

simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus), rotaviruses, Norwalk viruses, hantavirus, arenavirus, rhabdovirus (e.g. rabies virus), retroviruses (including HIV, HTLV-I and -II), papovaviruses (e.g. papillomavirus), polyomaviruses, and picornaviruses, and the like), and bacteria (including a wide variety of pathogenic and non-pathogenic prokaryotes of interest including *Bacillus*; *Vibrio*, e.g. *V. cholerae*; *Escherichia*, e.g. Enterotoxigenic *E. coli*, *Shigella*, e.g. *S. dysenteriae*; *Salmonella*, e.g. *S. typhi*; *Mycobacterium* e.g. *M. tuberculosis*, *M. leprae*; *Clostridium*, e.g. *C. botulinum*, *C. tetani*, *C. difficile*, *C. perfringens*; *Corynebacterium*, e.g. *C. diphtheriae*; *Streptococcus*, *S. pyogenes*, *S. pneumoniae*; *Staphylococcus*, e.g. *S. aureus*; *Haemophilus*, e.g. *H. influenzae*; *Neisseria*, e.g. *N. meningitidis*, *N. gonorrhoeae*; *Yersinia*, e.g. *G. lamblia Y. pestis*, *Pseudomonas*, e.g. *P. aeruginosa*, *P. putida*; *Chlamydia*, e.g. *C. trachomatis*; *Bordetella*, e.g. *B. pertussis*; *Treponema*, e.g. *T. palladium*; and the like); (2) enzymes (and other proteins), including but not limited to, enzymes used as indicators of or treatment for heart disease, including creatine kinase, lactate dehydrogenase, aspartate amino transferase, troponin T, myoglobin, fibrinogen, cholesterol, triglycerides, thrombin, tissue plasminogen activator (tPA); pancreatic disease indicators including amylase, lipase, chymotrypsin and trypsin; liver function enzymes and proteins including cholinesterase, bilirubin, and alkaline phosphatase; aldolase, prostatic acid phosphatase, terminal deoxynucleotidyl transferase, and bacterial and viral enzymes such as HIV protease; (3) hormones and cytokines (many of which serve as ligands for cellular receptors) such as erythropoietin (EPO), thrombopoietin (TPO), the interleukins (including IL-1 through IL-17), insulin, insulin-like growth factors (including IGF-1 and -2), epidermal growth factor (EGF), transforming growth factors (including TGF- α and TGF- β), human growth hormone, transferrin, epidermal growth factor (EGF), low density lipoprotein, high density lipoprotein, leptin, VEGF, PDGF, ciliary neurotrophic factor, prolactin, adrenocorticotrophic hormone (ACTH), calcitonin, human chorionic gonadotropin, cotrisol, estradiol, follicle stimulating hormone (FSH), thyroid-stimulating hormone (TSH), leutinizing hormone (LH), progeterone and testosterone; and (4) other proteins (including a-fetoprotein, carcinoembryonic antigen CEA, cancer markers, etc.).

[0042] In addition, any of the biomolecules for which antibodies may be detected may be detected directly as well; that is, detection of virus or bacterial cells, therapeutic and abused drugs, etc., may be done directly.

[0043] Suitable target analytes include carbohydrates, including but not limited to, markers for breast cancer (CA15-3, CA 549, CA 27.29), mucin-like carcinoma associated antigen (MCA), ovarian cancer (CA125), pancreatic cancer (DE-PAN-2), prostate cancer (PSA), CEA, and colorectal and pancreatic cancer (CA 19, CA 50, CA242).

[0044] Particularly preferred target analytes include cells. "Cell" or "cells" as used herein refers to all types of cells, including prokaryotic and eukaryotic cells, such as bacterial, fungal, plant, and animal cells. In one embodiment the cells are plant cells, including both monocots and dicots and both angiosperms and gymnosperms, which cells may or may not include the cell wall. In another embodiment the cells are animal cells such as blood cells, including: end stage white blood cell types, such as neutrophils, eosinophils, basophils, T lymphocytes, B lymphocytes, macrophages and their

monocyte antecedents; red blood cells and their reticulocyte antecedents; blood platelets and their megakaryocyte antecedents; intermediate forms; progenitor cells; and stem cells that give rise to all of these blood cells; other cells that may appear in the blood or other fluids from time to time such as blood vessel components, e.g. endothelial cells; fetal cells in pregnancy; and bacteria, protozoa and other parasites in blood.

[0045] The present invention provides microfluidic devices comprising solid supports. The "solid support" or "substrate" can be made of a wide variety of materials and can be configured in a large number of ways, as is discussed herein and will be apparent to one of skill in the art. In addition, a single device may comprise more than one substrate; for example, there may be a "sample processing" cassette that interfaces with a separate "detection" cassette; a raw sample is added to the sample processing cassette and is manipulated to prepare the sample for detection, which is removed from the sample processing cassette and added to the detection cassette. There may be an additional functional cassette into which the device fits; for example, a heating element which is placed in contact with the sample processing cassette to effect reactions such as PCR, or an electromagnet that produces a magnetic field across the chamber or magnetizes magnetic materials within the device. In some cases, a portion of the substrate may be removable; for example, the sample processing cassette may have a detachable detection cassette, such that the entire sample processing cassette is not contacted with the detection apparatus. See for example U.S. Pat. No. 5,603,351 and PCT US96/17116, hereby incorporated by reference.

[0046] The composition of the solid substrate will depend on a variety of factors, including the techniques used to create the device, the use of the device, the composition of the sample, the analyte to be detected, the size of the wells and microchannels, the presence or absence of electronic components, the choice of magnetic microchannels, etc. Generally, the devices of the invention should be easily sterilizable as well.

[0047] In a preferred embodiment, the solid substrate can be made from a wide variety of materials, including, but not limited to, silicon such as silicon wafers, silicon dioxide, silicon nitride, glass and fused silica, gallium arsenide, indium phosphide, aluminum, ceramics, polyimide, quartz, plastics, resins and polymers including polymethylmethacrylate, polydimethylsiloxane (PDMS), PMMA, epoxies, acrylics, polyethylene, polyethylene terephthalate, polycarbonate, polystyrene and other styrene copolymers, polypropylene, polytetrafluoroethylene, superalloys, zircaloy, steel, gold, silver, copper, tungsten, molybdeum, tantalum, KOVAR, KEVLAR, KAPTON, MYLAR, brass, sapphire, etc. In preferred embodiments, the solid support is non-magnetic. In addition, as outlined herein, portions of the internal surfaces of the device may be coated with a variety of coatings as needed, to reduce non-specific binding, to generate a high gradient magnetic field, etc.

[0048] Materials that make up the magnetic microchannel are preferably nonmagnetic and generally may include any of the substrate materials listed above. Plastics, resins, polymers are preferred. PDMS, PMMA, polycarbonate, epoxies, and silicon wafers are particularly preferred. Non-magnetic metals such as aluminum or titanium are also suitable.