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Real-time Detection of Nano-sized Magnetic Beads by Using Spin-valve Devices for Biological Applications

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We report the real-time detection of nano-sized magnetic beads for biological applications using highly sensitive spin-valve devices with nano-oxide layer (NOL) exhibiting an 8.5% magnetoresistance (MR) ratio. A combination of photolithography and lift-off process was employed to place nano-sized magnetic beads on the active area of a spin-valve device. The spin-valve device was found to show a signal voltage change of 0.28 μV in the presence of a cluster of nano-sized magnetic beads by comparing the signal voltage difference between the sensing spin-valve device and a reference spin-valve device. The real-time detection of nano-sized magnetic beads was found successfully achieved by direct measurement of the magnetic dipole fields emanating from clusters of nano-sized magnetic beads on the spin-valve device.

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I. INTRODUCTION

The development of magnetoresistance (MR) devices based on the detection of micron or nano-sized magnetic labels has recently attracted great interests, because they are capable of realizing a bio-assay system showing fast response time, high sensitivity, high performance, and portability [1–8]. In particular, the detection of nano-sized magnetic labels is one of the key issues for implementing a bio-assay system using MR devices because micron-sized magnetic labels will hinder bimolecular interactions [9]. Furthermore, nano-sized magnetic beads can be controlled to conjugate with one or a few bimolecular, which will allow a quantitative relationship with enough accuracy to be established between the number of the detected magnetic labels and the actual target bimolecular. However, most magnetic labels used in previous studies were micron-sized magnetic beads because the magnetic moments of the nano-sized magnetic beads were too small due to their limited volume. In order to detect such a small magnetic moments in real-time, a sensor should have characteristics such as high sensitivity, good signal-to-noise ratio (S/N) and low detection limit [10].

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Spin-valve devices are able to offer sufficiently these characteristics compared with other spintronic devices, such as anisotropic magnetoresistance (AMR) devices [4], Hall effect devices [5,6], and magnetic tunneling junction (MTJ) devices [8]. For these reasons, spin-valve devices may be good candidates to detect nano-sized magnetic beads for real-time detection of the nano-sized magnetic beads. The real-time detection of the nano-sized magnetic beads is essential for the development of chip-cytometers, which has recently attracted great interests, since they are capable of realizing both cell separation and cell counting on a chip at the same time. However, to date, no one has attempted yet to apply spin-valve devices as sensing elements in the real-time detection of nano-sized magnetic beads.

In the present work, we report on real-time detection of nano-sized magnetic beads by using highly sensitive spin-valve devices for biological applications. We describe the design and fabrication of spin-valve devices and discuss the real-time detection of nano-sized magnetic beads by using spin-valve devices.

II. EXPERIMENT

Spin valves were deposited on thermally oxidized Si(100) substrates in a dc/rf magnetron sputtering system at a base pressure of 4×10^{-8} Torr. The

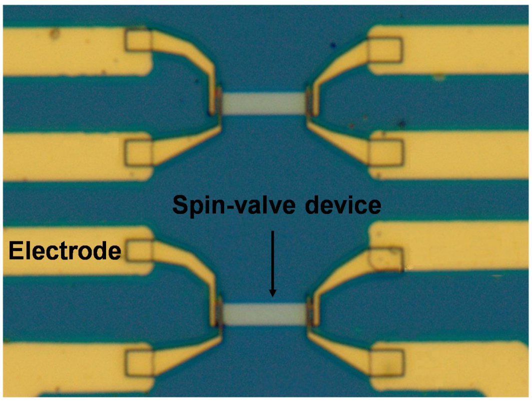

Fig. 1. Optical microscope image of an array of spin-valve devices with 6 × 30 μm^2. The spin-valve device consisted of a spin-valve strip and four electrodes fabricated by using a combination of electron beam lithography and lift-off process.

generic structure of the spin-valves was $Co_{84}Fe_{16}$ (20 Å)/NOL/$Ni_{81}Fe_{19}$ (25 Å)/$Co_{84}Fe_{16}$ (10 Å)/Cu (17 Å)/$Co_{84}Fe_{16}$ (20 Å)/$Ir_{22}Mn_{78}$ (75 Å)/Ta(50 Å). The nano-oxide layer (NOL) was employed in order to enhance the sensitivity of the spin valves [11]. As-deposited spin valves were found to exhibit about an 8.5% magnetoresistance (MR) ratio. An array of the spin-valve devices with dimension of 6 × 30 μm^2 were fabricated using a combination of electron-beam lithography and a lift-off process (see Fig. 1). The patterned spin-valve devices were measured to have an ∼8.5% MR as shown in Fig. 2, and were used to detect nano-sized magnetic beads. The surfaces of the spin-valve devices were passivated with a 200-nm-thick silicon dioxide layer deposited using a radio frequency (rf) sputtering system in order to prevent device corrosion due to deionized water.

III. RESULTS AND DISCUSSION

In order to place nano-sized magnetic beads on the active area of a spin-valve device among the spin-valve array, we adopted a photolithography and lift-off process. A conceptual drawing of this process is introduced in Fig. 3. A photoresist layer with a thickness of 1.1 μm was spin-coated on the surface of a spin-valve array. A window in the photoresist layer on the only one spin-valve device (sensing SV device) among the spin-valve array was patterned by using photolithography. After the dispersion of nano-sized magnetic beads on the photoresist layer, a cluster of nano-sized magnetic beads was found to be placed on the active area of sensing spin-valve device through the window as shown in Fig. 4(a). The remaining magnetic beads were placed on the photoresist layer, the magnetic dipole fields of which were too small to change the magnetic state of the other spin-valve devices with a photoresist layer (reference SV devices) because the maximum magnetic dipole fields (B^{max}) emanating from the magnetic beads decreased exponentially with increasing distance (z) between the reference SV devices and the center of the magnetic beads according to the equation of $B^{max} = -(\mu_0/4\pi)m_0/z^3$, where μ_0 and m_0 are the magnetic permeability and the magnetic moment of the magnetic beads, respectively [10].

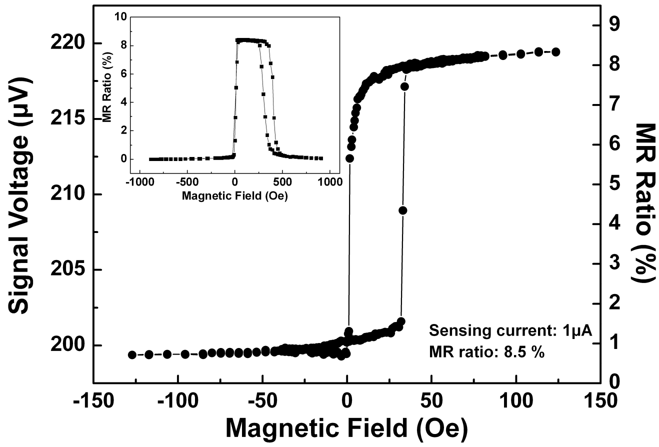

Fig. 2. Representative magnetoresistance (MR) curve of a spin-valve device. The spin-valve device was observed to exhibit about an 8.5% MR ratio. The inset shows the full MR curve. The best sensitivity in the MR of a spin-valve device was found to occur in the range of 25 – 50 Oe.

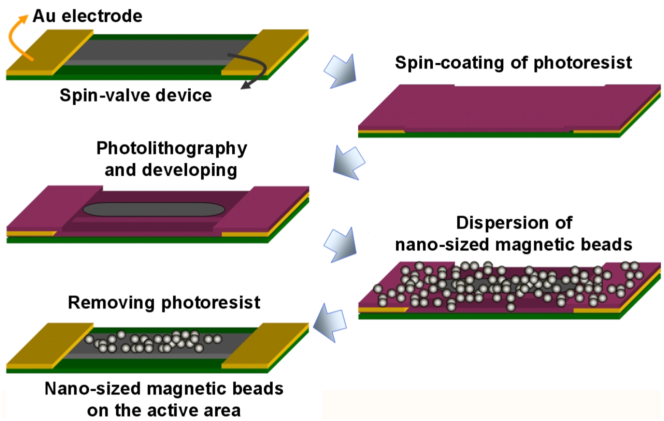

Fig. 3. A conceptual drawing of the process for patterning a window in the photoresist layer on the sensing spin-valve device.

In order to demonstrate the detection the nano-sized magnetic beads in real time, we dispersed a droplet containing superparamagnetic nano-sized magnetic beads on top of the spin-valve array while measuring the voltage of the sensing spin-valve device and reference spin-valve device, respectively. Superparamagnetic beads (Nanomag-D 250) with d = 250 nm and a susceptibility of 3.1 × 10^{-15} emu/Oe (10 < $|H|$ < 50 Oe) were utilized in this real-time detection. The most sensitive region in the MR curve of a spin-valve device was found to occur in the range of 25 – 50 Oe (see Fig. 2). A dc magnetic field of 30 Oe was applied in the longitudinal direction of the

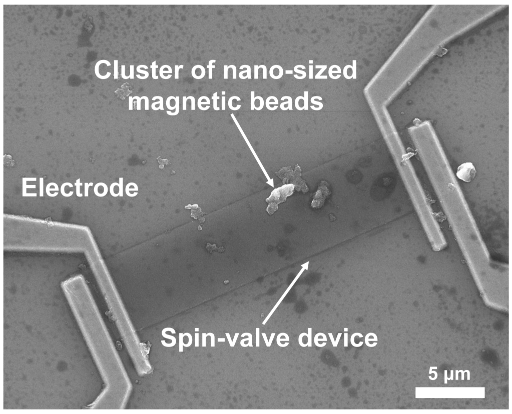

Fig. 4. A SEM image showing nano-sized magnetic beads on the active area of a sensing spin-valve device.

spin-valve devices in order to bias the free layer of the spin-valve devices and generate a magnetic dipole field of the nano-sized magnetic beads. At this applied magnetic field, the free layer of the spin-valve devices was not fully changed from parallel states to anti-parallel states, providing that the spin state of the free layer was reversible in the range of magnetic fields, which are external magnetic fields plus magnetic field emanating from the nano-sized magnetic beads

When nano-sized magnetic beads were placed on the active areas of the sensing spin-valve devices, the magnetic dipole field of the magnetic beads is expected to cancel out a small fraction of the applied field in the free layer of the spin-valve devices [12]. The reduction of the applied field in the free layer was found to result in a signal voltage drop. Fig. 5(a) presents the real-time voltage signals of the sensing spin-valve device and of the reference spin-valve device showing the detection of a cluster of nano-sized magnetic beads. As seen in Fig. 5(a), the signal voltage of the sensing spin-valve device was decreased when Nanomag-D 250 was added to the spin-valve array at a time of 110 sec., whereas the voltage signal of the reference spin-valve device was almost flat and had no substantial signal change This reveals that the photoresist layer on the reference spin-valve device was thick enough to keep the fringe field of the cluster of nano-sized magnetic beads from reducing the applied field in the free layer [13]. In Fig. 5(a), the slight perturbation of the signal voltage was caused by Joule heating created by the bias current. In order to compare clearly the signal change between the reference spin-valve device and the sensing spin-valve device caused by a cluster of nano-sized magnetic beads, the signal voltage difference between the sensing spin-valve device and reference spin-valve device was calculated. Fig. 5(b) present the signal voltage difference between the sensing spin-valve device and the reference spin-valve device.

A signal voltage change of 0.28 μV, caused by the cluster of nano-sized magnetic beads in Fig. 4(a), was clearly confirmed by $\Delta V = V_{reference} - V_{sensing}$, where

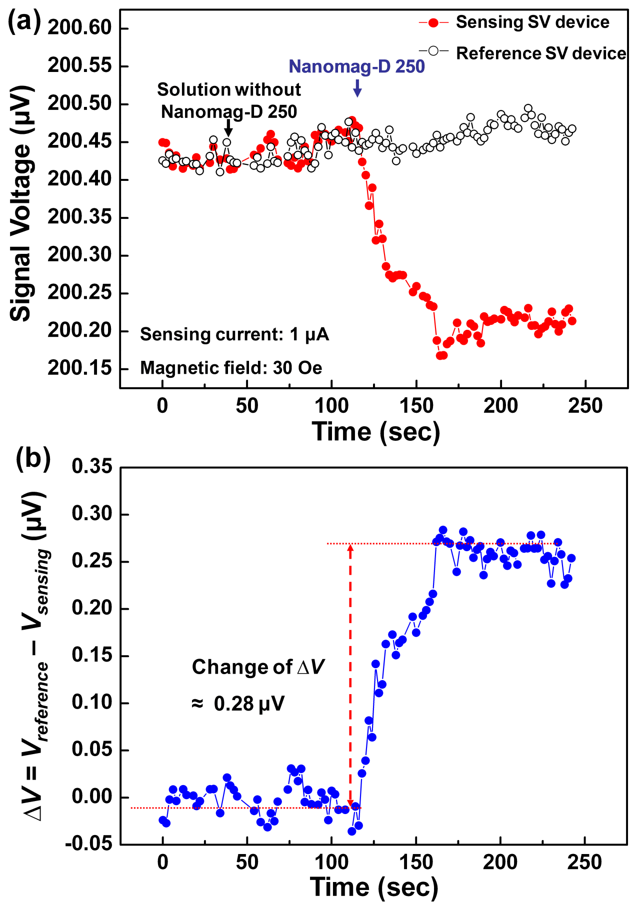

Fig. 5. Real-time signals of the sensing SV device and reference SV device showing the detection of a cluster of nano-sized magnetic beads. (a) The signal of the sensing SV device only decreased after dispersing Nanomag-D 250 superparamagnetic beads on the spin-valve array at 110 sec. (b) The signal voltage difference between the sensing SV device and the reference SV device.

$V_{reference}$ and $V_{sensing}$ are the signal voltages of the reference spin-valve device and of the sensing spin-valve device, respectively. A slow increase of ΔV after dispersing the magnetic beads occurred because the Nanomag-D 250 settled on the surface of the sensing spin-valve device after the solution had finished drying.

In addition, control experiments were carried out before adding nano-sized magnetic beads (Nanomag-D 250) on the spin-valve array in order to investigate the perturbation of the sensor signals caused by other parameter changes. In Fig. 5(a), the solution without beads was added at 40 sec in order to measure the perturbation of signal caused by adding the solution. As shown in Fig. 5(a), no significant signal change was observed in either the sensing spin-valve device or the reference spin-valve device after adding the solution without nano-sized magnetic beads. This result reveals that the signal voltage in Fig. 5(a) was only caused by adding nano-sized magnetic beads (Nanomag-D 250) on the spin-valve array.

Our results demonstrate that nano-sized magnetic beads can be detected using a highly sensitive spin-valve device in spite of their small magnetic moments.

IV. CONCLUSION

The highly sensitive spin-valve devices with a nano-oxide layer were designed and fabricated for the detection of nano-sized magnetic beads. The detection of the nano-sized magnetic beads by using an array of the spin-valve devices were demonstrated by comparing the signal voltage difference between a sensing spin-valve device and a reference spin-valve device. In the real-time measurements, the spin-valve device was found to show a signal voltage change of 0.28 μV in the presence of a cluster of nano-sized magnetic beads. Our results demonstrate the possibility of implementing a bio-assay system based on the detection of the nano-sized magnetic beads using the highly sensitive spin-valve devices. Further studies are planned to extend these results to integration of spin-valve sensors into microfluidic channel and quantitative real-time detection of moving nano magnetic particles in the fluidic channel for applications as a chip-cytometer

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