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Ferromagnetism, hysteresis and enhanced heat dissipation in assemblies of superparamagnetic nanoparticles

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In this paper, we develop theoretical frameworks to explain the emergence of ferromagnetism in suspensions and agglomerates of superparamagnetic (SPM) nanoparticles. In the limit of strong anisotropy, the super moments can be treated as a collection of two-state Ising spins. When adequate in number, they interact via dipole-dipole coupling to produce a dipolar field and subsequently a permanent dipole moment. As a result, this effectual ferromagnet exhibits hysteresis on the application of an oscillating magnetic field yielding heat dissipation that is several orders of magnitude larger than in a paramagnet. Using our frameworks, we provide a design for a magnetite-blood suspension that yields heat dissipation in the mW range. Its important physical application is in remedial procedures for destroying tumor and cancer cells. We are also able to explain many experiments reporting manifestations of ferromagnetism in the form of hysteresis loops, return point memory and large heat dissipation in suspensions and aggregates of SPM nanoparticles. Our frameworks can be used to manipulate heat dissipation in variety of combinations of particles and their embedding mediums. They impart a basis to the often used ad-hoc methodologies in this subject. © 2012 American Institute of Physics. [http://dx.doi.org/10.1063/1.4768904]

I. INTRODUCTION

The last decade has revealed the tremendous potential of magnetic nanoparticles (MNP) for diagnostic and therapeutic applications. The reasons behind their wide applicability are many. They can be easily detected and manipulated by the application of external magnetic fields. They can be prepared in varying sizes and bound to biological entities, such as cells, viruses, proteins and genes. As a result, MNP provides exciting opportunities for site-specific drug delivery, improved quality of magnetic resonance imaging, manipulation of cell membranes, etc.1,2 The presence of a magnetic moment opens up further avenues in biomedicine. When subjected to an oscillating magnetic field, the particles can be made to dissipate heat. This phenomenon results in selective warming of the target site and is usually referred to as hyperthermia in the medical literature. Therefore, when directed on malignant tumors, MNP hold the potential to destroy cells or introduce a modest rise in temperature to increase the efficacy of chemotherapy.3–5 Consequently, recent years have evidenced intense investigations and developments towards the understanding of heat dissipation in MNP to combat cancer. And promising results have emerged from clinical trials of magnetically mediated hyperthermia.3,6

The most commonly used MNP for remedial purposes are single domain, superparamagnetic (SPM) nanoparticles. There are many advantages associated with them. They can be intravenously injected and then magnetically targeted to affected tissues or organs. Another convenience offered by particles of this size is their easy clearance from the body by way renal and biliary excretions. This can be a menace though, if the process is very rapid. It often needs to be slowed down by conjugating nanoparticles with ligands, such as folic acid, avidin-biotin complex, peptides, and carbohydrates.2,7–9 Further, the particles get magnetized only after the application of a magnetic field. So the risks of aggregation and embolism are substantially lower for paramagnetic nanoparticles vis-a-vis their ferromagnetic counterparts. However, each nanomagnet dissipates only a femtowatt of heat when subjected to an oscillating magnetic field! An often-used rule of the thumb is that a heat deposition of 100 mW/cc is required to raise the tissue temperature to ~45 °C desired for hyperthermia and chemotherapy applications.1 Thus, substantially large concentrations are required, but then the dangers of aggregation and safe levels of toxicity are a matter of great concern. It is, therefore, a challenge to create a suspension of SPM nanoparticles, which yields the required heat dissipation but at the same time, is non-toxic and non-aggregating.

Of late, many experimentalists have reported the unusual emergence of ferromagnetism in distinct assemblies of SPM nanoparticles. Some recently studied systems of relevance are magnetite (Fe3O4) nanoparticles embedded in glue,10 maghemite (γ–Fe2O3) nanoparticles suspended in water11 and close-packed metallic iron nanoparticles.12 For large concentrations of nanoparticles, these systems exhibit hysteresis loops, return point memory (RPM), and enhanced heat dissipation. Further, there are wide discrepancies between experimental data and theoretical predictions from the conventionally used Stoner-Wolfarth (SW) model for such systems. These observations, therefore, remain a puzzle to date.

In this paper, we develop the theoretical framework to explain the emergence of ferromagnetic behavior in assemblies of SPM nanoparticles. In the limit of strong anisotropy, the super moments can be treated as a collection of two-state Ising spins. When adequate in number, they interact via
dipole-dipole coupling to produce a dipolar field and subsequently a permanent dipole moment.\textsuperscript{13-17} As a result, this effectual ferromagnet exhibits hysteresis on the application of an oscillating magnetic field yielding heat dissipation that is several orders of magnitude larger than in a paramagnet. Two complications arise in the case of suspensions of SPM nanoparticles. The first one is the possibility of magnetic decoherence due to the tumbling motion or the Brownian relaxation of the suspended particles. The second one is the possibility of aggregation of the nanoparticles due to their magnetic moment. From our theoretical calculations, we find that they can be prevented by size-selection. Fortunately, the range of particle sizes which avert both these phenomena are coincident! Using our frameworks, we provide a prototypical calculation to design a magnetite-blood suspension that yields heat dissipation in the mW range and at the same time, is non-aggregating and non-toxic. (We choose magnetite because it is most commonly used in therapeutic applications.) We are also able to explain many of the outstanding experimental issues in the suspensions and aggregates discussed in the preceding paragraph. Our frameworks provide excellent agreement between experimental and theoretical data in these systems. We emphasize that our procedures can be used to manipulate heat dissipation in a variety of combinations of particles and their embedding mediums, provided the limit of strong anisotropy (Ising) holds. Further, we believe that these procedures impart a basis to the often used ad-hoc methodologies in this subject.

The rest of the paper is organized as follows. In Sec. II, we develop the theoretical formalisms required to design a model suspension of SPM nanoparticles that has magnetic coherence, is non-aggregating, and exhibits enhanced heat dissipation. The relaxation mechanisms of SPM nanoparticle in a suspension and their control using size-selection are discussed in Sec. II A. The mechanisms of aggregation and fragmentation in clusters of nanoparticles are discussed in Sec. II B. In Sec. II C, we provide the formulation for calculation of heat dissipation in the SPM nanoparticle suspension influenced by dipolar interactions. We then proceed to create a suspension of magnetite particles, which has the aforementioned properties. In Sec. III, we explain using our framework the experimentally observed amplified magnetic response in three distinct ensembles of SPM particles: (i) magnetite nanoparticles embedded in glue, (ii) maghemite ($\gamma = Fe_2O_3$) nanoparticles suspended in water, and (iii) close-packed metallic iron nanoparticles. Finally, in Sec. IV, we conclude this paper with a summary of results.

II. THEORETICAL FORMULATION AND DESIGN

A. Relaxation mechanisms of SPM nanoparticles in a suspension

A ferromagnetic samples such as iron for instance, comprises of domains, each having spontaneous magnetization pointing in a different direction. If the size of the sample is reduced, there comes a point beyond which a single domain state becomes preferable. The direction of magnetization of the single domain particle does not remain fixed in time though, but undergoes fluctuations or “relaxations” as the magnetic moment rotates between the crystallographic anisotropy axes. As a result, the time averaged magnetization is still zero and the particle is paramagnetic. It is called “super paramagnetic” because each particle has a giant magnetic moment arising due to a large number ($\sim 10^5$) of individual atomic moments.

In the case of uniaxial anisotropy (in the z-direction say), the magnetic energy of a single-domain, SPM particle is given by\textsuperscript{18,19}

$$E = VK\sin^2\Phi,$$

where $V = 4\pi r_c^3/3$ is the magnetic volume of a particle with radius $r_c$, $K$ is the effective magnetic anisotropy constant, and $\Phi$ is the angle between the z-axis and direction of the “super” magnetic moment of the single-domain particle. Minimum energy occurs at $\Phi = 0$ and $\pi$ and these angles define the two equilibrium orientations of the magnetic moment. If $VK \gg k_BT$, where $k_B$ is the Boltzmann constant and $T$ the absolute temperature, the magnetic moment is mostly locked in two minimum energy orientations resulting in the so-called Ising limit. In this limit, $\Phi(t)$ may be viewed as a dichotomic Markov process in which it jumps at random between the angles $0$ and $\pi$. The jump rate is governed by the Arrhenius-Kramer formula

$$\lambda_{0\rightarrow\pi} = \lambda_{\pi\rightarrow0} = \lambda_o \exp\left(-\frac{VK}{k_BT}\right),$$

where $\lambda_o$ is the “attempt” frequency. The reciprocal of the jump rate is the Néel relaxation time and is given by

$$\tau_N = \tau_o \exp(VK/k_BT),$$

where $\tau_o$ is related to the inverse of the attempt frequency of magnetic reversal.

A suspended SPM particle can also relax due to Brownian rotation of the particle within the fluid. The associated Brownian relaxation time is given by

$$\tau_B = \frac{4\pi\eta r_h^3}{k_BT},$$

where $\eta$ is the viscosity of the carrier liquid and $r_h$ is the hydrodynamic radius defined as the sum of the core radius $r_c$ and the thickness $\delta$ of the surfactant coating, which prevents agglomeration and sedimentation of nanoparticles.

It is customary to define an effective relaxation time as follows:\textsuperscript{18,20}

$$\frac{1}{\tau_e} = \frac{1}{\tau_N} + \frac{1}{\tau_B}.$$ 

Naturally, the effective relaxation time is dominated by the smaller of the two relaxation times. As can be seen from Eqs. (3) and (4), the Néel and Brownian relaxation times can be manipulated by $K$, $r_c$, $\eta$, and $\delta$. In an earlier paper, we did a detailed analysis to understand the role played by these parameters on $\tau_N$, $\tau_B$, and $\tau_e$.\textsuperscript{21} We found that for specific values of $K$ and $\eta$, which is tantamount to choosing
nanoparticles and their suspending medium, the core radius $r_c$ affects the relaxation times the most. While $\tau_N$ increases exponentially with particle size, $\tau_B$ grows linearly with it. Size-selection, therefore, is most commonly employed to tailor $\tau_N$, $\tau_B$, and consequently $\tau_c$. However, any of the parameters $K$, $\eta$, and $\delta$ can be used to alter the relaxation times. Physically, this amounts to changing the composition or/and shape of nanoparticles, the viscosity of the suspending medium and the properties or/and the thickness of the surfactant coating. Thus, there are many ways to tailor relaxation times and consequently relaxation behavior of suspensions of SPM nanoparticles. In Ref. 21, we have studied the relaxation characteristics of magnetic nanoparticle suspensions for a variety of SPM nanoparticles, suspending mediums, and surfactant coatings. We refer an interested reader to this paper for further insights on tailored relaxation times in nanoparticle suspensions.

Table I summarizes the evaluations of $VK/k_B T$, $\tau_N$, $\tau_B$, and $\tau_c$, for a range of diameters of magnetite nanoparticles suspended in blood. Spherical particles of magnetite have an anisotropy constant $K = 4.68 \times 10^6$ ergs/cc and the viscosity of human blood at $37^\circ$C is $\eta \approx 0.03$ poise. In most applications, the surfactant coating is in the range 2–6 nm. We have used $\delta = 4$ nm in our calculations. The important conclusion from Table I is that the magnetic particles with diameters in the range 6–10 nm are in the Ising limit and that $\tau_c \approx \tau_N$ for these. The relaxation then takes place by rotation of the magnetic moment inside the particle. This observation provides the first step towards the design of the model suspension. For larger particles on the other hand, $\tau_c \approx \tau_B$ and the relaxation is due to a physical rotation of the particle in the suspension. We find that $\tau_c$ is unaffected by $\delta$ when the particle diameters are $\approx 10$ nm because in this range, Néel relaxation dominates.

### B. Aggregation and fragmentation mechanisms in SPM nanoparticle suspensions

Clustering of magnetic nanoparticles is rather common in dense suspensions, as observed in electron microscopy or light scattering experiments. Since the relaxation times are strongly size-dependent, the formation of clusters can significantly alter the response characteristics of the suspension. Further, for applications such as hyperthermia, clustering can endanger the flow of particles and could also lead to blockages in the arterial system. Therefore, in such applications, it is imperative to prevent clustering via parameters which are easy to manipulate.

There are several energies, attractive and repulsive, ubiquitous in suspensions of magnetic particles. Their relative strengths play an important role in the aggregation properties of the suspension.20,21–25 The primary interactions between a pair of spherical magnetic nanoparticles in a suspension are as follows:

1. Dipolar interaction: The dipolar interaction energy between two particles $i$ and $j$ with magnetic moments $m_i$ and $m_j$, respectively, is given by

$$E_d(s) = -\frac{\mu_0}{4\pi} \left( \frac{3}{s^3} \left( \frac{m_i \cdot m_j}{s^3} - \frac{m_i \cdot m_j}{s^3} \right) \right),$$

where $s$ is the center-to-center separation between them and $\mu_0$ is the permeability of free space. This interaction energy is attractive and reaches its maximum when the particles come in contact with one another. Its presence, therefore, promotes aggregation. Since the magnetic properties of the particles are affected by temperature, the dipolar interaction is also temperature dependent.

2. Van der Waal’s interaction: It arises spontaneously between neutral particles because of the fluctuating electric dipolar forces and is attractive in nature. Hamaker calculated this interaction for identical spheres separated by a surface-to-surface distance $l$ to be

$$E_v = \frac{A}{6} \left\{ \frac{2}{l^2 + 4l} + \frac{2}{(l + 2)^2} + \ln \left( \frac{l^2 + 4l}{l + 4l} \right) \right\},$$

where the Hamaker constant $A = 10^{-19}$ Nm. It should be noted that the $l^{-1}$ dependence in the above equation indicates that infinite energy is required to separate a particle pair while a finite energy is required in its formation. Therefore, aggregation of particles will occur as long as the Hamaker constant has a finite value. Van der Waal’s interaction, unlike dipolar interaction, is unaffected by temperature.

3. Steric interaction: The steric energy comes into play due to the presence of long chained surfactant molecules coating the particles. This mechanism prevents the particles from approaching very close to one another, thus preventing the van der Waal’s attraction to come into play. This repulsive interaction originates due to a compression of the surface-adsorbed surfactant molecules when the inter-particle separation is smaller than two times the thickness of the surfactant layer. For a sufficient thickness of the surfactant layer, the repulsion can grow large enough to avoid the contact between the magnetic particles. This interaction energy for spherical particles is given by

$$E_s = \frac{Y}{1.325} \left( 2\delta - \frac{s^2}{2} \right)^{5/2} \left( r_c + \delta \right)^{1/2},$$

where $Y$ is the Young’s modulus of the surfactant coating over the nanoparticles.

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### Table I. Evaluations of $VK/k_B T$, $\tau_N$, $\tau_B$, and $\tau_c$, for a range of diameters $d$ of magnetite nanoparticles suspended in blood. The parameters used for these evaluations are $K = 4 \times 10^6$ Jm$^{-3}$, $T = 37^\circ$C, $\eta \approx 0.03$ poise, and $\delta = 4$ nm. Diameters which yield the Ising limit and exhibit Néel relaxation as well are highlighted.

<table>
<thead>
<tr>
<th>$d$ (nm)</th>
<th>$VK/k_B T$</th>
<th>$\tau_N$ (s)</th>
<th>$\tau_B$ (s)</th>
<th>$\tau_c$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.05</td>
<td>$1.05 \times 10^{-9}$</td>
<td>$1.10 \times 10^{-6}$</td>
<td>$1.04 \times 10^{-9}$</td>
</tr>
<tr>
<td>4</td>
<td>0.37</td>
<td>$1.45 \times 10^{-9}$</td>
<td>$1.90 \times 10^{-6}$</td>
<td>$1.45 \times 10^{-9}$</td>
</tr>
<tr>
<td>6</td>
<td>1.25</td>
<td>$3.51 \times 10^{-9}$</td>
<td>$3.02 \times 10^{-6}$</td>
<td>$3.50 \times 10^{-9}$</td>
</tr>
<tr>
<td>8</td>
<td>2.97</td>
<td>$1.96 \times 10^{-9}$</td>
<td>$4.51 \times 10^{-6}$</td>
<td>$1.95 \times 10^{-9}$</td>
</tr>
<tr>
<td>10</td>
<td>5.81</td>
<td>$3.34 \times 10^{-7}$</td>
<td>$6.42 \times 10^{-6}$</td>
<td>$3.18 \times 10^{-7}$</td>
</tr>
<tr>
<td>12</td>
<td>9.72</td>
<td>$1.71 \times 10^{-5}$</td>
<td>$8.81 \times 10^{-6}$</td>
<td>$5.77 \times 10^{-6}$</td>
</tr>
<tr>
<td>14</td>
<td>15.51</td>
<td>$5.12 \times 10^{-3}$</td>
<td>$1.17 \times 10^{-5}$</td>
<td>$1.17 \times 10^{-5}$</td>
</tr>
</tbody>
</table>
Apart from the above energies, the thermal energy responsible for the Brownian motion of the suspended particles also plays an important role in the aggregation dynamics. An appropriate value of temperature (which depends on the size of the interacting particles) is capable of preventing aggregation. In principle, this condition may be expressed as a comparison between the attractive energy with the thermal energy of the two particles to yield a numerical value of the core radius $r_c$ at which this could happen. This exercise however is not straightforward when attractive forces are effective at different length scales, as in the present case. The attractive dipolar and van der Waal interactions cause aggregation of the particles to yield clusters. The steric repulsion in conjunction with the thermal energy $k_BT$ on the other hand hampers the aggregation process but may also lead to fragmentation or removal of particle(s) from the parent cluster. The mean cluster size can hence be expected to be governed by the relative strengths of the twin mechanisms of aggregation and fragmentation. A convenient parameter in this context, therefore, is the ratio of the strengths of the attractive and repulsive energies

$$\Omega = \frac{E_a + E_r}{E_a + k_BT}.$$  \hfill (9)

The description of non-equilibrium phenomena involving diffusion, aggregation, and fragmentation is a difficult problem. Two approaches have generally been employed in this context. The first one is a molecular dynamics (MD) approach in which the particles follow trajectories according to the explicitly chosen interaction energies.\textsuperscript{26,27} Arrangements, such as rings, chains, etc. of particles in aggregates can be obtained with precision in these simulations.\textsuperscript{28–30} However, the observation of aggregation events is computationally very expensive. As a result, MD procedures are employed when system sizes and observation times are small. The second approach uses the point-particle models introduced by Smoluchowski.\textsuperscript{31} They have become a standard tool to study growth processes involving the mechanisms of diffusion, aggregation, and fragmentation.\textsuperscript{32–34} The evolution is described in terms of rate equations, which enumerate all possible ways in which a cluster could change its size. The rate equations are easy to implement numerically using discretization techniques or Monte Carlo (MC) methods. Though simplistic in nature, they capture important qualitative and quantitative features of the growth phenomena.\textsuperscript{21,33,34} We use this approach to understand the dynamical evolution and steady-state properties of the aggregating-fragmenting suspension of SPM nanoparticles.

To begin with, we assume that the suspension contains $N$ identical, point particles. The particles aggregate on contact to form (point) clusters if the net interaction between them is attractive. A particle could break-off from clusters if the repulsive interactions can overcome the mutual attraction. These competing mechanisms result in clusters of varying sizes. Let $P(k,t)$ denote the probability of having a clusters containing $k$ particles. The time evolution of $P(k,t)$ is governed by the equations\textsuperscript{21}

$$\frac{\partial P(k,t)}{\partial t} = \sum_{i+j=k} K_{ij}P(i,t)P(j,t) - P(k,t) \sum_{j=1}^{\infty} K_{ij}P(j,t) + \omega P(k+1,t) - \omega P(k,t), \quad k > 1,$$  \hfill (10)

$$\frac{\partial P(1,t)}{\partial t} = -P(1,t) \sum_{j=1}^{\infty} K_{1j}P(j,t) + \omega \sum_{j=2}^{\infty} P(j,t), \quad k = 1.$$  \hfill (11)

In Eqs. (10) and (11), $K_{ij}$ describes aggregation of a cluster containing $i$ particles with another containing $j$ particles to yield an aggregate of $k=i+j$ particles. It is usually assumed to have a mass-dependent form defined by $K_{ij} = D(i^{-\mu} + j^{-\mu})$. If $\mu = 0$, the diffusion rate of clusters is mass-independent. If $\mu > 0$, larger clusters have lower mobility than smaller clusters. The parameter $\omega$, on the other hand, describes fragmentation of a particle from a cluster. Analogous to $\Omega$ in Eq. (9), we can define

$$R = \frac{D}{\omega},$$  \hfill (12)

to describe the relative strengths of the aggregation and fragmentation processes in the aggregation-fragmentation model. In fact, the correspondence between $R$ and $\Omega$ facilitates the contact between numerical results and experimental observations on cluster formation in magnetic nanoparticle suspensions.

We carried out detailed numerical simulations of the aggregation-fragmentation model described by Eqs. (10) and (11) to understand the role played by $R$ on the cluster-size distribution $\{P(k,t)\}$ in Ref. 21. Of particular significance in the present context is the dependence of the average cluster size in the steady-state $\langle k(R) \rangle$ on the ratio $R$. Our simulations yielded the power law

$$\langle k(R) \rangle \sim R^z,$$  \hfill (13)

with $z \approx 0.85 \pm 0.02$.\textsuperscript{21} In Table II, we present the values of $\langle k(R) \rangle$ corresponding to different values of $R$. We calculated $\Omega$ using Eqs. (6)–(8) for many magnetic nanoparticle suspensions with known statistics of aggregates. We got the same statistics using Eq. (13), which has lent credence to our model and interpretation of parameters therein.\textsuperscript{21}

We now perform these calculations for 10 nm diameter magnetite particles with a 4 nm coating of polyethylene glycol ($Y \sim 10^6$ Pascal), a commonly used biocompatible surfactant, suspended in blood. In Table III, we calculate $\Omega$ for different particle diameters and three values of concentrations: 1.0 $\mu$g/ml, 10.0 $\mu$g/ml, and 100 $\mu$g/ml. (The biologically safe limit of magnetic material in the human body is within 100 $\mu$g/ml). The corresponding particles/cc, the

| TABLE II. Variation of the average cluster size $\langle k(R) \rangle$ in the steady state as a function of $R$, the ratio of aggregation and fragmentation rates. |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| R   | 0.001 | 0.01 | 0.05 | 0.1  | 0.2  | 0.3  | 0.4  | 0.5  |
| $\langle k(R) \rangle$ | 1.03 | 1.12 | 1.34 | 1.56 | 2.08 | 2.59 | 3.09 | 5.8  |
Table III. Calculation of expected cluster size ($\langle k \rangle$) for different diameters and concentrations of magnetic particles with a 4 nm coating of polyethylene glycol ($T = 10^6$ pascal) suspended in blood at body temperature (37°C).

<table>
<thead>
<tr>
<th>$\rho$ (μg/cc)</th>
<th>d (nm)</th>
<th>N (particles/cc)</th>
<th>l (nm)</th>
<th>$\Omega$</th>
<th>$\langle k \rangle$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>6.0</td>
<td>$1.7 \times 10^{12}$</td>
<td>500</td>
<td>$10^{-4}$</td>
<td>1.0</td>
</tr>
<tr>
<td>8</td>
<td>7.2</td>
<td>$10^{11}$</td>
<td>490</td>
<td>$10^{-4}$</td>
<td>1.0</td>
</tr>
<tr>
<td>10</td>
<td>3.7</td>
<td>$10^{11}$</td>
<td>480</td>
<td>$10^{-4}$</td>
<td>1.0</td>
</tr>
<tr>
<td>10.0</td>
<td>6.0</td>
<td>$10^{13}$</td>
<td>400</td>
<td>$0.009$</td>
<td>1.08</td>
</tr>
<tr>
<td>8</td>
<td>7.2</td>
<td>$10^{12}$</td>
<td>380</td>
<td>0.01</td>
<td>1.2</td>
</tr>
<tr>
<td>10</td>
<td>3.7</td>
<td>$10^{12}$</td>
<td>360</td>
<td>0.04</td>
<td>1.28</td>
</tr>
<tr>
<td>100.0</td>
<td>6.0</td>
<td>$10^{14}$</td>
<td>250</td>
<td>0.04</td>
<td>1.28</td>
</tr>
<tr>
<td>8</td>
<td>7.2</td>
<td>$10^{13}$</td>
<td>230</td>
<td>0.08</td>
<td>1.47</td>
</tr>
<tr>
<td>10</td>
<td>3.7</td>
<td>$10^{13}$</td>
<td>200</td>
<td>0.1</td>
<td>1.56</td>
</tr>
</tbody>
</table>

The parameter $\Lambda$ contains all the constants. It fluctuates in sign and has a magnitude dependent on the volume fraction of the SPM nanoparticles in the suspension.

The equilibrium value of magnetization is given by

$$M_{eq} = \lim_{t \to \infty} M(t) = \mu N V \tanh \left( \frac{\mu V H_d}{k_B T} \right).$$

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Heat dissipation in magnetic systems results from the delayed response of the magnetic moment to an ac magnetic field. Suspended super moments relax via the Néel and Brownian mechanisms. When their effective relaxation time at most form dimers. Notice that in most cases, nanometer-sized suspensions provide the second step towards the design of our model suspension.

**C. Heat dissipation in SPM nanoparticle suspensions**

Heat dissipation in magnetic systems results from the delayed response of the magnetic moment to an ac magnetic field. Suspended super moments relax via the Néel and Brownian mechanisms. When their effective relaxation time (given by Eq. (5)) is larger than the period of the applied oscillating magnetic field, the super moments lag behind the oscillating field, causing heat dissipation. However, these relaxation losses are much smaller in magnitude than hysteresis losses in ferromagnetic samples. In this subsection, we obtain conditions under which a suspension of SPM nanoparticles can behave as an effective ferromagnet in order to yield amplified heat dissipation.

Discussions in the preceding subsections provide a practical approach to tailor relaxation times and aggregation in a suspension of SPM nanoparticles via size selection. We consider a suspension of $N$ SPM particles, which relax via the Néel mechanism and that at the same time, are non-aggregating. As seen from Tables I and III, these properties are satisfied by a range of particle sizes. When sufficiently large in number, the supermoms start interacting via dipole-dipole coupling. In order to incorporate the effects of dipolar interactions, it is essential to add the contribution due to the “dipolar Hamiltonian” to the magnetic energy of the particle defined by Eq. (1). In the limit of large anisotropy, the dipolar energy in Eq. (6) simplifies to the following form:

$$E_d = \frac{\hbar^2 \mu^2 V^2}{2} \sum_{i,j} \frac{(1 - 3 \cos^2 \theta_{ij})}{r_{ij}^3} \cos \Phi_i \cos \Phi_j.$$

Here, $\gamma_i$ and $\gamma_j$ are the gyromagnetic ratio of the $i$th and $j$th particle, respectively, $r_{ij}$ is the distance between the two particles, $\theta_{ij}$ is the angle between $\mathbf{r}_{ij}$ and the anisotropy axis, and $\Phi$ is as defined in Eq. (1). Note that the angular dependence $(1 - 3 \cos^2 \theta_{ij})$ implies that the interaction can change sign thereby switching from ferromagnetic for angles close to the anisotropy axis to antiferromagnetic for intermediate angles ($55^\circ \leq \theta_{ij} \leq 125^\circ$).

A mean-field approach is invoked to treat the complicated interaction in Eq. (14). Each particle is visualized to be experiencing an effective local magnetic field $H_d$ due to the surrounding (magnetic) medium. Further, the Ising limit allows for the replacement of $\cos \Phi$ by a two-state variable $\sigma$. These simplifications yield the mean-field dipolar energy

$$E_d^{MF} = \mu V \sigma H_d,$$

with the field $H_d$ evaluated self-consistently by the equation

$$H_d = \mu N V \langle \sigma \rangle = \mu N V \tanh \left( \frac{\mu VH_d}{k_B T} \right).$$

The parameter $\Lambda$ contains all the constants. It fluctuates in sign and has a magnitude dependent on the volume fraction of the SPM nanoparticles in the suspension.

Though small in magnitude, the emergence of $H_d$ introduces significant changes in the suspension. It alters the relaxation rate in Eq. (2), and under the assumption of large anisotropy yields the following generalized relaxation rates:

$$\lambda_{0 \to \pi} = \lambda_0 \exp \left( -\frac{V(K + H_d \mu)}{k_B T} \right),$$

$$\lambda_{\pi \to 0} = \lambda_0 \exp \left( -\frac{V(K - H_d \mu)}{k_B T} \right).$$

The relative populations of magnetic moments $n_0$ and $n_\pi$ aligned along and against the anisotropy axis (corresponding to $\Phi = 0$ and $\pi$) are now described by a pair of master equations for a two-state system

$$\frac{dn_0(t)}{dt} = -\lambda_{0 \to \pi} n_0(t) + \lambda_{\pi \to 0} n_\pi(t),$$

$$\frac{dn_\pi(t)}{dt} = \lambda_{0 \to \pi} n_0(t) - \lambda_{\pi \to 0} n_\pi(t),$$

with $N = n_0 + n_\pi$. Solving Eqs. (19) and (20) and defining $\lambda = \lambda_{0 \to \pi} + \lambda_{\pi \to 0}$ and $\Delta \lambda = \lambda_{0 \to \pi} - \lambda_{\pi \to 0}$ yields the time-dependent magnetization

$$M(t) = V \mu [n_0(t) - n_\pi(t)],$$

$$M(t) = M(t = 0) \exp(-\hat{\lambda} t) + \mu V N \frac{\Delta \lambda}{\hat{\lambda}} [1 - \exp(-\hat{\lambda} t)],$$

$$M(t = 0) \exp(-\hat{\lambda} t) + \mu V N \tanh \left( \frac{\mu VH_d}{k_B T} \right) [1 - \exp(-\hat{\lambda} t)].$$

The equilibrium value of magnetization is given by

$$M_{eq} = \lim_{t \to \infty} M(t) = \mu V N \tanh \left( \frac{\mu VH_d}{k_B T} \right).$$
The super moments are now aligned along $H_d$ and the assembly mimics a domain of a ferromagnet. At this juncture, the need to block Brownian rotations can be appreciated. Their presence will result in disordering and misalignment of the magnetic moments.

The emergence of the permanent dipole moment leads to new consequences. Consider this system subjected to an oscillating magnetic field $H(t) = H_o \cos \omega t$ where $H_o$ and $\omega$ ($= 2\pi f$) are the amplitude and frequency of oscillation. As $H(t)$ varies periodically in time, so does $M(t)$ with the same period. This time dependent magnetization can be obtained by replacing $H_d$ with $(H + H_d)$ in Eq. (24) (Ref. 14)

$$M(t) = \mu V N \tanh \left( \frac{\mu V (H + H_d)}{k_B T} \right). \quad (25)$$

For dilute suspensions, $H_d \approx 0$ and Eq. (25) reduces to the Langevin form as expected $^{18}$

$$M(t) = \mu V N \tanh \left( \frac{\sqrt{\mu H}}{k_B T} \right). \quad (26)$$

The hysteresis loop area $A = \frac{1}{2} M(t) dH(t)$ can be computed after a few field cycles to provide sufficient time for the transients to settle down. The area of the loop is a measure of the heat dissipation. More precisely, the volumetric power dissipation is given by

$$P = \mu_o f \int dH(t) M(t) = \mu_o f A. \quad (27)$$

We go back to the magnetite-blood suspension for the numerical evaluations of heat dissipation. We specifically choose particle sizes, which block Brownian rotations and guarantee a single-particle status as required for our formulation discussed above. The clinically safe range for frequency $f$ of the applied oscillating magnetic field is 50 to 1500 kHz and that for the field amplitude is 1 to 200 Oe. We have done our evaluations for $H_o = 100$ Oe and $f = 1000$ kHz. In Table IV, we present the calculations of the dipolar field $H_d$ and the corresponding volumetric power dissipation using Eq. (27) for different sizes and concentrations of magnetite nanoparticles. Careful inspection reveals pronounced heat dissipation, in the milliwatt range, for significant values of the dipolar field $H_d$. These arise for higher concentrations of magnetite nanoparticles. To further emphasize the consequences of the dipolar interactions, in Figure 1, we plot $M(t)$ vs. $H(t)$ using Eq. (25) for increasing concentrations of

![FIG. 1. Typical hysteresis loops corresponding to 10 nm diameter magnetite particles for increasing values of $N$, the number of particles/cc. The inset shows $M/M_s$ for the two lower concentrations to clarify the deviation from the Langevin response (for $N = 10^{10}$) to the emergence of hysteresis loops with increasing concentrations (interactions).](image)

TABLE IV. Calculation of the dipolar field $H_d$ and volumetric power dissipation $P$ in magnetite nanoparticles suspension for different diameters and concentrations. Values corresponding to significant increase in heat dissipation are indicated in bold.

<table>
<thead>
<tr>
<th>$N$ (particles/cc)</th>
<th>$H_d$ (Oe)</th>
<th>$P$ (mW/cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>6 $10^{12}$</td>
<td>0.007</td>
<td>0.17</td>
</tr>
<tr>
<td>8 $10^{12}$</td>
<td>0.024</td>
<td>0.31</td>
</tr>
<tr>
<td>10 $10^{12}$</td>
<td>0.088</td>
<td>0.67</td>
</tr>
</tbody>
</table>

III. COMPARISONS WITH EXPERIMENTAL DATA

Of late, many experiments have reported signs of ferromagnetism in dense assemblies of magnetic nanoparticles. It is manifested in the form of hysteresis loops and large heat dissipation in these systems. But wide discrepancies between experimental data and theoretical predictions from the conventionally used SW model have been observed $^{11,12,36,37}$ The SW model assumes the magnetic dipoles to be freely orientable or non-interacting. Dense assemblies of magnetic nanoparticles, on the other hand, are far from non-interacting. Therefore, quantitative discrepancies are not unexpected when the same theory is applied to interacting samples. We attend to some such experimental observations with our framework of Sec. II, which takes into account the dipolar interactions amongst the moments. In particular, we choose those observations, which are relevant in the context of hyperthermia and chemotherapy.

The first result pertains to measurement of $M(t)$ vs. $H(t)$ by Gudoshnikov et al. for a sample of magnetite nanoparticles dispersed in glue $^{10}$ Their anisotropy constant $K = 1.5 \times 10^5$ ergs/cc and concentration $N = 8.7 \times 10^{13}$ particles/cc. The sample is polydisperse, obeying a log-normal distribution with a mean particle size of 25 nm and variance $\sigma = 0.3$. A striking observation here is that of RPM exhibited by the hysteresis loops. If the field $h(t)$ is made to cycle with a reduced amplitude to generate a sub-loop, the system returns precisely to the same state from which it left the outer loop. This same memory effect extends to sub-cycles within cycles. The system thus remembers a hierarchy of states in its past external fields. $^{38,39}$ Figure 2(a) shows the RPM as observed by Gudoshnikov et al. These data are a reproduced
in Figure 2(b) using Eq. (25) for the same set of parameters used in the experiment. These parameters yielded \( t_N = 6.4 \times 10^{-5} \text{ s} \) and \( H_d = 0.85 \text{ Oe} \) using Eqs. (3) and (16), respectively. The slight discrepancy between Figures 2(a) and 2(b) can be attributed to the fact that our evaluations are for a monodisperse sample. Polydispersity introduces a distribution of relaxation times, which imparts a softness to the magnetization reversal. Figure 2(c) indicates the specific absorption rate (SAR) = \( A_f \), as a function of \( h_0 \), used to generate the minor loops for both sets of data. Their good agreement brings out the cogency and the robustness of our theoretical formulation.

A few comments regarding loop shapes are in order. The hysteresis loops in Ising ferromagnets are characterized by a sharp magnetization reversal under the action of the oscillating magnetic field. The loops observed in Figure 1 on the other hand are slanting, smooth, and continuous. Such loops are typical of systems with conflicting interactions. They lead to frustrated magnetic moments and consequently to complex free energy landscapes, which impede moment reversal.\(^{39-41}\)

We attribute similar behavior to our system of SPM nanoparticles due to the presence of the dipolar interactions. As seen from Eq. (14), these can be positive or negative in sign because of the cosine term. Further, we emphasize that RPM though unexplored in the context of hyperthermia and chemotherapy applications is a promising technique for gradual heating of a local area. Easy implementation in a clinical laboratory makes this protocol practical.\(^{14}\)

The second set of experimental results that we explain are measurements of heat dissipation by Fortin et al. for maghemite(\(\gamma-Fe_2O_3\)) nanoparticles in water with calculated values (\(P_s\)) using our theoretical framework incorporating inter-particle interactions. The corresponding dipolar field strength \(H_d\) for each case is also indicated.

**TABLE VI.** Comparison of \(P_E\) measured by Mehdaoui et al. for different particle sizes and concentrations of maghemite(\(\gamma-Fe_2O_3\)) nanoparticles in water with calculated values (\(P_s\)) using our theoretical framework incorporating inter-particle interactions. The corresponding dipolar field strength \(H_d\) for each case is also indicated.

<table>
<thead>
<tr>
<th>(d) (nm)</th>
<th>(\sigma)</th>
<th>(N) (particles/cc)</th>
<th>(P_E) (mW/cc)</th>
<th>(P_S) (mW/cc)</th>
<th>(H_d) (Oe)</th>
<th>(P_I) (mW/cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3</td>
<td>0.19</td>
<td>(1.73 \times 10^{15})</td>
<td>2.66</td>
<td>1.49</td>
<td>2.31</td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>0.20</td>
<td>(8.57 \times 10^{15})</td>
<td>4.41</td>
<td>1.58</td>
<td>3.89</td>
<td></td>
</tr>
<tr>
<td>8.1</td>
<td>0.21</td>
<td>(5.03 \times 10^{15})</td>
<td>7.15</td>
<td>1.67</td>
<td>6.53</td>
<td></td>
</tr>
<tr>
<td>10.2</td>
<td>0.28</td>
<td>(2.42 \times 10^{15})</td>
<td>56.2</td>
<td>1.71</td>
<td>43.26</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE V.** Comparison of power dissipation (\(P_E\)) measured by Fortin et al. for different particle sizes and concentrations of maghemite(\(\gamma-Fe_2O_3\)) nanoparticles in water with calculated values (\(P_s\)) using our theoretical framework incorporating inter-particle interactions. The corresponding dipolar field strength \(H_d\) for each case is also indicated.

<table>
<thead>
<tr>
<th>(d) (nm)</th>
<th>(\sigma)</th>
<th>(N) (particles/cc)</th>
<th>(P_E) (mW/cc)</th>
<th>(P_S) (mW/cc)</th>
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<td>43.26</td>
<td></td>
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</table>
of all the magnetic moments, i.e., \( M_s = \mu N \). The presence of dipolar interactions however, with ferromagnetic and antiferromagnetic couplings, preclude a complete alignment of the moments along the direction of the applied field. So, \( M_s < \mu N \) in this case. Our explanation is indeed supported by the hysteresis loops in Figures 1 and 2. They do not saturate for dense assemblies of magnetic systems.

IV. CONCLUSION

In this paper, we have developed an unified approach to study dilute and dense assemblies of SPM nanoparticles. The latter are characterized by the presence of dipolar fields, which induce ferromagnetism in them. The manifestations of this permanent magnetic moment are in the form of hysteresis loops, return point memory and enhanced heat dissipation on the application of an oscillating magnetic field. We have verified these properties in distinct physical systems characterized by diverse parameter values.

As our first example, we studied a magnetite-blood suspension. It is relevant in the context of remedial procedures for destroying tumor and cancer cells. Brownian relaxation and aggregation can be blocked if particles are a few nanometers in size. On account of the dipolar field, this suspension becomes a ferromagnetic domain for a range of particle diameters. When cycled through an oscillating magnetic field, it dissipates heat in the mW range on account of hysteresis causing a rise in temperature of the malignant cells.

Our next set of examples included magnetite nanoparticles embedded in glue, maghemite \( (\gamma - Fe_2O_3) \) nanoparticles suspended in water, and close-packed metallic iron nanoparticles. For large concentrations of nanoparticles, the systems exhibited hysteresis loops, return point memory, and enhanced heat dissipation. Our theoretical framework could explain these puzzling experimental observations and yielded an accurate quantitative agreement between theoretical and experimental observations. They could not be understood by the Stoner-Wolfarth model, which has conventionally been used for theoretical investigations of such systems.

The dipolar interactions between the supermoments played a major role in creating the effectual ferromagnet. The conflicting ferromagnetic and antiferromagnetic nature of these interactions have given rise to many interesting phases in magnetic spin systems. More unusual properties have been observed in mesoscopic systems where system sizes are shorter than the long-ranged dipolar interactions. Assemblies of superparamagnetic nanoparticles could provide a platform to probe fascinating new effects arising from the above interplay. We believe that our results will motivate further experimental and theoretical investigations in these systems.

8C. Minelli, S. B. Lowes, and M. M. Stevens, Small 6, 2336 (2010).