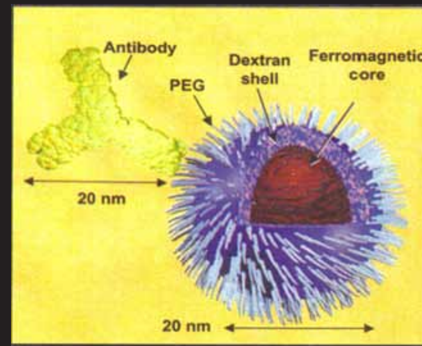
Magnetic Nanoparticle Metrology

Objective

We are developing best practice metrology for characterization of magnetic nanoparticle systems (e.g. blocking temperature, anisotropy, property distributions, T1 and T2 relaxation times, hysteretic energy loss, etc.) for use in biomedical applications. The emphasis is on the measurement methods to enable enhanced MRI imaging, drug delivery, and hyperthermia therapy. The tools provided will enable industry to more effectively design and develop new magnetic nanoparticles and provide guidelines to the FDA to properly compare systems when approving nanoparticle systems for clinical trials.



Impact and Customers

- Magnetic Resonance Imaging (MRI) is a $60 billion global industry. This imaging method, however, is only qualitative. More effective (through better contrast) and quantitative imaging would yield higher rates of detection, greater accuracy in detection, and earlier detection of diseases (e.g. cancer, heart disease, etc.) as well as better forms of treatment with potentially fewer side effects.
- Drug delivery and hyperthermia therapy for cancer treatment are still in the preclinical stages, but our input has the potential to significantly optimize the design and development of nanoparticles for these applications by eliminating the costly empirical approach currently used. This will help reduce the $1.7 billion price tag to bring a drug to the market.

ACR American College of Radiology · FDA Centennial 1906–2006 · National Cancer Institute · NIBIB · PhRMA · RSNA Radiological Society of North America Founded in 1915 · AAPM · International Society for ISMRM Magnetic Resonance in Medicine · National Institute on Aging · National Institutes of Health · TRITON BIOSYSTEMS Targeted Nano-Therapeutics™ for Cancer

Approach

Optimization of magnetic nanoparticle synthesis for a specific biomedical application necessitates a solid understanding of both fundamental magnetism and its measurement. Since most pharmaceutical companies employ biologists and chemists without such knowledge, we will aim to develop an ASTM standard for their use, applying established bulk and thin film techniques to nanoparticle systems for determining the appropriate magnetic properties of both individual and collections of nanoparticles.

In addition, two new measurement techniques will be developed: First Order Reversal Curve (FORC) models to correlate physical size distributions with magnetic property distributions, and transverse AC Susceptometry for determining interaction timescales for individual and collective systems.

There are also specific requirements for each medical application. For example, a novel variable field and frequency relaxometer will be developed for correlating the materials structure with T1 and T2 relaxation times to develop stable T1 and T2 SRMs for quantitative MRIs. For hyperthermia therapy, a microcalorimeter will be developed for accurately measuring temperature changes in a nanoparticle suspension under the influence of a high frequency alternating magnetic field.

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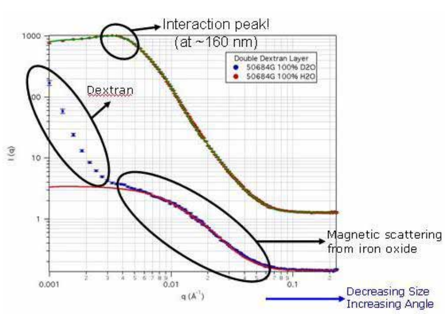
Accomplishments

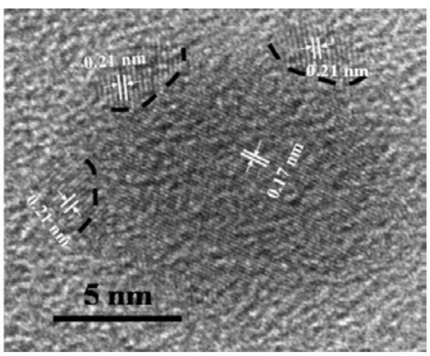
We recently determined that strongly interacting coated magnetic nanoparticles yield very large increases (by a factor of seven) in heat output as compared to nominally identical particles which are only weakly interacting, illustrating the enormous consequences of using improperly characterized nanoparticles for hyperthermia treatment. This behavior was found in two nanoparticle systems which were nominally identical physically (as determined by photon correlation spectroscopy, transmission electron microscopy, Mössbauer spectroscopy, and x-ray diffraction), and were very similar magnetically (although the nanoparticle system with the larger heating rate had the smaller saturation magnetization). The difference between the nanoparticle systems, identified through small angle neutron scattering, was the interaction radius, which was modified by changing the dextran stabilization layer. The more closely spaced nanoparticles interacted more strongly, utilizing a collective behavior to enhance the heating properties. This finding is a significant departure from "common knowledge" in the medical community, which has long contended that non-interacting magnetic nanoparticles are the ideal material for hyperthermia treatment.

Typically, conventional magnetic characterization methods reveal information about the "bulk" properties of a material. However, when combined with physical characterization methods like transmission electron microscopy (TEM), the same magnetic characterization methods can be used to separate and probe the details of magnetic nanoparticle growth and aging in a manner that neither technique can do alone. Recently, through this combination, we were able to determine the intermediate stage in Co nanoparticle growth to be Co cluster complexes formed with the surfactants. Meanwhile, after synthesis, a hysteresis loop shift along the field axis (exchange bias) is observed for the aged Co colloid, indicating the formation of anti-ferromagnetic/ferromagnetic (AFM/FM) interfaces in the aged Co nanoparticles. Although not measurable by x-ray diffraction, high-resolution TEM results confirm that a thin and inhomogeneous AFM face-centered cubic cobalt (II) oxide (CoO) grows on the surface of the FM Co nanoparticles, a configuration which is not sufficient by itself to produce exchange bias. This suggests that not only the AFM/FM coupling in individual aged nanoparticle matters, but also the strong magnetostatic coupling between the neighboring nanoparticles contributes to the exchange bias observed.

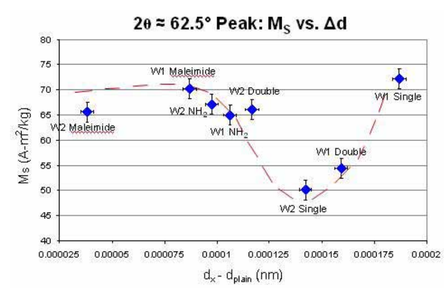
We recently demonstrated (with the help of SURF student Christine Lau) one effect of thermal, chemical, and/or mechanical processing on magnetic nanoparticles: the processing causes an expansion of the crystal lattice which in turn changes the bond angles between different elements in the Fe_3O_4 structure. This appears to partially change the magnetic coupling from ferromagnetic to antiferromagnetic, reducing the saturation magnetization. This had been observed previously in magnetite thin films, but never before in nanoparticles, and may be one origin of the significant variation in saturation magnetization of Fe_3O_4 nanoparticles from the bulk.



Small angle neutron scattering data showing interactions.



TEM image of Co nanoparticle, with dotted lines showing location of CoO patches.



Saturation magnetization data vs. change in lattice constant.

Learn More

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Publications

Dennis CL, Jackson AJ, Borchers JA, Ivkov R, Foreman AR, Lau JW, Goernitz E and Gruettner C *The Influence of Collective Behavior on the Magnetic and Heating Properties of Iron Oxide Nanoparticles* Journal of Applied Physics, 103: 07A319 (2008)

Dagata JA, Farkas N, Dennis CL, Shull RD, Hackley VA, Yang C, Pirollo KF and Chang EH *Physical Characterization Methods for Iron-oxide Contrast Agents Encapsulated Within a Targeted Liposome-based Delivery System* Nanotechnology, 19: 305101 (2008)

Dennis CL, Jackson AJ, Borchers JA, Ivkov R, Foreman AR, Hoopes PJ, Strawbridge R, Pierce Z, Goernitz E, Lau JW and Gruettner C *The Influence of Magnetic and Physiological Behavior on the Effectiveness of Iron Oxide Nanoparticles for Hyperthermia* Journal of Physics D: Applied Physics, 41:134020 (2008)

Dennis CL, Cheng G, Baler KA, Maranville BB, Hight Walker AR and Shull RD *The Influence of Temperature on the Magnetic Behavior of Colloidal Cobalt Nanoparticles* IEEE Transactions on Magnetism, 43:2448 (2007)