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Hydrodynamic core size extraction of magnetic nanoparticles using non-regularized non-negative inversion of combined real and imaginary magnetic responses

Ekstrakcja hydrodynamiczna wielkości rdzenia nanocząstek magnetycznych przy użyciu nieregularnej i nieujemnej inwersji połączonych rzeczywistych i urojonych odpowiedzi magnetycznych

***Abstract**. Accurate reconstruction of the hydrodynamic size distribution of magnetic nanoparticles (MNPs) is often hindered by assumptions about distribution shape and the neglect of imaginary components in magnetic response analysis. In this work, we propose a non-regularized, non-negative inversion method that incorporates both real and imaginary components of the magnetic response to improve size distribution reconstruction. The avoidance of regularization mitigates the risk of excessive smoothing, preserving fine distribution details, while the non-negative constraint ensures physically meaningful solutions. The method is validated using complex AC magnetic responses of three commercial MNP samples, including both multi-core and single-core types, with hydrodynamic diameters ranging from 38 nm to 130 nm. Measurements were conducted over a frequency range of 5 to 100 kHz. The reconstructed hydrodynamic sizes are compared with dynamic light scattering (DLS) measurements, a standard technique for size analysis, to assess the accuracy of the proposed approach. Our results demonstrate strong agreement with the DLS measurements, with a maximum deviation of 13.6%. Additionally, the AC magnetic response predicted from the reconstructed size distribution closely aligns with the measured data, underscoring the robustness and reliability of the method.*

***Streszczenie.** Dokładna rekonstrukcja hydrodynamicznego rozkładu wielkości nanocząstek magnetycznych (MNP) jest często utrudniona przez założenia dotyczące kształtu rozkładu i zaniedbanie składników urojonych w analizie odpowiedzi magnetycznej. W tej pracy proponujemy nieuregulowaną, nieujemną metodę inwersji, która uwzględnia zarówno rzeczywiste, jak i urojone składniki odpowiedzi magnetycznej, aby poprawić rekonstrukcję rozkładu wielkości. Unikanie regularyzacji zmniejsza ryzyko nadmiernego wygładzania, zachowując drobne szczegóły rozkładu, podczas gdy ograniczenie nieujemne zapewnia fizycznie znaczące rozwiązania. Metodę zweryfikowano na podstawie złożonych odpowiedzi magnetycznych prądu przemiennego trzech dostępnych na rynku próbek MNP, zarówno wielordzeniowych, jak i jednordzeniowych, o średnicach hydrodynamicznych w zakresie od 38 nm do 130 nm. Pomiary przeprowadzono w zakresie częstotliwości od 5 do 100 kHz. Zrekonstruowane rozmiary hydrodynamiczne porównuje się z pomiarami dynamicznego rozpraszania światła (DLS), standardową techniką analizy wielkości, aby ocenić dokładność proponowanego podejścia. Nasze wyniki wykazują silną zgodność z pomiarami DLS, z maksymalnym odchyleniem wynoszącym 13,6%. Ponadto odpowiedź magnetyczna prądu przemiennego przewidywana na podstawie zrekonstruowanego rozkładu wielkości jest ściśle zgodna z danymi zmierzonymi, co podkreśla solidność i niezawodność metody.*

Keywords: hydrodynamic core, complex magnetic response, non-negative inversion, magnetic nanoparticles
Słowa kluczowe: rdzeń hydrodynamiczny, złożona odpowiedź magnetyczna, nieujemna inwersja, nanocząstki magnetyczne

Introduction

Magnetic nanoparticles (MNPs) exhibit unique properties that have driven extensive research into their applications in biomedical fields such as magnetic particle imaging (MPI) [1], magnetic immunoassays [2], and magnetic hyperthermia [3]. These applications leverage the magnetic response of MNPs to facilitate physical interactions at the nanoscale, enabling non-invasive tracking and manipulation. The performance of MNPs in these applications is heavily influenced by key parameters, including the effective magnetic moment and magnetic relaxation properties, such as hydrodynamic size D_H and magnetic anisotropy energy ratio. Optimal MNP properties vary depending on the target application; for instance, magnetic immunoassays benefit from particles with large magnetic moments and superior relaxation characteristics. As a result, precise characterization of MNPs is essential for tailoring their properties to achieve optimal performance in specific applications [4].

AC magnetic susceptibility techniques provide a rapid and direct means of probing the magnetic properties of MNPs, offering insights into both magnetic and physical parameters [5]. These techniques are particularly useful for analyzing hydrodynamic size when MNPs are suspended in solution and for estimating magnetic anisotropy energy constants when the particles are immobilized [6]. However, accurate determination of hydrodynamic size from AC magnetic responses requires an inversion method that does not rely on prior assumptions about the particle size distribution. Furthermore, accounting for both the real and imaginary components of the magnetic response is critical for obtaining accurate size distributions.

Traditionally, the peak of the imaginary magnetic response has been employed to estimate hydrodynamic size. For more comprehensive size distribution reconstructions, a lognormal distribution is often assumed [7], [8]. While this approach can yield reasonable estimates, it may overlook finer distribution details and lead to inaccuracies if the true distribution deviates from the assumed model. Additionally, regularization techniques are typically applied to prevent overfitting; however, excessive regularization can excessively smooth the distribution, masking important features and limiting the accuracy of size reconstruction.

In this work, we propose a non-regularized, non-negative inversion method that combines real and imaginary magnetic responses to reconstruct hydrodynamic size distributions without relying on prior assumptions about distribution shape. The absence of regularization preserves finer details in the size distribution, while the non-negative constraint ensures physically meaningful solutions by preventing negative values that could distort the results. The method utilizes a non-negative least squares (NNLS) approach, segmenting the size distribution into distinct domains and subdomains to enhance resolution and accuracy.

The proposed technique is validated using experimental data from three commercial MNP samples, including both single-core and multicore particles, with hydrodynamic diameters ranging from 38 nm to 130 nm. Measurements were conducted over a frequency range of 5 to 100 kHz using an AC magnetometer [9], [10]. The reconstructed size distributions are compared with results obtained from dynamic light scattering (DLS), a standard technique for size characterization, to evaluate the accuracy and reliability of the method. Our approach aims to offer greater flexibility and accuracy by circumventing assumptions about distribution shape, allowing for the reconstruction of complex and potentially multi-modal distributions.

AC magnetic response of magnetic nanoparticles

The complex AC susceptibility of magnetic nanoparticles (MNPs) is typically described by the standard Debye model [7]:

$$\frac{\chi}{\chi_0} = \frac{1}{1+i\omega\tau} = \frac{1}{1+\omega\tau} - i\frac{\omega\tau}{1+\omega\tau}, \tag{1}$$

where $\omega = 2\pi f$, χ_0 represents the static susceptibility, and τ is the relaxation time. For particles that predominantly relax through Brownian relaxation rather than Néel relaxation ($\tau_B << \tau_N$), and exhibit a normalized volume-weighted hydrodynamic diameter distribution $f_V(D_H)$, the AC susceptibility can be derived as [11][12]:

$$\frac{\chi}{\langle\chi_0\rangle} = \left(1-\Phi_{HF}\right)\int_{D_{H,\min}}^{D_{H,\max}} \frac{f_V\left(D_H\right)dD_H}{1+i\omega\left(D_H{}^3\eta/2k_BT\right)} + \Phi_{HF}, \tag{2}$$

where $D_{H,\min}$, and $D_{H,\max}$ denote the minimum and maximum hydrodynamic sizes determined by the measurement frequency range using the relation $\omega D_H{}^3\eta/2k_BT = 1$. Here, k_B is the Boltzmann constant, T is the absolute temperature, and η is the viscosity of the carrier liquid. $D_{H,\min}$ is defined by the highest measurement frequency, and Φ_{HF} accounts for the fast-relaxation contributions from particles smaller than $D_{H,\min}$ within the measurement window [13]. The constant Φ_{HF} can be estimated by the normalized real susceptibility at the highest measured frequency.

To address inadequacies in reconstructing the AC susceptibility response, this study applied a non-negative least squares (NNLS) method to minimize errors and reconstruct $f_V(D_H)$ from the AC susceptibility curve of suspended MNPs.

Non-regularized non-negative inversion with combined real and imaginary magnetic responses

Following the subtraction of high-frequency contributions Φ_{HF}, the normalized AC magnetic response from Brownian MNPs at angular frequency ω_q can be expressed as:

$$\begin{aligned} X_q(\omega_q) &= \sum_{p=1}^{N} \frac{F_p}{1+i\omega_q\left(D_p{}^3\eta/2k_BT\right)} \\ &= \sum_{p=1}^{N}\left(\frac{1}{1+\omega_q\left(D_p{}^3\eta/2k_BT\right)} - i\frac{\omega_q\left(D_p{}^3\eta/2k_BT\right)}{1+\omega_q\left(D_p{}^3\eta/2k_BT\right)}\right)F_p \\ &= \sum_{p=1}^{N}\left(B_{qp}^{real} - iB_{qp}^{imag}\right)F_p \end{aligned}, \tag{3}$$

where B_{qp} is the complex Brownian coefficient of MNPs with hydrodynamic diameter D_H and F_p is the distribution weight. Direct computation of B_{qp} and solving for F_p can be computationally demanding. Conventionally, the imaginary component alone is used for F_p reconstruction to simplify the problem. However, in this work, we propose a novel approach that combines both real and imaginary components to improve accuracy and reduce computational burden.

By concatenating the real and imaginary AC magnetic responses into a single vector, the combined response can be represented as:

$$\mathbf{X}^* = \begin{bmatrix}\mathrm{Re}(\mathbf{X})\\ \mathrm{Im}(\mathbf{X})\end{bmatrix} = \begin{bmatrix}\mathrm{Re}(\mathbf{B})\mathbf{F}\\ \mathrm{Im}(\mathbf{B})\mathbf{F}\end{bmatrix} = \mathbf{B}^*\mathbf{F}^*. \tag{4}$$

This transformation effectively doubles the vector length from N to $2N$. The hydrodynamic size distribution FFF is obtained by minimizing the deviation $\xi^2 = \| \mathbf{X}^*_{\exp} - \mathbf{B}^*\mathbf{F}^* \|^2$ where $\mathbf{X}^*_{\exp}$ is the measured AC magnetic response. To ensure a non-biased reconstruction, a non-regularized non-negative inversion technique is applied [14]. It should be noted that similar components of **F** are repeated in **F*** from the N+1 to 2N elements so that the final **F** distribution can be obtained from 0 to N elements.

The hydrodynamic diameter D_H is segmented into k domains, each containing s subdomains. For each domain, one element is selected, forming a list of D elements. Their corresponding coefficients F are solved using the NNLS method [15]. This process is repeated s times to cover all elements, resulting in s solutions for **F**. The final distribution is obtained by combining all solutions and dividing their **F** intensity by s. Figure 1 illustrates the separation of hydrodynamic diameters into k domains and s subdomains.

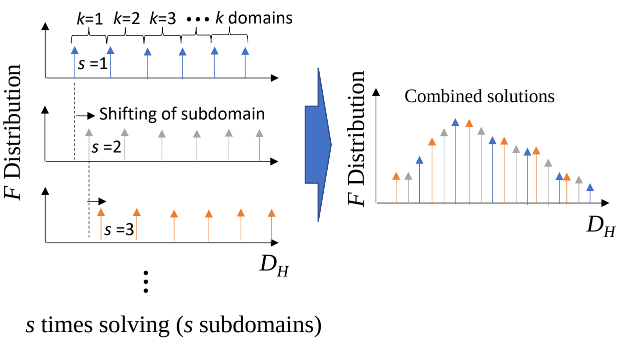

Fig. 1. Schematic representation of the hydrodynamic diameter D_H segmented into k domains and s subdomains.

One of the most widely used approaches is the assumption of a lognormal distribution, where the size distribution $f_V(D_H)$ is modeled as a lognormal function, and the parameters are estimated by fitting the model to the imaginary component of the magnetic susceptibility. This approach has been successful in providing reasonable estimates for many systems. However, it relies heavily on the assumption that the distribution takes a lognormal shape, which may not always hold true, especially in systems with complex or multimodal distributions. As a result, fitting to a single lognormal function can lead to biased or oversimplified reconstructions, missing finer details in the true size distribution. Another conventional method involves using only the imaginary component of the AC magnetic response, where the peak of the imaginary susceptibility is typically linked to the hydrodynamic size of the particles. While this approach is simpler and computationally less intensive, it often neglects the contributions from the real part of the magnetic susceptibility, which can lead to less accurate or incomplete reconstructions of the size distribution, especially for nanoparticles with more complex magnetic responses.

In contrast, our proposed method does not assume any specific shape for the size distribution, providing greater flexibility and accuracy. By combining both the real and imaginary parts of the magnetic response, the proposed technique incorporates more information from the data, which allows for a more precise reconstruction of the hydrodynamic size distribution. Furthermore, the non-regularized inversion avoids the smoothing effects that can distort the true distribution, providing a more accurate reflection of the underlying particle sizes. This approach represents a significant advancement over traditional methods by offering more detailed and robust results, especially in cases where the particle size distribution is not well-described by a lognormal function.

Experimental setup and sample preparation

In this study, the magnetic properties of multi-core and single-core MNPs were investigated. The samples included D130 (Micromod Partikeltechnologie GmbH), Resovist (FUJIFILM RI Pharma), and SHP30 (Ocean Nanotech). The hydrodynamic size distribution was analyzed using the dynamic light scattering (DLS) method with a Litesizer 500 particle analyzer (Anton Paar GmbH, Austria). Measurements were conducted in a low-field region (<0.5 mT) over a frequency range of 5 to 100 kHz. A sample volume of 1 mL was used for each measurement. Further details of the AC susceptibility measurement setup can be found in [9].

Table 1. The parameters of the MNP samples

Sample (type)	Fe concentration (mg/mL)	D_H, from DLS, Polydispersity index	$\langle D_H \rangle$ from AC susceptibility
D130	2.75	174.0 nm, 0.14	173.6 nm (0.2% deviation)
Resovist	0.26	61.0 nm, 0.17	69.3 nm (13.6% deviation)
SHP30	0.48	71.0 nm, 0.16	80.0 nm (12.7% deviation)

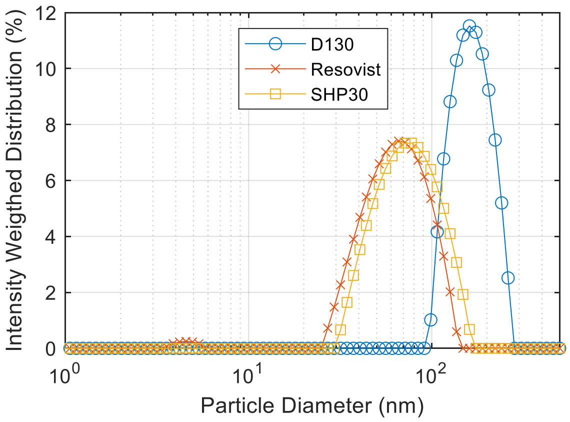

Fig. 2. Hydrodynamic sizes of MNP samples determined using the dynamic light scattering (DLS) method.

Results and discussion:

AC magnetic response and reconstruction of hydrodynamic size distribution

The hydrodynamic size distributions obtained using the DLS method are presented in Figure 2, with corresponding mean sizes and polydispersity indices (PDI) listed in Table 1. Although the PDI for all samples was below 0.2, the D130 sample exhibited the largest D_H compared to the other samples. This hydrodynamic size, determined by DLS, serves as a comparative baseline for sizes derived from Brownian relaxation under an alternating excitation field.

The measured real and imaginary AC magnetic responses of D130, Resovist, and SHP30 samples are illustrated by open markers in Figures 3, 4, and 5, respectively. Across all samples, the real part of the magnetic response decreases with increasing frequency, while the imaginary part demonstrates a characteristic peak. The frequency at which this peak occurs is often utilized to estimate the Brownian relaxation time, which can be further employed to derive the hydrodynamic size, assuming spherical particle shapes and known solution viscosity. However, due to the finite size distribution of the particles, Brownian relaxation frequencies also manifest as a distribution rather than a single peak.

By applying the proposed non-regularized inversion method, the hydrodynamic size distributions of each sample were reconstructed, as shown in Figure 6. For this analysis, the viscosity of water η=0.87 mPa·s at 26 °C was used. The hydrodynamic size D_H distribution was divided into 10 domains and 12 subdomains, with 60 D_H elements per decade on a logarithmic scale.

The reconstructed AC magnetic responses derived from the size distributions are superimposed as solid lines in Figures 3, 4, and 5, demonstrating the accuracy of the inversion process. The average hydrodynamic sizes $\langle D_H \rangle$ extracted from Figure 6 are summarized in Table 1.

The average hydrodynamic sizes calculated using the proposed inversion method show strong agreement with those obtained from DLS measurements. The D130 sample displayed a minimal deviation of 0.2%**,** while the Resovist and SHP30 samples exhibited deviations of 13.6% and 12.7%, respectively. The observed differences and broader distributions in Figure 6 as compared with in Figure 2 suggest the presence of non-negligible particle aggregation, potentially induced by the applied AC magnetic field. To further evaluate the accuracy of the proposed inversion method, the residual sum of squares between the reconstructed and measured magnetic responses was computed. As shown in Figure 7, the residual values remain relatively small across all samples, indicating high fidelity in reconstructing the complex magnetic response.

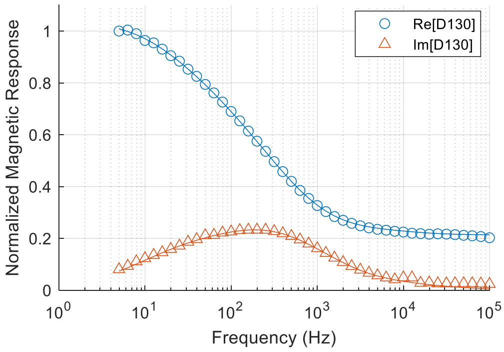

Fig. 3. Normalized real and imaginary magnetic response of the D130 sample. The solid lines show the reconstructed response from the hydrodynamic size distribution.

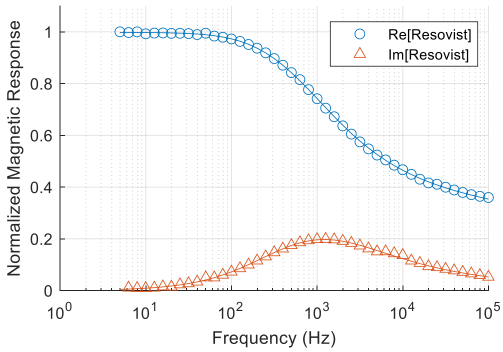

Fig. 4. Normalized real and imaginary magnetic response of the Resovist sample. The solid lines show the reconstructed response from the hydrodynamic size distribution.

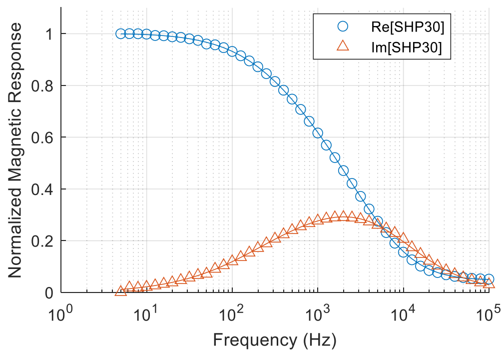

Fig. 5. Normalized real and imaginary magnetic response of the SHP30 sample. The solid lines show the reconstructed response from the hydrodynamic size distribution.

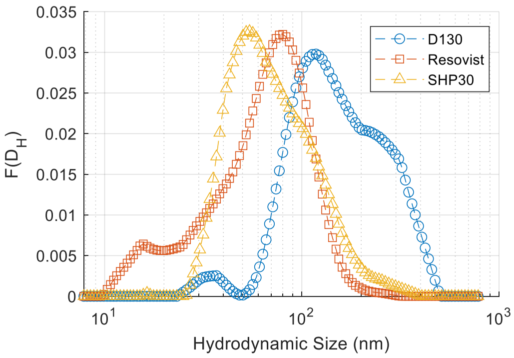

Fig. 6. Hydrodynamic size distributions of the D130, Resovist, and SHP30 samples.

Conclusions

In this work, the non-regularized inversion method to reconstruct the hydrodynamic core size of MNPs is presented. The proposed technique which utilized the non-negative least square technique, domains and subdomains division, and the combined real and imaginary magnetic responses showed that the hydrodynamic size of the commercial MNPs could be accurately reconstructed. The good agreement of the hydrodynamic size with the DLS method and the reconstructed AC magnetic response with the original data reflected the potential of the proposed technique with the benefit of the non-prior knowledge of the shape distribution.

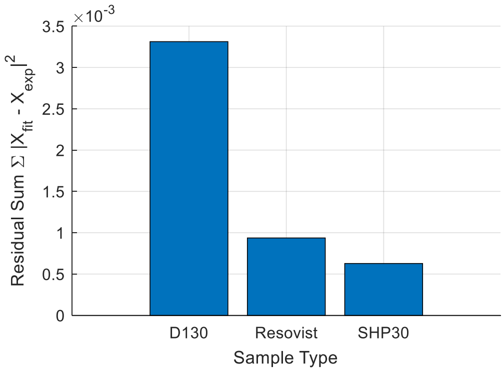

Fig. 7. Residual sum of the reconstructed AC magnetic responses for the D130, Resovist, and SHP30 samples.

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