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A prototype of ultrasonic micro-degassing device for portable dialysis system

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Abstract

The design, fabrication and evaluation of a micro-degasser are described. The intended use of the device is in portable dialysis systems. Degassing processes were based on ultrasound induced cavitation. The pattern of the degassing chamber was formed in a glass wafer and that of the gas-venting channels were formed in a silicon wafer. The entire flow path network was encapsulated by the anodic bonding of the Si to the glass wafer. A diaphragm (6 mm × 6 mm × 0.1 mm) was etched on the Si side for oscillation. The ultrasonic vibration originated from a bulk piezoelectric PZT ceramic (5 mm × 4 mm × 0.15 mm) which was excited by a 49 kHz square wave at 100 V (peak-to-peak). The gas-venting channels (2 μm wide and 2.7 μm deep) were hydrophobically passivated using a functional silicone. Cavitation occurred in a degassing chamber (6 mm × 6 mm × 0.02 mm) when the Si oscillating diaphragm was driven by the PZT. Water was used to demonstrate the degassing process. The entire process was recorded using a microscope equipped with a video camera. The gas bubbles were vented effectively and no gas bubble flowing out of the degassing chamber with water was observed. Thirty-eight percent of the dissolved oxygen was removed.

Keywords: Degassing; Dialysis; Ultrasound; Micromachine

1. Introduction

A portable dialysis system has long been awaited. Dialysis treatment is highly stressful to patients both mentally and physically. Generally, the patients must visit a clinic three times a week and lie in bed for 5 h during the dialysis treatment. The additional time required for commuting and preparing for treatment must also be considered. Thus, the entire day is taken up for the dialysis treatment. A portable system promises more freedom to patients. With the development of micromachining technology, such a system is close to being realized. Methods for creating networks of microchannels are well established for silicon, glass and polymeric substrates. PZT-actuated micropumps have achieved high performance [1], various microsensors have been reported, and temperature management devices are easily miniaturized to heat the dialysate to 38°C. However, the lack of a suitable vacuum pump to control the concentration of dissolved gases in dialysate is the obstacle in realizing a portable dialysis system. Micropumps are effective for powerful delivery of liquids but micro-vacuum pumps have rarely been reported.

The principle of dialysis is shown in Fig. 1. Instead of adding additional chemical drugs, this therapy uses physical diffusion and ultrafiltration to remove the chemicals as well as water from the blood. The important points for us are temperature and pressure. The dialysate must be heated up to body temperature and drawn into a dialyzer by negative pressure. The dissolved gases in dialysate will come out and form bubbles due to the heating up and the negative pressure. The bubbles inside the dialyzer result in the reduction of the effective exchange surface area. Therefore, the concentration of dissolved gases in dialysate should be kept low for efficient osmotic exchange with blood [2,3]. Oxygen is easily monitored using an oxygen electrode. The dissolved oxygen concentration is an index of the dissolved gases in liquid. The oxygen concentration in air-saturated water at 25°C is 8.2 ppm, which decrease to 6.6 ppm at 38°C. Dialysate with 6 ppm dissolved oxygen will not generate gas bubbles inside the dialyzer [3].

In principle, degassing can be classified into chemical and physical methods [4]. The N_2H_4 or NaHSO3 used in chemical degassing is limited to large-scale industrial production and is unsuitable for the treatment of dialysate in our application. The physical degassing methods present more choices. They can be classified into gas exchange, diffusion and ultrasonic cavitation. The gas-exchange method uses

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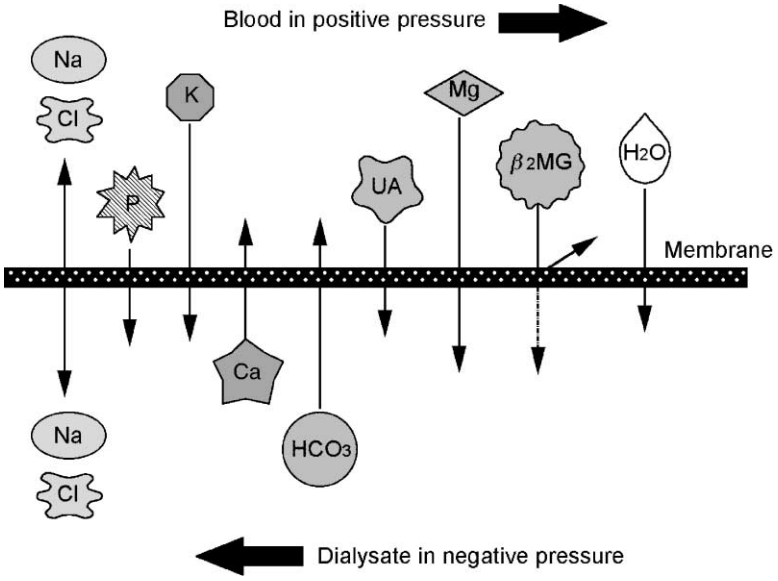

Fig. 1. The principle of hemodialysis therapy. The solutes were removed mainly by diffusion due to the concentration gradient and water was removed by ultrafiltration due to the pressure gradient between blood and dialysate.

less dissolved gases, such as N_2, Ar or He, to bubble the solution for degassing. The boiling of water is also an exchange method. It is widely used in laboratory experiments for temperature insensitive solutions. Water vapor is generated and is exchanged with the dissolved gases. The gas exchange method requires either additional gas supplies or high temperature. Thus, it is difficult to satisfy the demands of a portable system for medical purposes. The diffusion method makes use of the natural diffusion phenomena to decrease the amount of dissolved gases. The use of a vacuum pump is the most popular method of generating the concentration gradient. This method is widely used in current dialysis systems for the degassing of dialysate. However, vacuum pumps are difficult to miniaturize using micromachining technologies. To our knowledge, there is yet no report on the micro-vacuum pump. Degassing using ultrasound is an alternative technique. Dissolved gases are actively driven out by means of the cavitation phenomena induced by ultrasound. We use this principle to miniaturize the degassing unit for dialysate.

In this paper, we present an ultrasonic micro-degassing device for the first time. The design, fabrication and evaluation of the device are reported. The possible applications to a portable dialysis system and other instruments are also discussed.

2. Materials and methods

Conventional photolithographic methods were used in the fabrication of the device (Fig. 2a). Several channels of 2 μm width and 2.7 μm depth were etched into the silicon substrate using the RIE method (SLR730/740, Plasma-Therm, USA). These channels were designed to vent the gas bubbles. The patterns of the inlet, outlet and degassing chamber for dialysate were formed in Pyrex glass #7740 (Iwaki Glass, Japan) by HF isotropic etching (50% HF:69% HNO_3:H_2O in volume rate of 2:1:2) at room temperature [5]. A 200-Å-thick chromium layer, topped by a 1500-Å-thick gold layer, was evaporated as the etching mask.

The depth of the liquid flow channel was 20 μm into the glass substrate. The entire flow path was encapsulated by anodically bonding the silicon to the glass (Fig. 3). A diaphragm of 6 mm × 6mm × 0.1 mm was etched from the silicon side using DRIE (STS Technology, UK). A 9-μm-thick (postbaking at 150°C for 30 min) photoresist layer (S 1830, Shipley, USA) was used as the etching mask. The thick photoresist layer was spin-coated (1H-DX2, Mikasa, Japan) onto silicon at 3000 rpm for 1 s. After a Pt/Ti background electrode was sputtered onto the Si side, a piece of bulk piezoelectric PZT ceramic (5 mm × 4 mm × 0.15 mm) was adhered directly onto the oscillating diaphragm using an epoxy resin, XNR 3506 (Nagase-Ciba, Japan) (Fig. 4). PZT (Type C-82) was purchased from Fuji Ceramics Co. (Fujinomiya, Japan). A function generator (Sony Tektronix AFG320, Japan) connected to a power amplifier (NF Electronic Instruments 4010, Japan) was used to generate the square wave (100 V peak-to-peak at 49 kHz) for PZT excitation. After individual chips (10 mm × 10 mm × 0.9 mm) were diced, the 2 μm channels were treated by a chemical solution (KP801M, Shinetsu Silicone, Japan) for hydrophobic passivation from the side wall (the gas outlet parts in Fig. 3). The chemical is a kind of functional silicone [6]. It filled in the 2 μm channels automatically due to the capillary attraction.

Water was used to evaluate the performance of the device. External pressure of 10 kPa was applied to water using a fluid dispenser (custom-ordered from Musashi Engineering

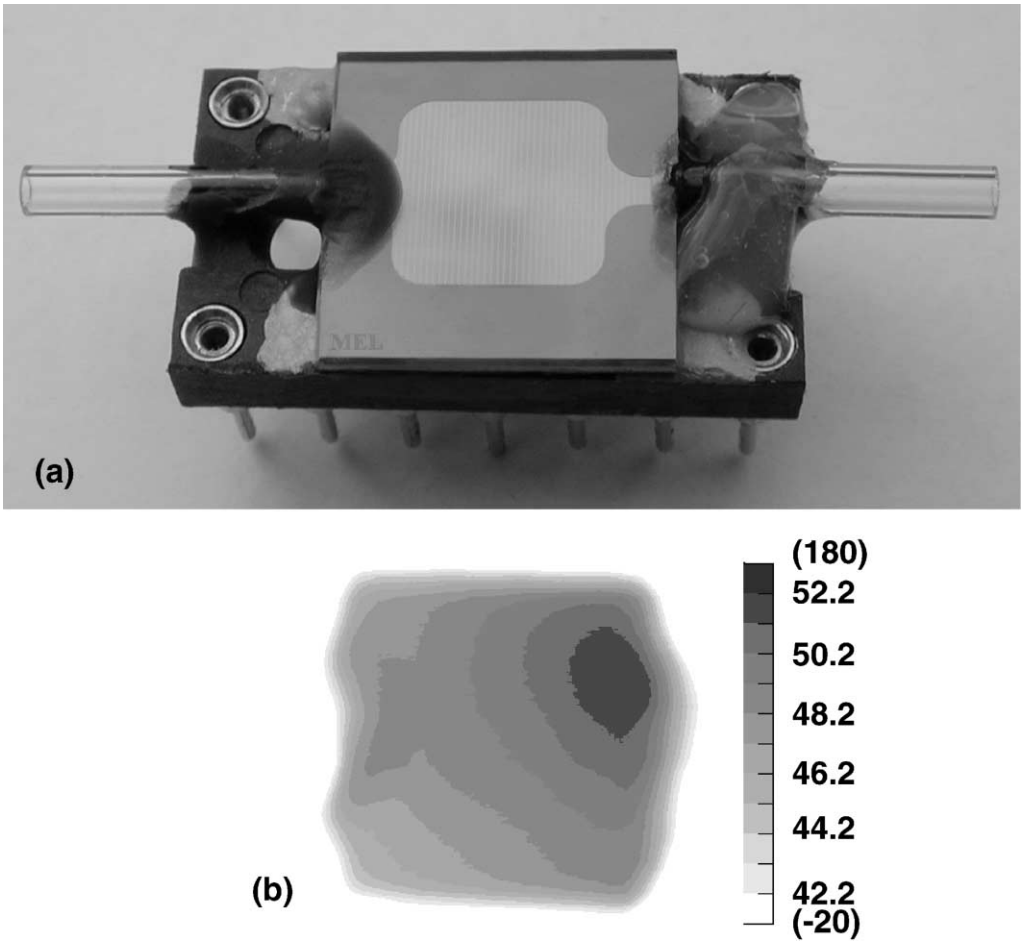

Fig. 2. (a) Photograph of the degassing device. The die size is 10 mm × 10 mm × 0.9 mm. (b) The thermo distribution on the surface of the working device. The highest temperature was 52°C and the lowest temperature was 42°C on the chip.

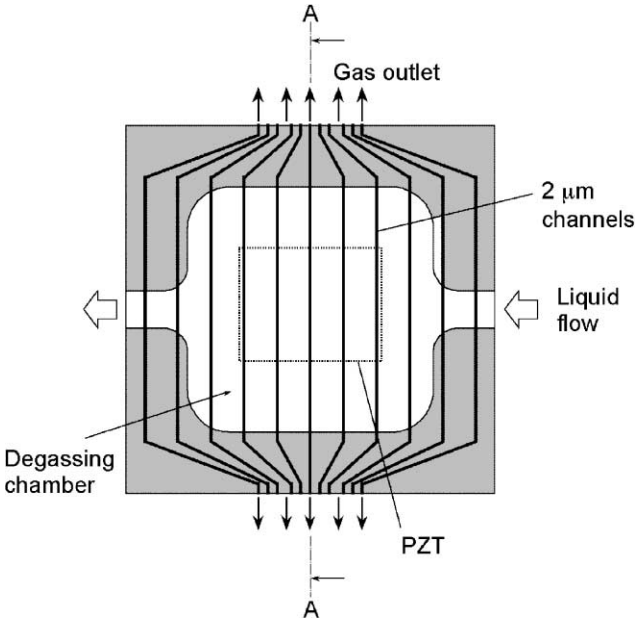

Fig. 3. Schematic drawing of the degassing device. The degassing chamber etched into glass is 6 mm × 6 mm × 0.02 mm. The gas-venting channels are arranged vertically to the flow direction.

Inc., Japan) to maintain a continuous flow (about 120 μl/min). Water flow was kept away from the passivated wall. A microscope (Olympus, Japan) with a video camera (KY-F55, Victor, Japan) was used for monitoring the degassing process (Fig. 5).

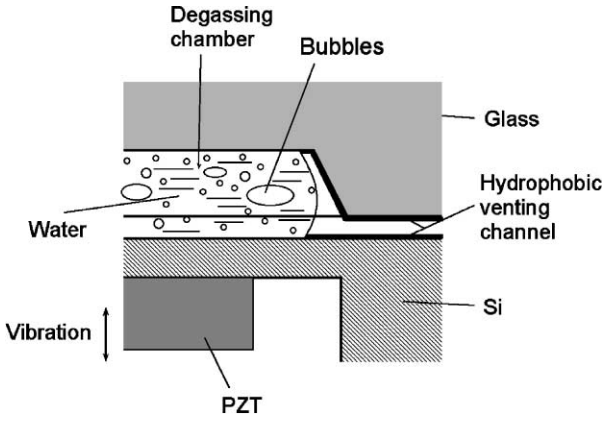

Fig. 4. Part of the cross section along the line AA in Fig. 3, to show the working principle. Water was blocked by the passivated wall and gas bubbles were generated by PZT vibration and vented out through the hydrophobic channels.

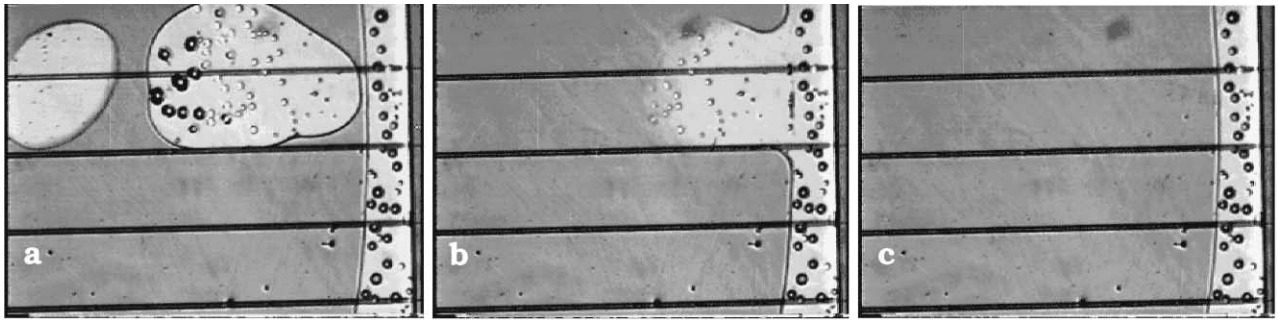

Fig. 5. Selected video-printings showing a degassing process. This process repeated with continuous water flow. (a) Gas bubble generation; (b) venting; (c) return to normal state for the next bubble generation.

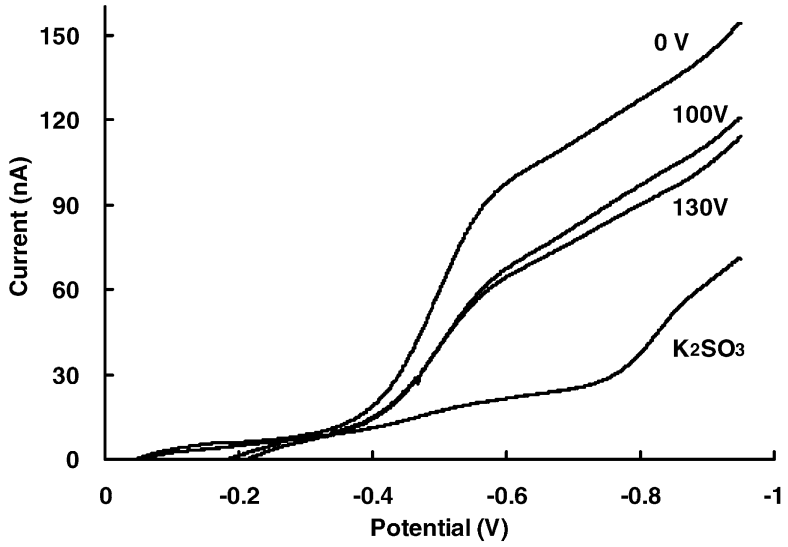

Fig. 6. The forward scans of the second voltammogram from the miniature oxygen electrode at various conditions. The electrode gave the highest response to water when the degassing device was off (0 V). Dissolved oxygen decreased when the device was actuated at 100 V. The more energy input into the degassing device, the more dissolved oxygen was removed. Thus, the electrode showed lower response at 130 V than that at 100 V. The electrode showed the lowest response to 2% K_2SO_3 solution for the dissolved oxygen concentration is 0.

The temperature of our device was monitored using a thermo-inspector (JTG-7200HR, JEOL, Japan). Two k-type thermo couplers were inserted into the inlet and outlet of the device respectively to monitor the temperature of water. The temperatures were measured after 5 min of continuous ultrasonic irradiation. The experiment was conducted at 16°C room temperature and the result was shown in Fig. 2b.

The dissolved oxygen concentration was measured using a miniature oxygen electrode (testing sample from FDK Corporation, Japan). The electrode was connected to an electrochemical analyzer (ALT 600, CH Instruments, USA) in the mode of voltammetry measurement. The potential was swept from 0 to −950 mV for two cycles. The forward scan current at −885 mV of the second voltammogram was used as the oxygen electrode's response [7]. The oxygen electrode has no built-in temperature compensation feature. Therefore, an additional 20 mm long stainless pipe (1/16 in. type) was inserted between the outlet of the degasser and oxygen electrode. With the help of forced air from a hair-blower, the temperature of the degassed water recovered at room temperature. A pump (600F, Waters, USA) was used to deliver water at 120 μl/min for this experiment. The experiment was conducted at 25°C room temperature and the results are shown in Fig. 6.

3. Results and discussion

A micro-degassing device with a very simple structure has been developed for the first time. The principle of employing ultrasonic cavitation was shown to be effective for degassing. The structure of our device vents gas bubbles effectively and the degassing process is shown in Fig. 5. Gas bubbles grew upon continuous ultrasonic irradiation (Fig. 5a), moved and vented out (Fig. 5b), and then resumed a normal state before the next bubble generation (Fig. 5c). This degassing process was repeated with a continuously

flow of water. The volume of gas bubbles stopped growing immediately when ultrasound was turned off (not shown). This verified that the gas bubbles were generated by ultrasonic irradiation.

The entire fabrication process was compatible with conventional microfabrication technologies. The prototype of micro-degasser shows great flexibility for integrated with micropumps, microvalves, micromixers and microchannels. This degassing device is dramatically decreased in size and power consumption compared with the use of a vacuum pump to remove the dissolved gases in the liquid. This is a significant step towards portable dialysis systems.

3.1. Degassing methods

Gas bubbles inside the dialyzer will decrease the exchange surface area and increase the possibility of serious problems arising, such as air embolization. First, we investigated the possibility of minimizing vacuum pumps, which are currently used for degassing of dialysate. We have not yet encountered any report on micromachined vacuum pumps. Micromachined motors have been developed for many years, but due to the friction and other problems, such micromotors have difficulty in supplying mechanical power. The motor-driven vacuum pump is difficult to minimize using micromachining technologies. Furthermore, the degassing process using a vacuum pump has low efficiency. The degassing process is not directly due to the vacuum pump, but is due to the natural diffusion resulting from the concentration gradient generated by the vacuum pump. Natural diffusion is a slow process. Most of the power consumed by the vacuum pump goes towards maintaining the vacuum level. Therefore, even if we succeed in minimizing the vacuum pump, it will be difficult to ensure a sufficient power supply for the vacuum pump in a portable system. Consequently, the ultrasonic method was chosen. It is compatible with micromachine technology. The dissolved gases are actively driven out by ultrasonic cavitation. Thus, its working efficiency is higher than that of natural diffusion. For a portable system, each individual component should be light and small. The energy required should also be affordable for a portable power supply. Therefore, degassing process depended on vacuum pump is not suitable for portable system.

We used positive pressure in the degassing device, which is different from the current dialysis systems which apply a negative pressure to the dialysate. Positive pressure is only applied to blood, as shown in Fig. 1. This method ensures that both the waste and water are efficiently removed from blood by ultrafiltration. However, in our device, a negative pressure will give rise to problems. The viscosity of air is significantly lower than that of liquid. Hence, air might enter into the degassing chamber through the gas-venting channels. The danger of viral or bacterial infection is difficult to avoid. Our gas-venting channel has a width of 2 μm, which is nearly the limit of our silicon fabrication process. Normally, the air filter used to prevent infection must be one order of magnitude lower, i.e. 0.2 μm. We believe a possible solution can be devised in the design of the dialysis system. A narrow channel can be set between the degasser and dialyzer. The flow rate is restricted by this narrow channel. Thus, it becomes possible to apply a negative pressure on the dialysate in the dialyzer while applying a low positive pressure in the degasser.

In general, ultrasound introduced cavitation is very harmful for bio-materials. However, for dialysis application, only dialysate needs to be degassed before entering into the dialyzer. Blood is completely isolated from any degassing device. Therefore, active degasser using ultrasound was a suitable choice.

3.2. Device design

In the design, we used 2-μm-wide venting channels and the hydrophobic chemical has the contact angle $\theta = 110$. According to Hosokawa et al., these hydrophobic channels (with the depth of 2.7 μm) can withstand a water pressure of 40 kPa [8]. Experimentally, we found that the hydrophobic area could act as a barrier to up to 30 kPa still pressure, which is very close to the theoretical value. With ultrasonic waves applied, our device can only withstand the pressure of 10 kPa. This might be sufficient for our application, because the dialysate will ultimately be introduced with a negative pressure into the dialyzer.

Basically, the gas-venting channels were only needed for connection to the degassing chamber. In our design, we extended the 2-μm-wide channels across the entire degassing chamber. These channels help to prevent the gas bubbles from flowing out of degassing chamber with dialysate. As shown in Fig. 5a, the resistance of gas bubbles to flow across the channel is relatively high. The gas bubbles deform along the channel, move parallel to the channels and are vented out.

We used an oscillating diaphragm in the degasser structure. Theoretically, the cavitation effect originates due to the ultrasonic irradiation. Thus, an oscillating diaphragm is not necessary for acoustic irradiation. We used the silicon oscillating diaphragm only to prevent ultrasonic radiation from escaping to other parts of the device and to focus it into the mixing chamber. The oscillating diaphragm structure was the easiest way to achieve ultrasonic isolation [9].

3.3. Device fabrication

In the fabrication process with DRIE, a thick layer (about 5.5 μm) of photoresist is needed as the etching mask. Our photoresist generally had the thickness of less than 4 μm (after postbaking). We modified the spin-coating condition to only 1 s to resolve this problem, and a 9 μm photoresist layer was formed.

We chose the silicon/glass structure in order to enable process visualization for evaluation. Silicon/silicon direct bonding or polymer structures are also possible for making

micro-degassing device. Hydrophobic passivation must be performed after the formation of flow channels. The passivation layer cannot exceed 400°C during the anodic bonding process.

(Heptadecafluoro-1,1,2,2-tetrahydrodecyl) triethoxysilane [10] was famous for a hydrophobic treatment. Hydrolysis in combination with polydimethoxysiloxane gives hard hydrophobic coatings [11]. The chemical solution for hydrophobic treatment we used was also a kind of silicone compound. KP801M can be applied to a substrate directly without dilution.

The same as most other kinds of microfluidic devices, priming with liquid should be considered [9]. First, we passivated the entire chip with the KP801M solution. Relatively high pressure was needed to prime the device, since the liquid flow channel was also hydrophobic. Under this pressure, the hydrophobic interface was destroyed at the inlet of the degassing device and then water flowed into the air-filled chamber. Water moved very fast at the moment of breakdown of the hydrophobic interface. We observed that some parts of gas-venting channels were also filled with water. As a result, the gas bubbles could not be vented efficiently. We, therefore, passivated the venting channel from the sidewall, the gas outlet parts in Fig. 3, making use of capillary phenomena. The device worked well because the water flow channels were left in the hydrophilic state. A pressure of 0.01 MPa was enough to prime the device. It is important to prime the liquid flow channel without destroying the hydrophobic barrier of gas-venting channels.

3.4. Heating problem

Because of the energy input into the degassing chamber, a temperature increase could not be avoided. We used the IR camera and thermo couplers to monitor both the temperature distribution of the working device and temperature of water before and after it flowed through the working device. The temperature of the device increased significantly, varying from 41 to 52°C. The temperature of water increased from 17°C at the inlet of the degassing device to 41°C at the outlet of the device. The temperature distribution on the device was special. The highest temperature point (52°C) was on the edge area instead of the central part of the device with PZT (Fig. 2b). We checked the package of our device and found the problem was caused by a silver paste layer used for connecting the backside electrode to the lead frame. The resistance of the silver paste layer is relatively high, about 16 Ω. Instead of the actuated PZT, the drop in the resistance of the silver paste layer generated a large amount of heating. The further improvement on package process is needed to achieve better heating performance.

3.5. Quantitative evaluation and further improvement

We verified the degassing process (bubble generation, venting and the recovery of the hydrophobic barrier) under microscope. Quantitative evaluation of the degassing process was successfully obtained using a miniature oxygen electrode. This electrode has its advantage over ordinary oxygen electrode on lower working current. This means that the miniature electrode consumes less oxygen. Ordinary oxygen electrode is not suitable for evaluating the sample of the order of micro liter at this point. The temperature increase during the degassing process is the first problem for applying the miniature oxygen electrode of evaluation.

Temperature increase directly affected the diffusion rate of dissolved oxygen through gas-permeable membrane. The output current from electrode shifts 1–6% for a rise of 1°C [12]. A stainless steel pipe, combined with forced air-cooling worked well in our system. The shift of the water temperature was less than 0.5°C at the outlet of the stainless steel pipe. Another problem for applying a miniature electrode was the relatively short working lifetime. This problem was compensated by choosing the voltammetry measurement method. Unlike the chronoamperometric method, the voltammetric method we used only cost 76 s for each measurement. As shown in Fig. 6, the saturated water gave the highest output from the miniature oxygen electrode. The electrode showed the lowest output for 2% K_2SO_3 solution, for the dissolved oxygen was completely reduced by SO_3^{-2} ion. This output was the background current from the electrode. The degassed water under different input energy level showed the middle level current output. The oxygen electrode was calibrated using a two-point method [12]. The current at −885 mV [7] of the saturated water was the response to oxygen of 8.2 ppm and that of 2% K_2SO_3 solution was the response to oxygen of 0 ppm at 25°C. With these calibration results, we could get the efficiency of our device (Table 1). It showed our device worked efficiently. The limit for dialysate on dissolved oxygen concentration of 6 ppm [3] was cleared. The degassing efficiency was also adjustable by changing the level of the input energy.

This prototype device can still be optimized. In addition to the dialysis system, degassers have been widely used in chemical analysis such as high performance liquid chromatography. In those applications, a micro-degasser will be advantageous for portable systems, but it must be able to withstand a relatively high pressure (of the order of mega Pascals). The hydrophobic treatment is not expected to be effective under such a high pressure. A polymer layer is an alternative barrier layer for gas-venting channels.

Table 1
The dissolved oxygen concentrations of water after passing the degassing device under different conditions

Peak-to-peak voltage on PZT (V)	Dissolved oxygen concentration (ppm)	The degassing efficiency (%)
0	8.2	0
100	5.1	38
130	4.1	50

4. Conclusions

Effective degassing was achieved using ultrasonic induced cavitation. It could satisfy the demand required for dialysis application to keep the dissolved oxygen concentration less than 6 ppm. The PZT/diaphragm structure worked in elastic mode. There are no other mechanical moving parts inside the device. Therefore, the degasser would be reliable for long-term operation. The power consumption of the ultrasonic actuator would be much lower than that of a vacuum pump. The device would be able to be driven by batteries. This device exhibits great potential for the integration of microchannels, micropumps, micromixers and other components. The results of this work confirmed that ultrasonic waves are a very powerful tool in microfluidic applications.

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