BASIC SCIENCE

Nanomedicine: Nanotechnology, Biology, and Medicine
12 (2016) 1253 – 1262

nanomedicine
Nanotechnology, Biology, and Medicine

nanomedjournal.com

Review Article

Iron oxide nanoparticles as magnetic relaxation switching (MRSw) sensors: Current applications in nanomedicine

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Received 13 October 2014; accepted 20 January 2016

Abstract

Since pioneering work in the early 60s on the development of enzyme electrodes the field of sensors has evolved to different sophisticated technological platforms. Still, for biomedical applications, there are key requirements to meet in order to get fast, low-cost, real-time data acquisition, multiplexed and automatic biosensors. Nano-based sensors are one of the most promising healthcare applications of nanotechnology, and prone to be one of the first to become a reality. From all nanosensors strategies developed, Magnetic Relaxation Switches (MRSw) assays combine several features which are attractive for nanomedical applications such as safe biocompatibility of magnetic nanoparticles, increased sensitivity/specificity measurements, possibility to detect analytes in opaque samples (unresponsive to light-based interferences) and the use of homogeneous setting assay. This review aims at presenting the ongoing progress of MRSw technology and its most important applications in clinical medicine.

Key words: Biosensors; Magnetic nanoparticles; Magnetic resonance; Nanodiagnostics; Nanomedical devices; Nanoengineering

Magnetic nanomaterials are an important and suitable source of labels for biosensing due to their strong magnetic properties, which are not found in biological systems.[1] Modification of the composition and size, alongside the smart manipulation of their magnetic properties enables their use in a wide range of devices in a diverse array of formats for biosensing.[2,3] Moreover, there are many potential clinical applications for localized drug delivery and magnetic relaxation switching (MRSw) sensing systems. Besides standard biocompatible experimental approaches, this evolving transition from *in vitro* diagnostics to innovative *in vivo* therapeutics is taking advantage of new computational models able to predict potential toxicities of new and modified magnetic nanoparticles (NPs).[4] In addition, new types of portable instrumentation are making feasible the use of nanoscale magnetic materials as point of care sensors for a variety of applications.[5,6] That is why, due to their distinctive features, magnetic biosensors are under active development and may soon rival established biological detection methods that use conventional surface-bond fluorescent tags.[7–9] In this sense, among the different magnetic nanosystems available, we will focus on iron oxide magnetic nanoparticles due to their wider use in biomedical research. These include Fe_3O_4 (magnetite), γ-Fe_2O_3 (maghemite), and non-stoichiometric magnetite.

Magnetic relaxation properties of iron oxide nanoparticles: rationale for tuning in biomedical applications

Accurate control over the conditions of synthesis and surface functionalization of iron oxide NPs is crucial because these steps determine their physicochemical properties, their colloidal stability, and their biological distribution, availability and clearance in living organisms. A key feature enabling iron oxide NPs for biomedical applications is the control and understanding of their magnetic properties, in particular, magnetic susceptibility and magnetic moment. For example, in the case of iron oxide superparamagnetic nanoparticles

Support was provided by the Spanish Ministry of Economy and Competitiveness with FEDER co-funding (FIS-PI14-1600 to DP), the Regional Ministry of Health (PI2013-375 to SL; PI2013-0559 to MPL), the Regional Ministry of Economy, Science and Innovation (P10-CTS-6928 and P11-CTS-8161 to DP), and the PAIDI Program from the Andalusian Government (CTS-677 to DP). DA holds a Marie Curie Fellowship (FP7-PEOPLE-2012-IEF, grant number 327151) from the European Commission.

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http://dx.doi.org/10.1016/j.nano.2016.01.005
1549-9634/

Please cite this article as: Alcantara D, et al, Iron oxide nanoparticles as magnetic relaxation switching (MRSw) sensors: Current applications in nanomedicine. *Nanomedicine: NBM* 2016;12:1253-1262, http://dx.doi.org/10.1016/j.nano.2016.01.005

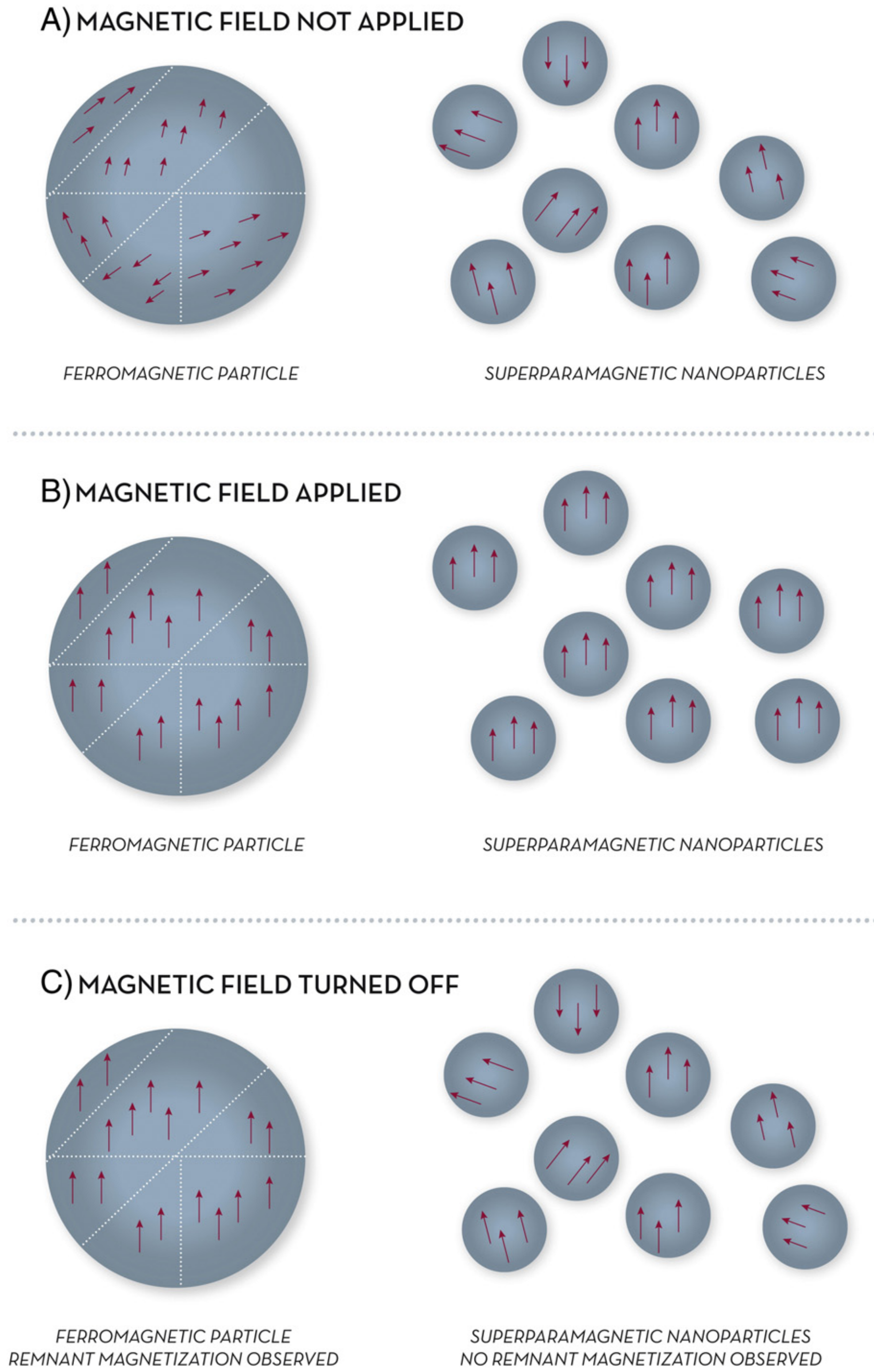

Figure 1. Superparamagnetic versus ferromagnetic particles in the absence (**A**) or presence (**B**) of an external magnetic field. The magnetic moment of superparamagnetic particles in the absence of an external field is time-averaged to zero, similar to the net magnetic moment of a superparamagnetic particle assembly. In the presence of an external field, the magnetic moments of the particles align to it. When the magnetic field is turned off (**C**), magnetic moments of superparamagnetic particles randomize and lack a remnant magnetization.

(SPIONs), the magnitude and characteristics of both parameters have consequences on the magnetic attraction between particles in solution, a key factor affecting the formation of aggregated clusters of NPs, with obvious implications for their potential applications in nanomedicine.

Magnetic materials when placed in a magnetic field with strength H exhibit an induced magnetization, M, characterized by $M = \chi H$, where χ is the so-called magnetic susceptibility, a dimensionless constant. Those particles with parallel aligned magnetic moments to a given magnetic field, and magnetic susceptibilities in a range between 10^{-10} and 10^{-1} are described as paramagnetic. Remarkably, iron oxide NPs with sizes below 20 nm produce crystal structures in which the oxygen ions form a closely packed cubic lattice with smaller iron cations placed at