Microfluid Nanofluid
DOI 10.1007/s10404-012-1036-1

RESEARCH PAPER

Design and characterization of a platform for thermal actuation of up to 588 microfluidic valves

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Received: 16 May 2012 / Accepted: 18 June 2012

Abstract In this paper, we describe a large-scale microfluidic valve platform for thermally actuated phase change (PC) microvalves. PC microvalves can be actuated by heat sources such as ohmic resistors, which can be highly integrated resulting in dense arrays of individually addressable microfluidic valves. We present a custom-made electronic platform with custom-written control software that allows controlling a total of 588 individually addressable resistors each of which can be used as the actuator for a separate PC valve. The platform is demonstrated with direct PC microvalve (the simplest example of a PC valve) where working fluid and phase change material are the same media. We present experimental results for single valve setups as well as for a 24 microvalve setup showing the scalability of the system. Furthermore, we demonstrate that precise and individual 'per-resistor' temperature profiles are required for valve actuation in order to decrease thermal latency and ensure that the time required for switching the valve state is independent from the "thermal history" (i.e. the duration of the previous valve state) of the valve. To the best of our knowledge, there is no such platform described in the literature, which offers an equal potential for individual valve operation (potentially up to 588 individual valves) as presented in this work.

Electronic supplementary material The online version of this article (doi:10.1007/s10404-012-1036-1) contains supplementary material, which is available to authorized users.

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Keywords Microfluidics · Microfluidic valves · Thermal actuation · Phase change

1 Introduction

Microfluidics deals with small amounts of liquids and their manipulation inside of technical systems. Microfluidic systems feature a number of advantages compared to macroscopic fluidic systems such as low sample consumption or faster analysis times due to short diffusion distances. This makes them extremely suitable for high-throughput biochemical experiments or molecular biology (Cho et al. 2011). Furthermore, microfluidic systems enable applications in clinical diagnostics with integrated sample preparation such as the extraction of particular molecules from clinical samples such as whole blood (Schulte et al. 2002). Demanding applications often require complex and reconfigurable microfluidic channel networks for pre-treatment of the sample or premixing such as in multi-step syntheses applications (Lee et al. 2005). Embedded microfluidic valves allow the regulation of the liquid flow within the microfluidic channels. For complex systems, the number of valves required on-chip can be as high as several hundreds (Melin and Quake 2007). The scientific literature describes a multitude of microfluidic valve types with different actuation principles such pneumatics, piezoelectricity, magnetism or phase changes (PC) (Oh and Ahn 2006). Pneumatic actuation is the most commonly used actuation principle especially if the microfluidic systems are created from soft materials such as elastomers (Melin and Quake 2007). On-chip pneumatic actuation is usually combined with external pneumatic pressure reservoirs and external pneumatic valves for actuation as the membrane valves created on chip do not include an, e.g., electrically addressable actuator. Therefore, it is possible to create a large number of microvalves with pneumatic actuation but those valves are usually not individually addressable because the number of actual actuators (in form of the external pressure vales) is limited to only a few. In these systems, one actuator usually actuates a number of on-chip membrane valves (Thorsen et al. 2002). This disadvantage is usually compensated by using multiplexers, which allow a lager number of on-chip valves to be actuated while sacrificing individual control (Unger et al. 2000). For example, 8 individually addressable external pneumatic valves can be used to set up an 8-bit multiplexer, which allows a total of $2^8 = 256$ on-chip valves to be actuated. However, by design, a multiplexer only has one output valve, which can be actuated at a time: if one valve is actuated, the other 255 valves are not. In technical terms, the number of individually addressable valves would still be 8.

In order to increase the number of individually addressable microfluidic valves it is mandatory to implement actuators that can be packed and integrated densely and which may be controlled, e.g., by means of digital electrical control signals outputted directly from a computer. It is furthermore advantageous, if the chosen actuation principle relies on such electrical signals solely and does not require additional actuation components such as pneumatic pressure. PC microvalves can be considered a suitable choice for such an actuation as they can be activated electronically with limited space demands and with few to no mechanically movable components. PC valves are usually activated by a heat source, typically implement as an ohmic resistor to which a voltage is applied. This voltage is the actual control signal. The integration and individual addressing of a large number of ohmic resistors is common practice in circuit design today.

There are two different kinds of PC microvalves: indirect and direct ones. In indirect PC microvalves, the fluid is separated from the actuator medium by a flexible membrane. For such valves, the volume expansion during the phase change of an actuator medium such as paraffin wax (Kabei et al. 1997) or hydrogel (Richter et al. 2004; Eddington and Beebe 2004) is used to deflect an elastic membrane and to block a microfluidic channel. An alternative to using the volume expansion is using the ability to displace the actuator medium in the liquid state by an outer pressure thus creating a latchable PC microvalve (Yang and Lin 2009). In general, indirect PC valves require additional components such as an elastic membrane and are therefore set up as multi-component systems that require bonding processes or the like during assembly. This may result in problems with leak-tightness and component failure due to insufficient bond strengths.

This problem is solved by direct PC microvalves where the channel is directly blocked by the actuator medium. This type of PC microvalve is especially advantageous as it has no mechanically moving parts at all, features minimal dead volumes and does not require any additional components besides the mere microfluidic channel. Therefore, no additional bonding and consequently no potentially leaking bonds have to be introduced. Furthermore, the valve can be directly addressed by means of digital electrical signal from a controlling computer. The fact that the valve is slower in reaction time compared to membrane valves due to the thermal nature of the actuation may be considered the primary disadvantage.

Direct PC valves may be set up in two ways: using a second material as actuator material or using the working fluid (the fluid which is transported in the microfluidic channels) directly as actuator material. Examples of the first case would be using a hydrogel (Richter et al. 2004) or disposable paraffin plugs (Liu et al. 2004) directly located in the channel and activated via a temperature change. Introducing a second material for actuation may lead to problems with (bio) chemical compatibility and contamination as the actuator material may chemically interact with the working fluid and lead to cross-contamination during the experiment. This problem is solved by using the working fluid directly as the actuator material. In this case, no extra material is required to be in contact with the working fluid. In general, the working fluid is frozen to block the channel and thawed to open it. The first examples using this kind of microvalves known from literature used liquid carbon dioxide directly sprayed onto the channel to freeze the liquid inside (Bevan and Mutton 1995). However, as only the environmental temperature was used to thaw the liquid the thawing and thus opening times of the valves were in the range of 5 min. Takagi et al. (1995) used Peltier elements around the channel for cooling and active heating of the channel. A PC microvalve with separate cooling and heating sources was presented by Colin and Mandrand (1999) using a thermoelectric cooler for freezing and ohmic heating of the microfluidic channels' metal walls for thawing.

As stated, PC microvalves offer the potential for high-density integration into large-scale microfluidic valve arrays, potentially with hundreds of individually addressable valves, due to the simplicity of their actuation principle. However, to the best of our knowledge, all systems known from literature describe valve systems with only one or only a small number of individually addressable microvalves. In this paper, we present a large-scale microvalve platform, which can potentially be used to operate 588 individually addressable thermally actuated microvalves, including direct and indirect PC valves as well as almost any valve type based on thermal actuators. In this work, we will describe the design and the setup of this valve platform showing first experimental results for the simplest case of a PC microvalve, a direct microvalve, using a total of 24 individually addressable PC microvalves.

Part of this work has been presented at µTAS 2011 (Neumann et al. 2011).

2 Experimental setup

Phase change valves require a temperature change for actuation. Using separate components for heating and cooling allows lower reaction times especially if only one Peltier element is used for cooling of multiple PC valves while using individually addressable ohmic resistors for heating. This allows the creation of individually addressable heating zones and therefore multiple PC valves. This general arrangement can be used for any kind of PC microvalve, direct as well as indirect ones. The fact that individual control of large numbers of ohmic resistors is a routine process in electronics makes this approach scalable, resulting in a platform with a high number of individually addressable microvalves. The easiest version of a direct PC valve is set up with the channel directly above a Peltier element as heat sink and an ohmic resistor inside of the fluidic channel as heat source. The heat sink is constantly active while the heat sources are temporarily switched on and off to trigger the valve opening and closing, respectively. This operation scheme is convenient because it is technically less challenging to constantly cool a larger area and create heat only locally than vice versa. This is due to the fact that a technical heat sink is mostly set up in form of a heat pump such as a thermoelement (usually a Peltier element). The latter has a cold and a hot contact zone requiring constant cooling of the hot contact zone for effective operation as heat sink on the cold contact zone. Using several Peltier elements locally (instead of only one large heat sink) would require equipping each those elements with a separate cooling which increases system complexity and decreases system performance because smaller Peltier elements usually provide less cooling efficiency than larger ones (Gui et al. 2011).

One important aspect of our setup is the fact that heat is constantly removed from the system. To avoid freezing of the whole working fluid (which is identical with the actuator medium) the channel is arranged in two levels with only the lower level being in direct contact with the heat sink. This small contact zone is the active zone of the valve. The rest of the channel is spaced from the heat sink, thus avoiding freezing of the working fluid in this section of the channel. This results in the microfluidic channel being U-shaped. Figure 1 shows the general operating principle of this direct PC microvalve. If the resistor is switched off (no voltage applied), the heat sink will permanently remove heat from the system. If the temperature from the heat sink is set below the freezing point of the working liquid, the latter will freeze in the active zone of the valve. To open the valve a voltage is applied to the resistor creating a heat source thus thawing the working medium. So the microvalve is switched to the open state by applying a voltage to the resistor. If the voltage is removed, the heat source is switched off and the valve closes.

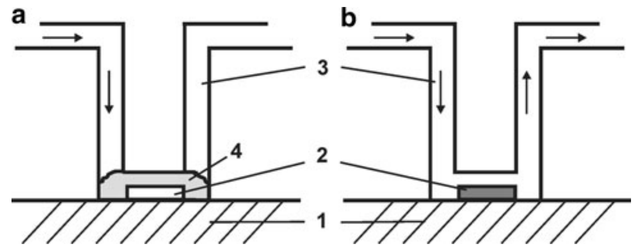

Fig. 1 Schematic view of the two operating modes of the PC microvalve. **a** No voltage is applied to the resistor thus the channel is frozen and the valve closed. **b** The channel opens when a voltage is applied to the resistor thereby creating a heat source which thaws the valve. *1* Constantly operating heat sink (in this work, a Peltier element is used), *2* ohmic resistor (*white* without voltage applied, thus in cold state, *grey* with voltage applied, therefore heated), *3* microfluidic channel, *4* plug of frozen working medium blocking the channel in the active valve zone (closed state)

2.1 System hardware and control software

The electronic setup for the thermal valve platform is custom-made. As heat sink a commercially available Peltier element (type DAC060-24-02 by Laird Technologies®, USA, purchased from Telemeter, Germany) was used. The Peltier element was complemented with a custom-developed electronic control board (termed system hardware) for controlling the Peltier temperature and the ohmic resistors used for thawing (see Fig. 2). The Peltier element was controlled by a microcontroller which measured and set the temperature by means of a temperature sensor (type TMP17, Analog Devices) in combination with a PI control circuit. The thermally actuated surface of the Peltier element is of size 6 × 12 cm. This dimensions given, a custom-designed circuit board layout was designed which allows a total of 588 SMD resistors (type 0603, size 1.6 × 0.8 mm, resistance 330 Ω) in 12 lines (denoted A–L) and 49 columns (denoted with the numeric values 1–49) with a column pitch of 2.4 mm and a line pitch of 4.6 mm on an area identical to the thermally modulated surface of the Peltier element. The chosen packaging density was determined in preliminary experiments as a good trade-off between high packaging density and minimal thermal cross-talk (see ESM, section 1). The circuit board with the ohmic resistors is termed heat pixel array. It is a multilayer

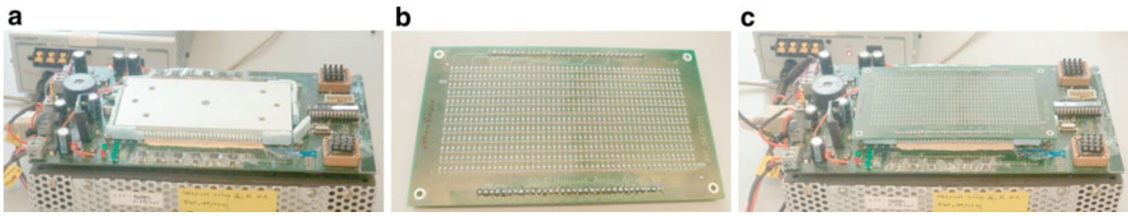

Fig. 2 Photographs of the experimental setup displaying the electronic components. The heat pixel array is displayed without the microfluidic polymer component. **a** Peltier element with the system hardware. The Peltier element has a thermally modulated surface of size 6 × 12 cm. The system hardware consists of a microcontroller and serial input latched sink drivers which are used to control the activation of the individual SMD resistors. In addition the system hardware features a TMP17 sensor which is used to control the temperature of the Peltier element. **b** Circuit board with 12 × 49 = 588 SMD individually addressable resistors (termed heat pixel array). **c** Heat pixel array mounted to the Peltier element. During experiments the microfluidic polymer component is mounted irreversibly to the heat pixel array (usually by gluing)

printed circuit board (PCB) with the line wires (A–L) and the column wires (1–49) located on different layers of the circuit board. At each intersection a resistor and a diode are located resulting in a classical diode matrix setup (see ESM, section 2). The microcontroller sequentially applies voltage to the line wires for about 1 ms each. If a specific line wire has voltage applied, the ohmic resistors located along this respective wire can be activated. Selection of the individual resistors to be activated is performed via the microcontroller and serial input latched sink drivers which allow each column line to either connect to ground (thus closing the electronic circuit and allowing a current to flow through the ohmic resistor) or to remain open (thus no current can flow). For each line, a different actuation pattern can be applied for a total duration of 1 ms. This actuation pattern can be defined by the user and instructs the microcontroller to set the respective resistors to connect to ground. It is implemented in the form of a bit field with a total of 49 entries (equivalent to the number of columns): if an entry is set to logical true, the respective resistor will be connected to ground (thus current can flow), if the entry is set to logical false, the resistor will not be connected to ground (thus no current will flow). After 1 ms the microcontroller switches to the next line. This results in current sequences being applied to the individual resistors. The thermal inertia of the ohmic resistors is high enough to only result in small pulsation over time (data not shown). Under the heat pixel array an aluminium substrate is located for enhanced heat coupling between the Peltier element and the heat pixel array. The Peltier element itself is equipped with a constantly operating cooling fan for effective heat removal from the hot contact zone of the Peltier stack. This setup is mounted with 4 screws and 2 electrical connectors (type precision-header 1X40 gold plated RM 2.54 and socket strip 1X36 gold plated RM2.54, purchased from BKL Electronic, Germany) to the system hardware. As the microfluidic polymer components (see Fig. 4) are usually mounted irreversibly to the heat pixel arrays it is convenient to be able to quickly mount and dismount different heat pixel arrays (with attached microfluidics) from the Peltier element. The whole system is operated with a 24 V power supply.

The system is controlled by means of custom-written software which is implemented in C#. The software communicates with the system hardware via a RS232 interface. The graphical user interface of the software is displayed in Fig. 3. It allows the user to set and monitor the Peltier temperature as well as to set each of the 588 resistors or groups thereof. The temperature of the SMD resistors is regulated by varying the total number of current pulses applied. As described the voltage is sequentially set to each of the 12 lines for a total duration of 1 ms each. If the voltage is applied to the respective line, then each resistor located along this line may be set to receive current (depending on the respective actuation pattern). If a resistor receives a current pulse every time its respective line is set to voltage, the resistor will heat up to its maximum value. If it receives a pulse once every two times, then the temperature of the resistor is approximately half of the maximum temperature. The software allows setting the heating power in steps of 10 %, which corresponds to the percentage value of the total applicable heating power. For example, if a value of 40 % is chosen, the resistor receives a current pulse in 4 out of 10 cycles. The software allows the definition of heating patterns (intensities over time) which can be set to individual resistors or definable groups of resistors.

2.2 Microfluidic components

The microfluidic structures were manufactured by stereo lithography in Accura 60®. The microfluidic channels have rectangular cross-sections of 1 mm width and 0.5 mm height. Stereo lithography allows the creation of microfluidic channels with arbitrary shapes within bulk polymer components (Waldbaur et al. 2011) and has been described as a suitable method for rapid prototyping in microfluidics (Rapp et al. 2009). The microfluidic structures were glued directly

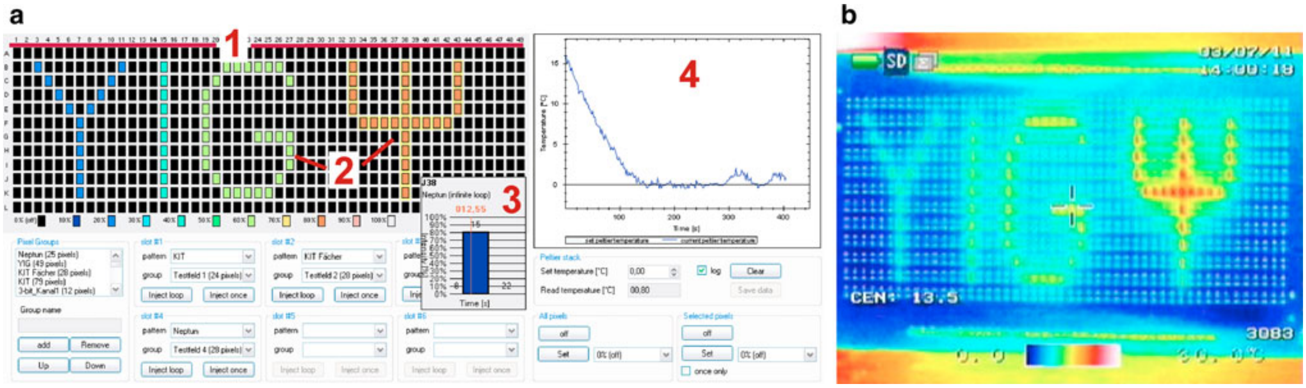

Fig. 3 **a** Screenshot of the custom-written control software. Each resistor is displayed in a matrix (*1*) and different power levels (in steps of 10 % measured as fraction of the full applicable heating power) can be applied to each resistor individually. It is also possible to define groups of resistors to which the same heating power or heating power pattern is applied (*2*). The heating power set is displayed in false-colour (with *black* corresponding to 0 % and *white* corresponding to 100 %). It is also possible to define heating patterns defined as sequences of heating power intervals (each of which has a specific duration and a specific heating power) which can be applied to individual resistors or groups (*3*). Additionally the software allows controlling the Peltier temperature (*4*) and monitors the actual Peltier temperature over time. **b** Infrared image of the heat pixel array visualizing that every SMD resistor can be controlled individually. The Peltier temperature was set at 0 °C and the temperature of the resistors in the 'YIG Ψ' pattern increases from *left* to *right*. The picture was taken at ambient temperature without microfluidic polymer component mounted on *top* of the heat pixel array

onto the heat pixel array with an epoxy adhesive (DELO-KATIOBOND 4552, purchased from Delo, Germany).

2.3 Experimental details

Figure 4 shows a picture of a 24 valve setup. The microfluidic chip is connected to a 20-channel microfluidic multiport connector (Rapp et al. 2010). For transport of the working liquid polytetrafluoroethylene tubes (PTFE tubes, inner diameter: 0.8 mm, outer diameter: 1.6 mm) and a peristaltic pump (type MC-MS/CA4/8, purchased from Ismatec, Germany) were used. Tetradecane (purchased from Merck, Germany), as a well suited liquid for indirect microfluidics (Rapp et al. 2009), was used as working liquid which has a melting point of 6 °C.

Tetradecane was chosen as a first liquid to demonstrate the platform with, because we have previously described tetradecane as a suitable intermediary liquid in indirect microfluidics exploiting the fact that tetradecane and aqueous solutions (most biological application samples are aqueous solutions) are non-miscible. It is therefore possible to create microfluidic valves by only blocking channels filled with tetradecane directing the flow (similar to a hydraulic system) in complex microfluidic channel networks. Furthermore, tetradecane is also a commonly employed substance in droplet microfluidic (Grodrian et al. 2004). However, the system described can also be used with aqueous solutions directly, provided that the repetitive cooling and heating does not damage the biological samples (if present). The volume expansion upon freezing is not critical as the active valve zone is of low volume and the slight expansion of the liquid upon freezing merely causes a small volume displacement along the channel. Other working liquids besides water and tetradecane can be used as well but the temperatures set to the Peltier element must be adapted accordingly. For tetradecane, we found that setting the Peltier element temperature to 0 °C was sufficient for freezing the active valve zones. All experiments were conducted with a flow rate of 40 µl/min. To determine the temperatures at the resistors with different power rates, the setup was monitored with an infrared camera (type Mikron MikroSHOT, purchased from Mikron Infrared Inc., USA). Experiments were conducted with a single valve setup and a 24 valve setup. The first allows for a more precise and refined characterization of the valve design and has been used for design optimization. The latter has been used to assess the suitability of the single valves for integration in arrays. In both systems one resistor activates one microvalve and each resistor can be controlled individually. Reaction times of both systems were measured by determining the time required for stopping and starting the flow of the working fluid. Starting and stopping of the flow were assessed visually and the time measured with a conventional stop watch.

2.3.1 *Single valve experiments*

As described before, the microfluidic channel has been laid out in U-shaped form in order to assure that only a small fraction of the channel (the active valve zone) is thermally modulated. This result in the creation of two layers of microfluidic channels being spaced by a particular distance called *H*. The single valve setup was primarily used for optimizing the distance variable *H* between the two channel

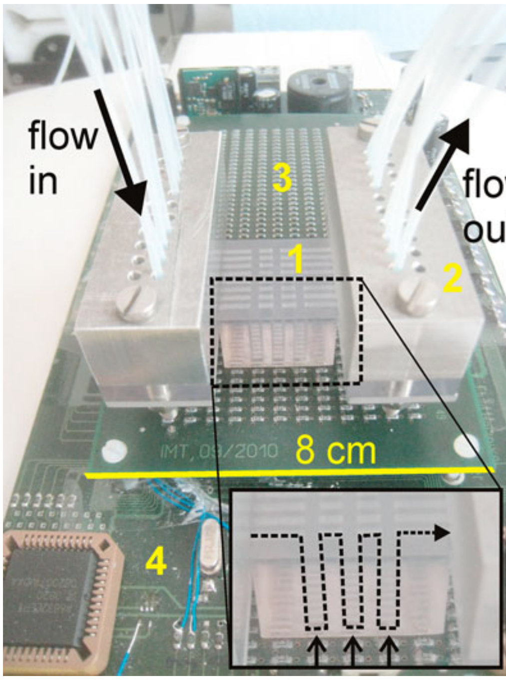

Fig. 4 Photograph of an experimental setup for a 24 valve setup. The valves are arranged in eight channels with three sequential valves per channel to test interlinking of several valves. The inlay shows the flow path along one of the eight channels with the location of the three valves indicated by *arrows*. Each of these 24 resistors can be controlled individually. The microfluidic chip (*1*) is connected to a microfluidic multiport connector (*2*) for interfacing the chip to the PTFE tubes and the pump, (*3*) heat pixel array with 12 × 49 SMD resistors, (*4*) system hardware, the Peltier element is located underneath the circuit board

levels. Due to heat dissipation in the chip material an influence of H on the reaction times of the system was expected. The reaction times during valve opening were determined for different values of H until increasing the value of H did not alter the reaction time of the system anymore. The best setup ($H = 12$ mm) was used for further experiments.

2.3.2 Microvalve platform

To test the electronic platform with numerous PC microvalves and therefore demonstrate the scalability of the system, a microfluidic setup with 24 microvalves–8 channels and 3 valves in line per channel was designed (see Fig. 4). The distance between the two channel levels was set to the value which yielded the best reaction times in the single valve experiments ($H = 12$ mm). In these experiments the 24 valves are addressed and controlled individually.

3 Results and discussion

As stated in the experimental setup description, the platform described allows the individual setting of the heating power of each resistor in the heat pixel array over time. If temperature values are given for resistors these values have been measured by means of an infrared camera in air. Due to the high IR absorbance of the polymeric flow cell and the working liquid in the system it is not possible to directly measure the temperature of each resistor during the experiment which would yield lower values than those measured in air.

3.1 Single valve experiments—optimization of the microfluidic channel level spacing H

In first experiments different single valve setups with varying distances H between the two channel levels (see Fig. 5) were tested. The spacing of the two levels greatly influences the opening times of the valve after a prolonged period in which the valve was closed. This is due to the fact that, as mentioned, the Peltier element is operated constantly which results in constant draining of heat from the valve. If H is too small, not only the active valve zone but also the upper microfluidic channel layers would freeze. This would significantly increase the opening times of the valve.

In this first set of experiments, the resistor of the respective valve was switched off and the valve was allowed to close. The experiment was started as soon as the flow stopped indicating that the valve was completely closed. The valve was left closed for varying intervals (called 'time valve was closed before switching') in order to assess the influence of the temperature drain on the valve opening times. The resistor was then set to the maximum temperature in order to open the valve. The experiment ended when the fluid flow through the valve started again. The results of these experiments showed that the time required for opening the valve decreases with increasing H until a value of about 12 mm. Increasing the spacing between the two microfluidic channel layers further did not reduce the time required for opening of the valve significantly. In order to keep the system as compact as possible, 12 mm was chosen as suitable value for H and all following experiments were performed with this geometry.

3.2 Microvalve platform experiments—temperature profiles

As stated, assessing the performance of a single valve setup was primarily intended for design optimization. For a more realistic application scenario, we set up a multiple valve array system consisting of eight microfluidic channels each of which contained three valves arranged sequentially along the respective channel (see Fig. 2, no. 1). The three valves of a chosen channel were always actuated as a software-defined group applying the same heating power to

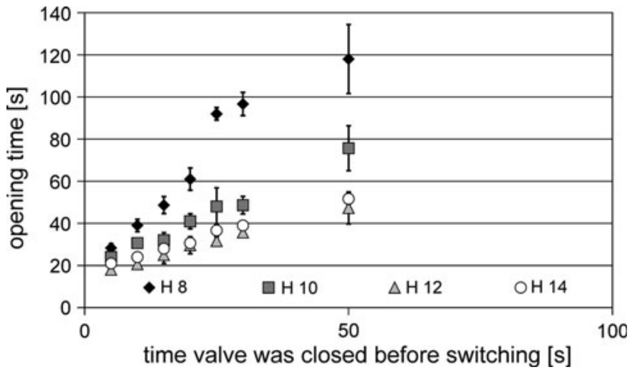

Fig. 5 Response times for valve opening in dependence of the time the valve was closed. This dependence is different for varying values of the distance (*H* in mm) between the two microfluidic channel levels. As stated, the Peltier element is constantly draining heat from the active valve zone which may cause freezing beyond the active valve zone potentially even in the upper microfluidic channel layer during prolonged periods in which the valve is closed. This significantly increases the valve reaction times for opening. Increasing *H* decreases this risk. In these experiments the working medium was tetradecane, the temperature of the Peltier element was set to 0 °C and the heating temperature of the resistor was set to maximum (100 % heating power). Starting from a value of 12 mm for *H*, the reaction times for valve opening do not decrease significantly indicating that 12 mm is a sufficient spacing to ensure only the active valve zone is frozen. Values displayed are mean values and standard deviation taken from three independent experiments

all three. It has to be noted that the grouping is merely software-based—there is no physical grouping of the three valves. The experimental procedure was analogous to the measurements of the single valve setup. For this setup the spacing between the microfluidic channel layers was again set to $H = 12$ mm.

Besides the dependency of the valve opening time on the spacing of the microfluidic channel levels Fig. 5 also shows that the time required for opening the valve increases for longer periods of valve closure prior to opening. This fact is undesired as reaction times for valve opening should not depend on the duration of the preceding closed state. This problem also occurs during valve closing: the longer the valve was opened the more the resistor will heat up the active valve zone thus extending the time required for valve closing.

In both cases the effect can be reduced by applying temperature profiles. Rather than applying maximum power during valve opening and minimum temperature (by switching off the resistor completely) during valve closing it is advantageous to only apply these extremes for a very short time in order to trigger the valve switching. After the valve reaches the desired state, the temperature is adjusted to a value that stabilizes the respective valve state, while keeping the temperature influx and outflux of the active valve zone to a minimum. The two temperature states are referred as trigger temperature and hold temperature, respectively.

For the opening of a valve this means that a strong heat pulse (maximum power) is applied for a short period of time to open this valve whereupon the temperature is reduced to a smaller value keeping the valve in the open state without further heating up the active valve zone. For closing a valve, the temperature would be set to a minimum (no current applied to the respective resistor) for a very short time in order to close this valve whereupon the resistor would be set to a low power value which compensates the constant heat drain of the Peltier element ensuring the valve zone is not cooled further (see Fig. 6).

The aim of these experiments was to establish temperature profiles for opening and closing of a valve that would ensure the time required for the respective switching operation is independent of the time the valve was in the previous state. This means the opening time of the valve should be independent from the time it was closed (frozen) before and the closing time should be independent from the time it was opened (heated before). Precise fluid control with this type of PC microvalve is not possible if this prerequisite is not met.

The measurements for valve opening are summarized in Fig. 7. For these experiments, the 3 valves of one selected fluidic channel (refer to Fig. 4) were set to the closed state whereupon the experiment was started once the working fluid stopped flowing. After 5 s the channel was then preheated at varying hold temperatures and kept in this state for varying time periods [termed 'pre-switch time (closed)']. In order to trigger valve opening, the temperature of the resistors was then set to the maximum temperature (here 19.2 °C, measured with an infrared camera in air as stated) while measuring the time between setting this temperature and the start of the fluid flow (termed 'reaction time/opening time'). The diagram shows that the opening times decrease with increasing preheating temperature. For preheating temperatures of 6.1 or 7.9 °C the opening times reach a plateau at 150 s which means that the time required for opening the valve is independent of the time the valve was closed before the switching.

The measurements for valve closing are displayed in Fig. 8. For these experiments all three valves were set to the maximum temperature (100 % heating power) until the fluid started flowing whereupon the time measurement was started. After 5 s the temperature of all valves was reduced to the respective hold value and kept for varying periods of time [termed 'pre-switch time (open)']. In order to trigger valve closing, the resistors of all three valves set to 0 % heating power (no current applied) and the time it took for the fluid to stop flowing was measured (termed 'reaction time/closing time'). The data shows that the closing time decreases with decreasing hold temperature. For all hold temperatures except the lowest value 9.4 °C (50 % heating power), the closing time of the channel was independent

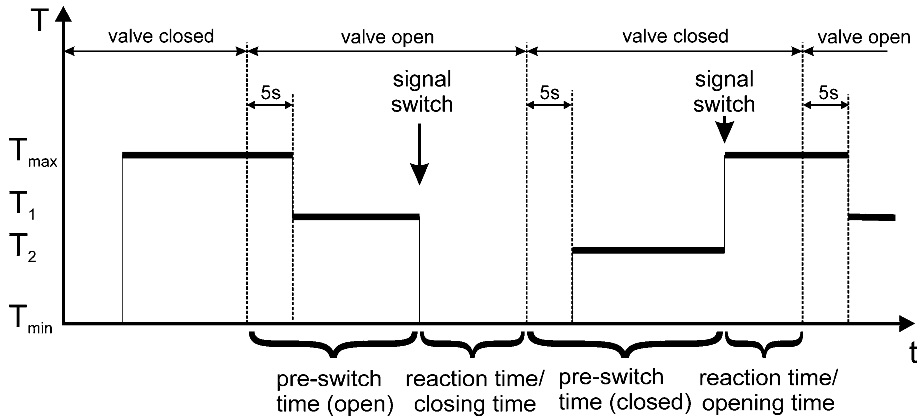

Fig. 6 Diagram of the temperature management of a resistor on a single PC microvalve. T_{max} and T_{min} are the trigger temperatures to initialize opening and closing of the valve. T_1 and T_2 are the respective hold temperatures, which were varied during the different experiments with the aim of establishing temperature profiles that would render the valve reaction times independent from the length of the preceding valve state duration. Signal switch is the moment the user sets the trigger temperature. Such temperature profiles can be set to each of the 588 resistors individually. The 5 s time delay after closing or opening of the valve and setting of the temperature to the respective hold value originates from the fact that the experiment is observed by eye and the temperature adjustment in the software is done by the user which may result in varying delays. In order to compensate this uncertainty, a fixed delay of 5 s was introduced which is sufficient to start the experiment and prepare the setting of the temperature on the user interface of the software

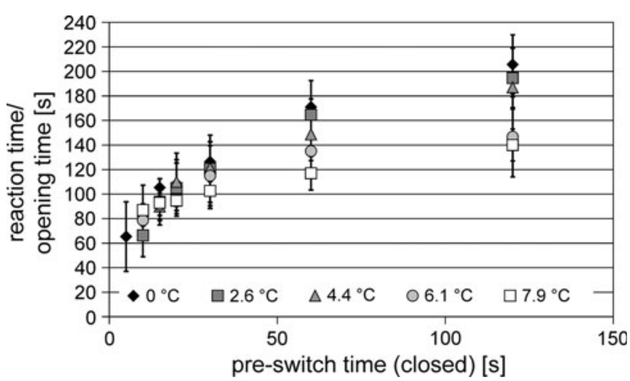

Fig. 7 Times required for opening one channel ('reaction time/opening time', see Fig. 6) with a total of three valves located sequentially along the channel as a function of the time the valves were closed before ['pre-switch time (closed)', see Fig. 6] and the selected hold temperature (0, 2.6, 4.4, 6.1 and 7.9 °C corresponding to a heating power of 0, 10 20, 30 and 40 %, respectively). In all experiments the resistors were first set to 0 °C (0 % heating power) in order to close the valve whereupon varying low heating power values were applied for preheating of the valve while keeping the closed state (hold state). Then the temperature was set to 19.2 °C (100 % heating power) in order to trigger the opening of the valves and the time required until the fluid started flowing again ('reaction time/opening time', see Fig. 6) was measured. The distance between the two channel levels was $H = 12$ mm, the working medium was tetradecane and the temperature of the Peltier element was set 0 °C. Values displayed are mean values and standard deviation taken from three independent experiments

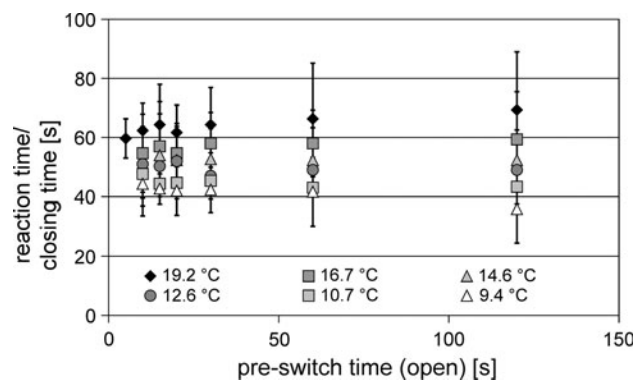

Fig. 8 Times required for closing one channel ('reaction time/closing time', see Fig. 6) with a total of three valves located sequentially along the channel as a function of the time the valves were open before ['pre-switch time (open)', see Fig. 6] and the selected hold temperature (19.2, 16.7, 14.6, 12.6, 10.7 and 9.4 °C corresponding to a heating power of 100, 90, 80, 70, 60 and 50 %, respectively). In all experiments the temperature of the resistors was 19.2 °C (100 % heating power) in order to open the channel whereupon varying low heating power levels were applied for keeping the channel open (hold state). Then the resistors were set to 0 % heating power (no current applied) in order to trigger the closing (freezing) of the valves and the time required until the fluid stopped flowing ('reaction time/closing time', see Fig. 6) was measured. The distance between the two channel levels was $H = 12$ mm, the working medium was tetradecane and the temperature of the Peltier element was set 0 °C. Values displayed are mean values and standard deviation taken from three independent experiments

from the time the channel was opened prior to closing. A temperature of 9.4 °C seems to be too low for holding the temperature of the valve zone constant.

The best result obtained for closing a channel with three sequential valves was found to be 40 s using a hold temperature of 10.7 °C (60 % heating power). This time is similar to the closing time measured for a single valve setup (see ESM, section 3) demonstrating that in fact the valve concept is scalable as the response times of the valve platform are independent from the number of valves operated.

4 Conclusions

We presented an electronic setup for a large number of individually addressable thermal PC microvalves. The suitability of the setup was demonstrated by using (as a first example) a direct PC microvalve with identical working PC medium (in this case tetradecane). It has been shown that with the fluidic layout presented, reaction times of 40 s for closing the valves and up to 150 s for opening could be achieved. For practical applications in microfluidics these values are still too high and require further optimization. Potential improvements include reducing the volume of the PC material in the valve zone and using materials with higher thermal insulation for the fabrication of the fluidic chip in order to reduce the thermal in- and outflux of the microfluidic chip and therefore reduce the overall thermal mass of the system. Another aspect to consider is the question whether the experiments have to be conducted in-flow as in the experiments presented. If valve opening and especially closing is conducted in no-flow condition, reaction times of the system can be decreased.

An additional aspect to be considered is the fact that opening and closing temperatures profiles, hold temperatures as well as the temperature value for the Peltier element need to be adapted if different working liquids or varying flow rates are to be used. If experiments are to be conducted in-flow, the reaction times for valve closing depend on the flow rate. Depending on the working medium, there may potentially be a maximum flow rate above which the valves cannot be closed because the temperature influx (due to the high flow velocity of the fluid flowing through the active valve zone) is too high. This is, of course, not the case for valve opening as well as for non-flow conditions.

However, the usage of direct PC microvalves was chosen primarily as an experimental demonstration of the versatility of the platform presented in this work which is intended as a generic platform for all types of thermally actuated microvalves including direct and indirect ones, as well as valves based on paraffin actuators (Yang and Lin 2009) or hydrogels (Richter et al. 2004). The system presented can be used to address a total of 588 resistors individually which would result in a total of 588 individually addressable PC microvalves because one resistor activates one microvalve. One important advantage of the system presented is the fact that individual temperature profiles can be applied to each resistor individually which is mandatory for a precise thermal modulation of the PC valves. We have shown this to be especially true for direct PC microvalves which require temperature profiles in order to "hide the thermal history" of the microvalve, which means making the reaction times for switching the valve state independent of the duration of the preceding state. This aspect is very important for any type of PC microvalve.

In general thermal PC microvalves may have slower reaction times compared to conventional microfluidic valves, such as the ones based on pneumatic actuation. However, they allow enhanced scalability as the parallel operation of small heat zones is technically less challenging than setting up a multitude of miniaturized pneumatic actuators. To the best of our knowledge, there is no report in the scientific literature of a microvalve platform based on pneumatic actuation that demonstrates individual addressability of more than a few pneumatic lines. Usually this fact is compensated by using multiplexing technology which allows increasing the number of total addressable valves while sacrificing individual addressability: a multiplexer allows the selection of only one output line at a time. We have demonstrated that several hundreds of individually addressable microvalves can be designed using thermal actuation which is a great leap in scalability.

We believe that the valve platform described in this work will allow setting up microfluidic systems with hundreds of individually controllable PC microfluidic valves resulting in systems that do not required the use and therefore don't suffer the limitations of multiplexing technology.

Acknowledgments This work was funded in part by the 'Concept for the Future' of Karlsruhe Institute of Technology (KIT) within the framework of the German Excellence Initiative, a Max-Buchner Research fellowship (DECHEMA, Gesellschaft für Chemische Technik und Biotechnologie e. V., Grant #2676) as well as a travelling grant provided by the Karlsruhe House of Young Scientists (KHYS).

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