Specific absorption rate determination of magnetic nanoparticles through hyperthermia measurements in non-adiabatic conditions

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ABSTRACT

An experimental setup for magnetic hyperthermia operating in non-adiabatic conditions is described. A thermodynamic model that takes into account the heat exchanged by the sample with the surrounding environment is developed. A suitable calibration procedure is proposed that allows the experimental validation of the model. Specific absorption rate can then be accurately determined just from the measurement of the sample temperature at the equilibrium steady state. The setup and the measurement procedure represent a simplification with respect to other systems requiring calorimeters or crucial corrections for heat flow. Two families of magnetic nanoparticles, one superparamagnetic and one characterised by larger sizes and static hysteresis, have been characterised as a function of field intensity, and specific absorption rate and intrinsic loss power have been obtained.

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1. Introduction

Hyperthermia [1] has been the subject of wide interdisciplinary interest in the last years, as one of the several approaches that could turn out to be viable for selective tumour cell destruction [2,3]. In particular, magnetic particles hyperthermia (MPH) has been regarded as particularly promising, and has therefore attracted significant research efforts [4,5]. In spite of the several advantages that magnetic hyperthermia could bring [6] (direct thermal effects on cancer cells, heat assisted chemotherapy and radiotherapy whose outcome is significantly improved when coupled with MPH [7]), several open questions still hinder the application of this methodology, such as the complex relationship between the intrinsic properties of the magnetic material and its specific power losses [8,9], or the difficulty of obtaining reliable estimates of specific absorption rates (SAR) of different kinds of magnetic particles in different media and under different measurement conditions [10]. Many recent studies have concentrated on the optimisation of the materials' properties, by exploring different shapes and anisotropy values for the particles [11], by deeply investigating crystalline properties of the materials [12], by analysing how interparticle interactions may affect hyperthermia losses [13], or by suggesting entirely new families of "particles",

such as nanorings [14], microdisks [15,16] or nanodisks [17].

However, the lack of standards in MPH has also led to many different experimental approaches and to results that are difficult to compare: one of the main issues is the need of performing MPH experiments, leading to the measurement of the SAR, in adiabatic conditions [10], or under suitable, well-calibrated corrections for compensating the non-ideal adiabatic conditions [18]. In this paper, we present an approach that does not require the development of an adiabatic or almost adiabatic experimental setup for magnetic hyperthermia. On the contrary, a simpler system is used that allows heat exchange with the surrounding environment. A modelling of the thermodynamics of the system, together with a suitable calibration procedure, allows for the accurate determination of the specific absorption rate (and its derived quantity intrinsic loss power) of hyperthermia agents such as magnetic particles. A detailed knowledge of the experimental details will be the basis for future standardisation of the hyperthermia treatment.

2. Magnetic nanoparticles

Fe-oxides particles are currently the most frequently used material for MPH [11]. In this work, Fe_3O_4 nanoparticles have been obtained by two different suppliers: Alfa Aesar (sample A, nominal particles diameter in the range 50–100 nm) and Politronica s.r.l. (sample P, nominal particles diameter in the range 10–20 nm). For

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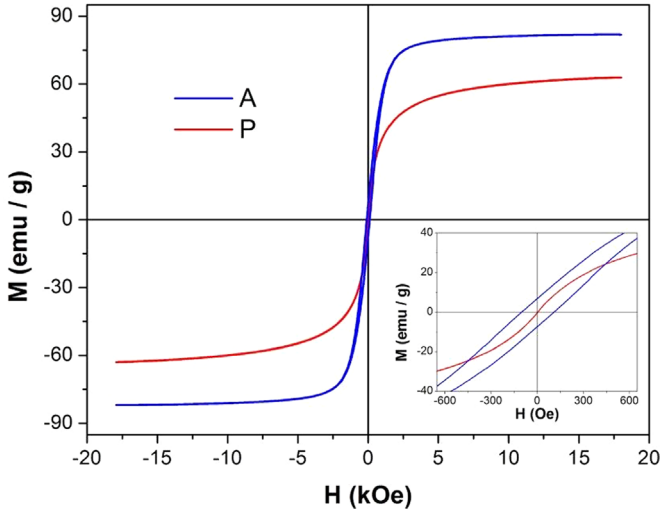
Fig. 1. Room temperature hysteresis loops of sample A (blue curve) and sample P (red curve). Inset: magnification at low fields to better show the coercivity. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this paper.)
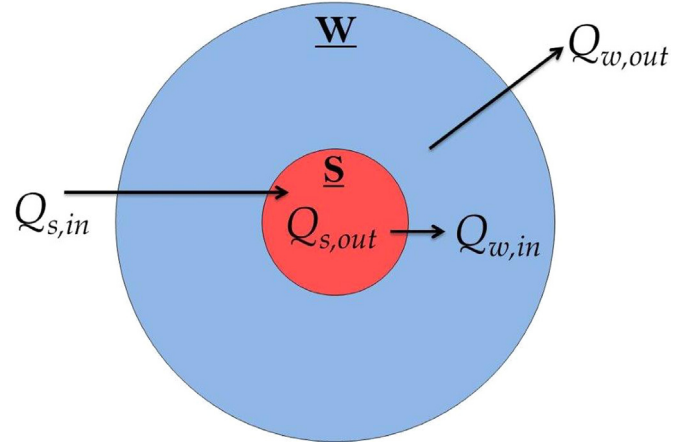
both samples, solutions containing 10 mg/ml of particles in deionised water have been prepared. Room temperature hysteresis loops of as-received dried particles have been measured with a LakeShore 7410 VSM: the results are reported in Fig. 1.

Sample A is constituted by larger particles, with a lower surface to volume ratio with respect to sample P; therefore, as expected, their saturation magnetisation is higher, and almost equal to the saturation of bulk magnetite. Sample P, instead, is characterised by smaller particles, with a higher surface to volume ratio leading to a reduced saturation, that display a superparamagnetic behaviour, with zero coercive field and a much slower approach to saturation. These two samples are representative of two different classes of particles often studied for MPH applications.

3. Hyperthermia setup: calibration and modelling

The hyperthermia setup used in our experiments consists in a water-cooled copper coil made of 4 turns, connected to a rf generator through a matching network, and able to generate electromagnetic fields with intensity up to 100 mT at a frequency of 100 kHz. Inside the coil, a PTFE sample holder hosts an Eppendorf test tube containing 1 ml of water into which known concentrations of magnetic nanoparticles are dispersed. At equilibrium and with no rf field applied, the sample remains at a constant temperature $T_a = 23.5$ °C thanks to the water-cooling of the coil. In order to measure the temperature of the water solution, a type-T (wires diameter 0.127 mm) thermocouple is available, that does not allow the measurement of the sample temperature during the rf irradiation process. However, it can be inserted in the test tube immediately after the rf field is switched off, in order to measure the time-dependent temperature decay of the sample towards T_a. As we will show, if a suitable calibration of the experimental setup is available, an accurate determination of the specific absorption rate (SAR), and consequently of intrinsic loss power (ILP), can be obtained by just knowing the two temperatures T_a and T_M, the latter being the equilibrium temperature reached by the nanoparticles solution at steady state during irradiation.

An accurate determination of SAR would require a hyperthermia setup operating in ideally adiabatic conditions [10,18], i.e. a calorimeter would be the optimum choice for this kind of measurements. However, such complex setups are often not

available and SAR is therefore determined by measuring the initial slope of the sample temperature vs. time when the rf field is switched on [11]. This procedure leads to approximate results that may be affected by how the temperature vs. time curve is analysed and by the accuracy of the adiabatic hypothesis in the actual experimental setup, and requires suitable corrections for compensating the heat exchange with the surrounding environment [12,13].

To avoid these problems, we opted to keep simple the hyperthermia experiment, while taking into account the heat exchange of the sample with the surrounding environment in the physical model that describes its thermodynamics. In this way, after a suitable calibration procedure, the SAR can be accurately measured even in non-adiabatic conditions.

The hyperthermia system can be modelled as described in Fig. 2. A heat source S (e.g. the nanoparticles inside the solution) provides energy $Q_{s,in}$ to the system (e.g. through the power losses of the magnetic particles excited by the rf field), and exchanges heat with the water W, $Q_{s,out}$ and $Q_{w,in}$ representing the same amount of heat, respectively, flowing out of the S subsystem and into the W one. Finally, the water exchanges heat $Q_{w,out}$ with the environment (at temperature T_a). At each instant of time, the heat exchange equations for the S and W subsystems are the following:

$$\frac{\delta Q_s}{dt} = \frac{\delta Q_{s,in}}{dt} + \frac{\delta Q_{s,out}}{dt} \tag{1a}$$

$$\frac{\delta Q_w}{dt} = \frac{\delta Q_{w,in}}{dt} + \frac{\delta Q_{w,out}}{dt} \tag{1b}$$

where each term is taken with its proper sign (positive for heat entering the subsystem, negative for heat released by the subsystem).

The first term $\frac{\delta Q_{s,in}}{dt}$ is given by the power P that is provided through the source. The two terms $\frac{\delta Q_{s,out}}{dt}$ and $\frac{\delta Q_{w,in}}{dt}$ are of opposite sign and given by the following expression:

$$\frac{\delta Q_{s,out}}{dt} = -\frac{\delta Q_{w,in}}{dt} = -\frac{c_s m_s}{\tau_s}[T_s(t) - T_w(t)] \tag{2}$$

where c_s is the specific heat of the source, m_s is its mass, τ_s is the time constant of the heat exchange process between the source and the water, T_s is the source temperature and T_w is the temperature of the water. Both quantities T_s and T_w depend on time, but in typical hyperthermia experiments involving magnetic

Fig. 2. Thermodynamic scheme of the hyperthermia system. S is the source subsystem (i.e. the magnetic nanoparticles). W is the water subsystem in which the nanoparticles are dispersed. P is the exciting power. Q terms represent the heat exchanged by the two subsystems with each other and with the environment.