Measurement of the distribution parameters of size and magnetic properties of magnetic nanoparticles for medical applications

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Abstract. Magnetic nanoparticles usually show a broad size distribution resulting in a corresponding distribution of the magnetic properties. One important goal of particle development is the reduction of the distribution width of the relevant quantities. In this contribution we show that for magnetic nanoparticles with sizes above the superparamagnetic range the measurement of remanence curves provides the required information. From these data we can obtain the remanence ratio and the switching field distribution which can be used as a quality criterion in the development of this type of magnetic nanoparticles.

1. Introduction
Magnetic nanoparticles (MNP) have been proposed for medical applications, e.g. hyperthermia [1] or drug-targeting [2]. As such applications require non-toxic material our work is focussed on the magnetic iron oxides $\gamma$-Fe$_2$O$_3$ and Fe$_3$O$_4$. The most common preparation technique of such particles is the wet-chemical precipitation which usually provides MNP with a broad distribution of their size resulting in corresponding distributions of the magnetic properties. This is a disadvantage for applications as only a small fraction of the MNP in a given sample shows the optimal properties. The focus of our current work is the preparation of MNP with a sharper distribution of the relevant properties. There are two possible ways to achieve this goal. Firstly, the development of modified preparation methods [3], and secondly, a physical aftertreatment by magnetic separation or centrifugation. The development of such materials requires measurement methods which provide information on the statistical properties of the samples. For small, i.e. superparamagnetic particles this information can be extracted from the Langevin-like magnetization curve using the method of Chantrell [4]. Assuming a lognormal distribution of the MNP size the method provides the mean value and the distribution width parameter. From the size distribution one can calculate the distribution of the Néel relaxation time which determines the heating effect of superparamagnetic particles in an ac magnetic field. Our current work, however, is focussed on larger particles, which show a hysteresis. Here the Chantrell method is not suitable. Moreover, the relevant magnetic parameter is no longer the relaxation time but the anisotropy field $H_K$ and its distribution. In addition, this type of material usually contains a certain fraction of superparamagnetic particles which is indicated by a reduced remanence ratio $M_{rs}/M_s$ (saturation magnetization $M_s$ and maximum remanent
magnetization $M_{rs}$). In this contribution we demonstrate the characterization of large MNP on the basis of these quantities.

2. Remanence Measurements and Switching Field Distribution

The measurement of the initial remanence curve is performed in the following way. A small field $H$ is applied to a demagnetized sample. Then the field is reduced to zero and the remanent magnetization is measured providing the first point $M_r(H)$ of the initial remanence curve. This procedure is repeated with successively increasing fields until the saturation remanence $M_{rs}$ is reached. In addition, the saturation magnetization $M_s$ is determined from a usual magnetization loop. The remanence curve contains information on the amount of particles which switch their magnetization irreversibly at the field $H$. Therefore differentiation provides the distribution of this switching field $\delta S(H) = \frac{1}{M_{rs}} \frac{dM_r(H)}{dH}$.

In the ideal case of monodisperse uniaxial MNP which are aligned parallel to the field $M_r(H)$ is 0 below $H_K$ and equal to $M_s$ above $H_K$ resulting in a remanence ratio $M_{rs}/M_s = 1$ and $S(H) = \delta(H-H_K)$. In general $S(H)$ is broadened by two effects, firstly the statistical orientation of the particles, and secondly, the distribution of $H_K$. In order to distinguish between these effects $M_r(H)$ and $S(H)$ were simulated for monodisperse (i.e. the same $H_K$ for all particles) statistically oriented samples consisting of particles with uniaxial or cubic anisotropy. For cubic particles two cases, positive or negative anisotropy constant, were regarded. The simulation is based on the minimization of the total energy of an ensemble of isotropically oriented particles. The energy consists of two contributions: the anisotropy energy and the energy of the particles in the external field. Fig. 1 and 2 show the results of the simulation. The switching field distributions were fitted by a lognormal distribution function

$$S(H) = \frac{1}{\sqrt{2\pi\sigma H}} \exp \left( -\frac{\ln^2(H/H_m)}{2\sigma^2} \right)$$

with the mean value $H_m$ and the width $\sigma$. Tab. 1 shows the fit parameters. Iron oxide MNP are represented by type N in Tab. 1 if the shape anisotropy is negligible. The lognormal function

![Figure 1](image1.png)  
![Figure 2](image2.png)
Table 1. Parameters of the simulated remanence curves and switching field distributions for aligned uniaxial particles (T) and statistically oriented particles of uniaxial (U) or cubic anisotropy with positive (P) or negative (N) anisotropy constant

|       | $M_r/M_s$ | $H_m/H_K$ | $\sigma$ |
|-------|-----------|-----------|----------|
| T     | 1.00      | 1.00      | 0.00     |
| U     | 0.50      | 0.52      | 0.05     |
| P     | 0.83      | 0.29      | 0.18     |
| N     | 0.86      | 0.20      | 0.35     |

Table 2. Parameters of the measured remanence curves and switching field distributions

| Sample | $M_r/M_s$ | $H_m$/Oe | $\sigma$ |
|--------|-----------|----------|----------|
| S      | 0.007     | 52       | 0.60     |
| C      | 0.064     | 135      | 0.67     |
| L      | 0.042     | 142      | 0.60     |
| M      | 0.272     | 161      | 0.51     |

does not fit to the simulated points very well. But we use it here for comparison with the experimental data where the lognormal distribution is suitable.

3. Experimental Investigations
In order to demonstrate the method we present remanence measurements of four iron oxide samples which were prepared by different methods. Three of them were made by alkaline precipitation and coated by carboxymethyl-dextrane. Sample S was prepared by fast precipitation with a strong base and consists mainly of superparamagnetic particles. Sample C was slowly precipitated with a weak base resulting in particle clusters [6]. For sample L a fast precipitation method with a weak base was used which leads to larger single domain particles. For comparison we investigated sample M which consists of magnetosomes [7], i.e. magnetite particles from magnetotactical bacteria. The remanence curves and the resulting switching field distributions as well as their lognormal fits are shown in Fig. 3 and 4. The remanence ratios and the distribution parameters are given in Tab. 2. The most significant difference between the samples is the remanence ratio. Even for the samples L and C which consist of relatively large particles (mean diameter 15 nm or 50 nm) it is one order of magnitude lower than the theoretical value (Tab. 1) indicating a large superparamagnetic fraction. Sample M is much closer to the theoretical values. The distribution width $\sigma$ is similar for all samples and differs from the theoretical value by less than a factor of 2. Also the mean values $H_m$ are similar except for sample S. These results show that a reduction of the superparamagnetic fraction is

![Image of remanence curves and switching field distributions](image-url)
Table 3. Fractionation with 10 mm gap:
O original sample, A inner fraction, B outer fraction, C final fraction

| fraction | \(M_r/M_s\) |
|----------|-------------|
| O        | 0.0074      |
| A        | 0.0037      |
| B        | 0.0041      |
| C        | 0.0109      |

Table 4. Fractionation with 17 mm gap:
O original sample, A inner fraction, B outer fraction, C final fraction

| fraction | \(H_m/Oe\) | \(\sigma\) |
|----------|------------|------------|
| O        | 36.6       | 0.70       |
| A        | 34.9       | 0.65       |
| B        | 33.5       | 0.69       |
| C        | 40.4       | 0.69       |

the most promising way to improve the material. Nevertheless, the reduction of the distribution width has some potential as well.

4. Characterization of Magnetically Fractionated Samples

Experiments were performed in order to find the optimum parameters (field gradient, flow velocity, particle concentration) for magnetic fractionation of a given particle type. The fractionation set-up consists of a glass tube of 10 mm diameter and 200 mm length which is placed between two oppositely oriented permanent magnets (6 x 10 x 200 mm³). After flowing through this quadrupole field the fluid is split into two fractions using concentric tubes at the end of the system. The inner part is fraction A, the outer one fraction B. A third fraction (C) is obtained at the end of the process from the last 10 ml of the fluid. The samples obtained by this method were characterized by remanence measurements. Tab. 3 and 4 show the results of two experiments with particles of type S and different gaps between the magnets where an effect of fractionation was observed, i.e. the fractions show increased or decreased values of the remanence ratio or the mean switching field. However, the effects are not very pronounced so far and further optimization of the process is necessary.

5. Conclusions

The measurement of remanence curves and the determination of the switching field distribution is a suitable method to characterize the statistical properties of large MNP samples. The most promising way of improvement of such samples is the reduction of the superparamagnetic fraction. The method was used to characterize samples obtained by magnetic fractionation. In two selected experiments a fractionation effect due to the remanence ratio or the mean switching field was shown.

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