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Using Alternating Gradient Field Magnetometers for the characterization of the mechanical and magnetic behavior of magnetic nanoparticles in biological samples

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The utility of magnetic nanoparticles (MNPs) has been proved with several in-vitro and in-vivo experiments. Their applications based on the interactions with static or time-varying magnetic fields, such as drug delivery, magnetic separation of labelled biological entities, magnetic resonance imaging contrast enhacement and, especially, the catabolism of tumours via hyperthermia, are currently some of the main and most promising focuses in biomedical investigation.

The characterization of the magnetic properties of the MNPs and their performance inside biological materials are improvable aspects, as well as the first steps for any experiment using them. At the moment there are no specific devices created for this purpose. As a consequence of this, the characterization of MNPs isn't good enough to determinate their behavior inside solid samples and biofluids. Therefore most of the results come from trial and error experiments.

Alternating gradient field magnetometers (AGFM) are fundamental instruments for characterizing magnetic materials. This type of magnetometer is extensively used in both laboratories and production environments for measuring the basic magnetic properties of materials as functions of magnetic field and, if desired, temperature. The AGFM is well-known because of its high sensitivity and low noise floor. Due to its features, the AGFM can be used for characterizing the magnetic and mechanical properties of MNPs.

The Princeton Measurements Corporation *MicroMag Model 2900 AGM System*®, installed in our laboratories as part of the Spanish Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine MNPs Characterization Platform, offers the best combination of performance capabilities and can accommodate a large range of samples of very different properties, such as tissues or biofluids.

We have carried out a large number of experiments to prove that the AGFM is able to characterize MNPs inside biological samples. Figure 1 presents hysteresis loops resulting from experiments with 250 nm dextran-coated MNPs suspended in water infused inside human glioblastoma cells. It can be seen the only contribution come from the probe and the MNPs. Figure 2 shows normalized hysteresis loops, which are different between cultures with or without MNPs. Therefore, the AGFM is able to characterize the particles.

As can been seen in Figure number 3, the AGFM is able to discriminate the mechanical behavior of MNPs in liquid and solid sample. Using engineered MNPs (Magnetite MNPs dispersed in Triethylene glycol), constant measurements were taken while the sample evaporated. The influence of this evaporation was analyzed. It can be checked on Figure 3 that the hysteresis loop reaches a higher saturation when the sample dries, as well as the superparamagnetism is accentuated.

It has been also proved that the AGFM is able to detect low-concentrated (500 μg/ml) nanoparticles (Kisker's PMAV-250) inside 1321N1 human glioblastoma cell lines incubated

for three days. The samples were cultured on plastic cover slips, and the cationic peptide "protamine sulfate (PS)" was used (5 µg/ml) to increase the uptake of MNPs. The differences in the MNPs can be appreciated between Figure 4 (without PS) and Figure 5 (with PS). As can be seen in Figure 6, the AGFM can be used for characterizing the magnetic and mechanical properties of MNPs acquired by cells even without using PS. These experiments are the first step to discriminate the behavior of MNPs acquired by cells or situated on the extracellular matrix.

At the moment, we are focusing on the study of the differences between the magnetic and the mechanical properties of cell cultures with nanoparticles infused inside and outside of them. This way, we will know when MNPs have been acquired by cells. The final goal is to use AGFM combined with other techniques for the detection and the identification of engineered MNPs as contaminant in ex-vivo samples.

References:

[1] V. Ferro, J.J. Serrano, C. Maestú, C. Sánchez, M.C. Maicas, C. Aroca, M.M. Sanz, F. del Pozo**,** *"El magnetómetro por gradiente alternante de campo: una nueva herramienta para la caracterización de nanopartículas magnéticas en biofluidos y tejidos biológicos"*, **Proceedings of the XXVIth Annual Congress of the Spanish Society of Biomedical Engineering (CASEIB 2008)**, Valladolid, October, 2008, pp.348-351, ISBN: 978-84-691-3640-9.

[2] V. Ferro, J.J. Serrano, T. Fernández, M. Ramos, F. del Pozo, *"Caracterización del comportamiento magnético y mecánico de nanopartículas en biofluidos y células con un AGFM"*, **Proceedings of the XXVIIth Annual Congress of the Spanish Society of Biomedical Engineering (CASEIB 2009)**, Cádiz, November, 2009, pp.285-288, ISBN: 978-84-608-0990-6.

Figures:

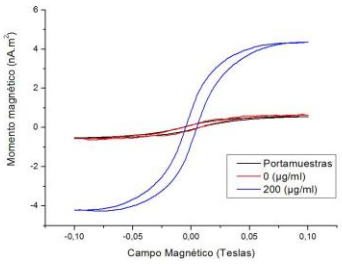

Figure 1

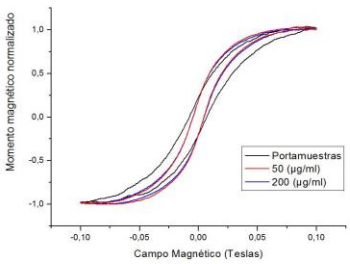

Figure 2

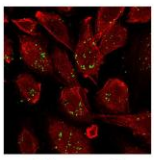

Figure 3

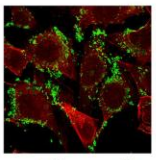

Figure 4

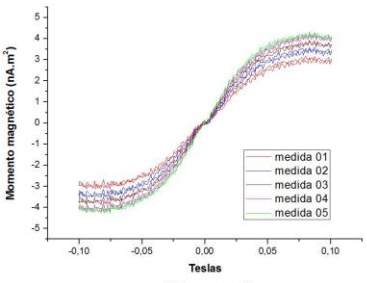

Figure 5

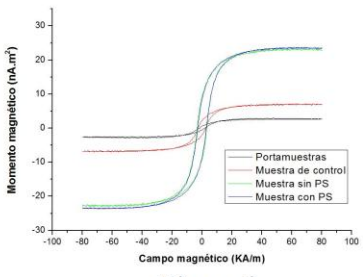

Figure 6