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Detection of single micron-sized magnetic bead and magnetic nanoparticles using spin valve sensors for biological applications

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We have fabricated a series of highly sensitive spin valve sensors on a micron scale that successfully detected the presence of a single superparamagnetic bead (Dynabeads M-280, 2.8 μm in diameter), and thus showed suitability for identifying biomolecules labeled by such magnetic beads. By polarizing the magnetic microbead on a spin valve sensor with a dc magnetic field and modulating its magnetization with an orthogonal ac magnetic field, we observed a magnetoresistance (MR) signal reduction caused by the magnetic dipole field from the bead that partially cancelled the applied fields to the spin valve. A lock-in technique was used to measure a voltage signal due to the MR reduction. A signal of 1.2 mV rms or 5.2 mΩ of resistance reduction was obtained from a 3 μm wide sensor and a signal of 3.8 mV rms or 11.9 mΩ from a 2.5 μm wide sensor. Micromagnetic simulations were also performed for the spin valve sensors with a single bead and gave results consistent with experiments. Further experiments and simulations suggested that these sensors or their variations can detect 1–10 Co nanoparticles with a diameter of ~11 nm, and are suitable for DNA fragment detection. © *2003 American Institute of Physics.* [DOI: 10.1063/1.1540176]

INTRODUCTION

In the past few years, giant magnetoresistive (GMR) structures like spin valve have become a potential sensing element in various biosensors for detection or identification of biomolecules.[1–5] In these biosensors, magnetic micron-sized particles were used as markers of biomolecules and the GMR elements detected the presence of the particles that were immobilized to the sensors through intermolecular interactions, e.g., DNA hybridization.[2] A major advantage of the magnetic labels over the fluorescent ones is the low requirement for sample amount, for which the tedious bioenrichment procedure may be avoided. Further, GMR sensors can be easily integrated so that multianalyte detection on a single chip becomes possible.[2,3] In this type of application, the detection of presence or absence of magnetic particles is a key issue. The detection methods used in prior reports are either magnetizing the magnetic particles by an out-of-plane ac magnetic field and measuring an ac signal from the GMR elements,[1–3] or applying an in-plane field to measure a dc signal change.[4] In this article, we demonstrate the detection of a single magnetic microbead by highly sensitive spin valve sensors in a different method, i.e., applying an in-plane biasing dc field and an orthogonal in-plane ac field and measuring the corresponding ac signal change from the spin valve sensors. The experimental results are also compared with micromagnetic simulations for magnetic microbeads and nanoparticles.

FABRICATION AND MEASUREMENT

A series of spin valve sensors with a width from 1 to 3 μm have been fabricated. The spin valve structure is Si/Ta 3 nm/seed layer 4 nm/PtMn 15 nm/$Co_{90}Fe_{10}$ 2 nm/Ru 0.85 nm/$Co_{90}Fe_{10}$ 2 nm/Cu 2.3 nm/ $Co_{90}Fe_{10}$ 2 nm/Cu 1 nm/Ta 4 nm with a magnetoresistance (MR) of 10.3% and a sheet resistance of 18.41 Ω. As shown in Fig. 1, rectangular spin valve strips were patterned out of blanket wafers so that the pinned magnetization of the spin valve lies in the transverse (width) direction of the strips and the easy axis of the free layer lies in the longitudinal direction. Thick (300 nm) Al leads were then deposited on the strips using liftoff technique. The Al leads also define the middle section of the strip as the active area of the spin valve. After that, half of spin valve strips

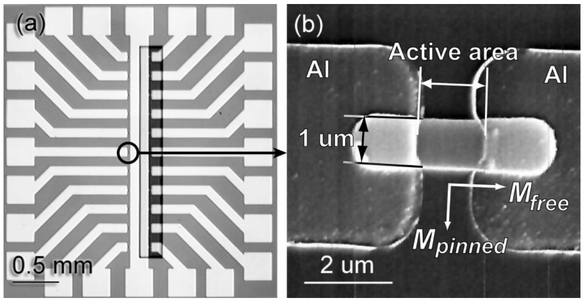

FIG. 1. (a) Optical microscope image of a 1 μm wide spin valve sensor array and (b) scanning electron microscope image of a 1 μm wide sensor strip (center). The dark bar in the center of image (a) is the photoresist passivation layer. The orientations of the free and pinned magnetizations M_{free} and M_{pinned}, are also shown in (b).

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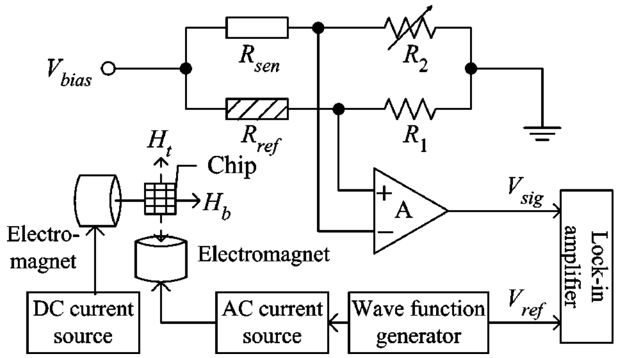

FIG. 2. Schematic of the measurement setup for spin valve sensors. The sensor chip is placed in the plane of a dc field H_b and an ac field H_t. A pair of sensor R_{sen} and reference R_{ref} strips form a Wheatstone bridge with two off-chip resistors R_1 and R_2. The signal is measured by a lock-in amplifier.

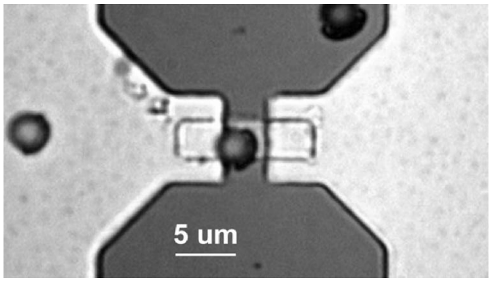

FIG. 3. An optical image of a 3×12 μm^2 spin valve sensor strip (center) with a single 2.8 μm diam magnetic bead (Dynabeads M-280).

were covered by a 1 μm thick photoresist layer that was then hard baked as a passivation. The passivated spin valve strips are effectively shielded from magnetic particles and therefore can serve as references to the unpassivated ones. The unpassivated and passivated strips are called sensor and reference strips, respectively.

Figure 2 shows the schematic diagram of the measurement setup. The sensor chip is placed in the gap of two orthogonal electromagnets in such a way that the longitudinal direction of the spin valve strips is aligned with a dc bias field H_b and the transverse direction parallel to an ac tickling field H_t. In this configuration, the spin valve is biased by the dc field H_b to its most sensitive and linear point. Meanwhile, magnetic particles on the chip are polarized by H_b and have their magnetizations modulated by the tickling field H_t. A pair of sensor (R_{sen}) and reference (R_{ref}) strips on the chip and two off-chip resistors (R_1 and R_2) form a Wheatstone bridge circuit. A voltage signal from the bridge is amplified and then measured by a lock-in amplifier at the frequency of H_t. In the linear region, the resistance of a spin valve strip under the ac tickling field may be expressed as $R=\overline{R}+\tilde{R}\sin(\omega t)$, where ω is the frequency of H_t. By tuning the variable resistor R_2, we may balance the difference between the sensor and reference strips and get a zero ac signal in the initial state when $R_2/R_1=\tilde{R}^0_{\mathrm{sen}}/\tilde{R}^0_{\mathrm{ref}}$. $\tilde{R}^0_{\mathrm{sen}}$ and $\tilde{R}^0_{\mathrm{ref}}$ are the ac parts of resistances of the sensor and reference strips in the initial state, respectively. If there is a magnetic particle sitting on the sensor strip, the magnetic dipole field of the particle will partially cancel the applied fields in the free layer, particularly in the transverse direction, reducing the MR response of the sensor strip. As a result, when a magnetic particle is added to or removed from the sensor strip, the balance between the sensor and reference strips will be broken and a nonzero ac signal will appear with an rms amplitude

$$V_{\mathrm{sig}}=A\frac{V_{\mathrm{bias}}}{\sqrt{2}R_2}(\tilde{R}_{\mathrm{sen}}-\tilde{R}^0_{\mathrm{sen}})=A\frac{V_{\mathrm{bias}}}{\sqrt{2}R_2}\Delta\tilde{R}_{\mathrm{sen}}, \quad (1)$$

where A is the gain of the differential amplifier, $\tilde{R}_{\mathrm{sen}}$ the ac part of resistance of the sensor strip in the detection state, and $\Delta\tilde{R}_{\mathrm{sen}}$ the resistance change of the sensor strip between the two states.

RESULTS AND DISCUSSION

We have tested the spin valve sensors for superparamagnetic beads with a diameter of 2.8 μm (Dynabeads M-280). These microbeads are polymer beads with an even dispersion of iron oxide (γ-Fe_2O_3) nanoparticles and are commonly used as magnetic labels for biomolecules.[1,2] Small amount of diluted water solution of Dynabeads was first dropped onto the sensor chips. Some beads would rest on the active area of sensor strips when the water evaporated. The strips with a single bead in the active area, such as the one shown in Fig. 3, were identified under an optical microscope, while a reference strip without any beads was also chosen. We then put the chip into the measurement setup and balanced the sensor strip with a single bead present and its reference in their initial states. The signal in the detection state was measured after removing the bead from the sensor strip by dissolving the beads back into water and blowing them off the chip. The measurement results for two spin valve sensors each with a single bead are listed in Table I. The frequency of H_t was 40 Hz and the gain A was 100. The noise levels were also measured by the lock-in amplifier with a 1 Hz equivalent noise bandwidth. The initial state signals V^0_{sig} were tuned as small as possible, below the noise level. When the beads were removed, we observed a jump in the signal V_{sig}, well above the noise level, which clearly indicated the difference be-

TABLE I. Experimental data for two spin valve sensors with a single 2.8 μm diam magnetic bead (Dynabeads M-280) and the micromagnetic simulation results. The voltages are all rms values. The 3 μm wide sensor is also shown in Fig. 3.

Sensor size (μm^2)	Active area (μm^2)	H_t (Oe rms)	H_b (Oe)	V_{bias} (V)	R_2/R_1 (kΩ/kΩ)	$V^0_{\mathrm{sig}}/V_{\mathrm{noise}}$ (mV/mV)	$V_{\mathrm{sig}}/V_{\mathrm{noise}}$ (mV/mV)	$\Delta\tilde{R}_{\mathrm{sen}}$ (mΩ)	$\Delta\tilde{R}_{\mathrm{sen,simu}}$ (mΩ)
3×12	3×4.1	32.0	120.0	30.0	9.134/9.532	0.03/0.09	1.2/0.1	5.2	5.6
2.5×10	2.5×3.8	38.0	94.0	100.0	22.202/24.862	0.04/0.15	3.8/0.3	11.9	13.3

tween the initial state (presence of a single bead) and the detection state (absence of the bead). In addition, the resistance changes of the sensor strips $\Delta\tilde{R}_{\text{sen}}$ were calculated using Eq. (1) and listed in Table I. The positive sign of V_{sig} or $\Delta\tilde{R}_{\text{sen}}$ confirmed that the magnetic bead reduced the MR responses of the sensor strips as expected. Since the detection of a bead's presence is simply the reverse of detecting its absence, it is apparent that the spin valve sensors are capable of detecting the presence of such a single magnetic bead.

In addition to the experiments, two-dimensional (2D) micromagnetic simulations for the spin valve sensors were also performed using the object oriented micromagnetic framework (OOMMF) software from National Institute of Standards and Technology.[6] Since the spin valve has a synthetic pinned layer, only the free layer will be affected by the magnetic fields in measurement. For that reason, we used OOMMF to simulate only the magnetization behavior of the $Co_{90}Fe_{10}$ free layer to obtain the corresponding MR responses. The saturation magnetization (1540 emu/cm^3) and exchange stiffness (1.53 μerg/cm) of $Co_{90}Fe_{10}$ were obtained from Ref. 7. By fitting the GMR transfer curves (not shown in this article), the uniaxial anisotropy field was found to be 40 Oe, close to the reference value of 32 Oe.[7] The cell size was chosen to be 25 nm for the micron-sized sensors. The Dynabeads are considered as a magnetic dipole, and their susceptibility was experimentally found to be $\sim$0.04. The resistance changes $\Delta\tilde{R}_{\text{sen,simu}}$, from simulations under the same conditions as in the experiments were listed in the last column of Table I for a comparison. We see that the simulations are consistent with the measurements.

Encouraged by the experiments on the Dynabeads, we tested the spin valve sensors for 11 nm diam Co nanoparticles.[8] A 1 μm wide spin valve sensor produced a signal of 0.4 mV rms or 1.9 mΩ of resistance change, which was very likely due to multiple Co nanoparticles, as the precise manipulation of the nanoparticles has not been achieved at the present time. Nevertheless, the micromagnetic simulations suggested that a smaller spin valve sensor could generate sufficient signal due to the presence of a single Co nanoparticle. For example, a single Co nanoparticle can cause a resistance change of 1.4 mΩ in a 0.2 μm wide spin valve sensor. Therefore it is possible to fabricate spin valve sensors that can detect 1–10 Co nanoparticles, which would dramatically reduce the sample amount needed for DNA fragments detection.

CONCLUSIONS

We fabricated a series of highly sensitive spin valve sensors on a micron scale and demonstrated that these sensors have successfully detected a single 2.8 μm diam magnetic bead. The micromagnetic simulations further confirmed the detection capability of the spin valve sensors. Therefore the spin valve sensors can be used for identification of biomolecules like DNA fragments labeled by such a magnetic particle. The experiments and simulations also suggested that a submicron spin valve sensor would be able to detect only a few Co nanoparticles and make the identification of a single DNA fragment possible, which is also the direction of our future research work.

ACKNOWLEDGMENTS

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