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Estimation of hydrodynamic size distribution of magnetic nanoparticles based on AC magnetization harmonics for magnetic immunoassay

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Abstract

Magnetic nanoparticles (MNPs) have been widely studied for use in biomedical applications such as magnetic immunoassay. The hydrodynamic size distribution is an important physical characteristic for estimating the binding behavior in magnetic immunoassay. In this study, we proposed a method to estimate the hydrodynamic size distribution of MNPs based on the AC magnetization harmonics. The matrix equation of hydrodynamic size distribution was constructed based on the Fokker-Planck equation dominated by Brownian relaxation, and inversed by a Tikhonov regularization least squares algorithm. The simulation results show that the proposed method can accurately estimate the hydrodynamic size distribution, which is expected to be useful for biosensor applications.

I. Introduction

Magnetic nanoparticles (MNPs) provide some unique advantages for use as readout labels in biological assays [1]. For example, magnetic immunoassay using biofunctionalized MNPs has been studied extensively for medical diagnosis to detect biological targets. With bound biomolecules onto the surface of MNPs, the effective hydrodynamic size of the MNPs enlarges. Therefore, we can estimate the binding behavior between biomolecules and MNPs if the hydrodynamic size distribution can be obtained. At present, dynamic light scattering (DLS) is an effective method to estimate the hydrodynamic size distribution of marker. However, the DLS based on optical principle is easily affected by external interferants, such as multiple scattering of colored samples and samples with large particles may lead to larger errors [2]. Magnetic immunoassay based on MNPs is to analyze markers by detecting the magnetization signals, which can avoid this problem of optical approaches.

In this study, we proposed a method for estimating the hydrodynamic size distribution of MNPs based on magnetization harmonics under an AC excitation magnetic field. The simulation results show that the proposed method can accurately estimate the hydrodynamic size distribution, which is expected to be useful for magnetic immunoassay.

II. Model

We assume that the magnetic nanoparticles have an ideal single core size, and the relaxation mechanisms are dominated by Brownian relaxation. The ensemble magnetization M can be described as follows [3]:

$$M(t) = M_s \int_{d_{h,\ min}}^{d_{h,\ max}} n(d_h) V_{dc} M_{FP}(d_h, d_c, H_{ac})\, d d_h, \tag{1}$$

where M_s is the saturation magnetization, $n(d_h)$ is the number of MNPs with hydrodynamic size d_h, V_{dc} is the volume of MNPs with core diameter d_c, $H_{ac} = H_0 sin(\omega t)$ is the excitation field, H_0 is the amplitude of excitation field, $\omega = 2\pi f t$ is the angular frequency, M_{FP} is the magnetization described by Fokker-Planck equation with Brownian relaxation dominated.

To obtain a numerical solution of the integral in Equation (1), d_h is given by discrete values and $M(t)$ can be rewritten as:

$$M(t) = M_s \sum_{i=1}^{N} n(d_{h,i}) V_{dc} M_{FP}(d_{h,i}, d_c) \Delta d_h, \tag{2}$$

where $\Delta d_h = (d_{h,\ max} - d_{h,\ min})/(N-1)$, and N denotes the number of sampling points used for the hydrodynamic size.

Fourier series expansion of Equation (2) allows $M(t)$ to be expressed as:

$$M(t) = \sum_{k=-\infty}^{\infty} (a_{2k-1} - i b_{2k-1}) e^{i(2k-1)\omega t}, \tag{3}$$

$$M_{FP}(d_{h,i}, d_c) = \sum_{k=-\infty}^{\infty} (c_{2k-1} - i d_{2k-1}) e^{i(2k-1)\omega t}, \tag{4}$$

where $A_{2k-1} = \frac{1}{2}\sqrt{c_{2k-1}^2 + d_{2k-1}^2}$ and $B_{2k-1} = \frac{1}{2}\sqrt{a_{2k-1}^2 + b_{2k-1}^2}$ are the $(2k$-1)-th harmonic amplitudes of magnetization with hydrodynamic size d_h and ensemble magnetization M, respectively. Here, the relationship between A_{2k-1} and B_{2k-1} can be expressed as follows:

$$B_{2k-1}(\omega) = M_s \sum_{i=1}^{N} n(d_{h,i}) V_{dc} A_{2k-1}(\omega, d_{h,i}) \Delta d_h. \tag{5}$$

As shown in Equation (5), the contribution of the magnetic nanoparticle with hydrodynamic size d_h to the harmonics' amplitude is given by the factor $n(d_{h,i})$. The matrix equation can be obtained as follows:

$$\mathbf{B} = \mathbf{A} \cdot \mathbf{X}, \tag{6}$$

$$\mathbf{B} = \begin{pmatrix} B_{2k-1}(\omega_1) & \cdots & B_{2k-1}(\omega_S) \end{pmatrix}^{\mathbf{T}}, \tag{7}$$

$$\mathbf{X} = \begin{pmatrix} n(d_{h,1}) V_{dc} \Delta d_h & \cdots & n(d_{h,N}) V_{dc} \Delta d_h \end{pmatrix}^{\mathbf{T}}, \tag{8}$$

$$\mathbf{A} = \begin{pmatrix} A_{2k-1}(d_{h,1}, \omega_1) & \cdots & A_{2k-1}(d_{h,N}, \omega_1) \\ \vdots & \ddots & \vdots \\ A_{2k-1}(d_{h,1}, \omega_S) & \cdots & A_{2k-1}(d_{h,N}, \omega_S) \end{pmatrix}. \tag{9}$$

The $S \times 1$ vector $\boldsymbol{B}$ is magnetization harmonics of ensemble MNPs. The $S \times N$ matrix $\boldsymbol{A}$ is the coefficient matrix of the magnetization harmonics of hydrodynamic d_h calculated with Fokker-Planck Equation dominated by Brownian relaxation [4]. The $N \times 1$ vector $\boldsymbol{X}$ is the hydrodynamic size distribution calculated by a Tikhonov regularization least squares algorithm [5].

III. Simulation and results

We performed simulations to verify the feasibility of estimating the hydrodynamic size distribution of MNPs through harmonics amplitudes. We assume that $n(d_{h,i})$ obeys log-normal distribution for the hydrodynamic size given by:

$$n(d_h) = \frac{1}{\sigma d_h \sqrt{2\pi}} e^{-\frac{(\ln d_h - \ln \mu)^2}{2\sigma^2}}, \tag{10}$$

where μ and σ are the mean and standard deviation, respectively.

In the simulations, the core diameter of MNPs was fixed at 30 nm, the hydrodynamic size d_h range over 10 - 150 nm with a step size 5 nm, and the saturation magnetization was 400 kA/m. The AC excitation field had a frequency from 1 to 10 kHz with a step of 1 kHz and an amplitude of 1 mT. The Brownian relaxation time was calculated by $\tau_B = \pi \eta {d_h}^3 / 2 k_B T$, where viscosity η is 0.947 mPas, the Boltzmann constant k_B is 1.38×10^{-23} J/K, the temperature T is 297 K.

The amplitudes of the harmonics of the ensemble magnetization and MNPs with hydrodynamic size d_h can be obtained based on the Fokker-Planck equation dominated by Brownian relaxation. The hydrodynamic size distribution was inversed by a Tikhonov regularization least squares algorithm based on the Equation (6) at a signal-to-noise ratio of 60 dB. Fig. 1 illustrates the estimated hydrodynamic size distribution, the solid line indicates the original distribution and symbol indicates the estimated distribution estimated with harmonic amplitudes. The mean μ and standard σ deviation of estimated hydrodynamic distribution is 90.31 and 0.14, respectively, very closed to the true values. The largest error is at the peak of distribution, which the relative error is less than 7 %. There is excellent agreement between the estimated distributions and the original ones. Moreover, we used the estimated hydrodynamic distribution to reconstruct the magnetization harmonics. As shown in Fig. 2a-d, the 1^{st}, 3^{rd}, 5^{th}, and 7^{th} harmonics reconstructed by estimated hydrodynamic distribution agree well with that of the original magnetization harmonics.

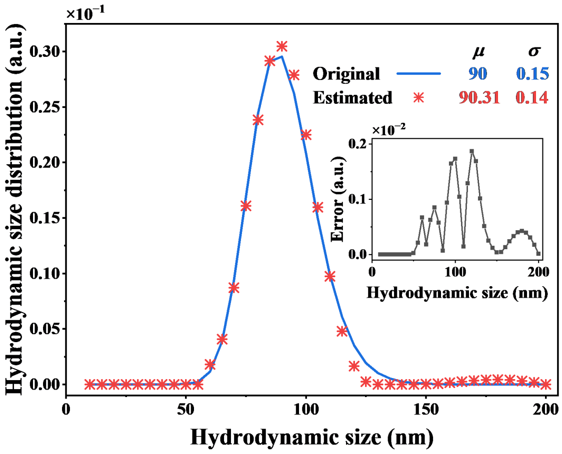

Figure 1: The estimated hydrodynamic size distributions using 1^{st}, 3^{rd}, and 5^{th} harmonics of MNPs magnetization. The illustration is the error between the original and reconstructed distribution.

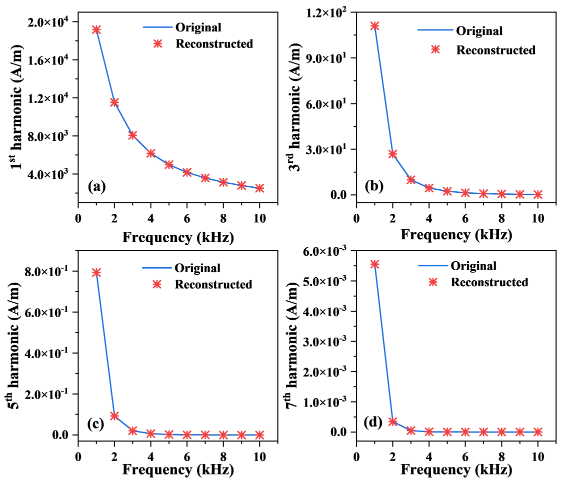

Figure 2: Reconstructed results of the (a) 1^{st}, (b) 3^{rd}, (c) 5^{th}, and (d) 7^{th} harmonics of MNPs magnetization.

IV. Conclusions

In this study, we reported a method for estimating the hydrodynamic size distribution of single core MNPs based on AC magnetization harmonics dominated by Brownian relaxation. We constructed the mathematical model between the harmonic amplitudes of MNPs' magnetization and the hydrodynamic size distribution under AC excitation field when the Brownian relaxation dominates. The estimated results and reconstructed harmonics show that the proposed method can accurately obtain the hydrodynamic size distribution. It is expected to apply to biologicals immunoassay.

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Author's statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study.

References

[1] L. F. Huergo, K. A. Selim, M. S. Conzentino, et al. *Magnetic bead-based immunoassay allows rapid, inexpensive, and quantitative detection of human SARS-CoV-2 antibodies*, ACS sensors, vol. 6(3), pp. 703-708, Jan. 2021.

[2] C. Li, J. Ma, Q. Fan, et al. *Dynamic light scattering (DLS)-based immunoassay for ultra-sensitive detection of tumor marker protein[J]. Chemical Communications*, 52(50), pp. 7850-7853, May. 2016.

[3] H. Remmer, J. Dieckhoff, M. Schilling, et al. *Suitability of magnetic single-and multi-core nanoparticles to detect protein binding with dynamic magnetic measurement techniques*. Journal of Magnetism and Magnetic Materials, vol. 380, pp. 236-240, Oct. 2014.

[4] J. L. Déjardin, Y. P. Kalmykov. *Nonlinear dielectric relaxation of polar molecules in a strong ac electric field: Steady state response*, Physical Review E, vol. 61(2), pp. 1211, Feb. 2000.

[5] P. Bender, C. Balceris, F. Ludwig, et al. *Distribution functions of magnetic nanoparticles determined by a numerical inversion method*. New Journal of Physics, vol. 19(7), pp. 073012, Jul. 2017.

