Journal of the Korean Physical Society, Vol. 52, No. 2, February 2008, pp. 513∼516

Detection of a Countable Number of Magnetic Particles for Biological Applications Using a Hall Device

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(Received 15 January 2008)

We fabricated a magnetic field sensor made of an InAs quantum-well. Various numbers of magnetic particles were located on the sensor and the stray field generated by the magnetic particles was detected using micro-Hall magnetometry at room temperature. A numerical calculation carried out for this device successfully explained the experimental results and a useful equation relating the signal of the device and the number of particles was deduced.

PACS numbers: 87.50.Mn, 07.55.Ge
Keywords: magnetic particle, Biosensor, Gradiometry

I. INTRODUCTION

The sensor for nano-scale magnetics has potential applications in the fundamental study of biological interactions and biomedical applications [1]. Micromagnetic sensors proposed thus far are based on magnetoresistive technologies, such as giant magnetoresistance [2,3] and spin-valve effect [4]. These magnetoresistive devices provide high sensitivity and good performance for single particle detection. However, they suffer from nonlinear response and saturation of the sensor material at low field, both of which are serious drawbacks for detecting the number of nano-scale particles.

Another kind of promising sensor is a micro-Hall device based on a semiconductor quantum-well structure, whose sensitivity is comparable with that of the magnetoresistive devices. Two features of the micro-Hall device can be advantages over magnetoresistive devices. Firstly, the sensor material does not magnetically saturate; secondly, the sensor-signal measuring the magnetic field shows linear response no matter how large the field range is.

The commercially used magnetic particles for biological application are composed of superparamagnetic materials to protect against aggregation. Thus, a relatively high external magnetic field is required to magnetize the particles. This field may lead to saturation of the magnetoresistive devices, but for the micro-Hall devices it does not affect the device performance. For biological applications, particles with nano-scale size are generally preferred. However, it is not easy to make nano-scale sensors for detection of individual nano-scale particles because the size of the sensor is limited by the fabrication process. Therefore, if nano-scale particles are to be detected, a reasonable choice would be to count the number of particles using a single sensor having a relatively large size. One requirement for measuring the number of particles is that the sensor signal is linear like that of the micro-Hall sensor.

In spite of the advantages of the micro-Hall device, a systematic study of its use to measure the number of magnetic particles has not been done so far. In this study, we fabricated micro Hall devices made of InAs quantum-well and located several different numbers of magnetic particles on the surface of the sensor. Using an AC modulated magnetic field superposed on a DC magnetic field, we obtained the magnetic susceptibility of the particle. The measured signals were proportional to the

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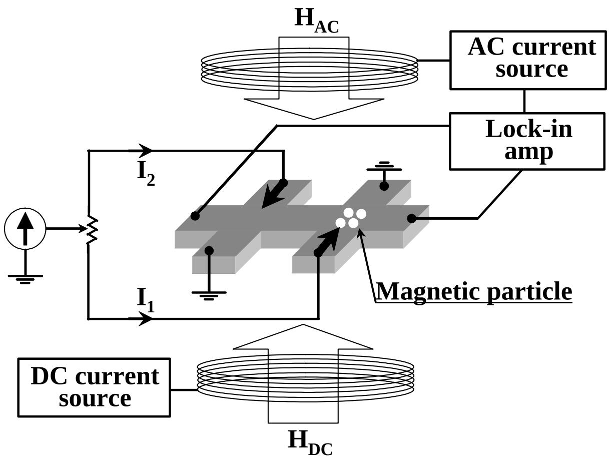

Fig. 1. Schematic illustration of the Hall gradiometry sensor. A DC magnetic field (H_{DC}) modulated by an AC field (H_{AC}) is applied perpendicular to the sensor. Magnetic particles are located on one of the two Hall crosses. The direction of current I_1 is opposite to that of I_2. By this geometry, a large background signal from the applied AC field can be canceled and the output signal is mainly the Hall resistance coming from the magnetization of the particles.

number of particles, which indicates successful detection of the number density of the particles on the sensor's surface.

II. EXPERIMENTS AND CALCULATIONS

The technique for detecting magnetic particles with our device is schematically illustrated in Figure 1. A mesa of two-dimensional InAs electron gas (2DEG) with two adjacent Hall crosses was patterned by using photolithography. A current channel resides 35.5 nm below the sensor surface and the mobility and the carrier density of the 2DEG at 300 K are 2.0 m^2/Vsec and 1.9×10^{16} m^{-2}, respectively. Several numbers of superparamagnetic particles (Dynabeads M280 of 2.8 μm in diameter) were placed on one of the Hall cross by lithographic technique, the remaining Hall cross being empty.

To detect the magnetic particles on the Hall cross, we employed the Hall gradiometric technique previously used by Li et al. [5] to detect Fe nano particles. Two Hall crosses were biased oppositely by DC currents of 100 μA so that the voltage difference between them gave a signal that came solely from the magnetization of the particles. A DC magnetic field (H_{DC}) was applied perpendicular to the sensor surface to align the magnetizations of the particles. A perpendicular AC excitation magnetic field (ΔH_{AC}) was also applied with frequency $f0$ and the voltage difference was measured at that frequency by using a lock-in amplifier. The ΔH_{AC} and the $f0$ in this study were 2 mT and 3.5 Hz, respectively.

The magnetization curve of the particle as a function of the DC magnetic field is similar to a Langevin function because of its superparamagnetic property. The magnitude of the particle's magnetization is determined by the DC magnetic field while the AC magnetic field caused a signal representing the slope of the magnetization curve. The linearity of the Hall sensor ensures that both stray field from the magnetized particle and the AC magnetic field itself contribute to the signal. The former gives information about the magnetic susceptibility of the particle and the latter adds a constant value to the signal. On the empty Hall cross only the constant Hall voltage caused by the AC magnetic field is measured. Therefore, by using the Hall gradiometric technique, which gives the difference in the Hall voltage between the Hall cross with the particles and the empty one, we can obtain a signal free from the influence of the AC magnetic field and caused only by the magnetization of the particles.

A differential resistance ΔR is defined as the measured voltage divided by the applied current (I_1 in Figure 1) and is related to the magnetic susceptibility χ of the particles as follows:

$$\frac{\Delta R}{\Delta H_{AC}} = \frac{\partial R_{Hall}}{\partial M}\chi, \tag{1}$$

where M is magnetization of the particle and R_{Hall} is Hall resistance, which depends on M and the number of the particles N. A numerical calculation confirmed that R_{Hall} was nearly proportional to N and M, as shown in Figure 3, which will be discussed later. Thus, $\partial R_{Hall}/\partial M$ in the above equation can be replaced by N times the geometric constant C_g and C_g is related the geometric factors of the device.

In order to elucidate our experimental data, we numerically calculated the output of our device in the diffusive transport regime. The magnetic field from a spherical particle is expected to be identical to the field from a point dipole with the same moment. The field perpendicular to the Hall cross is given by [6]

$$B_i(x,y) = \frac{\mu_0}{4\pi} m \frac{2d^2 - (x-x_i)^2 - (y-y_i)^2}{r^5}, \tag{2}$$

where $m = 3/4\pi a^3 M$ is the magnetic moment of the particle, a the radius of the particle, d the distance between the 2DEG and the center of the particle, $(x,\ y)$ the transverse coordinates in the 2DEG, $(x_i,\ y_i)$ the center position of the ith particle and $r = \sqrt{d^2 + (x-x_i)^2 + (y-y_i)^2}$. When N particles are placed on the surface of the sensor at (x_i, y_i) ($i = 1, ..., N$), the field profile given by $\sum B_i(x,y)$ leads to a Hall voltage on the voltage probes. The electrostatic potential and the current density were obtained by solving the continuity equation with the spatially dependent conductivity tensor [7–9]. In our numerical simulations, we took into account the number and the arrangement of the magnetized particles, as well as the device geometry and we calculated the R_{Hall} in Eq. (1) as a function of N and M.

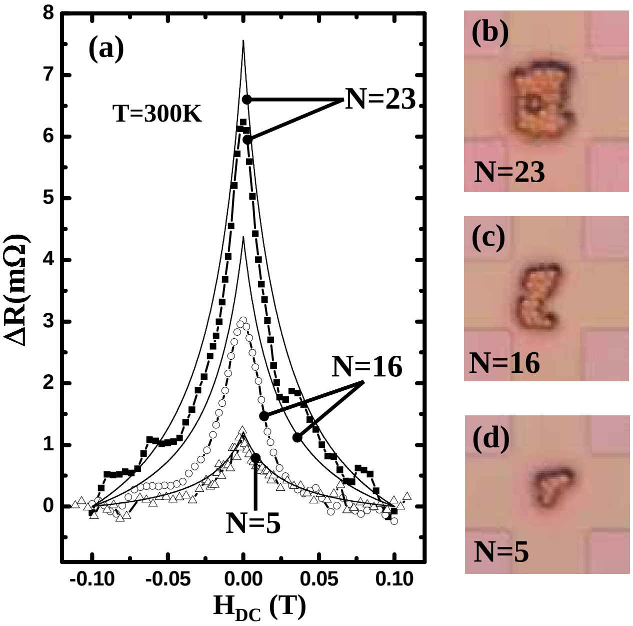

Fig. 2. (a) Signals of Hall gradiometry as a function of the DC field at room temperature. The number of particles (N) on the Hall cross is designated on each curve and the corresponding photos of the particles on the Hall cross are shown in (b), (c) and (d). The thin solid lines are the calculated values and show relatively good agreement with the experimental data. An offset is applied so that each curve is zero at $H_{DC} = \pm 0.1$ T.

M280 Dynabeads have a saturation magnetization (Ms) of 15.12 kA/m and a susceptibility of $\chi_0 = 0.756$ at zero field [10]. Generally, the dependence of the susceptibility on the magnetic field is a complicated tensor-function. Therefore, we adopted an approximate form for the calculation of χ in Eq. (1). We used the empirical Fröhlich-Kennelly relation expressed by

$$\chi(H_{DC}) = \frac{\chi_0 Ms}{Ms + \chi_0 |H_{DC}|}, \tag{3}$$

which was chosen by Smistrup as a good approximation for M280 Dynabeads [11].

III. RESULTS AND DISCUSSION

Figure 2(a) shows experimental signals at room temperature. Clearly distinguishable curves were observed for different numbers of particles and the magnitude of the curve increased as the number increased. The calculated signals are depicted as solid lines and are in relatively good agreement with the experimental data. The photos of the particles placed on the sensor surface are also shown in the figure. For the Hall voltage, all of the particles were located within the area of the active Hall

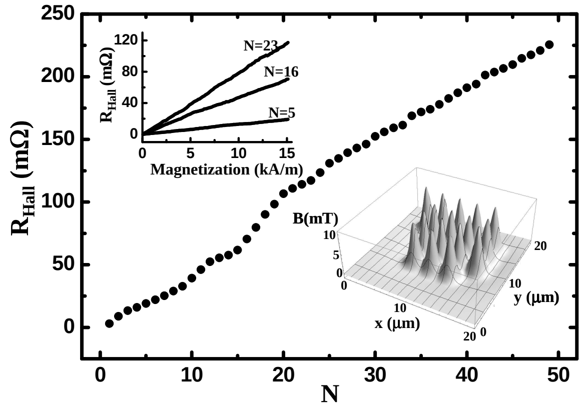

Fig. 3. Calculated Hall resistance (R_{Hall}) versus the number of magnetic particles (N) when the magnetization of the particles is saturated. The upper inset shows R_{Hall} as a function of the magnetization for various N. The lower inset depicts the perpendicular component of the field profile (B) made by the magnetically saturated particles for N=16.

cross. M280 Dynabeads were magnetized about 77 % at $H_{DC} = 0.1$ T [10]. To make a clear comparison between the curves, we displayed each curve with an offset so that the curve had a zero at $H_{DC} = 0.1$ T.

From the simulation, we know that the arrangement of particles on the Hall cross has a small effect on the signal whereas the number of particles has a significant affect on the signal. For a systematic study, the arrangement of the particles in our calculation was a little bit different from the experimental case. The particles were located on a square-shaped lattice mapped with 2.8 μm size onto the Hall cross. The first particle has a central position. Then, the remaining lattice points are occupied one by one with particles in the order of the nearest neighbor to the first, until N particles are placed on the Hall cross. An example of the field profile on a 2DEG resulting from this arrangement is shown in the lower inset of Figure 3. The peak positions of the profile correspond to the particle's positions.

For a given N, the R_{Hall} versus magnetization curve of the particles was investigated in our simulation. The upper inset of Figure 3 shows that R_{Hall} is almost proportional to the magnetization; *i.e.*, $R_{Hall} \sim M$. The proportionality constants are 1.3×10^{-3}, 4.5×10^{-3} and 7.9×10^{-3} Ωm/kA for $N = 5$, 16 and 23, respectively. On the other hand, when the magnetization is fixed, R_{Hall} is also nearly proportional to N, as shown in Figure 3. The asymmetric magnetic field profile produced by the particles adds a small component to the Hall voltage, which is different from the case of a symmetric profile. Since the field profile depends on the arrangement of particles, there is slight difference in the Hall voltage according to the particle's arrangement in spite of the fixed number of the particles. Thus, a different arrangement of the particles on the Hall cross will cause some deviation from linearity, but the effect is small enough to be negligible for applications as a particle-number detector.

A more simplified expression of Eq. (1) was obtained from the calculated results;

$$\Delta R \approx C_g N \chi \Delta H_{AC}, \tag{4}$$

where $C_g = 0.23$ for our device and the units of ΔR and ΔH_{AC} is Ω and T, respectively. The value of C_g is determined from the parameters of the device including the shape of the Hall cross, the electric properties of the 2DEG, *etc.* Once C_g for a given device is determined, Eq. (4) is practically useful. The number or magnetic susceptibility of the particles can be obtained experimentally from the device by making use of Eq. (4).

When the size of the particle is reduced, several factors contributing to the magnetic field in Eq. (2) can be considered. The distance d between the 2DEG and the center of the particle is approximately equal to the particles radius a, if the thickness of the insulation layer on the 2DEG is ignored. The field around a magnetic moment is inversely proportional to the cube of the distance from the center of the magnetic moment while the magnetic moment m is proportional to the cube of a. Thus, the contribution of m and d to the field strength cancel each other out. Thus, the maximum value of the magnetic field given by $\mu_0/(2\pi)m/d^3$ from Eq. (2), is independent of the particle's size. The magnetic field produced by a particle has a distribution over the Hall cross and Eq. (2) indicates that the degree of spread of the field distribution is determined by d (or the size of the particle). The Hall voltage is affected by this distribution. When the size of the particle is changed, a similar magnitude of the Hall voltage can be obtained if the Hall cross is replaced by one with a size proportional to the particle's size. Here is an example. In this study, the diameter of the particle is 2.8 μm and the size of Hall cross is 20 μm. If particles of 140 nm in diameter are to be detected, a Hall cross of 1 μm in size can be used, then a signal can be obtained whose magnitude is similar to this result.

IV. CONCLUSIONS

We have fabricated Hall gradiometric sensors based on InAs quantum-wells. A systematic study for various numbers of magnetic particles was carried out, including a numerical simulation. We confirmed that the number or magnetic susceptibility of the particles could be detected by using our device and we proposed a practical equation relating these quantities to the device signal. For quantitative detection of nano-scale biological particles, the size of the Hall cross should be reduced to sub-micron scale. Further miniaturization of our device to submicron dimensions will lead to a high-performance biological sensor for detection of nanometer-size particles.

ACKNOWLEDGMENTS

This work was supported by KIST vision 21 program, the electron Spin Science Center at POSTECH and a Korea Research Foundation Grant funded by the Korean Government(MOEHRD) (KRF-2007-313-D00327), in which main calculations were performed by using the supercomputing resource of the Korea Institute of Science and Technology Information(KISTI).

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