

microarray. The other solution, a blocking solution (pH=7.9), is a proprietary product from Surmodics (Eden Prairie, Minn.), primarily used to remove nonspecific binding sites in the test area. This process increases the likelihood of target molecules interacting with probes. The final addition to these solutions was the DNA (sonicated salmon sperm DNA) at a concentration of 0.1 mg/mL.

[0087] The performance of the spin valve sensor after DNA solution exposures was evaluated by measuring its magnetoresistance (MR) ratio, $\Delta R/R_0$. This parameter was tracked over time in solution. The first step of the experiment was to locate an active spin valve sensor (width of about 300 μm) with an MR ratio that was reasonably high, about 6-7%. The MR ratio was measured by use of a probe station setup that gave resistance data with respect to applied field. The chip was placed in contact with a selected DNA solution for repeated 30 minute cycles after which the chip was removed, washed with deionized water, air dried, and measured for MR. After 2 hours of cycling, the chip was left in solution for a total of 24 hours and tested a final time. Note that the sensor currents were turned off when the detectors were in the solutions because hybridization and signal detection could be done sequentially.

[0088] The testing results for the blocking solution are shown in FIG. 4. All of the MR values lie between 6-7% with the highest deviation from the 0th hour test being around 0.15%. The ΔR values deviate about $\pm 1 \Omega$ from the 0th hour value. Similarly, the results for the chip in hybridization solution show no dramatic difference from the blocking solution. The distribution of values is a bit wider for both MR and ΔR . The MR varies no more than 0.4% from the 0th hour and the ΔR scatter is within 4 Ω . Thus, the spin valve sensor maintains reasonable levels for MR and ΔR through all hours of testing. These results support the MagArray™ design strategy of using ultrathin passivation layer.

Example 3

Synthetic Ferrimagnetic Nanoparticles

[0089] Here we disclose novel magnetic nanoparticle tags that are fabricated by physical methods instead of chemical routes and are suitable for labeling the target biomolecules to be detected in MagArray™. The tags consist of at least two thin ferromagnetic layers, preferably $\text{Fe}_x\text{Co}_{1-x}$, $0.5 < x < 0.7$, or $\text{Fe}_x\text{Co}_{1-x}$ based alloys. It is well known that $\text{Fe}_x\text{Co}_{1-x}$ has the highest saturation magnetization (about 24.5 kGauss) among the known ferromagnetic materials (Bozorth, R. M., *Ferromagnetism*, D. Van Nostrand Company, 1951). These ferromagnetic layers are separated by nonmagnetic spacer layers such as Ru, Cr, Au, etc., or their alloys. The spacer layers are appropriately engineered to make the ferromagnetic layers coupled antiferromagnetically so that the net remnant magnetization of the resulting particles are zero or near zero, as shown in FIG. 5. A gold cap is added at the top of the antiferromagnetic stack so that the nanoparticle can be conjugated to biomolecules via the gold-thiol linkage or other chemical bonding. The edge of the nanoparticles can be passivated for chemical stability with Au or other thin inert layers. Many physical methods can be conceived by those familiar with the art to fabricate the nanoparticles described above.

Example 4

Additive Fabrication Method of Synthetic Ferrimagnetic Nanoparticles

[0090] An additive fabrication method is shown in FIG. 6. As shown therein, going from the top of the figure to the bottom in the direction of the arrows, the fabrication method begins with the deposition of a continuous thin layer (for releasing particles later) on an ultrasmooth substrate, then depositing a mask layer on the release layer. Finally, identical holes are patterned into the mask layer.

[0091] In the next step, the film stack is deposited on the mask layer. The film stack, similar to that shown in FIG. 5, includes the ferromagnetic layers, spacer layers, and the gold cap. Following the deposition, the mask layer is removed, lifting off the unwanted films deposited on the mask layer. Finally, the release layer is removed, lifting off the magnetic nanoparticles into a solution which can then be used as magnetic tags.

Example 5

Integration of Microfluidic Channels with Detectors

[0092] In order to improve the chemical sensitivity of the MagArray™, we have integrated microfluidic circuits (Thorsen, T., et al., *Science*, Vol. 298, p. 580 (2002)) directly on 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, thereby minimizing waste of DNA probes or DNA targets. The schematic of such systems are shown in FIGS. 7A and 7B. The DNA probes are attached specifically to detector surface. In FIG. 7A, the detector is made slightly longer than 20 μm which is the width of microfluidic channel. The long detector is suitable for relatively large quantities of DNA samples. In FIG. 7B, the detector is made shorter than the width of the microfluidic channel. The short detector is more suitable for relatively small quantities of DNA samples. In the latter case, applied electric field or magnetic field gradient, and hydrodynamic focusing schemes can be used to direct the DNA samples to the detector surface. It is also conceivable to make the microfluidic channel in FIG. 7B as wide as the detector length.

[0093] All of the compositions and/or methods and/or processes and/or apparatus disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and/or apparatus and/or processes and in the steps or in the sequence of steps of the methods described herein without departing from the concept and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the scope and concept of the invention.