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Fluid flow behavior and the rate of an enzyme reaction in deep microchannel reactor under high-throughput condition

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Abstract

Two different types of deep microchannel reactors, T- and To-types, were fabricated using glass substrates, and the reaction interface formed in each of them was observed using a flow visualization technique. The flow maldistribution was not observed even when the flow rate was increased to 100 mL/min in experiments using the To-type reactor. Analysis on the basis of a computational fluid dynamics simulation indicated that the flow maldistribution is caused by fabrication error, and it is strongly affected by the channel length and difference in the fluid properties. In an examination of the reactor performance using an enzyme reaction, it was shown that even at a high flow rate condition, the reaction rates in the deep microchannel reactors were higher than those in a beaker. It was concluded that To-type deep microchannel reactors are suited for building microreactor systems with a throughput in the order of 10^4 tons per year.

Keywords: Microreactor; Throughput; Maldistribution; Enzyme reaction: Computational fluid dynamics

1. Introduction

Microchannel reactors or microreactors are effective in improving the selectivity and yield of many chemical reactions. However, its application area is considered to be limited to pharmaceutical and a part of fine chemical industry, where small amount of highly expensive substances are produced. This is primarily because the maximum throughput of an ordinary single microchannel reactor is usually in the order of a few tons per year.

The numbering-up concept is often regarded as a technique suited for increasing the throughput of a microreactor system. In this concept, the throughput is increased by parallelizing many identical microreactors or microchannels. Numbering-up is sometimes regarded as one of the advantages of microreactor technology. When the optimal microreactor design and its operating conditions are found in laboratory experiments, a commercial scale production plant can be designed in this concept more quickly than in the conventional scaling-up approach, which requires repetitive performance testing and process modification at several different throughput levels.

However, there are several problems associated with realization of chemical processes by practicing numbering-up concept. In order to operate the hundreds of reactors at an identical condition, the control and monitoring system must be carefully designed. Also it is necessary to design a device to split feed stream into hundreds of small ones with an equal flow rate. The problem of equal flow splitting has been studied by several researchers [1–3] using numerical simulation. Tonkovich et al. [4] also derived a manifold design for uniform flow splitting and verified the results experimentally. These results are directly applicable to the microdevices with single feed for a single channel, such as micro-heat exchangers and microreactors for heterogeneous catalytic reaction with premixed feed. Schenk et al. [5,6] conducted an experimental study on a unit for splitting one feed into six equal streams for external numbering-up devices.

The task of increasing the throughput of the microreactors treating more than two reactants in one channel is more challenging than that of microdevices handling a single fluid in a single channel. This is because the quality of flow distribution is more important in the former case, and maldistribution of reactants results in variations in the inlet concentration and residence time, which often reduces conversion and selectivity.

Recently, several high-throughput microchannel devices that can handle more than two feed streams have been presented. In a study of mixing performance in an microreactor with interdigital contacting and flow focusing, Löb et al. showed that SuperFocus micromixer showed the throughput of 320 L/h at the pressure drop of 10 bar [7]. Werner et al. presented a

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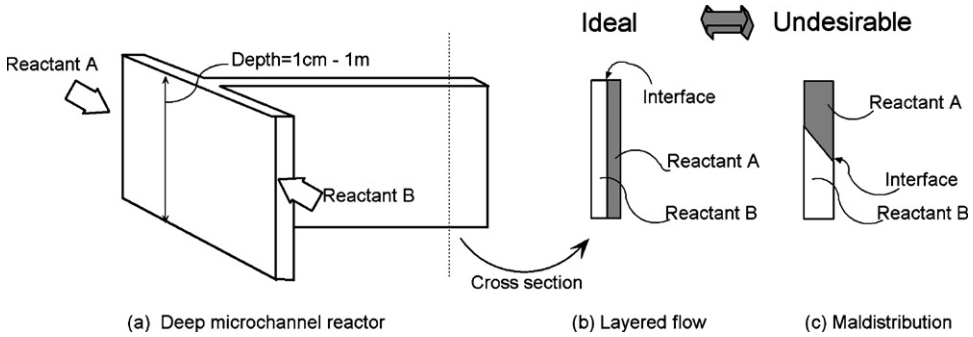

Fig. 1. The concept of deep microchannel reactor (FMR) and anticipated flow pattern.

high-throughput micromixer called StarLam 300 and StarLam 3000 [8]. The throughput of the StarLam 3000 was 3000 L/hr at a pressure drop of 0.7 bar, while that of StarLam 300 was 1000 L/h at 3 bar. Ehrfeld Mikrotechnik developed a mixing device called LH-1000, which is capable of handling 1000 L of liquid medium per hour at a pressure drop of 1 bar [9].

In the present study, we suggest use of a deep microchannel reactor (referred to as FMR in the followings), having a channel depth of few cm to 1 m (Fig. 1a) for treating more than two reactants at a high rate. In a FMR with a channel depth of 1 cm, the throughput can be increased 100 times greater than that of a microchannel reactor which is 100 μm in depth. By using a FMR with a channel depth of 1 m, or by parallelizing 10 FMRs with a depth of 10 cm, the production rate can be made 10000-fold greater than in normal microreactors. There are several reports that discuss microreactors developed on a similar idea [10,11]. Okamoto et al. [10] presented a planar type microreactor and conducted an addition reaction between phenylisocyanate and ethyl alcohol. Also a high-throughput process for a heterogeneously catalyzed reaction has been built by stacking plates with integrated slits [11].

Although FMR is simple in its concept, the problem of flow distribution needs to be treated carefully before it is realized in an industrial scale. In ordinary microchannels, the two reactants flow side by side and thus the diffusion length is shorter than in conventional vessels. Analogously, for a FMR to exhibit a good performance as observed in microchannel reactors, the reactants should form a layered flow as shown in Fig. 1b. However, due to the deep microchannel, a small disturbance in the flow or fabrication error would result in flow maldistribution as shown in Fig. 1c. This gives an adverse effect on the reactor performance since it reduces the interface area and extends the diffusion or mixing time. In the previous studies including those introduced above, however, no study has been conducted to investigate the fluid flow in deep microchannels, and the effect of channel geometry on it.

The objective of the present study is to clarify the performance of FMRs as a chemical reactor. As a first step, the fluid behavior in FMRs was studied by using flow visualization technique, and the channel geometry that is tolerant to fabrication error was investigated. CFD simulation was also conducted to examine the effects of channel geometry on the flow distribution. Also an enzyme reaction was carried out to study the performance of FMRs.

2. Reactor fabrication

2.1. Deep microchannel reactor

Two different types of FMRs were fabricated in this study and their outlines are depicted in Fig. 2. The figure shows the arrangement of glass plates for walls only, in order to avoid possible confusion. The top and bottom plates, which are not shown here, were also fixed to form a closed deep microchannel. Fig. 2a illustrates the T-type FMR, where two reactants are brought into contact in a deep T-intersection. The other (Fig. 2b) is referred to as To-type FMR, and a reactant is injected vertically to the stream of the other. Each FMR consisted of a main channel, two subchannels and two manifolds. The both main

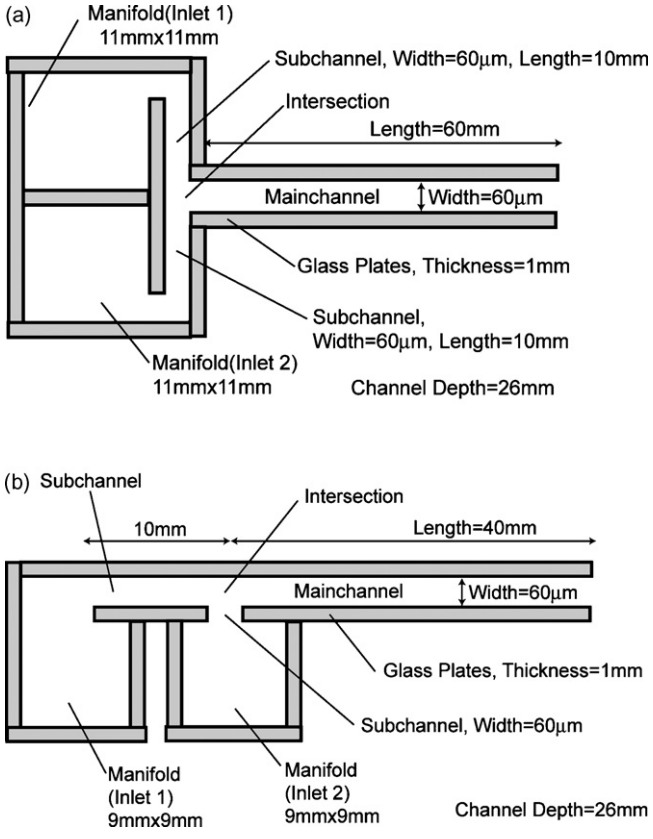

Fig. 2. Outlines of FMRs fabricated in the present study. To avoid possible confusion, only glass plates for walls are shown. (a) T-typeFMR. (b) To-type FMR.

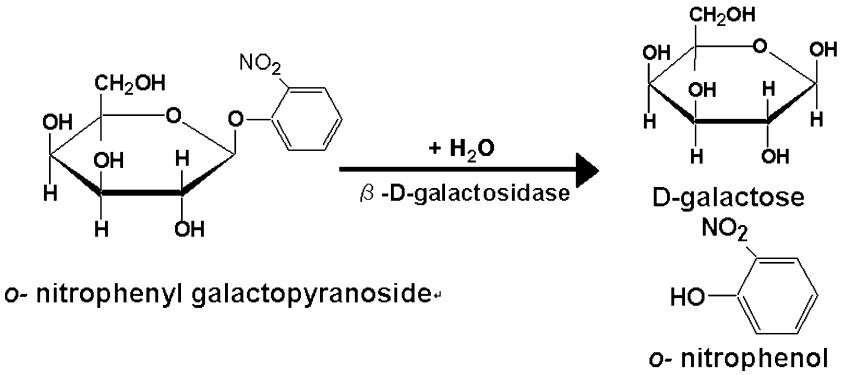

Fig. 3. Hydrolysis of *o*-nitrophenyl galactopyranoside.

and subchannels were 60 μm in width and 26 mm in depth. The cross-section of each manifold was approximately 1 cm^2. This was to realize uniform pressure distribution along the entrance to each subchannel by minimizing the mean velocity in the manifold.

Both FMRs were fabricated using glass substrates, which were 76 mm in width, 26 mm in depth and 1.0 mm in thickness. The substrates were cut into small pieces of appropriate sizes and manually assembled using epoxy resin adhesive. In order to feed the reagent to the FMR, teflon tubes, which were 0.5 and 1.6 mm in inner and outer diameters respectively, were inserted into the holes on the top plate, and fixed with epoxy resin adhesive.

2.2. Microreactor

A microreactor with a Y-shaped microchannel was also fabricated with glass substrates. This was used in the enzyme reaction experiments to obtain reference data to evaluate the performance of the FMRs. The microchannel was 500 μm in width, 200 μm in depth and 40 mm in length. A desktop machining system (EXG-300, Roland DG, Japan) was used to form the Y channel on a glass substrate which was 30 mm in width, 70 mm in length and 2 mm in thickness. Two holes for inlets and one hole for outlet were drilled on the substrate. The channel thus formed was sealed with another glass plate by fusion bonding technique. Teflon tubes, which were 0.5 and 1.6 mm in inner and outer diameter, respectively, were connected to these holes.

3. Experimental

3.1. Flow visualization experiment

The location of the interface between two fluids was observed by visualizing it by using reaction between a bromothymol blue (BTB) solution and a sodium hydroxide solution. Yellow BTB solution was prepared by adding few drops of acetic acid to a 0.04% BTB solution. The concentration of the sodium hydroxide solution used was 0.1 M. When these solutions were brought into contact, the interface changes its color to blue. In the experiments at low flow rates (≤2 mL/min), the solutions were fed to a microreactor or a FMR using a syringe pump (IC-3210, KdScientific, USA), while diaphragm pumps (DME-8-10A, Grundfos) were used in the high flow rate experiments (≥10 mL/min).

3.2. Enzyme reaction

Fig. 3 shows the enzyme reaction carried out in the present study. This is hydrolysis of *o*-nitrophenylgalactopyranoside (ONPG) by β-galactosidase. It was shown in a previous study that the reaction rate was faster in a microchannel than in a beaker [12]. The exact reason for the acceleration was not clarified yet. One of the suggested reasons for this was an increased surface to volume ratio in the microchannel, on which enzyme molecules may be adsorbed.

A phosphate buffer (0.15 M, pH 7) was prepared by dissolving sodium dihydrogen phosphate and di-sodium hydrogen phosphate in distilled water. The substrate and enzyme solutions were prepared by diluting ONPG (Lot PGK1448, Wako, Japan) and β-galactosidase (E.C.3.2.1.23, Lot CEU0261, Wako, Japan) using the buffer solution. The concentrations were 0.1 mg/mL and 0.01 mg/mL, respectively.

The enzyme reaction was conducted in three different types of reactors: a beaker, the microreactor, and the FMRs. In the beaker experiments, 20 mL of each solution was preheated in a water bath at 325 K. The reaction was initiated by mixing these solutions in a beaker in the water bath. 1 mL of sample was taken from the reaction mixture every 30 s. The sample was immediately mixed with 3 mL of a sodium carbonate solution (1.0 mol/L) in order to stop the reaction.

In the experiments using microreactor or FMRs, the reactor was immersed in a water bath that was kept at 325 K. The residence time was controlled by changing the length of the tube connected to the outlet. After steady state was reached, 1 mL of reaction mixture was taken from the tube outlet, and immediately mixed with 3 mL of a 1.0 mol/L sodium carbonate solution. Nitrophenol, which is one of the reaction products, absorbs light at 420 nm, and so the solution turns yellow after the reaction. Thus, the absorbance of the solution at 420 nm was measured using a UV-vis spectrophotometer (UV-2500, Shimadzu, Japan) to measure the concentration of the *o*-nitrophenol in the reacted mixture.

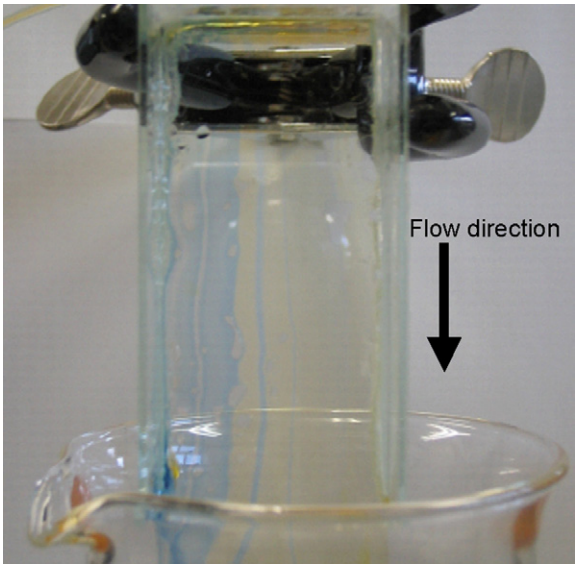

Fig. 4. Observed interface in To-type FMR (BTB = 1.0 mL/min, NaOHaq = 1.0 mL/min).

4. Results and discussion

4.1. Flow visualization experiment

Fig. 4 shows the flow pattern observed in the T-type FMR in a flow visualization experiment. It was observed that color change to blue was observed only in the left half, indicating maldistribution of the solutions in the main channel. This experiment was conducted by varying the orientation of the FMR. It was found that the area of blue color change was the largest when the reactor was placed in such a way that the fluid flowed to the direction of gravity. Five T-type FMRs of identical design were additionally fabricated and the experiment was repeated. However, the area of the blue color change did not extend to the entire area in any experimental runs.

In case of the To-type FMR, the color change to blue was observed in the entire area, as shown in Fig. 5a. This means the fluid flow in the To-type FMR is layered as shown in Fig. 1b. Additional four To-type FMR were fabricated and the experiment was repeated for each of them. It was revealed that in each experimental run, the color change was observed in the entire area.

In order to examine the distribution of the interface at high flow rate, another To-type FMR was fabricated. The only difference from the previous design was that the new reactor was connected a tube which was 6 mm in inner diameter. The BTB and sodium hydroxide solutions were fed at a rate of 50 mL/min each. Despite the presence of small pulsation in the fluid flow due to operation of diaphragm pumps, the blue color change was observed in the entire area as shown in Fig. 5b. It was revealed that the To-type FMRs can be used to increase the throughput without occurrence of flow maldistribution.

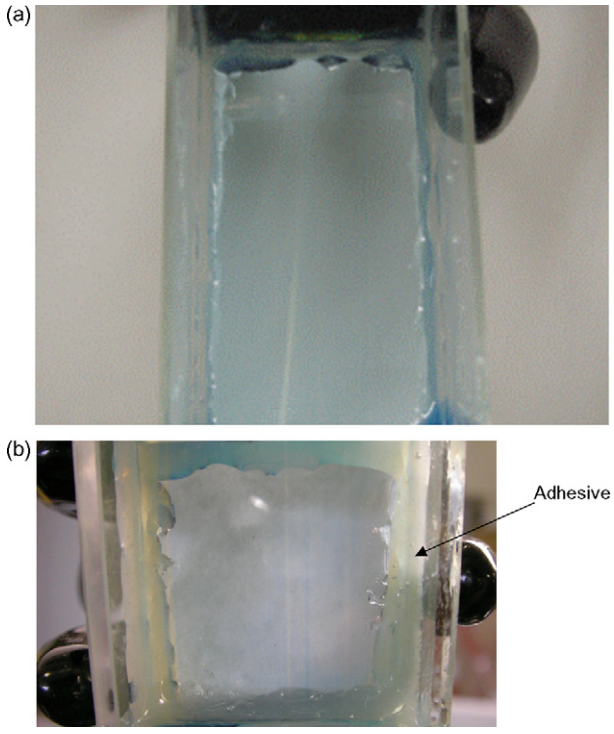

Fig. 5. Observed interface in To-type FMR. (a) Low flow rates (BTB = 2.0 mL/min, NaOHaq = 2.0 mL/min). (b) High flow rates (BTB = 50 mL/min, NaOHaq = 50 mL/min).

4.2. Enzyme reaction

The performance of the FMRs as a reactor was evaluated using the enzyme reaction. As a reference, the reaction was carried out in a beaker and a glass plate microreactor. Fig. 6 shows the evolution of *o*-nitrophenol concentration with the residence time.

In an experiment using the ordinary microreactor, the substrate and enzyme solutions were fed to the reactor at a rate of 0.1 mL/min each. The reaction rate observed in the microreactor was higher than that in the beaker, as reported previously [12]. The FMR was operated at the same flow rates, the reaction rate observed in the FMR was comparable to that of microreactors. Fig. 6 also shows the change in *o*-nitrophenol concentration,

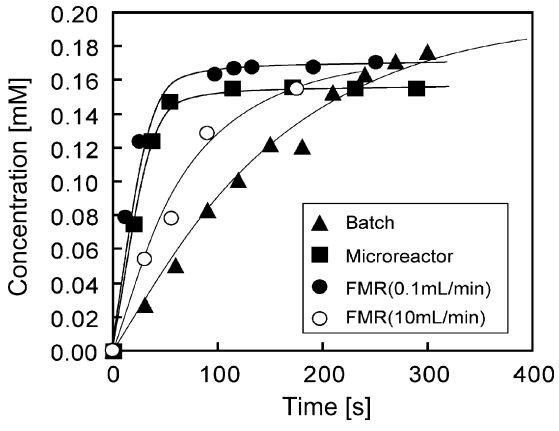

Fig. 6. Evolution of *o*-nitrophenol concentration in various reactors.

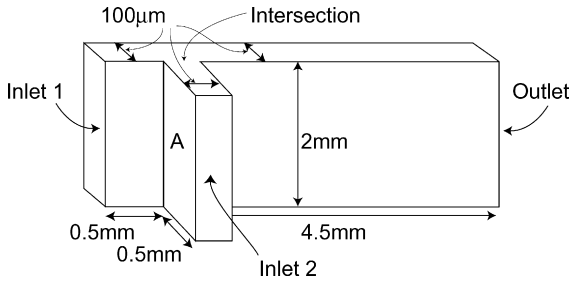

Fig. 7. Channel geometry assumed in CFD simulation.

when the flow rate of each solution was 10 mL/min, which was 100 times greater than that in the microreactor experiments. Although the measured reaction rate was smaller than that observed in the low flow rate operation, it was substantially higher than that in the beaker.

4.3. Fluid dynamics simulation

The performance of the reactor strongly depends on how the feed solutions are distributed in the main channel. When the channel walls of the T-type FMRs are sufficiently smooth, and are perfectly oriented, the fluid resistance and thus the flow distribution will be uniform. In reality, however, it is not possible to align the channel walls in parallel exactly in the process of assembling glass pieces. In this study, therefore, the effect of slanted channel wall on the flow distribution was examined using computational fluid dynamics (CFD) simulation.

Fig. 7 shows the channel geometry assumed in the numerical simulation. In order to reduce the computational load, the depth of the geometry was assumed to be 2 mm, and the main channel was assumed to be 4.5 mm in length. The distance from each inlet to the intersection was 0.5 mm. The channel width was assumed to be 100 μm. The computational grid consisted of approximately 200,000 nodes. The simulation was carried out using a commercial CFD software (Fluent 6.2, Fluent Inc, USA). The channel depth and the length assumed in the simulation were smaller than those in the channels used in the experimental work. To study the distribution in the channel the grid size must be in the order of 10 μm, while the channel depth and length were in the order of centimeters. When the channel geometry in the simulation was assumed to be exactly the same as that in the experiment, a large number of numerical grids were required, and thus the problem becomes computationally extremely expensive.

It was assumed that the channel wall marked A in Fig. 7 was slightly tilted inwards, and the top end of the subchannel was narrower. Fluids 1 and 2 were assumed to be entering from inlets 1 and 2, respectively. The density and viscosity of each fluid were 1000 kg/m^3 and 0.001 Pas, and the volmetric flow rate was 0.02×10^{-6} m^3/s. The diffusion constant was assumed to be 1×10^{-9} m^2/s.

When tilt is 0, both velocity and the fluids were uniformly distributed. Fig. 8a shows the distributions of velocity and Fluid 1 on the plane in the middle of the main channel. The tilt of 1° decreased the flow rate of Fluid 2 on the upper half, and caused uneven material distribution as shown in Fig. 8a. The velocity distribution was not uniform just after the intersection, but it became uniform in the downstream. This was because the channel walls in the downstream of the intersection were assumed to be exactly parallel to each other, and the both fluid had the same property.

The effect of fluid property on the uniformity of the distributions was examined. In this simulation, the density and viscosity of the Fluid 1 were assumed to be 791 kg/m^3 and 0.0003 Pas, respectively. The volumetric flow rate of each fluid was again 0.2×10^{-6} m^3/s, and the distributions of velocity and Fluid 1 were calculated. The results were summarized in Fig. 8b. Again, the uneven material distribution was observed. The velocity distribution was not uniform even in the downstream of the intersection.

It should be also noted that the velocity was higher in the upper half of the main channel, where flow rate of Fluid 2 was smaller. The uneven velocity distribution was caused by the difference in the viscosity of the fluids. In the upper half of the reactor, the fraction of Fluid 2 is smaller. Since Fluid 2 is more viscous than Fluid 1, the average viscosity is lower in the upper half than the other half. Since the uneven distribution was caused by the difference in the viscosity of the fluids, the distribution could become uniform only when the diffusion in the depth direction was complete and a homogeneous mixture was obtained. However, in the FMRs, where depth is longer than a few centimeters, the time needed for this diffusion is much longer than the residence time in the reactor. It can be concluded that the fluid property as well as the fabrication error gives rise to maldistribution of the flow.

The influence of the subchannel length on the fluid behavior was also examined. The fluid dynamics simulation was carried out for the case when the subchannel was 2.5 mm long. This is 5-fold longer than the previous cases. The tilt of wall A was assumed to be 1°, and the fluid properties were assumed to be the same as those in Fig. 8b. Fig. 8c shows the distributions of velocity and fraction of Fluid 2. As compared with Fig. 8b, the maldistribution appeared to be greater. When the subchannels were long, the flow resistance in the subchannels strongly influenced the total flow resistance. Therefore a small tilt of channel wall strongly influences the distribution of the flow resistance along the channel depth. Thus, the effects of fabrication error of the subchannels on the flow distribution can be minimized by employing short subchannels.

The fluid flow in a T-type FMR was also numerically simulated. Fig. 9 shows the fraction distribution of Fluid 2 under the condition similar to that of Fig. 8c except that the channel was of T-type. The simulation results showed that the flow maldistribution was more prominent in the T-type than the To-type FMR under the similar fabrication error.

These simulation results support the observation that the flow distribution was more uniform in the To-type than that in the T-type FMR. The shortest subchannel was only 1 mm in the To-type FMR, while that of T-type microreactor was 10 mm. This means that uniformity of the flow distribution of the T-type FMR used in the study was more vulnerable to the fabrication error

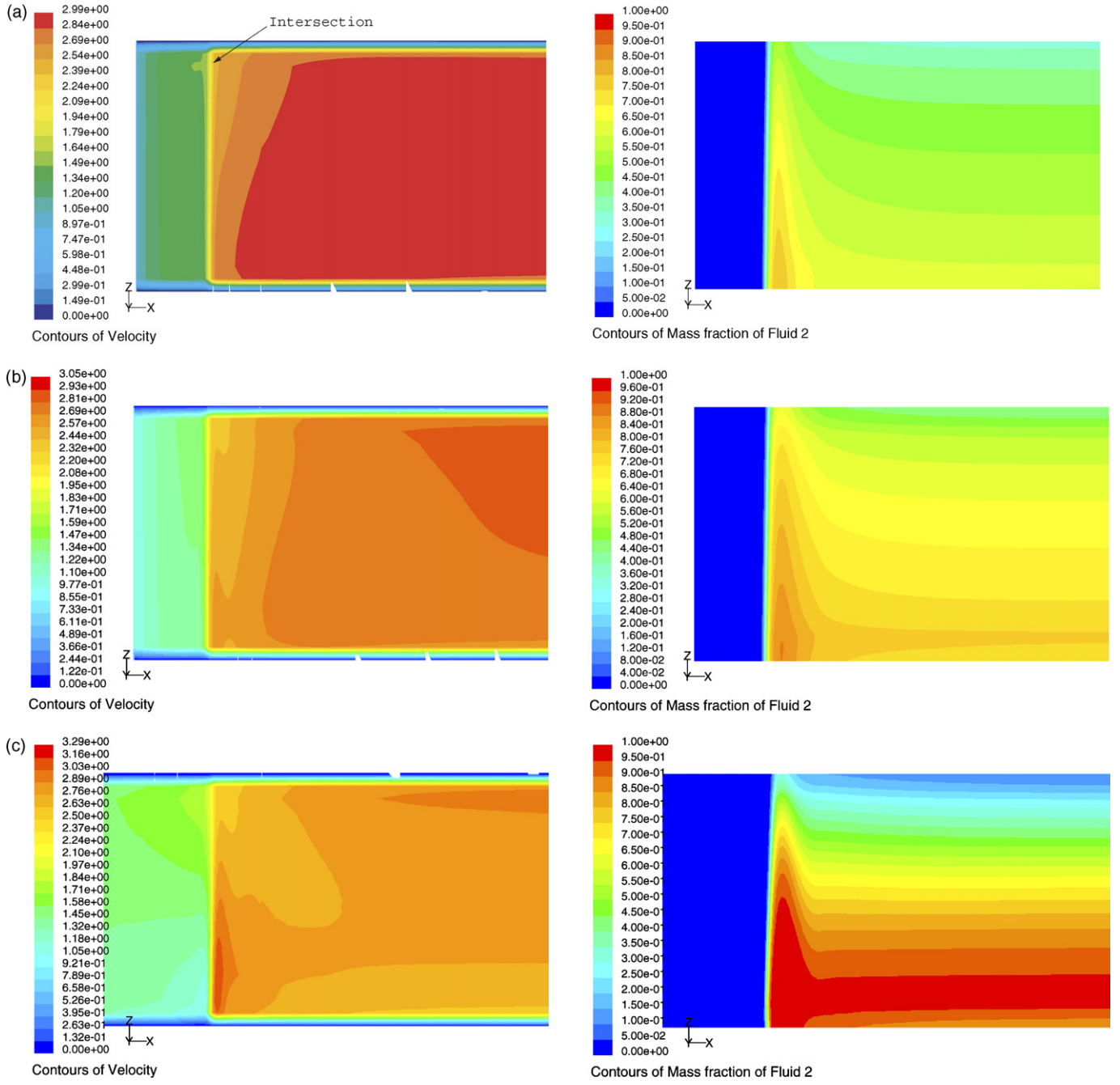

Fig. 8. Distributions of velocity and fraction of Fluid 2 in FMR. The unit of velocity is m/s. (a) The density and viscosity of both fluids were 1000 kg/m^3, 0.001 Pas, respectively. (b) The density and viscosity of fluid 1 were 791 kg/m^3, 0.0003 Pas, respectively. (c) Each subchannel was 5 mm in length.

than that in the To-type, because of both channel shape and the dimensions.

4.4. Pressure drop

When the properties of Fluid 1 is similar to that of Fluid 2, the pressure drop per channel length $\Delta P/L$ can be calculated by the following equation.

$$\frac{\Delta P}{L} = \frac{12\mu Q}{W^3 D} \quad (1)$$

where μ, Q, W and D are fluid viscosity, volumetric flow rate, width and depth of the channel, respectively. In case of the FMR in Fig. 5b the pressure drop across the reactor was calculated to be 2.0 bar, which higher than those reported for the case of LH-1000 or StarLam 3000. This is because the length of the microscale channels were longer in the FMRs. However, the pressure drop can be reduced easily by forming a deep microchannel in FMRs. The channel depth needed for a given pressure drop can be calculated from Eq. (1), and when the calculated depth is too great, several FMR should be used in parallel.

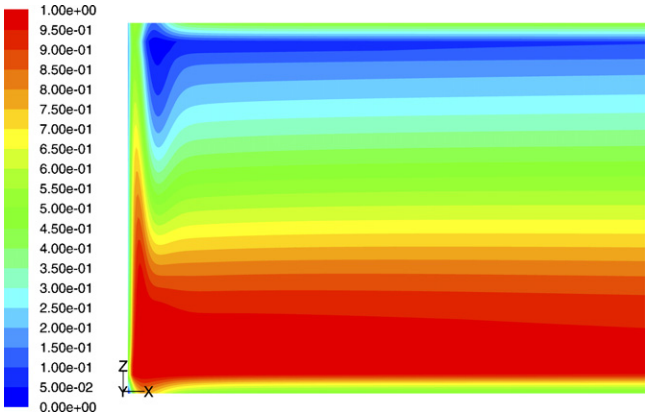

Fig. 9. Distribution of Fluid 2 in T-type FMR. The subchannels were 5 mm in length.

5. Concluding remarks

The performance of deep microchannel microreactor was examined. The flow visualization experiment revealed that by using To-type FMR, the flow maldistribution can be effectively suppressed. The simulation study supported this and indicated that the flow maldistribution is caused by fabrication error, and it is strongly affected by the channel length and difference in the fluid properties.

FMRs have a main channel and fluid manifolds, which, with a large cross-sectional area, made an even pressure distribution along the depth of the main channel. The results showed that the flow maldistribution arising from the fabrication error can be minimized by employing To-type geometry and a short subchannel, which can be easily realized in a practical setting, by forming the manifolds near the main channel.

An enzyme reaction was also conducted to examine the performance of FMR as a reactor. The FMR showed an enhanced reaction rate as was observed in the ordinary microchannel reactors. It was therefore concluded that the To-type FMR can be used to increase the throughput of the microreactor system. In the present study, the maximum flow rate used were 100 mL/min, which is approximately same as 50 m^3 per year. If 10 identical FMRs with a depth of 26 cm are used in parallel, the reactor system can process 5000 tons of aqueous solutions per year. Another advantage of To-type FMRs is that its design can be easily modified so that more than three reactants can be handled.

The FMR used in the study was manually assembled by members at the University of Tokushima. By using more sophisticated fabrication technique, FMR with smaller fabrication error can be obtained. Flows in such FMRs are expected to be more uniform than those observed in the present study. However, change in the effective channel geometry is anticipated after a long time of operation due to corrosion, fouling and mechanical deformation. The observations in the present study showed that in the To-type FMR, the flow distributions would remain uniform even after long time of operation.

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