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Journal of Magnetism and Magnetic Materials 290–291 (2005) 269–271
Journal of magnetism and magnetic materials
www.elsevier.com/locate/jmmm

Scanning force microspy study of biogenic nanoparticles for medical applications

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Available online 7 December 2004

Abstract

We present a combined atomic force microscopy (AFM) and magnetic force microscopy (MFM) study of bacterial magnetosomes, consisting of membrane-covered magnetite particles. AFM imaging unambiguously demonstrates the existence of single isolated magnetosomes with a size of about 40 nm, in addition to various clusters of magnetosomes. With MFM we have particularly addressed the magnetic properties of single magnetosomes. These nanoparticles behave like single mono-domain nanomagnets, as shown by the comparison of the MFM data to simple simulations. These simulations also provide information on the size of the magnetic kernel of the magnetosomes. Moreover, the invasiveness of the MFM tip is addressed.

PACS: 07.79.Pk; 75.50.Tt; 75.60.Ej

Keywords: Biomagnetism; Nanoparticles; Magnetic force microscopy

1. Introduction

Magnetic nanoparticles in diluted aqueous suspensions are an important tool in medical diagnostics as contrast agent for magnetic resonance imaging, and in therapy for magnetic drug targeting and hyperthermia. For these applications, special nanoparticles (so-called magnetosomes) were isolated, which consisted of a magnetite core covered by a protein-containing lipid membrane [1]. The properties of ensembles of these magnetosomes were investigated using spatially integrating measuring methods [2]. Yet, for many applications it is advantageous to use single magnetosomes. Consequently, one needs to clarify unambiguously whether single, isolated magnetosomes exist in ensembles. If so, the magnetic properties of the individual magnetosomes are of great interest. In particular, the remanent magnetization, coercivity, and domain structure need to be studied in detail. These issues can be addressed by atomic force microscopy (AFM) and magnetic force microscopy (MFM) thanks to the nanometer spatial resolution of these techniques [3,4]. In this paper we present a combined AFM and MFM study of single magnetite magnetosomes. It is shown that single magnetosomes exist and that they exhibit a magnetic mono-domain structure.

2. Material and measuring method

2.1. Magnetosomes

Magnetosomes are biogenic magnetic nanoparticles of sub-100-nm diameter consisting of cubo-octahedral

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doi:10.1016/j.jmmm.2004.11.206

magnetite crystals coated by a lipid–protein membrane. The magneotsomes were extracted from the magnetic bacterium *Magnetospirillum gryphiswaldense*, see Ref. [1]. Based on the results of macroscopic measurements, it can be concluded that they have much higher magnetic moments than most conventional magnetic particles prepared by precipitation reactions [2]. For AFM/MFM experiments, a very small drop of highly diluted aqueous suspension of magnetosomes was applied on a silicon wafer and then was allowed to dry.

2.2. Force microscopy

Measurements were performed with a nanoscope IIIa force microscope equipped with a bioscope scanner. To optimize the sensitivity of the MFM, the MFM measurements were done in non-contact phase detection mode. In a first scan an AFM image is taken in contact tapping mode to give a reference height line. The MFM scan is performed taking into account this reference line with a lifted cantilever driven at its resonance frequency. The shift of the phase of the driven cantilever is detected, which is a measure of dF_z/dz, where F is the force and z is the direction normal to the sample plane. Whisker tips (from NT-MDT, Russia) with a hard magnetic coating, i.e., Ni and a tip radius of 15 nm as well as ultrasharp soft magnetic tips coated with a thin film of Fe–Ni with a tip radius of about 25 nm (from NT-MDT, Russia) were used. For both types of tips the spatial resolution is 15 nm in magnetic field measurements. Since the tip length is much larger than the tip radius, both types of tips can be modelled as monopoles. As a result, the cantilever phase shift is a measure of dB_z/dz, where B is the magnetic flux density. The images detected by the system are low-pass filtered in Fourier space to remove features with a size of less than 1 nm.

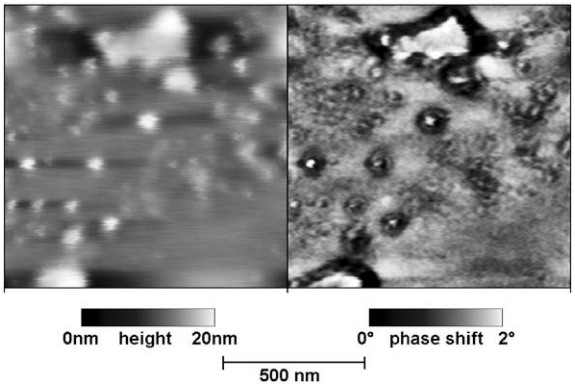

Fig. 1. AFM (left) and MFM (right) images of isolated magnetosomes and magnetosome clusters magnetized vertically to the plane before the measurement. In the MFM image, the white (black) color represents repulsion (attraction).

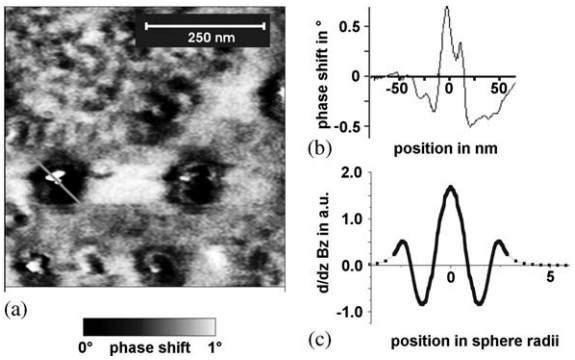

Fig. 2. (a) Enlarged MFM image of two single magnetosomes of Fig. 1. Bright colors represents repulsion, while dark colors represent attraction. (b) Cut through the MFM image of the left particle along the line in (a). (c) Cut through the calculated dB_z/dz image of a sphere that is homogeneously magnetized vertically to the sample plane.

3. Results

The AFM image of Fig. 1 clearly shows single, isolated magnetosomes along with magnetosome clusters of various sizes.

From the analysis of such images, the size of a single magnetosome is determined to be typically 40–45 nm.

First MFM measurements were performed with a hard magnetic whisker tip. The samples were magnetized by an external field oriented vertically to the substrate plane prior to the measurement. The MFM image of single magnetosomes consists of a dark ring around a white center (see Fig. 1, right image). The dark ring corresponds to attraction between the magnetosome and the MFM tip, while the white center corresponds to repulsion. For further analysis, a line cut was taken across a single magnetosome (see Fig. 2b). The position and direction of the cut are indicated in the close-up of the MFM image displayed in Fig. 2a. The measured line cut is compared to the calculated dB_z/dz response of a sphere with a homogeneous magnetization oriented normal to the sample plane, i.e., in the z direction (see Fig. 2c). Good agreement is found between the measured and calculated data. This comparison demonstrates that single magnetosomes exhibit a magnetic mono-domain structure with a dipole moment oriented normal to the substrate plane under our experimental conditions. The small tilt of the measured profile can be related to a slight tilt of the magnetization axis.

From the analysis, the size of the magnetic kernel of the magnetosomes can be estimated as well as preliminary information about their long-time stability. As

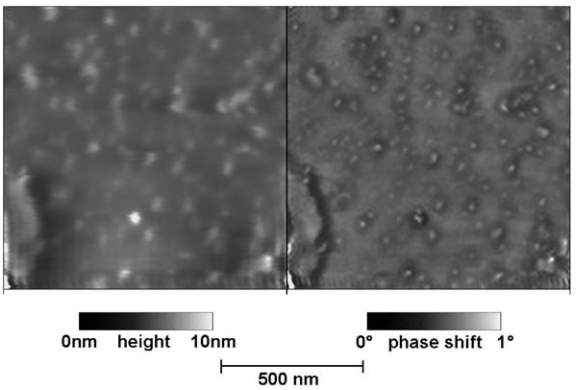

Fig. 3. AFM (left) and MFM (right) images of single magnetosomes and magnetosome clusters magnetized vertically to the plane before the measurement. In the MFM image the white (black) color represents repulsion (attraction). The measurement was performed 1 month after the measurement of Fig. 1.

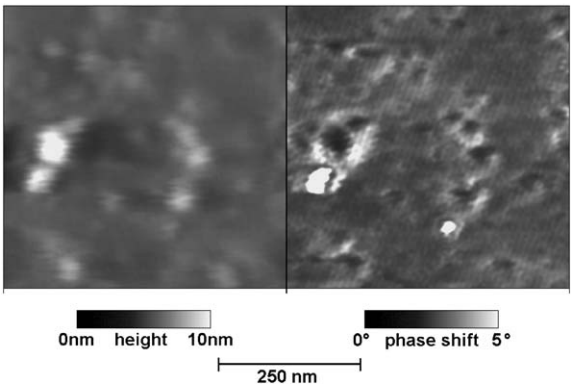

Fig. 4. AFM (left) and MFM (right) images of magnetosomes and magnetosome clusters magnetized in plane before the measurement. In the MFM image the white (black) color represents repulsion (attraction). The white areas are not in the center but on the lower right corner of the magnetosomes, whose magnetization lies in the plane.

a measure of the particle size, we take the diameter of the homogenously magnetized model sphere that yields the best fit to the measured line. Evaluating 25 particles we find a diameter of 21 nm $\pm$ 2.5 nm from the data of Fig. 2. Measurements done 1 month later showed the same general features as before (see Fig. 3), yet the diameter of the magnetic kernel—this time averaged over 30 particles—has slightly decreased to 18 nm $\pm$ 3 nm. This result suggests that the magnetic kernel of the magnetosomes slightly shrinks with time.

In general, the magnetic MFM tip may affect the magnetization of a sample during image acquisition. To address this issue, magnetosome samples were magnetized by an in-plane external field prior to the measurement. In these measurements, the external field was normal to the main direction of the field generated by the MFM tip. MFM images taken with a hard magnetic whisker tip showed the MFM pattern of a vertical, out-of-plane magnetization, i.e., normal to the direction of the external field. MFM images with hard magnetic tips reveal the magnetic properties of the magnetosomes in the external field generated by the MFM tip.

Using an ultrasharp tip with soft magnetic coating the magnetization initially stays in plane (see Fig. 4), but changes to the vertical direction after several scans. As expected, the influence of the soft magnetic ultrasharp tips is weaker than the influence of the hard magnetic whisker tip [5]. It is currently not clear whether the reorientation of the magnetization is solely due to the tip field or involves thermal excitation. The latter cannot be excluded since the blocking temperature of 21 nm large magnetosomes is in the order of magnitude of the room temperature [2].

4. Conclusion

We have presented AFM measurements, which show that magnetosome ensembles consist of single, isolated magnetosomes with diameters between 40 and 45 nm and magnetosome clusters. With MFM we have particularly addressed the magnetic properties of single magnetosomes. It is found that the magnetosomes exhibit a magnetic mono-domain structure in the field generated by the MFM tip. The dipole moment of the particles is oriented normal to the sample plane in these measurements. The comparison between the MFM data and a simple model calculation has yielded information on the size of the magnetite kernel of the magnetosomes. Based on this data, the issue of long-time stability of the magnetosomes can be addressed. These results demonstrate that AFM and MFM are powerful tools for the development of magnetosomes for medical applications.

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