

current (power) to the electrodes 27, and in conjunction with the aforementioned means for monitoring of fluid flow velocity, a closed loop fluid flow control system can be realized. Such an implementation opens up many possibilities for very well controlled reactions, as the fluid velocity (and hence residence times at various reaction regions), at various points in the processing cycle can be independently controlled and monitored.

[0141] FIG. 6 shows a schematic, cross sectional view of a preferred microfabricated chip 20 to be used as the flow through component in the cartridge of FIG. 2. The chip 20 is used to capture a desired analyte, e.g. nucleic acid, from a fluid sample and to provide a highly concentrated eluate of the analyte. The chip 20 includes a body having formed therein an inlet port 28, an outlet port 30, and an extraction chamber 26 for extracting the analyte from the fluid sample as the fluid sample flows through the body. The chamber 26 is in fluid communication with the inlet and outlet ports 28 and 30, and the ports are preferably positioned on opposite sides of the chamber 26 to permit continuous fluid flow through the chamber.

[0142] The body preferably comprises a base substrate 22 and a top substrate 24 bonded to the base substrate 22. The substrates 22 and 24 may comprise any suitable substrate materials, such as silicon, glass, silicon dioxide, plastics, or ceramics. In the preferred embodiment, the chamber 26 is formed in the base substrate 22, and the fluid ports 28 and 30 are formed in the top substrate 24. In alternative embodiments, however, many different configurations are possible, e.g., the chamber 26 may be partially or completely formed in the top substrate 24, the fluid ports may be formed in bottom or sides of the base substrate 22, etc. Several of these alternative embodiments will be described below.

[0143] The chamber 26 has internal attachment surfaces having sufficiently high surface area and binding affinity with the target analyte to capture the analyte as the fluid sample flows through the chamber. In the preferred embodiment, the internal attachment surfaces are formed by an array of internal microstructures, preferably high aspect ratio columns 32, integrally formed with a wall of the chamber 26 and extending into the chamber. For simplicity of illustration, only twenty-five columns are shown in the schematic view of FIG. 6. It is to be understood, however, that the chip of the present invention may include many more columns. In general, it is preferred to fabricate the chip with at least 100 columns, and more preferable to fabricate the chip with 1,000 to 10,000 columns. The number of columns depends, inter alia, on the amount and concentration of analyte in the sample, the dimensions of the chamber, the spacing of the columns, the flow rate of fluid through the chamber, etc. Specific techniques for fabricating the chip are described below.

[0144] FIG. 8 shows a portion of the array of columns 32 extending from a bottom wall 23 of the extraction chamber. The columns 32 preferably have an aspect ratio (ratio of height to width or diameter) of at least 2:1, and more preferably have an aspect ratio of at least 4:1. The high aspect ratio columns 32 provide a large surface area for capturing the analyte. As the fluid sample flows through the chamber, the analyte contacts and adheres to the surfaces of the columns 32. To elute the analyte, an elution fluid is forced to flow through the chamber, releasing the analyte, e.g. nucleic acid, from the surfaces of the columns 32 into the elution fluid. In the preferred embodiment, the columns 32 have a height equal to the depth of the extraction chamber, preferably at

least 100  $\mu\text{m}$ . In alternative embodiments, the extraction chamber may have a shallower depth, but depths of less than 100  $\mu\text{m}$  may cause excessively slow fluid flow through the chamber.

[0145] FIG. 9 shows a schematic view of the array of columns 32 disposed in the chamber 26. Fluid enters the chamber 26 through the inlet port 28 and flows between the columns 32 to the outlet port 30. The columns 32 are preferably arranged in an array that optimizes fluid interaction with the surfaces of the columns as the fluid flows through the chamber 26. The optimization of the column arrangement permits faster flow rates of fluids through the chamber without losing efficiency of extraction.

[0146] In the preferred embodiment, the columns 32 are disposed in rows, with each of the columns in a row spaced a uniform distance from adjacent columns in the row, i.e. the columns in a row preferably have uniform center to center spacing. For example, FIG. 9 illustrates ten horizontal rows of uniformly spaced columns 32. In addition, adjacent rows are preferably offset from each other such that the columns in each row are misaligned with the columns in an adjacent row. For example, each row of columns in FIG. 9 is offset horizontally from an adjacent row.

[0147] Also in the preferred embodiment, the rows are offset such that the columns in each row are misaligned with the columns in at least two previous and/or successive rows. The misalignment may be in a pattern of successive rows, where the chamber includes one pattern or a repeated pattern. For example, the pattern may repeat every three to ten rows. In the alternative, the misalignment of columns may be random from row to row.

[0148] Generally, any two adjacent rows in the array should not be offset from each other such that the columns in the first row are aligned exactly halfway between the columns in the second row. Instead, it is presently preferred to offset adjacent rows a distance greater than or less than 50% of the center to center spacing between the columns. This arrangement provides for an asymmetrically split flow pattern through the chamber to ensure that each branch of the fluid stream interacts as strongly as possible with the surfaces of the columns.

[0149] A specific example of a suitable arrangement of columns will now be given with reference to FIG. 9. In each row, the center to center spacing between adjacent columns is 15  $\mu\text{m}$ . The columns are arranged in a pattern that repeats every five rows. In particular, each of the top five rows is offset 6  $\mu\text{m}$  from a previous/and or successive row. The bottom five rows (the sixth-through tenth rows) repeat the pattern of the top five rows, with the sixth row being aligned with the top row, e.g., column 32A is aligned with column 32B. Of course, this is just one example of a suitable array of columns and is not intended to limit the scope of the invention. It will be apparent to one skilled in the art from this description that the columns may be arranged in many other patterns, preferably within the general guidelines set forth above.

[0150] FIG. 10 shows a top plan view of two adjacent columns 32 in a row. The columns 32 preferably have a cross sectional shape and size which maximizes fluid contact with the surfaces of the columns while still allowing for smooth fluid flow through the chamber. In the preferred embodiment, this is achieved by fabricating columns having a long and thin cross sectional shape, preferably a streamlined shape, such as the hexagonal shapes shown in FIG. 10. In particular, each column 32 preferably has a ratio of cross sectional length L to cross sectional width W of at least 2:1, and more preferably of