VERTICAL MICROFLUIDIC PROBE HEADS

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ABSTRACT

Non-contact scanning microfluidic technologies such as the microfluidic probe (MFP) are of great interest for microscale (bio)chemical and biological applications on surfaces, which cannot be processed in closed microfluidic systems. Here we present a new type of MFP heads that have their main axis normal to the processed surface. Vertical MFP heads have in-plane-fabricated microchannels and are assembled by anodically bonding a microfabricated Si chip with a glass layer. These heads are easier to fabricate, package and position than standard MFP heads that are operated parallel to a surface.

KEYWORDS: MFP, Microfluidic Probe, Microfluidics

INTRODUCTION

The MFP is a versatile microfluidic technology for depositing and removing biomolecules on and from surfaces, forming surface density gradients, staining cells, and removing selected adherent cells from a surface [1,2]. Recent approaches also showed that the MFP technology can be used to stain tissue sections [3] and that related technologies using dual capillaries are capable of collecting RNA from cells [4]. The main component of a MFP is its head, typically microfabricated in a Si wafer and bonded to a Si lid or a poly(dimethylsiloxane) block comprising vias for connection to capillaries and pumps. During operation, the MFP head is brought within micrometers over a surface where it focuses a processing solution in the presence of an immersion liquid by means of injection and aspiration apertures, figure 1. Challenges posed by MFP heads are (1) the precise fabrication of the apertures which have to be etched through the Si wafer, (2) the bonding of the Si lid or the PDMS connection block to the head and (3) the large footprint of the heads. This paper presents new MFP heads having strongly reduced complexity, small footprint and that are easy to fabricate with high precision and yield.

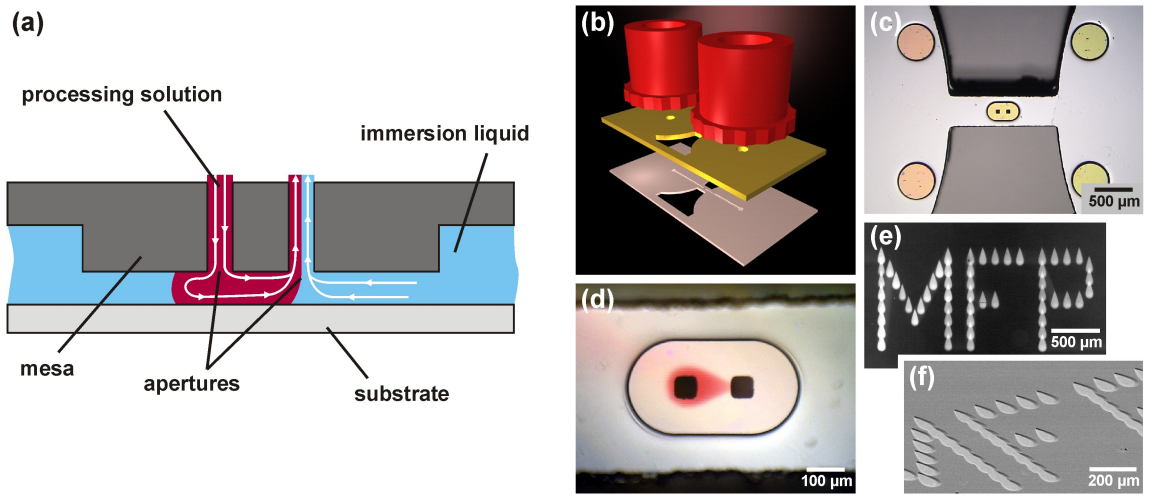

Figure 1: Working principle of the MFP. (a) Flow confined by a MFP head brought close to a substrate. (b) A standard MFP head consists of three parts: (i) an etched chip with channels and apertures (ii) a Si lid with vias and (iii) ports for fluidic connection. (c) Bottom view of a MFP head showing the mesa and the apertures. (d) Flow confinement between the injecting aperture (left) and the aspirating aperture (right). (e) Local deposition of fluorescent antibodies. (f) Exposed photoresist, developed locally using an MFP.

EXPERIMENTAL

The new MFP heads operate in a vertical position. They are made of a microfabricated Si chip that is anodically bonded to a glass lid (Borofloat® 33, SCHOTT). Microfluidic paths are patterned in the plane of the Si chip so as to reach the tip of the chip. These channels form the micro-apertures after bonding the glass onto the Si wafer (450 °C, 1.25 kV) and separating the chips by dicing. Cutting off the tips to generate a flat area is performed directly during the dicing step. Through holes (vias) etched into the Si at the beginning of the microchannels allow fluidic connections with pumps and valves to be established, figure 2.

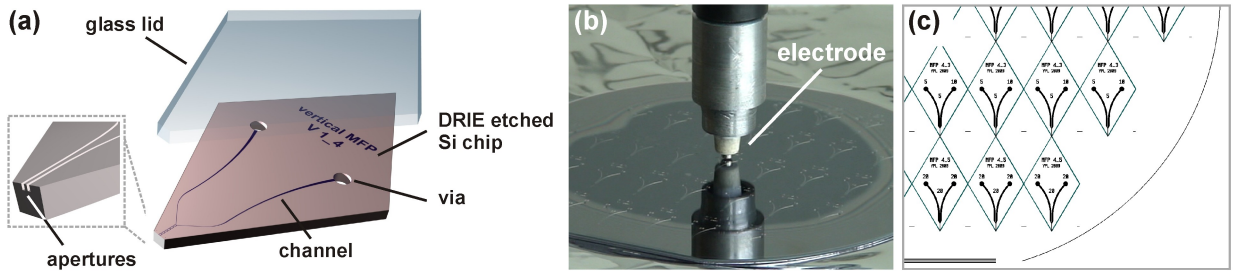

Figure 2: Fabrication of vertical MFP heads. (a) A Si chip comprising channels and vias is closed with a glass lid using anodic bonding. The side of the chip where the channels converge, is cut and polished to define the apertures. (b) Snapshot of the anodic bonding step. (c) Wafer layout showing the dicing lines for easy chip separation.

The quality of the tips after the dicing step is not sufficient for proper operation of the MFP, figure 3a. To improve the surface quality and to ensure well opened apertures, a lapping and polishing step of the tip is performed. First, the channels are protected from debris generated during lapping and polishing by partially filling their apertures with molten wax. Therefore, a wax that melts at ~80 °C is liquefied on a hot plat and pulled into the apertures using a silicone tube connected to a vacuum pump, figure 3b and 3c. Two to four chips are clamped and aligned using a special holder to fix them onto the lapping and polishing machine (Logitech, Scotland). During the lapping process (using 1 µm Al_2O_3 polishing slurry) typically about 200 µm of the tip is removed. The following polishing process (SF1 polishing solution, Logitech) then removes ~10 µm of material. After polishing, well defined apertures are obtained and the flat tip has a footprint of ~1.5 mm^2, figure 3d. Removal of the wax is done by heating the chips to ~ 110 °C while applying a vacuum at the vias. After an initial opening of the apertures, the residual wax in the channels is removed using heptane.

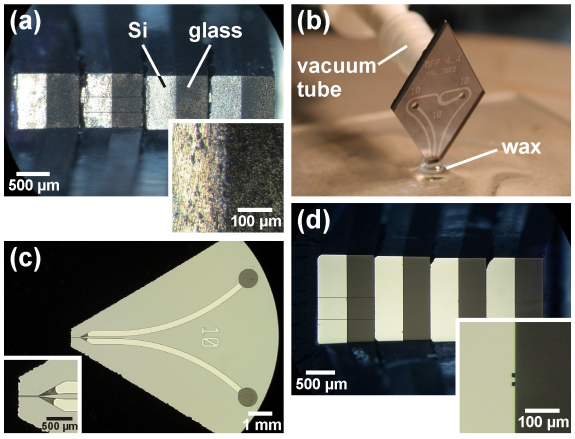

Figure 3: Polishing procedure for vertical MFP heads. (a) Micrographs of unpolished MFP heads clamped into a custom-made holder for lapping and polishing. (b, c) Vacuum assisted filling of the channels with molten wax (140 °C) to protect the channels from debris entering during lapping and polishing. (d) Micrographs of MFP heads after the polishing procedure yielded the well defined apertures.

RESULTS

Vertical MFP heads provide major improvements to the MFP technology. They are not only easier to fabricate with high precision and easy to assemble at high yields but they are also more convenient to connect to peripherals (holder, pumps). With a custom-made holder, an individual vertical MFP head is connected to high-precision pumps and the positioning stage within less than a minute. Two O-rings seal the vias of the MFP head with the holes of the holder, figure 4a and b. Different designs were made for the channels geometries, in which the widths of the channels vary between 5 and 20 µm and two different depths (10 and 20 µm) of channels were made, figure 4c. In figure 4d, an operational vertical MFP head was positioned ~10 µm above a transparent substrate and colored water (black) was injected at a flow rate of 1 µL min^{-1}, while aspirating at 5 µL min^{-1}. There, the immersion liquid was water and the micrographs were taken through the transparent substrate using an inverted microscope. The width of the flow confinement was roughly 50 µm. Smaller or larger widths of the flow confinement could be achieved by changing the either the gap distance between the head and the substrate or changing the injection and aspiration flow rates. Feasible confinement sizes are between 20 µm and 75 µm in width.

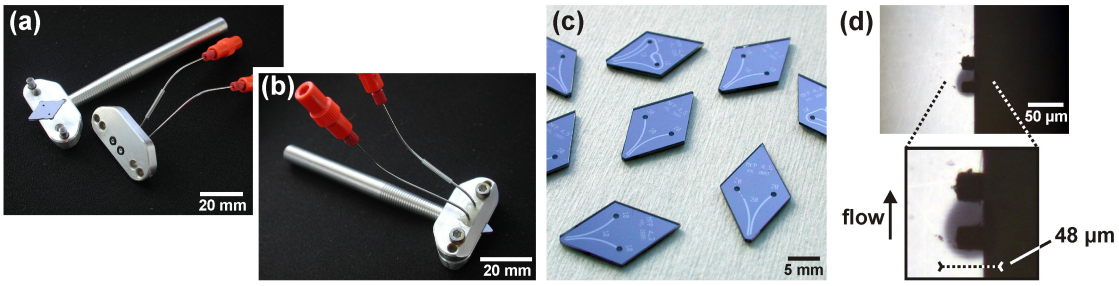

Figure 4. Testing of vertical MFP heads. (a, b) Photographs of a vertical MFP head mounted in a custom made holder comprising connectors for tubes from the pumps. Two rubber O-rings ensure proper sealing. (c) Five different channel/aperture designs were fabricated with channels depths of 10 µm and 20 µm. (d) Micrograph of an operational vertical MFP head, showing the flow confinement using colored water as processing solution and water as immersion liquid.

CONCLUSION

Because vertical MFP heads have their microfluidic structures fabricated in plane, these heads are simple to fabricate and assemble at high yields. They are robust and amenable to confine liquids on surfaces with very high precision. These new heads should therefore strongly contribute to the adoption of the MFP technology for processing and analyzing samples using non-contact, scanning microfluidics.

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