AA01

Design, Fabrication, and Application of Nanomagnetic Biosensors and Biochips

Shan X. Wang*[1,2]

[1]Department ofMaterials Science and Engineering, Stanford University, Stanford, CA 94305-4045, USA
[2]Department of Materials Electrical Engineering, Stanford University, Stanford, CA 94305-4045, USA

*Corresponding author: sxwang@stanford.edu, Phone: +1 650 723 8671

Magnetic nanotechnology is finding wide applications in medicine, most notably in magnetic resonance imaging and magnetic separation. However, even more exciting applications of nanotechnology in fighting cancer, heart diseases, and infectious diseases are emerging. We are developing nanomagnetic biosensors and biochips which are sensitive and quantitative molecular detection devices based on magnetic nanotags (nanoparticles, 10-100 nm in mean diameter) and spin valve sensor arrays. The magnetic biochips can be used for rapid and portable DNA fingerprinting, pathogen detection, and proteomics.

We have designed and fabricated several types of such magnetic biochips (MagArray) consisting of arrays of spin valve detectors with appropriate dimensions, surface chemistry, and microfluidics. An ASIC circuit with a footprint of 2 mm by 2 mm and including row and column addressing decoders and parallel fast readout schemes have been designed and fabricated (Fig. 1). The MagArray chips feature redundant and high density of sensors, with a sensor density as high as 0.1 million sensors per squared cm. An advanced electronic test station has been set up as a demonstration vehicle for the integrated evaluation of our magnetic biochips with the custom magnetic nanotags and DNA-based biochemistry. The system is capable of detecting down to 1-30 nanotags.

Real-time detection of biological events in the context of DNA and protein assays has been successfully performed in laboratories, suggesting that MagArray holds unparalleled capabilities as compared to existing biochip technologies. Several practical issues need to be addressed in time for MagArray to emerge as a killer application for biomedicine and biodefense in the near future.

This work is supported in part by US Navy/ DARPA and National Cancer Institute.

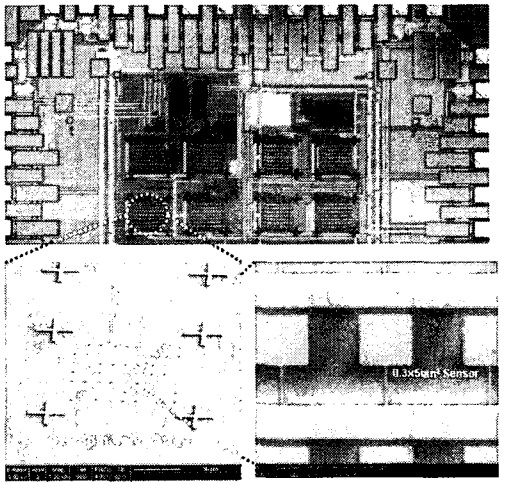

Fig. 1. high density CMOS-integrated nanomagnetic biochip with 1008 sensors on a footprint of 2 mm by 2 mm..

REFERENCES

[1] G. Li, V. Joshi, R. L. White, S. X. Wang, J. T. Kemp, C. Webb, R. W. Davis, J. Appl. Phys., 93, 7557-9, 2003.
[2] S.-J. Han, H. Yu, L. Xu, R. J. Wilson, N. Pourmand, and S. X. Wang, Proceedings of International Electron Device Meeting (IEDM), Paper #28.2, San Francisco, CA, USA, December 11-13, 2006.

AA02

Magnetoresistive Sensors and Magnetic Nanoparticles for Biotechnology

G. Reiss, A. Hütten, A. Thomas, J. Schmalhorst, M. Schilling, A. Weddemann

Bielefeld University, Department of Physics, P.O. Box 100 131, 33501 Bielefeld, Germany

The detection as well as the manipulation of single molecules on a common technological platform is of great interest for both basic research on biological or chemical systems as well as for applications in, e.g., antibody detection. A promising approach is the detection of small magnetic carriers[1] with the newly developed magnetoresistive sensors which would be capable of creating a completely electronic measurement system[2]. Moreover, this system would be addtionally compatibe[1] with an important development in microelectronics, namely the so called MRAM. Both the principles of the measurement technique as well as new achievements in the preparation of magnetic carriers are demonstrated.

It is shown that paramagnetic beads can be detected by highly sensitive magnetoresistive sensors yielding a purely electronic signal. New materials like magnetic Heusler alloys and MgO tunneling barriers have recently increased the potential capabilities of these sensors dramatically. Even the magnetic switching by direct spin transfer from the current running through the devices seems now applicable, avoiding problems with downscaling and power consumption(Fig.1).

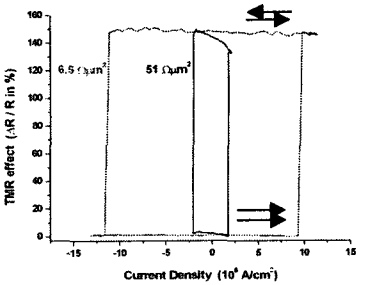

Fig. 1. Dependence of the resistance of magnetic tunneling cells on the density of current pulses applied prior to the resistance measurement at 19mV bias voltage.

The two curves are for extremely low (red) resistive and medium resistive (black) tunneling cells with MgO barriers[3].

The high resistance state corresponds to antiparallel and the low resistance state to parallel alignement of the magnetization of the ferromagnetic electrodes (indicated by arrows).

Besides the use of such devices in storage or logic microelectronic circuits, they can measure magnetic fields with a high sensitivity. In particular, stray fields arising from magnetic markers from biomolecules and thereby the molecules themselves can be detected[2]. Different configurations are discussed and the results for Giant Magnetoresistance sensors are compared to an analysis of the same biological systems marked with fluorescence dyes. This shows, that down to a conentration of about 10 pg/µl of, e.g., DNA molecules, the magnetoresistive technique is competitive to nowadays standard analysis methods. The capability of the Tunneling Magnetoresistance sensors to detect even single markers is additionally demonstrated.

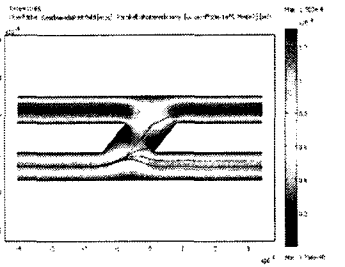

Fig. 2. Two micofluidic channels with different flow velocities (color bar) connected by a small bridge with a magnetic gradient field. The traces of the particles are shown as black lines. The gradients of the flow velocity and the magnetic field separate the particles coming from the left side into small particles in the lower and large ones in the upper channel.

The magnetic carriers detected by the sensors are mostly paramagnetic magnetite beads embedded in a polymer matrix with sizes from some µm down to about 100nm. They are linked to, e.g., DNA or proteins (often by a avidin-biotin bond) and thereby enable highly specific detection of complementary molecules. These magnetic particles often suffer from their broad size distribution and the relatively small magnetic moment. With the new colloidal synthesis of superparamagnetic or ferromagnetic Co, CoFe and FePt nanocrystals by, e.g., pyrolythic decomposition of CVD precursor molecules, magnetic markers with superior magnetic moments, smaller size and size distribution can be produced[1]. Here, the question about their potential to replace magnetite is addressed. Starting from a magnetic analysis of the corresponding magnetophoretic mobility of Co and FeCo based alloys their synthesis and resulting microstructural and magnetic properties as function of the underlying particle size distribution and the stability of the oleic acid ligand are discussed.

Moreover, the magnetic particles offer an additional feature: They can be manipulated on chip via magnetic field gradients running through specially designed line patterns[4]. If additionally a microfluidic environment is used for transportation, even the separation of different species within one fluid seems possible[3](Fig. 2)

We show, that this manipulation can be performed in a precise and reproducible manner, enabling locally enhanced concentration or even the measurement of binding forces with very low loading rates.

Thus, magnetic markers in combination with magnetoresistive sensors are a promising choice for future integrated lab-on-a-chip Systems.

REFERENCES

[1] Guenter Reiss and Andreas Huetten, Nature Materials-News and Views, 4 (2005) 725
[2] Guenter Reiss, Hubert Brueckl, Andreas Huetten, Joerg Schotter, Monika Brzeska, M. Panhorst, D. Sudfeld, Anke Becker, Paul B. Kamp, Alfred Puehler, K. Wojczykowski, Peter Jutzi, J. Mater. Res., **20** (2005) 3294
[3] Singulus Technologies, Semiconductor Equipment/TMR-MRAM, Hanauer Landstrasse 103, 63796 Kahl am Main, Germany (TIMARIS coating tool)
[4] M. Panhorst, P. Kamp, G. Reiss, H. Brückl, Biosens. Bioelectron., **20** (2005) 1685
[5] A. Weddemann, Diploma thesis, Bielefeld University (2006)