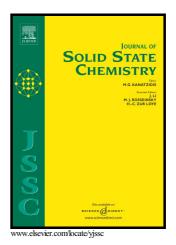
### Author's Accepted Manuscript

Threshold heating temperature for magnetic hyperthermia: controlling the heat exchange with the blocking temperature of magnetic nanoparticles

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#### Threshold heating temperature for magnetic hyperthermia: controlling the heat exchange with the blocking temperature of magnetic nanoparticles

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 $La_{0.75}Sr_{0.25}MnO_3$  nanoparticles with average diameter close to 20.9 nm were synthesized using a sol-gel method. Heating measurements show that the heating process stops at the blocking temperature, lying significantly below the Curie temperature. Measurements of Specific Absorption Rate (SAR) as a function of AC magnetic field revealed a superquadratic power law, indicating that, in addition to the usual Néel and Brown relaxation, the hysteresis also has an important role on the mechanism of heating. The ability to control the threshold heating temperature, a low remanent magnetization and a low field needed to achieve the magnetic saturation are the advantageous properties of this material for therapeutic magnetic hyperthermia.

#### Keywords:

magnetic nanoparticles, hyperthermia, self-controlled inductive heating, self-regulating magnetic hyperthermia

#### I. Introduction

Cancer remains a major cause of death throughout the world [1]. New treatment modalities are aimed to improve the efficacy of tumor damage with minimal injury to the surrounding healthy tissues [2-6]. In this direction, physical methods using nanoparticles have been extensively studied in recent years [7]: in particular, the development of magnetic nanoparticles for antitumor hyperthermia is under way [8-11]. This technique uses magnetic nanoparticles dispersed into a fluid (ferrofluid); and then an external AC magnetic field (respecting the Brezovich limit [12]) is used to heat the body or an area of the body.

Magnetic heating can be generated by three types of mechanisms: Néel relaxation, Brown relaxation, and hysteresis losses. For Néel relaxation, the magnetic moments of nanoparticles are consistently inverted due to AC magnetic field and then energy is dissipated when the magnetic moments relax around the equilibrium position [8]. Brown relaxation presumes that, before the coherent reversal of magnetization (by Néel relaxation), the nanoparticles gain freedom of movement in the fluid due to external AC magnetic field [11]. The friction between the surface of nanoparticles and the surrounding liquid causes heat release to the medium. The hysteresis losses are associated with the power dissipated in one cycle of magnetization [13, 14].

A common parameter for quantitative characterization of magnetic hyperthermia is the Specific Absorption Rate (SAR). This value is of clinical importance for calculation of dose and duration of treatment [9]; and it is generally believed that optimization of SAR means simply to increase its value. However, one can avoid a tissue overheating, that leads to an undesired side-effect, by a self-regulating (or self-controlled) hyperthermia concept [15-16] It consists of an internal mechanism that provides the high heating rate to the body and a saturation of heating at higher temperatures. The most natural way is to use the ferromagneticparamagnetic phase transition: the temperature of nanoparticles heated under a magnetic field can not exceed the Curie temperature [17-18]. Current materials are the superparamagnetic iron oxide nanoparticles; however, their Curie temperatures are far from what the clinical magnetic hyperthermia needs [19].

An alternative family of compounds for magnetic hyperthermia has been introduced [16,20-23], namely,  $La_{1.}$  <sub>x</sub>Sr<sub>x</sub>MnO<sub>3</sub> (LSMO) nanoparticles. The physical parameters of these compounds, like Curie temperature, magnetic saturation and effective magnetic moment can be easily managed and therefore one can avoid overheating and damage of the surrounding tissues. It is usually supposed that the main factor limiting the excessive heating in magnetic

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