

**METHODS AND APPARATUS FOR
MANIPULATION AND/OR DETECTION OF
BIOLOGICAL SAMPLES AND OTHER OBJECTS**

**CROSS-REFERENCES TO RELATED
APPLICATIONS**

[0001] The present application claims the benefit, under 35 U.S.C. §119(e), the following U.S. provisional applications:

[0002] Ser. No. 60/561,704, filed Apr. 13, 2004, entitled “Programmable Integrated Biochip;”

[0003] Ser. No. 60/611,370, filed Sep. 20, 2004, entitled “An I/C Microfluidic Hybrid Microsystem for 2D Magnetic Manipulation of Individual Biological Cells;” and

[0004] Ser. No. 60/627,940, filed Nov. 15, 2004, entitled “Methods and Apparatus for Manipulation and/or Detection of Biological Samples and Other Objects.”

[0005] Each of the foregoing applications is hereby incorporated herein by reference.

GOVERNMENT SPONSORED RESEARCH

[0006] Some of the research relating to the subject matter disclosed herein was sponsored by the following government grants, and the government has certain rights to some disclosed subject matter: NSF-PHY-0117795, NSF-DMR-98-09363, NSF-PHY-9871810, NSF-DMR-98-02242, DARPA-DAAD 19-01-1-0659, ONR-N0014-95-1-0104, and ONR-N00014-99-1-0347.

FIELD OF THE DISCLOSURE

[0007] The present disclosure relates generally to methods and apparatus for manipulating, detecting, imaging, and/or identifying particles or objects via electromagnetic fields. In various examples, integrated microsystem methods and apparatus are disclosed, involving electric and/or magnetic field-generating devices fabricated using conventional semiconductor techniques (e.g., Si, SiGe, CMOS, GaAs, InP) and configured to direct, sense, image, and/or identify particles or objects of interest via electric and/or magnetic field interactions. In some examples, such field-generating devices are integrated together with a microfluidic system to further facilitate movement, sensing, imaging and/or identification of particles or objects of interest.

BACKGROUND

[0008] In biological and medical sciences, it is often useful to be able to manipulate (e.g., move or direct) a biological sample (e.g., one or more cells) along a prescribed path. Manipulation of biological systems based on magnetic fields is one conventionally used method to accomplish this task. In one conventional implementation involving magnetic fields, a small magnetic bead with a chemically modified surface can be coupled to a target biological system, such as a particular cell or microorganism. Depending on the type of coating of a given bead, and the relative sizes of the bead and the target cell or microorganism, the bead may be bound to the surface of the cell or organism (exterior coupling), or ingested by the cell or organism (interior coupling). Such a “bead-bound” sample then may be suspended in a host liquid to constitute a “microfluid,” and the suspended sample in the microfluid can then be manipulated

using an external magnetic field. Devices based on this principle often are referred to as “magnetic tweezers” and have been conventionally used, for example, to trap small particles (e.g., DNA) suspended in a liquid for study.

[0009] Because magnetic fields and the magnetic beads themselves are typically biocompatible, this process is non-invasive and generally not damaging to the sample. However, conventional magnetic tweezers fail to provide individual control of multiple magnetic beads because these devices typically produce only a single field peak that may be moved; thus only a single bead or, simultaneously, a group of beads in close proximity, may be conventionally controlled within a microfluid.

[0010] Another area related to the movement and manipulation of biological samples, particles, or other objects suspended in liquid involves a phenomenon referred to as “dielectrophoresis.” Dielectrophoresis occurs when an inhomogeneous electric field induces a dipole on a particle suspended in liquid. The subsequent force on the dipole pulls the particle to either a minimum or a maximum of the electric field. Almost any particle, without any special preparation, can be trapped or moved using dielectrophoresis when it is exposed to the proper local electric field. This is an advantage of electric field-based operation over the magnetic field-based manipulation described above, as the latter mandates marking biosamples or other objects of interest with magnetic beads. However, a potential disadvantage of the dielectrophoresis is that a relatively strong electric field may damage the cell, particle or other object of interest in some circumstances.

[0011] Yet another area related to the movement and manipulation of biological samples that enables various applications in medical diagnostics and life sciences is referred to as “microfluidics.” Microfluidics is directed to the containment and/or flow of small biological samples by providing a micro-scale biocompatible environment that supports and maintains physiological homeostasis for cells and tissues. Microfluidic systems may be configured as relatively simple chambers or reservoirs (“bathtubs”) for holding liquids containing cells/biological samples of interest; alternatively, such systems may have more complex arrangements including multiple conduits or channels in which cells, particles, or other objects of interest may flow. By controlling the flow of fluids in micro-scale channels, a small quantity of samples can be guided in desired pathways within a microfluidic system. Integration of various microfluidic devices, such as valves, filters, mixers, and dispensers, with microfluidic channels in a more complex microfluidic system facilitates sophisticated biological analysis on a micro-scale. Fabrication of even some complex conventional microfluidic systems generally is considered to be cost-effective, owing to soft-lithography techniques that allow many replications for batch fabrication.

[0012] Once fabricated, however, conventional microfluidic systems (especially more complex systems) do not offer an appreciable degree of flexibility, and specifically suffer from insufficient programmability and controllability. In particular, conventional microfluidic systems that are used for analytic operations such as cell sorting are manufactured to have a specific number and arrangement of fixed channels and valves. Operation of the valves controls the flow of cells into the channels, thereby sorting them. Function of the