removal modules, cell concentration modules, and cell separation or capture modules. In addition, as for all the modules of the invention, the cell handling module is in fluid communication via a flow channel with at least one other module of the invention.

[0121] In a preferred embodiment, the cell handling module includes a cell lysis module. Cells need to be lysed in order for the target analytes inside the cells to be magnetically labeled and processed in the magnetic microchannel. Alternatively, cells that have been separated by the magnetic microchannel need to be lysed before a target analyte within the cells can be detected.

[0122] As is known in the art, cells may be lysed in a variety of ways, depending on the cell type. In one embodiment, as described in EP 0 637 998 B1 and U.S. Pat. No. 5,635,358, hereby incorporated by reference, the cell lysis module may comprise cell membrane piercing protrusions that extend from a surface of the cell handling module. As fluid is forced through the device, the cells are ruptured. Similarly, this may be accomplished using sharp edged particles trapped within the cell handling region. Alternatively, the cell lysis module can comprise a region of restricted cross-sectional dimension, which results in cell lysis upon pressure.

[0123] In a preferred embodiment, the cell lysis module comprises a cell lysing agent, such as guanidium chloride, chaotropic salts, enzymes such as lysozymes, etc. In some embodiments, for example for blood cells, a simple dilution with water or buffer can result in hypotonic lysis. The lysis agent may be solution form, stored within the cell lysis module or in a storage module and pumped into the lysis module. Alternatively, the lysis agent may be in solid form, that is taken up in solution upon introduction of the sample.

[0124] The cell lysis module may also include, either internally or externally, a filtering module for the removal of cellular debris as needed. This filter may be microfabricated between the cell lysis module and the subsequent module to enable the removal of the lysed cell membrane and other cellular debris components; examples of suitable filters are shown in EP 0 637 998 B1, incorporated by reference.

[0125] In a preferred embodiment, the cell handling module includes a cell separation or capture module. This embodiment utilizes a cell capture region comprising binding sites capable of reversibly binding a cell surface molecule to enable the selective isolation (or removal) of a particular type of cell from the sample population, for example, white blood cells for the analysis of chromosomal nucleic acid, or subsets of white blood cells. These binding moieties may be immobilized either on the surface of the module or on a particle trapped within the module (i.e. a bead) by physical absorption or by covalent attachment. Suitable binding moieties will depend on the cell type to be isolated or removed, and generally includes antibodies and other binding ligands, such as ligands for cell surface receptors, etc. Thus, a particular cell type may be removed from a sample prior to further handling, or the assay is designed to specifically bind the desired cell type, wash away the non-desirable cell types, followed by either release of the bound cells by the addition of reagents or solvents, physical removal (i.e. higher flow rates or pressures), or even in situ lysis.

[0126] In a preferred embodiment, as described above, cell separation or capture can be achieved within the magnetic microchannel.

[0127] Alternatively, a cellular "sieve" can be used to separate cells on the basis of size. This can be done in a variety of ways, including protrusions from the surface that allow size exclusion, a series of narrowing channels, a weir, or a diafiltration type setup.

[0128] In a preferred embodiment, the cell handling module includes a cell removal module. This may be used when the sample contains cells that are not required in the assay or are undesirable. Generally, cell removal will be done on the basis of size exclusion as for "sieving", above, with channels exiting the cell handling module that are too small for the cells.

[0129] In a preferred embodiment, the cell handling module includes a cell concentration module. As will be appreciated by those in the art, this is done using "sieving" methods, for example to concentrate the cells from a large volume of sample fluid prior to lysis.

[0130] In a preferred embodiment, the devices of the invention include a separation module. Separation in this context means that at least one component of the sample is separated from other components of the sample. Like the magnetic microchannel, the separation module can comprise the separation or isolation of the target analyte, or the removal of contaminants that interfere with the analysis of the target analyte, depending on the assay. The separation module may comprise one or more dielectrophoresis electrodes for separating sample components based on their dielectrophoretic response. Suitable separation modules for manipulating sample components via dielectrophoresis are described in U.S. Patent Application "Method and Apparatus for Manipulating Polarizable Analytes via Dielectrophoresis", filed Jul. 22, 2002, incorporated herein by reference.

[0131] In a preferred embodiment, the separation module includes chromatographic-type separation media such as absorptive phase materials, including, but not limited to reverse phase materials (e.g. C_8 or C_{18} coated particles, etc.), ion-exchange materials, affinity chromatography materials such as binding ligands, etc. See U.S. Pat. No. 5,770,029, herein incorporated by reference. Suitable choromatographic set ups for microfluidic devices include HPLC, CEC (capillary electrochromatography), as reviewed in Regnier et al., TIBTECH, March 1999, vol. 17.

[0132] In a preferred embodiment, the separation module utilizes binding ligands, as has been described above. When the sample component bound by the binding ligand is the target analyte, it may be released for detection purposes as described above.

[0133] In some embodiments, preferential binding of molecules to surfaces can be achieved using coating agents or buffer conditions; for example, DNA and RNA may be differentially bound to glass surfaces depending on the conditions.

[0134] In a preferred embodiment, the separation module includes an electrophoresis module, as is generally described in U.S. Pat. Nos. 5,770,029; 5,126,022; 5,631,337; 5,569,364; 5,750,015, and 5,135,627, all of which are hereby incorporated by reference. In electrophoresis, mol-