Giant Magnetoresistance Material and Its Potential for Biosensor Applications

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Abstract: In the future, devices based on lab-on-a-chip, compact and inexpensive detection units are required that directly translate the abundance of certain biomolecules into an electronic signal. By detecting specifically bound magnetic labels with magnetoresistive sensors, a versatile platform can be designed that fulfils those requirements and even enables on-chip manipulation of biomolecules by suitable magnetic gradient fields. In this paper, sensitive recognition of magnetic label by magnetoresistive sensor based on giant magnetoresistance (GMR) have been discussed.
Keyword: Giant Magnetoresistance, Biosensor, Biomolecules, lab-on-a-chip, magnetic label.

I. INTRODUCTION

The discovery of biosensors began in early 1960s, when Clark and Lyons firstly reported on amperometric glucose detection using the enzyme glucose oxidize [1]. Later, biosensors found a wide area of applications in industry, clinical diagnostics, and ecology. At the same time, biosensor science became an independent area of modern analytical chemistry involving approaches of biochemistry and physical chemistry. A biosensor is generally defined as an analytical device, which makes use of a biological molecular recognition component connected to a transducer to generate a quantifiable electronic output signal, in response to a biological or chemical analyte [2].

Biosensors promise to provide analytically powerful and inexpensive alternatives to standard bacteriological methods used today for bacteria detection. Biosensors are analytical devices that respond selectively to analytes or bacteria by use of a combination of a biological recognition system and a physical transducing element. The biological response is converted by the transducer to an electrical or optical signal that is directly related to the concentration of the analyte of interest or bacteria. A biosensor's recognition system may consist of one of many biological components including: enzymes, antigens, antibodies, nucleic acids, cells, cell organelles or receptor molecules. All of these biological components are capable of interacting very specifically with an analyte of interest or with bacteria and to give a biosensor its unique specificity.

Nowadays, accurate, rapid, cheap and selective analysis is required for clinical and industrial laboratories. Magnetoresistive biosensors seem to be among the best candidates to meet these criteria. Since the late 1990s, magnetoelectronics [3] has emerged as one of several new platform technologies for biosensor and biochip development. This technology is based on the detection of biologically functionalized micrometer or nanometer-sized magnetic labels, using high-sensitivity microfabricated magnetic-field sensors.

Another concept for DNA detection was introduced in 1998 by Baselt et al. [4]. It is based on detecting the stray field of magnetic labels by embedded magnetoresistive sensors. Such a technique, apart from being sensitive, flexible and compatible with standard CMOS fabrication, also has the advantage of directly providing an electronic signal that is suitable for automated on-chip analysis. Furthermore, the possibility to attract the magnetic labels by suitable gradient fields also opens up a completely new prospect that is not possible in such a way for any of the competing detection schemes, i.e. the selective on-chip manipulation of desired biomolecules [5]. This option could be used, for example, to reduce incubation times during hybridization, or to test binding forces of adhered molecules [6]. Due to these opportunities, magnetoresistive biosensors represent a very promising alternative detection unit for lab-on-a-chip devices, and since the first publication in 1998, a number of research groups initiated work on that subject [7].

A group at the Naval Research Laboratory (NRL) and NVE Corporation in the US first demonstrated a magnetic biosensor system which they called BARC [4,8]. Their detector employed a giant magnetoresistive multilayer stack that is less sensitive than properly designed spin valve (SV) or magnetic tunnel junction (MTJ) detectors [9]. Another group in Germany demonstrated that giant magnetoresistive (GMR) multilayer biodetection was superior to fluorescent biodetection [10]. Groups in Portugal and Netherlands have deployed SV sensors coupled with coils at proximity for rapid molecular detection [11, 12]. The commercially available magnetic tags used by these groups tend to have a mean diameter in the range from 0.1 μm to 3 μm, including the paramagnetic polystyrene beads and similarly sized ferromagnetic particles.

The unique feature of the magneto-nano biochip were developed by Wang [13] that it use magnetic nanoparticles (also called NanoTags or nanotags) with a mean diameter of only 100-1000 Å as the tags. Since the tag dimensions are more comparable to those of the target biomolecules to be assayed, they expect better performance in real biological assays.

II. THEORETICAL BACKGROUND

A. GMR Effect

Magnetoresistance is defined as the change in the resistance of a material in response to an externally applied magnetic field. The first announcement of the GMR effect was reported in 1988 by Baibich and co-workers [14]. They discovered that the resistance of a sandwich type multilayer with magnetizations aligned initially (in the magnetic field H = 0) antiparallel decreased more than 50% after applying an external magnetic field. Because this decrease of resistance was very large they called this effect giant magnetoresistance (GMR) and this nomenclature is still in use today.

The GMR effect relies on the experimentally established fact that electron spin is conserved over distances of up to several tens of nanometers, which is greater than the thickness of a typical multilayer. Therefore, the electric current in the trilayer flows in two channels, one corresponding to electrons with spin projection ↑ and the other to electrons with spin projection ↓. Since the ↑ and ↓ spin channels are independent (spin is conserved) they can be regarded as two wires connected in parallel and the GMR can be explained using a simple resistor model, as shown in Fig. 1. The essential ingredient is that electrons with spin projections parallel and antiparallel to the magnetization of the ferromagnetic (FM) layer are scattered at different rates when they enter the ferromagnetism. Let us assume that electrons with spin antiparallel to the magnetization are scattered more strongly. In the ferromagnetic configuration Fig. 1 (a) of the trilayer, electrons with spin ↑ are weakly scattered both in the first and second ferromagnet, whereas the ↓ spin electrons are strongly scattered in both ferromagnetic layers. This is modelled by two small resistors in the spin ↑ spin channel and by two large resistors in the spin ↓ channel in the equivalent resistor network. Since the ↓ and ↑ spin channels are connected in parallel, the total resistance of the trilayer is determined by the low resistance ↑ spin channel which shorts the high-resistance ↓ spin channel. Therefore the total resistance of the trilayer in the ferromagnetic configuration is low. On the other hand, ↓ spin electrons in the antiferromagnetic configuration are strongly scattered in the first ferromagnetic layer but weakly scattered in the second ferromagnetic layer. The ↑ spin electrons are weakly scattered in the first ferromagnetic layer and strongly scattered in the second. This is modelled in Fig. 1 (b) by one large and one small resistor in each spin channel. There is no shorting and the total resistance in the antiferromagnetic configuration is much higher than in the ferromagnetic configuration.

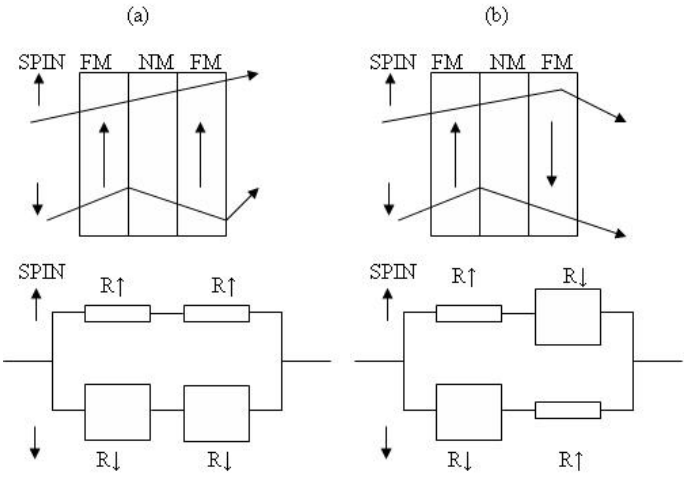

Fig.1. Resistor model of GMR [15]

Fig. 2. shows the original results obtained by Baibich and coworkers. The (001)Fe/(001)Cr *bcc* superlattices were grown by the MBE method. The magnetoresistance was measured at 4.2K for different thicknesses of the Cr spacer. The authors explained the GMR effect as follows. The resistivity drops when the magnetic external field overcomes the antiferromagnetic coupling and the alignment of magnetizations becomes a parallel arrangement. It was supposed that the spin-dependent scattering of the conduction electrons in the magnetic layers or at their interfaces was responsible for the GMR effect. The scattering in antiparallel alignment is much larger than in the parallel case.

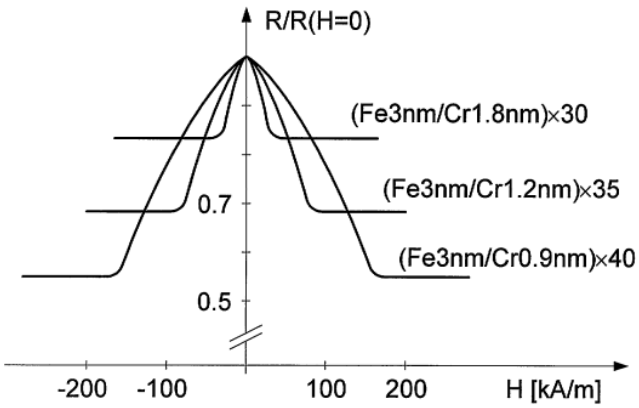

Fig. 2. The first announcement of GMR effects – results obtained by Baibich and co-workers [14].

In this field, we also have been developed GMR material with sandwich structure [16]. Recently, we have successfully developed GMR thin film with sandwich structure using dc-opposed target magnetron sputtering, and we obtained about 65 % MR value at room temperature in NiCoFe/Cu/NiCoFe sandwich [17,18,19]. The GMR ratio curve for NiCoFe/Cu/NiCoFe sandwich are shown in Fig. 3, 4, 5 and 6.

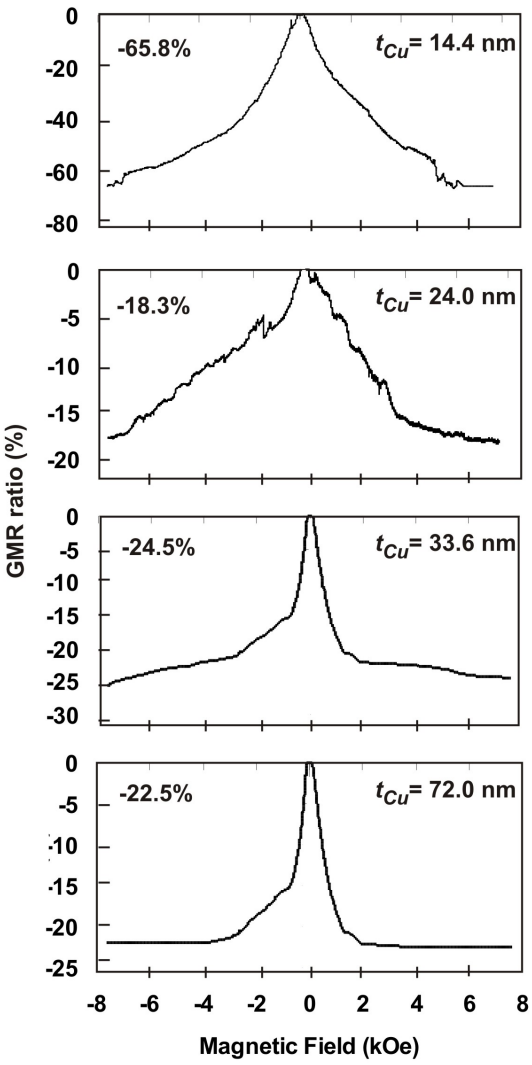

Fig. 3. The dependence of GMR ratio on the spacer layer thickness (t_{Cu}) with fixed NiCoFe layer thickness, t_{NiCoFe} = 62.5 nm.

Fig 4 show variation of GMR ratio vs. Cu layer thickness at room temperature.

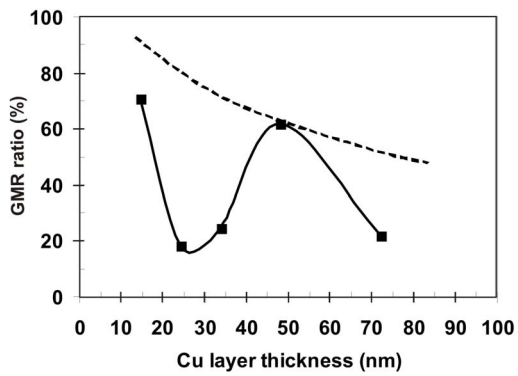

Fig 4 Variation of magnitude of GMR ratio versus Cu layer thickness. The dotted line shows the decay of GMR ratio with increasing of Cu layer thickness.

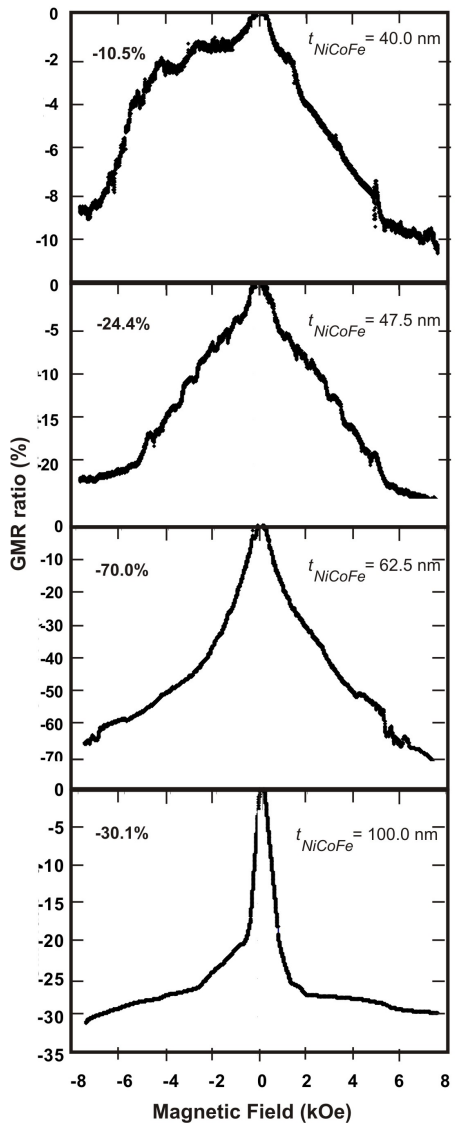

Fig. 5. The dependence of GMR ratio on the ferromagnetic layer thickness (*tNiCoFe*) with fixed Cu layer thickness (*tCu* = 14.4 nm).

Fig 6 shows variation of GMR ratio vs. NiCoFe layer thickness at room temperature.

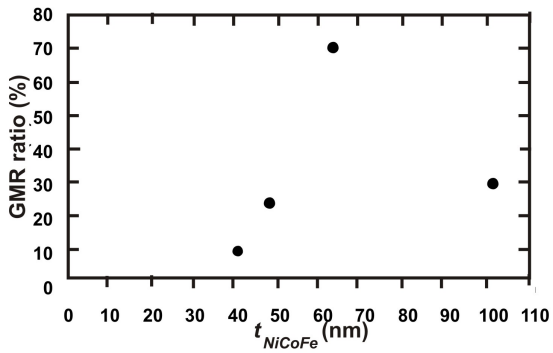

Fig 6. Variation of magnitude of GMR ratio versus NiCoFe layer thickness.

We found that the GMR ratio changes with variation of the thickness of ferromagnetic and non magnetic layers. The thickness of both ferromagnetic and non magnetic layers of NiCoFe/Cu/NiCoFe sandwich influences the spin-dependent scattering in the film, which can be explained using Valet-Fert model as can be found in other paper [20].

B. GMR Sensor

Generally, sensors for measuring the magnetic field include fluxgate sensor, Hall sensor, induction coil, GMR sensor, and SQUID sensor. Due to advantages of GMR materials for magnetic field measurements, such as: high sensitivity and quick response under low magnetic field, more attentions have been paid on developing GMR material for magnetic field sensors. Table 1 illustrates the differences between GMR and other magnetic field sensors [21].

Since 1988, giant magnetoresistance sensors (GMRs) have become one of the most heavily used tools for the detection of magnetic fields. While almost universally employed as compact, high-density, and high speed read heads in computer hard drives [22], GMRs have also found specialty applications in several other areas [23,24,25] including antilock brakes [26], magnetic imaging [27] and galvanic isolators [28].

TABLE 1 COMPARISON OF MAGNETIC FIELD SENSORS COMMONLY USED[21]

	***H* range (T)**	**Sensivity (V/T)**	**Response time**	**Power consumption**	**Sensor head size**
GMR	10^{-12}-10^{-2}	120	1 MHz	10 mw	10-100μm
Hall	10^{-6}-10^{2}	0.65	1 MHz	10 mw	10-100μm
SQUID	10^{-14}-10^{-6}	10^{-14}	1 MHz	10 mw	10-100μm
Flux gate	10^{-12}-10^{-2}	3.2	5 kHz	1 w	10-20 mm

C. Magnetic Label

Magnetic labels or carriers, also referred to as microspheres, microbeads and nanoparticles, have found wide-ranging scientific and clinical application in biotechnological and biomedical research, most notably in the areas of bioseparations, molecular biology and drug delivery [29]. The most important characteristics of magnetic labels that are used in biosensor or biochip devices are size and shape, chemical and magnetic composition, surface properties, stability and ease of chemical functionalization for the immobilization of biomolecules.

D. GMR Device for Biosensor

The pioneering work in the field of magnetoresistive biosensors was done by the Naval Research Laboratory (NRL) [4,30], which developed the first prototype magnetoresistive biosensor called bead array counter (BARC). It consists of 8 separate arrays, each incorporating 8 rectangular (5 μm × 80μm) sensor elements per probe DNA spot. A single sensor element is capable of detecting a single magnetic marker (Dynal Inc., M-280, mean diameter 2.8 μm). They have shown good selectivity and sensitivity (10 times better than the unspecific signal) to an unspecified amount of single-stranded *Francisella tularensis* DNA oligomers [31].

A first model for the detection of magnetic markers by GMR-type magnetoresistive sensors was published by Tondra, et.al, 1999 in NVE Inc.[32]. He concluded that single magnetic markers of any size can be detected as long as the sensor has about the same size as the marker and the insulating protection layer is thin enough.

J. Schotter, et.al., 2004 [10] present recent results on large area magnetoresistive biosensors. The guideline for the design of the sensor elements is the size of a single probe DNA spot, which is typically from 70 to 150 μm in diameter for standard microarray spotters. Other than the NRL group, they do not resolve the distribution of the magnetic markers within a single probe DNA spot, but are only interested in the average signal. Therefore, they design the sensor elements large enough to cover the entire area of a single probe DNA spot [33].

Like in the case of standard fluorescent DNA microarrays, the magnetoresistive biosensor is based on the principle of molecular recognition between specific known DNA sequences immobilized locally at the sensor surface (so-called probe DNA) and the DNA sequences that are to be analyzed (so-called analyte DNA). The only differences between the fluorescent and the magnetoresistive biosensor are the markers (magnetic instead of fluorescent) and the method of detection.

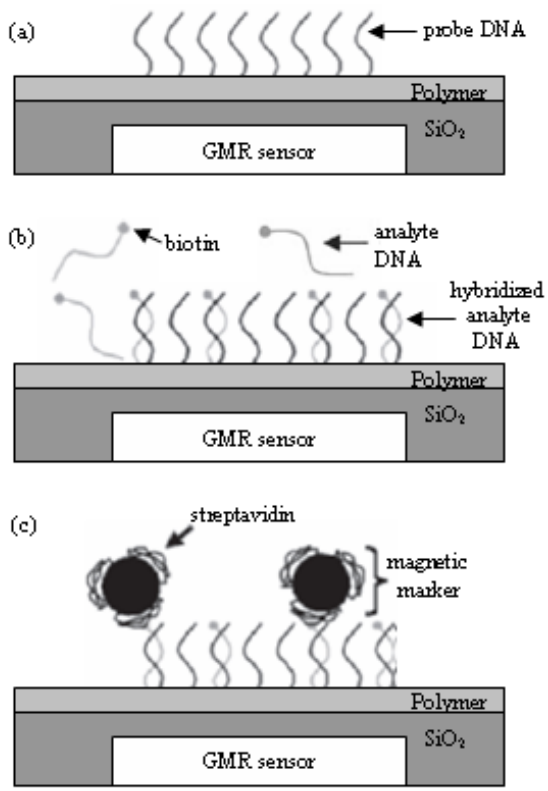

Fig. 7. Principle of the giant magnetoresistive biosensor: (a) immobilization of the probe DNA; (b) hybridization of the analyte DNA; (c) binding of the magnetic markers and detection of their stray field by the GMR-sensor [10].

Fig. 7 displays the different steps involved in DNA detection by the magnetoresistive biosensor. First, samples of probe DNA are spotted onto the sensor surface and are immobilized via epoxy groups embedded into the top polymer layer.

Second, the biotin-labeled analyte DNA is added and hybridizes to complementary probe DNA. In the final step, streptavidin-coated magnetic markers are introduced and bind specifically to the biotin of the hybridized analyte DNA. After each step, washing removes unbound DNA or markers. The magnetic stray field of the markers is detected as a resistance change in a GMR-based magnetoresistive sensor embedded underneath the probe DNA spot.

The incorporation of GMR structures in bacteria sensing is illustrated in Fig. 8 by Millen, et. al, 2005 [34]. Generally, the surface of the GMR sensing region is modified to allow the binding of capture antibody. When the GMR structure is exposed to a sample solution that contains target antigens, complex binding between the target antigen and antibody occurs. This is followed by the addition of antibody-coated magnetic particles that subsequently label the target antigens and form a series of sandwich-like structures.

In order to detect the magnetic particles bound on a GMR structure surface, an external magnetic field is applied in the z-direction, as illustrated in Fig. 9 [35]. Bound magnetic particles that are exposed to a magnetic field will generate magnetic induction in the x-direction, as shown in the Fig.8. Since the GMR structure detects only the x-component of the magnetic field, the external magnetic field in the z-direction does not have any effect on the detection.

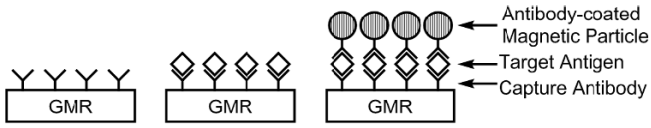

Fig. 8. Bacteria sensing using a GMR structure [34]

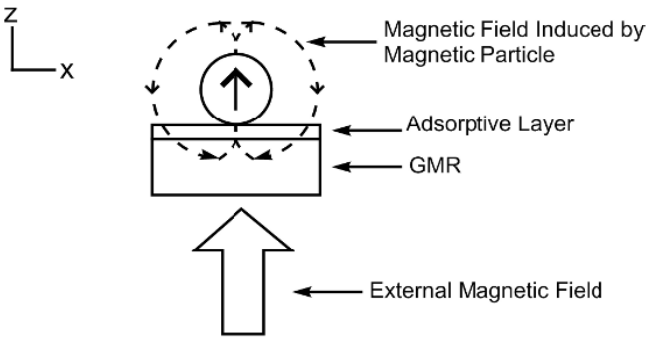

Fig. 9. Detection of magnetic particle on GMR structure [35].

As indicated in Fig. 2, increasing the magnetic field in either direction will reduce the resistance of a GMR material. Hence, the magnetic induction in both directions generated by magnetic particles will subsequently lower the resistance of the GMR structure. The induced magnetic field in the x-direction can be described as [34]:

$$B_x = \mu_0 M \frac{a^3 (a+t) d}{\left[(a+t)^2 + d^2\right]^{5/2}} \qquad (1)$$

where M is the external magnetic field, a is the radius of the magnetic particle, t is the distance of the magnetic particle to the GMR structure separated by the top layer, and d is the distance of B_x along the trace and relative to the center of the magnetic particle.

J. Nordling et.al, 2008 [36], have been exploring the use of GMRs, focusing on chip-scale applications in both flow detection and immunosorbent assays. The integrated sensor is a passive circuit consisting of four GMRs, deposited in a serpentine pattern and wired together as a Wheatstone bridge, as shown in Fig. 10.

Nordling et.al, has demonstrated the potential value of GMR sensors in the detection of bioactive magnetic particles by using a scanning readout method that takes advantage of a sample stick design, which includes on-chip magnetic reference addresses. Results were also presented that showed streptavidin-modified superparamagnetic particles (MPs) can potentially be used as a universal magnetic label.

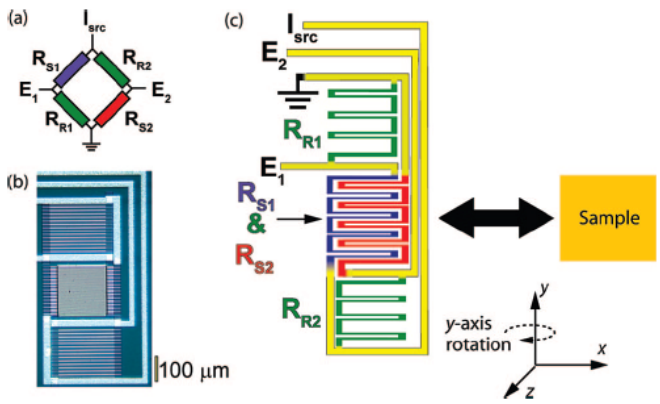

Fig. 10 a) Electronic schematic of the Wheatstone bridge. (b) Photomicrograph of the GMR sense pad showing the reference GMR traces (top and bottom) and the GMR sense pad (center). (c) Schematic illustration of the Wheatstone bridge GMR sensor shown in (b) depicting the circuit as well as the direction of the external magnetic field and the motion of the GMR relative to the sample. After J. Nordling et.al [36].

III. CONCLUSION

The giant magnetoresistance sensor has been used in sensing of bacteria and DNA.The GMR biosensor are best candidates for future device based on lab-on a-chip, compact and inexpensive detection units that directly translate the abundance of certain biomolecules into an electronic signal.

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