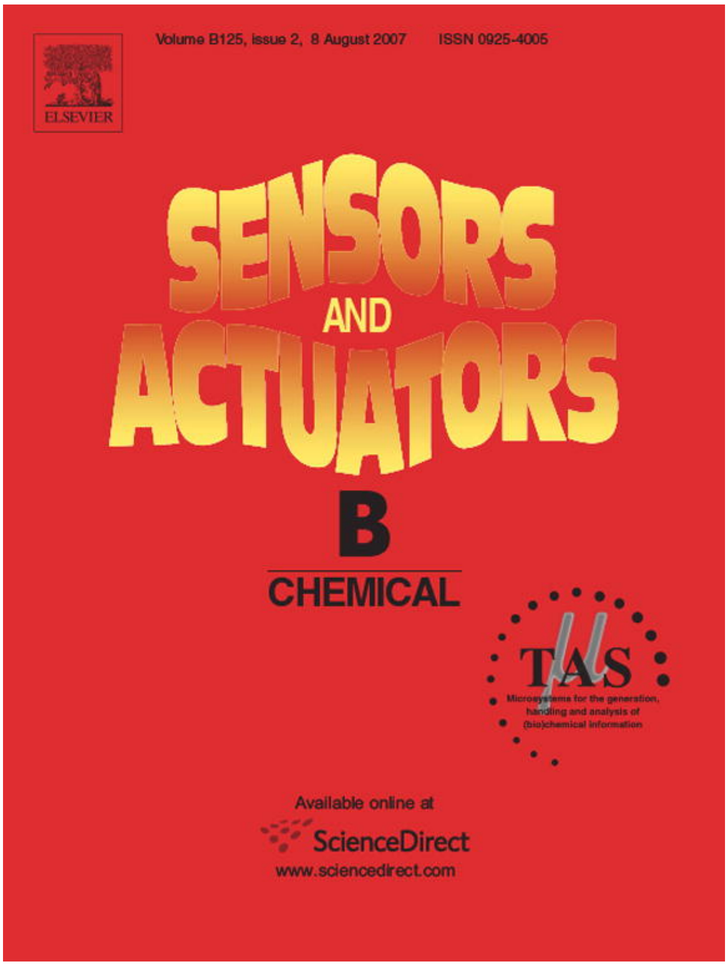
Volume B125, issue 2, 8 August 2007
ISSN 0925-4005
ELSEVIER
SENSORS AND ACTUATORS
B
CHEMICAL
µTAS
Microsystems for the generation, handling and analysis of (bio)chemical information
Available online at
ScienceDirect
www.sciencedirect.com

Available online at www.sciencedirect.com
ScienceDirect
Sensors and Actuators B 125 (2007) 569–573
SENSORS AND ACTUATORS B CHEMICAL
www.elsevier.com/locate/snb

Mechanically adjustable chemostats based on stimuli-responsive polymers

Andreas Richter [a,b,*], Jan Wenzel [b], Katja Kretschmer [c]

[a] *Physical Chemistry of Polymers, Technische Universität Dresden, 01062 Dresden, Germany*
[b] *Institute of Electromechanical and Electronic Design, Technische Universität Dresden, 01062 Dresden, Germany*
[c] *Macromolecular Chemistry and Textile Chemistry, Technische Universität Dresden, 01062 Dresden, Germany*

Received 25 January 2007; received in revised form 1 March 2007; accepted 5 March 2007
Available online 12 March 2007

Abstract

A method for a mechanical operating point adjustment of hydrogel-based devices performing closed loop control has been developed. These so-called chemostats automatically control certain chemical and energy-based conditions of a liquid. The adjustment of the controlled condition is provided by a defined change of the triggering point by the activation unit of the device and the hydrogel actuator determining the basic functional relationship. The antagonistic principles of automatic valve chemostats were introduced, which can alternatively realize a normally open or a normally closed function. Using the hydrogel poly(*N*-isopropylacrylamide) the chemostat's switching concentration of ethanol in aqueous solution can be adjusted in the range of 5 and 20 wt.% with a practically relevant precision of 1 wt.%. The controllability of an energy-based condition by the chemostat was investigated on the process temperature control. We found that this temperature can be mechanically adjusted in a range of 25 and 35 °C with a standard deviation below 0.75 K.

Keywords: Chemostat; Hydrogel; Poly(*N*-isopropylacrylamide); Automatic flow control

1. Introduction

Concentration control of certain chemical substances is a key problem in liquid phase based processes. Devices able to regulate a chemical or physical condition of a liquid automatically are therefore of common interest. In microbiology a concept of such a device is known as chemostat maintaining the concentration of special chemical nutrient components in a bioreactor [1,2]. This device acts as an open loop control continuously supplying these chemical compounds, the so-called growth factors, which causes a defined growth rate of a bacterial population. Due to the high cost closed loop chemical control, consisting of sensors, data processing and actuator units, is rarely realized.

However, stimuli-responsive polymers and hydrogels respectively provide the probably simplest realization of closed loop chemostats applying both, actuator and chemical sensor properties. The material-based concept is based on a reversible change of volume in response to small alterations of the chemical [3–7] and energy-based [8–11] conditions of liquids. Valves that automatically control the ion and solvent concentration in aqueous solutions have been demonstrated on the example of various alcohols [12,13] and on the pH value [12,14,15]. Devices responsible to energy-based values were described for temperature [12,16,17] and light of a specific wavelength [18]. Also automatic pH [19] and temperature [20] controlled pumps are known. Devices able to regulate biochemical substances such as that of the pancreas [21] could be realized and are of particular interest because of substitution of body functions.

However, the disadvantage of hydrogel-based devices is the difficult adaptation to the application's requirements. In fact each application would require a stimuli-responsive polymer with an adapted phase transition behavior, usually realized by special polymer synthesis. This inhibits the broad practical use of hydrogel-based chemostats. A first adjustment method of chemostats without need to change the actuator material is described for hydrogels with a special double-sensitivity [22].

Herein, we describe a mechanical adjustment method of the chemostat's operating condition, which does not require special hydrogel properties. Using the hydrogel poly(*N*-isopropylacrylamide) (PNIPAAm) the antagonistic principles of automatic chemostats acting as valve are introduced, which

* Corresponding author. Tel.: +49 351 463 32025.
E-mail address: Andreas.Richter@chemie.tu-dresden.de (A. Richter).

0925-4005/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.snb.2007.03.002

realize alternatively either normally open or normally closed function. Furthermore, the closed loop control of chemical and energy-based conditions of liquids is investigated and demonstrated.

2. Experimental

2.1. Synthesis of hydrogel

PNIPAAm hydrogel was prepared as follows. Monomer *N*-isopropylacrylamide was recrystallized from *n*-hexane solution. Crosslinking agent was *N*,*N*′-methylenebisacrylamide. Initiator and accelerator for the polymerization reaction were potassium peroxidisulfate and *N*,*N*,*N*′,*N*′-tetramethyl-ethylenediamine (all from Aldrich Chemical Co.). *N*-Isopropylacrylamide and 4 mol% *N*,*N*′-methylenebisacrylamide were dissolved in deionized water. The total monomer concentration was 0.53 mol/l. To initiate the polymerization reaction 0.3 mol% of potassium peroxidisulfate and *N*,*N*,*N*′,*N*′-tetramethyl-ethylenediamine, respectively, were added to the oxygen free solution (bubbled with N_2). After polymerization (ca. 12 h at room temperature) the PNIPAAm gel was immersed in deionized water for about 1 week to wash out non-reacted reagents. After drying the PNIPAAm gel the particles were obtained by milling and subsequent fractionating into different particle sizes using test sieves. Particles possess an irregular shape. Particle size fraction used for experiments is (300 ± 100) μm.

2.2. Design and fabrication of the normally closed chemostat

The device shown in Fig. 1a involves two parts (1,2) forming a hydrogel chamber (5). Both parts are made of brass. Metal gauzes (mesh size 53 μm, wire diameter 24 μm) used as semi-permeable chamber walls (3) were adhered to inner and outer part using an epoxy based adhesive. The inner part can be screwed into the outer part using a metric fine thread (4). The chamber diameter is 5 mm. The length of chamber can be varied between 0 and 12 mm. To avoid a leakage flow between both parts the fit has a sealing ring (not shown in Fig. 1a). The chamber was filled with 24.4 mg dry hydrogel particles which correlates with a filling degree of about 30% of the chamber volume.

2.3. Design and fabrication of the normally open chemostat

This valve (see Fig. 1b) involves also two main parts (1,2). The valve body (1) (made from stainless steel) involves a conical valve seat (9) and a membrane (8) separating the two media circuits. Furthermore, the valve body possesses a metric fine thread (4). In this thread the position member (6) can be screwed in. This part consisting of the hydrogel, a flexible diaphragm (7) (polyurethane foil Walopur 4201, 25 μm thickness, from Epurex Films GmbH), and a metal gauze (mesh size 53 μm, wire diameter 24 μm) used as semi-permeable chamber wall (3). Gauze and elastic film were adhered to position member (6) using epoxy based adhesive. Before closing into the chamber 53.7 mg dry

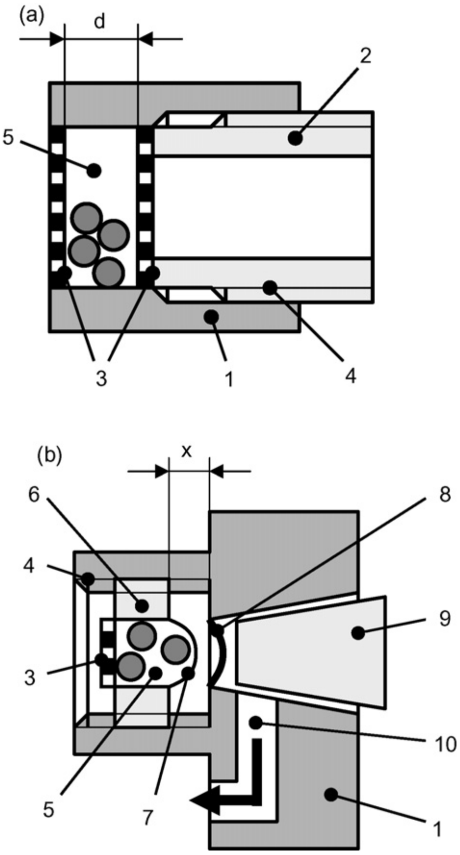

Fig. 1. Schematic designs of the mechanically adjustable chemostats. (a) Normally closed chemostat. (b) Normally open chemostat. 1, outer part; 2, inner part; 3, metal gauze; 4, fine thread; 5, actuator chamber filled with hydrogel; 6, position member; 7, flexible membrane of the actuator chamber; 8, flexible membrane separating the liquid circuits; 9, conic valve seat; 10, outlet; *d*, adjustable chamber length; *x*, adjustable distance.

PNIPAAm particles were filled (equal to 60% of the chamber volume).

3. Results and discussion

3.1. Hydrogel behavior

PNIPAAm shows sensitivities towards special organic solvents. Contents of alcohols in the aqueous solution cause a drastic change of hydrogel volume. As shown in Fig. 2a two phase transition concentrations of PNIPAAm at room temperature can be observed. Small amounts of alcohols cause a collapse of the gel. With increasing the length of the alcohol chain the lower phase transition concentration decreases. This lower critical alcohol concentration is 17.5 wt.% for methanol, 14 wt.% for ethanol and 6 wt.% for 1-propanol at 21 °C (see Fig. 2b). If the alcohol content is higher than 25 wt.% the hydrogel is completely shrunken in each case. In the range of the upper phase transition concentration the PNIPAAm shows an inverse behavior, that means, the hydrogel swells by increasing alcohol content. In pure alcohol the gel exhibits a swelling degree, which is comparable with that in pure water.

PNIPAAm is also a well-known temperature sensitive hydrogel exhibiting lower critical solution temperature behavior. As

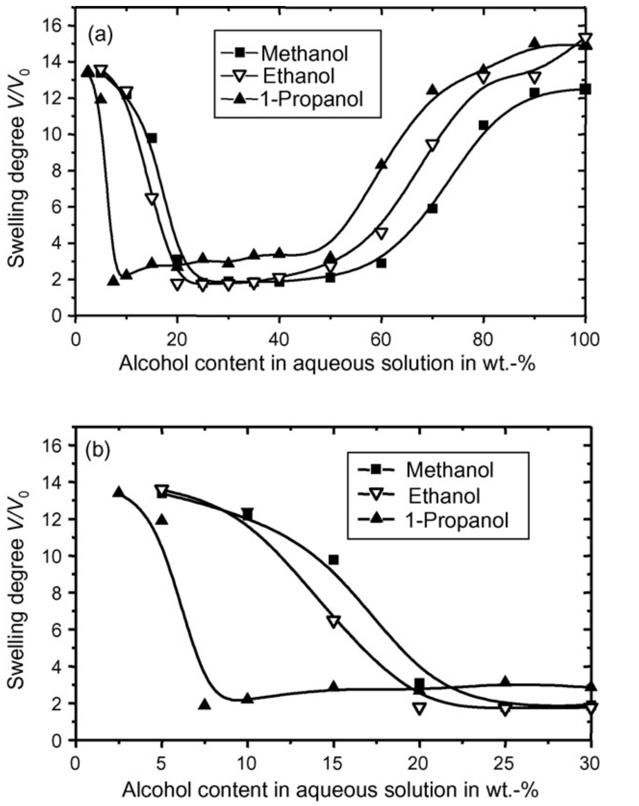

Fig. 2. Swelling behavior of PNIPAAm depending on the alcohol content in aqueous solution at 21 °C. (a) shows the general swelling behavior, while (b) zooms the range of the lower phase transition concentration. V, swollen volume; V_0, dry volume.

shown in Fig. 3, below a volume phase transition temperature T_t the hydrogel is swollen, while by exceeding this temperature the hydrogel shrinks delivering swelling agent. T_t of the homopolymer PNIPAAm is 33.8 °C in pure water measured by turbidity and 35.3 °C by DSC measurements, respectively.

3.2. Function of the normally closed chemostat

As presented in Fig. 1a the hydrogel actuator is directly placed inside the flow channel trapped between two semi-permeable chamber walls (3). In the swollen state the actuator seals the channel and the liquid flow is terminated. A shrinking of the hydrogel opens the valve seat and enables a liquid flow. The operating point of the device is exactly the point, on which the chemostat closes. This means that in this point the chamber volume equals the hydrogel volume. In the ranges of the lower and upper phase transition regions the particular swelling degree is assigned to one defined alcohol concentration. The metric fine thread (4) allows to change the size of the chamber (5) mechanically and thereby to adjust the swelling degree of hydrogel and accordingly the alcohol concentration at which the chemostat actuates. The adjustability of the chemostat switching an alcohol concentration is shown in Fig. 4a on the example of ethanol. The device is calibrated to an ethanol content of 30 wt.% in aqueous solution [Δd (30 wt.%) = 0 mm]. In the range of 10–20 wt.% ethanol the chemostat characteristic is nearly linear. The operating point of the device can be adjusted with a calculative precision of 0.133 wt.% per 0.1 mm. The obtained standard deviation indicates an applied adjustment precision of 1 wt.%. Above and below this range the changes in the swelling degree of the actuator are too small to obtain a considerable adjustment of the device's operating point.

Fig. 4b presents the chemostat's adjustability of the switching temperature. Between 25 and 35 °C the characteristic possesses an average calculative precision of 0.143 K per 0.1 mm by non-negligible variations of the linearity. The obtained standard deviation is below 0.75 K.

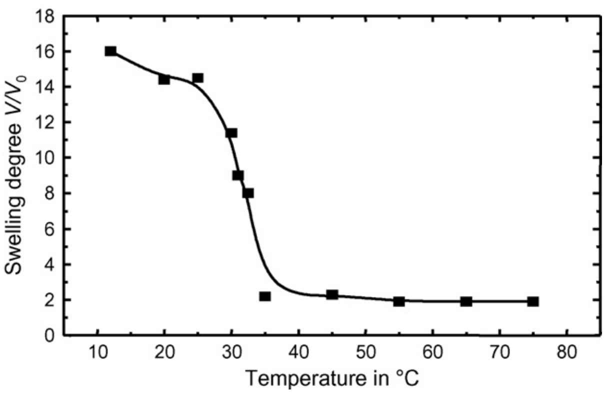

Fig. 3. Swelling behavior of PNIPAAm in aqueous solution depending on the environmental temperature.

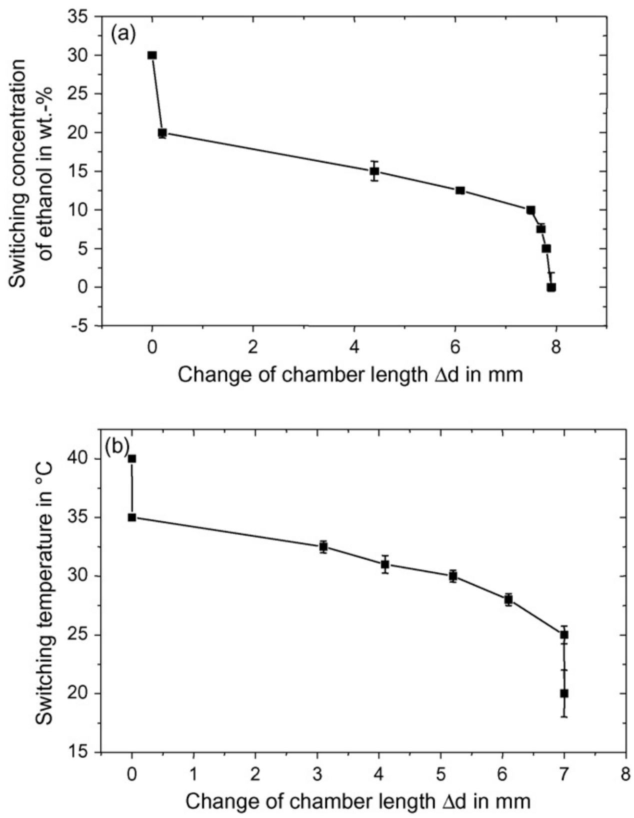

Fig. 4. Operating conditions of the chemostat with normally closed valve function depending on the adjusted change of actuator chamber length Δd. (a) Ethanol switching concentration and (b) switching temperature.

Above and below this region an adjustment of the device's operating point is hardly obtainable.

The operating point of the device depends on the required pressure resistance. For the presented measurements, the pressure drop was 0.2 bar. A higher pressure drop needs a more packed hydrogel actuator, which is reached by a further manual decrease of the chamber size.

3.3. Function of the normally open chemostat

In the design shown in Fig. 1b the hydrogel actuator (5) is placed within a position member (6). When the actuator swells a flexible membrane (7) is moved. In the swollen state the actuator pushes the conic valve seat (9), opens the valve and enables a liquid flow through the outlet (10). When the hydrogel shrinks the valve seat throttles or stops the flow. The operating point of the chemostat is the point, on which the actuator starts to push the valve seat. The metric fine thread (4) allows to change the distance between position member and valve seat and accordingly the membrane displacement, which actuates the valve seat.

The adjustability of the chemostat's ethanol switching concentration is presented in Fig. 5a. Calibrated at an ethanol content of 25 wt.% in aqueous solution [Δd (25 wt.%) = 0 mm] the chemostat can be adjusted to a concentration lower than 20 wt.%. Between 20 and 5 wt.% ethanol the characteristic of the chemostat is nearly linear with a calculative precision of 0.83 wt.% per 0.1 mm. The standard deviation indicates an applied adjustment precision of 1 wt.%. Above and below this region no values can be adjusted.

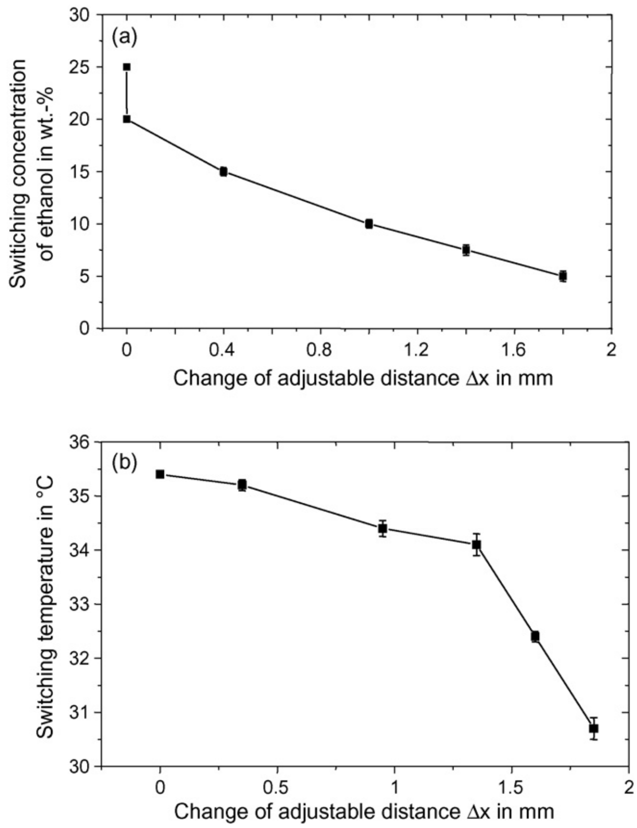

Fig. 5. Operating conditions of the chemostat with normally open valve function depending on the adjustable distance of the position member. (a) Ethanol switching concentration and (b) switching temperature.

Fig. 5b shows the chemostat characteristic of the adjustable switching temperature. The curve strongly corresponds to the swelling characteristic of the PNIPAAm. Between 35.4 and 34.1 °C the curve possesses a good adjustment precision of 0.1 K per 0.1 mm with a standard deviation of maximal 0.2 K. From 34.1 to 30.7 °C a linear behavior with a change of 0.68 K per 0.1 mm (S.D. = 0.2 K) can be observed. At 30.7 °C, the adjustability of the chemostat is limited by the design of the device because the maximal displacement of the membrane is achieved. The operating point of the chemostat is independent of the required pressure resistance.

PNIPAAm-based valves show a long-lasting durability. No changes in mechanical, actuator and sensor properties are observed on 9 years old devices. Furthermore, more than 450 temperature-controlled cycles were performed without any adverse effect. However, hydrogels can lose their actuator properties if they are exposed to aqueous solutions with high ionic strength for a long time. Probably, this effect is caused by ion and material enrichment within the gel, which affects the collapse of polymer chains. Systematic rinsing with deionized water can avoid this.

4. Conclusion

The results show that it is possible to adjust the chemostat mechanically to a defined quantity value of both, chemical and energy-based conditions of a liquid. By variation of the device design alternatively a normally open or a normally closed function can be realized using the same hydrogel and condition. Although the manually adjusted distance for the operating point are quite different, both types possess a similar precision of adjustability. The normally open chemostat shows more significantly the swelling characteristic of the hydrogel than the normally closed device.

The mechanical adjustability of the chemostat's operating point can be applied for each stimuli-responsive polymer. We believe that this possibility will provide a broad use of hydrogel-based chemostats in practice. In microbiology, biochemistry and medical science the adjustable case-sensitive drug release can open many new possibilities, e.g. in cancer research and medical treatment. The level regulation of standard media, such as chemicals, buffers and substrates, is also a helpful feature for these disciplines. Particularly the printing industry and processes in surface treatment, e.g. cleaning and finishing, but also applications in pharmacy can benefit from chemostats. Furthermore, the principle can be applied in sensing devices, fluidic drives and others.

Acknowledgments

Financial support has been provided by the Deutsche Forschungsgemeinschaft (Collaborative Research Center SFB 287 "Reactive Polymers"). Epurex Films GmbH granted polyurethane foils.

References

[1] A. Novick, L. Szilard, Experiments with the chemostat on spontaneous mutations of bacteria, Proc. N.A.S. 36 (1950) 708–719.

[2] A. Novick, L. Szilard, Description of the chemostat, Science 112 (1950) 715–716.

[3] T. Tanaka, Collapse of gels and critical endpoint, Phys. Rev. Lett. 40 (1978) 820–823.

[4] W. Li, H. Zhao, P.R. Teasdale, R. John, S. Zhang, Synthesis and characterisation of a polyacrylamide–polyacrylic acid copolymer hydrogel for environmental analysis of Cu and Cd, React. Funct. Polym. 52 (2002) 31–41.

[5] K.-F. Arndt, A. Richter, S. Ludwig, J. Zimmermann, J. Kressler, D. Kuckling, H.-J. Adler, Poly(vinyl alcohol)/poly(acrylic acid) hydrogels: FT-IR spectroscopic characterization of crosslinking reaction and work and transition point, Acta Polym. 50 (1999) 383–390.

[6] K. Kataoka, H. Miyazaki, M. Bunya, T. Okano, Y. Sakurai, Totally synthetic polymer gels responding to external glucose concentration: their preparation and application to on-off regulation of insulin release, J. Am. Chem. Soc. 120 (1998) 12694–12695.

[7] T. Miyata, N. Asami, T. Uragami, A reversibly antigen-responsive hydrogel, Nature 399 (1999) 766–769.

[8] K.-F. Arndt, T. Schmidt, R. Reichelt, Thermo-sensitive poly(methyl vinyl ether) micro-gel formed by high energy irradiation, Polymer 42 (2001) 6785–6791.

[9] A. Suzuki, T. Tanaka, Phase-transition in polymer gels induced by visible-light, Nature 346 (1990) 345–347.

[10] T. Tanaka, I. Nishio, S.-T. Sun, S. Ueno-Nishio, Collapse of gels in an electric field, Science 218 (1982) 467–469.

[11] Y. Osada, J.-P. Gong, Soft and wet materials: polymer gels, Adv. Mater. 10 (1998) 827–837.

[12] K.-F. Arndt, D. Kuckling, A. Richter, Application of sensitive hydrogels in flow control, Polym. Adv. Technol. 11 (2000) 496–505.

[13] A. Richter, S. Howitz, D. Kuckling, K.-F. Arndt, Influence of volume phase transition phenomena on the behaviour of hydrogel-based valves, Sens. Actuators, B. Chem. 99 (2004) 451–458.

[14] D.J. Beebe, J.S. Moore, J.M. Bauer, Q. Yu, R.H. Liu, C. Devadoss, B.-H. Jo, Functional hydrogel structures for autonomous flow control inside microfluidic channels, Nature 404 (2000) 588–590.

[15] D. Kuckling, K.-F. Arndt, A. Richter, Temperature and pH dependent swelling behavior of poly(*N*-isopropylacrylamide)-copolymer hydrogels and their use in flow control, Macromol. Mater. Eng. 288 (2003) 144–151.

[16] E.C. Peters, F. Svec, J.M.J. Frechét, Thermally responsive rigid polymer monoliths, Adv. Mater. 9 (1997) 630–633.

[17] M.E. Harmon, M. Tang, C.W. Frank, A microfluidic actuator based on thermoresponsive hydrogels, Polymer 44 (2003) 4547–4556.

[18] S.R. Sershen, G.A. Mensing, M. Ng, N.J. Halas, D.J. Beebe, J.L. West, Independent optical control of microfluidic valves formed from optomechanically responsive nanocomposite hydrogels, Adv. Mater. 17 (2005) 1366–1368.

[19] D.T. Eddington, D.J. Beebe, A valved responsive hydrogel microdispensing device with integrated pressure source, J. Microelectromech. Syst. 13 (2004) 586–593.

[20] K. Kobayashi, H. Suzuki, A sampling mechanism employing the phase transition of a gel and its application to a micro analysis system imitating a mosquito, Sens. Actuators, B Chem. 80 (2001) 1–8.

[21] A. Baldi, Y. Gu, P.E. Loftness, R.A. Siegel, B. Ziaie, A hydrogel-actuated environmentally sensitive microvalve for active flow control, J. Microelectromech. Syst. 12 (2003) 613–621.

[22] A. Richter, A. Türke, A. Pich, Controlled double-sensitivity of microgels applied on electronically adjustable chemostats, Adv. Mater. 19 (2007) 1109–1112.

Biographies

Andreas Richter received the Dipl.-Ing. degree in electromechanical and electrical engineering from Technische Universität Dresden in 1996, and the PhD degree in electrical engineering from the same university in 2002. His work is focused on the development of hydrogel based applications in chemical sensorics, medical engineering, micro fluidic devices, and tactile communication.

Jan Wenzel obtained the Dipl.-Ing. degree in electromechanical and electrical engineering from Technische Universität Dresden in 2007. His field of interest is the design and investigation of mechanical and electronic systems.

Katja Kretschmer received the Dipl.-Chem. from Technische Universität Dresden in 2002, and the PhD in macromolecular chemistry from the same university in 2005. The synthesis and characterization of stimuli-responsive polymers are some of her main research interests.