

formed using any well known technique, e.g., thermal growth, chemical or electrochemical growth, or deposition.

[0175] An electrically conductive material, e.g., aluminum, gold, or copper, is then deposited and patterned on the back-side of the substrate to form the resistive heating element, temperature sensor, and bond pads. Different materials may be used to form the heating element and sensor. Specific techniques for patterning metal on a substrate are well known in the art. The substrate is then anodically bonded to a thin, e.g., 500 μm , Pyrex™ glass cover. The glass cover has holes fabricated in it, e.g., by ultrasonic milling, which form the fluid ports to the chamber. After bonding, the substrate pair may be diced using a diamond saw. The resulting structure is shown schematically in FIG. 6.

[0176] The exact dimensions and structure of the microfluidic chip may be varied to suit the chip to a particular application. A specific example of one possible device according to the present invention is as follows. The device is 4.0 mm square and 0.9 mm thick. The extraction chamber has a depth of 200 μm and a length and width of 2.8 mm. The fluid ports each have a width of 0.4 mm. The device has a dense array of columns occupying an area 2.0 mm \times 2.8 mm within the chamber. The columns have a height of 200 μm , a cross sectional length of 50 μm and a cross sectional width of 7 μm , a gap distance of 8 μm between adjacent columns in a row, and a center to center spacing of 15 μm . There are roughly 7,000 columns in the array. Of course, these dimensions are exemplary of just one possible embodiment and are not intended to limit the scope of the invention. The specific dimensions of each material of the device may be varied in alternative embodiments, preferably within the general guidelines set forth earlier in this description.

[0177] The chip may be incorporated into a region of the cartridge with a flexible, polymeric coating, such as a silicone glue. Alternatively, a gasket may be fabricated with matching holes to the fluidic ports on the chip and a sealed fluidic assembly made between the microfluidic domain (the chip) and the macrofluidic domain (the cartridge body). The chip may be pressed tightly and sealed against the gasket material by bonding another plastic piece over the chip, thus completely encapsulating the chip within the cartridge.

[0178] Alternatively, the chip may be fused or welded to the cartridge directly without the use of a gasket. In a particularly advantageous embodiment, a portion of the cartridge itself may be the cover for the chip rather than using a separate substrate, e.g., the Pyrex™ glass, to form the cover. In this embodiment, the substrate 22 is inserted into the cartridge and sealed to a wall of the cartridge. The wall has holes in it forming the fluid ports to the extraction chamber.

[0179] One technique used to make integrated chip and plastic cartridges uses recessed regions in the plastic to accept the silicon/glass micromachined chip(s). The recessed regions are precisely dimensioned to accept and accurately locate the silicon/glass chip. This technique allows the small silicon/glass microfluidic chip(s) to be easily aligned to the macrofluidic channels, ports, and other fluidic regions molded into the plastic. The recess itself may contain a fluid port to connect with a fluid port on the bottom of the silicon/glass chip.

[0180] In addition, the use of recessed regions allows another plastic molded component to be easily laminated on top of the first silicon/glass/plastic assembly. This second technique is especially suitable for interfacing the molded fluid paths in the plastic to the small microfluidic openings

(typically about 0.5 mm in diameter) which emerge onto the flat surfaces (on either side of the chip) of the silicon/glass chip. This technique can also provide a convenient means for accessing electrical contacts on the microfluidic chip, if necessary. In this case, a region in the laminated plastic is left open to allow easy access for wire bonding to the silicon/glass chip.

[0181] A third technique is the forming of molded plastic regions that are the inverse shape of anisotropically etched pyramidal pits in (100) silicon. This technique has several advantages. It allows for easy alignment between the silicon and the plastic and at the same time, minimizes the fluid dead volume where the plastic must be connected to an anisotropically etched fluid pit in a silicon chip.

[0182] A fourth technique is the use of laminated or patterned adhesive films to make fluid-tight seals between the various plastic and silicon/glass pieces. Materials such as polyimide or Mylar® can be formed in very thin sheets (on the order of 0.0254 mm) and coated on both sides with adhesive (curable by ultra violet or by temperature). The adhesive not only joins the two components, but also forms fluid-tight seals. Such sheets can be cut or punched into various shapes, thereby providing access holes or other shapes, then laminated onto the plastic and/or silicon/glass. For some applications, screen-printed adhesives may be more appropriate as fluid-tight seals.

[0183] FIG. 15 illustrates one type of integration between a silicon microfluidic chip 7 and a recess 3 within a cartridge 1. The precisely-dimensioned recess 3 is molded into the middle plastic portion 5 into which the chip 7 is inserted. The chip 7 has a glass portion 9 and silicon portion 11 and is accessible to wire connection 13. A channel 15 is molded into the middle plastic portion 5 and lower plastic portion 17. A laminated interface 19 aligns the channel of the middle and lower plastic components. A gasket or an adhesive 93 allows for fluid-tight lamination, sealing, and integration of the plastic portion and silicon-glass chip 7.

[0184] FIG. 12 shows an alternative embodiment of the microfabricated chip in which the chip has fluid ports 28 and 30 formed in the base substrate 22 rather than the top substrate 24. The chip also includes electrodes 48A and 48B for heating the internal surfaces of the chamber 26. The electrodes are preferably positioned on opposite sides of the bottom wall 23 of the extraction chamber 26. The base substrate 22 is fabricated from a thermally conductive material, preferably silicon, so that the bottom wall 23 and integrally formed columns may be heated by applying an appropriate voltage across the electrodes 48A and 48B.

[0185] As in the previous embodiment, the chip may be used in combination with the cartridge, as previously described with reference to FIG. 2. The operation of the chip is analogous to the operation described above, except that the internal surfaces of the chamber 26 are heated by applying a voltage across the electrodes 48A and 48B. The bottom wall 23 functions as a resistive heating element for heating the chamber 26.

[0186] The microfluidic chip of FIG. 12 may be fabricated using a variety of techniques, including photolithography and/or micromachining. A preferred method for fabricating the chip will now be described.

[0187] A 100 mm, n-type (100), silicon wafer is used as starting material for the base substrate 22. The wafer preferably has a resistivity of 1 to 100 ohm-cm, depending on the desired final resistance between the electrodes 48A and 48B.