

Size Characterization of Magnetic Nanoparticles Based on Magnetic Particle Spectroscopy for Bio-Analytical Applications

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論 文 名 : Size Characterization of Magnetic Nanoparticles Based on Magnetic Particle Spectroscopy for Bio-Analytical Applications
(磁性粒子分光法による磁性ナノ粒子の粒径評価とバイオ分析応用)

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論 文 内 容 の 要 旨

Magnetic nanoparticles (MNPs) exhibit unique physicochemical characteristics owing to their comparable dimensions with important biological substances, high surface-to-volume ratios, size-dependent magnetic properties, magnetocaloric effect, and temperature sensitivity. In recent years, MNPs have become increasingly important in biosensor technology and biomedical applications, such as carriers for targeted drug delivery, nano-tracers for magnetic particle imaging (MPI), nano-markers for magnetic immunoassays, and nano-heaters for cancer hyperthermia. The size distribution, including core size and hydrodynamic size, is an essential physical characteristic of MNPs because it seriously affects biomedical and biological applications. A fast and accurate method for estimating size distributions is needed to optimize MNP applications. Notably, conventional size characterization methods cannot simultaneously obtain the core diameter and hydrodynamic particle size distribution of MNPs.

The purpose of the present study is to develop a high-precision, high-stability magnetic particle spectroscopy (MPS) system to measure the dynamic magnetization response of MNPs, and establish a method for simultaneous characterization of the core size and hydrodynamic size distributions of MNPs through the harmonics of dynamic magnetization. Based on the method for simultaneous characterization of the core size and hydrodynamic size distributions, an analysis framework for bio-analytical applications is proposed.

Chapter 1 introduced the background of the present study.

Chapter 2 reviewed the theoretical models of steady-state and dynamic magnetization responses of MNPs under the DC and AC excitation fields, analyzing and comparing the advantages and disadvantages of different models.

Chapter 3 presents the design, construction, and testing of a high-precision, high-stability MPS system. This MPS system is specifically developed to detect low concentrations of MNPs and to measure their dynamic magnetization responses under alternating magnetic fields. The developed MPS primarily comprises an excitation generation device, a weak magnetic detection device, and a signal acquisition device. A balanced structure of the detection coils is introduced to eliminate feedthrough interference from the excitation magnetic field and the influence of diamagnetic substances (e.g., water) in liquid samples. Helmholtz coil structure is used as detection coils to improve volume consistency during sample detection. Additionally, by connecting different capacitance groups in series, this system can generate excitation magnetic fields with frequencies ranging from 0.1 kHz to 20 kHz and a maximum strength of 20 mT, with a

detection limit of 1 ng Fe for MNP samples.

In Chapter 4, an improved methods for independent estimation of core size distribution and hydrodynamic size distribution of MNPs were presented. The first, third, and fifth magnetization harmonics under different excitation field strengths were used to estimate the core size distribution, rather than using all the available magnetization harmonics at a single excitation magnetic field. The core size distributions can be obtained without assuming any distribution function. The harmonic amplitudes of the MNP magnetization reconstructed from the estimated distribution agree well with experimental results. Using this method, the distributions of large core sizes can be more accurately and quickly estimated than by the static $M-H$ curve method. For the hydrodynamic size distribution, a mathematical model between the harmonic amplitudes of MNPs magnetization and the hydrodynamic size distribution under the AC excitation field was constructed for MNPs dominated by Brownian relaxation. The estimated results and reconstructed harmonics show that the proposed method can accurately obtain the hydrodynamic size distribution.

In Chapter 5, a method for simultaneous estimation of the magnetic moment and Brownian relaxation time distributions of MNPs using AC magnetization harmonics was proposed. The estimated results agreed well with the core size distribution reconstructed from $M-H$ curves and the hydrodynamic size distribution measured by DLS. Under the conditions of low-frequency and small excitation magnetic fields, the magnetization response of MNPs primarily originates from the larger particles and the macroscopic relaxation mechanism is dominated by those particles. Based on the estimated distribution results of magnetic moment and Brownian relaxation, the effective relaxation time of the entire MNP sample can be obtained, and the relationship between the core size and hydrodynamic size can be analyzed.

In Chapter 6, a method to specifically functionalize the surface of MNPs for the target analyte Anti-IgG was developed and its direct detection in solution using an MPS system was successfully demonstrated. The proposed wash-free detection method is user-friendly, requires minimal training, and enables rapid testing by non-specialists. The upper and lower detection limits of functionalized MNPs were also systematically investigated. The detection mechanism is based on the change in Brownian relaxation time, where the binding of target molecules increases the relaxation time, leading to a reduction in harmonic amplitude. The custom-built MPS system achieves a detection sensitivity for iron content as low as 1 ng, and experimental results demonstrated a detection limit for Anti-IgG of 25.5 ng (approximately 0.17 pmole).

Chapter 7 is a summary of the present thesis, and proposes some possible future works based on this study.