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Magnetic manipulation and optical monitoring of magnetic nanoparticles in solution

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Abstract*— Magnetic nanoparticles (MNPs) have been extensively studied as functional materials in the field of biotechnology and medicine, and have been applied to magnetic immunoassays, drug delivery, hyperthermia, magnetic particle imaging, and so on. It has been assumed that manipulation of MNPs by an external magnetic field is directly applied to the control of aggregation and dispersion in solution. In this study, a device that can manipulate and monitor MNPs in solution was developed using magnets and laser sensors. Using this device, the dynamic behavior of MNPs under the external magnetic field was evaluated. As a result, the movement by the magnetic manipulation depended on the magnetic field gradient difference achieved by the magnet arrangement. In addition, it depended on the magnetization and dispersibility, relative magnetic nanoparticle size, and overall size of MNPs.

***Index Terms*—laser, magnetic nanoparticles, manipulation, monitoring.**

I. BACKGROUND

Magnetic nanoparticles (MNPs) are magnetic particles, a few nanometers in size with super paramagnetism, and have been widely studied as functional materials in the field of biotechnology and medicine. Recently, MNPs have been investigated not only as markers for magnetic measurements [1], [2], such as magnetic immunoassays (MIAs) [3]–[6] but also as therapy carrier agents to the target location using magnetism [7]. They can be manipulated by an external magnetic field, which has direct applications to the control of aggregation and dispersion in solution, including hyperthermia, and magnetic particle imaging [8], [9]. In this study, a device that can magnetically manipulate and monitor MNPs was developed using the magnets and laser sensors to evaluate the dynamic behavior of magnetic nanoparticles in the solution.

II. METHODS

The system namely consists of a transmission-type laser sensor (IB-10, KEYENCE Corp.) for sample detection, an optical cell, neodymium magnets, an x-axis stage, and a reflection-type laser sensor for position detection. The transparency in the central part of the fixed optical cell (13 × 4 × 45 mm^3) with a 300 µL MNP solution was monitored by the transmission-type laser sensor while the magnets which were mounted on an x-axis stage were periodically moved in the left and right direction (Fig. 1).

The laser (with a wavelength of λ~660 nm) was used to locally irradiate an area of 3 × 8 mm^2 through a slit. The sensor output was acquired using DAQ device (National Instruments) and the sampling frequency was 100 Hz. The flux density on the surface of the magnet (15 × 10 × 10 mm^3) was approximately 470 mT. The MNPs (Micromod nanomag®-D-spio), which were iron oxide particles coated with dextran, were used in a concentration of 25 mg/mL. The behavior of the MNPs in a solution was investigated with various magnetic field gradients by changing the polarity of the magnet. Additionally, the particle diameter dependence from the MNP movement in a solution was investigated by changing stage speed.

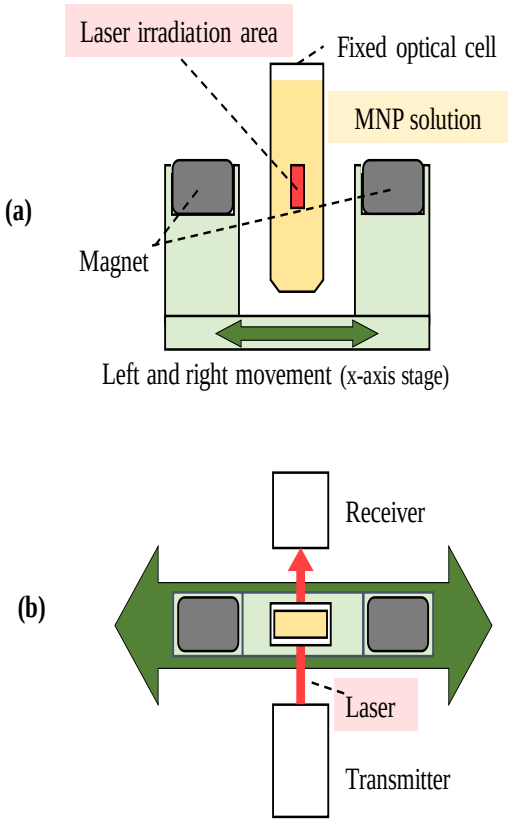

Fig. 1. System configuration:
(a) Front view, and (b) Top view.

III. RESULTS AND DISCUSSION

First, MNPs with 20-nm average particle diameter were

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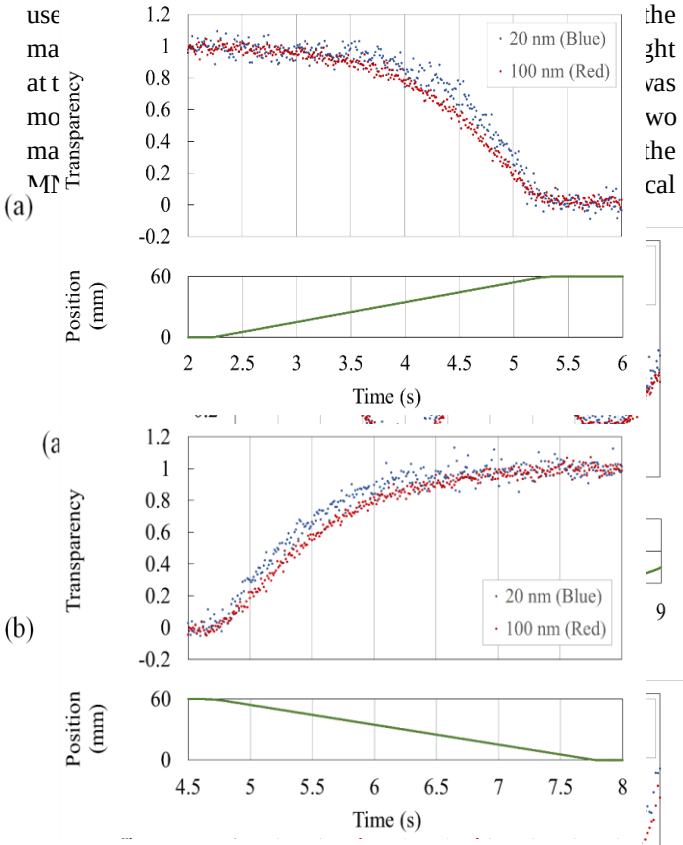

Fig. 3. Comparison of position dependence of transparency between 20 nm sample and 100 nm sample: (a) approaching and (b) departing

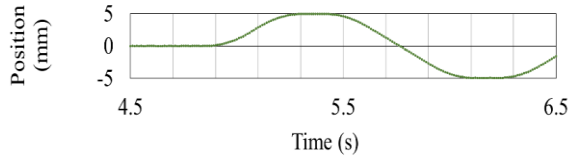

Fig. 2: Comparison of the particle diameter dependence of the movement of the MNPs: (a) stage speed 5 mm/s and (b) stage speed 20 mm/s.

transparency becomes higher and the output voltage of the photodiode will be larger.

In case that the two magnets were placed such that the same magnetic poles face each other, when one magnet approached to the cell, the magnetic field gradient of that approaching magnet was large. After that, as many MNPs were aggregated, the output voltage decreased (Fig. 2 (a)). On the other hand, when the cell was placed in the middle position between the two magnets, zero magnetic gradient existed to the center of the cell, and the output voltage was large. When two magnets were placed such that the opposite magnetic poles face each other, the magnetic field between the two magnets was almost uniform. As shown in Fig. 2 (b), when each magnet approached the cell, the signal change was very small, and the movement of the MNPs was not observed, compared with the case of repelling.

In another magnet arrangement, the magnet was placed on only one side. It was periodically moved 60 mm to the left and right at the speed of 5 mm/s, and the particle movement was monitored. Here, the position 60 mm away from the position where the magnet and the cell were at their closest to each other was set to 0 mm. In this case, the magnetic field becomes large when the magnet is close to the cell. Therefore, as shown in Fig. 2 (c), the output of laser sensor was large at the starting position where the magnet was away from the cell. On the other hand, the magnetic field gradient increased when the magnet was close to the cell, and then the MNPs were aggregated.

Next, the particle diameter dependence was investigated using two different diameters (20 nm and 100 nm) of the MNPs under the same conditions as repelling. Here, the transparencies of 20 nm and 100 nm samples were different. Therefore, the output in the bright state and the dark state was normalized and set to be 1 and 0, respectively. As shown in Fig. 3 (a), in both diameters, their behavior was similar to that obtained in Fig. 2 (a) and apparent difference was not observed. Therefore, the moving speed of stage was changed from 5 to 20 mm/s. However, as shown in Fig. 3 (b), the diameter difference was still not observed. It was considered to be due to the large magnetic gradient of repelling position. Therefore, the magnet was placed on only one side, the magnet approached the cell from a position 60 mm away from the cell at the speed of 20 mm/s, and the diameter dependence was monitored again. As shown in Fig. 4 (a), the transparency of 100 nm sample reached 0.5 about 0.2 s earlier compared with the 20 nm sample. It was due to the large magnetic force by the large magnetic moment of the 100 nm MNPs particles. On the other hand, the transparency of 20 nm sample reached 0.5 about 0.2 s earlier compared with the 100 nm sample in the case of receding motion of the magnet (Fig. 4 (b)). It was due to the rapid diffusion by the small diameter of 20 nm MNPs.

To consider the influence of magnet arrangement, magnetic field gradient difference of repelling, attracting direction of the magnets, and one magnet were simulated (Fig. 5). In the case where two magnets were placed such that the same magnetic poles face each other, the magnetic field lines were described to be released radially from each magnet and the magnetic field gradient around the middle region was large because the magnetic field bends. The magnetic flux density was large near each of the magnets, and the density was small in the middle between two magnets. On the other hand, in the case where two magnets were placed such that the opposite magnetic poles face each other, the magnetic field lines were described to go from one magnet to the other.

Therefore, the gradient was almost uniform. In the case of placing a magnet on one side, the magnetic field lines were described to be released radially from the magnet, and the closer to the magnet, the larger the magnetic flux density.

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IV. CONCLUSION

Magnetic manipulation of the MNPs in the solution was monitored by the laser sensor unit. Magnetic movement by the magnetic manipulation depended on the magnetic field gradient difference by the magnet arrangement. The repelling direction made the largest magnetic field gradient and can easily move the MNPs. In addition, large magnetization of the large size MNPs made large magnetic force. On the other hand, the diffusing force was large for the small size MNPs.

This paper is a basic report of magnetic manipulation and optical monitoring of MNPs in solution. The dynamic behavior of the MNPs conjugated with antibodies that connect with antigens, and the MNPs in serum under an external magnetic field will be investigated.

As future enhancements, to monitor the localized concentration distribution of agglomerated MNPs, the developed device will be improved by using an optical system.

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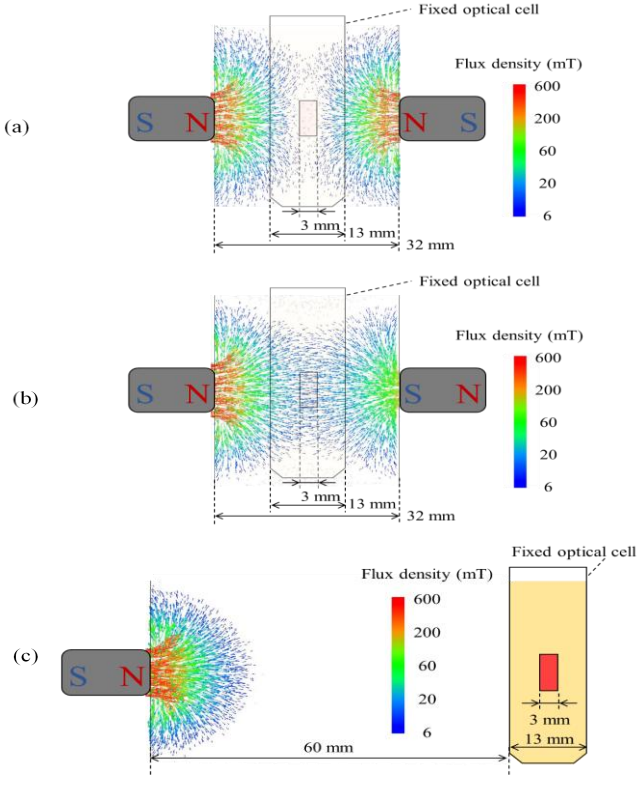

Fig. 4: Simulation of magnetic field lines: (a) repelling direction of the magnet, (b) attracting direction, and (c) one magnet

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