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COMMUNICATION

Precise temperature control in microfluidic devices using Joule heating of ionic liquids

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Microfluidic devices for spatially localised heating of microchannel environments were designed, fabricated and tested. The devices are simple to implement, do not require complex manufacturing steps and enable intra-channel temperature control to within ± 0.2 °C. Ionic liquids held in co-running channels are Joule heated with an a.c. current. The nature of the devices means that the internal temperature can be directly assessed in a facile manner.

Introduction

The use of microfluidic reactors in chemical and biological synthesis is an area of high research interest.[1] A continuing theme within this field is the ability to control and monitor temperature within microchannel environments. For example, the ability to perform high-efficiency PCR (polymerase chain reaction) within microfluidic environments is critically dependent on rapid and precise thermal transfer.[2] The difficulty encountered with many procedures for on-chip heating is a dilemma between accuracy and complexity. Accurate zonal heating may be achieved through the use of complex on-chip resistive heater networks, requiring additional fabrication steps.[3] Conversely, general non-zonal heating may be easily accomplished using a Peltier device or a laboratory hotplate.[4] This latter approach, although successful, does pose restrictions on optical interrogation of microchannels enforced by such a method.

Approaches to accurate temperature control within micro-fluidic systems have been varied. For example, Guijt *et al.* have recently reported an elegant approach to on-chip heating and cooling.[5] In these studies the authors exploit the use of endothermic or exothermic processes within microchannels to respectively cool or heat solutions contained in an adjacent microchannel. Although, elegant and highly-flexible, this approach requires the continuous addition of reagents (such as sulfuric acid and acetone). In addition, in electrokinetically-pumped systems intrachannel Joule heating can be used to control and vary temperature.[6] However, it should be noted that this approach may introduce unwanted electrochemical effects into the reactor, and is largely inapplicable to systems utilising organic solvents.

In this communication, we investigate the possibilities of using Joule heating of liquids as a method of on-chip heating. Joule heating in capillary electrophoresis (CE) or electroosmotic flow (EOF) systems has long been a cause of distress in the analytical community.[7] This process, whereby an electric current flowing through a conductive liquid heats the medium through which it passes, causes axial temperature gradients within the channel or capillary and thus band broadening and potential bubble formation which may disrupt EOF. Nevertheless, the use of Joule heating of a liquid in a co-running channel to heat a central microfluidic structure should provide a simple route to the precise control of local temperature, without the electrochemical problems encountered when heating the channel itself.

Experimental

Initial studies were performed using a lagged glass microfluidic device, consisting of a working channel structure surrounded by a separate but co-running (parallel) heating channel. Microfluidic devices were produced in-house *via* standard lithographic, wet chemical etching and thermal bonding procedures.[8] Briefly, a soda lime glass substrate (thermal conductivity -0.937 W m^{-1} K^{-1}) precoated with a positive photoresist (AZ 1518) and a low reflective chromium layer (Nanofilm, Westlake Village, California) was exposed using a DWL system (DWL2.0, Heidelberg Instruments, Heidelberg, Germany) to transfer the channel design. After the photoresist was developed (Microposit 351, Shipley Europe Ltd, Coventry, UK), channels were etched into the glass substrate using a buffered oxide etching solution (HF/NH$_4$F) and external access holes were drilled. To form enclosed channels, a glass cover plate cleaned with concentrated H$_2$SO$_4$ was thermally bonded in a furnace (Heraeus Instruments GmbH, Hanau, Germany) at 585 °C. The reactor channel pattern is schematically described in Fig. 1.

Heating and working channel dimensions were typically 150 μm wide by 50 μm deep. Reservoirs were cemented (using Araldite 1014 2-part epoxy resin) to the chip surface above the heating channel inlets to act as electrical contact points. Chips were embedded in a layer of polydimethylsiloxane (PDMS) so that the upper surface was lagged to a depth of 75 mm, the lower surface being unlagged. The PDMS layer was formed by mixing PDMS base and curing agent (Sylgard 184; Dow Corning, Wiesbaden, Germany) in a ratio of 10:1 w/w, and curing overnight in an oven at 40°C. Temperatures were recorded using a k-type thermocouple (RS Components, Corby, UK) embedded flush with the surface of a poly-dimethylsiloxane block. Temperature measurements were
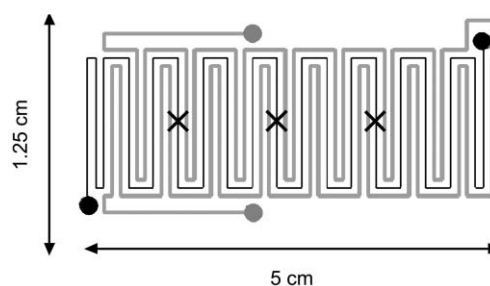

Fig. 1 Schematic of microfluidic device incorporating co-running heating channels. The working (sample) channel is shown in black and the co-running heating channel in grey. Both channels are 150 μm wide and 50 μm deep. Crosses mark position of thermocouples for temperature measurements.

taken at three positions across the device area (Fig. 1). Thermocouple readings were averaged from readings taken along the chip midline at three points representing the geometric centre and the two centroids of the rectangle. The central region of the chip showed a uniformity of temperature. Readings taken at the outer edges of the device show the expected gradient due to a reduced heating channel density. Electrical current was applied using either a high voltage d.c. power supply (FUG HCL 140, FUG Electronik, Rosenheim, Germany) or a home-built variable a.c. power supply (0–10000 V, 50 Hz, 500 mA). Current was recorded in series using a digital multimeter (Fluke 179E, RS Components, Corby, UK)

Initial experiments involved filling the co-running heating channel with a concentrated potassium chloride solution and application of d.c. current (500 µA, 12.5 kV). However, it was rapidly discovered that heating of potassium chloride or other aqueous solutions produced point boiling, followed by arcing. The resulting high-energy chlorine plasma rapidly etches glass microstructures. Consequently, ionic liquids were investigated as possible heating media. Ionic liquids are an emerging technology in separation science, catalysis, and chemical synthesis.[9] Since they are composed entirely of ions, ionic liquids are conducting (with typical conductivities of the order of 1–20 mS cm^{-1}) and are normally electrochemically stable.[9f] *Ambient temperature ionic liquids* are typically moderately viscous liquids (*ca.* 30–200 cP) at room temperature and are often thermally stable at temperatures above 300 °C.[10] Also, of great importance in the current context, ionic liquids exhibit negligible vapour pressure (and thus do not boil) below their decomposition temperatures. Two ionic liquids were synthesised and used in subsequent studies: 1-butyl-3-methylimidazolium *bis*(trifluoromethylsulfonyl)imide ([C$_4$C$_1$im][Tf$_2$N] and 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM]-[PF$_6$]). The ionic liquids were prepared according to the following procedures.

1-Butyl-3-methylimidazolium chloride – [BMIM]Cl

To a vigorously stirred solution of 1-methylimidazole (1.25 mol) in toluene (125 cm^3) at 0 °C was added 1-chlorobutane (144 cm^3, 1.38 mol). The solution was heated to reflux at *ca.* 110 °C for 24 h, after which it was placed in a freezer at *ca.* −20 °C for 12 h. The toluene was decanted and the remaining viscous oil/semi-solid re-crystallized from acetonitrile and then repeatedly re-crystallized from ethyl acetate to yield a white crystalline solid, which was dried *in vacuo* to give [BMIM]Cl in approximately 86% yield. 1H-NMR (270 MHz, Chloroform-d) d: 10.54 (1H, s, NCHN), 7.55 (1H, m, CH$_3$NCHCHN), 7.40 (1H, m, CH$_3$NCHCHN), 4.26 (2H, t, J = 7.3 Hz, NCH$_2$(CH$_2$)$_2$CH$_3$), 4.11 (3H, s, NCH$_3$), 1.82 (2H, m, NCH$_2$CH$_2$CH$_2$CH$_3$), 1.30 (2H, m, N(CH$_2$)$_2$-CH$_2$CH$_3$), 0.89 (3H, t, J=7.3 Hz, N(CH$_2$)$_3$CH$_3$). Mass spectrum (FAB +ve) *m/z*: 139 [M − Cl]$^+$

1-Butyl-3-methylimidazolium ionic liquids

[Anion] = PF$_6$, Tf$_2$N. The respective metal salt (0.32 mol), required to give the desired ionic liquid, was added to a solution of [BMIM]Cl (0.29 mol) in dichloromethane and stirred for 24 h. The suspension was filtered to remove the precipitated chloride salt and the organic phase repeatedly washed with small volumes of water (*ca.* 30 cm^3) until no precipitation of AgCl occurred in the aqueous phase on addition of a concentrated AgNO$_3$ solution. The organic phase was then washed a further two times with water to ensure complete removal of the chloride salt. The solvent was removed *in vacuo* and the resulting ionic liquid stirred with activated charcoal for 12 h, after which the ionic liquid was passed

through a short alumina column(s) (acidic and/or neutral) to give a colourless ionic liquid, which was dried at *ca.* 100 °C *in vacuo* for *ca.* 24 h or until no visible signs of water were present in the IR spectrum. Yields were generally 70 to 80%.

[BMIM][PF$_6$]

Salt: NaPF$_6$. ^{1}H-NMR (270 MHz, Chloroform-*d*) δ: 8.68 (1H, s, NCHN), 7.25 (1H, m, CH$_3$NCHCHN), 7.10 (1H, m, CH$_3$NCHCHN), 4.16 (2H, t, J = 7.4 Hz, NCH$_2$(CH$_2$)$_2$CH$_3$), 3.94 (3H, s, NCH$_3$), 1.86 (2H, m, NCH$_2$CH$_2$CH$_2$CH$_3$), 1.36 (2H, m, N(CH$_2$)$_2$CH$_2$CH$_3$), 0.95 (3H, t, J=7.3 Hz, N(CH$_2$)$_3$CH$_3$). Mass spectrum (FAB +ve) *m/z*: 139 [BMIM]$^+$

[BMIM][(Tf$_2$N] [BMIM](Imide)

Salt: Li(CF$_3$SO$_2$)$_2$N. ^{1}H-NMR (270 MHz, Chloroform-*d*) δ: 8.70 (1H, s, NCHN), 7.29 (2H, m, CH$_3$NCHCHN), 4.14 (2H, t, J = 7.4 Hz, NCH$_2$(CH$_2$)$_2$CH$_3$), 3.92 (3H, s, NCH$_3$), 1.89 (2H, m, NCH$_2$CH$_2$CH$_2$CH$_3$), 1.34 (2H, m, N(CH$_2$)$_2$CH$_2$CH$_3$), 0.93 (3H, t, J = 7.2 Hz, N(CH$_2$)$_3$CH$_3$). Mass spectrum (FAB +ve) *m/z*: 139 [BMIM]$^+$

Results

Fig. 2 illustrates sample results from initial heating experiments. With both ionic liquids (BMIM Imide and BMIM PF$_6$) heating was not accompanied by boiling, bubbling or arc discharges. The applied voltage has a significant influence on the rate of heating as well as the expected effect on the eventual temperature reached. Application of low voltages (below 3 kV) produced the expected hyperbolic curve expressing the relationship between heat generation and the rate of heat loss. More interestingly at higher applied voltages (above 3.5 kV) an s-shape relationship between temperature and time is observed, with an increased rate of heating occurring after an initial induction period. This effect is attributed to a decrease in liquid viscosity as temperature is increased. Furthermore, it is noted that the use of a constant current to heat the channels results in fouling and degradation of the electrode. In these studies interactions of the ionic liquid with the electrode-material play an important role. Pt-electrodes are used together with a disubstituted imidazolium species. The acidic C2-hydrogen of imidazolium-species can be reduced to yield the corresponding carbene which will then form a stable ligand for platinum species leading to a marked variance in local viscosity and conductivity.
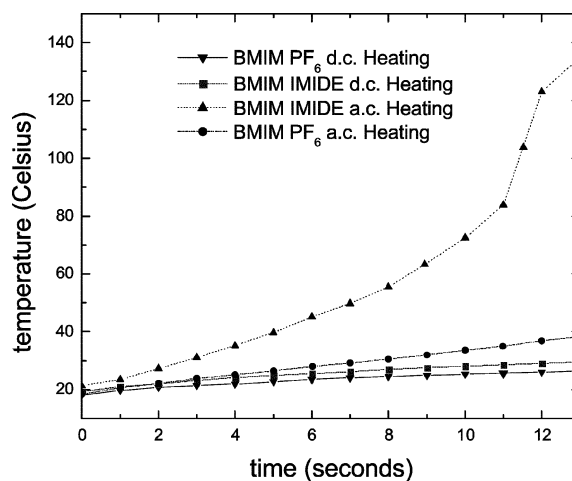

Fig. 2 Variation of temperature as a function of time after application of 3.75 kV across ionic liquid filled heating channels. Ionic liquids: [BMIM][PF$_6$] and [BMIM] [Tf$_2$N]. Voltages: d.c. and 50 Hz a.c. Heating channel: 150 µm wide and 50 µm deep.
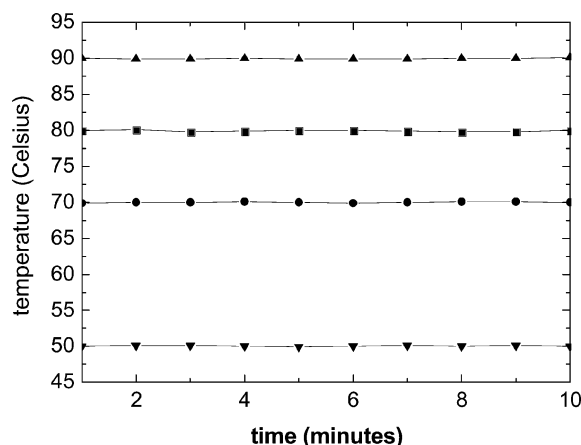
Fig. 3 Variation of set temperature as a function of time for temperatures of 50, 70, 80 and 90 °C. Ionic liquid: [BMIM][PF$_6$]. Heating channel: 150 μm wide and 50 μm deep.

Heating using an alternating current (50 Hz) resulted in smooth and contollable heating with little or no degradation of the heating medium near the electrodes. This in part is attributed to the high stability of ionic liquids as electrochemical media.[11] Examination of the a.c. heating data (Fig. 2) shows that once a certain critical temperature is reached the rate of heating at a fixed voltage increases rapidly. This rate then drops off at higher temperatures to yield the sigmoidal curve described above. At higher temperatures more rapid ion transport takes place within the heating medium, thus increasing the power consumption. As the temperature further increases the expected equilibrium point between heat input and heat loss to the surroundings is reached, causing the rate of change of temperature to reduce. In the current studies, the rate of heating for devices containing [BMIM] [Tf$_2$N] was much greater than when using [BMIM] [PF$_6$] under similar conditions. Power consumption for these devices was typically on the order of 1 Watt

Variable rates of heating could be achieved with precision between 0 and 5 °C min^{-1}. This range was chosen to minimise thermal shock on the glass substrate, though much faster heating rates (in excess of 100 °C min^{-1}) were achievable. Through simple feedback control, microfluidic channels could be maintained at a specific temperature to within 0.2 °C (between ambient and 140 °C). Fig. 3 illustrates the use of the heating system to maintain microchannels at fixed temperatures between 50 and 90 °C. Results demonstrate that microchannel elements can be maintained at a fixed temperature (± 0.2 °C) for extended periods of time with no degradation of the heating medium. Significantly, the conductivities of the ionic liquids used vary with temperature in a predictable way. As illustrated in Fig. 4, this variation of conductivity with temperature allows precise monitoring and calibration of intra-channel temperatures.

Conclusions

Joule heating of ionic liquids is shown to be an effective method of controlling temperatures with high precision and accuracy within microchannel environments. The concordance between temperature and conductivity of the ionic liquids allows for internal temperature measurement and negates the use of on-chip thermocouples. Microfluidic devices incorporating such fluidic heaters are simple to manufacture, use very little ionic liquid ($\sim$750 pL per channel), and are completely transparent (affording efficient optical interrogation of sample). Devices
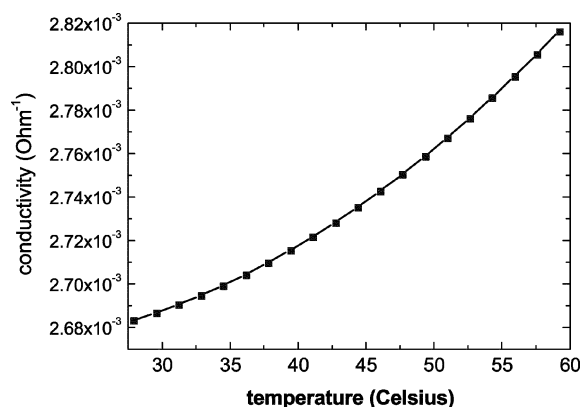

Fig. 4 Variation of ionic liquid conductivity as a function of temperature. Ionic liquid: [BMIM][PF$_6$].

can be heated rapidly or slowly depending on the applied voltage, and temperatures can be maintained to within ± 0.2 °C. This approach will be of particular use in thermocycling applications, where integration of multiple heating channels along a co-running reaction microchannel should allow efficient and localised temperature control. In addition, the approach requires no manipulation or replenishment of the heating medium once introduced into the heating microchannel and initial estimates indicate operational lifetimes of the order of hundreds of hours. Current studies are addressing the use of such heaters in microfluidic systems for small molecule synthesis within temperature controlled environments. Furthermore, a more precise assessment of intra-channel temperatures is being investigated using anti-Stokes fluorescence imaging of temperature sensitive fluorescent dyes within microchannels.

Acknowledgements

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