

“MALDI” is used herein to refer to a process wherein analyte is embedded in a solid or crystalline “matrix” of light-absorbing molecules e.g., nicotinic, sinapinic, or 3-hydroxypicolinic acid), then desorbed by laser irradiation and ionization from the solid phase into the gaseous or vapor phase, and accelerated as intact molecular ions towards a detector. The integration of MALDI into a microfluidic device is taught by U.S. Pat. No. 5,716,826.

[0283] In a preferred embodiment, the detection is carried out while the target analytes are captured within the microchannel. For example, the target analyte can be labeled by both magnetic labels and a detection label such as a fluorescent group. When the target analyte is captured in the magnetic microchannel, preferably on the lateral surfaces of the channels, the detection labels attached to the target analytes can be detected by a detection device such as a fluorescent microscope.

[0284] In a preferred embodiment, optics are included near the channel, so that light can be coupled into and out of the channel. For example, diffractive optical lenses, beam splitters, and other optical elements can be fabricated into the channel. See Quake et al., *Science* 290, 1536.

[0285] The devices of the invention are generally made as outlined herein and using techniques well known in the art.

[0286] In a preferred embodiment, a device comprising “embedded channels” is made by modification of conventional techniques for fabricating microchannel structures, for example, the technique disclosed in U.S. Pat. No. 6,176,962. Suitable substrates for this embodiment include, but is not limited to, plastics, PDMS and other materials, as outlined above. In a preferred embodiment, with devices prepared from a plastic material, a silica mold master which is a negative for the channel structure can be prepared by etching or laser micromachining. A polymer precursor is first impregnated with magnetic beads. The beads are generally deposited in a monolayer or near a monolayer at the channel surface. Their higher density generally keeps them in place and at the channel surface if the beads are on top of the channel mold. The impregnated precursor can then be thermally cured or photopolymerized between the silica master and support planar plate, such as a glass plate. After the planar substrate has been fabricated, a cover plate may be placed over, and sealed to, the surface of the substrate, thereby forming an integrated device. The cover plate may be sealed to the substrate using any convenient means, including ultrasonic, welding, adhesive, etc. Alternatively, the planar substrate can be sealed with a flexible cover as described in PCT US01/02664, incorporated herein by reference. It should be clear to the skilled in art that the cover plate may also be prepared from a precursor impregnated with magnetic beads, thus making channels surrounded by the magnetic beads.

[0287] In a preferred embodiment, a device comprising “coated channels” is made by modification of conventional techniques for fabricating microchannel structures. For example, a substrate with microchannel can be fabricated using any convenient means, such as molding and casting techniques. The microchannel are then coated with magnetic beads impregnated into a coating material. The coating material includes, but is not limited to, polycarbonate, polypropylene, acrylics, epoxies, PDMS, etc, even agarose or acrylamide. Upon coating, the substrate is then sealed

with a cover plate, as described above. One advantage of this technique includes that fabrication can be done for any pre-existing channel, for example, injection-molded devices.

[0288] In a preferred embodiment, the device comprising magnetic microchannel filled with magnetic beads are made using techniques well known in the art. For example, with devices prepared from a plastic material, a silica mold having at least one raised ridges for the position of the magnetic microchannel can be prepared. Next, a polymer precursor formulation can be thermally cured or photopolymerized between the silica master and support planar plate. After the planar substrate is fabricated, filled-channels, prepared in a separate device, can then be placed into the cavity and connected to other parts of the device. Finally, a cover plate is placed over the planar substrate and sealed to the substrate as outlined above, thereby forming an integrated device. Alternatively, the channels are first made with conventional techniques, and magnetic beads are subsequently filled into the magnetic channel.

[0289] In a preferred embodiment, the magnetic microchannel comprises gradient inducing features coated with magnetic materials. The magnetic material is preferably electroplated onto gradient-inducing features, however, other methods such as sputtering and evaporation may be used. Similar fabrication methods to those used to fabricate channels, discussed above, may be used to fabricate gradient inducing features including photolithography techniques, wet and dry etching, laser drilling, etc. Gradient inducing features may be fabricated directly. Alternatively, a ‘negative mold’ may be fabricated and used to form the gradient inducing features, for example using injection molding techniques.

[0290] In a preferred embodiment, shown in FIG. 7, negative mold 71 comprising ridges 72 and 74 (defining valley 73) and pits 76 and 78 is fabricated from silicon using an etchant comprising hydrofluoric acid (HF), nitric acid (HNO₃), and acetic acid (CH₃COOH) in a ratio of 1:3:8, generally known as HNA. A layer of SiO₂ is preferably used to mask the silicon, although other materials, such as silicon nitride may be used. The masking material is removed above valley 73, pit 78 and pit 76. Briefly, exposure to HNA results in isotropic etching, that is etching that proceeds both down into the silicon and laterally under the masking material. The etching rate is affected by the size of the mask opening. The distance between ridges is significantly greater than the width of pits, accordingly the area between ridges, valley 73, is etched deeper than the pits 76 and 78. A preferred embodiment is described in greater detail in the example below. It is to be understood that these measurements are by way of example, and that the inventive process would apply to a variety of ridge and pit dimensions. After negative mold 70 is formed, it may be used in, for example, an injection molding process to generate a device comprising a microchannel containing a dome structure. Ridges 72 and 74 correspond to resultant microchannels, and pits 78 and 76 to a dome within each microchannel.

[0291] Once made, the devices of the invention find use in a number of applications.

[0292] In principle, any biological samples that contain magnetic components or components that can be magnetically labeled can be processed by the microchannel. The