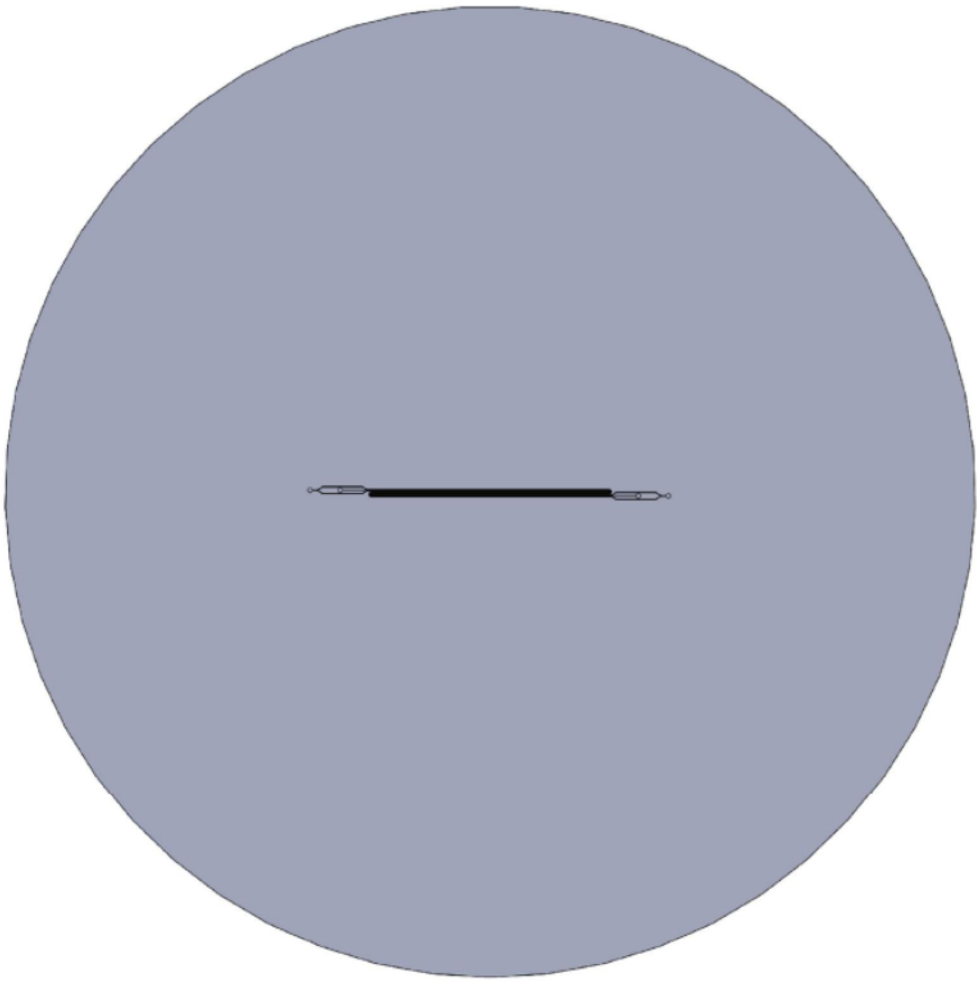
Application of Joule heating for temperature control in microfluidic devices



Matt Nitzken, Emily Cox, Joel Graham

Bio-Engineering Department

University of Louisville

April 29th, 2010

Introduction

The ability to monitor and control temperature in microfluidic devices is a continuing issue in the micro-electro-mechanical-systems (MEMS) field. Many applications require precise temperature control and detection. For example, the ability to perform high-efficiency polymerase chain reactions (PCR) in a microfluidic environment is critically dependent on rapid and precise thermal transfer. PCR is a technique to amplify a single of a few copies of DNA several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence. It relies on thermal cycling, consisting of cycles of repeated heating and cooling of the reaction for DNA melting and enzymatic replication of the DNA. As PCR process progresses, the DNA that it generates is itself used as a template for replication, which allows a chain reaction in which the DNA template is exponentially amplified. PCR is now a common and essential technique used in medical and laboratory settings for a wide range of applications. PCR applications include DNA cloning for sequencing, functional analysis of genes, diagnosis of hereditary diseases, and detection and diagnosis of infectious diseases [1]. Most DNA-based assays (eg. PCR, restriction endonuclease reaction, temperature gradient gel electrophoresis (TGGE) and PCR-sequence-specific oligonucleotide polymorphism (SSOP)) are extremely temperature sensitive and require precise temperature control [2].

Surface plasmon resonance (SPR) detection is also highly temperature sensitive and requires precise temperature control. SPR detection relies on the measurement of a refractive index change at a metal surface that has had probe molecules applied to the surface. The light source is applied at a specific angle to excite a surface plasmon. At this angle, the reflection intensity for the light significantly decreases to a local minimum. Slight changes in the dielectric environment on the opposite side of the sensor surface will reflect the beam of light back at different angles. SPR provides excellent sensitivity and can detect remarkably small changes with high accuracy. However, SPR detection has been difficult to miniaturize and to take to a portable environment. One limitation that could be addressed is the temperature dependence. Temperature affects the surface plasmon resonance angle and, thus, temperature control is a critical feature of SPR implementation.

Joule heating has been a problem in capillary electrophoresis (CE) and electroosmotic flow (EOF) systems [2]. Joule heating is created when an electric field is applied across conductive liquids. This heats the medium through which the current is passing, causing axial temperature gradients within the channel or capillary [3]. In CE, such heat generated is rejected through the channels walls and the downstream end of the channel to the surrounding. The temperature elevation of the buffer and the induced temperature gradient affect the electroosmotic flow (EOF) and the electrophoretic transport of solutes by influencing the temperature sensitive buffer and solute properties such as viscosity, dielectric constant, electric conductivity, mass diffusivity, electroosmotic and electrophoretic mobilities, and pH value. The negative consequences of this in CE include sample peak dispersion and peak band broadening. This results in low column separation efficiency and a reduction of analysis resolution. Additionally, severe temperature rises could cause decomposition of thermally labile samples and even formation of vapor bubbles [4].

Various cooling methods such as liquid coolants in well-thermostated systems and air by natural/forced convection in nonthermostated systems have been developed to maintain an acceptable temperature to minimize the effects of Joule heating. However, the use of Joule heating effects for precise temperature control in microfluidic applications that rely upon a stable temperature (i.e. PCR and SPR) provides a novel way to approach the current limitations of temperature control on the micro scale.

Joule heating generates a radial temperature profile across the channel that can be determined by the following equation (created for a conventional fused-silica capillary with an external polyimide coating):

$$T(x) = T_{ext} + \frac{W}{2}\left[\frac{(0.5 * ID)^2 - x^2}{2k_b} + \frac{(0.5 * ID)^2}{k_{SiO2}}\ln\left(\frac{OD_{SiO2}}{ID}\right) + \frac{(0.5 * ID)^2}{k_{pol}}\ln\left(\frac{OD_{pol}}{OD_{SiO2}}\right) + \frac{(0.5 * ID)^2}{0.5 * OD_{pol} * h}\right]$$

The heat transfer from the outside wall to the surroundings (the last term in the brackets of the above equation, see reference for variable definitions) is usually the dominant factor that determines the temperature rise of the solution [5].

The goal is to develop a simple and low-cost joule heating device that provides a stable heating solution for point-of-care (POC) applications. The proposed design also allows for a degree of flexibility without the need for changes to the device structure. The device will be capable of heating a solution using either counter-current heating or concurrent heating (Figure 1). This would enable the device to provide double the heating range of a single directional flow device. The design would also enable a uniform heating distribution across the channel due to equal heating on both sides of the device. Such a simple design with no rare-metal components would also allow for a low-cost of fabrication. Harvesting the effects of joule heating provides a safe and reliable method of microchannel heating.

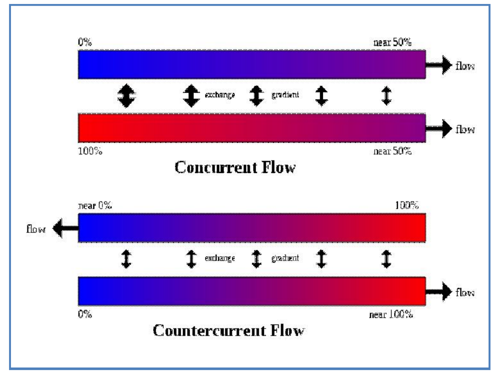


Figure 1 - Concurrent and countercurrent flow. [14]

Background

In creating our low-cost point-of-care temperature stabilization device, we examined other proposed methods of heating liquids in microchannels. Other proposed methods include photothermal control through utilization of a laser diode, micro heat-pipe exchanging, micro-traditional and microchannel hotplates and epoxy resistive heating.

In a laser diode based photo-thermal control, the laser was used to directly heat the substance [6]. The incoming fluid passed through the absorbing target point and exited the system via a drain with detection in between (Figure 2). Some of the problems discussed with this system include that there was often oxidation and discoloring problems in the current setup. The system also involved the use of a higher cost laser diode to accurately control the temperature. Also, if the flow rate through the absorbing target was too fast or too slow the solution would not be heated evenly. In this system many components had to be finely controlled to achieve a uniform heating. As long as

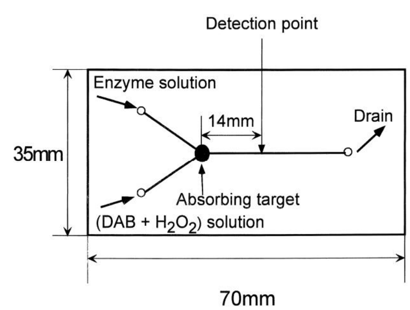


Figure 2 - Layout and dimensions of the photo-thermal laser diode microchip. [6]

conditions were kept stabilized, the system was said to offer stable temperature control, but the necessity for fine tuned control would make it difficult for usage in a POC application.

In our decision to pursue a joule based heating device, examining a heat-pipe based design was a logical conclusion as these two devices share many similar qualities. While there were not many applications published in this area, a paper by Zhiquaun et al. introduces a possible micro heat-pipe based exchanger [7]. The proposed system involves a complex heat source and condenser (Figure 3). It also involves electronic control through the usage of a several thermocouples. The system operates in a way similar to a macro-scale heat-pipe exchanger. The paper discusses that accurate heat control can be gained through the system. It also notes that there is some issue with temperature control due to the system having more difficulty stabilizing than a macro-scale counterpart. This system does show the potential for a micro-scale heat exchanger to be a valid option. The main problem is that the heat generation is due to a complex system. Due to the high cost in manufacturing such a complex heat controller, this would not be a viable option for use in a POC application either.

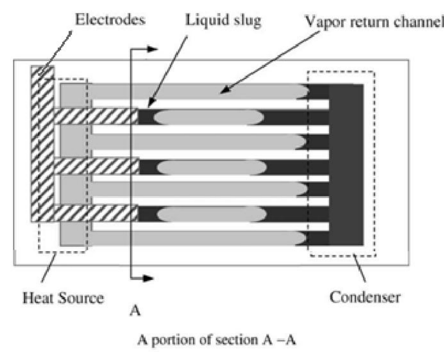


Figure 3 - The schematic configuration of the EHD micro heat pipes. [7]

A third technique proposed for temperature control is the creation of a micro hotplate [8]. This system is a miniaturized heater that can be connected to various micro-systems. This type of heating system has been used as standard laboratory equipment for years and has been a reliable heating technique in macro-scale. A fabrication of the device can be seen in Figure 4. While the system provides a fine-tuned control mode of heating, the traditional hotplate method has a number of disadvantages. A hotplate heats from only one side of a sample; thus, the heating is not uniform across the chamber being heated, creating an unwanted gradient. In a system which has constant flow through a microchannel, it is undesirable to having a heat gradient in your material. Hotplate electronics are also very

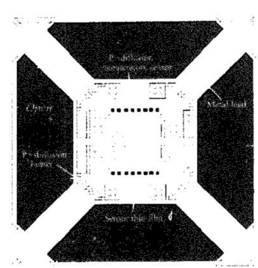


Figure 4 - Layout of revised micro-hotplate design after the thermal analysis. [8]

complex and both difficult and expensive to produce making this unfeasible for a low cost disposable chip application.

Sun et al. proposed a modified hotplate for usage in heating microchannels for a PCR [9]. This heating system is composed of three different layers. The cover layer provides the inlet and outlet for the microchannel. The middle layer contains the actual microchannel and the bottom layer is covered in ITO film and gold electrodes as shown in Figure 4. This system works on the traditional hotplate method with liquid running through the microchannels and being heated from below as shown in Figure 5. The advantages to this technique are that the material is protected within an enclosed microchannel and that ITO film can provide a reliable and durable heating mechanism. This type of system would be able to provide uniform heating even in a many environments due to the even heating of the ITO film and the large surface area for heat transfer. While this method also shares the same disadvantages as a traditional hotplate, the system also uses gold and ITO film which are both expensive.

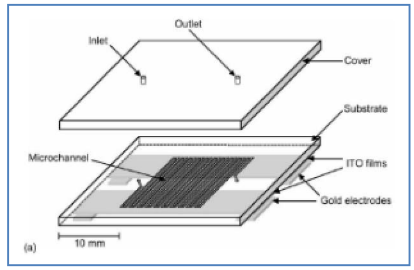


Figure 6 - The structure of the microchannel chip for PCR. [9]

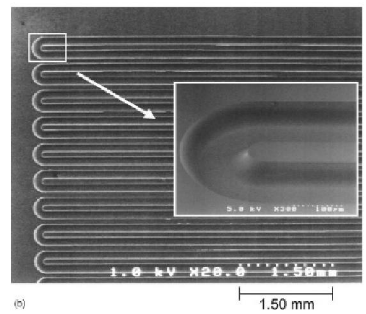


Figure 5 - SEM image of microchannel hotplate. [9]

An article by Vigolo et al. demonstrates an epoxy heating system that with a design that resembles a potential joule heating application [10]. In this a tube of epoxy is formed around the sample channel. The hardened epoxy then has a voltage passed through it which produces heat that can be used. The concept uses the hardened epoxy like a resistor in a circuit to generate heat. Disadvantages to this method are that the temperature distribution throughout the epoxy is not uniform as can be seen in the images and according to the paper the device always results in a gradient due to the current flow path. The device is capable of maintaining a stable elevated

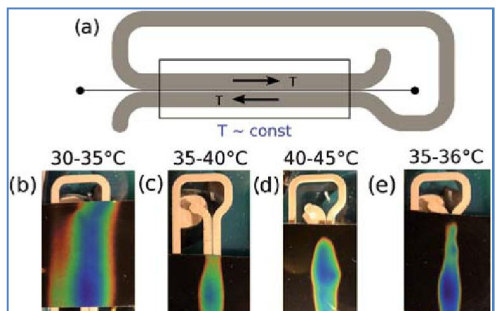


Figure 7 - Bias currents for different temperatures. [10]

temperature, but it is very difficult to change the temperature and also very slow. Once the device has heated up, it cools in a method similar to a ceramic. Thus, this device has problems for quick temperature changes.

Materials and Methods

Typical rapid prototyping techniques are used for construction of the device, which include the photolithography technique for master fabrication followed by use of the soft lithography technique for PDMS replication of the master, dry etching and bonding procedures.

Design

The proposed design is a simple MEMS device that sandwiches two heating channels around a sample channel seen in Figure 4. The heating channels have an applied voltage that heats the sample through the joule heating effect. The voltage and diameter of the channels determine the amount of heating possible. The device is 7 cm in total length with a straight 5 cm portion of the channel that bends back upon itself twice.

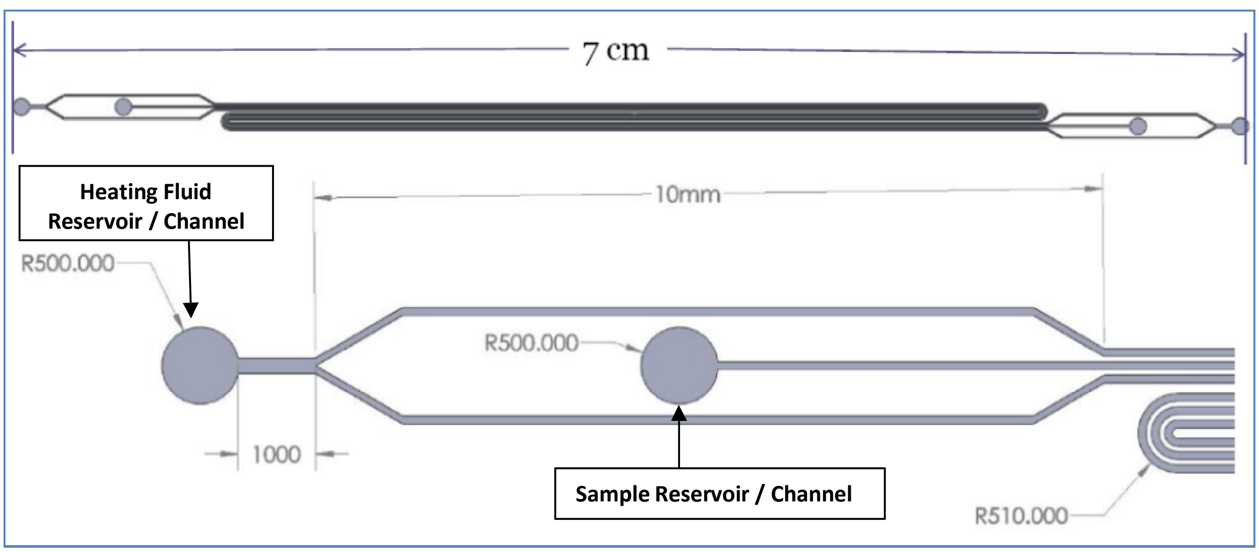


Figure 8 - Proposed design for heat exchange in microfluidic devices.

Based from established studies on joule heating, a channel width and depth of 100 µm by 50 µm, respectively, with a separation of 70 µm between sample and heating channels was chosen (Figure 5). The bends are rounded to prevent uneven heating and aide in uniform flow. Electrodes are placed in the heating channel and sample reservoirs to deliver the voltage potentials; though in the proposed experiment, the electrodes for the sample channel are not used as the fluid is driven pneumatically. The simple design is versatile and allows for a variety of experiments.

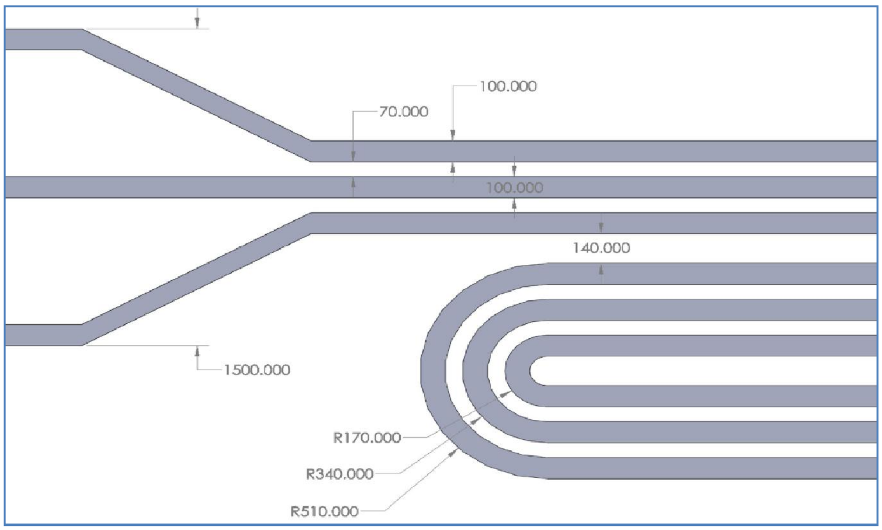


Figure 9 - Close up of design. The rounded bends aid in even heating of the sample fluid.

Fabrication

A soda lime glass substrate wafer is sufficiently cleaned of any organic residues before being coated with a barrier layer and a positive photoresist layer. When exposed to UV light, a positive photoresist undergo chain scission and degrade. The developer solution removes only the portions of the photoresist that have been exposed to UV light, forming a master with a geometry that is specific to the mask developed on the substrate. Before exposure, the wafer is soft-baked to remove solvents, remove stresses, and to promote adhesion. A mask with the mircofluidic design is aligned onto the wafer to dictate which areas are exposed to light. To transfer the mask pattern to the substrate, there are three methods available: contact mode, proximity mode, and projection mode. Proximity mode would be a good selection because it minimizes the amount of damage to the mask (which can be high in contact printing) and it also has a good resolution (unlike projection mode).

Once the mask is aligned, the pattern is exposed using UV light to transfer the mask onto the photoresist. Finally, the photoresist is developed and both the sample and the device geometry is etched into the substrate via dry etching.

Dry etching uses a gas in contact with a solid material to react and form chemical compounds that are soluble in the gas. It has good anisotropy, which will help to carve geometry with sharp edges. It also efficiently transfers the lithographically defined photoresist patterns into the underlying layers, has high resolution, better process control, and ease of automation. Specifically, deep reactive ion etching (DRIE), accompanied by ionic bombardment, will be used. Finally, the exposed photoresist is removed with a developer solution. This master wafer is then hard baked to remove residual solvents, promote interfacial adhesion of the resist, and to improve the hardness of the film.

A mixture of PDMS is then poured over the positive master wafer and allowed to harden. The PDMS microfluidic device is then removed from the surface and placed onto a glass slide. The glass slide will have electrodes deposited on the glass surface so that the voltage maybe applied across the channels. A wet-deposited metal film technique can be used, as described by Ebina et al. [12]. To form the enclosed channels, the PDMS and glass slide are bonded using an oxygen plasma technique. Circular holes are created using a needle to poke through the PDMS and provide access to the channels and serve as fluid reservoirs.

Testing

To test the device, exterior tubing will be connected to the inlet and outlet ports. A syringe pump will be used to drive the sample channel. The heating channels would be attached to reservoirs using similar tubing. For power, the electrodes on the device would be connected to an external, user-configurable power supply with positive and negative contacts. We would undergo two different modality tests to examine the effectiveness of the microchannel joule heating device. Counter-current and concurrent flow for the sample channel would be examined. The flow type could be easily changed by altering which input the syringe pump is connected to. The flow rate for the heating channel would be driven using the voltage gradient in the device. An applied voltage will give a specific flow rate. The sample channel flow rate would be driven by the syringe pump system. This would allow fine-tuned control of the flow rate of the sample itself. It would be necessary to examine the heating effects of different voltages (heat channel flow rates) and different sample channel flow rates. It would also be necessary to examine the effects of different ionic solutions and different molar concentrations for the heating liquids [11]. This would determine the heating limits of the channels before reaching melting point. Current data has shown that the usage of different concentrations of the same solution produce differing results in heating [11].

Temperature acquisition would be done using a Micro-Epsilon CS Series Infrared Thermometer or a comparable micro- infrared thermometer to measure the temperature at the inlet port, midway point of the channel and outlet port of the sample channel. Temperature for the heat channels would be measured similarly to ensure that heat distribution remains constant throughout the channels. The use of an infrared thermometer would enable temperature acquisition without the need for temperature sensors physically embedded in the device and is a viable solution because our materials are penetrable by infrared waves. To further characterize the temperature gradient profiles, rhodamine B dye Solution would also be injected into each of the channels to examine the temperature [13]. This fluorescent dye is temperature dependant and can be imaged using a fluorescent microscope. This would allow acquisition of detailed temperature gradients in the sample and heating channels and visual detection of uneven heating or problematic areas. We would also examine the stability of the heating in different external environments.

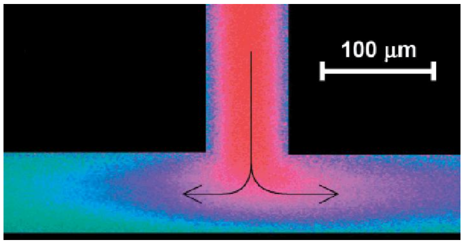


Figure 10 - False color image of buffer temperature in T-shaped microchannel [12]

Summary/Discussion:

It is important to note some limitations of the device. First, the fluid must not get so hot that it has harmful or degradative effects on the substrate. Also, there is a chance of developing a non-uniform axial temperature gradient across the channel width. However, this gradient should be small with the center of the channel being slightly cooler than the area near the walls. Both the heating and electrical conducting / insulating properties of the materials are affected by the thickness of the materials. The effect and optimization of these properties will be needed in future studies.

Future work for this device could include cooling applications as the device functions as a heat exchanger. In addition, channel dimensions, voltages, and flow rates will need to be optimized. Future applications could be in precise temperature control in microreactors. Different geometries and channel widths allow for tight control of temperature as a fluid is flowed through the device. Another promising application is in point of care SPR applications.

The advantages the proposed device includes its low cost of fabrication, ease of use, and its ability to be used for point of care applications. Disadvantages include limitations in measurement of the temperature gradients depending on the method used. The device also requires an external power supply and the sample channel must be powered through an external pump. There is also no internal storage reservoir for the heat channels making them dependant on external fluid supplies. For use in an integrated system this would these would not be significant disadvantages but they would be disadvantages for usage of the system as a standalone device.

This simple heat exchanger design offers a low cost and flexible solution to current heat stabilization issues in the field of microfluidics. Due to the simple design, there is a broad range of applications available for this technique.

Bibliography

[1] Zhang, C., Xu, J., Ma, W., Zheng,W. PCR microfluidic devices for DNA amplification. *Biotechnology Advances*. (2006) 24:243-284.

[2] Zhang, C and D Xing. Miniaturized PCR chips for nucleic acid amplification and analysis: latest advances and future trends. *Nucleic Acids Research*. (2007) 35:13:4223-4237.

[3] Tang, G., Yang, C., Chai, C., Gong, H. Modeling of electroosmotic flow and capillary electrophoresis with the Joule heating effect: The Nernst-Plank equation versus the Boltzmann distribution. *Langmuir*. (2003). 19: 10975-10984.

[4] Tang, G., Yan, D., Yang, C., Gong, H., Chai, J., Lam, Y. Assessment of Joule heating and its effects on electroosmotic flow and electrophoretic transport of solutes in microfluidic channels. *Electrophoresis*. (2006). 27: 628-639.

[5] Peterson, N., Nikolajsen, R., Mogensen, K., Kutter, J. Effect of Joule heating on efficiency and performance for microchip-based and capillary-based electrophoretic separation systems: A closer look. *Electrophoresis*. (2004). 25: 253-269.

[6] Tanaka, Y, Slyadnev, MN, Hibara, A, Tokeshi, M, Kitamori, T (2000). Non-contact photothermal control of enzyme reactions on a microchip by using a compact diode laser. *J Chromatogr A*, 894, 1-2:45-51.

[7] Zhiquan Yu,, Kevin P. Hallinan and Reza A. Kashani. Temperature control of electrohydrodynamic micro heat pipes. Experimental Thermal and Fluid Science. Volume 27, Issue 8, October 2003, Pages 867-875

[8] Samuel K.H Funga, Zhenan Tangb, Philip C.H Chana, Johnny K.O Sina and Peter W Cheunga. Thermal analysis and design of a micro-hotplate for integrated gas-sensor applications. Sensors and Actuators A: Physical. Volume 54, Issues 1-3, June 1996, Pages 482-487

[9] Kai Suna, Akira Yamaguchib, Yutaka Ishidac, Shigeki Matsuoa and Hiroaki Misawa. A heater-integrated transparent microchannel chip for continuous-flow PCR. Sensors and Actuators B: Chemical. Volume 84, Issues 2-3, 15 May 2002, Pages 283-289

[10] Vigolo, D, Rusconi, R, Piazza, R, Stone, HA (2010). A portable device for temperature control along microchannels. *Lab Chip*, 10, 6:795-8.

[11] G. Y. Tang, C. Yang, , J. C. Chai and H. Q. Gong. Joule heating effect on electroosmotic flow and mass species transport in a microcapillary. International Journal of Heat and Mass Transfer. Volume 47, Issue 2, January 2004, Pages 215-227

[12] Wataru Ebina, Amy C. Rowat, David A. Weitz. Electrodes on a budget: Micropatterned electrode fabrication by wet chemical deposition. Biomicrofluidics. 2009 September; 3(3): 034104

[13] Ross, D, Gaitan, M, Locascio, LE (2001). Temperature measurement in microfluidic systems using a temperature-dependent fluorescent dye. Anal. Chem., 73, 17:4117-23.