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Gas chromatography of the future: columns whose time has come

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Currently a new technology for the manufacture of chromatographic columns is being developed on the basis of methods designed to create microelectromechanical systems. This technology allows reducing the column size and also opens up prospects for developing a unique process for manufacturing columns without human intervention. The review presents data on the use of this technology for manufacture of gas chromatography capillary columns. The methods for preparation of capillaries and the influence of their shape and configuration on the chromatographic properties of the columns are considered. The methods for stationary phase introduction into capillaries, both traditional for capillary gas chromatography and borrowed from the semiconductor and microelectromechanical technologies are discussed. The unique properties of semi-packed columns obtained using microelectromechanical techniques are considered. The possible applications of such columns and the ways of their further development are discussed.
The bibliography includes 179 references.

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I. Introduction

Gas chromatography is one of the few versatile methods for qualitative and quantitative analysis of complex mixtures of organic compounds. The key element of this method is a chromatographic column, which defines the scope and largely the equipment background of the method. During the long history of chromatography, the design of the column has substantially transformed.

A new technology for the manufacture of chromatographic columns is currently being developed. It is based on methods designed initially for fabrication of microelectromechanical systems (MEMS). These methods enable significant reduction in size for the majority of typical items around us including analytical instruments. The methods are based on etching chromatographic channels in silicon wafers or other materials.

The information discussed in this review is relatively new to the Russian reader, so the question arises of how to

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name these columns. The terms 'MEMS Columns' and, very rarely, 'Planar Columns' are used in the English literature to describe the columns manufactured by forming a capillary on a surface. Columns that are described in this review are called MEMS columns, *i.e.*, columns manufactured using technologies designed for the fabrication of microelectromechanical systems. To date, the only review has been published on the subject,[1] considering insertion of the chromatographic material into the channels of MEMS columns. However, the authors of that review did not consider the methods for forming capillaries and did not compare the chromatographic properties of MEMS columns of various types.

In 1979, the first miniature chromatographs appeared, most of their elements being made on chips.[2] Such devices are portable, have low power consumption and are suitable for performing analyses in locations where standard laboratory equipment is inapplicable. As noted above, the most important element of any chromatographic system is the column, which determines the separation quality and time. There are various types of gas chromatography microcolumns which are prepared using MEMS technology. Their important feature is high reproducibility of determination and low cost of replication.

The modern process of manufacturing fused silica capillary chromatographic columns comprises many steps, each of which may introduce an error. Therefore, the market receives only columns qualified against the chromatographic parameters; it is obvious that this is only a part of the total number of columns prepared. Using rigidly standardized MEMS technologies for the manufacture of columns, these limitations can be overcome. Moreover, the existing MEMS technologies are able to form phase and sorbent layers on the inner surface of the channels without human intervention. This is in line with the modern trend of technology, that is, development of methods that exclude human error in the manufacturing process.

This review deals with chromatographic columns prepared by etching of silicon wafers. The methods for forming channels on silicon wafers and for coating the channel surface by films of chromatographic materials are described. Various types of columns that can be manufactured using MEMS technologies are considered as well as some chromatographic properties of such columns; examples of separation of mixtures with their application are given.

II. Methods of forming channels on the surface of a silicon wafer

Methods of forming channels† in MEMS columns are typically based on etching of a silicon wafer by photolithography techniques.[3,4] It should be noted that similar techniques may be used to fabricate not only columns, but also items in which gas communication routes need to be made.[5] Before conducting the etching process, one should clearly conceive the required shape of the channel. For this, it is necessary to apply a pattern of the item (in this case, the channel) onto the prepared template. The mask is a glass plate or a polymer film with a pattern formed on its surface by some material (for example, chromium film) that is impervious to a certain type of radiation.[6]

After fabrication of the mask, the pattern from its surface is transferred to the substrate surface. The substrate material may have various chemical compositions[7–14] Silicon and glass are used most often. Regardless of the nature of the material, the surface to be treated is polished and a photoresist layer is applied onto it during centrifuging of the wafer.[15] When this application method is used, film thickness can be controlled by varying the rotation speed.[4] After the substrate is coated with a photoresist, the pattern is transferred to the substrate surface by irradiating the substrate (*e.g.*, with UV light) through the mask. The general diagram of patterning of a photoresist-coated substrate is shown in Fig. 1. After the development, the exposed area becomes soluble and is destroyed (positive photoresist) or polymerizes and becomes insoluble and only the unexposed regions are dissolved (negative photoresist). A positive photoresist (*e.g.*, AZ 9260) is used most often to prepare MEMS columns.[15,17,18]

Note that, if necessary, the application of the photosensitive layer may be preceded by an additional procedure for deposition of a sublayer of functional material on the substrate surface. In the case of silicon wafer substrates, silica obtained by thermal oxidation of the surface or epitaxial deposition is used most often as a sublayer between the substrate and photoresist.[16,19] The sublayer of the functional material can serve, for example, to improve adhesion of the photoresist to the substrate or to enhance resistance to etching agents or to etching method. In the latter case, the sublayer acts as a mask, which protects the silicon wafer surface from exposure to etching substances.[20]

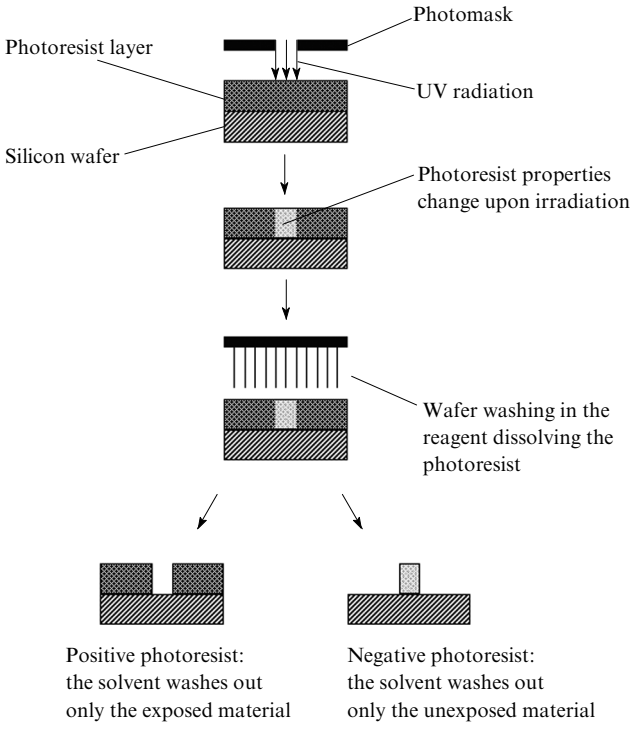


Figure 1. Patterning of the silicon surface.[16]

† By the word 'channel' is meant an open trench etched on the surface of any material. Sealing of the channel by a plate produces a capillary. The capillary in which a stationary phase is deposited on the inner surface is called a column.

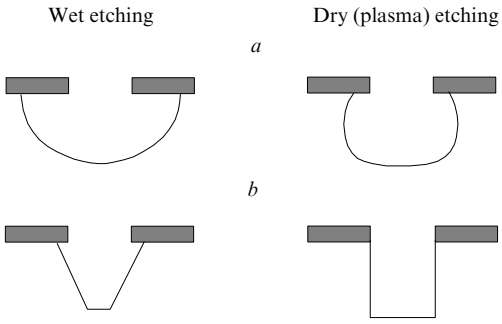


Figure 2. Examples of channel profiles obtained with isotropic (*a*) and anisotropic (*b*) etching using wet and dry etching technologies.[16]

After the pattern is formed on the silicon surface, the etching process can be started to obtain a channel that will be used as a chromatographic column.

There are two main etching techniques, liquid (wet) and dry ones (Fig. 2). Depending on the technology used, the channels have various cross-sectional shapes.[21] The channel shape also depends on whether etching is isotropic or anisotropic (see Fig. 2). In the case of isotropic etching, the etching rate is the same in any direction, whereas anisotropic etching occurs faster in one direction than in the other directions.

Both dry and wet etching and their combinations are currently used to produce channels with a characteristic size of 50 – 500 μm required for the preparation of MEMS columns.

II.1. Wet etching

Wet etching consists in dissolving substrate areas not covered by the protective photoresist layer according to the predetermined pattern on the surface. This method provides a high etching rate and enables the process control by changing the temperature and concentration of the etching solution. Wet etching can be either isotropic or anisotropic (see Fig. 2). A mixture of acids, *e.g.*, hydrofluoric and nitric, is used for the isotropic etching of silicon;[2, 21 – 25] anisotropic etching is performed with potassium hydroxide or tetramethylammonium hydroxide.[2, 21, 26 – 28] The advantages of wet etching are the simplicity of the equipment, low cost of materials and no need for highly skilled personnel. The drawback is that with this method, it is impossible to precisely control the etching depth and to create compact (< 10 μm in size) elements within the channels (including the channels themselves).[29] Nevertheless, wet etching is used to form the channels of circular and semicircular cross-section. The depth of the obtained channels depends on the temperature, etching time and width of the opening for the access of etching substances, while the shape depends on the composition of the etching solution. A typical example of wet etching has been reported;[23] the authors used a mixture of hydrofluoric acid (49.5%), nitric acid (69.5%) and acetic acid in a volume ratio of 0.5 : 85.5 : 10 and applied a mask based on a chromium film. The etching was carried out at 20 °C for 67 min. Under the conditions described above, it became possible to etch the channels of cross-section representing a semi-ellipse with major and minor axes of 100 and 10 μm, respectively.

Further development of the techniques to prepare MEMS columns using wet etching was aimed at finding ways to form channels of circular cross-section instead of an asymmetric semi-circular one. This required the use of elements of dry etching. Two methods proposed by de Boer and co-workers [21, 22] were mainly used for the formation of circular channels. One method consists in bonding of two substrates, in which semicircular channels have already been formed by isotropic etching. Methods for bonding silicon wafers have been described in the literature.[30, 31] In such a way, columns with mean capillary diameters of 44 – 58 μm were prepared. A detail section of this column is shown in Fig. 3.

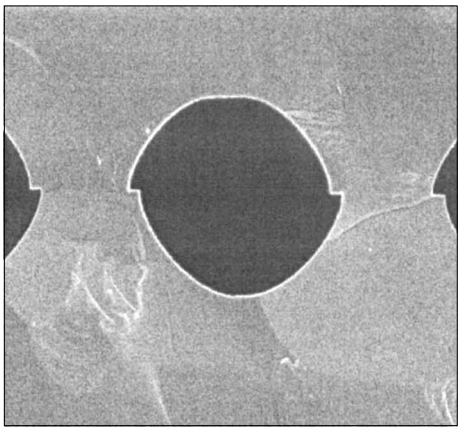


Figure 3. Cross-section of a channel of capillary MEMS column obtained by isotropic wet etching and bonding of two wafers.[21]

A significant limitation of this method is that the channel diameters for different parts of the substrate may vary (typically, the holes in the middle of the wafer are somewhat narrower than the edge ones). Bonding the substrates with channels of different diameter distorts the capillary shape, and, hence, deteriorates the properties of chromatographic columns. Upon bonding, the wafers, even having equal diameters of the channels, may shift relative to each other (see Fig. 3), and this is also reflected in the quality of the columns.

These defects can be avoided by using the method called Buried Channel Technology (BCT), which is based on the formation of circular channels within a silicon wafer.[21, 22] A scheme to prepare the channel using this technique is shown in Fig. 4.

The process begins with the application of silicon nitride layer on a silicon wafer by the chemical vapour deposition (CVD) method;[32] this layer serves as a mask during etching (step *1*). Then, a long, narrow trench (*e.g.*, 4 μm wide) is formed in the resulting layer and in the silicon wafer using the reactive-ion etching (RIE) method [33] (step *2*). After that, a silicon nitride layer is applied again to cover the trench walls and bottom (step *3*). In the next step, silicon nitride is removed from the bottom of the trench using RIE and the silicon surface becomes available for wet etching (step *4*). Then the isotropic wet etching is carried out: the substrate is placed in an aqueous solution containing a mixture of hydrofluoric and nitric acids (step *5*). After etching, the channel is washed with water. Further, the channel walls

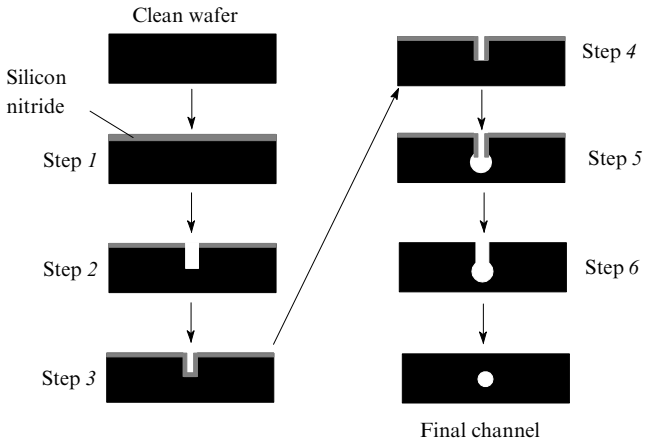


Figure 4. Diagram of fabrication of MEMS columns using BCT method.[22]

and the wafer surface are cleaned from silicon nitride by immersing the substrate into a 50% solution of hydrofluoric acid (step *6*). At the final step, a layer of material that covers the wall of the channel and closes the narrow trench is introduced into the capillary. Silica, silicon nitride and polysiloxane can be used as such materials. Fragment of the column section prepared according to the BCT method is shown in Fig. 5. One can see that the channel shape deviates from circular. The deviation is due to the accumulation of etching products within the channel and the reduction of concentration of active substance.[34]

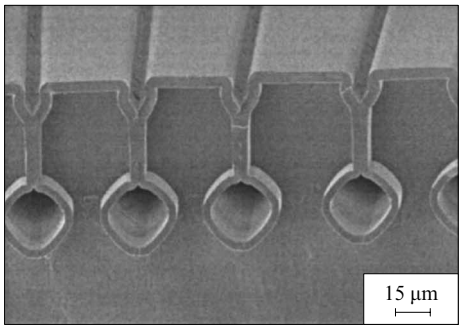


Figure 5. Fragment of a column manufactured using BCT.[21]

It should be noted that the separation power of the columns is not given in the papers[21,22] which describe the BCT fabrication of MEMS columns.

In 2009, an improved BCT was proposed,[19] according to which one can obtain a round channel located partially inside the wafer [partially BCT (p-BCT)]. The block diagram of this method is shown in Fig.6.

Many stages of the p-BCT process are similar to those of BCT. A protective layer is deposited on the silicon wafer (in this case, a silica layer; Fig. 6 *a*). After photoresist deposition (Fig. 6 *b*), holes are formed inside the protective layer for the access to the silicon wafer, but this time to a small depth of 11 μm (Fig. 6 *c*). Then, using CVD method, a silica layer is deposited (Fig. 6 *d*); after removal of this layer from the bottom by reactive-ion etching (Fig. 6 *e*), the side walls

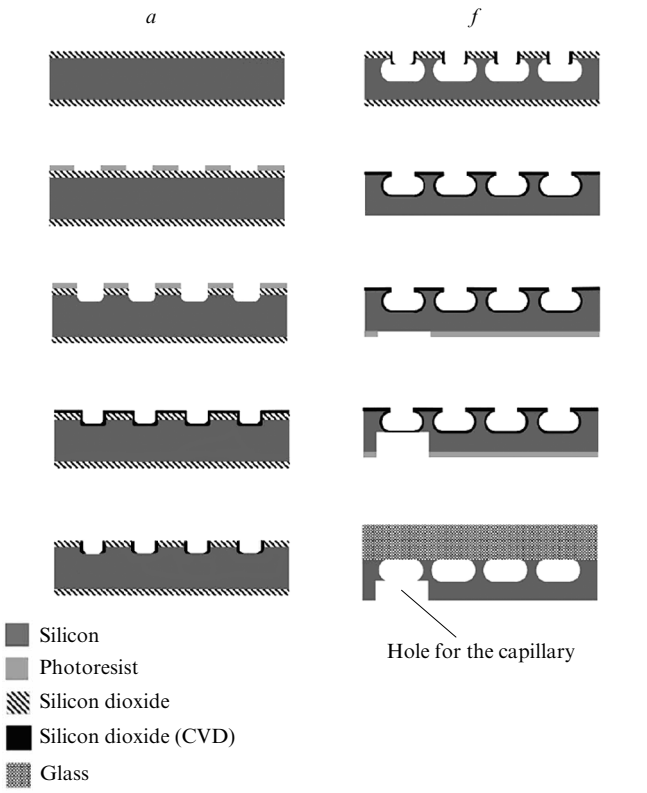


Figure 6. Diagram of fabrication of MEMS columns using p-BCT.[19]
For *a*–*j*, see text.

of the channel remain protected during etching (Fig. 6 *f*). Dry rather than wet isotropic etching is used in p-BCT, unlike the BCT (see the next section). The diagram provides additional procedures consisting in the formation of the outlets on the reverse side of the wafer required for connecting the column to a chromatograph. The formed column channel is covered by a protective silica layer (CVD) to prevent it from being affected during the preparation of outlets (Fig. 6 *g*) . A layer of photoresist is applied on the reverse side of the wafer, to which a pattern with predetermined parameters of the holes is transferred by lithography (Fig. 6 *h*). Then the wafer part not protected by the photoresist is dry-etched (Fig. 6 *i*). Thereafter, the wafer is freed from silica and photoresist, and the channel is covered by a Pyrex plate (Fig. 6 *j*).

This gave a channel, the cross-section of which is shown in Fig. 7. It is evident that the cross-section is not circular. Nevertheless, columns prepared by this procedure are suitable for separation of multicomponent mixtures of chemically different compounds.

Wet etching, especially in combination with other methods, is a rather labourious process that does not guarantee the reproducibility of the size of prepared columns. The desire to create a column of circular cross-section of the channel is a kind of stereotype formed when working with fused silica capillary columns of circular capillary cross-sections.

The capillaries prepared by the wet etching of silicon were later used to manufacture chromatographic columns; however, most of the works in this field were carried out using capillaries fotmed by the dry etching method.

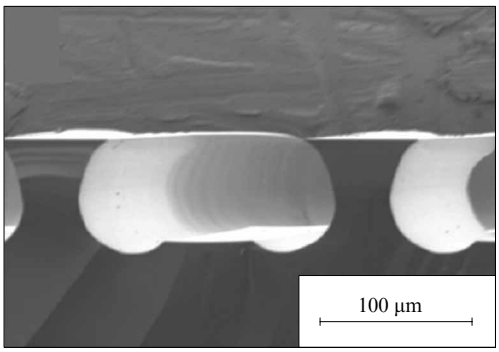


Figure 7. Channel cross-section fabricated using p-BCT.[19]

II.2. Dry etching

Currently, techniques for forming channels in a silicon wafer that do not require the use of a liquid for etching are most popular. Most often, reactive-ion etching is used. This is a kind of dry etching in which the photoresist-coated wafer is exposed to plasma of the etching substance. A specially selected photoresist is not affected by plasma, which etches the bare surface of silicon. The removal of the substrate material occurs as a result of both the chemical reaction and the physical bombardment (sputtering) by plasma ions and radicals. An appropriate reactive gas is selected for each material subjected to dry etching. Silicon and its compounds are etched by chlorine- and, more often, fluorine-containing plasma.[35] In the case of reactive-ion etching, the process is isotropic and the channel profile will not have clear vertical boundaries (see Fig. 2).

Deep reactive-ion etching (DRIE) is used to make etching anisotropic.[36–40] This method differs from reactive-ion etching in that the sidewalls are passivated during the formation of channels, thereby mainly the bottom of the channel is etched. There are several approaches to the implementation of the method.

II.2.a. The cryogenic dry etching process

In this process, passivation of the sidewalls is based on oxidation of the silicon surface at 173 K.[35] Oxygen radicals required for surface oxidation of silicon are formed in oxygen plasma. The oxidation produces a passivating silica film, which prevents interaction of fluorine with the surface during subsequent etching of the silicon wafer by fluorine-containing plasma. The main disadvantage of cryogenic process is the need to use low temperatures. In this regard, the use of photoresists is impeded, as they can crack and delaminate at low temperature. Furthermore, defects can form on the silicon wafer at a large temperature difference between the substrate surface and plasma.[35]

II.2.b. Bosch-process

The basis for this process of anisotropic dry etching is alternation of plasma dry etching with sulfur hexafluoride plasma and the plasma passivation with a precursor gas.[36] Hexafluoropropylene or octafluorocyclobutane is used as the precursor gas. A passivation film resembling Teflon in the structure is formed in the reaction of these compounds with plasma. The etching and passivation gases are fed alternately into the reaction chamber. The interaction of plasma with the wafer material and material carry-over from the reacting surface occur in each cycle of plasma treatment of the surface. Each passivation cycle yields a thin Teflon film coating the channel bottom and sidewalls. The deposited film is removed from the bottom of the channel using ion bombardment. Currently, Bosch-process is used most widely in the fabrication of MEMS columns.

The advantages of dry etching are high reproducibility of the channel dimensions and the possibility of their different positions on a silicon wafer. However, implementation of this method requires expensive equipment and highly qualified personnel. Nevertheless, once developed technology allows for a reproducible replication of the same type of product without human intervention.

The vast majority of MEMS columns use channels of square or rectangular cross-section. For the preparation of columns with such cross-section, a $\sim$2 μm thick photoresist layer is deposited on a silicon substrate. The channel pattern is formed by photolithographicy on the photoresist, followed by dry etching of silicon wafer areas from which the photoresist was removed.[20]

II.3. Anode bonding

The cross-section of a wafer with rectangular open channels obtained this way is shown in Fig. 8. For the formation of a capillary, it is necessary to seal the channel; this is done by anode bonding of the matrix with a glass plate, usually made of Pyrex.[17,19,20,42] Anode bonding is a method for attaching a silicon wafer to glass under the effect of high temperature (200 – 500 °C) and applied electric field.[43] In an electric field, Na^+ cations in the heated glass diffuse to the cathode and O^- anions move toward the silicon wafer surface. External pressure is applied to form a close contact between the silicon wafer and the glass. In such a way it is possible to reliably seal the adjacent rectangular channels and to provide the flow of gases only along the formed capillary.

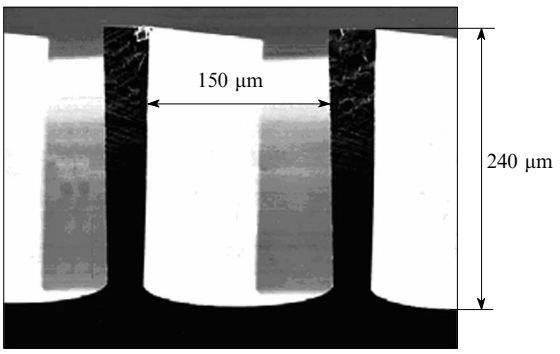


Figure 8. Photograph of the cross-section of a wafer with rectangular channels not closed from the top.[41]

There are other less common methods and materials for sealing the column channels, for example, a silicon wafer can be used instead of glass.[30,31,44]

II.4. Inclusion of MEMS columns into the chromatography path

It was noted above that MEMS technology can provide systems in which most of the chromatograph elements, including the chromatographic column, are arranged on a single chip. In this case, chromatograph elements are

interconnected by communication routes formed directly in the wafer by etching methods that are also based on MEMS technology. However, in the design of MEMS columns with new stationary phases, it is important to evaluate their suitability for chromatographic analysis. For this purpose, there is no need to fabricate the entire device on the wafer, but it is sufficient to connect in some way the finished column to a standard laboratory instrument. This can be done using fused silica capillaries with an inner diameter of 100–250 μm and a length of about 5–30 cm, which will serve as adapters between the column and the instrument communications.[19, 23, 42] The inlet and outlet ports for capillaries are made on the reverse side of the wafer to connect the column to the chromatograph (see Fig. 6 *g*–*j*). Normally these ports are formed before the channels are sealed with Pyrex or other material. This is done as follows. The etched holes are sealed with a protective layer such as silica. Then, a photoresist layer is applied to the reverse side of the plate and the pattern of the holes with the required parameters is transferred photolithographically from the template. The template is attached to the wafer so that the future holes precisely coincide with the column channel. The holes are formed by DRIE etching of the silicon wafer areas unprotected by the photoresist. After that, the photoresist and the protective layer are removed from both sides and the channels are sealed with a Pyrex plate. The capillaries are attached to the inlet–outlet holes thus obtained by epoxy resin[42] or polyimide[23] or connected by means of special holding devices such as Nanoport (Fig. 9).[19, 45]

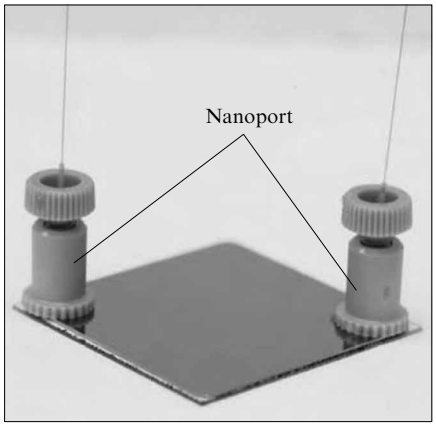


Figure 9. MEMS column connected to fused silica capillaries *via* Nanoport.[45]

After the capillaries are attached, the MEMS column is connected to an instrument as a conventional fused silica capillary column. The procedure of capillary attachment is also required for introducing the stationary phase in a number of ways, for example, using a static or dynamic method (see below).

III. Efficiency and expected properties of MEMS columns

III.1. Dependence of the efficiency of columns with rectangular cross-section channels on the carrier gas velocity

The most important quality characteristic of any chromatographic column is its efficiency measured by the number of effective theoretical plates (N) or by the height equivalent to a theoretical plate (HETP), denoted by H. The values of N and H are related by the equation

$$H = \frac{L}{N}$$

where L is the length of the column.

We will consider what HETP values can be obtained using a rectangular capillary as a chromatographic column and how much these values differ from those obtainable using conventional circular cross-section capillary columns.

The following expression for calculating the HETP for a rectangular cross-section capillary column with a film of a liquid stationary phase, taking into account the pressure drop correction factors, was reported:[46, 47]

$$H = \frac{2D_g}{\bar{u}} f_1 f_2 + \frac{(1 + 9k + 25.5k^2)}{105(1+k)^2} \frac{w^2 \bar{u} f_1}{D_g f_2} + \frac{2}{3} \frac{k}{(k+1)^2} \frac{(w+h)^2 d_f^2}{D_s h^2} \bar{u} \quad (1)$$

Here, D_g and D_s are the diffusion coefficients of the substance in the mobile (gas) and stationary phases, respectively, $\bar{u}$ is the average linear velocity of the carrier gas, f_1 and f_2 are the Giddings–Golay and Martin–James gas compressibility factors, respectively, d_f is the stationary phase thickness, k is the capacity factor that shows how long molecules of the substance occur in the stationary phase relative to the time they spend in the mobile (gas) phase, w is the channel width and h is the channel height.

The first term of Eqn (1) describes the chromatographic band broadening caused by longitudinal diffusion, the second term describes the resistance to mass transfer from the gas phase to the liquid phase and the third one describes the diffusion in the stationary phase. It is assumed that the phase film thickness is the same over the entire perimeter of the rectangular cross-section. Meanwhile, there are reasons to believe that the film may be thicker around the rectangle corners because of the liquid phase surface tension.[19] Note that the values of h and w for which Eqn (1) is valid are not specified in the publications.[46, 47]

The minimum HETP for the optimal carrier gas velocity for a rectangular cross-section column is given by[48]

$$H_{min} = w f_1 \sqrt{\frac{8(1 + 9k + 25.5k^2)}{105(1+k)^2}} \quad (2)$$

If the pressure drop is small, the f_1 value remains constant and equal to 1. Thus, expression (2) can be converted to

$$H_{min} = w \sqrt{\frac{8(1 + 9k + 25.5k^2)}{105(1+k)^2}} \quad (3)$$

In this case, the H_{min} value is related to the capillary width w and capacity factor k. From Eqn (3), it follows that for a non-sorbing substance, *i.e.*, when $k = 0$,

$$H_{min} = w \sqrt{\frac{8}{105}} = 0.28\, w \quad (4)$$

For strongly retained substances at $k > 100$

$$H_{\min} = w\sqrt{\frac{8 \times 25.5}{105}} = 1.39\,w \qquad (5)$$

This means that at the optimal carrier gas velocity, the efficiency (N) for a rectangular cross-section capillary column relative to a non-sorbing component is maximal, while that for compounds with high retention times tends to a constant value. For a rectangular cross-section column, the efficiency will be close to the corresponding HETP value of about $1.39\,w$. Similar trends are also typical of conventional round capillary columns (see below).

It is essential that the minimum HETP value for a rectangular capillary depends only on the channel width but not on its height. Hence, the capillary height can be varied without the loss of efficiency, which can be used to increase the loading of the column.

III.2. Comparison with capillary columns of circular cross-section

For a capillary of circular cross-section, the HETP value is found from the expression [47]

$$H = \frac{2\,D_g}{u} f_1 f_2 + \frac{(1 + 6k + 11k^2)}{24(1+k)^2}\frac{r^2\,\bar{u} f_1}{D_g f_2} + \frac{2}{3}\frac{k}{(k+1)^2}\frac{d_f^2}{D_s}\bar{u} \qquad (6)$$

where r is the capillary radius.

The minimum value of HETP at the optimal carrier gas velocity for capillary columns of circular cross-section is determined by the expression [49]

$$H_{\min} = r\sqrt{\frac{1 + 6k + 11k^2}{3(1+k)^2}} \qquad (7)$$

It follows from Eqn (7) that the value of $H_{\min}$ is proportional to the capillary radius r and is a function of the capacity factor k. By substituting the boundary k values, we find the minimum HETP values. For a non-sorbing substance (at $k = 0$)

$$H_{\min} = 0.58\,r \qquad (8)$$

for high k values ($k > 100$)

$$H_{\min} = 1.9\,r \qquad (9)$$

Comparison of the expressions describing the HETP at the optimal carrier gas velocity for rectangular [see Eqns (4) and (5)] and circular [see Eqns (8) and (9)] columns shows that for equal r and w, the columns of rectangular cross-section are more efficient.

Radadia *et al.*[19] reported an experimental comparison of the performance of a MEMS column of a 100 μm × 100 μm square cross-section and a round cross-section column fabricated by p-BCT. The authors concluded that the round column is more efficient. However, they did not consider the fact that the column cross-section was a 65 × 165 μm oval rather than a circle; perhaps, this was the reason for the observed increased performance of the round column.

IV. Types of MEMS columns

To date, there is no common view about the configuration required for a MEMS column for the highest separation performance. Meanwhile, channel etching technologies are suitable for not only arranging the channel in an arbitrary manner on the wafer but also fabricating columns that are difficult or impossible to manufacture by other methods.

IV.1. Configurations of the capillary MEMS columns

It should be noted that before the advent of MEMS columns, the question of the spatial configuration (shape) of columns was barely addressed. The shape of the traditional capillary (or packed) columns has been settled long ago. Capillary columns produced commercially represent narrow cylindrical capillaries rolled into rings that form a coil. The issue of the design of capillary columns was reduced to find the optimal coil size.[50 – 52] On the one hand, its radius should be large enough (not less than 8 – 10 cm) to reduce the contribution to band broadening caused by mass transfer resistance in the gas. On the other hand, the column must fit into the thermostat of the chromatograph.

In the design of micro gas chromatography systems, it is important to take into account that 1 – 3 m long channels must fit in a wafer with a small area (2 – 10 cm^2).[2] Thus, there is a need to manufacture a capillary with a lot of twists. Hence, studies have been conducted to search for the optimal channel configuration of MEMS columns on a silicon wafer. Examples of studied configurations are shown in Fig. 10.

The serpentine configuration of MEMS columns described in a number of papers [9, 45, 54 – 58] consists of long, straight channels (segments) and curved sections (180° turns) (Fig. 10 *a*). Other papers [2, 10, 23, 45, 59, 60] discuss columns with the channels shaped like a circular spiral (Fig. 10 *b*). Columns of another type, square spiral ones, contains rather extended straight segments with many 90° turns (Fig. 10 *c*).[14, 25, 40, 45, 61 – 64] A column shaped like a polygonal spiral was proposed [53] (Fig. 10 *d*). This configuration was used only for liquid chromatography.

Radadia *et al.*[45] compared the chromatographic properties of 3 m long MEMS columns of rectangular (100 × 100 μm) cross-section and of different shapes. Evaluation of serpentine, circular-spiral and square-spiral columns (with polysiloxane as the stationary phase) was based on comparison of efficiency and separation parameters. It turned out that, according to all criteria, the serpentine-shaped column had the best performance. Figure 11 shows the plots for specific efficiency on the pressure at the column inlet for the columns being considered.

It can be seen that the maximum specific efficiency of the serpentine column is close to 20 000 TP m^{-1}, which is approximately twice the specific efficiency for the spiral columns (11 000 and 10 500 TP m^{-1} for the circular and square spiral columns, respectively).

Deterioration of the separation performance of the circular- and square-spiral columns is attributable to the influence of column configuration on the uniformity of stationary phase (polysiloxane) film thickness. Moreover, the serpentine configuration allows reducing the number of turns per unit length of the capillary, which should also enhance the separation performance.

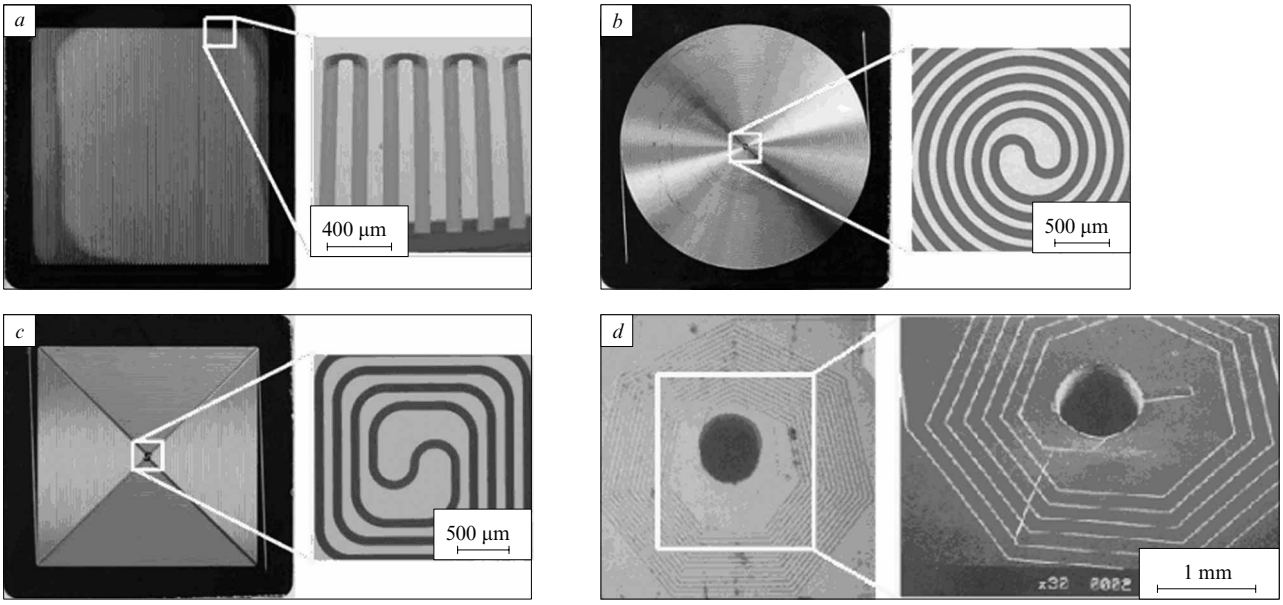


Figure 10. MEMS columns of various configurations.[45, 53]
Configuration: (*a*) serpentine, (*b*) circular spiral, (*c*) square spiral, (*d*) polygonal spiral.

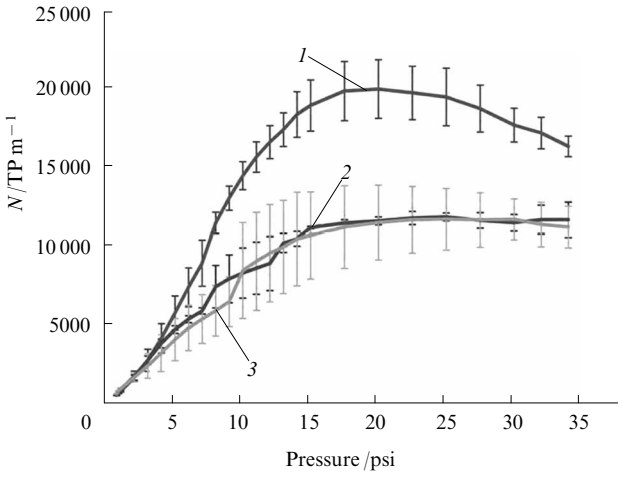


Figure 11. Dependences of the specific efficiency on the inlet pressure for serpentine (*1*), circular spiral (*2*) and square spiral (*3*) columns.[45]
The substance used for measurements was isooctane; the column temperature was 40 °C; the carrier gas was hydrogen; TP is theoretic plate.

In the case of separation of mixtures of compounds under the same conditions, it was noted that at the optimal carrier gas velocity, the elution from the serpentine column is faster than that from the spiral column, which is also attributed to a more uniform film thickness in the former case.

IV.2. Multicapillary columns

Miniaturization of the chromatographic system implies a decrease in every part, including the chromatographic column. However, this decreases the internal surface area of the column and, consequently, the amount of a mixture that can be effectively separated.

According to an approaches, this problem is solved by using multicapillary columns (MCC) consisting of several narrow capillaries operating simultaneously within the same column.[65 – 69] Multicapillary columns retain the speed and performance at high sample loading.[67]

One of the first mentions of a multicapillary column based on capillaries arranged in one plane and used for chromatography purposes dates back to 2001.[68] The author considered the theoretical possibility of application of a diffraction grating as a template for the manufacture of a flat column. However, the column he proposed had design flaws and could not be used in practice.

Further development of flat MCC is associated with the advent of MEMS technology, which led to fabrication of MCC micrometre-sized capillaries (m-MCC). Currently, there exist m-MCC with stationary phases based on polysiloxane,[70] modified gold [17, 71, 72] and silica.[73]

Like monocapillary MEMS columns, m-MCC have various configurations such as serpentine or spiral. A serpentine column has an advantage over the spiral one.[45] However, in the case of m-MCC, the serpentine configuration plays a different role than in a monocapillary MEMS column. The serpentine shape can compensate for the difference between the lengths of parallel segments caused by capillary bends. Thus it is possible to achieve the same length for external and internal capillaries of m-MCC (Fig. 12); this cannot be done using a spiral column. To make the compensation of the capillary lengths happen, the number of serpentine loops in m-MCC should be even.

A specific feature of m-MCC is the sample injection system. To attain high performance, the injection system should ensure the entry of approximately the same amount of the mixture into each capillary. A flow splitter ensuring even injection of the sample into the m-MCC consisting of eight capillaries has been proposed [70, 74] (Fig. 13). It was shown experimentally that the performance of m-MCC with

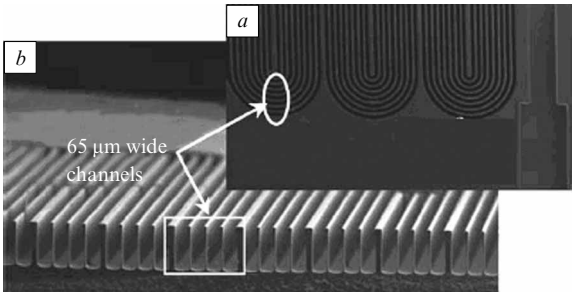


Figure 12. Position of serpentine m-MCC on a wafer (*a*) and a fragment of channel cross-section (*b*).[70]

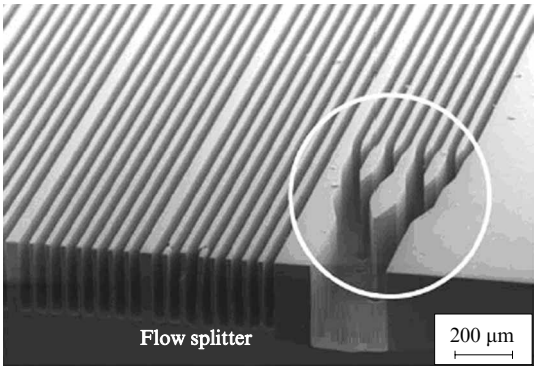


Figure 13. Flow spplitter for m-MCC.[70]

this flow splitter is 20% higher than that without the splitter.

For a multicapillary column consisting of rectangular cross-section capillaries, the equation for HETP can be generally represented as: [75]

$$H = H_0 + \left(\Delta_h^2 + \Delta_\omega^2\right) L \qquad (10)$$

where H_0 is the HETP of the capillary average in the cross-section distribution out of the bundle of capillaries, Δ_h^2 and Δ_ω^2 are the relative variances of the height and width distributions, respectively, for each capillary of the column, L is the column length.

For multicapillary columns representing a bulky bundle of circular cross-section capillaries, the variance in the capillary cross-sections is 3% – 4%.[76] This fact, together with the dependence of the carrier velocity in each capillary on its cross-section, leads to an additional chromatographic band broadening.

When using the package of capillaries produced by MEMS technology, the variance of the capillary geometric parameters does not exceed 1%.[70] For this reason, in Eqn (10), the terms that take into account the variance of the height and width vanish, and the MCC efficiency becomes approximately equal to those of columns composed of average-size rectangular cross-section capillaries. As a result, the column efficiency depends on how identically each capillary has been coated by the stationary phase. Most coating methods do not produce a uniform film of the stationary phase in narrow capillaries, which decreases the efficiency. Nevertheless, using phases based on octadecanethiol-modified gold, one can fabricate m-MCC with efficiency up to 7000 TP m^{-1} (Ref. 17). However, the range of phases that can be used for this purpose is limited.

IV.3. Semi-packed columns

In addition to MCC fabrication, MEMS technologies can be applied to another approach increasing the loading capacity of columns. This approach implies embedding micro-pillars with a height equal to the capillary depth within the channel, thus increasing the inner specific surface area of the column. This type of columns proposed for the first time by Ali *et al.*[77] is called semi-packed columns (SPC). An image of a fragment of this type of column is shown in Fig. 14. The fabrication of these columns is based on the same principles as fabrication of monocapillary columns.

In the semi-packed column described by Nakai *et al.*,[78] the micro-pillars 20 μm in diameter are arranged in a row one behind another at a distance of 30 μm. Semi-packed columns can be located on platinum or silicon surfaces as a serpentine or spiral.[77, 79, 80] Semi-packed columns with a polysiloxane-,[77] polyethylene glycol-,[81] inorganic oxide-[18, 79] or parylene-based [78, 80] stationary phases are known. To date, semi-packed columns prepared using MEMS technologies have no analogues in the traditional gas chromatography. Several papers [82 – 84] were published on the use of columns, similar in configuration to semi-packed ones, in liquid chromatography and capillary electrophoresis.

Owing to the presence of pillars in the capillaries, SPC have the following features that distinguish them from columns of other types:

— SPC can significantly increase the internal surface area and thus increase the sample loading compared with monocapillary MEMS columns;[77]

— the ordered arrangement of pillars in the semi-packed column reduces the pressure drop at the column inlet and outlet, as well as the contribution of eddy diffusion in comparison with the same parameters of packed columns;[79]

— the pillars in the column reduce the diffusion path and mass transfer from the gas to stationary phase, while the column design (alternating capillary sections with and without the pillars) contributes to decrease in the longitudinal diffusion input and to alignment of the carrier gas velocity profile, which increases the performance.[77]

The calculated profile of the carrier gas velocity through semi-packed column is shown in Fig. 15. The mass transfer is reduced due to lateral diffusion as the carrier gas flow passes through the column area containing micro-pillars

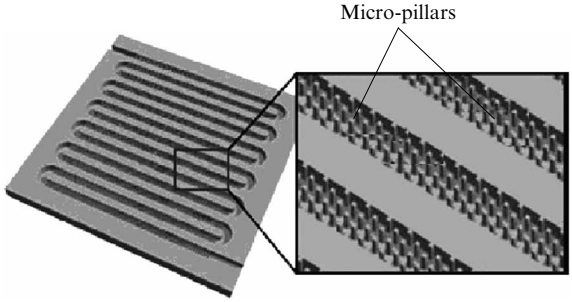


Figure 14. Semi-packed column.[78]

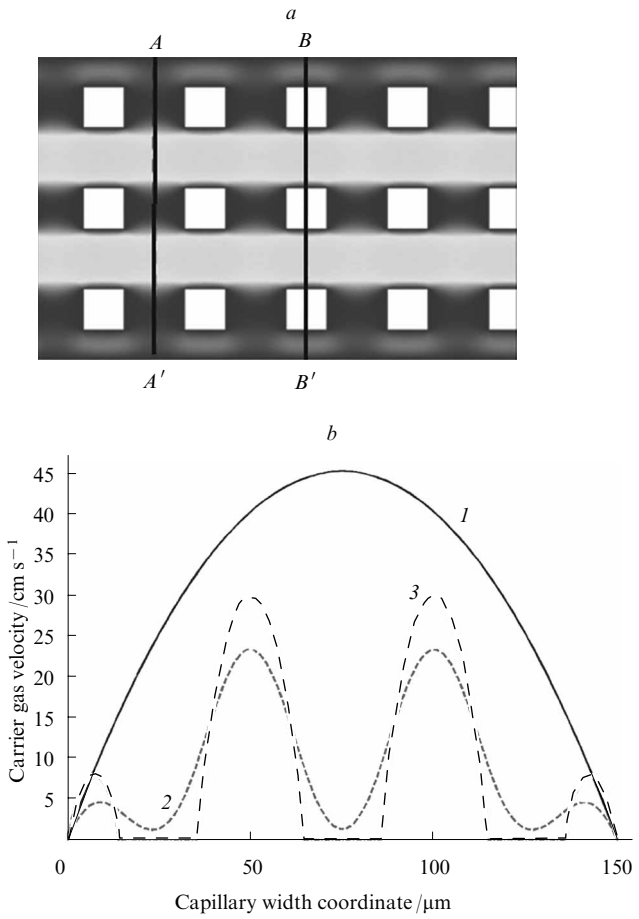


Figure 15. Cross-section of an SPC column (*a*) and carrier gas velocity profiles through capillary and semi-packed columns (*b*).[77] (*1*) MEMS column, (*2*) SPC along section AA', (*3*) SPC along section BB'.

(section BB'), which reduces chromatographic band broadening. Chromatographic band broadening upon passage of the gas through the pillar-free area (section AA') is minor, being substantially smaller than that in the case of a parabolic velocity profile for the open capillary column. The chromatographic band broadening in the case of the semi-packed column is smaller than in the case of the capillary one; hence its performance is higher (see Fig. 15). This conclusion was confirmed experimentally.[79]

Thus, semi-packed columns represent a new type of columns that can be regarded as packed ones with an ordered internal structure.

It was shown experimentally that with increasing number of pillars in the column, the performance increases.[80] Ali[85] considered columns with various cross-sectional shapes of the pillars (square, rhombus, hexagon) but made no conclusions about benefit of any of the shapes. Sun *et al.*[81] showed that a uniform carrier gas velocity profile in the column can be achieved (*i.e.*, the separation efficiency can be increased) if the distance between the wall and the pillar is greater than that between adjacent pillars. It was found that the serpentine form of the semi-packed column has advantages over the spiral one.[55] However, the presence of pillars in the bends of the serpentine semi-packed column leads to additional band broadening.[81] Therefore, for better separation, the bends in a serpentine column are to be vacant (free from pillars).

V. Methods for coating of stationary phases on the walls of MEMS column capillaries

The advent of MEMS columns initiated research aimed at loading of stationary phases into these columns. A variety of ways are used, depending on the column designation: a porous sorbent layer is formed on the capillary wall to fabricate a gas-solid column; a film of stationary liquid phase is applied on the channel surface to provide columns for gas chromatography.

This section provides an overview of the methods of coating of stationary phases on the channel walls of MEMS columns by both classical and specially developed methods.

V.1. Loading of stationary liquid phases

The coating of stationary liquid phases on MEMS capillary wall is performed using static and dynamic methods employed conventionally for the preparation of classical capillary columns for gas chromatography.[86] In most studies on capillary MEMS columns, polydimethylsiloxane (PDMS) polymers were used as stationary liquid phases.[2, 7, 19, 20, 40, 45, 46, 60, 61, 63, 77, 87 – 94]

Most often, a stationary liquid phase film is loaded by a low static pressure method. This method is as follows: the entire column is filled with a solution of the stationary phase in a volatile solvent, one end of the column is sealed, and the open end is attached to a vacuum pump. The solvent is evaporated upon pressure decrease, and the stationary phase remains on the channel walls as a film.

An optimized procedure for static low pressure deposition of stationary liquid phases as applied to the capillary MEMS columns (Fig. 16) is described by Reidy *et al.*[62] First of all, fused silica capillaries are attached to the inlet and outlet channels of a column formed on the silicon wafer. Then a stationary phase solution in a volatile solvent is prepared. The most suitable solvent is methylene chloride. The contents of polysiloxane stationary liquid phase in methylene chloride can vary from 0.1 mass % to 0.5 mass %, which leads to the formation of a 0.2 to 0.5 μm thick film in the channels. Dicumyl peroxide in the amount of 0.1 mass % (relative to the stationary liquid phase) was added to the prepared mixture for the radical binding of the polysiloxane polymer. The prepared solution is passed, under pressure, through the capillaries attached to the column (see Fig. 16 *a*). After the column channel is filled with the solution (as evidenced by appearance of the solution from the outlet), the channel is sealed so that no air bubbles are left. The column is transferred to a thermostat, which is maintained at a temperature a few degrees below the boiling point of the solvent used (see Fig. 16 *b*). In the case of methylene chloride, it is 40 °C. The open end of the column is connected to a vacuum pump. The volatile solvent evaporates, and the high-boiling liquid phase remains as a film on the capillary surface. The details of this method described for the first time by Bouche and Verzele[95] for various liquid phases and depositions conditions can be found in the literature.[49, 96 – 98]

The duration of the deposition procedure was ~15 min for a 1 m long MEMS column with the channel cross-section of 150 × 240 μm.[62] After removal of the solvent,

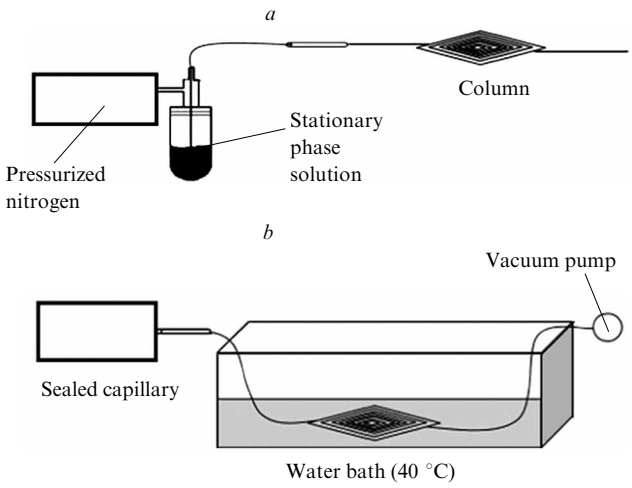


Figure 16. Static low pressure method applied to a MEMS column.[62]
(*a*) Filling of the column with a solution of stationary phase, (*b*) solvent removal from the column.

the column was evacuated for two hours (to remove solvent traces). Then the column was purged with nitrogen in a thermostat with programmed heating from room temperature to 180 °C at a 5 °C min^{-1} rate and maintained at 180 °C for four hours. This leads to activation of dicumyl peroxide molecules in the stationary liquid phase and, hence, binding of the siloxane polymer molecules. After these procedures, the column is ready for operation. The considered method is versatile: it can be used for deposition of any non-polar or weakly polar phase.

The dynamic method for deposition of stationary liquid phases is based on formation of a plug of a solution of the stationary phase in a low-boiling solvent in the beginning of the column, and then the plug is pushed through the column under an inert gas pressure. As the plug moves along the column, it leaves a film of the stationary phase material on the capillary wall. The film thickness depends on the velocity of plug movement along the channel and on the concentration of the phase in the solution. Once the plug exits the column, the residual solvent is removed by a gas stream, the film remaining on the capillary wall. This method is suitable for fabrication of non-polar columns (for example, based on PDMS) and medium polar columns {for example, based on poly[trifluoropropyl(methyl) siloxane]}.[20, 61, 99, 100]

It was noted above that the authors of the majority of works related to the MEMS columns used PDMS phases. The static and dynamic methods, common for the traditional capillary chromatography, are used for the stationary liquid phase deposition in the fabrication of these columns. Both methods are implemented after the anode bonding procedure, *i.e.*, after sealing of the column channels. The columns obtained by these methods can be used for the separation of multicomponent mixtures of compounds of different chemical nature.

However, there are objects for chromatographic analysis for which no satisfactory results can be obtained by using columns with stationary liquid phases. In particular, they include light hydrocarbons and volatile oxides. To solve the problems encountered in the analysis of such specimens, one needs a sorbent within the chromatographic column.

V.2. Deposition of stationary solid phases

Few investigations are dedicated to the use of ready-made sorbents as stationary phases in the MEMS columns. One can mention publications[101, 102] describing packing of a MEMS column by carbon-based molecular sieves for the separation of aromatic compounds. A spiral column was filled under vacuum with a fine fraction of the sorbent, one end of the column was connected to a vacuum pump, and the sorbent powder was fed through the other end. It should be noted that in this case, the size of the column was greater than the size of the column used for liquid phase deposition: the column length was 75 cm, the channel width was 1000 μm, and the channel depth was 750 μm.

There is a group of methods for sorbent deposition on the channel wall of MEMS columns before the anode bonding process. These are methods commonly used to impart functional properties to a silicon surface. These methods also can be ued to fabricate MEMS columns in which the sorbent is located on the inner surface of the capillary to form porous layers of various chemical natures.

V.2.a. Carbon nanotubes

Nakai *et al.*[103] described the fabrication of MEMS columns with a porous layer based on carbon nanotubes (CNTs).[104] The first step in manufacturing a column is the formation of channels by etching a silicon wafer (Fig. 17 *a*). A carbon nanotube layer is grown on the channel bottom by CVD. The process is catalyzed by cobalt and molybdenum. The catalysts are deactivated when applied on silicon; hence, silicon-on-insulator wafers are used,[105] *i.e.*, silicon – insulator (silica) – silicon three-layer substrates are utilized.[106] An ethanol solutions of metal acetates (0.01 mass %) was prepared to form a catalyst layer inside the channels; the solution was introduced into the channels at room temperature. The substrate was then dried at 400 °C (Fig. 17 *b*). The porous layer of carbon nanotubes is formed by heating the wafer to 800 °C in a quartz tube (Fig. 17 *c*). For this purpose, the substrate with a catalytic layer is first heated in an argon stream with 3% hydrogen. As 800 °C is reached, the argon flow is stopped and ethanol vapour is introduced

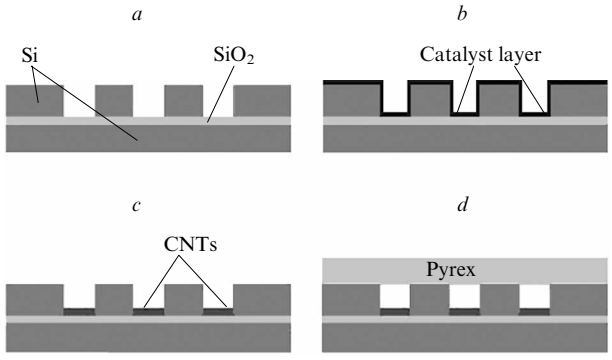


Figure 17. Fabrication of capillary MEMS columns with a porous layer of CNT-based sorbent.[103]
(*a*) Formation of column channels; (*b*) catalyst deposition on the column surface; (*c*) formation of the CNT layer; (*d*) sealing of the column channels with Pyrex.

into the system under pressure to decompose on the channel bottom to give CNTs. Since the catalysts are inactive on the silicon surface, no CNT layer is formed on the channel walls or the outer surface. After the formation of the CNTs layer, the channels are sealed by a Pyrex plate using anode bonding (Fig. 17 *d*). A similar method of application was used in other studies.[9, 107]

Columns based on CNTs are suitable for separation of C_6-C_{14} n-alkanes [103, 107] and oxygenates.[9] The maximum separation efficiency of a 1-m long column with 160×250 μm channels was 2500 TP m^{-1} (Ref. 103).

Despite the high efficiency of the columns obtained by the described method, it has a significant drawback: only one side of a rectangular capillary can be coated by the sorbent. Therefore, when using such columns for the separation of mixtures containing polar compounds, excessive sorption by the material of column walls free from CNT is possible, resulting in a very moderate separation efficiency.

V.2.b. Coatings based on gold

For the separation of hydrocarbons with >10 carbon atoms in the molecule, one can use MEMS columns with channel surfaces being covered with a layer of modified gold.[71, 108] The fabrication of these columns includes etching of microchannels, formation of a thin gold film by electrodeposition, anode bonding and binding of gold by octadecanethiol.[71, 108] During the electrodeposition, gold particles can be deposited not only on the channel walls but also on the upper surface of the wafer. Mechanical cleaning of the wafer surface usually brings about damage to the thin walls and narrow channels of the column. In addition, incomplete removal of gold leads to a loose bonding of the wafer to Pyrex.[71] A method for selective electrodeposition of gold was developed to solve this problem; in this case, the upper surface of the wafer remained without a gold coating.[17, 71]

Single-doped self-patterned and double-doped self-patterned processes were proposed for stationary phase deposition. They were designed for the preparation of a 25 cm long 16-channel m-MCC with rectangular channels and dimensions of 30×250 μm. In accordance with the former method, after the formation of channels (Fig. 18 *a*,*b*), the wafer was placed in an oven for 10 hours to perform doping of channel surface with phosphorus at 950 °C (Fig. 18 *c*). This procedure was carried out in order to reduce the electric resistance of silicon and to improve the conductivity between the cathode (micro-channel of the column) and anode (platinized titanium electrode). The electrodeposition of gold proceeds at a temperature of 55 °C and under constant stirring of the gold plating solution (TG-25 RTU, Technic Inc, USA). The electrodeposition conditions are experimentally selected in such a way that the gold layer is deposited only on the vertical sidewalls of the channels (Fig. 18 *d*) and not on horizontal surfaces.[17]

In accordance with the double-doped self-patterned method, the procedure of gold deposition begins with doping of the silicon wafer with phosphorus (950 °C, 10 h), which is carried out before the formation of the column channels (Fig. 19 *a*). Thereafter, a ~220 nm thick silica layer is applied to the upper surface of the doped wafer using chemical deposition from the gas phase. The silica acts as a mask during the electroplating of gold and does not affect the process of anode bonding of the wafer to Pyrex. The next step is the formation of the column

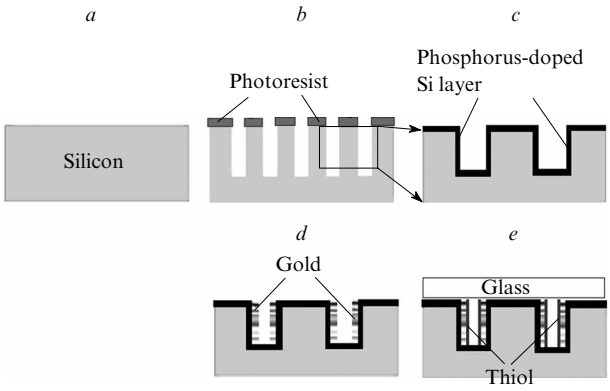


Figure 18. Fabrication of m-MCC using one-doped self-patterned method.[17]
(*a*) Silicon sublayer, (*b*) formation of channels, (*c*) doping of the silicon surface with phosphorus, (*d*) gold electroplating, (*e*) anode bonding, thiol modification.

channels (Fig. 19 *b*). Thereafter, the silicon wafer is again doped with phosphorus (950 °C, 10 h) (Fig. 19 *c*). Upon electroplating, a gold layer covers the entire inner surface of the channels, while the outer area of the wafer remains uncovered (Fig. 19 *d*). The electroplating conditions are described elsewhere.[17] Gold layer deposition is followed by sealing of the column channels with a Pyrex plate and subsequent application of thiol groups to the surface of gold (Fig. 19 *e*).

To modify the gold coating, the channel is filled with a solution of octadecanethiol in hexane, the capillary is sealed and maintained at room temperature for 40 h. During this time, the addition reaction of thiol to gold occurs to form a thiolate. Thus, a monolayer of the modified gold serves as the stationary phase.

The described method for deposition of a gold layer affords efficient columns with similar properties. The maximum efficiency achieved for these columns was 7300 TP m^{-1} against 5400 TP m^{-1} for the column fabricated by the single-doped self-patterned method. The differ-

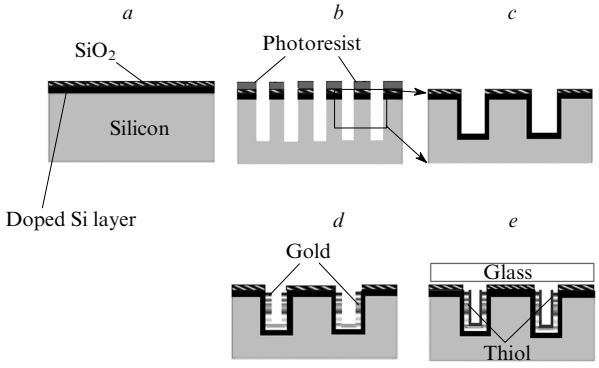


Figure 19. Fabrication of m-MCC using double-doped self-patterned method.[17]
(*a*) Doping of the silicon surface with phosphorus and silica deposition (CVD), (*b*) formation of channels, (*c*) repeated doping with phosphorus, (*d*) gold electroplating, (*e*) anode bonding and modification.

ence in the efficiency is associated with capillary coverage by the stationary phase.

It was proposed [72] to enhance the separation performance of the columns by using an additional procedure of Pyrex deactivation by octadecyltrichlorosilane. For imparting various properties to the gold layer, chemical modification is possible.[72] Thus, with the use of 6-sulfanylhexan-1-ol as a modifier, one can prepare a column suitable for separating polar compounds such as alcohols ($C_4 - C_9$).

V.2.c. Porous layers based on inorganic oxides

In addition to the methods conventionally used in capillary chromatography for stationary phase deposition on channel walls of MEMS columns, techniques borrowed from MEMS technology are used; they are based on sputtering materials of various chemical nature above the wafer with etched channels.

Sputtering methods used in MEMS technology were previously reduced to application of conductive layers (metals, alloys, graphite) to the surface. The application of insulating materials such as oxides or nitrides did not usually lead to the creation of uniform layers because of charge accumulation on the non-conductive material. To overcome this phenomenon, an approach was developed based on high-frequency anode – cathode polarization. A method was described to obtain uniform films by sputtering silica,[109, 110] nickel or titanium,[111] aluminium oxide,[112, 113] graphite,[114] magnesium oxide [115, 116] and titanium oxide.[117, 118]

With regard to chromatography, the use of sputtering process is described by Vial *et al.*[79] The block diagram of formation of capillary MEMS columns with a film of silica prepared by sputtering within the channels is shown in Fig. 20. A photoresist layer is deposited on the wafer (Fig. 20 *a*). Then the column channels are formed by DRIE (Fig. 20 *b*). After the formation of channels, a thin film of silica is sputtered on their inner surface (Fig. 20 *c*). The sputtering concept is based on the collision of gas ions with the target resulting in sputtering of the target material with its subsequent precipitation on the silicon wafer. The target consists of a material that is to be applied to the column. After completion of sputtering, the photoresist is removed with acetone (Fig. 20 *e*) and the column channels are sealed with Pyrex (Fig. 20 *f*).

The capillary MEMS columns with a layer of silica obtained by this method were used to separate light $C_1 - C_4$ hydrocarbons with efficiency of up to 2500 TP m^{-1}.

It should be noted that this method of silica deposition was used to prepare a sorbent layer in the channels of semi-packed columns; the efficiency of such columns reaches 5000 TP m^{-1} (Ref. 79). With this deposition method, one can also fabricate semi-packed columns with an alumina layer; the efficiency of such columns is 4500 TP m^{-1} (Ref. 119).

Another approach to fabrication of porous layers based on inorganic oxides in the channels of MEMS columns is disclosed by Shakeel and co-workers.[18, 73] It is based on precipitation of the corresponding oxides or their precursors from the liquid [73] or gas [18] phase. In one study,[73] the deposition process was started with immersing the wafer into an aqueous solution of poly(allylamine hydrochloride), which formed the positive charge on the channel wall. Then, this wafer was immersed into an aqueous suspension of silica and the negative charge was localized on the silica particles. The procedure of immersion was repeated several times. As a result, a thin film consisting of alternating oppositely charged layers held together by electrostatic forces was formed inside the channels. Thereafter, the plate was calcined at 500 °C for 4 h to remove the polymer. At the final stage, the channels of the column were sealed by a Pyrex plate and active silanol groups were deactivated using chlorosilanes. As a result, the methylated silica layer was obtained on the channel wall. The efficiency reached 930 TP m^{-1} for the capillary columns and 4750 TP m^{-1} for the semi-packed MEMS columns.

Shakeel *et al.*[18] implemented a new approach to the preparation of stationary phase as alumina film using atomic layer deposition from the gas phase. It is based on a sequence of chemical reactions between the vapour and the solid.[120] Most reactions of atomic layer deposition

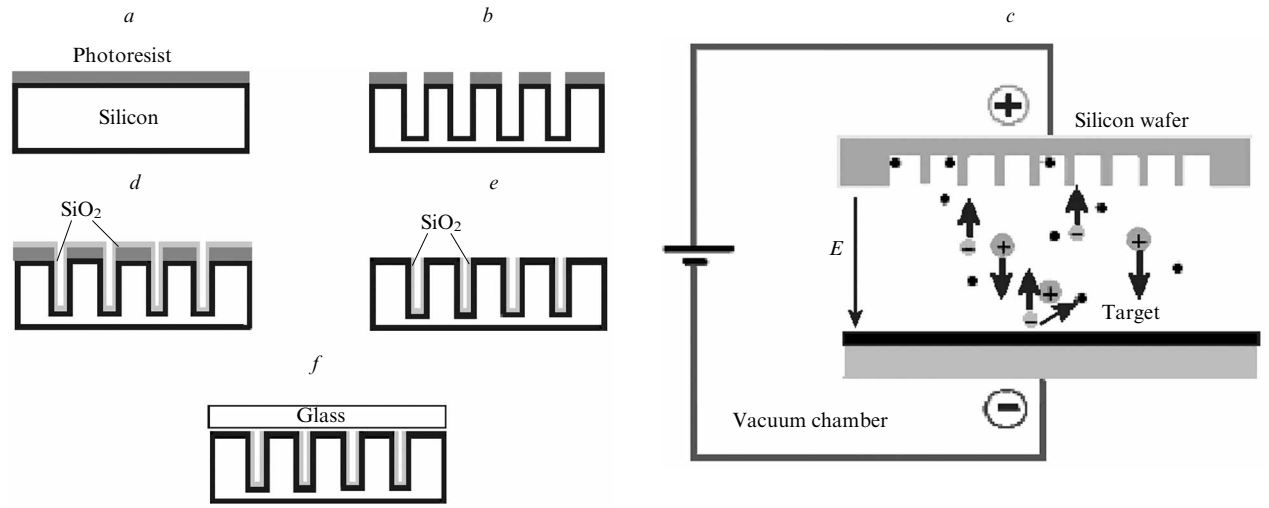


Figure 20. Fabrication of silica-coated planar columns.[79]
(*a*) Photoresist deposition, (*b*) formation of channels, (*c*) general scheme of sputtering, (*d*) silica sputtering, (*e*) photoresist removal, (*f*) anode bonding.

involve two chemical compounds that are commonly referred to as precursors. In the study cited,[18] trimethylaluminium and water were used as the precursors. The buildup of the aluminium oxide layer on the surface is described by two consecutive reactions

$$\sim SiOH + AlMe_3 \longrightarrow \sim SiOAlMe_2 + CH_4 \quad (11)$$

$$\sim SiOAlMe_2 + 2\,H_2O_{(gas)} \longrightarrow \sim SiO - Al(O^*)OH \quad (12)$$

In reaction (12), the oxygen atom marked with an asterisk is common to the neighbouring aluminium atoms on the surface. The hydroxyl group on the surface provides for deposition of one more layer of aluminium oxide. After each stage, the system was purged with an inert gas. To obtain the layer of the desired thickness, the deposition is repeated several times. After completion of the deposition and anode bonding to a glass substrate, the oxide film and glass surfaces are deactivated by dimethyl(octadecyl)chlorosilane. All steps of the preparation of the columns by this method are described in detail.[18] The efficiency of the obtained semi-packed columns reached 4200 TP m^{-1}.

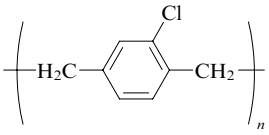
There are other methods to form the stationary phase of a desired composition.[121] One of them is based on sol – gel technology,[122 – 125] which allows easy adjustment of the polymer properties such as porosity and specific surface area of the layer within the capillary.[126] Columns prepared using this method are suitable for analysis of light hydrocarbons; the efficiency of such columns reaches 8000 TP m^{-1} (Ref. 127).

V.2.d. Organic sorbents

For the first time, the deposition of an organic sorbent was reported by Hannoe *et al.*[23] It was proposed to use sputtering of Teflon onto open channels before the anode bonding of the silicon wafer to Pyrex. However, this publication does not describe any chromatographic data characterizing the possibilities of the columns, which were obtained by this method of stationary phase deposition.

The deposition of a porous layer based of parylene C functionalized by amine into the MEMS columns is described.[78, 80] Parylene C [poly(chloro-*p*-xylylene)] has the following structure

Structure 1



Parylene films were deposited from the gas phase at low pressure according to the diagram shown in Fig. 21. Parylene C and poly(aminomethyl[2,2]paracyclophane) were used as the precursors. The layer of the stationary phase based on amine-functionalized parylene C film was deposited separately on both the silicon wafer with etched channels and the Pyrex plate (Fig. 21 *b*). Then they were glued together by anode bonding (Fig. 21 *c*).

The columns prepared in this way allow separation of $C_6 - C_{10}$ n-alkanes with an efficiency of up to 2500 TP m^{-1}. Although parylene can be used to separate various classes of chemical compounds, no experiments on separation of any other compounds except for the hydrocarbons were reported by the authors.[78, 80]

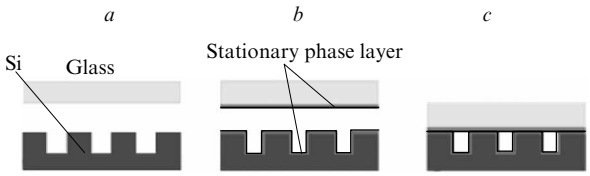


Figure 21. Sequence of the formation of MEMS columns with a stationary phase based on the functionalized parylene C.[78] (*a*) Formation of channels in the wafer, (*b*) stationary phase film deposition, (*c*) anode bonding.

It is noteworthy that the deposition methods described in this section were performed before the anode bonding procedure. Coating methods are on the shelf or specifically designed for MEMS technology and they are not used in traditional gas chromatography.

V.3. Synthesis of monoliths in the capillaries of MEMS columns

In addition to deposition of a sorbent or a liquid phase on the capillary surface, it is possible to form a monolith, that is, a continuous three-dimensional material synthesized directly in the column.[128] The monolith fills the entire internal volume of the column and has a developed pore system comprising macropores (transport pores) and meso(micro) pores. The transport pores provide permeability to the monolithic column, *i.e.*, the carrier gas with the analytes passes through these pores. The meso (micro) pores form a porous solid structure on the surface of the solid base and are responsible for analyte sorption – desorption processes. In accordance with the nature of the material, the monoliths are divided into two groups: organic and inorganic ones. The key organic materials for monoliths are divinylbenzene copolymers.[129 – 131] However, the most widely used monolithic columns are based on inorganic oxides.[130, 132 – 137] The methods based on sol – gel technology are at the heart of creation of such columns.[138] The properties of the obtained monolith depend essentially on the reactant ratio in the feed mixture and the time of gel ageing. By varying these parameters, one can achieve the desired structural properties of the resulting monolith. An advantage of monolithic columns used in gas chromatography is the ability to handle large sample volumes.[131]

Azzouz[139] described a 1 m long MEMS capillary column with 75×75 μm capillary cross-section with a monolith based on silica. The monolith was prepared using sol – gel process. With the use of this column, a $C_1 - C_4$ hydrocarbon mixture was separated in two minutes; the column efficiency was 1750 TP m^{-1}. However, such columns are characterized by the same drawback as the conventional micro-packed columns: their operation requires a significant pressure drop across the inlet and outlet of the column.[131, 140 – 143]

Thus, for the deposition of stationary phases on the MEMS columns, both conventional methods of capillary gas chromatography and the methods borrowed from the depot of MEMS technology are used. In the latter case, films of stationary liquid phases and porous layers of sorbents of various chemical nature can be formed inside the columns. Therefore, MEMS columns can be used in virtually all areas of gas chromatography that employ traditional capillary columns.

VI. Properties of MEMS columns

Since MEMS columns are relatively new, their chromatographic properties have not been so well investigated compared to those of other types of columns. This Section provides an overview of works on the chromatographic properties of MEMS columns.

VI.1. Dependence of the height equivalent to a theoretical plate on the carrier gas velocity

To maximize the chromatographic performance, the column must be operated at an optimal carrier gas velocity corresponding to the minimum HETP. The dependences of HETP on the carrier gas velocity were determined for MEMS columns of various types with stationary phases based on inorganic oxides, CNTs, gold, parylene and PDMS.[17, 18, 62, 73, 80, 103] A typical plot of this dependence for MEMS columns of rectangular cross-section is shown in Fig. 22. The curve shown in Fig. 22 is similar to the HETP curve for capillary columns of circular cross-section. The optimal carrier gas velocity for the majority of known MEMS columns is in the range from 5 to 20 cm s^{-1}; however, the velocity is greater for some columns. It should be noted that the optimal velocity depends on the nature, thickness and deposition uniformity of the stationary phase, structural characteristics of the sorbent as well as on the configuration of the column itself.

A somewhat different pattern of HETP dependence on the carrier gas velocity is observed for the multicapillary and semi-packed MEMS columns. Figure 23 *a* presents the dependences of HETP on the carrier gas velocity for multicapillary and capillary columns with a stationary phase based on modified silica.[73] A 16-channel multicapillary column of 25 cm length and 30×240 μm capillary size was used in this work. The capillary column had a length of 1 m, the channel parameters were 150×240 μm. In the case of a smaller capillary size inherent in m-MCC, chromatographic band broadening was less pronounced, resulting in a higher efficiency of the column.[144] However, the identity of the column capillaries has the greatest influence on the MCC efficiency.[66, 145] Therefore, the observed efficiency of the MCC is 2.5 times higher than that of the capillary column, despite the fact that the capillary width differs 5-fold. It is worth noting that a more gently sloping right-hand branch of the Van Deemter curve is characteristic of the MCC. This relationship is known also for glass MCC with a large number of capillaries.[146]

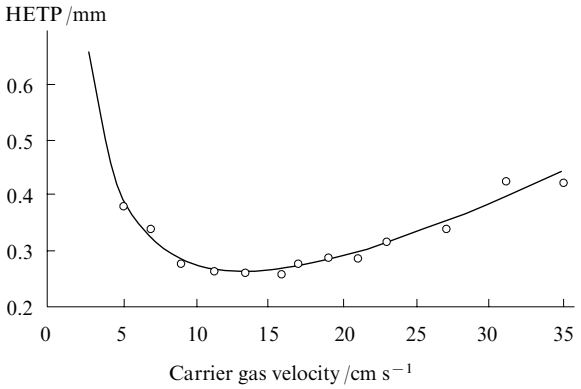


Figure 22. HETP *vs.* carrier gas velocity for a MEMS column measured for n-octane at 40 °C.[62]
Stationary liquid phase PDMS; column length 3 m; channel size 150×250 μm; square spiral configuration.

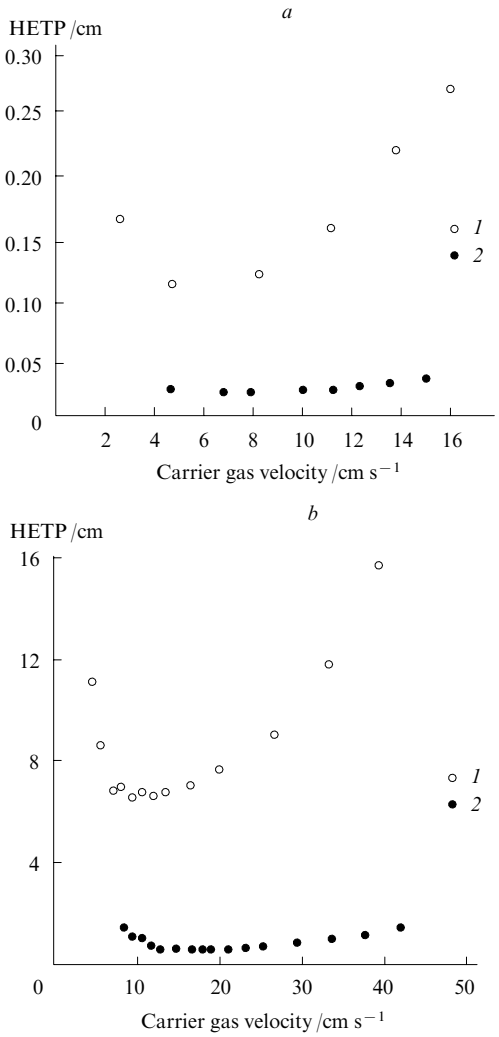


Figure 23. HETP *vs.* carrier gas velocity for multicapillary (*a*) and semi-packed (*b*) MEMS columns.[73, 78]
(*a*) The stationary phase is modified silica, measurements were made against dodecane at 65 °C; (*1*) capillary column, (*2*) multicapillary column; (*b*) the stationary phase is parylene C, measurements were carried out against octane at 30 °C; (*1*) capillary column, (*2*) semi-packed column.

The dependences of HETP on the carrier gas velocity for semi-packed and capillary columns with parylene C stationary phases are shown in Fig. 23 *b*.[78] The micro-pillars with the size of 30×30 μm are located inside the semi-packed column. The capillary column has a length of 1 m and the channel parameters are 160×230 μm. The columns characterized by the data of Fig. 23 *b* are not highly efficient; however, since the stationary phases in these columns were deposited by the same method, they can be compared with each other. It can be seen that the efficiency of the semi-packed columns is an order of magnitude higher than that for the capillary ones. The more gently sloping branch of the curve observed for the semi-packed column is attributable to lower time required for the gas – stationary

phase equilibrium to establish [owing to the small distance (30 μm) between the micro-pillars inside the channel] compared to the same time in the capillary column of the open type. It should be noted that m-MCC and semi-packed columns have a wider range of optimal carrier gas velocities; hence, they can be operated at higher speed without the loss of separation performance.

VI.2. Sample loading possibilities of MEMS columns of various types. Comparison with traditional capillary columns

Any chromatographic process involves sample injection into the column and recording of a chromatogram in the form of resolved peaks. The minimum amount of sample to be introduced is determined by the detector sensitivity and the maximum sample capacity is determined by the greatest sample volume that can be injected into a column without changing its separation properties. The upper loading limit problem consits in the following. When working with small amounts of samples, one can see well resolved peaks of a Gaussian shape in the chromatogram; the increase in the sample volume decreases the column efficiency and the peak shape changes due to various physicochemical reasons. This phenomenon is called column overload. The sample capacities for the capillary MEMS columns with polysiloxane stationary phase are given in Table 1.

Table 1. Loading of MEMS columns of different types measured against dodecane.[70]

Column type	Rectangular channel widths /μm	Sample capacity without overload /ng
Capillary	25	6
	50	10
	125	12
	250	19
Multicapillary		
2 channels	250	50
4 channels	250	200

The sample capacity depends primarily on the amount of stationary phase in the column. It is obvious that the more phase in the column, the more sample can be introduced; however, overload of the column is possible. Columns with wider capillaries (250 μm) contain more stationary phase, so their loading characteristics are higher than those for the columns with narrow capillaries (25 μm). A comparison of the sample capacities for capillary MEMS columns and conventional capillary columns[144] showed that their loading properties are comparable (provided that the capillary diameter of the circular column is equal to the width of the capillary of the MEMS column).

Investigations of the loading properties of multicapillary MEMS columns confirmed, quite expectedly, the possibility of handling an order of magnitude greater amounts of samples than the amount of samples for monochannel MEMS columns. If one compares multicapillary MEMS columns with the glass multicapillary columns, the capacity for the latter is an order of magnitude greater than that for m-MCC.[67] First of all, it is connected with a large number of capillaries (up to 1500) in the glass package type MCC.

The sample capacity of semi-packed columns were investigated by Ali *et al.*[77] The capacity was measured against dodecane for semi-packed column and MEMS column with PDMS. The study showed that one can introduce 20 μg of a substance into the MEMS column without overload and 30 μg into the semi-packed one. These values are abnormally high for standard capillary chromatography columns. The authors[77] did not provide a detailed description of the procedure for determining the properties of the column loading; hence, the provided result cannot be treated as reliable. Nevertheless, the maximum loading of semi-packed columns certainly exceeds that for capillary MEMS columns.

VI.3. Comparison of the efficiency of MEMS columns

Characteristics of MEMS columns with different stationary phases are shown in Table 2. It may be noted that columns with polysiloxane as the stationary phase were used in most of publications as data sources. The values of efficiency of these columns are usually lower than for the classical capillary columns of circular channel cross-section.[144]

For semi-packed columns, it is possible to increase not only the sample capacity, but also the efficiency. According to the presented data, the specific efficiency of semi-packed columns is roughly twice the efficiency of MEMS columns with smaller channels. The efficiency of m-MMC is similar to the efficiency of capillary MEMS columns. In most cases, the efficiency of columns with a channel cross-section other than rectangle is lower than that for a rectangular cross-section.

Methods of deposition of the layers of carbon nanotubes, inorganic oxides and gold with thiol groups on the capillary wall used in MEMS technologies are also suitable for obtaining columns with satisfactory efficiency. However, it should be kept in mind that in some cases, the efficiencies given in Table 2 do not adequately characterize the quality of the stationary phase deposition. This is due to the fact that the column efficiency is dependent on the carrier gas velocity[47, 144, 147] and the data presented in Table 2 were not always collected at the optimal velocities for all columns. In addition, the column efficiency depends on the capacity factor of the compound used to determine the efficiency. To properly characterize the column efficiency, it is necessary to measure this parameter for a compound with a capacity factor of >5;[148] this condition was not always obeyed in the studies on MEMS columns. In the light of the foregoing, the data in Table 2 should be taken as a reference material for MEMS columns rather than as a guide for choosing the type of the column with the most efficient separation. An adequate conclusion of which of the deposition methods leads to the best results can be drawn only provided that all conditions of the experiment used to measure the efficiency are known.

VII. Applications of MEMS columns

The possible applications of miniaturized chromatographic systems obtained using MEMS technology are related to monitoring of air quality, detection of toxic and explosive compounds, toxic industrial compounds, as well as biomedicine.[149 – 163]

To date, numerous procedures for introducing stationary phases of various chemical nature into the channels of MEMS columns have been developed. We will consider examples of separation of mixtures on MEMS columns as well as the possible ways of inclusion of such columns into a chromatographic path.

Table 2. Efficiency of MEMS columns of various types.

Channel sizes /μm	Column configuration	Column length /cm	Stationary phase	Efficiency /TP	Specific efficiency /TP m^{-1}	HETP /mm	Ref.
			Channel of circular cross-section				
100	Circular spiral	560	Polysiloxane	40 000	7140	0.14	89
90	The same	100	"	2000	2000	0.50	63
320	"	140	"	56 100	18 700	0.05	45
320	"	140	"	2000	1430	0.70	7
			Channel of oval cross-section				
165 × 65	Serpentine	34	Polysiloxane	870	2560	0.39	19
			Channels of square and rectangular cross-sections				
230 × 30	Circular spiral	150	Polysiloxane	2300	1530	0.65	2
150 × 250	Square spiral	300	"	8000	2660	0.38	40
150 × 240	The same	300	"	6500	2160	0.46	87
150 × 250	"	25	"	630	2500	0.40	46
150 × 250	"	300	"	12 500	4260	0.25	62
150 × 180	SPC, square spiral	100	"	10 000	10 000	0.10	77
200 × 100	Circular spiral	856	"	35 000	4090	0.24	92
100 × 100	Serpentine	600	"	4850	800	1.24	20
100 × 100	"	300	"	56 100	18 700	0.05	45
300 × 360	SPC, serpentine	200	"	19 000	9500	0.11	81
180 × 230	The same	100	Parylene	2500	2500	0.40	80
180 × 230	"	100	"	170	170	6	78
30 × 250	Serpentine	25	Au-Tiol	1800	7200	0.14	72
30 × 250	m-MCC, serpentine	25	Au-Tiol	1700	6800	0.15	71
30 × 250	The same	25	Au-Tiol	1830	7300	0.14	17
75 × 75	Serpentine	100	SiO_2 (monolith)	1750	1750	0.57	139
160 × 250	The same	100	Nanotubes	2500	2500	0.40	103
100 × 100	"	220	SiO_2	5500	2500	0.40	79
225 × 125	SPC, serpentine	110	SiO_2	5500	5000	0.20	79
80 × 80	Circular spiral	133	SiO_2	11 000	8000	0.12	127
200 × 100	SPC, serpentine	110	Al_2O_3	4950	4500	0.22	119
150 × 240	Square spiral	100	SiO_2 – silane	9300	930	1.1	73
30 × 240	m-MCC	25	SiO_2 – silane	1190	4750	0.20	73
190 × 180	SPC, serpentin	100	Al_2O_3 – silane	4200	4200	0.24	18

VII.1. Examples of separation on MEMS columns

As traditional capillary columns, MEMS columns are classified into columns for gas liquid and gas solid chromatography. The former type of columns, in which the stationary phase is a film of viscous liquid, are used to analyze different chemical classes of compounds with 5 to 200 carbon atoms in the molecule. A typical example of separation of a mixture of organic compounds on MEMS columns of this type is shown in Fig. 24.

This separation is not very different from what can be obtained using a packed column or a short capillary column. Some of the peaks could not be resolved due to insufficient column efficiency. The use of fast temperature programming leads to a more rapid separation process. Figure 25 displays the chromatograms of fast separation of a mixture of $C_5 - C_{16}$ hydrocarbons with a different programming rate of column temperature.[46]

In the isothermal mode, the efficiency of the considered column is 800 TP. With a short length of the column (25 cm), one can achieve the separation at a high speed; however, as seen in Fig. 25 *a*, elution of high-boiling components is hampered at room temperature. The use of rapid temperature programming (300 – 600 °C min^{-1}) allows for a significant acceleration of the process of separation, but its quality starts to deteriorate.

Let us consider examples of separation on MEMS columns with a sorbent layer. We should recall that the columns for gas adsorption chromatography are mainly used in cases where the use of gas liquid columns is complicated, for example, for analysis of light hydrocarbons. Figure 26 shows the chromatogram obtained in the separation on a gas adsorption MEMS column with a porous layer based on silicon dioxide; the layer was formed by sputtering SiO_2 on the silicon wafer. A fast column with good separation performance was obtained by this sorbent deposition method. It was noted above that the sorbent deposition method is not related to chromatography but is specially designed to meet the challenges in creating microelectromechanical systems.

A monomolecular layer of the stationary phase is formed by gold electrodeposition and subsequent modification. Figure 27 shows the chromatogram for the separation on the column with a stationary phase prepared by grafting octadecanethiol molecules to a gold layer.[17] All separations

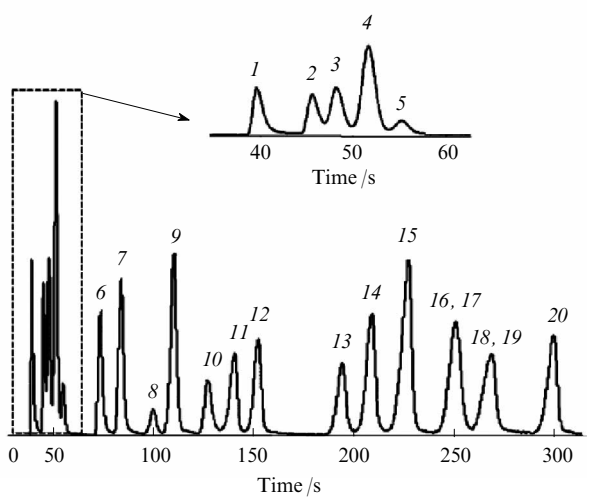


Figure 24. Chromatograms obtained in the separation of an organic mixture on a MEMS column with PDMS stationary liquid phase.[40]
Column length 3 m, channel size 150 × 250 μm; T = 30 °C for 1 min, further temperature change at 5 °C min^{-1} for 5 min; (*1*) methanol, (*2*) ethanol, (*3*) acetone, (*4*) pentane, (*5*) dichloromethane, (*6*) butan-2-one, (*7*) ethyl acetate, (*8*) 1,1,1-trichloroethane, (*9*) benzene, (*10*) pentan-2-one, (*11*) trichlorethylene, (*12*) heptane, (*13*) 1-chloropentane, (*14*) toluene, (*15*) 2-fluorotoluene, (*16*) cycloheptane, (*17*) ethyl butyrate, (*18*) octane, (*19*) butyl acetate, (*20*) chlorobenzene.

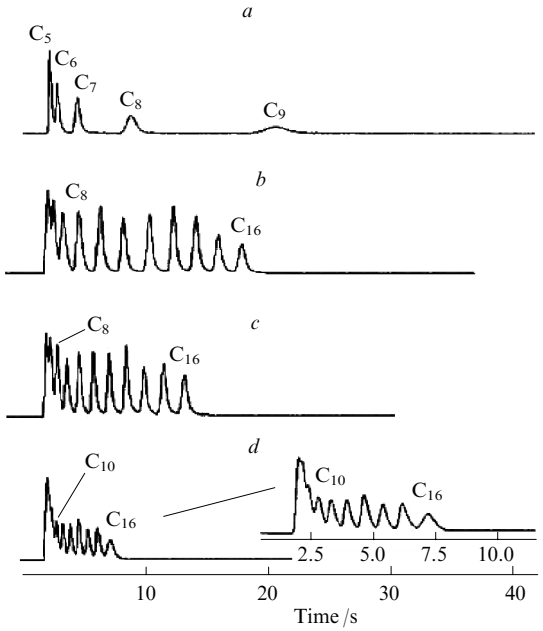


Figure 25. Chromatograms obtained in the separation of C_5–C_{16} hydrocarbon mixture on a MEMS column with PDMS stationary liquid phase.[46]
Column length 25 cm, channel size 150 × 200 μm, carrier gas velocity (helium) 25 cm s^{-1};
(*a*) Isothermal separation at room temperature; separation with programmed temperature rise (ΔT).

Fig.	*b*	*c*	*d*
T/°C	25–130	25–130	50–130
ΔT/°C min^{-1}	300	600	600

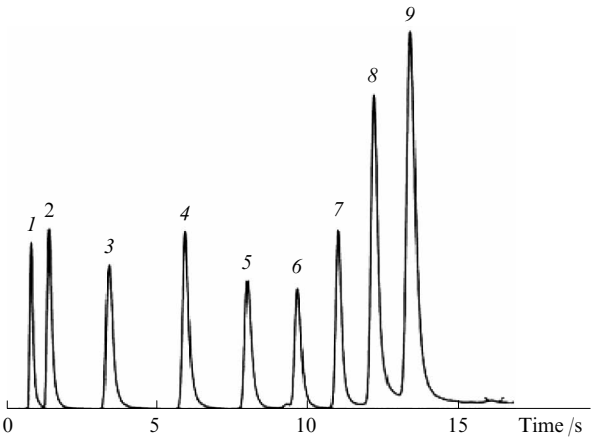


Figure 26. Chromatogram obtained in the separation of C_1–C_9 hydrocarbon mixture on a MEMS column with silica-based stationary phase.[164]
Column length 2.2 m, channel size 100 × 100 μm; T = 15–200 °C, heating rate 15 °C s^{-1}; (*1*) methane, (*2*) ethane, (*3*) propane, (*4*) butane, (*5*) pentane, (*6*) hexane, (*7*) heptane, (*8*) octane, (*9*) nonane.

on such columns were performed for model mixtures of hydrocarbons, which do not have excessive sorption properties. The application of other modifiers of gold surface in MEMS columns is also possible.[72]

Thus, using MEMS columns one can separate mixtures like in short capillary columns of circular cross-section. In addition to the stationary phase deposition methods used in capillary chromatography, it is possible to deposit films by methods designed for the application in MEMS technology. The prepared MEMS columns have satisfactory chromatographic properties and can be used for the separation of mixtures of compounds of various chemical nature.

VII.2. Two-dimensional chromatography

The examples of separation of organic mixtures given in the previous section were obtained for the classical scheme of capillary column application: the sample is injected into the

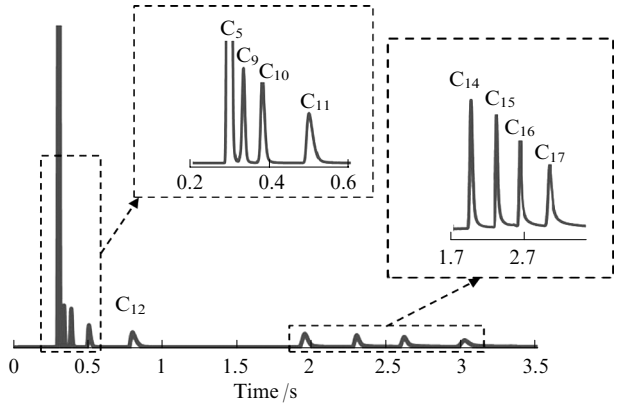


Figure 27. Chromatogram obtained in the separation of C_5–C_{17} hydrocarbons on a MEMS column with a modified gold layer.[17]
T = 50 °C for 0.7 min, further temperature rise at 17 °C min^{-1} up to 120 °C.

column together with the carrier gas and the separated components enter the detector at the column outlet.

Modern chromatography solves many problems related to the separation processes. In most cases, chromatographic analysis should ensure the separation of a large number of components, and this requires a high-performance column. One can achieve high efficiency using long columns. The length of MEMS columns does not exceed 5 – 6 m, while the length of the classical capillary column may reach 100 m. It is obvious that it is difficult to achieve the separation of good quality for a multicomponent mixture on a short column. In this regard, the question arises: how to improve the separation performance of MEMS columns? There are several ways, the easiest of which is to reduce the channel cross-section. With the application of this method, the specific efficiency of the column increases and, hence, the column length and separation time can be decreased;[145, 165] however, the quantity of stationary phase thus decreases, and this may cause column overload by the sample and, as a consequence, a decrease in efficiency.[144] In this regard, other ways of increasing the separation performance of MEMS columns are relevant.

One of such methods is two-dimensional gas chromatography.[166, 167] In accordance with this method, two columns of different phase polarity are used for separation.[168] The compounds partially separated in the first column are fed in portions into the second column in which the final separation occurs. To implement this flow diagram, a modulator is installed between the columns that accumulates compound from the first column and injects it into the second one.[169 – 172] Extensive bibliography is devoted to two-dimensional chromatography in standard capillary columns (*e.g.*, [170, 171, 173, 174]).

There are known examples of intermediate variants of two-dimensional chromatography using MEMS columns. Thus, Lambertus and Sacks [99] separated critical (*i.e.*, hardly separable) pairs of volatile organic compounds by connecting a column with a nonpolar stationary phase and a column with a stationary phase of moderate polarity using a valve. When the valve is closed, the flow was continuously fed from the first column into the second one; opening of the valve stopped the flow in the first column and increased the flow rate in the second one. If the compounds were poorly divided on the first column, the valve was opened. Thereby one peak had time to pass into the second column, while the other one remained in the first column. The described method provided resolved peaks in the chromatogram and separation of pairs of critical compounds.

Reidy [41] described a two-column separation with the use of successively connected MEMS columns with different polarity of the stationary phases. The separation of a multicomponent mixture was achieved by means of independent temperature programming in each of the columns.[40, 46, 63]

Whiting *et al.*[175] showed for the first time the possibility of application of MEMS columns for fast two-dimensional chromatography. In this paper, MEMS columns with varying polarity of stationary phases [PDMS and polyethylene glycol (PEG)] were connected *via* a pneumatic modulator.[176] An example of high-speed separation achieved in this work is shown in Fig. 28.

Reidy [41] investigated the air [176, 177] and cryogenic [170] modulators for two-dimensional chromatography on MEMS columns. Both types of modulators have shown

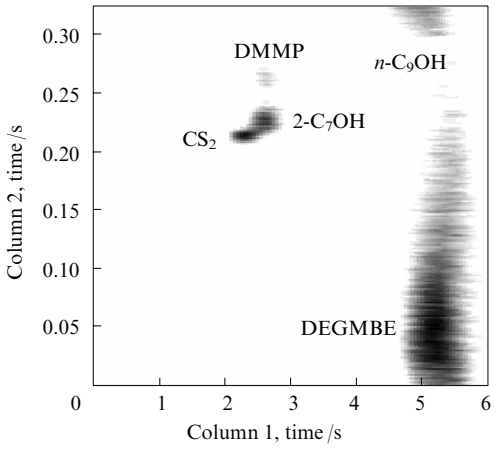


Figure 28. Chromatogram obtained in the separation of a mixture of polar compounds [isoheptanol + n-nonanol + diethylene glycol monobutyl ether (DEGMBE)] in dimethyl methylphosphonate (DMMP) by two-dimensional chromatography using MEMS columns.[175]
Column 1: stationary phase PDMS, length 90 cm, channel size 30 × 686 μm; column 2: stationary phase PEG, length 30 cm, channel size 30 × 686 μm.

good (approximately equivalent) results in the separation of a multicomponent test mixture. Note that for portable devices based on MEMS technology, the use of air modulator is most promising because of its lower power consumption and no need for the use of cooling gases.[41, 175]

The results of studies in which the authors used MEMS columns fabricated on glass wafers [7, 178] for two-dimensional chromatography do not differ significantly from the results obtained with the use of silicon wafers, but here we will not discuss details of these works.

Small dimensions of MEMS columns and the ability to connect to other chromatographic elements, which are also manufactured on the basis of MEMS technology, are the factors that can be utilized for developing new principles of assembly of chromatographic instruments. One way of such design has been considered by Liu *et al.*[179] Since the MEMS technology can produce multiple columns on a single silicon wafer, it is possible to construct a device comprising three, four or more columns rather than two. The columns should differ from one another in some parameter: length, shape, nature of the stationary phase, carrier gas flow rate, temperature of the analysis. Figure 29 shows a possible flow diagram for separation of a mixture of eight (or more) compounds. The operation of this device is based on the fact that the stream with the sample enters column 1, after which it is analyzed by detector 1, and this accompanied by recording of the chromatogram by a personal computer. When there appears a peak composed of several components, the computer switches the carrier gas flow with unseparated compounds to the second column. Furthermore, the flow from the column 1 may either enter one column 2 or be distributed between several secondary columns (2A, 2B, 2C, *etc.*). Each secondary column is connected to a separate detector. The result is a more complete separation of multicomponent mixtures. The disadvantage of the described parallel system is the increase in analysis time. However the authors cited [179] suggested that, owing to the absence of the energy-consuming modulator in

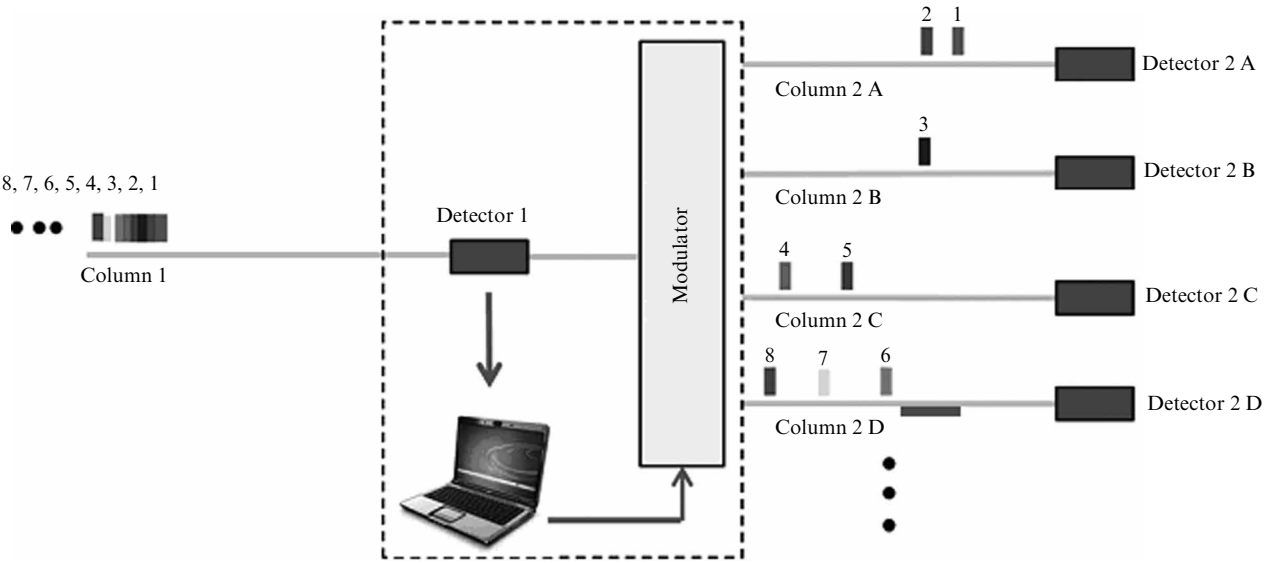


Figure 29. Flow diagram of parallel fast two-dimensional chromatography.[179]

their design, the power consumption is lower than that of the instrument used in conventional two-dimensional chromatography.

* * *

The given analysis of published papers provides the conclusion that the new compact MEMS columns are in many ways similar to short capillary columns in their separation characteristics. However, unlike the preparation of conventional capillary columns, in the fabrication of MEMS columns, manual operations can be eliminated. This is in line with the trend of modern technologies. The possibility of manufacturing small-sized columns and other chromatographic elements using MEMS technology provides a basis for the search for new design concepts in the field of chromatography. As regards development of investigations in the fabrication of MEMS columns, they are just beginning to leave the stage of laboratory research. One may believe that over time, these columns will be a common tool like the conventional capillary columns, which have already occupied their niche in gas chromatography.

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