Development of microfluidic chip manufacturing technology for human sweat analysis

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Abstract. A technology for manufacturing a microfluidic chip for analyzing the composition of human sweat is proposed. Microfluidic chips can be made of various materials, and, depending on this, can be made by various methods. The analysis of the materials of the constituent components of the product. Equipment was selected for each operation, modes were selected.

1. Introduction
A microfumed chip (also called a lab-on-chip) is a miniature device designed for instant analysis of biological fluids. One of the advantages of this technology is the small volume of liquid for analysis, which makes it very easy to use in medicine and veterinary diagnostics [1].

The project is supposed to modernize the existing analogue, to develop a technology for microfluidic chip production. Unlike the chip for blood analysis, the new development is designed for the analysis of sweat. Changes to the object of analysis will avoid some of the shortcomings of the existing technology.

One of the important parts of the device being developed is the conductive layer. This layer is necessary for transmitting a signal from a biomarker to an electronic device, and is obtained by applying a thin film on the base material.

This chip is supposed to be manufactured using vacuum technological methods. This will increase the purity of the internal surface of the microchannels. Also, a vacuum is necessary for applying a conductive layer, which is responsible for transmitting the change in resistance, when an analyte is in contact with it, on an analytical device. This will ensure the absence of contamination of the material and allow you to apply a thin layer of metal with the necessary range of resistance.

2. Structure of the microfluidic chip under development
The microfluidic chip can be divided into 4 main components, shown in Figure 1:
The main structure, for analysis, is located in module 3, so the most stringent requirements are imposed on the body material. The main analysis device in a microfluidic chip is a biomarker, which is placed on the conductive layer to read the results from the microfluidic chip to an electronic carrier.

3. Selection of materials components microfluidic chip

Microfluidic chips are made mainly from polymers, less often from glass and silicon, sometimes from metals and ceramics. Polymethyl methacrylate, cycloolefin copolymer, polymethylsiloxane, polyether ether ketone is among the most commonly used polymers. In addition, the module material must be a hydrophobic dielectric that is not susceptible to corrosion. The cover material should also be a hydrophobic dielectric, but its main characteristic is transparency. The cover material should be a transparent plate so that you can observe the movement of the sample under study, as well as monitor the state of the internal structure and replace it in case of a malfunction [2].

The material significantly affects the parameters of the modules. Comparison of materials is presented in Table 1.

Table 1. Analysis of housing materials for the MFC

| Parameter                  | Polymers | Glass     | Silicon   |
|----------------------------|----------|-----------|-----------|
| Optical properties         | Good     | Excellent | Good      |
| Mechanic properties        | Satisfactorily | Good     | Excellent |
| Chemical resistance        | Unsatisfactory | Excellent | Good      |
| Temperature properties     | Unsatisfactory | Excellent | Good      |
| Cost effectiveness         | Unsatisfactory for prototyping, excellent for large-scale production | Excellent for prototyping, satisfactory for large-scale production | Excellent for prototyping, satisfactory for large-scale production |
| Recycling                  | Disposable | Excellent | Satisfactorily |
| Life time                  | Satisfactorily | Good     | Good      |
The material significantly affects the parameters of the modules. In laboratory conditions, it is better and more economical to use glass. However, if, in the future, it is planned to release this sample to the market, all research should be carried out immediately on the polymer [3].

Silicon was chosen for the base material, since its parameters (mechanical and temperature properties) satisfy all the conditions set. This material is also suitable for economic parameters.

It is recommended to use polymer for the module material, since it is difficult to find a sample of silicon of the thickness required to obtain a system of capillaries on the material. A polymer can also be used to make the lid, but glass may also be suitable for this role.

The material of the conductive layer must have the highest conductivity, since the film thickness must be the smallest, which is caused by the need to reduce the roughness, as well as the size of the chip. After analyzing the literature, it can be concluded that for a metallized layer, a thickness of 500-900 nm is sufficient. This element is very important in the operation of the device, as it affects the accuracy of the transfer of the result to the electronic device [4].

Table 2 presents a comparison of the two most common metals to create this layer.

| Characteristic                              | Copper          | Gold + Titan    |
|--------------------------------------------|-----------------|-----------------|
| Electrical conductivity, S/m               | 5.96*10⁻⁴       | 4.1*10⁻⁴       |
| Resistance, μΩ*cm                          | 1.7             | 2.3             |
| Specific thermal conductivity, W/(m*K)     | 398             | 318             |
| Economic component, rub/g                  | 0.375           | 2717            |

By all measures, most of all, for a given chip element, copper is suitable. This metal has the highest conductivity and less resistance than gold. Copper is the most profitable from the economic point of analysis, it is much cheaper. Also, it does not need, in contrast to gold, an additional component to improve adhesion. The most important disadvantage of copper is high oxidability, but this disadvantage will not have a strong impact on the work, since the conductive element is easily replaced.

4. The choice of the method of forming a nanoscale conductive layer length microfluidic chip
One of the key operations is to create a conductive layer for transferring analysis data to an electronic device. There are several ways to create metallic nanoscale copper layers on the surface of the base: magnetron sputtering, laser ablation, thermal evaporation, arc deposition, schemes of which are shown in Figure 2.
Figure 2. Application scheme: a) Magnetron deposition. b) Laser evaporation. c) Thermal evaporation. d) Arc deposition.

The result of the analysis of these methods is presented in Table 3:

| Mode                  | Sedimentation rate, μm/h | Operating pressure, Pa | Material utilization | Substrate temperature, K | Adhesion strength, MPa |
|-----------------------|--------------------------|------------------------|----------------------|---------------------------|------------------------|
| Magnetron sputtering  | $10^{-2}$-5x$10^{-1}$    | $10^{3}$-10^{2}        | Low                  | 800                       | Until 150              |
| Laser evaporation     | 0,1-1                    | $10^{-1}$-10^{3}       | Low                  | 400                       | Until 100              |
| Thermal evaporation   | 0,1-1                    | $10^{3}$-10^{2}        | High                 | 1000                      | Until 100              |
| Arc deposition        | 0,1-50                   | $10^{2}$-10^{3}        | Medium               | 500                       | Until 310              |

Table 3. Comparison of film application methods

Based on the available data on the methods required by the parameters of the conductive layer, as well as on the available equipment, the most appropriate method is the magnetron sputtering method, which is implemented on the UVN-1M installation.

5. Technology development and equipment selection

Based on the analysis of suitable materials, the microfluidic chip manufacturing technology was developed. It can be divided into three stages.

The first stage involves the creation of a conductive base. To do this, clean the polymer plate. This will reduce the substrate roughness, due to contamination on the surface, and also to avoid deterioration of adhesion, and contamination of the film structure.

This operation will be performed on a low-pressure plasma installation using ion-plasma etching. The estimated process time is 30 minutes.

The formation of a conductive layer is a key operation for the first stage of manufacturing a microfluidic chip. This operation is performed on a vacuum deposition unit UVN-1M by
magnetron sputtering at an operating pressure of $5 \times 10^{-1}$ Pa in the working gas medium (argon). The approximate pumping time is 10 minutes.

In the second stage, an analysis block is created. As in the first stage, it begins with the cleaning of the polymer plate. Then, to create a system of capillaries, the method of photolithography was chosen. A positive photoresist is applied to the cleaned plate using a centrifuge to further etch certain areas of the polymer.

Next is the formation of the mask. This operation consists of several stages, and is necessary for giving the photoresist a given structure for further etching. First of all, it is necessary to dry the photoresist using a thermostat, for the best adhesion to the surface of the plate. The operation time is 30 minutes. Then the photomask is combined with the sample.

After combining the photomask and the surface of the polymer plate with a photoresist applied to it, the photoresist is illuminated through the photomask using ultraviolet radiation. After the photoresist is exposed, the photomask is removed. Then a photoresist is developed, during which the lighted part of the photoresist is removed, leaving a non-lighted photoresist on the substrate surface of the required topology. Operation time 30 s.

After creating the mask of the required pattern, areas of the polymer plate are etched, which are not hidden under the photoresist layer.

The photoresist plate is placed in the chamber of the etching unit, where the polymer is etched by reactive ion etching in CHF$_3$ medium, for 60 minutes.

After forming the desired structure, remove the layer of the remaining photoresist. Alkali solution is best for its removal. Alkali solution concentration: 5%.

After removing the photoresist, we obtain the necessary structure in the polymer plate - a polymer stamp.

The third stage is packaging. After creating the first and second main parts of the microfluidic chip housing, you can proceed to their connection. The simplest method of bonding will be diffusion glue, since this substance must be transparent and also have the properties of a dielectric.

After applying the glue around the perimeter of the polymer plate, it should be left in the air for 40-60 seconds, then attach the polymer template. Then, in the same way, a sealing cap is attached. This operation, for greater accuracy of alignment, it is recommended to make along the guides. After bonding both parts, leave the chip for a day, for complete solidification.

An illustration of this technology is presented in Figure 3.
The developed technology is a sequence of operations, enlarged in stages - there are three of them. As a result of the implementation of this technology, it is possible to create a microfluidic chip, which allows determining the main components of human sweat: ammonia, iodine and urea.

6. Setting up and conducting an experiment to obtain the dependence of resistance on process parameters.

To study the dependence of the dimensional and electrical characteristics of the conductive layer, a series of experiments was carried out.

After studying the materials of the base, the conductive layer, as well as the methods of applying a thin film coating, the following components were selected:

- silicon substrates, since further work with the microfluidic chip will be carried out on the basis of silicon, the experiment should be carried out immediately on this material;
- copper, to create a conductive layer;
- installation supporting the magnetron sputtering method.

Pre-cleaned substrates, using an alcohol solution, were placed separately in a vacuum chamber. The spraying was carried out according to the given data of time and distance from the substrate to the source. Photos of the samples, as well as the values of time and distance are shown in Figure 4.
To obtain the parameters of the electrical network conductivity and resistance, an immittance meter was used, also called an RLC meter. The measurement was carried out according to the scheme shown in Figure 5.

After all measurements, the following melon
for sample 1 (3 min, 30 mm) the resistance is 4583.66 mOhm;
for sample 2 (6 min, 30 mm) resistance is 28x103 mOhm;
for sample 3 (3 min, 60 mm) the resistance is 991.6 mOhm;
for sample 4 (6 min, 60 mm) the resistance is 7.61 x 103 mOhm.

According to the measurement data on the RLC meter, a mathematical model was built of the dependence of the resistance of the copper coating on the application time and the distance from the substrate to the source:

\[ R = 10304 + 7516 \cdot t - 6003 \cdot h - 4207 \cdot t \cdot h \]  

(1)

where \( h \) is the distance from the source to the substrate, \( t \) is the process time.

After analyzing the obtained mathematical model of the process, we can conclude that both the distance from the source to the substrate and the deposition time affect quite significantly. And also, the interaction of these two factors has a significant impact on the value of resistance. The mathematical model confirmed its adequacy, the experiments were reproducible.

7. Conclusions
In the course of this work, an analysis of the base materials and the current-conducting layer of the microfluidic chip was carried out. The most suitable materials are: for the case - polymer or glass, for the conductive layer - copper. Conductive layer can be applied in vacuum using magnetron deposition.

The proposed technology, at the moment is a theoretical development, and is being tested for feasibility in MSTU. N. E. Bauman.

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