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Measurements of Brownian relaxation of magnetic nanobeads using planar Hall effect bridge sensors

F.W. Østerberg[a], G. Rizzi[a], T. Zardán Gómez de la Torre[b], M. Strömberg[b], M. Strømme[b], P. Svedlindh[b], M.F. Hansen[a,*]

[a] Department of Micro- and Nanotechnology, Technical University of Denmark, DTU Nanotech, Building 345B, DK-2800 Kongens Lyngby, Denmark
[b] Department of Engineering Sciences, Uppsala University, The Ångström Laboratory, Box 534, SE-751 21 Uppsala, Sweden

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ABSTRACT

We compare measurements of the Brownian relaxation response of magnetic nanobeads in suspension using planar Hall effect sensors of cross geometry and a newly proposed bridge geometry. We find that the bridge sensor yields six times as large signals as the cross sensor, which results in a more accurate determination of the hydrodynamic size of the magnetic nanobeads. Finally, the bridge sensor has successfully been used to measure the change in dynamic magnetic response when rolling circle amplified DNA molecules are bound to the magnetic nanobeads. The change is validated by measurements performed in a commercial AC susceptometer. The presented bridge sensor is, thus, a promising component in future lab-on-a-chip biosensors for detection of clinically relevant analytes, including bacterial genomic DNA and proteins.

1. Introduction

In recent years, the interest in using magnetic particle-based biosensors has increased (Göransson et al., 2010; Jaffrezic-Renault et al., 2007; Koh and Josephson, 2009; Wang and Li, 2008). One of the main reasons for this is the lack of magnetic background in most biological samples. Furthermore, magnetic particles of dimension in the sub-micrometer range, so called nanobeads, have high physical and chemical stability, are inexpensive to produce, and can easily be made biocompatible.

Brownian relaxation was first proposed for biosensing by Connolly and St Pierre (2001). The principle behind using Brownian relaxation for biodetection is that a naked magnetic particle will have a smaller hydrodynamic diameter than the same particle bound to a biomolecule. This means that the naked particle will relax faster than a particle bound to a biomolecule. Brownian relaxation has been demonstrated to work for both detection of DNA (Strömberg et al., 2008) and proteins (Astalan et al., 2004; Öisjöen et al., 2010; Zardán Gómez de la Torre et al., 2012). Traditionally, Brownian relaxation is measured in a SQUID magnetometer, which is expensive and requires cryogenic liquids for cooling; other methods include inductive setups and fluxgates (Ludwig et al., 2005). None of these methods are easily integrated into a lab-on-a-chip system, thus there is a need for a sensor suited for integration onto a lab-on-chip platform. We have previously demonstrated that Brownian relaxation can be measured using a cross-shaped planar Hall effect (PHE) sensor without the need for any externally applied field since the beads are magnetized by the field generated by the alternating sensor bias current (Dalslet et al., 2011; Østerberg et al., 2010).

In the present work, we compare results obtained from measurements of Brownian relaxation of 40 nm magnetic beads using two different PHE sensor geometries; the traditional cross geometry and the newly proposed bridge (PHEB) geometry (Henriksen et al., 2010; Persson et al., 2011). We first show that the two sensor types yield the same frequency dependence of the measured signal from magnetic nanobeads and that the signals measured by the bridge sensor are six times as large as those measured by the cross-shaped sensor. We then present results of the first on-chip experiments, where functionalized magnetic nanobeads are mixed and hybridized to DNA coils formed in a rolling circle amplification (RCA) process. These results are found to compare well with those obtained in experiments carried out using a commercial AC susceptometer. The presented findings open up for the development of inexpensive on-chip magnetic read-out devices for detection of clinically relevant analytes including bacterial genomic DNA and proteins.

2. Theory

Below, the theoretically expected signals from magnetic beads when they are magnetized by the sensor self-field for both the

* Corresponding author. Tel.: +45 45256338.
E-mail addresses: frederik.osterberg@nanotech.dtu.dk (F.W. Østerberg), Mikkel.Hansen@nanotech.dtu.dk (M.F. Hansen).

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cross and bridge geometries of planar Hall effect sensors are derived. It is also described how the dynamic magnetic bead response can be extracted using lock-in technique.

2.1. Low-field sensor response

The sensors rely on the anisotropic magnetoresistance (AMR) effect measured in the cross and bridge geometries shown in Fig. 1. The cross consists of two orthogonal arms each of width w. The bridge consists of four arms of width w and length l that form angles $\pm\pi/4$ to the x-axis as illustrated in Fig. 1. The sensors consist of a ferromagnetic layer exhibiting the AMR effect, which is exchange pinned along the positive x-direction in zero external magnetic field by an antiferromagnet. The sensors are connected in series and are biased by a current I applied in the positive x-direction. The resulting sensor output voltages V_C and V_B of the cross and the bridge, respectively, are measured along the y-direction. In zero magnetic field both sensors will ideally give zero output voltage. Upon application of a small magnetic field H_y in the y-direction, the magnetization of the ferromagnetic layer will rotate resulting in non-zero values of V_C and V_B due to the AMR effect. The cross sensor is usually termed planar Hall effect sensor because it shares the geometry with ordinary Hall sensors. The bridge sensor presented here has recently been shown to have exactly the same response as the cross sensor except for a geometrical amplification factor and hence this particular class of AMR sensors was termed planar Hall effect bridge sensors (Henriksen et al., 2010). For both sensors, the output for low applied magnetic fields can be written as

$$V_C = IS_{C,0}H_y, \tag{1}$$

$$V_B = IS_{B,0}H_y, \tag{2}$$

where $S_{C,0}$ and $S_{B,0}$ are the low-field sensitivities of the cross and bridge sensors, respectively. When the two sensors have the same value of w, the two sensitivities are ideally related as $S_{B,0} = (l/w)S_{C,0}$ (Henriksen et al., 2010).

2.2. Response to sensor self-field and magnetic beads

We consider the self-field H_{sf} acting on the sensor in the directions indicated in Fig. 1 due to the applied sensor bias current. For the present sensors, part of the sensor bias current is shunted in the antiferromagnetic layer. This gives rise to an effective in-plane magnetic field acting on the ferromagnetic layer aligned perpendicular to the direction of the current I_c through the conductor. We write this effective field as $I_c\gamma_0$, where γ_0 is a constant that depends on the sensor stack and sensor geometry. Likewise, magnetic beads that are present on and near the conductor will be magnetized by the field from the sensor bias current and give rise to a net positive field acting on the conductor. This we write as $I_c\gamma_1\chi$, where γ_1 depends on the sensor geometry and bead distribution and χ is the magnetic bead susceptibility (Hansen et al., 2010). Hence, we write the total self-field acting on the sensor due to the applied bias current as

$$H_{sf} = I_c\gamma_0 + I_c\gamma_1\chi. \tag{3}$$

For the cross sensor, the entire current passes through the sensor and the self-field acts in the positive y-direction. Inserting $I_c = I$ and $H_y = H_{sf}$ in Eq. (1) yields the expected self-field signal:

$$V_C = I^2 S_{C,0}(\gamma_0 + \gamma_1\chi). \tag{4}$$

For the bridge sensor, only half of the bias current passes through each branch and the sensor is sensitive only to the y-component of the self-field. Inserting $I_c = I/2$ and $H_y = H_{sf}/\sqrt{2}$ in Eq. (2) yields the expected self-field signal:

$$V_B = 2^{-3/2} I^2 S_{B,0}(\gamma_0 + \gamma_1\chi), \tag{5}$$

where we have implicitly assumed that γ_0 and γ_1 are the same for the two sensor types. Combining Eqs. (4) and (5), we find that the ratio of the self-field signals for the two sensors is

$$V_B/V_C = 2^{-3/2}(S_{B,0}/S_{C,0}) \tag{6}$$

and that, ideally, $V_B/V_C = 2^{-3/2}(l/w)$.

2.3. Dynamic magnetic susceptibility measurements

To probe the dynamic magnetic properties of magnetic nanobeads, we apply an alternating sensor bias current $I(t) = I_{AC}\sin(2\pi ft)$, where I_{AC} is the current amplitude, f is the frequency and t is the time. The response of a bead ensemble to the alternating magnetic field is described by the complex magnetic susceptibility:

$$\chi = \chi' - i\chi'' \equiv |\chi|\cos\phi - i|\chi|\sin\phi, \tag{7}$$

where χ' and χ'' are the components of χ in-phase and out-of-phase with the magnetic field, respectively, and ϕ is the phase lag of the magnetic response with respect to the magnetic field. As the self-field signals are proportional to I^2, the signals must be detected at twice the frequency ($2f$) of the bias current. This can be achieved by measuring the 2nd harmonic signal $V_2 = V_2' + iV_2''$ using lock-in technique, where V_2' and V_2'' are the in-phase and out-of-phase signals, respectively. We have previously shown (Dalslet et al., 2011; Østerberg et al., 2010) that the 2nd harmonic signals for the cross sensor are

$$V_{C,2}' = -2^{-3/2} I^2 S_{C,0}\gamma_1\chi'', \tag{8}$$

$$V_{C,2}'' = -2^{-3/2} I^2 S_{C,0}(\gamma_0 + \gamma_1\chi'). \tag{9}$$

Hence, $V_{C,2}{}'$ is directly proportional to the out-of-phase susceptibility χ'' and $V_{C,2}''$ depends linearly on the in-phase susceptibility χ'. The corresponding expressions for the bridge sensor can be found using Eq. (6).

2.4. Brownian relaxation of magnetic beads

We consider a magnetic bead, where the superparamagnetic relaxation time due to internal flipping of the magnetic moment of the bead is much longer than the Brownian relaxation time due to a physical rotation of the bead (Brown, 1963). Hence, we assume that Brownian relaxation is the dominating relaxation mechanism in the investigated frequency window. Brownian relaxation is characterized by the Brownian relaxation frequency

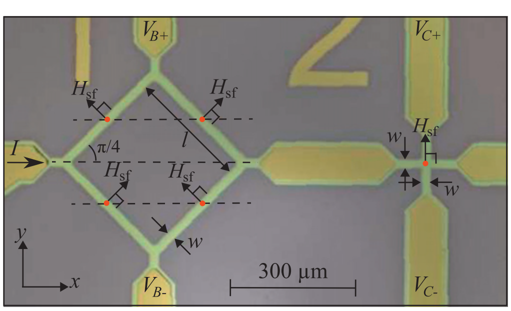

Fig. 1. Picture of a bridge and a cross sensor connected in series with definition of geometric variables and the orientation of self-fields acting on the sensor. The current is applied in the x-direction, while sensor signals are measured across the sensors in the y-direction.