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BACTERIAL MAGNETOSOMES AS A NEW TYPE OF BIOGENIC MPI TRACER

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Introduction & Objective

Biomineralization is the process whereby minerals are formed by living organisms. Biominerals exhibit extraordinary material properties such as the combination of extreme mechanical robustness and extreme lightweight as in the case of nacre. Another amazing example are so-called magnetosomes, membrane-enclosed iron oxide nanoparticles biomineralized by magnetotactic bacteria as magnetic sensor for magnetotaxis [1]. Such magnetosomes are characterized by distinctive monodispersity in size and shape and consist of a monocrystalline magnetite (Fe_3O_4) phase. Magnetic Particle Imaging (MPI) is a new and promising imaging technology that requires the use of a magnetic tracer material. Different theories and approaches exist, involving iron oxide nanoparticles comprising, on the one hand, particles of crystal clusters [2] and, on the other hand, monocrystalline particles of large size [3]. For the first time, we present the investigation of the MPI performance of magnetosomes isolated from the bacterium *Magnetospirillum gryphiswaldense.* Magnetic particle spectroscopy (MPS) studies as well as static M/H-measurements are performed and compared with the current MPI gold-standard, Resovist®.

Materials & Methods

Magnetospirillum gryphiswaldense strains were grown under anoxic conditions in modified FSM medium [4] at 25° C in a Biostat C fermentor (B. Braun Biotech International, Melsungen, Germany). Magnetosome isolation was performed as described previously [5]. To evaluate the results, the current MPI gold-standard, Resovist®, was used for comparison (Resovist is no longer a marketed product but was still stocked in the author's lab).
TEM images were taken using a Zeiss EM 912 Ω operated at an acceleration voltage of 120 kV. Dynamic light scattering (DLS) was performed using a Submicron Particle Sizer Model 370 from Nicomp Particle Sizing Systems. The magnetic particle spectra were recorded at a drive field with an amplitude of 25 mT/μ_0 and a frequency of f_0=25.25 kHz with a commercial MPS system (Bruker BioSpin MRI GmbH, Germany). The M/H-curves were recorded with a SQUID magnetic property measurement system (MPMS XL, Quantum Design, USA).

Results & Discussion

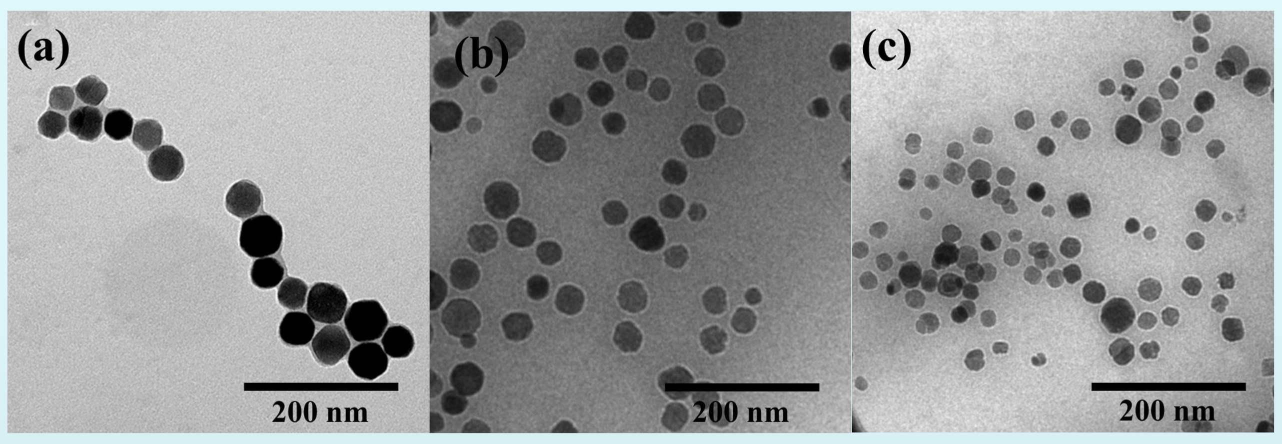


Fig. 1: *TEM image of the magnetosome samples a) LMU01, b) LMU02, and c) LMU03*

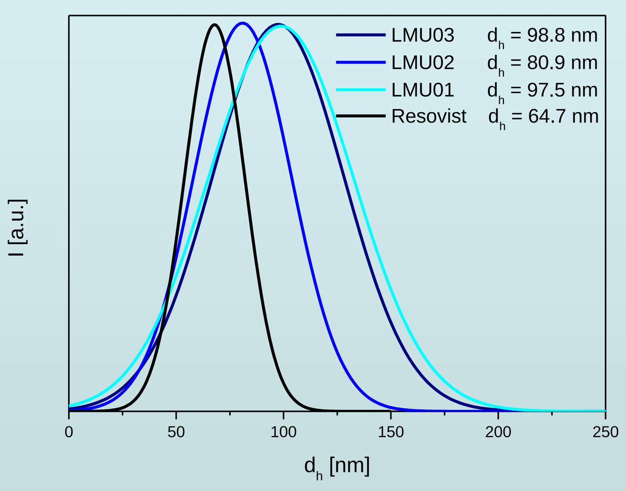
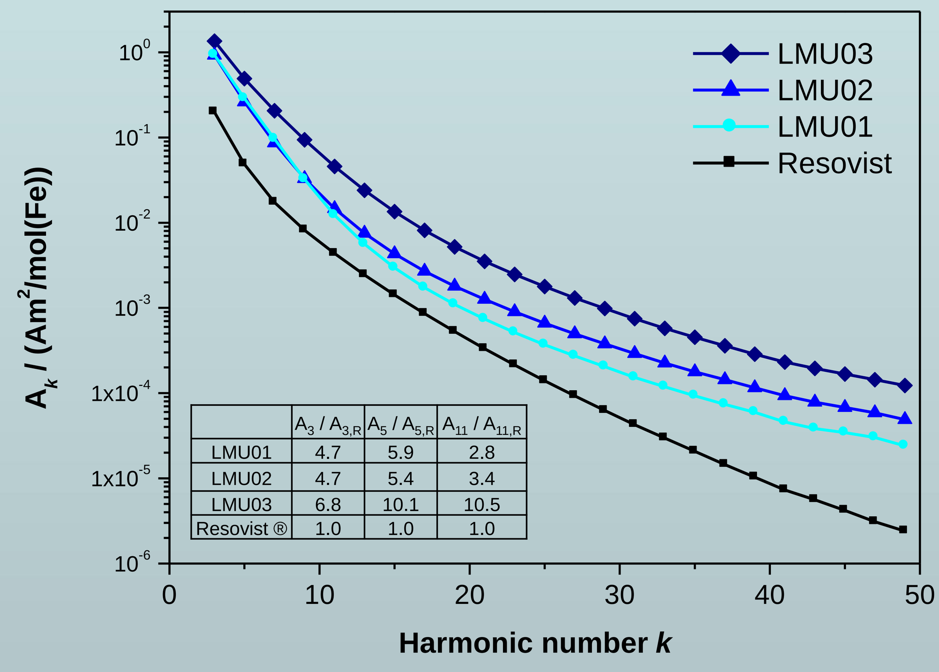


Fig. 2: *Intensity weighted Gaussian distribution and mean values of d_h of the* magnetosomes and Resovist.

TEM images highlight the presence of large and non-interacting particles (Fig. 1). Samples LMU02 and LMU03 mainly consist of randomly distributed particles whereas the TEM image of sample LMU01 shows, besides single particles (not present in Fig. 1a), also the typical chain alignment of biological magnetosomes. The crystal size, here designated as average core diameter d_c, is determined at values of 33.0 nm, 30.5 nm, and 25.7 nm for LMU01, LMU02 and LMU03, respectively. All samples provide sufficient colloidal stability attributed to the magnetosome membrane, which stabilizes the particles in aqueous media. The hydrodynamic diameter d_h is measured by DLS. The d_h of all samples is in the range of 80 – 100 nm indicating only minor interactions/aggregation in aqueous media (Fig. 2). The results confirm the TEM findings where mostly separated particles are visible. MPS spectra of the measured magnetosome suspensions in comparison to Resovist are shown in Fig. 3. It can be clearly seen, that the amplitudes of the magnetosomes over the entire range of the harmonics exceed that of Resovist by far, with a reduced decay of the amplitudes at higher harmonics. The third harmonic of the magnetosomes is at least about 4.7 times higher compared to that of Resovist, in which the sample with the smallest core diameter LMU03 exhibits the strongest amplitude. The amplitude of LMU03 is, in fact, higher by a factor of about 6.8; and is indeed one of the highest values found so far.

The decay of the harmonic spectrum of the magnetosome suspensions decreases with decreasing core diameter. In particular, in comparison to Resovist, a 10.5-fold increase of the amplitude of the 11th harmonic of LMU03 is observed. To classify the MPS results, static M/H-measurements were performed (Fig. 4). Compared to Resovist, the magnetosomes posses already a high magnetization (steeper magnetization curve) at low fields indicating larger effective magnetic moments. LMU01 offers the steepest slope whereas LMU02 and LMU03 are almost comparable. Interestingly, the saturation magnetization is reached at M_S = 480 kA/m, which is the theoretical bulk-value of magnetite. Considering these findings only, LMU01 should provide the best MPS spectrum. This contradiction can be explained by the fact that M/H is a quasi-static method and, in contrast to MPS, neglects particle dynamics. Here LMU03, with the smallest magnetosome particles, can follow the excitation field best without a major phase delay and, therefore, provides the best MPI performance.



	$A_3 / A_{3,R}$	$A_5 / A_{5,R}$	$A_{11} / A_{11,R}$
LMU01	4.7	5.9	2.8
LMU02	4.7	5.4	3.4
LMU03	6.8	10.1	10.5
Resovist ®	1.0	1.0	1.0

Fig. 3: *Odd harmonics of the MPS spectra of the magnetosomes in comparison to Resovist. Spectra were measured using 5 mmole Fe suspensions and were subsequently normalized to 1 mole Fe.*

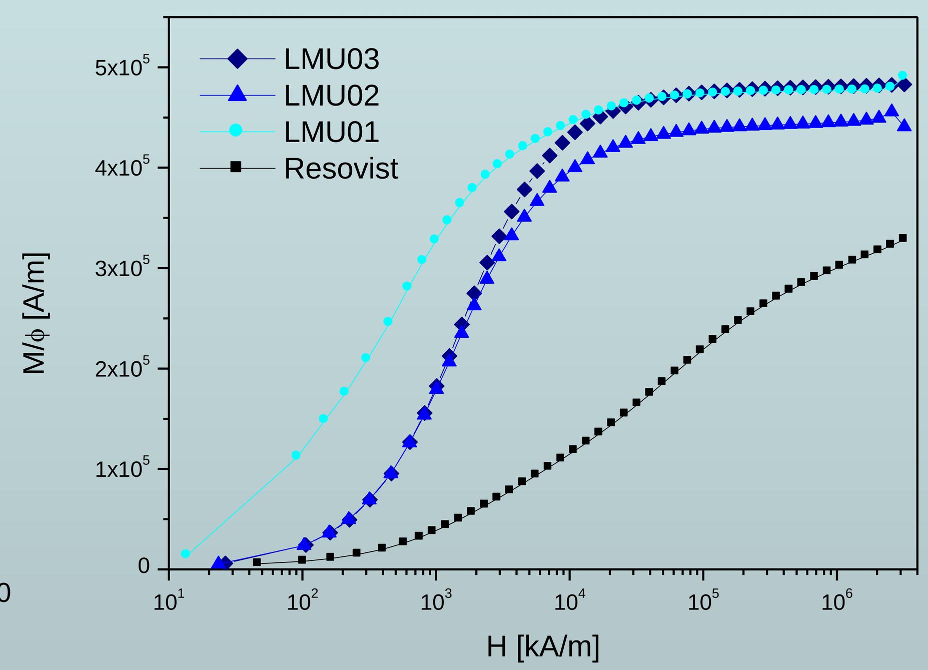


Fig. 4: *M/H-curves of magnetosome suspensions and Resovist. Magnetization values are normalized to the volume fraction of magnetite.*

Conclusion

We show that the MPS signal exhibited by the magnetosomes is highly improved compared to Resovist, the hitherto gold-standard in MPI. This is made possible through the magnetosomes' structural features such as high crystallinity and large crystal size, which result in large magnetic moments and negligible magnetic anisotropy. Furthermore, we observe a size-dependence of the MPS signal with the highest signal for the smallest magnetosome particles, showing that not only a strong magnetic moment but also dynamic aspects are important for a good MPI performance. Although technical applications of magnetosomes have been hampered due to their technically challenging bioproduction, our contribution proves their great potential as tracers and may stimulate new research efforts to synthesize such particles in the lab by biological and biomimetic synthetic routes [6].

Acknowledgements

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