

MAGNETOELECTRONICS, MAGNETIC LABELS AND BIOMOLECULAR DETECTION

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INTRODUCTION: The Bead Array Counter (BARC) is a magnetic-label-based system for the detection of biomolecules. Central to this system is a microfabricated sensor chip containing giant magnetoresistance (GMR) magnetic field sensors. The third-generation sensor chip (BARC III) shown in Fig. 1 consists of 64 probe sites with a sensing area of approximately 30,000 μm^2 per site. Currently, BARC is configured as a “DNA-chip” that detects the presence of magnetically-labeled DNA samples.

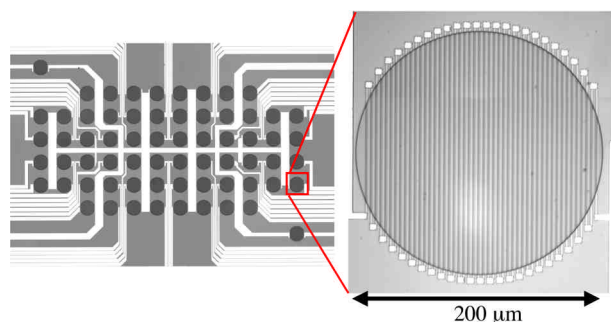


Fig. 1: A micrograph of the BARC III chip containing 64 sensor areas (dark circles). On the right is an expanded view of an individual sensor.

METHODS: The BARC III chips are an evolution of a lower density prototype (BARC II) chip that has been described elsewhere [1]. Briefly, thiolated, single-stranded DNA capture probes are arrayed on a gold surface above the embedded GMR sensors. An assay is performed by flowing biotinylated DNA samples over the probe areas and hybridization with the complementary probes occurs. Streptavidin-coated magnetic microbeads (2.8 μm diameter Dynal M-280) are then introduced into the flow cell and bind to the biotin at the hybridized DNA spots. The immobilized microbeads are detected by the GMR sensors.

The BARC III chip represents a compromise in which the sensor detection threshold was sacrificed for a nearly 10-fold increase in sensing area/probe and an 8-fold increase (to 64) in the number of probes over that of the BARC II. While BARC II was capable of detecting a single Dynal M-280 microbead, BARC III has a detection threshold of about 15 microbeads. Nevertheless, we have

demonstrated the ability to detect 30-mer samples of anthrax lethal factor (ALF) at concentrations as low as 10 fM in about 30 minutes.

DISCUSSION: Currently the electronic noise background (~15 beads) is below the chemical “noise” background (~50 beads) due to non-specific binding. Furthermore, the magnetic variability [1,2] within a sample of the Dynabeads makes ensemble averaging necessary; i.e., single-bead detection is unreliable. As the chemical background is lowered the electronic detection threshold will become a greater issue and must be addressed. Simply substituting solid, soft-ferromagnetic labels such as NiFe for the polymer-ferrite composite labels will yield a 10-fold increase in magnetoelectronic sensitivity due to larger effective magnetization [1]. Additionally, these ferromagnetic labels will be magnetically uniform [1]. With a narrowly defined range of label diameters single-bead detection will be meaningful. We are currently developing techniques for sizing and functionalizing these materials for this purpose.

Finally, it has been shown that improved signal-to-noise can be realized when the sensors have lateral dimensions comparable to those of magnetic labels [3]. However, as sensor dimensions are reduced, magnetostatic barriers become increasingly important and magnetic sensitivity is compromised [4]. Using solid ferromagnetic labels and more efficient sensor designs utilizing ring-shaped structures that are currently being developed for non-volatile computer memory should further enhance the magnetoelectronic sensitivity as well as increase the number of different biomolecules that can be simultaneously detected [4]. Such an approach provides a reasonable path to a robust, massively-arrayed biosensor.

REFERENCES: ¹M.M. Miller *et al* (2001) *J. Magn. Magn. Mat.* **225**, 138. ²D.R. Baselt *et al* (1998) *Biosens. Bioelectron.* **13**, 731. ³M. Tondra *et al* (2000) *J. Vac. Sci.* **A18**, 1125. ⁴J.J. Krebs (1996) *J. Appl. Phys.* **79**, 6087. ⁵US Patent Application 09/497,754.