

Direct Detection of SPIO Labeled Stem Cells

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Introduction

Stem cell tracking is being performed in NMR as an indirect measurement of effects caused by iron nanoparticles which suffers from ambiguity and strong background dependency of the observed signal changes. Recently a method for direct imaging of magnetic particles has been introduced [1]. We present a setup for spectroscopic detection of magnetic nanoparticles along with measurements to characterize those particles and to detect labeled stem cells.

Methods

In order to perform a direct detection of magnetic particles, the response of their magnetization to an applied radio frequency (rf) is observed. The response manifests in higher harmonics of the excitation frequency. This enables to unambiguously detect and quantify magnetic particles. An rf transmit/receive unit has been assembled which operates between 1 and 100kHz and is capable of generating magnetic fields between 1 and 30mT. As SPIOs we used Endorem (Guerbet S.A.), Resovist (Bayer Schering Pharma AG) and SPIO -D 100nm (Nanomag).

Results

Figure 1 shows the Fourier transform of the typical signal received from super-paramagnetic particles. In the absence of additional fields only odd harmonics can be observed in the signal. Its field dependency is shown in figure 2 for excitation fields B_{ac} up to 26mT. Simulated results are included in figure 2 as dash dotted lines.

The signal was proportional to the concentration which suggests that inter-particle interactions are negligible. When stepping through higher excitation frequencies the signal decreased slightly. Furthermore it can be efficiently suppressed by applying offset fields of about 30mT. These also take influence on the observable harmonics: offset components parallel to the excitation field disturb the symmetry and generate additional even harmonics. Figure 3 shows the signal detected from Resovist labeled stem cells (c) and d), 5×10^5 cells, 44pg Fe/Cell). For comparison scans on pure water (a), unlabeled cells (b), and a suspension of SPIO -D 100nm in water (e) are shown.

Conclusion

Though only at the very beginning of using this new technique, good insights into the response of magnetic particles to different environments could be gathered. These data enable to optimize transmitters and detectors in order to enhance the signal gain and develop suitable models and theory. Furthermore even at this stage we were able to clearly distinguish labeled from unlabeled stem cells in spectroscopic studies.

References

[1] B.Gleich, J.Weizenecker: Tomographic imaging using the nonlinear response of magnetic particles. Nature 435,1214-1217,2005

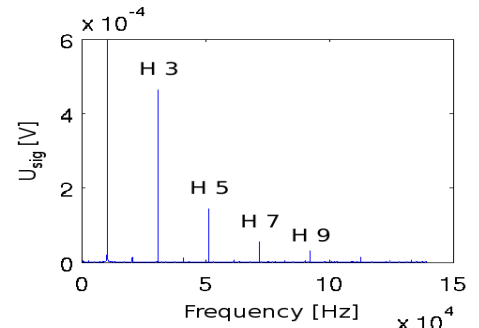


Figure 1: Fouriertransform of the typical received signal. H_n denotes the n^{th} harmonic.

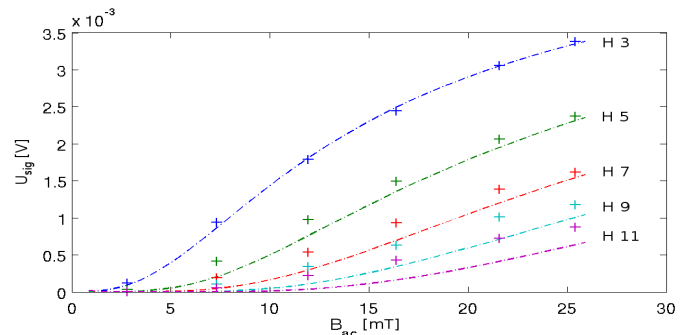


Figure 2: Field dependency of the harmonics as shown in figure 1: B_{ac} is the magnitude of the excitation field. No static offset field is applied. H_n denotes the n^{th} harmonic. The crosses are measurements, the dash dotted lines show simulated results according to the theory of Langevin.

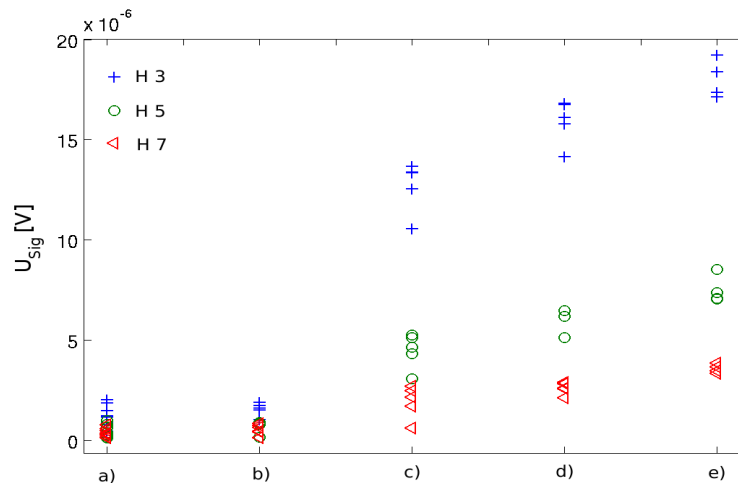


Figure 3: Signal from labeled stem cells and reference scans: a) pure water, b) unlabeled stem cells, c) and d) labeled stem cells, e) suspension of SPIOs. Blue crosses denote the 3rd harmonic, green circles the 5th, red triangles the 7th. In d) the sample of labeled stem cells contained the same amount of iron as the cells in c) but had a different morphology, which resulted in a better filling factor of the used receiver coil. The homogeneous distribution of the reference suspension in e) did also result in a better filling factor compared to c) and d).