

Electronic Supplementary Information

DIPOLAR INTERACTIONS AMONG MAGNETITE NANOPARTICLES FOR MAGNETIC HYPERTHERMIA: A RATE-EQUATION APPROACH

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I. RATE EQUATIONS

Magnetic nanoparticles (NPs) with predominant uniaxial anisotropy can be described as double-well systems (DWS). The model is exploited to draw and analyze the hysteresis loops of particles submitted to cyclic magnetization. Here, the main assumptions leading to the rate equations are given.

Each magnetic nanoparticle has size D , effective volume $V = (\pi/6)D^3$ and magnetic moment $\mu = M_s V$ where M_s is the saturation magnetization of the material; in the absence of magnetic field, the magnetic moment is aligned by to the easy axis by uniaxial anisotropy of amplitude K_{eff} . The easy directions of NPs are assumed to be evenly distributed in space; in Figure 1 the plane containing the rotation of the μ vector is defined by the applied field H and the easy axis of a nanoparticle.

Let N_ϕ be the number (per unit volume) of particles of magnetic moment μ whose easy axis forms an angle ϕ with respect to H . For easy-axis directions evenly distributed in space, $N_\phi = N/2\pi$, N being the total number (per unit volume) of particles in the system. For each angle ϕ the occupancy numbers in the two wells are $N_{1\phi}$ and $N_{2\phi}$ ($N_{1\phi} + N_{2\phi} = N_\phi$).

The energy of a single DWS, $E(\theta, \phi)$ is:

$$E(\theta, \phi) = K_0(T)V \sin^2(\theta) + \alpha M_s^2 V \left(1 - \frac{|m_0|}{2}\right) f_V - 2HM_s(T)V \cos(\theta - \phi)$$

where θ is the angle between the magnetic moment direction and the easy axis. The

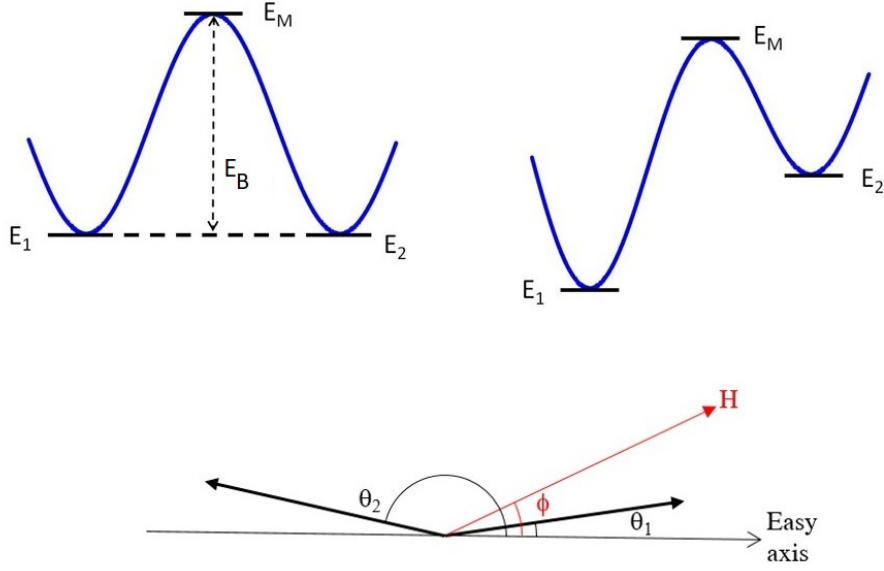


FIG. 1. Top: energy of the DWS without and with applied field; bottom: reference system (easy axis parallel to the x-axis).

dipole-dipole interaction term is included. The angles of minimum energy $\theta_1(\phi)$, $\theta_2(\phi)$ (see Figure 1) are found by requiring that the derivative of $E(\theta, \phi)$ with respect to θ be equal to zero; the magnetization along the field direction at the temperature T is therefore:

$$M(T, \phi) = N_{1\phi}(T)M_s(T)V\cos(\theta_1(\phi) - \phi) + N_{2\phi}(T)M_s(T)V\cos(\theta_2(\phi) - \phi).$$

The redistribution of particles in the two wells is ruled by the rate equations:

$$\begin{aligned} \frac{dN_{1\phi}}{dt} &= -\frac{1}{\tau_1(t)}N_{1\phi} + \frac{1}{\tau_2(t)}N_{2\phi} = \frac{N_\phi}{\tau_2(t)} - \left(\frac{1}{\tau_1(t)} + \frac{1}{\tau_2(t)}\right)N_{1\phi} \\ \frac{dN_{2\phi}}{dt} &= \frac{1}{\tau_1(t)}N_{1\phi} - \frac{1}{\tau_2(t)}N_{2\phi} = \frac{N_\phi}{\tau_1(t)} - \left(\frac{1}{\tau_1(t)} + \frac{1}{\tau_2(t)}\right)N_{2\phi}. \end{aligned} \quad (1)$$

In the standard Arrhenius picture the time-dependent escape frequencies are:

$$\tau_i^{-1}(t) = \tau_0^{-1}\exp\left(-\frac{E_{Bi}(t)}{k_B T}\right) = \tau_0^{-1}\exp\left(-\frac{E_M(t) - E_i(t)}{k_B T}\right) \quad (i = 1, 2)$$

where $E_{B1,2}(H, \phi)$ are the total energy barriers for $1 \rightarrow 2$ transitions and viceversa, $E_i(t)$ ($i = 1, 2$) are the energies of the two energy minima, $E_M(t)$ is the energy at the top of the barrier (see Figure 1). The total energy barriers are defined in Equation (4) of the main text.

The energies $E_{i,M}$ depend on time when $H = H(t)$. The problem's symmetry dictates the general relationship $\tau_1(-H) = \tau_2(H)$ that holds at all angles ϕ .

In high-frequency measurements τ_{meas} is conventionally taken as the reciprocal of measurement frequency. In this case the sweep rate is no longer a constant; nevertheless, it is still possible to introduce a r.m.s sweep rate R_{RMS} defined as $R_{RMS} = (\pi/\sqrt{2})H_v f$ where H_v is the vertex field. The dimensionless rate equations (1) can be rewritten in terms of the magnetic field H :

$$\begin{aligned} \frac{dN_{1,\phi}}{dH} &= \mp \frac{1}{R_{RMS}} \left[\frac{N_\phi}{\tau_2(H)} - \left(\frac{1}{\tau_1(H)} + \frac{1}{\tau_2(H)} \right) N_{1,\phi} \right] \\ \frac{dN_{2,\phi}}{dH} &= \mp \frac{1}{R_{RMS}} \left[\frac{N_\phi}{\tau_1(H)} - \left(\frac{1}{\tau_1(H)} + \frac{1}{\tau_2(H)} \right) N_{2,\phi} \right]. \end{aligned} \tag{2}$$

where the \mp sign refers to the upper/lower loop branch.

The behavior of a DWS assembly with randomly distributed easy axes is obtained by averaging the solutions of the full rate equations (2) over all ϕ angles.

In three dimensions, the average of a ϕ -dependent quantity $g(\phi)$ is the sum: $\sum_1^N g(\phi_i) \sin(\phi_i) / \sum_1^N \sin(\phi_i)$ over N angles in the interval $-\pi/2 \leq \phi_i \leq \pi/2$. In this work, N has been fixed to 181; the relative difference between the average done with $N = 181$ and with $N = 1801$ is negligible ($< 2 \times 10^{-3}$).

The rate-equation approach is a simplifying approximation to the Fokker-Planck equation for the double-well problem. For magnetic nanoparticles, rate equations naturally emerge from the Fokker-Planck equation when the ratio $K_{eff}V/k_B T$ is significantly larger than unity; therefore the validity of the approach at a given temperature depends on both magnetic anisotropy and nanoparticle size.

In rate equations containing time-dependent escape frequencies, as the ones studied here, detailed balancing is achieved only when $\omega\tau_c \ll 1$ where τ_c is the characteristic relaxation time of the system. In magnetic nanoparticles, the free diffusion time of magneti-

zation is $\tau_c = M_s V(1 + \alpha^2)/2\gamma\alpha k_B T$ where γ is the electron gyromagnetic ratio and α is the Gilbert's damping constant appropriate to describe systems with intermediate-to-high damping ($\alpha \approx 1$) such as magnetic nanoparticles. Using $\alpha = 0.5$ one gets $\tau_c = 1.06 \times 10^{-9}$ s for $D = 15$ nm. A similar figure is valid for all particle diameters considered in this work. Therefore, the driving-field frequency should be much lower than $\approx 1 \times 10^8$ Hz to guarantee detailed balancing. In fact, the highest driving-field frequency used in the paper ($f = 1 \times 10^6$ Hz) ensures that rate equations can be confidently applied for all studied nanoparticle sizes.

II. MAXIMUM LOOP AREA AND PARTICLE VOLUME

The behavior of the maximum loop area A_L^{MAX} (i.e., the area of the loops calculated when $f_V = f_V^{(Max)}$) with the volume of particles can be studied following the time evolution of the magnetization $M(t)$ driven by the applied field $H(t)$, which is directly obtained by the rate equations. An example is given in Figure 2, where the magnetization of 16-nm particles (green line) is compared to the one of 13-nm particles (black line). As a matter of fact, the two curves are observed to merely differ by a scale factor. This clearly results in a corresponding difference in the loop's area.

The proportionality between maximum loop area and V can be explained by means of a simple analytical treatment valid when the magnetic field is sufficiently small. For any angle ϕ between the magnetization and the easy axis, the condition for the maximum area is $\tau = 1/f$ where $\tau = \tau_0 \exp(E_B/k_B T)$ is the typical relaxation time *at zero magnetic field*. In the presence of a magnetic field, the relaxation times τ_i ($i=1,2$) entering the rate equations (see previous Section) become:

$$\begin{aligned}\tau_1 &= \tau e^{-\alpha H(t)} \simeq \tau(1 - \alpha H(t)) \\ \tau_2 &= \tau e^{\alpha H(t)} \simeq \tau(1 + \alpha H(t))\end{aligned}\tag{3}$$

where $\alpha = \frac{M_s V}{k_B T}$ and the last equality holds when $\alpha H_V \ll 1$. In these conditions, the rate equation for $n_1 = N_{1,\phi}/N_\phi$ becomes (to the first order in αH):

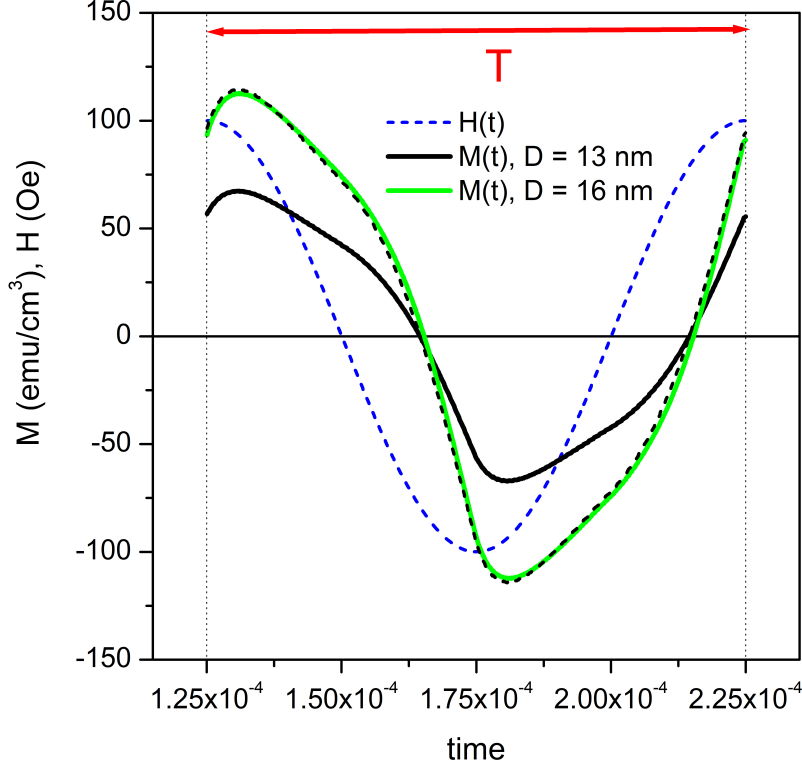


FIG. 2. Time evolution of the applied magnetic field (dashed blue line) and of magnetization during one period $T = \frac{1}{f}$, for two monodisperse systems with $D = 13$ and 16 nm (full black/green lines, respectively). The dashed black line almost perfectly superimposed to the green line is obtained multiplying the curve for $D = 13$ nm by a constant factor.

$$\frac{dn_1}{dt} = \frac{1}{\tau_2} - \left(\frac{1}{\tau_1} + \frac{1}{\tau_2}\right)n_1 \simeq f(1 - \alpha H) + 2fn_1. \quad (4)$$

Rearranging terms, and taking $H(t) = H_V e^{i\omega t}$:

$$\frac{dn_1}{dt} - 2fn_1 = f(1 - \alpha H_V e^{i\omega t}) \quad (5)$$

which admits the general solution:

$$n_1(t) = C e^{-2ft} + \frac{1}{2} - \frac{\alpha H_V}{4} \frac{1}{1 + \pi i} e^{i\omega t}. \quad (6)$$

The steady state solution after the initial transient is therefore:

$$n_1(t) = \frac{1}{2} - \frac{\alpha H_V}{4} \frac{1}{1 + \pi i} e^{i\omega t}. \quad (7)$$

Note that there is a phase shift between $n_1(t)$ and $H(t)$, and the system's response is proportional to V through the α factor. A similar equation holds for n_2 :

$$n_2(t) = \frac{1}{2} + \frac{\alpha H_V}{4} \frac{1}{1 + \pi i} e^{i\omega t}. \quad (8)$$

so that the magnetization, which is a just linear combination of n_1 and n_2 , turns out to be indeed proportional to the particle volume V .

Although this explicit proof is valid when $\alpha H_V \ll 1$ only, the proportionality between magnetization and V is maintained also for higher values of the vertex field (see Figure 2 of the ESI and panel *c* of Figure 2 of the main text).

Finally, note that such a proportionality only holds at, or very close to $f_V = f_V^{(Max)}$, because only there it is possible to set $\tau = 1/f$ and write the rate equation in the form of equation 4.

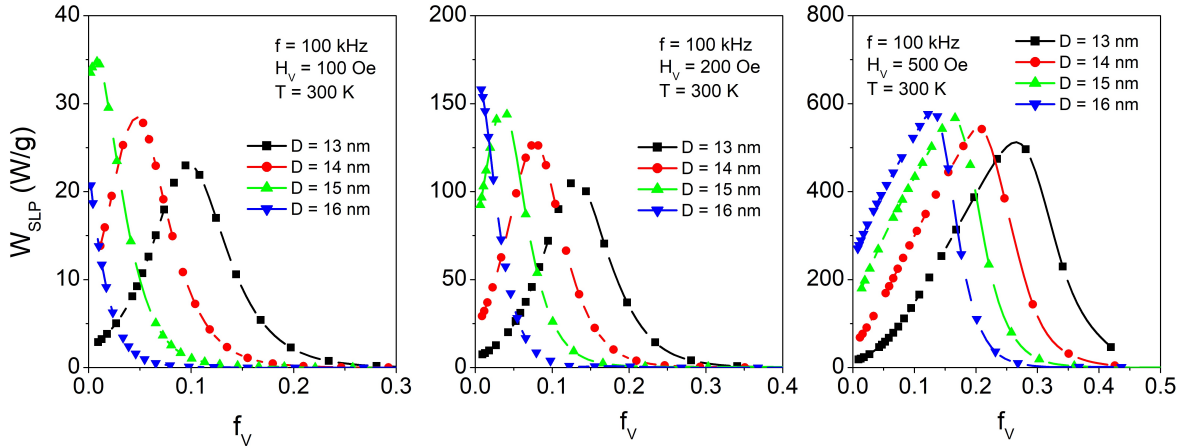


FIG. 3. Behavior of the room-temperature Specific Loss Power of interacting magnetite nanoparticles of different diameters as a function of the volume fraction f_V for different vertex field values.

III. SPECIFIC LOSS POWER AND PARTICLE VOLUME FRACTION

One of the most important consequences of the presence of dipole-dipole interactions among magnetic nanoparticles is the fact that the Specific Loss Power (SLP) $W_{SLP} = (f/\rho_{NP})A_L$ where f is frequency, ρ_{NP} is the mass density of magnetic material and A_L is the hysteresis loop's area, cannot be considered as a sort of label associated to a given type of magnetic nanoparticles but becomes a function of how many interacting particles are contained in the host medium, i.e., a function of f_V . This is shown in Figure 3, where the SLP obtained at room temperature under a field of 100 kHz is reported for some typical nanoparticle diameters and three values of the vertex field H_V . In all cases, the SLP has a maximum for a volume fraction whose value depends on both nanoparticle size and vertex field. At high particle concentrations, the interaction becomes so strong that the SLP almost disappears. The bell-shaped form of the $W_{SLP}(f_V)$ curves found for $H_V = 100$ and 200 Oe is slightly deformed when $H_V = 500$ Oe, which is however a value exceeding the typical range used in hyperthermia applications.

IV. FACTORS AFFECTING THE VARIATION OF W_{eff} WITH TEMPERATURE

The specific loss power W_{eff} is not only a function of f_V at a given temperature, but also of T for a given particle concentration. Two different factors concur to determine the behavior of W_{eff} as a function of temperature, a fact which has important consequences on the heat effectively released by magnetic nanoparticles to a host material: first, the magnetic properties are not constant, but they are monotonically decreasing functions of T , as briefly discussed in the main text; second - and most important: the kinetics of redistribution of the population of the two-level systems between the two wells is strongly influenced by temperature.

The key point is that we are mainly interested in the temperature behavior of *minor* hysteresis loops. Let us recall that in a minor loop the maximum magnetization (i.e., the magnetization measured at the vertex field) is very far from technical saturation, whereas in a *major* hysteresis loops the maximum magnetization is in the region of reversible approach to saturation. For biomedical applications, the vertex field must be low in order to avoid discomfort or nuisance to patients, so that one is compelled to make use of minor loops.

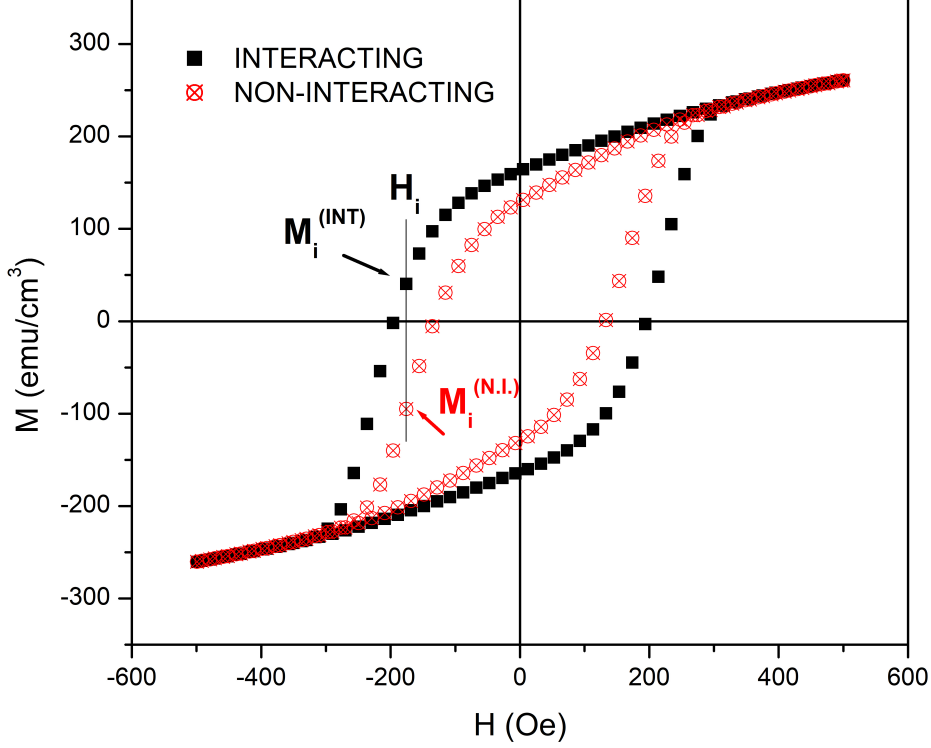


FIG. 4. Graphical representation of the way the quantity Σ is determined

Minor symmetric hysteresis loops of monodisperse random NP systems exhibit a non-monotonic temperature behavior of both shape and enclosed area A_L . A sharp maximum of A_L appears between room temperature and the material's Curie point, its position being dependent on particle size D . The temperature where W_{eff} is a maximum (T_{MAX}) can be predicted considering that the largest loop area occurs when the typical time of jump across the barrier $\tau(T)$ becomes equal to the time $1/(2f)$ taken to reverse the driving field:

$$\tau(T) = \tau_0 e^{\frac{E_B}{k_B T}} = \frac{1}{2f}. \quad (9)$$

As a consequence, T_{MAX} is found solving the implicit equation:

$$T_{MAX} = \frac{E_B(T_{MAX})}{k_B \ln\left(\frac{1}{2f\tau_0}\right)} \quad (10)$$

where E_B is a function of temperature because it contains temperature-dependent quan-

tities such as K_0 and M_s , and also depends on particle size because it is proportional to the volume V .

When $\tau \ll 1/(2f)$ the two-level systems are very close to thermal equilibrium and the hysteresis loop is very narrow; on the contrary, when $\tau \gg 1/(2f)$ the redistribution of magnetic moments in the energy wells is almost suppressed, and the magnetization only rotates towards the field direction giving rise to a nearly anhysteretic curve. Only when $\tau \approx 1/(2f)$ does the redistribution most effectively keep the double-well systems out of equilibrium during the loop, resulting in the largest enclosed area.

V. PROCEDURE TO DETERMINE THE QUANTITY Σ : A GRAPHICAL EXAMPLE

The parameter Σ defined in Equation 11 of main text is determined by selecting a large number n of magnetic field values H_i in the range $\pm H_V$, as shown in Figure 4 (in this work, $n = 1000$). For each i , the magnetization on the hysteresis loop is calculated in the case of an assembly of interacting particles (black symbols in Figure 4) and in the non-interacting case (red symbols). The square of the difference ($M_i^{(INT)} - M_i^{(N.I.)}$) is summed for $i = 1$ to n . The quantity Σ is obtained by taking the square root of the sum and by dividing it by the saturation magnetization of magnetite NPs.