Micropumps operated by swelling and shrinking of temperature-sensitive hydrogels†

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Received 17th June 2008, Accepted 31st October 2008
First published as an Advance Article on the web 20th November 2008
DOI: 10.1039/b810256b

This paper describes two types of polymeric micropumps based on the temperature-sensitive hydrogel poly(*N*-isopropylacrylamide). The gel actuators are realised as photopolymerised patterns and microgels. They are electrothermically controlled by resistive heating elements. The diffusion-based micropump contains a photopatterned monolithic actuator, which is placed within the pump chamber, and provides a valveless single layer set-up. The diffusion micropump is intended for low performance applications and can operate in two modes: peristaltic or pulsatile. The maximum operating parameters are a flow rate of 2.8 ± 0.35 µl min^{-1} and a back pressure of 1.28 kPa. The second type, a displacement pump, provides a higher performance (maximal 4.5 µl min^{-1} and 15 kPa). The pump comprises a microgel-based actuator, which is placed within a separate actuator layer, and active microvalves. The specific features of the design and performance of the pumps are discussed.

Introduction

Due to their unique properties and excellent fabrication facilities stimuli-sensitive hydrogels are discussed as materials, which could induce a significant progress in microelectromechanical systems (MEMS).[1,2] Liquid handling fluidics and microfluidics can especially benefit from a hydrogel-based technology. Within this area, gels offer a multi-functionality which is only known from silicon in microelectronics. They provide two general applications, automatic and electronically controlled systems, respectively.

Automatic systems are based on the great number of various stimuli-sensitive hydrogels which offer specific sensitivities across physical values such as temperature,[3] electrical field values,[1] light,[4] and chemical parameters, *e.g.* pH, solvent composition and the concentration of specific ions.[5–7] Due to their phase transition behaviour, gels can change their volume significantly in response to small alterations of certain environmental parameters. These volume changes can be more than hundred-fold, based on the absorption or on the release of aqueous solution accompanied by considerable swelling forces if an external force is applied.[8] Automatic fluidic systems involve fixed[9–14] and adjustable[15] chemostat valves (performing feedback control to keep a concentration on a constant level), fluidic drives[16–19] and lenses.[20–22] Furthermore, the manifold sensitivities of gels were used in chemical liquid sensors.[23]

Electronically controllable components are intended as basement for liquid handling of a gel-based technology of fully polymeric integrated fluidic circuits (IFC). To minimise the complexity of IFC, which are also called lab-on-a-chip (LOC) or micro total analysis systems (µTAS),[24] it is desirable to realise all active components with only one type of hydrogel. Such multi-functionality is known from poly(*N*-isopropylacrylamide) (PNIPAAm). The temperature-sensitive PNIPAAm is typically electrothermically controlled by heating elements. Controllable valves,[25–27] adjustable chemostat valves[28] and liquid sensors[29] are realised with this hydrogel. However, hydrogel-based electronically controllable fluidic drives, so-called micropumps,[17] are not yet known.

Here, we describe two types of hydrogel-based micropumps distinguished by the placement of the hydrogel actuators. In this paper we show how both, the swelling and shrinking process of hydrogel actuator, can be used to generate a liquid flow. Furthermore, two types of PNIPAAm actuators, photopolymerised monolithic actuators and microgels, are discussed.

Materials and methods

Materials

N-Isopropylacrylamide (NIPAAm), crosslinking agent *N,N′*-methylenebis(acrylamide) (99%) (BIS), photoinitiator 2-hydroxy-4′-(2-hydroxyethoxy)-2-methylpropiophenone (98%), potassium peroxidisulfate (KPS), *N,N,N′,N′*-tetramethyl-ethylenediamine (TEMED), n-hexane and pure ethanol (99.9%) were obtained from Aldrich. Distilled water was used to prepare photopolymerisable solution. Poly(dimethylsiloxane) was received as RTV 615 from Momentive Performance Materials.

Design of micropumps

Diffusion micropump. To provide a simple single-layer set-up the photopolymerised monolithic PNIPAAm actuator is directly placed within the pump chamber (Fig. 1A and 1B). The actuator is photolithographically partitioned into five independently movable segments. In the swollen state the actuator tenses the

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† Electronic supplementary information (ESI) available: Supplementary video S1. See DOI: 10.1039/b810256b

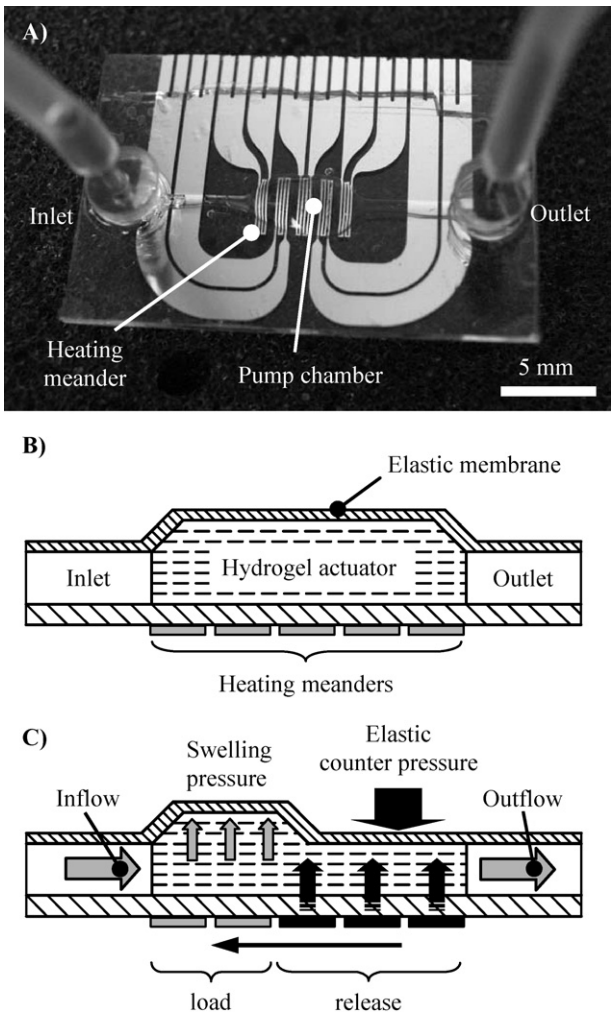

Fig. 1 Diffusion micropump. (A) Photograph. (B) Schematic set-up. (C) Operating principle.

elastic cover membrane. A sequence of five resistive platinum heating meanders is located below the pump chamber.

Displacement micropump. Comparable to reported fluidic drives,[16–19] the hydrogel actuator is placed within an actuator chamber which is part of a separate layer (Fig. 3A and 3B). This layer contains a swelling agent supply and is placed above the channel structure involving the pump chamber. As actuator material PNIPAAm microgel is used. The actuator chamber is formed by a movable membrane separating the actuator chamber from the pump chamber and the gauze permeable for the swelling agent. The SMT circuit board, which consists of the heating resistors, is placed on top of the pump.

Device fabrication. The hydrogel-based micropumps consist of two main parts, which are an electrical control circuit and the fluidic channel structure.

Electrical control circuit. The electrical control circuits are realised with a platinum thin film technology and a surface mount technology (SMT).

The platinum heating elements (110 nm thickness, resistance 50 Ω) of the control circuit of the diffusion pump are plated onto the SiO_2 substrate (4″, type Pyrex 7740, 500 μm thickness) by MSBA-400SP (Malz & Schmidt), lift-off patterned and covered by a Si_3N_4 passivation.

To fabricate the SMT circuit board a 50 μm thick copper sheet (one-sided coated with glue EF 8791 (Eurofol Neuss)) is laminated onto a transparent polyester substrate. The conducting pathways are patterned by photoengraving the copper sheet. Resistors (100 Ω, 0.8 W) were surface mounted on the copper sheet. To create an even surface the gaps around these heating elements were mounted with PDMS.

Fluidic channel structure. The fluidic channel structures are fabricated by PDMS replica-moulding[30] and multilayer soft lithography.[31]

Prototyping of master mould. The prototyping of the masters is based on a dry photoresist technology, which has its origin in the printed circuit board fabrication. This technology is inexpensive, rapid and does not need microfabrication facilities. After laminating the dry photopolymer Dynamask 5030 onto the copper-coated standard board material FR 4 (0.2m min^{-1} at 105 °C, Bungard RLM 419P) the photoresist has been exposed to UV light through a photomask, developed by KOH rinsing and finally dried.

The smallest realisable features (spacing and width) are 50 μm while the thickness of one layer is a maximum of 75 μm. Up to four layers can be laminated and separately photolithographically patterned to form three-dimensional structures.

Fabrication of PDMS components. Each of the PDMS structure layers is separately cast and cured from a master mould. The mixing ratio of base and curing agent of PDMS is 3 : 1 or 30 : 1 requiring a curing time at 80 °C of about 40 min (3 : 1) or 2 h (30 : 1), respectively. To seal and interconnect the PDMS layers they have to be combined with alternating mixing ratios. Each layer has an excess of one of the two components so that reactive molecules remain at the interface between the layers. Further curing bonds the layers irreversibly.

The membranes consist of PDMS 3 : 1 because this material is more stable than the 30 : 1 polymer. To fabricate a 50 μm thick membrane the PDMS solution was spin-coated on polycarbonate at 1.500 rpm and than cured at 80 °C for 50 min. If a thicker membrane is required the spin-coating process for the membrane has to be repeated. This second curing process should last for 20 min at 80 °C. The membrane should be pre-stressed before bonding with another layer.

The monofilament polyester gauze (wire diameter 100 μm, mesh size 200 μm, obtained from Schwegmann Filtrations-Technik GmbH, Germany) is cast into a PDMS matrix and further processed as a common PDMS layer.

Fabrication of hydrogel actuators

Photo-patterning. The photolithographic polymerisation of PNIPAAm is performed *in-situ*. The channel structure involving the pump chamber is rinsed with argon and filled with polymerisable aqueous solution consisting of 2.223 mol% NIPAAm, 0.033 mol% crosslinking agent BIS, and 0.022 mol%

photoinitiator. To pre-stress the working membrane of the diffusion pump a pressure is applied which is about 20% higher than the working pressure of the membrane. Now the solution has to be polymerised by UV exposure (75 mW cm^{-2}) through a photomask at 5 °C. Finally, non-polymerised residues can be removed by a rinsing step with ethanol and water. Due to the outstanding hydrophobicity of PDMS, PNIPAAm does not polymerise directly at the PDMS surface without additional treatment. We do not pre-treat the PDMS, because the pre-stressed membrane places the actuator within the pump chamber safely by deformation.

Microgels. Microgels are fabricated by free radical bulk polymerisation of NIPAAm. Monomer NIPAAm is recrystallised from n-hexane solution. NIPAAm and 4 mol% BIS are dissolved in deionised water. The total monomer concentration is 0.53 mol l^{-1}. To initiate the polymerisation reaction 0.3 mol% of KPS and TEMED, respectively, are added to the oxygen free solution (rinsed with N_2). After the polymerisation (*ca.* 12 h at room temperature) the PNIPAAm gel is immersed in deionised water for about seven days to wash out non-reacted reagents. After drying the bulk gel microgels are obtained by milling and subsequent fractionating into different microgel sizes using sieves. Microgels possess an irregular shape.[10,25] The dry PNIPAAm microgel particles are manually incorporated into the actuator chamber. The filling degree of particles within the chamber is adjusted by volumetric dosing. After inserting the microgels, the PDMS layers are interconnected.

Results

Behaviour of diffusion micropump

The special feature of stimuli-sensitive hydrogels to change their volume absorbing or releasing aqueous solution has been used advantageously to realise displacement free valves.[32] However, this gel property inhibits its use as directly acting actuator of pumps. Therefore, our hydrogel actuator uses its swelling pressure to tense an elastic membrane acting as a pressure accumulator (Fig. 1C). If the swollen PNIPAAm actuator is sequentially heated by the heating meanders above its phase transition temperature of approx. 34 °C (starting with the outlet-side), then the actuator shrinks releasing the swelling agent. The released solution is immediately pushed to the outlet by the pressure of the elastic membrane because the inlet is sealed by a swollen actuator segment. To re-load the pump the heating meander has to be switched-off incipient inlet-sided so that the PNIPAAm cools down below the phase transition temperature and swells by absorbing the liquid.

The pump can perform two different operational modi (Fig. 2A). A peristaltic operation (see also video S1)† provides a continuous and relatively homogeneous pumping. As illustrated in detail by the inset of Fig. 2A the peristaltic wave has a characteristic which is determined by the loading and releasing processes of the actuator segments. In our example, the first two actuator segments pump powerfully, whereas the performance decreases at the beginning of the activation of the third segment. At this moment the heating of the first segment is finished. Its temperature falls below the phase transition temperature and causes the segments to swell. The simultaneous loading and releasing processes of the first and third segments counteract and reduce the effective flow rate.

To obtain an optimised peristaltic operation the time necessary for both release and reload has to be considered. An optimal control of our device (Fig. 2B) is achieved by applying a heating power of 130 mW per heating element. Every 15 s a new heating element is activated and heated with a constant power during the following 30 s. This schedule provides a reload time of 30 s for each segment. With these parameters the device has a flow rate of 0.54 ± 0.016 µl min^{-1}. Shorter reload times result in a decrease of the pumping performance because the segments can not obtain their complete loading.

A pulsatile operation of the pump (Fig. 2A) is realised by emptying the pump chamber completely. To achieve an undisturbed discharge of the solution the actuator is heated in two steps (Fig. 2C) of 30 s. After a complete discharge of the pump chamber the pump is reloaded within 75 s. With a volume of 10.3 µl of the pump chamber (in the shrunken hydrogel state) each stroke pumps 2.8 ± 0.35 µl within one minute.

The maximum flow rate of a pumping stroke is determined by the shrinking kinetics of the hydrogel. This process is strongly influenced by the applied heating power of the heating meanders. Beginning at an initial heating power of approx. 100 mW the flow rate increases with increasing heating power up to an optimal value of 130 mW (operating voltage 4 to 7 V). Further rising of heating power only slightly enhances the flow rate. Furthermore, the gel's shrinking kinetics depends on the properties of the elastic PDMS membrane. The higher the pressure of the membrane the faster the gel actuator shrinks. The pressure of the membrane is equal to the pumping pressure. As shown in Fig. 2D that pressure increases with increasing thickness of the elastic membrane. On the other hand, the increase of the thickness increases the reload time of the pump sharply and decreases the maximal swelling volume of the hydrogel actuator. The pump performing the characteristics shown in Fig. 2A is equipped with a 70 µm thick membrane which generates a pumping pressure of 0.43 kPa and provides a reload time of 75 s. The maximum pressure obtained with a 190 µm thick membrane is 1.28 kPa accompanied by a long reload time of 465 s.

For some applications the diffusion pump is not usable. For example, some solvents can affect the actuator functionality of the hydrogel, particles can not pass the actuator chamber, or the pressure of the pump can be insufficient. Therefore, we present a second pump type with a characteristic that avoids these problems.

Behaviour of displacement micropump

The hydrogel actuator of this pump type is separated from the process medium by a movable membrane (Fig. 3A).

The supply of swelling agent, which is stored inside the separate actuator layer, is granted by the water permeable gauze. A low mesh size can constrain the swelling agent supply. With a large mesh size and a large gauze area a low flow resistance is provided, which does not affect the actuator's response time. Due to its mechanical stability the polyester gauze acts as a non-deformable support of the actuator. While pumping, the actuator displaces the volume of the pump chamber. The swelling of the gel actuator

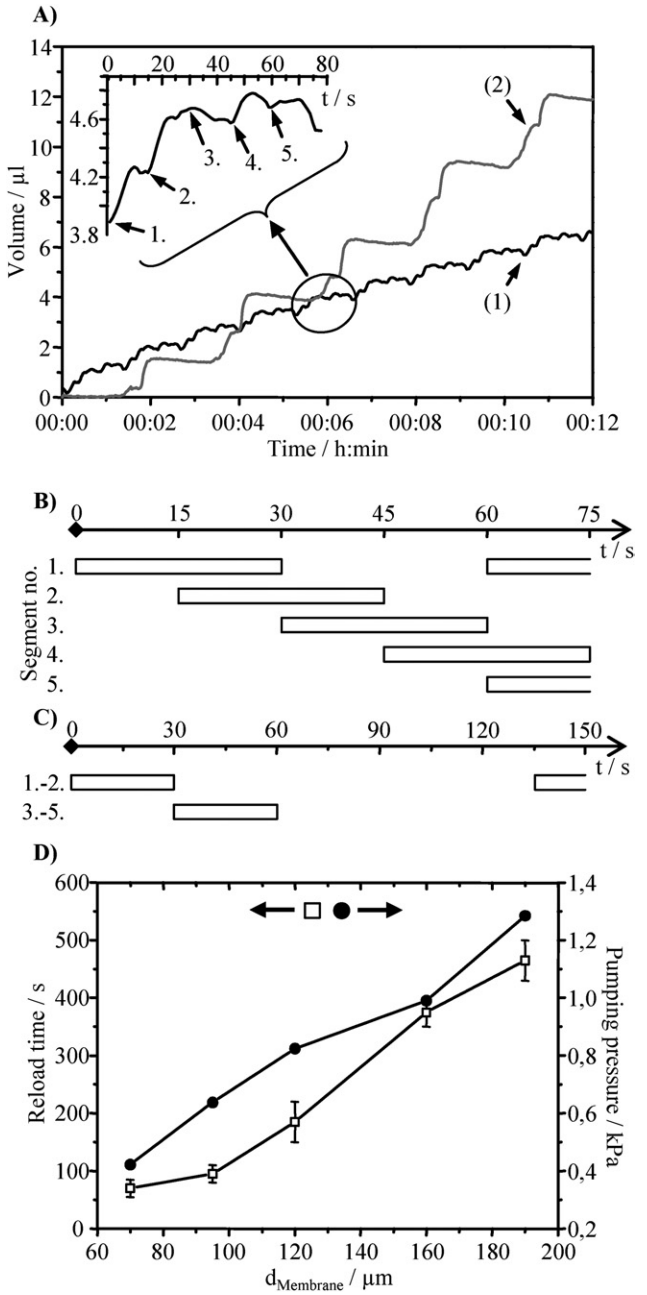

Fig. 2 Behaviour of the diffusion micropump. (A) Pump characteristics; (1) peristaltic operation; (2) pulsatile operation. (B) Schedule of the segment control during peristaltic operation. (C) Schedule of the segment control during pulsatile operation. (D) Influence of the thickness of the elastic membrane on the reload time and the pumping pressure (each measurement is performed five times).

leads to a displacement of the membrane, which results in an emptying of the pump chamber (Fig. 3B).

The electrothermic control of the actuator is realised by the resistive heaters of the SMT circuit board placed on top of the pump, which apply a heating power of 180 mW each. Because the actuators consist of numerous versatile microgels a segmented control for the peristaltic mode is not recommended. Instead, a pulsatile mode should be preferred. To define the

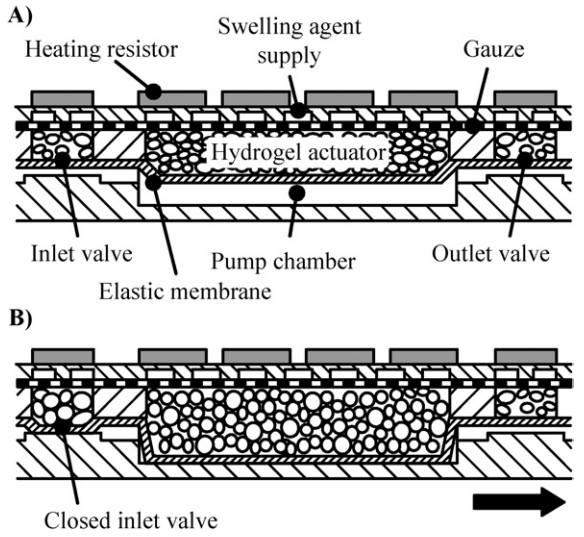

Fig. 3 Displacement micropump. (A) Schematic set-up. (B) Operating principle.

pump direction, two electronically controllable valves are placed inlet- and outlet-sided.

In contrast to the diffusion pump, the displacement device pumps at increasing actuator volume and fills the pump chamber at hydrogel shrinkage. Hence, the flow rate per pumping stroke is determined by the swelling of the gel actuator after switching off the heating and cooling below the phase transition temperature.

The time behaviour of the actuator's swelling can be described by the characteristic time constant

$$\tau \sim \frac{d^2}{D_{\mathrm{Coop}}} \tag{1}$$

which depends on a material specific collective diffusion constant $\{D_{\mathrm{Coop}}$ (PNIPAAm) $= 2.3 \times 10^{-7}$ cm^2 s$^{-1}\}$ and the square of the smallest effective dimension d.[33] In our case d correlates with the radius of the microgels[10,32] and provides

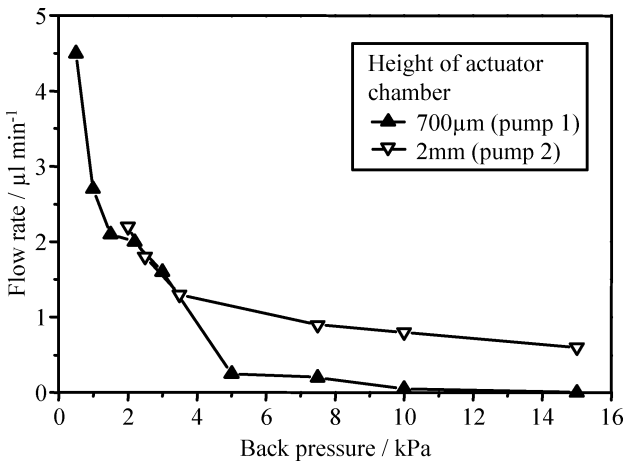

Fig. 4 Characteristics of the displacement micropump. The pump chamber volume of each device is 30 µl. The actuator volume of pump 1 is 105 µl; the actuator volume of pump 2 is 300 µl. Each measurement is performed five times.

a large independency of the swelling time from the thickness of the actuator. This effect is observable in Fig. 4. While the ratio of the characteristic time constants of the pumps is

$$\frac{\tau_{\text{pump2}} = f\left(d_2 = \frac{2\text{mm}}{2}\right)}{\tau_{\text{pump1}} = f\left(d_1 = \frac{700\mu\text{m}}{2}\right)} = \frac{d_2^2}{d_1^1} = 8.16 \quad (2)$$

the flow rates of both pumps do not differ significantly at low back pressure.

We found an optimal PNIPAAm microgel size of 450 ± 50 μm at a filling degree of the actuator chamber of 50% in the dry state. The usage of smaller microgels does not generally lead to a faster swelling due to the increasing flow resistance of the swelling agent supply, which is caused by the diameter-dependent packing density of the microgels.[32] An increase of the microgel diameter above the optimal size increases the swelling time significantly.

The pumping pressure of the displacement pump is generated by the swelling force of the hydrogel actuator. Besides the elastic membrane, the back pressure of the system counteracts the swelling pressure. Increasing back pressure decreases the flow rate of the device drastically (pump 1, Fig. 4). Maximal values of the pumping parameters are 4.5 μl min^{-1} at 0.5 kPa back pressure and 7.5 kPa at 0.2 μl min^{-1}. The pumping pressure can be increased by increasing the actuator's thickness. A threefold thicker actuator (pump 2, Fig. 4) provides at 7.5 kPa a flow rate of 0.8 μl min^{-1} and at a back pressure of 15 kPa a flow rate of 0.6 μl min^{-1}. In principle, the correlation between the pumping pressure and the actuator thickness is a linear scaling law. As an advantageous feature, the performance and pumping volume of the micropumps can be exactly tailored to the requirements of a special LOC application by rating the pumping unit, which consists of the actuator and the pump chamber.

The pressure resistance of the pump depends on the device's microvalves (Fig. 3). The set-up and operating principle of the valves corresponds with the pumping unit. Due to their function, which is to switch the liquid flow, the filling degree of the valve's actuator chamber is higher than that of the pump actuator. By using PNIPAAm microgel with a diameter of 450 ± 50 μm, the filling degree of the actuator chamber of the valve is about 80% in the dry state. Hydrogel-based microvalves show an outstanding pressure resistance up to 0.84 MPa without any leakage flow.[25]

The maximum flow rate of the displacement pump at low back pressure is linearly dependent on the volume of the pump chamber, if the ratio of the volumes of actuator and pump chamber is fixed. Therefore, an increase of the chamber at a defined factor leads to an increase of the flow rate at the same factor. As previously reported the maximum flow rate of a single stroke can be significantly improved by a dynamic pressure mode provided by an actuator swelling prior to the outlet valve opening.[17]

The swelling process of the gel actuator can be described by an exponential function.[33] To obtain maximised flow rates we use only 80 to 90% of the change in hydrogel volume. Therefore, the pump chamber is usually not fully emptied. The elastic membrane is not completely pressed to the side walls of the chamber and a residual volume of about 3 to 5 μl remains inside the pump. When the gel actuator achieves its swelling equilibrium, which typically occurs within some hours, the pump chamber is then completely emptied.

The behaviour of the pumps is not significantly affected by performing several dozen strokes. The electrothermic control of the micropumps requires room temperature conditions or an active cooling. Environmental temperatures above 27 °C could disturb the functionality of the device.

Conclusions

Compared to other micropumps, hydrogel-based devices can be classified as pumps with a small dead volume suitable for low (diffusion micropump) and medium (displacement micropump) performance applications.[34,35]

Due to the inexpensive design, the simple electrothermic control and the soft lithographic fabrication, our micropumps are particularly suitable for on-chip components of polymeric lab-on-a-chip devices that are intended for disposable use.

The active polymer PNIPAAm offers a unique variety of electronically controllable elementary microfluidic components. This includes not only the standard elements of liquid handling (microvalves and micropumps) but also hydrogel-specific active components such as chemostat valves and chemical sensors. These components can be monolithically integrated on a substrate. Such properties are unknown from other technologies. Therefore we believe that the hydrogel-based platform will influence the development of integrated microfluidic systems.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft within the Collaborative Research Centre 287 "Reactive Polymers", RI 1294/2-1, RI 1294/3-1, and the Heisenberg Fellowship of A.R.

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