Characterization of Water/Organic Biphasic System in Liquid-Liquid Slug Flow under Hydrothermal Conditions: Solvation, Vorticity, and Hydrophobicity

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The microcapillary was combined with the liquid-liquid slug flow to build the separation field. The partition behavior of seventeen kinds of substrates was investigated by using six kinds of water/organic biphasic systems under hydrothermal conditions (25 – 190°C at 10 MPa). The scale of hydrophobicity ($H_F$) of water/organic biphasic system was estimated. The $H_F$ value for the biphasic system used here was comparable to the conventional aqueous two-phase systems and depended on the (de)solvation of substrates by water and organic solvent. Besides, the vortex field in the slug contributed to the enhanced mass transfer of substrates. Those results are available for the selection of water/organic biphasic system as the reactive separation of target materials.

1. Introduction

Biomasses have recently come to an attention because they yield the value-added materials such as 5-hydroxymethylfurfural (HMF) [1-5], 2,5-furandicarboxylic acid (FDCA) [4,6], and lactic acid [7,8]. Those value-added materials are obtained from cellulose. Cellulose that is a typical woody biomass is resistant to chemical and biological catalysts. The degradation treatment of cellulose has been then reported: an enzymatic hydrolysis [9], a microwave pyrolysis [10], and a hydrothermal treatment [11-16]. The utilization of the biomass as the chemical platform requires not only a design of the catalytic reaction process, but also an adequate separation method of the value-added materials from the residues. The effective separation method applicable under the wide operational conditions including subcritical water condition has been therefore demanded.

Many types of reaction processes has been developed by considering the separation stage [17,18]. For examples, the reaction process combined with the countercurrent extraction by water/methyl isobutyl ketone (MIBK) achieved high yield of HMF (~99%). The capillary typed-reactor has been also developed to avoid the production of by-products. Thereby, a rapid temperature control allows us to achieve the improved yield of lactic acid under the hydrothermal reaction condition (453 K, 10 MPa) [19]. The capillary-type reactor is easy to combine with the water/organic biphasic system to achieve the selective separation of target compounds during the reaction process. The continuous reaction and separation of HMF has been achieved with avoiding its degradation in water phase [20,21], despite that the conversion of glucose or fructose to
HMF affords many by-products in the reaction pathway \([22]\) and decomposability of HMF in water \([1,11,22]\). Thus, a combination of capillary-typed reactor with the biphasic system as the separation field is promising from the viewpoints of the process intensification as well as the reactive extraction column \([17,18]\).

In the method to form the biphasic system in a capillary-typed reactor, mixing of two liquids through a Y- or T-junction has been utilized because these methods require lower energy consumption for the formation of biphasic interface \([23,24]\). Thereby, several types of biphasic system have been developed: the emulsion system (oil-in-water or water-in-oil droplet with micrometers in diameter) \([25]\), the laminar flow \([26]\), or liquid-liquid slug flow \([20,21,27]\). Of these two-phase systems, the liquid-liquid slug flow is one of the most promising biphasic systems. The prominent feature is that the surface-to-volume ratio of the liquid-liquid biphasic system is controllable by the volume flow ratio \([23,24]\). Accordingly, the liquid-liquid slug flow exhibits excellent mass transfer characteristics and provides a well-defined interfacial area relative to the emulsion system \([27-29]\).

The reaction and separation operation is simultaneously performed in the capillary-typed reactor \([30]\). The prominent feature of the capillary-typed reactor combined with the liquid-liquid slug flow is the improved yield due to the rapid temperature control including the hydrothermal conditions \([19-21]\). In our previous studies, the fundamental characteristics of liquid-liquid slug flow for the water/MIBK biphasic system under the hydrothermal conditions has been examined based on the aqueous two-phase partitioning method \([31]\). This method allows us to quantitatively compare the partitioning behavior of the variety of substrates and to give the quantitative index for the adequate selection of hydrophilic and hydrophobic liquids. However, other biphasic systems of the liquid-liquid slug flow under the hydrothermal conditions have not far been completely characterized in details.

In this study, we characterized the water/organic biphasic system of liquid-liquid slug flow in the capillary under the high temperature and pressurized conditions. Previously, it was confirmed that the concentration ratio of the substrate between organic and water phases \((K_{ex})\) was not the intrinsic partition coefficient \([31]\). This was because the partition behavior of thirteen substrates in water/MIBK biphasic system depended the operational conditions. The resulting \(K_{ex}\) value was again defined as the apparent partition coefficient \([31]\). Whether the \(K_{ex}\) value obtained in other biphasic systems was the index responding the partition behavior was then examined in terms of velocity of liquid-liquid slug flow, the temperature, and pressurized conditions. The advantages of the slug flow as the separation field were also discussed by using the variety of substrates including HMF derivatives, amino acids, and sugars. These substrates are typical to the molecular conversion of cellulose as biomass. Finally, the generality of the present biphasic system was discussed, taking into consideration the application to the biomass conversion process.

2. Experimental

2.1 Reagents

Methyl isobuthyl ketone (4-methyl-2-pentanone; MIBK), decane, octanoic acid, 2-butanol, and dimethylsulfoxide (DMSO) were purchased from Wako Pure Chemical Industry. Ltd. (Osaka, Japan). Seventeen substrates shown in Table 1 were purchased from Sigma Aldrich (Tokyo, Japan). Other chemical reagents were of analytical grade. Polyetheretherketone (PEEK) tubes and SUS316 tubes were obtained from GL Science, Co. Ltd. (Tokyo, Japan).
2.2 Set up of the partitioning system

The flow system used in this study is shown in Figure 1. In short, 1.5 g/L of HMF solution was prepared without a pH adjustment by an acid or alkali ne because the activity coefficient of solutes could be approximated to be unity. Thereafter, the solution was injected to mix with the organic MIBK solvent. The mixture was incubated in a heating bath (25 - 190°C) and thereafter cooled to 20°C. The pressure was elevated to 10 MPa by controlling the back pressure valve. The time for the partition of HMF was defined as the residence time, which was determined by the flow rate. The same operation was performed for other substrates. The distribution was monitored for 400 seconds to quantify the amount of HMF in the MIBK phase. No significant influence of either cooling bath or the separation at the terminal to the partition behavior of substrates had been confirmed in advance. The same was true for the measurement of other substrates shown in Table 1. Notably, the pH value of the solution for amino acids bearing the individual isoelectric point (pI) might affect their partition behavior. The amino acid was solved in distilled water to indicate pH 6 of the solution. The temperature shift to 190°C reduced the pH into 5.8 [32]. Therefore, it was considered that the hydrothermally induced-pH shift at the heating bath made it possible to adjust the pH to near pI of amino acids shown in Table 1 (referred from literature [33]). Likewise, other biphasic systems were prepared by changing both water and organic solutions as summarized in Table 2.

2.3 Determination of the concentration of substrates and reaction

The concentration of substrates in the water and organic phases was analyzed by the high performance liquid chromatography. The column used was a COSMOSIL 5C18-AR-II Packed Column (4.6 × 250 mm, Nacalai Tesque Co. Ltd., Japan). 5 μL of the sample was loaded to the column (equilibrated at 40°C) at a flow rate of 1.0 mL/min. The mobile phase was MeOH/H₂O = 20/80 (wt/wt). The HMF in the sample was detected by a peak at 254 nm in wave length, by using the photodiode array detector (SPD-M20A, Shimadzu Co. Ltd.). The peaks derived from the water and the MIBK phases were eluted at 10 and 45 min. Some substrates were detected by the refractive index (RI) detector. The hydrothermal HMF conversion from fructose in the presence of hydrochloric acid was performed according to the previous procedure [20,21]. The maximal yield of HMF in several water/organic biphasic systems was recorded.
Table 1. Partition behavior under high temperature and pressure (25 and 180°C at 10 MPa, \(V_{\text{MIBK}}/V_{\text{water}} = 1\)).

| Entry | Substrate         | MW [g/mol] | \(\log P_{ow}^*\) | \(K_{ex}[-]\) | \(25^\circ C\) | \(180^\circ C\) |
|--------|-------------------|------------|-------------------|--------------|----------------|-----------------|
| S1     | 2-Acetylfuran     | 110.1      | 0.50              |              | 5.24           | 5.27            |
| S2     | Furfural          | 96.09      | 0.41              |              | 5.35           | 5.83            |
| S3     | Furfuryl alcohol  | 98.1       | 0.28              |              | 2.38           | 2.43            |
| S4     | HMF               | 126.1      | -0.15             |              | 0.91           | 0.92            |
| S5     | Lactic acid       | 90.08      | -0.62             |              | 0.081          | 0.087           |
| S6     | FDCA              | 156.1      | -0.91             |              | 0.008          | 0.010           |
| S7     | Tryptophan        | 204.2      | -1.05 (5.89)      |              | 0.37           | 0.40            |
| S8     | Phenylalanine     | 165.2      | -1.38 (5.48)      |              | 0.31           | 0.38            |
| S9     | Valine            | 117.2      | -2.26 (5.96)      |              | 0.28           | 0.32            |
| S10    | Threonine         | 119.1      | -2.94 (6.16)      |              | 0.25           | 0.27            |
| S11    | Glycine           | 75.07      | -3.21 (5.97)      |              | 0.24           | 0.26            |
| S12    | Glucose           | 180.2      | -3.10             |              | 0.014          | 0.014           |
| S13    | Fructose          | 180.2      | -3.20             |              | 0.018          | 0.022           |
| S14    | Sucrose           | 342.3      | -3.70             |              | 0.017          | 0.016           |
| S15    | Cellobiose        | 342.3      | -4.70             |              | 0.014          | 0.014           |
| S16    | Maltose           | 342.3      | -5.03             |              | 0.014          | 0.015           |
| S17    | Treharose         | 342.3      | -5.48             |              | 0.014          | 0.015           |

* The \(\log P_{ow}\) value that is the concentration ratio of substrate in octanol to water phase represents the hydrophobicity of individual substrate. The value in parenthesis is pI value [33].

Table 2. Properties of various biphasic system in slug flow.

| Entry | Water phase | Organic phase   | \(T\Delta S_0\) [kJ/mol] | \(\alpha\) [-] | \(HF(180^\circ C)\) [mol/kJ] |
|-------|-------------|-----------------|--------------------------|----------------|--------------------------|
| T1    | water       | MIBK            | -0.14                    | 0.93           | 0.035                    |
| T2    | water       | MIBK+2-butanol  | 0.05                     | 0.92           | 0.033                    |
| T3    | water +DMSO | MIBK            | -0.39                    | 0.93           | 0.036                    |
| T4    | water+DMSO  | MIBK+2-butanol  | -0.1                     | 0.91           | 0.035                    |
| T5    | water       | Octanoic acid   | -2.5                     | 0.92           | 0.050                    |
| T6    | water       | Decane          | -7.9                     | 0.93           | 0.084                    |

2.4 Numerical calculation of liquid-liquid slug flow

A mathematical method was adopted to simulate the liquid-liquid slug flow with a free surface and in
order to study and predict slug generation, shape and hydrodynamics. The hydrodynamics were calculated by the finite-volume method [27,28] and implemented in the open source software OpenFoam. The fluids were described using the incompressible Navier-Stokes equations. The governing equations of the volume-of-fluid method formulations for the liquid-liquid are comprised of the equation of continuity, the equation of motion, and the volume fraction equation.

3. Results and Discussion

3.1 Partition behavior of HMF in the liquid-liquid slug flow under various conditions

In the first series of experiments, the partition behavior of HMF (entry S4 in Table 1) previously confirmed in the liquid-liquid slug flow of water/MIBK biphasic system (T1 in Table 2) [31] was investigated by using five other types of biphasic systems (T2 – T6, shown in Table 2). Octanoic acid and decane were selected in terms of solubility to water. In addition, 2-butanol or DMSO was added to vary the dielectric constant of solvent, anticipating their contribution to the partition behavior of substrates with the variety of hydrophobicity (log $P_{ow}$ in Table 1). In our previous report [20,31], the vortex field in slug promoted the partition behavior of HMF in the T1 system. The formation of the vortex field depended on operational conditions such as the temperature, the flow rate ratio, and the line velocity [20,27,28,34-36]. Therefore, the partition behavior of HMF in T1 – T6 systems was examined under the operation conditions mentioned above.

The concentrations of HMF in organic and water phases for each biphasic system ($C_{org}$ and $C_{water}$) were measured to estimate the concentration ratio $C_{org}/C_{water}$ (Figure 2(a)). The residence time defined as the contact time of both phases during the passage of heating bath determines the partition behavior of HMF (Figure 1). As shown in Figure 2(a), the $C_{org}/C_{water}$ value increased as prolonging the residence time and was saturated in the constant value after passing 60 seconds. This characteristic time was likely to depend on the type of water/organic biphasic system. Thereby, the concentration ratio at 60 seconds was tentatively defined as $K_{ex}$ for the further investigation in the same manner as the previous report [31]. The $K_{ex}$ value for HMF indicated the same extent in the concentration range of 0.15 – 1.5 g/L of HMF, suggesting that the influence of the activity coefficient was negligible. Thereby, the concentration of 1.5 g/L was adopted in the present study. The $K_{ex}$ values for T1 – T6 systems were almost constant in the range of pressure drop up to 10 MPa (Figure 2(b)), indicating $d(ln K_{ex})/dP \sim 0$ at 180°C. The same was true for other temperature conditions (data not shown). In the case of the constant-temperature liquid phase system, the intrinsic partition coefficient $K$ bears $d(ln K)/dP = -\Delta V^d/RT$ where $\Delta V^d$ is the change in the partial molar volume of the solute associated with the partition process. Defining $V_{water}^d$ and $V_{org}^d$ as the partial molar volume of the solute in water and organic solvent, one can denote as $\Delta V^d = V_{org}^d - V_{water}^d$. The network of hydrogen bondings formed in water molecules is considerably reduced under the high temperature and pressurized conditions like the present experimental ones [37]. Therefore, such water indicates the solvent property similar to the organic solvent. For this, both the $V_{org}^d$ and $V_{water}^d$ would indicate the similar value, that is, $\Delta V^d \sim 0$ cm$^3$/mol. Thus, the result of $d(ln K_{ex})/dP \sim 0$ is considered to be a certain experimental form of the $d(ln K)/dP = -\Delta V^d/RT$ in the partition system.
Next, the ratio \( V_{\text{org}}/V_{\text{water}} \) determines the dimension of the liquid-liquid slug flow and the strength of the vortex field in the slug [27,31,34-36]. Accordingly, the influence of \( V_{\text{org}}/V_{\text{water}} \) on the \( K_{\text{ex}} \) value was examined in biphasic systems of T1 – T6. Overall, the \( K_{\text{ex}} \) value decreased with increasing the \( V_{\text{org}}/V_{\text{water}} \) value and indicated the maximum value of \( K_{\text{ex}} \) at \( V_{\text{org}}/V_{\text{water}} = 1 \) (Figure 2(c)). The smaller \( V_{\text{org}}/V_{\text{water}} \), the stronger the vorticity [20,31]. Therefore, the results in Figure 2(c) represent the effect by the vortex field to the partition behavior of HMF. The dependency of \( K_{\text{ex}} \) on \( V_{\text{org}}/V_{\text{water}} \) was weakened in the higher temperature range (180 and 190°C), as compared with the lower temperature range (25°C). This was probably because high temperature and pressurized conditions reduce the difference in the solvent property between water and

![Figure 2. (a) Time-course of concentration ratio of HMF in organic phase to water phase, \( C_{\text{org}}/C_{\text{water}} \), for T1, T5, and T6. The \( C_{\text{org}}/C_{\text{water}} \) value after 60 sec later was defined as the apparent partition coefficient \( K_{\text{ex}} \). Relationship between the apparent partition coefficients of HMF in the slug flows and (b) pressure drop \( \Delta P \), (c) the flow rate ratios, and (d) line velocity of fluid \( U \). All the experiments were, at 10 MPa, 180°C, and \( Re = 1.1 – 44 \), performed at least three times.](image)
organic solvents. Alternatively, the line velocity \( U \) is also a factor to affect the vortex field [34-36]. The increase of \( U \) elevated the \( K_{ex} \) value at \( V_{org}/V_{water} = 1 \), as shown in Figure 2(d). The temperature was unlikely to obviously affect the \( K_{ex} \) value as a function of the line velocity in every biphasic system. The effect of the vorticity affected by both the \( V_{org}/V_{water} \) and line velocity is again discussed in the section of 3.3.2.

Thus, the \( K_{ex} \) value depended, in this study, on operational conditions other than the pressure drop. Bearing in mind that the intrinsic partition coefficient is originally independent of the operational conditions, the \( K_{ex} \) value should be regarded as just the apparent index regarding the partition behavior of the solute.

### 3.2 Comparison of the present method with the conventional biphasic systems

The hydrophobicity of a biphasic system determines the partition behavior of substrates [38]. Therefore, the evaluation of hydrophobicity of biphasic systems used herein helps us to understand the partition behavior of substrates shown in Table 1. The characteristics of the biphasic system based on the partition behavior of amino acids were investigated at pH equivalent to the isoelectric point (pI) of each amino acid, according to the previous publications [31,38]. Accordingly, the ionization equilibrium and association equilibrium for five amino acids could be neglected.

Amino acid has the relative hydrophobicity scale defined as relative hydrophobicity (\( RH \)) by Nozaki and Tanford [39]. The \( K_{ex} \) value for amino acids (entries S7-S11 in Table 1) were plotted against the corresponding \( RH \) value (Figure 3(a)). The slope of \( \ln K_{ex} \) to \( RH \) affords the hydrophobic factor (\( HF \)) of the two phase system [40]: \( \ln K_{ex} = HF \cdot (RH + a) \) where \( a \) is the constant. The \( HF \) value for the six types of biphasic systems are shown in Figure 3(b). The increased temperature overall elevated the \( HF \) value especially in any system.

For a comparison of the \( HF \) value of liquid-liquid slug flow with the conventional biphasic system, a ladder of \( HF \) for various partitioning fields was shown in Figure 3(c). Interestingly, the hydrophobicity (\( HF \) value) of biphasic systems tested here (Figure 3(b)) was comparable with the conventional aqueous two-phase systems such as the ATPS(1) [40], liposome membrane system (LMS) [40,41], the biphasic system prepared by the aqueous poly(ethylene glycol) (PEG)/salts (ATPS(2)) and reversed micellar system (RVMS) [23]. The \( HF \) value of liquid-liquid slug flow was lower than those for the ATPS(2) and RVMS systems.

From these results, it was likely that the conventional analytical method used in the aqueous two-phase systems was applicable to the present biphasic systems. The hydrophobic factor for the present biphasic systems was comparable to the conventional biphasic systems. The physicochemical interpretation of \( HF \) in liquid-liquid slug flow is required from other viewpoints, as stated below.
Figure 3. (a) Relationship between the relative hydrophobicity of amino acids and their partition coefficient $K_{ex}$. All the experiments (180°C at 10 MPa) were performed three times. Correlation coefficient $r^2$ values for T1 - T6 were 0.988, 0.981, 0.993, 0.985, 0.978, 0.980, respectively. (b) Hydrophobic factor for T1, T5, and T6 at 25 to 190°C and for T2 –T4 at 25 and 180°C. (c) Comparison of the present partition systems with the conventional biphasic systems. Data with error bar represent that the experiments were performed at least three times.

### 3.3 Possible contributions of three factors to the partition behavior

Previously, it has been reported that the hydrophobicity of flow system was greater than that of the batch system [31], suggesting that the advantage of the slug flow system. The $K_{ex}$ value mainly depended on the $HF$ value, $V_{org}/V_{water}$, and $U$ (Figures 2 and 3). The $HF$ value is the thermodynamic parameter characterizing the biphasic system, implying the contribution of the thermodynamic cost of (de)solvation to the mass transfer of substrates across the interface of water/organic phase. Also, the response of $K_{ex}$ value
against the $V_{\text{org}}/V_{\text{water}}$ and $U$ appeared the induction of the increase in surface-to-volume for the mass transfer and the increased convection for vorticity [31], suggesting the need for the investigation from the fluid dynamic aspect. Then, we discussed the enhanced distribution of substrates from the viewpoints of solvation, vorticity, and hydrophobicity of substrates.

### 3.3.1 Effect of solvation

The van’t Hoff equation is the equation to describe the temperature dependency of the intrinsic partition coefficient $K$ and affords the thermodynamic information for the partitioning of substrates between the organic and water phases:

$$\ln K = \frac{\Delta S}{R} - \frac{(\Delta H/R)}{T}$$

where $\Delta H$ and $\Delta S$ are the enthalpy and entropy for the partitioning of substrates between two phases, respectively. $T$ is the absolute temperature [K] and $R$ is the gas constant.

The van’t Hoff equation requires the $\Delta H$ to be constant. In the partition system, the $\Delta H$ value can be interpreted as the heat change in the (de)solvation process from water to organic phases. This solvation process is also characterized by the change in partial molar volume of the solute between water and organic solvent ($\Delta V^o$), as stated in the section 3.1. Under the high temperature and pressurized conditions, forty percent of hydrogen bonding between water molecules disappeared, implying the weakening of solvation by water (hydration) [37]. Then, it was considered that the exchange of solvation structure required low energy (low $\Delta H$). The result of $\Delta V^o \sim 0 \text{ cm}^3/\text{mol}$ was observed in the temperature conditions between 160 and 190°C. When it comes to this, the $\Delta H$ value might be constant in this temperature range. Therefore, we assume that van’t Hoff equation can be formally adopted, although the $K_{\text{ex}}$ value is not an intrinsic partition coefficient.

In any $V_{\text{org}}/V_{\text{water}}$ value, the linear relationship between the $\ln K_{\text{ex}}$ of HMF and $1/T$ was observed as shown in Figure 4(a), which is comparable with the previous result with respect to the water/MIBK biphasic system [31]. The $\Delta H$ and $T\Delta S$ estimated from Figure 4(a) are shown as a function of $V_{\text{org}}/V_{\text{water}}$ value (Figure 4(b)). Both the $\Delta H$ and $T\Delta S$ values increased with an increase in $V_{\text{org}}/V_{\text{water}}$ value. A similar trend between the $\Delta H$ and $T\Delta S$ values suggested that the partitioning of HMF determined the balance between enthalpic and entropic factors. Furthermore, the $\Delta H$ value was plotted against the corresponding $T\Delta S$ and the linear relationship between both was observed (the enthalpy-entropy compensation) as shown in Figure 4(c). The compensation was observed regardless of the condition of $V_{\text{org}}/V_{\text{water}}$ value and the six types of biphasic systems, suggesting that the partition behavior of substrates was thermodynamically driven by the same mechanism. These linear relationships can be discussed in terms of the slope of the compensation and its $y$-intercept.

First, the plot of $\Delta H$ value against the corresponding $T\Delta S$ affords the slope $\alpha$, meaning the conformational change of solvation structure (of solvent molecules) surrounding substrate [6]. In all systems, the $\alpha$ value was almost same ($\alpha \sim 0.9$), suggesting the intrinsically same (de)solvation of substrate over the mass transfer in biphasic system. Second, focusing on the $y$-intercept, the $\Delta H$-$T\Delta S$ relationship for biphasic system was almost identical in the case of water/MIBK, water/(MIBK + 2-buthanol), (water + DMSO)/MIBK, and (water + DMSO)/(MIBK + 2-buthanol). In contrast, water/octanoic acid/ and water/decane systems differed from the biphasic systems including MIBK. To clarify the difference between these compensations, the $y$-intercept obtained by the extrapolation of $\Delta H$ to 0 ($T\Delta S_0$) is discussed. It is noted that the $T\Delta S_0$ value is the index for the desolvation of molecule [30] and the (de)solvation property of substrate across the interface.
The $\Delta S_0$ values for T1 – T4 were almost zero (Table 2), indicating that the entropy gain in the water phase balanced the entropy loss in the organic phase. The alteration of organic phase from MIBK to octanoic acid and decane reduced the $\Delta S_0$ value (-2.5 and -7.9 kJ/mol), strongly suggesting the amplification of entropy loss due to the solvation of substrates in the organic phase. In other words, the $\Delta S_0$ value means there is an advantage to mass transfer of substrates from water to organic phases. In addition, the addition of DMSO to water and 2-butanol to MIBK altered no significant variation in $K_{ex}$ value, $\Delta H$-$T\Delta S$ relationship, and $\Delta S_0$ value (see Figures 2, 4, Table 2). These results suggested that both the water and MIBK determined the main property of the biphasic system in the low volume ratio of DMSO and 2-butanol.

Figure 4. (a) van’t Hoff plot of HMF under various conditions. The correlation coefficients were $r^2 = 0.923$, 0.935, 0.914 for T1 at $V_{org}/V_{water} = 1, 3, 5$, respectively. The $r$ values for T2 – T6 were 0.977, 0.960, 0.982, 0.968, 0.971, respectively. (b) Relationship between the thermodynamic parameters and flow rate ratios. (c) Enthalpy-entropy compensation of HMF in the continuous biphasic system. (d) Relationship between $T\Delta S_0$ and $HF$ for various systems. Conditions: 10 MPa. The $HF$ values at 180°C were used as the representative value. Data with error bar represent that the experiments were performed at least three times.

The $T\Delta S_0$ value for each biphasic system was again plotted against the corresponding $HF$ value at 180°C (Figure 4(d)). Thereby, both were negatively correlated. This implies that the $HF$ value as a
thermodynamic aspect can be interpreted: the thermodynamic solvation property determined the
hydrophobicity of the biphasic system. Therefore, the \( HF \) value indicated the resistance to the mass transfer
of substrates in the liquid-liquid biphasic systems of slugs.

### 3.3.2 Effect of vorticity

Previous theoretical calculation experiment supported that the velocity field in the liquid-liquid slug
flow of the water/MIBK biphasic system assisted the mass transfer of substrates [20,31]. As stated before,
the \( K_{ex} \) value depended on both the \( V_{org}/V_{water} \) and \( U \) values (that are a key factor for the vorticity of the liquid-
liquid slug). To discuss the impact of vorticity on the \( K_{ex} \) value, we experimentally estimated the vorticity
based on the determination method using the dimension of slugs: the \( U/(d + 2l) \) value was the index for the
vorticity of slugs with the dimension \( d \) and \( l \) shown in Figure 5(a) (top) [34-36]. The resulting \( U/(d + 2l) \)
value was then estimated. Since the vorticity is estimated from each slug, the statistical error should be ruled
out by the histogram analysis of vorticity as shown in Figure 5(a) (bottom). This index showed the single
peak with a certain width and its mean value would be applicable as the statistical parameter. The vorticity
distribution increased with an increase in the line velocity. This trend was almost identical in other biphasic
systems. Furthermore, the \( K_{ex} \) value of HMF measured at 25\(^\circ\)C was compared the corresponding mean value
for vorticity. The \( K_{ex} \) value for T1, T5 and T6 was elevated by the increase in vorticity, as shown in Figure
5(b).

The formation of vortex field in slug at 180\(^\circ\)C and 10 MPa was confirmed by using OpenFoam as the
supplemental discussion. The liquid-liquid slug flow using the water/MIBK biphasic system (T1, \( HF = 0.035; \)
\( V_{org}/V_{water} = 1 \)) was selected as a representative example. The wall film of organic phase was neglected to
simplify the numerical calculation. The velocity of organic and water phases was also lowered by 1/10 times
as a real condition, since the \( K_{ex} \) value at 60 seconds was almost same as that at 600 seconds. These
simplifications could reduce the calculation cost. The calculated results on the slug flow generations were
shown in Figures 5(c). The velocity vector in the liquid-liquid slug flow was, in the calculation, visualized in
the condition of 180\(^\circ\)C and 10 MPa where the visualization like Figure 5(a) was difficult. The velocity vector
field for the absolute velocity showed the parabolic velocity distribution typical to the laminar flow (Figures
5(c)). Considering the relative velocity (= absolute velocity – mean velocity), the definite vortex field that
top and bottom were symmetric was observed in the liquid-liquid slug flow. This calculation suggested the
generation of vortex field as schematically illustrated in Figure 5(c) validated the results of Figure 5(a) and
(b).

From the results, it was plausible that the vorticity at the hydrothermal conditions would promote the
mass transfer to elevate the \( K_{ex} \) value, as was stated in the previous reports [20,31,34-36].

### 3.3.3 Effect of hydrophobicity of substrates

The partition behavior of substrates in the biphasic water/organic systems of liquid-liquid slug flow is
also predominated by the hydrophobicity of substrates. In this section, the effect of hydrophobicity of
substrates was discussed.
Figure 5. (a) Vorticity distribution for liquid-liquid slug flow. The vorticity was estimated by the equation $U/(d + 2l)$ where $U$, $d$, and $l$ are the line velocity, diameter of slug and its length, respectively. (b) Relationship between vorticity and the apparent partitioning coefficient at 25°C. Error bar of data for vorticity originated from the dispersion of histogram in Figure 5(b). (c) Flow analysis of water/MIBK. (top) A time-course of liquid-liquid slug flow calculated by OpenFoam. (middle) Magnified images of absolute velocity field of the region underlined by white bar, in the slug flow at $t = 5s$. (bottom) Relative velocity field recalculated from the absolute velocity field. Calculated conditions: the line velocity was 5 mm/s. $Re = 40; V_{org}/V_{water} = 1.36; 180°C$ and 10 MPa.

Table 1 shows the apparent partition coefficient of various substrates. The $K_{ex}$ value ranged from 0.008 (entry S6) to 5.35 (entry S2) at 25°C. Overall, an elevation of temperature to 180°C resulted in enhancement
of $K_{\text{ex}}$ values. Furfural and its derivatives (entries S1-S5) had the higher $K_{\text{ex}}$ value, by comparison of other substrates such as amino acids (entries S7-S11) and saccharides (entries S12-S17). In general, the partition behavior of substrates in the two phase system is caused by its hydrophobicity [21]. The hydrophobicity of chemical molecules are defined as the partition coefficient of the substrate in the water/octanol system ($\log P_{\text{ow}}$). The hydrophobicity of various materials are in the order: furfural derivatives > amino acids > saccharides. Meanwhile, the $K_{\text{ex}}$ value for various substrates overall scattered against the corresponding $\log P_{\text{ow}}$ value, as shown in Table 1. This result suggested that the partition behavior of substrates in the liquid-liquid slug flow depended not only on the operational conditions (e.g. the flow rate and temperature), but also on the selection of water/organic biphasic system (e.g. the $HF$ value). Therefore, the $K_{\text{ex}}$ value is more plausible than the $\log P_{\text{ow}}$ value in order to quantify the partition behavior influenced by the operational conditions that determined the residence time, dimension of a slug, and vorticity.

3.4 Possible selection of water/organic biphasic system for hydrothermal HMF conversion

The systematic investigation of the $K_{\text{ex}}$ value for the variety of substrates and the $HF$ value for the biphasic systems would be useful for selecting the reactive separation field. A possible application is our previous investigation that fructose was converted into HMF to recover into MIBK phase [20,21]. Fructose (entry S13; $K_{\text{ex}} = 0.022$) as a reactant is soluble in the water phase. In contrast, HMF (entry S4; $K_{\text{ex}} = 0.92$) as a product is soluble not only in water but also in MIBK phases. A use of water/organic biphasic system induces a conversion of fructose into HMF in the water phase, followed by a partition of HMF into MIBK phase [20]. The yield of HMF is controlled by the reactive separation in slug flow because of its easy degradable propensity in the water phase [1,11,22]. Figures 3(b) and (c) suggest the comparison of HMF yield among T1, T5, and T6. For examples, the water/MIBK biphasic system (T1) bearing the smallest $HF$ value of biphasic systems tested here resulted in the most effective recovery of the product HMF into the MIBK phase (yield: 88.5%) [20]. In contrast to T1, a use of T5 and T6 bearing the higher $HF$ values gave the lower recovery of HMF to organic phases (yield: 78.0 and 62.4%). This was because the high $HF$ values of biphasic system gave the large resistance to the mass transfer of HMF from water to organic phases (see the section 3.3.1). Thus, the quantitative index such as $K_{\text{ex}}$ and $HF$ values helps to build the reactive separation process of HMF. In such a sense, the present study concerning the liquid-liquid slug flow as the separation field would contribute to the process intensification although the further investigations are required.

4. Conclusion

The fundamental property of the liquid-liquid slug flow generated in the water/organic phase in the capillary was discussed. The experimental treatment on the $K_{\text{ex}}$ value used in water/MIBK biphasic system [31] could be extended to other types of water/organic biphasic systems, suggesting that the slug flow of water/organic biphasic system could be used as the two-phase system for the separation field. The hydrophobic scale ($HF$) as the characteristic parameter for the separation field was comparable with those for the conventional aqueous two-phase system and the liposome membrane system. From some aspects, it was likely that the increased $K_{\text{ex}}$ value resulted from the reduction of the resistance to the mass transfer across the interface of both phases and the convection effect due to the vortex field. Finally, the optimal reactive separation field for HMF from fructose was successfully selected by using the $K_{\text{ex}}$ and $HF$ values. Therefore, the present findings would afford the optimization of water/organic biphasic systems and the process
intensification of the reactive separation process.

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