Detection of magnetic microbeads and ferrofluid with giant magnetoresistance sensors

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Abstract. Giant magnetoresistance sensors based on multilayers [Cu/NiFeCo]_{10}/ Ta were fabricated by microfabrication technology. A GMR-bridge was used to detect the magnetic MyOne beads and Ferro fluid. The dependence of the GMR-bridge signals on the surface coverage of MyOne beads was studied. The results show that the GMR sensor is capable of detecting the magnetic beads. The detectable limit of MyOne beads is about 100, and the corresponding signal output is 8 μV. The GMR bridge signal is proportional to the surface coverage of the MyOne beads. The sensitivity of the GMR bridge is inversely proportional to the feature size of the GMR sensor. The GMR bridge integrated with microfluidic channel was also used for dynamic detection of ferrofluid (suspension of Fe_{3}O_{4} particles). The results show that the GMR bridge is capable of detecting the flow of ferrofluid, and the sensor signals are proportional to the concentration of the ferrofluid. The detection limit of concentration of the ferrofluid is 0.56 mg/ml, and the corresponding signal is 6.2 μV.

1. Introduction

Cheap, reliable and portable biosensing technologies for medical applications have received growing attention. Different techniques are employed to develop lab-on-a-chip system, such as fluorescent labels with an exciting laser and detection optics and electrochemical detections. In these techniques, micro-arrays can be integrated to detect the multi analytes simultaneously.

Recently magnetic particles have been developed as labels for biosensing, due to their several advantages over other labels [1,2]. Magnetoresistance devices including giant magnetoresistance (GMR) sensor [3-5], spin-valve GMR sensor [6-8], tunneling magnetoresistive sensor [9], and Hall Effect sensor [10] are widely studied and employed for detection of magnetic labels. The GMR sensors can be integrated into micro-arrays for multi-analyte detection. The GMR sensors can also be integrated with microfluidics to realize more complex bioassay [11]. By applying a magnetic field on chip, the bio-molecules bound with magnetic labels can be manipulated and separated on chip and finally detected by the integrated GMR sensors [12].

In this study, multilayer-based GMR sensors were fabricated. A GMR-bridge was constructed and employed to detect the magnetic MyOne beads. The GMR sensor was also integrated with microfluidic channel for dynamic detection of ferrofluid. The dependence of the GMR-bridge signals on the surface coverage of MyOne beads and the concentration of ferrofluid were studied.
2. Experiment

Giant magnetoresistance (GMR) multilayers were deposited by dc magnetron sputtering onto 3 inch-Si wafers with the structure of NiFeCo 6nm[Cu 2.1nm/NiFeCo 1.5nm]_{10}/Ta 100nm. The sensors based on the GMR multilayers were fabricated by lithography, ion beam etching and lift-off technology. The sensors were covered with a 200 nm thick sputtered SiO₂ passivation layer to protect it from environmental corrosion. Finally a layer of SU-8 photoresist was coated on the chip. A micro channel on the GMR sensor with 200 μm wide and 50 μm in depth was formed by photo lithography. The structure of a GMR sensor element is shown in figure 1(a), and the magnetoresistance response to an in-plane magnetic field of the sensor element is displayed in figure 1(b). The GMR sensors revealed magnetoresistance ratio of ~9.8%. The resistances of the sensor elements are ~5 kΩ and ~3 kΩ for the sensors with the feature line width of 3 μm and 5 μm respectively.

A GMR-bridge, resembling a Wheatstone bridge, was constructed by connecting two GMR sensors and two external adjustable resistors for the detection of magnetic beads and ferrofluid. One of the two GMR sensors was used as sensing element and the other one was used as reference. The GMR-bridge was biased by 1-2 V DC current generated by 2400 Sorcemeter. The voltage signal across the bridge was measured directly using an Agilent multimeter and the acquired data fed to a computer. A vertical magnetic field of 240 Oe generated by a Helmholtz coil was applied as induced field in the detection of magnetic beads, while an in-plane magnetic field of 70 Oe was applied in ferrofluid detection. These magnetic fields were applied to induce a moment within the superparamagnetic particles. In dynamic detection of ferrofluid, a GMR sensor chip was embedded in a PDMS base at first, after the PDMS base solidified the micro channel was constructed by aligned bonding SU-8 layer and PDMS base to PDMS lid.

3. Results and discussion

3.1. Detection of magnetic beads

The superparamagnetic MyOne beads from Invitrogen Company with diameter of 1 μm were used and a DC magnetic field of 240 Oe normal to the sensor plane was applied in this section. Because of the demagnetizing effect, GMR sensors do not respond to the vertical magnetic field. When the sensing area of GMR bridge was free of magnetic beads, almost no resistance change in sensing element and no voltage output in GMR bridge was observed even if the normal magnetic field increased from 0 to 240 Oe. The calibration of GMR bridge was performed by adjusting the external resistor at first. When no magnetic beads are on the sensing area, the voltage output of the GMR bridge at this time is considered to be zero point of signal. Then some MyOne beads were settled on the surface of the
sensing area, a vertical magnetic field of 240 Oe was applied. A signal output of the GMR bridge was observed owing to the occurrence of the MyOne beads, which means that the GMR bridge is capable of detecting the existence of the MyOne beads.

The magnetic liquid with various concentrations of MyOne beads was dropped and various content of MyOne beads were settled on the surface of the GMR sensors. The signal response of GMR-bridge to the MyOne beads that were on the surface of the sensing area was measured. Figure 2 is the dependence of the signal output on the surface coverage of MyOne beads. The surface coverage of MyOne beads was calculated by Photoshop software. The GMR bridge signal is almost proportional to the surface coverage of the MyOne beads. In figure 2, deviations of the signal to the linearity can be observed. The deviations to the linearity can be attributed to several factors, such as the tilt of the induced magnetic field, the deviation of the position of the beads from the central area of the sensor strip, and the aggregation of MyOne beads as shown in figure 3.

Figure 2. The dependence of the output signal on the surface coverage of MyOne beads.

The impact of feature size of the GMR sensor on its detection sensitivity was also studied, and the signals of the GMR sensors with line width of 5 μm and 3 μm are all displayed in figure 2. The result shows that the GMR sensor with line width of 3 μm is more sensitive than that one with line width of 5 μm. The sensor sensitivity increases while the feature size of the GMR sensor decreases.

Figure 3 is the images of the MyOne beads on the surface of sensing area with different surface coverage and signal output. The more the beads covered the sensing area, the larger the signal output of GMR bridge was. The beads number was counted directly when the surface coverage was 1.37%, and the MyOne beads number was about 100, and the corresponding signal output of GMR bridge was 8 μV. In this study, the detection limit of the number of MyOne beads is about 100, which is in agreement with the reported results [5]. Target biomolecules such as DNA can be marked with MyOne beads by hybridization assays, therefore the GMR sensors can be applied in biosensor system to detect the biomolecules by measuring the density of magnetic beads.

Figure 3. The images of the MyOne beads on the surface of sensing area and the output signals.
3.2. Dynamic detection of ferrofluid

In order to dynamically detect the magnetic particles in flow, the GMR sensors were integrated with a microfluidic channel which was constructed by bonding SU-8 channel layer to PDMS lid. Figure 4 is sectional schematic illustration of a GMR sensor bound with a microfluidic channel. The width of the microfluidic channel is 200 $\mu$m and the depth is 50 $\mu$m. The GMR sensing element is directly under the microfluidic channel, while the reference GMR sensor is away from the channel. Ferrofluid (suspension of ~10 nm Fe$_3$O$_4$ superparamagnetic particles) was used in this section.

Syringe pump was connected to microfluidic channel by capillaries via access ports that were formed in the PDMS lid. A ferrofluid plug and a water plug were pushed into micro channel and passed through the GMR sensing area alternately. The flow rate of ferrofluid was 5 $\mu$l/s. An in-plane magnetic field was applied to induce the stray field of magnetic particles. The signal of GMR bridge is proportional both to the sensitivity of the GMR sensor and to the stray fields of magnetic particles. Because an external field of 70 Oe can induce larger stray fields of magnetic particles than the magnetic field of 50 Oe, an in-plane magnetic field of 70 Oe was applied, even if the sensitivity of the GMR sensor is larger at the magnetic field of ~50 Oe. The dynamic detection was performed by directly detecting the stray fields generated by Fe$_3$O$_4$ particles in the ferrofluid plug while it passed through the sensing area. Real time GMR bridge signals were directly measured using a GPIB-controlled multimeter and the acquired data fed to a computer.

Figure 5 shows the real time response of the GMR bridge to the ferrofluid. When a ferrofluid plug passed through the sensing area, a voltage signal of ~40 $\mu$V was observed. The four signal peaks in figure 5 indicate the four ferrofluid plug passing through the GMR sensing area serially. We repeated the dynamic detection with ferrofluid of different concentration. Figure 6 shows the relationship of the GMR signal to the concentration of ferrofluid. The GMR bridge signals are proportional to the concentration of the ferrofluid.

![Figure 4. The schematic illustration of a GMR sensor bound with a microfluidic channel.](image)

![Figure 5. The real time response of the GMR bridge to the ferrofluid.](image)

![Figure 6. The relationship of the GMR signal to the concentration of ferrofluid.](image)
As a control test, distilled water plugs were pushed into micro channel, and the real time output of bridge voltages were in the range of ±3 μV, which is considered to be system noise. The detection limit of concentration of the ferrofluid is 0.56 mg/ml, and the corresponding signal is 6.2 μV. Because DC magnetic field was applied in this study, a base line drift was observed in measurement. It should be more suitable to apply an AC magnetic field as an induced magnetic field to increase the sensitivity of detection system [4, 11].

4. Conclusions
The GMR sensors based on the [Cu/NiFeCo]×10/ Ta multilayers are applicable to detection of magnetic microbeads and the detectable MyOne beads are about 100 at least. The GMR bridge signal is proportional to the surface coverage of the magnetic beads. The sensitivity of the GMR sensor is inversely proportional to the feature size of the sensor.

The GMR sensor is also capable of detecting the flow of ferrofluid, and the output signals are proportional to the concentration of the ferrofluid. Because of the drift of the zero point in DC magnetic field, an AC magnetic field mode of measurement should be more suitable especially for dynamic detection of ferrofluid.

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