

## DEVICES AND METHODS TO FORM A RANDOMLY ORDERED ARRAY OF MAGNETIC BEADS AND USES THEREOF

### CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 60/223,125, filed Aug. 7, 2000, which is incorporated herein by reference in its entirety for all purposes. Inventors' U.S. Provisional Application No. 60/202,357, filed May 5, 2000, is also incorporated herein by reference in its entirety.

[0002] This invention was made with U.S. Government support pursuant to grant no. HG 00205 from the National Institutes of Health. The U.S. Government may have certain rights in this invention.

### FIELD OF THE INVENTION

[0003] Embodiments of the invention relate to devices and methods for forming arrays of magnetic particles, arrays of such particles, and uses of the arrays.

### BACKGROUND OF THE INVENTION

[0004] Progress in biology and in chemistry is leading to an ever-increasing demand for high-throughput, cost-effective analysis of complex mixtures. This demand has in turn stimulated the development of compact, high-density array devices. These devices are used to perform a wide variety of assays in a number of different contexts. Such assays typically involve classes of molecules including nucleic acids, proteins, antibodies, small organic molecules, etc. Applications include genotyping, immunodiagnosics, and screening of drug candidates. For example, the complete DNA sequence of a number of organisms including humans has been determined or will be determined in the near future. The next step is to quantify and understand the DNA sequence variation within particular individuals, thereby enabling identification and possibly treatment of genetic diseases, personalized selection of medications based on an individual's genetic makeup (pharmacogenomics), and a deeper understanding of the genetic basis for phenotypic variability. Arrays will play a key role in developing the massively parallel technologies needed to realize these possibilities.

[0005] Although diverse in terms of the specific molecules and assays involved, a common conceptual scheme underlies most array technologies. In general, a probe or sensor molecule is attached in some fashion to a substrate. The probe is contacted with a sample (typically, though not necessarily, a complex mixture) and an interaction takes place between the probe or sensor and a component of the sample (a target), which is then detected. In many array-based assays the target is bound (either covalently or non-covalently) to the probe, and binding is detected via a range of different approaches, thereby revealing the presence, identity, or other features of the target.

[0006] In most array technologies, the identity of a probe is positionally encoded, i.e., the probe is attached either directly or indirectly to a typically planar surface, and the position of the probe on the surface serves to encode the identity of the probe. For example, oligonucleotide arrays

are used to understand the DNA sequence variation between individuals, e.g., by performing single nucleotide polymorphism (SNP) genotyping. DNA obtained from an individual can be labeled (possibly after or during an amplification step) and then contacted with an array consisting of thousands of oligonucleotides attached to a substrate. Each of the oligonucleotides has a known sequence and is present at a known location on the substrate. The location of the hybridized nucleic acid molecule can be determined, e.g., by observing a fluorescent signal coming from the label. This location can be used to determine the sequence of the oligonucleotide bound to the DNA, which in turn reveals the sequence of the DNA. Similar approaches are widely used for determining mRNA expression patterns, and applications involving detection of proteins are contemplated. The current and potential future impact of DNA biochips is reviewed in Brown, P. and Botstein, D., "Exploring the new world of the genome with DNA microarrays", *Nat. Genet.*, 21 (1 Suppl):33-37, 2000 and in Lockhart, D. and Winzeler, E., "Genomics, gene expression and DNA arrays", *Nature*, 405(6788):827-826, 2000.

[0007] Arrays such as substrate-bound oligonucleotide arrays have been fabricated using ink-jet printing and high-speed robotics, which individually deposit the oligonucleotides on a substrate as spots. The oligonucleotides are then permanently bound to the substrate. Oligonucleotide arrays have also been fabricated using photolithography and light-directed combinatorial chemical synthesis. Other array manufacturing techniques include screen printing and photodeposition. These techniques typically require multiple fabrication steps, are labor-intensive and time-consuming, and are subject to variability. In addition, the identity of each probe on the array must generally be "pre-registered" by its position on the array. Such arrays are not easily adaptable or reusable as the probes are permanently bound to the substrate. In addition, these arrays suffer from a significant lack of flexibility since a new fabrication protocol is needed to change any of the probe sequences or to add new probes to the array.

[0008] Thus while array designs and manufacturing techniques such as those described above have already proven to be highly effective tools for genetic analysis and diagnostic applications, there is considerable room for improvement. The present invention addresses some of the limitations of currently existing array technologies.

### SUMMARY OF THE INVENTION

[0009] Embodiments of the invention are directed to devices and methods for forming random arrays of magnetic particles, to arrays formed using these devices and methods, and to methods of using the arrays. As described further below, the invention provides an assembly comprising magnetic domains that produce localized magnetic fields capable of immobilizing magnetic particles such as commercially available magnetic beads. Probe or sensor molecules can be coupled to the beads, which are then dispersed on the assembly, forming a random order array. The arrays can be used for analyzing samples, targets, and/or the interaction between samples and targets. The invention finds particular use in processes such as high-throughput genotyping and other nucleic acid hybridization based assays. The invention offers a number of significant advantages in comparison with traditional DNA arrays in which probes are bound to a substrate.