Specific loss power of magnetic nanoparticles: a machine learning approach

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Abstract. A machine learning approach has been applied to the prediction of magnetic hysteresis properties (coercive field, magnetic remanence, and hysteresis loop area) of magnetic nanoparticles for hyperthermia applications. Trained on a dataset compiled from numerical simulations, a neural network and a random forest were used to predict power losses of nanoparticles as a function of their intrinsic properties (saturation, anisotropy, and size) and mutual magnetic interactions, as well as of application conditions (temperature, frequency, and applied field magnitude), for values of the parameters not represented in the database. The predictive ability of the studied machine learning approaches can provide a valuable tool toward the application of magnetic hyperthermia as a precision medicine therapy tailored to the patient's needs.

Introduction. Cancer being one of the most important causes of death, its fight is a challenge that involves many different disciplines. Recently, machine learning has joined them by helping aggregate and analyze the data and results emerging from many different research fields; as such, it offers a new paradigm for their interpretation and for extracting valuable information to the benefit of final users, including medical doctors and clinicians and, eventually, patients [1].

In recent years, the possibility to exploit the properties of nanoparticles to offer a different approach for cancer treatment has been investigated under a multitude of approaches. Among them, magnetic nanoparticles have been identified as potentially relevant in precision medicine through magnetic hyperthermia [2], a technique aimed at delivering heat to tumor cells by inducing power losses into the magnetic nanoparticles by means of an externally applied electromagnetic field and therefore by releasing heat into the surrounding tissues. The heat, selectively released in the cancerous tissues, directly destroys them, or weakens them to improve the effectiveness of chemotherapy or radiotherapy, or helps to release a suitable drug locally.

With this work, we aim at showing how machine learning can be exploited to predict the power losses of magnetic nanoparticles with different magnetic properties in a multitude of application conditions (e.g., temperature, mutual magnetic interactions, applied magnetic field intensity, and frequency), starting from an available database [3]. In perspective, this approach will offer a fast, reliable, and easy to use tool available to medical doctors and magnetic hyperthermia operators for precisely and effectively tailoring the therapy to their patients' needs. In its present form, it provides a novel and viable method to model the magnetic properties of nanoparticles from an initial dataset. To eventually bring this approach to end users (e.g., medical doctors in hospitals), the property dataset will need to be expanded with additional simulated and experimental data on magnetic nanoparticles as well as with relevant information concerning the environment where the nanoparticles are expected to operate (e.g., kind of tissue where they are injected and its thermal transport properties), obtained either experimentally or by numerical simulations.

Results and discussion. In a typical magnetic hyperthermia application, magnetic nanoparticles are either injected or carried into the cancerous tissue and then submitted to an alternating electromagnetic field of suitable intensity and frequency, submitted to biocompatibility constraints, with the aim to induce in the target tissue an increase of temperature capable of killing, or at least weakening, the tumor cells. Many different parameters contribute in determining the end result; all need to be under the control of the operator, otherwise, either an insufficient or excessive amount of heat is released, which respectively turns out to be ineffective or dangerous. Among the involved parameters, the more relevant ones can be collected into three different groups: i) *application conditions:* temperature T at which the nanoparticles power losses are exploited; vertex field H_V, i.e., the maximum applied magnetic field, in absolute value, representing the field extrema between which the hysteresis loop is cycled and the power losses are exploited; frequency f at which the applied field cycles; ii) *material:* saturation magnetization M_S, magnetic anisotropy K, nanoparticles diameter D, and magnetic interaction parameter *Int* (defined as $Int = D / d$, where d is the average centre-to-centre distance of the particles); iii) *loop shape:* coercive field H_C, magnetic remanence M_R, and hysteresis loop area, intimately linked to the specific loss power, SLP, and interaction parameter.

All these quantities are subjected to multiple non-linear relationships: for example, the temperature directly affects M_S and K values; however, these quantities are not entirely defined by T. In turn, M_S, together with the interaction parameter, affects the loop shape, but the interaction parameter plays with K and D as well, directly affecting the coercive field H_C, which, in turn, plays a role in determining the whole loop shape. Similarly, H_V and f, together with the magnetic anisotropy, also affect the final loop shape. All these relationships are often highly non-linear. Under specific constraints, some of these non-linear relationships can be analytically modeled, but in general an analytical representation of the non-linear relationships among these quantities is not available. To overcome this limitation, numerical models are often developed, which try to take into account as many parameters as possible, at the expense of their complexity or of computation time.

In this work, we developed a simple two-well model to generate a large number of magnetic hysteresis loops of nanoparticles in different measurement conditions and for different material property values. In total, ~4000 simulations were carried on, and their

data (the quantities listed above) were collected. A few examples of the hysteresis loops generated with the two-wells model are reported in Fig. 1(b). While large, the simulated dataset cannot cover any possible scenario where the prediction of the hysteresis loop details of an ensemble of nanoparticles with given properties and in a given experimental condition would be important. Exploiting the two-well model to generate the simulations in the desired conditions requires both a specific expertise on the model and on the required numerical tools and sufficient computation time. In fact, the calculation of a hysteresis loop of magnetic systems, especially in conditions far from magnetic saturation, is a task that cannot be significantly parallelized, since the magnetization processes are characterized by a memory that is often *non-persistent* (and therefore depends on the rate at which the applied magnetic field is varied) and *non-local* (and therefore not only the present state but the whole past history of the magnetic material need to be known to calculate its future states). As a consequence, except for very simple models and systems, the accurate calculation of the magnetic configuration or of the hysteresis loop of a magnetic system, under given conditions, is computationally heavy. On the contrary, innovative machine learning approaches seem particularly apt at overcoming these severe obstacles.

Therefore, we decided to use the set of 4000 simulations obtained with the two-well model to train and test a neural network and a random forest, both having the quantities reported in "application conditions" and "material" groups as inputs, and those in the "loop shape" group as outputs. Both systems were randomly initialized each time and trained with a random subset of the whole simulated dataset, made of 90% of it. Then, the two machine learning systems have been tested on the remaining 10% of the whole dataset. Each result has been repeated 30 times with a different (random) initialization of the machine learning system and training-testing splitting of the whole dataset. Scores and predicted values are then averaged and their standard deviation is calculated to give the final results and their respective error bars.

Fig. 1 (a) reports the relative difference between the predicted value p_V (by the machine learning system) and the expected value e_V for H_C, M_R, and loop area, normalized to the expected value and to the standard deviation. The vast majority of the predicted data are within 3σ of the expected value, as indicated by the dashed line in Fig. 1(a). However, the random forest has much lower σ values, indicating that it is more precise in its predictions, and its computing time is on average 300 times shorter than for the neural network. As a consequence, the random forest system appears to be both quicker and more precise for this kind of problem.

The power of the machine learning approach can now be fully exploited to generate results for input parameter values that were not previously simulated, for example for a temperature of 42 °C (315 K), or for a stimulation frequency f (100 kHz) or field amplitude H_V (150 Oe) that were not part of the training dataset. Fig. 2(a) reports predicted (by the random forest) loop area as a function of nanoparticles size at the given input values (none of which were previously simulated). Panels (b) and (c) report similar data as a function of the simulating field intensity and of the interactions among the nanoparticles.

A systematic numerical study of these effects would be difficult and time consuming, whereas machine learning approaches could help exploring how the different parameters of the magnetic nanoparticles affect their specific loss power in a more effective way. Moreover, the predictions reported in Fig. 2 are accurate and physically sound. The results were produced almost in real time and could be triggered with a user interface hiding the complexity of the details, suitable for the in-field application. By contrast, qualitatively similar results obtained with the two-well model require extremely longer computation times and a specific expertise in the subject.

In perspective, the aim is to build an improving-over-time knowledge base that will make machine learning systems more accurate in their predictions. The approach presented in this paper can therefore pave the way toward a breakthrough in the application of magnetic hyperthermia for cancer treatment.

References

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Figures

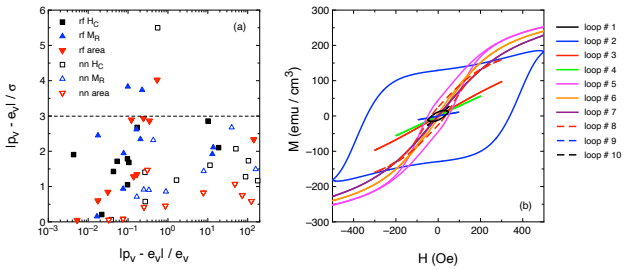

Figure 1. (a) Deviation of the predicted value p_V from the expected one e_V, divided by the standard deviation, for selected simulated loops. Full symbols refer to the random forest, open symbols to the neural network. (b) Respective simulated hysteresis loops.

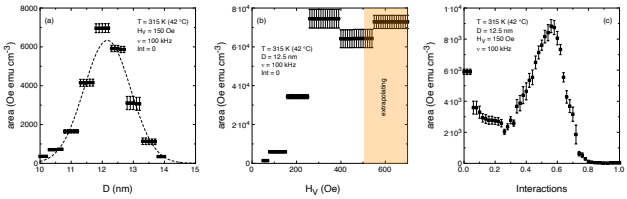

Figure 2. (a) Loop area as a function of nanoparticles diameter for the reported measurement conditions. The dashed line is a guide to the eye. (b) Loop area as a function of the vertex field. (c) Loop area as a function of the interaction parameter.