Technologies and Microstructures for Separation Techniques in Chemical Analysis

Vincent.L. Spiering[1], Theo S.J. Lammerink, Henri V. Jansen,
Jan H.J. Fluitman, and Albert van den Berg

MESA Research Institute, University of Twente,
P.O. Box 217, 7500 AE Enschede, the Netherlands
tel: xx31 53 489 2805 fax: xx31 53 489 3343
email: v.l.spiering@el.utwente.nl http://www/el.utwente.nl/tdm/mmd/projects/mutas/mutas.htm

ABSTRACT

The possibilities for microtechnology in chemical analysis and separation techniques are discussed. The combination of the materials and the dimensions of structures can limit the sample and waste volumes on the one hand, but also increases the performance of the (chemical) system. Especially in high performance chromatography separation systems, where the separation quality is directly depending on the length to width ratio of the fluid channels, there is a large potential for applications. Novel technologies as well as demonstrator devices for different applications will be presented in this paper. Finally, a modular concept for microfluidic systems, in which these micromachined structures can be incorporated, is described and illustrated with a demonstrator.

Keywords: microtechnology, chromatography channels, chemical analysis system, modular system.

1. 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) realise 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 volumes associated with interconnections.

Up to now, only few 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], who used electroosmotic flow to drive the liquid chromatography carried out in an etched glass structure, and an isotropically etched column in silicon with a (hybridly) integrated electrochemical detector [3]. Besides the work on liquid chromatography structures, most work has been focused on planar structures for (high performance)

[1] Currently working at Twente MicroProducts, P.O. Box 217, 7500 AE Enschede

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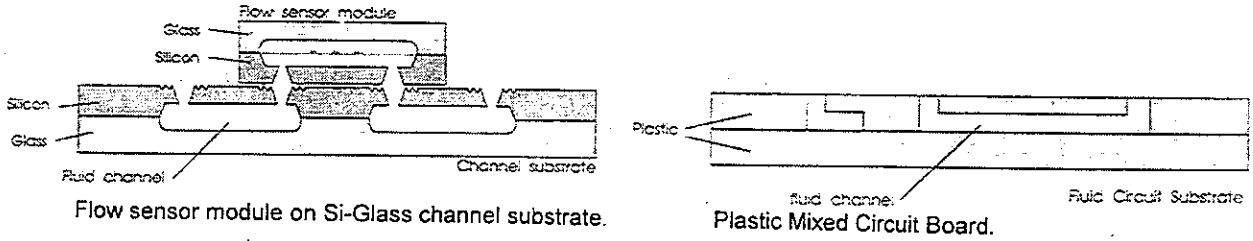
capillary electrophoresis (HPCE). Manz and Harrison [4,5] were the first to use planar etched glass structures for this purpose. An elegant example of the potential advantages of using this technology was demonstrated by Burggraf et al. [6] who presented a quartz structure where a very good separation 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. We will describe our planar Micro Fluid System (MFS) concept as a potential solution for this. Secondly, it is important to dispose of a technique that enables the fabrication of microchannels with a virtually arbitrary cross section. For this, the so-called Black Silicon Method will be described. 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 made using silicon etching techniques. Particular emphasis is laid on a technology that enables the realisation of a closed, all-insulator microchannel.

2. MODULAR FLUID SYSTEM

Over the past few years there has been an increasing interest in the development and realisation of miniaturised total analysis systems (μTAS) [7,8,9]. This growth is partly due to the rapid developments in fluid handling devices such as micropumps, -valves, -filters and -mixers [10], but is also explained by the need for complex (bio)chemical sensor systems with integrated self-test and calibration features. This has led to attempts to fabricate miniaturised flow systems [8,9] and microfabricated parts for separation systems. However, since such systems typically comprise a variety of components, materials and technologies, considerable attention has to be paid to the integration-concept of such systems. The two extreme forms of integration are hybrid and monolithic. An example of a hybrid analysis systems is the stacked phosphate analyser, as developed by Van der Schoot *et al.* [11], whereas the liquid dosing system of Lammerink *et al.* [12] is an example of a monolithic system. In practice, most systems will consist of a combination of these two forms. In [13], Lammerink *et al.* showed a concept that enables a modular mixed integration of different system components or subsystems on a planar backplane: the Mixed Circuit Board. This MCB serves at the time as mechanical support for the system components (modules), it has the necessary electrical connections (Printed Circuit Board) and contains the microchannels for fluid transport connecting the different modules (Channel Circuit Board) (see figure 1).



Flow sensor module on Si-Glass channel substrate. Plastic Mixed Circuit Board.

Figure 1. Examples of Mixed Circuit Boards based on glass-bonded silicon (left) and plastic substrates (right).

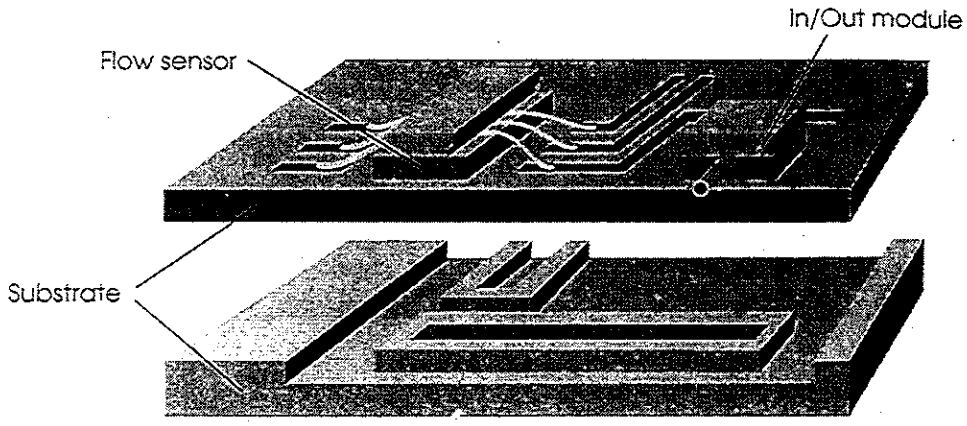


Figure 2. Artist's impression of laminated Mixed Circuit Board with mounted flow sensor and in/out module.

Standardization of components, materials and technology is important to make the modular concept successful. It enables system integrators to combine components from different suppliers into one system, which is of particular importance when assembling microanalysis systems with a large variety of components. As substrate or backplane material, up to now often an anodically bonded Pyrex glass-silicon structure has been used, mainly because of the simplicity to fabricate microchannels in silicon by isotropic or anisotropic etching. However, when aiming at economic production, polymer materials are preferred, and hot-embossing methods, using micromachined silicon moulds, to structure plastics have been investigated (see figure 3 [14]).

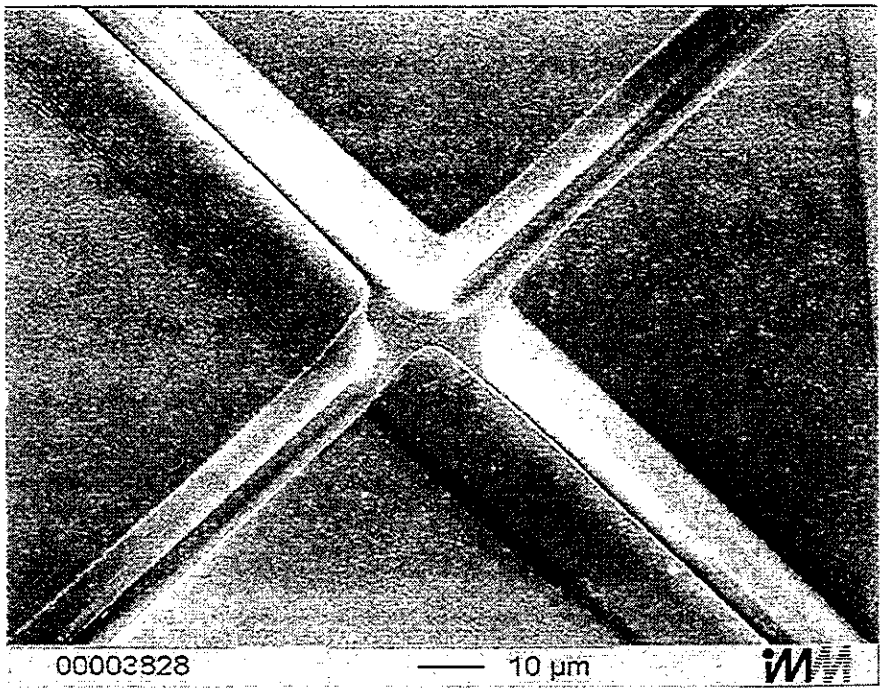
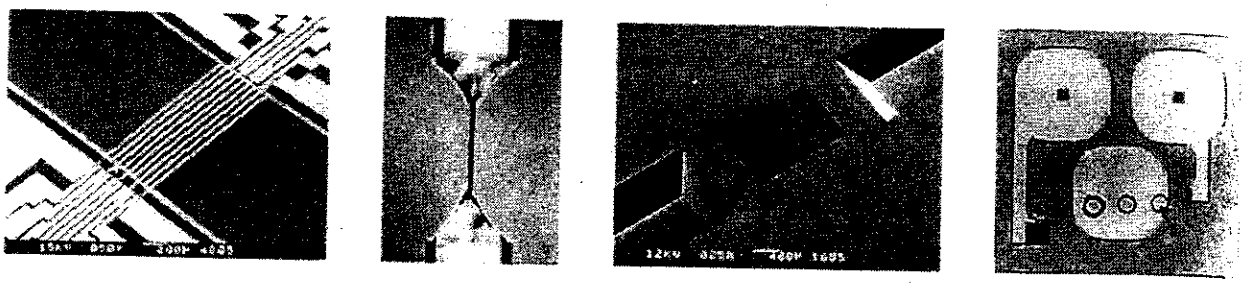


Figure 3. Micrograph of hot-embossed polycarbonate structures, using silicon as mold insert.

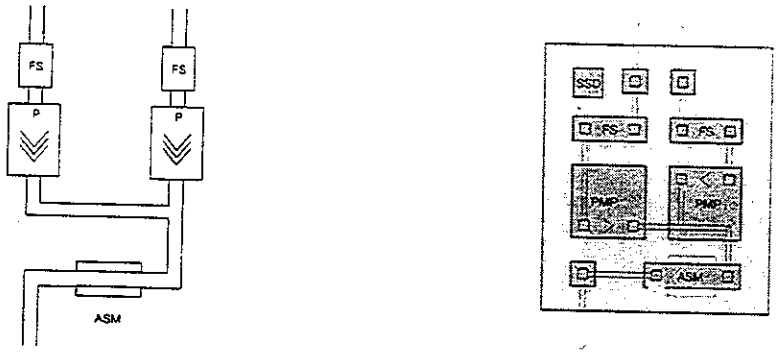


a) b) c) d)

Figure 4. a) Beam type flow sensor (the fluid channel width is 1 mm). b) Hydraulic resistor made of anisotropically etched V-groove. c) Mixer and/or filter module. d) Micropump (top-view).

For the realisation of fluid handling microsystems a wide variety of modules is needed. Many of them, like pumps, flow sensors and filters, were already developed before, but for integration into the modular system new designs have been made. In figure 4, SEM and/or optical photographs of some of the realised system modules are shown. These are all based on the standard fluid port pitch of 5 mm.

In figure 5, a schematic diagram of the demonstrator chemical analysis system, fabricated according to the MFS-concept, is given. The MCB comprises three in/outlets, two micro-pumps, two flow sensors and an optical absorption detector module. The purpose is to measure chemical reaction products by detection of the (spectral) absorption intensity. Sample and reagent liquids are mixed in the appropriate amounts on-board (currently the actual mixing takes place during the propagation in channels) and the optical absorption is measured at the detector side. The electronic control circuitry is situated in two levels below the MCB layer with the modules. It is based on a microcontroller system for the micro liquid handling and the chemical analysis data. Implemented in the electrical circuitry are driving circuits for the micro pumps, sensing circuits for the flow sensors, optical absorption measurement circuitry, power management and communications using an RS232 interface.



a) b)

Figure 5. Micro Analysis System (MAS). a) Structure of MAS with two flow sensors, two pumps and an absorption sensor module. b) Component lay-out of MAS.

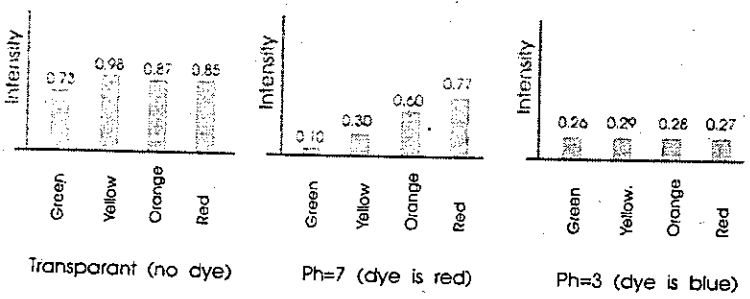


Figure 6. Measured light intensities with four coloured LED's.

The absorption cell is a glass silicon glass sandwich component (15x1x0.4 mm) where optical intensities from different coloured LED's are measured by a 64 pixel CCD detector. The operation of the absorption detection is demonstrated by recording absorption intensities. This was done at four different wavelengths for three liquids: a transparent fluid, the Congo red indicator at pH=7 (red-coloured), and the Congo red indicator at pH=3 (blue-coloured). In agreement with the literature the red LED detector shows the largest extinction, see figure 6.

An overview of the demonstrator system with a total system volume of about 50 ml is given in figure 7. Note that the largest part of the system is consumed by two electronic boards mounted under the fluidic system, which can be integrated in one or more ASICs if needed. This realization gives a clear view of the perspective of future μTAS realizations: the whole system can be realized on a plastic planar board with dimensions slightly larger than the size of a credit card.

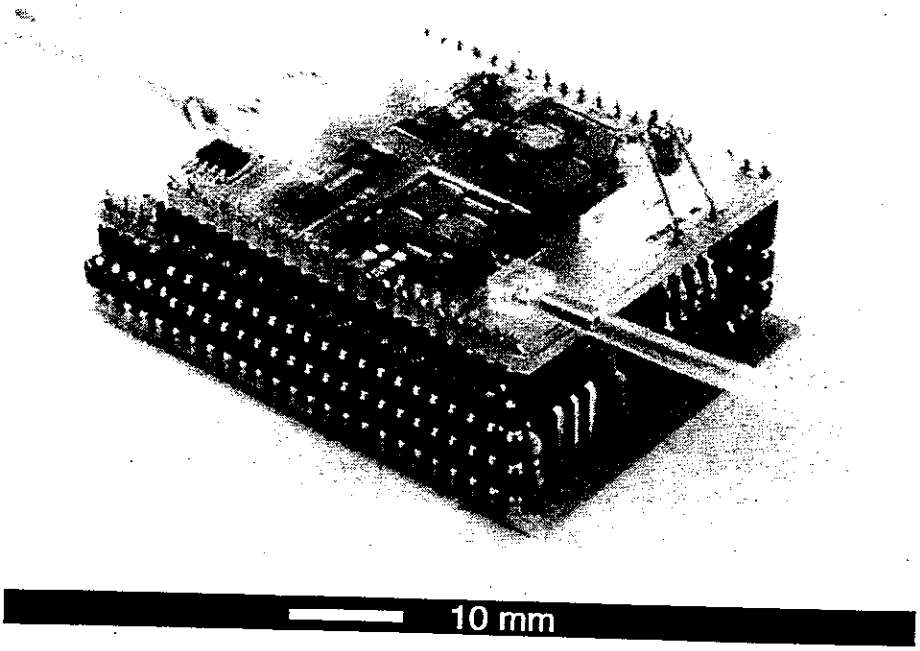


Figure 7. Demonstrator MAS modules mounted on a MCB.

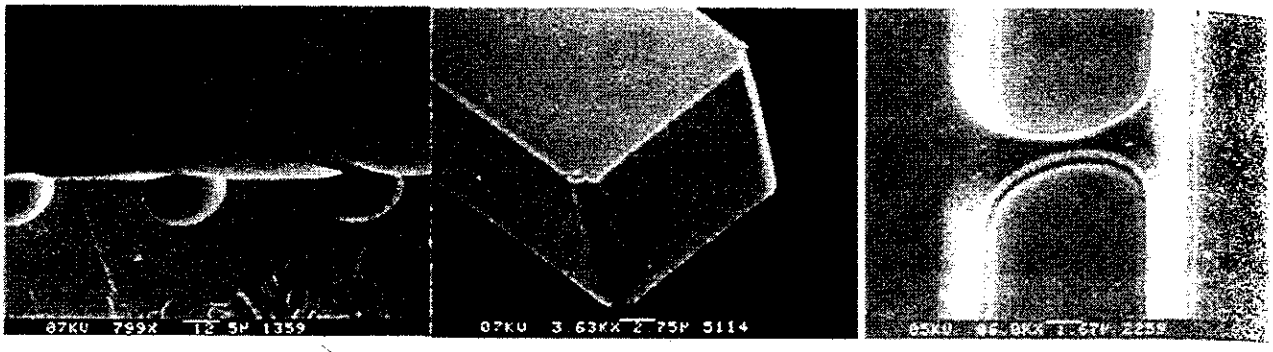


Figure 8: Typical products of the three basic mechanisms of dry plasma etching. Left: Chemical RE. Mid: Synergetic IBARE. Right: Physical IBE.

3. MICROMACHINING OF SILICON

Silicon micromachining has become a fundamental tool for the fabrication of micromechanical devices and, in general, miniature sensors and actuators. Micromachining techniques include firstly the basic processing steps of IC technology, namely film formation, doping, lithography and etching. In addition, they incorporate special etching and bonding processes which allow for the sculpturing of three-dimensional microstructures. Due to the good mechanical characteristics of silicon these technologies appeared to be useful for the fabrication of a variety of structures. However, the brittleness of silicon and the need for materials with specific properties (e.g. optical or electrical properties) stimulated the microstructuring of different materials as well.

The development of the so-called LIGA technology has given an impetus with respect to high aspect ratio structuring of different materials. The materials range from metals such as nickel, gold, alloys such as nickel iron up to polymers such as polyoxymethylene, polymethylmethacrylate polysterene, polycarbonate and others. However, the use of synchrotron radiation and the resulting complicated mask making make the LIGA technology economically less attractive and time consuming. Therefore, a variety of alternatives have been developed, such as UV-lithography, laser ablation, ion milling and spark erosion. Also, the innovations in etching techniques enabled the fabrication of micromoulds in silicon. This mould can subsequently be electroplated resulting in a metal micromould [14]. Some micromachining processes yield single-crystal silicon (SCS) moulds using crystal-orientation-dependent wet chemical etchants such as EDP, KOH_3 and hydrazine. However, the type, shape and size of the SCS structures that can be fabricated are severely limited. So, processes capable of fabricating structures with arbitrary orientations are desired. A way to achieve this is plasma-assisted etching.

The basis of plasma-assisted etching is simple; use a gas glow discharge to dissociate and ionisate relatively stable molecules forming chemically reactive and ionic species and choose the chemistry such that these species react with the solid to be etched to form volatile products. Plasma etching can be divided into three main groups (fig.8); 1) the *chemical* radical etching (RE), 2) the *synergetic* ion beam assisted radical etching (IBARE=RIE), and 3) the *physical* ion beam etching (IBE). Generally, IBE shows only positively tapered profiles, low selectivity and low etch rates, whereas RE gives rise to isotropic profiles, high etch rates and high selectivity. IBARE, currently the most important plasma configuration, enables the achievement of profile control due to the synergetic combination of physical sputtering with chemical activity of reactive species with high etch rate and high selectivity. Ion-enhanced etching can be divided into two main groups; ion-induced (reaction-controlled etching) and ion-inhibitor (desorption-controlled etching) IBARE.

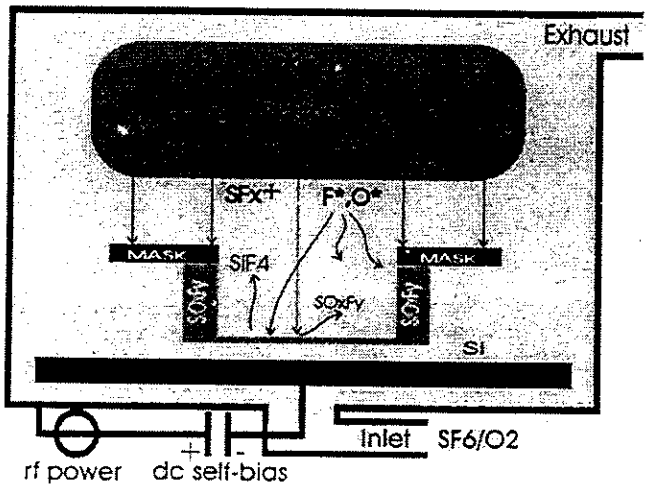


Figure 9. Basic IBARE system.

A basic ion-inhibitor IBARE system is illustrated in figure 9. Very deep trenches in silicon are etched using a fluorine-based plasma (SF_6/O_2). Generally, chromatography channels require vertical walls and a convenient way to find this condition is described below; the so-called Black Silicon Method [15].

In an SF_6/O_2 plasma, each gas has a known specific function and influence, so the etched profile is easily controlled just by changing the flow rate of one of these gasses. The functions of the gasses are: SF_6 produces the F^* radicals for the chemical etching of the silicon, O_2 creates the O^* radicals to passivate the silicon surface with SiO_xF_y, and SF_6 is the source for the SF_x^+ ions which etches the SiO_xF_y layer in the direction normal to the substrate due to the directional ion bombardment. Isotropic, positively and negatively tapered as well as fully vertical walls with smooth surfaces are achieved by controlling the plasma chemistry. Increasing the oxygen content will decrease the chemical etching and the etch mechanism will become more physical i.e. positively tapered as found in fig.10 left [16]. Even negatively tapered profiles can be obtained at lower oxygen content due to ion bowing of incoming ions (fig.10 right). At zero oxygen concentrations, there is no passivating layer which results in a more isotropic profile.

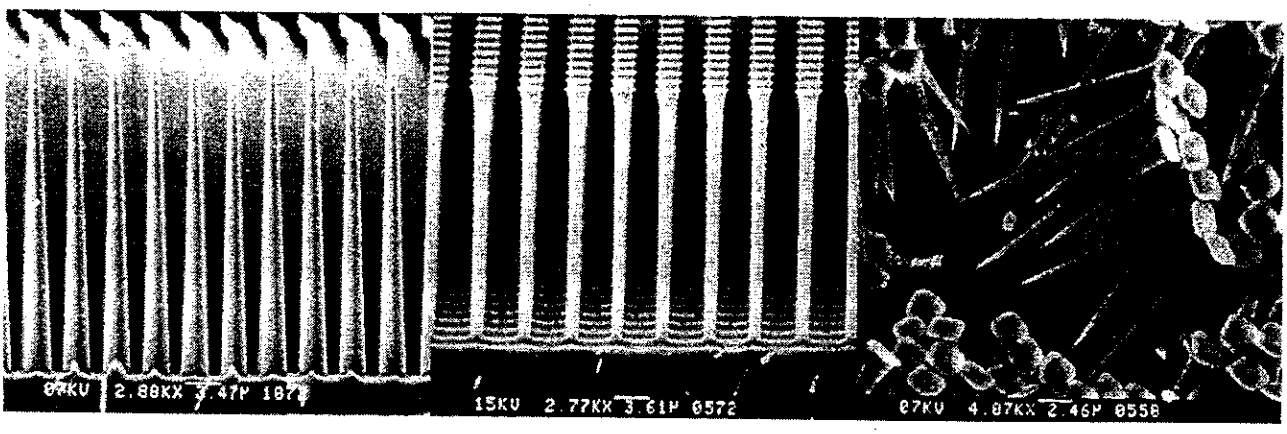


Figure 10: An array of silicon pillars for filter applications. The pillars are etched with the SF6/O2 chemistry at decreasing oxygen concentration in the feed from the left to the right.

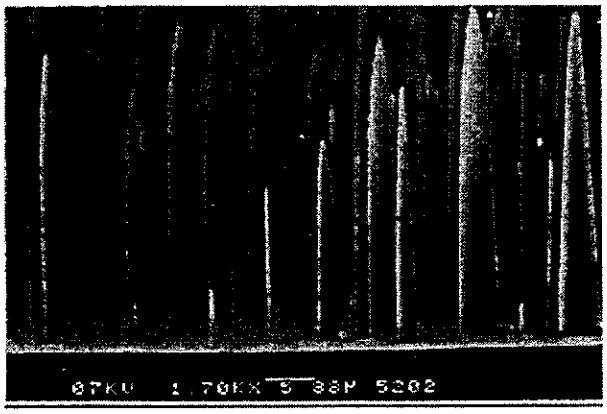
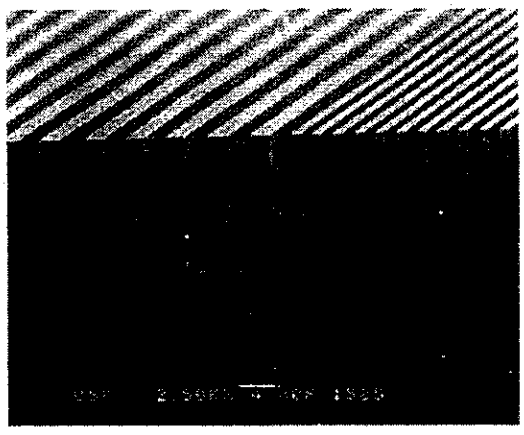


Figure 11. Black silicon surrounding etched structures.

At a certain oxygen content there is such a balance between the etching and the passivation that a nearly vertical wall results. At the same time, small particles such as native oxide, dust and resputtered mask material act as a micro mask. Because of the directional etching, spikes will appear as shown in figure 11. The appearance of such a surfaces is very black and is known as black silicon. This explains the name given to this method: the Black Silicon Method. The black silicon is used to find the etch parameters and gas concentrations needed to obtain high aspect ratios. Note that once the anisotropic region is found, spikes can be avoided by slightly decreasing the oxygen content in the feed.

4. SILICON AND GLASS MICROCHANNELS.

The abovementioned etching technique has been used to etch vertical channels with relatively high aspect ratios in silicon (see figure 12). Vertical channels have the advantage that they allow a high density of channels per area, and provide for a long (vertical) absorption path length for optical detection. The high channel density is illustrated by the channel structure for chromatography containing over 300 m of 2.5 μm wide and 25 μm deep channels on one single 3" wafer (see figure 13).



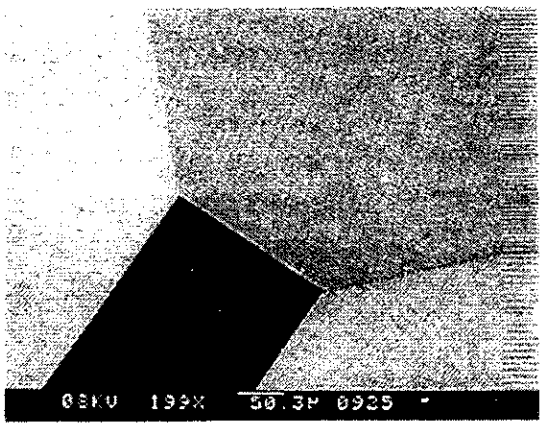


Figure 12 (left). Vertical channels made with RIE.
Figure 13 (right). Anisotropically etched microchannels for chromatography.

The wafers containing the etched trenches are anodically bonded to Pyrex glass to form closed channels. The bond strength thus formed is strong enough to withstand pressures up to 250 bar. At that point a breakdown even takes place in the monocrystalline silicon and not at the bonded interface. Clearly, the indicated structures are useful for HPLC applications. However, for capillary electrophoresis typically voltages of several kV's are applied, and completely isolating materials such as quartz are used [5]. Unfortunately, wet etching of quartz is not trivial, and little is known about dry etching techniques of quartz. Thus there is an interest to transform the etched silicon structures into isolating structures. For this purpose, the etched trenches are filled with silicon oxide and anodically bonded. Subsequently, the backside of the silicon is etched back until the oxide is reached, and in such way closed, all-glass microchannels are formed (see figure 14).

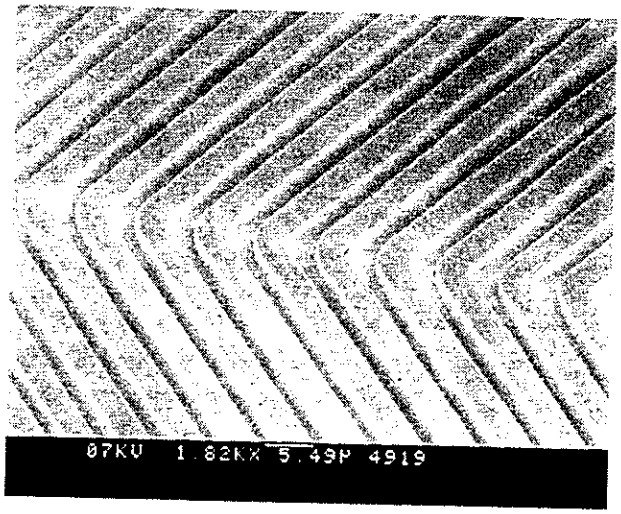


Figure 14a. All-glass microchannels formed by RIE with back-etched silicon.

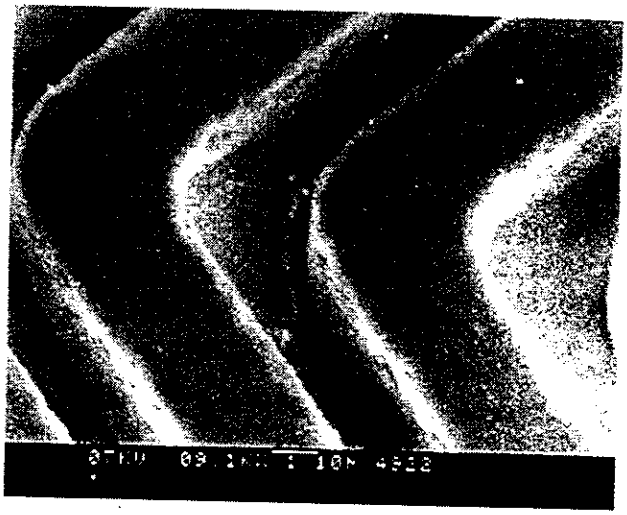


Figure 14b. Detailed micrograph of glass-micro-channels.

5. CONCLUSIONS

We have shown that reactive ion etching (RIE) is particularly suited for the fabrication of microchannels for chromatography. The etching technique allows for the fabrication of rectangular channel cross-sections, enabling a high channel density. With the modular fluidic system (MFS) concept, silicon components can be assembled onto a planar channel board, which can be made of glass-bonded silicon or being replicated in plastic using silicon moulds. In addition to the RIE, a novel technology to fabricate the microchannels in glass/silicon-oxide is proposed which makes these devices available for separation based on electrophoresis. concept of microfluidic systems [2], other components such as detectors but also pumps, flow sensors, mixers and inlet/outlet-connectors can be integrated. Using planar waveguides, an integrated optical detector with very long optical interaction length combined with a small detection volume can be realised. Finally, a capillary connector with very small dead volume has been realised.

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