

within a region to enable cross-flow or tangential flow of fluids. Because the papers can simultaneously physically entrap target cells, lyse cells, and bind either target analytes or competing contaminants or analytical reaction inhibitors, they provide for multiple modes of activity at a single interactive region within the cartridge.

[0088] Reagents can be contained as liquids within specific regions of the cartridge; using conventional pouching or packaging techniques, the designs of which are optimized to allow integration into the cartridge. Reagents containing compounds that are thermally unstable when in solution can be stabilized by drying using common techniques such as lyophilization. Additives, such as simple alcohol sugars, methylcelluloses, and bulking proteins may be added to the reagent before drying to increase stability or reconstitutability. For these reagents, reagent activity is reconstituted by rehydration with the fluid sample or with a separate reconstitution fluid, either by pre-mixing or preferably during sample flow.

[0089] A variety of techniques may be employed which provide for solid reagent deposition patterns that facilitate uniform reconstitution. The reagent may be deposited in a parabolic pattern mirroring the flow pattern of the fluid front in a wide, narrow channel, thereby increasing the likelihood of uniform exposure of the sample contents to the reagent. The selection of sheets of dried reagents, layers of reagents, or individual spot arrays depends on the desired reconstitution event, the rate of reconstitution, and on whether additional mixing is employed.

[0090] For reagent spot arrays, ink-jet printing and piezo-coupled micropipette tips can dispense drops of liquid reagent in a variety of uniform or non-uniform patterns on the surface of an active region, and deposition of separate reagents in separate areas of the active region can be achieved if sequential modification of the fluid sample is desired, or if combined reagents cannot be dried as a single reagent. If the active region is a high surface-to-volume ratio structure, the region may be dipped into, sprayed with, or otherwise exposed to a reagent, and dried before incorporation into the cartridge.

[0091] The operations enabled by specific chemical interactions include specimen volume dilution; pH adjustment; biochemical solubilization; molecular aggregation; cellular or viral lysis; agglutination of target cells or capture-particles; filtration; neutralization; specific analyte extraction and purification; contaminant extraction and separation; precipitation of specific molecules; binding of analyte to reporter moieties; and dried reagent reconstitution.

[0092] The overall geometry of the cartridge may take a number of forms. For example, the cartridge may incorporate a plurality of interactive regions, e.g. channels or chambers, and storage regions, arranged in series, so that a fluid sample is moved serially through the regions, and the respective operations performed in these regions. Alternatively, the cartridge may incorporate a central fluid interactive region connected to peripheral reagent or diluent storage chambers.

[0093] Generally, a single cartridge includes at least two distinct interactive regions, and preferably, at least three or more distinct interactive regions. Individual regions and regions may vary in size and shape according to the specific function of the region or region. In some cases, elongated or spherical interactive regions or chambers may be employed.

In general, the interactive regions may vary in dimensions from microscale (microns) to mesoscale (submillimeters) to macroscale (millimeters).

[0094] In some cases, a separate region may be used as a volumetric region, e.g., to precisely measure fluid volumes for introduction into an adjacent region. In such cases, the volume of the region is dictated by volumetric needs of a given reaction. Further, the cartridge may be fabricated to include a series of regions having varied dimensions and volumes in comparison to each other.

[0095] Cross-sectional areas of the regions dictate the fluid resistance, pressure, and volumetric flow rates. The regions have dimensions or properties (e.g., internal diameter, surface friction, materials, embedded chips, temperature, or other factors) that precisely control the volumetric flow rate, dwell times in the regions, processing efficiencies of on-board, pre-packaged reagents, and efficiencies of sensors and detectors. Consequently, precise dwell times, reagent reconstitution rates, flow rates, flow directions, and all of the flow-through elements and parameters may be implemented.

[0096] The cartridge may be fabricated using one or more of a variety of methods and materials suitable for microfabrication techniques. For example, in preferred aspects, the cartridge may comprise a number of planar members that may individually be sheets or injection molded parts fabricated from a variety of polymeric materials, or may be silicon, glass, or the like. In the case of substrates like silica, glass or silicon, methods for etching, milling, drilling, etc., may be used to produce wells and depressions which make up the various regions, chambers and fluid channels within the cartridge capable of receiving inserts such as pouches, chips, papers, beads, gels, porous materials, tablets, and the like.

[0097] Microfabrication techniques, such as those regularly used in the semiconductor and microelectronics industries, are particularly suited to these materials and methods. These techniques include, e.g., electrodeposition, low-pressure vapor deposition, glass bonding, photolithography, wet chemical etching, reactive ion etching (RIE), laser drilling, and the like. Where these methods are used, it will generally be desirable to fabricate the planar members of the cartridge from materials similar to those used in the semiconductor industry, i.e., silica glass, silicon, gallium arsenide, polyimides, metal films and the like. In additional embodiments, the cartridge may comprise a combination of materials and manufacturing techniques described above. In some cases, the cartridge may include some parts of injection molded plastics, and the like, while other portions of the body may comprise etched glass or silicon members, and the like.

[0098] The cartridge may also incorporate one or more filters for capturing sample components, e.g., cells, spores, or microorganisms to be lysed. The filters may also be used for removing particulates, cell debris, and protein solids from the sample. The filters may be within any region, e.g., within the fluid passages or channels leading between regions or within a particular interactive region. A variety of filter media may be used, including, e.g., cellulose, nitrocellulose, polysulfone, nylon, vinyl copolymers, glass fiber, micromachined structures, and the like. Similarly, separation media, e.g., ion exchange resins, affinity resins or the like, may be included within the cartridge.

[0099] The surfaces of the fluid interactive regions that contact the fluid sample and reagents may be made hydrophobic or hydrophilic depending upon the particular application. Where reagents involved in a particular analysis are