Evaluation of Microvalves Developed for Point-of-Care Testing Devices Using Shape-Memory Polymers

Chenyang Jiang, Hiroaki Takehara, Koichiro Uto*, Mitsuhiro Ebara*,
Takao Aoyagi* and Takanori Ichiki

*Department of Bioengineering, School of Engineering,
The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan*
**Smart Biomaterials Unit, National Institute for Materials Science (NIMS)
1-2-1 Sengen, Tsukuba-city, Ibaraki 305-0047, Japan*

A temporal change in temperature in an actuating shape-memory polymer (SMP) valve has been measured by analyzing the fluorescence spectrum of sulforhodamine B in the aqueous solution. The SMP microvalve used in this study was recently developed by the authors. It is actuated by the shape recovery of poly(ϵ -caprolactone) (PCL), which is triggered by heat from a microheater. To obtain information about temperature rise during operation, we measured “temperature quenching” of the fluorescence from sulforhodamine B using laser-induced fluorescence (LIF) spectroscopy. The maximum temperature during valve actuation was approximately 60 °C and was slightly higher than the phase transition temperature 52 °C of the PCL material used in this study. The results indicate that the present microvalve is potentially applicable to practical point-of-care testing devices.

Keywords : microvalve, shape memory polymer, laser-induced fluorescence spectroscopy

1. Introduction

In recent years, microfluidic devices have emerged as important tools in the fields of life science and medicine, with the potential for integrating complex analytical procedures on a chip [1-5]. One of the essential technologies for the construction of fully integrated microfluidic systems is a microfluidic valve [6-9]. To fulfill the requirements of microfluidic valves for practical use in disposable integrated microfluidic devices, the use of a shape-memory polymer (SMP) [10-12] as the primary element of microfluidic valves has been proposed. We have recently developed a prototype SMP microvalve using the solid-solid phase transition of poly (ϵ -caprolactone) (PCL), whose actuation is triggered by heat from a microheater, and successfully demonstrated its good performance for valve actuation [13]. Moreover, SMP microfluidic valves have several desirable features for use in disposable devices, including compatibility with plastic microfluidic devices, low-cost mass producibility, and integration with electrical control systems. However, further study was needed on the effect of the local heating of microvalves to minimize the

risk of unfavorable temperature increases in analyte samples or reagents during microvalve actuation.

In this paper, we report the real-time temperature measurement of a liquid sample during SMP microvalve actuation by laser-induced fluorescence (LIF) spectroscopy and discuss the effect of actuation conditions on the sample temperature and the design of SMP microvalves with the minimum necessary temperature rise.

2. Experimental

2.1 Shape-memory polymer microvalve

Figure 1 shows a schematic diagram of the normally open (N/O)-type SMP microvalve used in this study. The structure comprises three layers: a poly(dimethylsiloxane) (PDMS) sheet having microfluidic channels, a PCL sheet, and a microheater-integrated glass plate. The PCL sheet can be locally heated by the microheater to actuate the valve. The cross section of the microchannel was 45 μ m in height and 100 μ m in width. The distance between two adjacent microchannels was

Figure 1. (a) Schematic of SMP microvalve (N/O type). A valve actuates with heat from the microheater. (b) Micrographs of SMP microvalve in open state and closed state.

100 μm. The concave structure of 300 μm diameter and 45 μm depth was hot-embossed on the flat 200-μm-thick PCL sheet. A thin-film microheater, which had the same diameter as the concave structure, was integrated immediately below the concave structure. PCL has covalently cross-linked semicrystalline networks and reverts to its original shape at the transition temperature, which can be controlled by changing the cross-linking density. Details of the fabrication process of the microvalve were described previously [13].

2.2 Actuation of the microvalve

A programmable dc power source was used to control the electric current flowing through the microheater, and an epi-fluorescence microscope (Ti-U, Nikon Corp., Tokyo, Japan) equipped with a 130 W mercury lamp (Intensilight C-HGFIE, Nikon Corp.) was used to monitor the microvalve actuation. By applying various voltages to the microheater, the actuation of the N/O microvalve was tested. A fluorescent aqueous solution of 0.05% (w/w) sulforhodamine B (Kanto Chemical Co., Inc., Tokyo, Japan) was introduced into the microvalve, and the change in fluorescence intensity was monitored at the central position (volume-changing space located between the adjacent microchannels) of the microvalve to monitor the valve actuation. The fluorescence emission excited by green light was delivered through an iris (ID15/M, Thorlabs, Newton, NJ, USA) and a lens (LA1805, Thorlabs) to an avalanche photodiode (APD) (C5460, Hamamatsu Photonics KK, Hamamatsu, Japan). The analog signal from the APD was converted to a digital

signal using the data acquisition module (NIUSB-6008, National Instruments, Corp., TX, USA). The response time was evaluated from the evolution of fluorescence intensity. The response time was defined as the time from the switching-on of the microheater to the moment when the fluorescence intensity decreases to zero. In addition, the heating power of the microvalve was calculated from the applied voltage and the resistance of the microheater.

2.3 Temperature measurement by LIF spectroscopy

Measuring the temperature of a very small amount of liquid is not straightforward, and a promising approach to addressing this issue is to use the temperature-dependent fluorescence intensity of dyes [14-19]. Generally, fluorescence intensity decreases with increasing temperature owing to the increase in collision frequency between dye and solvent molecules, and this phenomenon is called “temperature quenching”. Lavielle et al. reported the temperature measurement of droplets using the ratio of fluorescence intensity from the same dye at two different wavelengths [20]. According to Lemoine et al., the temperature dependence of the fluorescence intensity I_f is expressed as follows:

$$I_f = K_{\text{opt}} K_{\text{spec}} V_c I_0 C \exp\left(\frac{\beta}{T}\right), \quad (1)$$

where K_{opt} and K_{spec} are optical and spectroscopic constants, respectively. V_c is the measured volume of the aqueous solution excited by laser radiation, I_0 is the incident laser intensity, C is the molecular concentration of the fluorescent tracer, and T is the absolute temperature. The coefficient β indicates the temperature sensitivity of the fluorescence intensity, and depends on the physical properties of the fluorescent molecule. By applying Eq. (1) to two different wavelengths and considering the ratio of fluorescence intensity R_f , R_f can be written as a function of temperature as follows.

$$\ln\left(\frac{R_f(T_0)}{R_f(T)}\right) = (\beta_1 - \beta_2) \left(\frac{1}{T_0} - \frac{1}{T}\right) \quad (2)$$

Here, β_1 and β_2 are the temperature sensitivity coefficients at the two different wavelengths, which can be experimentally determined. T_0 is the reference temperature.

LIF spectra were excited using a blue excitation filter set (EX 460-500, DM 505 nm) without an emission filter and measured using a multichannel photodetector (MCPD-7000, Otsuka Denshi Inc., Osaka, Japan) which had a resolution of 1.2 nm.

The spectra were recorded every 20 ms.

Figure 2 shows the fluorescence spectra of low-concentration sulforhodamine B solution (0.005%, w/w) measured at 25 °C and 60 °C. By applying Eq. (1) at these two temperatures, β was calculated as also shown in Fig. 2, and was found to have maximum and minimum values at 582 nm and 617 nm, respectively. By calculating the ratio of fluorescence intensity at these two wavelengths and using Eq. (2), the unknown temperature of the aqueous solution can now be calculated.

Using LIF spectroscopy described above, the temperature change in the microvalve during its actuation was measured. To compare the temperature change under different conditions, the measurement was conducted in the microvalve actuated at different voltages.

Figure 2. Fluorescence spectra of sulforhodamine B measured at 25 °C and 60 °C. Quenching with increasing temperature is observed. The temperature sensitivity coefficient β is a function of the wavelength.

3. Results and discussion

Firstly, the evolution of the fluorescence intensity in N/O microvalves during actuation was measured to monitor the actuation speed. As shown in Fig. 3, the fluorescence intensity decreased immediately after switching-on of the microheater. Although the intensity change is originated from both the reduced microvalve's space and the temperature quenching, the drop to zero indicates the perfect closure of microvalves. As expected, a higher heating power enables a shorter response time. Moreover, the relationship between the heating power and the response time was investigated systematically as plotted in Fig. 4. By changing the voltage applied to the microheater, the response time changed markedly from ~300 ms

Figure 3. Change in fluorescence intensity measured at central position of N/O-type SMP microvalves actuated by supplying voltages of 5 V, 6 V, and 7 V to microheater. The heating power was calculated from the applied voltage and the resistance of the microheater. A higher heating power results in a shorter response time.

Figure 4. Relationship between heating power and response time. An asymptotic relationship was found between the two factors. The asymptotic value of the actuation time is approximately 290 ms. The minimum heating power required for valve actuation is estimated to be approximately 130 mW.

to ~1400 ms. An asymptotic relationship was found between the heating power and the response time, and the experimental data could be fitted by the linear-fraction function shown in the Figure.

The asymptotic value of the actuation time of approximately 290 ms is considered to be the time necessary for the elastic deformation of PCL after the phase transition. In addition, the minimum heating power required for valve actuation is estimated to be approximately 130 mW. These two values are rather larger than those reported previously [13]. This discrepancy is considered to be resulted from the difference in thickness of PCL sheets used for the valves.

Subsequently, the changes in liquid sample temperature in N/O valves during actuation were investigated as shown in Fig. 5. Here, the heating time was set to ensure the perfect closure of microvalves at each voltage, namely it was selected to be longer than the response time shown in Fig. 3. A faster temperature increase was observed at a higher voltage. It is interesting that the maximum temperature during actuation was almost the same (approximately 60 °C) irrespective of the heating conditions.

Although an increase in temperature to 60 °C, higher than body temperature, has a risk of denaturing biological samples such as proteins to some extent, the period is relatively short (less than 1000 ms). Therefore, the effect on sample analytes

Figure 5. Changes in liquid sample temperature in N/O-type SMP microvalves. The heating times of 1000 ms, 800 ms, and 500 ms were selected for heating conditions of 5 V, 6 V, and 7 V, respectively, ensuring sufficient time for perfect closure of microvalves. Regardless of the heating conditions, the maximum temperature was approximately 60 °C.

may be limited. The phase transition temperature T_{trans} for the PCL used in the present study was 52.3 °C and can be lowered, if necessary, by tuning the mixing ratio of macromonomers used as raw materials [21–23]. The use of PCL with low- T_{trans} will enable the realization of SMP valves with a small temperature increase during actuation.

4. Conclusion

New microfluidic valves based on the solid-solid phase transition of a thermally responsive

shape-memory polymer have been developed for use in point-of-care testing devices. To assess the applicability of these microvalves to biological samples, we evaluated their performance, focusing on the temporal temperature change during actuation. The temperature change of aqueous samples in SMP microvalves was optically measured by LIF spectroscopy of sulforhodamine B. The maximum temperature during valve actuation was approximately 60 °C, which was slightly higher than T_{trans} for the PCL material used in the present study. The temperature rise hardly varied with the heating conditions, and hence, tailoring T_{trans} for the PCL material is considered to be the most suitable approach to lowering the temperature increase if necessary. We believe that this novel SMP microvalve can be applied in practical microfluidic devices owing to its advantages such as compatibility with plastic microfluidic devices, low-cost mass producibility, and integration with electrical control systems.

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