incorporated into an instrument, and such radiation used for specific purposes within the cartridge, such as the enhancement of reactions or detection of specific fluid components or properties.

[0120] The cartridge may be fabricated in such a way that specific regions or regions may interact with the external environment via magnetic forces. For example, a region of the cartridge may contain a reservoir of magnetic beads. Such beads can be functionalized with various binding agents. By applying a series of magnetic fields to the cartridge (e.g. by means of switchable electromagnets) these beads may be vibrated or moved from one region to another. Using AC electromagnetic fields, such beads may be caused to circulate within a small region of the cartridge to mix fluids within the cartridge.

[0121] Magnetic forces may also be used to operate small valves within the cartridge for fluid control. A small strip of magnetic material may be incorporated into the cartridge to divert the fluid flow along one particular flow path. Another possibility is to fabricate the magnetic strip in such a way that it returns to the first position when the field is removed. The strip could be fabricated in such a way as to be mechanically bistable. Application of a magnetic pulse to the strip causes a mechanical transition from the initial bistable state to the second state. In this second state, the strip diverts the fluid flow to an alternative path. An array of such valves allows complete control of the fluid motion.

[0122] The cartridge may be fabricated so that specific regions may interact with the external instrument via electric fields. By fabricating very thin regions within the cartridge, and by mating these with corresponding conductive areas within the instrument, electric fields may be applied to the fluid without the need for any electrical connections to the cartridge itself. Such electric fields may be used to move charged molecules from one surface to the other within the cartridge. By proper design of the fluidic paths, such a configuration may be used to separate charged from uncharged molecules, or to attract and hold charged molecules while other unwanted molecules are flushed from the system.

[0123] A number of the operations performed by the various interactive regions of the cartridge require a controllable-temperature. For example, PCR amplification requires cycling of the sample among a strand separation temperature, an annealing reaction temperature; and an extension reaction temperature. A number of other reactions, including isothermal DNA amplification techniques, ligand binding, enzymatic reactions, extension, transcription and hybridization reactions are also generally carried out at optimized, controlled temperatures.

[0124] Temperature control is generally supplied by resistive heaters which are prepared using methods that are well known in the art. For example, these heaters may be fabricated from thin metal films applied within or adjacent to channels or chambers using well known methods such as sputtering, controlled vapor deposition, screen printing and the like. The heater is electrically connected to a power source which delivers a current across the heater. The electrical connections may be fabricated using methods similar to those described for the heaters.

[0125] In one embodiment, a controllable heater is disposed within or adjacent to a region for thermal control of the sample. Thermal control is carried out by varying the current supplied to the heater to achieve the desired temperature for the particular stage of the reaction. Alternatively, thermal control may be achieved by transferring the fluid sample among a number of different reaction regions or regions of the same cartridge, having different, constant temperatures, or by flowing the sample through a serpentine channel which travels through a number of varied temperature zones. Heating may alternatively be supplied by exposing the region to a laser or other radiation source.

[0126] Resistive heater elements may also be incorporated into regions of the cartridges by diffusing silicon into the regions or by depositing thin-film metal, carbon, or polysilicon at selected regions. Controlled heating provides additional functional capabilities, such as mixing, dissolution of solid reagents, lysing, thermal denaturation of proteins and nucleic acids and lysis of cells, elution of bound molecules, enhanced diffusion rates of molecules in the sample, and modification of surface binding coefficients, as well as high efficiency thermal cycling for polymerase and ligase chain reactions. Cooling features may also be exploited in high surface area regions, for example, with external cooling fins.

[0127] Preferably, the heaters are capable of producing temperatures in excess of 100° C. without suffering adverse effects as a result of the heating. The heaters may be provided as a layer on one surface of an interactive region or other region, or may be provided as molded or machined inserts for incorporation into a region or region. Control of the power source is typically carried out by an appropriately programmed processor, such as the processor in the external instrument. The heaters may be incorporated within the cartridge by depositing a resistive conductive film or insert on a surface of the cartridge, or alternatively, the heaters may be provided externally, e.g. in the instrument, and applied to the exterior of the cartridge, adjacent to a particular region, so that heat is conducted into the region.

[0128] Temperature controlled regions may also include miniature temperature sensors for monitoring temperatures and thereby controlling the application of current across the heater. A wide variety of microsensors are available for determining temperatures, including, e.g., thermocouples having a bimetallic junction which produces a temperature dependent electromotive force (EMF), resistance thermometers which include material having an electrical resistance proportional to the temperature of the material, thermistors, IC temperature sensors, quartz thermometers and the like. Alternatively, the temperature coefficient of resistance of the heater itself may be monitored to control the heat input.

[0129] The temperature measured by the temperature sensor and the input for the power source will typically be input to a processor, e.g. a microprocessor or microcontroller in the external instrument, which is programmed to receive and record this data. The same processor will typically include programming for instructing the delivery of appropriate current for raising and lowering the temperature of the interactive region or regions. For example, the processor may be programmed to take the interactive region through any number of predetermined time/temperature profiles, e.g., thermal cycling for PCR, and the like. Given the small size of the cartridges of the invention, cooling of an interactive region will typically occur through exposure to ambient temperature. However, additional cooling elements may be included if desired, e.g., coolant systems, Peltier coolers, water baths, heat pipes, and the like.

[0130] In alternate aspects, mixing may be accomplished by the incorporation of ferromagnetic elements within the cartridge which may be vibrated by supplying an alternating