

DNA fragments. To utilize the substrate area efficiently, we have employed a scheme that appears similar to magnetic random access memory (MRAM), but in fact the MagArray™ detector is distinctively different from MRAM in that the MagArray™ detector does not require conduction lines for write currents and that the signal levels in the MagArray™ detector are much smaller. The cells in the MagArray™ detector need to share preamplifiers and a lock-in amplifier (or a narrowband pass filter) so that signals as small as about 1 μ V can be reliably detected. Each detector is connected to the drain of a switching transistor and each cell framed by one row conduction line (word line) and one column conduction line. We can read an individual detector by turning on the corresponding transistor and passing a sense current through the detector. The voltage change in the column lines are detected by the preamplifier and the lock-in amplifier.

[0080] A typical block with 1024 cells in the MagArray™ detector has been designed. Each block consists of a row decoder, a column decoder, a preamplifier, current sources, and an array of cells. At least one column of cells are covered with thick polymers, rendering them insensitive to magnetic nanoparticles, and thus can be used as reference detectors in a bridge circuit or a subtraction circuit. We estimate that the MagArray™ detector can have a density of as high as about 10^6 cells/cm² (one detector per cell).

[0081] The DNA probes can be immobilized on the MagArray™ detector chips by conventional spotting or ink-jet printing. Each circular feature of DNA probes (or binding molecules) spans over a multiplicity of cells, but the probes bind only to the active detector area of each sensor within the feature. There is at least one feature per DNA probe to capture a corresponding DNA target. Unspecifically bound probes are then washed away without cross contamination. After hybridization with magnetically tagged DNA target samples, each detector within the same DNA feature will be interrogated individually, the resulting average signal is used to identify and quantify the DNA target captured by the DNA probes at a given site. In spite of the high density of chemically active sensor surfaces, they still occupy only a fraction of the cell area because a detector is much smaller than a cell.

[0082] Alternatively, to improve the chemical sensitivity of the MagArray™ detector, we have integrated microfluidic circuits directly onto the detector array so that DNA probes and target samples are only attached or directed at the detector surfaces which are sensitive to magnetic tags. Here we may achieve one detector (instead of one feature) per DNA probe, maximizing the number of different DNA probes which can be accommodated on a chip. Several methods exist to attach DNA probes specifically to surfaces such as silicon dioxide or gold which are selectively deposited on active detector surfaces only. This approach will greatly boost the overall chemical sensitivity, allowing us to detect minute amount of biomolecules, e.g., 1-10 target DNA fragments, to minimize the amount of DNA probes spotted on the MagArray™ detector, and to speed up the detection process.

[0083] The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques

discovered by the inventors to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the scope of the invention.

EXAMPLES

Example 1

Detection of Magnetite Nanoparticles

[0084] A series of experiments was carried out to demonstrate that in addition to Co, Fe, and their alloys, ferrite such as magnetite and Mn-ferrite can also serve as biological tags, in accordance with the present invention. A monolayer of 16-nm Fe₃O₄ nanoparticles (NP) on 0.3- μ m wide spin valve sensors was coated using polyethylenimine (PEI)-mediated self-assembly method (see, S. Sun, et al., *J. Am. Chem. Soc.*, 124, 2884 (2002)), as shown in FIG. 3A. It was found that the voltage signal from a spin valve covered magnetite nanoparticles are nearly proportional to the bias voltage applied to the sensor as expected, shown in FIG. 3B, while the signal from a reference spin valve not covered with any magnetite nanoparticles is nearly zero. The voltage signals were measured from a Wheatstone bridge circuit by a lock-in amplifier at different bridge circuit biases. Furthermore, it is demonstrated that the measured signals could be well described by an analytical model, such as described by G. X. Li and S. X. Wang in *IEEE Trans. Magn.*, 39(5), 3313-5, (2003).

[0085] The detection of hundreds of magnetite nanoparticles in a patterned monolayer by a spin valve sensor was also demonstrated. It was found, using an experiment similar to that described above, that the maximum resistance change of the spin valve due to about 630 magnetite particles self assembled at the top surface of the spin valve was about 1.3 Ω . In other words, the signal per particle was roughly 2 m Ω , which is equivalent to 2 μ PV of signal voltage if the sense current is 1 mA. The detection limit in this experiment was approximately 55 m Ω , suggesting that the minimum detectable number of the magnetite nanoparticles is about 30. However, it seems apparent that with a more sensitive sensor, such as magnetic tunnelling junctions and higher moment nanoparticles such as FeCo, an even lower detection limit of nanoparticles is reachable. Consequently, it is readily evident from this example that it is realistic to detect from tens of magnetic nanoparticles to single magnetic nanoparticles.

Example 2

Spin Valve Sensors with Ultrathin Passivation

[0086] The reliability of a 4 nm passivation layer has been studied through a series of passive corrosion studies. A prototype MagArray™ chip was submerged into one of two DNA solutions that are currently used in standard DNA microarrays. The first solution, a hybridization buffer (pH=7.5), consists of a mixture of 0.6 M NaCl, 0.06 M C₆H₅Na₃O₇ (sodium citrate), and 0.1% SDS (sodium dodecyl sulfate). As its name indicates, this solution is the primary medium for the actual hybridization step in the