Publishing House
AKAPIT

COMPUTER METHODS IN MATERIALS SCIENCE
Informatyka w Technologii Materiałów

Vol. 9, 2009, No. 1

NUMERICAL SIMULATIONS OF DIAMOND MICROFLUIDIC DEVICE FOR THE BIOMOLECULES ELECTROPHORETIC SEPARATIONS

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Abstract

Microfluidic devices known also as labs-on-chip, capillary electrophoresis microchips or micro total analysis systems (µ-TAS) were introduced in 1990's for the first time. These devices have attracted much attention over the last years. They transfer tiny quantities of samples and reagents, through a system of microchannels and microchambers manufactured on the surface of a small plate. They are made up of different materials, most often of polymers (PDMS, PMMA), glass or silicon. Microfluidic devices are applied in many areas including separations of biomolecules (DNA or proteins), DNA amplification and sequencing, chemical synthesis, single cell analysis, environmental monitoring etc. They often integrate many steps of analysis such as sample preparation, separation and detection on a small, single chip.

In this paper we study electrophoresis microchips. Joule heating and its effects, i.e., the temperature growth leading to temperature gradients in microfluidic devices, lead to many problems during chip electrophoresis. Sample band dispersion (low column separation efficiency), reduction of analysis resolution, destruction of thermally labile biomolecules or formation of vapor bubbles are the negative effects of Joule heating. In our research we compare diamond, glass and PDMS microfluidic devices. Microchips of different geometries and of different materials have been analyzed by the Conventor™ software. Diamond reveals exceptionally good electro-thermo-opto-chemical parameters, is very useful in the range of biomolecular separations (such as electrophoresis) and for optical detection methods. Among them, the most important are: the highest-ever thermal conductivity coefficient, good optical transparency, very high electrical breakdown voltage, good chemical resistance and mechanical durability.

Diamond microfluidic devices are very advantageous over glass or polymer microfluidic devices commonly used. They dissipate Joule heat much more efficiently because of the highest-ever thermal conductivity coefficient of diamond.

Key words: diamond microfluidic device, electrophoresis, numerical simulations, Joule heat

1. INTRODUCTION

"It is hoped that many of the large, expensive chemical and biological analyses that are currently being performed can be replaced by integrated microfluidic devices, often called labs-on-chip…" was written by Erickson in his review paper concerning numerical simulations of microfluidic devices, [1]. Microfluidic devices, which are known from the beginning of 1990's, [2-4], transfer tiny quantities of samples and reagents through a system of microchannels and microchambers manufactured on the surface of a small plate. They are fabricated from different materials: glass, quartz, silicon and polymers (mainly PDMS or PMMA).

ISSN 1641-8581

Diamond, because of its exceptional physical, bio-chemical and mechanical properties, has been recognized recently as a very promising material for different biological sensing systems, [5-13]. Its highest known thermal conductivity makes diamond the best choice of material for the applications in different microfluidic devices based on electrophoresis process (microchip electrophoresis – MCE), [14]. Electrophoresis is widely used for the separation of biomolecules. However, because of the high electric field applied to the electrodes, the Joule heat produced during the electrophoresis process has to be efficiently dissipated. Diamond ideally fits this requirement and opens new horizons in biomedical sensing.

An important issue in designing new microfluidic devices (or electrophoretic chips) is a profound analysis of the processes present during the microchip electrophoresis. This leads to the optimal selection of the electrophoretic chip material and its optimal geometry, [10]. Numerical simulations of microfluidic devices reduce cost and time of device development - from the concept to an application of the ready microchip, [1]. The results are very useful during the designing process and bring information about the influence of geometry and physical parameters affecting the device performance. The simulations were focused on the heat transfer and temperature profile due to Joule heat generation.

There are some papers dealing with numerical simulations of microfluidic devices, [1,14-18]. Erickson, et al., [15], have presented their results of numerical simulations, compared with experiments, to examine Joule heat generation and transfer in the microfluidic devices made-up from PDMS (polydimethylsiloxane), and hybrid PDMS/glass.

In the recent project (MNT-ERA NET, the project acronym DIAMID: "Diamond Microfluidic Devices for Genomics and Proteomics"), [13], a diamond microfluidic device was designed for fast and accurate electrophoretic separations of DNA and protein molecules. A moulding technique was applied to form polycrystalline diamond microfluidic chips. A Silicon microelectronic technological facility and equipment, especially an Adixen plasma reactor (Bosh process) were used to form silicon moulds, whereas microwave plasma CVD was used for the thick polycrystalline diamond layer deposition, chemical solution was used to remove silicon mould, and finally, a laser was used to cut diamond chip edges. The experimental part of the project gave samples of the CVD polycrystalline diamond mcrofluidic chips with open channels, (figure 1) [19].

a) b)

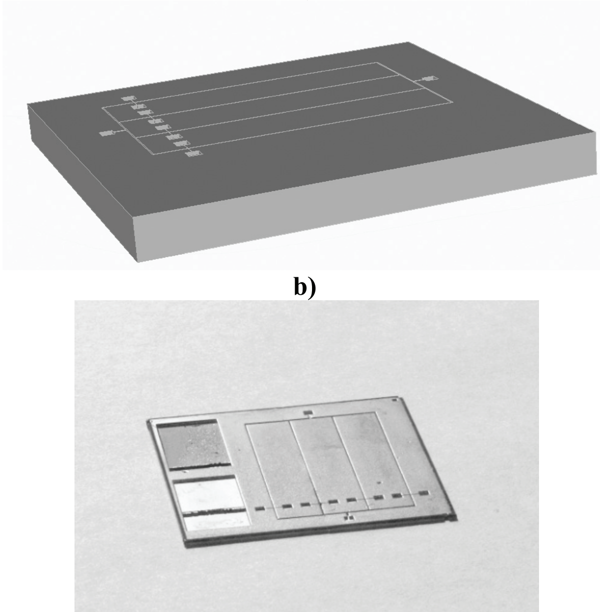

Fig. 1. (a) Model of the diamond chip with four parallel channels and ten reservoirs; (b) real diamond chip after the Si substrate removal and laser edge treatment.

The results of the computer modelling and simulations apply the same geometrical dimensions as in the real chip of the diamond microfluidic device. The profiles of the temperature distribution calculated for the diamond are compared to the profiles calculated for PDMS and glass devices of the same geometry.

2. EXPERIMENT

2.1. Design

The project consists of four different versions of microfluidic chips (33 mm × 33 mm) which were placed side-by-side on the 4"-diameter silicon wafer area. One of the chips contains 8 individual microchannels 25 μm wide, with 4 reservoirs (1 mm × 1 mm) each. Other three chips contain four channels with 10 reservoirs each, as shown in figure 1. Each of these three chips is characterized by different channel width - 10 μm, 25 μm or 50 μm, respectively. Two reservoirs (the external ones) are applied to fill microchannels with the fluid and to insert electrodes for electrophoresis. Other pairs of the reservoirs and cross-channels, located at the 1/5 of the channel length, were designed for the sample introduction into the volume of the channel crossing. Several test structures were also designed and placed on the peripheral areas of the chips.

2.2. Technology

The technology concept is based on the mould technique [4,5,20]. 4"-diameter, 3mm-thick (non-standard) silicon wafers of arbitrary electronic parameters, were used to fabricate silicon moulds on the CMOS IC technological line. At the beginning, wafers were washed and oxidized in the diffusion furnace. Because of the non-standard wafers thickness, special teflon/quartz cassettes, boxes and holders had to be used (this requirement refers to the almost all subsequent technological steps). After the oxidation step, thin Al layer was sputtered to serve as a sacrificial, masking layer. Photolithography was used to transfer shapes from the glass mask on the wafers covered by photoresist, followed by the wet etching of the Al/SiO_2 sacrificial layers. Plasma etching (Bosch process) was used for the deep (250 μm) trenches formation with vertical walls in the Si substrates. Finally, masking layers SiO_2/Al were chemically etched-off and wafers were diced with use of the high speed disk saw with diamond blade. A polycrystalline diamond layer was deposited on each of the silicon mould with a plasma microwave CVD reactor. After the poly-diamond layer deposition, the silicon mould was chemically etched-off and the laser trimming was used to cut and form diamond chip edges.

2.3. Modeling and simulation

Modeling and simulations were created out with the CoventorWare™ software, [21,22], on the standard PC. The most important questions were related to the thermo-electro-chemo-mechanical properties of the diamond and their impact on the microfluidic, microphoretic device functional parameters, mainly – an impact on the temperature distribution inside the microchannels and across whole chips. The parameters, which were applied in the calculations, are collected in table. 1.

Several assumptions had to be made to conduct calculations:

1. In every case the chip thickness was 3 mm and the cap cover - 0.5 mm,
2. Three channel widths (10 μm, 25 μm, and 50 μm) and two channel depths were simulated (150 μm, 250 μm),
3. Three materials were chosen for simulations: diamond, glass and PDMS (parameters are summarized in Tab. I),
4. The same electrical current density was applied in every simulation to enable a comparison of the results,
5. Chips were surrounded by a thick air cushion. The air flow velocity was fixed at the very low level (1000 $\mu m^3/s$) with the flow vector perpendicular to the channels,

Table. 1. *Material properties of air, fluid, diamond, glass and PDMS.*

PARAMETER	UNIT	AIR	FLUID	DIAMOND	GLASS	PDMS
Density	$\left[\frac{kg}{\mu m^3}\right]$	$1.16\cdot10^{-18}$	10^{-15}	$3.51525\cdot10^{-15}$	$2.225\cdot10^{-15}$	$9.7\cdot10^{-17}$
TCE	$\left[\frac{1}{K}\right]$	$3.66\cdot10^{-3}$	$1.8\cdot10^{-4}$	$1.05\cdot10^{-6}$	$5\cdot10^{-7}$	0
Thermal cond.	$\left[\frac{pW}{\mu m\cdot K}\right]$	$2.62\cdot10^{4}$	$6\cdot10^{5}$	$1.5\cdot10^{9}$	$1.4\cdot10^{6}$	$1.5\cdot10^{5}$
Specific heat	$\left[\frac{pJ}{kg\cdot K}\right]$	$1.007\cdot10^{15}$	$4.1\cdot10^{15}$	$4.715\cdot10^{14}$	$8.35\cdot10^{14}$	$1.46\cdot10^{15}$
Electric cond.	$\left[\frac{pS}{\mu m}\right]$	1	$1.288\cdot10^{7}$	0	0	$2.5\cdot10^{-8}$
Diele. constant	[–]	1	78	5.7	8	2.55
Viscosity	$\left[\frac{kg\cdot s}{\mu m}\right]$	$1.86\cdot10^{-11}$	$1.002\cdot10^{-9}$	0	0	0

6. Temperature of the bottom wall of the chip, air, upper and inlet walls was fixed at 300K,
7. The same meshing scheme was applied in every model – "Manhattan Bricks", min. 5 elements per edge, element linear order, no biasing,
8. Test elements were removed from the layout to simplify the model.

3. RESULTS

The computer simulations, [21,22], were used for the fast calculation of the temperature distribution along and across the channels as a function of:

- geometry,
- material properties (thermal conductivity coefficient, heat capacity),
- time,
- electrical power (Joule heat).

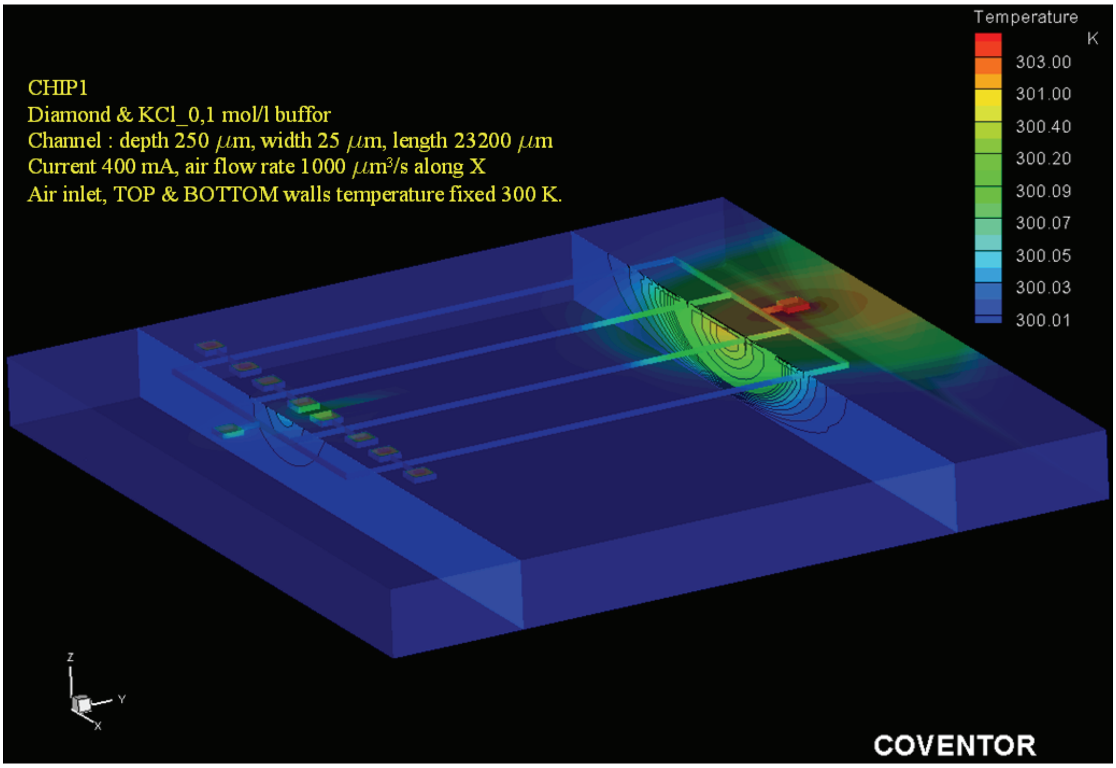

Fig. 2. *Temperature distribution in four microchannels in diamond microfluidic device.*

As an example, figure 2 shows simulation results of the temperature distribution across the diamond chip (no.1). Two additional planes of the cross section, perpendicular to the OY axis, enable a closer view on the XZ temperature maps with isothermal lines. It was assumed that microchannel dimensions on chip no. 1 were: w = 25 μm, l = 2320 μm, d = 250 μm. Thase microchannels were filled with the KCl/H_2O 0.1mol/dm^3. The Joule heat was generated by the electrical current (400mA) flow through the electrolyte, which corresponds to the voltage estimated to 30 kV. The diamond microchip was cooled by the air cushion with the enforced flow rate of 1000 μm^3/s along the OX axis. In the model, the temperature of selected walls was fixed at 300K. The simulations generally have confirmed the correctness of the project idea, showing that diamond microfluidic chips during the electrophoresis remain much cooler than the same microfluidic chips made-up of glass or PDMS, as well as that the temperature profiles in every direction are very planar, due to much better heat conductivity and dissipation.

The graphs in figure 3 reveal significant differences in the temperature levels and profiles extracted along the channels between diamond, glass and PDMS chips. This is obviously due to the difference in thermal conductivity coefficients – diamond has about 10^3 time higher thermal conductivity than the other two materials under consideration. The temperature profile across the diamond chip is almost flat and contained in the scale range of 1K only. One may also observe a difference between the temperature profiles between the channels located on the same chip. Supposed it is caused by an interaction between neighbouring sources of the Joule heat. This phenomenon is also well seen on the following diagrams (figure 4), where internal channels (no. 2, 3) of the microfluidic system are slightly overheated in comparison to the external ones (no. 1, 4).

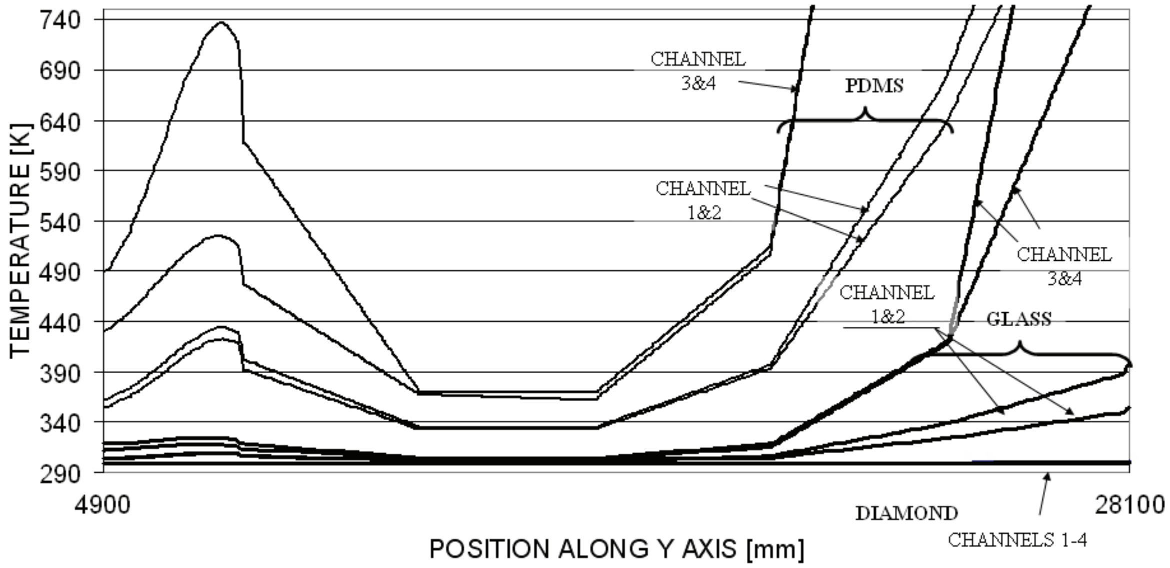

Fig. 3. Temperature profiles along the channels - simulation results for PDMS, glass and diamond microfluidic devices.

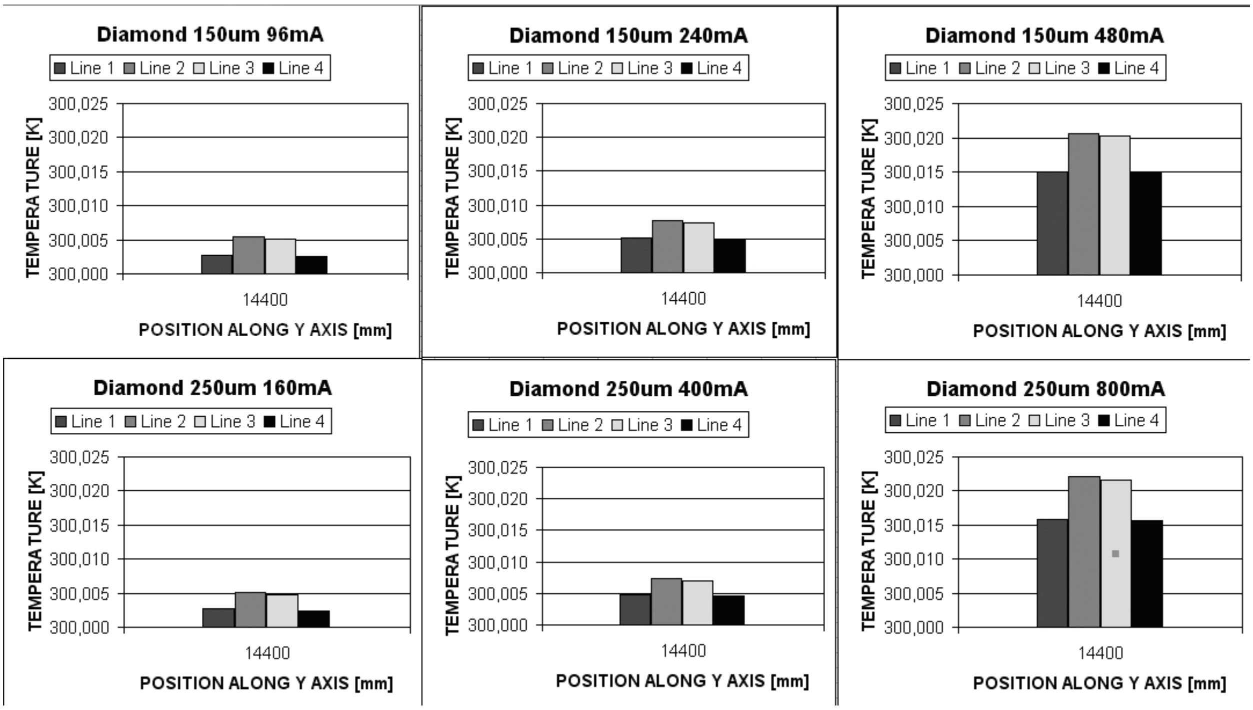

Fig. 4. Diagrams illustrating the temperature distribution between the channels 1-4 (lines 1-4, respectively) for different channel widths/depths and electrical current.

4. DISCUSSION

Joule heat is a very significant but undesirable phenomenon occurring during the process of electrophoresis. It leads to the temperature and temperature gradient growth across the microfluidic chips and channels, decreasing the quality of separation in a number of ways (sample band dispersion or peak broadening, deterioration of analysis resolution and even decomposition of thermally sensitive samples or creation of vapor bubbles in the microchannels), [16]. A proper selection of the material with a high thermal conductivity coefficient for chips, optimization of the chip geometry, as well as an efficient cooling system, may reduce all the above mentioned thermal effects, [10-13]. The calculations were focused on different aspects of the electrophoretic chips design, with respect to minimizing an influence of Joule heating. Wu, et al., [14], in one section of their review paper concerning microchip electrophoresis also discussed the Joule heating effects in MCE. They have shown three aspects of the temperature growth - an overall temperature increase of the buffer solution inside the microchannels, radial temperature gradient within the microchannel and inhomogeneous temperature distribution in the axial direction. They have underlined thermal properties of glass and silica chips, in comparison to plastic chips. With the same electric field, microchannel geometries and running buffer, electrophoresis in the glass and silicon microchips leads to slightly higher temperature in comparison to the plastic ones. They have concluded that an application of PDMS microchips requires highly reduced electric fields than in case of glass devices. These conclusions are in a very good agreement with the results obtained in this research for a new generation material for the MCE application - diamond.

Polycrystalline diamond reveals several extreme, very beneficial properties - the highest thermal conductivity, remarkable biocompatibility, high electrical breakdown voltage and chemical resistance against the majority of chemical solutions applied in the solid-state technology. This makes polycrystalline diamond thick layers the best choice for this type of application.

5. CONCLUSIONS

On the basis of the numerical simulations and the analysis performed, it can be stated that diamond is the best material solution for the MCE application. Diamond is characterized by the highest-ever thermal conductivity coefficient (about 2000 W/m·K), high breakdown voltage, good optical parameters enabling optical detection of biomolecules, and satisfactory mechanical strength. In comparison to the standard glass or plastic devices, diamond offers a significant temperature reduction during the MCE. The electric field necessary for electrophoresis may be increased to accelerate the separation process and to improve the detection selectivity, repeatability and reliability. One may observe an additional effect - internal channels in comparison to the external ones are slightly overheated in every simulated case. Fortunately, for the diamond devices, temperature differences between the channels is of secondary importance.

ACKNOWLEDGEMENTS

Supported by project ERA-NET MNT/98/2006 “Diamond Microfluidic Devices for Genomics and Proteomics”.

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NUMERYCZNE SYMULACJE MIKROFLUIDYCZNEGO DIAMENTOWEGO PRZYRZĄDU DO SEPARACJI BIOMOLEKUŁ METODĄ ELEKTROFOREZY

Streszczenie

W publikacji są omawiane przyrządy mikrofluidyczne, znane również jako laboratorium na strukturze (ang. lab-on-chip, LoC), elekroforetyczne mikrostruktury kapilarne lub miniaturowe układy do całościowej analizy biochemicznej (ang. micro total analysis systems, µ-TAS). Były one wprowadzone do użytku po raz pierwszy w latach 1990, a ponad to skupiały na sobie dużo uwagi w ciągu minionych ostatnich lat. Do pomiarów z ich użyciem potrzebne są bardzo małe objętości próbek i odczynników (bardzo kosztowne). Są one transportowane przez system mikrokanałów i mikrokomór wytworzonych na powierzchni małych płytek podłożowych z różnego rodzaju materiałów. Najczęściej z polimerów (PDMS, PDMA), szkła lub krzemu. Przyrządy mikofluidyczne są stosowane w wielu dziedzinach, obejmujących rozdziały biomolekuł (DNA., lub białek), powielanie i sekwencjonowanie DNA, syntez chemicznych, monitorowania zjawisk biochemicznych zachodzących w pojedynczych komórkach, monitorowania środowiska naturalnego itp. Często łączą w sobie wiele operacji analitycznych, takich jak przygotowanie próbki, separacja i detekcja biomolekuł w małych pojedynczych strukturach. W tej publikacji przedstawiono mikrostruktury do separacji biomolekuł metodą elektroforezy. Zjawisko ciepła Joule'a i jego wpływ, tj. wzrost temperatury prowadzący do dużych gradientów, w przyrządach mikorfluidycznych powoduje wiele problemów metrologicznych - rozmycie pasm (niska wydajność rozdziału kolumny), zmniejszenie rozdzielczości pomiarowej, uszkodzenie niestałych termicznie biomolekuł lub uwolnienie z cieczy gazów w formie pęcherzyków. W zaprezentowanych wynikach badań porównano parametry przyrządów mikrofluidycznych wykonanych z diamentu, szkła i PDMS-u. Mikrostruktury o różnych proporcjach wymiarów geometrycznych i wykonane z różnych materiałów były analizowane z użyciem oprogramowania komputerowego Coventor (metoda elementów skończonych, FEM). Diament posiada wybitnie dobre parametry elektro-termo-optochemiczne, które są bardzo użyteczne w zaprezentowanej metodzie analizy biomolekularnej (w szczególności przy elektroforezie). Najważniejszymi parametrami są: bardzo duży współczynnik przewodnictwa cieplnego, dobra przezroczystość optyczna, bardzo duże napięcie przebicia elektrycznego, dobra odporność chemiczna i duża wytrzymałość mechaniczna.

Diamentowe przyrządy mikrofluidyczne mają wiele zalet względem swoich powszechnie stosowanych odpowiedników wykonywanych ze szkła lub polimerów. Znacznie wydajniej przewodzą one ciepło Joule'a z powodu największego znanego współczynnika przewodnictwa cieplnego diamentu.

Submitted: September 30, 2008
Submitted in a revised form: December 8, 2008
Accepted: December 8, 2008