Thermal management in microfluidics using micro-Peltier junctions

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We report refrigeration and heating of nanoliter fluid volumes with micro-Peltier junctions. The temperature of small liquid reservoirs can be rapidly changed and controlled within a range between −3 °C to over 120 °C with good long-term stability. These thermal management systems enable the fabrication of complex chip-based chemical and biochemical reaction systems in which the temperature of many processes can be controlled independently. © *2005 American Institute of Physics*. [DOI: 10.1063/1.2089174]

The dense integration of microfluidic components for the construction of compact and monolithic chip-sized laboratories and reaction systems requires many different functions to be miniaturized and combined on the same substrate. Some useful chip-based operations could include mixing, filtering, metering, pumping, reacting, sensing, heating, and cooling of nanoliter volumes of fluids.[1–3] In such systems, smaller amounts of samples can be analyzed in less time, as little material is lost by transferring samples from one reaction vessel to another. So far, much work has been performed on defining and integrating fluidic components that can perform such on-chip mixing, sorting, and reacting of fluids. By combining thousands of lithographically defined pumps and valves into chip-based systems, it is possible to obtain unprecedented control over reagent concentrations and perform many reactions in parallel. However, one largely unexplored area for microfluidic devices has been the miniaturization of thermal management systems,[4–7] such as refrigerators and heaters to control the local temperature of a reaction. Typically, the entire chip must be heated or cooled, which seriously limits the kind of independent operations that can be performed on such chips. As a result of the recent demand for performing more complex procedures with greater temperature flexibility and accuracy, as well as the need for sample accumulation and chromatographic analysis, we have investigated methods for independent thermal control over individual reaction chambers on a fluidic chip.

Many different approaches have so far been explored for thermal control, including the construction of resistive heating elements within fluidic chambers, and immersing the entire chip into coolant. For example, polymerase chain reaction (PCR) systems for deoxyribonucleic acid (DNA) amplification have been fabricated with volumes as small as 12 nanoliters based on lithographically defined resistive tungsten heaters.[8,9] We believe that the use of micro-Peltier junctions provides an even more versatile method of thermal control, which permits both local heating and cooling of reaction chambers and the controlled redistribution of heat loads on microfluidic chips. Here, we demonstrate the integration of such refrigeration systems with microfluidic valves and pumps, and describe the temperature dependence on the current applied to the thermoelectric cooler as well as the microfluidic heat exchange flow. The technology described here is expected to be particularly useful for the definition of micro-PCR systems, as well as for many analytical biochemical reaction and testing systems.

Figure 1 shows a picture of a micro-Peltier cooler encapsulated within a replication molded elastomeric chip. In the resulting chips, the Peltier junction is used as a heat pump to transfer heat from a microfluidic chamber into an adjacent channel which uses water as a microfluidic heat exchanger. The Peltier device is embedded within a standard polydimethylsiloxane (PDMS) replication mold, making this device compatible with the most common microfluidic material. The molds for this device are made by three-dimensional fabrication, which allows for a large surface area to be presented to the face of the Peltier device while still minimizing volumes of the chamber and channel. A copper busbar joins *p* and *n* junctions in the Peltier chamber to improve thermal transfer, while a similar copper/fluid heat exchanger was introduced on the cooling channel side to maximize the thermal transfer from the warm side of the Peltier device to the heat sink. Thermal isolation is achieved through the low thermal conductivity of PDMS. The Peltier device itself is a $0.6 \times 0.6 \times 1.0\ \mathrm{mm}^3$ diced pieces of *p*- and *n*-type thermoelectric materials with nickel and gold applied to the end faces to facilitate solder connections, obtained from Marlow Industries Incorporated and soldered to wires that are sealed and isolated through two-component elastomer and connected to a constant current power supply. To conduct measurements of the refrigeration temperature and rate, one side of the Peltier junction is heat sunk with a microfluidic flow channel in which the flow rate was measured to observe the effect of heat exchange on this device. The sample side of

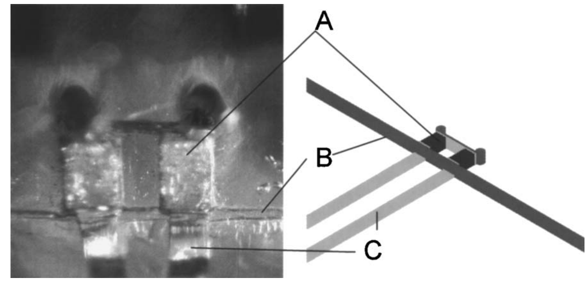

FIG. 1. Optical micrograph of the 168 nL chamber Peltier cooler embedded between the PDMS chamber and the 200 μm heat exchanging channel. A three-dimensional drawing of the device is depicted with A pointing to one of the Peltier devices, B pointing to the heat exchange channel, and C points to the copper heat sink and electrical connection. The two holes at the top of the picture allow access to the chamber for fluid and the thermocouple.

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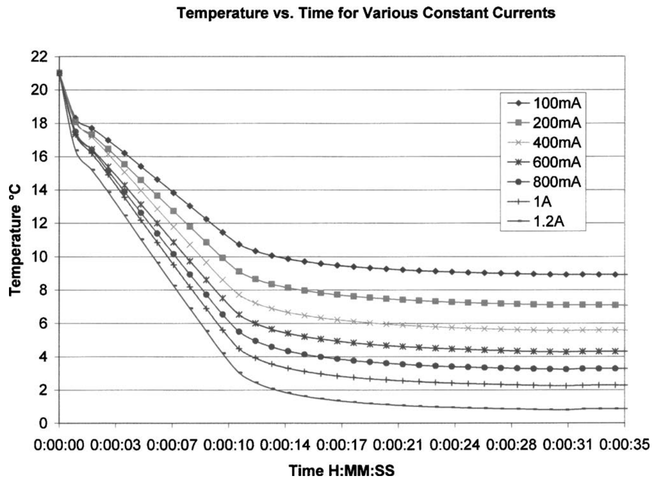

FIG. 2. Time dependence of the sample temperature as a function of the current applied to the thermoelectric junction.

the junction consists of a small fluidic chamber, 169 nl in volume, which also contains a .001 in. diameter bare wire type K thermocouple to measure the temperature of the refrigerated material. As a current is applied to the micro-Peltier junction, the chamber can be cooled down within approximately 10 s (Figs. 2 and 4). The ultimate temperature depends on the current applied to the thermoelectric cooler, as well as the flow rate and temperature of the heat exchanger liquid. Figure 3 demonstrates such a temperature dependence of the refrigerated liquid as a function of current and flow rate with the cooling water kept at 25 °C. Several temperature curves are shown for various heat exchange flow rates as the Peltier current is increased in steps of 200 mA. As the cooling water flow is increased, the better the effectiveness of the Peltier junctions at lowering the temperature in the chamber. The effect of no cooling water flow is shown by the curve which heats up after 800 mA, in which case the resistive heating overwhelms the cooling power due to the lack of an effective heat sink. A subzero temperature can be obtained when the highest heat exchange flow rates and large currents (of approximately 1.2 A) are applied to the cooler. Ultimately, this temperature is limited by a balance between

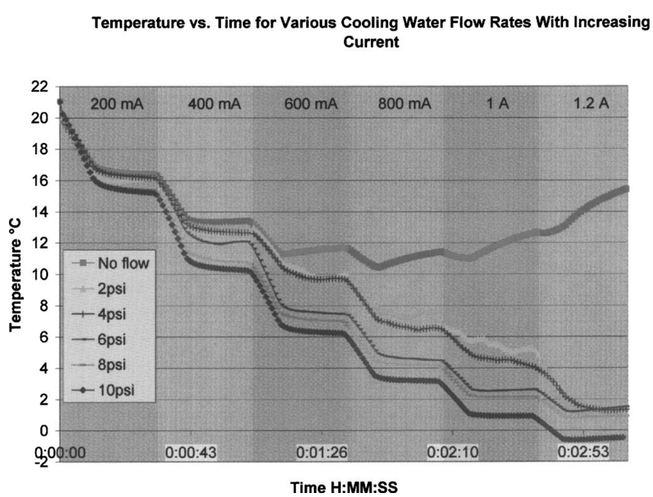

FIG. 3. Time-dependent plot showing several temperature curves for different thermal transfer cooling rates. The applied current was incrementally increased by 200 mA every ~30 s. Note the curve which increases at 600 mA was with no cooling water flow showing, and that increased cooling water flow leads directly to improved cooling.

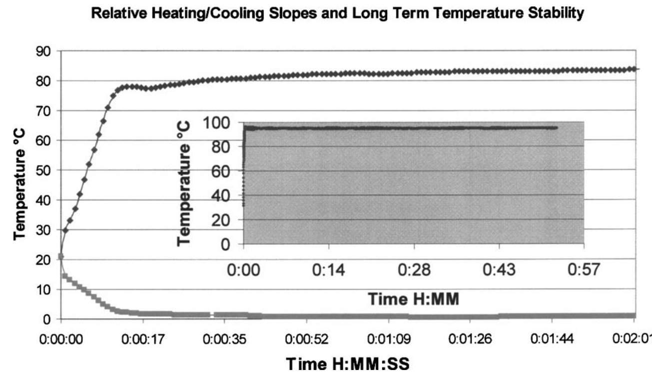

FIG. 4. Temperature ramp rates for both thermoelectric heating and cooling. Inset graph shows a heating run at 94.7 °C with a standard deviation of 0.2° over almost 1 h.

the resistive heating of the junctions at high applied currents and the cooling action from the Peltier effect, as described in the following equation:[10]

$$q_c = \alpha_n I T_1 - \frac{\lambda A \Delta T}{L} - \frac{I^2 R}{2},$$

where R is the resistance, I is the applied current to the Peltier device, α is the Seebeck coefficient, λ is the thermal conductivity, A is the surface area, and L is the length.

During our measurements, the chamber temperature was monitored by a thermocouple embedded in the chamber, to obtain response results as functions of electrical current, heat exchange fluid flow, and time. The resulting curves can be used to optimize the temperature and ramp rate of the micro-Peltier device. For many applications, such as quantitative PCR, it is also important to demonstrate constant temperatures with accuracies of 0.1 °C, and we have measured the time-dependent response of the chamber temperature over several hours of refrigeration or heating. The inset graph of Fig. 4 shows a typical thermal stability plot for our refrigerator when operated with a simple labview program to control temperature. These preliminary temperature control results are already promising, reaching an average temperature of 94.7 °C with a standard deviation of .2° over almost an hour, however the goal of a temperature control of 0.1° C will require more complex active feedback to adjust the Peltier current.

We report an on-chip refrigerator and heat exchanger for microfluidic devices. The microfluidic chamber was cycled between −3 and over 120 °C, thus spanning water freezing and boiling, and the entire PCR temperature range. For smaller chambers, we also show that it is possible to cool reagent from room temperature to freezing within 10–20 s, and to obtain relatively good temperature ($<\pm.2$ °C) stability over long periods of time. The ability to localize heating and cooling in microfluidic chambers and channels will enable massive parallelization of chemical reactions in which the temperature of each reaction vessel can be independently controlled. This enables more complex chemical and biochemical reactions, which require precise temperature schedules, to be performed on miniaturized fluidic chips. Moreover, important analytical and functional temperatures can be changed very rapidly or held constant. For instance, one chamber can be frozen in order to store a cell, while another can be boiled in order to sterilize it, whereas yet another chamber can cycle the temperature in order to perform a PCR reaction.

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[1] J. P. Brody and P. Yager, *Proceedings of the Solid State Sensor and Actuator Workshop, Hilton Head, SC, June 1996*, pp. 105–108.
[2] S. R. Quake and A. Scherer, Science **290**, 1536 (2000).
[3] H. P. Chou, M. A. Unger, A. Scherer, and S. R. Quake, Biomed. Microdevices **3**, 323 (2001).
[4] J. Lee and I. Mudawar, Int. J. Heat Mass Transfer **48**, 928 (2005).
[5] J. Lee and I. Mudawar, Int. J. Heat Mass Transfer **48**, 941 (2005).
[6] A. M. Clark, N. A. Miller, A. Williams, S. T. Ruggiero, G. C. Hilton, L. R. Vale, J. A. Beall, K. D. Irwin, and J. N. Ullom, Appl. Phys. Lett. **86** 173508 (2005).
[7] X. Fan, G. Zeng, C. LaBounty, J. E. Bowers, E. Croke, C. C. Ahn, S. Huxtable, A. Majumdar, and A. Shakouri, Appl. Phys. Lett. **78** 1580 (2001).
[8] J. Liu, M. Enzelberger, and S. R. Quake, Electrophoresis **23**, 1531 (2002).
[9] E. T. Lagally, P. C. Simpson, and R. A. Mathies, Sens. Actuators B **63**, 138 (2000).
[10] H. J. Goldsmid, in *CRC Handbook of Thermoelectrics*, edited by D. M. Rowe (CRC Press, Boca Raton, FL, 1995), p. 20.