

[0034] The methods and systems disclosed herein are much more sensitive than the previously reported optical detection systems and the other magnetic detection schemes of the known prior art. The inventive systems are more efficient and sensitive than BARC, since they involve spin valve or MTJ detector designs. Additionally, nanometer-scale particles of high magnetic moment are used as biomolecule tags instead of larger particles with more dilute magnetic material. The systems are more sensitive than functional MRI (fMRI) systems. Calculations indicate that the amount of gadolinium required for detection by fMRI far exceeds the amount of magnetic nanotags that can be detected with the inventive systems. Finally, the inventive systems do not require the sophisticated cooling apparatuses required for detection by SQUID (Superconducting Quantum Interference Device) detector systems.

[0035] Aspects of the invention include magnetic nanoparticles, detectors, detection systems, and methods for their use. Various aspects of the invention are discussed below. U.S. Trademark Application Serial No. 78285336 was filed on Aug. 9, 2003 for the mark MAGARRAY (Applicant Sunrise Associates).

[0036] Nanoparticles

[0037] Nanoparticles useful in the practice of the present invention are preferably magnetic (i.e., ferromagnetic) colloidal materials and particles. The magnetic nanoparticles can be high moment magnetic nanoparticles which are small in size so as to be superparamagnetic, or synthetic antiferromagnetic nanoparticles which contain at least two layers of antiferromagnetically-coupled high moment ferromagnets. Both types of nanoparticles appear "nonmagnetic" in the absence of magnetic field, and do not normally agglomerate. In accordance with the present invention, magnetizable nanoparticles suitable for use comprise one or more materials selected from the group consisting of paramagnetic, superparamagnetic, ferromagnetic, and ferrimagnetic materials, as well as combinations thereof.

[0038] The magnetic nanoparticles preferably possess the following properties: (1) their remnant magnetization is as small as possible so that they preferably will not agglomerate in solutions (either superparamagnetic particles or antiferromagnetic particles can satisfy this requirement); (2) the tags display high magnetic moments under a modest magnetic field of about 100 Oe so they can be readily detected; (3) the size of the tags preferably is comparable to the target biomolecules so that they do not interfere with the DNA hybridization process and other biological processes; (4) the tags preferably are uniform and chemically stable in a biological environment; and/or (5) the tags preferably are biocompatible, i.e., water soluble and functionalized so that they are readily attached to DNA fragments or other biomolecules.

[0039] The nanoparticles are preferably high moment magnetic nanoparticles such as Co, Fe or CoFe nanocrystals which are superparamagnetic at room temperature. They can be fabricated by chemical routes such as salt reduction or compound decomposition in appropriate solutions. Examples of such magnetic nanoparticles have been published in the literature (S. Sun, and C. B. Murray, *J. Appl. Phys.*, 85: 4325 (1999); C. B. Murray, et al., *MRS Bulletin*, 26: 985 (2001)). These particles can be synthesized with

controlled size (e.g., 5-12 nm), are monodisperse, and are stabilized with oleic acid. In accordance with the present invention, it is also possible to fabricate high magnetic moment nanoparticles in a nanocluster deposition system (D. J. Sellmyer, et al., Chap. 7, *Handbook of Thin Film Materials*, edited by H. S. Nalwa, Academic Press (2002)). These particles have been developed for applications in bioconjugation. Magnetic nanoparticles and nanopowders suitable for use with the present invention include but are not limited to Co, Co alloys, ferrites, Cobalt nitride, Cobalt oxide, Co—Pd, Co—Pt, Iron, Iron alloys, Fe—Au, Fe—Cr, Fe—N, Fe<sub>3</sub>O<sub>4</sub>, Fe—Pd, Fe—Pt, Fe—Zr—Nb—B, Mn—N, Nd—Fe—B, Nd—Fe—B—Nb—Cu, Ni, and Ni alloys. Alternatively and equally acceptable, a thin layer of gold can be plated onto a magnetic core, or a poly-L-lysine coated glass surface can be attached to a magnetic core. Suitable nanoparticles are commercially available from, e.g., Nanoprobes, Inc. (Northbrook, Ill.), and Reade Advanced Materials (Providence, R.I.).

[0040] Magnetic nanoparticle tags can be fabricated by physical methods instead of chemical routes, and are suitable for labeling the target biomolecules to be detected. The tags comprise at least two thin ferromagnetic layers, preferably Fe<sub>x</sub>Co<sub>1-x</sub>, wherein x is 0.5 to 0.7, or Fe<sub>x</sub>Co<sub>1-x</sub> based alloys. Fe<sub>x</sub>Co<sub>1-x</sub> has the highest saturation magnetization (about 24.5 kGauss) among the known ferromagnetic materials (R. M. Bozorth, *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. The antiferromagnetic coupling can be achieved via RKKY exchange interaction (S. S. P. Parkin, et al., *Phys. Rev. Lett.*, 64(19): 2304 (1990)) and magnetostatic interaction (J. C. Slonczewski, et al., *IEEE Trans. Magn.*, 24(3): 2045 (1988)) as practiced in the magnetic data storage industry. However, the antiferromagnetic coupling strength preferably is moderate so that the particles can be saturated (i.e., magnetization of all layers become parallel) by an external magnetic field of about 100 Oe. This can be achieved by adjusting layer thicknesses and by alloying the spacer layer.

[0041] To facilitate the bio-conjugation of the nanoparticle, a gold cap can be added at the top of the antiferromagnetic stack so that the nanoparticle can be conjugated to biomolecules via the gold-thiol linkage. Furthermore, appropriate surfactants can also be readily imparted to the nanoparticles, rendering them water-soluble. The edge of the nanoparticles can be passivated for chemical stability with Au or other thin inert layers.

[0042] Many physical methods can be conceived by those familiar with the art to fabricate the nanoparticles described above. A film stack can be made of nanometer-scale ferromagnetic and spacer layers, so they need to be deposited on ultrasmooth substrates (or release layer). The mask layer can be formed by imprinting, etching, self assembly, etc. Sub-