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Wheatstone bridge giant-magnetoresistance based cell counter

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ABSTRACT

A Wheatstone bridge giant magnetoresistance (GMR) biosensor was proposed here for the detection and counting of magnetic cells. The biosensor was made of a top-pinned spin-valve layer structure, and it was integrated with a microchannel possessing the function of hydrodynamic focusing that allowed the cells to flow in series one by one and ensured the accuracy of detection. Through measuring the magnetoresistance variation caused by the stray field of the magnetic cells that flowed through the microchannel above the GMR biosensor, we can not only detect and count the cells but we can also recognize cells with different magnetic moments. In addition, a magnetic field gradient was applied for the separation of different cells into different channels.

1. Introduction

Magnetism provides great opportunities for researchers to remotely control and detect small biological samples for biomicrofluidic applications. Since last decade, there has been some research on magnetic biochips (Pamme, 2006) such as magnetic micromixing (Rida and Gijs, 2004; Roy et al., 2009; Wei and Lee, 2009), sample separation (Rong et al., 2006; Drogoff et al., 2008; Lee and Lai, 2010), and magnetic manipulation of biological samples (Vieira et al., 2009; Lai et al., 2010; Lee et al., 2012). Besides, quantitative detection of biological samples using magnetic approaches is also an important topic of research.

Magnetic immunoassay is one novel type of immunoassays that can quantitatively detect biomolecules. The mechanism of magnetic immunoassay is that magnetic labels/beads are conjugated to either an antibody or an antigen that is specifically binding to the antibody. The quantity of the analyte is proportional to the magnetic beads, whose quantity can be determined by a magnetic measurement, such as measuring the remanent magnetic flux (Enpuku et al., 1999) or the magnetization relaxation time (Matz et al., 2001) of magnetic particle clusters, measuring the reduction of AC magnetic susceptibility of the mixture (Krause et al., 2007; Nikitin et al., 2007), and using an optical approach to measure the amount of two-particle structures created by the conjugation between antigens and antibodies (Ranzoni et al., 2011).

In addition to the methods mentioned above, magnetoresistance (MR) can also be used for determining the quantity of the analyte in magnetic biosensing. The amount of target biomolecules/cells can be estimated by measuring the MR signal variation of the MR-based biosensor caused by the magnetic micro- or nanoparticles that are attached on the target sample. In 2008 Osterfeld et al. proposed a prototypical MR-based biosensor (Osterfeld et al., 2008) that can detect the target molecules attached with magnetic nanoparticles through MR measurement. Similarly, Vavassori et al. utilized magnetic domain walls of patterned ferromagnetic films to attract nanomeric magnetic beads, and estimated the amount of beads according to the MR variation of the ferromagnetic films (Vavassori et al., 2008). So far, cell detection using MR-based biosensors is seldom referred to in the literature partly because it is more challenging than biomolecule detection (Huang et al., 2013). In this study, we designed an MR-based biosensor that can be used to count flowing magnetically-labeled cells in a microfluidic channel. In addition, the sorting of different cells was also demonstrated in our experiment.

Flow cytometer, which can rapidly count and separate cells that belong to different populations, is one of the most important instruments in the field of basic and clinical medicine (Vignali, 2000), and it has been widely used for the research on cell immunoassay, cell cycle, ploidy analysis (Tzur et al., 2011), and so on. Today, most of the flow cytometers are based on the fluorescent sensing technology. This technology is mature and practical, but the cost is very high. Therefore, the purpose of this study is to develop an alternative technique that is more economical for cell counting by the integration of the highly-developed spintronics and microfluidics.

2. Experiment details

2.1. Cell counter design

Fig. 1 shows the schematic of the magnetic cell counter setup. The cell counter was composed of a giant-magnetoresistance (GMR)

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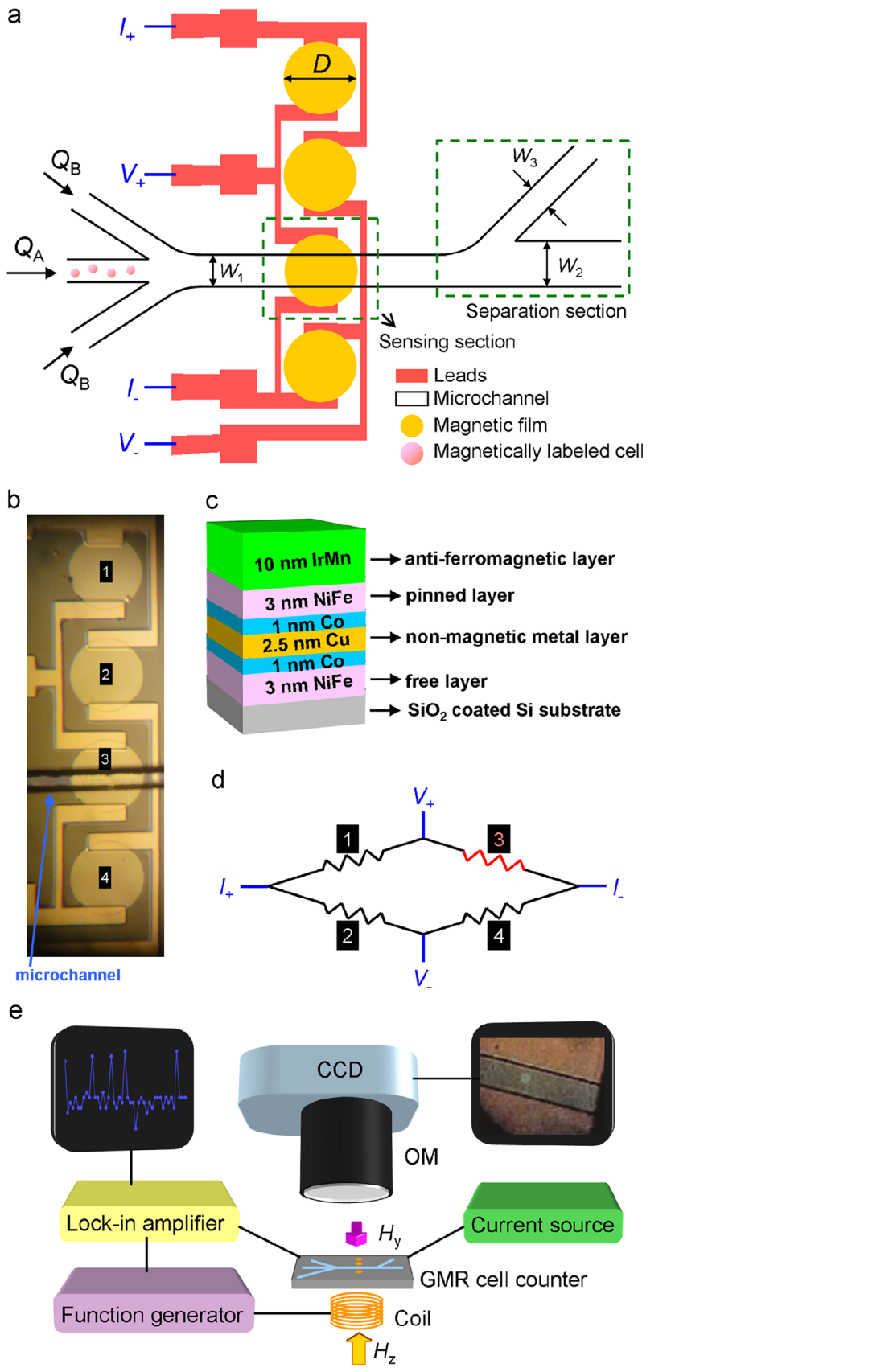

Fig. 1. (a) Schematic of the spin-valve GMR cell counter structure. (b) Micrograph of the Wheatstone bridge composed of four GMR discs, the third of which is traversed by the microchannel. (c) The layer structure of the spin valve used in this study. (d) Equivalent circuit of the Wheatstone bridge in (a) and (b), in which I_+, I_-, V_+ and V_- indicate the current and voltage connecting points for the electrical measurements. (e) Experimental setup for the cell detection. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)