solid lines represent the best fit of the data in the full range of particle concentration, i.e. according to Eq. (2). The ratio of the K_3 values for BMF1 and BMF2 (0.91) indicates that dipole-dipole interaction is roughly the same for both samples. However, the ratio of the B values for BMF1 and BMF2 (1.3) indicates that particle-particle coupling, due to the coating molecular layer, is quite different in both samples. Finally, the ratio of the K_1 values for BMF1 and BMF2 (0.88) indicates that the particle-core diameter (effective values) is slightly different in both samples.

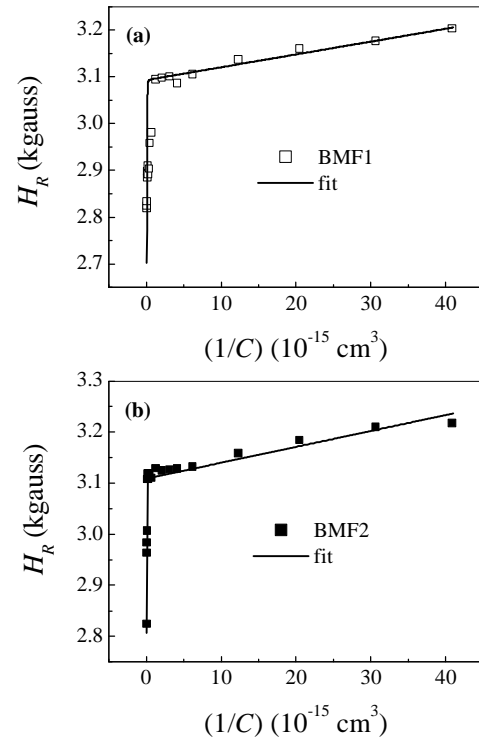


Fig. 3: Resonance field versus the inverse of particle concentration for samples (a) BMF1 and (b) BMF2.

CONCLUSIONS: In summary, magnetic resonance has been used to investigate magnetic fluids based on magnetite nanoparticle coated with two biocompatible molecular species (dextran and DMSA). Whereas the resonance field shift by about

the same amount in both samples, the shift in the resonance linewidth in the dextran-coated sample is twice the shift observed in the DMSA-coated sample. This aspect would favor the use of the DMSA-coated MF sample to probe biodistribution after injection in animals. In particular, concentration of DMSA-coated magnetite nanoparticles in specific organs could be signaled through line splitting in MR measurements.

REFERENCES: ¹L.M. Lacava, Z.G.M. Lacava, M.F. Da Silva, O. Silva, S.B. Chaves, R.B. Azevedo, F. Pelegri, C. Gansau, N. Buske, D. Sabolovic, and P.C. Morais (2001) *Biophys. J.* **80**:2483-2486. ²D. Günther and N. Buske (1993) DE patent Nr. 4325386. ³K. Nagata and A. Ishihara (1992) *J. Magn. Magn. Mater.* **104**:1571-1573. ⁴A.F. Bakuzis, P.C. Morais, and F. Pelegri (1999) *J. Appl. Phys.* **85**:7480-7482. ⁵E. Kneller (1969) *Fine particle theory* in Magnetism and Metallurgy (eds A.E. Berkowitz and E. Kneller), Academic Press, pp. 365-471. ⁶P.C. Morais, M.C.F.L. Lara, A.L. Tronconi, F.A. Tourinho, A.R. Pereira, and F. Pelegri (1996) *J. Appl. Phys.* **79**:7931-7935.

ACKNOWLEDGEMENTS: This work was partially supported by the Brazilian agencies CNPq and CAPES.