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Novel microstructures and technologies applied in chemical analysis techniques

Vincent L. Spiering[2], Johannes N. van der Moolen[3], Gert-Jan Burger[2], Albert van den Berg[1]

[1] MESA Research Institute, University of Twente
PO Box 217, 7500 AE Enschede, the Netherlands

[2] Twente MicroProducts, PO Box 217, NL-7500 AE Enschede; tmp@eltn.utwente.nl

[3] University of Amsterdam, Nieuwe Achtergracht 166, NL-1018 WV Amsterdam

SUMMARY

Novel glass and silicon microstructures and their application in chemical analysis are presented. The micro technologies comprise (deep) dry etching, thin layer growth and anodic bonding. With this combination it is possible to create high resolution electrically isolating silicon dioxide structures with aspect ratio's similar to those possible in silicon. Main applications are chemical separation methods such as High Performance Liquid Chromatography (HPLC) or Electrophoresis (HPCE). Beside these channel structures, a capillary connector with very low dead and mixing volume has been designed and fabricated for use in (correlation) electrophoresis, and tested by means of precision of consecutive single injections.

Keywords: Materials and Technology, Chemical Analysis, Fluid Systems

INTRODUCTION

In the field of chemical analysis. especially in the important area of separation techniques, planar microstructures have a large potential, because they offer a number of advantages as compared to fused silica capillary-based systems. Microfabrication techniques give the possibility to (i) fabricate very small reproducible fluid channels, eventually with a large length, (ii) realize channels with variable cross-section in depth, (iii) vary the width (mask design) of the channels, (iv) integrate detection components into the fluid channels, and (v) decrease the dead and mixing volumes associated with interconnections.

Up to now, some groups have been working on the fabrication of planar structures for chromatography purposes. Manz et al. [1] was the first to use anisotropically etched channels in silicon for liquid chromatography, later followed by work from Ramsey et al. [2] and Cowen et al. [3]. Simultaneously, work was concentrated on High Performance Capillary Electrophoresis (HPCE), whereas Manz and Harrison [4, 5] were the first to use planar etched glass structures for this purpose. An elegant example of the potential advantages of using this technology was demonstrated by Burggraf et al. [6] who presented a quartz structure where a very good separation between two components was obtained through synchronised switching of the separation potential.

Despite all these interesting results, there are still several shortcomings of the use of planar separation structures up to now. First of all, the microchannels need to be interconnected to the other system components such as an injector, sample (micro)vial, and detector and waste. For this, interconnection techniques and system concept are of crucial importance. Our planar Micro System Fluid (MFS) concept was described earlier [7], and in this paper a capillary connection to microchannels is described. This technique can also be used to connect two capillaries.

Secondly, it is important to dispose of a technique that enables the fabrication of the fabrication of microchannels with a virtually arbitrary cross-section. For this, the so-called Black Silicon Method (BSM) [8] is applied. With the BSM technology, deep high aspect ratio channels can be dry etched. The cross-sectional shape can be varied by means of process variable control (type and flow of gasses, pressure). In this way channels shapes from square until isotropic round can be fabricated.

Finally, it is interesting to see whether structures for capillary electrophoresis, where high voltages in the order of several kV's are used, can be fabricated using silicon etching techniques. Particular emphasis is laid on a technology that enables the realization of a closed, all insulator microchannel.

GLASS MICROSTRUCTURES/CHANNELS

The conventional (MST) way to fabricate glass microchannels is to etch these in one or two glass wafers and bond these on top of each other [9, 10]. This method has the disadvantage that in glass only isotropically etched channels are feasible to make. Therefore, we developed an alternative technology, where the variety of cross-sectional shape acquired by the BSM technology is combined with anodic bonding in such a way that all-glass channels are fabricated [11]. This transfer from a high resolution/high aspect ratio silicon dry etched structure to a complete (inverse) glass microstructure is explained in detail.

Transparent glass micro channel fabrication

The main process steps are as follows:

1. Channel etching in silicon
2. Channel material depositing on silicon
3. Machining of the pyrex wafer
4. Anodic bonding pyrex wafer on top of silicon wafer
5. Etch back of sandwich in KOH
6. Protection/planarization layer over the channels

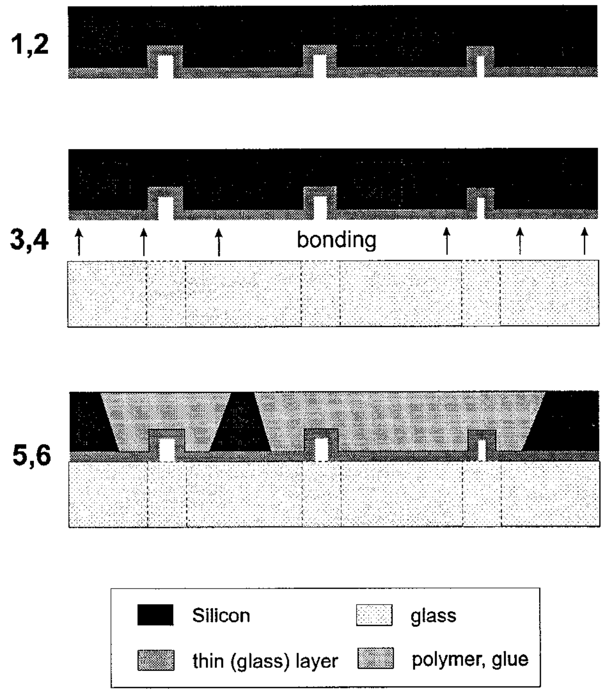


Fig. 1. Process scheme for glass microchannels.

1. Channel etching in silicon

With the BSM technology, deep channels with a variable cross-sectional can be etched.

2. Channel material depositing on silicon

Materials applied for structures are usually low stress LPCVD silicon-nitride, and/or TEOS oxide, sometimes combined with a thin layer of polysilicon. Functions of these layer are mechanical, electrically isolation, and etch stop for backside KOH-etching. The polysilicon prevents locally release at <111> faces of silicon during the KOH etch back process. Constraint on the layers is the total thickness for anodic bonding reasons.

3. Machining of pyrex wafer

By means of conventional precision machining techniques, inlet/outlet holes are drilled in the glass wafer.

4. Anodic bonding pyrex wafer on top

The machined glass wafer is bonded to the silicon wafer with intermediate layer of oxide and/or nitride.

5. Etch back of sandwich in KOH

This step can be done without patterns (total etch back of the silicon wafer, but also with a pattern in silicon to acquire more mechanical strength of the total structure. Especially in combination with the next step, this will prevent breaking of the tiny glass channels walls.

6. Protection/planarization layer over the channels

Several layers/materials like, thin films, polymers, glue cam be applied for this purpose. If a transparent material is used, the whole structure remains transparent from top and bottom side, which enables several types of optical detection techniques.

Relevant steps are the thin layer deposition followed by an anodic bonding process. Important for success are the mechanical *and* electrically isolating properties of the thin layers [12].

Figure 2 shows the outside of a complete glass covered channel on a glass substrate (step 5 carried out without mask). These structures are of great interest in the field of electrophoresis and other applications where electrical isolation of the structure is essential. Currently, specially shaped glass microchannels are to be tested for their fluid resistance and electrical isolation in concentration experiments for pre-separation applications.

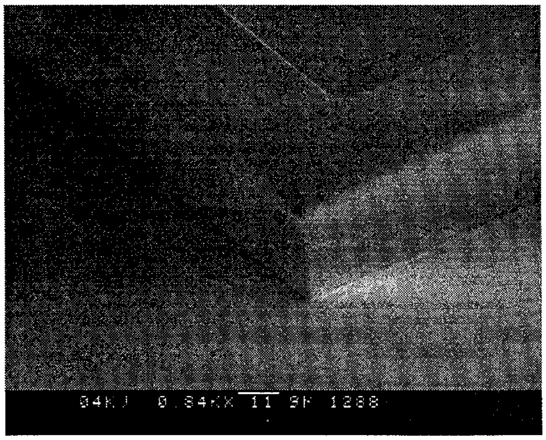


Fig. 2. Complete closed glass microchannel on glass substrate.

CAPILLARY CONNECTOR

Connections between capillary and sample injector or between several capillary's are realized via micro channels in silicon. The capillary connection chips were designed and fabricated by Twente MicroProducts [13]. The sample injection holes, channels, and wafer-through holes are realized by a combination of dry and wet etching steps in a silicon substrate. The channel dimensions are matched to the inner diameter of the capillary, thus minimizing the dead and mixing volume of the connection. The channels are electrically isolated with a thin layer of silicon oxide and they are covered by a glass plate. The structure was able to sustain voltages up to 250V/cm across the channel, and pressures up to 120 bar. Figures 3 and 4 show a lay-out and a SEM of a cross-section of a glued capillary connection with a micro channel.

The electrically isolated connectors are fabricated in a very reproducible way. Essential for a suitable connection are the application of high performance dry etch techniques, the design of a pre-aligned connection, and the glueing technique.

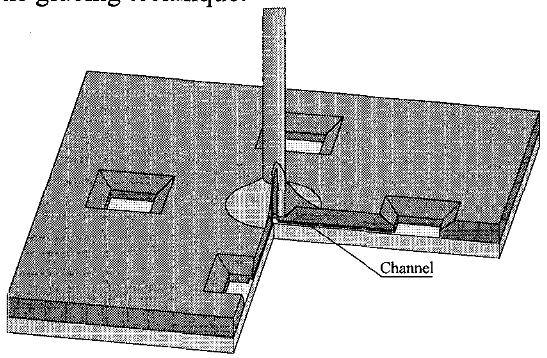


Fig. 3. Capillary connector combined on-chip with sample injector holes.

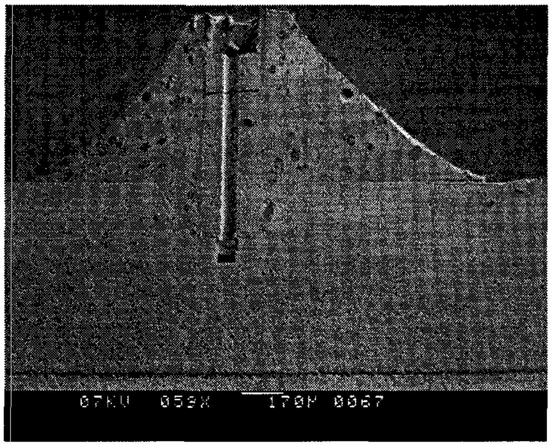


Fig. 4. Cross section of glued 280/75 μm capillary

The electrically isolated connectors are fabricated in a very reproducible way. Essential for a suitable connection are the application of high performance dry etch techniques, the design of a pre-aligned connection, and the glueing technique.

Capillary connector specifications:
dead/mixing volume: < 0.5 nl
max. pressure: to about $150 \cdot 10^5$ Pa
alignment: within 5 μm
Voltages: up to 250 V/cm

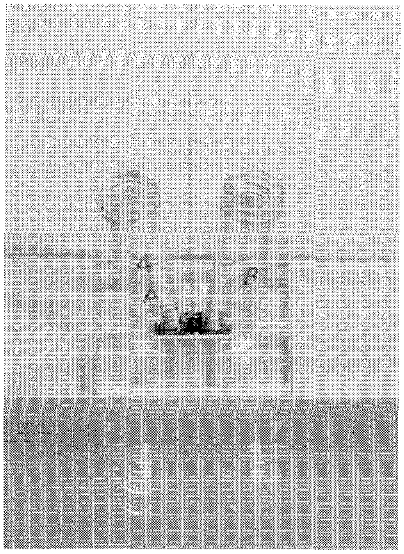
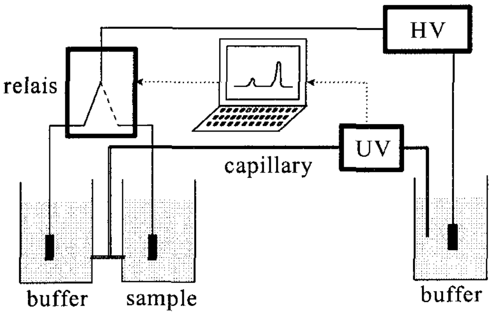


Fig. 5. Photograph of capillary and two sample injectors connected via the chip in a test set-up.

RESULTS

The connector has been tested by the Laboratory of Analytical Chemistry at the University of Amsterdam with a set-up as given in figure 6 [14].

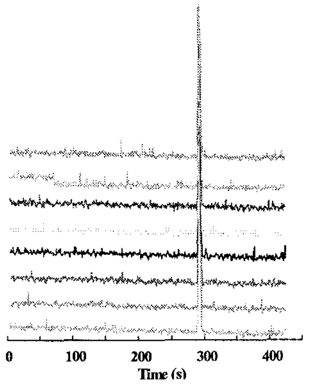


Injection Device: •No Dead-Volume

•Short Channels

Fig. 6. Correlation CZE system connection with a micro channel.

After proven precision of 8 consecutive injections (see fig. 7) the so-called correlation capillary zone electrophoresis (CCZE) technique was applied [15]. The capillary connector showed a very good reproducible behavior.



☞ RSD:

Time < 0.3 %

Height < 1 %

Area < 1 %

Fig. 7. Precision of 8 consecutive injections

The results in figure 8 show the improvement of detection limit in case of the CCZE technique: the detection signal to noise improves with a factor of 8.

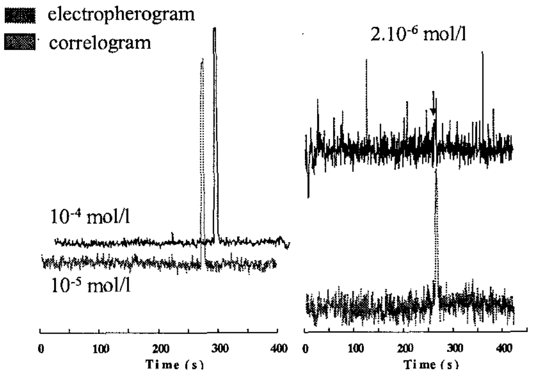


Fig. 6. Electropherogram vs. Correlogram

CONCLUSIONS

Microchip technology is very well suited for accurate fabrication of complex structures. Beside the fabrication of glass micro channels, it is demonstrated that connecting a microchip injection device to a fused silica capillary can be done quit easily. SEM photographs proved that the connection is excellent, with extremely low dead-volume. The repeatability in peak height and peak area of the electrokinetic injection was very good, with RSD-values better than 1.1 %. An improved repeatability with the microchip injection device compared to conventional injections has been demonstrated. With correlation CZE, the injection repeatability was even better than the repeatability with conventional CZE with the microchip injection device. Correlation experiments showed a considerable improvement in S/N ratio at high as well as low concentration. An 8-fold improvement in detection limit has been demonstrated.

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