Accuracy increase of blood viscoelasticity measurement of the microfluidic Wheatstone bridge

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Abstract. Development of methods for the analysis and control of biomaterials goes to the most important task level in the field of modern medicine. Blood viscoelasticity measurement in the microfluidic Wheatstone-bridge is one of the most promising method today. Nowadays this measurement parameter does not meet the requirements of laboratories, so the method is not used widely. We propose to improve the method by changing geometry of microfluidic Wheatstone bridge. Our method allows increase the accuracy due to statistical processing of obtained data. Designed device can be used not only to measure blood parameters, but also for other types of fluid.

1. Introduction

The microfluidic Wheatstone bridge (MWB) is used for a long time for measuring of various parameters. For example, the authors of [1] use it to measure the viscoelasticity of blood, the authors of [2] use the system, which facilitates rapid, on-demand fluid sampling in the bridge. The authors of [3] use a similar microfluidic system for electrokinetic study of miscellaneous liquid–solid interfaces. In [4], we proposed the use of a simple form of the MWB for measurement of pressure with high accuracy. In general such the microfluidic devices use in different areas for high precision measurements. The purpose of the future device determines its material. For example, one of the most popular materials for all microfluidic devices is different polymer and epoxy resins. This choice is due to the characteristics of these materials, such as chemical resistance, strength of the material, ease of manufacture, availability and cost. Also microfluidic devices are made of silicon [5]. The article deals with the configuration of the standard MWB [1] for measuring the viscosity and elasticity of blood. The creators of this design make a measurement of the parameters, based on the visual position of the boundary between the two liquids. In this article, we describe the results of an experiment of such a structure. And also draw conclusions about the performance of the standard MWB. And we offer an improved design of the MWB, which takes into account many of the shortcomings of the already created device.

2. Description of the principle of the simple the microfluidic Wheatstone bridge for measuring of the blood viscoelasticity

To measure the viscoelasticity of blood, the authors of [1] use a system of the MWB. The system contains two input channels for blood and PBS solution. These two streams have different flow rates, different consumption and hydraulic pressures. As the fluids pass through the channels, they collide in a bridge microchannel. Different flow rates make it possible to compare the physical parameters of a liquid. The PBS solution presses on the blood with certain strength. The blood under this influence starts to move in the opposite direction and acquires an acceleration of the flow. At some point in time, the system comes to a stable equilibrium, the position of the two liquids stops relative to each other. Then the camera fixes this position. Digital imaging techniques allow to measure the area of the blood in the bridging channel. The viscoelasticity of the blood is calculated according to the size of this area. Such a system is simple but not sufficiently accurate. In this case there are measurement errors, which are caused by defects in the channels shape (imperfect geometry). In addition interphase interaction between blood and the PBS solution leads to meniscus appearance near the wall of the channel. It is possible to carry out these measurements repeatedly, in order to increase accuracy and obtain an average result after statistical data processing. But the action increase measurement time and volume of blood and PBS solution per one experiment (Fig 1).
3. Technique of the experiment

The microfluidic plate was manufactured for behavior studies of measurement system, which was described in the article [4]. The plate has several structure tests; one of this is a structure of the microfluidic measurement bridge. It has four outputs, two inputs and two outputs for two different liquid (A – no color, B – black color). Width of measurement channel is 8 mm, length is 40 mm, and depth of channel is 1 mm. Appearance of this structure test and its outputs during operation is shown in the Fig 2.

The essence of the experiment is as follows. Initially, the system is filled with liquid A, after which the second part is filled with a liquid B, while still pumping liquid A through the system. As a result, equilibrium is established and forms a boundary between liquids A and B. This boundary is distinguishable and this is shown in the Fig 2.

A flow occurs in the channel, when there is a pressure difference at the ends of the measuring channel. The pressure difference is due to various factors such as viscosity, flow velocity, hydraulic resistance and other characteristics of the liquids properties. The apparent boundary between liquids A and B begins to move, can be fixed visually or by another method. This motion is the output signal of the measuring system, which must be processed.
Specialized photographic equipment is used to test the system detection of the movement of liquids in the measuring channel; images are processed using computer methods. The experiment was as follows. At the beginning the system was brought into this state, when the measuring channel was completely filled with liquid B. After that increase the flow of liquid A, so that in the measuring channel the reverse movement began. The dynamics of this movement was observed in time. Fig 3 shows the image of the measuring channel at different times. They visually see the movement of the interface of the liquid, which indicates the presence of a flow in the measuring channel.

![Image of the measuring channel at different times.](image)

**Figure 3.** Image of the measuring channel at different times.

In the observed experiment, each photo was processed to obtain a normalized output signal by brightness. This became the basis of numerical analysis. The values of the output signal were averaged over the width of the entire channel. As a result, for each frame, the distribution of the normalized output signal along the length of the measuring channel over time has been obtained. These results are shown in Fig 4(a).

![Distribution of the normalized output signal along the length of the measuring channel over time; The average flow rate for each output level.](image)

**Figure 4(a, b).** (a) Distribution of the normalized output signal along the length of the measuring channel over time; (b) The average flow rate for each output level.

The results of the measurements show that for the outermost regions a constant value of the output signal is observed (within the noise level). This corresponds to the region of pure liquids flows A and B from their inputs to the outlets in the microfluidic structure under consideration. For the central area of the measuring channel it is convenient to consider the movement of a point with a fixed level of the output signal. For levels from 0.6 to 0.2, considerable movement can be observed at a distance of 1 to 1.5 cm during the observation time 45 s. To quantify the speed, you can calculate the movement along the measuring channel of a local point, which gives an output signal of a given level. These data are shown in Figure 4 for the output signal levels from 0.2 to 0.6. If you know the movement in time, you can calculate the average flow rate for each of the levels of the output signal. These results are shown in Fig 4(b).

The presented data are very ambiguous and difficult to use to obtain information about the flow in the measuring bridge. The presence of local kinks in the graph 3 and the inequality of the rates for different levels of the output signal (in Fig 5) speak about this.
Figure 5. Indicators of different levels of the output signal.

Consider the reasons for the appearance of these difficulties. Such phenomena as the volatility of the fluxes of substances A and B during the measurement make some contribution. Minor pulsations in the liquid flow lead to pressure pulsations at the ends of the measuring channel and as a consequence this leads to an uneven flow rate in it. From this it follows that the measuring system must have a stable source of fluxes of substances. In addition, the measurement time should be less to reduce the negative impact of this factor.

However, the main source of the problems considered is the poor design of the measuring channel. The channel has a large width; therefore, a parabolic flow profile develops in it. Proof of this is shown in Figure 6.

In this case, depending on the direction of flow in the measuring channel, the parabola has a convex part either in the liquid A or in the liquid B. The presence of a parabolic profile is harmful for two reasons:

1) Intensification of diffusion of substances into each other. With a parabolic profile, the total length of the interface of the two liquids is greater than at the direct boundary, and then the total diffusion flux is also greater. Secondly, the parabolic profile near the channel walls contributes to the formation of a thin boundary layer which diffuses rapidly into another liquid.

2) In the experimental procedure, averaging of the signal over the entire width of the channel is assumed. Accordingly, in the presence of a parabolic interface, such averaging will give an incorrect picture. This leads to a significant distortion in the level of the output signal and to the contradictory results shown above.

The transition from a parabolic profile to a direct one is a solution to this problem. Physically, this can be done with the appearance of slippage of the flow at the boundary. But such an effect cannot be precisely regulated; therefore its use in the measuring system is unjustified.

Another solution involves with obtaining output profiles along the measuring channel, if there is no averaging over the width. In this case a line with a width of 1 pixel will have a flat boundary between the liquids A and B. But in this case the noise in the measuring channel is significantly increased.

In this way we come to the conclusion, need to create a system which would not have a wide measuring channel, to keep the phase boundary as clear as possible, but at the same time it would be possible to carry out averaging of the measured signal to reduce the noise to an acceptable level. From this condition we arrive at the structure of the measuring bridge with a lot of narrow measuring channels. The scheme of such a microfluidic structure is shown in Figure 1.
4. Proposed solution

We propose to increase the number of measuring channels in microfluidic structure. In this way we can provide statistical data processing and keep reagents consumption on one level.

To provide a realization of this approach we propose to use an advanced form of the MWB. The MWB system has new elements in its composition. The elements are additional bridge channels in the structure of the MWB, which provides a multiple measurement.

In our new design the MWB has special expanded chambers (pressure equalizers) between which all bridge channels are situated. This is aimed at reducing the effect of the pressure difference between inlets of bridge channels. If these chambers are absent, vortices can be formed and pressure near the inlets of channels has strong nonuniformity.

The flow of two liquids in the improved structure of the MWB was simulated. Depending on the ratio of flow rate and viscosity the behavior of the interface between liquids was investigated. The simulation results show the correct operation of the improved structure, because both systems have a similar function (Fig 7).

![Velocity in the bridge channels: (a) total liquid flow; (b) current lines through the structure](image)

Figure 7(a, b). Velocity in the bridge channels: (a) total liquid flow; (b) current lines through the structure

5. Conclusions

This work is devoted to microfluidic structure blood viscoelasticity measurement. Considering this question, we have found and have eliminated the critical moments. In this case there are measurement errors, which are caused by defects in the channels shape (imperfect geometry). In addition interphase interaction between blood and the PBS solution leads to meniscus appearance near the wall of the channel. We proposed a method of increase in accuracy of measurement at preservation of the minimum volume of tests of blood. The method consists in change of geometry of microfluidic structure for the purpose of increase in accuracy by carrying out statistical processing of results. The advanced system is presented in Fig. 1. Such structure contains the big field of alignment of pressure; this ensures the same pressure at all the inputs to the bridge channels. The behavior of the proposed microfluidic structure by methods of mathematical modeling is studied. Its operability and possibility of application in laboratory practice is shown.

In the future we are planning to make a prototype of MWB for experimental investigation. The planned experiments will be based on the operation of real working fluids. After successful results, certified patenting is planned. The possibility of applying an improved design will be considered in a wide range of applications.

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