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Magnetic performance of Synomag nanoparticles in various environments

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Abstract

This work is an assessment of changes in magnetic properties of magnetic nanoparticles in various biological environments. To mimic variations in biological conditions, we have evaluated magnetic performance of Synomag® nanoparticles in two experiments: the effect of viscosity by varying the ratio of glycerol/water mixture and the effect of immobilization after blocking the Brownian relaxation by freeze-drying (to mimic uptake in macrophages). The magnetic response was measured with the Superparamagnetic quantifier. Synomag® exhibits a slight decrease (7.9 %) of magnetic response under increased viscosity from $\eta_1 = 0.95$ to $\eta_6 = 259.71$ mPa.s, and a dramatic magnetic signal drop (78.2 %) after freeze-drying. Synomag® nanoparticles are less sensitive to viscosity due to an additional relaxation mechanism of disordered spins within the nanoflowers. However, the magnetic performance has been reduced due to the blocking of Brownian relaxation after immobilization.

I Introduction

Superparamagnetic iron oxide nanoparticles (SPIONs) have been extensively studied for use in biomedical applications, e.g. magnetic particle imaging (MPI), magnetic resonance Imaging (MRI), hyperthemia, and sentinel lymph node biobsy [1]. Additionally, several formulations of magnetic tracers with the nonlinear magnetic response have been approved for clinical application [2]. The change of biological medium around SPIONs could affect their magnetic performance (and therefore affect clinical applications) due to change of viscosity environment (tissue or blood) and immobilization into macrophages [3], see Figure 1.

Generally, SPIONs exhibit two distinct relaxation mechanisms: The Brownian relaxation due to the rotation of the whole particle, and internal Néel relaxation within the single domain where the magnetization relaxes without any physical rotation [4]. Recently, an additional relaxation echanism has been described for a new particle (dextran coated iron-oxide with a nanoflower shape: mixture of γ-Fe_2O_3 and Fe_3O_4), Synomag® (micromod Partikeltechnologie GmbH, Germany). It is a fast relaxation mechanism attributed to the relaxations of disordered spins within the nanoflowers [5]. In this study, we investigated the effect of viscosity and immobilization of Synomag® on magnetic performance.

II Material and methods

II.I Viscosity experiment

Six samples of Synomag® nanoparticles, each containing 200 μg of iron, have been mixed with glycerol and water to a total volume of 300 μl. The viscosity was adjusted to $\eta_1 = 0.95$, $\eta_2 = 2.1$, $\eta_3 = 5.04$, $\eta_4 = 74.2$, $\eta_5 = 167.56$, and $\eta_6 = 259.71$ mPa.s, using the Cheng formula [6], by changing the weight ratio of Synomag®, distilled water, and glycerol. The range of viscosity was chosen with respect to the viscosity of various biological environments [7].

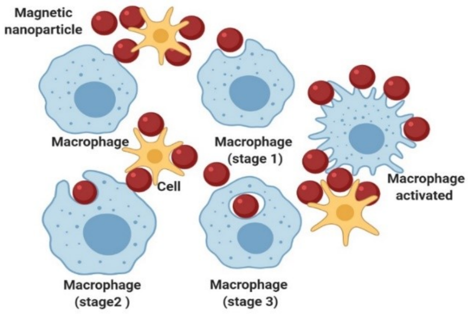

Figure 1: The different stages of cellular uptake by macrophages.

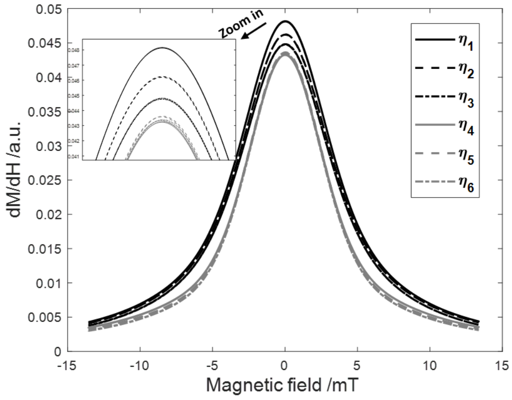

Figure 2: The dM/dH response vs offset field for the Synomag® in different viscosities at a definite frequency 2.5kHz.

II.II Immobilization experiment

Magnetic properties of a 200 μl Synomag® sample containing 5μg/μl iron have been evaluated before and after immobilization via the process of freeze-drying.

II.III Measurement principle

The magnetic response for all samples has been assessed using the SuperParamagnetic Quantifier (SPaQ) [8]. An alternating field (1.33 mT) in combination with an offset field ($\leq$ 13.3 mT) was applied to each sample, time of measurements was set to 1 second, and the excitation frequency was to 2.5 kHz. This resulted in a measurement

Table 1: Percentage magnetic drop of dM/dH maximum for all samples.

Viscosity (mPa.s)	η_1 to η_2	η_1 to η_3	η_1 to η_4	η_1 to η_5	η_1 to η_6
ΔA (%)	4.1	6.3	9.33	7.97	7.97

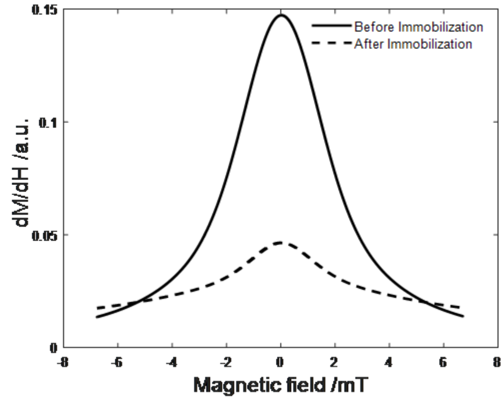

Figure 3: The dM/dH response vs offset field for the Synomag® before and after Freeze-drying at a frequency 2.5kHz.

of the derivative of the nonlinear magnetization curve of SPIONs (dM/dH). A relative change in the magnetic signal was reported [9]: $\Delta A\% = -\frac{A'-A}{A}\cdot 100$ With A': the dM/dH max value of each viscosity ranging from η_2 to η_6 and A: the dM/dH max value of sample η_1 (in water).

III Results

Figure 2 illustrates dM/dH curves for Synomag® nanoparticles for different viscosity values. All curves are symmetrical around zero magnetic field confirming the superparamagnetic nature of all samples. For low-viscosity values (η_1, η_2 and η_3), we observed a change of the maximum value in dM/dH curves. In contrast, for high-viscosity values (η_4, η_5 and η_6), we observed an increase of dM/dH$|_{max}$ values. All percentage of magnetic drop are listed in Table 1.

Figure 3 represents the magnetic response of Synomag® particles before and after Freeze-drying. A dramatic drop of amplitude (78.2 %) has been observed after immobilization.

IV Discussion

The dM/dH curves slightly decrease with increasing viscosity. This shows that the magnetization of Synomag® nanoparticles is nearly independent of the viscosity of the surrounding medium. Our results are consistent with the study of Bender et al. [5], in which similar independence of viscosity for same nanoparticles for hyperthermia application was observed, and underlined that the mechanism of relaxation is generated by internal process not only the Brownian relaxation. The immobilization by freeze-drying of Synomag® nanoparticles totally blocks the Brownian relaxation and keeps only the internal relaxation. The dramatic drop of signal in Figure 3 demonstrates that Synomag® nanoparticles are dominated by

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Brownian relaxation and the fast relaxation of disordered spins within the nanoflowers.

V Conclusion

Clinical applications aim to preserve the magnetic performance when particles are transferred from a laboratory to in vivo environment. Even though immobilization has an effect on the magnetic properties of Synomag®, the limited sensitivity to varying viscosity is promising for clinical application. The fact that the changes in viscosity of the medium almost do not affect the change in magnitude between dM/dH curve at magnetic field of 0 and 10 mT demonstrates that the Synomag® particle is a promising candidate for in vivo use, for instance in sentinel lymph node procedures for cancer patients.

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