

[0022] Other embodiments of the present disclosure are directed to sensing/imaging methods and apparatus utilizing one of the IC-based magnetic and/or electric field generating arrays as introduced above, or other arrangements of magnetic and/or electric field-generating devices. For example, in various aspects of these sensing embodiments, a micro-coil array, a micropost array, or other arrangement of field-generating devices (e.g., see the various structures described in PCT Application No. PCT/US02/36280, filed Nov. 5, 2002, entitled "System and Method for Capturing and Positioning Particles," International Publication No. WO 03/039753 A1) may be controlled using signals of various frequencies so as to be capable of detecting one or more cells, particles or objects of interest, and even the type of particle or object of interest, by measuring resonance characteristics associated with interactions between samples and one or more of the field-generating devices.

[0023] In some embodiments, radio frequency (RF) signals are employed to facilitate detection, imaging and/or identification. One of the principles underlying these RF embodiments is that an RF field is capable of interacting with virtually any particle (biological or otherwise) that conducts electricity at the RF signal frequency, or is polarizable electrically or magnetically. Accordingly, in these RF sensing embodiments, the interaction between an RF field and an object in the vicinity of the RF field may be exploited to determine the position of one or more objects of interest so as to facilitate imaging of the object(s). In this manner, semiconductor-based/microfluidic hybrid systems and methods as disclosed herein may be configured to detect and image biological cells, particles and other objects of interest via purely electrical/magnetic means using RF signals, and without resorting to chemical agents or optical techniques. Based on such RF imaging techniques, various implementations of a hybrid system according to the present disclosure may incorporate feedback control mechanisms, whereby samples of interest may be manipulated based on acquired images of the samples.

[0024] In some aspects, the RF techniques disclosed herein may be used not only to detect and image particles, but also to identify different types of particles/objects of interest. This type of identification may be accomplished, for example, by measuring spectral responses of RF field/particle interactions over a broad range of frequencies and comparing these responses to known frequency dependent behavior of various materials in electromagnetic fields. In other aspects, RF techniques disclosed herein also may be used to conduct local measurements of magnetic resonance (including ferromagnetic resonance) in a uniform magnetic field applied to a sample or object of interest to thereby identify the material of the sample based on characteristic oscillating frequencies of spins (e.g., Electron Spin Resonance or "ESR") or magnetic domains (e.g., Nuclear Magnetic Resonance or "NMR"). Accordingly, methods and apparatus according to various embodiments of the present disclosure may be employed to effectively implement a Magnetic Resonance Imaging (MRI) system on a chip.

[0025] In view of the manipulation, detection, imaging and identification techniques discussed above and in greater detail below, Applicants have recognized and appreciated that semiconductor-based/microfluidic hybrid systems and

methods as disclosed herein facilitate a wide variety of new types of investigations in biomedicine and systems biology, as well as other applications.

[0026] For example, another embodiment of the present disclosure is directed to cell sorting methods and apparatus by employing IC/microfluidic hybrid methods and apparatus, as well as RF sensing/imaging methods and apparatus as introduced above. In one aspect, cell sorting methods and apparatus according to this embodiment facilitate molecularly-precise identification and rapid, highly-accurate sorting of cells. In particular, biological cells may be sorted individually with ultrahigh accuracy and with molecularly-precise identification. Such precision sorting facilitates the separation of specific (e.g., "rare") cell types or pathogens (e.g., stem cells for bone marrow reconstitution procedures in cancer patients) for clinical applications. Such precision sorting also facilitates parsing a tissue's demographics and evaluating each cell type separately, rather than collecting gene expression data on tissue from an ensemble of different cell types.

[0027] Yet another embodiment of the present invention is directed to methods and apparatus for assembling micro-scale engineered tissues. In one aspect of this embodiment, a two-dimensional cell trap array based on an IC/microfluidic hybrid system is configured to be capable of micro-scale tissue assembly with precise control of cellular demographics and spatial distribution (e.g., artificial tissues from heterotypical distributions of cells may be assembled one cell at a time). Such a technique according to one embodiment of the present disclosure represents a new way to develop novel in vitro assays for studying communication networks amongst different cell types, drug efficacy, and for fundamental physiological study in a standardized, repeatable manner.

[0028] Semiconductor-based IC/microfluidic hybrid systems and methods according to various embodiments of the present disclosure have several important technological advantages. First, a semiconductor-based/microfluidic hybrid system may be fabricated in an appreciably cost-effective manner with high yield using a mature CMOS technology and inexpensive lithographic techniques for formation of the microfluidic system portion. Such CMOS implemented systems may be made significantly small in size and appropriately packaged to withstand various environmental hazards. Advanced low-power integrated circuit techniques also facilitate the fabrication of battery-powered devices. In view of the foregoing, such systems can be made as rugged single-use disposable devices, and may be employed in a variety of applications, including potentially adverse and/or emergency situations, that would otherwise be precluded using conventional methods and apparatus. For example, small, inexpensive, battery-powered, rugged hybrid systems according to various embodiments of the present disclosure may be easily and effectively employed in emergency medical situations to quickly screen an individual's health using saliva, breath, sweat, or blood samples. Such systems also may be employed to detect biologically harmful substances in a given environment.

[0029] Additionally, as compared to conventional magnetic manipulation methods using simple magnetic tweezers or external magnets, or conventional dielectrophoresis techniques, semiconductor-based/microfluidic hybrid systems