[0110] The mechanical disruption of target cells or viruses can be accomplished with interactive regions designed to tear the surface membrane or cell wall of the target organism via shearing or vibration. Vibration can be accomplished by containing glass or other beads in a chamber, and by coupling to the chamber a piezomembrane also incorporated into the cartridge. Alternatively, an ultrasonic transducer, such as an ultrasonic horn, may be coupled to a wall of the chamber to transfer ultrasonic energy to the cells. The frequency and amplitude of the ultrasound is tuned to correspond with the resonant frequency of the target cells and optimized to effect lysis with minimal heating or cavitation, though the latter may be required for efficient lysis.

[0111] Microfabricated chips can be designed to effect one or more modes of physical or chemical disruption of host cell walls or membranes. In one embodiment, the chip has an integral heater and high surface area microstructures derivitized with amino-silane to allow the chemical conjugation of antibodies with specificity and avidity for the surface proteins of a target cell or virus. When a fluid sample containing the target cell or virus flows through the chip, the target cell or virus is bound by antibodies linked to the high-surface area microstructures and removed from the flowing fluid stream. The microstructures are heated to 95° C. at a later time causing the viruses to lyse.

[0112] Other methods of cell extraction may also be used, e.g., employing a channel with restricted cross-sectional dimensions so that shear stress causes cell lysis when the sample is passed through the channel at sufficiently high pressure. Alternatively, cell extraction and denaturing of contaminating proteins may be carried out by applying an alternating electrical current to the sample. Numerous other methods may be utilized within the cartridge to effect lysis and extraction.

[0113] Following extraction, it will often be desirable to separate the nucleic acids from other elements of the crude extract, e.g., denatured proteins, cell membrane particles, and salts. Removal of particulate matter is generally accomplished by filtration, flocculation and the like. A variety of filter types may be readily incorporated into the chemically and/or mechanically interactive regions of the cartridge. Further, where chemical denaturing methods are used, it may be desirable to desalt the sample prior to proceeding to the next step. Desalting of the sample and isolation of the nucleic acid may be carried out, e.g., by binding, the nucleic acids to a solid phase and washing away the contaminating salts, or by performing gel filtration chromatography on the sample, by passing salts through dialysis membranes, and the like. Suitable solid supports for nucleic acid binding include, e.g., filters, beads, fibers, membranes, glass wool, filter paper, polymers, and gel exclusion media.

[0114] In some embodiments, enzymes, such as a polymerase enzyme, may be present within an amplification region, coupled to a suitable solid support, or to the walls and surfaces of the region. Suitable solid supports include those that are well known in the art, e.g., agarose, cellulose, silica, divinylbenzene, polystyrene, etc. Coupling of enzymes to solid supports has been reported to impart stability to the enzyme in question, which allows for storage of days, weeks or even months without a substantial loss in enzyme activity, and without the necessity of lyophilizing the enzyme. Monoclonal antibodies are available which bind the enzyme without affecting its polymerase activity. Consequently, covalent attachment of the active polymerase enzyme to a solid support, or the walls of the amplification region may be carried out by using the antibody as a linker between the enzyme and the support.

[0115] In another aspect of the invention, ligand binding methods can be used in the cartridges for binding and capturing specific cell types and/or other analytes. Ligand binding entities, such as nucleic acids and proteins, may be located at selected capture regions, attached to the surface(s) of the analyte capture components, to form a specific analyte-reacting region. Ligand coupling chemistries, such as silane-based chemistries, may be used. Homo- or hetero-bifunctional linkers, with one functionality binding to the internal surface and the other to a target in the test sample, may be employed. A sample containing the target analyte is passed continuously through the cartridge and the analyte binds to the ligand covered surface. After subsequent washing with one or more wash solutions, the ligand-analyte complexes can be eluted. Alternatively, a secondary anti-analyte molecule conjugated to a reporter molecule may be passed through the cartridge, so that the conjugate is captured by the analyte. This complex may also be eluted.

[0116] In particularly preferred embodiments, the cartridge is made from at least one injection molded, press molded or machined polymeric part that has one or more wells or depressions manufactured into its surface to define several of the walls of the interactive regions. Examples of suitable polymers for injection molding or machining, include, e.g., polycarbonate, polystyrene, polypropylene, polyethylene, acrylic, and commercial polymers such as Kapton®, Valox®, Teflon®, ABS, Delrin® and the like. A second part that is complementary in shape is mated to the surface of the first part to define the remaining wall of the cartridge. The mating part or a third part may be a printed circuit board for implementing electrical contact directly with the fluid or indirectly via the cartridge.

[0117] The cartridge may be fabricated in such a way that specific regions or regions interact with an external instrument via exchange of electromagnetic radiation. Many plastics commonly used for such cartridges (e.g. polypropylene and polycarbonate) are optically transparent. In general, insulating materials allow electromagnetic radiation to pass over a wide frequency range. Such radiation may be of any frequency consistent with the intended application. For example, radio waves may be used as an alternative means of communicating with the cartridge. Radio waves may also be used to supply small amounts of power to any internal circuitry within the cartridge. Microwave frequencies may be used to induce heating of the fluid sample. Infrared signals may be used for heating, or for data exchange via an IR link, similar to those used in personal computers.

[0118] Optical frequencies, using light emitting diodes (LEDs) and photodetectors, such as photodiodes, are useful for detection of fluid presence (by detecting changes in optical transmittance), and for monitoring of chemical reactions (by, e.g., measuring absorption, fluorescence, or luminescence at specific wave lengths). Optical, as well as ultraviolet frequencies may be used to excite fluorescence of reaction products for detection. These frequencies may also be used to induce or accelerate chemical reactions.

[0119] Higher frequency radiation, such as deep UV or x-ray radiation, is also possible for specific applications, although the sources for these types of radiation may not always be practical in a small instrument. Sources of ionizing radiation (such as radioactive materials) could be reasonably