

The microstructures preferably comprise an array of columns integrally formed with at least one wall of the chamber and extending into the chamber. In an alternative embodiment, the flow-through component comprises a channel or chamber in the cartridge containing at least one solid support for capturing the analyte. Suitable solid supports include, e.g., filters, beads, fibers, membranes, glass wool, filter paper, polymers and gels.

**[0014]** A flow path for carrying elution fluid is also formed in the cartridge. The elution flow path passes through the flow-through component, thereby releasing captured analyte from the component into the elution fluid. The elution flow path diverges from the sample flow path after passing through the component. In the preferred embodiment, the cartridge also includes, or may be coupled to, a heating element for heating the component, thereby increasing elution efficiency.

**[0015]** The cartridge also includes at least one flow controller, e.g., one or more valves, flow diverters, or fluid diodes, for directing the fluid sample into the sample flow path after the sample flows through the capture component and for directing the elution fluid and eluted analyte into the elution flow path, after the elution fluid flows through the capture component. In the preferred embodiment, the cartridge further includes a waste chamber at the end of the sample flow path for collecting the remaining fluid sample and a second-chamber at the end of the elution flow path for receiving the eluted analyte. The second chamber may alternatively be a reaction chamber formed in a separate reaction vessel coupled to the cartridge to receive the eluted analyte for further processing.

**[0016]** In contrast to prior fluidic cartridges that process a fluid sample as a bolus, the continuous-flow cartridge of the present invention permits the rapid processing of a fluid sample that is larger in volume than any interactive region within the cartridge. The ability to process larger sample volumes allows increased sensitivity in the detection of low copy concentrations of analytes, such as nucleic acid.

**[0017]** In a preferred mode of operation, the cartridge is used to separate nucleic acid, e.g. DNA or RNA, from a fluid sample and to concentrate the nucleic acid into a smaller volume of elution fluid. In these applications, it is preferred that the sample flow path formed in the cartridge include a lysing region, e.g. a channel or chamber, for lysing cells, spores, or microorganisms in the fluid sample. Preferably, an ultrasonic transducer, such as an ultrasonic horn, is coupled to the cartridge for transferring ultrasonic energy to the fluid sample in the lysing region, thereby effecting lysis of the cells, spores, or microorganisms. The lysing channel or chamber may additionally include particles or beads for rupturing the cells, spores, or microorganisms as the ultrasonic energy is applied.

**[0018]** The lysing channel or chamber preferably contains a solid phase for capturing the cells, spores, or microorganisms as the sample flows through the chamber. Suitable solid phases include, e.g., filters, beads, fibers, membranes, glass wool, filter paper, polymers and gels. Lysing is accomplished by applying ultrasonic energy to the cells, spores, or microorganisms captured on the solid phase. The ultrasonic energy may be supplied from, e.g., an ultrasonic horn coupled to a wall of the lysing chamber or built into the cartridge. The cartridge may also contain, or be coupled to, a heating element in thermal contact with the lysing chamber for heating the fluid sample as the ultrasonic energy is applied.

**[0019]** In another embodiment of the cartridge, the lysing region comprises a lysing chamber positioned upstream of

the capture region, and the cartridge further includes a reagent chamber in fluid communication with the lysing chamber for holding a lysing reagent. In this embodiment, a fluid motive source, such as a pump, is also provided for forcing the lysing reagent to flow into the lysing chamber to contact the sample. Lysing reagents may also be used in combination with the ultrasonic lysing embodiments described above.

**[0020]** In the preferred embodiment, the invention also provides an external instrument for receiving one or more of the cartridges. The external instrument includes a fluid motive source, e.g., one or more pumps, vacuums, or pressure sources, that interface with one or more ports or vents formed in the cartridge, to force the sample to flow through the cartridge. Either the instrument or the cartridge may also include processing electronics, e.g., one or more microprocessors, microcontrollers, or memory chips, for controlling the operation of the cartridge.

#### BRIEF DESCRIPTION OF THE DRAWINGS

**[0021]** FIG. 1 is a plot of analyte concentration (copy number) versus sample volume showing the minimum volume required for statistically significant detection of analyte.

**[0022]** FIG. 2 is a schematic, plan view of a cartridge for processing a fluid sample according to a first embodiment of the invention.

**[0023]** FIG. 3 is a perspective view of an instrument holding several cartridges for processing.

**[0024]** FIG. 4 is an exploded view of a fluid diode for the prevention of backflow.

**[0025]** FIG. 5A is a schematic, plan view of an electrolytic pump.

**[0026]** FIG. 5B is a schematic side view of the pump of FIG. 5A.

**[0027]** FIG. 6 is a schematic, cross sectional view of a flow-through chip for extracting analyte from a fluid sample according to a preferred embodiment of the invention.

**[0028]** FIG. 7 is a bottom plan view of the chip of FIG. 6.

**[0029]** FIG. 8 is a three-dimensional view of microcolumns formed in an extraction chamber of the chip of FIG. 6.

**[0030]** FIG. 9 is a schematic, plan view of the microcolumns in the chip of FIG. 6.

**[0031]** FIG. 10 is a plan view of two adjacent microcolumns in the chip of Fig. G.

**[0032]** FIG. 11 is a schematic view of an etch mask defining a chamber pattern and a column pattern used in the fabrication of the chip of FIG. 6.

**[0033]** FIG. 12 is a schematic, cross sectional view of an alternative microfabricated chip for extracting analyte from a fluid sample.

**[0034]** FIG. 13 is a schematic, cross sectional view of another microfabricated chip for extracting analyte from a fluid sample.

**[0035]** FIG. 14 is a schematic, cross sectional view of a microfabricated chip for extracting analyte from a fluid sample according to a further embodiment of the invention.

**[0036]** FIG. 15 is a partially exploded, cross-sectional view of a microfabricated chip embedded in a plastic cartridge.

**[0037]** FIG. 16 is a partially exploded view of another cartridge showing a bottom plate, interactive regions, connecting channels, flex circuitry, fluid pouches, and a top plate with a fluid inlet port.

**[0038]** FIG. 17 is a cross-sectional view of a region of the cartridge of FIG. 16 containing filter paper for capturing analyte.