probes are bound to beads. Using the magnetic chip of the present invention it is possible to perform one or more steps of a multistep assay prior to dispersing the beads on the chip surface, while other steps may be performed after dispersal. This possibility enhances the flexibility of the system. For example, one could perform a series of hybridizations under different conditions (e.g., different temperatures), assemble a random array of beads, and then perform additional steps (e.g., enzymatic reactions such as ligation and then detection) under uniform conditions.

[0191] VII. Detection

[0192] Numerous detection methods are known in the art and are suitable for detecting beads, probes, targets, and the interaction between probes and targets. In general, an appropriate detection scheme will depend upon the method used to encode or label the beads, probes, and/or targets. For example, where a labeling or encoding scheme employs optically detectable moieties, e.g., fluorescent dyes, confocal scanning or CCD detection may be appropriate. If oligonucleotide tags are employed direct sequencing, as described above, may be used. Various detection methods that are useful in the context of the invention are described below. These methods are, in general, known in the art and the descriptions provided below are not intended to be limiting in any way. Different embodiments of the invention may employ different detection techniques or combinations thereof.

[0193] A. Confocal Scanning

[0194] This method is now in standard use to perform fluorescence scans of microarrays. After forming a random order array on the magnetic chip, the chip is inserted into a commercially available fluorescence scanner for data collection. As mentioned above, a density of 10,000 oligonucleotide probes/mm^2 surface area is readily achievable. Typically, a 2.8 μm diameter bead may contain about 100,000 molecules that are covalently bound to the surface. Assuming a worst case hybridization and signal collection efficiency of only 1%, this results in approximately 1000 fluors/bead. Detection thresholds for most commercial scanners are close to one fluor/bead, yielding three orders of magnitude in the signal dynamic range for each site (bead) on the array.

[0195] B. CCD Detection

[0196] This detection scheme is an alternative to confocal scanning. Advantages include continuous data collection over the entire chip. When using a method such as pyrosequencing to decode the beads, CCD detection may be the method of choice although signal to noise ratios may be slightly better with confocal scanning.

[0197] C. Direct Sequencing

[0198] On-bead sequencing of tags and/or probes is discussed above.

[0199] D. Integrated Photodetectors

[0200] Fabrication and use of on-chip photodetectors is discussed above.

[0201] E. Detecting Beads Having Varying Magnetization

[0202] As discussed above, an encoding/decoding scheme for magnetic beads may involve detecting differences between populations of beads having different magnetization. Magnetic fields (and hence the magnetic particles) are detectable with spin valve technology. This technology is at the core of the multi-billion dollar computer hard-drive industry. Briefly, the spin valve sensors consist of materials whose resistance changes in response to a magnetic field. Thus, by passing a current through a strip of such material and measuring the resistance, once can detect the local magnetic field. Data is read from a spinning hard drive by such sensors. Advances in such materials (Giant MagnetoResistive—GMR) have enabled the fabrication of micron-scale sensors with very high magnetic field detection sensitivities. This technology has been applied to detect magnetic bead particles by hybridization of the bead particles to an array of fabricated sensors as described, for example, in R. L. Edelstein, et al., "The BARC biosensor applied to the detection of biological warfare agents", *Biosensors and Bioelectronics,* 14 (2000) pp. 805 813 (See also WO0061720). As described therein, the presence or absence of a magnetic bead above a fabricated spin valve is detected by attachment of the bead to the surface above the valve. In our setup, we would use the magnetic bead chip to form arrays of such beads, and use the spin valve read-head to scan the magnetic fields (and encoding) of the various beads by the response. In the context of the present invention, a similar detection scheme could use a single read head (spin valve) which would scan the magnetic chip for magnetic fields and variation on the fields. Great sensitivity can be obtained using schemes such as lock-in detection. The chip may also be slowly spun in a configuration like a hard drive to leverage this highly developed technology.

[0203] Other embodiments of the invention will be apparent to those skilled in the art from a consideration of the specification or practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with the true scope and spirit of the invention being indicated by the claims that follow the Examples.

EXAMPLES

Example 1

Fabricating Magnetic Chips

[0204] (1) Cobalt film approximately 700-1000 nm thick was deposited on a silicon wafer with a diameter of approximately 3.0 inches. The cobalt layers were sputtered sequentially without breaking vacuum using a UHV DC magnetron sputtering system at 2×10^{-8} torr. The deposition rate was 0.39 nm/sec. An e-beam lithographic pattern was written using a Hitachi HL-700F instrument, a direct write patterning tool with a minimum feature size of 50 nm, and a UVN30 photoresist at 5.5 Krpm spin for 40 sec. The resulting photoresist layer was approximately 500 nm thick. The photoresist was then developed with MF-CD 26 for 30 sec. The chip configuration defined by the mask resulted in a pattern of diamond-shaped magnetic regions.

[0205] To fabricate the magnetic islands, argon sputter etching was performed in an ion-milling etcher without breaking vacuum and with the photoresist as the mask. Time intervals of 10 min etching/10 min cooling were used for a total of 80 min. The remaining photoresist was stripped