Continuous flowing micro-reactor for aqueous reaction at temperature higher than 100 °C

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Some aqueous reactions in biological or chemical fields are accomplished at a high temperature. When the reaction temperature is higher than 100 °C, an autoclave reactor is usually required to elevate the boiling point of the water by creating a high-pressure environment in a closed system. This work presented an alternative continuous flowing microfluidic solution for aqueous reaction with a reaction temperature higher than 100 °C. The pressure regulating function was successfully fulfilled by a small microchannel based on a delicate hydrodynamic design. Combined with micro heater and temperature sensor that integrated in a single chip by utilizing silicon-based microfabrication techniques, this pressure regulating microchannel generated a high-pressure/high-temperature environment in the upstream reaction zone when the reagents continuously flow through the chip. As a preliminary demonstration, thermal digestion of aqueous total phosphorus sample was achieved in this continuous flowing micro-reactor at a working pressure of 990 kPa (under the working flow rate of 20 nl/s) along with a reaction temperature of 145 °C. This continuous flowing microfluidic solution for high-temperature reaction may find applications in various micro total analysis systems. © 2013 AIP Publishing LLC. [<http://dx.doi.org/10.1063/1.4807463>]

INTRODUCTION

With the development of microfabrication, microfluidics that handles fluid flow at micro-scale receives more and more attention, especially in biological and chemical fields.^{1–4} By scaling the flow domain down to microliter-scale (or even smaller), microfluidics possesses several attractive characteristics, such as low sample consumption, rapid heat/momentum transfer, and has been utilized to develop various micro-reactors.^{5–9} A variety of functional components have been integrated into a single microfluidic chip to meet the requirements from different target reactions. For example, a microheater and a temperature sensor were fabricated inside a polydimethylsiloxane (PDMS) chip to implement rapid heating along with precise temperature control for DNA amplification.¹⁰ Thermoelectrics were also used to realize ice-valving and thermocycling for polymerase chain reaction in an integrated centrifugal microfluidic platform.¹¹ Conductive PDMS was developed to achieve pressure measurement in microfluidic chip,¹² which could be used for reaction condition monitoring. Besides the above applications with the temperature lower than the boiling point of reagents at the atmosphere condition, reaction at a more elevated temperature, for example, higher than 100 °C for an aqueous system, attracts particular interests in the microfluidics community because of its signification in chemical engineering.^{13–15} To avoid the unwanted phase transition, the conventional high-temperature reaction is usually fulfilled in an autoclave reactor, where the system pressure is elevated to

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raise the boiling-point of the reagent. While the reported microfluidic high-temperature reactor, which is generally designed based on an engineering perspective, achieves the required high system-pressure by an off-chip back pressure regulator.^{16–19} Although this scheme saves space compared to the traditional autoclave one, it is still too large for some *in situ* applications.^{20,21} For example, wireless sensor network for water-quality monitoring,²² one of the most important applications of micro total analysis system, only leaves very small space for its sensor unit. The sensor for water-quality monitoring usually requires a digestion pretreatment of the aqueous sample with a temperature higher than 100 °C to decompose the dissolved organic compounds into ionic radicals for indicative species detection.^{23–28} Therefore, it is in high demands to integrate all the functional components including pressure regulator, heater, and temperature sensor into a single device.

This work presents a continuous flowing micro-reactor prepared by silicon-based microfabrication techniques for aqueous reaction at a temperature higher than 100 °C. To verify the chip performance, an on-chip thermal digestion of standard total phosphorus sample, a standard sample for total phosphorus analysis in water quality monitoring, was preliminarily demonstrated.

WORKING PRINCIPLE

As schematically illustrated in Figure 1, the present continuous flowing micro-reactor has three functional zones for reagent mixing, high-temperature reaction, and pressure regulating, which are separated by two thermal isolation trenches. Reagents are loaded into the chip from two inlets and mixed in a long microchannel. An integrated temperature control system, including micro heater/temperature sensor, provides the required high temperature in the reaction zone. A microchannel with a small width serves as an integrated pressure regulator to raise the upstream pressure when sample continuously flows through the channel.

According to Hagen–Poiseuille law,²⁹ the relationship between the pressure drop and the flow rate is

FIG. 1. Schematic of the working principle of the present continuous-flowing micro reactor. Top: Temperature distribution profile along the microchannel; Middle: Pressure distribution profile along the microchannel; Bottom: Basic design of the present chip.

$$\Delta p = 3\mu QL/4a^3b \left[1 - \frac{192a}{\pi^5b} \sum_{n=1,3,5,\dots}^{\infty} \frac{1}{n^5} \tanh\left(\frac{n\pi b}{2a}\right) \right], \quad (1)$$

where p is the pressure, μ is the fluid viscosity, L is the channel length, a and b are half width and half depth of the channel, respectively. Therefore, the pressure drop of a fluid flowing through a channel is strongly affected by the channel size (roughly in a fourth power inversely proportional relationship) and is in a linear proportion to the flow rate. A small channel, as showed in the pressure regulating zone in Figure 1, dramatically increases the pressure in the upstream channel and provides the required high boiling-point condition based on the Antoine relationship,³⁰

$$\log_{10}p = 8.14 - 1810.94/(244.48 + T_b), \quad (2)$$

where T_b is the boiling point of the water. For example, when p is higher than 500 kPa, the boiling-point of water can be raised up to 145 °C, which satisfies the requirement in the demonstrative thermal digestion experiment. Meanwhile, at a given flow rate, a wider channel design in the reaction zone will slow down the fluid speed and provide a longer high-temperature reaction time. Furthermore, the larger channel design in the reaction zone is also helpful to reduce the unnecessary pressure drop.

HYDRODYNAMIC DESIGN

Hydrodynamic phase chart of the present chip is shown in Figure 2. The chip was designed based on Hagen-Poiseuille law with some geometric parameters set in advance. For example, the channel depths (D_0) were set as 40 μm after a trade-off consideration between the high-temperature reaction time and the operable flow rate, as shown in the inset of Figure 2. Given a pressure drop of 4 atm, when the channel depths varies from 20 μm to 40 μm , the period of the fluid in the reaction zone will decrease from 50.3 s to 46.0 s, while the flow rate will increase from 6.37 nL/s to 13.90 nL/s. Based on the acceptable space, the reaction channel was designed as 208 mm long and 100 μm wide, the mixing channel was 270 mm long and 40 μm wide, and the length of the pressure regulating channel (L_p) was set as 42 mm. The most pressure sensitive parameter, the width of the pressure regulating channel (W_p), was the geometric variable for the chip design. In order to keep the time of collecting 50 μL samples (volume required for the

FIG. 2. Hydrodynamic phase chart of the chip design (physical properties were taken at 50 °C). Inset figure shows the effects of the channel depth on the high-temperature reaction time and the operable flow rate.

off-chip absorbance measurement in the demonstration experiment) within three hours, the minimum flow rate (Q_{min}) was set as 5 nl/s. Based on the Antoine relationship, the minimum working pressure is 500 kPa to make sure the boiling-point of water higher than 145 °C, required by the demonstration experiment in this work. However, the maximum working pressure was suggested as 1100 kPa to guarantee that the present glue-based package worked safely. The working pressure in this hydrodynamic design is defined as the fluid pressure at the end of the reaction zone, i.e., the entrance of the pressure regulating zone. Considering that the fluid viscosity varied noticeably with the temperature, all physical properties were calculated at 50 °C, which was exactly the temperature of the pressure regulating zone when the reaction temperature was 145 °C. According to the phase chart in Figure 2, W_p was finally set as 5 μ m.

FABRICATION AND PACKAGE

Layout of the chip and its fabrication process is schematically shown in Figure 3. The real chip layout is different with the basic design showed in Figure 1. Considering the temperature variations of the three functional zones, the reagent mixing zone is put in between of the high-temperature reaction zone and the pressure regulating zone to reduce the thermal interference. The chip was fabricated as following steps: First, a 400 μ m-thick, 4 in. silicon (100) wafer was etched by deep reactive ion etching (DRIE) to the target channel depth (D_0) with a patterned photoresist as the etching mask. After removing the photoresist and passivating the wafer with a 100-nm-thick thermally grown oxide, the etched wafer was bonded with a Pyrex glass (550 μ m thick) by anodic bonding. The prepared microchannel was on the bonding interface. Then, the silicon wafer was thinned to 100 μ m from its back-side by a 150-min wet etching in an 80 °C KOH-bath. After depositing a 500-nm-thick SiO_2 as the dielectric layer by pressure enhanced chemical vapour deposition (PECVD), a lift-off process was applied to form the Cr/Pt (15 nm/300 nm thick) heating/sensing resistors on the silicon wafer. Another DRIE etched through the residual silicon to form the inlets/outlet along with the isolation trenches. Finally, the wafer was diced into pieces in size of 11 mm $\times$ 13 mm.

Hand-made PMMA gadgets were used to connect the chip and the tubing system with the help of a high-temperature/high-pressure silicone (704, Nanjing University). A MEMS sensor (YX-PS500-A with 1 μ m thick Parylene C for water-proof, 0.1–3 MPa, the First MEMS Comp., China) was connected between one inlet and the pump for pressure monitoring. To demonstrate the on-chip pressure regulating and the high-temperature/pressure reaction capabilities of the present microreactor, a syringe pump (TS-2 A, Lange Comp. China; maximum pressure capability of 5 MPa) was used to provide high-pressure fluid flows just for simplicity. As there are

FIG. 3. Layout of the present chip (a) and its fabrication process (b). Inserted figures in (a) showed the detail of the key components of the chip. Inserted SEM photos (from top to bottom) showed the cross section of the final isolation trench, the inlet with 5 μ m/20 μ m filters, and the pressure regulating microchannel and the outlet. All the scale bars were 300 μ m.

already many off-the-shelf products and various integration solutions of micropump,^{31,32} by further integrating an on-chip or in-package pumping function with the present chip in the future, a real miniaturized micro reactor could be finally achieved. The input power was supplied by a constant-voltage source (DH1718G-4, Dahua Comp. China) and all electrical read-outs were recorded by Agilent 34970A. Typical power supply for the present microfluidic reactor is around 1.5 W.

HYDRODYNAMICS AND THERMAL DIGESTION EXPERIMENTS

De-ionized (DI) water was used as the working fluid to evaluate the hydrodynamic performance of the present chip. As mentioned above, the increased temperature in the pressure regulating zone can reduce the fluid viscosity considerably and thereby lower down the flow resistance. In order to get a quantitative understanding of this thermal issue, micro heater/temperature sensor was also integrated in the pressure regulating zone to actively and independently control the temperature there. During the experiment, instead of being heated by the thermal cross-talk from the high-temperature reaction zone, the pressure regulating zone was purposely heated to different temperatures without powering the heater in the reaction zone. In addition, saturated sodium chloride (NaCl) in water (at room temperature) was used as the working fluid to test the function failure induced by phase-transition.

In the thermal digestion experiment, standard phosphorus solution (provided by Institute for Environmental Reference Materials, Ministry of Environmental Protection, China) and the potassium peroxodisulfate ($K_2S_2O_8$) buffer (the oxidant in the digestion) were pumped into the chip with different concentrations and different flow rates. After the reaction in the present chip, the product was incubated with ascorbic acid (100 g/l) and molybdic acid solutions (digested sample: ascorbic acid: molybdic acid solution = 8:1:1) for 10 min following the standard protocol.³³ Then the absorbance of the incubated mixture at 700 nm was measured by a spectrophotometer (Biospec-nano, Shimadzu Corp., Japan). All chemicals were purchased from Sigma with analytical grade unless otherwise stated.

RESULTS AND DISCUSSION

The experimental system and the fabricated chip are shown in Figure 4. Reagents, including DI water for the hydrodynamic evaluation, saturated NaCl solution for the boiling test and standard phosphorus solution along with $K_2S_2O_8$ buffer for the thermal digestion demonstration, were pumped into the chip from inlets, as shown in Figures 4(a) and 4(b).

Thermal isolation trenches successfully reduced the temperature increment in the pressure regulating zone which was caused by the cross-talk from the heated reaction zone. As shown in the infrared photos of the chips (Figure 5), the temperature of the pressure regulating zone (T_p)

FIG. 4. Photos of the experimental system and the fabricated chip. (a) Photo of the experimental set-up with a packaged chip as inset figure. (b) Photo of the chips with glass (left) and silicon (right) sides upwards.

FIG. 5. Infrared photos of the chips without (a) and with (b) thermal isolation trenches before package. The photos were taken by an infrared thermograph (FLIR SC7300) from the glass side of the chip.

was decreased from 90 °C (without thermal isolations) to 50 °C (with these trenches) when the reaction zone was heated to around 145 °C. T_P has an important effect on the pressure elevating performance since a high temperature here will dramatically decrease the water viscosity, and thereby make the pressure in the reaction zone drop correspondingly. For example, when T_P varies from 50 °C to 90 °C, the viscosity will decrease from 5.52×10^{-4} kg/ms to 3.18×10^{-4} kg/ms,³⁴ and the pressure at the reaction zone decreases from 1025.5 kPa to 591.7 kPa at a flow rate of 20 nl/s. To evaluate this T_P -sensitive working pressure characteristic, a microheater was placed on top of the pressure regulating zone to actively and independently tune the local temperature, i.e., T_P . Figure 6 showed the pressure regulating performance measured at different T_P with water as the working fluid. A reasonable consistence was found between the experimental measurements and the numerical calculation that extracted from the chip design. This T_P -sensitive working pressure characteristic could also be applied to actively and independently control the pressure regulating performance, which further expands the pressure adjustability of the present chip.

FIG. 6. Experimental and numerical pressure variation in the reaction zone with the flow rates at different T_P . The dashed circles indicated that the circumscribed line and marker stand for the same group, with lines for the numerical simulation results and markers for the experimental measurements. For the case with T_P of 50 °C, only numerical results were included. DI water was used as the working fluid. Error bar stands for three independent trials.

FIG. 7. Variation of the absorbance with the total phosphorus concentration at 700 nm. Inset figure showed the comparison of the chip (with different flow rates, i.e., different digestion times) and off-chip thermal digestion performances.

Saturated NaCl solution was used to evaluate the operability of the present continuous flowing micro reactor under the high temperature. As shown in the videos in the supplementary material,³⁵ the chip was capable of running the saturated NaCl solution at flow rate of 5 nl/s without phase transition at the reaction temperature of 145 °C. However, phase transition was found when the reaction temperature was raised to 180 °C, which led the chip failed soon by drying out the solution.

In the thermal digestion experiment, the reaction temperature was set at 145 °C. The ratio of the oxidant (the $K_2S_2O_8$ buffer) to the phosphorus sample was optimized in advance. The results indicated that a ratio of 4:1 had the highest digestion efficiency within the present experiment. Samples with different total phosphorus concentrations were digested by the present chip and the conventional method (5 b-1 COD Analyzer, Lianhua Tech., China) in parallel. Sample that flew through the chip, but without being heated, was also tested as a negative control. After the optimization which is shown in the inset of Figure 7, the total flow rate was set as 20 nl/s and the pressure at the reaction zone was elevated to 990 kPa (measured, also consistent with the calculation) to avoid the phase transition. The digestion time was calculated as 48 s based on the chip geometric size and the flow rate, only 3% of the time (30 min) required in the conventional autoclave based thermal digestion. The mechanism for this fast on-chip digestion still calls for further studies. A possible reason could be the short diffusion length of the present chip scheme, which leads to a rapid reagent mixing, compared to the conventional autoclave one. Based on the absorbance results, the digestion efficiency of the present chip was around 42% of the conventional method. As shown in Figure 7, the absorbance values of chip digestion showed a good linear relationship with the total phosphorus concentrations varying from 1 mg/l to 5 mg/l with the linear correlation coefficient of 0.996.

CONCLUSIONS

In summary, this work reported a continuous flowing micro reactor for high-temperature reaction. By utilizing silicon-based microfabrication techniques, pressure regulating function which resulted in an elevated boiling-point for the high-temperature reaction was successfully integrated with micro heater and temperature sensor in a small chip (11 mm × 13 mm). As a demonstration, thermal digestion of aqueous total phosphorus sample with pressure of 990 kPa (at flow rate of 20 nl/s) and temperature of 145 °C without phase transition was successfully

achieved. The present continuous flowing micro-reactor also preliminarily demonstrated its capability of controlling the working pressure independently by tuning the local pressure regulating temperature, T_p . Meanwhile, the reaction time can be adjusted by setting the flow rate corresponding. Combining the above two adjustments, the proposed micro-reactor scheme is able to fulfill a reasonable range of on-chip reactions.

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